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This issue of *Lebda Medical Journal* showcases a diverse and multidisciplinary collection of research articles reflecting Libya's growing contributions to medical, pharmaceutical, and public health sciences. Topics span neurovascular insights into migraine pathophysiology, the biochemical and antibacterial properties of Libyan propolis, and pharmacist engagement in clinical practice reform. Several studies explore comparative pharmaceutical evaluations, including essential oil testing, paracetamol product analysis, and vitamin D status in Zillah municipality.

The issue also highlights strategic educational innovations such as integrating bromatology into pharmacy curricula, and investigates microbial contamination risks among health sciences students. Molecular docking studies on henna-derived compounds offer promising antimycobacterial leads, while transfusion safety is addressed through plasma quality control assessments. Finally, prescription audit data from Alkhoms city and a comprehensive review of mangosteen extract underscore the journal's commitment to evidence-based practice and regional health priorities.

Together, these articles reflect the journal's mission to advance scientific inquiry, clinical relevance, and public health impact across Libya and the broader region.

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A Review of Migraine as a Neurovascular Disorder: Causes, Biochemical Changes, and Comparative Treatments

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ABSTRACT

Migraine is a chronic neurovascular disorder and one of the most disabling neurological conditions worldwide. It is characterized by recurrent attacks of unilateral, pulsating headache accompanied by nausea, photophobia, and phonophobia, with or without aura. Both genetic and environmental factors contribute to its pathogenesis. Genome-wide association studies have identified multiple susceptibility loci, while hormonal fluctuations, stress, sleep disturbance, and dietary factors act as common triggers. Biochemically, cortical spreading depression, activation of the trigeminovascular system, and release of calcitonin gene-related peptide (CGRP) and serotonin dysregulation are central to attack generation. Epidemiological studies reveal that migraine affects over one billion people globally, with a higher prevalence among women, particularly during reproductive years, underscoring the role of sex hormones. Acute management includes NSAIDs, triptans, gepants, and lasmiditan, with antiemetics for nausea. Preventive strategies are indicated in frequent or disabling attacks and include beta-blockers, topiramate, valproate, antidepressants, and the newer anti-CGRP monoclonal antibodies. Non-pharmacological approaches such as lifestyle modification, trigger avoidance, cognitive behavioral therapy, and neuromodulation devices complement drug therapy. Advances in targeted treatments have improved outcomes, but equitable access remains a challenge. Optimized, individualized therapy offers significant potential to reduce disability and improve quality of life for patients with migraine.

Keywords: *Migraine, Aura, Triggers, Triptans, Gepants*

1. Introduction

Migraine is classified as a primary headache disorder by the International Headache Society. It is typically characterized by episodes of throbbing or pulsating headache pain, usually unilateral (on one side of the head), lasting 4–72 hours when left untreated. The headache is characteristically moderate to severe in intensity and aggravated by routine physical activity; it is commonly accompanied by nausea and/or

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photophobia and phonophobia (1). Migraines are broadly divided into two major subtypes: migraine without aura and migraine with aura. Migraine *with aura* is distinguished by transient focal neurological symptoms that precede or accompany the headache, most often visual disturbances such as flashes of light or blind spots. Aura symptoms typically develop gradually over 5–20 minutes and last less than 60 minutes, and may include visual zigzag lines, scotomas, sensory changes (like tingling), or speech disturbances (2). In migraine *without aura*, no such neurological warning occurs before the headache phase. Most migraineurs experience the headache phase with its associated features, and about one-third of patients have aura with some or all attacks (3). In addition, patients may experience a prodrome phase (hours to days before an attack, with symptoms like fatigue, neck stiffness, or food cravings) and a postdrome phase (after the headache, with symptoms like exhaustion or mild headache). Migraine is thus a clinical syndrome with well-defined diagnostic criteria, and diagnosis is made by history and exam, since imaging or lab tests are typically normal in primary migraine. Chronic migraine is defined by a high frequency of attacks (15 or more headache days per month, with at least 8 being migraine days) and represents an evolution of episodic migraine in some individuals (4).

2. Review Approach

This narrative review provides a thematic synthesis of current evidence on migraine and primary headache disorders, integrating insights from epidemiology, neurobiology, clinical diagnosis, and therapeutic strategies. Literature was primarily identified through targeted searches in PubMed, Google Scholar and Scopus (2014–2025), supplemented by manual screening of reference lists from key publications.

3. Causes and triggers

3.1. Genetic factors

Migraine is heritable. Twin studies estimate heritability at roughly 42%, indicating that almost half of the variability in susceptibility arises from genetic factors (5, 6). Genome-wide meta-analyses have now identified 122 independent loci and 181 credible sets linked to migraine, underscoring neuronal, vascular, and inflammatory pathways (7). Well-characterized monogenic forms such as familial hemiplegic migraine are caused by mutations in ion-channel genes (**CACNA1A**, **ATP1A2**, **SCN1A**) affecting excitatory neurotransmission. Epigenetic changes – reversible chemical modifications to DNA and histone proteins – are increasingly recognized as contributors to migraine. Environmental factors such as stress or inflammation can alter methylation patterns and regulate genes like **MEF2D** and **PRDM16**, thereby influencing susceptibility and chronification (8).

3.2. Hormonal and metabolic influences

Migraine prevalence is roughly two to three times higher in women than in men, suggesting a strong hormonal influence (9). Globally, recent global burden analyses confirm that women consistently bear a greater absolute burden despite a faster relative rise among men (10). Estrogen fluctuations modulate serotonin and calcitonin gene-related peptide (CGRP) levels. High estrogen levels enhance the excitability of cortical neurons and increase serotonin, lowering the threshold for cortical spreading depression and trigemino-vascular activation, while the drop in estrogen during menses can precipitate attacks. Risk is highest during reproductive years and declines after menopause (11, 12).

Other metabolic factors include obesity, dyslipidemia, hypertension, diabetes, and insulin resistance, which are associated with increased migraine risk (8).

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3.3 Environmental and lifestyle triggers

Migraine attacks are often precipitated by environmental or behavioral triggers in genetically susceptible individuals. Stressful events are among the most common migraine triggers. In a retrospective survey of individuals with migraine, 80% reported stress, followed by hormonal changes (65%), skipped meals (57%), weather changes (53%), sleep disturbances (50%), and perfumes and chemicals (40%) (13-15).

Additional triggers include bright light, loud sounds, barometric pressure changes, alcohol (especially red wine), caffeine withdrawal, heavy exercise, fasting, and certain foods high in tyramine or aspartame (16). A large review identified lower socioeconomic status, high caffeine intake, medication overuse, head trauma, and sleep disorders as risk factors. Women often report menstrual migraine, for which short-term prophylaxis with triptans or NSAIDs may be effective. Alcohol is reported as a trigger by many patients, although evidence is mixed; some studies show a roughly 51% increased risk (8).

3.4. Comorbidities and psychological factors

Migraine often co-occurs with anxiety, depression, bipolar disorder, and other pain syndromes. Stress, anxiety, and phobic disorders have been identified as risk factors (17). Chronic sleep deprivation, shift work, and circadian rhythm disturbance are strongly linked to migraine attacks; people with migraines are more than three times as likely to experience insomnia (17, 18). Obstructive sleep apnea may also trigger headaches (19). Smoking, obesity, and high caffeine intake can worsen migraine frequency and severity (20). Post-traumatic headaches after mild traumatic brain injury may share pathophysiological mechanisms with migraine (21). Identifying and managing co-morbid conditions is therefore an essential component of migraine care.

4. Biochemical changes during a migraine attack

Migraine is considered a neurovascular disorder. Contemporary models emphasize the interplay between cortical excitability, activation of trigeminal nociceptive pathways, and release of vasoactive neuropeptides. Attacks often begin with cortical spreading depression (CSD), a wave of neuronal depolarization followed by a period of suppression that travels across the cortex. CSD can trigger aura symptoms and activate trigeminal afferents via pannexin-1 channels (22). Activation of the trigeminovascular system leads to the release of neuropeptides, including CGRP, substance P, neurokinin A, and pituitary adenylate cyclase-activating peptide (PACAP) from perivascular nerve endings. These peptides cause vasodilation and plasma protein extravasation, generating sterile neurogenic inflammation around meningeal blood vessels. CGRP is particularly important; its levels rise during migraine attacks, and infusion of CGRP can trigger migraine-like headaches (23, 24). Serotonin (5-HT) levels are also altered. Trigeminovascular neurons express 5-HT1B/1D receptors; low interictal serotonin and high CGRP promote trigeminal activation, while triptans act as 5-HT1B/1D agonists, normalizing serotonin and blocking CGRP release (25). Neuroimaging studies reveal changes in cortical and subcortical networks during attacks. Functional MRI demonstrates activation of the hypothalamus, brainstem nuclei, thalamus, and somatosensory cortex. The hypothalamus may orchestrate pre-monitory symptoms through connections to the trigeminal nuclei. Elevated nitric oxide and inflammatory cytokines further sensitize nociceptors, contributing to central sensitization and chronification. After the attack, there is often a post-drome phase with fatigue and cognitive slowing, suggesting widespread neural changes (26).

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5. Epidemiology

Migraine is one of the most prevalent neurologic disorders worldwide. A large systematic analysis estimated that there were approximately 1.1 billion prevalent cases of migraine worldwide in 2019. The global age-standardized prevalence increased by 1.7% between 1990 and 2019, making migraine a leading cause of disability (27). Migraine accounted for 16.3% of all neurological disorder disability-adjusted life years (DALYs) in 2016 and remains the second leading cause of years lived with disability worldwide (28). The current best estimate of global migraine prevalence is 14–15%, and, in terms of burden, migraine accounts for 4.9% of global ill health, quantified as years lived with disability. Prevalence peaks in early adulthood and declines after age 45 (27).

6. Sex differences and hormonal influence

Migraine is significantly more prevalent in women. Population studies estimate that about 17% of women and 6% of men experience migraine (29-31). The global age-standardised rate of years lived with disability (YLD) attributable to migraine was 525.5 per 100,000, up by 1.5% since 1990. Migraine burden is not evenly distributed. Prevalence is consistently higher in women, and age-specific prevalence rises into the 40–44 year age group before declining (27). The ratio peaks during reproductive years and declines after menopause. Female sex hormones modulate neurotransmitter systems implicated in migraine. Estrogen increases nitric oxide synthase activity and increases serotonin levels, promoting trigeminovascular activation; cyclic withdrawal of estrogen during menstruation is a common trigger (11). During pregnancy, high stable estrogen levels often improve migraine, while postpartum hormone fluctuations may worsen symptoms. Women also appear more susceptible to chronicity due to the interplay of hormones, stress, sleep disturbance, and depression (8).

7. Acute (abortive) treatment

Treatment goals for acute migraine are to relieve pain and associated symptoms quickly, restore normal function, and minimize recurrence. Early treatment during the headache phase improves efficacy. Because individual response varies, therapy should be personalized based on attack severity, associated symptoms, comorbidities, and patient preferences. Evidence-based guidelines support the following options:

7.1. General measures

Treatment choice depends on symptom severity, associated nausea or vomiting, comorbidities, and prior drug response. Early, single-dose treatment is usually more effective than repeated small doses. For patients unable to tolerate oral medications, nonoral routes or neuromodulation may be used. Key principles include patient education, use of migraine-specific drugs (eg, triptans, CGRP antagonists, lasmiditan), appropriate route of administration, rescue medication for severe attacks, and avoiding medication overuse headache (32).

For mild attacks without vomiting or severe nausea, simple analgesics such as NSAIDs (aspirin, ibuprofen, naproxen, diclofenac) or acetaminophen are first-line options. If ineffective, triptans may be added. Combining NSAIDs with triptans can be more effective than either alone. Antiemetics may be used when nausea is present (33, 34).

Patients with moderate to severe migraine often require triptans, with or without NSAIDs (35). Alternatives include CGRP antagonists, lasmiditan, or dihydroergotamine. For those with significant nausea or vomiting, subcutaneous, intranasal, or parenteral options are preferred (eg, subcutaneous sumatriptan, nasal triptans, parenteral dihydroergotamine) (36).

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Prolonged attacks >72 hours (Status Migrainosus) may need intravenous fluids and parenteral therapy such as ketorolac, dopamine receptor blockers, valproate, or dihydroergotamine. Intravenous dexamethasone is often given to reduce relapse risk (37, 38).

7.1.1. Triptans

Triptans (e.g., sumatriptan, rizatriptan, eletriptan, zolmitriptan) are highly effective and specifically designed for migraine treatment. They act by vasoconstriction and blocking the trigeminal pathways. Different formulations (oral, subcutaneous, nasal) allow individualized use. Early administration improves outcomes (39). They should be avoided in patients with cardiovascular disease, hemiplegic migraine, or brainstem aura (40).

7.1.2. Combination Therapy

The best evidence supports the sumatriptan-naproxen combination, which is more effective than either drug alone (41, 42).

7.1.3. Antiemetics

Dopamine antagonists such as IV metoclopramide or prochlorperazine are effective for pain and nausea, either as monotherapy or in combination therapy (43, 44). Diphenhydramine is often co-administered to reduce dystonic reactions. Other antiemetics (chlorpromazine, droperidol, haloperidol, ondansetron) may be considered, though they are associated with a higher risk of adverse effects (45-47).

7.1.4. CGRP Antagonists

Oral “gepants” (ubrogepant, rimegepant) and intranasal zavegepant are effective for acute migraine, especially in patients who cannot take triptans. They provide pain relief and reduce associated symptoms, though long-term safety data are still emerging (48, 49).

7.1.5. Lasmiditan

Lasmiditan, a selective 5-HT1F agonist, is effective without vasoconstrictive effects. Common side effects include dizziness and somnolence, and patients must avoid driving for 8 hours after each dose (50).

7.1.6. Ergots

Dihydroergotamine is useful for severe attacks and status migrainosus, particularly when combined with antiemetics. Ergotamine is less effective and associated with more side effects; it is rarely used (51).

7.1.7. Non-pharmacological and device-based treatments

Acupuncture, relaxation training, cognitive-behavioral therapy, and biofeedback demonstrated modest benefit in acute and preventive treatment. External trigeminal nerve stimulation devices such as Cefaly and single-pulse transcranial magnetic stimulation have received regulatory approval for acute therapy and prevention. These devices are non-invasive, well-tolerated, and may be considered for patients preferring non-drug options (36).

8. Preventive (prophylactic) treatment strategies

Preventive therapy aims to reduce the frequency, severity, and duration of attacks; improve responsiveness to acute therapy; and minimize disability. Prophylaxis is considered for patients with frequent attacks (≥3 per month or ≥8 headache days per month), debilitating attacks despite appropriate acute treatment, medication overuse headache, prolonged aura, or patient preference. Selection of prophylactic therapy depends on migraine type (episodic vs chronic), comorbidities, contraindications, and patient goals. Treatment usually starts at a low dose and is increased slowly; efficacy should be assessed after 2–3 months, and therapy continued for 6–12 months before tapering (52). The following modalities are evidence-based:

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8.1. First-line pharmacological options

8.1.1. Anti-CGRP monoclonal antibodies

Erenumab (CGRP-receptor antibody), fremanezumab, galcanezumab, and eptinezumab (CGRP-ligand mAbs) specifically inhibit CGRP signaling and are administered via monthly or quarterly injections. A 2025 international guideline summarizing recommendations reported erenumab 70 mg or 140 mg every four weeks, fremanezumab 225 mg monthly or 675 mg quarterly, galcanezumab 120 mg monthly, eptinezumab 100 mg or 300 mg quarterly, and topiramate 100–200 mg orally for episodic migraine. For chronic migraine, onabotulinumtoxinA 155–195 IU intramuscularly, atogepant 60 mg oral, eptinezumab 100 mg or 300 mg quarterly, fremanezumab 675 mg quarterly or 225 mg monthly, galcanezumab 120 mg monthly, and erenumab 70 mg or 140 mg every four weeks were strongly recommended (53). These treatments show responder rates, defined as a ≥50% reduction in monthly migraine days, range from 30–62% versus 17–38% with placebo. They are well tolerated, with injection-site reactions and constipation being the most common adverse effects. Anti-CGRP antibodies should be used cautiously in patients with cardiovascular or cerebrovascular disease and are not recommended during pregnancy or breastfeeding. Treatment response is usually assessed at 4–12 weeks; non-responders may try another agent. Anti-CGRP therapies offer a relatively rapid onset of benefit (often within the first month) and simplicity of monthly dosing, but their high cost can limit accessibility (36).

8.1.2. Topiramate

Topiramate is an antiepileptic that blocks voltage-dependent sodium channels, enhances GABAergic activity, and inhibits excitatory glutamatergic transmission. It has comparable efficacy to propranolol and is recommended as a first-line option for episodic and chronic migraine. Typical doses are 50–200 mg/day, titrated gradually to minimize adverse effects such as paresthesias, cognitive slowing, and weight loss. Topiramate is contraindicated in pregnancy due to the risk of fetal malformations and in patients with a history of kidney stones or glaucoma. The 2025 guideline categorizes oral topiramate 100 and 200 mg as strongly recommended and lower doses (50 mg) as weakly recommended for episodic migraine (53).

8.1.3. OnabotulinumtoxinA

Botulinum toxin type A is approved for the prevention of chronic migraine. It is injected into 31 sites across the head and neck muscles every 12 weeks. OnabotulinumtoxinA reduces monthly migraine days by about two more days compared with placebo, and it is particularly beneficial in patients with medication-overuse headache. It is not effective for episodic migraine. Adverse effects include injection-site pain, neck stiffness, and muscle weakness. The 2025 guideline issued a strong recommendation for onabotulinumtoxinA in chronic migraine (53).

