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The Impact of a Short Online Medical Leadership Competencies Framework (MLCF)-based Leadership Training Program on Leadership Competencies Development of Healthcare Students and Junior Professionals: A Pre-Post Study.

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Abstract

Background: Leadership competencies are crucial for the students of medical, nursing, and other health disciplines due to their prospective roles in decision-making, teamwork, communication, and health crisis management. However, the contribution of the formal teaching sessions in health professions curricula to leadership and communication skills is inconsistent globally, including within the Palestinian undergraduate education system. To address this gap, the researchers evaluated the effectiveness and impact of the online leadership training program on the participants' leadership competencies, aiming to identify effective adjuncts to formal curricula. **Methods:** This study employed a one-group pretest–post-test design. The intervention was an online training program conducted via Zoom Meetings Platform for a duration of 2 hours. The training curriculum was designed in accordance with the Medical Leadership Competency Framework (MLCF). Participants were recruited through a call for registration posted on the website of the International Medical Education Trust 2000. Pre-training/post-training impact assessment was conducted using the Medical Leadership Competence Scale (MeLeCoS). Data

were analyzed using descriptive statistics and paired t-tests. **Results:** A total of 76 participants (65.8% undergraduates and 34.2% postgraduates) were enrolled in the study. The training significantly enhanced the participants' leadership competencies, as evidenced by the increase in the mean MeLeCoS score from 3.65 (± 0.54) to 3.98 (± 0.55) out of 5 (mean difference 0.33; 95% CI 0.20–0.45; $p < 0.001$). Significant improvements were observed in five MeLeCoS factors (all $p < 0.001$). No significant differences in the MeLeCoS scores between both sexes, study discipline, or training phase (p -values > 0.05). **Conclusion:** The online leadership training program markedly improved the participants' leadership competencies and emerged as a potential adjunct to formal curricula.

Keywords: Competencies, Curriculum, Healthcare, Leadership, Online, Training.

1. Introduction

Leadership is essential for students in the healthcare fields, considering their future involvement in ethical decision-making, teamwork, communication, and the management of health crises [1,2]. Many physicians assume a leadership role during their careers, making it essential for leadership training to be integrated into medical education [3,4]. Similarly, leadership is integral to nursing practice at all levels and is essential for enhancing the continuous improvement of the nursing practice, thereby improving the quality of the patient care [5,6]. However, the time assigned for leadership training in medical and nursing school curricula is limited. For example, data from the Leadership in Undergraduate Medical Education National Survey (LUMENS), which included thirty medical schools in the United Kingdom (UK), showed that only 2% of the total duration of undergraduate medical education in the UK is spent on leadership training [7].

Early-career physicians have demonstrated low confidence in their preparedness to assume medical leadership roles, particularly during their transition from students to professionals who are expected to be responsible and accountable decision-makers [3]. The stress endured by the newly graduated physicians is not only attributed to the lack of leadership training and competence, but also to the lack of self-assessment. Self-assessments influence career choice and performance, which, in turn, help identify one's own true incompetencies [8]. Consequently, it is crucial for leadership training to be integrated into undergraduate health sciences education to promote the preparedness of the emerging healthcare professionals and strengthen their performance in their future roles.

The techniques used for developing leadership in healthcare settings vary widely [9,10]. Some studies have discussed the fact that leadership programs vary in consistency and have heterogeneous and poor-quality methods, and, as a result, they highlighted the need for well-designed, accredited, and integrated leadership programs [10]. This includes integrating training in leadership skills, such as providing feedback, conflict resolution, and technical knowledge, as well as personal development, into post-graduate curricula [11]. Along with the increase in leadership training, the development of leadership competency assessment tools and frameworks has also become common in the health professions. An example of these frameworks is the one developed by the Academy of Medical Royal Colleges, which is the Medical Leadership Competency Framework (MLCF), which consists of the following five categories [12,13]: 'setting direction', 'demonstrating personal qualities', 'working with others', 'managing services', and 'improving services'. It aims to help design leadership training curricula, promote personal development, and highlight strengths through self-assessment [12–15]. Another tool is the 4Cs Framework of influence, which emphasizes the importance of 'character', 'competence', 'connection', and 'culture' in leadership and influence development [16].

The approaches used in evaluating leadership training programs were mostly subjective, non-standardized, and variable. When it comes to assessment, most studies on leadership training programs used either post-curriculum or pre/post surveys [17]. Integrating leadership curricula with comprehensive and standardized program evaluation methodologies, such as the Kirkpatrick framework and the Medical Leadership Competence Scale (MeLeCoS), facilitates standardized assessment of outcomes, thereby enhancing the measurement of participants' leadership competencies [12,14]. While numerous studies indicated enhancement in leadership skills across participants, the external validity and generalization of those findings were limited due to the heterogeneity in assessment methods across studies [14].

Evidence from various studies has shown that leadership training programs may enhance the leadership competencies of healthcare practitioners, thereby improving healthcare outcomes [15]. These programs have been shown to enhance decision-making abilities, teamwork, and patient care [18,19]. Despite this evidence, formal leadership training for healthcare professionals remains greatly absent globally [20,21], and in Palestine, this absence is evident. As Katoute et al. stated that the health systems in the Middle East and North Africa (MENA) region not only lack leadership training, but they also face multiple leadership challenges, including the insufficient development of leadership skills, a lack of information for thorough and comprehensive decision-making, and the fact that leadership support is mostly confined to senior executives [20,21]. This lack of structured training underscores the pressing need to integrate leadership development into the Palestinian healthcare education, thereby enhancing both confidence and the patient care.

The literature on medical leadership training in Palestine is notably limited. That is, no studies directly investigated the leadership competencies of Palestinian healthcare workers. This gap highlights the need for the development of a leadership training program tailored to Palestinian institutions. The sparse literature reveals a knowledge gap emphasizing the need for developing new programs to address these deficiencies. The proposed online leadership training program was designed to address the leadership training gap in the curricula of the undergraduate medical and nursing education in Palestine. Alongside promoting leadership training within the Palestinian medical institutions, the program aims to advocate for a culture of leadership training that is currently lacking in the region [20]. The online training modality provides a feasible and accessible approach to leadership development, especially in under-resourced environments. Although the effectiveness of online leadership training has not been studied in Palestine, remote learning methods may address the operational and resource challenges faced by the Palestinian medical institutions.

The comprehensive aim of this study is to evaluate the effectiveness and impact of the online leadership training program on participants' leadership competencies. We aim to enhance Palestinian literature in the context of leadership competencies development in health sciences educational settings by showing data and practical insights. Therefore, this study contributes to bridge the gap in the medical education literature in Palestine, and supports the forthcoming leadership training initiatives by the healthcare institutions in Palestine and other low-to middle-income countries (LMICs). Through this study, we aim to enrich the literature on the effectiveness of an online MLCF-based, affordable, and applicable training program, which may be an effective solution to bridge the gap in leadership training in LMICs.

2. Methods

2.1 Study Design and Setting:

A pre-post study design was implemented from June 3, 2025, to June 20, 2025 to evaluate the impact of a brief synchronous online training program on the development of leadership competencies among undergraduate medical and nursing students and junior practitioners. The participants' self-assessed leadership competencies were evaluated one week before and one week after the online training program. A study information sheet was shared with the participants, and the participants who voluntarily agreed to participate in the study signed an electronic informed consent. This study adhered to the Declaration of Helsinki. Ethical approval to conduct this study was obtained from the Institutional Review Board (IRB) at An-Najah National University (Reference number: Nurs. Sep.2025/36). The report of this study was drafted according to the Defined Criteria To Report INnovations in Education (DoCTRINE) [22] and the newly developed CheckList Of Standards of reporting in Education Research (CLOSER) and the Checklist for Intervention Description of Education Research (CIDER) [23].

2.2 Participants and Recruitment:

The target population included the undergraduate medical and nursing students and the junior practitioners in the Palestinian institutions. A call for participation in the training program was shared online on the Facebook page and the official website of the International Medical Education Trust 2000-Palestine (IMET2000-PAL) three weeks before the training. The participants' eligibility criteria included: [1] being an undergraduate medical or nursing student enrolled in the Palestinian medical or nursing faculties, or a junior practitioner recently graduated from the Palestinian medical or nursing faculties, and [2] filling out the pre-training and post-training surveys.

A total of 80 participants attended the online training session, 76 (95%) of whom met the eligibility criteria and were included in this study. The sampling nature would lead to a potential selection bias; students and junior practitioners with an interest in leadership and access to the Facebook page and the official IMET2000-PAL website would be more likely to participate in this program. The limitation of the generalization of this study's findings, due to this potential bias, is partially alleviated by the sufficient and representative sample included in this study.

3. Leadership Training Curriculum Development Process

3.1 Description of the Intervention Design:

The intervention was a short synchronous online training program titled the "Leadership Skills Training Program for Healthcare Students and Junior Healthcare Professionals". The training program was designed according to an outcome-based education (OBE) framework, which ensured alignment among the learning objectives, educational activities, and evaluation outcomes. The curriculum of this training program was designed using Kern's Six-Step Approach to Curriculum Development [24], as follows:

Steps 1 and 2: Problem identification, general needs assessment, and targeted needs assessment

Leadership competencies are essential for physicians and nurses; however, formal training on leadership competencies is often limited in the Palestinian undergraduate curricula. A scoping literature review was conducted to identify research work targeting leadership competencies development in the undergraduate medical and nursing education in Palestine. Literature on this field is notably limited; no studies directly investigated the leadership competencies of the Palestinian medical and nursing students or healthcare workers. Moreover, observations from faculty members and a revision of the curricula of the medical and nursing faculties in the major Palestinian institutions revealed a gap in the formal curricula, highlighted by the lack of structured training for leadership development. This gap prompts the need for the development of a leadership training program tailored to the Palestinian institutions.

Step 3: Goals and Objectives.

The proposed online leadership training program aims to enhance the quality of the Palestinian healthcare system by developing the leadership competencies of undergraduate medical and nursing students and newly graduated healthcare professionals. The specific objectives of this program were: [1] to introduce the participants to the importance of the effective communication in healthcare leadership, [2] provide them with different leadership styles and demonstrate their impact on healthcare teams and patient outcomes, [3] equip the participants with essential leadership and communication competencies, and [4] provide practice strategies for resolving conflicts and building consensus in healthcare teams.

By the end of the training program, participants were expected to demonstrate a measurable improvement in the following domains taken from the Medical Leadership Competency Framework (MLCF) [12,14]:

- [1] Achieving learning and reflecting on performance
- [2] Demonstrating responsible behaviour and shaping relations
- [3] Fostering personal development and promoting quality improvement
- [4] Developing self-management and supporting management in healthcare
- [5] Promoting improvement and innovation in undergraduate medical and nursing education
- [6] Introducing systemic perspectives into organizations

Step 4: Educational Strategies.

The educational strategies of this training program curriculum included an interactive lecture and case-based discussions to facilitate experiential learning and introduce the essential principles of the effective leadership in healthcare to the participants. The content of the online lecture was organized around the stages of leadership competencies development, based on the MLCF, and focusing on the main leadership competency domains: demonstrating personal qualities (such as self-awareness, emotional intelligence, and self-regulation), managing oneself (such as time management, adaptability, and resilience), acting with integrity (such as ethical decision-making and cultural sensitivity), and working with others (such as teamwork, empathy, and communication). The participants were introduced to diverse leadership styles, including transformational and shared leadership, through interactive discussions and case-based activities. Moreover, real-world clinical scenarios were used to facilitate the practical application of leadership theories.

Step 5: Implementation.

The program was implemented in an online, synchronous training session for 2 hours via the Zoom Meetings platform. The training was organized by the International Medical Education Trust 2000-Palestine (IMET2000-PAL). The training was delivered by the Dean of the Faculty of Medicine at the Arab American University of Palestine (AAUP). The training developer and instructor has a Master's degree in Medical Education, and was selected as the instructor to bridge the content created with the experience in both academic and healthcare leadership.

Step 6: Evaluation and Feedback.

An online survey using Google Forms was used to assess the impact of this training program and collect participants' feedback. The participants were required to complete the pre-training online survey one week prior to the training session, and the post-training online survey one week after the training session. The evaluation form consisted of two sections: [1] training evaluation and participants' feedback (from the post-training survey), and [2] the Medical Leadership Competence Self-Assessment Scale (MeLeCoS), which was included in the pre- and post-training surveys [14]. The MeLeCoS self-assessment tool used included six factors with a total of 37 items. The six MeLeCoS factors relate to different aspects of leadership: factor 1 ('Achieving learning and reflecting on performance') and factor 2 ('Demonstrating responsible behaviour and shaping relations') focus on assessing the leadership of students, individually, factor 3 ('Fostering personal development and promoting quality improvement') and factor 4 ('Developing self-management and supporting management in healthcare') reflect students' leadership performance in the management and improvement of healthcare facilities, and lastly, factor 5 ('Promoting improvement and innovation in undergraduate medical education') and factor 6 ('Introducing systemic perspectives into organisations') portray students' overall leadership involvement during undergraduate studies and their contribution to providing a leadership-promoting environment.

While the validity of the MeLeCoS was established in a previous study[14], the content validity of this tool in assessing the leadership competencies in medical and nursing students, as well as junior practitioners, was ensured by a panel of experts in medical education. The pretest and post-test reliability of the questionnaire were determined by calculating Cronbach's Alpha. The Cronbach's Alpha values for the pre-test and post-test were 0.931 and 0.953, respectively, indicating excellent internal consistency. This means that the MeLeCoS questionnaire is a reliable instrument for medical and nursing students, as well as junior practitioners, to self-assess their leadership competence, with good content validity.

The evaluation of the training program followed the Kirkpatrick Model of training evaluation[25]. Level 1 (Reaction) was measured using a post-training online survey that assessed participants' perceptions of content, delivery, overall satisfaction, and likelihood of recommending the program. Level 2 (Learning) was evaluated through pre- and post-training administration of the Medical Leadership Competence Self-Assessment Scale (MeLeCoS), a validated instrument that measures leadership competencies across six domains. The instrument demonstrated excellent reliability in this study (Cronbach's $\alpha = 0.931$ pre-test; 0.953 post-test), supporting its suitability for detecting changes in competence. Level 3 (Behavior) was indirectly assessed through items measuring participants' self-reported likelihood of applying acquired leadership skills in future clinical or academic settings. While direct organizational outcomes were not measured, the evaluation indirectly addressed Level 4 (Results) by assessing improvements in leadership domains related to innovation, quality improvement,

and systemic thinking. These domains collectively represent competencies that contribute to long-term system-level impact. This evaluation approach provided a comprehensive assessment of participants' immediate reactions, learning gains, anticipated behavior change, and potential broader influence on educational and healthcare environments.

3.2 Outcomes

The primary outcome of this study includes a measurable improvement in the participants' total MeLeCoS score and scores of the MeLeCoS domains. Secondary outcomes include the participants' self-reported effectiveness of the program, likelihood of applying the learned skills in practice, and the likelihood of recommending the training program to colleagues.

3.3 Statistical Analysis

Data were analyzed using SPSS version 27.0. Univariate analysis using descriptive statistics was conducted to describe the variables and summarize them in the form of means, standard deviations, frequencies, and percentages. A paired t-test was used to compare the mean scores of the MeLeCoS scale and its domains pre- and post-training. Subgroup analysis using an independent sample t-test was conducted to compare the mean improvement in the MeLeCoS (post minus pre MeLeCoS scores) among the study groups (males versus females, medical versus nursing, and undergraduate versus postgraduate). The significance level was set at 5%, and any p-value below 0.05 was considered statistically significant.

4. Results

4.1 Sociodemographic Characteristics of the Participants

The study included a total of 76 participants, 44 (57.9%) were female, and 32 (42.1%) were male. 54 (71.1%) participants were in the field of Medicine, and 22 (28.9%) participants were in the field of nursing and midwifery. 50 (65.8%) of the total participants were undergraduate students, while the remaining 26 (34.2%) participants were postgraduate and junior practitioners. The characteristics of the participants are summarized in Table 1 and Figure 1.

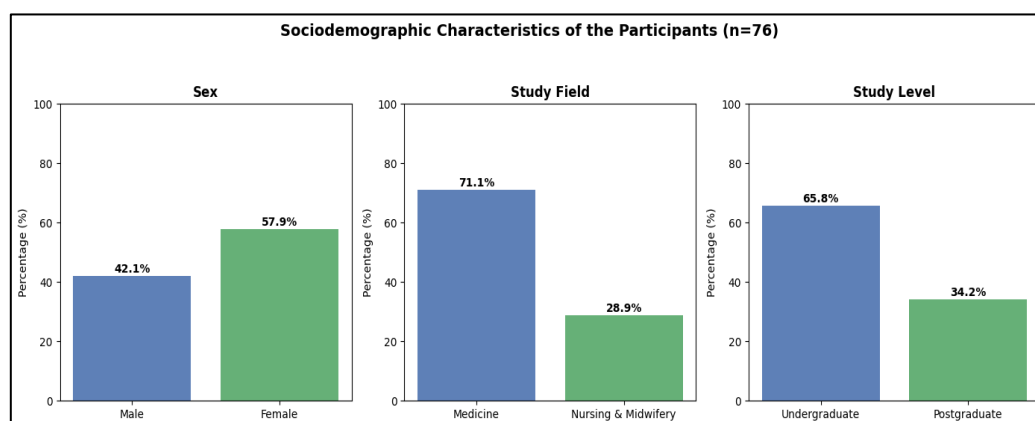


Figure 1. Sociodemographic Characteristics of the Participants (n=76).

Table 1. Sociodemographic Characteristics of the Participants (n=76).

Variable	Frequency (n)	Percentage (%)
Sex:		
Male	32	42.1
Female	44	57.9
Study Field:		
Medicine	54	71.1
Nursing and Midwifery	22	28.9
Study Level:		
Undergraduate	50	65.8
Postgraduate	26	34.2
Total	76	100

4.2 Online Leadership Training Impact Assessment using the MeLeCoS Self-Assessment

The participants' post-training overall mean of the MeLeCoS was significantly higher than the pre-training overall mean score (mean (SD) 3.98 (± 0.55) out of 5 vs. 3.65 (± 0.54) out of 5, mean difference = 0.33; 95% CI [0.20-0.45], p-value <0.001). These results indicate that the training session positively impacted the overall participants' leadership competence. Moreover, the training significantly and positively enhanced the self-reported participant's competences' rating in the following factors of the MeLeCoS: factor 1 achieving learning and reflecting on performance (mean (SD) 3.98 (± 0.59) out of 5 vs 3.67 (± 0.56) out of 5, mean difference = 0.31; 95% CI [0.15-0.46], p-value <0.001), factor 3 fostering personal development and promoting quality improvement (mean (SD) 4.02 (± 0.56) out of 5 vs 3.70 (± 0.64) out of 5, mean difference = 0.32; 95% CI [0.16-0.48], p-value <0.001), factor 4 developing self-management and supporting management in healthcare (3.67 vs 4.01, p-value <0.001), (mean (SD); 4.01 (± 0.63) out of 5 vs 3.67 (± 0.70) out of 5, mean difference = 0.34; 95% CI [0.17-0.50], p-value <0.001), factor 5 promoting improvement and innovation in undergraduate medical education (mean (SD) 3.64 (± 0.91) out of 5 vs 3.19 (± 0.95) out of 5, mean difference = 0.45; 95% CI [0.27-0.63], p-value <0.001), and factor 6 introducing systemic perspectives into organizations (mean (SD); 3.87 (± 0.79) out of 5 vs 3.42 (± 0.82) out of 5, mean difference = 0.45; 95% CI [0.28-0.62], p-value <0.001). However, the training did not significantly impact the self-reported participant's competences' rating in factor 2 of the MeLeCoS demonstrating responsible behaviour and shaping relations (mean (SD) 4.33 (± 0.58) out of 5 vs 4.22 (± 0.57) out of 5, mean difference = 0.11; 95% CI [-0.02-0.26], p-value =0.10) (Table 2 and Figure 2).

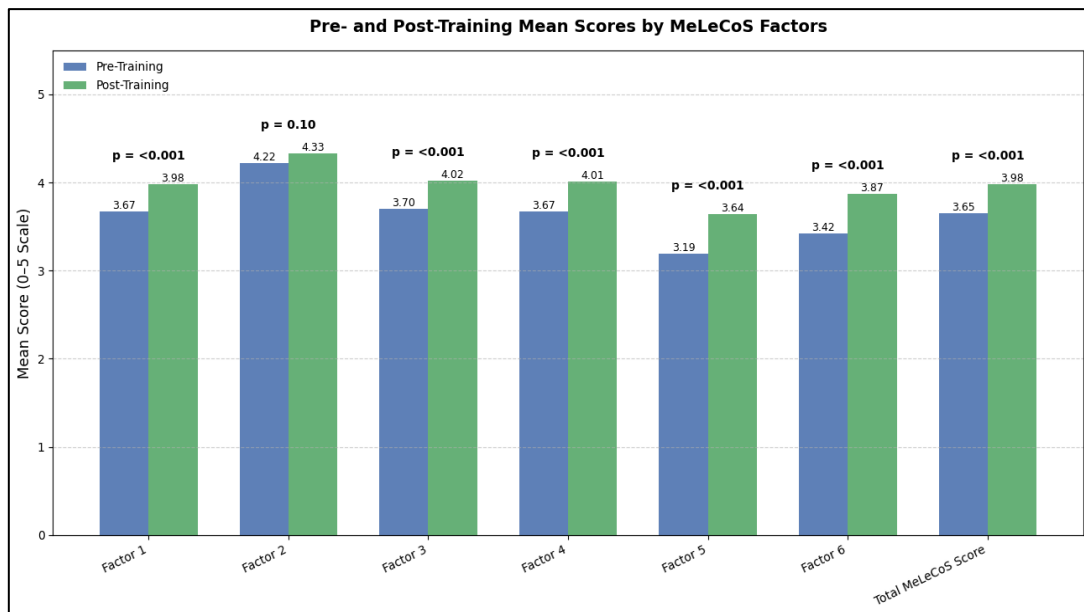


Figure 2. Pre- and post-training mean scores by the MeLeCoS Factors (n=76).

Table 2. Results of the Leadership Training Program Impact Assessment using the MeLeCoS (n=76).

MeLeCoS-Questionnaire Factors	Pre-Session Mean ($\pm$ SD)	Post-Session Mean ($\pm$ SD)	Mean Difference	95% CI	p-value α
[1] Achieving learning and reflecting on performance.	3.67 ($\pm$ 0.56)	3.98 ($\pm$ 0.59)	0.31	[0.15-0.46]	<0.001
[2] Demonstrating responsible behaviour and shaping relations.	4.22 ($\pm$ 0.57)	4.33 ($\pm$ 0.58)	0.11	[-0.02-0.26]	0.1
[3] Fostering personal development and promoting quality improvement.	3.70 ($\pm$ 0.64)	4.02 ($\pm$ 0.56)	0.32	[0.16-0.48]	<0.001
[4] Developing self-management and supporting management in healthcare.	3.67 ($\pm$ 0.70)	4.01 ($\pm$ 0.63)	0.34	[0.17-0.50]	<0.001
[5] Promoting improvement and innovation in undergraduate medical education.	3.19 ($\pm$ 0.95)	3.64 ($\pm$ 0.91)	0.45	[0.27-0.63]	<0.001
[6] Introducing systemic perspectives into organisations.	3.42 ($\pm$ 0.82)	3.87 ($\pm$ 0.79)	0.45	[0.28-0.62]	<0.001
Total MeLeCoS	3.65 ($\pm$ 0.54)	3.98 ($\pm$ 0.55)	0.33	[0.20-0.45]	<0.001
α Paired t-test. * Statistically significant (p-value < 0.05) MeLeCoS: medical students' leadership competence self-assessment scale. SD: Standard deviation. 95% CI: 95% Confidence Interval Scores range = 0-5					

Participants' pre-training and post-training scores per individual items of the MeLeCoS Self-Assessment are summarized in Supplementary Material, Table 3.

Table 3. Results of the Leadership Training Program Impact Assessment using the Individual Items of the MeLeCoS (n=76).

Items	Pre-Session Mean ($\pm$ SD)	Post-Session Mean ($\pm$ SD)	Mean Difference	95% CI	p-value α	Factor
I question whether I have delivered the best possible performance.	3.79 ($\pm$ 0.85)	4.18 ($\pm$ 0.79)	0.39	[0.16-0.63]	0.002*	1
I reflect on my performance at the end of each study period or semester.	3.98 ($\pm$ 0.96)	4.17 ($\pm$ 0.81)	0.19	[-0.06-0.43]	0.137	
I can control my self-learning well (e.g. I start studying early for exams).	3.45 ($\pm$ 1.02)	3.77 ($\pm$ 1.01)	0.32	[0.09-0.56]	0.007*	
I compare my knowledge and practices with those of my peers to question both content and actions.	3.34 ($\pm$ 1.15)	3.59 ($\pm$ 1.01)	0.25	[-0.02-0.52]	0.066	
I communicate goals clearly in working or learning groups so that we can work together to achieve them.	3.81 ($\pm$ 1.06)	4.18 ($\pm$ 0.79)	0.37	[0.08-0.65]	0.012*	
In controversial discussions, I make sure that the views of all participants are heard before decisions are made.	4.12 ($\pm$ 0.88)	4.28 ($\pm$ 0.80)	0.16	[-0.09-0.40]	0.203	2
I take responsibility for the active role assigned to me in a team (e.g. minute taker).	4.04 ($\pm$ 0.88)	4.19 ($\pm$ 0.81)	0.15	[-0.06-0.37]	0.147	
I motivate others in group work.	4.13 ($\pm$ 0.85)	4.33 ($\pm$ 0.77)	0.20	[-0.01-0.41]	0.062	
I behave responsibly during my studies (e.g. I contribute to a good working atmosphere during group work).	4.11 ($\pm$ 0.89)	4.29 ($\pm$ 0.76)	0.18	[-0.06-0.40]	0.145	
I behave ethically towards fellow students and teachers (e.g. I do not discriminate against anyone on the basis of cultural origin).	4.63 ($\pm$ 0.70)	4.55 ($\pm$ 0.66)	-0.08	[-0.28-0.12]	0.442	
I behave responsibly during clinical training, e.g. during a clinical clerkship.	4.41 ($\pm$ 0.80)	4.45 ($\pm$ 0.76)	0.04	[-0.18-0.26]	0.727	
I behave ethically towards patients in clinical situations (e.g. I treat all patients equally, regardless of their social background).	4.51 ($\pm$ 0.89)	4.58 ($\pm$ 0.70)	0.07	[-0.16-0.29]	0.549	

I can build a professional relationship with patients.	3.93 ($\pm$ 0.85)	4.26 ($\pm$ 0.66)	0.33	[0.11-0.55]	0.004*	
In history taking, I encourage patients to share their perspective.	4.07 ($\pm$ 0.91)	4.08 ($\pm$ 0.92)	0.01	[-0.18-0.20]	0.887	
I use information from others, e.g. feedback, to continue my learning.	3.75 ($\pm$ 0.95)	4.01 ($\pm$ 0.86)	0.26	[-0.01-0.53]	0.064	3
If I recognize the influence of poor performance on the quality of results, then I discuss this with the people involved.	3.78 ($\pm$ 0.95)	4.07 ($\pm$ 0.88)	0.29	[0.05-0.52]	0.018*	
In groups, I try to discuss identified problems further.	3.82 ($\pm$ 0.84)	4.09 ($\pm$ 0.85)	0.27	[0.04-0.51]	0.019*	
After critical incidents, I voluntarily participate in the review of work processes in the affected work area.	3.41 ($\pm$ 1.00)	3.96 ($\pm$ 0.86)	0.55	[0.25-0.86]	0.002*	
I look for role models from whom I can learn something about the healthcare system or healthcare organizations.	3.95 ($\pm$ 0.91)	4.16 ($\pm$ 0.71)	0.21	[-0.01-0.43]	0.053	
I organize additional extracurricular learning opportunities for myself (e.g. study groups with fellow students).	3.55 ($\pm$ 1.06)	3.87 ($\pm$ 0.90)	0.32	[0.07-0.56]	0.012*	
In emotional situations, e.g. when receiving very critical feedback, I communicate in a controlled and objective manner.	3.63 ($\pm$ 0.91)	3.92 ($\pm$ 0.89)	0.29	[0.03-0.55]	0.032*	4
I am involved in research (e.g. through my own research projects or research supporting activities).	3.37 ($\pm$ 1.16)	3.58 ($\pm$ 1.00)	0.21	[-0.04-0.46]	0.092	
I seek additional learning opportunities to recognize how decisions are made in the light of new knowledge and information.	3.95 ($\pm$ 1.03)	4.16 ($\pm$ 0.90)	0.21	[-0.03-0.45]	0.088	
I support other students in their studies (e.g. as a mentor or by providing learning materials).	3.93 ($\pm$ 1.12)	4.07 ($\pm$ 0.91)	0.14	[-0.15-0.42]	0.361	
I seize learning opportunities to understand the basic principles of healthcare financing.	3.70 ($\pm$ 1.05)	4.17 ($\pm$ 0.85)	0.47	[0.20-0.74]	0.001*	
During my clinical training, I contemplate the use of resources (e.g. when ordering laboratory diagnostics).	3.63 ($\pm$ 0.98)	4.01 ($\pm$ 0.76)	0.38	[0.13-0.64]	0.004*	
I discuss the opportunities and limitations of change projects in student groups (e.g. the introduction of digital medical records).	3.53 ($\pm$ 0.92)	3.96 ($\pm$ 0.86)	0.43	[0.19-0.67]	<0.001*	

When changes are introduced in medical procedures (e.g. shortening the length of inpatient treatment), I keep myself informed about their effectiveness.	3.64 (±1.07)	4.20 (±0.83)	0.56	[0.27-0.84]	<0.001*	
I am involved in the student council and/or committees.	3.41 (±1.16)	3.51 (±1.09)	0.10	[-0.16 - 0.37]	0.427	5
I take part in projects or committees to improve undergraduate medical studies and teaching.	3.25 (±1.17)	3.70 (±1.01)	0.45	[0.19-0.70]	0.001*	
I am involved in student groups to improve the general conditions for studying (e.g. support for students with children).	3.12 (±1.15)	3.66 (±1.04)	0.54	[0.30-0.78]	<0.001*	
I take on leadership roles in a student group to implement teaching innovations (e.g. ultrasound tutorials).	3.16 (±1.25)	3.67 (±1.00)	0.51	[0.24- 0.79]	<0.001*	
I am involved in student groups to implement teaching innovations (e.g. ultrasound tutorials).	3.04 (±1.15)	3.68 (±0.96)	0.64	[0.37-0.92]	<0.001*	
I take responsibility for finances or resource planning in an organization (e.g. in a club or a group).	2.91 (±1.21)	3.54 (±1.12)	0.63	[0.40-0.86]	<0.001*	6
I am actively involved in a change project (e.g. a reorganization in a club).	3.16 (±1.23)	3.71 (±1.06)	0.55	[0.29- 0.81]	<0.001*	
I share information so that others can understand me better.	4.00 (±0.86)	4.17 (±0.89)	0.17	[-0.05- 0.40]	0.134	
I am able to steer group dynamic processes (e.g. by involving quieter group participants).	3.64 (±0.99)	4.08 (±0.86)	0.44	[0.21-0.66]	<0.001*	
α Paired t-test.						
* Statistically significant (p-value < 0.05)						
MeLeCoS: medical students' leadership competence self-assessment scale.						
SD: Standard deviation.						
95% CI: 95% Confidence Interval						
Scores range = 0-5						

4.3 Online Leadership Training Program Impact Assessment according to Sex, Study Field, and Study Level

The mean Post/Pre difference in the MeLeCoS score was slightly lower in males compared to females; however, this difference was statistically insignificant (mean (SD) 0.30 (±0.60) out of 5 vs 0.35 (±0.51) out of 5, mean difference = -0.50; 95% CI [-0.30-0.21], p-value =0.719). The participants in the field of medicine had a slightly higher mean Post/Pre difference in the MeLeCoS score compared to the participants in the field of nursing and midwifery; however, the result was statistically insignificant (mean (SD); 0.36 (±0.56) out of 5 vs 0.24 (±0.53) out of 5, mean difference = 12; 95% CI [-

0.15-0.41], p-value =0.363). Similarly, undergraduate students had a slightly higher mean Post/Pre difference in the MeLeCoS score compared to postgraduate participants; however, the result was statistically insignificant (mean (SD) 0.36 (± 0.62) out of 5 vs 0.26 (± 0.39) out of 5, mean difference = 0.10; 95% CI [-0.17-0.37], p-value =0.452) (Table 4 and Figure 3).

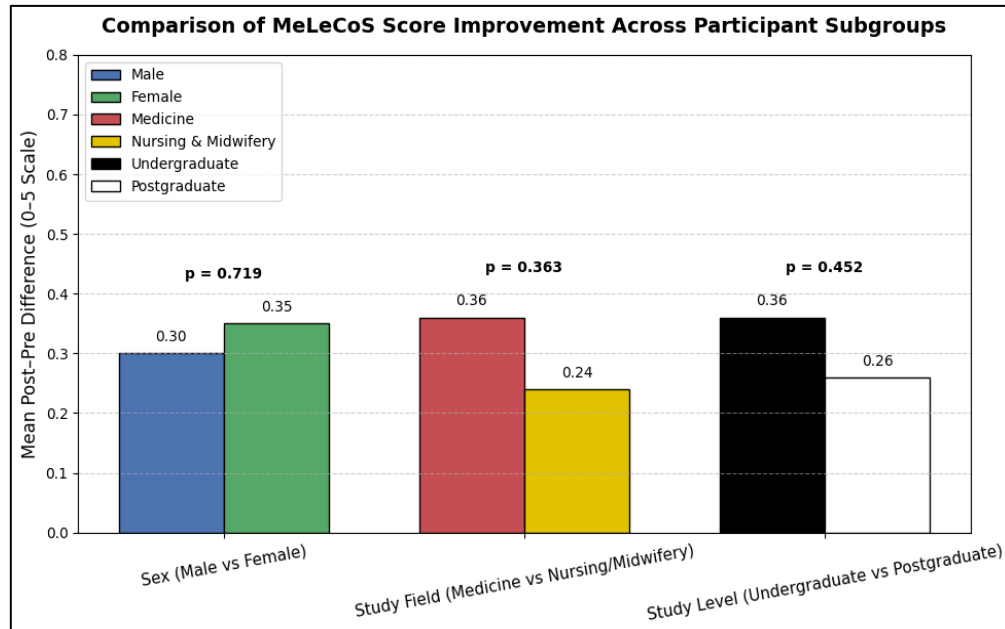


Figure 3. Comparison of MeLeCoS Score Improvement Across Participant Subgroups (n=76).

Table 4. Results of the Online Leadership Training Program Impact Assessment according to Sex, Study Field, and Study Level, using the Post-Pre Difference in the MeLeCoS (n=76).

MeLeCoS- Questionnaire Factors	Mean of Post/Pre Difference in MeLeCoS By Sex ($\pm$ SD)				Mean of Post/Pre Difference in MeLeCoS By Study Field ($\pm$ SD)				Mean of Post/Pre Difference in MeLeCoS By Study Level ($\pm$ SD)			
	Male	Female	MD [95% CI]	p-value α	Medicine	Nursing and Midwifery	MD [95% CI]	p-value α	Undergraduate	Postgraduate	MD [95% CI]	p-value α
[1] Achieving learning and reflecting on performance.	0.28 (± 0.86)	0.33 (± 0.50)	-0.05 [-0.40-0.29]	0.760	0.34 (± 0.75)	0.23 (± 0.42)	0.11 [-0.16-0.28]	0.425	0.30 (± 0.69)	0.31 (± 0.65)	-0.01 [-0.33-0.32]	0.982
[2] Demonstrating responsible behaviour and shaping relations.	0.11 (± 0.56)	0.12 (± 0.65)	-0.01 [-0.30-0.28]	0.944	0.11 (± 0.58)	0.14 (± 0.68)	-0.03 [-0.35-0.28]	0.823	0.14 (± 0.67)	0.07 (± 0.48)	0.07 [-0.23-0.37]	0.645
[3] Fostering personal development and promoting quality improvement.	0.32 (± 0.66)	0.31 (± 0.72)	0.01 [-0.31-0.33]	0.955	0.35 (± 0.68)	0.22 (± 0.72)	0.13 [-0.22-0.48]	0.467	0.34 (± 0.77)	0.28 (± 0.51)	0.06 [-0.28-0.39]	0.753

[4] Developing self-management and supporting management in healthcare.	0.32 (±0.81)	0.34 (±0.69)	-0.02 [-0.36-0.33]	0.913	0.38 (±0.74)	0.22 (±0.72)	0.16 [-0.21-0.54]	0.376	0.42 (±0.84)	0.17 (±0.45)	0.25 [-0.11-0.60]	0.101
[5] Promoting improvement and innovation in undergraduate medical education.	0.24 (±0.74)	0.60 (±0.80)	-0.36 [-0.72-0.00]	0.053	0.47 (±0.77)	0.39 (±0.86)	0.08 [-0.32-0.49]	0.682	0.48 (±0.88)	0.38 (±0.61)	0.10 [-0.29-0.48]	0.608
[6] Introducing systemic perspectives into organisations.	0.53 (±0.91)	0.38 (±0.57)	0.15 [-0.20-0.49]	0.434	0.54 (±0.79)	0.22 (±0.51)	0.31 [-0.06-0.68]	0.096	0.49 (±0.80)	0.35 (±0.60)	0.14 [-0.22-0.49]	0.437
Total MeLeCoS	0.30 (±0.60)	0.35 (±0.51)	-0.50 [-0.30-0.21]	0.719	0.36 (±0.56)	0.24 (±0.53)	0.12 [-0.15-0.41]	0.363	0.36 (±0.62)	0.26 (±0.39)	0.10 [-0.17-0.37]	0.452
α Independent Samples t-test. * Statistically significant (p -value < 0.05) MeLeCoS: medical students' leadership competence self-assessment scale. SD: Standard deviation. MD: Mean difference 95% CI: 95% Confidence Interval Scores range = 0-5												

4.4 Participants' Evaluation of the Online Leadership Training Program

Data from the participants' evaluation of the online leadership training program showed a perceived potential benefit from the training session. Overall, on a scale from 0 to 5, the participants rated the session as effective to highly effective in developing their leadership and communication skills, with a mean of 4.14 (± 0.72) out of 5. Additionally, on a scale from 0 to 5, where 5 indicated highly likely, they reported that they are likely to apply the learned skills and information into their practice, with a mean of 4.27 (± 0.66) out of 5. Moreover, on a scale from 0 to 5, where 5 indicated highly likely, they reported that they would likely recommend this session to a colleague, with a mean of 4.45 (± 0.79) out of 5 (Figure 4).

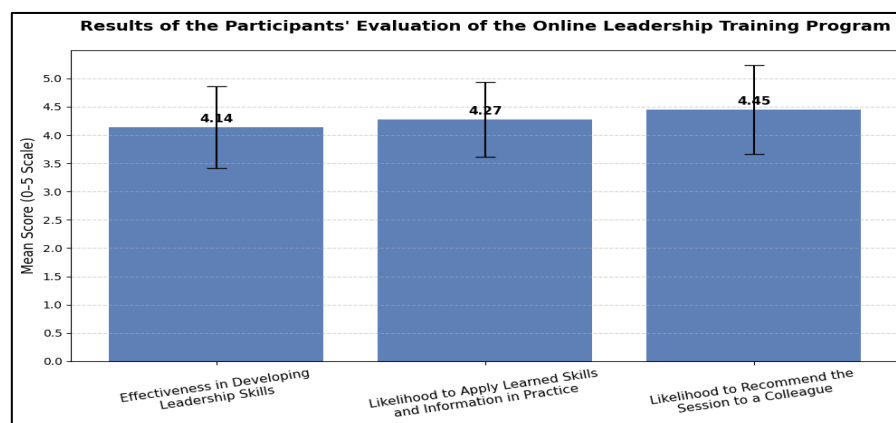


Figure 4. Results of the Participants' Evaluation of the Online Leadership Training Program.

5. Discussion

In this study, the researchers evaluated the impact of an online MLCF-based leadership training program on the self-reported leadership competencies of medical and nursing students, as well as postgraduate junior practitioners, using the MeLeCoS model, which encompasses six key leadership domains. The researchers found that this online training program effectively enhanced the self-reported leadership competencies of the participants, regardless of their sex, study field, or level of training highlighting the effectiveness of such training in developing the leadership competencies in future healthcare practitioners. The researchers also demonstrated that the MeLeCoS Self-Assessment tool could be used to assess the leadership competencies of the nursing students and the postgraduate junior practitioners, not just for undergraduate medical students.

The training program improved the participants' leadership competencies across most domains of the MeLeCoS score indicating its promising role in developing the leadership competencies of the future healthcare practitioners. Similar improvements were reported in previous studies, where structured leadership development programs led to enhanced self-assessed knowledge and expertise among participants [15]. While the debate on whether leaders are born or made is still ongoing, these findings supported the role of leadership development programs in developing the leadership competencies of the future healthcare practitioners [26,27]. Generally, effective clinical leadership could be developed through systematic leadership training programs, leading to enhanced clinical outcomes and greater satisfaction for both the patients and the providers [28].

The improvement in leadership competencies' score was consistent across different groups, regardless of their sex, study field, or level of training. This finding indicated the effectiveness of the online training program in developing the leadership competencies of future healthcare practitioners. This is particularly important because healthcare program graduates are expected to take on leadership roles, yet they often lack adequate preparation during their undergraduate education. While a graduate leadership curriculum is missing in the Palestinian context, a systematic review of leadership training curricula in graduate medical education programs worldwide revealed that these programs were inconsistent and had limited effectiveness [29]. In contrast, the suggested online leadership training program effectively enhanced the perceived leadership competencies of postgraduate, junior healthcare practitioners. Moreover, the induced improvement in leadership competencies in both disciplines, medicine and nursing, makes this training program a suitable option for institutions with limited resources and those prioritizing interprofessional education.

Improvements were observed across most of the MeLeCoS factors, with factor 5 (promoting innovation in undergraduate medical education) and factor 6 (introducing systemic perspectives into organizations) showing the greatest improvement. This reflects the training impact on the participants' motivation and willingness to contribute to the development of their institutions as leaders. Similarly, improvements were also observed in specific domains, such as 'achieving learning and reflecting on performance', 'fostering personal development and promoting quality improvement', and 'developing self-management and supporting management in healthcare'. This highlights the effectiveness of such a training program in developing the leadership competencies of the participants across multiple factors of the MLCF. On the other hand, no significant improvement was observed in factor 2 (demonstrating responsible behaviour and shaping relations). The minimal change likely reflects students' prior high levels of self-perceived competence in professional responsibility and teamwork, leaving a limited room for further measurable improvement in this domain. Overall, the online training program demonstrated its effectiveness in developing the participants' leadership competencies, providing foundational evidence

for policy-makers in health professions education in Palestine to integrate similar MLCF-based leadership development programs into formal curricula.

The participants' evaluation of the training program generally yielded promising perspectives (Level 1: Reaction). They perceived potential benefits from the training, and the majority indicated their willingness to apply the learned concepts in their practice. This finding corresponds to an early indicator of level 3 (Behavior change) suggesting that the program promoted readiness for behavioral change even though long-term follow-up was not conducted. Additionally, they were willing to recommend this online training program to their colleagues. The consistent high scores in these areas highlight the utility of the program and support its acceptance as an effective method for developing foundational leadership competencies for future healthcare practitioners.

6. Implications

Based on these findings, this proposed online leadership training program is affordable, short, and easy to deliver; it is an impactful tool for developing leadership competencies not only among the medical and nursing students but also among the graduate professionals. Therefore, the researchers confidently propose this course as an adjunct to the formal curricula for the undergraduate health professions education programs in Palestine and similar contexts. Moreover, the findings might lay, for the first time, foundational evidence that supports the integration of leadership development training into the formal curriculum. Such integration is pivotal because leadership skills are not only essential for productive clinical practice but also for creating positive workplace cultures and improving the patient's outcomes [5,30]. To optimize the impact of leadership training programs, educational institutions should integrate a competency-based framework for leadership development into the core curriculum. Moreover, they should ensure that leadership training, both theoretical and practical, is introduced early and reinforced throughout the educational journey [5,6]. By implementing a combination of training strategies, such as direct teaching, experiential learning, mentorship, and opportunities for students to experience real-life leadership responsibilities, the institutions can prepare future healthcare leaders to assume their roles in the healthcare system [31,32]. Future research may focus on the long-term impact of the leadership training and identify the potential barriers to integrating effective leadership training programs into the formal curriculum.

7. Strengths and Limitations

The pre-post design of this study enabled us to measure the direct impact of the online leadership training program. By establishing baseline measures, this design facilitated the understanding of the added value of the online leadership training program. Moreover, all participants received the same intervention from the same instructor, further enhancing the internal validity of this study in demonstrating the connection between the training program and the improved self-perceived leadership competencies. Furthermore, the use of the MeLeCoS, a valid and reliable self-assessment tool for a comprehensive set of leadership competency domains, adds to the strengths of this study. Additionally, including a diverse and representative sample of undergraduate healthcare students and junior postgraduate practitioners enhances the external validity of the study's findings, allowing for more generalizable results.

On the other hand, this study has some limitations. The short duration of the training program, combined with the lack of practical and situation-based learning strategies, such as role-playing, limits the competency development to the lower levels of Miller's pyramid model for competency development. This is particularly important because when participants

successfully execute the learned leadership behaviors through role-playing and simulations, they contribute to strengthening their beliefs in leadership capabilities [33]. Additionally, the online modality of the training limits interpersonal interaction, leading to reduced engagement, diminished motivation, and communication barriers [34–36]. Moreover, while the MeLeCoS is a valid and reliable leadership self-assessment tool, assessing leadership competencies through practical tools, such as peer evaluation during role plays, would further strengthen the objectivity of the leadership competencies assessment. Furthermore, the voluntary registration in the training program and participation in the study might have attracted individuals with an interest in developing leadership skills, thereby introducing a selection bias. The inclusion of a sufficient and representative sample may have compensated for this potential bias.

8. Recommendations

Based on the findings of this study, several recommendations can be made to improve leadership development in health professions education. Firstly, leadership training should be integrated early and longitudinally within curricula, using a competency-based approach that is reviewed and strengthened at multiple stages of training [5,6,31]. Secondly, educational strategies should include a combination of didactic lectures, experiential learning, interprofessional education, and opportunities for students to adopt leadership skills in both academic and clinical settings [31,32]. Thirdly, faculty development initiatives to equip the educators with the skills necessary to teach effective leadership behaviors would strengthen the impact of such leadership training programs [32]. Fourthly, the assessment of leadership competency domains should utilize multiple formats, integrating self-assessment, peer review, and faculty feedback to capture a thorough, comprehensive picture of student progress [5,31]. Finally, future studies should focus on multi-organizational research with longer follow-up to assess the long-term impact of leadership training and to identify the most effective approaches for program implementation and assessment.

9. Conclusion

Leadership training can contribute to the development of the leadership competencies of healthcare students and practitioners. This brief online leadership training program demonstrated an acceptable efficacy in developing the leadership competencies of the participants. The findings support its role as an adjunct to the formal curriculum, supporting the efforts of faculties in building the leadership competencies of their students. Integrating leadership training into the formal undergraduate curriculum, at early stages and in a longitudinal fashion, may ensure that future healthcare practitioners are well-equipped to assume leadership roles and enhance the quality of healthcare. It is necessary to design and implement leadership development training programs for junior healthcare practitioners to prepare them for real-life situations where leadership competencies may be life-saving.

10. Declarations

Acknowledgments

Not applicable.

Ethical consideration

This study adhered to the principles of the Declaration of Helsinki. Ethical approval to conduct this study was obtained from the Institutional Review Board (IRB) at An-Najah National University (Reference number: Nurs.

Sep.2025/36). A study information sheet was shared with the participants, and those who voluntarily agreed to participate signed an electronic informed consent form. Participation was entirely voluntary, and participants were informed that they could withdraw from the study or exit the survey at any time without any repercussions. To maintain confidentiality, no personally identifiable information was collected at any stage of the study.

Consent to participate

All participants enrolled in this study received an information sheet that explained the study's purpose and details about their involvement. The first page of the Google Form contained the written consent form. Participants electronically consented to this study by answering a multiple-choice question that confirmed their understanding of the information sheet and their voluntary agreement to participate. This method was deemed valid by the Institutional Review Board (IRB).

Conflicts of interest

The author (Prof. Malik Zaben) is a member of the Editorial Board for the AAUP Journal of STEM and Health Sciences. To maintain a transparent and unbiased peer-review process, Prof. Malik was not involved in the selection of reviewers or any editorial decisions regarding this manuscript. The peer-review process was handled independently by other editors of the journal. Otherwise, the authors have no conflicts of interest to declare that are relevant to the content of this article.

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Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Authors Contributions

Conceptualization: Ahmad Rjoub, Fadi Zaben, and Malik Zaben. **Formal analysis:** Ahmad Rjoub. **Investigation:** Ahmad Rjoub, Zainah Amjad Issa, Asala Khalil Rezeq, Zeina Daoud Salhi, Fadi Zaben, and Malik Zaben. **Methodology:** Ahmad Rjoub, Fadi Zaben, and Malik Zaben. **Supervision:** Fadi Zaben and Malik Zaben. **Visualization:** Zainah Amjad Issa, Asala Khalil Rezeq, and Zeina Daoud Salhi. **Writing – original draft:** Zainah Amjad Issa, Asala Khalil Rezeq, Zeina Daoud Salhi, and Ahmad Rjoub. **Writing – review & editing:** Ahmad Rjoub, Fadi Zaben, and Malik Zaben.

References

- [1] Fattah L, Bloom L, Ventura C Della, Gabrilove J. Building leadership capacity among junior faculty: Evaluating multi-level outcomes of a leadership program. *J Clin Transl Sci.* 2023;7[1].
- [2] Smith KA, Morassaei S, Ruco A, Bola R, Currie KL, Cooper N, et al. An evaluation of the impact for healthcare professionals after a leadership innovation fellowship program. *J Med Imaging Radiat Sci.* 2022;53[4].
- [3] Ogurek B, Harendza S. Development of medical leadership competence during undergraduate medical students' final year – a cross-sectional cohort study. *BMC Med Educ.* 2025;25[1].

- [4] Vo A, Torti J, Haddara W, Sultan N. Exploring medical students' perspectives of physician leadership. *BMC Med Educ.* 2023;23[1].
- [5] Costa P, Sousa JP, Nascimento T, Cruchinho P, Nunes E, Gaspar F, et al. Leadership Development in Undergraduate Nursing Students: A Scoping Review. *Nursing Reports.* 2025;15.
- [6] Scammell JME, Apostolo JLA, Bianchi M, Costa RDP, Jack K, Luiking ML, et al. Learning to lead: A scoping review of undergraduate nurse education. *J Nurs Manag.* 2020;28[3].
- [7] Aldersley K, Gibb J, Grainger C, Abou-el-Ela-Bourquin B, Badhrinarayanan S, Bhanot R, et al. Medical leadership training varies substantially between UK medical schools: Report of the leadership in undergraduate medical education national survey (LUMENS). *Med Teach.* 2023;45[1].
- [8] Ochsmann EB, Zier U, Drexler H, Schmid K. Well prepared for work? Junior doctors' self-assessment after medical education. *BMC Med Educ.* 2011;11[1].
- [9] Curry LA, Ayedun AA, Cherlin EJ, Allen NH, Linnander EL. Leadership development in complex health systems: a qualitative study. *BMJ Open.* 2020;10[4].
- [10] Johnson O, Begg K, Kelly AH, Sevdalis N. Interventions to strengthen the leadership capabilities of health professionals in Sub-Saharan Africa: A scoping review. *Health Policy Plan.* 2021;36[1].
- [11] Omar A, Shrestha A, Fernandes R, Shah A. Perceived barriers to medical leadership training and methods to mitigate them in the undergraduate medical curriculum: A mixed-methods study of final-year medical students at two medical schools. *Future Healthc J.* 2020;7[3].
- [12] Medical leadership competency framework: enhancing engagement in medical leadership. Coventry: NHS Institute for Innovation and Improvement; 2010.
- [13] Nicol. Improving clinical leadership and management in the NHS. *J Healthc Leadersh.* 2012.
- [14] Ogurek B, Harendza S. Medical students' leadership competence in health care: development of a self-assessment scale. *BMC Med Educ.* 2024;24[1].
- [15] Frich JC, Brewster AL, Cherlin EJ, Bradley EH. Leadership Development Programs for Physicians: A Systematic Review. *J Gen Intern Med.* 2015;30[5].
- [16] Do V, Maniate JM, Sultan N, Sonnenberg L. The 4C's of influence framework: fostering leadership development through character, competence, connection and culture. *Leadership in Health Services.* 2023;36[4].
- [17] Lyons O, Su'a B, Locke M, Hill A. A systematic review of leadership training for medical students. *New Zealand Medical Journal.* 2018;131.
- [18] Cheney AM, Baltrushes N, Gehlbach D, Navarro A. Becoming a leader for underserved patients—the importance of student run free clinics. *Frontiers in Health Services.* 2024;4.
- [19] Webb AMB, Tsipis NE, McClellan TR, McNeil MJ, Xu MM, Doty JP, et al. A First Step Toward Understanding Best Practices in Leadership Training in Undergraduate Medical Education: A Systematic Review. *Academic Medicine.* 2014;89.
- [20] Katoue MG, Cerda AA, García LY, Jakovljevic M. Healthcare system development in the Middle East and North Africa region: Challenges, endeavors and prospective opportunities. *Front Public Health.* 2022;10.
- [21] Chavan AK, Bendriss R. Leadership Curriculum in Medical Education: Exploring Student and Faculty Perceptions in a US Medical School in Qatar. *J Healthc Leadersh.* 2022;14.