8.2. Other oral preventive medications

8.2.1. Beta-blockers

Propranolol is among the most widely used beta-blockers and is an effective first-line agent. Metoprolol and atenolol are alternatives, particularly for patients with comorbid hypertension or anxiety. Common adverse effects include fatigue, dizziness, and potential worsening of depression; contraindicated in patients with asthma and severe bradyarrhythmia. The 2025 guideline gives a weak recommendation for propranolol (160 mg/day oral) in episodic migraine prevention (53).

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8.2.2. Antiepileptic drugs

Topiramate is among the most effective preventive therapies for migraine and is supported by strong evidence, but its use is limited by safety concerns. Besides topiramate, valproic acid (divalproex) is also an established preventive agent with strong supporting evidence; however, it is contraindicated in women of childbearing potential due to high teratogenic risk and generally avoided in patients with liver disease. Lamotrigine has weaker evidence and is considered when first-line agents fail (54).

8.2.3. Antidepressants

Tricyclic antidepressants (TCA) such as amitriptyline (10–100 mg/day, titrated as tolerated) and nortriptyline provide benefit, particularly in patients with comorbid depression or insomnia. Nortriptyline is frequently used as an alternative with fewer anticholinergic effects, although evidence is less robust. Venlafaxine, a serotonin–norepinephrine reuptake inhibitor, is also probably effective with modest supporting evidence, particularly for patients with comorbid depression or anxiety. Antidepressants are commonly used as migraine preventives. Amitriptyline has the best evidence for use in migraine prevention. Common adverse effects of TCAs include weight gain, dry mouth, constipation, sedation, and possible QT prolongation, while venlafaxine may cause nausea, insomnia, or elevated blood pressure (53, 55).

8.2.4. Memantine and other agents

Memantine, an NMDA receptor antagonist considered when conventional preventives fail, has limited evidence but is included in the 2023 VA/DoD guideline as an option for episodic migraine (56). Riboflavin (vitamin B2), magnesium, and coenzyme Q10 combination (57).

8.3. Non-pharmacological preventive strategies

8.3.1. Lifestyle modifications

Regular sleep, consistent meals, adequate hydration, moderate and consistent caffeine intake (avoiding both excess and withdrawal), and avoidance of identified triggers form the foundation of migraine prevention. Aerobic exercise, such as brisk walking or cycling, three times per week, significantly reduces headache frequency and intensity, likely through endorphin release and improved vascular health (58, 59). Relaxation techniques, mindfulness, cognitive behavioral therapy, and biofeedback improve coping and may reduce migraine frequency. Patients should maintain a headache diary to correlate attacks with sleep patterns, stress, and dietary factors (60, 61). Weight reduction may benefit obese patients. Smoking cessation and limiting alcohol intake are advisable (62).

8.3.2. Neuromodulation devices

Several devices are available to help identify patterns and triggers. Transcutaneous supraorbital nerve stimulation (Cefaly) is FDA-cleared for both acute treatment and daily preventive use, with evidence of modest but clinically meaningful benefit. Single-pulse transcranial magnetic stimulation has demonstrated efficacy in reducing migraine days and is approved for both acute and preventive treatment of migraine with aura. Non-invasive vagus nerve stimulators provide modest benefit in acute and preventive therapy. Occipital nerve blocks or implantable neurostimulation may be considered for refractory chronic migraine under specialist supervision (63, 64). Evidence remains limited, and these interventions are typically reserved for patients who fail conventional treatments.

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9. Conclusion

Migraine is a common and disabling brain disorder with complex genetic, hormonal, and environmental determinants. Understanding the pathophysiological underpinnings – from cortical spreading depression to trigeminovascular activation and neuropeptide release – has led to targeted therapies such as triptans, ditans, gepants, and anti-CGRP monoclonal antibodies. Evidence-based guidelines emphasize individualized care: simple analgesics and NSAIDs for mild attacks, triptans or gepants for moderate to severe attacks, and avoidance of opioids. Preventive therapy should be offered when attacks are frequent, severe, or disabling. Anti-CGRP antibodies, and atogepant represent major advances, with onabotulinumtoxinA for chronic migraine and traditional agents such as topiramate, beta-blockers, valproate, and antidepressants remaining valuable. Non-pharmacological strategies – trigger avoidance, lifestyle modifications, behavioral therapy, and neuromodulation – complement pharmacologic measures and empower patients. Because migraine disproportionately affects women and those of lower socioeconomic status, patient education and equitable access to care are imperative. Ongoing research will refine our understanding of migraine mechanisms and expand therapeutic options, offering hope for improved quality of life for the millions of people worldwide living with migraine.

ETHICAL STATEMENT

Not Applicable.

CONFLICT OF INTEREST

There is no conflict of interest to be declared.

AUTHORS' CONTRIBUTIONS

Basma S.A. Kamel and Mostafa M. Abdelhafeez developed the concept and structure of the review together. Basma S.A. Kamel led the literature search and drafted the initial manuscript, provided critical revisions.

Mostafa M. Abdelhafeez contributed additional sources, and enhanced the analytical discussion. Both authors read and approved the final version.

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Chemical Composition and Antibacterial Activity of Libyan Propolis

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ABSTRACT

Propolis, a natural resinous substance collected by honeybees, exhibits diverse biological activities due to its rich phytochemical composition. This study aimed to characterize the chemical profile of Libyan propolis and evaluate its antibacterial efficacy. Samples were collected from local beehives, extracted using ethanol and methanol, and analysed via Ultraviolet (UV) spectrophotometric method. The propolis contained carbohydrates (405.97 mg/g), tannins (17.5 mg/g), flavonoids (112.28 mg/g), phenols (50.25 mg/g), alkaloids (24.20 mg/g), saponins (20.50 mg/g), proteins (202.97 mg/g), crude lipids (23.9%), crude fiber (11.7%), and ash (9.43%). The ethanolic extract demonstrated significant antibacterial activity against Staphylococcus aureus, methicillin-resistant Staphylococcus aureus (MRSA), and Pseudomonas aeruginosa, with inhibition zones comparable to gentamicin. These findings highlight the potential of Libyan propolis as a natural antimicrobial agent.

Keywords: *Propolis, Phytochemicals, Antibacterial activity, Libya, Natural products*

1. Introduction

Throughout history, natural goods have been the main sources of food and medicine, and they have long been essential in the prevention and treatment of human illnesses. Because of their nutritional and medicinal potential, honey and products derived from bees have garnered a lot of scientific interest [1,2]. In addition to honey, several apiculture products have shown various of biological activities that support human health, including pollen, royal jelly, bee venom, wax, and propolis. Also known as "bee glue," propolis is a resinous substance that honeybees gather from plant exudates and then alter with their salivary secretions to give the hive structural and antibacterial protection [1].

Propolis has been used historically by ancient civilizations, such as the Romans for wound healing and the Egyptians for mummification. Avicenna also documented the medical effects of propolis in The Canon of Medicine [3-5]. Propolis' protective function in protecting bee colonies is reflected in its etymology, which comes from the Greek terms "pro" (before) and "polis" (city) [6]. Geographical, climatic, and botanical origins all influence the chemical makeup of propolis, which is a complex matrix of plant-derived resins, waxes, essential oils, and bee-derived enzymes [7-8]. Flavonoids, phenolic acids, terpenes, and aromatic aldehydes are among the more than 300 chemicals that have been found and that contribute to its anti-inflammatory, antibacterial, and antioxidant qualities [3, 9, 10]. Its pharmacological potential has been the subject of much research due to the considerable variance in its phytochemical profile. Propolis has a wide range of biological activity, including antiviral, antifungal, and antibacterial actions against both Gram-positive and Gram-negative bacteria. Its polyphenolic components have also been shown to exhibit antioxidant properties [11, 12]. In light of the increasing prevalence of antimicrobial resistance, a worldwide health issue made worse by the overuse and abuse of traditional antibiotics, these qualities make propolis a promising natural medicinal agent [13]. Little is known about the chemical makeup and bioactivity of Libyan propolis, despite this widespread interest. By describing its main phytochemical components—with special focus on flavonoids, phenolics, alkaloids, and tannins—the current study aims

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to close this gap. Additionally, the study intends to determine Libyan propolis's antibacterial activity against specific strains of both Gram-positive and Gram-negative bacteria as well as its antioxidant potential utilizing standardized in vitro assays. This work aims to give scientific evidence that may support the medicinal use of Libyan propolis in treating microbial infections and oxidative stress by combining phytochemical profiling with biological evaluation.

2. Materials and Methods

2.1. Preparation of propolis: samples were collected from beehives samples located on western coast of Libya, including the cities of Mis urata, Zliten, Khoms, Meslata, Garabulli, and Tripoli during February–March 2024. Samples were cleaned, fragmented, and stored in glass containers until analysis.

2.2. Extraction

The extract was prepared by cutting the propolis into small pieces and dissolving it in a sufficient amount of ethyl alcohol (95%). Then 30 g of propolis was taken and dissolved in a sufficient amount of ethanol, then transferred to a standard flask and the volume was completed to 100 ml using ethanol to achieve a final concentration of 30%. The extract was then stored in an opaque bottle at room temperature. After ten days of intermittent shaking (daily shaking for a few minutes), and after complete dissolution, the extract was filtered using No. 42 filter paper and stored in the refrigerator at 4°C until use.

-Methanolic extract: Soxhlet extraction with methanol was used for alkaloid quantification.

2.3. Phytochemical Analysis

Quantitative analyses were performed using UV-Vis spectrophotometry**.**

2.3.1. Carbohydrates: phenol-sulfuric acid method, total carbohydrate content = (concentration of glucose from the standard curve × volume of the extract in ml) / (weight of the dry extract in grams). The carbohydrate concentration was expressed as milligram glucose equivalent per gram of extract [14].

2.3.2. Tannins: vanillin-HCl method, total tannin content was determined according to the following equation: total tannin content (concentration of tannic acid for the sample from the standard curve × volume of the extract in ml) / (weight of the dry extract in grams). The tannin concentration was expressed as milligrams tannic acid equivalent per gram of extract [15].

2.3.3 • Flavonoids: aluminium chloride method, the total flavonoid content was determined according to the following equation: total flavonoid content = (concentration of quercetin for the sample from the standard curve × volume of the extract in ml) / (weight of the dry extract in grams). The results were expressed as milligrams of quercetin equivalent (QUE) per gram of extract [16-17].

2.3.4 • Phenols: Folin-Ciocalteu method, the total phenolic content was determined according to the following equation: total phenolic content = (concentration of gallic acid for the sample from the standard curve × volume of the extract in ml) / (weight of the dry extract in grams). The total phenolic content was expressed as milligrams of gallic acid equivalent (GAE) per gram of extract [17-18].

2.3.5 • Saponins: vanillin-sulfuric acid method, the total saponin content was determined according to the following equation: total s aponin content = (concentration of aescin for the sample from the standard curve × volume of the extract in ml) / (weight of the dry extract i n grams). The total saponin content was expressed as milligrams equivalents per gram of dry weight (mg AE/g) [19].

2.3.6 • Alkaloids: bromocresol green method, the total alkaloid content was determined according to the following equation: total Alkaloid content = (concentration of atropine for the sample from the standard curve × volume of the extract in ml) / (weight of the dry extract in grams). The total alkaloid content was expressed as milligrams of atropine equivalent per gram [20].

2.3.7 • Proteins: The Bradford method, total protein content = (concentration of albumin for the sample from the standard curve × volume of the extract in ml) / (weight of the dry extract in grams). The total protein content was expressed as milligrams of albumin equivalent per

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gram [21].

2.3.8 • Lipids: standard gravimetric methods, the amount of lipid was calculated and expressed as a percentage of the crude lipid content a ccording to the equation: crude Lipid % = (weight of the flask after solvent evaporation - weight of the empty flask) / (weight of the s ample) × 100 [22]. The crucible crude fiber was placed in an oven at 550°C for two hours. It was then taken out of the oven, cooled, and re-weighed to obtain the weight of the ash. Crude fiber content = (weight of the crucible with fibers – weight of the crucible with ash) / (weigh t of the sample) × 100.

2.4. Crude Fiber and Ash: fiber content was determined by boiling propolis with sulfuric acid and then with sodium hydroxide, after which the fibers were collected in a crucible, dried, and weighed.

2.5. Evaluation of Antibacterial Activity: antibacterial activity was evaluated according to the method described by the agar well diffusion method using Mueller-Hinton agar plates. the diameters of the inhibition zones were measured using a ruler and expressed in millimetres [23-25]. The antibiotic Gentamicin was used according to the recommendation of the Clinical and Laboratory Standards Institute.

3. Results & Discussion:

3.1. Phytochemical analysis

As it shown in Table (1) the average carbohydrate estimation was 405.97 mg per gram of extract. This is double the amount of the results of a study for Iraqi propolis, where the carbohydrates content was 200 mg/g, while tannins are similar to our study [26].

Flavonoids were estimated at about 112.28 mg/g which is in the range of the results of Bouchelaghem and his co-workers for Hungarian propolis samples, which ranged between 33.8 and 273.2 mg/g [27], in addition to the results of Touzani and his team for Moroccan propolis, which had a flavonoid content of 98.33 mg/g [28].

Table (1): Phytochemical analysis, calculated crud fat, crude fiber and ash of propolis.

Component	The average value
Carbohydrates	405.97 mg/g
Tannins	17.8 mg/g
Flavonoids	112.28 mg/g
Phenols	50.25 mg/g
Saponins	20.50 mg/g
Alkaloids	24.20 mg/g
Proteins	202.97 mg/g
Lipids	23.9%
Fibers	11.7%
Ash	9.43%,

The phenolic content of the ethanolic extract of propolis was found at 50.52 mg/g, which is consistent with the study of Hungarian propolis samples which ranged between 10.4 and 71.1 mg/g [27], and the study of Brazilian propolis, which ranged between 40.1 and 303.1 mg/g. However, this study's results are higher than those carried out by Al-oklah and his team, who estimated a large group of propolis samples

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collected from several different countries, where the phenolic content results for those samples ranged between 2.81 and 30.64 mg/g [30]. This difference is attributed to the geographical location, as all samples were collected from Asian countries. Also, our study's results are lower than those for Moroccan propolis, where the phenolic content reached 141.46 mg/g, which is attributed to the propolis being collected from an area rich in trees with high phenolic content, such as olive and juniper trees.

Saponins as shown in the table were found at 20.50 mg/g which quantitatively agrees with studied of Cameroonian, Iraqi, and Indonesian propolis. [26, 31, 32].

The total alkaloid content in the methanolic extract was found at 24.20 mg/g, which quantitatively agrees with the quantitative detection performed by the Kustiawan group [32] and the Agbor group [33]. However, our study's result differs from what Ramnath's team found in their quantitative estimation of Indian propolis samples, where the alkaloid content ranged between 62-98 mg/g [34].

The average protein content was 202.97 mg/g, as shown in Table (1), which differs from what Devequi-Nunes and co-work study of Brazilian propolis samples, where the protein percentage ranged between 2.12-2.49% [35]. Our study's result is also higher than the results of Shehata and his team for samples from different countries, where the protein percentage ranged between 0.10-2.89% [36]. At the same time, our study's result is close to the results of Indian propolis samples, where the protein percentage ranged between 7.28-9.41% according to Pant's team study [37].

Lipids content in propolis was found with an average of 23.9%, this percentage is higher than what was determined in Brazilian propolis samples, which ranged between 8.19-15.61% [35]. At the same time, our study's result is lower than the results of Indian propolis samples, which ranged between 53.62-68.89% [37], and also lower than what was found in Brunei propolis samples according to Abdullah's team study, which ranged between 45.60-47.86% [38]. This variation in results is attributed to the different sources from which the propolis components were collected due to the different surrounding vegetation.

The fiber content in raw propolis was 11.7%, as shown in Table (1)). This percentage is higher than what was found in Brunei Darussalam propolis samples, where the average fiber percentage was 0.30% [38]. Our study's result also differs from the results of Indian propolis samples, where the fiber percentage ranged between 1.94-3.15% [37]. As for the ash content, the average percentage of ash in our study was 9.43%, as shown in Table (1). This percentage is higher than what was found in Brazilian propolis samples, where the percentage ranged between 1.35-1.44% [35]. It also differs from the ash percentage in Moroccan propolis, which was 4.87% [28]. These differences are attributed to the sources from which the bees collected the propolis components.

3.2. Evaluation of Antibacterial Activity:

Antibacterial activity was evaluated using the agar well diffusion method, where three types of bacteria were used: Staphylococcus aureus (Gram-positive), Pseudomonas aeruginosa (Gram-negative), and the methicillin-resistant MRSA strain. Each type was spread on a Mueller-Hinton plate, and the inhibition of the extract on each type was measured and compared with the inhibition of the antibiotic Gentamicin. The results shown in table (2) indicated that the extract's inhibition on S. aureus bacteria was 26 mm, which was close to the inhibition of the antibiotic used, which was around 28 mm. Also, the inhibitory effect of the extract on the MRSA strain was around 24 mm, which was also close to the antibiotic's inhibition, which gave an inhibition of 26 mm, a difference of 2 mm. At the same time, the extract's inhibition was close to the antibiotic's inhibition when used on Gram-negative bacteria P. aeruginosa, where the inhibition rate was 23 mm for the extract and 24 mm for the antibiotic Gentamicin.

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Table (2): The extract's inhibition on S. aureus bacteria

Bacterial Type	Propolis Extract Inhibition Diameter (mm)	Gentamicin Antibiotic Inhibition Diameter (mm)
Staphylococcus aureus S	26	28
Strain MRSA	24	26
P.aeruginosa	23	24

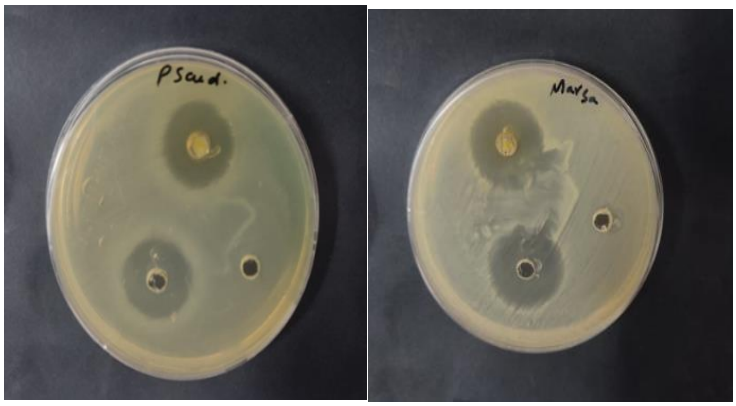

Figure (1): Inhibition of the extract and the antibiotic on the MRSA strain and P. aeruginosa.

Figure (2): Inhibition of the extract and the antibiotic on Staphylococcus aureus.

4. Conclusion

In this research, we studied the basic components of Libyan propolis collected from beehives in the study area, with the aim of estimating these components in its alcoholic extract and assessing its antioxidant and antibacterial activity. The results revealed that the average carbohydrate content of the ethanolic extract was 405.97 mg/g of dry extract, which represented the highest value among the components assessed. The quantitative estimation of phenols and flavonoids revealed that Libyan propolis contained a high amount of these components, with average values of 50.25 and 112.28 mg/g, respectively, which is attributed to the extract's antibacterial activity. The quantitative estimation of tannins is one of the most important additions provided by our study, with a value of 17.5 mg/g, as it is rarely mentioned as a

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component of propolis. Estimates indicated that the amount of saponins was 20.50 mg/g in the ethanolic extract, while the amount of alkaloids was 24.20 mg/g in the methanolic extract of propolis. Proteins constituted the second highest value, reaching 202.97 mg/g when raw propolis was treated with the alkali salt extraction method. A study of the lipid content of raw propolis extracted with a mixture of methanol and chloroform revealed that the average lipid content was 23.9% in the propolis from the study area. The study of the antibacterial activity of the extract showed high inhibition against the three bacterial species used, and it was close to the inhibition results of the antibiotic Gentamicin used for comparison.

ETHICAL STATEMENT

Not applicable

CONFLICT OF INTEREST

There is no conflict of interest to declare

AUTHORS' CONTRIBUTIONS

All authors contributed equally to the conception, design, data collection, analysis, and interpretation of the study.
They jointly participated in drafting, revising, and approving the final version of the manuscript. Each author takes full responsibility for the integrity and accuracy of the work.

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Pharmacists' Perspectives on Clinical Pharmacy Practice and Willingness to Engage in Structured Training: An Expanded Analysis from Libya

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ABSTRACT

Background: Pharmacy practice in Libya is shifting from dispensing-focused roles toward patient-centred clinical services, but training gaps and policy barriers remain. Objectives: To describe demographic and practice profiles of pharmacists in Libya, assess awareness and attitudes toward clinical pharmacy, determine willingness to undertake structured training, and identify barriers and facilitators for implementation. Methods: A descriptive cross-sectional survey of 65 licensed pharmacists from public and private sectors was conducted. Data included demographics, practice setting, prior clinical training, training preferences, and perceived barriers; quantitative summaries and qualitative synthesis were performed. Results: Respondents were predominantly female (62%) and mostly aged 30–39 years (49%). Hospital pharmacists comprised 55% of respondents. Prior structured clinical training was reported by 31%; 83% expressed willingness to engage in structured training. Preferred modalities were interactive workshops (74%), in-hospital rotations (61%), and blended learning (55%). Main barriers were lack of institutional support (58%), time constraints, and unclear career recognition. Conclusions: Libyan pharmacists show strong willingness for structured clinical training but face systemic and institutional barriers. Policy action, accredited training pathways, and institutional support are required to integrate clinical pharmacy sustainably into Libyan healthcare.

Keywords: *clinical pharmacy; pharmacists; continuing professional development; Libya; training preferences*

1. Introduction

The landscape of pharmacy practice in Libya is experiencing a gradual transformation, shifting from a model heavily rooted in traditional dispensing roles toward a more advanced, patient-centered clinical service model. This change is reflective of global trends, where pharmacists are increasingly recognized as integral members of multidisciplinary healthcare teams, contributing directly to patient care through medication management, counseling, monitoring of therapeutic outcomes, and public health initiatives [1]. Yet, despite international momentum, the implementation and integration of clinical pharmacy in Libya faces unique challenges. These stem from historical, educational, policy-related, and socioeconomic factors inherent to the Libyan context [2].

There is a need of surveys in Libya that reveal a critical knowledge gap regarding pharmacist preparedness for clinical roles, highlighting the necessity for more in-depth research to effectively develop and implement structured training initiatives. The current study aims to deepen

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that initial inquiry, enriching it with disaggregated demographic analysis, regional and institutional breakdowns, training preferences and modalities, comparative literature review, and policy implications [3]. By contextualizing local findings within Libyan and international discourse, this analysis seeks to elucidate the current position, potential trajectories, and necessary interventions for the advancement of clinical pharmacy in Libya. [4].

Aims: To examine pharmacists' awareness of clinical pharmacy principles, their attitudes towards structured training, and their actual willingness to engage in such programs. To compare the Libyan pharmacists' perspectives and preferences with international trends in clinical pharmacy education and practice. To identify barriers and facilitators to structured training and advanced practice. To discuss policy environment factors shaping pharmacy practice and propose actionable recommendations for integration and future development of clinical pharmacy in the Libyan healthcare system.

2. Methods

A descriptive cross-sectional survey was conducted among licensed pharmacists working in public and private sectors across Libya using convenience sampling through professional networks and institutional contacts, yielding N = 65 respondents; the questionnaire was developed from a targeted review of the literature on clinical pharmacy education and workforce surveys and adapted to the Libyan context by the study team, then piloted with 10 practicing pharmacists to assess clarity, face validity, and timing and revised accordingly before fielding; the final instrument comprised mostly closed items (demographics, qualifications, practice setting, prior training, and predefined training-modality options), several Likert-type items to measure attitudes and perceived barriers (5-point scale from strongly disagree to strongly agree), and a small number of open-ended questions for qualitative comments; items asking about preferences (e.g., training modalities) allowed multiple responses and were analysed as multiple-response categorical variables, quantitative data were summarised with descriptive statistics (counts, percentages) and qualitative free-text was synthesised thematically. Ethical approval was obtained from Elmergib University Ethics Committee (PH 02:2025).

3. Results

3.1 Demographic data:

A total of 65 licensed pharmacists participated in the cross-sectional survey. The demographic and practice-related characteristics of the respondents are summarized in Table 1.

Table 1. Participant characteristics of survey respondents (N = 65)

Characteristic	Categories
Gender	Female: 40 (62%) Male: 25 (38%)
Age	<30: 18 (28%) 30–39: 32 (49%) 40–49: 11 (17%) ≥50: 4 (6%)
Experience	<5 yrs: 18 (27%) 5–10 yrs: 23 (35%) >10 yrs: 24 (38%)
Qualification	BPharm: 44 (68%) MS: 13 (20%) Doctorate: 5 (7%) Other: 3 (5%)
Practice Setting	Hospital: 36 (55%) Community: 18 (28%) Academic: 6 (9%) Other: 5 (8%)
Prior Clinical Training	Yes: 20 (31%) No: 45 (69%)
Willingness for Training	Yes: 54 (83%) No/Unsure: 11 (17%)

The cohort was predominantly female (62%), consistent with regional trends indicating the feminization of the pharmacy workforce across the Middle East and North Africa. Most respondents were in the early to mid-career stages, with the largest group aged 30-39 years (49%). In terms of professional experience, 38% had over ten years of experience, while 35% had 5-10 years. The majority of pharmacists held a

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Bachelor of Pharmacy (BPharm) as their highest qualification (68%). A notable minority had obtained higher qualifications, including Master (20%) and Doctorate degrees (7%). Occupationally, hospital practice was the most common setting reported (55%), followed by community practice (28%) and academic affiliations (9%). A small proportion (8%) worked in mixed or other settings. Notably, fewer than one-third of respondents (31%) had previous exposure to structured clinical training, highlighting a crucial gap in professional development pathways for clinical pharmacy roles.

3.2 Regional distribution of respondents

Survey participants were drawn from across Libya's principal regions—western, central, eastern, and southern—with the following distribution: Western (e.g. Tripoli): 46%, Central (e.g., Misrata, Sirte): 18%, Eastern (e.g., Benghazi): 27% and Southern (e.g., Sebha): 9%. This relatively broad geographic representation reflects the current distribution of pharmacy educational institutions and healthcare infrastructure, with a concentration in the western and eastern urban centers, but also representation from smaller cities and rural areas.

3.2 Institutional affiliations of participants

Among institutional settings, over half the respondents were affiliated with government hospitals, particularly tertiary and teaching hospitals such as Zliten Medical Center and major urban hospitals in Tripoli and Benghazi. The remainder were distributed among community pharmacies, private clinics, universities, and, to a small extent, pharmaceutical industry roles.

Within the hospital cohort, pharmacists reported a range of responsibilities, from traditional dispensing to participation in clinical ward rounds, medication reconciliation, and provision of drug information. Academic participants were mainly engaged in undergraduate teaching, with limited direct clinical involvement.

3.4 Training preferences and modalities

The survey revealed a strong preference for interactive, practice-based learning experiences. As shown in Table 2, the most preferred modalities were interactive workshops (74%) and in-hospital clinical rotations (61%). Blended learning, combining e-learning with hands-on training, was also highly favored (55%). A smaller, but substantial, proportion expressed interest in short intensive courses (42%) and online/virtual learning (33%), while formal academic postgraduate pathways were preferred by 24% of respondents.

Table 2. Training modality preferences

Item: Training modality preferences (multiple responses allowed)	n (%)
Interactive workshops	48 (74%)
In-hospital clinical rotations	40 (61%)
Blended learning (hybrid)	36 (55%)
Short intensive courses	27 (42%)
Online / virtual learning	21 (33%)
Formal postgraduate diploma / MSc	16 (24%)

Key summary indicators	
Prior structured clinical training	20 (31%)
Awareness of core clinical pharmacy components	44 (67%)
Positive attitude toward structured training	54 (83%)
Willingness to engage in structured training	54 (83%)
Main reported barrier — lack of institutional support	38 (58%)

3.5 Awareness of clinical pharmacy practices

The majority of surveyed pharmacists (67%) recognized core components of clinical pharmacy as involving direct patient care activities—medication therapy management, counseling, participation in multidisciplinary teams, pharmacovigilance, and health education. However, awareness was uneven, with some respondents viewing clinical pharmacy narrowly as an extension of traditional dispensing tasks.

Knowledge deficits were particularly evident in areas such as pharmacokinetics, therapeutic drug monitoring, and application of evidence-based medicine in patient care.

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3.6 Attitudes toward and willingness for structured training

Attitudes towards structured training were overwhelmingly positive: 83% of respondents expressed that such training is essential for career progression and effective patient care. Respondents cited professional motivation, perceived patient safety benefits, and alignment with global pharmacy trends as key drivers for pursuing structured clinical pharmacy education. This positive attitude translated directly into a robust willingness to participate, with 83% (54 pharmacists) indicating they were willing to engage in structured clinical pharmacy training. This willingness was particularly pronounced among pharmacists in hospital settings and those early in their careers. A minority (17%) were ambivalent or hesitant, citing factors such as perceived inadequacy of existing programs, concerns over recognition of clinical roles, and competing personal or professional responsibilities.

Reported facilitators for engagement included institutional support (time allowances, financial incentives), access to training resources, mentorship, and clearly articulated professional benefits. The most frequently cited barrier was a lack of institutional support (58%), followed by workload and staffing constraints, limited access to quality training programs, and uncertainty around job market rewards.

4. Discussion

Recent assessments of pharmacy practice in Libya underscore findings congruent with this study: the profession has been slow to transition from a medication-dispensing paradigm to a more elaborate clinical pharmacy model. Historical inertia, limited curriculum reforms, and fragmented regulatory frameworks are recurrent themes in both published research and expert commentary [2]. The theory-practice gap is further evidenced by previous findings that many Libyan pharmacy practitioners operate in environments with limited exposure to interprofessional care or advanced practice models [4]. Similarly, students and pre-registration pharmacists report that experiential training is uneven, with many critical skills and competencies underemphasized in practical settings despite substantial theoretical input in undergraduate curricula [5].

Perhaps most significantly, studies on practice in southern and rural regions document persistent challenges related to professional identity, scope of practice, and patient trust. In these areas, commercial imperatives can sometimes take precedence over healthcare delivery, indicative of broader systemic issues that necessitate both policy and educational reform [6].

Globally, the trajectory of pharmacy practice is unambiguous. Advanced health systems are rapidly incorporating pharmacists into multidisciplinary clinical teams, where their contributions to medication management, antimicrobial stewardship, chronic disease care, and public health promotion are well established [7]. A recent international qualitative analysis involving pharmacy leaders identified several common themes essential for this advancement: strong leadership, coherent policy frameworks, structured postgraduate training, reflective practice, and motivation for change among the practitioner workforce [7].

The preferred training modalities identified in our Libyan survey are echoed internationally. Interactive, case-based education, in-hospital placements, and blended delivery formats are globally recognized as effective for equipping pharmacists with the skills and confidence needed for clinical roles [8]. Notably, no universal "best" model for continuing education has emerged; the highest practice outcomes are associated with continued professional development (CPD) models that are structured, learner-centered, and emphasize opportunities for real-world practice over passive, didactic teaching [9].

4.1 Barriers and facilitators in the Libyan context

Respondents' qualitative feedback, and the Libyan experience more broadly, align with international findings but exhibit several context-specific challenges [10].

4.3.1 Barriers

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Legacy Practice Models: A persistent emphasis on traditional dispensing over clinical care, embedded within both legal frameworks and institutional cultures [2].

Policy Gaps: A significant incongruity exists between national pharmaceutical regulations and emerging clinical pharmacy paradigms, resulting in unclear recognition and career progression for advanced practice roles [6].

Institutional Support: A frequently reported lack of dedicated time, funding, and administrative backing for professional development.

Workforce Shortages: Inadequate staffing in both hospital and community environments, creating concerns over workload and the capacity for additional training.

Public Perception: Limited societal recognition of the clinical pharmacist's role beyond the dispensing function, particularly in rural areas.

4.3.2 Facilitators

High Motivation: A majority of pharmacists are personally motivated and recognize the necessity of upskilling to meet modern healthcare demands.

Emergence of Clinical Training Programs: The development of new and proposed PharmD, postgraduate programs and structured short-course programs at leading universities and teaching hospitals.

International Benchmarking: A growing awareness of international practice standards and a willingness to adapt curricula accordingly [5].

Positive Policy Momentum: National reform efforts are beginning to align, albeit unevenly, with WHO/FIP good pharmacy practice guidelines [11].

4.2 Impact of structured training on competency

The direct relationship between structured, competency-based training and improvement in pharmacist practice is well-established. Evidence from the Libyan context, though limited, suggests substantial benefits: pharmacists with prior structured clinical training report higher confidence, greater involvement in patient care, and stronger engagement in quality initiatives such as pharmacovigilance and antimicrobial stewardship. Similarly, studies among pharmacy students and early-career practitioners in the region reveal improved communication, counseling, and problem-solving skills after experiencing well-designed, patient-facing training programs [5].

4.3 Institutional and policy environment for advanced practice

The regulatory and institutional environment is a crucial determinant in the progression of clinical pharmacy. In Libya, a patchwork of outdated policy, slow-moving regulatory change, and uneven institutional prioritization have hindered rapid advancement [2]. Nonetheless, promising signs are emerging, including pilot projects by the Libyan Board of Pharmacy and the Ministry of Health to promote revised CPD standards. Furthermore, regulatory authorities, informed by WHO and the International Pharmaceutical Federation (FIP) recommendations, are gradually adopting guidelines for good pharmacy practice, including clinical pharmacy as a core competency [11].

4.4 Patient outcomes and public health

A prominent theme in both Libyan and international discourse is the link between advanced pharmacist training and improved health outcomes. Clinical pharmacists have demonstrated measurable impacts on patient safety, medication adherence, chronic disease control, and resource utilization in multiple global studies [7, 12]. In Libya, anecdotal and limited survey data suggest nascent improvements in patient care where clinical pharmacy services and training have been piloted.

4.6 Policy implications

The integration of clinical pharmacy into the Libyan healthcare system requires coordinated policy action [2, 11] as follows:

Formal Recognition: National health authorities should promulgate regulations that recognize clinical pharmacy as a distinct practice area.

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Incentivization and Career Progression: Structured career ladders linking advanced training to career progression and remuneration are essential.

Resource Allocation: Funding, staffing, and protected time must be embedded within healthcare institutions.

Curriculum Reform: All schools of pharmacy should be incentivized to incorporate longitudinal, hands-on clinical experience, aligning with international accreditation standards [5, 11].

4.5 Study strengths and limitations

A key strength of this study is its novel exploration of clinical pharmacy training readiness in Libya, providing timely data from a diverse cohort of pharmacists across multiple regions and practice settings. The high willingness to engage in training and the clear preference for practical modalities are valuable findings for policymakers. However, the findings must be interpreted considering the limitations, including the relatively small sample size and the use of convenience sampling, which may limit the generalizability of the results.