- [22] Blanco M, Prunuske J, Dicorcia M, Learman LA, Mutcheson B, Huang GC. The DoCTRINE Guidelines: Defined Criteria to Report INnovations in Education. *Academic Medicine*. 2022;97[5].
- [23] Upsher R, Dommett E, Carlisle S, Conner S, Codina G, Nobili A, et al. Improving reporting standards in quantitative educational intervention research: introducing the CLOSER and CIDER checklists. *J New Approaches Educ Res*. 2025;14[1].
- [24] Thomas PA, Kern DE. Curriculum development for medical education: a six-step approach. John Hopkins University Press. 2022.
- [25] Kirkpatrick DL. Evaluating training programs: The four levels. 1998.
- [26] Warren OJ, Carnall R. Medical leadership: Why it's important, what is required, and how we develop it. *Postgrad Med J*. 2011;87.
- [27] Sonnino RE. Health care leadership development and training: Progress and pitfalls. *J Healthc Leadersh*. 2016;8.
- [28] Blumenthal DM, Bernard K, Bohnen J, Bohmer R. Addressing the leadership gap in medicine: Residents' need for systematic leadership development training. *Academic Medicine*. 2012;87[4].
- [29] Sadowski B, Cantrell S, Barelski A, O'Malley PG, Hartzell JD. Leadership Training in Graduate Medical Education: A Systematic Review. *J Grad Med Educ*. 2018;10.
- [30] van Diggele C, Burgess A, Roberts C, Mellis C. Leadership in healthcare education. *BMC Med Educ*. 2020;20.
- [31] Evans MA, James EJ, Misa Mi. Leadership Training in Undergraduate Medical Education: A Systematic Review. *Int J Med Students*. 2023;11[1]:58–66.
- [32] Ekayani NWD, Findyartini A, Anugrapaksi E, Nadarajah VDV. Integration of leadership training in the medical and health profession education curricula. *Jurnal Pendidikan Kedokteran Indonesia*. 2023;12[1].
- [33] Lawrance L, McLeroy KR. Self-efficacy and Health Education. *J Sch Health*. 1986;56[8].
- [34] Sawant NS, Vinchurkar P, Kolwankar S, Patil T, Rath K, Urkude J. Online teaching, learning, and health outcomes: Impact on medical undergraduate students. *Ind Psychiatry J*. 2023;32[1].
- [35] Forde C, OBrien A. A Literature Review of Barriers and Opportunities Presented by Digitally Enhanced Practical Skill Teaching and Learning in Health Science Education. *Med Educ Online*. 2022;27.
- [36] Naciri A, Radid M, Kharbach A, Chems G. E-learning in health professions education during the COVID-19 pandemic: A systematic review. *J Educ Eval Health Prof*. 2021;18.



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Integrating Sentiment Analysis and Topic Modeling for Actionable Business Intelligence: A Comparative Study of Machine Learning and Deep Learning Architectures for Arabic Company Reviews

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Abstract

Background: This study presented a comprehensive framework for Arabic Sentiment Analysis (ASA) integrated with Topic Modeling to support actionable Business Intelligence (BI) from company reviews. **Methods:** Using 5-fold stratified cross-validation, the researcher compared traditional Machine Learning (ML) classifiers (Logistic Regression, Support Vector Machine, Naive Bayes, and Random Forest) with Deep Learning (DL) architectures (Bidirectional LSTM and Bidirectional GRU) and a Transformer-based model (AraBERT). **Results:** The experiments demonstrated that no single model dominated across all evaluation metrics. Logistic Regression achieved the highest Macro F1-score (0.6212 ± 0.0036 ; 95% CI: 0.6180–0.6243), indicating the most balanced performance under class imbalance. Naive Bayes obtained high accuracy (0.8350 ± 0.0029 ; 95% CI: 0.8324–0.8376) and weighted F1-score (0.8140 ± 0.0029 ; 95% CI: 0.8115–0.8165), reflecting strong performance on the dominant sentiment class. **Conclusion:** Deep learning models achieved competitive accuracy (Bi-LSTM: 0.8386 ± 0.0020 ; 95% CI: 0.8369–0.8404) but did not surpass linear models in Macro F1. AraBERT outperformed all

models with accuracy (0.8598 ± 0.0044 ; 95% CI: 0.8560–0.8636) and Macro F1 (0.6382 ± 0.0100 ; 95% CI: 0.6294–0.6469). Topic Modeling using Latent Dirichlet Allocation (LDA) complemented sentiment classification by extracting interpretable strengths and weaknesses for each company. Precision-Recall curves across models confirmed the impact of class imbalance, with high Average Precision (AP) for the positive class (~ 0.92 – 0.96) and very low AP for neutral (~ 0.09 – 0.20). These findings supported actionable BI insights from Arabic company reviews.

Keywords: Arabic NLP, Sentiment Analysis, Bi-LSTM, Support Vector Machines, Topic Modeling, Business Intelligence, Class Imbalance

1. Introduction

The rapid proliferation of digital platforms and e-commerce across the Middle East and North Africa (MENA) has transformed how consumers interact with brands. In the contemporary digital economy, customer feedback – expressed through reviews, tweets, and comments – has become a rich source, providing raw, unstructured data that contains the key to understanding consumer behavior and market trends [1]. However, the sheer volume of this data makes manual moderation and analysis impossible. Consequently, Automated Sentiment Analysis (ASA) has emerged as a vital tool for Business Intelligence (BI), allowing organizations to monitor their brand reputation in real-time [2]. Arabic is the fifth most spoken language globally, with over 400 million speakers. Despite its global significance, Arabic Natural Language Processing (NLP) has historically lagged behind English, primarily due to the unique morphological and orthographic characteristics of the language. While English sentiment analysis is often a matter of identifying polarity words, Arabic sentiment is deeply embedded in complex grammatical structures and cultural nuances. For businesses operating in Arab markets, the ability to accurately "sense" the emotion behind a review is not just a technical task but a strategic necessity for survival in a competitive landscape. The challenges of Arabic NLP can be categorized into three distinct layers: morphological, orthographic, and dialectal.

Morphological Complexity: Arabic is a highly inflected, derivational language based on a root-and-pattern system. A single word can contain a root, prefixes, suffixes, and even infixes that change its meaning from a verb to a noun or a possessive statement. For instance, the word "وسيعجبهم" (and they will like it) contains a conjunction, a future tense marker, a root verb, and a plural pronoun. For a Machine Learning model, these "clitics" increase the size of the vocabulary exponentially, leading to data sparsity issues where the model sees many variations of the same root but fails to connect them.

Orthographic Variation and Noise: In informal settings, such as company reviews on Google Maps or Facebook, Arabic speakers rarely use diacritics (Tashkeel). Furthermore, they often use character elongation (Tatweel) for emphasis (e.g., "ممتاز" instead of "ممتاز") or interchange different forms of the letter Alef (أ, إ, آ). Without a robust preprocessing layer, such as the one implemented in this study using pyarabic, these variations create "noise" that significantly degrades model accuracy.

Dialectal Diversity: While Modern Standard Arabic (MSA) is used in formal writing, reviews are frequently written in various dialects (Egyptian, Levantine, Gulf, etc.). These dialects often utilize different negations and vocabulary. A "Positive" word in one dialect might be "Neutral" in another, requiring models that can capture contextual dependencies rather than relying on static sentiment lexicons.

For over a decade, traditional Machine Learning (ML) served as the backbone of ASA. Models such as Support Vector Machines (SVM) and Naive Bayes, paired with TF-IDF (Term Frequency-Inverse Document Frequency)

vectorization, were the gold standard. These models are mathematically robust and computationally efficient. As demonstrated in our implementation, SVM remains a powerful contender because it handles high-dimensional sparse data – typical of text – extremely well. However, traditional ML has a major limitation: it is "bag-of-words" oriented. It treats words as independent entities and often fails to capture the long-range dependencies and the "flow" of a sentence. The advent of Deep Learning (DL) and Recurrent Neural Networks (RNNs) marked a paradigm shift. Unlike traditional classifiers, architectures like the Bidirectional Long Short-Term Memory (Bi-LSTM) and Bidirectional Gated Recurrent Unit (Bi-GRU) process text as a sequence. By reading a review both from left-to-right and right-to-left, these models can understand the context of a word based on what preceded it and what followed it. This is particularly crucial for Arabic, where the placement of a negation word can occur far before the adjective it modifies.

While classification accuracy is a primary metric for researchers, it is often insufficient for business stakeholders. A company does not only need to know that a review is "Negative"; it needs to know why. Is the negativity directed at the customer service, the price, or the product quality? This research bridges the gap between raw classification and actionable insight. By integrating Latent Dirichlet Allocation (LDA) for topic modeling, the researcher has moved beyond polarity. The system automatically extracts the "strengths" and "weaknesses" of a brand by identifying the most frequent themes within positive and negative feedback subsets. This transforms a simple NLP task into a Comprehensive Business Intelligence Report, enabling decision-makers to identify specific operational areas that require improvement. The primary objective of this study was to provide a comprehensive comparative analysis of various computational architectures for ASA. Specifically, the researcher aimed to:

evaluate traditional ML models (SVM, Random Forest, Naive Bayes, Logistic Regression) against Deep Learning models (Bi-LSTM, Bi-GRU) and a Transformer-based model (AraBERT) using the "Arabic Company Reviews" dataset.

develop a standardized preprocessing pipeline that addresses the specific needs of the Arabic language, including normalization and noise reduction.

propose a Business Intelligence framework that uses unsupervised learning (LDA) to provide granular insights into brand perception.

visualize performance trade-offs using Precision-Recall curves and learning curves to determine the most cost-effective architecture for industrial deployment.

employ 5-fold stratified cross-validation to ensure robust and reproducible performance estimation, addressing limitations of single train/test splits and severe class imbalance in the exploited dataset.

By addressing these objectives, this research contributed and provided a scalable and interpretable framework for Arabic-speaking markets, providing both high-accuracy sentiment detection and deep-dive thematic analysis.

2. Related Work

The field of Arabic Sentiment Analysis (ASA) has evolved through distinct computational eras: from early rule-based systems and manual lexicons to the rise of statistical Machine Learning (ML), and finally to the current dominance of Deep Learning (DL) and Transformer-based architectures.

2.1 Theoretical Foundations of Arabic Sentiment Analysis

Early research in ASA was primarily constrained by the lack of large-scale, annotated datasets. Early pioneers like Abbasi et al. [8] focused on "Affect Analysis," which combined stylistic and structural features to identify sentiment in extremist forums. Their work laid the groundwork for feature engineering in Arabic, proving that language-specific preprocessing—such as handling the "root-and-pattern" morphology—was essential for reducing feature sparsity.

Unlike English, where sentiment is often explicitly carried by adjectives, Arabic sentiment is frequently embedded in verbal morphology. For instance, the research by Farra et al. [9] highlighted how sentence-level sentiment in Arabic is heavily influenced by the "Mood" (I'rab) and the specific grammatical constructs used in dialectal vs. Modern Standard Arabic (MSA). They noted that simple bag-of-words models often miss the nuances of negation and intensification in complex Arabic sentences.

2.2 Traditional Machine Learning: The Statistical Era

The mid-2010s saw a surge in the application of supervised learning for ASA. Support Vector Machines (SVM) and Naïve Bayes (NB) became the standard benchmarks for the industry [4].

Support Vector Machines (SVM): El-Halees [10] proposed a multi-stage approach using SVM, which remains a highly relevant methodology. His research demonstrated that SVMs, when paired with TF-IDF vectorization and N-gram features (unigrams and bigrams), could achieve accuracies exceeding 80% on news datasets. Our implementation leverages this historical success by utilizing the LinearSVC architecture, which excels in high-dimensional text spaces where the number of features often exceeds the number of samples.

Random Forests and Ensembles: Al-Kabi et al. [3] conducted a comprehensive survey of 14 different classifiers on a large dataset of Arabic reviews. Their findings suggested that while Naïve Bayes is computationally efficient, Ensemble methods like Random Forest provide better robustness against the "noise" of dialectal Arabic. This informed our decision to include Random Forest in our comparative pipeline to evaluate its performance against high-variance user reviews.

2.3 The Deep Learning Revolution: RNNs, LSTM, and GRU

The shift toward Deep Learning (DL) addressed the fundamental weakness of ML: the inability to capture sequential context [7]. Traditional ML treats "ليس جيد" (not good) as two independent tokens, whereas DL architectures maintain a "memory" of previous tokens.

Bi-LSTM Architectures: Research by Al-Smadi et al. [11] on Aspect-Based Sentiment Analysis (ABSA) for Arabic hotels and restaurants revealed that Bidirectional Long Short-Term Memory (Bi-LSTM) networks significantly outperform traditional models by capturing dependencies in both directions. This is particularly crucial for Arabic, where the subject often follows the verb, and negation markers can appear several words before the target adjective. Our study builds on this by implementing a 64-unit Bi-LSTM layer to handle these long-range semantic dependencies.

Gated Recurrent Units (GRU): While LSTMs are powerful, Gated Recurrent Units (GRU) have emerged as a computationally efficient alternative with fewer parameters and comparable representational capacity. Dahou et al. [12] demonstrated the effectiveness of distributed Word2Vec embeddings combined with deep neural architectures for Arabic sentiment classification, highlighting the benefits of neural sequence modeling over

traditional machine learning approaches. In parallel, Cho et al. [17], who originally introduced the GRU architecture, showed that GRUs achieve faster convergence and competitive performance compared to LSTMs due to their simplified gating mechanism. Motivated by these findings, our comparative framework explicitly evaluates both Bi-LSTM and Bi-GRU architectures to identify the optimal accuracy-to-computational-cost trade-off for industrial Arabic sentiment analysis applications.

2.4 Word Embeddings and Vector Space Models

The transition from one-hot encoding (TF-IDF) to dense vector representations revolutionized ASA. Early models relied on static embeddings like Word2Vec and GloVe.

Soliman et al. [13] introduced AraVec, a pre-trained distributed word representation specifically for Arabic. Their research demonstrated that utilizing pre-trained embeddings on large corpora of tweets and news articles allowed models to understand semantic similarity (e.g., understanding that "رائع" (wonderful) and "جميل" (beautiful) share a similar sentiment space). However, our current study focuses on training domain-specific embeddings to capture the unique vocabulary of corporate reviews, which often differs from social media slang.

2.5 The Role of Preprocessing in Sentiment Accuracy

A recurring theme in the literature is that the "quality of cleaning" is often more important than the "complexity of the model."

Normalization and Stemming: The work of Duwairi et al. [14] emphasized that without normalizing the "Hamza" and "Yaa" and stripping "Tashkeel" (diacritics), the vocabulary size becomes unmanageable. They argued that light stemming (removing common prefixes and suffixes) is superior to root stemming for sentiment analysis because root stemming can conflate words with opposite polarities (e.g., "مقبول" - acceptable and "قبل" - before). This research justifies our use of the pyarabic and tashaphyne libraries in the preprocessing.py module.

Handling Sarcasm and Dialects: Sarcasm remains one of the "Grand Challenges" of ASA. Abu Farha and Magdy [15] noted that Arabic sarcasm is often dialect-specific. They developed the ArSarcasm dataset, highlighting that even the most advanced DL models struggle with figurative language. While our current research focuses on polarity, their work underscores the need for the future integration of Transformer models like AraBERT.

2.6 Sentiment Analysis for Business Intelligence (BI)

In the corporate sector, sentiment analysis is often the first step toward Topic Modeling. Latent Dirichlet Allocation (LDA) has been widely used to identify the "aspects" of a business that customers are discussing.

Blei et al. [5] explored the integration of sentiment scores with LDA to create "Brand Perceptual Maps." Their work showed that by filtering reviews into positive and negative buckets before applying LDA, companies could identify specific "pain points" (e.g., slow delivery) vs. "competitive advantages" (e.g., friendly staff). Our insights.py module implements this specific theoretical framework by generating automated "Strength/Weakness" reports for brands in the MENA region.

2.7 Recent Trends: Transformers and Large Language Models (LLMs)

The current state-of-the-art involves Transformer architectures, specifically AraBERT. Antoun et al. [16] demonstrated that AraBERT, through its self-attention mechanism, achieves unprecedented results on ASA benchmarks. While this study focuses on the comparative analysis of lighter ML/DL architectures suitable for edge deployment or resource-constrained environments, the literature clearly points toward a hybrid future where Transformers provide the "gold standard" and RNNs provide "efficiency."

Despite the wealth of research, two significant gaps remain:

Industrial Scalability: Most research focuses on academic datasets (like LABR or ArSarcasm) rather than real-world corporate review streams which contain a mix of formal and highly informal text.

Actionable Intelligence: Few studies bridged the gap between "Classification Report" and "Business Report."

This research contributed to the field by providing a head-to-head comparison of five distinct architectures (SVM, RF, NB, Bi-LSTM, Bi-GRU) specifically on the Fahd Seddik company reviews dataset [6], paired with an unsupervised insight generation layer that translates computational metrics into managerial value. In addition, the researcher included AraBERT as a Transformer baseline to evaluate its performance against traditional ML and DL models using 5-fold stratified cross-validation, addressing limitations of single-split experiments and providing more reliable performance estimates under class imbalance.

3. Methodology

The methodology of this study followed a structured computational pipeline designed to move from raw, unstructured Arabic text to high-level business intelligence. The process was divided into four major phases: Data Preprocessing, Feature Engineering, Model Implementation (Machine Learning and Deep Learning), and Insight Extraction. In Figure 1, the researcher provided a high-level architecture of the proposed methodology, including the employed models and 5-fold stratified cross-validation loop.

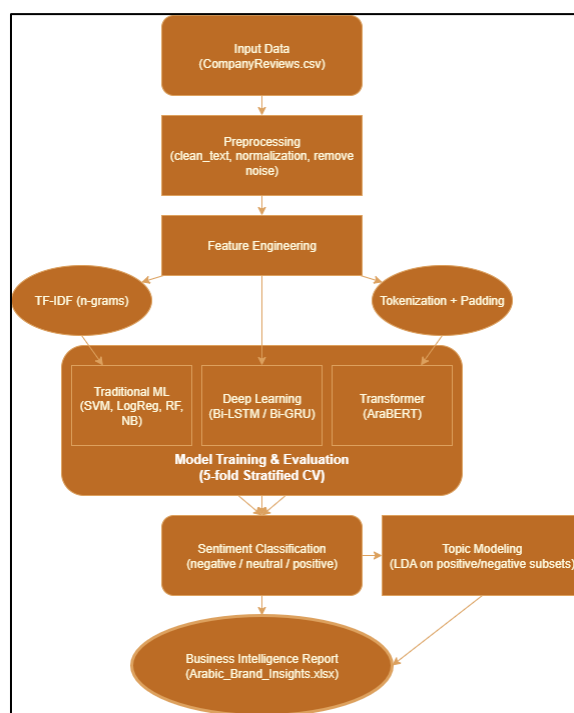


Figure 1. High-level Architecture of the Employed Methodology

3.1 Data Preprocessing and Normalization

Given the morphological richness of Arabic, the preprocessing layer (implemented in preprocessing.py) is critical. The researcher defined the cleaning function $\mathcal{C}(R)$ such that for any raw review R , the cleaned output R' is:

$$\mathcal{C}(R) = \text{Normalize}(\text{Strip}(\text{Filter}(R))) \dots (1)$$

Algorithmic Steps for Preprocessing:

1. Noise Reduction: Removal of non-Arabic characters, URLs, and punctuation using Regular Expressions.
2. Orthographic Normalization: * Standardizing Alef variants (أ, إ, ؤ) to a bare Alef (ا).
 - Standardizing Yaa (ي) and Alef Maksura (ى).
3. Tashkeel and Tatweel Removal: Using the pyarabic library to strip diacritics and character elongations (e.g., "جميل" becomes "جميل").
4. Token Normalization: Reducing character repetitions (e.g., "رائع" to "رائع") to prevent vocabulary explosion.

3.2 Feature Engineering: Vectorization and Embeddings

The researcher employed two distinct types of mathematical representations for the text data depending on the model architecture.

3.2.1 TF-IDF Vectorization (for ML Models)

For traditional models, the researcher used the Term Frequency-Inverse Document Frequency (TF-IDF) weight. The weight W of a term t in document d is calculated as:

$$W_{t,d} = tf_{t,d} \times \log\left(\frac{N}{df_t}\right) \dots (2)$$

Where N is the total number of reviews and $\{df\}_t$ is the number of reviews containing term t . We implement unigrams and bigrams ($n=1, 2$) to capture local word orderings.

3.2.2 Sequence Padding and Word Embeddings (for DL Models)

For Deep Learning, the text was converted into sequences of integers $S = [w_1, w_2, \dots, w_n]$. To ensure uniform input for the neural network, the researcher applied zero-padding $\mathcal{P}(S)$ such that all sequences have length $L=100$:

$$\mathcal{P}(S) = [0, 0, \dots, w_1, w_2, \dots, w_n] \dots (3)$$

3.3 Exploited Model Architectures

The researcher compared five distinct models, each representing a different mathematical approach to classification. Additionally, AraBERT was included as a Transformer-based baseline to evaluate modern pre-trained contextual embeddings against traditional ML and DL approaches.

3.3.1 Support Vector Machines (SVM)

The SVM seeks to find the optimal hyperplane that maximizes the margin between classes. In this implementation (LinearSVC), the researcher solved the following optimization problem:

$$\min \frac{1}{2} \|w\|^2 + C \sum_{i=1}^n \xi_i \dots (4)$$

Subject to: $y_i (w \cdot x_i + b) \geq 1 - \xi_i$. The parameter C controls the trade-off between margin maximization and error minimization.

3.3.2 Naive Bayes (Multinomial)

Based on Bayes' Theorem, this model assumes conditional independence between features:

$$P(y | x_1, \dots, x_n) = (P(y) \prod_{i=1}^n P(x_i | y)) / P(x_1, \dots, x_n) \dots \dots \dots (5)$$

Despite the "naive" assumption, it is highly effective for high-dimensional Arabic text where term frequencies are the primary signals.

3.3.3 Random Forest (RF)

An ensemble learning method that constructs N decision trees during training. The final sentiment $\hat{y}$ is determined by majority voting:

$$\hat{y} = \text{mode}\{T_1(x), T_2(x), \dots, T_N(x)\} \dots \dots \dots (6)$$

3.3.4 Bidirectional LSTM (Bi-LSTM)

LSTMs use "gates" to manage the flow of information, solving the vanishing gradient problem. A cell at time t consists of a Forget Gate f_t , Input Gate (i_t), and Output Gate (o_t):

$$f_t = \sigma(W_f \cdot [h_{t-1}, x_t] + b_f) \dots \dots \dots (7)$$

The Bidirectional component allows the network to have both forward ($\rightarrow h_t$) and backward ($\leftarrow h_t$) hidden states, concatenating them to capture full context:

$$H_t = [\rightarrow h_t; \leftarrow h_t] \dots \dots \dots (8)$$

The architecture of this model is depicted in Figure 2. To handle class imbalance, class weights (computed as inverse class frequency) were applied during training.

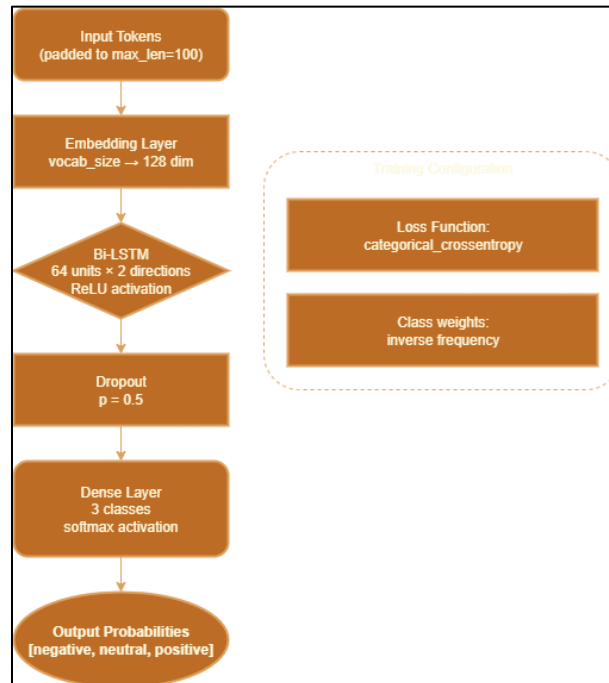


Figure 2. Architecture of the employed Bi-LSTM model

3.3.5 Bidirectional GRU (Bi-GRU)

The Gated Recurrent Unit (GRU) simplifies the LSTM by merging the forget and input gates into a single "Update Gate" (z_t) and adding a "Reset Gate" (r_t):

$$z_t = \sigma(W_z \cdot [h_{t-1}, x_t] + b_z) \dots\dots\dots (9)$$

$$r_t = \sigma(W_r \cdot [h_{t-1}, x_t] + b_r) \dots\dots\dots (10)$$

This reduces the parameter count, often leading to faster training times on smaller Arabic datasets without significant loss in accuracy.

3.3.6 Transformer Model (AraBERT)

AraBERT is a BERT-based model pre-trained on large Arabic corpora. The researcher fine-tuned the aubmindlab/bert-base-arabertv2 checkpoint using the Hugging Face Transformers library. The key settings included:

- Maximum sequence length: 128 tokens
- Batch size: 32
- Epochs per fold: 3
- Optimizer: AdamW (learning rate scheduler with warmup)
- Mixed precision (fp16) enabled with GPU.
- Evaluation strategy: per epoch
- No model checkpoint saving during training to reduce disk usage

AraBERT was trained using the Trainer API with stratified 5-fold cross-validation. Class imbalance was implicitly handled by the pre-trained contextual embeddings and the large capacity of the model.

3.4 Unsupervised Insight Generation (LDA)

The final stage of the methodology involved Latent Dirichlet Allocation (LDA) to extract themes from the classified reviews. LDA assumes each document d is a mixture of topics θ_d and each topic k is a distribution over words ϕ_k .

$$P(w | d) = \sum_{k=1}^K P(w | z = k) P(z = k | d) \dots\dots\dots (11)$$

By applying LDA separately to the "Positive" and "Negative" subsets for each company, the researcher generated a Business Intelligence Report that highlighted specific operational strengths and weaknesses.

3.5 Experimental Setup and Evaluation Metrics

The dataset was evaluated using 5-fold stratified cross-validation (StratifiedKFold, shuffle=True, random seed=42) to maintain class distribution across folds and ensure robust performance estimation. All models were trained and evaluated on the same folds for fair comparison. Metrics included:

1. Macro F1-Score: Primary metric to account for class imbalance and minority class performance.
2. Accuracy and Weighted F1-Score: To reflect overall and majority-class performance.
3. Precision-Recall Curves: Generated from the last fold to visualize model confidence and imbalance effects (Average Precision reported per class and micro-averaged).
4. Learning Curves (optional): To detect overfitting vs. underfitting in DL models.

Computational notes: ML models run on CPU (<1 min/fold), DL models run on GPU (RTX 4060, 1–3 min/fold), AraBERT runs on GPU (20–30 min/fold).

Algorithm 1: The Proposed ASA-BI Framework

Input: Raw Arabic Company Reviews CSV

Output: Classification Metrics & Brand Insights Report

1. Load dataset: $\rightarrow \text{prepare_dataset}()$
2. For each review R : Apply $\mathcal{C}(R)$ (Normalization & Cleaning)
3. Split data into 5 stratified folds (StratifiedKFold)
4. Train ML Pipeline:
 - a. TF-IDF (1,2) n-grams
 - b. Fit SVM, RF, NB, LogReg
5. Train DL Pipeline:
 - a. Tokenize and Pad sequences
 - b. Fit Bi-LSTM and Bi-GRU (20 epochs max, Adam optimizer, early stopping, class weights for imbalance)
6. Train Transformer Pipeline:
 - a. Tokenize with AraBERT tokenizer
 - b. Fine-tune AraBERT (3 epochs/fold, batch_size=32, fp16 on GPU)
7. **Evaluate:** Generate Confusion Matrices and PR Curves
8. Insight Mining: For each company, run LDA on $\{R_{\{pos\}}\}$ and $\{R_{\{neg\}}\}$
9. **Export** Final_Business_Report.xlsx

4. Experimental Setup

Experiments were conducted on an Arabic company reviews dataset. The data were split using 5-fold stratified cross-validation to preserve class distribution and ensure robustness across folds. Evaluation metrics included Accuracy, Macro F1-score, and Weighted F1-score. Macro F1 was used as the primary metric due to its robustness under class imbalance.

4.1 Experimental Environment and Dataset Partitioning

The experiments were conducted using a Python-based pipeline leveraging Scikit-learn for traditional models and TensorFlow/Keras for deep learning architectures. To ensure reliability, the researcher employed 5-fold stratified cross-validation on the dataset [6]. This maintained proportional representation of classes, preventing bias. The results reported averages $\pm$ standard deviations with 95% confidence intervals (normal approximation). Figure 3 shows the sentiment percentage per company.

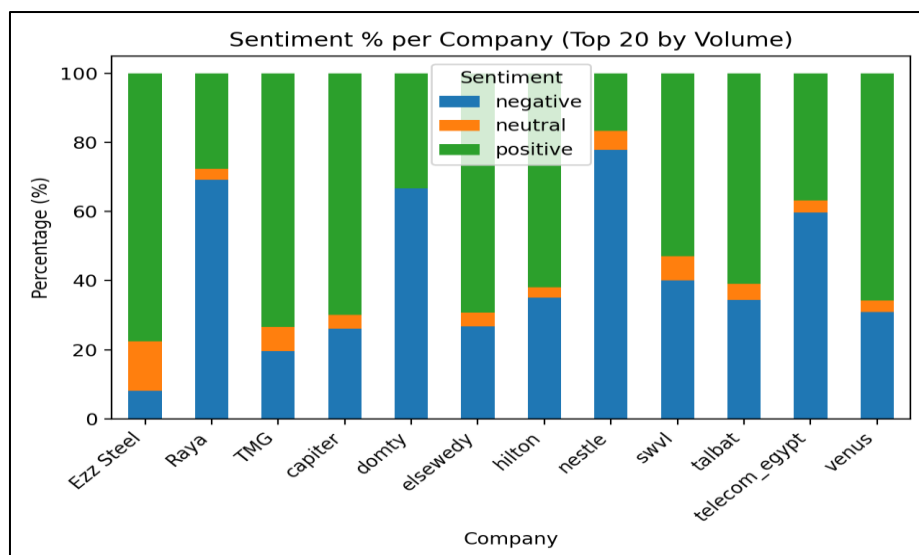


Figure 3. Sentiment percentage per company

4.1.1 Dataset Details

The Arabic Company Reviews dataset [6] contained 38,097 valid reviews after cleaning and filtering (original size ~40,046 reviews) from 12 companies: talbat (32,073), swvl (4,693), telecom_egypt (2,090), venus (281), Raya (268), TMG (250), elsewedy (147), hilton (100), capiter (73), Ezz Steel (49), nestle (18), domty (4). The overall sentiment distribution was positive (70%, ~28,032 reviews), negative (20%, ~8,009), and neutral (10%, ~4,005). Review lengths varied with an average ~50 words, where the minimum review size was 1, and the maximum review size was 200. Table 1 shows the sentiment class distribution, review length statistics, and sample reviews.

Table 1. Dataset Overview

Category	Details
Total Reviews	38,097
Number of Companies	12
Sentiment Class Distribution	
Positive	Positive: ~70% (~26,668 reviews)
Negative	Negative: ~20% (~7,619)
Neutral	Neutral: ~10% (~3,810)
Review Length Statistics (approximate word count after preprocessing)	
Average length	~50 words
Median length	~38 words
Minimum length	1 word
Maximum length	200 words
25th percentile	~18 words
75th percentile	~68 words
Sample Reviews (illustrating typical language, dialectal features, and noise)	
Sample 1 (Positive)	Arabic: الخدمة ممتازة وسريعة جداً، التوصيل في وقت قياسي English: The service is excellent and very fast, delivery in record time

	Rating/Sentiment: Positive (1) Company: talabat Length: ~12 words
Sample 2 (Negative)	Arabic: الإنترنت سيء جداً و دائماً ينقطع، مش عارف أتصفح حتى English: The internet is very bad and always cuts off, I can't even browse Rating/Sentiment: Negative (-1) Company: telecom_egypt Length: ~18 words
Sample 3 (Neutral)	Arabic: المنتج عادي، السعر مناسب بس الجودة متوسطة English: The product is average; the price is reasonable but the quality is medium Rating/Sentiment: Neutral (0) Company: swvl / Raya (similar style) Length: ~14 words

It is important to point out that the labels are derived from user ratings (stars >3 positive). As user-generated data, no inter-rater reliability is available; potential biases from dialects are noted as a limitation.

4.2 Hyperparameter Configuration

The models were configured to balance computational efficiency with classification depth as follows:

Traditional ML: The SVM was implemented using a LinearSVC with a regularization parameter $C=1.0$ and $dual=False$ to optimize performance for a sample size where $n > \{features\}$. The TF-IDF vectorizer utilized a range of (1, 2) n-grams with a maximum of 5,000 features.

Deep Learning: Both the Bi-LSTM and Bi-GRU models utilized an Embedding layer (input dim: 5,000, output dim: 128) followed by a Bidirectional layer with 64 units. A Dropout rate of 0.5 was applied to the dense layer to mitigate overfitting, a common challenge when dealing with the high morphological variance of Arabic text.

Optimizer: Adam ($lr=0.001$, $\beta_1=0.9$, $\beta_2=0.999$), with batch size=32 and early stopping with patience=3, max epochs=20. Class weights (inverse class frequency) were applied during training to address severe imbalance.

Transformer (AraBERT): Fine-tuned aubmindlab/bert-base-arabertv2 using Hugging Face Trainer with batch_size=32, epochs=3 per fold, max_length=128, eval_strategy="epoch", fp16 enabled on GPU (RTX 4060). No additional class weighting was applied, as the pre-trained contextual embeddings implicitly handle imbalance.

4.2.1 Hyperparameter Optimization

Hyperparameters were selected via grid search on a validation set (20% of train). For SVM, searched $C=[0.1,1,10]$; best $C=1$. For DL, units=[32,64,128] (64 chosen for balance); dropout=[0.3,0.5,0.7] (0.5 best). Embedding dim=128, which is standard for semantics. Ablation results in Table 2 show sensitivity (reducing units to 32 drops Macro F1 by 0.02) for Bi-LSTM as example.

Table 2. Ablation on Key Hyperparameters (Bi-LSTM)

Hyperparameter	Value	Macro F1 Change
Units	32	-0.02
Dropout	0.3	-0.01
Embedding Dim	64	-0.015

4.3 Results Analysis

Based on the 5-fold cross-validation results and Precision–Recall curves generated from the last fold of each model, distinct performance characteristics were observed across the examined architectures, as summarized in

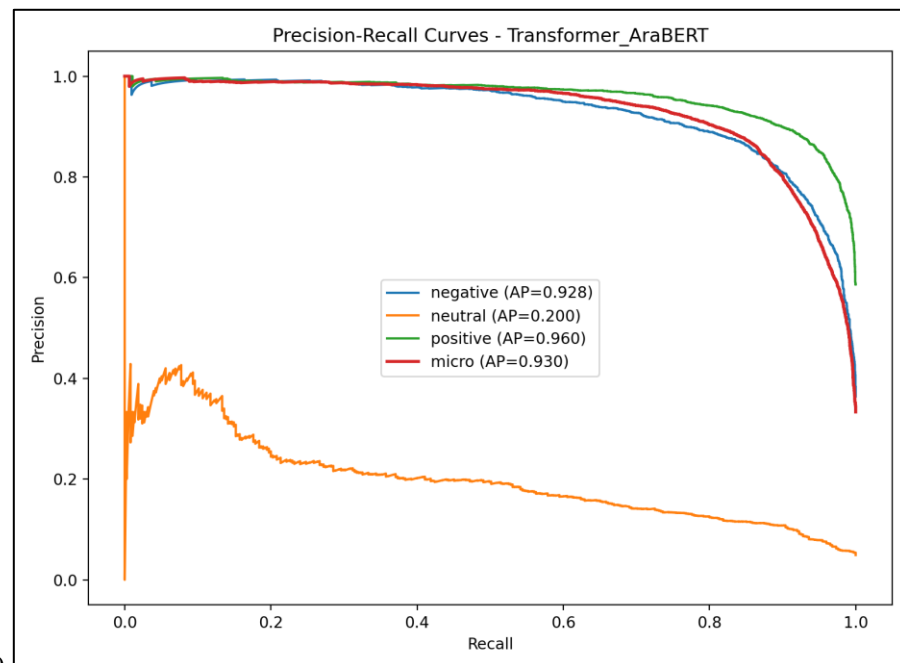


Table 3 and Figures 4-10.

Figure 4. Precision/Recall of the AraBERT Model

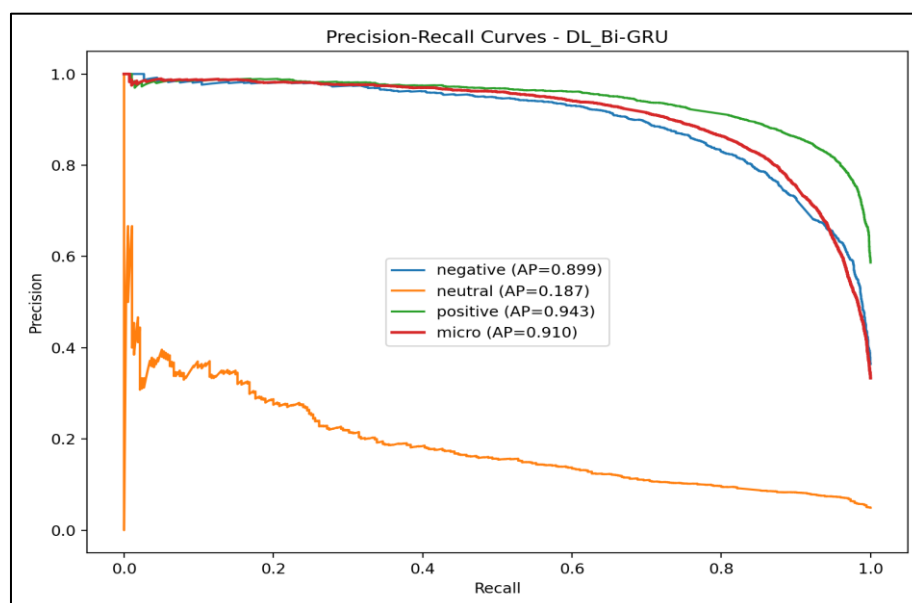


Figure 5. Precision/Recall of the Bi-GRU Model

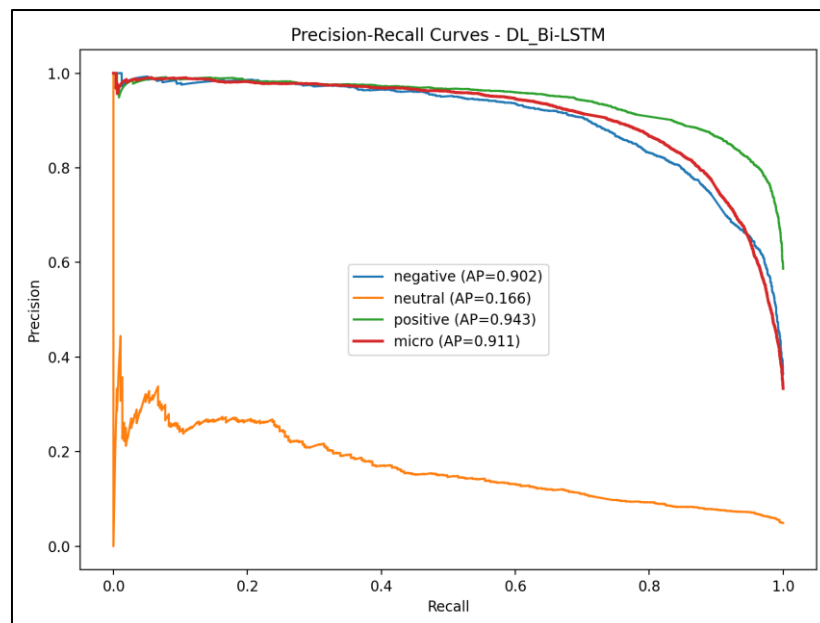


Figure 6. Precision/Recall of the Bi-LSTM Model

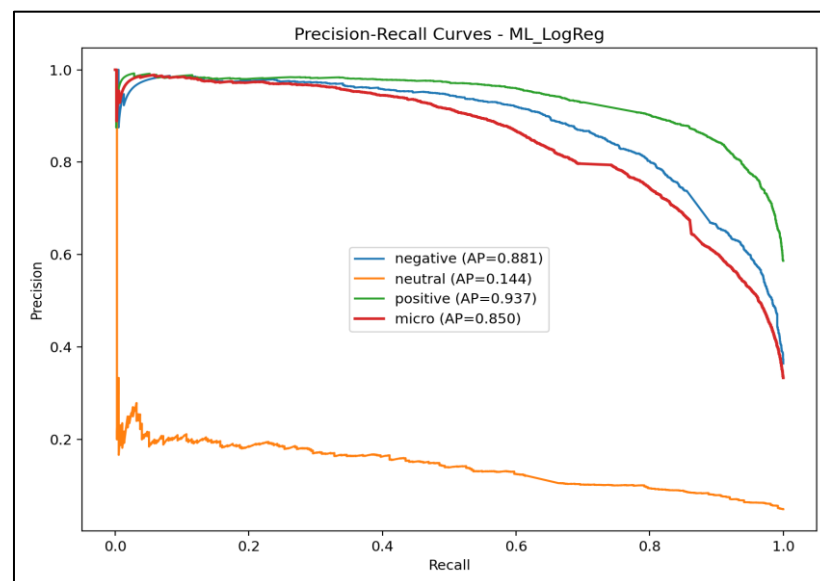


Figure 7. Precision/Recall of the Logistic Regression Model

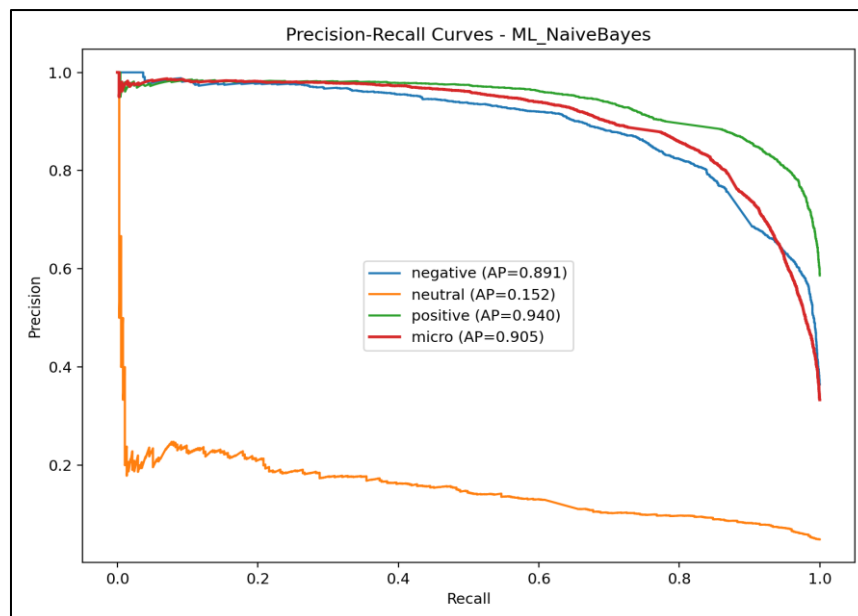


Figure 8. Precision/Recall of the Naive Bays Model

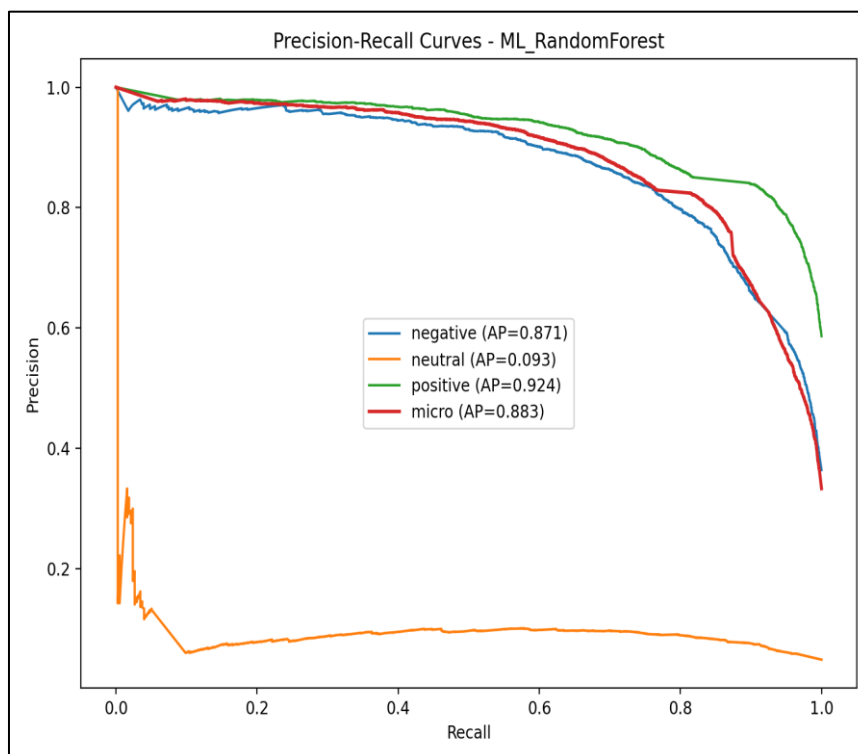


Figure 9. Precision/Recall of the Random Forest Model

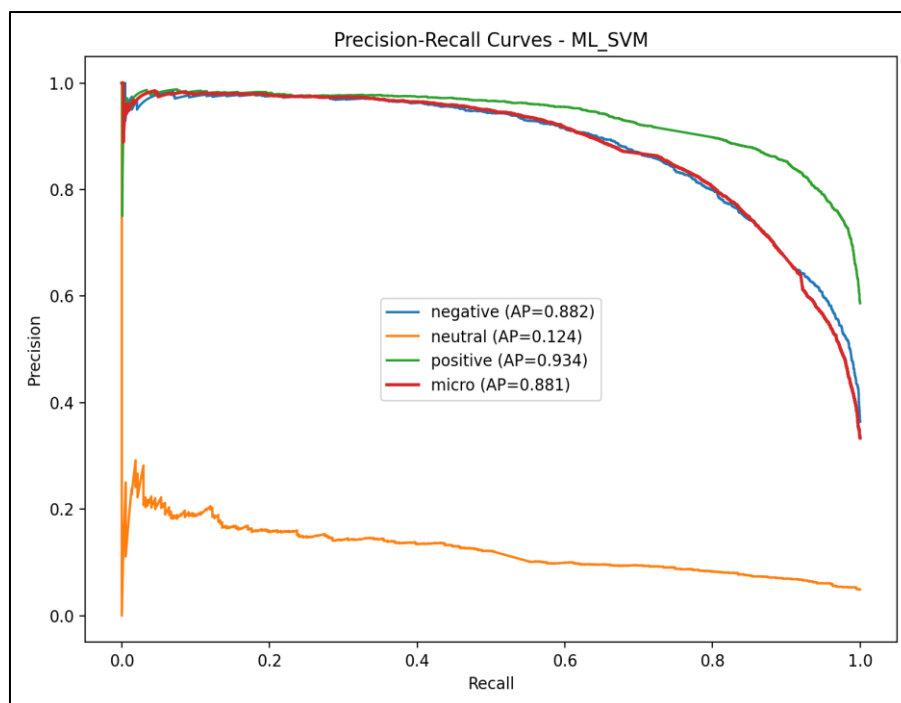


Figure 10. Precision/Recall of the SVM Model

Table 3. Comparative 5-Fold CV Performance (Mean $\pm$ Std; 95% CI)

Model	Accuracy	Macro F1	Weighted F1
SVM	0.8036 $\pm$ 0.0049 (0.7993–0.8079)	0.6205 $\pm$ 0.0058 (0.6154–0.6256)	0.8103 $\pm$ 0.0042 (0.8066–0.8140)
RandomForest	0.8158 $\pm$ 0.0032 (0.8130–0.8186)	0.5689 $\pm$ 0.0055 (0.5641–0.5737)	0.7990 $\pm$ 0.0028 (0.7965–0.8015)
NaiveBayes	0.8350 $\pm$ 0.0029 (0.8324–0.8376)	0.5673 $\pm$ 0.0022 (0.5654–0.5692)	0.8140 $\pm$ 0.0029 (0.8115–0.8165)
LogReg	0.7683 $\pm$ 0.0036 (0.7651–0.7714)	0.6212 $\pm$ 0.0036 (0.6180–0.6243)	0.7965 $\pm$ 0.0031 (0.7937–0.7993)
Bi-LSTM	0.8386 $\pm$ 0.0020 (0.8369–0.8404)	0.5681 $\pm$ 0.0020 (0.5663–0.5698)	0.8171 $\pm$ 0.0025 (0.8149–0.8194)
Bi-GRU	0.8365 $\pm$ 0.0011 (0.8355–0.8375)	0.5741 $\pm$ 0.0059 (0.5689–0.5793)	0.8162 $\pm$ 0.0022 (0.8143–0.8182)
AraBERT	0.8598 $\pm$ 0.0044 (0.8560–0.8636)	0.6382 $\pm$ 0.0100 (0.6294–0.6469)	0.8479 $\pm$ 0.0043 (0.8441–0.8516)

As shown in Table 3, AraBERT achieved the highest overall Accuracy and Macro F1-score, demonstrating the advantage of pre-trained contextual embeddings. Naive Bayes and Bi-LSTM/Bi-GRU models showed high accuracy and weighted F1, reflecting strong performance on the dominant positive class. In contrast, Logistic Regression obtained the highest Macro F1 among non-Transformer models, indicating a more balanced treatment of minority and majority sentiment classes. This behavior highlights the trade-off between overall correctness and class-balanced performance in highly imbalanced sentiment datasets. Although the deep learning models (Bi-LSTM and Bi-GRU) consistently improved Accuracy and Weighted F1 compared to linear baselines, they did not surpass Logistic Regression in terms of Macro F1. This suggests that increased model capacity primarily benefits majority class recognition rather than improving minority class discrimination. The Support Vector Machine demonstrated competitive performance across all metrics, serving as a strong classical

baseline that balances robustness and computational efficiency. Random Forest, while achieving reasonable accuracy, exhibited comparatively weaker class-balanced performance, consistent with its known limitations in high-dimensional sparse text representations.

Precision-Recall curves across all models highlighted severe class imbalance: positive class Average Precision (AP) ranged from 0.924 (RandomForest) to 0.960 (AraBERT), while neutral class AP remained very low (0.093–0.200). Negative class AP was moderate (0.871–0.929). Micro-averaged AP was high (~0.85–0.93), driven by the dominant positive class. These curves visually confirmed the need for class weighting and justify Macro F1 as the primary balanced metric.

4.4 Automated Business Intelligence Output

A unique component of this experiment is the generation of the Arabic_Brand_Insights.xlsx report. By analyzing the "Sentiment Score" (mean rating) per company, the system identified that companies with the lowest scores frequently had negative reviews associated with specific latent topics.

For example, for a specific telecom provider in the dataset, the top negative keywords extracted were (تغطية / سيء), clearly pointing to "Network Coverage" issues. Conversely, high-scoring retail brands showed positive keywords such as (سريع / توصيل / ممتاز), highlighting "Logistics Speed" as their primary competitive advantage. With the addition of AraBERT, the report benefited from more accurate sentiment classification, leading to higher-quality topic extraction and more reliable BI insights.

5. Discussion

The results demonstrated that model performance varied significantly depending on the evaluation metric. Naive Bayes achieved the highest accuracy and weighted F1-score, suggesting strong performance on the majority sentiment class. However, its lower Macro F1-score indicated limited effectiveness in minority-class prediction.

Logistic Regression achieved the highest Macro F1-score, making it the most balanced classifier across sentiment classes. This confirms that linear models with TF-IDF features remain highly effective for Arabic sentiment analysis, particularly when fairness across classes is required.

Deep learning models (Bi-LSTM and Bi-GRU) produced competitive accuracy, reflecting their ability to capture contextual information. Nevertheless, their Macro F1-scores did not surpass those of linear models, likely due to dataset size constraints and the absence of pretrained Arabic embeddings. These findings highlighted the importance of aligning model choice with data characteristics and evaluation objectives.

The 5-fold stratified cross-validation results (Table 3) confirmed and strengthened these observations, with minor numerical differences from the original single-split experiments attributable to averaging across folds (e.g., Logistic Regression Macro F1 0.6212 ± 0.0036 vs. original 0.6257). Confidence intervals were narrow (e.g., Macro F1 CI width ~0.006–0.012), indicating stable performance and reduced variance compared to single splits. AraBERT achieved the highest overall performance (accuracy 0.8598 ± 0.0044 ; Macro F1 0.6382 ± 0.0100), outperforming all ML and DL models. This demonstrates the advantage of pre-trained contextual

embeddings for Arabic, which better handle dialectal variation and long-range dependencies without explicit feature engineering. However, AraBERT requires significantly higher computational resources (~20–30 min/fold on GPU) compared to ML (<1 min/fold on CPU) or DL (1–3 min/fold on GPU), highlighting a trade-off between accuracy and deployability in resource-constrained environments. Precision-Recall curves across all models revealed severe class imbalance: positive class Average Precision (AP) was consistently high (0.924–0.960), driven by the dominant positive reviews (~70%). Negative class AP was moderate (0.871–0.929), while neutral class AP remained very low (0.093–0.200), explaining the gap between high accuracy/weighted F1 and lower Macro F1. Micro-averaged AP (0.85–0.93) was inflated by the majority class, reinforcing Macro F1 as the primary balanced metric. These curves visually confirmed that even top models struggle with neutral sentiment, a common challenge in real-world Arabic reviews.

6. Conclusions and Future Work

This study presented an integrated ASA and BI framework for Arabic company reviews. Experimental evaluation showed that while deep learning architectures achieved strong accuracy, Logistic Regression delivered the best-balanced performance as measured by Macro F1-score. Naive Bayes remained an effective option when overall accuracy was prioritized. The integration of topic modeling enhanced interpretability, enabling organizations to identify actionable insights from sentiment-labeled reviews.

Future work should explore the incorporation of pretrained Arabic language models (e.g., AraELECTRA, MARBERT), data augmentation strategies (e.g., back-translation for minority classes), class-aware loss functions, and ensemble methods (e.g., stacking AraBERT with LogReg) to further improve minority-class sentiment detection and overall robustness under imbalance. Additional directions could include multi-label ASA, sarcasm detection, and real-time deployment on edge devices.

7. Declarations

Acknowledgments

Not applicable.

Ethical consideration

Not applicable.

Consent to participate

Not applicable

Conflicts of interest

The author (Maree) is a member of the Editorial Board for the AAUP Journal of STEM and Health Sciences. To maintain a transparent and unbiased peer-review process, Maree was not involved in the selection of reviewers or any editorial decisions regarding this manuscript. The peer-review process was handled independently by other editors of the journal. Otherwise, the authors have no conflicts of interest to declare.

Data availability

The Arabic Company Reviews dataset analyzed in this study is publicly available through Kagglei.

Code availability

The full source code, preprocessing pipeline, and scripts used to reproduce the reported experiments and figures are available from the author upon request and can be provided to reviewers during the evaluation process.

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Authors Contributions

All authors contributed to Conceptualization; Formal analysis; Investigation; Methodology; Supervision; Writing – original draft; Writing – review & editing and their roles in the paper were distributed accordingly.

References

- [1] Maree, M.; Eleyat, M. and Rabayah, S. *Pertanika Journal of Science & Technology*, Volume 32, Issue 3, April 2024. DOI: <https://doi.org/10.47836/pjst.32.3.05>
- [2] Alawneh, H.; Hasasneh, A.; Maree, M. On the Utilization of Emoji Encoding and Data Preprocessing with a Combined CNN-LSTM Framework for Arabic Sentiment Analysis. *Modelling* 2024, 5, 1469–1489. DOI: <https://doi.org/10.3390/modelling5040076>
- [3] Al-Kabi MN, Gigieh AL, Al-Smadi IM, et al. Opinion mining and sentiment analysis for Arabic language: a comprehensive survey. *Int J Comput Appl*. 2014;101(15):24-35.
- [4] Joachims T. *Learning to Classify Text Using Support Vector Machines*. 2nd ed. Norwell: Kluwer Academic Publishers; 2002.
- [5] Blei, D. M., Ng, A. Y., & Jordan, M. I. (2003). Latent Dirichlet Allocation. *Journal of Machine Learning Research*, 3, 993–1022.
- [6] Seddik F. Arabic Company Reviews Dataset. Kaggle. 2021 [cited 2025 Jan 5]. Available from: <https://www.kaggle.com/datasets/fahdseddik/arabic-company-reviews>
- [7] Zhang, L., Wang, S., & Liu, B. (2018). Deep learning for sentiment analysis: A survey. *WIREs Data Mining and Knowledge Discovery*, 8(4), e1253. DOI: <https://doi.org/10.1002/widm.1253>
- [8] Abbasi A, Chen H, Salem A. Sentiment analysis in multiple languages: Feature selection for opinion classification in Web forums. *ACM Trans Inf Syst*. 2008;26(3):1-34.
- [9] Farra N, et al. Sentence-level and document-level sentiment analysis for Arabic. *Proceedings of IEEE Workshop on Spoken Language Technology*. 2010;233-238.
- [10] El-Halees A. Arabic opinion mining: A hybrid approach. *Al-Aqsa Univ J*. 2011;15(1):101-122.
- [11] Al-Smadi, M., Talafha, B., Al-Ayyoub, M., & Jararweh, Y. (2019). Using long short-term memory deep neural networks for aspect-based sentiment analysis of Arabic reviews. *International Journal of Machine Learning and Cybernetics*, 10, 2163–2175. DOI: <https://doi.org/10.1007/s13042-018-0799-4>
- [12] Dahou A, et al. Word Embeddings and Convolutional Neural Networks for Arabic Sentiment Classification. *Proceedings of COLING 2016*.
- [13] Soliman AB, Eissa K, El-Beltagy SR. AraVec: A set of Arabic Word Embedding Models for use in Arabic NLP. *Procedia Comput Sci*. 2017;117:256-265.

-
- [14] Duwairi RM, et al. Sentiment Analysis for Arabic Dialects. Proc. of 9th Int. Conf. on Information and Communication Systems (ICICS). 2018.
- [15] Abu Farha I, Magdy W. ArSarcasm: A New Arabic Sarcasm Detection Dataset. Proceedings of the Fourth Arabic Natural Language Processing Workshop. 2020.
- [16] Antoun W, Baly F, Hajj H. AraBERT: Transformer-based Model for Arabic Language Understanding. LREC. 2020.
- [17] Cho, K., Van Merriënboer, B., Gulcehre, C., Bahdanau, D., Bougares, F., Schwenk, H., & Bengio, Y. Learning Phrase Representations using RNN Encoder–Decoder for Statistical Machine Translation. Proceedings of the 2014 Conference on Empirical Methods in Natural Language Processing (EMNLP), 1724–1734.
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ⁱ <https://www.kaggle.com/datasets/fahdseddik/arabic-company-reviews>



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Food as Medicine in Prophetic and Greco-Arab Traditions: Historical Perspectives and Modern Scientific Evidence

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Abstract

The idea of using food as a form of medicine has deep roots in Prophetic, Greco-Arab, and Islamic medical traditions. Those systems regarded dietary therapy as the first and most natural methods of preserving health and treating diseases. The renowned physician Al-Razi (Rhazes, 864–930) once said, “As long as you can treat with food, do not treat with medicine,”. This definitely underlined the gist of the classical Greco-Arab medical principle that prioritized diet and physical therapy without resorting to drugs or surgery. In terms of the Prophetic Medicine, food played a dual role of life- sustaining and healing. More specifically, Prophet Muhammad (Peace Be Upon Him) recommended several diets, including honey, olive oil, dates, black seeds, barley, and camel milk for their preventive and healthy features. Recent advances in nutrition research and biomedical research provided cell biological and molecular evidence that supported many of these traditional perceptions. That is, foods rich in antioxidants, essential fatty acids, vitamins, and other bioactive compounds have shown to improve immune function and reduce the risk of chronic conditions, such as cardiovascular disease, diabetes, cancer, and age-related ailments. This study outlined the historical background and traditional uses of some selected wild edible Arab and Islamic plants and foods highlighted in the Prophetic Medicine, and discussed their pharmacological actions in light of the current scientific understanding. Furthermore, it aimed to bridge the gap between traditional and modern biomedical perspectives on maintaining health and preventing diseases through diet.

Keywords: Diet therapy, Prophetic medicine, Arab medicinal plants. Antioxidant, Anti-microbial, Anti-inflammatory.

1. Introduction

Chronic diseases remain among the most serious public health challenges of the twenty-first century. A growing body of evidence links plant-based diets and medicinal herbs to improved health outcomes and a lower risk of metabolic and chronic disorders, including obesity, cardiovascular disease, diabetes, and certain cancers [1]. Such diets are typically low in saturated fats yet rich in fiber, antioxidants, active compounds, and vitamins. They also contain whole grains, legumes, nuts, and soy-based proteins, foods that have been consistently associated with reduced risk of chronic diseases [2, 3].

Over the past five decades, epidemiological evidence has constantly shown that people who consume bigger amounts of olive oil, fruits and vegetables tend to experience fewer cardiovascular events, cancers, and metabolic complications [4]. These protective effects are attributed largely to the combined action of dietary fiber, polyphenols (natural antioxidants), and a broad spectrum of bioactive phytochemicals present in natural products. Many of these compounds act as antioxidants and influence key metabolic pathways and regulate immune activity. Because proper immune function protects against infections and cancers, it is central to maintaining health. Unfortunately, immune capacity can decline with age, stress, poor nutrition, and other lifestyle factors. Incorporating foods with immune-modulating properties into the diet is therefore considered an effective strategy to preserve immune functions and prevent disease [5, 6].

People in Mediterranean regions generally have lower rates of cardiovascular diseases compared with populations in Northern Europe and North America [7, 8]. The traditional Mediterranean diet, abundant in fruits, vegetables, wild herbs, bread, nuts, seeds, and olive oil, is recognized as one of the healthiest dietary patterns in the world. Its richness in carotenoids, vitamin C, tocopherols, α -linolenic acid, and essential minerals, together with numerous non-nutrient components such as polyphenols, anthocyanins, and dietary fiber, contribute to its protective effects [7, 8, 9, 10]. Dietary fiber encompasses a variety of soluble and insoluble components that exert different physiological functions. That is to say, soluble fiber slows digestion and nutrient absorption, helping to prolong satiety and stabilize blood glucose and lipid levels, whereas insoluble fiber accelerates intestinal transit and enhances carbohydrate metabolism [11, 12]. Both types appear to influence body weight through their effects on gut hormones that regulate appetite and energy balance. Ghrelin, a peptide primarily secreted by the stomach, stimulates appetite and food intake; its levels rise during fasting and fall after meals. Animal studies indicate that elevated ghrelin promotes weight gain by enhancing hunger and reducing fat oxidation, shifting metabolism toward carbohydrate use [11, 12, 13, 14].

Studies containing migrant populations suggested that the lower rates of chronic disease seen in Mediterranean societies are mainly attributable to diet and lifestyle rather than genetic background. For example, comparisons between indigenous Arab and immigrant Jewish populations in Israel revealed that differences in the rate of incidence of cancer were largely linked to dietary habits [15, 16]. Nutritional factors can thus act as either risk or protective elements depending on their composition and balance. In many Arab communities, olive oil serves as the primary source of dietary fat [17]. Among Bedouin tribes, for instance, traditional diets are centered on olive oil, milk, wild plants, and wheat bread, with a low overall fat intake. Such dietary patterns provide sufficient essential fatty acids like linoleic and linolenic acids while keeping total fat consumption modest [15, 16].

1.1 Historical Background

The use of natural products (e.g., medicinal plants, camel milk, and honey) for healing represented one of the oldest medicinal practices known to humankind. Long before the emergence of modern pharmacological medicine, physicians and healers in ancient civilizations recognized that natural products played a central role in maintaining health and restoring balance. Similar to the Greek, Persian, and Ayurvedic traditions, pre-Islamic medicine viewed dietary regulation as fundamental to disease prevention and treatment [17]. Within the Islamic worldview, however, food acquired an even deeper meaning—it was not only a physiological necessity but also a matter of spiritual and moral discipline [17]. The Holy Qur'an outlines a complete framework of dietary guidance for believers, permitting (halal) most foods while forbidding (haram) those explicitly prohibited by divine command. As the Islamic empire rapidly expanded from the Arabian Peninsula to Persia, Egypt, the Maghreb, and the Iberian Peninsula, Arab and Muslim scholars encountered a notable range of medical and food customs. This exchange of ideas and

produced a distinctive Islamic approach to dietary therapy that harmonised Qur'anic principles, pre-Islamic medical knowledge, and Greek philosophical concepts [1, 17].

Prophetic sayings (Hadiths) further lighten the spiritual and therapeutic dimensions of food in Prophetic medicine and in Arab and Islamic medicine. Prophet Muhammad (Peace Be Upon Him) emphasized certain foods—such as dates, honey, olive oil, and black seeds—for their health beneficial effects. He stated, “Eat olive oil and massage it over your bodies, for it is from a blessed (mubarak) tree,” and described black seed (*Nigella sativa*) as “a cure for every disease except death.” Dates occupy a particularly valued place in Islamic tradition, being mentioned twenty times in the Qur'an. The Prophet also advised: “*If anyone of you is fasting, let him break his fast with dates; and if he does not have them, then with water, for water is a purifier.*” [18].

Both the Qur'an and the Hadith contain numerous references to natural products-based foods derived from plants and animals—among them dates, black seeds, olive oil and leaves, honey, and camel milk [1, 17]. These foods formed the foundation of the Prophet's daily diet and were employed for both nourishment and healing. Over time, they became essential parts of the *Prophetic Medicine (Al-Tibb al-Nabawi)*, a comprehensive system that combined preventive care, therapeutic practice, and spiritual guidance based on the teachings of the Prophet Muhammad (Peace Be Upon Him).

Two of the Prophet's Hadiths — “*The one who sent down the disease sent down the remedy*” and “*For every disease, Allah has given a cure*”—became guiding principles that inspired generations of Muslim physicians and scholars to seek remedies for all illnesses [17, 18]. These teachings strongly influenced the evolution of Greco-Arab and Islamic medicine during the Golden Age of the Arab-Islamic civilisation (7th–15th centuries CE). This period was marked by flourishing scientific, cultural, and philosophical activity that stretched from Andalusia and North Africa to Central Asia and India. The principal centres of medical scholarship—Egypt, Bilad al-Sham (Greater Syria), and Baghdad—played pivotal roles in shaping the advancement of medical knowledge [17, 18].

The Book of Medicine (Kitab al-Tibb) found in *Sahih al-Bukhari* (810–870 CE) is considered one of the most authoritative collections of the Prophet's Hadiths and practices. The interpretation and scope of the Prophetic Medicine were later elaborated by leading scholars, such as Ibn Hajar al-‘Asqalani (d. 1449) and Abu Muhammad al-‘Ayni (d. 1452). Living during the height of Arab-Islamic intellectual achievement, these scholars contextualized the Prophetic Medicine not merely as a reflection of early Islamic life but as a timeless framework applicable to their own era, integrating moral, medical, and philosophical insights [17, 18].

The Prophetic Medicine is different from purely empirical medical traditions. Rather than relying exclusively on experimentation, it draws upon divine inspiration and the accumulated wisdom of earlier civilizations. One Hadith highlights the centrality of nutrition to well-being: *“The stomach is the central basin of the body, and the veins are connected to it. When the stomach is healthy, the veins convey health; when it is diseased, they transmit disease.”* This saying encapsulates the holistic view of health deeply rooted in early Islamic thought.

In his practice, Prophet Muhammad (Peace Be Upon Him) often prescribed foods rather than complex herbal mixtures or animal-based substances. His advice included simple yet powerful natural remedies—barley soup for weakness, honey for various ailments, and camel milk for vitality [17, 18]. Dietary adjustments were frequently advised as preventive and therapeutic strategies, reflecting an understanding that food itself is among humanity’s most ancient forms of medicine. Among his favorite foods—honey, camel’s milk, dates, olive oil, and black seeds—each possessed unique therapeutic and symbolic importance. The Prophet repeated endorsement of olive oil and black seeds, as noted earlier, reflected his recognition of their exceptional curative power [17, 18].

The following subsections emphasize these natural products that were extensively studied in modern biomedical research and remained central to traditional medical practice in many Islamic cultures [19, 20, 21].

2. Traditional and Pharmacological Properties of the Prophetic Medicine-Based Diet

Honey: Honey, a natural product produced by bees from floral nectar, contains a complex mixture of nutritional and medicinal substances—many of which yet remain to be fully identified [22]. Its chemical composition depends heavily on its botanical origin, with sugar forming about 95% of its dry weight. In addition, honey includes organic acids, amino acids, proteins, polyphenols, vitamins, minerals, and aromatic compounds [22].

In the Arab-Islamic medicine, as in other traditional medical systems, honey is valued both as nourishment and as a curative agent—particularly for wound care [1, 23]. The Holy Qur’an explicitly acknowledges its therapeutic qualities: “And thy Lord has inspired the Bees, to build their hives in hills, on trees and in man’s habitations. From within their bodies comes a drink of varying colours, wherein is healing for mankind. Verily in this is a Sign for those who give thought.” (An-Nahl-68). Islamic scholars, such as Al-Razi (Rhazes, AD 864–932) and Ibn Sina (Avicenna) praised honey’s medicinal virtues in their seminal works. In Al-Hawi (The Comprehensive Book on Medicine), Al-Razi recommended the use of honey ointments for skin disorders and nerve injuries and recommended honey water for bladder wounds [1, 17, 23]. He stated: “Honey is the best treatment for the gums. To keep the teeth healthy mix honey with vinegar and use as a mouthwash daily... Honey does not spoil and could also be used to preserve cadavers.” Similarly, Ibn Sina stated in The Canon of Medicine: “Honey is good for prolonging life, preserving activity in old age... If you are above the age of 45, eat honey regularly, especially mixed with chestnut powder.” He further recommended honey for wound healing, tuberculosis, and insomnia [17, 23].

Over the last four decades, extensive research has confirmed honey’s efficacy in treating wounds, burns, and infections. Its antimicrobial, anti-inflammatory, and immunomodulatory properties were well documented, leading to renewed clinical interest in honey-based therapeutics [22, 23, 24, 25, 26]. Manuka honey, derived from *Leptospermum* species in New Zealand and Australia, exhibited strong antibacterial effects independent of

hydrogen peroxide. Therapeutic-grade honeys such as Medi-honey and Active Manuka Honey have been approved for medical use [17, 23].

Honey's antimicrobial mechanism differs from that of conventional antibiotics. It dehydrates bacteria through its hygroscopic properties, inhibits microbial growth via osmotic pressure and acidity, and maintains antibacterial potency even when diluted. Studies show inhibitory activity against over 60 bacterial species and several fungi, including *Aspergillus* and *Penicillium* [22, 23, 27]. Furthermore, the antibacterial potency of honey may vary up to 100-fold depending on floral origin and processing. Laboratory analyses confirm that *Staphylococcus aureus* is among the most sensitive pathogens to honey's antimicrobial effects [22, 24]. Experimental and clinical research indicated that honey enhances wound healing and tissue regeneration in burns and ulcers [28]. Its antioxidant activity also contributes to reducing oxidative stress. Honey's antioxidant enzymes and compounds such as ascorbic acid, flavonoids, and phenolic acids exhibit strong radical-scavenging activity. A direct correlation exists between honey's phenolic content and its antioxidant potential, as shown in oxygen radical absorbance capacity (ORAC) studies [29, 30]. In recent studies [31, 32], the physicochemical characteristics, polyphenolic composition, antioxidant potential, antibacterial activity, and wound healing effects of Palestinian alfalfa honey avocado honey were evaluated. Results obtained revealed that both honeys exhibit potent antioxidant, anti-inflammatory, antibacterial, and wound healing properties. Both honeys are high ellagic acid content, dose-dependent effects on keratinocyte proliferation, and broad antibacterial activity highlight its potential as a natural therapeutic agent in wound management. Furthermore, Molecular Docking Analysis revealed strong binding of key compounds to targets mediating antioxidant, antibacterial, and anti-inflammatory effects.

Camel Milk: Milk generally contains proteins and peptides vital for immune defense and growth. These include lactoferrin, casein, glycomacropeptide, α -lactalbumin, and lysozyme—each demonstrating antimicrobial, antiviral, anticancer, and immunostimulatory activities [33, 34]. Camel milk, however, possesses a unique nutritional and medicinal profile distinct from that of other ruminant milks. It is lower in cholesterol and sugar yet higher in essential minerals (Na, K, Fe, Cu, Zn, Mg), vitamins (A, B2, C, E), and insulin. It is hypoallergenic, suitable for lactose-intolerant individuals, and beneficial for immune-compromised patients. Traditionally, camel milk and butter have been used in Saharan and Bedouin medicine for both therapeutic and cosmetic purposes. In India, camel milk is used to manage conditions such as jaundice, spleen disorders, asthma, tuberculosis, anemia, piles, and diabetes. Clinical trials have demonstrated a 30–35% reduction in insulin requirements among type 1 diabetic patients consuming raw camel milk [33, 34].

Prophet Muhammad (Peace Be Upon Him) endorsed camel milk and urine for their medicinal value, permitting their use when necessary for treatment. Bedouins have long relied on camel milk to address disorders including osteoporosis, hepatitis, respiratory infections, and metabolic conditions [35, 36].

Olive Oil: The olive tree (*Olea europaea*), native to the Mediterranean basin, is one of humanity's oldest cultivated plants. Archaeological evidence dated olive cultivation back to 39,000 years ago on the Aegean island of Santorini and to 12,000 B.C. in the Sahara Desert [37, 38]. Qur'anic texts reference the olive tree's sanctity and healing properties: "The fruit thereof shall be for meat and the leaf thereof for medicine." "God is the light of the heavens and the earth... lit by a blessed olive tree, neither Eastern nor Western, whose oil almost glows, even without fire touching it—light upon light." (An Nur 35). The Prophet Muhammad (Peace Be Upon Him) advised: "Eat olive oil and massage it over your bodies since it is a holy (mubarak) tree," and stated that it "cures seventy diseases" [17, 23].

Olive oil, a cornerstone of the Mediterranean diet, is increasingly recognized not only for its cardiovascular benefits but also for its potential role in cancer prevention and therapy. Among its bioactive constituents, several phenolic compounds—tyrosol, hydroxytyrosol, oleuropein, oleacein, and oleocanthal—have demonstrated promising anticancer activities in various experimental models. These compounds act synergistically through diverse mechanisms, including antioxidant, anti-inflammatory, and immunomodulatory effects, as well as modulation of cell proliferation, apoptosis, angiogenesis, and metastasis. Notably, oleocanthal selectively induces cancer cell death via lysosomal membrane permeabilization, while hydroxytyrosol and oleuropein exhibit potent radical-scavenging and anti-proliferative properties. Olive oil's cardioprotective effects are attributed largely to its MUFA and phenolic constituents. These compounds exhibit antioxidant, anti-inflammatory, antithrombotic, and vasodilatory effects, improving lipid profiles and reducing oxidative stress [38]. Phenolic compounds in virgin olive oil—such as hydroxytyrosol, tyrosol, and oleuropein—protect endothelial function, enhance nitric oxide production, and suppress platelet aggregation. They also upregulate antioxidant enzymes such as glutathione peroxidase. In vivo studies confirm that olive phenolics delay atherosclerosis progression in animal models [39]. While oleic acid contributes to these benefits, evidence suggested that phenolic compounds played an equally vital role. Thus, olive oils rich in phenolics—typically virgin or extra virgin—offer superior protective effects, though their stronger flavor may not appeal to all consumers. These oils should be integrated into a balanced and enjoyable dietary pattern [39].

Olive polyphenols exhibit antimicrobial activity against intestinal and respiratory pathogens, including *Helicobacter pylori*, *Escherichia coli*, *Listeria monocytogenes*, and *Salmonella enteritidis*. This bioactivity may contribute to olive oil's preventive effects on gastrointestinal and infectious diseases [39].

Dates (*Phoenix dactylifera*): The date palm (*Phoenix dactylifera*) is considered one of humanity's earliest cultivated fruit trees. Its fruit, the date, is rich in carbohydrates—primarily glucose and fructose—comprising 44–88% of its total composition, which makes it an excellent source of quick energy. A 100-gram serving of date flesh provides approximately 314 kcal. Besides sugars, dates contain proteins, fats, essential minerals, vitamins, and about 8 g of dietary fibre per 100 g, with insoluble fibre forming the major portion. Both the flesh and the seed include a variety of fatty acids—saturated and unsaturated. While the seed contains 14 fatty acid types, only eight occur in the flesh and in small quantities. Unsaturated fatty acids such as palmitoleic, oleic, linoleic, and linolenic acids are among the main types found [40]. Ten key minerals have been identified in dates, with selenium, copper, potassium, and magnesium being the most abundant. A 100 g portion supplies more than 15% of the recommended daily allowance of these minerals. Trace elements such as aluminum, cadmium, chloride, lead, and sulfur are also present [40]. Fluorine, known to protect teeth from decay, is another important element. Dates further contain vitamins C, A, and B-complex (B₁, B₂, and niacin), with vitamins C and the B-complex group being the most prominent. The fruit also exhibits strong antioxidant potential due to its carotenoid and phenolic contents [41, 42].

Although the precise origin of the date palm is uncertain due to its long history of cultivation, it is believed to have originated near the Persian Gulf. Its domestication dates back to ancient Mesopotamia and possibly prehistoric Egypt, with archaeological evidence of cultivation in eastern Arabia as early as 6000 BCE (Alvarez-Mon, 2006). Arab traders later disseminated the plant throughout South and Southeast Asia, North Africa, and parts of Europe such as Spain and Italy. The tree typically grows 15–25 m tall, with a trunk diameter of 20–40 cm. It may form clusters of multiple trunks or grow singly. The pinnate leaves, reaching 3–5 m in length, have spines along the

petiole and about 150 leaflets, forming a crown spread of up to 10 m. Dates have served as a staple food in Middle Eastern diets for millennia [43].

In the Islamic tradition, dates hold religious and cultural significance. The fruit is mentioned around 20 times in the Quran, and Prophet Muhammad (Salallahu Alayhi Wasalim Peace Be Upon Him) is reported to have said: “If any of you is fasting, let him break his fast with dates; if he does not have them, then with water, for water is purifying.” Consequently, during Ramadan, Muslims often break their fast with dates accompanied by milk or yogurt. Dates are eaten fresh or dried, sometimes stuffed with almonds, walnuts, or marzipan, and used in both sweet and savory preparations—such as ka’ak (Arab cookies), Moroccan tajines, and puddings. They are also processed into various products, including date paste (‘Ajwa’), syrup (dibs), powder (date sugar), and spreads. Prophet Muhammad also emphasised their medicinal and protective value, saying: “Whoever takes seven ‘Ajwa dates in the morning will not be affected by magic or poison that day.” [17].

Due to their high tannin content, dates have long been used in traditional medicine as cleansing and astringent agents for digestive ailments. Preparations such as date infusions, syrups, and pastes have been used to relieve sore throats, colds, bronchial conditions, and fevers, and to mitigate alcohol intoxication. Date seed powder is also employed in some traditional remedies [17, 23]. In addition, dietary fibre in dates supports digestive health, as it consists of indigestible plant components beneficial to gut function. Health authorities recommend adequate daily fiber intake from plant-based foods. Additionally, dates’ antioxidants—particularly phenolics and carotenoids—are believed to contribute to the prevention of cardiovascular diseases, cancers, neurodegenerative disorders (e.g., Alzheimer’s and Parkinson’s), inflammation, and aging. Phenolic contents in fresh dates range around 193.7 mg/100 g, increasing to 239.5 mg/100 g in dried fruit. Their Oxygen Radical Absorbance Capacity (ORAC) averages 1656 μmol trolox/100 g in fresh dates and 1025 μmol /100 g when dried. Compared with other dried fruits (340 μmol /100 g for apricot and 3383 μmol /100 g for figs), dates are a strong antioxidant source [39, 40, 42].

Several in vitro studies have confirmed the antioxidant potential of date extracts. For example, aqueous extracts show dose-dependent inhibition of superoxide and hydroxyl radicals. In tests, 0.8 mg/mL and 2.2 mg/mL concentrations achieved 50% inhibition of superoxide and hydroxyl radicals, respectively, while complete inhibition occurred at 1.5 mg/mL and 4.0 mg/mL. Furthermore, 1.9 mg/mL extracts inhibited lipid peroxidation by 50%, and 2.3 mg/mL inhibited protein carbonyl formation by half. These results demonstrate that dates possess potent antioxidant and antimutagenic compounds [44, 45, 46]. Furthermore, date fruit extract also inhibited benzo(α)pyrene-induced mutagenicity in Salmonella strains TA-98 and TA-100, with 50% inhibition achieved at 3.6 mg/plate and 4.3 mg/plate, respectively, suggesting significant free-radical-scavenging activity [44, 45, 46].

Carob (*Ceratonia siliqua*): The carob tree (*Ceratonia siliqua*), known in Arabic as Kharob, has been cultivated for centuries for its eatable pods. Historically, the uniform weight of carob seeds inspired the term “carat,” a unit once used to measure gold and gemstones. Its nutritious pods is sometimes referred to as “St. John’s Bread.” Both pods and seeds are edible and processed for various purposes—ground seeds serve as cocoa substitutes and food stabilisers, while the pulp produces molasses (debs) and drinks, especially consumed during Ramadan [47, 48].

Carob is rich in carbohydrates, making it naturally gummy and capable of thickening and binding, particularly in the treatment of diarrhoea. It also contains about 8% protein, vitamins, tannins, and dietary fibre. Carob fibre, high in insoluble fibre and polyphenols, has been shown to lower serum cholesterol and triglyceride levels while

promoting antioxidant activity [48, 49]. Dietary fibre from carob were found to influence body weight by modulating gut hormones such as ghrelin, which controls hunger and fat metabolism [48]. Studies indicate that consuming polyphenol-rich carob fibre reduces postprandial triglycerides and free fatty acids and shifts metabolism toward greater lipid oxidation. This is also associated with decreased acylated ghrelin levels after consuming carob-enriched meals [48, 49].

Carob's tannins also show antimicrobial and antiviral activity. Clinical research carried out in Turkey assessed the efficacy of carob bean juice (CBJ) as an adjunct to oral rehydration solution (ORS) in treating childhood diarrhea. Among 80 children with acute diarrhea, those receiving ORS + CBJ experienced a 45% reduction in diarrhoea duration, 44% lower stool output, and 38% less ORS intake compared with the ORS-only group [50, 51]. No adverse metabolic effects were reported, and mild hyponatremia occurred only in the control group. These findings confirmed that CBJ was an effective and safe supplement to standard ORS treatment [50, 51].

Black seed (*Nigella sativa*): *Nigella sativa*, commonly known as black seed or Habbatul Barakah in Arabic, is a plant rich in diverse nutritional and bioactive compounds. Its seeds contain monosaccharides such as glucose, rhamnose, xylose, and arabinose, as well as a significant amount of non-starch polysaccharides, which serve as an important source of dietary fibre [52, 53]. The seeds are also abundant in fatty acids, particularly the essential and unsaturated types, including alpha-linolenic acid (omega-3) and linoleic acid (omega-6). Furthermore, *Nigella sativa* seeds provide eight of the nine essential amino acids, which, like essential fatty acids, cannot be synthesised endogenously and must therefore be obtained through diet [52, 53]. In addition to these macronutrients, black seeds contain carotene (a precursor that the liver converts into vitamin A), a nutrient known for its anticancer properties. They also contain minerals such as calcium, iron, sodium, and potassium, which, although needed only in trace amounts, play a crucial role as cofactors in enzymatic reactions. Moreover, black seeds contain active constituents such as thymoquinone, dithymoquinone, thymohydroquinone, and thymol—compounds primarily responsible for the plant's therapeutic potential [17, 52, 53].

Often referred to as black cumin or Habbatul-Barakah, the seeds were prescribed in Greco-Arab, Islamic, Indian, and Chinese traditional systems for treating a wide range of disorders, including asthma, headaches, dysentery, infections, obesity, back pain, hypertension, and gastrointestinal disturbances [17]. Prophet Muhammad (Peace Be Upon Him) was reported to have said, "The black seed can heal every disease except death." Similarly, Ibn Sina (Avicenna) 980–1037 AD, referred to the seed in his Canon of Medicine as a stimulant of energy that aids recovery from fatigue and melancholy [44, 45, 46]. Regular consumption of black seed may thus contribute to overall well-being, strengthening the immune system and promoting the body's natural ability to prevent and recover from disease [38]. In traditional Eastern Mediterranean practices, black seed has also been utilized to promote lactation. Preparations combining black seed with toasted flour, sesame, and honey are consumed to nourish both mother and infant. Its immune-boosting properties further enhance resistance to illness, while scientific studies confirm its lactogenic benefits [17].

The Prophet's statement regarding its healing potential was confirmed by plenty of scientific papers dealing with the pharmacological effects of black seeds. A Medline and Google Scholar search for "*Nigella sativa*" and "medicine" resulted in over 2,000 studies highlighting its antioxidant, anti-inflammatory, antimicrobial, hypotensive, analgesic, choleric, uricosuric, antidiabetic, antihistaminic, immunomodulatory, anticancer, and fertility effects. Both the seed oil and its bioactive constituents demonstrate broad-spectrum antimicrobial

activity—antibacterial, antifungal, antiparasitic, and antiviral—effects that are believed to be partly due to the immunomodulatory actions of its compounds [17, 52].

Common fig (*Ficus carica*): Common fig (Teen in Arabic), is a large deciduous shrub or small tree native to Southwest Asia and the Eastern Mediterranean region. The Fig has a long history of safe consumption and traditional impact. In addition to its nutritional value, the fruit has been used for its medicinal properties in Greco-Arab and Islamic medicine, as well as in Ayurvedic and Traditional Chinese Medicine systems [17]. The fig is notably mentioned in several verses of the Holy Qur'an, including a chapter named after the tree itself, highlighting its importance. The Prophet Muhammad (Peace Be Upon Him) is reported to have said: "If I had to mention a fruit that descended from paradise, I would say this is it because the paradisiacal fruits do not have pits... Eat from these fruits for they prevent hemorrhoids, piles, and help with gout." Nutritionally, figs are rich in dietary fiber, potassium, and vitamin B6. Their high fiber content supports digestive health by promoting stool bulk, thereby reducing the risk of constipation, hemorrhoids, and colon cancer [17, 54, 55].

Scientific research confirmed that different species of fig trees exhibit notable anti-inflammatory, cancer-preventive, and cancer-therapeutic effects derived from their bark, roots, leaves, fruits, and latex [56, 57]. Ancient and medieval medical texts document their use in treating carcinomas, inflammatory swellings, "hard swellings," and tumors. Historically, fig-based preparations were often applied externally, even for internal ailments such as intestinal tumors, and were frequently combined with other medicinal ingredients like blue flag (*Iris versicolor* L.), barley, and fenugreek. Both the latex and the fruits were also administered orally [56, 57].

Greek and Arabic manuscripts contain early descriptions of fig trees, and later European texts provide detailed illustrations that help identify species, primarily *Ficus carica* and *Ficus sycomorus*. These records document the use of various plant parts—including fruits (fresh or dried, at different ripening stages), bark, leaves, twigs, young shoots, and latex—for treating inflammatory and tumorous conditions. Additionally, ashes from fig trees, stalks, and lye made from the branches and wood were utilized medicinally, as was wine prepared from the fruit [54]. Although historical terminology often does not align precisely with modern diagnostic categories, the consistency and specificity of these references support the long-standing recognition of *Ficus carica* for treating inflammation and tumors. Contemporary pharmacological studies have validated these traditional uses, demonstrating both anti-neoplastic and anti-inflammatory effects of crude extracts and isolated compounds. Of particular interest are phenanthroindolizidine alkaloids and triterpenoids containing C-18 carboxylic acid groups, which show potent cytotoxic activity against several cancer cell lines and are under investigation as potential anticancer agents [58, 59]. In addition, figs contain flavonoids such as anthocyanins, phenolic compounds, and lectins with antioxidant, anti-inflammatory, and immunomodulatory effects. Sterols contribute to immune enhancement and inhibit inflammatory processes and cellular invasion while promoting apoptosis and differentiation. Moreover, coumarins exhibit selective cytotoxicity toward cancer cells and possess antioxidant and anti-inflammatory properties through inhibition of lipoxygenase-derived 5-HETE formation [58, 59].

Beyond their therapeutic promise, *Ficus carica* fruits hold significant potential in the development of functional foods and beverages. This potential arises from their favorable safety profile, pleasant taste, and rich antioxidant content [60].

The antioxidant activity of figs also contributes to reducing chronic inflammation and improving insulin sensitivity, making them valuable in functional food strategies aimed at mitigating metabolic syndrome and enhancing general wellness. In addition to these metabolic benefits, figs continue to be recognised for their

traditional roles in promoting digestive health, providing natural energy, and serving as a nutritious and accessible food source [60].

Pomegranate (*Punica granatum*): The pomegranate is a deciduous fruit-bearing shrub or small tree native to the region extending from Persia to northern India. It is now naturalized throughout the Mediterranean basin and many other parts of the world. The fruit consists of three main structural components—the seeds, juice, and peel—each possessing distinct nutritional and medicinal properties. A notable derivative, pomegranate molasses (*dibs rumman* in Arabic), is a thick, tangy syrup widely used in Middle Eastern cuisine for its characteristic flavor and health [17, 61, 62].

Pomegranate had a long-standing role in Greco-Arab and Islamic traditional medicine, where it was prescribed for ailments such as sore throat, inflammation, and rheumatism. Across the Middle East, Iran, and India, its traditional therapeutic uses also included treatment of diarrhoea, colic, and intestinal worms in children. Moreover, pomegranate was used to relieve bladder discomfort, strengthen gums, and soothe oral ulcers. Beyond its medicinal relevance, the fruit had deep symbolic importance across major world religions—including Judaism, Christianity, Islam, Buddhism, and Zoroastrianism. In the Islamic tradition, the Qur'an describes pomegranates as among the fruits that grow in the gardens of paradise [17, 61].

From a phytochemical standpoint, pomegranate juice is rich in polyphenolic compounds, particularly hydrolyzable tannins known as punicalagins, which are recognised for their strong antioxidant activity. These compounds are bioavailable and contribute to the fruit's dietary and pharmacological value. Additional bioactive constituents include beta-carotene, catechins, gallocatechins, and various anthocyanins such as prodelphinidins, delphinidin, cyanidin, and pelargonidin. The fruit also provides vitamin C at a concentration of approximately 0.47 mg per 100 g [61]. In addition, pomegranate and its extracts are diverse pharmacological activities. These include anti-inflammatory effects, hormone replacement support, allergy symptom management, cardiovascular protection, maintenance of oral hygiene, ophthalmic treatment, and cosmetic uses such as weight-loss soaps. Pomegranate derivatives have also been investigated as adjunct agents for enhancing the bioavailability of radioactive tracers in diagnostic imaging. [17, 61, 62]. The potent antioxidant activity of pomegranate compounds helps regulate inflammatory pathways, thereby reducing oxidative stress and inflammation-related damage. This mechanism is supposed to underlie the fruit's chemo preventive and chemotherapeutic potential against certain cancers [61, 62, 63, 64].

Garlic (*Allium sativum* L.): Garlic, along with onion (*Allium cepa* L.), is ranked among the oldest cultivated plants known for both culinary and medicinal uses. Garlic has been appreciated for its therapeutic potential for millennia [65, 66]. Ancient Sanskrit texts mentioned its medicinal applications as early as 5,000 years ago, and it was a component of Chinese medicine for at least 3,000 years. Civilizations such as the Egyptians, Babylonians, Greeks, and Romans also used garlic for its healing properties. In 1858, Louis Pasteur first documented garlic's antibacterial effects, and it was subsequently used as an antiseptic during World War I and World War II to prevent gangrene. Across various cultures, garlic was traditionally used to manage hypertension, and [65, 66]. Both, garlic and onion are both rich in bioactive compounds, key components of the Mediterranean diet, and are widely recognized for their role in preventing and treating several diseases. These include cancer, coronary heart disease, obesity, hypercholesterolemia, type 2 diabetes, hypertension, cataracts, and several gastrointestinal disorders (e.g., colic pain, flatulence, and dyspepsia). The pharmacological activity of garlic is primarily attributed to thiosulfates, sulfur-containing compounds, of which allicin is the most prominent. Allicin

is produced enzymatically when alliin, a sulfur-rich amino acid, reacts with the enzyme alliinase during chopping, crushing, or chewing of raw garlic. The antimicrobial, hypolipidemic, antioxidant, and antithrombotic effects associated with garlic are largely linked to allicin and its various breakdown products [67, 68]. In addition, both garlic and onion contain more polar phenolic and steroidal compounds, often found in glycosylated forms, that exhibit significant therapeutic properties. These compounds are advantageous compared to thiosulfates because they are non-pungent and more stable when exposed to heat, making them suitable for consumption in cooked dishes. Contemporary research has increasingly focused on these stable, health-promoting constituents and their potential applications in disease prevention and management [67, 68].

Fenugreek (*Trigonella foenum-graecum* L): Fenugreek, is a leguminous plant widely cultivated in India, North Africa, and the Mediterranean region. The seeds of fenugreek are particularly rich in bioactive compounds, including galactomannans, proteins rich in lysine and tryptophan, lipids, and pyridine-type alkaloids such as trigonelline, choline, gentianine, and carpaine. Additionally, the seeds contain flavonoids (apigenin, luteolin, orientin, quercetin, vitexin, and isovitexin), free amino acids, minerals such as calcium and iron, saponins, and glycosides that yield steroidal sapogenins upon hydrolysis, including diosgenin, yamogenin, tigogenin, and neotigogenin. Other notable constituents are cholesterol, sitosterol, vitamins A, B1, and C, nicotinic acid, and volatile oils [69].

The medicinal properties of fenugreek reside mainly in its seeds, which were used for centuries in Greco-Arab and Islamic medicine, as well as in Indian and Chinese traditional systems. The Prophet Muhammad (Peace Be Upon Him) and generations of herbalists highly valued this plant for its therapeutic effects. One Hadith recounts that when the Prophet visited his companion Sa'ad bin Abi Waqqas during an illness, he instructed that the patient be given a soup made from dates and fenugreek, declaring that it would aid his recovery. In another Hadith, the Prophet stated, "If my community knew the benefits of fenugreek, they would value it as highly as gold." [17].

Fenugreek seeds, when crushed or powdered, have long been used externally as poultices to treat boils, ulcers, eczema, and hives, while internally they are used to reduce blood sugar, promote lactation, and treat a wide range of ailments such as pellagra, loss of appetite, indigestion, bronchitis, fever, hernia, vomiting, respiratory tract catarrh, and gastric ulcers. Additionally, fenugreek is traditionally believed to enhance female breast development and regulate hormonal imbalances [70, 71]. Furthermore, according to the German Commission E, fenugreek seeds possess secretolytic (anti-mucous) and mild antiseptic properties. Similarly, the British Herbal Pharmacopoeia identifies their hypoglycemic activity. Empirical evidence supports these claims: adults consuming half a teaspoon of fenugreek seeds with water three times daily often experience rapid and notable relief of symptoms. Experimental and clinical studies have further demonstrated the antidiabetic, anti-inflammatory, and antitumor properties of the seeds, including significant hypoglycemic effects in patients with type 1 diabetes [72, 73, 74]. Although clinical studies on fenugreek use in type 2 diabetes remain limited and of generally lower methodological quality, results consistently indicate beneficial outcomes. Most studies, though small and uncontrolled, report improvements in glycemic control with the inclusion of fenugreek seed powder in daily meals such as unleavened bread. One randomized crossover study involving healthy volunteers (n = 38) compared various seed preparations, including raw whole seeds, extracted powders, gum isolates, and cooked seeds. All forms produced reductions in postprandial glucose levels. Other trials following patients for up to six months have similarly demonstrated sustained improvements in blood glucose management without any reported adverse effects [72, 73, 75, 76].

3. Concluding Remarks

The merging of Prophetic, Greco-Arab, and Islamic medical traditions with contemporary medicine and nutritional science highlights an enduring reality. In addition, the historical focus on balance in diet and the healing properties of natural foods is well-supported by current biological and medical studies. More importantly, foods, like honey, olive oil, dates, black seeds, and diverse wild edible plants, are now approved for their abundant antioxidants, essential fatty acids, vitamins, and bioactive substances that support immune regulation, metabolic equilibrium, and disease prevention.

Current scientific investigations are revealing the cell biological, biochemical, and molecular pathways through which diet-derived active compounds promote health, offering evidence for dietary principles established centuries ago by physicians such as Al-Razi, Ibn Sina, and Ibn Albaitar echoed from the Prophetic teachings.

With chronic illnesses placing growing pressure on healthcare systems globally, there is a revived recognition of food-focused preventive approaches that provide a sustainable, culturally relevant, and scientifically supported way ahead. Combining knowledge from traditional Arab-Islamic medicine with modern nutritional science can enhance contemporary healthcare methods, linking historical wisdom with present advancements. In the end, acknowledging and utilizing the healing power of food could be crucial in reinstating a comprehensive perspective on health—one that integrates body, mind, and spirit through equilibrium, moderation, and organic sustenance.

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Ethical consideration

This study adhered to the principles of the Declaration of Helsinki.

Consent to participate

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Conflicts of interest

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References

- [1] Saad, B. "History, Present and Prospect of Greco-Arab and Islamic Herbal Medicine." *History, Present and Prospect of World Traditional Medicine*. 2024. 235-300. https://doi.org/10.1142/9789811282171_0004
- [2] Wang Y., Liu B., Han H., Hu Y., Zhu L., Rimm E. B., Hu F. B., Sun Q. (2023/2024). Associations between plant-based dietary patterns and risks of type 2 diabetes, cardiovascular disease, cancer, and mortality – a systematic review and meta-analysis. *Nutrition Journal*, 22, Article number: 46
- [3] Tan H., Zhang Y., Jiang L., Li R., Yang Q., et al. (2024). Plant-based diet and risk of all-cause mortality: a systematic review and meta-analysis. *Journal of Epidemiology & Community Health*.
- [4] Saad, B. Prevention and Treatment of Obesity-Related Inflammatory Diseases by Edible and Medicinal Plants and Their Active Compounds. *Immuno* 2022, 2, 609–629. <https://doi.org/10.3390/immuno2040038>
- [5] Lee Y-H, Lee J-H, Jeon S-M, Park I-K, Jang H-B, Kim S-A, et al. The Effect of Organic Vegetable Mixed Juice on Blood Circulation and Intestine Flora: Randomized, Double-Blinded, Placebo-Controlled Clinical Trial. *Diseases*. 2024;12(9):223.
- [6] Connolly EL, Liu AH, Radavelli-Bagatini S, et al. Cruciferous vegetables lower blood pressure in adults with mildly elevated blood pressure in a randomized, controlled, crossover trial: the vegetableS for vascular health (VESSEL) study. *BMC Medicine*. 2024;22:353.
- [7] Immonen V, Virtanen JK, Mursu J, Tuomainen TP. Mediterranean Diet in Older Adults: Cardiovascular Outcomes and Mortality from Observational and Interventional Studies — A Systematic Review and Meta-Analysis. *Ageing Res Rev*. 2023;86:101850. doi:[10.1016/j.arr.2023.101850](https://doi.org/10.1016/j.arr.2023.101850).
- [8] Schwingshackl L, Christoph M, Hoffmann G. Effect of Mediterranean Diets on Cardiovascular Risk Factors and Disease in Overweight and Obese Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Clin Nutr*. 2024;43(1):21-39. doi:[10.1016/j.clnu.2023.09.004](https://doi.org/10.1016/j.clnu.2023.09.004).
- [9] Bonaccio M, Di Castelnuovo A, Costanzo S, De Curtis A, Persichillo M, Cerletti C, Donati MB, de Gaetano G, Iacoviello L. Effect of Mediterranean Diet on Lifespan: A Treatment-Effect Survival Analysis of a Population-Based Prospective Cohort Study in Southern Italy. *Int J Epidemiol*. 2021;50(1):245-255. doi:[10.1093/ije/dyaa163](https://doi.org/10.1093/ije/dyaa163)
- [10] Nettleton JA, Steffen LM, Loehr LR, Rosamond WD, Folsom AR. Mediterranean Diet Adherence and Risk of All-Cause Mortality in Women. *JAMA Netw Open*. 2020;3(12):e2029335. doi:[10.1001/jamanetworkopen.2020.29335](https://doi.org/10.1001/jamanetworkopen.2020.29335).
- [11] Xie Y, Zhang Y, Zhang Y, Chen X, Zhang Y, Li X, et al. Effects of soluble fiber supplementation on glycemic control in adults with type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials. *Clin Nutr*. 2021;40(4):1800-1810. doi:[10.1016/j.clnu.2020.10.032](https://doi.org/10.1016/j.clnu.2020.10.032).

- [12]Hartvigsen ML, Gregersen S, Lærke HN, Bach Knudsen KE, Hermansen K. Effects of concentrated arabinoxylan and β -glucan compared with refined wheat and whole grain rye on glucose and appetite in subjects with the metabolic syndrome: a randomized study. *Eur J Clin Nutr.* 2014;68(1):84-90. doi:10.1038/ejcn.2013.236.
- [13]Clark MJ, Slavin JL. The effect of fiber on satiety and food intake: a systematic review. *J Am Coll Nutr.* 2013;32(3):200-211. doi:10.1080/07315724.2013.791194.
- [14]Santaliestra-Pasías AM, Moreno LA, González-Gross M, Gracia-Marco L, Rodríguez G, Molnar D, et al. Effect of two bakery products on short-term food intake and satiety in children: a randomized controlled crossover trial. *Eur J Clin Nutr.* 2016;70(4):459-463. doi:10.1038/ejcn.2015.212.
- [15]Markellos C, Konstantinidou V, Panagiotakos DB, Antonopoulou S, Kontogianni MD. Olive oil intake and cancer risk: A systematic review and meta-analysis. *Nutrients.* 2022;14(5):1456. doi:10.3390/nu14051456.
- [16]Carruba G. Nutrition, aging and cancer: Lessons from dietary intervention studies. *Immun Ageing.* 2016;13:1-11. doi:10.1186/s12979-016-0069-9.
- [17]Saad B, & Said O. *Greco-Arab and Islamic Herbal Medicine: Traditional System, Ethics, Safety, Efficacy and Regulatory Issues*, Wiley-Blackwell John Wiley & Sons, Inc 2011.
- [18]Saad B. Integrating traditional Greco-Arab and Islamic herbal medicine in research and clinical practice. In *Phytotherapies: safety, efficacy, and regulation*, Ed. Iqbal Ramazan. Wiley-Blackwell John Wiley & Sons, Inc 2015
- [19]Khaliq A, and Ali Z. A Research Review of the Concepts, Necessity and Importance of Prophetic Medicine. *ASSAJ.* 2025 Jun 13;3(02):1541-52.
- [20]Almutairi K, De Santis J. Prophetic Medicine in the Context of Middle Eastern Culture: A Concept Analysis. *Research & Theory for Nursing Practice.* 2025 Jan 1;39(1).
- [21]Mogharbel GH, Badawi AS, Zaman AY, Abd Elmoniem MM, Abdel-Rahman IM, Alenazi ME, Shah FA, Aly MA, Imam SN, Alenazi NE, El Sayed SM. Therapeutic benefits of prophetic medicine remedies in treating hematological diseases (A review article). *American Journal of Blood Research.* 2023 Aug 15;13(4):130.
- [22]Ilia G, Simulescu V, Merghes P, Varan N. The health benefits of honey as an energy source with antioxidant, antibacterial and antiseptic effects. *Science & Sports.* 2021 Sep 1;36(4):272-e1.
- [23]Saad, B. Immunomodulatory and Anti-Inflammatory Properties of Honey and Bee Products. *Immuno.* 2025 May 30;5(2):19.
- [24]Almasaudi S. The antibacterial activities of honey. *Saudi journal of biological sciences.* 2021 Apr 1;28(4):2188-96.
- [25]Abu-Farich B, Hamarshi H, Masalha M, Aboulghazi A, El Ouassete M, Kmail A, Imtara H, Badiia Lyoussi B, Saad B. Polyphenol Contents, Antibacterial and Antioxidant Effects of Four Palestinian Honey Samples, and their Anticancer Effects on Human Breast Cancer Cells. *J Pure Appl Microbiol.* 2024;18(2):1372-1385
- [26]Imtara H, Abujaber, F., Siouri, F., Tumeh, A., & Saad, B. (2025). Chemical composition, antioxidant, and anticancer activities of *Thymus capitatus* essential oil: Experimental and computational approaches. *Phyton-Int J Exp Bot.* 2025; Doi:10.32604/phyton.2025.063403

- [27] Abu-Farich B, Masalha M, Hamarshi H, El Ghouizi A, Aboulghazi A, El Ouassete M, Weldali D, Lyoussi B, Saad B. In vitro evaluation of Hyphaene thebaica honey as a multitarget therapeutic product, *Microbes Immun.* 2025;doi:10.36922/mi.4994.
- [28] Tashkandi H. Honey in wound healing: An updated review. *Open life sciences.* 2021 Oct 6;16(1):1091-100.
- [29] Akanda MK, Mehjabin S, Parvez GM. Honey for nutrition and health benefits: an overview. *Honey in Food Science and Physiology.* 2024 Jul 19:33-56.
- [30] Mărgăoan R, Topal E, Balkanska R, Yücel B, Oravec T, Cornea-Cipcigan M, Vodnar DC. Monofloral honeys as a potential source of natural antioxidants, minerals and medicine. *Antioxidants.* 2021 Jun 25;10(7):1023.
- [31] Jarar D, Kmail A, Masalha M, Abu-Farich B, Weldali D, Touzani S, Lyoussi B, Saad B. Wound Healing Mechanisms of Medicago sativa Honey: Antioxidant, Anti-inflammatory, Antibacterial and Phytochemical Characterisation. *Journal Of Natural Remedies*, DOI: 10.18311/jnr/2025/50943
- [32] Jarar D, Imtara H, Kmail AS, Masalha M, Aouji M, Weldali D, Aboulghazi A, Lyoussi B, Saad B, Experimental evaluation of avocado honey's wound healing properties: Physicochemical, antibacterial, anti-inflammatory, and proliferative effects combined with in silico toxicity and molecular docking analysis, *Journal of Ethnopharmacology*, 2026, 358:121038
- [33] Kumar D, Verma AK, Chatli MK, Singh R, Kumar P, Mehta N, Malav OP. Camel milk: Alternative milk for human consumption and its health benefits. *Nutrition & Food Science.* 2016 Mar 14;46(2):217-27.
- [34] Muthukumaran MS, Mudgil P, Baba WN, Ayoub MA, Maqsood S. A comprehensive review on health benefits, nutritional composition and processed products of camel milk. *Food Reviews International.* 2023 Aug 18;39(6):3080-116.
- [35] Pal M, Tariku F, Rebuma T, Molnar J, Pinto S. Growing importance of camel milk in human health. *J. Nutrition and Food Processing.* 2024;7(7).
- [36] Behrouz S, Saadat S, Memarzia A, Sarir H, Folkerts G, Boskabady MH. The antioxidant, anti-inflammatory and immunomodulatory effects of camel milk. *Frontiers in immunology.* 2022 Apr 12;13:855342.
- [37] Chiavarini M, Rosignoli P, Giacchetta I, Fabiani R. Health outcomes associated with Olive oil intake: an umbrella review of meta-analyses. *Foods.* 2024 Aug 21;13(16):2619.
- [38] Xiong Y, Shi X, Xiong X, Li S, Zhao H, Song H, Wang J, Zhang L, You S, Ji G, Liu B. A systematic review and meta-analysis of randomized controlled trials: effects of mediterranean diet and low-fat diet on liver enzymes and liver fat content of NAFLD. *Food & Function.* 2024;15(16):8248-57.
- [39] Saad, B., Kmail A. Olive Oil Polyphenols in Cancer: Molecular Mechanisms and Therapeutic Promise. *Immuno* 2025, 5, 36
- [40] Al-Alawi RA, Al-Mashiqri JH, Al-Nadabi JS, Al-Shihi BI, Baqi Y. Date palm tree (*Phoenix dactylifera* L.): natural products and therapeutic options. *Frontiers in plant science.* 2017 May 23;8:845.
- [41] Bentrad N, Hamida-Ferhat A. Date palm fruit (*Phoenix dactylifera*): Nutritional values and potential benefits on health. In *The Mediterranean Diet* 2020 Jan 1 (pp. 239-255). Academic Press.