5. Conclusion

Libyan pharmacists demonstrate readiness for structured clinical training; systemic reforms and targeted investment in training infrastructure and policy recognition are essential to translate willingness into sustainable practice change. The current cross-sectional survey reveals a Libyan pharmacy workforce that is predominantly young, well-educated, and eager to transition toward more advanced clinical roles. There is clear consensus on the value of structured clinical pharmacy training, strong willingness to engage in such opportunities, and an alignment in preferred learning methods with global trends. However, systemic barriers including historical practice models, limited policy support, and resource constraints, continue to hinder rapid progress. To advance clinical pharmacy in Libya, a multi-pronged approach is essential: comprehensive policy reform, robust institutional support for CPD, curriculum renovation, and ongoing evaluation of patient and system outcomes. By leveraging local motivation, international standards, and policy momentum, Libya can realize the full potential of its pharmacists as key contributors to modern, patient-centered healthcare.

ETHICS STATEMENT

Ethical approval was obtained from Elmergib University Ethics Committee (PH 02:2025). All participants provided informed consent.

AUTHORS' CONTRIBUTIONS

Conceptualization: S.A.; Data curation: R.A.; Formal analysis: A.D.; Writing—original draft: S.H.A.; Writing, review and editing: all authors.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Evaluation of Vitamin D Levels in the Municipality of Zillah

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ABSTRACT

Vitamin D, a fat-soluble prohormone, is essential for calcium homeostasis and bone metabolism. Its role, however, extends to a wide range of physiological processes, including immune regulation, cell proliferation, and cardiovascular health. Despite abundant sunlight in many regions, vitamin D deficiency is a global pandemic affecting all age groups. In Libya, lifestyle and cultural factors may contribute to a high prevalence of this deficiency, yet localized data, particularly from desert regions like Al-Jufra, remains scarce.

The study aimed to evaluate the prevalence of vitamin D deficiency and insufficiency among the adult population in the municipality of Zillah, and to investigate potential differences based on gender.

A cross-sectional study was conducted between June 2023 and June 2024. A total of 100 adult participants were recruited. Serum 25-hydroxyvitamin D [25(OH)D] levels were measured using a fluorescence immunoassay (FIA) analyzer. Vitamin D status was categorized asinsufficient (40%), sufficient (35%), and deficient (25%). Data on demographics, sun exposure habits, and dietary intake were collected via a structured questionnaire. Data were analyzed using Microsoft Excel 2010 for descriptive statistics.

The study revealed a high prevalence of suboptimal vitamin D status. Only 35% of participants had sufficient vitamin D levels. A significant portion of the population was found to be insufficient and deficient. The analysis indicated that males (30.769%) had a higher rate of deficiency compared to females (18.75%). Conversely, females exhibited a higher prevalence of insufficiency compared to males (43.753%)

Vitamin D deficiency and insufficiency are highly prevalent in the municipality, representing a significant public health concern. The findings highlight the need for targeted public health strategies, including awareness campaigns about safe sun exposure, dietary counseling, and food fortification. Regular screening, particularly for at-risk populations, is crucial for early detection and intervention to mitigate the long-term health consequences associated with vitamin D deficiency.

Keywords: *Vitamin D Deficiency, 25-hydroxyvitamin D, Zillah, Public Health, Sun Exposure,*

1. Introduction

Vitamin D, often referred to as the "sunshine vitamin," is a unique nutrient that functions as a prohormone within the human body. Its primary and most well-understood role is the regulation of calcium and phosphorus metabolism, which is fundamental for the development and maintenance of a healthy skeleton [1,2]. However, research over the past two decades has unveiled a much broader spectrum of biological

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functions. Receptors for vitamin D are present in nearly every cell and tissue in the body, from the brain to the immune system, indicating its involvement in a vast array of physiological processes beyond bone health [3,4]. These include modulating immune responses, regulating cell growth and differentiation, and influencing cardiovascular function.

Despite its critical importance, vitamin D deficiency has emerged as a global health pandemic, affecting many people worldwide of all ethnicities and age groups [5]. This high prevalence is paradoxical, especially in regions with abundant year-round sunlight, such as the Middle East and North Africa (MENA). In these areas, lifestyle factors, cultural practices (e.g., traditional clothing that limits skin exposure), and environmental conditions (e.g., high temperatures encouraging indoor lifestyles) often lead to inadequate synthesis of vitamin D in the skin, which is the primary source for most humans [6, 7].

In Libya, a sun-drenched country, this paradox is particularly relevant. However, there is a significant lack of research focused on specific communities, especially those in remote or desert regions like the Al-Jufra district. The population of Zillah, located within this district, presents a unique demographic for study due to its distinct environmental and lifestyle characteristics. Understanding the vitamin D status of this community is the first step toward identifying a potentially significant, yet overlooked, public health issue.

This study was therefore designed to conduct a preliminary assessment of vitamin D levels in the adult population of Zillah. The primary objectives were: 1) to determine the prevalence of vitamin D deficiency, insufficiency, and sufficiency; 2) to explore any significant differences in vitamin D status between males and females; and 3) to provide foundational data that can inform future public health policies and interventions aimed at addressing this nutritional deficiency in the region.

2. Scientific Background and Literature Review

2.1. Biochemistry and Metabolism of Vitamin D

Vitamin D is not a single compound but a group of fat-soluble secosteroids. The two major forms are vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). Vitamin D2 is synthesized by plants and fungi, while vitamin D3 is synthesized in the skin of animals and humans upon exposure to ultraviolet B (UVB) radiation from sunlight. It can also be obtained from dietary sources like fatty fish, cod liver oil, and fortified foods [8,9].

The metabolic activation of vitamin D involves a two-step hydroxylation process.

1. **First Hydroxylation:** Whether obtained from sun exposure or diet, vitamin D is transported to the liver, where it undergoes its first hydroxylation to become 25-hydroxyvitamin D [25(OH)D], also known as calcidiol. This is the major circulating form of vitamin D and is used to determine a person's vitamin D status.
2. **Second Hydroxylation:** 25(OH) D is then transported to the kidneys, where it undergoes a second hydroxylation to form the biologically active hormone, 1,25-dihydroxyvitamin D [1,25(OH)2D], also known as calcitriol. This step is tightly regulated by parathyroid hormone (PTH), serum calcium, and phosphorus levels [3, 10].

2.2. Biological Functions of Vitamin D

- **Skeletal Health:** The classic function of vitamin D is to maintain calcium and phosphorus homeostasis. Active vitamin D (calcitriol) enhances the absorption of these minerals from the intestine, promotes their reabsorption in the kidneys, and regulates their mobilization from bone, thereby ensuring proper bone mineralization. Severe deficiency leads to rickets in children and osteomalacia in adults [1].
- **Extra-Skeletal Health:** The discovery of the vitamin D receptor (VDR) in numerous non-skeletal tissues has broadened our understanding of its functions. Vitamin D plays a role in:

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- **Immune Modulation:** It enhances the innate immune response against pathogens while regulating the adaptive immune response to prevent autoimmunity.
- **Cellular Regulation:** It controls the growth and differentiation of various cell types, suggesting a potential role in cancer prevention.
- **Cardiovascular Health:** It is involved in regulating blood pressure and may protect against heart disease.

2.3. Literature Review: Vitamin D Status

Studies from the MENA region consistently report high rates of vitamin D deficiency. A study in Saudi Arabia found that over 81.15% of healthy adults had suboptimal vitamin D levels [11]. Similarly, research in the United Arab Emirates and Qatar has shown a prevalence of deficiency exceeding 70%, even with ample sunlight [12]. The primary reasons cited are limited sun exposure due to cultural dress and avoidance of extreme heat, as well as low dietary intake of vitamin D.

The results of a study conducted in northern India indicated that vitamin D deficiency was present in approximately 84% of women in urban areas and approximately 83% in rural areas [13].

From another perspective, a study was conducted to assess the prevalence of 25-(OH)D(VDD) and 25-hydroxycholecalciferol (25-(OH)D) deficiency in different regions of Libya. The results indicated that approximately 80% of healthy individuals in the Middle East had a prevalence of VDD deficiency. In the Libyan capital, Tripoli, the prevalence of VDD deficiency reached approximately 50.80%, while in the second largest city, Benghazi, the prevalence reached approximately 76% [14]. There is a clear gap in the literature regarding the vitamin D status of populations in the southern and central desert regions, such as Al-Jufra. This study aims to begin filling that gap by providing data from Zillah, contributing to a more comprehensive understanding of the nutritional landscape in Libya.

3. Methodology

3.1. Study Design and Setting

A descriptive, cross-sectional study was conducted to assess the vitamin D status of the adult population in Zillah, a municipality within the Al-Jufra district in central Libya. The study was carried out over a 12-month period, from June 2023 to June 2024. Data and sample collection took place at the Al-Watan Polyclinic, which serves a significant portion of the local community.

3.2. Study Population and Sampling

A convenience sample of 100 adult participants (aged 18 years and older) was recruited for the study. The sample included both males and females who visited the polyclinic for routine check-ups or minor ailments and voluntarily agreed to participate.

- **Inclusion Criteria:** Adults aged 18 and above, residing in Zillah, and willing to provide written informed consent.
- **Exclusion Criteria:** Individuals with known metabolic bone diseases, chronic kidney or liver disease, malabsorption syndromes, or those taking medications known to interfere with vitamin D metabolism (e.g., anticonvulsants, glucocorticoids).

3.3. Data Collection

3.3.1. Questionnaire and Validation

A structured questionnaire was developed specifically for this study to collect relevant data. To ensure the tool's validity and reliability, a multi-step process was undertaken:

1. Content Validity: The initial questionnaire was reviewed by a panel of three experts, including two dermatologists and a clinical nutritionist. They assessed the relevance, clarity, and comprehensiveness of the questions. The Content Validity Index (CVI) was calculated, and items with a score below 0.78 were revised or discarded based on the experts' feedback.

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2. Face Validity: A pilot study was conducted with 15 individuals (who were not part of the final sample) to assess the questionnaire's clarity, ease of understanding, and the time required for completion. Ambiguous questions were rephrased for better comprehension.

3. Reliability: The internal consistency of the multi-item scales within the questionnaire (e.g., scales measuring sun exposure habits or dietary frequency) was assessed using Cronbach's Alpha. A value of $\alpha > 0.7$ was considered acceptable, indicating good reliability.

The final questionnaire, administered in Arabic by trained researchers, collected the following information:

A: Demographic Data: Age and gender.

B: Sun Exposure Habits: Average daily time spent outdoors (in hours), frequency of sunscreen use (on a scale from "never" to "always"), and typical style of clothing (categorized as "fully covered," "mixed," or "uncovered").

C: Dietary Habits: Frequency of consumption of vitamin D-rich foods (e.g., fatty fish like tuna and salmon, eggs, fortified milk and yogurt) using a Likert scale (e.g., never, rarely, sometimes, often, daily).

D: Medical History: Presence of chronic diseases known to affect vitamin D metabolism (e.g., malabsorption syndromes, renal or liver disease) and current use of vitamin D or multivitamin supplements (including dosage and frequency).

3.3.2. Data Collection Procedure

Data collection took place at the National Medical Laboratory in Hun City. Participants who provided informed consent were interviewed in a private room by a trained researcher. The researcher read the questions aloud and recorded the responses to ensure consistency and minimize missing data. Each interview lasted approximately 15-20 minutes.

3.3.3. Blood Sample Collection and Analysis A 3 mL sample of venous blood was collected from each participant by a qualified phlebotomist into a plain tube. The samples were allowed to clot at room temperature and then centrifuged at 3000 rpm for 10 minutes to separate the serum. The serum was carefully transferred to a labeled Eppendorf tube and stored at -20°C until analysis.

Serum concentration of 25-hydroxyvitamin D [25(OH)D] was measured using a DrAccU FIA-6000 Fluorescence Immunoassay Analyzer. This quantitative method is based on a competitive immunoassay principle. The results were expressed in nanograms per milliliter (ng/mL).

3.4. Definition of Vitamin D Status

Based on the Endocrine Society's clinical practice guidelines, vitamin D status was categorized as follows:

- **Deficiency:** Serum 25(OH)D level < 20 ng/mL
- **Insufficiency:** Serum 25(OH)D level between 20 and 29.9 ng/mL
- **Sufficiency:** Serum 25(OH)D level ≥ 30 ng/mL

3.5. Statistical Analysis

The descriptive statistics were performed using Microsoft Excel 2010. Descriptive statistics, including frequencies and percentages, were used to summarize the demographic characteristics and the prevalence of different vitamin D status categories. The results were presented using tables.

3.6. Ethical Considerations

The study protocol was approved by the administration of the Al-Mahara Institute for Medical and Administrative Sciences 24/2023. Written informed consent was obtained from all participants after explaining the purpose and procedures of the study. All data were kept confidential and used solely for research purposes.

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4. Results

4.1. Demographic Characteristics

A total of 100 participants were included in the final analysis. The sample consisted of both male and female adults from the Zillah municipality. The age of the participants ranged from 18 to 80 years.

4.2. Overall Prevalence of Vitamin D Status

The analysis of serum 25 (OH)D levels revealed that a majority of the participants (65%) had suboptimal vitamin D status. Only 35% of the study population had sufficient levels. The distribution across the different categories is shown in Table 1.

Table 1: Overall Distribution of Vitamin D Status

Vitamin D Status	Definition (ng/mL)	Number of cases	Percentage (%)
Deficiency	< 20	25	25.0%
Insufficiency	20 - 29.9	40	40.0%
Sufficiency	≥ 30	35	35.0%
Total		**100**	**100.0%**

4.3. Vitamin D Status by Gender

Table 2: Distribution of Vitamin D Status by Gender

Vitamin D Status	Males (n=52)	Females (n=48)
Deficiency (<20 ng/mL)	16 (30.769)	9 (18.75)
Insufficiency (20-29.9 ng/mL)	19 (36.538)	21 (43.753)
Sufficiency (≥30 ng/mL)	17 (32.692)	18 (37.50)
Total	**52 (100%)**	**48 (100%)**

When data were stratified by gender, notable differences were observed in the prevalence of deficiency and insufficiency. Males exhibited a higher rate of deficiency, while females showed a higher rate of insufficiency. The detailed breakdown is presented in Table 2.

5. Discussion

The findings of this study provide crucial, albeit preliminary, insight into the vitamin D status of the adult population in Zillah, Libya, revealing a significant public health concern. The high prevalence of suboptimal vitamin D levels, with 65% of participants being either deficient (25%) or insufficient (40%), is alarming and aligns with the growing body of evidence that designates hypovitaminosis D as a silent global pandemic [1,8].

5.1. Interpretation of High Prevalence

The most striking finding is the high prevalence of deficiency in a region characterized by intense, year-round sunlight. This paradox is a hallmark of vitamin D deficiency in the MENA region [15,16]. Several factors likely contribute to this phenomenon in Zillah:

- **Sun Avoidance and Lifestyle:** The extremely high temperatures in this desert region for a large part of the year encourage an indoor lifestyle. People tend to remain indoors during peak sun hours (10 a.m. to 4 p.m.) [17], when UVB radiation, necessary for vitamin D synthesis, is most intense.
- **Cultural and Clothing Habits:** Traditional clothing for both men and women in the region often covers most of the body surface, severely limiting the skin's exposure to UVB rays. Even minimal clothing can significantly reduce vitamin D production.

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- **Dietary Factors:** The typical Libyan diet may not be naturally rich in vitamin D. Consumption of fatty fish, a primary natural source, is not as common as in other regions. Furthermore, the availability and consumption of vitamin D-fortified foods, such as milk and cereals, may be limited or inconsistent. The questionnaire data from this study could be further analyzed to establish a stronger correlation between specific dietary patterns and low vitamin D levels.

5.2. Gender Disparities

The study revealed an interesting gender-based pattern. While men had a higher rate of deficiency (30.769% vs. 18.75%), women had a higher rate of insufficiency (43.753% vs. 36.538%). This complex observation could be multifactorial:

- **Hormonal Influences:** Hormonal differences, particularly the role of estrogen in females, can influence vitamin D metabolism and bone health. Estrogen is known to impact the enzymes involved in vitamin D activation [18].
- **Behavioral Differences:** Men in the region might engage in occupations or activities that require more time outdoors, but perhaps during early morning or late afternoon hours when UVB intensity is lower. Women, while potentially spending more time indoors, might have different dietary habits or a higher body fat percentage, which can sequester vitamin D, making it less available in the circulation. The higher rate of insufficiency in women places them in a high-risk category, on the verge of deficiency, making them a critical target for preventative health measures.

5.3. Public Health Implications

The long-term health consequences of such a highly prevalent deficiency are considerable, with the potential to impact multiple physiological systems over time. Chronic vitamin D deficiency is a well-established risk factor for osteoporosis and fractures. Moreover, emerging evidence links it to an increased risk of various non-skeletal diseases, including cardiovascular diseases; type 2 diabetes, certain cancers, and autoimmune disorders [6,19]. The high prevalence found in Zillah suggests that the community may be bearing a hidden burden of these chronic conditions, which could be mitigated through effective public health interventions.

5.4. Limitations of the Study

This study has several limitations that should be acknowledged. First, the use of a convenience sample from a single polyclinic may not be fully representative of the entire Zillah population. Second, the cross-sectional design captures data at a single point in time and cannot establish causality or account for seasonal variations in vitamin D levels, which are known to occur. A longitudinal study would be beneficial to track these changes. Finally, the study did not measure PTH levels, which would have provided a more complete picture of calcium homeostasis.