- [42] Mahomoodally MF, Khadaroo SK, Hosenally M, Zengin G, Rebezov M, Ali Shariati M, Khalid A, Abdalla AN, Algarni AS, Simal-Gandara J. Nutritional, medicinal and functional properties of different parts of the date palm and its fruit (*Phoenix dactylifera* L.)—A systematic review. *Critical reviews in food science and nutrition*. 2024 Aug 28;64(22):7748-803.
- [43] Chao CT, Krueger RR. The date palm (*Phoenix dactylifera* L.): overview of biology, uses, and cultivation. *HortScience*. 2007 Aug 1;42(5):1077-82.
- [44] Al-Shwyeh HA. Date palm (*Phoenix dactylifera* L.) fruit as potential antioxidant and antimicrobial agents. *Journal of Pharmacy and Bioallied Sciences*. 2019 Jan 1;11(1):1-1.
- [45] Zineb G, Boukouada M, Djeridane A, Saidi M, Yousfi M. Screening of antioxidant activity and phenolic compounds of various date palm (*Phoenix dactylifera*) fruits from Algeria. *Mediterranean Journal of Nutrition and Metabolism*. 2011 Oct 28;5(2):119-26.
- [46] Asdaq SM, Almutiri AA, Alenzi A, Shaikh M, Shaik MA, Alshehri S, Rabbani SI. Unveiling the Neuroprotective Potential of Date Palm (*Phoenix dactylifera*): A Systematic Review. *Pharmaceuticals*. 2024 Sep 17;17(9):1221.
- [47] Basharat Z, Afzaal M, Saeed F, Islam F, Hussain M, Ikram A, Pervaiz MU, Awuchi CG. Nutritional and functional profile of carob bean (*Ceratonia siliqua*): A comprehensive review. *International Journal of Food Properties*. 2023 Sep 22;26(1):389-413.
- [48] Azab A. Carob (*Ceratonia siliqua*): Health, medicine and chemistry. *Eur Chem Bull*. 2017 Dec 5;6(10):456-69.
- [49] Benyaich A, Nouayti A, El Mekki O, Errafia R, Bahtat F, Aksissou M. Phytochemical and pharmacological properties of *Ceratonia siliqua* L.: A comparative review of Moroccan and Mediterranean varieties. *Journal of Applied Pharmaceutical Science*. 2025 Sep 5;15(10):022-42.
- [50] Abdulkareem RS, Yaseen Al-Hayali WR, Ibrahim II. Antimicrobial activity of *Ceratonia siliqua* L. extract against diarrheagenic E-coli. *Systematic Reviews in Pharmacy*. 2020 Dec 1;11(12).
- [51] Najem NA, Alhamdani HA. Evaluation the Antifungal Activity of the Alcoholic Extract of Carob (*Ceratonia siliqua* L) Plant Against Fungal Isolates Obtained from the Mouths of Infants in Ramadi City. *InIOP Conference Series: Earth and Environmental Science* 2025 Oct 1 (Vol. 1538, No. 1, p. 012015). IOP Publishing.
- [52] Hannan MA, Rahman MA, Sohag AA, Uddin MJ, Dash R, Sikder MH, Rahman MS, Timalsina B, Munni YA, Sarker PP, Alam M. Black cumin (*Nigella sativa* L.): A comprehensive review on phytochemistry, health benefits, molecular pharmacology, and safety. *Nutrients*. 2021 May 24;13(6):1784.
- [53] Abbas M, Gururani MA, Ali A, Bajwa S, Hassan R, Batool SW, Imam M, Wei D. Antimicrobial properties and therapeutic potential of bioactive compounds in *Nigella sativa*: A review. *Molecules*. 2024 Oct 17;29(20):4914.
- [54] Barolo MI, Mostacero NR, López SN. *Ficus carica* L.(Moraceae): An ancient source of food and health. *Food chemistry*. 2014 Dec 1;164:119-27.
- [55] Rasool IF, Aziz A, Khalid W, Koraqi H, Siddiqui SA, Al-Farga A, Lai WF, Ali A. Industrial application and health prospective of fig (*Ficus carica*) by-products. *Molecules*. 2023 Jan 18;28(3):960.
- [56] Nuri ZN, Uddin MS. A review on nutritional values and pharmacological importance of *Ficus carica*. *Journal of Current Research in Food Science*. 2021;2(1):07-11.

- [57] Soltana H, Pinon A, Limami Y, Zaid Y, Khalki L, Zaid N, Salah D, Sabitaliyevich UY, Simon A, Liagre B, Hammami M. Antitumoral activity of *Ficus carica* L. on colorectal cancer cell lines. *Cellular and Molecular Biology*. 2019 Jul 31;65(6):6-11.
- [58] Park S, Han J, Im K, Whang WK, Min H. Antioxidative and anti-inflammatory activities of an ethanol extract from fig (*Ficus carica*) branches. *Food Science and Biotechnology*. 2013 Aug;22(4):1071-5.
- [59] Ali B, Mujeeb M, Aeri V, Mir SR, Faiyazuddin M, Shakeel F. Anti-inflammatory and antioxidant activity of *Ficus carica* Linn. leaves. *Natural product research*. 2012 Mar 1;26(5):460-5.
- [60] Mopuri R, Ganjari M, Meriga B, Koorbanally NA, Islam MS. The effects of *Ficus carica* on the activity of enzymes related to metabolic syndrome. *Journal of food and drug analysis*. 2018 Jan 1;26(1):201-10.
- [61] Dogara AM, Hama HA, Ozdemir D. Update on the potential of *Punica granatum* L. traditional uses and pharmacological uses: A review. *Advances in Pharmacological and Pharmaceutical Sciences*. 2024;2024(1):6523809.
- [62] Machado JC, Ferreira MR, Soares LA. *Punica granatum* leaves as a source of active compounds: A review of biological activities, bioactive compounds, food, and technological application. *Food Bioscience*. 2023 Feb 1;51:102220.
- [63] Dimitrijevic J, Tomovic M, Bradic J, Petrovic A, Jakovljevic V, Andjic M, Živković J, Milošević SD, Simanic I, Dragicevic N. *Punica granatum* L. (Pomegranate) extracts and their effects on healthy and diseased skin. *Pharmaceutics*. 2024 Mar 26;16(4):458.
- [64] Mohan M, Mohanavarshaa CA, Priya D. Review of pharmacological and medicinal uses of *punica granatum*. *Cureus*. 2024 Oct 15;16(10).
- [65] Tesfaye A. Revealing the therapeutic uses of garlic (*Allium sativum*) and its potential for drug discovery. *The Scientific World Journal*. 2021;2021(1):8817288.
- [66] Choudhary S, Noor MU, Hussain MS, Mishra M, Tyagi S. Pharmacological properties and phytoconstituents of garlic (*Allium sativum* L.): A review. *Biological Sciences*. 2022 Dec 25;2(4):338-46.
- [67] Loría Gutiérrez A, Blanco Barrantes J, Porras Navarro M, Ortega Monge MC, Cerdas Vargas MJ, Madrigal Redondo GL. General aspects about *Allium sativum*—a review. *Ars pharmaceutica*. 2021 Oct 1;62(4).
- [68] Okoro BC, Dokunmu TM, Okafor E, Sokoya IA, Israel EN, Olusegun DO, Bella-Omunagbe M, Ebubechi UM, Ugbogu EA, Iweala EE. The ethnobotanical, bioactive compounds, pharmacological activities and toxicological evaluation of garlic (*Allium sativum*): A review. *Pharmacological Research-Modern Chinese Medicine*. 2023 Sep 1;8:100273.
- [69] Ruwali P, Pandey N, Jindal K, Singh RV. Fenugreek (*Trigonella foenum-graecum*): Nutraceutical values, phytochemical, ethnomedicinal and pharmacological overview. *South African Journal of Botany*. 2022 Dec 1;151:423-31.
- [70] Singh U, Chamoli M, Singh KP, Ram L, Jangir S, Maheshwari RK. Amazing health benefit of fenugreek (*Trigonella foenum-graecum* LINN.). *International Journal of Environment and Health Sciences*. 2022;4:19-27.
- [71] Arya P, Kumari N, Wani SA, Kumar P. *Trigonella foenum graecum*. Herbs, spices and their roles in nutraceuticals and functional foods. 2023 Jan 1:133-48.

- [72] Saad B, Zaid H, Shanak S, & Kadan S. Anti-diabetes and Anti-obesity Medicinal Plants and Phytochemicals Safety, Efficacy, and Action Mechanisms. Springer 2017
- [73] Sarker DK, Ray P, Dutta AK, Rouf R, Uddin SJ. Antidiabetic potential of fenugreek (*Trigonella foenum-graecum*): A magic herb for diabetes mellitus. *Food Science & Nutrition*. 2024 Oct;12(10):7108-36.
- [74] Rahman S, Husen A. *Trigonella foenum-graecum* L.: A useful medicinal plant for diabetes and other diseases. In *Antidiabetic medicinal plants and herbal treatments 2023* Jul 17 (pp. 145-157). CRC Press.
- [75] Kashif M, Nasir A, Gulzaman, Rafique MK, Abbas M, ur Rehman A, Riaz M, Rasool G, Mtewa AG. Unlocking the anti-diabetic potential of *Gymnema sylvestre*, *Trigonella foenum-graecum*, and their combination thereof: An in-vivo evaluation. *Food Science & Nutrition*. 2023 Dec;11(12):7664-72
- [76] Saad, B. Management of obesity-related inflammatory and cardiovascular diseases by medicinal plants: From traditional uses to therapeutic targets. *Biomedicines* 2023 5;11(8):2024.



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Artificial Intelligence in Digital Implant Planning: A Narrative Review of Current Trends and Future Prospects

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Abstract

Background: Artificial intelligence (AI) has emerged as a streaming technology in dental implant planning that addresses workflow complexity and enhances diagnostic precision across multiple treatment stages. **Objective:** This narrative review synthesizes current evidence on AI applications throughout the implant planning continuum, examining accuracy metrics, clinical implementation considerations, and future directions. **Methods:** In 2015-2025, AI applications in implant dentistry, including anatomical segmentation, virtual patient creation, presurgical planning, computer-assisted surgery, prosthetic design, and outcome prediction, were examined. **Results:** AI demonstrates high accuracy in anatomical segmentation (>90%), edentulous site identification (96% mandibular accuracy, 83% maxillary accuracy), and virtual implant placement (95% clinical acceptability). Compared with human clinicians, deep learning models automate labor-intensive processes, reduce the segmentation time from hours to seconds, and achieve expert-level planning with 2.2-fold faster execution. Compared with conventional guided approaches (1.0 mm), robotic-assisted surgery powered by AI achieves superior positional accuracy (0.5 mm coronal, 0.5 mm apical deviation). AI-powered CAD/CAM systems enhance prosthetic design efficiency and customization. However, significant limitations persist: data heterogeneity reduces generalizability, interference from metal artifacts degrades segmentation, algorithmic opacity undermines clinical trust, and external validation studies remain insufficient. Ethical concerns regarding data privacy, algorithmic bias, and healthcare disparities require careful consideration. **Conclusions:** AI functions most effectively as a clinical decision support system that augments human expertise rather than replacing clinician judgment. Emerging technologies, including explainable AI frameworks, augmented reality visualization, and hybrid models, promise enhanced clinical integration. Prospective multicenter trials with standardized metrics and transparent validation are essential before widespread clinical deployment. AI-augmented implant planning represents a paradigm shift toward precision, personalized, and predictable implant dentistry.

Keywords: Artificial intelligence, dental implants, implant planning, deep learning, computer-assisted surgery, clinical decision support, surgical accuracy

1. Introduction

The digitalization of dental workflows represents one of the most significant paradigm shifts in contemporary implant dentistry[1]. Digital technologies now facilitate comprehensive treatment planning, from initial data acquisition through final prosthetic design, offering substantial improvements in predictability and clinical outcomes[2,3]. This integration encompasses multiple technologies, including cone-beam computed tomography (CBCT) for three-dimensional anatomical visualization, intraoral scanners (IOSs) for capturing dental and soft tissue geometry, facial scanning for aesthetic planning, and computer-aided design/computer-assisted manufacturing (CAD/CAM) systems for prosthetic fabrication[4,5]. These multimodal digital systems enable customized implant planning, supporting innovations, such as patient-specific implants, personalized titanium meshes for guided bone regeneration, and CAD/CAM scaffolds for bone augmentation, ultimately allowing clinicians to transition from generic protocols toward individualized treatment strategies[6,7].

However, the complexity inherent in these digital workflows presents significant challenges. Multiple sequential steps, encompassing image acquisition, multimodal image registration, anatomical landmark identification, segmentation of critical structures, implant position planning, and prosthetic design, require substantial operator expertise and remain time-consuming and user-dependent processes[8]. The extended duration and technical complexity of these workflows can limit their accessibility and consistency across clinical practices, necessitating approaches to streamline procedures and reduce the training burden on clinicians[9].

Artificial intelligence (AI) has emerged as a supportive force in dental implant planning, fundamentally reshaping diagnostic workflows, treatment predictability, and surgical precision[8]. AI techniques, particularly deep learning methodologies grounded in artificial neural networks, offer promising solutions to address these workflow limitations[10]. AI systems have the capacity to automate repetitive tasks, enhance diagnostic accuracy, reduce human error, and improve procedural efficiency, thereby potentially minimizing complications and optimizing treatment outcomes[11]. The significance of AI in implant dentistry extends beyond simple task automation; these technologies can extract complex patterns from imaging data[12], facilitate rapid and consistent anatomical structure segmentation[13], and support evidence-based clinical decision-making at multiple treatment stages[14–20].

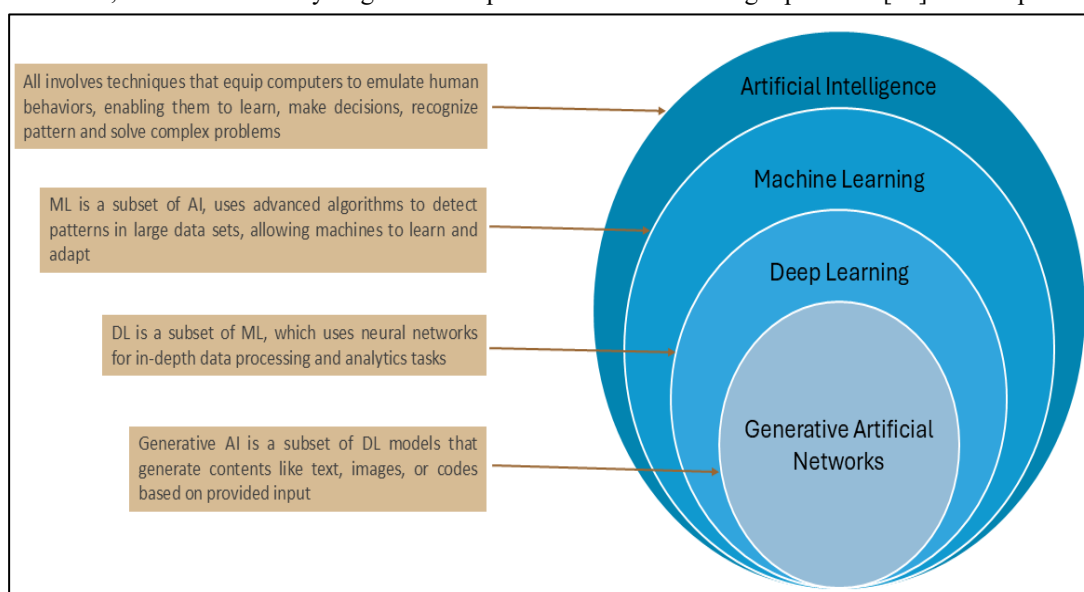
Previous studies have documented the potential of AI models in specific implant dentistry applications, including dental implant recognition[21], peri-implant bone loss detection[22], implant failure prediction[23], and automated assessment of bone dimensions for implant site selection on CBCT images[24]. Currently, the scientific literature has comprehensive evidence regarding how AI can be strategically integrated throughout the presurgical implant planning process. This necessitates a detailed analysis of specific treatment planning steps, how AI technologies can increase planning accuracy and efficiency, and what clinical outcomes result from AI-augmented planning compared with conventional approaches. This narrative review addresses these questions by synthesizing current evidence on AI applications across the implant planning continuum, examining reported accuracy metrics, discussing implementation considerations for clinical practice, and identifying future research directions and clinical opportunities. This narrative review synthesizes current evidence on AI applications throughout the

implant planning continuum, from anatomical assessment to outcome prediction, while examining accuracy metrics, clinical implementation challenges, and future directions.

2. The role of the AI in anatomic landmark segmentation

The initial phase of digital implant planning focuses on generating 3D virtual reconstructions of dentomaxillofacial structures from CT or CBCT scans. These digital models are essential for virtual surgical planning and designing patient-specific components, such as surgical guides and prostheses[5]. Traditionally, segmentation is performed manually, which is labor intensive and requires significant anatomical and imaging expertise [25]. To reduce time and workload, semiautomatic segmentation methods have been introduced. These rely on defining threshold values of Hounsfield or grayscale intensities to differentiate between tissues [26]. Although semiautomatic processes allow quicker segmentation, they are prone to certain limitations, such as a steep learning curve, the need for excessive manual postprocessing in the presence of high-density material artifacts, and interobserver variability due to manual threshold value selection that differs for each patient and anatomical region, depending on the bone density [27].

Recent advances in AI (Figure 1) have emerged as powerful alternatives to these traditional methods. Modern AI algorithms, especially deep learning models such as convolutional neural networks (CNNs) and U-Net architectures, can automatically segment complex structures with high precision[28]. Their performance is



typically evaluated via metrics such as accuracy, recall, precision, Dice score, and intersection over union (IoU), with most studies reporting results exceeding 90% accuracy for CBCT-based segmentation of the mandible, maxilla, teeth, nerves, dental implants, and airway spaces [29–47].

Figure 1. Artificial intelligence model types and their evolution.

Compared with manual or semiautomatic methods, AI segmentation is faster, more consistent, and independent of observer variability; in fact, segmentation tasks that once took clinicians up to several hours can now be completed within seconds [30,38]. Additionally, AI demonstrates robustness in cases affected by metal artifacts, accurately distinguishing anatomical structures even under low-contrast conditions [48].

The integration of AI into cloud-based platforms has further simplified clinical workflows by eliminating the need for high-performance computing hardware [29]. These automated systems increase the efficiency of computer-assisted surgical planning (CASP) in fields such as dental implantology, orthognathic surgery, and navigational procedures. Nevertheless, challenges persist regarding generalizability; AI models may perform inconsistently across data from different scanners and imaging protocols. To overcome this limitation, large, multicenter datasets are needed to train and validate algorithms for broader clinical applicability [49]. Figure 2 shows an example of a cloud-based AI platform that automatically segments anatomical structures from uploaded 3D data of patients.

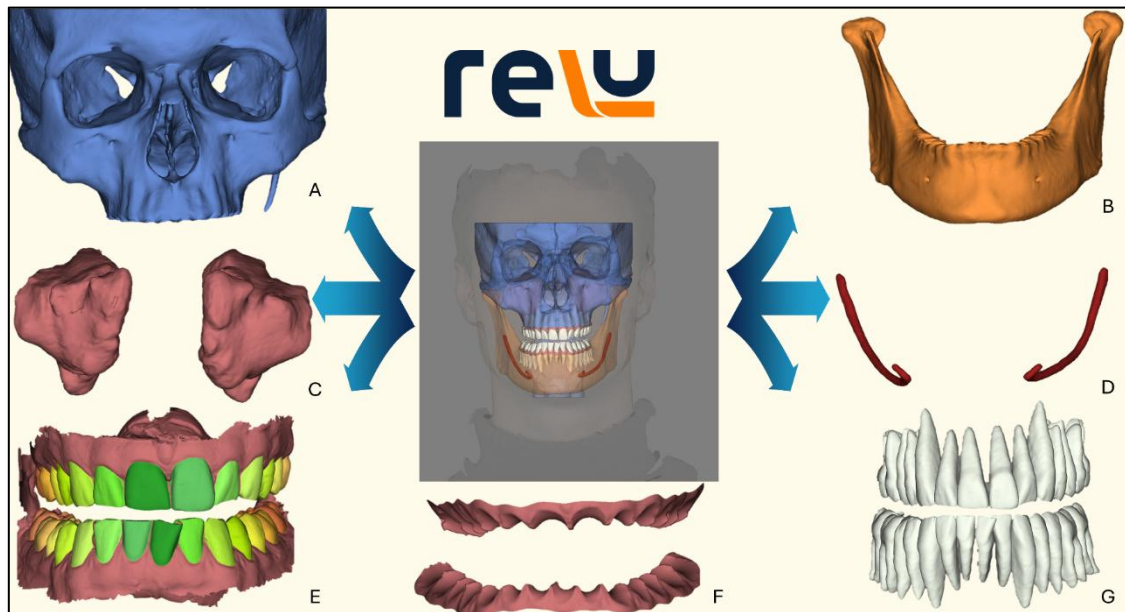


Figure 2. Example of a cloud-based AI platform for automatic anatomical segmentation from CBCT and the IOS. A) Maxillary complex segmented model, B) segmented model of the mandible, C) bilateral maxillary sinus segmented model, D) bilateral mandibular nerve segmentation, E) teeth segmentation from the IOS, F) gingiva segmentation from the IOS, and G) teeth crowns from the IOS fused with roots from CBCT.

3. Virtual patient creation

Image registration is the superimposition of three-dimensional images from different imaging modalities into a unified coordinate frame. It has become fundamental to CASP in oral and maxillofacial procedures. Accurate registration ensures optimal alignment of anatomical structures, preventing misalignments that could compromise surgical outcomes[50]. By combining complementary imaging modalities, such as CBCT, intraoral scanners, and facial scans, clinicians gain comprehensive views of both osseous and soft tissue anatomy, which is essential for successful implant placement, orthognathic surgery, and maxillofacial reconstruction[51,52].

Conventional registration approaches employ either extrinsic methods, which rely on physical markers or fiducial devices placed on the patient during imaging, or intrinsic methods, which identify anatomical or mathematical landmarks for alignment. Although established, these traditional techniques are hindered by substantial drawbacks: metal artifacts obscure critical anatomical details, manual registration demands considerable time investment, and outcomes depend heavily on operator expertise, introducing variability and observer bias. These limitations have prompted a shift toward automated and AI-driven solutions[48,53].

Recent advances in AI have revolutionized image registration by automating previously labor-intensive processes. AI-based registration algorithms now achieve accuracy comparable to or exceeding that of manual landmark-based approaches, with landmark distance errors reduced to less than 0.5 mm and superior performance over existing software algorithms, reducing error distances by 30–70%[54]. The integration of AI-aided segmentation with registration has proven particularly effective; automated registration of CBCT-derived panoramic images with optically scanned dental models yields landmark and surface deviations as low as 0.5 mm, substantially better than manual methods, which typically exceed 1 mm[55]. These advances address longstanding limitations, including labor intensiveness and observer variability, while dramatically improving robustness against metal artifacts and image distortions.

The creation of reliable 3D virtual patient models from CBCT, IOS, and face scans represents a cornerstone of modern surgical planning. Studies have demonstrated that integrated CNN-based segmentation can simultaneously process multiple anatomical structures from CBCT, IOS, and face scans with exceptional precision, achieving Dice similarity coefficients of 99.3% and requiring minimal manual refinement[13,56]. Furthermore, automated fusion of CBCT-derived dental roots with intraoral scanner-derived crowns has proven both robust and clinically efficient, operating over 30 times faster than manual fusion approaches while maintaining accuracy well below 1 voxel in surface discrepancies[57].

AI-powered registration tools offer clear clinical advantages by delivering accurate, rapid, and reproducible multimodal image alignment, eliminating the need for specialized technical expertise [51,52]. These capabilities are essential for planning treatment procedures, designing patient-specific surgical guides and implant-supported restorations, where precision directly impacts functional and aesthetic outcomes. The convergence of advancing algorithms, validated computational tools, and demonstrated clinical utility suggest that automated registration will become standard practice in digital dentistry and maxillofacial surgery. As these technologies mature and gain wider acceptance, they promise to reduce manual workload, minimize operator-dependent variability, and ultimately enhance patient outcomes through precise, standardized surgical planning.

4. Presurgical dental implant planning

AI models have extended beyond anatomical mapping to predict optimal surgical protocols on the basis of bone characteristics. Machine learning algorithms can analyze CBCT images to predict jawbone mineral density and recommend appropriate drilling protocols, achieving accuracy rates of 93.8%, with area under the curve (AUC) values exceeding 0.98[58,59]. This capability enables clinicians to predict bone quality and adjust surgical approaches before making an incision, potentially enhancing primary implant stability and reducing intraoperative complications.

For edentulous site assessment, pooled meta-analytic data indicate 96% accuracy (95% CI: 94–98%) for mandibular implant planning and 83% accuracy (95% CI: 82–84%) for maxillary planning via AI-based detection systems[60]. These measurements encompass bone height and width determinations that directly inform implant size selection and positioning. Notably, AI measurements of bone height in premolar and molar regions show no statistically significant differences compared with manual expert measurements, validating their clinical reliability[24].

The integration of AI into digital implant workflows (Figure 3) enables truly prosthetically driven treatment planning by merging CBCT data with intraoral scans to visualize ideal implant positioning relative to the planned restoration.

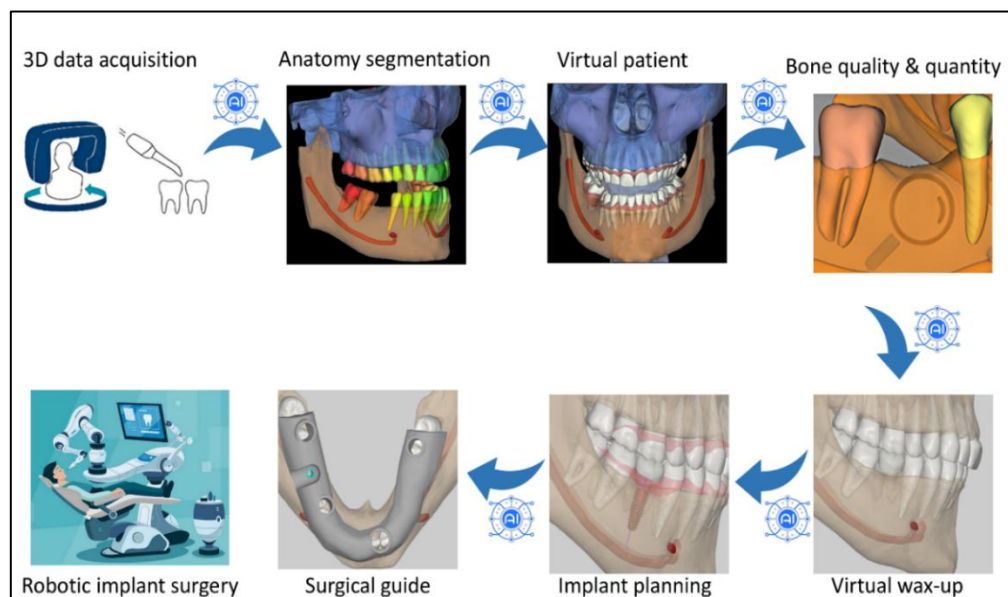


Figure 3. Traditional artificial intelligence-enhanced digital workflow for digital implant planning.

Compared with the HI-based method, AI achieves expert-quality, clinically acceptable single-implant planning (Figure 4) with greater time efficiency and consistency[11]. AI-powered automated virtual implant placement tools have been rigorously evaluated against human experts in preclinical studies[61–63]. These AI systems complete implant planning in approximately 198 seconds compared with 435 seconds for human planners, a 2.2-fold improvement in time efficiency. Remarkably, 95% of AI-generated plans require no significant modifications, nearly matching the 96% clinical acceptability rate of human-generated plans[61,64].



Figure 4. AI-driven digital implant planning for a single maxillary right canine. The AI-based platform first A) segments the anatomical structures followed by B) designing wax-up to follow the concept of prosthetically driven implant planning; then, C) the implant is planned on the basis of the available bone analysis and wax-up design; additionally, the platform designs a temporary crown for provisionalization starting from D) detecting the emergence line for the prosthesis, E) selecting the appropriate abutment, and F) designing the final crown; finally, after treatment approval by the clinician, the platform designs a surgical guide to transfer the digital planning to the real world.

Current evidence demonstrates that AI can achieve expert-level, clinically acceptable implant planning; however, the translation of these plans into surgical execution remains underexplored. Existing studies have focused primarily on static-guided demonstrations with limited quantification of placement accuracy and few evaluations of safety or prosthetic outcomes[61,65,66]. Moreover, most validation has been restricted to single posterior mandibular implants, leaving the generalization of AI planning to anterior, maxillary, immediate, and multi-implant scenarios untested.

Future research should bridge the gap between AI planning and clinical execution through well-designed prospective studies. Key priorities include determining whether AI-generated plans achieve noninferior accuracy and safety compared with clinician plans; assessing how reliably different execution modalities, static guides, navigation, and robotics can be used; transferring the same AI plan to the patient; and quantifying the impact of local registration errors on surgical deviation. Long-term registries should capture outcomes in complex and varied indications, whereas uncertainty-aware AI models that integrate real-world tolerances should be tested for their potential to increase safety without compromising prosthetic precision. Standardized definitions, metric reporting, and transparent error budgets are essential to ensure comparability across studies. Together, these initiatives will enable a rigorous, end-to-end validation of AI-driven implant workflows, linking digital planning accuracy to surgical safety and long-term restorative success.

5. Computer-assisted and robotic implant surgery

Computer-assisted implant surgery (CAIS) has become a major innovation in implant dentistry, improving the precision, predictability, and safety of implant placement by accurately transferring virtual plans into the patient's oral environment[9]. Guided systems are classified as static or dynamic. In static CAIS, prefabricated 3D-printed guides containing metal sleeves and depth stops direct drilling to the planned osteotomy site. Teeth, mucosa, or bone may support these guides and can be designed as single-piece or stackable systems to accommodate complex procedures such as osteotomy or sinus floor elevation [67].

In contrast, dynamic CAIS functions similarly to GPS navigation, using stereoscopic cameras to continuously track fiducial markers on the patient and handpiece, displaying the real-time drill trajectory on CBCT images[68]. Unlike static systems, dynamic navigation does not require a physical template and provides an unobstructed surgical field, enabling intraoperative adjustments and enhanced soft-tissue management. Modern navigation systems integrate both surgical and prosthetic considerations, aiming for site-specific accuracy and immediate provisionalization to improve functional and aesthetic outcomes [69].

The next evolution, robot-assisted computer-aided implant surgery (r-CAIS), incorporates AI, machine vision, sensor fusion, and 3D visualization to further reduce deviations between planned and executed implant positions [70,71]. Robotic systems operate across defined autonomy levels, from semiactive, operator-controlled arms (Level 1) to autonomous systems (Level 2, ADIR) capable of performing osteotomy and implant placement independently [72,73]. In autonomous mode, the robotic arm follows a predefined path within an infrared-guided visual field, executing drilling and implant insertion with visual-force feedback to maintain precision while minimizing operator variability[72].

Recent clinical studies have confirmed the superior accuracy of AI-driven robotic systems, reporting mean coronal deviations of approximately 0.5 mm, apical deviations of 0.5 mm, and angular deviations near 1°, significantly outperforming both static and dynamic guided approaches, which typically show platform deviations of approximately 1.0 mm and angular errors of 3–4° [74–77]. These results demonstrate the potential of autonomous robotics to standardize implant placement accuracy across jaw types and anatomical sites, representing a critical step toward fully digital, precision-guided implantology.

6. The role of AI in prosthetic design and occlusion

AI-powered CAD/CAM systems have transformed dental crown and implant restoration workflows by automating the design process through deep learning and advanced 3D modeling[78]. Platforms such as 3Shape Automate (3Shape A/S, Denmark), Fastdesign.io (Glidewell, USA), Dentbird (Imagoworks, Inc., Republic of Korea), Relu automate (Relu BV, Belgium), and Exocad AI Design (Exocad GmbH, Germany) use neural networks trained on extensive datasets of expert-designed crowns to identify margins, segment teeth, and generate restorations within minutes. These systems achieve high first-fit accuracy, minimize chairside adjustments, and significantly reduce turnaround times, enabling same-day or next-day delivery of precisely milled crowns[79].

Beyond efficiency, AI enhances customization and aesthetic optimization by analyzing patient-specific factors such as facial structure, gum lines, occlusion, and ethnic traits. Machine learning algorithms generate highly personalized prosthetic designs and simulate bite dynamics to ensure natural integration with the patient's existing

dentition[80]. For implant-supported restorations, AI assists in designing custom abutments and crowns that align precisely with implants and surrounding tissues[81].

AI applications include removable and complex prosthetics, biomechanical analysis, and automated manufacturing. In removable and full-arch restorations, AI-driven generative design ensures optimal strength, comfort, and aesthetics while allowing virtual treatment visualization. Biomechanical simulations predict stress distribution and implant stability, reducing complications and improving long-term success. Integrated manufacturing systems employ robotic milling and surface measurement for automated quality assurance, achieving micrometer-level precision. Although clinical studies have shown that AI enhances efficiency and accuracy, slight differences remain compared with expert human designs, indicating ongoing refinement toward full clinical parity[78,82].

7. Predictive Modeling for Implant Success and Complications

Machine learning models have been developed to predict implant survival, osseointegration success, and complication risk by integrating patient-specific factors, including demographics, medical history, bone quality, implant characteristics, and surgical variables[83]. For peri-implant disease detection. Machine learning approaches, including random forest, support vector machine, and neural network models, can predict peri-implantitis onset with accuracies ranging from 0.70--1.00, depending on the algorithm and outcome definition. However, systematic reviews note that most prediction models have limited external validation and methodological quality concerns, indicating the need for more rigorous development and testing[22].

8. Clinical Implementation and Workflow Efficiency

The real-world clinical deployment of AI systems in implant dentistry has demonstrated measurable benefits in workflow efficiency and diagnostic consistency. AI-powered CBCT interpretation reduces the average assessment time by 1.19 minutes (6.78%) per scan through automated dental charting and pathology detection. These time savings, while seemingly modest per case, accumulate significantly across high-volume practices. Moreover, AI systems facilitate standardized documentation and reduce interobserver variability, addressing a persistent challenge in radiological interpretation[84]. Studies examining clinician acceptance have revealed that dental professionals prefer AI to function as an augmentative tool complementing human expertise rather than as an autonomous decision-maker. The key facilitators of AI adoption include high diagnostic accuracy, real-time processing speed, and compatibility with existing digital workflows[85,86].

9. Current Limitations and Challenges

Despite promising accuracy metrics, several limitations constrain widespread AI adoption in implant planning. Data heterogeneity across CBCT devices, imaging protocols, and patient populations limits model generalizability. Many AI models are trained on datasets from single institutions or specific equipment, resulting in reduced performance when applied to external data sources. The scarcity of large, diverse, annotated datasets remains a fundamental bottleneck, particularly for less common anatomical variations and pathologies[87,88].

Technical limitations include challenges with cross-sectional bone measurements[89], interference from metal artifacts[28], and the detection of subtle anatomical variations[39]. The "black box" nature of deep learning models raises concerns about interpretability and clinical trust, particularly when diagnostic errors could have serious consequences. Additionally, there is a 17% miss rate and 2.8% false positive rate in certain applications, such as stent marker localization, indicating room for improvement[90,91].

Ethical considerations include data privacy, algorithmic bias, accountability for AI-generated errors, and potential exacerbation of healthcare disparities if training datasets lack demographic diversity. Regulatory frameworks often lag behind technological innovation, creating uncertainty around approval processes and liability. Furthermore, most published studies demonstrate high or unclear risk of bias due to methodological limitations, and only a minority have undergone external validation[92–95]. AI integration into clinical workflows faces significant logistical challenges. High costs, infrastructure requirements, and training needs remain prohibitive for smaller practices[96].

10. Future Directions and Emerging Technologies

The future of AI in implant planning will likely involve substantial progress in implant materials and digital technologies alongside persistent barriers to clinical translation. Smart implants with piezoelectric biosensors enable real-time monitoring when coupled with artificial intelligence, although standardization remains lacking[97]. FEMs in personalized dentistry have the potential to significantly improve treatment precision and efficacy, optimize outcomes and reduce complications. Their integration underscores the need for interdisciplinary collaboration and advancements in computational techniques to enhance personalized dental care[98].

Explainable AI (XAI) frameworks that provide transparent reasoning for algorithmic decisions are critical for building clinician trust and facilitating clinical adoption. Augmented reality applications for surgical visualization and hybrid AI models that combine multiple architectural approaches represent additional frontiers. The convergence of AI with 3D printing, photogrammetry, and light-field imaging may further refine accuracy and expand capabilities[99].

11. Conclusion

AI has demonstrated remarkable capabilities across the implant planning workflow, from anatomical segmentation and bone quality assessment to surgical guidance and outcome prediction. Current evidence supports AI's role as a clinical decision support system that enhances diagnostic accuracy, improves workflow efficiency, and augments, rather than replacing clinician expertise. While challenges related to data quality, model generalizability, algorithmic transparency, and ethical implementation persist, ongoing technological advances and interdisciplinary collaboration are progressively addressing these barriers. As AI systems mature and become integrated into routine clinical practice, they hold substantial promise for advancing precision, personalization, and predictability in dental implantology, ultimately improving patient outcomes and expanding access to high-quality implant care.

12. Declarations

Acknowledgments

Not applicable.

Ethical consideration

This study adhered to the principles of the Declaration of Helsinki.

Consent to participate

Not applicable

Conflicts of interest

Not applicable.

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The authors did not receive support from any organization for the submitted work.

Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Author(s) Contribution

Eslam Abdelwahab Dawood: Conceptualization, Methodology, Resources, Data Curation, Visualization, Investigation, Writing – original draft, **Bahaaeldeen M. Elgarba:** Formal analysis, Visualization, Investigation, review & editing, **Rochardes Cavalcante Fontenele:** Visualization, Investigation, review & editing, **Reinhilde Jacobs:** Conceptualization, Methodology, Supervision, Writing – review & editing

References

- [1] Elgarba BM, Fontenele RC, Tarce M, et al. Artificial intelligence serving presurgical digital implant planning: A scoping review. *J Dent* 2024;143:104862. <https://doi.org/10.1016/J.JDENT.2024.104862>.
- [2] Flügge T, Kramer J, Nelson K, et al. Digital implantology—a review of virtual planning software for guided implant surgery. Part II: Prosthetic setup and virtual implant planning. *BMC Oral Health* 2022 22:1 2022;22:1–11. <https://doi.org/10.1186/S12903-022-02057-W>.
- [3] Joda T, Zarone F, Ferrari M. The complete digital workflow in fixed prosthodontics: a systematic review. *BMC Oral Health* 2017 17:1 2017;17:1–9. <https://doi.org/10.1186/S12903-017-0415-0>.
- [4] (PDF) Stresses transmitted by two different implant angulations in All-on-Four supporting fixed detachable prosthesis. (In vitro study) n.d. https://www.researchgate.net/publication/353413381_Stresses_transmitted_by_two_different_implant_angulations_in_All-on-Four_supporting_fixed_detachable_prosthesis_In_vitro_study (accessed November 12, 2025).
- [5] Shujaat S, Bornstein MM, Price JB, et al. Integration of imaging modalities in digital dental workflows - possibilities, limitations, and potential future developments. *Dentomaxillofacial Radiology* 2021;50. <https://doi.org/10.1259/DMFR.20210268>.

- [6] Jacobs R, Salmon B, Codari M, et al. Cone beam computed tomography in implant dentistry: recommendations for clinical use. *BMC Oral Health* 2018 18:1 2018;18:1–16. <https://doi.org/10.1186/S12903-018-0523-5>.
- [7] Elfahl BN, Mostafa TMN, Ghalwash D, et al. A novel full digital positioning guide for autogenous bone grafting in the esthetic zone. *J Dent* 2025;163. <https://doi.org/10.1016/j.jdent.2025.106102>.
- [8] Elfahl BN, Mostafa TMN. Polyetheretherketone custom CAD-CAM splint for treatment of periodontally affected mobile anterior teeth. *Journal of Prosthetic Dentistry* 2022;127:210–2. <https://doi.org/10.1016/j.prosdent.2020.08.031>.
- [9] Andrade-Bortoletto MFS, Du X, Dawood EA, et al. What is the role of AI-driven automation in static surgical guide design? A scoping review. *J Dent* 2025;163:106193. <https://doi.org/10.1016/J.JDENT.2025.106193>.
- [10] Revilla-León M, Gómez-Polo M, Vyas S, et al. Artificial intelligence applications in implant dentistry: A systematic review. *Journal of Prosthetic Dentistry* 2023;129:293–300. <https://doi.org/10.1016/j.prosdent.2021.05.008>.
- [11] Elgarba BM, Fontenele RC, Mangano F, et al. Novel AI-based automated virtual implant placement: Artificial versus human intelligence. *J Dent* 2024;147:105146. <https://doi.org/10.1016/J.JDENT.2024.105146>.
- [12] Preda F, Nogueira-Reis F, Stanciu EM, et al. Validation of automated registration of intraoral scan onto Cone Beam Computed Tomography for an efficient digital dental workflow. *J Dent* 2024;149:105282. <https://doi.org/10.1016/J.JDENT.2024.105282>.
- [13] Nogueira-Reis F, Morgan N, Suryani IR, et al. Full virtual patient generated by artificial intelligence-driven integrated segmentation of craniomaxillofacial structures from CBCT images. *J Dent* 2024;141:104829. <https://doi.org/10.1016/J.JDENT.2023.104829>.
- [14] Fontenele RC, Jacobs R. Unveiling the power of artificial intelligence for image-based diagnosis and treatment in endodontics: An ally or adversary? *Int Endod J* 2025;58:155–70. <https://doi.org/10.1111/IEJ.14163>;SUBPAGE:STRING:FULL.
- [15] Gracea RS, Winderickx N, Vanheers M, et al. Artificial intelligence for orthodontic diagnosis and treatment planning: A scoping review. *J Dent* 2025;152:105442. <https://doi.org/10.1016/J.JDENT.2024.105442>.
- [16] Hendrickx J, Gracea RS, Vanheers M, et al. Can artificial intelligence-driven cephalometric analysis replace manual tracing? A systematic review and meta-analysis. *Eur J Orthod* 2024;46. <https://doi.org/10.1093/EJO/CJAE029>.
- [17] Grigoriadis A, Saadi SB, Munirji L, et al. Development and validation of an AI-driven tool to evaluate chewing function: a proof of concept. *J Dent* 2025;153:105525. <https://doi.org/10.1016/J.JDENT.2024.105525>.
- [18] Vranckx M, Van Gerven A, Willems H, et al. Artificial Intelligence (AI)-Driven Molar Angulation Measurements to Predict Third Molar Eruption on Panoramic Radiographs. *Int J Environ Res Public Health* 2020;17. <https://doi.org/10.3390/IJERPH17103716>.

- [19] Leite AF, Gerven A Van, Willems H, et al. Artificial intelligence-driven novel tool for tooth detection and segmentation on panoramic radiographs. *Clin Oral Investig* 2021;25:2257–67. <https://doi.org/10.1007/S00784-020-03544-6>.
- [20] Ver Berne J, Saadi SB, Oliveira-Santos N, et al. Automated classification of panoramic radiographs with inflammatory periapical lesions using a CNN-LSTM architecture. *J Dent* 2025;156:105688. <https://doi.org/10.1016/J.JDENT.2025.105688>.
- [21] Ibraheem WI. Accuracy of Artificial Intelligence Models in Dental Implant Fixture Identification and Classification from Radiographs: A Systematic Review. *Diagnostics* 2024;14:806. <https://doi.org/10.3390/DIAGNOSTICS14080806/S1>.
- [22] Mugri MH. Accuracy of Artificial Intelligence Models in Detecting Peri-Implant Bone Loss: A Systematic Review. *Diagnostics (Basel)* 2025;15. <https://doi.org/10.3390/DIAGNOSTICS15060655>.
- [23] Alqutaibi AY, Algabri RS, Alamri AS, et al. Advancements of artificial intelligence algorithms in predicting dental implant prognosis from radiographic images: A systematic review. *Journal of Prosthetic Dentistry* 2024. <https://doi.org/10.1016/j.prosdent.2024.10.036>.
- [24] Qiu S, Yu X, Wu Y. Application of artificial intelligence in bone quality and quantity assessment for dental implant planning: A scoping review. *J Dent* 2025;162:106027. <https://doi.org/10.1016/J.JDENT.2025.106027>.
- [25] Leite AF, Vasconcelos K de F, Willems H, et al. Radiomics and Machine Learning in Oral Healthcare. *Proteomics Clin Appl* 2020;14. <https://doi.org/10.1002/PRCA.201900040>.
- [26] Singh GD, Singh M. Virtual Surgical Planning: Modeling from the Present to the Future. *J Clin Med* 2021;10. <https://doi.org/10.3390/JCM10235655>.
- [27] Hung K, Yeung AWK, Tanaka R, et al. Current Applications, Opportunities, and Limitations of AI for 3D Imaging in Dental Research and Practice. *International Journal of Environmental Research and Public Health* 2020, Vol 17, Page 4424 2020;17:4424. <https://doi.org/10.3390/IJERPH17124424>.
- [28] Shujaat S, Riaz M, Jacobs R. Synergy between artificial intelligence and precision medicine for computer-assisted oral and maxillofacial surgical planning. *Clin Oral Investig* 2023;27:897–906. <https://doi.org/10.1007/S00784-022-04706-4>.
- [29] Verhelst PJ, Smolders A, Beznik T, et al. Layered deep learning for automatic mandibular segmentation in cone-beam computed tomography. *J Dent* 2021;114. <https://doi.org/10.1016/j.jdent.2021.103786>.
- [30] Shaheen E, Leite A, Alqahtani KA, et al. A novel deep learning system for multiclass tooth segmentation and classification on cone beam computed tomography. A validation study: Deep learning for teeth segmentation and classification. *J Dent* 2021;115. <https://doi.org/10.1016/j.jdent.2021.103865>.
- [31] Gerhardt M do N, Fontenele RC, Leite AF, et al. Automated detection and labeling of teeth and small edentulous regions on cone-beam computed tomography using convolutional neural networks. *J Dent* 2022;122. <https://doi.org/10.1016/j.jdent.2022.104139>.
- [32] Morgan N, Van Gerven A, Smolders A, et al. Convolutional neural network for automatic maxillary sinus segmentation on cone-beam computed tomographic images. *Scientific Reports* 2022 12:1 2022;12:1–9. <https://doi.org/10.1038/s41598-022-11483-3>.

-
- [33] Preda F, Morgan N, Van Gerven A, et al. Deep convolutional neural network-based automated segmentation of the maxillofacial complex from cone-beam computed tomography: A validation study. *J Dent* 2022;124. <https://doi.org/10.1016/j.jdent.2022.104238>.
 - [34] Ayidh Alqahtani K, Jacobs R, Smolders A, et al. Deep convolutional neural network-based automated segmentation and classification of teeth with orthodontic brackets on cone-beam computed-tomographic images: a validation study. *Eur J Orthod* 2023;45:169–74. <https://doi.org/10.1093/EJO/CJAC047>.
 - [35] Fontenele RC, Gerhardt M do N, Picoli FF, et al. Convolutional neural network-based automated maxillary alveolar bone segmentation on cone-beam computed tomography images. *Clin Oral Implants Res* 2023;34:565–74. <https://doi.org/10.1111/CLR.14063>;WGROU:STRING:PUBLICATION.
 - [36] Morgan N, Shujaat S, Jazil O, et al. Three-dimensional quantification of skeletal midfacial complex symmetry. *International Journal of Computer Assisted Radiology and Surgery* 2022 18:4 2022;18:611–9. <https://doi.org/10.1007/S11548-022-02775-0>.
 - [37] Oliveira-Santos N, Jacobs R, Picoli FF, et al. Automated segmentation of the mandibular canal and its anterior loop by deep learning. *Scientific Reports* 2023 13:1 2023;13:1–9. <https://doi.org/10.1038/s41598-023-37798-3>.
 - [38] Elgarba BM, Van Aelst S, Swaity A, et al. Deep learning-based segmentation of dental implants on cone-beam computed tomography images: A validation study. *J Dent* 2023;137:104639. <https://doi.org/10.1016/J.JDENT.2023.104639>.
 - [39] Jindanil T, Marinho-Vieira LE, de-Azevedo-Vaz SL, et al. A unique artificial intelligence-based tool for automated CBCT segmentation of mandibular incisive canal. *Dentomaxillofacial Radiology* 2023;52:20230321. <https://doi.org/10.1259/DMFR.20230321/7491455>.
 - [40] Swaity A, Elgarba BM, Morgan N, et al. Deep learning driven segmentation of maxillary impacted canine on cone beam computed tomography images. *Scientific Reports* 2024 14:1 2024;14:1–8. <https://doi.org/10.1038/s41598-023-49613-0>.
 - [41] Wang X, Alqahtani KA, Van den Bogaert T, et al. Convolutional neural network for automated tooth segmentation on intraoral scans. *BMC Oral Health* 2024 24:1 2024;24:1–9. <https://doi.org/10.1186/S12903-024-04582-2>.
 - [42] Elsonbaty S, Elgarba BM, Fontenele RC, et al. Novel AI-based tool for primary tooth segmentation on CBCT using convolutional neural networks: A validation study. *Int J Paediatr Dent* 2025;35:97–107. <https://doi.org/10.1111/IPD.13204>.
 - [43] Slim ML, Jacobs R, de Souza Leal RM, et al. AI-driven segmentation of the pulp cavity system in mandibular molars on CBCT images using convolutional neural networks. *Clinical Oral Investigations* 2024 28:12 2024;28:1–11. <https://doi.org/10.1007/S00784-024-06009-2>.
 - [44] Fontenele RC, Gerhardt M do N, Pinto JC, et al. Influence of dental fillings and tooth type on the performance of a novel artificial intelligence-driven tool for automatic tooth segmentation on CBCT images – A validation study. *J Dent* 2022;119. <https://doi.org/10.1016/j.jdent.2022.104069>.
 - [45] Lahoud P, Diels S, Niclaes L, et al. Development and validation of a novel artificial intelligence driven tool for accurate mandibular canal segmentation on CBCT. *J Dent* 2022;116. <https://doi.org/10.1016/j.jdent.2021.103891>.

-
- [46] Shujaat S, Jazil O, Willems H, et al. Automatic segmentation of the pharyngeal airway space with convolutional neural network. *J Dent* 2021;111. <https://doi.org/10.1016/j.jdent.2021.103705>.
 - [47] Lahoud P, EzEldeen M, Beznik T, et al. Artificial Intelligence for Fast and Accurate 3-Dimensional Tooth Segmentation on Cone-beam Computed Tomography. *J Endod* 2021;47:827–35. <https://doi.org/10.1016/J.JOEN.2020.12.020>.
 - [48] Elgarba BM, Ali S, Fontenele RC, et al. An AI-based tool for prosthetic crown segmentation serving automated intraoral scan-to-CBCT registration in challenging high artifact scenarios. *Journal of Prosthetic Dentistry* 2025;134:191–8. <https://doi.org/10.1016/j.prosdent.2025.02.004>.
 - [49] Iacob AM, Verdecchia A, García-Mesa Y, et al. Effectiveness of automated segmentation of maxillofacial structures in cone-beam computed tomography images using artificial intelligence: A systematic review. *Int Orthod* 2025;24:101081. <https://doi.org/10.1016/J.ORTHO.2025.101081>.
 - [50] El-Gamal FEZA, Elmogy M, Atwan A. Current trends in medical image registration and fusion. *Egyptian Informatics Journal* 2016;17:99–124. <https://doi.org/10.1016/J.EIJ.2015.09.002>.
 - [51] Elgarba BM, Fontenele RC, Ali S, et al. Validation of a novel AI-based automated multimodal image registration of CBCT and intraoral scan aiding presurgical implant planning. *Clin Oral Implants Res* 2024;35:1506–17. <https://doi.org/10.1111/CLR.14338>;ISSUE:ISSUE:DOI.
 - [52] Jindanil T, Gracea RS, Claessens N, et al. Three-dimensional facial scanning: quantitative and qualitative assessment of five different modalities with CBCT as a reference. *J Dent* 2025;163:106179. <https://doi.org/10.1016/J.JDENT.2025.106179>.
 - [53] Qin C, Mai Y, Chen X. Registration in oral and maxillofacial surgery. *Computer-Aided Oral and Maxillofacial Surgery: Developments, Applications, and Future Perspectives* 2021:29–54. <https://doi.org/10.1016/B978-0-12-823299-6.00002-X>.
 - [54] Jang TJ, Yun HS, Hyun CM, et al. Fully automatic integration of dental CBCT images and full-arch intraoral impressions with stitching error correction via individual tooth segmentation and identification. *Med Image Anal* 2024;93:103096. <https://doi.org/10.1016/J.MEDIA.2024.103096>.
 - [55] Marinho-Vieira LE, Fontenele RC, Elgarba BM, et al. Artificial Intelligence-Based CBCT Segmentation in the Presence of Metallic Artifacts for 3D Virtual Orofacial Patient Generation. *J Dent* 2025:106223. <https://doi.org/10.1016/J.JDENT.2025.106223>.
 - [56] Jindanil T, Burlacu-Vatamanu OE, Meyns J, et al. Automated orofacial virtual patient creation: A proof of concept. *J Dent* 2024;150:105387. <https://doi.org/10.1016/J.JDENT.2024.105387>.
 - [57] Baldini B, Papasratorn D, Fagundes FB, et al. Validation of a novel tool for automated tooth modeling by fusion of CBCT-derived roots with the respective IOS-derived crowns. *J Dent* 2025;153. <https://doi.org/10.1016/j.jdent.2024.105546>.
 - [58] Xiao Y, Liang Q, Zhou L, et al. Construction of a new automatic grading system for jaw bone mineral density level based on deep learning using cone beam computed tomography. *Sci Rep* 2022;12. <https://doi.org/10.1038/S41598-022-16074-W>.
 - [59] Sakai T, Li H, Shimada T, et al. Development of artificial intelligence model for supporting implant drilling protocol decision making. *J Prosthodont Res* 2023;67:360–5. https://doi.org/10.2186/JPR.JPR_D_22_00053.