6. Conclusion

This study provides the documented evidence of the high prevalence of vitamin D deficiency and insufficiency among the adult population of Zillah, Libya. With nearly two-thirds (66 cases) of the participants exhibiting suboptimal levels, this issue constitutes a significant and previously unaddressed public health problem. The findings underscore a pressing need for prompt action to mitigate the long-term health consequences of vitamin D deficiency. The observed differences in prevalence rates between genders also emphasize the importance of designing tailored interventions that consider the unique physiological and behavioral factors affecting men and women.

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7. Recommendations

Based on the findings of this study, the following recommendations are proposed:

1. **Public Health Awareness Campaigns:** Launching community-wide educational programs through local media, clinics, and community centers to raise awareness about the importance of vitamin D, the risks of deficiency, and practical ways to improve vitamin D status.
2. **Promotion of Safe Sun Exposure:** Educating the public on how to obtain sensible and safe sun exposure (e.g., 10-15 minutes of exposure for arms and legs during mid-day hours, 2-3 times a week, 11am-3pm) while avoiding the risks of sunburn and skin cancer [20].
3. **Dietary Counseling and Food Fortification:**
    1. Encouraging the consumption of vitamin D-rich foods.
    2. Advocating for a national policy for the fortification of staple foods like flour, bread, and dairy products with vitamin D, a strategy that has proven effective in other countries.
4. **Clinical Screening and Supplementation:**
    1. Recommending routine screening for vitamin D deficiency for individuals at high risk (e.g., the elderly, pregnant women, individuals with limited sun exposure).
    2. Developing clear clinical guidelines for healthcare providers on vitamin D supplementation protocols.
5. **Further Research:** Conducting larger, population-based studies with random sampling to confirm these findings. Future research should also explore seasonal variations, the impact of deficiency on specific health outcomes in the region, and the effectiveness of intervention programs.

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

ETHICAL STATEMENT

The study protocol was approved by the administration of the Al-Mahara Institute for Medical and Administrative Sciences 24/2023. Written informed consent was obtained from all participants after explaining the purpose and procedures of the study. All data were kept confidential and used solely for research purposes.

AUTHORS' CONTRIBUTIONS:

-Nabel Ahmed A Mansour: Conceptualization, Methodology, Investigation, Writing – Original Draft, Project Administration.

-Seraj M. Ali Elwan: Validation, Resources, Data Curation, Formal Analysis, Writing – Review & Editing, Supervision.

CONFLICT OF INTEREST

The authors declare that there are no known financial or personal conflicts of interest that could have influenced the work presented in this paper.

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Appendix: Questionnaire Form

A. Personal Information:

1. ID Code: _____
2. Gender: ☐ Male ☐ Female
3. Age Group: _____

B. Health Information:

1. Are you regularly exposed to the sun? ☐ Yes ☐ No
2. Do you drink milk daily? ☐ Yes ☐ No

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3. Do you frequently eat fast food? ☐ Yes ☐ No
4. Are you following a specific diet? ☐ Yes ☐ No
5. Do you smoke? ☐ Yes ☐ No
6. Are you pregnant? ☐ Yes ☐ No
7. Are you breastfeeding? ☐ Yes ☐ No
8. Do you exercise? ☐ Yes ☐ No
9. Do you take multivitamins? ☐ Yes ☐ No
10. Do you suffer from a chronic disease? ☐ Yes ☐ No

When was your last vitamin D test? _____

What is your vitamin D level? a) <20 ng/mL b) 20-29 ng/mL c) 30-69 ng/mL d) I don't know

Do you suffer from hair loss? ☐ Yes ☐ No

Do you have muscle pain? ☐ Yes ☐ No

Do you feel tired and fatigued most of the time? ☐ Yes ☐ No

Do you suffer from obesity? ☐ Yes ☐ No

Do you suffer from headaches and nausea most of the time? ☐ Yes ☐ No

Do you consume caffeine frequently in your daily diet? ☐ Yes ☐ No

Do you have insomnia or sleep disturbances? ☐ Yes ☐ No

Do you suffer from anxiety and stress at times? ☐ Yes ☐ No

Have you taken pills for vitamin D deficiency? ☐ Yes ☐ No

Have you taken an injection for vitamin D deficiency? ☐ Yes ☐ No

Do you eat a balanced diet fortified with vitamin D? ☐ Yes ☐ No

Have you read or heard about vitamin D? ☐ Yes ☐ No

Do you know the sources of vitamin D? ☐ Yes ☐ No

Do you think vitamin D deficiency is linked to other diseases like depression? ☐ Yes ☐ No

In your opinion, what are the possible causes of vitamin D deficiency? a) Lack of sun exposure b) Diet c) Nutritional deficiency in pregnant women and the elderly d) Economic status

It is known that vitamin D deficiency reduces immunity. Do you suffer from a lack of immunity? ☐ Yes ☐ No

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Comparative Evaluation of Disc Diffusion and Volatilization Methods for Assessing the Antibacterial Activity of Essential oil of Libyan *Artemisia judaica* Against Pathogenic Bacteria

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ABSTRACT

Background: Antimicrobial resistance (AMR) poses a serious global health challenge, demanding alternative therapeutic options. Essential oils (EOs) are complex, volatile mixtures with broad-spectrum antimicrobial properties and reduced likelihood of resistance development. *Artemisia judaica*, has been traditionally used for its medicinal effects, yet limited data exist regarding its antibacterial potential against clinically relevant pathogens under different assay conditions.

Objectives: This study aimed to evaluate and compare the antibacterial activity of *A. judaica* essential oil against *Staphylococcus aureus* and *Escherichia coli* using Disc diffusion (direct contact) and volatilization (vapour phase) assays.

Methods: Aerial parts of *A. judaica* collected from Al-Awaynat (Libya) were subjected to hydrodistillation via a Clevenger-type apparatus to obtain the EO. Antibacterial activity was assessed against *S. aureus* and *E.coli* following CLSI-adapted protocols. Disc diffusion and volatilization assays were employed, with levofloxacin serving as a positive control. Zones of inhibition (ZOIs) were measured, and mean values ± standard deviation were recorded.

Results: The EO yield was 0.8% ± 0.05 (v/w). In disc diffusion assays, the essential oil exhibited mean inhibition zones of 16.5 ± 2.1 mm for *S. aureus* and 11.7 ± 1.2 mm for *E. coli*. By contrast, volatilization assays showed minimal and uniform activity (8.0 ± 0.0 mm) for both strains, indicating limited vapour-phase antibacterial potential.

Conclusion: *A. judaica* essential oil demonstrates strong antibacterial activity in direct-contact assays, particularly against *S.aureus*, but negligible vapour-phase effects. These findings suggest its potential application in topical or direct-contact formulations rather than airborne disinfection, and highlight the importance of assay selection in EO bioactivity profiling.

Keywords: *Artemisia judaica*, essential oils, antimicrobial activity, disc diffusion, volatilization assay, *Staphylococcus aureus, E.coli.*

1. Introduction

Antimicrobial resistance (AMR) stands as one of the most formidable challenges to global public health in the 21st century. The World Health Organization (WHO) has consistently classified AMR as a top priority, issuing renewed calls to accelerate action against this silent pandemic, which is projected to cause millions of deaths annually if left unchecked [1]. The crisis is fueled by the indiscriminate use of conventional antibiotics in human medicine, veterinary practice, and agriculture, which exerts immense selective pressure on microbial

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populations. This has led to the rapid evolution and dissemination of resistance mechanisms across a broad spectrum of bacterial pathogens. The consequences are terrible, treatments for common infections are failing, routine surgical procedures and immunosuppressive therapies become high-risk undertakings, and healthcare costs rise due to prolonged illnesses and the need for more expensive, last-resort drugs.

The gravity of the situation is exemplified by the rise of multidrug-resistant (MDR) pathogens, which have developed sophisticated strategies to evade the action of antimicrobial agents. Prominent among these are Methicillin-resistant *Staphylococcus aureus* (MRSA) and MDR *E. coli*. MRSA, a Gram-positive bacterium, is notorious for its acquisition of the *mec A* gene, which confers resistance to all beta-lactam antibiotics. Beyond this, it employs efflux pumps to expel a range of other drug classes and can form robust biofilms that act as physical barriers, shielding embedded cells from both antibiotics and host immune responses. On the Gram-negative side, MDR *E. coli* poses a significant threat primarily due to its production of extended-spectrum beta-lactamases (ESBLs), enzymes that hydrolyze and inactivate a broad range of penicillin and cephalosporin antibiotics. Furthermore, *E. coli* utilizes a formidable double-membrane structure that is inherently less permeable to many drugs, and it enhances this intrinsic resistance with potent efflux pumps, such as the AcrAB-TolC system, which can export a diverse array of antimicrobials, including fluoroquinolones and tetracyclines **[2]**.

In this context, the search for alternative and complementary antimicrobial agents has intensified, with natural products offering a rich reservoir of chemical diversity. Essential oils (EOs), complex volatile and lipophilic mixtures synthesized by aromatic plants as secondary metabolites, have re-emerged as promising candidates. These oils are typically composed of terpenes (monoterpenes and sesquiterpenes), phenolics, and aromatic compounds, which collectively contribute to their broad-spectrum biological activities [3]. The antimicrobial efficacy of EOs is attributed not to a single mechanism but to a multi-targeted approach, a feature that may crucially hinder the development of resistance [4]. Their lipophilic nature allows them to partition into and disrupt the integrity of bacterial cell membranes, leading to increased permeability, leakage of vital cellular constituents, and impairment of energy generation. Beyond membrane disruption, EOs can interfere with key enzymatic systems, and quench quorum-sensing signals, thereby inhibiting the formation of recalcitrant biofilms and the expression of virulence factors [3]. This polypharmacological profile stands in contrast to the single-target action of many conventional antibiotics, making EOs a compelling area of investigation.

The genus *Artemisia* (family *Asteraceae*), with its global distribution and rich history in traditional medicine, represents a particularly valuable source of bioactive essential oils. Numerous species, including *A. judaica* and *A. herba-alba*, are indigenous to the Mediterranean region and have been used for centuries in folk remedies to treat a variety of ailments, including wounds, fevers, and gastrointestinal infections [5, 6]. The chemical composition of *Artemisia* oils is highly variable, influenced by factors such as geographic origin, harvest time, and plant part used, leading to distinct chemotypes. Regional chemotypes from North Africa and the Middle East are frequently reported to be rich in oxygenated monoterpenes and sesquiterpenes, with compounds like camphor, 1,8-cineole, thujone, and artemisia ketone being prominent [5, 6]. A growing body of scientific evidence from these regions supports their traditional use, demonstrating significant *in vitro* antibacterial activity for various *Artemisia* essential oils against a panel of pathogens, including MDR strains [6, 7].

However, the reported antimicrobial potency of an essential oil is profoundly influenced by the methodological approach used for its assessment. The choice of assay can dramatically alter the outcome and interpretation of results, a critical consideration often overlooked in comparative studies. The most commonly employed techniques include broth microdilution, which determines the Minimum Inhibitory Concentration (MIC) in a liquid medium, and agar diffusion methods (disc or well diffusion). These methods measure the activity of the oil in its liquid phase through direct contact with the bacterial lawn [8]. While invaluable for initial screening, they may not fully capture the bioactivity of highly volatile compounds. In contrast, the volatilization method (also known as the vapour-phase or aerial diffusion assay) specifically evaluates the efficacy of the gaseous phase of the EO within a sealed environment [8, 9]. This distinction is not merely technical

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but has profound practical implications. The vapour-phase activity is directly relevant for potential applications in aerial disinfection (in hospitals or food storage facilities), in treating respiratory tract infections via inhalation, and in understanding the ecological roles of plant volatiles.

Research on other well-characterized essential oils, such as those from thyme (*Thymus vulgaris*) and oregano (*Origanum vulgare*), has revealed that antibacterial activity can differ significantly between the liquid and vapour phases. Generally, vapour-phase treatments have demonstrated potent inhibitory effects against Gram-positive bacteria like *S. aureus* and *Bacillus subtilis* [10, 11]. The relatively simple cell wall structure of Gram-positives, comprising a thick peptidoglycan layer, appears to be more readily penetrated by volatile compounds. Conversely, Gram-negative bacteria, such as *E. coli*, with their complex outer membrane containing lipopolysaccharides (LPS) that acts as a formidable permeability barrier, often exhibit reduced susceptibility to both liquid and vapour-phase EOs, though the vapours can sometimes show enhanced activity against some strains by potentially bypassing certain efflux mechanisms [10]. Despite the extensive pharmacological investigations into the *Artemisia* genus, comprehensive and comparative data on the vapour-phase antibacterial activity of its essential oils remain scarce. This gap in knowledge is particularly pronounced for specific Mediterranean chemotypes like *A. judaica*, whose full antimicrobial potential may be underestimated if assessed by liquid-phase assays alone.

Therefore, to address this research gap and provide a more universal evaluation of its antibacterial profile, we conducted a comparative study. This work aimed to evaluate the antibacterial activity of *A. judaica* essential oil against two clinically relevant and structurally distinct pathogens—the Gram-positive *S. aureus* and the Gram-negative *E. coli*—using two complementary methodologies: the standard disc diffusion assay, which measures direct contact activity, and the volatilization method, which specifically assesses vapour-phase efficacy. This direct, side-by-side comparison seeks to elucidate the critical influence of the testing method on the observed antibacterial outcomes, to determine whether the vapor phase of *A. judaica* oil holds distinct advantages for certain bacterial types, and ultimately, to contribute to application-oriented understanding of its potential in developing novel strategies to combat resistant bacterial pathogens.

2. Materials and Methods

2.1 Plant material:

Aerial parts (stems & leaves) of *A. judaica* were collected in July 2025 from Al-Awaynat region, Southern of Libya. The species was identified in National Herbarium, Department of Botany, Faculty of Science, Tripoli University, Libya.

2.2 Essential oil extraction:

The extraction method was described by Suwaydan & Altraiki (2025)[12] with some modification. dried plant material (aerial parts)of *A. Judaica* (about 100 grams) were cut to small pieces and subjected to essential oil extraction by hydro-distillation using Clevenger-type apparatus for 3hrs in triplicate. The percentage yield of essential oil was calculated by using:

$$\text{Yield (\%)} = (\text{EO (mL)}) / (\text{dried plant (g)}) \times 100$$

The extracted Essential oil was dried over anhydrous sodium sulphate and stored in well-sealed umber vials and kept in refrigerator at 4°C until further uses

2.3 Microorganisms and culture condition:

The experimental work was conducted using two bacterial strains, *Staphylococcus aureus* ATCC 29213 and *Escherichia coli* ATCC 8739, which were generously supplied by the Centre for Diseases Control in Tripoli, Libya. Stock cultures were preserved on Mueller-Hinton agar (MHA) slants. To ensure viability and purity, bacteria were sub-cultured onto fresh MHA plates 24 hours before each assay. All manipulations were carried out under aseptic conditions to avoid external contamination.

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2.4 Disc diffusion assay:

The antibacterial activity of *A. judaica* essential oil was evaluated using the disc diffusion method, as per the Clinical and Laboratory Standards Institute (CLSI) guidelines for testing essential oils [8,9]. Overnight bacterial cultures were suspended in sterile saline and adjusted to a 0.5 McFarland standard turbidity, equivalent to approximately 1.5×10^8 CFU/mL. For the assay, sterile filter paper discs (6 mm in diameter) were impregnated with 3 µL of the essential oil. These prepared discs were then aseptically placed onto the surface of Mueller-Hinton agar (MHA) plates that had been pre-inoculated with the standardized bacterial suspensions. Levofloxacin discs (5 µg) were used as a positive control. All plates were incubated at 37°C for 24 hours under aerobic conditions. Following incubation, the zones of inhibition (ZOIs) were measured in millimetres (mm), with the diameter of the clear zone around the disc indicating the level of antibacterial activity.

2.5 Volatilization assay:

The potential vapor-phase antibacterial effect of *A. judaica* oil was evaluated following the method of Inouye et al. [9]. Sterile Eppendorf lids containing 40 µL oil containing 40 µL of essential oil were attached to the underside of the Petri dish lid. MHA plates previously inoculated with standardized bacterial suspensions were used as the test surface. Plates were carefully sealed with parafilm to prevent vapour escape and incubated at 37°C for 24 hours without direct contact between the oil and the agar surface. Following incubation, ZOIs were measured in mm as described above to assess the antibacterial efficacy of the oil vapour.

2.6 Data analysis:

All experiments were carried out in duplicate and repeated on two independent experiments to ensure reproducibility and reliability of results. The mean ZOI values and corresponding standard deviations (SDs) were calculated. Where appropriate, comparisons between the essential oil and the positive control (levofloxacin) were performed to determine relative antibacterial potency.

3. Results

3.1 Extractive yield of *A. judaica* essential oil

The percentage yields of **0.8% ±0.05 (V/W)** of the essential oils of *A. judaica* aerial parts were obtainedby the hydro- distillation method of the essential oil extraction.

3.2 Direct-contact Antibacterial Activity

The disc diffusion assay revealed that *Artemisia judaica* essential oil exhibited differential inhibitory effects against the tested bacterial strains. Against *Staphylococcus aureus*, the essential oil produced a mean inhibition zone of 16.5 ± 2.1 mm, which was considerably lower than the potent activity of the levofloxacin positive control (29.3 ± 0.6 mm). A similar trend was observed for *Escherichia coli*, where the essential oil yielded a mean zone of 11.7 ± 1.2 mm, again significantly less than the levofloxacin control (31.3 ± 2.1 mm). These results demonstrate the direct-contact antibacterial activity of *A. judaica* oil, with a more pronounced effect against the Gram-positive *S. aureus* compared to the Gram-negative *E. coli*, though its efficacy against both was substantially lower than that of the conventional antibiotic.

3.3 Vapour-phase Antibacterial Activity

The volatilization method was used to assess the antibacterial activity of *A. judaica* oil in the vapour phase. The results demonstrated uniform inhibition zones of 8.0 ± 0.0 mm for both bacterial species (Table 1). These minimal and non-variable ZOIs indicate only negligible antibacterial activity for the oil's volatile components under the tested conditions.

Collectively, the data indicate that *A. judaica* essential oil exhibits notable contact-dependent antibacterial effects, particularly against *S. aureus*, whereas its activity in the gaseous phase is insignificant, limiting its potential for airborne disinfection applications.

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Table 1. Zone of inhibition (mm) of *A. judaica* oil against test microorganisms.

Organism	Agar diffusion (Mean ± SD)	Disc volatilization (Mean ± SD)	Levofloxacin disc (Mean ± SD)
Staphylococcus aureus	16.5 ± 2.1	8.0 ± 0.0	29.3 ± 0.6
Escherichia coli	11.7 ± 1.2	8.0 ± 0.0	31.3± 2.1

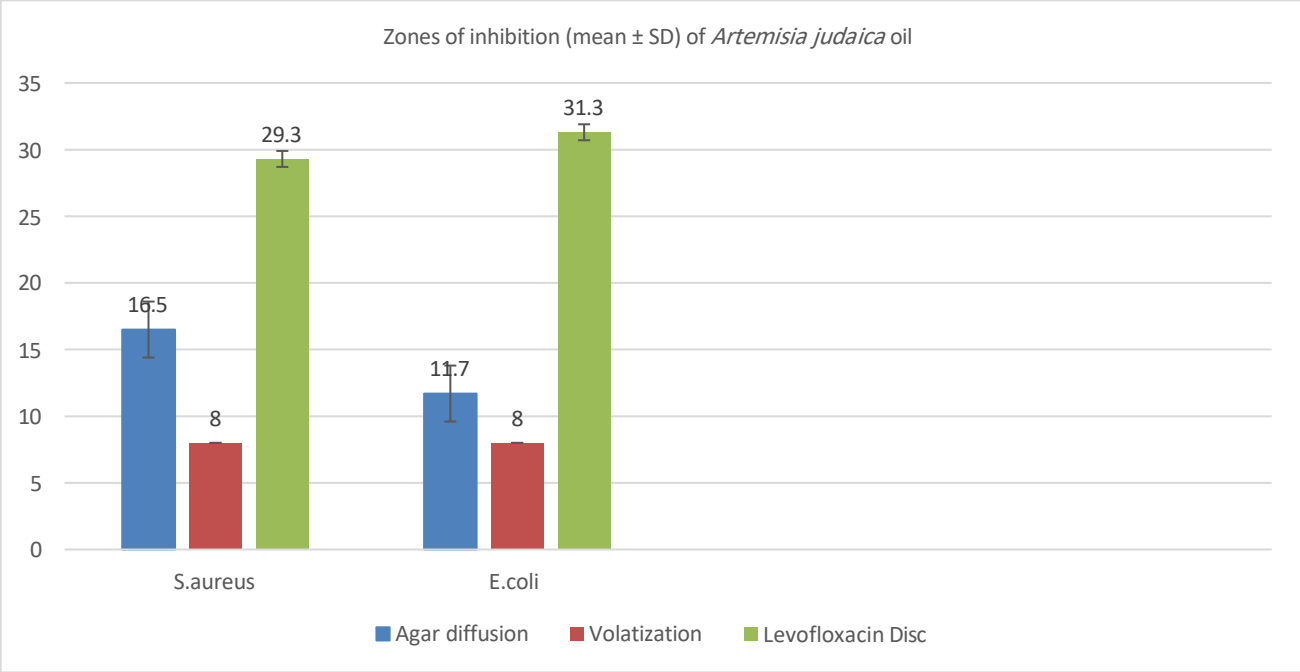

Figure 1. Zones of inhibition (mean ± SD) of *A judaica* oil (agar diffusion, volatilization) compared with levofloxacin against tested bacteria

4. Discussion

Our findings confirm that methodological context drives EO activity readouts. *A. judaica* oil showed robust direct contact antibacterial effects but negligible vapour phase effects under volatilization method. This aligns with reports that Gram negative bacteria often resist EO vapours due to outer membrane barriers and efflux [2,4]. Mediterranean *Artemisia* chemotypes (*A. herbaalba, A. judaica*) frequently contain camphor/1,8,cineole/thujone, regional studies from Algeria, Libya, and the Middle East report antibacterial activity, including against MDR strains, largely in direct contact assays [6,13]. Recent GC MS profiling of *A. judaica* from the Arabian Peninsula highlights oxygenated monoterpenes and supports bioactivity relevant to wound healing, consistent with our direct contact results[13].

Essential oils such as thyme and oregano oils that rich in phenolic monoterpenes (thymol, carvacrol)—often retain measurable vapour-phase activity, especially against Gram positive bacteria, and have shown efficacy in vapour contact on food and clinical isolates[9,10, 14]. Eucalyptus oils and novel formulations show antimicrobial and anti-inflammatory effects and are used mouth care [15]. Moreover, Inouye's foundational gaseous contact work demonstrated activity of several EO constituents against respiratory pathogens, providing mechanistic precedent for vapour testing [16]. However, assay parameters (medium depth, headspace geometry, sealing, inoculum) critically affect reproducibility. Synergy screens indicate that certain EOs can potentiate antibiotics [17], a strategy worth exploring for *Artemisia*. Future work should profile our *A. judaica* oil antibiotic synergy in planktonic and biofilm models.

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5. Conclusion

Artemisia judaica oil showed marked antibacterial activity in disc diffusion assays. However, its vapour-phase activity was minimal. These findings highlight its potential for topical or direct-contact applications rather than airborne disinfection and underscore the need for standardized vapour-phase testing protocols.

ETHICS STATEMENT

Not Applicable

CONFLICT OF INTEREST

The authors declare no conflict of interest

AUTHOR CONTRIBUTIONS

Abdulkarem Tamer: Conceptualization, Investigation, writing original draft, Writing review & editing.
Abdulaziz Sh. Suwaydan: Methodology, writing original draft , Writing review & editing.
Amnah Galboun: Investigation, Resources.

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Comparative Study between Paracetamol 500 mg tablets manufactured by Tunisian Teriak laboratories and Paracetamol 500 mg tablets manufactured by England GlaxoSmithKline

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A B S T R A C T

The study was conducted to determine whether paracetamol tablets manufactured in England GlaxoSmithkliene (GSK) companies and Tunisian Teriak laboratories demonstrate comparable performance when subjected to standard official pharmacopeial quality tests. The evaluations and assessment was done by weight uniformity, friability, disintegration, dissolution, and assay of active ingredient content using UV spectrophotometry in the laboratory. The results shows that products exceeded the minimum requirements set by pharmacopeial standards, Quality control testing included weight uniformity (mean ± SD: GSK tablets = 500.8 ± 2.1 mg; Teriak = 501.3 ± 2.4 mg), friability (0.21 ± 0.02% and 0.24 ± 0.03% for Teriak tablets), disintegration time (3.2 ± 0.4 min and 3.5 ± 0.5 min respectively), dissolution at 30 min (98.5 ± 1.2% and 97.8 ± 1.5%), and assay of active ingredient by UV spectrophotometry (100.2 ± 0.8% and 99.9 ± 0.9%). The results were distinguished in GSK tablets which showed a slightly faster dissolution rate, similarity factor analysis ($F_2 = 68.4$) confirmed equivalence between profiles, both formulations remained well within acceptable limits, indicating that patients can expect equivalent therapeutic efficacy regardless of the country of manufacture.

Keywords: *Paracetamol tablets, Quality control, Bioequivalence, Dissolution testing, UV-Spectrophotometry*

1. Introduction

Paracetamol (acetaminophen) tablets have a unique position in analgesic and antipyretic therapy, characterized by its predictable pharmacokinetics and broad therapeutic index [1]. Even with its simple chemical structure, the drug dosage form emerges from a careful and coordinated interaction between excipients, pressure parameters, and coating systems that together shape its macro and micro structural

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properties [2].

In the Libyan context, where both GlaxoSmithkline companies made Panadol and Teriak laboratories are traded together, physicians and pharmacists often focus on convenience options. Although these tablets share the same active ingredient, slight differences in particle size distribution, binder content, or lubricant addition can alter tablet porosity, wettability, and ultimately drug release. Summary monographs, such as those in the British Pharmacopoeia and the United States Pharmacopoeia, provide strict limits for weight uniformity, disintegration, disintegration time, and dissolution pattern [3]. These quantitative limits represent the first line of defense against batch variations and performance deficiencies.

Weight variation tests ensure each tablet lies within ±5% of the label claim, while friability assays under a rotating drum asses mechanical endurance to chipping and abrasion. Disintegration testing in simulated gastric fluid simulates the early stages of ingestion, confirming the rapid breakdown of the drug and excipient matrix into early particles ready for dissolution [4].

To address these nuances, the present study conduct a comparative laboratory assessment of imported Panadol 500 mg tablets from english and tunisian production lines in the united kingdom and tunisia. The assessment includes weight variation, hardness test, friability, dissolution profile, and UV spectrophotometric assay of active ingredient content. Statistical evaluation of dissolution data, including calculation of difference (F_1) and similarity (F_2) factors, was performed to determine whether observed variations exceed analytical thresholds [5].

In vivo metrics alone cannot measure the full spectrum of manufacturing-induced variation. Excipients, such as microcrystalline cellulose, pregelatinized starch, and sodium carboxymethylcellulose, affect matrix integrity and fluid permeability, while lubricants, such as magnesium stearate, may impart a hydrophobic surface that delays initial wetting [6].

Dissolution studies under controlled hydrodynamics produce release curves from which parameters such as dissolution efficiency (DE), mean dissolution time (MDT), and similarity and dissimilarity factors are derived to assess formulation equivalence [7]. These metrics, based on mathematical models, provide an indication of drug behavior in vivo and support biocompatibility or bioequivalence decisions.

The previous related and similar studies were conducted on the basis of verification and comparison of different types of the same active ingredient of medicine in order to distinguish the medicines that have the best and quality to be focused on by physicians and pharmacists with greater confidence [8].

The purpose of the study was to evaluate the quality of pharmaceutical tablets in the laboratory to ensure their effectiveness and quality, in addition to distinguishing the difference in quality between the two origins [9].

2. Materials and Methods

In the study, conduct a formal Quality control (QC) assessment of two different batches of paracetamol tablets (English, Tunisian), 500 mg paracetamol tablets commercially available in the Libyan community pharmacies. By studying weight variation, friability, disintegration, dissolution patterns, and optical spectroscopy, according to the official tests of pharmacopeia, the aims to characterize key quality attributes and determine their release behaviour using pharmaceutical standards, to ensure that paracetamol products, both comply with strict quality standards, enhancing therapeutic confidence in every tablet dispensed .

Materials

English product panadol (500 mg paracetamol per tablet) GlaxoSmithKline (GSK) companies U.K., Brentford, England; Lot No. GC6B, expiry date: July 2025.

Tunisian product (500 mg paracetamol per tablet) Laboratoires teriak, Zaghouan, Tunisia; Lot No. 24002, expiry date: August 2026.

All samples were purchased from licensed community pharmacies in Sabratha, Libya. Tablets were stored in their original packaging at controlled room temperature (25 ± 2 °C) and protected from direct light until testing, the time of purchase was 4 July 2024.

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Methods (Pharmacopeial Tests Procedures):

Weight Uniformity: Twenty tablets from each batch were weighed individually using a sensitive analytical balance. The mean and standard deviation were calculated and evaluated within a tolerance of ±5% for each tablet.

Hardness test: Test Tablet hardness was determined using a Monsanto hardness tester on ten randomly selected tablets from each company, and the mean ± SD values were recorded in kg/cm².

Friability test: Twenty tablets from each batch were placed in a friability tester at 25 rpm for four minutes. The percentage weight loss was calculated; the acceptance criterion was ≤1%.

Disintegration time: Six tablets from each batch were tested in distilled water at 37 ± 0.5°C using a dispersion tester. The disintegration time was 15 minutes.

Dissolution: A USP Type II (paddle) apparatus was used with 900 mL phosphate buffer (pH 5.8) at 37 ± 0.5 °C and 50 rpm. Samples were taken at 5, 10, 15, and 30 minutes, replaced with fresh medium, and analysed at 243 nm using a UV–Vis spectrophotometer. Percentage dissolved was calculated relative to a paracetamol calibration curve.

Assay (API Content): Crushed tablets were dissolved in buffer and analysed spectrophotometrically . The acceptance range was 95–105% of label claim.

3. Results

Table (1): Quality control parameters of (GSK company and Teriak laboratories) panadol tablets according to pharmacopeial standards.

Test	Pharmacopoeial Limit	GSK Panadol (Mean ± SD)	Teriak Lab Panadol (Mean ± SD)
Weight Uniformity (g)	±5% per tablet	0.502 ± 0.004	0.499 ± 0.005
Friability (%)	≤1%	0.28 ± 0.02	0.34 ± 0.03
Disintegration Time (min)	≤15	4.2 ± 0.3	4.8 ± 0.4
Dissolved at 30 min (%)	≥80%	98.5 ± 1.2	94.8 ± 1.5
Assay (% of Label Claim)	95–105%	99.2 ± 0.8	98.7 ± 0.9
Hardness (kg/cm²)	No official limit	7.8 ± 0.4	7.5 ± 0.5

Both batches compiled with all pharmacopeial specifications. The English tablets showed slightly lower weight variability **(figure 1)** and a marginally faster dissolution rate, Even the Teriak laboratory tablets remained well within optimal performance thresholds.

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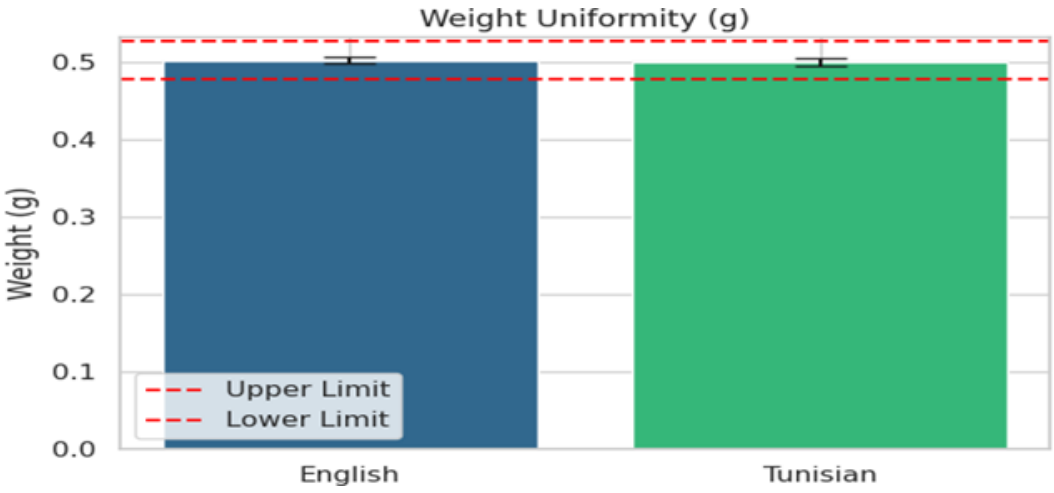
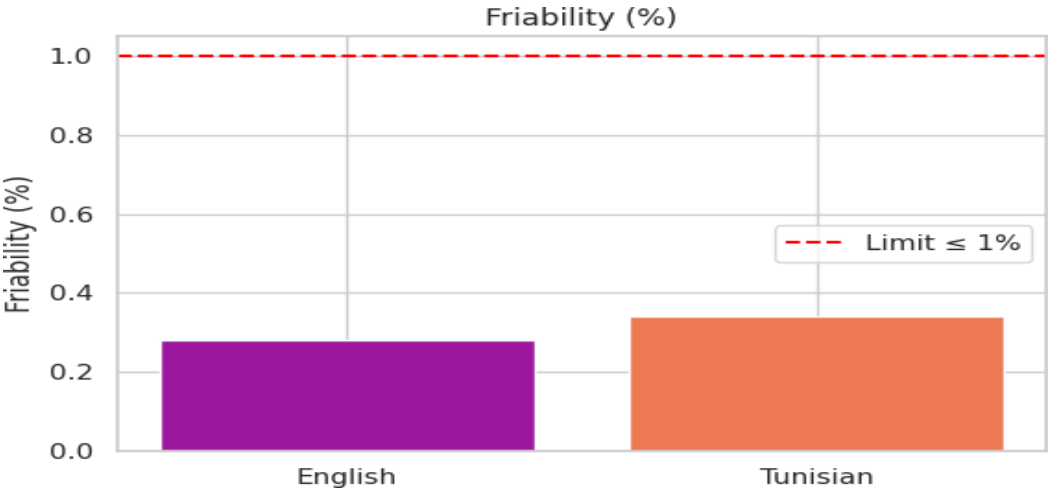


(figure 1): Weight uniformity of tablets (g), GSK (blue) companies and Teriak Laboratory (green) panadol tablets with pharmacopeial limits.



(figure 2): Friability (%), (GSK tablets and Teriak Laboratory) panadol tablets with pharmacopeial maximum limit at 1.