-
- [60] Alqutaibi AY, Algabri R, Ibrahim WI, et al. Dental implant planning using artificial intelligence: A systematic review and meta-analysis. *Journal of Prosthetic Dentistry* 2024. <https://doi.org/10.1016/j.prosdent.2024.03.032>.
 - [61] Elgarba BM, Fontenele RC, Du X, et al. Artificial Intelligence Versus Human Intelligence in Presurgical Implant Planning: A Preclinical Validation. *Clin Oral Implants Res* 2025;36:835–45. <https://doi.org/10.1111/CLR.14429>;JOURNAL:JOURNAL:16000501;WGROU:STRING:PUBLICATION.
 - [62] Schiavon L, Benkeser SM, Settecase E, et al. Can AI assistants improve time efficiency in digital dataset preparation in virtual implant planning? A comparative study. *J Dent* 2025;163:106152. <https://doi.org/10.1016/J.JDENT.2025.106152>.
 - [63] Cai G, Wen B, Gong Z, et al. Intelligent Virtual Dental Implant Placement via 3D Segmentation Strategy. *J Dent Res* 2025. <https://doi.org/10.1177/00220345251332511>;SUBPAGE:STRING:FULL.
 - [64] Ntovas P, Marchand L, Schnappauf A, et al. Comparison Between Conventional and Artificial Intelligence-Assisted Setup for Digital Implant Planning: Accuracy, Time-Efficiency, and User Experience. *Clin Oral Implants Res* 2025;36:290–7. <https://doi.org/10.1111/CLR.14382>;WGROU:STRING:PUBLICATION.
 - [65] Satapathy SK, Kunam A, Rashme R, et al. AI-Assisted Treatment Planning for Dental Implant Placement: Clinical vs AI-Generated Plans. *J Pharm Bioallied Sci* 2024;16:S942–4. https://doi.org/10.4103/JPBS.JPBS_1121_23.
 - [66] Zhou L, Zhao W, Chu M, et al. Accuracy of Two Robotic Computer-Aided Implant System Registration Methods for Dental Implantation: A Prospective Study. *Clin Implant Dent Relat Res* 2025;27:e70037. <https://doi.org/10.1111/CID.70037>;WGROU:STRING:PUBLICATION.
 - [67] Carosi P, Lorenzi C, Lio F, et al. Accuracy of Computer-Assisted Flapless Implant Placement by Means of Mucosa-Supported Templates in Complete-Arch Restorations: A Systematic Review. *Materials (Basel)* 2022;15. <https://doi.org/10.3390/MA15041462>.
 - [68] Pozzi A, Hansson L, Carosi P, et al. Dynamic navigation guided surgery and prosthetics for immediate loading of complete-arch restoration. *J Esthet Restor Dent* 2021;33:224–36. <https://doi.org/10.1111/JERD.12710>.
 - [69] Wang X, Shujaat S, Meeus J, et al. Performance of novice versus experienced surgeons for dental implant placement with freehand, static guided and dynamic navigation approaches. *Sci Rep* 2023;13. <https://doi.org/10.1038/S41598-023-29633-6>.
 - [70] Li P, Chen J, Li A, et al. Accuracy of autonomous robotic surgery for dental implant placement in fully edentulous patients: A retrospective case series study. *Clin Oral Implants Res* 2023;34:1428–37. <https://doi.org/10.1111/CLR.14188>.
 - [71] Zhang S, Cai Q, Chen W, et al. Accuracy of implant placement via dynamic navigation and autonomous robotic computer-assisted implant surgery methods: A retrospective study. *Clin Oral Implants Res* 2024;35:220–9. <https://doi.org/10.1111/CLR.14216>.
 - [72] Wang W, Xu H, Mei D, et al. Accuracy of the Yakebot dental implant robotic system versus fully guided static computer-assisted implant surgery template in edentulous jaw implantation: A preliminary clinical study. *Clin Implant Dent Relat Res* 2024;26:309–16. <https://doi.org/10.1111/CID.13278>.
-

-
- [73] Yang GZ, Cambias J, Cleary K, et al. Medical robotics-Regulatory, ethical, and legal considerations for increasing levels of autonomy. *Sci Robot* 2017;2. <https://doi.org/10.1126/SCIROBOTICS.AAM8638>.
 - [74] Wang X, Shaheen E, Shujaat S, et al. Influence of experience on dental implant placement: an in vitro comparison of freehand, static guided and dynamic navigation approaches. *Int J Implant Dent* 2022;8. <https://doi.org/10.1186/S40729-022-00441-3>.
 - [75] Chen J, Zhuang M, Tao B, et al. Accuracy of immediate dental implant placement with task-autonomous robotic system and navigation system: An in vitro study. *Clin Oral Implants Res* 2024;35:973–83. <https://doi.org/10.1111/CLR.14104>.
 - [76] Wu XY, Shi JY, Qiao SC, et al. Accuracy of robotic surgery for dental implant placement: A systematic review and meta-analysis. *Clin Oral Implants Res* 2024;35:598–608. <https://doi.org/10.1111/CLR.14255>.
 - [77] Yimarj P, Subbalekha K, Dhanesuan K, et al. Comparison of the accuracy of implant position for two-implants supported fixed dental prosthesis using static and dynamic computer-assisted implant surgery: A randomized controlled clinical trial. *Clin Implant Dent Relat Res* 2020;22:672–8. <https://doi.org/10.1111/CID.12949>.
 - [78] Karnik AP, Chhajer H, Venkatesh SB. Transforming Prosthodontics and oral implantology using robotics and artificial intelligence. *Frontiers in Oral Health* 2024;5:1442100. <https://doi.org/10.3389/FROH.2024.1442100/BIBTEX>.
 - [79] Kong HJ, Kim YL. Application of artificial intelligence in dental crown prosthesis: a scoping review. *BMC Oral Health* 2024;24:937. <https://doi.org/10.1186/S12903-024-04657-0>.
 - [80] Lemos LM, Ribeiro AKC, Vasconcelos BC do E, et al. Accuracy and time efficiency of deep learning-based method for single-crown design compared with a conventional CAD software program: A systematic review. *J Prosthet Dent* 2025. <https://doi.org/10.1016/J.PROSDENT.2025.10.046>.
 - [81] Zheng M, Yang X, Li X, et al. Text condition embedded regression network for automated dental implant abutment design. *Expert Syst Appl* 2026;299:130160. <https://doi.org/10.1016/J.ESWA.2025.130160>.
 - [82] MVG B, Aneja S, Rani KD, et al. Role of artificial intelligence in transforming prosthodontics and oral implantology: in vivo study. *Bioinformation* 2025;21:1275. <https://doi.org/10.6026/973206300211275>.
 - [83] Nazari Y, Lngeroodi PF, Maddahi M, et al. Artificial intelligence models and predicting implant success. *Biomedical Research and Therapy* 2025;12:7029–38. <https://doi.org/10.15419/BMRAT.V12I1.949>.
 - [84] Ezhov M, Gusarev M, Golitsyna M, et al. Clinically applicable artificial intelligence system for dental diagnosis with CBCT. *Scientific Reports* 2021 11:1 2021;11:1–16. <https://doi.org/10.1038/s41598-021-94093-9>.
 - [85] Cozmescu AF, Cernega A, Mincă DG, et al. Embracing Artificial Intelligence in Dental Practice: An Exploratory Study of Romanian Clinicians' Perspectives and Experiences. *Dent J (Basel)* 2025;13:390. <https://doi.org/10.3390/DJ13090390/S1>.
 - [86] Altalhi AM, Alharbi FS, Alhodaithy MA, et al. The Impact of Artificial Intelligence on Dental Implantology: A Narrative Review. *Cureus* 2023;15:e47941. <https://doi.org/10.7759/CUREUS.47941>.
 - [87] Lal A, Nooruddin A, Umer F. Concerns regarding deployment of AI-based applications in dentistry – a review. *BDJ Open* 2025 11:1 2025;11:1–6. <https://doi.org/10.1038/s41405-025-00319-7>.

-
- [88] Panahi O. Artificial Intelligence in Oral Implantology, Its Applications, Impact and Challenges. *Advances in Dentistry & Oral Health* 2024;17:1–4.
 - [89] Bayrakdar SK, Orhan K, Bayrakdar IS, et al. A deep learning approach for dental implant planning in cone-beam computed tomography images. *BMC Med Imaging* 2021;21. <https://doi.org/10.1186/S12880-021-00618-Z>.
 - [90] Zaww K, Abbas H, Vanegas Sáenz JR, et al. AI-driven innovations for dental implant treatment planning: A systematic review. *J Prosthodont Res* 2025. https://doi.org/10.2186/JPR.JPR_D_24_00338.
 - [91] Teng Q, Liu Z, Song Y, et al. A survey on the interpretability of deep learning in medical diagnosis. *Multimed Syst* 2022;28:2335. <https://doi.org/10.1007/S00530-022-00960-4>.
 - [92] Zhu Y, Du M, Li P, et al. Prediction models for the complication incidence and survival rate of dental implants—a systematic review and critical appraisal. *Int J Implant Dent* 2025;11:5. <https://doi.org/10.1186/S40729-025-00590-1>.
 - [93] Hanna MG, Pantanowitz L, Jackson B, et al. Ethical and Bias Considerations in Artificial Intelligence/Machine Learning. *Modern Pathology* 2025;38:100686. <https://doi.org/10.1016/J.MODPAT.2024.100686>.
 - [94] Zhang S, Li Y, Liu W, et al. A decade of review in global regulation and research of artificial intelligence medical devices (2015–2025). *Front Med (Lausanne)* 2025;12:1630408. <https://doi.org/10.3389/FMED.2025.1630408>.
 - [95] Morone G, De Angelis L, Martino Cinnera A, et al. Artificial intelligence in clinical medicine: a state-of-the-art overview of systematic reviews with methodological recommendations for improved reporting. *Front Digit Health* 2025;7:1550731. <https://doi.org/10.3389/FDGTH.2025.1550731/BIBTEX>.
 - [96] Ahmed MI, Spooner B, Isherwood J, et al. A Systematic Review of the Barriers to the Implementation of Artificial Intelligence in Healthcare. *Cureus* 2023;15:e46454. <https://doi.org/10.7759/CUREUS.46454>.
 - [97] James JR, Kharat A, Chinnakutti S, et al. The Future of Dental Implants: A Narrative Review of Trends, Technologies, and Patient Considerations. *Cureus* 2025;17:e90380. <https://doi.org/10.7759/CUREUS.90380>.
 - [98] Lahoud P, Faghihian H, Richert R, et al. Finite element models: A road to in-silico modeling in the age of personalized dentistry. *J Dent* 2024;150:105348. <https://doi.org/10.1016/J.JDENT.2024.105348>.
 - [99] Brankovic A, Cook D, Rahman J, et al. Benchmarking the most popular XAI used for explaining clinical predictive models: Untrustworthy but could be useful. *Health Informatics J* 2024;30. <https://doi.org/10.1177/14604582241304730;CTYPE:STRING:JOURNAL>.



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Measurement of Radioactivity in Some Liquid Foodstuffs Samples Collected from Palestinian Markets

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Abstract

Background: Natural radionuclides such as radon (^{222}Rn) and radium (^{226}Ra) may enter liquid foodstuffs through environmental transfer from soil and water, creating potential radiological exposure through ingestion. **Objective:** This work aims to measure the concentration of radon and radium contents and other radiological effects in 57 samples of liquid foodstuffs collected from Palestinian markets. **Methods:** passive technique were applied that contain Solid State Nuclear Track Detectors SSNTDs (CR 39). **Results:** The results showed that average radon concentration levels in fruit juice, soft drink, milk and other liquid foodstuff samples were: 152.0, 162.0, 142.6 and 135.3 Bq/m³, respectively, and the average concentration of radium contents were: 2.12, 2.28, 2.00 and 1.90 Bq/kg for fruit juice, soft drink, milk and other liquid foodstuff samples, respectively. The obtained values provided the levels of radon and radium concentration in most samples which were less than the safe limits as recommended by ICRP (200- 600 Bq/m³). Therefore, there is no risk of taking these drinks and no health hazards related to radiation. **Conclusion:** It is worth noting that the measurements obtained in this study establish a foundational database of activity levels and provide a valuable reference for future research evaluating the potential impacts of forthcoming events.

Keywords: Liquid foodstuff, radon, CR-39 detector, Palestinian markets, Palestine.

1. Introduction

Radon (^{222}Rn) is a chemical radioactive noble gas, and it is the product of decay series of uranium and radium as a transitional stage in the typical radioactive decays over thorium and uranium, which slowly decay into a variety of transient radioactive nuclides and lead with half-life of only 3.82 days. This gas, which cannot be observed or seen or felt through the senses (taste, smell or sight), can only be detected using of special equipment and protocols because it is a radioactive gas that is colorless, invisible, odorless, and tasteless [1].

Airborne Radon attached to dust particles rests onto the ground, or falls to the ground by rain. As a result, both soil and vegetation might be contaminated due to the decomposition of radon in the soil through rain or dust deposition and the deposited radon becomes strongly attached to the foliar of the plant, or the radon transferred throughout the plant by the absorption of foliar for radon [2].

The concentration of radon varies from plant to another due to its different chemical composition and vegetation. For example, silage cattle or fresh food transfers activity of radon to animals by eating. In addition, the radon concentration radioactivity depends on the area in which the animals are grazed. For example, dairy products, such as powdered milk, contain certain concentrations of radon, as a result of the production of lactating animals that eat contaminated grass [3]. In general, the environmental cover complements each other. Contaminated soil will pollute plants, and this pollution is transmitted to both animals and humans through eating meat, plants and juice. The food chain can pass radiation pollution that is present in the soil and water on to people and other animals. Humans can become contaminated with various radioactive isotopes (^{226}Ra , ^{222}Rn , ^{238}U) when they consume plants, animal meat, or liquid foodstuffs. Plants have radioactive isotopes in them that come from the soil, where they are absorbed together with other natural materials [4].

When radon enters the body, it can be held for a long time in the lungs, skin, and stomach before entering the circulation and accumulating in the fatty tissues. Radon and its progeny create their respective decay progeny during this period because of their short half-lives, and they are subsequently predominantly deposited in these organs. Some of the radon and progeny can provide significant doses to these organs prior to diffusion by depositing alpha decay energy [5]. Bronchial epithelial tissue receives the largest alpha doses from the breathed radon decay progeny, followed by the upper respiratory tract and skin, whereas other organs such as red bone marrow, liver, and kidney receive considerably low doses. Outside of the respiratory tract, radon and its decay products deliver the highest dose to the kidney [6].

The stomach, on the other hand, receives the largest alpha radiation dosage from radon dissolved in drinking water, followed by the oesophagus and other digestive system organs. Because radon is tiny and selectively soluble in tissues with a greater fat content, the fatty tissues in the yellow bone marrow and female breast may get comparatively large doses from radon and its offspring rather than other organs. Because alpha particles have a high LET, they can cause severe local ionization in irradiated tissues by depositing a considerable amount of energy and thereby causing damage to the targeted tissues. As a result, it is obvious that long-term exposure to radon can cause a variety of malignant or non-malignant health effects in various sections of the human body such as lung cancer. It causes health effects largely by causing local damage as a result of alpha-particle contact with the tissue atoms or molecules [7,8]

Radium is a radioactive element that occurs naturally in crusts of earth (soil and rocks) with little concentrations. It exists in nature in different forms isotopes. The two most common and abundant isotopes are: ^{226}Ra , which forms as the product of decay in ^{238}U chains and the second is ^{228}Ra , which forms as the product of ^{232}Th chains decay. Radium exists widely in environment, generally with low concentrations in plants, animals, ground surface water, soil, and rocks. Radium can enter the human body by ingestion or by inhaled air that enters the bloodstream after several months of inhaled radium that remains in lungs [1,9]. The potential for health impacts is proportional to the radiation of radium to which a person is exposed.

In general, the larger your overall radium radiation exposure, the more probable we are to produce a detrimental health result. Long-term radiation exposure may increase the risk of certain cancers, such as bone cancer. Higher radium dosages have been linked to the effects on the blood (anaemia), cataracts (eye growths), teeth (shattered teeth and cavities) and bones (reduced bone development, and therefore exposure to excessive levels of radium is considered hazardous [8].

In order to assess the radiological hazards, the researchers aimed to use the passive technique containing SSNTDS type (CR 39) to explore the radon concentration, radium concentrations and annual effective dose in 57 samples of liquid foodstuffs collected from different markets in west bank- Palestine.

2. Materials and Methods

2.1 Types of liquid foodstuff samples and classifications

In this work, various samples of liquid foodstuffs were collected from various markets in the West Bank on a daily basis as classified in Tables 1 and 2. 400 milliliters were taken from each sample. The passive technique of solid-state nuclear track detectors using the "sealed can technique" was used to measure the radon concentrations and radium contents in liquid foodstuff samples collected from the Palestinian markets. The samples were carefully sealed for 90 days in cylindrical containers composed of a good kind of plastic that measured 6.0 cm in diameter and 12.5 cm in depth. The CR-39 detectors (1 cm $\times$ 1 cm) were suspended above the plastic container at a specific distance (approximately 1.5 cm) from the surface of the liquid sample in each container [12,13].

As illustrated in Figure (1), each sample container was securely closed to an inverted cylindrical plastic cover, and the detector's sensitive portion was oriented toward the radon-emitting liquid sample. During the exposure period, the CR-39 detector was bombarded by radon decay particles and their daughters in the air volume of the cylindrical containers [13,14].



Figure 1. Schematic Diagram of the close vessel technique

2.2 Collecting Detectors and Chemical Etching and Detectors counting tracks

When alpha particles were formed in close proximity to the detecting material by radon or radon decay products, they could strike to create tiny areas of damage called alpha tracks as shown in figure (2). The shape and size of these tracks revealed information about the particles' mass, charge, energy, and direction of motion.

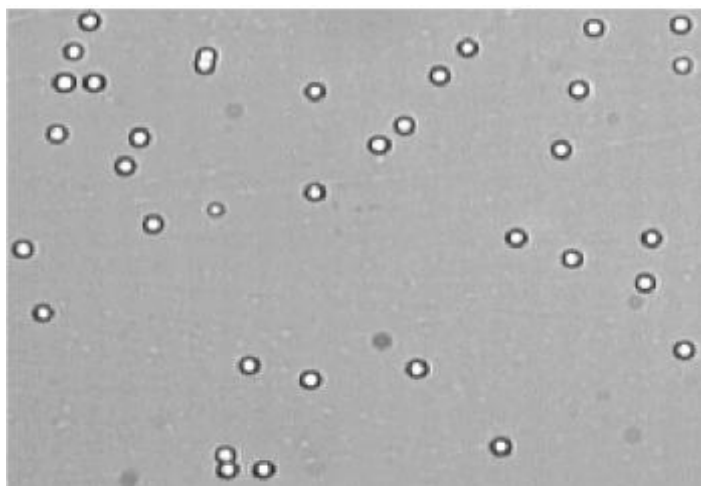


Figure 2. Tracks of alpha particles.

After the exposure period had expired, detectors were removed from the dosimeters. The detectors were chemically etching in 6.25 M NaOH at 70°C for 4 hours. The detectors were then washed by distilled water followed by drying to remove any remaining etchant from the detectors' surfaces [15,16]

A digital optical microscope with 400 times the magnification was utilized to count the tracks per field of vision, by ten times moving the microscope stage from left to right to make sure no tracks were missed. Track densities were computed based on the number of tracks collected, and the liquid foodstuffs radon concentration was then determined [14]

3. Theoretical Calculations

3.1 The activity concentration of radon

The formula of *Radon* – 222 concentration of the liquid foodstuffs samples in unit (Bqm^{-3}) is:

$$C_{Rn}(Bq/m^3) = \frac{c_0 t_0}{\rho_0} \left(\frac{\rho}{t} \right) = k \left(\frac{\rho}{t} \right) \quad (1)$$

Where C_{Rn} is the activity concentration of *Rn* – 222 in a liquid foodstuffs sample, ρ_0 is (*number of tacks/cm²*) track density in detectors exposed to *Ra* – 226, c_0 is the activity concentration of the (*Ra* – 226) is equal $800 Bqm^{-3}$, t_0 is the time of exposure to *Ra* – 226, roughly 90 days, ρ is track density (*number of tacks/cm²*) and t exposure time (in days) of detectors (Thabayneh, and Gharaybeh, 2023; Thabayneh, 2015).

3.2 The effective radium contents

The effective radium content in the unit of the liquid samples will be calculated from the formula [14] $Ra_{eff}(Bq/kg)$

$$Ra_{eff} = \frac{\rho V K}{M(T - \lambda^{-1}[1 - e^{-\lambda T}])} \quad (2)$$

Where ρ is the air space volume in unit, ρ is track density in unit, M is the mass of the liquid sample in unit, K is the calibration factor in unit, λ is decay radon constant is equal and T is total exposure length (days) [14]. The effective radium content has been calculated from the relation [17]: $V m^3 \rho (Tracks/cm^2) M kg (Bqm^{-3}). days/tracks/cm^2 \lambda (0.19 days^{-1}) TRa_{eff} (Bq/L)$

$$Ra_{eff} = \frac{C_{Rn} V}{V_W (T - \lambda^{-1}[1 - e^{-\lambda T}])} \quad (3)$$

Where V is the cup effective volume in m^3 and V_W is the sample volume in (L).

3.3 The annual effective dose

3.3.1 The annual effective dose due to the inhalation of radon

The following formula was used to determine the annual effective dosage of radon during inhalation due to the amount of radon present in liquid foods [14,18]: (H_{inh})

$$H_{inh} (nSv/yr) = C_{Rn} \times F \times R \times T \times 9 nSv (Bqhm^{-3})^{-1} \quad (4)$$

where C_{Rn} is the average radon concentration indoor air in unit Bqm^{-3} , F is the factor equilibrium between indoor radon and its progeny is equal 0.4, R is the ratio air–water concentration is equal 10^{-4} , T is the time exposure to this concentration in *hours* assumed to be $7000h/year$ and $9 nSv (Bqhm^{-3})$ is the factor of dose conversion.

3.3.2 The annual effective dose due to the ingestion of radon

The annual effective dose due to the ingestion of radon from liquid foodstuffs samples, was calculated from the formula [14]: (H_{ing})

$$H_{ing} (mSv/yr) = C_{Rn} \times D_{ing} \times L \quad (5)$$

Where H_{ing} is the effective dose in unit mSv/yr , C_{Rn} is concentration of radon in liquid samples in unit Bq/m^3 , D_{ing} is factor conversion equal to for adult, $D_{ing} = 1$, L is annual liquid consumption by an adult, child and infant in liters [19]. (H_{ing}) mSv/yr^{-1} , C_{Rn} $q\ell^{-1}$ D_{ing} $1 \times 10^{-8} SvBq^{-1}$ $2 \times 10^{-8} SvBq^{-1}$ for child and $7 \times 10^{-8} SvBq^{-1}$ for infant L

3.4 The annual exposure to potential alpha energy (effective dose equivalent)

The following relationship connects both of potential alpha energy E_p and average concentration radon C_{Rn} is:

$$E_p = \frac{8760 \times n \times C_{Rn} \times F}{170 \times 3700} (WLM.y^{-1}) \quad (6)$$

Where F represent the fraction of time spent indoors, n represent number of hours in years, F is the number of hours in working months and breathing in air and C_{Rn} radon concentration [19]. n 8760 1703700

4. Results

4.1. Radon concentrations and radium contents for liquid foodstuff samples:

Tables 1 and 2 provides the $Rn-222$ concentrations and radium contents for all types of liquid foodstuff samples collected from Palestinian markets. As shown in Table 1, the values of C_{Rn} for fruit juice were between $51.0 Bq/m^3$ ($0.051 Bq/l$) to $278.8 Bq/m^3$ ($0.279 Bq/l$) with an average value of $152.0 Bq/m^3$ ($0.152 Bq/l$). However, the values of C_{Rn} for soft drink samples were between $64.6 Bq/m^3$ ($0.065 Bq/l$) to $224.4 Bq/m^3$ ($0.224 Bq/l$) with an average value of $162.5 Bq/m^3$ ($0.163 Bq/l$). Figure 3 clarifies that the C_{Rn} of fruit juice samples was the highest at orange $278.8 Bq/m^3$, whereas the lowest value was Grapefruit $51.0 Bq/m^3$. As depicted in Table 1, the values of C_{Ra} for fruit juice were between $0.71 Bq/kg$ to $3.9 Bq/kg$ with an average values of $2.12 Bq/kg$, and for soft drink samples were between $0.90 Bq/kg$ (apple sample) to $3.14 Bq/kg$ (orange sample) with an average values of $2.28 Bq/kg$. From the results obtained, the researchers noticed that the average concentrations of soft drink samples were higher than those of fruit juice samples.

Table 1. Results of $Rn - 222$ concentrations and $Ra - 226$ contents in fruit juice and soft drink samples.

Samples	Types	Trade mark	C_{Rn} (Bq/m^3)	C_{Rn} (Bq/l)	C_{Ra} (Bq/kg)
	Juice Up	Candia	64.6	0.065	0.90
	Guava Nectar	Domty	71.4	0.071	0.99
	Manga Nectar	Domty	251.6	0.252	3.52
	Red cherry	Cappy	176.8	0.177	2.47

Fruit Juice Samples	Grapefruit	Cappy	51.0	0.051	0.71
	Orange	Cappy	190.4	0.190	2.66
	Lemon mint	Cappy	217.6	0.218	3.04
	Grape	Cappy	142.8	0.143	1.99
	Kiwi, cactus	Cappy	163.2	0.163	2.28
	Pomegranate	Cappy	142.8	0.143	1.99
	Manga	Cappy	129.2	0.129	1.80
	Black tea	Mathieu Teisseire	210.8	0.211	2.95
	Cocktail	Al-juneidi	61.2	0.061	0.85
	Grapefruit	Tabuzina	207.4	0.207	2.90
	Apple	Tabuzina	217.6	0.218	3.04
	orange	Tabuzina	278.8	0.279	3.90
	Lemon mint	Tabuzina	74.8	0.075	1.04
	Orange	Tabuzina	132.6	0.133	1.85
	Fruit Juice	Domty	57.8	0.058	0.80
	Tamarindus indica	Al-zahraa	81.6	0.082	1.14
	Black Grape	Enjoy	268.6	0.269	3.76
	Average		152.0	0.152	2.12
Soft Drink Samples	Pepsi	Pepsi	214.2	0.214	3.01
	sprite	Coca-cola	112.2	0.112	1.57
	Coca cola	Coca-cola	180.2	0.180	2.53
	XL	Xl	180.2	0.180	2.52
	BLU	BLU	200.6	0.201	2.81
	Blueberry	Fanta	166.6	0.170	2.33
	Grape	Fanta	95.2	0.095	1.33
	Orange	Fanta	224.4	0.224	3.14
	Pomegranate	Bavaria	187.0	0.187	2.62
	Apple	Bavaria	64.6	0.065	0.90
	Average		162.5	0.163	2.28

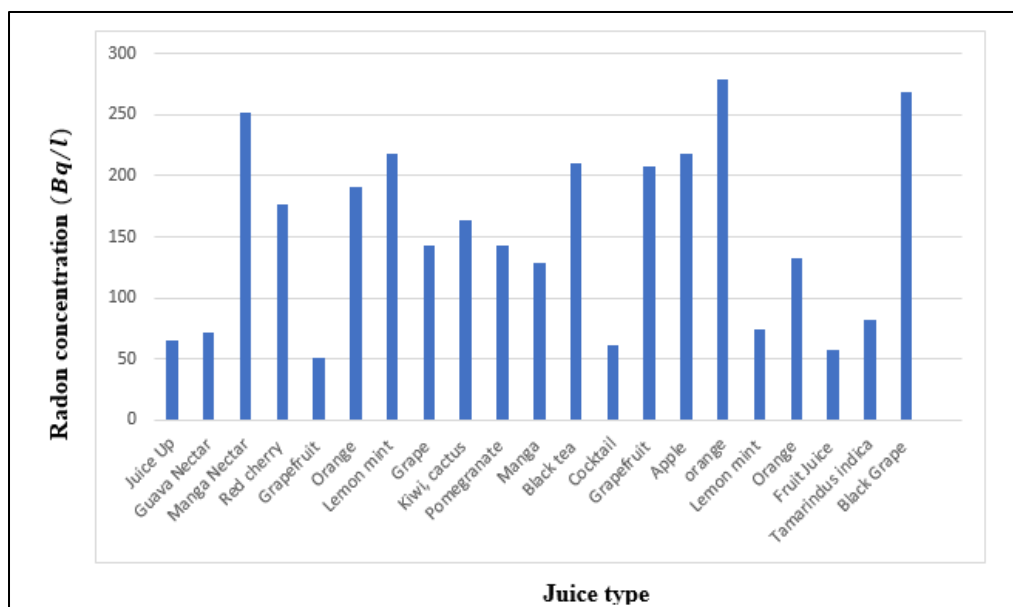


Figure 3. $Rn - 222$ concentrations in juice samples.

Table 2 shows the radon concentrations and radium contents in milk, milk with fruit and yogurt (milk up) samples and other liquid foodstuff samples collected from different Palestinian markets. The values of C_{Rn} of milk, milk with fruit and yogurt samples ranged between 61.2 Bq/m^3 (0.061 Bq/l) to 258.4 Bq/m^3 (0.258 Bq/l) with an average values of 142.6 Bq/m^3 (0.143 Bq/l). Also, the average concentrations of other liquid foodstuff samples ranged between 71.4 Bq/m^3 (0.071 Bq/l) to 207.4 Bq/m^3 (0.207 Bq/l) with an average values of 135.3 Bq/m^3 (0.135 Bq/l). The results provided that the average concentrations of different milk samples were higher than those of other liquid foodstuff samples. Figure 4 shows that the highest radon concentrations for full fat milk was with 258.4 Bq/m^3 and the lowest value for Choco milk was with 61.2 Bq/m^3 . As depicted in Table 2, the values of C_{Ra} for different milk samples ranged between 0.85 Bq/kg to 3.61 Bq/kg with an average values of 2.00 Bq/kg ; however, other liquid foodstuff samples ranged between 1.00 Bq/kg (Handmade sample) to 2.91 Bq/kg (Sesame sauce) with an average values of 1.90 Bq/kg .

Table 2. Results of $Rn - 222$ concentrations and radium contents $Ra - 226$ in milk, milk with fruit, yogurt and others liquid foodstuff samples.

Samples	Types	Trade mark	$C_{Rn}(\text{Bq/m}^3)$	$C_{Rn}(\text{Bq/l})$	$C_{Ra}(\text{Bq/kg})$
Milk, Milk with Fruit and Yogurt	Milk with vitamins	Candia	176.8	0.177	2.47
	Milk with fruit	Candia	156.4	0.156	2.18
	Full fat milk	Al-juneidi	258.4	0.258	3.61
	Free fat milk	Al-juneidi	146.2	0.146	2.04
	Banana milk	Al-rabie	78.2	0.078	1.09
	Chocolate milk	Candia	176.8	0.177	2.47
	Free lactose milk	Candia	105.4	0.105	1.47
	High pasteurized milk	Candia	91.8	0.092	1.28

Samples	Strawberry milk	Al-maraei	125.8	0.126	1.76
	Chocolate milk	Al-jebrini	190.4	0.190	2.66
	Choco milk	Al-juneidi	108.8	0.109	1.52
	Choco milk	Fresca	61.2	0.061	0.85
	Choco fresh	Sky candy	115.6	0.116	1.61
	Choco milk	Candy	122.4	0.122	1.71
	Strawberry milk	Al-maraei	105.4	0.105	1.47
	Yogurt	Candia	149.6	0.150	2.09
	Yogurt	Shanina	112.2	0.112	1.57
	Yogurt	Al-jebrini	159.8	0.160	2.23
	Fruit milk	Hi fresh	180.2	0.180	2.52
	Fresh up	Candy	180.2	0.180	2.52
	Yogurt	Al-juneidi	193.8	0.194	2.71
Average			142.6	0.143	2.00
Others Liquid Foodstuff Samples	Crataegus Molasses	Handmade	71.4	0.071	1.00
	Grape Molasses	Handmade	108.8	0.109	1.52
	Maize oil	Al-safi	91.8	0.092	1.29
	Sesame sauce	Shawar	207.4	0.207	2.91
	White vinegar	Al-tayebat	197.2	0.197	2.76
Average			135.3	0.135	1.90

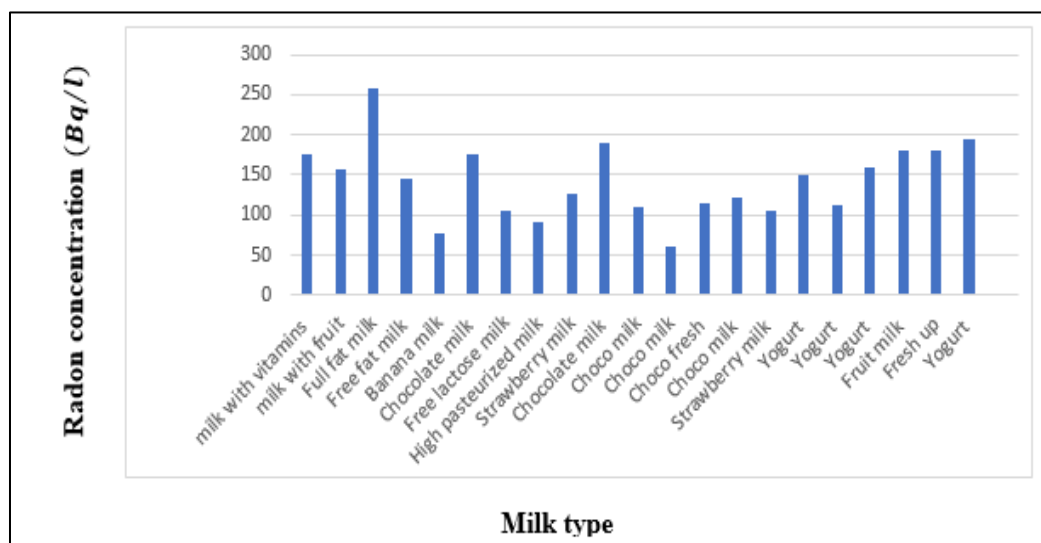


Figure 4. Rn – 222 concentrations in milk samples.

4.2. The annual effective doses (Hing and Hinh) and effective dose equivalent (Ep) for all types of liquid foodstuff samples:

Radon and its decay products enter the body mostly by inhalation through several ways like liquid foodstuff. The annual effective doses for the inhalation and ingestion of radon from liquid foodstuffs are listed in Tables 3 and 4, for all types of adults, children, and infant were determined using UNSCEAR guidelines.

Table 3 shows the annual effective dose ingestion H_{ing} and inhalation H_{inh} and effective dose equivalent for fruit juice and soft drink samples. For fruit juice samples, the average annual effective dose ingestion H_{ing} for adult, child and infant was $1.52 \mu\text{Sv/yr}$, $3.05 \mu\text{Sv/yr}$ and $10.64 \mu\text{Sv/yr}$, respectively, and for soft drink samples, the average annual effective dose ingestion for adult, child and infant was $1.62 \mu\text{Sv/yr}$, $3.25 \mu\text{Sv/yr}$ and $11.37 \mu\text{Sv/yr}$, respectively. The annual effective dose inhalation H_{inh} for fruit juice samples ranged between $0.12 \mu\text{Sv/yr}$ to $0.70 \mu\text{Sv/yr}$ with an average values of $0.38 \mu\text{Sv/yr}$; and for soft drink samples ranged between $0.16 \mu\text{Sv/yr}$ to $0.56 \mu\text{Sv/yr}$ with an average value of $0.40 \mu\text{Sv/yr}$. The average effective dose equivalent (E_p) for fruit juice and soft drink samples was 0.71 WLM.y^{-1} and 0.76 WLM.y^{-1} , respectively.

Table 3. Results of annual effective dose and effective dose equivalent in fruit juice and soft drink samples.

Samples	Types	Average of $H_{ing}(\mu\text{Sv/yr})$			Average of $H_{inh}(\mu\text{Sv/yr})$	E_p (WLM.y^{-1})
		Adult	Child	Infant		
Fruit Juice Samples	Juice Up	0.64	1.29	4.52	0.16	0.30
	Guava Nectar	0.71	1.42	4.99	0.17	0.33
	Manga Nectar	2.51	5.03	17.61	0.63	1.18
	Red cherry	1.76	3.53	12.37	0.44	0.83
	Grapefruit	0.51	1.02	3.57	0.12	0.23
	Orange	1.90	3.80	13.32	0.47	0.89
	Lemon mint	2.17	4.35	15.23	0.54	1.02
	Grape	1.42	2.85	9.99	0.35	0.67
	Kiwi, cactus	1.63	3.26	11.42	0.41	0.76
	Pomegranate	1.42	2.85	9.99	0.35	0.67
	Manga	1.29	2.58	9.04	0.32	0.60
	Black tea	2.10	4.21	14.75	0.53	0.99
	Cocktail	0.61	1.22	4.28	0.15	0.28
	Grapefruit	2.07	4.14	14.51	0.52	0.97
	Apple	2.17	4.35	15.23	0.54	1.02
	orange	2.78	5.57	19.51	0.70	1.31
	Lemon mint	0.74	1.49	5.23	0.18	0.35
	Orange	1.32	2.65	9.28	0.33	0.62
	Fruit Juice	0.57	1.15	4.04	0.14	0.27
	Tamarindus indica	0.81	1.63	5.71	0.20	0.38
	Black Grape	2.68	5.37	18.80	0.67	1.26
Average		1.52	3.04	10.64	0.38	0.71
Soft Drink Samples	Pepsi	2.14	4.28	14.99	0.53	1.00
	sprite	1.12	2.24	7.85	0.28	0.52
	Coca cola	1.80	3.60	12.61	0.45	0.84
	XL	2.00	4.01	14.04	0.50	0.94
	BLU	1.66	3.33	11.66	0.41	0.78
	Blueberry	0.95	1.90	6.66	0.23	0.44

	Grape	2.24	4.48	15.70	0.56	1.05
	Orange	1.80	3.60	12.61	0.45	0.84
	Bavaria Pomegranate	1.87	3.74	13.09	0.47	0.87
	Bavaria Apple	0.64	1.29	4.52	0.16	0.30
	Average	1.62	3.25	11.37	0.40	0.76

Table 4 provides, the annual effective dose ingestion H_{ing} and inhalation H_{inh} and effective dose equivalent for different milk samples and other Liquid foodstuff samples. For milk samples, the average annual effective dose ingestion H_{ing} for adult, child and infant was $1.42 \mu Sv/yr$, $2.85 \mu Sv/yr$ and $9.98 \mu Sv/yr$, respectively; and for other Liquid foodstuff samples, the average annual effective dose ingestion for adult, child and infant was $1.35 \mu Sv/yr$, $2.70 \mu Sv/yr$ and $9.47 \mu Sv/yr$, respectively. The annual effective dose inhalation H_{inh} for different milk samples ranged between $0.15 \mu Sv/yr$ to $0.65 \mu Sv/yr$ with an average values of $0.35 \mu Sv/yr$, and for other liquid foodstuff samples ranged between $0.17 \mu Sv/yr$ to $0.52 \mu Sv/yr$ with an average value of $0.34 \mu Sv/yr$. The average effective dose equivalent (E_p) for milk and others liquid foodstuff samples was $0.67 WLM.y^{-1}$ and $0.63 WLM.y^{-1}$, respectively.

Table 4. Results of annual effective dose and effective dose equivalent in milk, milk with fruit, yogurt and others liquid foodstuff samples.

Samples	Types	Average of $H_{ing}(\mu Sv/yr)$			Average of $H_{inh}(\mu Sv/yr)$	E_p ($WLM.y^{-1}$)
		Adult	Child	Infant		
Milk, Milk with Fruit and Yogurt Samples	Milk with vitamins	1.76	3.53	12.37	0.44	0.83
	Milk with fruit	1.56	3.12	10.94	0.39	0.73
	Full fat milk	2.58	5.16	18.08	0.65	1.21
	Free fat milk	1.46	2.92	10.23	0.36	0.68
	Banana milk	0.72	1.56	5.47	0.19	0.36
	Chocolate milk	1.76	3.53	12.37	0.44	0.83
	Free lactose milk	1.05	2.10	7.37	0.26	0.49
	High pasteurized milk	0.91	1.83	6.42	0.23	0.43
	Strawberry milk	1.25	2.51	8.80	0.31	0.59
	Chocolate milk	1.90	3.80	13.32	0.47	0.89
	Choco milk	1.08	2.17	7.61	0.27	0.51
	Choco milk	0.61	1.22	4.28	0.15	0.28
	Choco fresh	1.15	2.31	8.09	0.29	0.54
	Choco milk	1.22	2.44	8.56	0.30	0.57
	Strawberry milk	1.05	2.10	7.37	0.26	0.49
	Yogurt	1.49	2.99	10.47	0.37	0.70
	Yogurt	1.12	2.24	7.85	0.28	0.52
	Yogurt	1.59	3.19	11.18	0.40	0.75
	Fruit milk	1.80	3.60	12.61	0.45	0.84

	Fresh up	1.80	3.60	12.61	0.45	0.84
	Yogurt	1.93	3.87	13.56	0.48	0.91
Average		1.42	2.85	9.98	0.35	0.67
Others Liquid Foodstuff Samples	Crataegus Molasses	0.71	1.42	4.99	0.17	0.33
	Grape Molasses	1.08	2.17	7.61	0.27	0.51
	Maize oil	0.91	1.83	6.42	0.23	0.43
	Sesame sauce	2.07	4.14	14.51	0.52	0.97
	White vinegar	1.97	3.94	13.80	0.49	0.92
Average		1.35	2.70	9.47	0.34	0.63

5. Discussions

^{226}Ra is extensively distributed in the environment in varying concentrations in air, liquids, rocks, and sediments, and is significant radiologically because it acts chemically like calcium and is deposited on bone surfaces and locations where minerals are metabolized. Radium uptake in plants is increased by raising the concentration of organic acids mostly citric acid, significant impact in ^{226}Ra uptake by plants due to pH lowering and complex formation of organic acids with elements in the soil. Most of the components of radium are quickly eliminated after ingestion, but because of radium's chemical behavior, which is similar to that of calcium, it is absorbed into the blood. Lungs or intestinal-Gastro, like calcium, are deposited primarily in the bones [3,20].

All effective radium content levels for all liquid foodstuffs samples did not exceed the ICRP recommended value. The average values of annual effective dose in mSv/y were within the recommended limit of ICRP values. The results showed that all types of liquid foodstuffs which were analyzed in this work were safe for using daily in our kitchens. The findings indicated that the majority of ^{222}Rn concentration values in most analyzed samples were below the permissible limit established by the International Commission on Radiological Protection (ICRP, 1993), which suggests a recommended range of 200 to 600 Bqm-3 for residential environments. However, it is important to note that the measured radon-222 levels in most samples exceeded the updated reference level of 100 Bqm-3 set by the World Health Organization in 2015 [16,21].

According to ICRP, the limit values for annual effective dose is 3 mSvy-1 to 10 mSvy-1. The results revealed that the overall annual effective dosage from all liquid foodstuffs samples was lower than the ICRP's recommended limits (Thabayneh, and Shawamreh, 2024; ICRP, 1993). The average values of annual exposure to effective dose equivalent ranged between 0.63 WLMMy-1 to 0.76 WLMMy-1 which is consistent to the defined limit values by ICRP for annual exposure to potential alpha energy (effective dose equivalent) is 4.0 WLMMy-1, which confirms that these values are within the acceptable level [22].

Figure 5 shows the relationship between radon concentrations with radium contents (juice samples), a positive correlation has been observed between radium and radon with linear correlation coefficient equal to 0.99. The results of this study confirmed that there is a positive correlation between radium and radon, in addition to a relationship

between radium and radon which is positive with a perfect linear correlation. This result leads us to the fact that radium is a perfect source of radon in all samples.

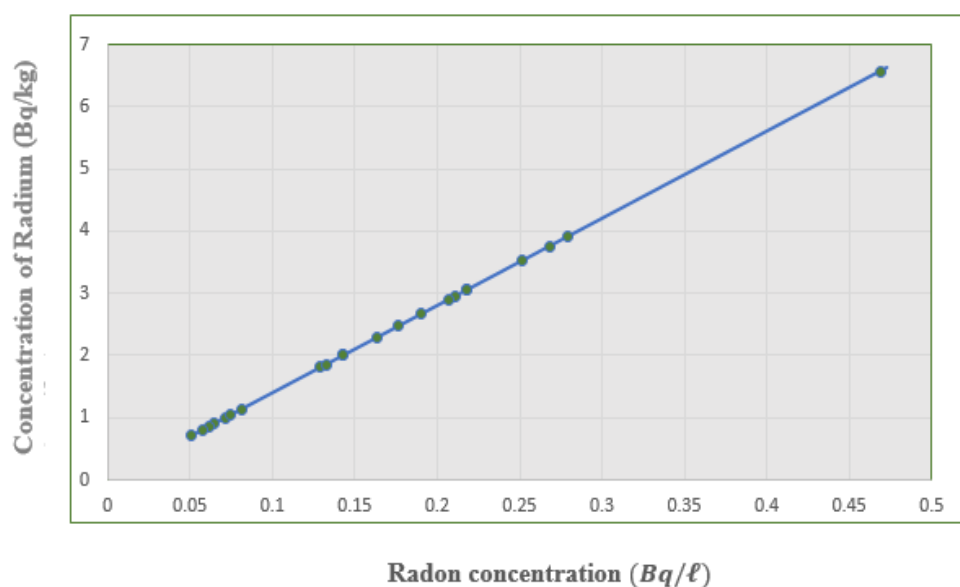


Figure 5. Correlation between $Rn - 222$ concentration and $Ra - 226$ content in juice samples.

6. Conclusions

The passive technique containing SSNTDS type (CR-39) was used in this study to assess radon concentration, radium contents and annual effective dose in 57 samples of liquid foodstuffs samples collected from different markets in the West Bank- Palestine, to assess the radiological hazards.

The levels of radon concentration in fruit juice samples are given in tables 1 and 2. The average radon concentration levels in fruit juice, soft drink, milk and other liquid foodstuff samples were: 152.0, 162.0, 142.6 and 135.3 Bq/m^3 , respectively, and the average concentration of radium contents was 2.12, 2.28, 2.00 and 1.90 Bq/kg for fruit juice, soft drink, milk and other liquid foodstuff samples, respectively. The average radon concentration and radium contents were found to be the highest in soft drink samples and the lowest in other liquid foodstuff samples.

The annual effective dose ingestion H_{ing} for adults, child's and infants, annual effective dose inhalation H_{inh} , and effective dose equivalent for all liquid foodstuff samples were calculated. The results revealed that the overall annual effective dosage from all liquid foodstuffs samples was lower than the ICRP's recommended limits. Therefore, there are no health hazards from drinking the liquid foods studied in this region. To the best of authors' knowledge, this research is the first to be done in the field of liquid foodstuffs in Palestine, and the results obtained from the measurements provide a baseline database of radioactivity levels in this area, that can serve as a benchmark for studies in the future to determine the effects of future occurrences.

6. Declarations

Acknowledgments

Not applicable.

Ethical consideration

This study adhered to the principles of the Declaration of Helsinki.

Consent to participate

Not applicable

Conflicts of interest

Not applicable.

Funding Statement

The authors did not receive support from any organization for the submitted work.

Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Author(s) Contribution

All authors contributed to: Conceptualization, Methodology, Resources, Data Curation, Visualization, Investigation, Writing – original draft, Writing – review & editing, and Formal analysis,

References

- [1] ATSDR, Agency for Toxic Substances and Disease Registry. (2015). Toxicological profile for radon archived at the Wayback Machine. Public Health Service, in collaboration with U.S. Environmental Protection Agency. <https://www.atsdr.cdc.gov/toxprofiles/tp145-p.pdf>
- [2] International Commission on Radiological Protection (ICRP). (2023). Protection against Rn-222 at home and work.
- [3] Tayseer, I., Al-Naggar, A., & Shabaan, D. H. (2020). Radon in foods. In Recent techniques and applications in ionizing radiation research (pp. 77–79). IntechOpen. <https://www.intechopen.com/chapters/72752>
- [4] World Health Organization (WHO). (2010). Guidelines for indoor air quality: Selected pollutants. <https://www.who.int/publications/i/item/9789289002134>
- [5] Bowie, C. (1991). Radon and health. *The Lancet*, 337, 409–413. [https://doi.org/10.1016/0140-6736\(91\)91177-V](https://doi.org/10.1016/0140-6736(91)91177-V)
- [6] Kendall, G. M., & Smith, T. J. (2002). Doses to organs and tissues from radon and its decay products. *Journal of Radiological Protection*, 22, 309–406. <https://doi.org/10.1088/0952-4746/22/4/304>
- [7] Chadwick, A. (1995). Basic principles of radiation biology (PhD thesis). University of Manchester.
- [8] Brugge, D., & Buchner, V. (2012). Radium in the environment: Exposure pathways and health effects. *Reviews on Environmental Health*, 27, 1–17. <https://doi.org/10.1515/reveh-2012-0001>

- [9] International Atomic Energy Agency (IAEA). (1984). The behavior of radium in waterways and aquifers. IAEA.
- [10] International Atomic Energy Agency (IAEA). (2023). What is radon and how are we exposed to it? IAEA Office of Public Information and Communication.
- [11] Thabayneh, K. M. (2015). Measurement of Rn-222 concentration levels in drinking water and the associated health effects in the southern part of West Bank – Palestine. *Applied Radiation and Isotopes*, 103, 48–53. <https://doi.org/10.1016/j.apradiso.2015.05.007>
- [12] Thabayneh, K. M. (2016). Determination of alpha particles concentration in some soil samples and the extent of their impact on the health. *Sains Malaysiana*, 45, 699–707.
- [13] Thabayneh, K. M. (2018). Determination of radon exhalation rates in soil samples using sealed can technique and CR-39 detectors. *Journal of Environmental Health Science & Engineering*, 16, 121–128. <https://doi.org/10.1007/s40201-018-0298-2>
- [14] Thabayneh, K. M., & Gharaybeh, A. (2023). Determination of the radiation dose from radon ingestion and inhalation in different types of drinking water samples collected from Bethlehem province – Palestine. *Applied Radiation and Isotopes*, 200, 110972. <https://doi.org/10.1016/j.apradiso.2023.110972>
- [15] Thabayneh, K. M., & Doweik, S. I. (2023). Measurement of radon concentration levels and radium contents in some foodstuff samples collected from Palestinian markets. *Hebron University Research Journal*, 12, 71–92.
- [16] Thabayneh, K. M., & Shawamreh, R. J. (2024). Measurement of some natural radioactive isotopes concentrations in soil samples in the northern part of West Bank – Palestine. *Radioprotection*, 59, 306–316. <https://doi.org/10.1051/radiopro/2024012>
- [17] Hashim, A. K., & Najam, L. A. (2015). Radium and uranium concentrations measurements in vegetables samples of Iraq. *Detection*, 3, 21–28. <https://doi.org/10.4236/detection.2015.34004>
- [18] Sujo, L. C., Montero, M. E., Villalba, L., Rentería, V. M., Torres, M. E., García, L. M., García, T. R., Mireles, G. F., Herrera, P. E., & Sánchez, A. D. (2004). Uranium-238 and thorium-232 series concentrations in soil, radon-222 indoor and drinking water concentrations and dose assessment in the city Aldama, Chihuahua, Mexico. *Journal of Environmental Radioactivity*, 77, 205–219. <https://doi.org/10.1016/j.jenvrad.2004.03.008>
- [19] United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). (2000). Sources and effects of ionizing radiation: Report to the General Assembly. United Nations.
- [20] Pourhabib, Z., Binesh, A., & Mohammadi, S. (2011). Determination of radon and radium in springs, wells, rivers and drinking water samples of Ramsar in Iran.
- [21] World Health Organization (WHO). (2015). WHO handbook on indoor radon: A public health perspective. <https://www.who.int/publications/i/item/9789241547673>
- [22] VKM Report. (2017). Risk assessment of radioactivity in food: Opinion of the Scientific Committee of the Norwegian Scientific Committee for Food Safety.



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In Silico Evaluation for the Inhibitory Action of Curcumin Derivatives on the CD14 Proteins

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Abstract

Background: Autoimmune thyroid diseases (AITD) are a class of immune disorders that target the thyroid gland. Two forms of the disease predominate: Graves' disease and Hashimoto Thyroiditis. The major symptoms of the diseases include hyperthyroidism and hypothyroidism, respectively. **Objectives:** One target protein of the immune system that is a hot spot in drug discovery is the CD14 protein (or cluster of differentiation 14). CD14 is a cell membrane protein that is highly expressed in macrophages, monocytes, and neutrophils and is a crucial receptor for gram-negative lipopolysaccharide (LPS). The CD14 monocytes produce high levels of HLA-DR, which may contribute to AITD. Single Nucleotide Polymorphisms (SNPs) in CD14 were previously identified to be risk factors to GD and HT diseases. However, the mechanistic involvement of CD14 protein or its relation to the AITD is not yet clear. **Methods:** In this study, the researchers shed light on targeting CD14 protein in silico for the aim of alleviating autoimmune thyroid diseases. Docking experiments and ADME/Tox (Absorption, distribution, metabolism and elimination) properties were performed to predict the mechanistic insights for the plausible inhibitory effect of recently produced synthetic derivatives of curcumin on CD14, as well as the estimation of drug likeness and bioavailability. **Results:** Most of the compounds showed variable levels of inhibition on the CD14 protein and good bioavailability scores. **Conclusion:** The results indicated that curcumin derivatives could be effective drugs against autoimmune thyroid diseases.

Keywords: Area of Interest: Drug Discovery, Docking, Structural bioinformatics, chem-informatics

1. Introduction

Autoimmune thyroid diseases (AITD) are a set of ailments that target the thyroid glands [1]. Two of the most prevalent forms of the AITD diseases are the Graves' Disease (GD) and Hashimoto Thyroiditis (HT), which cause hyperthyroidism and hypothyroidism, respectively [2]. More clearly, patients with Graves' Disease (GD) may suffer from anxiety, increased sensitivity to heat, weight loss, among other symptoms [3]. The prevalence of GD is 24.8 per 100,000 population per year [4], and it ranges from 21 per 100,000 population to 120 per 100,000 population per year [5]. Patients with Hashimoto Thyroiditis (HT) disease, on the other hand, suffer from fatigue, increased sensitivity to cold, increased sleepiness, muscle weakness, plus many other symptoms [6]. HT ranges from 27 per 100,000 per year to 448 per 100,000 per year in general populations [5]. The older ages and females normally show higher incidence of the diseases [7].

As is the case for many diseases, genes and some environmental factors increase the susceptibility and predisposition of AITD. Several genes were characterized to be connected to AITD, including the HLA-DR gene locus and the non-MHC genes, e.g., CD14, CD40, CTLA-4, PTPN22, thyroglobulin, and TSH receptor genes [8, 9]. The major environmental triggers of AITD include iodine, infection, medications, smoking, and stress [10]. GD and HT diseases are caused by a faulty outbreak for the autoantibodies of the immune system against the thyroid gland. This attack by GD or HT results in an increase in the thyroid gland volume and a consequent increase in thyroid hormones or a decreased thyroid volume and a decrease in thyroid hormones, respectively. Complications of GD include problems with fertility, the menstrual cycle, as well as pregnancy. Additional complications are heart failure, muscles problems, palpitations, and thinning bones [3]. HT is associated with heart disease, heart failure, high blood pressure, and high cholesterol [6].