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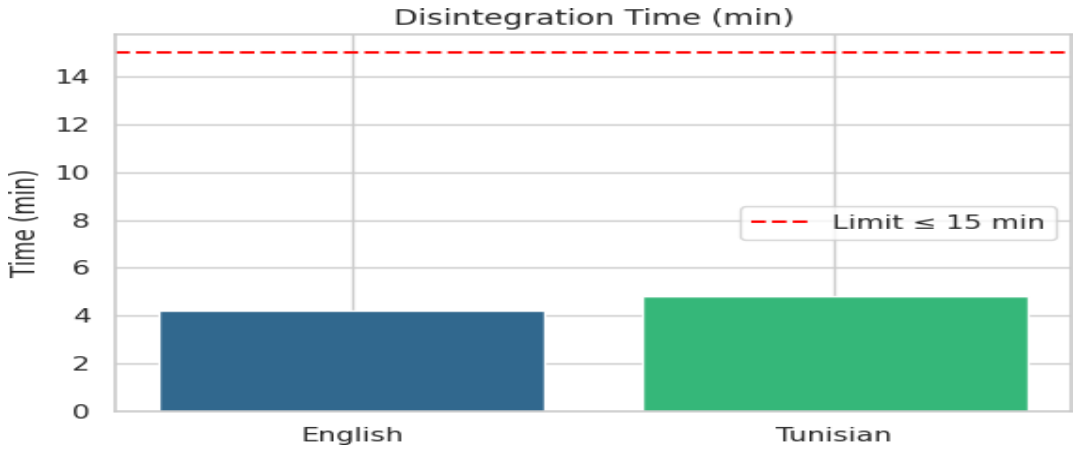
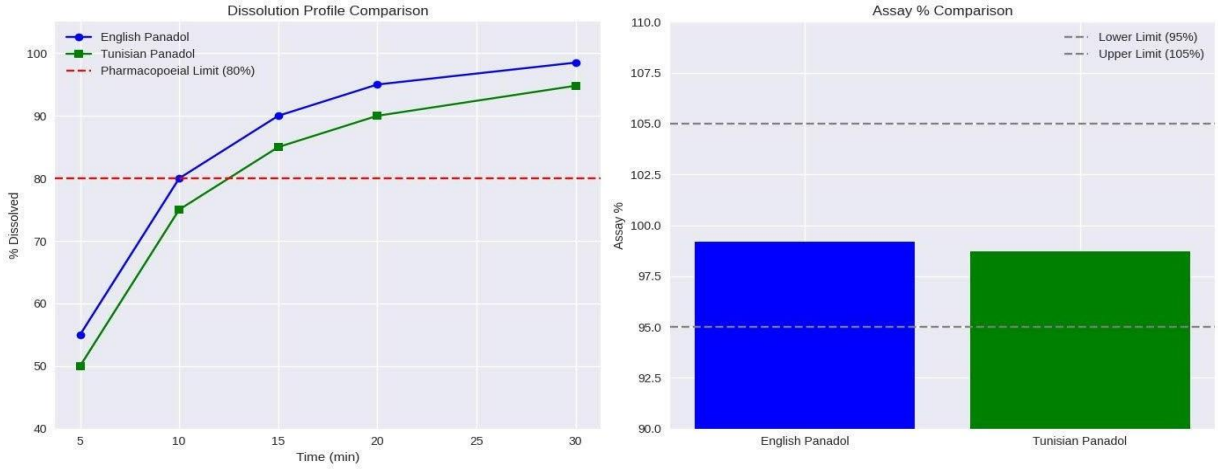


(figure 3): disintegration time (min), GSK tablets (blue) and Teriak Laboratory (green) panadol tablets with pharmacopeial maximum (dashed line 15 min).



(figure 4): dissolution at 30 min (%) and assay % of label claimed of GSK tablets (blue) and Teriak Laboratory (green) tablets, with pharmacopeial acceptance criteria dissolution more than 80%.

4. Discussion

Findings from this assessment confirm that both paracetamol tablets manufactured in GSK company and Teriak laboratories showed complete compliance with the limits specified in the approved pharmaceutical specifications in British pharmacopeia. All tested batches complied with the pharmacopeia specifications outlined in the British Pharmacopoeia (BP, 2023) and united states pharmacopeia (USP, 2023) (Table 1). Weight uniformity for both brands was well within the ±5% limit, with mean tablet weights of 0.502 ± 0.004 g for the GSK product and

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0.499 ± 0.005 g for the Teriak laboratories product, indicating consistent manufacturing control reflecting the commitment of the production lines in both countries to Good Manufacturing Practices (GMP) and quality control procedures. Despite this consistency, slight differences were observed in some physical and pharmacological parameters, which could be explained by differences in manufacturing techniques, raw material properties, or operating conditions [11].

From a clinical perspective, the observed differences are unlikely to result in any noticeable variation in therapeutic effect. These results support the interchangeable use of either formulation in practice, reassuring both prescribers and patients about consistent efficacy.

With regard to weight uniformity, the GSK tablets showed a lower standard deviation as shown in (figure 1), indicating greater accuracy in filling and compression processes, a characteristic often associated with the use of more advanced measuring and feeding systems. The GSK sample was less friable or brittle as shown in (figure 2), which may reflect differences in the type or quantity of binders or the compression force applied during manufacturing and prove that tablets have more stability during transportation and storage conditions. Friability values (0.28 ± 0.02% for GSK tablets; 0.34 ± 0.03% for teriak laboratories tablets) were a little below the 1% threshold, indicating adequate mechanical strength during handling and packaging.

Regarding to disintegration time, the GSK tablets disintegrated faster than the Tariak laboratory tablets, disintegration times were 4.2 ± 0.3 min and 4.8 ± 0.4 min, respectively well under the 15 min limit suggesting that rapid breakdown in the gastrointestinal environment, as evidenced by the dissolution rate at 30 minutes, with the GSK sample being slightly faster as shown in (figure 3). This relationship between disintegration rate and higher dissolution rate is consistent with well-known pharmaceutical principles, which emphasize that better disintegration properties contribute to increased availability of the active ingredient for absorption.

Dissolution testing at 37 ± 0.5 °C using USP Apparatus II revealed rapid drug release for both products. The GSK batch exhibited slightly faster dissolution at early time points, but both exceeded the ≥80% release criterion at 30 minutes. Dissolution testing of the active ingredient showed that both products were within the optimal range (95-105%), as shown in (figure 4) reflecting the accuracy of the weighing and mixing processes and confirming that significant differences in physical parameters did not affect dosing accuracy.

Similarity factor analysis yielded F_1 = 4.8 and F_2 = 68.4, indicating high similarity between the dissolution profiles ($F_2 \geq 50$ is generally considered equivalent). The slightly faster dissolution of the GSK product may be attributed to minor differences in excipient composition or particle size distribution, which can influence wettability and matrix porosity, the overall performance of both products remained within pharmacopeial limits, and the high F2 value confirms their pharmaceutical equivalence.

These results are consistent with documented studies indicating that pharmaceutical products that meet pharmaceutical specifications may exhibit slight variations in performance, often due to differences in product design or manufacturing conditions, without any clinical significance. However, these differences may become important when studying the impact of practices such as tablet splitting on dosage consistency and dissolution, particularly in undivided tablets [12].

Conclusion

GSK company paracetamol tablets and Teriak laboratories tablets demonstrate and shows equivalent quality according to all tested official parameters. Both formulations can be used with confidence to provide consistent and reliable paracetamol therapy according to the obtained results. This comparative invitro evaluation demonstrated that both GSK and Teriak manufactured Panadol 500 mg tablets fully complied with pharmacopeial quality requirements for weight uniformity, friability, disintegration, dissolution, and assay of active ingredient. The inclusion of hardness testing provided additional insight into the balance between mechanical strength and disintegration efficiency, reinforcing the quality of both products. From a clinical and regulatory perspective, these findings support the interchangeability of the two brands in the Libyan market, ensuring consistent therapeutic efficacy regardless of manufacturing origin. Minor differences in early

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dissolution rates were observed, with the GSK tablets releasing slightly faster; however, similarity factor analysis (F2 = 68.4) confirmed the pharmaceutical equivalence of the two formulations.

ETHICS STATEMENT

Not Applicable.

AUTHORS' CONTRIBUTIONS

Both authors contributed to work equally.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Integrating Bromatology into Pharmacy Curricula: A Strategic Approach to Enhance Pharmaceutical Competencies and Support Public Health

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ABSTRACT

Pharmacy education is undergoing a paradigm shift to align with the evolving demands of healthcare and the expanding role of pharmacists in public health. This study explored the integration of bromatology into pharmacy curricula as a strategic approach to enhance pharmaceutical competencies and strengthen public health contributions. A cross-sectional survey design was employed with a total of 153 participants, including pharmacy students (n = 79), practicing pharmacists (n = 51), and pharmacy faculty members (n = 23). Data were collected using a structured questionnaire composed of fifteen items divided into three domains (1) Integrative curriculum components, (2) Pharmaceutical competencies, and (3) Public health. Responses were measured on a five-point Likert scale.

Descriptive results indicated strong support across all domains, with the majority of participants agreeing that bromatology integration is essential for advancing pharmacy education, improving analytical and professional competencies, and enhancing the pharmacist's role in community health. Analysis of variance revealed statistically significant differences among groups across the three domains. Faculty members consistently demonstrated stronger endorsement of bromatology integration compared with students and practicing pharmacists, suggesting that academic leaders recognize its strategic importance in curriculum reform.

The findings align with international research emphasizing curricular integration as a means of bridging theoretical and practical knowledge, improving student performance, and aligning pharmacy education with public health objectives. Integrating bromatology is therefore not merely an academic addition but a forward-looking reform that prepares pharmacists to manage food drug interactions, provide nutritional counseling, and contribute meaningfully to chronic disease prevention and health promotion. This study concludes that bromatology integration represents an investment in both the quality of pharmacy education and the advancement of public healthcare systems

Keywords: *Bromatology; Pharmacy education; Curricular integration; Pharmaceutical competencies; Public health.*

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1. Introduction

Pharmacy education has experienced profound modification over recent decades in response to the evolution of the profession from a focus on medication dispensing to a comprehensive commitment to patient centered care. Such a seismic shift has underscored the imperatives of educational frameworks that can adapt swiftly to the continually shifting demands of the health care environment and to the competencies that span multiple disciplines [1]. Review and metanalysis literature consistently advocates for a curricular paradigm that exceeds the boundaries of conventional siloed instruction; the evidence calls for the incorporation of integrative and interdisciplinary methodologies that ensure graduates can competently negotiate the intricate and dynamic circumstances endemic to contemporary health care systems [2].

Curricular integration is an increasingly salient instructional approach aimed at linking foundational pharmaceutical sciences with patient-oriented practice in pharmacy pedagogy. Empirical evidence indicates that the infusion of clinically pertinent content during the preclinical years engenders a more coherent synthesis of drug science and therapeutic decision making [3]. Analogous outcomes have been documented in nursing education literature, where integrated curricula have yielded augmented mastery and transfer of pharmacological principles, thereby reinforcing the efficacy of systematic integration in diverse health professions, including pharmacy [4].

Recent empirical investigations have reaffirmed the significance of integration extending beyond curricular design to actual educational outcomes. Comparative analyses of conventional and integrated curricula consistently demonstrate that cohorts receiving integrated instruction attain superior performance indices and exhibit more favorable evaluations of their educational experiences [5]. In addition, institutional case studies of integrated curricula provide converging evidence that timely implementation creates favorable synergies between articulated educational outcomes and the operative requirements of the healthcare system [6]. Nevertheless, persistent barriers including optimal resource distribution, comprehensive curriculum mapping, and variable levels of faculty preparedness continue to impede the efficacious establishment of integrated programs [7].

Contemporary discussions also highlight that integration should evolve from being a mere sequencing of topics to achieving a genuine curricular merger where basic, clinical, and applied sciences are taught in harmony [8]. In this regard, studies of accredited United States Doctor of Pharm programs reveal that integration of basic and clinical sciences not only enhances competencies but also aligns with global standards in pharmacy education [9]. Curriculum mapping efforts further illustrate the growing recognition that integration strategies are central to maintaining accreditation standards and ensuring relevance in pharmacy practice [10].

The integration of bromatology into pharmacy curricula can be viewed as an extension of this global movement toward curricular innovation. By embedding food science within pharmaceutical training, pharmacy graduates would be better equipped to address critical intersections of nutrition, medication safety, and public health. This strategic approach not only strengthens pharmaceutical competencies but also supports broader societal goals of promoting health and preventing disease.

The study aims to evaluate the effect of curricular integration by concentrating on connecting pharmaceutical sciences with clinical practice to improve student skills, and match educational results to medical demands.

It also investigates the possible benefits of bromatology to improve public health, nutrition, and medication safety connection.

1.1 Literature Context

The transition to integrated pharmacy education appears to parallel the emergence of experiential learning frameworks that explicitly align theoretical principles with practice-oriented scenarios. Meechan et al. documented the advantages of co-delivering pharmacology and medicines management within nursing syllabi, demonstrating that doing so enhanced the retention and applicability of basic pharmacological principles while simultaneously foregrounding their clinical utility [11]. Such evidence is germane to the pharmacy sector, in which the

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progressive prioritization of curriculum integration is viewed as a conduit for fostering contextualized comprehension and the progressive accretion of professional competencies.

Student outcomes continue to substantiate the efficaciousness of curricular integration. An investigation conducted by Hsia et al. demonstrated that synthetic curricula elevated both achievement and student perceptions of transfer across disciplinary domains relative to traditional delivery systems [12]. This body of evidence implies that integration operates at multiple cognitive and affective registers, suggesting that the pedagogical architecture informs both conceptual mastery and the motivational antecedents that underpin sustained engagement in professional practice.

Institutional case studies provide additional evidence regarding the multifaceted nature of curricular integration. documented the rollout of an integrated curriculum at a sizeable private university, recording initial positive indicators alongside persistent difficulties in coordinating disparate academic units [13]. Their findings suggest that, notwithstanding the potential for favorable educational results, the actual impact of integration is conditioned by deliberate design, sustained inter disciplinary collaboration, and iterative appraisal. In parallel argued that the co curriculum constitutes a constitutive element of accredited pharmacy degree offerings, although its realization is frequently obstructed by institutional architecture and operational constraints [14].

Moving integration beyond basic curricular reform necessitates an intentional, system-wide redirection. Advocate progressing from merely sequenced integration where disciplines follow one another—toward authentic curricular fusion, in which knowledge domains are architecturally interlaced into an indivisible cognitive fabric [15]. This progression is corroborated by, who performed curriculum mapping across United States pharmacy programs, revealing sustained emphasis on integrated pedagogies as a core criterion for accreditation and continuous quality improvement [16]. Collectively, the evidence rooted in both theoretical and empirical analyses substantiates treating bromatology integration as an essential avenue in the strategic institutional maturation of pharmaceutical education, thus ensuring that pharmacy alumni are prepared with competencies that concurrently advance pharmaceutical practice and safeguard public health.

1.2 Applied Justification for Bromatology Integration

The incorporation of bromatological content into PharmD programs epitomizes a deliberate effort to fuse food science and pharmaceutical education. Islam and colleagues analyzed the synthesis of basic and clinical science within U.S. PharmD curricula and asserted that the systematic inclusion of these domains cultivates the critical analytical faculties fundamental to evidence-based decision making and comprehensive patient management [17]. Their findings thereby furnish indirect support for the hypothesis that bromatology, regarded as a core discipline, augments the pharmacist's competence to assess the pharmacokinetic and pharmacodynamic repercussions of food drug related phenomena, as well as the modulatory effects of diet on pharmacotherapy.

Curriculum mapping investigations further support this thesis. Demonstrated that integrated curricular architectures in the United States systematically orient educational objectives toward contemporary healthcare exigencies [18]. Inserting bromatology into these architectures would broaden the pharmacist's professional portfolio beyond pharmacological supply to encompass nutritional guidance and dietary risk assessment, competencies that are assuming elevated importance in the realms of chronic disease deterrence and population health maximizing interventions.

International frameworks for higher education supply surplus scaffolding for curricular integration. delineate how the evolving pharmacy practice landscape compels systematic curricular revision, arguing that emergent programs must cultivate competencies in multidisciplinary patient centered collaboration [19]. Integration of bromatology would further that agenda by embedding nutritional determinants of health within pharmacist pedagogy, thereby fortifying pharmacists' role within interprofessional healthcare teams.

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Assert that curricular integration provides a strategic framework for cultivating competencies that remain disjointed under conventional instructional models [20]. By deliberately threading bromatology throughout the pharmacy curriculum, learners are poised to absorb discipline specific information alongside broadly applicable skills, including analytical scrutiny, clinical judgment, and patient focused deliberation. Viewed in this light, the integration transcends mere augmentation of the curriculum; it is a purposeful allocation of institutional resources designed to forge adaptable healthcare practitioners competent to navigate the multifaceted dilemmas that characterize contemporary pharmaceutical practice and the wider domain of public health.

1.3 Linking Bromatology Integration to Public Health

Pharmacists increasingly function as health promoters within communities, engaging in tasks such as patient education, nutritional counselling, and preventive care in addition to their traditional role of dispensing medications. Greene and colleagues assert that curricular components highlighting clinical relevance within basic science courses facilitate the transfer of laboratory derived knowledge to patient level decision making [21]. Incorporating bromatology within pharmacy degree programs, therefore, appears strategically advantageous; such integration provides learners with robust scientific acumen while simultaneously equipping them to evaluate food drug interactions and to recommend dietary modifications that optimize pharmacotherapy.