CD14 (or cluster of differentiation 14) is a membrane cell-surface protein that is highly expressed on monocytes, macrophages, and neutrophils [11]. However, it is lowly expressed on other hematopoietic and stromal cells. CD14 is a recognition receptor of the innate immune system. It recognizes gram-negative cells and acylated microbial products and alerts the immune cells to their presence [12, 13]. The CD14 monocytes have been shown to express high levels of HLA-DR, which may cause AITD [14]. Several SNPs in CD14 gene were found to be associated with the genetic predisposition to GD with a statistical significance in the analysed populations [8]. In a study by Xin and colleagues, genome-wide methylation was compared between GO patients and negative controls. Differential methylation was detected in 148 loci, among which CD14 was a major gene [15]. Other studies concluded an enrichment of monocytes with CD14 and TLR2 expressions in HT disease compared to healthy controls [16, 17]. Thus, to treat AITD, specialists can use drugs that reduce the levels of CD14. Numerous routes are followed to alleviate AITD, where the production of thyroid hormones or their effects are aimed at being blocked. Patients with Graves' disease (including pregnant women) are administered medications like 6-n-propyl-2-thiouracil (PTU) that stop the production of the thyroid hormone [18]. Additionally, Graves' disease can be treated by beta-blockers, inorganic iodide, and lithium. Beta-Blockers can decrease the symptoms of hyperthyroidism [19]. Inorganic iodide could decrease the vascularity of the thyroid gland. As a result, it can be administered prior to surgery [20]. When drugs and radioactive iodine fail to treat the diseases, surgical intervention is followed, where all or part of thyroid gland is removed [21]. Levothyroxine (LT4) and hormone replacement therapy (via the introduction of triiodothyronine (T3)) may be prescribed to treat the Hashimoto Thyroiditis [6].

A few anti-thyroid drugs, such as amiodarone, carbimazole, and propylthiouracil, are confined by their narrow action and pharmacokinetic effect and have side effects. Traditional medicine utilizes herbal-based remedies by about 80% of the world's population. A wide range of herbal-derived compounds or chemically modified herbal phytochemicals are used to produce safe pharmaceutically active drugs with reduced or no side effects [22, 23].

Curcumin is a phytopolyphenol pigment produced by the plant turmeric of the ginger family (*Curcuma longa*) and other *Curcuma* species. *Curcuma longa* has been traditionally used in the Middle East and the Far East in traditional medicine due to its anticancer, anti-inflammatory, antimicrobial, anti-mutagenic, and antioxidant properties [24, 25]. Exemplary antioxidants present in turmeric include curcuminoids, used to alleviate oxidative stress and other illnesses including COVID19 [26-29].

Curcumin was shown to play a major role in the treatment of AITD by regulating inflammatory cytokines, such as IL-1beta, IL-6, IL-12, TNF-alpha and IFN-gamma. Curcumin was also linked to several pathways in immune cells including the JAK-STAT, AP-1, and NF-kappaB signalling pathways [30].

The process of drug discovery is time, money and effort consuming. Normally, it takes 10 to 14 years to launch a new drug on the market. The cost of a new drug ranges between \$300 million and \$2.8 billion dollars [31]. Using docking in drug discovery can decrease the time, money and efforts needed to launch a new drug [32].

Docking acts at the atomic resolution for the screening of robust ligand-protein interactions. Several calculation are carried out that help in resolving the ligand orientation, inhibition constants, as well as the binding affinities [33]. Additionally, drug likeness and bioavailability help to understand drug likeness via studying the ADME (Absorption, distribution, metabolism and elimination) properties of the drug [34, 35]. In this study, docking protocols and ADME/Tox studies were carried out to demonstrate the effects of several phytochemicals in the curcumin extract on CD14 molecule. To achieve this purpose, the researchers used the crystal structure of human soluble CD14 (PDB ID: 4GLP) [13].

2. Materials and Methods

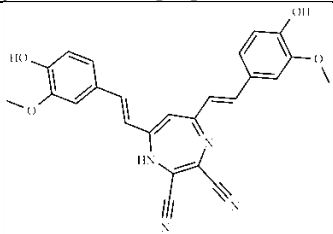
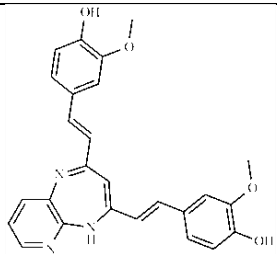
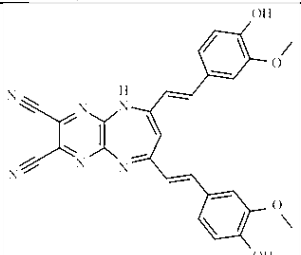
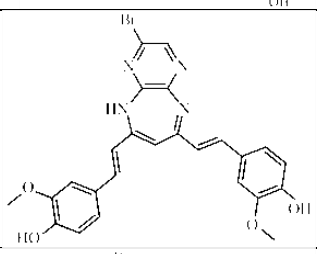
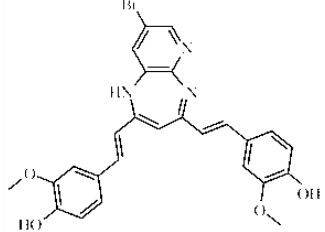
The researchers based the study on docking novel curcumin derivatives, which were synthesized by Qneibi et al. (Table 1)[36]. Herein, input PDB files were set up. To this aim, the SMILES structures of the compounds were processed based on the systemic IUPAC structures[37]. The Open Babel server was used to generate the PDB structures[38]. The compounds were docked against the apo form for the CD14 protein (PDB: 4GLP)[13] using the AutoDock Vina program, version 4.2[39]. AutoDock Vina is considered among the software choices with best scores for docking and top-ranked qualities[40].

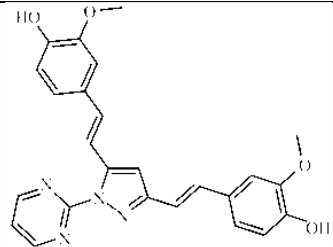
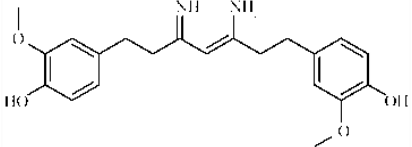
In each docking experiment, the receptor protein was kept rigid. Polar hydrogen atoms were added to the protein structure and heteroatoms were removed. Input files for docking were prepared using the AutoDock tools[39]. Parallel rectangular grid boxes of 50Å×50Å×80Å dimensions were prepared. The center of the grid was based on the center of mass of the protein. Starting from random coordinates, 20 independent docking runs were performed for the protein against each compound using the Lamarckian genetic algorithm[41]. The initial maximum energy was set to zero, and up to 1000 retries were permitted. The genetic algorithm employed a population size of 150 and a maximum of 2,500,000 energy evaluations. A total of 27,000 generations were executed. The mutation and crossover rates were fixed at 0.02 and 0.8, respectively, with a window size of 10. Local optimization was carried out using the Solis and Wets method for 300 iterations. The thresholds for

consecutive successes and failures before adjusting the step size (ρ) were both set to 4. The Cauchy distribution parameters were assigned as $\alpha = 0.0$ and $\beta = 1.0$. The resulting PDB files were extracted after the runs. Docking results were assessed as the best fit of the ligand-protein interactions in each of the compounds.

As a part of the process of drug discovery, the researchers used SwissADME to evaluate the pharmacokinetics, bioavailability, drug-likeness, and medicinal chemistry friendliness of the ligands. Molecules are input by drawing them using a molecular sketcher or by adding SMILES structures[42]. Accordingly, SwissADME then predicts several physicochemical properties[42]. One major property in the prediction of bioavailability is the Lipinski's rule of five (RO5)[43, 44]. The rule states that poor absorption is more possible when there are more than 5 H-bond donors, the ligand weighs over 500 daltons, the log P partition coefficient (octanol/water) is above 5, the molecule has more than 10 H-bond acceptors and more than 10 rotatable bonds. Violation of three or more rules decreases the chance of oral bioavailability. Yet, several orally administered drugs violate two to three rules[45].

Table 1. The seven curcumin derivatives introduced by Qneibi et al [36].

(a) S1: 5,7-bis[(E)-2-(4-hydroxy-3-methoxyphenyl)ethenyl]-1H-1,4-diazepine-2,3-dicarbonitrile	
(b) S2: 4-[(E)-2-(2-[(E)-2-(4-hydroxy-3-methoxyphenyl)ethenyl]-5H-pyrido[2,3-b][1,4]diazepin-4-yl)ethenyl]-2-methoxyphenol	
(c) S3: 6,8-bis[(E)-2-(4-hydroxy-3-methoxyphenyl)ethenyl]-5H-pyrazino[2,3-b][1,4]diazepine-2,3-dicarbonitrile	
(d) S4: 4-[(E)-2-(3-bromo-8-[(E)-2-(4-hydroxy-3-methoxyphenyl)ethenyl]-5H-pyrazino[2,3-b][1,4]diazepin-6-yl)ethenyl]-2-methoxyphenol	
(e) S5: 4-[(E)-2-{8-bromo-4-[(E)-2-(4-hydroxy-3-methoxyphenyl)ethenyl]-1H-pyrido[2,3-b][1,4]diazepin-2-yl}ethenyl]-2-methoxyphenol	

(f) S6: 4-[(E)-2-(5-[(E)-2-(4-hydroxy-3-methoxyphenyl)ethenyl]-1-(pyrimidin-2-yl)-1H-pyrazol-3-yl)ethenyl]-2-methoxyphenol	
(g) S7: 4-[(4Z)-5-amino-7-(4-hydroxy-3-methoxyphenyl)-3-iminohept-4-en-1-yl]-2-methoxyphenol	

3. Results

3.1. Binding Free Energies and Inhibition Constants for CD14 Protein

The binding free energies, inhibition constants as well as the root mean square deviation (RMSD) values for the ligand structures upon docking to the reference structures are shown in table 2. The inhibition constants (K_i) for the CD14 binding interface to the S1 – S3, S5 – S6 ligands were in the range (1.19 - 10.26 μ M), with higher values of inhibition constants for the CD14:S4 and CD14:S7 interfaces (K_i = 234.97, 463.37 μ M, respectively). Binding free energies of the CD14 protein to the several curcumin derivatives were in the range of (–4.55 - –8.08 Kcal/mol). The root mean square deviations (RMSD) of the ligand crystal structures from the reference ones were in the range of (32.05-78.63 Å), except for S4, with an unidentified value.

Table 2. Binding free energies, inhibition constants and RMSD values for the binding interfaces of the best fit between S1-S7 ligands and the CD14 protein.

Protein	Ligand	AutoDock binding free energy (Kcal/mol)	AutoDock inhibition constant, K_i (μ M)	RMSD for the ligand from the reference structure (Å)
CD14	S1	-7.23	4.99	67.859
	S2	-6.81	10.26	66.001
	S3	-7.66	2.43	32.054
	S4	-4.95	234.97	-
	S5	-7.09	6.34	73.609
	S6	-8.08	1.19	69.522
	S7	-4.55	463.37	78.630

3.2. Binding Interface for the CD14 Protein

For the CD14 protein (PDB ID: 4GLP) [13], and in all seven ligand-protein interaction interfaces, moderate-ranged (3.6 - 4.0 Å) electrostatic interactions had higher contribution than the short-ranged (2.5 - 3.5 Å) interactions at the ligand-protein interface in the binding energies (Figure 1). Few longer bonds contributed to the binding process at the binding interface. Nonpolar amino acids at the binding interfaces were prominent (e.g., Leu, Pro, Trp, Phe, Val, and Ala). These amino acids were more noticeable at the binding interfaces for all phytochemicals, with the least contribution at the S2:CD14 interface. Additionally, several polar contacts were found at the binding interfaces (e.g., Asn, Arg, Ser, Arg, Glu, Gln, Asn and Lys) for all phytochemicals excepting at the S5:CD14 interface, which was totally established by non-polar contacts.

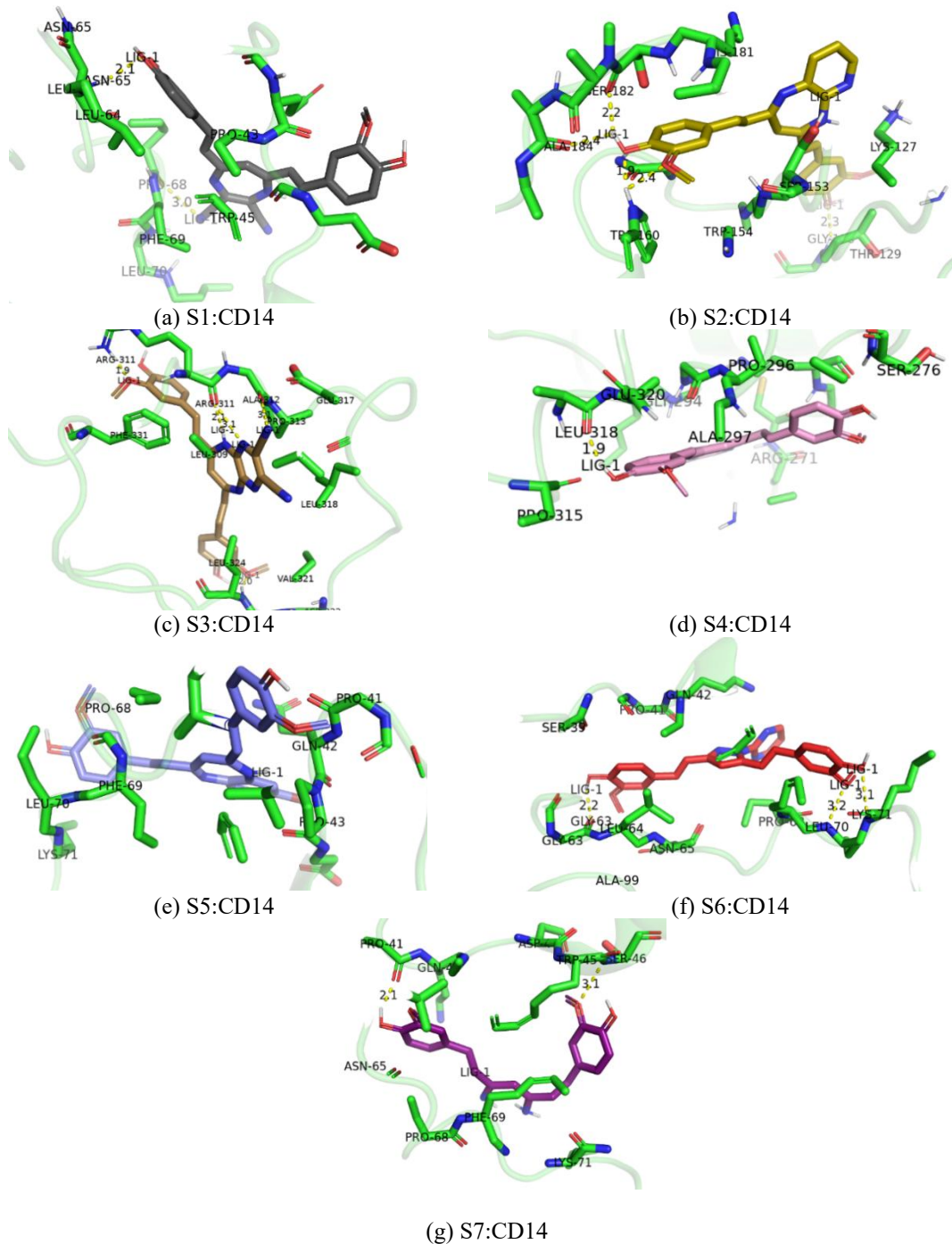


Figure 1. Binding interfaces for the curcumin derivatives to the CD14 protein (PDB ID: 4GLP [13]). (a) S1-CD14; (b) S2-CD14; (c) S3-CD14; (d) S4-CD14; (e) S5-CD14; (f) S6-CD14; (g) S7-CD14. Yellow color was used for polar contacts, while blue color for nonpolar ones.

3.3. ADME/Tox and Bioavailability of the Seven Ligands

Drug likeness was evaluated via examining the ADME properties. For a ligand to have the properties of a successful drugs, it is expected to have a good solubility, to obey the Lipinski's rule of 5 (RO5). Additionally, it is expected not to inhibit CYP450 enzymes or to cause problems related to elimination or excretion [46]. Table 3 shows that all seven ligands obey the Lipinski's RO5; with no violation (S1-S3, S6, S7) or at most one violation

(S4, S5), where the latter two molecules slightly exceeded the maximum molecular weight of 500 g/mol. Since none of the molecules broke three or more of the Lipinski's RO5, all ligands are orally active [43, 44].

Table 3. ADME analysis -Physicochemical properties (Lipinski rule of five of ligands)

Phytochemical	Physicochemical properties (Lipinski rule of five)					Lipinski
	Molecular weight (g/mol)	H-bond acceptor	H-bond donor	Log P	No of rotatable bond	
S1	440.45	7	3	2.88	6	Yes (0 violations)
S2	441.48	6	3	3.86	6	Yes (0 violations)
S3	492.49	9	3	3.07	6	Yes (0 violations)
S4	521.36	7	3	4.07	6	Yes (1 violation; MW >500)
S5	520.37	6	3	4.48	6	Yes (1 violation; MW >500)
S6	442.47	7	2	3.57	7	Yes (0 violations)
S7	370.44	5	4	3.04	9	Yes (0 violations)

To measure the ratio of an orally administered compound that passes to the systemic circulation, the bioavailability score was used (see table 4). It ranges from 0 to 1, where higher scores indicate higher fractions of the ligands to reach the systemic circulation. The researchers examined the five phytochemicals that showed the good docking results (S1 – S3, S5 – S6) as well as the other two phytochemicals for their bioavailability scores. All showed an intermediary bioavailability score (0.55). However, the prediction of aqueous solubility by three methods: ESOL logD, (ALI) logS, and (SILICOS- IT) logS presented moderate to poor solubility for the vast majority of phytochemicals [42].

During their first pass to the liver, a great percentage of drugs are metabolized by Cytochrome P450 enzymes, in a condition called the first pass effect [47]. In screening CYP450 inhibitors, all seven phytochemicals showed possible inhibition of some CYP450 enzymes. The inhibition of these enzymes by the selected ligands proposes a contribution to the drug-drug interaction [48].

Table 4. Drug-likeness analysis of bioactive compounds

Phytochemical	Bioavailability score	Solubility			Pharmacokinetics	
		Log S (ESOL)	Log S (Ali)	Log S (SILICOS-IT)	GI absorption	CYP enzymes inhibitors
S1	0.55	Moderately soluble	Poorly soluble	Moderately soluble	High	CYP2C19, CYP2C9, CYP3A4
S2	0.55	Moderately soluble	Poorly soluble	Poorly soluble	High	CYP2C19, CYP2C9
S3	0.55	Moderately soluble	Poorly soluble	Poorly soluble	Low	CYP2C9, CYP3A4
S4	0.55	Poorly soluble	Poorly soluble	Poorly soluble	High	CYP2C19, CYP2C9

S5	0.55	Poorly soluble	Poorly soluble	Poorly soluble	High	CYP2C19, CYP2C9,
S6	0.55	Moderately soluble	Poorly soluble	Poorly soluble	High	CYP2C9
S7	0.55	Soluble	Moderately soluble	Moderately soluble	High	CYP2C9, CYP2D6, CYP3A4

4. Discussion

Curcumin derivatives were lately synthesized by Qneibi and coworkers [36]. Being major components of curcumin extracts, these compounds are predictable to act against a wide-ranging number of disease-causing agents [36].

Curcumin, the main active polyphenol compound in *Curcuma longa*, was found to be potent in treating AITD by controlling inflammatory cytokines [30]. Some studies showed a direct association via in vitro experiments between the treatment of nontoxic concentrations of curcumin and the alleviation of inflammation in orbital fibroblast derived from Graves' patients [49]. Additionally, other studies showed curcumin to be among effective herbal medicines in the treatment of Hashimoto Thyroiditis [50]. Curcumin can interact with proteins and induce inhibitory actions. Herein, we aimed to shed light on the effect curcumin derivatives have on the protein CD14, which is a hub protein that contributes majorly to the innate immune response. Thus, in silico studies using curcumin derivatives in targeting CD14 are uncovered. Docking experiments were conducted to appreciate the plausible action mechanism by which the curcumin derivatives would inhibit the CD14 protein. Lead compounds were previously synthesized from the curcumin derivatives [36]. Screening protocols were followed that aid in checking the inhibitory potentials, binding free energies at the binding interfaces, and structural fluctuations for the ligands at the binding interfaces from the reference structures.

Previous studies concluded an inhibitory action of some flavonoids to CD14⁺ monocytes. An example is chrysin, a flavonoid that was found to inhibit the receptor-mediated endocytosis of CD14⁺ monocyte-derived immature dendritic cells [51]. This suggests an antagonistic action of chrysin on the CD14 protein, which controls the endocytosis process of toll-like receptor 4 [52]. It also attenuated the expression of CD80, CD83 and Cd86 [51]. Apigenin is another flavonoid that was also found to inhibit the expression of other clusters of differentiation, including the CD80 and CD86 [53].

Docking experiments showed good results in terms of the binding free energies, inhibition constants as well as the root mean square deviation (RMSD) values for the ligand structure upon docking from the reference structure (Table 2). In reference to literature, a scoring scheme of a binding free energy lower than -5 kcal/mol and an inhibition constant less than 100 μ M indicates a strong binding between the ligand and the protein [54]. All compounds, excepting S4 and S7 showed potent binding to CD14 (PDB ID: 4GLP [13]). Indeed, the inhibition constants (K_i) for the CD14 binding interface to the S1 – S3, S5-S6 ligands were in the low range (1.19 - 10.26 μ M), indicating a strong inhibition. Higher inhibition constants were found for the CD14:S4 and CD14:S7 interfaces (K_i = 234.97, 463.37 μ M), what shows comparably weaker inhibition. Binding free energies of the CD14 protein to the several curcumin derivatives were in the range of (-4.55 - -8.08 Kcal/mol), indicating stable contacts. The root mean square deviations (RMSD) of the ligand crystal structures from the reference ones were

in a reasonable range from the reference structures (32-78 Å) while bindings to the several ligands, except for S4, which showed an unidentified value.

The 3D structure for the best fit results of binding for the seven ligands to the CD14 (PDB ID: 4GLP) [13] showed moderate-ranged (3.6 - 4.0 Å) electrostatic interactions, and a slight contribution for the short-ranged (2.5 - 3.5 Å) interactions at the ligand-protein interface (Figure 1). A balanced contribution of both nonpolar amino acids (e.g., Leu, Pro, Trp, Phe, Val, and Ala) as well as polar amino acids (e.g., Asn, Arg, Ser, Arg, Glu, Gln, Asn and Lys) at all binding interfaces was noticed. The only exception was the S5:CD14 interface, where the contribution was merely non-polar. These results indicate a good drug likeness for the ligands, due to their capability to bind to water and to cross biological membranes. These results were further reinforced by ADMETox studies, especially the logP values that indicated balanced lipophilicities and hydrophilicities of the drugs. All seven ligands were also found to follow the Lipinski's RO5 and to show intermediary bioavailability scores (0.55). However, their inhibition of CYP450 suggests further needed modifications that alleviate drug-drug interactions[48].

Based on our previous work on curcumin derivatives and other phytochemicals targeted in our drug discovery protocols [22, 55, 56], the researchers predict that the phytochemical might bind several targets in different tissues, all with a high specificity. In addressing the plausible side effects of the off-target effect, nanoparticles are developed that induce an active targeting to the tissue under study, with a very high targeted localization of the drug in precision medicine. This additionally improves the toxicity profile by reducing side effects related to the unspecific binding of the phytochemicals [57, 58].

Docking is a well-established method used to understand the mechanistic insights of the protein-ligand plausible binding. However, some limitations to the performed docking study include the confined sampling for the conformational space of the protein and ligand. Additionally, the scoring schemes for the binding affinities and free energies are approximated. However, the results herein can be utilized in understanding the comparative binding affinities of the several phytochemicals to the protein under study [59, 60]. One more limitation is the limited crystallographic evidence with positive controls to serve in the validation process for the experiments held. It is necessary to handle further in vitro, in vivo and human-based research to test the clinical potential of the several phytochemicals and decipher these findings into the production of effective drugs for improving patient outcomes in treating autoimmune diseases.

5. Conclusion

It was previously suggested that the inhibition of CD14 protein can reduce the inflammatory responses [61]. Compounds derived from curcumin are robust in the treatment of a wide range of illnesses [24, 25]. This study emphasizes the mechanistic binding of compounds derived from curcumin to the CD14 protein. A special interest can be directed to the S1 – S3 and S6-S7 curcumin derivatives, which showed the best docking results. These results were based on the binding affinities, binding interfaces, and inhibition constants. Additionally, ADMETox results and the bioavailability scores indicated good drug likeness for the several curcumin derivatives. Taken together, these in silico results serve as good basis for ongoing in vitro and in vivo studies and drug identification for the treatment of autoimmune diseases.

6. Declarations

Acknowledgments

Not applicable.

Ethical consideration

This study adhered to the principles of the Declaration of Helsinki.

Consent to participate

Not applicable

Conflicts of interest

The authors (Siba Shanak and Hilal Zaid) are members of the Editorial Board for the AAUP Journal of STEM and Health Sciences. To maintain a transparent and unbiased peer-review process, Shanak and Zaid were not involved in the selection of reviewers or any editorial decisions regarding this manuscript. The peer-review process was handled independently by other editors of the journal. Otherwise, the authors have no conflicts of interest to declare that are relevant to the content of this article.

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Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Authors Contributions

Conceptualization: Hassan Shroof and Siba Shanak. **Formal analysis:** Hassan Shroof and Siba Shanak. **Investigation:** Hassan Shroof and Siba Shanak. **Methodology:** Hassan Shroof and Siba Shanak. **Supervision:** Hilal Zaid. **Visualization:** Hilal Zaid **Writing – original draft:** Hassan Shroof and Siba Shanak. **Writing – review & editing:** Siba Shanak

References

- [1] M. J. Simmonds and S. C. L. Gough, "Unravelling the genetic complexity of autoimmune thyroid disease: HLA, CTLA-4 and beyond," *Clinical and Experimental Immunology*, vol. 136, no. 1, pp. 1-10, Apr 2004, doi: 10.1111/j.1365-2249.2004.02424.x.
- [2] N. Stathatos and G. H. Daniels, "Autoimmune thyroid disease," *Current Opinion in Rheumatology*, vol. 24, no. 1, pp. 70-75, Jan 2012, doi: 10.1097/BOR.0b013e32834ddb27.
- [3] T. Davies et al., "Graves' disease," *NATURE REVIEWS DISEASE PRIMERS*, vol. 6, 2020-07-02 2020, doi: 10.1038/s41572-020-0184-y.
- [4] Y. S. Hussain, J. C. Hookham, A. Allahabadia, and S. P. Balasubramanian, "Epidemiology, management and outcomes of Graves' disease-real life data," *Endocrine*, vol. 56, no. 3, pp. 568-578, Jun 2017, doi: 10.1007/s12020-017-1306-5.
- [5] D. S. A. McLeod and D. S. Cooper, "The incidence and prevalence of thyroid autoimmunity," *Endocrine*, vol. 42, no. 2, pp. 252-265, Oct 2012, doi: 10.1007/s12020-012-9703-2.

- [6] J. Klubo-Gwiezdzinska and L. Wartofsky, "Hashimoto thyroiditis: an evidence-based guide to etiology, diagnosis and treatment," *Polish Archives of Internal Medicine-Polskie Archiwum Medycyny Wewnetrznej*, vol. 132, no. 3, Mar 2022, Art no. 16222, doi: 10.20452/pamw.16222.
- [7] T. Bjoro et al., "Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The Health Study of Nord-Trondelag (HUNT)," *European Journal of Endocrinology*, vol. 143, no. 5, pp. 639-647, Nov 2000, doi: 10.1530/eje.0.1430639.
- [8] X. Jia, B. Wang, Q. M. Yao, Q. Li, and J. N. Zhang, "Variations in CD14 Gene Are Associated With Autoimmune Thyroid Diseases in the Chinese Population," *Frontiers in Endocrinology*, vol. 9, Jan 2019, Art no. 811, doi: 10.3389/fendo.2018.00811.
- [9] A. Huber, F. Menconi, S. Corathers, E. M. Jacobson, and Y. Tomer, "Joint Genetic Susceptibility to Type 1 Diabetes and Autoimmune Thyroiditis: from Epidemiology to Mechanisms," *Endocrine Reviews*, vol. 29, no. 6, pp. 697-725, Oct 2008, doi: 10.1210/er.2008-0015.
- [10] Y. Tomer and A. Huber, "The etiology of autoimmune thyroid disease: A story of genes and environment," *Journal of Autoimmunity*, vol. 32, no. 3-4, pp. 231-239, May-Jun 2009, doi: 10.1016/j.jaut.2009.02.007.
- [11] H. W. L. Zieglerheitbrock and R. J. Ulevitch, "CD14 - CELL-SURFACE RECEPTOR AND DIFFERENTIATION MARKER," *Immunology Today*, vol. 14, no. 3, pp. 121-125, Mar 1993, doi: 10.1016/0167-5699(93)90212-4.
- [12] J. Pugin et al., "CD14 IS A PATTERN-RECOGNITION RECEPTOR," *Immunity*, vol. 1, no. 6, pp. 509-516, Sep 1994, doi: 10.1016/1074-7613(94)90093-0.
- [13] S. L. Kelley, T. Lukk, S. K. Nair, and R. I. Tapping, "The Crystal Structure of Human Soluble CD14 Reveals a Bent Solenoid with a Hydrophobic Amino-Terminal Pocket," *Journal of Immunology*, vol. 190, no. 3, pp. 1304-1311, Feb 2013, doi: 10.4049/jimmunol.1202446.
- [14] W. T. Ma, F. Gao, K. Gu, and D. K. Chen, "The Role of Monocytes and Macrophages in Autoimmune Diseases: A Comprehensive Review," *Frontiers in Immunology*, vol. 10, May 2019, Art no. 1140, doi: 10.3389/fimmu.2019.01140.
- [15] Z. Xin et al., "A genome-wide DNA methylation analysis in peripheral blood from patients identifies risk loci associated with Graves' orbitopathy," *JOURNAL OF ENDOCRINOLOGICAL INVESTIGATION*, vol. 41, pp. 719-727, 2018-06-01 2018, doi: 10.1007/s40618-017-0796-6.
- [16] M. Klatka et al., "The Role of Toll-like Receptor 2 (TLR2) in the Development and Progression of Hashimoto's Disease (HD): A Case Study on Female Patients in Poland," *INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES*, vol. 24, 2023-03-01 2023, Art no. 5344, doi: 10.3390/ijms24065344.
- [17] Q. Zhang et al., "Lymphocyte infiltration and thyrocyte destruction are driven by stromal and immune cell components in Hashimoto's thyroiditis," *NATURE COMMUNICATIONS*, vol. 13, 2022-02-09 2022, Art no. 775, doi: 10.1038/s41467-022-28120-2.
- [18] R. T. Zoeller and K. M. Crofton, "Mode of action: Developmental thyroid hormone insufficiency - Neurological abnormalities resulting from exposure to propylthiouracil," *Critical Reviews in Toxicology*, vol. 35, no. 8-9, pp. 771-781, Oct-Nov 2005, doi: 10.1080/10408440591007313.

- [19] E. Martino, L. Bartalena, F. Bogazzi, and L. E. Braverman, "The effects of amiodarone on the thyroid," *Endocrine Reviews*, vol. 22, no. 2, pp. 240-254, Apr 2001, doi: 10.1210/er.22.2.240.
- [20] D. D. Streetman and U. Khanderia, "Diagnosis and treatment of Graves disease," *Annals of Pharmacotherapy*, vol. 37, no. 7-8, pp. 1100-1109, Jul-Aug 2003, doi: 10.1345/aph.1C299.
- [21] M. Smithson, A. Asban, J. Miller, and H. Chen, "Considerations for Thyroidectomy as Treatment for Graves Disease," *Clinical Medicine Insights-Endocrinology and Diabetes*, vol. 12, Apr 2019, Art no. 1179551419844523, doi: 10.1177/1179551419844523.
- [22] S. Shanak, N. Bassalat, R. Albzoor, S. Kadan, and H. Zaid, "In Vitro and In Silico Evaluation for the Inhibitory Action of *O. basilicum* Methanol Extract on alpha-Glucosidase and alpha-Amylase," *Evidence-Based Complementary and Alternative Medicine*, vol. 2021, Jul 2021, Art no. 5515775, doi: 10.1155/2021/5515775.
- [23] L. Lu et al., "Traditional Medicine in the Treatment of Drug Addiction," *American Journal of Drug and Alcohol Abuse*, vol. 35, no. 1, pp. 1-11, 2009, Art no. Pii 907873875, doi: 10.1080/00952990802455469.
- [24] S. J. Hewlings and D. S. Kalman, "Curcumin: A Review of Its Effects on Human Health," *Foods*, vol. 6, no. 10, Oct 2017, Art no. 92, doi: 10.3390/foods6100092.
- [25] S. C. Gupta, S. Patchva, and B. B. Aggarwal, "Therapeutic Roles of Curcumin: Lessons Learned from Clinical Trials," *Aaps Journal*, vol. 15, no. 1, pp. 195-218, Jan 2013, doi: 10.1208/s12248-012-9432-8.
- [26] A. Sahebkar, C. Serban, S. Ursoniu, and M. Banach, "EFFECT OF CURCUMINOIDS ON OXIDATIVE STRESS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS," *Atherosclerosis*, vol. 241, no. 1, pp. E189-E190, Jul 2015, doi: 10.1016/j.atherosclerosis.2015.04.931.
- [27] V. P. Menon and A. R. Sudheer, "Antioxidant and anti-inflammatory properties of curcumin," *Molecular Targets and Therapeutic Uses of Curcumin in Health and Disease*, vol. 595, pp. 105-125, 2007.
- [28] A. Marchiani, C. Rozzo, A. Fadda, G. Delogu, and P. Ruzza, "Curcumin and Curcumin-like Molecules: From Spice to Drugs," *Current Medicinal Chemistry*, vol. 21, no. 2, pp. 204-222, Jan 2014.
- [29] B. A. C. Rattis, S. G. Ramos, and M. R. N. Celes, "Curcumin as a Potential Treatment for COVID-19," *Frontiers in Pharmacology*, vol. 12, May 2021, Art no. 675287, doi: 10.3389/fphar.2021.675287.
- [30] J. J. Bright, "Curcumin and autoimmune disease," *Molecular Targets and Therapeutic Uses of Curcumin in Health and Disease*, vol. 595, pp. 425-451, 2007.
- [31] O. J. Wouters, M. McKee, and J. Luyten, "Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018," *Jama-Journal of the American Medical Association*, vol. 323, no. 9, pp. 844-853, Mar 2020, doi: 10.1001/jama.2020.1166.
- [32] R. E. Amaro et al., "Ensemble Docking in Drug Discovery," *Biophysical Journal*, vol. 114, no. 10, pp. 2271-2278, May 2018, doi: 10.1016/j.bpj.2018.02.038.
- [33] H. Park, J. Lee, and S. Lee, "Critical assessment of the automated AutoDock as a new docking tool for virtual screening," *Proteins-Structure Function and Bioinformatics*, vol. 65, no. 3, pp. 549-554, Nov 2006, doi: 10.1002/prot.21183.
- [34] S. Schneckener et al., "[Prediction of Oral Bioavailability in Rats: Transferring Insights from in Vitro Correlations to (Deep) Machine Learning Models Using in Silico Model Outputs and Chemical Structure

- Parameters]," in JOURNAL OF CHEMICAL INFORMATION AND MODELING vol. 59, ed, 2019, pp. 4893-4905.
- [35] A. Vo, T. Van Vleet, R. Gupta, M. Liguori, and M. Rao, "[An Overview of Machine Learning and Big Data for Drug Toxicity Evaluation]," in CHEMICAL RESEARCH IN TOXICOLOGY vol. 33, ed, 2020, pp. 20-37.
- [36] M. Qneibi et al., "The inhibitory role of curcumin derivatives on AMPA receptor subunits and their effect on the gating biophysical properties," European Journal of Pharmaceutical Sciences, vol. 136, Aug 2019, Art no. 104951, doi: 10.1016/j.ejps.2019.06.005.
- [37] D. M. Lowe, P. T. Corbett, P. Murray-Rust, and R. C. Glen, "Chemical Name to Structure: OPSIN, an Open Source Solution," Journal of Chemical Information and Modeling, vol. 51, no. 3, pp. 739-753, Mar 2011, doi: 10.1021/ci100384d.
- [38] N. M. O'Boyle, M. Banck, C. A. James, C. Morley, T. Vandermeersch, and G. R. Hutchison, "Open Babel: An open chemical toolbox," Journal of Cheminformatics, vol. 3, Oct 2011, Art no. 33, doi: 10.1186/1758-2946-3-33.
- [39] G. M. Morris et al., "AutoDock4 and AutoDockTools4: Automated Docking with Selective Receptor Flexibility," Journal of Computational Chemistry, vol. 30, no. 16, pp. 2785-2791, Dec 2009, doi: 10.1002/jcc.21256.
- [40] P. Agu et al., "Molecular docking as a tool for the discovery of molecular targets of nutraceuticals in diseases management," SCIENTIFIC REPORTS, vol. 13, 2023-08-17 2023, Art no. 13398, doi: 10.1038/s41598-023-40160-2.
- [41] G. M. Morris et al., "Automated docking using a Lamarckian genetic algorithm and an empirical binding free energy function," Journal of Computational Chemistry, vol. 19, no. 14, pp. 1639-1662, Nov 1998, doi: 10.1002/(sici)1096-987x(19981115)19:14<1639::aid-jcc10>3.0.co;2-b.
- [42] A. Daina, O. Michielin, and V. Zoete, "SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules," Scientific Reports, vol. 7, Mar 2017, Art no. 42717, doi: 10.1038/srep42717.
- [43] C. A. Lipinski, F. Lombardo, B. W. Dominy, and P. J. Feeney, "Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings (Reprinted from Advanced Drug Delivery Reviews, vol 23, pg 3-25, 1997)," Advanced Drug Delivery Reviews, vol. 46, no. 1-3, pp. 3-26, Mar 2001, doi: 10.1016/s0169-409x(00)00129-0.
- [44] T. K. Karami, S. Hailu, S. X. Feng, R. Graham, and H. J. Gukasyan, "Eyes on Lipinski's Rule of Five: A New "Rule of Thumb" for Physicochemical Design Space of Ophthalmic Drugs," Journal of Ocular Pharmacology and Therapeutics, vol. 38, no. 1, pp. 43-55, Jan 2022, doi: 10.1089/jop.2021.0069.
- [45] L. Z. Benet, C. M. Hosey, O. Ursu, and T. I. Oprea, "BDDCS, the Rule of 5 and drugability," Advanced Drug Delivery Reviews, vol. 101, pp. 89-98, Jun 2016, doi: 10.1016/j.addr.2016.05.007.
- [46] W. L. Jorgensen and E. M. Duffy, "Prediction of drug solubility from structure," Advanced Drug Delivery Reviews, vol. 54, no. 3, pp. 355-366, Mar 2002, Art no. Pii s0169-409x(02)00008-x, doi: 10.1016/s0169-409x(02)00008-x.

- [47] L. Furge and F. Guengerich, "[Cytochrome P450 enzymes in drug metabolism and chemical toxicology]," in *BIOCHEMISTRY AND MOLECULAR BIOLOGY EDUCATION* vol. 34, ed, 2006, pp. 66-74.
- [48] M. Deodhar et al., "Mechanisms of CYP450 Inhibition: Understanding Drug-Drug Interactions Due to Mechanism-Based Inhibition in Clinical Practice," *PHARMACEUTICS*, vol. 12, 2020-09-01 2020, Art no. 846, doi: 10.3390/pharmaceutics12090846.
- [49] J. Lee, J. Kim, E. Lee, and J. Yoon, "Therapeutic Effect of Curcumin, a Plant Polyphenol Extracted From *Curcuma longae*, in Fibroblasts From Patients With Graves' Orbitopathy," *INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE*, vol. 60, pp. 4129-4140, 2019-10-01 2019, doi: 10.1167/iovs.19-27376.
- [50] J. Luo et al., "Herbal medicine for Hashimoto's thyroiditis: A systematic review and network meta-analysis," *JOURNAL OF ETHNOPHARMACOLOGY*, vol. 323, 2024-01-06 2024, Art no. 117663, doi: 10.1016/j.jep.2023.117663.
- [51] K. Zhang et al., "Chrysin suppresses human CD14⁺ monocyte-derived dendritic cells and ameliorates experimental autoimmune encephalomyelitis," *JOURNAL OF NEUROIMMUNOLOGY*, vol. 288, pp. 13-20, 2015-11-15 2015, doi: 10.1016/j.jneuroim.2015.08.017.
- [52] I. Zanoni et al., "CD14 Controls the LPS-Induced Endocytosis of Toll-like Receptor 4," *CELL*, vol. 147, pp. 868-880, 2011-11-11 2011, doi: 10.1016/j.cell.2011.09.051.
- [53] L. Jiang, G. Zhang, Y. Li, G. Shi, and M. Li, "Potential Application of Plant-Based Functional Foods in the Development of Immune Boosters," *FRONTIERS IN PHARMACOLOGY*, vol. 12, 2021-04-20 2021, Art no. 637782, doi: 10.3389/fphar.2021.637782.
- [54] C. Shivanika, S. D. Kumar, V. Raguathan, P. Tiwari, A. Sumitha, and P. B. Devi, "Molecular docking, validation, dynamics simulations, and pharmacokinetic prediction of natural compounds against the SARS-CoV-2 main-protease," *Journal of Biomolecular Structure & Dynamics*, vol. 40, no. 2, pp. 585-611, Jan 2022, doi: 10.1080/07391102.2020.1815584.
- [55] A. Jaradat, Y. Salameh, H. Zaid, and S. Shanak, "In Silico Evaluation for the Inhibitory Action of Curcumin Derivatives on the SARS-COV2," *Journal of Biosciences and Medicines*, vol. 10, no. 4, pp. 63-76, 2022.
- [56] S. Tahayneh, B. Qasem, H. Zakarneh, S. Shanak, and H. Zaid, "Ligand-Protein Docking of Gundelia tournefortii and Ocimum basilicum Derivatives in Scanning Hub Protein Targets (PI3K, PDK1, AKT, and RAC1) of the Insulin Signaling Pathway and ADME/Tox Drug Properties," *New Emirates Medical Journal*, vol. 5, 2024.
- [57] M. Manzari, Y. Shamay, H. Kiguchi, N. Rosen, M. Scaltriti, and D. Heller, "Targeted drug delivery strategies for precision medicines," *NATURE REVIEWS MATERIALS*, vol. 6, pp. 351-370, 2021-02-02 2021, doi: 10.1038/s41578-020-00269-6.
- [58] J. Yang, C. Jia, and J. Yang, "Designing Nanoparticle-based Drug Delivery Systems for Precision Medicine," *INTERNATIONAL JOURNAL OF MEDICAL SCIENCES*, vol. 18, pp. 2943-2949, 2021-01-01 2021, doi: 10.7150/ijms.60874.

-
- [59] K. Elokely and R. Doerksen, "Docking Challenge: Protein Sampling and Molecular Docking Performance," JOURNAL OF CHEMICAL INFORMATION AND MODELING, vol. 53, pp. 1934-1945, 2013-08-01 2013, doi: 10.1021/ci400040d.
- [60] T. Painsar and A. Poso, "Binding Affinity via Docking: Fact and Fiction," MOLECULES, vol. 23, 2018-08-01 2018, Art no. 1899, doi: 10.3390/molecules23081899.
- [61] L. Lupu et al., "Simultaneous C5 and CD14 inhibition limits inflammation and organ dysfunction in pig polytrauma," Frontiers in Immunology, vol. 13, Aug 2022, Art no. 952267, doi: 10.3389/fimmu.2022.952267.



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The Relationship between Nursing Informatics Competency and Caring Behaviors among Nurses in Intensive Care

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Abstract

Background: Intensive care nursing increasingly relies on information and communication technologies (ICT) and electronic medical records (EMRs), yet caring behaviors remain central to quality nursing practice. **Objectives:** The purpose of this study was to examine the relationship between nursing informatics competency and caring behaviors among ICU nurses in governmental hospitals in the West Bank, Palestine. **Methods:** A cross-sectional descriptive correlational study was conducted (Aug 1–Sep 1, 2025) among ICU nurses (N=224) recruited by convenience sampling from 10 governmental hospitals in the West Bank. Nursing informatics competency was measured using SANICS and caring behaviors using CBAN-SF. Data were analyzed using Pearson correlations, an independent t- test, and multiple linear regression. **Results:** Participants' mean age was 34.1±8.3 years; 75.9% were male, 79.0% held a bachelor's degree, and nurses spent 3.6±1.8 hours/shift using EMRs. Informatics competency was moderate overall (M=3.1±0.2), with the lowest subdomain in applied computer skills (M=2.3±0.5). Caring behaviors were high (M=103.9±14.6). Caring behaviors correlated strongly with SANICS (r=.867, p<.001) and EMR time (r=.716, p<.001). In regression, SANICS (B=50.17, p<.001), EMR time (B=1.22, p=.002), rotating shift (B=3.37, p=.001), and master's degree or higher (B= 2.61, p=.038) predicted caring behaviors; the model explained 78.3% of variance (R²=0.783). **Conclusion:** Among ICU nurses, higher nursing informatics competency especially alongside greater EMR engagement was associated with stronger caring behaviors. Strengthening applied informatics skills might help ensure technology functions as an enabler of patient-centered care rather than a barrier.

Keywords: Intensive Care Units, Nursing Informatics, Caring Behaviors, Patient-Centered Care

1. Introduction

The integration of information and communication technologies (ICT) into healthcare delivery has transformed nursing practice worldwide, particularly in intensive care units (ICUs), where critically ill patients require rapid, precise, and coordinated interventions [1,2]. Over the past two decades, the increasing adoption of electronic health records (EHRs), clinical decision support systems, patient monitoring technologies, and telehealth applications has underscored the importance of nursing informatics competency [3,4]. Nursing informatics competency refers to the knowledge, skills, and attitudes that enable nurses to effectively use health information systems to support evidence-based decision-making, improve care coordination, and ensure patient safety [5,6]. In the ICU setting, where patient conditions can deteriorate within minutes, strong informatics skills are indispensable for supporting timely interventions, enhancing interdisciplinary communication, and reducing preventable medical errors [7,8].

At the same time, the essence of nursing practice remains rooted in caring behaviors [9,10]. Caring in nursing is not only a professional value but also a relational process that encompasses empathy, emotional presence, advocacy, and holistic support for patients and their families [11,12]. Even in highly technological environments, patients and families consistently identify nurses' caring behaviors such as attentive listening, reassurance, and emotional support as critical determinants of satisfaction and trust in healthcare [13–14]. The ICU presents unique challenges to caring, as nurses must balance the technical demands of advanced monitoring and treatment with the psychosocial needs of vulnerable patients [15–16]. In this context, the interplay between technology and caring behaviors becomes highly significant [17].

1.1 Background

Despite the advantages of health technologies, concerns remain about their potential to depersonalize care [18]. Studies have reported that excessive documentation requirements, prolonged system navigation, and continuous interaction with monitoring devices can contribute to nurse frustration, burnout, and reduced opportunities for compassionate patient interactions [19]. For some nurses, the reliance on electronic systems creates a perceived barrier to establishing meaningful nurse patient relationships, raising fears of a decline in the humanistic aspects of care [20]. Conversely, research also suggests that high levels of informatics competency may empower nurses to streamline clinical processes, minimize medication errors, and allocate more time for therapeutic communication, thereby strengthening rather than diminishing caring behaviors [21].

1.2 Objectives

The purpose of the current study was to examine the relationship between nursing informatics competency and caring behaviors among ICU nurses in governmental hospitals in the West Bank, Palestine.

2. Related Work

Globally, a growing body of research has begun to explore the relationship between informatics proficiency and nursing care quality, yet findings remain inconsistent and context-dependent [22,23]. Some studies reported a positive association between informatics skills and nurses perceived caring efficacy, while others emphasized the risks of technological overload [2,19,21]. However, in Palestine, limited empirical evidence exists on this issue. Most local studies to date have examined either nursing informatics training and barriers to technology adoption, or nurses' caring behaviors and patient perceptions in isolation, without integrating the two domains. The Palestinian healthcare system presents additional contextual factors that make this inquiry important. ICUs in the West Bank often operate under resource constraints, with limited staffing, high patient acuity, and variable access to advanced health technologies [24]. Ultimately, the findings may guide the development of targeted educational strategies, capacity-building initiatives, and supportive policies that balance the dual imperatives of informatics and caring, ensuring that technology serves as an enabler rather than a barrier to patient-centered nursing practice.

3. Methodology

3.1 Design, Setting, Population, and Sample

A cross-sectional, descriptive correlational study was conducted among ICU nurses in the West Bank, Palestine, between August 1 and September 1, 2025. The sample size was calculated using Raosoft software with the following parameters: a population size of 500, a 50% response distribution, a 5% margin of error, and a 95% confidence interval, yielding a required sample of 218 participants. To accommodate potential non-responses, a convenience sample of 240 ICU nurses was initially recruited from 10 governmental hospitals across the West Bank. Ultimately, 224 nurses completed and returned the questionnaires. Governmental hospitals were selected because they play a pivotal role in delivering public healthcare services to a wide and diverse patient population. Moreover, these hospitals function under unified regulations and often face resource limitations, making them ideal for exploring the practical application of caring behaviors and nursing informatics in settings where efficiency and adaptability are essential.

To ensure that the participants had completed unit orientation/preceptorship and sufficient exposure to ICU workflows and routine EMR use, it was determined that the eligible participants should be full-time ICU nurses with at least six-month experience. This, in turn, would provide stable self-assessments of informatics competency and caring behaviors and willingness to participate. Nurses who were on leave or absent during the data collection period were excluded.

3.2 Study instruments

A structured self-administered survey was used to collect data from participants. The survey consisted of three main components:

Socio-demographic variables (i.e., age, gender, education level, years of ICU experience, work shift, and time spent using EMRs during a shift).

The SANICS, developed by Yoon et al. (2009) [25], was used to evaluate nurses' self-perceived informatics competencies across five domains: basic computer knowledge and skills, wireless device skills, clinical informatics knowledge, clinical informatics attitudes, and applied computer skills for clinical practice. The scale contains 30 items rated on a 5-point Likert scale, ranging from 1 (not competent at all) to 5 (very competent), with higher scores indicating greater informatics competency. Competency levels were categorized using mean scores as follows: low/novice (1.00–2.59), moderate/beginner (2.60–3.39), and high/competent (3.40–5.00) [26]. The SANICS has demonstrated strong validity and reliability [25,26]. Additionally, it has been culturally validated for use in Palestine [27,28]. In the current study, the tool showed excellent internal consistency, with a Cronbach's alpha of 0.90.

The CBAN-SF, developed by Akgün et al. (2020) [29], was used to evaluate participants' perceptions of caring behaviors. This instrument comprises 27 items rated on a five-point Likert scale (1 = least important to 5 = most important), covering seven domains: humanism/faith-hope/sensitivity, helping/trust, expression of positive/negative feelings, supportive/protective/corrective environment, teaching/learning, human needs assistance, and existential/phenomenological/spiritual forces. Total scores range from 27 to 135, with higher scores indicate higher perceived importance of caring behaviors. The CBAN-SF has demonstrated strong psychometric validity, with an overall Cronbach's alpha of 0.97 and subscale alphas ranging from 0.79 to 0.90 [29]. Additionally, it has been culturally validated for use in Palestine [9,30]. In the current study, the tool showed excellent internal consistency, with a Cronbach's alpha of 0.92.

3.3 Data Collection

Following ethical approval from the relevant institutional review board, the researchers visited the selected hospitals and identified the head nurses responsible for ICUs. During the initial meetings, the researchers explained the study's purposes and procedures and requested staff rosters and work schedules to facilitate participant recruitment.

Face-to-face sessions were subsequently conducted with ICU nurses to present the study objectives and methodology in detail. Nurses who agreed to participate were asked to sign an informed consent form, confirming their voluntary participation.

The researcher also used anonymous questionnaires, in which no personally identifiable information is recorded, stored, or linked to a participant's responses, which were then returned in sealed envelopes to a locked collection box accessed by the researcher only. This safeguarded the participants' privacy and the confidentiality of the process. Those paper-based questionnaires were distributed in person during nurses' break times to minimize disruption to clinical duties and were answered in English since the Palestinian nurses are proficient in English.

3.4 Analysis Methods

Data were analyzed using IBM SPSS Statistics version 28. Prior to analysis, the dataset was examined for completeness, missing values, and normality to ensure the integrity of inferential tests. The data met the assumptions of normality, and no missing values were identified. Descriptive statistics (means, standard

deviations, frequencies, and percentages) were used to summarize participants' demographic characteristics, nursing informatics competency, and caring behaviors scores. To identify significant predictors of caring behaviors, multiple linear regression analysis was conducted. Variables showing significant associations or differences in the bivariate analysis ($p < 0.05$) were included in the regression model using the enter method. Statistical significance was set at $p < 0.05$.

4. Experiments and Results

A total of 224 out of 240 participants completed the study, yielding a response rate of 93.3%. The mean age of participants was 34.1 ± 8.3 years, with the majority being male 170 (75.9%). Most participants held a bachelor's degree 177 (79.0%), and their average nursing experience was 9.6 ± 7.7 years. Additionally, 155 participants (69.2%) reported working rotating shifts. On average, they spent 3.6 ± 1.8 hours per shift using EMRs, as shown in Table 1.

Table 1. Demographic Characteristics of the Study Sample (N=224)

Characteristics	Categories	N (%)	M (SD)
Age			34.1(8.3)
Gender	Male	170 (75.9)	
	Female	54 (24.1)	
Educational Level	Bachelor's	177 (79.0)	
	Master's and above	47 (21.0)	
Experience in ICU			9.6(7.7)
Work Shift	Day Shift	69 (30.8)	
	Rotation Shift	155 (69.2)	
Time Spent on EMR during Shift			3.6(1.8)

The analysis revealed that that participant reported a moderate level of nursing informatics competency ($M = 3.1 \pm 0.2$). Among the subdomains, the highest mean score was in Clinical informatics role ($M = 3.8 \pm 0.9$), while the lowest was in Applied computer skills for clinical informatics ($M = 2.3 \pm 0.5$). Concerning caring behaviors, the average score was ($M = 103.9 \pm 14.6$), reflecting a strong satisfaction with caring behaviors. The highest mean scores were in the dimensions of Expression of Positive/Negative Feelings ($M = 4.0 \pm 0.4$) and Human Needs Assistance ($M = 4.0 \pm 0.8$), while Teaching/Learning had the lowest mean score ($M = 3.7 \pm 0.7$) and Helping/Trust ($M = 3.7 \pm 0.8$), as seen in Table 2.

Table 2. Levels of Nursing Informatics Competency and caring behaviors among participants

Variable	M (SD)	Range
SANICS	3.1(0.2)	1-5
Basic computer knowledge and skills	2.6(0.2)	1-5
Wireless device skills	3.2(0.2)	1-5
Clinical informatics role	3.8(0.9)	1-5
Clinical informatics attitude	3.1(0.2)	1-5
Applied computer skills for clinical informatics	2.3(0.5)	1-5
Caring Behaviors	103.9(14.6)	27-135
Humanism/Faith-hope/Sensitivity	3.9(0.5)	1-5
Helping/Trust	3.7(0.8)	1-5
Expression of Positive/Negative Feelings	4.0(0.4)	1-5
Teaching/Learning	3.7(0.7)	1-5
Supportive/Protective/Corrective Environment	3.8(0.7)	1-5
Human Needs Assistance	4.0(0.8)	1-5

Existential/Phenomenological/Spiritual Forces	3.9 (0.4)	1-5
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M: Mean; SD: Standard Deviation

The analysis revealed that caring behaviors were strongly and positively correlated with SANICS scores ($r = .867$, $p < .001$) and time spent on EMRs during shifts ($r = .716$, $p < .001$), while they were negatively correlated with age ($r = -.358$, $p < .001$) and ICU experience ($r = -.347$, $p < .001$). Caring behaviors were significantly higher among nurses working rotating shifts compared to those on fixed day shifts ($p = .006$) and among those with a master's degree or higher compared to bachelor's degree holders ($p = .020$), as seen in Table 3.

Table 3. Factors Correlating with caring behaviors among the Participants

Variable		N	M	SD	Statistical test	P. Value
SANICS					$r = .867^{**}$	$p < .001$
Age					$r = -.358^{**}$	$p < .001$
Time Spent on EMR during Shift					$r = .716^{**}$	$p < .001$
Experience in ICU					$r = -.347^{**}$	$p < .001$
Gender	Male	170	102.8941	14.74961	$t = -1.878$	.064
	Female	54	107.0185	13.83664		
Work Shift	Day	69	99.6522	15.62504	$t = -2.805$	.006
	Rotation	155	105.7742	13.77441		
Educational level	Bachelor	177	102.7345	14.60163	$t = -2.378$	.020
	Master and above	47	108.2340	13.95834		

Table 4 shows the unstandardized regression coefficients for predictors of caring behaviors. The model was statistically significant ($p < .001$), explaining 78.3% of the variance in caring behaviors. For every one-unit increase in SANICS, caring behavior scores increased by 50.2 points ($p < .001$). Time spent on EMRs during shifts also had a positive effect, with each additional hour associated with a 1.2-point increase ($p = .002$). Nurses working rotating shifts scored 3.4 points higher than those on day shifts ($p = .001$). Additionally, having a master's degree or higher was associated with a 2.6-point increase in caring behavior scores ($p = .038$).

Table 4. Predictors of caring behaviors

Predictors	B	Beta	t. test	p-value	95.0% CI		Collinearity	
					Lower	Upper	Tolerance	VIF
SANICS	50.171	.780	15.038	$p < .001$	43.596	56.747	.371	2.697
Age	-.452	-.257	-1.269	.206	-.250	1.154	.024	4.942
Time Spent on EMR during Shift	1.223	.153	3.133	.002	.454	1.993	.420	2.380
Experience in ICU	-.438	-.231	-1.159	.248	-1.183	.307	.025	3.861
Work Shift (Rotation)	3.371	.107	3.230	.001	1.314	5.428	.914	1.094
Educational Level (Master or above)	2.606	.073	2.092	.038	.151	5.060	.825	1.212
R= 0.885, R ² = 0.783, Adjusted R ² = 0.777, F = 130.830, $p < .001$, Durbin-Watson= 0.357								

5. Discussion

This study found moderate nursing informatics competency alongside high perceived caring behaviors. Importantly, caring behaviors showed a strong positive correlation with informatics competency and with time spent using EMRs during the shift. In the multivariable model, SANICS and EMR time remained significant predictors, and the model explained a large proportion of variance in caring behaviors. These findings suggest that, in this sample, informatics capability is not competing with caring; rather, it is statistically aligned with nurses' perceptions of caring practice. A rational interpretation is that informatics competency may function as an "enabler" of caring in technology-dense ICU work. When nurses can navigate documentation, retrieve information efficiently, and use systems confidently, cognitive load and workflow friction may decrease freeing attention for presence, communication, and responsiveness. This aligns with broader evidence that ICTs can influence multiple dimensions of nursing care (including time management, documentation quality, and nurse patient relationship), with effects depending on implementation and users' competence [2]. The ICU context is especially relevant: digital systems and bedside devices shape rounds and interprofessional work, and nurses' ability to integrate these tools into clinical routines affects both efficiency and human interaction [1]. From a caring-science perspective, technology is ethically acceptable when it supports, rather than replaces, the relational and humanistic core of nursing so competence becomes a practical pathway for protecting caring values under technological pressure [12].

In the Palestinian context, the strong association observed in this study was plausible because governmental hospitals often face intense workload and system constraints; in such environments, being "fluent" with EMRs and digital workflows may be one of the few immediately modifiable factors that helps nurses preserve caring behaviors under pressure. The Palestinian Ministry of Health has explicitly pursued digital transformation and strengthened health information management, while also acknowledging ongoing challenges such as limited technical staffing and insufficient staff capacity/skills in information technology[31]. When workforce capability is uneven, informatics competency can become a differentiator: nurses who are more competent may experience fewer delays, fewer documentation backlogs, and smoother coordination conditions that plausibly support more consistent caring behaviors.

The results also showed caring behaviors were negatively correlated with age and ICU experience in bivariate analysis. One reasonable explanation is not that older/more experienced nurses "care less," but that prolonged exposure to high-acuity environments plus repeated administrative burdens can erode perceived caring performance or the time available for visible caring behaviors (a pattern discussed in the broader literature on technology burden and work strain). In the West Bank, evidence from other recent hospital studies highlights the importance of patient-centered communication and the reality of resource-limited settings, where staffing and workload issues can shape nursing care experiences [32]. In such conditions, informatics competency may partially buffer the "time squeeze" by making required system tasks faster and less disruptive, thereby protecting caring behaviors.

Finally, the finding that nurses spent an average of 3.6 hours per shift using EMRs reinforces how central digital work has become in ICU nursing. In Palestine, efforts to strengthen and integrate electronic records and national health information systems continue to evolve, including initiatives to unify records within national information platforms [31]. At the same time, published work on EHR development in Palestine emphasizes persistent barriers such as interoperability, infrastructure, and governance factors that can either amplify or reduce

documentation burden at the bedside [33]. Therefore, beyond individual training, system-level usability, workflow design, and policy support are essential to ensure technology strengthens (rather than fragments) caring practice in Palestinian ICUs.

6. Strengths and limitations

This study's strengths include its multi-center sample from 10 West Bank governmental hospitals, a high response rate (93.3%), and the use of validated, reliable instruments with strong internal consistency in this sample (SANICS $\alpha=0.90$; CBAN-SF $\alpha=0.92$), alongside multivariable regression to identify predictors of caring behaviors.

Limitations include the cross-sectional, convenience-sampling design (limiting causality and generalizability), exclusive focus on governmental hospitals in the West Bank (excluding other Palestinian settings), and reliance on self-reported measures collected at one time point, which increases risk of social desirability and common-method bias especially relevant given the very strong correlation between informatics competency and caring behaviors ($r=.867$).

Future research should use longitudinal or prospective designs and multi-source/objective indicators (e.g., supervisor ratings, chart audit/usage logs, patient outcomes) to reduce shared-method variance and clarify directionality. Mechanisms could be tested by examining whether variables such as workload, unit culture, training exposure, or self-efficacy mediate or moderate the relationship between informatics competency and caring behaviors, and by evaluating targeted educational interventions using experimental or quasi-experimental designs.

7. Conclusions and Future Work

Among ICU nurses in West Bank governmental hospitals, nursing informatics competency was moderate overall with a notable deficit in applied clinical computer skills, while caring behaviors were high. Nursing informatics competency showed a strong positive association with caring behaviors and remained the most influential predictor in multivariable analysis, alongside EMR time, rotating shifts, and higher education. These findings support prioritizing practical informatics capacity-building in Palestinian ICUs paired with workflow improvements so that expanding digital health systems strengthens (rather than constrains) patient-centered caring

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9. Declarations

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Consent for publication

Not applicable.

Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest/Competing interests

Researcher declares no conflict of interest with any organization regarding the materials discussed in this paper.

Ethics approval and consent to participate

Ethical approval for this study was granted by the Arab American University (IRB: J-2025/A/36/N). Prior to distributing consent forms, the researcher clearly explained the study's purpose, voluntary nature, and the participants' right to withdraw at any time without consequences. Only those who provided written informed consent were included in the study. Participants' confidentiality was strictly maintained throughout the research process. No names or identifying personal information were collected or disclosed. All data were handled securely and used solely for research purposes.

Author(s) Contribution

Ahmad Ayed conducted the study and wrote the manuscript. The author read and approved the final manuscript.

References

- [1] Plumb, J. J., Hains, I., Parr, M. J., Milliss, D., Herkes, R., & Westbrook, J. I. (2017). Technology meets tradition: The perceived impact of the introduction of information and communication technology on ward rounds in the intensive care unit. *International Journal of Medical Informatics*, 105, 49–58. <https://doi.org/10.1016/j.ijmedinf.2017.04.004>
- [2] Rouleau, G., Gagnon, M. P., Côté, J., Payne-Gagnon, J., Hudson, E., & Dubois, C. A. (2017). Impact of information and communication technologies on nursing care: results of an overview of systematic reviews. *Journal of Medical Internet Research*, 19(4), e122. <https://doi.org/10.2196/jmir.6686>
- [3] Ge, S., Song, Y., Hu, J., Tang, X., Li, J., & Dune, L. (2022). The development and impact of adopting electronic health records in the United States: A brief overview and implications for nursing education. *Health Care Science*, 1(3), 186. <https://doi.org/10.1002/hcs2.21>
- [4] McGrow, K. (2025). *Empowering Nurses with Technology: A Practical Guide to Nurse Informatics*. CRC Press.
- [5] Hussey, P., & Hannah, K. J. (2021). Nursing informatics: a core competency for the profession. In *Introduction to Nursing Informatics* (pp. 55–85). Springer. https://doi.org/10.1007/978-3-030-58740-6_3
- [6] McGonigle, D., & Mastrian, K. (2024). *Nursing informatics and the foundation of knowledge*. Jones & Bartlett Learning.
- [7] Gopalan, P. D., & Pershad, S. (2019). Decision-making in ICU—a systematic review of factors considered important by ICU clinician decision makers with regard to ICU triage decisions. *Journal of Critical Care*, 50, 99–110. <https://doi.org/10.1016/j.jcrc.2018.11.027>
- [8] Yee, A. (2023). Clinical decision-making in the intensive care unit: a concept analysis. *Intensive and Critical Care Nursing*, 77, 103430. <https://doi.org/10.1016/j.iccn.2023.103430>

- [9] Ayed, A., Ejheisheh, M. A., Salameh, B., Batran, A., Obeyat, A., Melhem, R., & Alkhatib, S. (2024). Insights into the relationship between professional values and caring behavior among nurses in neonatal intensive care units. *BMC Nursing*, 23(1), 692. <https://doi.org/10.1186/s12912-024-02343-8>
- [10] Labrague, L. J., & Obeidat, A. A. (2025). Pedagogical approaches to foster caring behaviors among nursing students: A scoping review. *Nurse Education Today*, 146, 106547. <https://doi.org/10.1016/j.nedt.2024.106547>
- [11] Atta, M. H., Hammad, H. A., & Elzohairy, N. W. (2024). The role of empathy in the relationship between emotional support and caring behavior towards patients among intern nursing students. *BMC Nursing*, 23(1), 443.
- [12] Watson, J. (2009). *Assessing and measuring caring in nursing and health science* (2nd ed.). Springer.
- [13] Abou Hashish, E. A. (2025). Compassion through technology: Digital empathy concept analysis and implications in nursing. *Digital Health*.
- [14] Sedighi, S., Sadeghi, A., Roshanaei, G., & Purfarzad, Z. (2025). The relationship between nurses' caring behaviors and patient loyalty: trust towards nurses as a mediating role. *BMC Nursing*.
- [15] Al-Anzi, M. L., Al-Ruwaili, I. A., Al-Anzi, S. L., Al-Radini, N. A., Al-Ruwaili, N. A., Aljohani, A. M., Aljohani, S. M., Alharbi, W. S., Aljohani, J. S., & Alrashidy, A. M. (2024). Improving patient outcomes in critical care: The impact of nursing interventions. *Journal of International Crisis and Risk Communication Research*.
- [16] Henriksen, K. F., Hansen, B. S., Wøien, H., & Tønnessen, S. (2021). The core qualities and competencies of the intensive and critical care nurse: a meta-ethnography. *Journal of Advanced Nursing*.
- [17] Campo, A. M., Avolio, B., & Carlier, S. I. (2021). The relationship between telework, job performance, work-life balance and family supportive supervisor behaviours in the context of COVID-19. *Global Business Review*.
- [18] Marion, S., Ghazal, L., Roth, T., Shanahan, K., Thom, B., & Chino, F. (2024). Prioritizing patient-centered care in a world of increasingly advanced technologies and disconnected care. *Seminars in Radiation Oncology*.
- [19] Baxi, V. V., Banerjee, S., Patel, M. A., Sinha, R., & Khan, S. (2024). Enhancing patient safety in critical care: Challenges, strategies, and emerging innovations. *Journal of Medical and Dental Frontiers*.
- [20] Wahyuningtyas, E. S., & Abd-Elrazek, M. N. (2024). Nurses are never gone or forgotten: Breaking barriers to enhance nursing care with technology. *Journal of Holistic Nursing Science*.
- [21] Meissen, H., Gong, M. N., Wong, A. K., Zimmerman, J. J., Nadkarni, N., Kane-Gil, S. L., Amador-Castaneda, J., Bailey, H., Brown, S. M., DePriest, A. D., & Eche, I. M. (2022). The future of critical care: optimizing technologies and a learning healthcare system to potentiate a more humanistic approach to critical care. *Critical Care Explorations*.
- [22] Dang, Q., & Li, G. (2025). Unveiling trust in AI: The interplay of antecedents, consequences, and cultural dynamics. *AI & Society*.
- [23] Ng, J. J., Wang, E., Zhou, X., Zhou, K. X., Goh, C. X., Sim, G. Z., Tan, H. K., Goh, S. S., & Ng, Q. X. (2025). Evaluating the performance of artificial intelligence-based speech recognition for clinical documentation: a systematic review. *BMC Medical Informatics and Decision Making*.

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- [24] Bardhia, M., Batran, A., Ayed, A., Ejheisheh, M. A., Alassoud, B., & Abu-Siam, I. (2025). The relationship between the nurse practice environment and perceived patient-centered care in intensive care units. *SAGE Open Nursing*.
- [25] Yoon, S., Yen, P., & Bakken, S. (2009). Psychometric properties of the self-assessment of nursing informatics competencies scale. *Studies in Health Technology and Informatics*.
- [26] Mohamed, L. K., & Abouzaied, M. T. (2021). Self-assessment of nursing informatics competencies and attitudes among baccalaureate-nursing students. *Egyptian Nursing Journal*.
- [27] Amer, B., Ayed, A., Malak, M., & Bashtawy, M. (2025). Nursing informatics competency and self-efficacy in clinical practice among nurses in Palestinian hospitals. *Hospital Topics*.
- [28] Batran, A., Al-Humran, S. M., Malak, M. Z., & Ayed, A. (2022). The relationship between nursing informatics competency and clinical decision-making among nurses in West Bank, Palestine. *Computers, Informatics, Nursing*.
- [29] Akgün, M., Turan Kavradım, S., Boz, İ, Özer Z (2020). Development and psychometric properties of the Caring Behaviors Assessment Tool Nursing Version-Short Form. *International Journal for Quality in Health Care*. 32(10):701-707. <https://doi.org/10.1093/intqhc/mzaa134>
- [30] Ejheisheh, M. A., Ayed, A., Salameh, B., Ali, A. M., Alkubati, S. A., Batran, A., Jafari, W., & Alkhatib, S. (2025). Understanding the relationship between professional values and caring behavior among nurses in intensive care units: a cross-sectional study from Palestine. *BMC Nursing*.
- [31] Nemer, M., Araj, M., Basha, H., Wahdan, Y., & Abu-Rmeileh, N. (2025). Health system and policy response to climate change in the West Bank, Palestine: Current situation and priority actions. *PLOS Global Public Health*.
- [32] Smerat, H., Abu Ejheisheh, M., Ayed, A., Aqtam, I., & Batran, A. (2025). Patient satisfaction with the quality of nursing care in critical care units and medical wards in West Bank hospitals, Palestine. *PLOS ONE*.
- [33] El Jabari, C., Macedo, M., & Al-jabari, M. O. (2020). Towards a new paradigm of federated electronic health records in Palestine. *Informatics*.



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Relaxation Dynamics of QDLs Subjected to Optical Feedback

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Abstract

Background: Quantum dot lasers (QDLs) are promising semiconductor laser devices due to their discrete energy levels and strong carrier confinement, which enable high-speed operation and improved performance in applications such as optical communications, sensing, and quantum information processing. The interaction of these lasers with optical feedback significantly affects their dynamic behavior and stability. **Objectives:** This study aims to investigate the relaxation dynamics and stability characteristics of quantum dot lasers subjected to optical feedback by analyzing the influence of injection rate and detuning frequency on the system behavior. **Methods:** A theoretical analysis based on a rate-equation model describing the complex electric field, carrier density in the wetting layer, and occupation probability in quantum dots was employed. The steady-state conditions were obtained, and the Jacobian matrix was used to derive an analytical expression for the growth rate. Numerical simulations were then performed to evaluate the relaxation oscillation frequency and damping rate and to compare the dynamics of QDLs with and without optical feedback. **Results:** The results show that optical feedback increases the relaxation oscillation frequency and decreases the damping rate as the injection rate increases, leading to reduced system stability and the emergence of instability regions. For negative detuning frequency, bistability regions appear, enabling potential applications in optical switching and optical data storage. **Conclusions:** Optical feedback significantly influences the dynamical response of QDLs, modifying their stability and oscillatory behavior. These findings provide insights for controlling laser dynamics and improving the design of quantum dot laser systems for advanced photonic applications.

Keywords: Quantum dot lasers, stability, relaxation oscillation, damping rates, rate -equation approach.

1. Introduction

In the realm of modern photonics, the development of novel semiconductor lasers has been a key point for researchers aiming to enhance device performance and functionality. Among them, Quantum dot lasers with their unique electronic structure and discrete energy levels have emerged as promising candidates for a wide range

of applications [1], from optical communications [2] to quantum information processing [3]. One critical factor that significantly influences the dynamic response of these lasers is their interaction with optical feedback. Such optical feedback may be originated from external mirrors, optical source or unwanted reflections from the laser's operating environment. Understanding the interaction between quantum dot lasers and optical feedback has become important to meet the demands of advanced applications. Rate equations provide a fundamental framework for understanding the dynamics of quantum dot lasers (QDLs) by examining various factors. A lot of efforts have been directed toward formulating suitable rate equations for solitary QDLs [4,5,6,7,8]. Refining these rate equations, researchers can extend them to incorporate the effects of optical feedback, offering a more comprehensive view of the complex behaviours of QDLs [9,10,11,12].

The objective of this paper was to manipulate appropriate rate equations to study the dynamic response of QDLs under optical feedback, by finding an analytical expression of growth rate σ which in turn gives valuable insight about damping rate and relaxation oscillation frequency. In addition, a simulation method was used to validate the results by studying the response of QDL of a five-layer structure grown by solid-source MBE to optical feedback.

The rate equations for a QDLs subject to optical feedback were formulated by D. Goulding [14], which include three equations for the complex electric field E , the occupation probability in a dot ρ , and the carrier density n in the wetting layers. The complete set of equations are:

$$E' = \frac{1}{2}(1 + i\alpha)[-1 + g(2\rho - 1)]E + re^{i\Delta t} \quad (1.1)$$

$$\rho' = \eta[Bn(1 - \rho) - \rho - (2\rho - 1)E^2] \quad (1.2)$$

$$n' = \eta[J - n - 2Bn(1 - \rho)] \quad (1.3)$$

where the prime means differentiation with respect to $t = \frac{t'}{\tau_{ph}}$. α is the linewidth enhancement factor. Γ : injection rate. Δ : detuning frequency. $B = \tau\tau_{cap}^{-1}$ Dimensionless capture rate, where τ is the carrier recombination time and τ_{cap} is the capture time. $\eta = \tau_{ph}\tau^{-1}$ is the ration between photon lifetime τ_{ph} and the recombination time τ . the factor $1 - \rho$ is the Pauli blocking factor. The factor 2 in eq 1.3 accounts for the spin degeneracy in the QD energy level.

The previous rate equations were analyzed. This involved examining the effect of small perturbations around the steady state condition by taking derivatives of the rate equations and setting them equal to zero to find the steady state condition. After that, the partial derivative with respect to the state variables were used to construct the jacobian matrix. The characteristic equation was applied to evaluate the eigenvalues of this matrix at the steady state. These eigenvalues would provide valuable insight about relaxation oscillation and damping rate.

2. Reduced Rate Equations

The researchers first reduced the rate equation by introducing $\epsilon = g - 1$, $\rho = 1 + \epsilon u$, $s = \epsilon t$, $\gamma = \epsilon^{-1}\Gamma$, $\delta = \epsilon^{-1}\Delta$

Then the following equation was obtained:

$$E' = \frac{1}{2}(1 + i\alpha)[2u(1 + \epsilon)]E + \gamma e^{i\epsilon\delta\epsilon^{-1}s} \quad (2.1)$$

$$u' = \eta\epsilon^{-2}[-Bnu\epsilon - 1 - \epsilon u - (2\epsilon u + 1)E^2] \quad (2.2)$$

$$n' = \eta\epsilon^{-1}[J - n + 2Bn\epsilon u] \quad (2.3)$$

the prime means differentiation with respect to s . Since $\epsilon^{-2} \gg \epsilon^{-1}$ as $\epsilon \rightarrow 0$, u is faster than n and it could be eliminated adiabatically from equation (2.2) then

Also, the complex electric field was composed of both the real part, which is related to the amplitude, and the imaginary part which is related to the phase. It could be substituted as:

$$E = R e^{i\delta s + i\varphi} \quad (2.4)$$

Then the reduced rate equations were:

$$R' = \frac{1}{2} \left[1 - \frac{2(1 + R^2)}{Bn\epsilon} \right] R + \gamma \cos\varphi \quad (2.5)$$

$$\varphi' = -\delta + \frac{1}{2}(\alpha) \left[1 - \frac{2(1 + R^2)}{Bn\epsilon} \right] - \frac{\gamma \sin\varphi}{R} \quad (2.6)$$

$$n' = \eta\epsilon^{-1}[J - n - 2(1 + R^2)] \quad (2.7)$$

Understanding the impact of these parameters on the dynamical properties of a QD laser was precisely the objective of our work.

3. Growth Rate

From equations 2.5 to 2.7, the researchers determined the steady states and conditions. For simplicity, they introduced:

$$F = \frac{1}{2} \left[1 - \frac{2(1 + R_s^2)}{B\epsilon(J - 2(1 + R_s^2))} \right] \quad (3.1)$$

Then, the steady state conditions were:

$$FR_s = (\gamma \cos\varphi)_s \quad (3.2)$$

$$(-\delta + \alpha F)R_s = (\gamma \sin\varphi)_s \quad (3.3)$$

$$n_s = J - 2(1 + R^2) \quad (3.4)$$

By taking the square of both sides of (3.2) and (3.3) and adding them the researchers found:

$$(F^2 + (-\delta + \alpha F)^2)R_s^2 = \gamma^2 \quad (3.5)$$

From the linearized equations, the researchers then formulated the characteristic equation for the growth rate [16]: σ

$$\sigma^3 + a_1\sigma^2 + a_2\sigma + a_3 = 0 \quad (3.6)$$

Where:

$$a_1 = -(G - F - \eta\epsilon^{-1}) \quad (3.7)$$

$$\begin{aligned} a_2 = & -(FG + G\eta\epsilon^{-1} - F\eta\epsilon^{-1}) \\ & + ((\delta - \alpha F)\alpha(F - G) + (\delta - \alpha F)^2) \\ & + (1 - 2F)(F - G)B\eta \end{aligned} \quad (3.8)$$

The researchers could expand in powers of ϵ since it did not appear in steady state expressions [13], the researchers introduced ϵ in jacobian matrix, then they equated each coefficient of ϵ to zero, which led to set of equation in term of ϵ and η . Solving these equations, the researchers obtained: $\sigma\eta\sigma = \eta^{\frac{1}{2}}\lambda_0 + \eta\lambda_1 + \dots \eta\lambda_0\lambda_1$

$$\begin{aligned} \sigma_1 \approx & \pm i \sqrt{(F - G) \left(\frac{2 \frac{(1 - 2F)B - 2\epsilon^{-1}}{5} \pm}{5} \sqrt{\frac{((1 - 2F)B - 2\epsilon^{-1})^2}{-5\epsilon^{-1}(\epsilon^{-1} + (1 - 2F)B)}} \right) \eta} \\ & + \left(\frac{(1 - 2F)B - 2\epsilon^{-1}}{5} \right. \\ & \left. \pm \frac{1}{5} \sqrt{\frac{((1 - 2F)B - 2\epsilon^{-1})^2}{-5\epsilon^{-1}(\epsilon^{-1} + (1 - 2F)B)}} \right) \eta \end{aligned} \quad (3.10)$$

the real part represents the damping rate which is related to the stability of the mode while the imaginary part represents the RO frequency of the mode. When the real part is negative, the mode exhibits stability and the excited oscillations damped out for a time development with frequency determined from the imaginary part. However, a positive real part means the unstability of the mode and the laser exhibits regular or irregular oscillations with a frequency corresponding to the imaginary part [15].

Table 1. Physical parameters used in the simulation of the QDL model unless stated otherwise.

Parameter	Value
g	1.01
ϵ	0.01

B	10^2
J_{th}	4
α	1.2
η	2×10^{-3}

4. Numerical Results

In order to investigate the previous results, the researchers examined the response of QDL of a five-layer structure grown by solid-source MBE to optical feedback. This QDL consist of 2.4 InAs monolayers topped with 5 nm GaInAs stacked in a 400 nm thick optical cavity. A GaAs spacer of 35 nm is also used between the QD layers. The constants shown in table 1 below are used in the following discussion [17].

The researchers characterized the dynamics of QDL subjected to the optical feedback that operate above threshold region $J \Rightarrow J_{th}$. The control parameters that are varied are the detuning frequency and the injection rate.

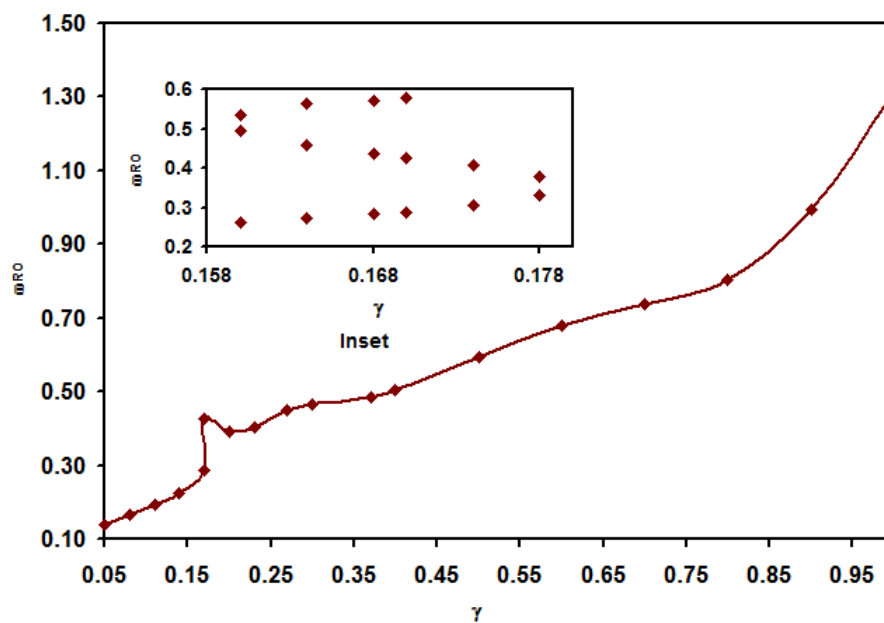


Figure 1. RO frequency ω_{RO} versus injection rate γ for $\delta = -0.4$. The inset represents different value of RO frequency ω_{RO} in bistability region.

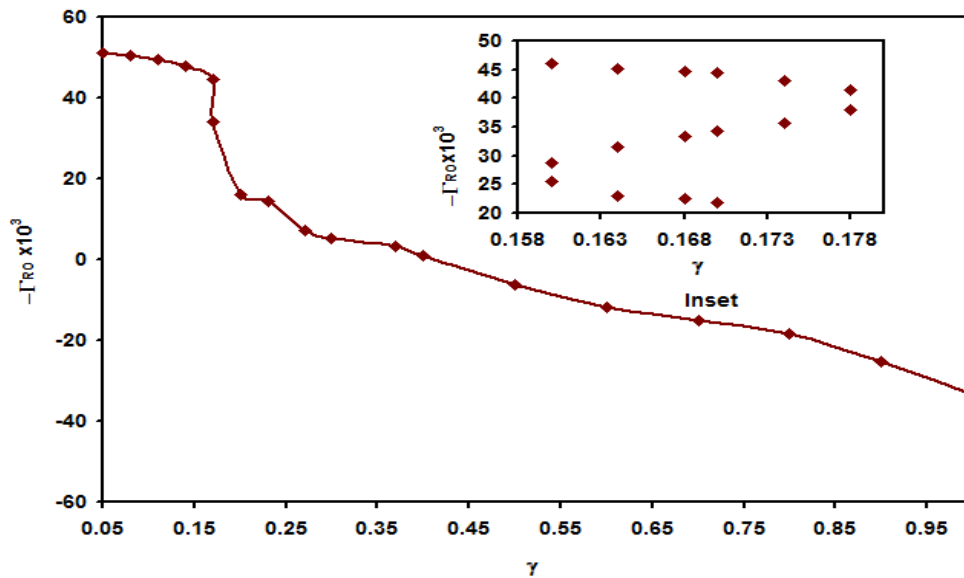


Figure 2. Damping rate Γ_{RO} versus injection rate γ for $\delta = -0.4$. The inset represents different value of damping rate Γ_{RO} in bistability region.

To visualize the effect of changing the injection rate in the dynamics of the system, the researchers manipulated two cases: one for negative and other for positive ($=$) detuning frequency by varying the injection rate up to. For each negative and positive detuning frequencies, the RO frequency increased and the damping rate decreased as illustrated in figures 1, 2 and 3. This implied that further increasing of the injection rate, the system tends toward instability and chaotic behaviour. In both cases, the solution gave a negative damping rate for low injection rate, which implied the stability of the system (Yamada, 2014). Further increasing of injection rate, the damping rate becomes positive and so the system goes to instabilities. It is worth noting that for ($=$) the system exhibits stability over a wide range of injection rate than . In the case of , different values of both damping rate and relaxation oscillation for the same injection rate in the inset of figure 1 and 2 indicated the appearance of bistability or excitability. While it is absent for Bistability means the ability of the system to operate at two stable states with different intensities [18], which enables the system to transit from one state to another at specific conditions. This provides the opportunities for control and manipulation the laser output which can be utilized in various optical technologies such as optical switching [19] and optical memory. ($\delta = -0.4$) $\delta = 0.4$ (1) $\delta = 0.4$ ($\delta = -0.4$) ($\delta = -0.4$) ($\delta = 0.4$).

At constant injection rate ($\gamma = 0.2$) , the RO frequency and the damping rate were plotted versus the detuning frequency as shown in figures 4 (a) and (b), respectively. Increasing the detuning frequency at constant injection rate had a noticeable effect on the RO frequency and the damping rate. Specifically, as the detuning frequency increased, the RO frequency decreased, and the damping rate increased. This pattern indicated an improvement in the stability of the system. In this context, the detuning frequency is defined as the difference between the master laser and the slave laser frequencies. In our scenario, this detuning frequency δ corresponds to the difference between the frequency of the laser reflected back into the cavity ω_L and the resonance frequency of the cavity ω_0 . It's worth noting that the resonance frequency depends upon the cavity length. Consequently, controlling the detuning can be achieved by adjusting the cavity length. Therefore, enhancing stabilization can be accomplished through precision manufacturing processes.

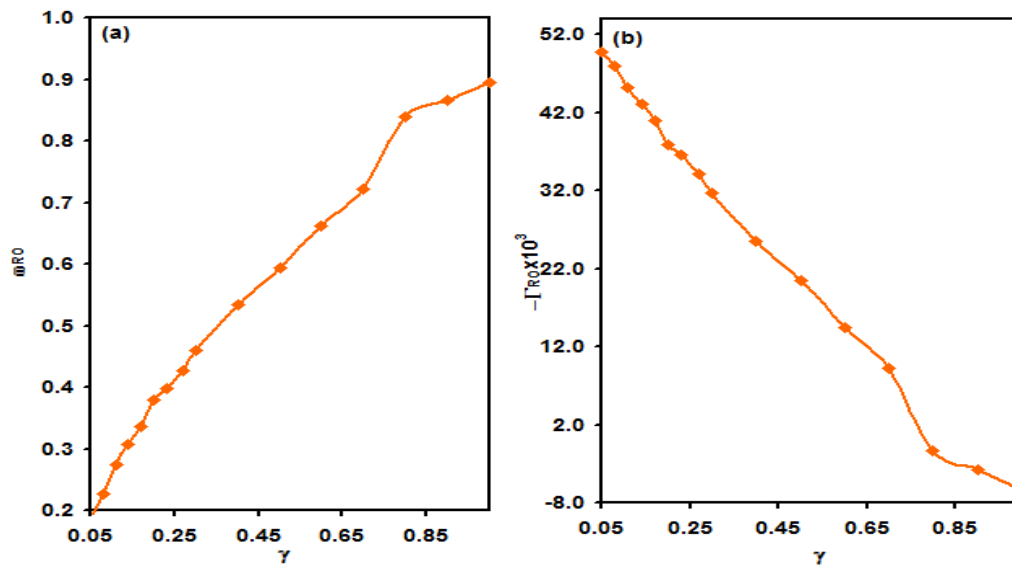


Figure 3. (a) RO frequency ω_{RO} versus the injection rate γ for $\delta = 0.4$ and (b) Damping rate Γ_{RO} versus injection rate γ for $\delta = 0.4$.

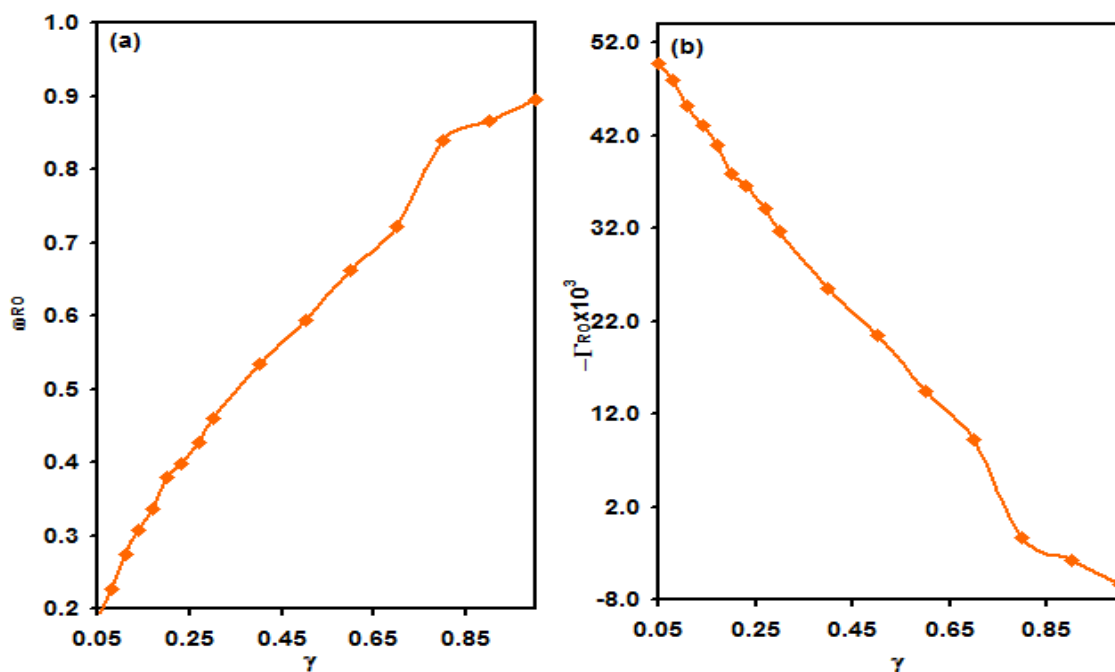


Figure 4. (a) RO frequency ω_{RO} versus the detuning frequency δ at constant injection rate γ . And (b) Damping rate Γ_{RO} versus the detuning frequency δ at constant injection rate γ .

5. Numerical Comparison between Dynamics of solitary and subjected to optical feedback QDLs.

In this section, the researchers aimed to compare the impact of optical feedback on the dynamics of QDLs for one case where ($\delta = -0.4$) with those of solitary QDLs. It is well known that the RO frequency in the presence of

optical feedbacks shifts from that of solitary oscillation (Ohtsubo, 2013). However, in our case it took larger value than that of the solitary oscillation at the same value of steady state intensity as shown in figures 5(a).

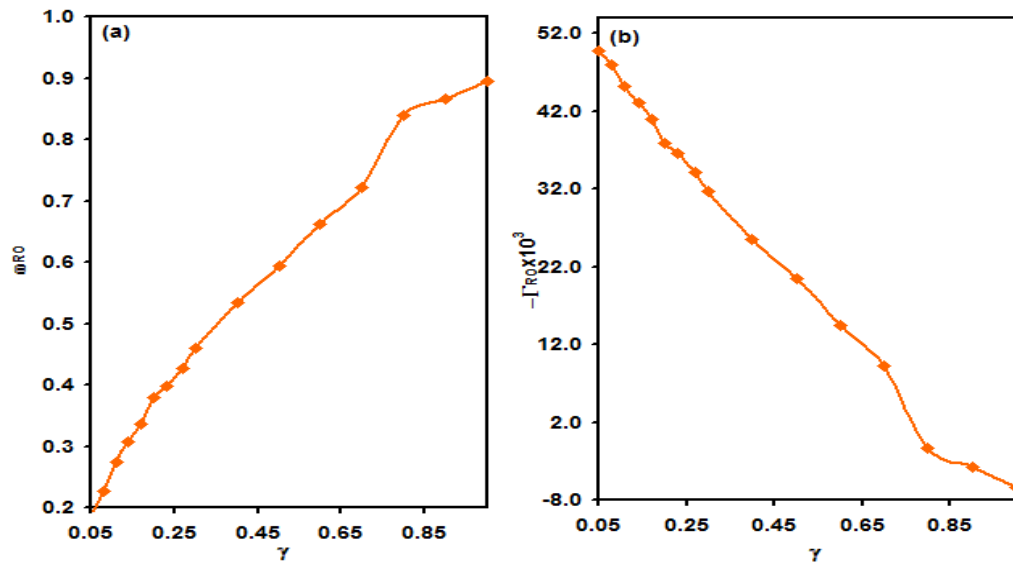


Figure 5. (a) RO frequency ω_{RO} versus steady state intensity I_s for solitary and under optical feedback QDL and (b) Damping rate Γ_{RO} versus steady state intensity I_s for solitary and under optical feedback QDL.

In a stability regime, the damping rate of the oscillations was lower than the damping in the solitary oscillation which indicated that the system is less stable than predicted from solitary model. Moreover, there was an instability regime indicated by positive damping rate. Furthermore, as explained previously, the optical feedback provides bistability phenomena, which provide an ability to use as optical switch.

6. Conclusions

In this work, the dynamic response of QDLs subjected to optical feedback was explored analytically utilizing a rate equation model developed by O'Brien et al. An expression for the growth rate was derived analytically in terms of the eigenvalues of the Jacobian matrix evaluated at steady state. Our findings were numerically validated by studying the reaction of a five-layer structure generated by solid-source MBE to optical feedback. The computation revealed that under optical feedback at constant detuning frequency the RO frequency increased while the damping rate decreased as the injection rate increased. For small injection rate, the system was still stable. However, with further increasing of the injection rate the system went to instabilities and chaotic region. Moreover, for negative detuning frequency, there was a bistability region which enables to use the laser in various applications such as optical switch and optical data storing. Comparing to solitary QDLs, the analysis revealed that the system is less stable than predicted from solitary model.

8. Declarations

Acknowledgments

Not applicable.

Ethical consideration

Not applicable.

Consent to participate

Not applicable

Conflicts of interest

Not applicable

Data availability

Declared upon request

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Author(s) Contribution

Conceptualization (C): M Abusaa and AA Saleh. **Methodology (M):** Haneen NM Jaradat, M Abusaa and AA Saleh. **Formal Analysis (FA):** Haneen NM Jaradat. **Writing – Original Draft (WO):** Haneen NM Jaradat. **Writing – Review & Editing (WR):** Haneen NM Jaradat, M Abusaa and AA Saleh. **Visualization (Vi):** Haneen NM Jaradat **Supervision (Su):** M Abusaa and AA Saleh.

References

- [1] Huang, H. (2004). Theoretical study of gallium arsenide-based quantum dot lasers and microcavity light emitting diodes (Doctoral dissertation, The University of Texas at Austin).
- [2] Huang, H. (2017). Optical nonlinearities in quantum dot lasers for high-speed communications (Doctoral dissertation, Télécom ParisTech).
- [3] Coleman, J. J., Young, J. D., & Garg, A. (2010). Semiconductor quantum dot lasers: A tutorial. *Journal of Lightwave Technology*, 29, 499–510. <https://doi.org/10.1109/JLT.2010.2098849>
- [4] Abusaa, M., Danckaert, J., Viktorov, E. A., & Erneux, T. (2013). Intradot time scales strongly affect the relaxation dynamics in quantum dot lasers. *Physical Review A*, 87, 063827. <https://doi.org/10.1103/PhysRevA.87.063827>
- [5] Abusaa, M., Danckaert, J., & Viktorov, E. A. (2017). Lasing due to the excited state in quantum dot lasers. *Journal of Physics: Conference Series*, 869, 012008. <https://doi.org/10.1088/1742-6596/869/1/012008>
- [6] Fiore, A., & Markus, A. (2007). Differential gain and gain compression in quantum-dot lasers. *IEEE Journal of Quantum Electronics*, 43, 287–294. <https://doi.org/10.1109/JQE.2006.890399>
- [7] Malić, E., Ahn, K. J., Bormann, M. J. P., Hövel, P., Schöll, E., Knorr, A., Kuntz, M., & Bimberg, D. (2006). Theory of relaxation oscillations in semiconductor quantum dot lasers. *Applied Physics Letters*, 89, 101107. <https://doi.org/10.1063/1.2346224>
- [8] Uskov, A. V., Boucher, Y., Le Bihan, J., & McInerney, J. (1998). Theory of a self-assembled quantum-dot semiconductor laser with Auger carrier capture: Quantum efficiency and nonlinear gain. *Applied Physics Letters*, 73, 1499–1501.
- [9] O'Brien, D., Hegarty, S. P., Huyet, G., & Uskov, A. V. (2004). Sensitivity of quantum-dot semiconductor lasers to optical feedback. *Optics Letters*, 29, 1072–1074. <https://doi.org/10.1364/OL.29.001072>

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- [10] Oleiwi, M. O., & Emsary, C. A. (2014). The dynamical characteristics of InAs/InGaAs quantum dot semiconductor laser under optical feedback. *Basrah Journal of Science*.
- [11] Otto, C. (2013). Dynamics of quantum dot lasers subject to optical feedback and external optical injection (Doctoral dissertation, Technische Universität Berlin).
- [12] Otto, C., Lüdge, K., & Schöll, E. (2010). Modeling quantum dot lasers with optical feedback: Sensitivity of bifurcation scenarios. *Physica Status Solidi B*, 247, 829–845.
- [13] Otto, C., Lüdge, K., Viktorov, E., & Erneux, T. (2011). Quantum dot laser tolerance to optical feedback. In *Nonlinear Laser Dynamics: From Quantum Dots to Cryptography*. Wiley-VCH.
- [14] Kelleher, B., Goulding, D., Hegarty, S. P., Huyet, G., Viktorov, E. A., & Erneux, T. (2012). Optically injected single-mode quantum dot lasers. In *Lecture Notes in Nanoscale Science and Technology*. Springer.
- [15] Van Tartwijk, G. H., & Agrawal, G. P. (1998). Laser instabilities: A modern perspective. *Progress in Quantum Electronics*, 22, 43–122.
- [16] Erneux, T., et al. (2007). Laser dynamics and growth rate analysis in semiconductor lasers.
- [17] Erneux, T., et al. (2010). Numerical simulations of quantum dot laser dynamics.
- [18] Oliver, E. C. (2004). Optical bistability and soliton switching in an optical ring cavity (Doctoral dissertation, Acadia University).
- [19] Mehmannaavaz, M. R., & Sattari, H. (2015). A quintuple quantum dot system for electrical and optical control of multi/bistability in a telecommunication window. *Laser Physics Letters*, 12, 025201. <https://doi.org/10.1088/1054-660X/25/12/125201>



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Euler-Lagrange Equations with Generalized ABC and ABR Nabla Fractional Differences

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Abstract

Background: Discrete fractional calculus has emerged as an important mathematical framework for modeling dynamical systems with memory and nonlocal behavior. In particular, nabla fractional differences with Mittag–Leffler kernels have been widely used in discrete fractional variational problems and their associated Euler–Lagrange equations. **Objectives:** This study aims to derive new discrete fractional Euler–Lagrange equations involving generalized Atangana–Baleanu Caputo (ABC) and Atangana–Baleanu Riemann (ABR) nabla fractional differences with generalized Mittag–Leffler kernels. **Methods:** First, new summation-by-parts formulas for generalized ABC and ABR nabla fractional differences with a three-parameter Mittag–Leffler kernel are established. These formulas are then employed within the framework of discrete fractional calculus of variations to derive Euler–Lagrange equations for functionals containing generalized ABC nabla left and right fractional differences. **Results:** New discrete fractional Euler–Lagrange equations are obtained for variational problems involving generalized ABC nabla fractional differences with generalized Mittag–Leffler kernels. The proposed results extend previously known Euler–Lagrange formulations based on one-parameter kernels. Illustrative examples are presented to demonstrate the applicability of the theoretical findings. **Conclusions:** The results provide a generalized framework for discrete fractional variational problems and contribute to the development of Euler–Lagrange theory with generalized ABC and ABR nabla fractional operators, opening new directions for future research in discrete fractional calculus.

Keywords: Discrete fractional Euler–Lagrange equations; nabla fractional differences; discrete nabla Mittag–Leffler function; generalized ABC nabla fractional difference; summation by parts; discrete calculus of variations.

1. Introduction

The curiosity about continuous fractional calculus, in which the orders of differentiation and integration may be any real or complex numbers, is as old as ordinary calculus; it began in 1695 when Guillaume de l'Hôpital asked Gottfried Wilhelm Leibniz about the one-half derivative of x . The answer led to the name fractional calculus, which was considered a misnomer because the order of the derivative could be any number, not only rational numbers. Nevertheless, the firm foundation of continuous fractional calculus was not established until the late nineteenth century [1]. Due to its advantages and widespread applications in physics [2], medical science and computational biology [3], economics [4], control theory [5], and epidemiology [6], continuous fractional calculus has been studied extensively since the nineteenth century [7]. In addition, fractional-order derivatives have proven to be more suitable for modeling scientific and engineering problems than integer-order derivatives [7, 8]. This could be attributed to the fact that unlike integer-order derivatives and integrals, fractional operators are non-local, meaning that they depend on all historical values of the function, not only on its value at a single point. An encyclopedic reference for the different definitions and applications is provided in [8]. Nevertheless, the study of discrete fractional calculus has not attracted the same interest until quite recently.

Broadly speaking, discrete fractional calculus is defined as the study of sums and differences of arbitrary order, i.e., $\Delta^\alpha f(x)$ and $\nabla^\alpha f(x)$ on time scales—non-empty closed subsets of $\mathbb{R}$ —where $\alpha \in \mathbb{R}$. There are two types of difference operators: the delta operator, $\Delta f(x) = f(x+1) - f(x)$, which is the forward difference operator, and the nabla operator, $\nabla f(x) = f(x) - f(x-1)$, which is the backward difference operator. In recent years, discrete fractional calculus has been applied successfully in various fields [9, 10], for instance in modeling porous materials [11], in signal processing and diffusion problems [12], and in cancer tumor growth [13].

The earliest definition of the discrete fractional difference, to the best of the authors' knowledge, appeared in 1910 by Chapman [14] as an infinite series known as the delta fractional sequential difference; however, serious interest in discrete fractional sums and differences defined on the time-scale sets $\mathbb{N}_a$ was stimulated by the pioneering work of Miller and Ross [1]. Other contributors to the theory of discrete delta fractional calculus include Atici and Eloe [15], and Abdeljawad and Baleanu [16].

This paper lies within the scope of discrete nabla fractional differences. Gray and Zhang in 1988 [17] were the first to introduce the definition of the nabla left fractional sum as a finite sum based on the repeated summation formula of $f(t)$, which is analogous to Cauchy's formula for repeated integrals; they also defined the corresponding fractional difference. Later, Abdeljawad and Atici in [18] observed that starting the summation from $a+1$ instead of a in the definition of the nabla left fractional sum proposed by Gray and Zhang is more consistent with the general framework of fractional calculus on time scales; hence, they refined the nabla left fractional sum operator defined in [17]. Furthermore, they introduced the nabla right fractional sum and difference. Correspondingly, Ahrendt in [19] established a unification of the nabla left fractional sum and difference introduced in [18]. All these definitions of fractional differences are called the Riemann–Liouville nabla fractional differences. There are other definitions of the nabla fractional difference, known as the Caputo nabla fractional differences. Abdeljawad in [20] further introduced new definitions of the Caputo nabla left and right fractional differences.

In continuous case, a new fractional difference was obtained by Caputo and Fabrizio in [21] by replacing the kernel of the integration with an exponential function, which is non-singular, to better describe some systems dynamics and the behavior of some materials. Subsequently, another definition was established by Atangana and Baleanu in [22] just by changing the exponential kernel with the M–L function since it is considered as a generalization of the exponential function. Following the same procedure in discrete fractional setting, Abdeljawad and Baleanu [23] introduced new definitions of the nabla fractional differences and sums, where the kernel of the summation in the fractional differences is non-singular with the nabla M-L function of one parameter. These new definitions are called the Atangana-Baleanu Caputo (ABC) nabla fractional differences, the Atangana-Baleanu Riemann (ABR) nabla fractional differences, and the Atangana-Baleanu (AB) nabla fractional sums. Subsequently, Abdeljawad and Baleanu in [24] traced the steps of continuous fractional calculus and introduced the nabla fractional differences and sums with the discrete nabla exponential kernel, which are called the Caputo–Fabrizio Caputo (CFC) nabla fractional differences and Caputo–Fabrizio Riemann (CFR) nabla fractional differences and the Caputo–Fabrizio (CF) nabla fractional sums. Later on, Abdeljawad [25] generalized the definitions given in [23] with the generalized nabla M-L function of three parameters.

Variational principles could be applied nicely in the framework of the discrete fractional calculus. Calculus of variations is a generalization of the theory of finding extrema of a function of several independent variables, where one seeks a vector in $\mathbb{R}^n$ such that the function $f: \mathbb{R}^n \rightarrow \mathbb{R}$ attains an extremum. In the calculus of variations, a functional is optimized rather than a function. Hence, instead of finding a point $(x_1, x_2, \dots, x_n)$ at which the function $f(x_1, x_2, \dots, x_n)$ has a maximum or minimum, one aims to find a function at which the functional attains an extremum [26]. The first discrete delta difference fractional Euler-Lagrange equation was derived by Atici and Sengul [13]. Then, Abdeljawad and Baleanu in [16] introduced different versions of the delta fractional Euler-Lagrange equation using a different definition of the delta right fractional difference. After that, Abdeljawad [27] established the first nabla Euler-lagrange equations. More recently, Abdeljawad and Baleanu [23] derived the ABC nabla fractional Euler-Lagrange equation. And naturally the Euler-Lagrange equations with Caputo-Fabrizio fractional differences were introduced by Abdeljawad and Baleanu in [24].

Since Abdeljawad in [25] introduced the generalized ABC nabla left fractional difference, the main objective of this paper is to obtain summation by parts identities for the generalized ABC nabla fractional differences and use them to derive the generalized ABC nabla fractional Euler-Lagrange equations.

2. Preliminaries

In this section, some basic definitions related to nabla calculus were given. Throughout this paper, the function $f(t)$ was considered real-valued and defined on the following sets:

$$\mathbb{N}_a =: \{a, a + 1, a + 2, \dots\},$$

where $a \in \mathbb{R}$, or

$${}_b\mathbb{N} = \{b, b - 1, b - 2, \dots\},$$

where $b \in \mathbb{R}$, or

$$\mathbb{N}_a^b =: \{a, a + 1, a + 2, \dots, b\},$$

where $a, b \in \mathbb{R}$ and $b > a$.

The gamma function is an essential tool, which is used to define the discrete fractional operators and it is defined as follows:

Definition 2.1 (Gamma function). [28]

The gamma function can be expressed as follows: for any $z \in \mathbb{C}$, $\Re(z) > 0$

$$\Gamma(z) = \int_0^\infty e^{-t} t^{z-1} dt$$

Definition 2.2 (Forward Jump Operator). [29] Let $x \in \mathbb{N}_a$. The forward jump operator σ is defined as

$$\sigma(x) := x + 1$$

Also, let $f^\sigma = f \circ \sigma$.

Definition 2.3 (Backward Jump Operator). [29] The backward jump operator ρ is defined on $\mathbb{N}_{a+1}$ as

$$\rho(x) := x - 1$$

Also, let $f^\rho = f \circ \rho$.

Definition 2.4 (Rising Factorial). [28] Let $n \in \mathbb{N}$. For any $t \in \mathbb{R}$, the rising factorial function $t^{\overline{n}}$ takes the form:

$$t^{\overline{n}} := t(t+1)(t+2) \dots (t+n-1)$$

Also, $t^{\overline{0}} = 1$.

Definition 2.5 (Generalized Rising Factorial). [28] The generalized rising factorial function is defined as follows:

$$t^{\overline{\alpha}} = \begin{cases} \frac{\Gamma(t+\alpha)}{\Gamma(t)}, & \text{if } t, t+\alpha \notin -\mathbb{N}_0, \\ 1, & \text{if } t = \alpha = 0, \\ 0, & \text{if } t \in -\mathbb{N}_0 \text{ and } t+\alpha \in \mathbb{Z}^+, \\ \text{undefined,} & \text{otherwise.} \end{cases}$$

Definition 2.6 (Delta Difference Operator). [1] Let $f: \mathbb{N}_a^b \rightarrow \mathbb{R}$. The delta operator Δ , also called the forward difference operator, is defined as follows:

$$\Delta f(x) = f(x+1) - f(x), \quad x \in \mathbb{N}_a^{b-1}.$$

Moreover, for $n \in \mathbb{Z}^+$,

$$\Delta^n f(x) = \Delta(\Delta^{n-1} f(x)), \quad x \in \mathbb{N}_a^{b-n}.$$

Also, $\Delta^0 f(x) = f(x)$; the identity operator.

Definition 2.7 (Nabla Difference Operator). [29] Let $f: \mathbb{N}_a \rightarrow \mathbb{R}$. The nabla operator, also called the backward difference operator ∇ , is defined as:

$$\nabla f(x) = f(x) - f(x-1), \quad x \in \mathbb{N}_{a+1}.$$

Moreover, for $n \in \mathbb{Z}^+$,

$$\nabla^n f(x) = \nabla(\nabla^{n-1} f(x)), \quad x \in \mathbb{N}_{a+n}.$$

Also, $\nabla^0 f(x) = f(x)$; the identity operator.

The following two theorems state the delta and the nabla summation by parts formulas, which allow moving the delta or the nabla operator from one function to another:

Theorem 2.1 (Delta Summation by Parts). [28] Consider real-valued functions on $\mathbb{N}_a^b$, and let $c, d \in \mathbb{N}_a$ with $c < d$. The delta integration by parts formulas can be stated as follows:

$$\sum_{t=c}^{d-1} g(\sigma(t)) \Delta f(t) = g(t) f(t) \Big|_c^d - \sum_{t=c}^{d-1} f(t) \Delta g(t). \quad (1)$$

Theorem 2.2 (Nabla Summation by Parts). [28] Let $f, g: N_a^b \rightarrow \mathbb{R}$ be two functions and $b, c \in N_a$ with $c < d$. The nabla integration by parts formulas are:

$$\sum_{t=c+1}^d g(\rho(t)) \nabla f(t) = g(t)f(t)|_c^d - \sum_{t=c+1}^d f(t) \nabla g(t). \quad (2)$$

Before moving to the definitions of the fractional differences, let us introduce the M-L function. In the continuous setting, the classical M-L function generalizes the exponential function, which is a solution of a linear ordinary differential equation with constant coefficients. Similarly, the M-L function serves as a solution of a fractional order differential equation [30]. In discrete fractional calculus, the discrete M-L function is a solution of a fractional difference equation [20].

Definition 2.8 (Discrete Nabla M-L). [20] Assume that $\alpha, \beta, t \in \mathbb{C}$, $\Re(\alpha) > 0$ and $\forall \lambda \in \mathbb{R}$ with $|\lambda| < 1$. The discrete nabla M-L function of two parameters α and β takes the form:

$$E_{\alpha, \beta}(\lambda, t) = \sum_{k=0}^{\infty} \lambda^k \frac{t^{\overline{k\alpha + \beta - 1}}}{\Gamma(k\alpha + \beta)}. \quad (3)$$

Notice that for $\beta = 1$, the M-L function of one parameter α is obtained:

$$E_{\alpha}(\lambda, t) := E_{\alpha, 1}(\lambda, t) = \sum_{k=0}^{\infty} \lambda^k \frac{t^{\overline{k\alpha}}}{\Gamma(k\alpha + 1)}. \quad (4)$$

Definition 2.9 (Nabla Discrete Generalized M-L). [20] Assume that $\alpha, \beta, \gamma, t \in \mathbb{C}$, $\Re(\alpha) > 0$ and $\forall \lambda \in \mathbb{R}$ with $|\lambda| < 1$. The discrete nabla generalized M-L function of three parameters α, β, γ is expressed as:

$$E_{\alpha, \beta}^{\gamma}(\lambda, t) = \sum_{k=0}^{\infty} \lambda^k \frac{t^{\overline{k\alpha + \beta - 1}} \gamma^{\overline{k}}}{\Gamma(k\alpha + \beta) k!}. \quad (5)$$

Notice that if $\gamma = 1$, the discrete M-L function of two parameters for the nabla operator is recovered:

$$E_{\alpha, \beta}^1(\lambda, t) = E_{\alpha, \beta}(\lambda, t).$$

Theorem 2.3 [25] For $n = 1, 2, \dots$, the following relations hold:

- $\nabla^n E_{\alpha, \beta+n}^{\rho}(\lambda, z) = E_{\alpha, \beta}^{\rho}(\lambda, z);$
- $\nabla E_{\alpha}(\lambda, z) = \lambda E_{\alpha, \alpha}(\lambda, z).$

The core of discrete fractional calculus lies in the definitions of the discrete fractional operators. These definitions are not unique, which gives the subject some flexibility. Some of these definitions are outlined as follows:

Definition 2.10 (Nabla Left and Right Fractional Sums)

1. [18] Let $f: N_a \rightarrow \mathbb{R}$, $\alpha \in \mathbb{R}^+$. Then the nabla left fractional sum of order α can be defined as follows:

$${}_a \nabla^{-\alpha} f(t) = \frac{1}{\Gamma(\alpha)} \sum_{k=a+1}^t (t - \rho(k))^{\overline{\alpha-1}} f(k), \quad t \in N_{a+1}, \quad (6)$$

2. [18] Let $f: {}_b \mathbb{N} \rightarrow \mathbb{R}$ and $\alpha \in \mathbb{R}^+$. Then the nabla right fractional sum of order α can be defined as follows:

$$\nabla_b^{-\alpha} f(t) = \frac{1}{\Gamma(\alpha)} \sum_{k=t}^{b-1} (k - \rho(t))^{\overline{\alpha-1}} f(k), \quad t \in {}_{b-1} \mathbb{N} \quad (7)$$

Definition 2.11 (Riemann-Liouville Nabla Left and Right Fractional Differences)

1. [18] Let $f: \mathbb{N}_a \rightarrow \mathbb{R}, \alpha \in \mathbb{R}^+$ and let $N \in \mathbb{N}$ such that $N = [\alpha] + 1$. Then the Riemann-Liouville nabla left fractional difference of order α can be defined as follows:

$${}_a \nabla^\alpha f(t) = \nabla^N {}_a \nabla^{-(N-\alpha)} f(t), \quad t \in \mathbb{N}_{a+1}, \quad (8)$$

$$= \frac{\nabla^N}{\Gamma(N-\alpha)} \sum_{k=a+1}^t (t - \rho(k))^{\overline{N-\alpha-1}} f(k), \quad (9)$$

The authors [19] stated the following alternative definition when $\alpha \notin \mathbb{N}$:

$${}_a \nabla^\alpha f(t) = \frac{1}{\Gamma(-\alpha)} \sum_{k=a+1}^t (t - \rho(k))^{\overline{-\alpha-1}} f(k), \quad \alpha \in \mathbb{R}^+ \setminus \mathbb{N}, \quad t \in \mathbb{N}_{a+1}, \quad (10)$$

2. [18] Let $f: {}_b \mathbb{N} \rightarrow \mathbb{R}, \alpha \in \mathbb{R}^+$ and let $N \in \mathbb{N}$ such that $N = [\alpha] + 1$. Then the Riemann-Liouville nabla right fractional difference of order α is defined as follows:

$$\nabla_b^\alpha f(t) = (-1)^N \Delta^N \nabla_b^{-(N-\alpha)} f(t), \quad t \in {}_{b-1} \mathbb{N} \quad (11)$$

$$= \frac{(-1)^N \Delta^N}{\Gamma(N-\alpha)} \sum_{k=t}^{b-1} (k - \rho(t))^{\overline{N-\alpha-1}} f(k), \quad (12)$$

Moreover, when $\alpha \notin \mathbb{N}$

$$\nabla_b^\alpha f(t) = \frac{1}{\Gamma(-\alpha)} \sum_{k=t}^{b-1} (k - \rho(t))^{\overline{-\alpha-1}} f(k), \quad \alpha \in \mathbb{R}^+ \setminus \mathbb{N}, \quad t \in {}_{b-1} \mathbb{N}. \quad (13)$$

Now, the nabla fractional differences with discrete nabla M-L kernel of one parameter in the Riemann sense are expressed as follows:

Definition 2.12 (ABR Nabla Left and Right Fractional Differences). [23]

1. Let $f: \mathbb{N}_a \rightarrow \mathbb{R}, \alpha \in [0,1], \lambda = \frac{-\alpha}{1-\alpha}$, and let B be a normalization function such that $B(0) = B(1) = 1$.

Then the ABR nabla left fractional difference is defined as follows:

$$({}^{ABR} \nabla_a^\alpha f)(t) = \nabla_t \frac{B(\alpha)}{1-\alpha} \sum_{s=a+1}^t E_{\overline{\alpha}}(\lambda, t - \rho(s)) f(s), \quad t \in \mathbb{N}_a. \quad (14)$$

2. Let $f: {}_b \mathbb{N} \rightarrow \mathbb{R}, \alpha \in [0,1], \lambda = \frac{-\alpha}{1-\alpha}$, and let B be a normalization function such that $B(0) = B(1) = 1$.

Then the ABR nabla right fractional difference is defined as follows:

$$({}^{ABR} \nabla_b^\alpha f)(t) = \Delta_t \frac{-B(\alpha)}{1-\alpha} \sum_{s=t}^{b-1} E_{\overline{\alpha}}(\lambda, s - \rho(t)) f(s), \quad t \in {}_b \mathbb{N}. \quad (15)$$

Notice that the t in Δ_t and ∇_t indicates that the delta and nabla differences are with respect to t .

next, the nabla fractional differences with discrete nabla M-L kernel of one parameter in the Caputo sense are presented as follows:

Definition 2.13 (ABC Nabla Left and Right Fractional Differences). [23]

1. Let $f: \mathbb{N}_a \rightarrow \mathbb{R}, \alpha \in [0,1], \lambda = \frac{-\alpha}{1-\alpha}$, and let B be a normalization function such that $B(0) = B(1) = 1$.

Then the ABC nabla left fractional difference is defined as follows:

$$({}^{ABC} \nabla_a^\alpha f)(t) = \frac{B(\alpha)}{1-\alpha} \sum_{s=a+1}^t E_{\overline{\alpha}}(\lambda, t - \rho(s)) \nabla_s f(s), \quad t \in \mathbb{N}_a. \quad (16)$$

2. Let $f: {}_b\mathbb{N} \rightarrow \mathbb{R}, \alpha \in [0,1], \lambda = \frac{-\alpha}{1-\alpha}$, and let B be a normalization function such that $B(0) = B(1) = 1$.

Then the ABC nabla right fractional difference is defined as follows:

$$({}^{ABC}\nabla_b^\alpha f)(t) = \frac{-B(\alpha)}{1-\alpha} \sum_{s=t}^{b-1} E_{\alpha}^{-\lambda}(\lambda, s - \rho(t)) \Delta_s f(s), \quad t \in {}_b\mathbb{N}. \quad (17)$$

Notice that the s in Δ_s and ∇_s indicates that the delta and nabla differences are with respect to s .

The following definitions are the generalized Atangana-Baleanu Riemann (ABR) nabla fractional differences, the generalized Atangana-Baleanu Caputo (ABC) nabla fractional differences, and the generalized Atangana-Baleanu (AB) nabla fractional sums. These definitions were obtained by changing the kernel of summation in the fractional difference operators with the M–L function of three parameters:

First, the generalized nabla fractional differences with discrete nabla M–L kernel of three parameters in the Riemann sense are defined as:

Definition 2.14 (Generalized ABR Nabla Left and Right Fractional Differences). [25]

1. Let $f: \mathbb{N}_a \rightarrow \mathbb{R}, \alpha \in (0, \frac{1}{2}), \lambda = \frac{-\alpha}{1-\alpha}, \gamma \in \mathbb{R}, \operatorname{Re}(\mu) > 0$, and let B be a normalization function such that $B(0) = B(1) = 1$. Then the generalized ABR nabla left fractional difference is defined as follows:

$$({}^{ABR}\nabla_a^{\alpha, \mu, \gamma} f)(t) = \nabla_t \frac{B(\alpha)}{1-\alpha} \sum_{s=a+1}^t E_{\alpha, \mu}^{\gamma}(\lambda, t - \rho(s)) f(s), \quad t \in \mathbb{N}_a. \quad (18)$$

2. Let $f: {}_b\mathbb{N} \rightarrow \mathbb{R}, \alpha \in (0, \frac{1}{2}), \lambda = \frac{-\alpha}{1-\alpha}, \gamma \in \mathbb{R}, \operatorname{Re}(\mu) > 0$, and let B be a normalization function such that $B(0) = B(1) = 1$. Then the generalized ABR nabla right fractional difference is defined as follows:

$$({}^{ABR}\nabla_b^{\alpha, \mu, \gamma} f)(t) = \Delta_t \frac{-B(\alpha)}{1-\alpha} \sum_{s=t}^{b-1} E_{\alpha, \mu}^{\gamma}(\lambda, s - \rho(t)) f(s), \quad t \in {}_b\mathbb{N}. \quad (19)$$

Notice that the t in Δ_t and ∇_t indicates that the delta and nabla differences are with respect to t .

Next, the generalized nabla fractional differences with discrete nabla M–L kernel of three parameters in the Caputo sense can be presented as follows:

Definition 2.15 (Generalized ABC Nabla Left and Right Fractional Differences). [25]

1. Let $f: \mathbb{N}_a \rightarrow \mathbb{R}, \alpha \in (0, \frac{1}{2}), \lambda = \frac{-\alpha}{1-\alpha}, \gamma \in \mathbb{R}, \operatorname{Re}(\mu) > 0$, and let B be a normalization function such that $B(0) = B(1) = 1$. Then the generalized ABC nabla left fractional difference is defined as follows:

$$({}^{ABC}\nabla_a^{\alpha, \mu, \gamma} f)(t) = \frac{B(\alpha)}{1-\alpha} \sum_{s=a+1}^t E_{\alpha, \mu}^{\gamma}(\lambda, t - \rho(s)) \nabla_s f(s), \quad t \in \mathbb{N}_a. \quad (20)$$

2. Let $f: {}_b\mathbb{N} \rightarrow \mathbb{R}, \alpha \in (0, \frac{1}{2}), \lambda = \frac{-\alpha}{1-\alpha}, \gamma \in \mathbb{R}, \operatorname{Re}(\mu) > 0$, and let B be a normalization function such that $B(0) = B(1) = 1$. Then the generalized ABC nabla right fractional difference is defined as follows:

$$({}^{ABC}\nabla_b^{\alpha, \mu, \gamma} f)(t) = \frac{-B(\alpha)}{1-\alpha} \sum_{s=t}^{b-1} E_{\alpha, \mu}^{\gamma}(\lambda, s - \rho(t)) \Delta_s f(s), \quad t \in {}_b\mathbb{N}. \quad (21)$$

Notice that the s in Δ_s and ∇_s indicates that the delta and nabla differences are with respect to s .

Finally, the generalized nabla fractional sums with discrete nabla M–L kernel of three parameters are expressed as follows:

Definition 2.16 (Generalized AB Nabla Left and Right Fractional Sums). [25]

1. Let $f: \mathbb{N}_a \rightarrow \mathbb{R}$, $\alpha \in (0, \frac{1}{2})$, $\lambda = \frac{-\alpha}{1-\alpha}$, and let B be a normalization function such that $B(0) = B(1) = 1$.

Then the generalized AB nabla left fractional sum is defined as follows:

$$\begin{aligned} ({}^{AB} \nabla_a^{-(\alpha, \mu)} f)(t) &= \frac{1-\alpha}{B(\alpha)} ({}_a \nabla^{-(1-\mu)} f)(t) \\ &+ \frac{\alpha}{B(\alpha)} ({}_a \nabla^{-(1-\mu+\alpha)} f)(t), \quad t \in \mathbb{N}_a. \end{aligned} \quad (22)$$

2. Let $f: {}_b \mathbb{N} \rightarrow \mathbb{R}$, $\alpha \in (0, \frac{1}{2})$, $\lambda = \frac{-\alpha}{1-\alpha}$, and let B be a normalization function such that $B(0) = B(1) = 1$.

Then the generalized AB nabla right fractional sum is defined as follows:

$$\begin{aligned} ({}^{AB} \nabla_b^{-(\alpha, \mu)} f)(t) &= \frac{1-\alpha}{B(\alpha)} (\nabla_b^{-(1-\mu)} f)(t) \\ &+ \frac{\alpha}{B(\alpha)} (\nabla_b^{-(1-\mu+\alpha)} f)(t), \quad t \in {}_b \mathbb{N}. \end{aligned} \quad (23)$$

The operators ${}_a \nabla^{-\alpha}$ and $\nabla_b^{-\alpha}$ are defined as in (6) and (7), respectively.

3. Summation by Parts and Euler-Lagrange Equations with Generalized M–L Function of One Parameter

The study of discrete fractional calculus has gained increasing attention over the last decades, motivated by its applications in variational principles and dynamical systems. A thorough understanding of the subject requires not only the formal definitions of fractional sums and differences but also an awareness of the historical development of the variational principles in the discrete fractional setting. This section reviews some integration by parts formulas within the scope of discrete fractional calculus, followed by the formalism of discrete fractional Euler–Lagrange equations with ABC and ABR nabla fractional differences. Finally, the review identifies how the thesis extends previous findings to derive different types of Euler–Lagrange equations.

3.1 Discrete Fractional Summation by Parts Formulas For ABC Fractional Differences

Integration by parts formula plays an important role in classical continuous calculus, and it is no exception in continuous fractional calculus. In continuous fractional calculus there are various integration by parts formulas due to having several definitions of the fractional-order integral. The same is applied in discrete fractional calculus, as the definitions of the fractional sums and differences are not unique. Thus, different fractional summation by parts expressions have been obtained. Notice that the integration becomes summation in the discrete setting. These summation by parts formulas are essential in discrete fractional calculus of variations, since they allow one to move the fractional operator from one function to another and hence free the function that appears due to doing perturbations around the extremum of a functional. Two nabla fractional summation by parts formulas are reviewed in this subsection.

First, the summation by parts formula for the ABC nabla left fractional difference with M-L function of one parameter is discussed in the next theorem.

Theorem 3.1 [23] Assume that f and g are two functions whose domains are $\mathbb{N}_a^b$, with $a < b$ and $a \equiv b \pmod{1}$. Assume that $\alpha \in (0, 1)$, then the following summation by parts identity holds:

$$\begin{aligned} \sum_{t=a}^{b-1} f(t)({}^{ABC}\nabla_a^\alpha g)(t) &= \sum_{t=a}^{b-1} g(t)({}^{ABR}\nabla_{b-1}^\alpha f)(s) \\ &+ g(\rho(s)) \frac{B(\alpha)}{1-\alpha} \sum_{t=s}^{b-1} E_{\bar{\alpha}}(\lambda, t - \rho(s)) f(t) \Big|_{s=a}^b. \end{aligned} \quad (24)$$

Second, the summation by parts formula for the ABC nabla right fractional difference with M-L function of one parameter is presented in the following theorem.

Theorem 3.2 [23] Assume that f and g are two functions whose domains are $\mathbb{N}_a^b$, with $a < b$ and $a \equiv b(\text{mod}1)$. Suppose that $\alpha \in (0,1)$, then the following summation by parts formula applies:

$$\begin{aligned} \sum_{t=a+1}^b f(t)({}^{ABC}\nabla_{b+1}^\alpha g)(t) &= \sum_{t=a+1}^b g(t)({}^{ABR}\nabla_{a+1}^\alpha f)(t) \\ &- g(\sigma(s)) \frac{B(\alpha)}{1-\alpha} \sum_{t=a+1}^s E_{\bar{\alpha}}(\lambda, s - \rho(t)) f(t) \Big|_{s=a}^b. \end{aligned} \quad (25)$$

Having reviewed the main definitions of delta and nabla fractional sums and differences, along with various summation by parts formulas, one can now consider their role in variational calculus. The following subsection presents two versions of the Euler–Lagrange equations depending on the type of fractional difference used in the functional.

3.2 Discrete Fractional Nabla Euler-Lagrange Equations with ABC and ABR Fractional Differences

The framework of calculus of variations was first extended to the continuous fractional setting by Agrawal in 2002 [31]. This approach has been further explored by various researchers such as Frederico and Torres [32]. This extension is achieved by replacing integer-order derivatives with various types of fractional derivatives.

Regarding the discrete fractional setting, Bohner [33] appears to be the first to study the variational problem in the discrete setting, replacing the usual derivative with the delta derivative. Subsequently, discrete fractional variational problems on general time scales have been investigated by other researchers [34].

It seems that the first delta fractional Euler-Lagrange equation on the domain $\mathbb{N}_a$ was first derived by Atici and Sengul in [13]. Another delta Euler-Lagrange equation, with the more recent and refined definition of the right delta fractional difference, is studied by Abdeljawad and Baleanu [16]. Turning to the nabla fractional Euler-Lagrange equation, Abdeljawad in [27] derived the nabla fractional Euler-Lagrange equations when the Lagrangian includes the nabla Riemann and Caputo left fractional differences. As new definitions of nabla fractional difference were obtained, new Euler-Lagrange equations were derived as well. Abdeljawad and Baleanu in 2016 and 2017 [23, 24], found the discrete nabla Euler-Lagrange equations for Lagrangians that depend on the ABC and CFC nabla fractional differences, respectively.

The next theorems present the nabla fractional Euler-Lagrange equation when the Lagrangian contains the ABC nabla left fractional difference as done in [23].

Theorem 3.3 [23] Assume that

$$S = \{y: \mathbb{N}_{a-1}^{b-1} \rightarrow \mathbb{R}: y(a-1) = A, y(b-1) = B\}$$

with $\alpha \in (0,1)$, $a, b \in \mathbb{R}$, $a < b$, and $a \equiv b(\text{mod}1)$. Moreover, suppose that

$$J(y) = \sum_{t=a}^{b-1} L(t, y^\rho(t), {}^{ABC}_{a-1} \nabla^\alpha y(t)),$$

where $L: \mathbb{N}_{a-1}^{b-1} \times \mathbb{R} \times \mathbb{R} \rightarrow \mathbb{R}$. Let $y \in S$ be a local extremum of the given discrete functional. Then the discrete nabla Euler-Lagrange equation is given by:

$$L_1(t) + {}^{ABR}_{b-1} \nabla^\alpha L_2(t) = 0, \quad \text{for all } t \in \mathbb{N}_{a-1}^{b-1}, \quad (26)$$

$$\text{where } L_1(t) = \frac{\partial L}{\partial y^\rho}(t) \text{ and } L_2(t) = \frac{\partial L}{\partial ({}^{ABC}_{a-1} \nabla^\alpha y)}(t).$$

Allowing the Lagrangian to include the ABC nabla right fractional difference results in a new nabla fractional Euler-Lagrange equation:

Theorem 3.4 [23] Consider the following functional

$$J(f) = \sum_{t=a+1}^b L(t, y^\sigma(t), {}^{ABC}_{b+1} \nabla^\alpha y(t)),$$

where $L: \mathbb{N}_{a+1}^{b+1} \times \mathbb{R} \times \mathbb{R} \rightarrow \mathbb{R}$. Suppose that

$$S = \{y: \mathbb{N}_{a+1}^{b+1} \rightarrow \mathbb{R}: y(a+1) = A, y(b+1) = B\}$$

with $\alpha \in (0,1)$, $a, b \in \mathbb{R}$, $a < b$, and $a \equiv b \pmod{1}$. Let $y \in S$ be a local optimizer of J , then the Euler-Lagrange condition takes the form:

$$L_1(t) + {}^{ABR}_{a+1} \nabla^\alpha L_2(t) = 0, \quad \text{for all } t \in \mathbb{N}_{a+1}^b, \quad (27)$$

$$\text{where } L_1(t) = \frac{\partial L}{\partial y^\sigma}(t) \text{ and } L_2(t) = \frac{\partial L}{\partial ({}^{ABC}_{b+1} \nabla^\alpha y)}(t).$$

In Theorems 3.3 and 3.4, the ABC nabla fractional differences used are associated with the one-parameter M–L function defined in [23]. All these results can be generalized by using the generalized ABC fractional difference with the generalized three-parameter M–L function defined in [25]. In order to derive the Euler–Lagrange equations with the generalized ABC and ABR nabla fractional differences, one needs summation by parts formulas. That is what will be done in the next section.

4. Summation by Parts and Euler-Lagrange Equations with Generalized M–L Function of Three Parameters Results

Some summation-by-parts formulas are given in the first subsection; these formulas are essential for establishing the main results of this thesis. Second, the generalized Euler–Lagrange equations obtained through the use of the generalized ABC nabla left and right fractional differences, in which the kernel is the three-parameter generalized M–L function, instead of the ABC nabla fractional difference with the one-parameter nabla M–L function studied in [23].

4.1 Summation by Parts for Discrete Generalized ABC Nabla Fractional Differences

This subsection presents our first results, which are the summation-by-parts formulas corresponding to the generalized ABC nabla left and right fractional differences with M-L function of three parameters, which can be seen as generalizations of the formulas obtained by Abdeljawad and Baleanu in [23], where they used the discrete nabla M-L function of one parameter.

Theorem 4.1 (Summation by Parts Formula for the Generalized ABC Nabla Left Fractional Difference) For the functions $f, g: \mathbb{N}_a^b \rightarrow \mathbb{R}$, with $a \equiv b(\text{mod } 1)$ and $0 < \alpha < \frac{1}{2}$, one has the following formula:

$$\begin{aligned} \sum_{s=a+1}^{b-1} g(s) ({}^{ABC}_a \nabla^{\alpha, \mu, \gamma} f)(s) \\ = \sum_{s=a+1}^{b-1} f(s) ({}^{ABR}_b \nabla^{\alpha, \mu, \gamma} g)(s) + f(s) \left(\sum_{r=s+1}^{b-1} \frac{B(\alpha)}{1-\alpha} g(r) E_{\alpha, \mu}^{\gamma}(\lambda, r-s) \right) \Big|_{s=a}^{b-1}. \end{aligned} \quad (28)$$

Proof. By the definition of the generalized ABC nabla left fractional sum (20),

$$\text{L. H. S.} = \sum_{s=a+1}^{b-1} g(s) \frac{B(\alpha)}{1-\alpha} \sum_{r=a+1}^s E_{\alpha, \mu}^{\gamma}(\lambda, s-\rho(r)) \nabla_r f(r).$$

Since $a+1 \leq s \leq b-1$ and $a+1 \leq r \leq s$,

Then $a+1 \leq r \leq s \leq b-1$.

Hence, $a+1 \leq r \leq b-1$ and $r \leq s \leq b-1$.

changing the order of summation yields

$$\text{L. H. S.} = \sum_{r=a+1}^{b-1} \nabla_r f(r) \left(\sum_{s=\rho(r)+1}^{b-1} \frac{B(\alpha)}{1-\alpha} g(s) E_{\alpha, \mu}^{\gamma}(\lambda, s-\rho(r)) \right).$$

By the summation by parts formula (2) of nabla difference,

$$\begin{aligned} \text{L. H. S.} &= f(r) \left(\sum_{s=r+1}^{b-1} \frac{B(\alpha)}{1-\alpha} g(s) E_{\alpha, \mu}^{\gamma}(\lambda, s-r) \right) \Big|_{r=a}^{b-1} \\ &\quad - \sum_{r=a+1}^{b-1} f(r) \nabla_r \left(\sum_{s=r+1}^{b-1} \frac{B(\alpha)}{1-\alpha} g(s) E_{\alpha, \mu}^{\gamma}(\lambda, s-r) \right). \end{aligned}$$

Since $\nabla f(r) = \Delta f(r-1)$

$$\begin{aligned} \text{L. H. S.} = & \sum_{r=a+1}^{b-1} f(r) \left(\Delta_r \frac{-B(\alpha)}{1-\alpha} \sum_{s=r-1+1}^{b-1} g(s) E_{\alpha,\mu}^{\gamma}(\lambda, s - \rho(r)) \right) \\ & + f(r) \left(\sum_{s=r+1}^{b-1} \frac{B(\alpha)}{1-\alpha} g(s) E_{\alpha,\mu}^{\gamma}(\lambda, s - r) \right) \Big|_{r=a}^{b-1}. \end{aligned}$$

And using the definition of the generalized ABR nabla right fractional difference (19), it follows:

$$\text{L. H. S.} = \sum_{r=a+1}^{b-1} f(r) ({}^{ABR}\nabla_b^{\alpha,\mu,\gamma} g)(r) + f(r) \left(\sum_{s=r+1}^{b-1} \frac{B(\alpha)}{1-\alpha} g(s) E_{\alpha,\mu}^{\gamma}(\lambda, s - r) \right) \Big|_{r=a}^{b-1} = \text{R. H. S.}$$

Note, the right-hand side is reached by changing the name of the variables.

Now, the summation-by-parts formula for the generalized ABC nabla right fractional difference is stated in the following theorem:

Theorem 4.2 (Summation-by-Parts Formula for the Generalized ABC Nabla Right Fractional Difference)

Consider the real-valued be functions f and g whose domains are $\mathbb{N}_a^b$, on which $a \equiv b(\text{mod } 1)$. Suppose that $\alpha \in (0, \frac{1}{2})$, the formula below is then valid:

$$\begin{aligned} & \sum_{s=a+1}^{b-1} g(s) ({}^{ABC}\nabla_b^{\alpha,\mu,\gamma} f)(s) \\ & = \sum_{s=a+1}^{b-1} f(s) ({}^{ABR}\nabla_a^{\alpha,\mu,\gamma} g)(s) \left(\sum_{r=a+1}^{s-1} \frac{-B(\alpha)}{1-\alpha} g(r) E_{\alpha,\mu}^{\gamma}(\lambda, s - r) \right) \Big|_{s=a+1}^b. \end{aligned} \quad (29)$$

Proof. Starting with the definition of the generalized ABC nabla right fractional sum (21),

$$\text{L. H. S.} = \sum_{s=a+1}^{b-1} g(s) \frac{-B(\alpha)}{1-\alpha} \sum_{r=s}^{b-1} E_{\alpha,\mu}^{\gamma}(\lambda, r - \rho(s)) \Delta_r f(r).$$

Since $a+1 \leq s \leq b-1$ and $s \leq r \leq b-1$,

Then $a+1 \leq s \leq r \leq b-1$.

Hence, $a+1 \leq r \leq b-1$ and $a+1 \leq s \leq r$.

Thus, by changing the order of summation, one obtains

$$\begin{aligned} \text{L. H. S.} = & \sum_{r=a+1}^{b-1} \Delta_r f(r) \left(\sum_{s=a+1}^r \frac{-B(\alpha)}{1-\alpha} g(s) E_{\alpha,\mu}^{\gamma}(\lambda, r - \rho(s)) \right) \\ & = \sum_{r=a+1}^{b-1} \Delta_r f(r) \left(\sum_{s=a+1}^{\sigma(r)-1} \frac{-B(\alpha)}{1-\alpha} g(s) E_{\alpha,\mu}^{\gamma}(\lambda, \sigma(r) - s) \right). \end{aligned}$$

By the summation by parts formula (1) of delta difference,

$$\text{L. H. S.} = f(r) \left(\sum_{s=a+1}^{r-1} \frac{-B(\alpha)}{1-\alpha} g(s) E_{\alpha,\mu}^{\gamma}(\lambda, r-s) \right) \Big|_{r=a+1}^b + \sum_{r=a+1}^{b-1} f(r) \Delta_r \left(\sum_{s=a+1}^{r-1} \frac{B(\alpha)}{1-\alpha} g(s) E_{\alpha,\mu}^{\gamma}(\lambda, r-s) \right).$$

Since $\Delta f(r) = \nabla f(r+1)$

$$\begin{aligned} \text{L. H. S.} = & \sum_{r=a+1}^{b-1} f(r) \left(\nabla_r \frac{B(\alpha)}{1-\alpha} \sum_{s=a+1}^r g(s) E_{\alpha,\mu}^{\gamma}(\lambda, r-\rho(s)) \right) \\ & + f(r) \left(\sum_{s=a+1}^{r-1} \frac{-B(\alpha)}{1-\alpha} g(s) E_{\alpha,\mu}^{\gamma}(\lambda, r-s) \right) \Big|_{r=a+1}^b. \end{aligned}$$

Using the definition of the generalized ABR nabla left fractional difference (18), one obtains

$$\text{L. H. S.} = \sum_{r=a+1}^{b-1} f(r) ({}^{ABR}_a \nabla^{\alpha,\mu,\gamma} g)(r) + f(r) \left(\sum_{s=a+1}^{r-1} \frac{-B(\alpha)}{1-\alpha} g(s) E_{\alpha,\mu}^{\gamma}(\lambda, r-s) \right) \Big|_{r=a+1}^b = \text{R. H. S.}$$

Note, the right-hand side is reached by changing the name of the variables.

Since the required summation-by-parts formulas have been presented, the discrete nabla fractional difference Euler-Lagrange equations with the generalized M-L function of three parameters will be studied in the next subsection.

4.2 Discrete Fractional Nabla Euler-Lagrange Equations with Generalized ABC and ABR Fractional Differences

the Euler-Lagrange equation for the case in which the Lagrangian contains the generalized ABC nabla left fractional difference is studied in the next Theorem.

Theorem 4.3 [Euler–Lagrange Equation with Generalized ABC Nabla Left Fractional Difference in the Lagrangian] Let $S = \{y: \mathbb{N}_a^b \rightarrow \mathbb{R}, y(a) = A, y(b-1) = B\}$, where a, b are real numbers, such that $a \equiv b \pmod{1}$ and $a < b$. Assume that $\alpha \in (0, \frac{1}{2})$. Consider the following discrete fractional functional

$$J(y) = \sum_{t=a+1}^{b-1} L(t, y(t), {}^{ABC}_a \nabla^{\alpha,\mu,\gamma} y(t)),$$

where $L: \mathbb{N}_a^b \times \mathbb{R} \times \mathbb{R} \rightarrow \mathbb{R}$. Suppose that $y \in S$ is a local extremum of J . Then the y fulfills the following Euler-Lagrange condition

$$L_1(t) + {}^{ABR}_b \nabla_b^{\alpha,\mu,\gamma} L_2(t) = 0, \quad \forall t \in \mathbb{N}_{a+1}^{b-1}, \quad (28)$$

where $L_1(t) = \frac{\partial L(t)}{\partial y}$ and $L_2(t) = \frac{\partial L(t)}{\partial ({}^{ABC}_a \nabla^{\alpha, \mu, \gamma} y)}$.

Proof. Let $(X, \|\cdot\|)$ be the space of functions, on which the discrete functional J is defined. Without loss of generality, suppose that $y \in S$ is a local maximum of the discrete functional J . Therefore, there exists $\varepsilon > 0$ for which

$$J(\hat{y}) - J(y) \leq 0, \quad (29)$$

for all $\hat{y} \in S$, with $\|\hat{y} - y\| < \varepsilon$.

For any $\hat{y} \in S$, there is an $\eta \in H := \{y: \mathbb{N}_a^b \rightarrow \mathbb{R}, y(a) = y(b-1) = 0\}$ such that $\hat{y} = y + \varepsilon \eta$.

Since that the ABC nabla fractional difference is linear then

$${}^{ABC}_a \nabla^{\alpha, \mu, \gamma} \hat{y}(t) = {}^{ABC}_a \nabla^{\alpha, \mu, \gamma} y(t) + \varepsilon {}^{ABC}_a \nabla^{\alpha, \mu, \gamma} \eta(t).$$

Also,

$$L(t, \hat{y}(t), {}^{ABC}_a \nabla^{\alpha, \mu, \gamma} \hat{y}(t)) = L(t, y(t) + \varepsilon \eta(t), {}^{ABC}_a \nabla^{\alpha, \mu, \gamma} y(t) + \varepsilon {}^{ABC}_a \nabla^{\alpha, \mu, \gamma} \eta(t)).$$

By the ε -Taylor's theorem,

$$\begin{aligned} L(t, \hat{y}(t), {}^{ABC}_a \nabla^{\alpha, \mu, \gamma} \hat{y}(t)) &= L(t, y(t), {}^{ABC}_a \nabla^{\alpha, \mu, \gamma} y(t)) + \varepsilon \left[\eta(t) \frac{\partial L}{\partial y}(t) + ({}^{ABC}_a \nabla^{\alpha, \mu, \gamma} \eta(t)) \frac{\partial L}{\partial ({}^{ABC}_a \nabla^{\alpha, \mu, \gamma} y)}(t) \right] \\ &\quad + O(\varepsilon^2). \end{aligned}$$

Therefore,

$$J(\hat{y}) - J(y) = \varepsilon \sum_{t=a+1}^{b-1} [\eta(t) L_1(t) + ({}^{ABC}_a \nabla^{\alpha, \mu, \gamma} \eta(t)) L_2(t)] + O(\varepsilon^2).$$

The sign of $J(\hat{y}) - J(y)$ is determined by the sign of the first variation $\delta J(\eta, y)$. But, if $\eta \in H$ then $-\eta \in H$ as well. And, $\delta J(\eta, y) = -\delta J(-\eta, y)$, which implies that the first variation should be zero for all $\eta \in H$. That is to say:

$$\delta J(\eta, y) = \sum_{t=a+1}^{b-1} [\eta(t) L_1(t) + ({}^{ABC}_a \nabla^{\alpha, \mu, \gamma} \eta(t)) L_2(t)] = 0, \quad \forall \eta \in H. \quad (30)$$

By applying the summation by parts formula (28), it follows that for all η in H :

$$\delta J(\eta, y) = \sum_{t=a+1}^{b-1} \eta(t) [L_1(t) + ({}^{ABR}_b \nabla^{\alpha, \mu, \gamma} L_2(t))] + \eta(t) \left(\sum_{r=t+1}^{b-1} \frac{B(\alpha)}{1-\alpha} L_2(r) E_{\alpha, \mu}^{\gamma}(\lambda, r-t) \right) \Big|_{t=a}^{b-1} = 0.$$

Applying the boundary conditions $\eta(a) = \eta(b-1) = 0$ leads to

$$\delta J(\eta, y) = \sum_{t=a+1}^{b-1} \eta(t) [L_1(t) + {}^{ABR}\nabla_b^{\alpha, \mu, \gamma} L_2(t)] = 0 \quad \forall \eta \in H$$

Consider a special choice of η :

$$\eta(t) = \begin{cases} 1, & t = a + 1 \\ 0, & \text{otherwise} \end{cases}$$

This implies that

$$L_1(t) + {}^{ABR}\nabla_b^{\alpha, \mu, \gamma} L_2(t) = 0, \quad \text{at } t = a + 1.$$

Another choice of η is:

$$\eta(t) = \begin{cases} 1, & t = a + 2 \\ 0, & \text{otherwise} \end{cases}$$

This implies that

$$L_1(t) + {}^{ABR}\nabla_b^{\alpha, \mu, \gamma} L_2(t) = 0, \quad \text{at } t = a + 2.$$

Go on on the same manner until the last choice of η :

$$\eta(t) = \begin{cases} 1, & t = b - 1 \\ 0, & \text{otherwise} \end{cases}$$

This implies that

$$L_1(t) + {}^{ABR}\nabla_b^{\alpha, \mu, \gamma} L_2(t) = 0, \quad \text{at } t = b - 1.$$

In other words: one deduces that

$$L_1(t) + {}^{ABR}\nabla_b^{\alpha, \mu, \gamma} L_2(t) = 0, \quad \forall t \in \mathbb{N}_{a+1}^{b-1}.$$

The following theorem is devoted to the case in which the Lagrangian is a function of the generalized ABC nabla right fractional difference. The previous theorem together with the following theorem can be viewed as a generalization of the work of Abdeljawad and Baleanu in [23].

Theorem 4.4 [Euler–Lagrange Equation with Generalized ABC Nabla right Fractional Difference in the Lagrangian] Let J take the following form:

$$J(y) = \sum_{t=a+1}^{b-1} L(t, y(t), {}^{ABC}\nabla_b^{\alpha, \mu, \gamma} y(t)),$$

where $L: \mathbb{N}_a^b \times \mathbb{R} \times \mathbb{R} \rightarrow \mathbb{R}$ and a, b are real values such that $a < b$ and $a \equiv b \pmod{1}$. Assume further that $0 < \alpha < \frac{1}{2}$ and

$$S = \{y: \mathbb{N}_a^b \rightarrow \mathbb{R}, \quad y(a+1) = A, y(b) = B\}$$

If $y \in S$ is a local extremum of J , then y is subject to the following Euler-Lagrange condition:

$$L_1(t) + {}^{ABR}_a \nabla^{\alpha, \mu, \gamma} L_2(t) = 0, \quad \forall t \in \mathbb{N}_{a+1}^{b-1}, \quad (31)$$

where $L_1(t) = \frac{\partial L(t)}{\partial y}$ and $L_2(t) = \frac{\partial L(t)}{\partial ({}^{ABC}_a \nabla^{\alpha, \mu, \gamma} y)}$.

Proof. Assume that J is a discrete fractional functional with domain $(X, \|\cdot\|)$. Assume that $y \in S$ is a local maximum of the functional J ; the case of a minimum follows analogously. Then, for some $\varepsilon > 0$

$$J(\hat{y}) - J(y) \leq 0, \quad (32)$$

for all $\hat{y} \in S$, with $\|\hat{y} - y\| < \varepsilon$.

For any $\hat{y} \in S$, there is an $\eta \in H := \{y: \mathbb{N}_a^b \rightarrow \mathbb{R}, y(a+1) = y(b) = 0\}$ for which $\hat{y} = y + \varepsilon \eta$.

As in Theorem 4.3, the first variation is found by applying ε -Taylor's theorem. Then, to ensure that (34) is satisfied, one obtains the following:

$$\delta J(\eta, y) = \sum_{t=a+1}^{b-1} [\eta(t) L_1(t) + {}^{ABC}_b \nabla^{\alpha, \mu, \gamma} \eta(t) L_2(t)] = 0, \quad \forall \eta \in H. \quad (33)$$

Summation by parts formula (29) leads to the following:

$$\delta J(\eta, y) = \sum_{t=a+1}^{b-1} \eta(t) [L_1(t) + {}^{ABR}_a \nabla^{\alpha, \mu, \gamma} L_2(t)] + \eta(t) \left(\sum_{r=a+1}^{t-1} \frac{-B(\alpha)}{1-\alpha} L_2(r) E_{\alpha, \mu}^{\gamma}(\lambda, t-r) \right) \Big|_{t=a+1}^b, \\ \forall \eta \in H.$$

But, $\eta(a+1) = \eta(b) = 0$. Thus,

$$\delta J(\eta, y) = \sum_{t=a+1}^{b-1} \eta(t) [L_1(t) + {}^{ABR}_a \nabla^{\alpha, \mu, \gamma} L_2(t)] = 0, \quad \forall \eta \in H.$$

Since η is arbitrary, certain choices of α similar to the proof of Theorem 4.3 yield

$$L_1(t) + {}^{ABR}_a \nabla^{\alpha, \mu, \gamma} L_2(t) = 0, \quad \forall t \in \mathbb{N}_{a+1}^{b-1}.$$

Finally, to illustrate the results, two examples of physical interest, corresponding to Theorems 4.3 and 4.4, are presented.

Example 4.1 Consider the following discrete fractional functional

$$J(y) = \sum_{t=a+1}^{b-1} \frac{1}{2} ({}^{ABC}_a \nabla^{\alpha, \mu, \gamma} y(t))^2 - V(y, t).$$

Let $\alpha \in (0, \frac{1}{2})$, $y(a) = A$, and $y(b-1) = B$, where $A, B \in \mathbb{R}$ and $m \in \mathbb{R}$ is any constant. By Theorem 4.3, the Euler-Lagrange equation for this functional is given by

$${}^{ABR}_b \nabla^{\alpha, \mu, \gamma} ({}^{ABC}_a \nabla^{\alpha, \mu, \gamma} y)(t) - \frac{\partial V}{\partial y}(t) = 0, \quad \forall t \in \mathbb{N}_{a+1}^{b-1}.$$

Example 4.2 Let

$$J(y) = \sum_{t=a+1}^{b-1} \frac{1}{2} \left({}^{ABC}\nabla_b^{\alpha,\mu,\gamma} y(t) \right)^2 - V(y, t),$$

with $0 < \alpha < \frac{1}{2}$, $y(a+1) = A$, and $y(b) = B$, where A, B are real constants, and $m \in \mathbb{R}$ is any constant. By Theorem 4.4, the corresponding Euler-Lagrange equation reads

$${}^{ABR}\nabla_a^{\alpha,\mu,\gamma} \left({}^{ABC}\nabla_b^{\alpha,\mu,\gamma} y \right)(t) - \frac{\partial V}{\partial y}(t) = 0, \forall t \in \mathbb{N}_{a+1}^{b-1}.$$

5. Conclusion and Future Directions

This paper is devoted to the study of discrete fractional variational problems involving ABC and ABR nabla fractional differences with the generalized M–L kernels. It is known that integration by parts is essential in calculus of variations as well as in fractional calculus of variations. The same is applied in discrete fractional calculus of variations thus new summation by parts formula for ABC nabla left and right fractional differences are obtained to use them in getting new discrete nabla Euler–Lagrange equations.

New discrete fractional Euler–Lagrange equations were derived for functionals involving the generalized ABC nabla left and right fractional differences with the generalized M–L function of three parameters. These results extend already existing Euler–Lagrange equations with ABC and ABR fractional differences and provide a more general formulation within a broader setting. Some illustrative examples of physical interest were also established to demonstrate the viability of the obtained theoretical results.

Even though the present work establishes several theoretical results, a number of important research directions is still open for further investigation. One natural extension is to study discrete fractional variational problems with delay terms since such terms frequently arise in applications, and can significantly affect the stability and dynamical behavior of solutions. The problems studied in this thesis are formulated with fixed end-point boundary conditions thus future work may address discrete fractional variational problems with more general types of constraints, including isoperimetric constraints by applying Lagrange multiplier techniques. Further promising extensions may include the development of ABC and ABR delta fractional sums and differences, together with the derivation of the corresponding Euler–Lagrange equations.

ASA, sarcasm detection, and real-time deployment on edge devices.

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Ethical consideration

Not applicable.

Consent to participate

Not applicable

Conflicts of interest

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References

- [1] Miller KS and Ross B. Fractional Difference Calculus. Proceedings of the International Symposium on Univalent Functions, Fractional Calculus and their Applications. Nihon University, Koriyama, Japan, 1989:139–52
- [2] Hilfer R. Threefold Introduction to Fractional Derivatives. Anomalous Transport: Foundations and Applications. Wiley-VCH, 2008 :17–73. DOI: 10.1002/9783527622979.ch2
- [3] Boukhouima A, Hattaf K, Lotfi EM, Mahrouf M, Torres DFM, and Yousfi N. Lyapunov functions for fractional-order systems in biology: Methods and applications. Chaos, Solitons & Fractals 2020; 140:110224. DOI: 10.1016/j.chaos.2020.110224
- [4] Skovranek T. The Mittag-Leffler fitting of the Phillips curve. Mathematics 2019; 7:589. DOI: 10.3390/math7070589
- [5] Silva MF, Machado JAT, and Barbosa RS. Using fractional derivatives in joint control of hexapod robots. Journal of Vibration and Control 2008; 14:1473–85. DOI: 10.1177/1077546307087436
- [6] Barros LC, Lopes MM, Pedro FS, Esmi E, Santos JPC, and Sánchez DE. The memory effect on fractional calculus: An application in the spread of COVID-19. Computational and Applied Mathematics 2021; 40:72. DOI: 10.1007/s40314-021-01456-z
- [7] Podlubny I. Fractional Differential Equations: An Introduction to Fractional Derivatives, Fractional Differential Equations, to Methods of Their Solution and Some of Their Applications. Elsevier, 1999 :368. DOI: 10.1016/s0076-5392(99)x8001-5
- [8] Samko SG, Kilbas AA, and Marichev OI. Fractional Integrals and Derivatives: Theory and Applications. Philadelphia: Gordon and Breach Science Publishers, 1993
- [9] Suwan I, Owies S, Abussa M, and Abdeljawad T. Monotonicity Analysis of Fractional Proportional Differences. Discrete Dynamics in Nature and Society 2020; 2020:Article ID 4867927, 11 pages
- [10] Suwan I, Owies S, and Abdeljawad T. Fractional Differences with Exponential Kernels and Their Monotonicity Properties. Mathematical Methods in the Applied Sciences 2021; 44:8432–46
- [11] Bachher M, Abbas IA, and Sarkar N. Fractional Order Generalized Thermoelastic Infinite Porous Material Having Cylindrical Pores Subject to Ramp-Type Heating. Enlightenment of Pure and Applied Mathematics 2016
- [12] Benkhettou N, Hassani S, and Torres DFM. A Conformable Fractional Calculus on Arbitrary Time Scales. Journal of King Saud University - Science 2015. DOI: 10.1016/j.jksus.2015.05.003

- [15] Atici FM and Şengül S. Modeling with fractional difference equations. *Journal of Mathematical Analysis and Applications* 2010; 369:1–9. DOI: 10.1016/j.jmaa.2010.02.009
- [16] Chapman S. On non-integral orders of summability of series and integrals. *Proceedings of the London Mathematical Society* (2) 1910; 9:369–409. DOI: 10.1112/plms/s2-9.1.369
- [17] Atıcı FM and Eloe PW. A transform method in discrete fractional calculus. *International Journal of Difference Equations* 2007; 2:165–76
- [18] Abdeljawad T and Baleanu D. Fractional Differences and Integration by Parts. *J. Comput. Anal. Appl.* 2011; 13:574–82
- [19] Gray HL and Zhang NF. On a new definition of the fractional difference. *Mathematics of Computation* 1988; 50:513–29. DOI: 10.1090/s0025-5718-1988-0929549-2
- [20] Abdeljawad T and Atici FM. On the definitions of nabla fractional operators. *Abstract and Applied Analysis* 2012; 2012:13pp. DOI: 10.1155/2012/406757
- [21] Ahrendt K, Castle L, Holm M, and Yochman K. Laplace transforms for the nabla-difference operator and a fractional variation of parameters formula. *Communications in Applied Analysis* 2012 Jul; 16
- [22] Abdeljawad T. On Delta and Nabla Caputo Fractional Differences and Dual Identities. *Discrete Dynamics in Nature and Society* 2013; 2013:12pp. DOI: 10.1155/2013/406910
- [23] Caputo M and Fabrizio M. A New Definition of Fractional Derivative without Singular Kernel. *Progress in Fractional Differentiation and Applications* 2015; 1:73–85
- [24] Atangana A and Baleanu D. New Fractional Derivatives with Nonlocal and Non-Singular Kernel: Theory and Application to Heat Transfer Model. *Thermal Science* 2016; 20:763–9. DOI: 10.2298/TSCI160111018A
- [25] Abdeljawad T and Baleanu D. Discrete fractional differences with nonsingular discrete Mittag-Leffler kernels. *Advances in Difference Equations* 2016; 2016. DOI: 10.1186/s13662-016-0949-5
- [26] Abdeljawad T and Baleanu D. On Fractional Derivatives with Exponential Kernel and Their Discrete Versions. *Reports on Mathematical Physics* 2017; 80. DOI: 10.1016/s0034-4877(17)30059-9
- [27] Abdeljawad T. Fractional difference operators with discrete generalized Mittag-Leffler kernels. *Chaos, Solitons & Fractals* 2019; 126:315–24. DOI: 10.1016/j.chaos.2019.06.012
- [28] Brunt Bv. *The Calculus of Variations*. Universitext. New York, NY: Springer, 2004 :XIV+292. DOI: 10.1007/b97436
- [29] Abdeljawad T. Nabla Euler–Lagrange equations in discrete fractional variational calculus within Riemann and Caputo. *International Journal of Mathematics and Computation* 2014; 22:144–53. DOI: <https://doi.org/10.48550/arXiv.1703.06751>
- [30] Goodrich C and Peterson AC. *Discrete Fractional Calculus*. Vol. 1350. *Lecture Notes in Mathematics*. Berlin: Springer, 2015. DOI: 10.1007/978-3-319-25562-0
- [31] Bohner M and Peterson AC. *Dynamic Equations on Time Scales*. Boston: Birkhäuser, 2001. DOI: 10.1007/978-1-4612-0201-1
- [32] Kilbas AA, Srivastava HM, and Trujillo JJ. *Theory and Applications of Fractional Differential Equations*. Vol. 204. *North-Holland Mathematics Studies*. Amsterdam: Elsevier Science B.V., 2006. DOI: 10.1016/S0304-0208(06)80001-0

-
- [33] Agrawal OP. Formulation of Euler–Lagrange equations for fractional variational problems. *Journal of Mathematical Analysis and Applications* 2002; 272:368–79. DOI: 10.1016/S0022-247X(02)00180-4
 - [34] Frederico GSF and Torres DFM. A formulation of Noether’s theorem for fractional problems of the calculus of variations. *Journal of Mathematical Analysis and Applications* 2007; 334:834–46. DOI: 10.1016/j.jmaa.2007.01.013
 - [35] Bohner M. Calculus of variations on time scales. *Dynamics of Continuous, Discrete and Impulsive Systems Series A: Mathematical Analysis* 2004; 13:339–49
 - [36] Bastos NRO, Ferreira RAC, and Torres DFM. Discrete-time fractional variational problems. *Signal Processing* 2011; 91:513–24. DOI: 10.1016/j.sigpro.2010.05.001