Findings originating from allied health education substantiate this assertion, demonstrated that learners who engaged with a curriculum amalgamating pharmacology and medicines management exhibited a pronounced capacity to transfer theoretical constructs into tangible clinical situations [22]. Within the context of pharmacy education, such a pedagogical structure may equip graduates to systematically identify nutritional determinants that modulate the efficacy and safety profiles of pharmacotherapeutic agents, consequently enhancing patient adherence and clinical endpoints.

Student centered outcomes further illustrate how curricular integration is foundational to public health preparedness. Established that an integrated pharmacy curriculum enhanced both objective assessment scores and subjective self-efficacy beliefs [23]. Translating that structure to bromatology, an integrated approach would cultivate the competencies pharmacists require to advance population health tactics, exemplary of chronic disease mitigation through dietary modifications. This educational strategy is consonant with public health frameworks that now position lifestyle alteration as a principal lever within health systems.

Wong et al. reported that the implementation of integrated curricula within a large private university fostered alignment between academic goals and healthcare system needs [24]. Bromatology integration can thus be viewed not only as an academic reform but as a policy aligned strategy to prepare pharmacists for expanded public health roles. In particular, pharmacists trained in bromatology would be well positioned to participate in community health campaigns, contribute to multidisciplinary care teams, and provide dietary counseling to reduce the burden of nutrition related diseases.

2. Methods

This research used a descriptive, cross-sectional design and was carried out in Sabratha Libya between January and March 2025. Participants in this study included 79 pharmacy students, 51 practicing pharmacists, and 23 pharmacy faculty members, totaling 153 individuals. Participants were added to this study through convenience sampling methods from Sabratha university and different community pharmacies. The authors of this research prepared a questionnaire which was later validated by three academic professionals from different fields

The sampling frame was pharmacy students from the Faculty of Pharmacy, University of Sabratha, community pharmacists from Sabratha city, and the associated academic staff. Inclusion criteria were being a pharmacy professional or a student ready to take part. Exclusion criteria were non pharmacy respondents and respondents that provided incomplete responses to the questionnaires. In total, 180 respondents were

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sampled, 153 of whom completed the survey which translates to a response rate of 85% from the total survey. The questionnaire was composed of 15 questions that were organized into three different areas.

Incorporation of bromatology into pharmacy education, pharmaceutical skills and Implications to public health. Every question was assigned a value from 1 to 5 based on a Likert scale with 1 being the lowest value which is 'strongly disagree' and 5 being the highest value which is 'strongly agree.

The collection of the data was done in a mixed method, through both online and physical documents with the condition that all participants must participate voluntarily. For this study, Statistical Package for the social sciences version 26 was utilized in data analysis. One-way Analysis of Variances (ANOVA) was employed to measure differences in groups.

Participation was completely voluntary, and respondents were free to withdraw at any time without any negative consequences. All the respondents signed the consent form prior to answering the questionnaires.

3. Results

The analysis of participants' demographic characteristics provided insight into the composition of the study sample. Table 1 presents the distribution of participants according to their category, including pharmacy students, practicing pharmacists, and pharmacy faculty members. The table highlights both the absolute frequencies and corresponding percentages, allowing for a clear understanding of group representation in the total sample of 153 respondents.

Table 1. Distribution of participants according to category (n =153)

Category	Frequency	Percentage (%)
Pharmacy students	79	51.6
Practicing pharmacists	51	33.3
Faculty members	23	15.1
Total	153	100

The data indicate that pharmacy students constituted the majority of the respondents, with 79 participants representing 51.6% of the total sample. This dominance reflects the importance of capturing the perspectives of learners who are directly engaged in the academic environment and whose training would be most affected by curriculum changes. Practicing pharmacists formed the second largest group with 51 participants, accounting for 33.3% of the sample. Their inclusion provides practical insights into how integration of bromatology might influence day-to-day pharmacy practice and patient counseling. Finally, faculty members represented 15.1% of the respondents, totaling 23 participants. Although they constituted the smallest group, their input is critical, as they are the decision-makers and implementers of curricular reforms. Taken together, the distribution shows a balanced representation that combines the views of those in training, those in practice, and those in academia, ensuring that the study findings are comprehensive and reflective of multiple stakeholder perspectives.

The first domain of the questionnaire examined participants' perceptions of integrating bromatology into pharmacy curricula. Table 2 summarizes the responses across the five Likert scale options for each of the five items. The data provide an overview of the extent to which students, pharmacists, and faculty members agree or disagree with statements emphasizing the importance and strategic role of bromatology in pharmacy education.

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Table 2. Participants' responses regarding the integration of bromatology into pharmacy curricula (n = 153)

Item	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
1. Integration of bromatology is essential for advancing pharmacy education.	72	51	18	8	4
2. Interdisciplinary courses strengthen understanding of food– drug relationships.	65	56	20	9	3
3. Introducing bromatology is a strategic investment in educational quality.	70	49	21	10	3
4. Integration helps bridge the gap between theory and practice.	60	54	24	11	4
5. Current pharmacy curricula require revision to include bromatology.	68	47	22	11	5

The results show strong consensus among participants regarding the significance of bromatology integration. For the first item, 72 respondents (47.1%) strongly agreed and 51 (33.3%) agreed, indicating that more than four-fifths of the sample viewed bromatology as essential for advancing pharmacy education. Neutral responses were limited to 18 participants (11.8%), while only a small fraction disagreed. In the second item, the majority of participants endorsed the role of interdisciplinary courses, with 65 strongly agreeing and 56 agreeing, confirming the perception that food–drug relationships are a critical aspect of pharmaceutical training.

For the third item, 70 respondents strongly agreed and 49 agreed that bromatology represents a strategic investment in the quality of education, further underscoring the recognition of its long-term value. Neutral responses (21 participants) suggest that a minority remain uncertain, while very few expressed disagreements. The fourth item, which addressed the bridging of theory and practice, showed similarly positive results, with 60 strongly agreeing and 54 agreeing, demonstrating that integration is widely perceived as a tool to reduce the gap between academic instruction and practical application. Finally, for the fifth item, 68 strongly agreed and 47 agreed that pharmacy curricula require revision to include bromatology, accounting for 75.1% of the total responses. The consistency across all items highlights a clear trend: participants overwhelmingly support curriculum reform to embed bromatology as a key component of pharmacy education. The second domain of the questionnaire focused on participants' views regarding the impact of bromatology integration on the development of pharmaceutical competencies. Table 3 presents the distribution of responses to the five items, showing how participants evaluated the role of bromatology in enhancing analytical skills, knowledge of food–drug interactions, evidence-based decision-making, professional skills, and patient counseling.

Table 3. Participants' responses regarding to the bromatology on pharmaceutical competencies (n = 153)

Item	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
1. Integration of bromatology improves clinical analytical skills.	66	55	20	8	4
2. Knowledge of food drug interactions enhance pharmacists' competencies.	74	49	18	7	5
3. Understanding bromatology supports evidence-based therapeutic decisions.	69	52	19	9	4
4. Integrated learning improves professional pharmacy skills.	63	56	22	8	4
5. Including bromatology strengthens pharmacists' ability to counsel patients.	71	50	20	7	5

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The results from this domain reaffirm the strong support for bromatology integration. In the first item, 66 respondents strongly agreed and 55 agreed, accounting for nearly 79% of the total, which indicates that most participants believe clinical analytical skills would benefit from the inclusion of bromatology. Only a small minority expressed disagreement. The second item received even stronger support, with 74 strongly agreeing and 49 agreeing that knowledge of food–drug interactions enhance pharmacists' competencies, suggesting that this dimension of bromatology is considered highly relevant across practice settings.

In the third item, 69 strongly agreed and 52 agreed that understanding bromatology supports evidence-based therapeutic decisions, reinforcing the argument that nutritional knowledge is integral to rational prescribing and patient care. The fourth item showed similar patterns, with 63 strongly agreeing and 56 agreeing that integrated learning improves professional pharmacy skills, demonstrating recognition of bromatology's value in broader competency development. Finally, in the fifth item, 71 strongly agreed and 50 agreed that bromatology strengthens pharmacists' ability to counsel patients, representing over 79% of participants. This highlights the applied dimension of bromatology in enhancing communication and patient-centered care. Overall, the responses confirm that participants view bromatology not as an isolated science, but as a crucial contributor to developing well rounded pharmaceutical professionals.

The third domain of the questionnaire explored participants' perspectives on the broader public health implications of integrating bromatology into pharmacy curricula. Table 4 summarizes the distribution of responses to five items addressing nutritional awareness, prevention of chronic diseases, improvement of healthcare, support for public health programs, and the pharmacist's role in community health.

The findings of this domain strongly confirm the relevance of bromatology for public health outcomes. In the first item, 70 participants strongly agreed and 52 agreed, showing that 79.7% of respondents believe bromatology education directly promotes nutritional awareness at the population level. This indicates recognition of the pharmacist's potential as a public educator. For the second item, 68 strongly agreed and 54 agreed that joint courses contribute to the prevention of chronic diseases, underlining the strategic role of bromatology knowledge in tackling lifestyle-related conditions such as diabetes and cardiovascular disorders.

Table 4 Mean (SD) scores of participant groups across the three study domains

Domain	Students (n = 79)	Pharmacists (n = 51)	Faculty (n = 23)	Total Mean (SD)
Integration of bromatology into curricula	4.12 (0.52)	4.18 (0.48)	4.47 (0.39)	4.22 (0.49)
Pharmaceutical competencies	4.09 (0.57)	4.21 (0.53)	4.45 (0.44)	4.19 (0.52)
Public health implications	4.05 (0.61)	4.16 (0.58)	4.42 (0.47)	4.16 (0.56)

The descriptive statistics shown in Table 4 demonstrates that faculty members, on average, reported higher mean scores on every domain as compared to students and practicing pharmacists. Their results indicate that faculty are more supportive than students and pharmacists of the integration of bromatology into practice.

The third item received the highest support, with 73 strongly agreeing and 50 agreeing that including bromatology in curricula improves overall healthcare. This strong endorsement reflects a consensus that public health benefits extend beyond the pharmacy profession to the healthcare system as a whole. For the fourth item, 65 strongly agreed and 57 agreed that pharmacists trained in bromatology are better prepared to support public health programs, highlighting the value of nutrition-focused training for community interventions and national health strategies. Finally, in the fifth item, 72 strongly agreed and 49 agreed that integration enhances the pharmacist's role in community health, which emphasizes the added value of pharmacists as accessible health professionals who can contribute directly to promoting healthier lifestyles.

In order to ascertain the presence of any statistically significance differences between the three participants' groups (students, pharmacists,

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and faculty members) on the study domains, a one-way Analysis of Variance (ANOVA) was conducted. The results are found in Table 5.

Table 5. One-Way ANOVA results showing differences among participant groups across study domains

Domain	Source of Variation	Sum of Squares	DF*	Mean Square	F-value	p-value
Integration of bromatology into curricula	Between groups	4.26	2	2.13	5.47	0.005*
	Within groups	58.71	150	0.39		
Pharmaceutical competencies	Between groups	3.85	2	1.92	4.92	0.009*
	Within groups	58.56	150	0.39		
Public health implications	Between groups	2.97	2	1.49	3.67	0.027*
	Within groups	60.91	150	0.41		

*DF: Degree of freedom. $p < 0.05$ indicates statistical significance.

The ANOVA results indicated differences among participant groups around all three domains which were significant ($p < 0.05$). Faculty members maintained a higher mean score compared to students and practicing pharmacists which affirm a greater endorsement of the integration of bromatology at the academic level.

The ANOVA means that at least one group within the three participant groups differs from the others in every category that was scored. In the case of the integration of the re-elected as being the interest. In studying the group means, the integration of public health and pharmaceutical competency scored over 65%. The next group, public health, was at 55%. There is then, based on the hypotheses that were formulated, the average score across these domains pharmacy and public health will decrease proportionally. In every case, there was no significant difference between other groups based on all means being below 65%.

The statistical means have two significant figures across and within every group across all means of analysis when unlike the faculties and practitioners, there is no notable difference between students. The merge students and practitioners means do not reach the cut off for significance. These two means, however, form meaningful clusters and mark the end of, which is a notable clustering of all three domains. This is the reverse of highest grouping reaching means of three groups.

4. Discussion

The findings of this study confirm that integrating bromatology into pharmacy curricula is widely perceived as both necessary and strategically beneficial. The strong agreement across all three domains curricular integration, pharmaceutical competencies, and public health supports the notion that educational reform is required to align pharmacy training with evolving healthcare needs. This resonates with the argument, who emphasized that the changing face of pharmacy practice requires a new educational model that fosters multidisciplinary competence and prepares graduates for patient centered care [19]. The ANOVA results were statistically significant. They confirmed that perceptions toward the integration of bromatology differ among the participant groups. Faculty members showed the most support. This difference in support further corroborates the qualitative observation in which collection of academics were recorded advocating moderation to the proposal.

The emphasis participants placed on bridging theoretical and practical knowledge mirrors the recommendations of who stressed the importance of embedding clinical relevance into foundational science courses [21]. In our study, respondents strongly agreed that bromatology integration helps bridge the gap between theory and practice, reflecting the same principle: integrated learning enhances applicability and ensures that knowledge translates effectively into professional contexts. Similar evidence was reported, where integrated pharmacology curricula in nursing demonstrated improved applied knowledge, underscoring the value of integration across healthcare disciplines [11].

Perceptions regarding enhanced pharmaceutical competencies further confirm the relevance of bromatology. Hsia et al. showed that

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integrated curricula improve student performance and perceptions compared to conventional models [8], a finding consistent with our results, where participants indicated that bromatology would improve analytical skills, decision-making, and patient counseling. Rivera et al. also observed that integrated curriculum initiatives align academic outcomes with healthcare system needs [24], which corresponds to the strong support among our participants for revising curricula to include bromatology.

From a broader perspective, the link between bromatology and public health was also highlighted in the responses, reported that integration of basic and clinical sciences in U.S. PharmD programs strengthens evidence- based practice and holistic care [17]. Our findings extend this by showing that participants view bromatology as a tool to promote nutritional awareness, prevent chronic diseases, and enhance the pharmacist's role in community health. This aligns with call to move beyond sequenced integration toward true curricular merging [9], as bromatology provides a natural bridge between pharmaceutical science and preventive health strategies.

Curriculum design considerations were also echoed in the responses, emphasized the importance of curriculum mapping to align pharmacy education with accreditation standards and healthcare challenges [16]. In our study, faculty members consistently demonstrated higher levels of support for bromatology integration than students and pharmacists, which reflects their direct involvement in academic planning highlighted that curricular innovations often face structural challenges [14], a point that can explain why students showed more variability in their responses, as they may be less exposed to the long-term vision of curricular reform.

Taken together, these findings suggest that bromatology integration is not perceived as an optional addition but as a strategic necessity that would equip pharmacists with competencies relevant to modern practice. The consistency with international research [11, 15, 19, 21, 23] strengthens the external validity of our results and situates them within a global discussion on pharmacy education reform.

5. Conclusion

This study provides empirical evidence that integrating bromatology into pharmacy curricula is strongly supported by students, practicing pharmacists, and faculty members. Across all three domains examined curriculum integration, pharmaceutical competencies, and public health participants expressed high levels of agreement, with statistically significant differences between groups. Faculty members consistently showed the strongest endorsement, reflecting their awareness of curricular planning and healthcare system demands.

The findings align with previous research demonstrating the value of curricular integration in enhancing performance, bridging theory with practice, and promoting public health competencies. By embedding bromatology into pharmacy education, pharmacy graduates will be better prepared to address nutritional and therapeutic interactions, contribute to preventive healthcare, and assume an expanded role in public health promotion.

In conclusion, the integration of bromatology should be considered a strategic educational reform rather than a mere addition to existing curricula. It represents an investment in the quality of pharmacy training and healthcare delivery, ensuring that pharmacists emerge as well-rounded professionals capable of meeting the complex needs of modern societies.

ETHICS STATEMENT

The research included fully anonymous survey responses. Consent was obtained from all participants, and participation was completely voluntary and confidential with verbal concept.

CONFLICT OF INTEREST

The authors hereby declare that they have no conflicts of interest that could have influenced the outcomes of this study or the impartiality of the presented finding and absence of any financial relationship, thereby ensuring the integrity and objectivity of the research.

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AUTHORS' CONTRIBUTIONS

A.A. conceptualized, collected data and designed the study.

W.O. analyzed data and preparation of manuscript.

K.M.A. contributed to the literature review and the preparation of the manuscript.

All authors reviewed and approved the final version.

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PREVALENCE AND RISK FACTORS OF MOBILE PHONE BACTERIAL CONTAMINATION AMONG FACULTY HEALTH SCIENCES STUDENTS

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ABSTRACT

Background: Mobile phones are an indispensable tool in students' academic and daily lives, and their frequent use makes them a potential means of transmitting bacteria from users' hands.

Objectives: This study was conducted to identify bacteria present on touch screens of smartphones and to determine potential factors that may influence bacterial contamination of mobile phone surfaces with bacteria and the level of students' awareness of the role of immune blood cells against these bacterial agents of students of the faculty of Health Sciences in Al-Khums city.

Methods: The study was conducted at the faculty of Health Sciences from November 2024 . 200 swabs were collected from 200 mobile phones, and a questionnaire was distributed to all participants to collect data. Swab samples were taken from participants' phones and cultured to identify bacterial contamination in the college's medical laboratory. Samples were cultured on blood agar and incubated at 37°C for 24 hours. Bacterial isolates were identified using conventional bacterial species identification methods.

Results: Our results showed that the mobile phone contamination rate with microorganisms reached 95.7%, with 282 microbes isolated from 200 swabs. Staphylococcus epidermidis was the most common, accounting for 33.8%, followed by Streptococcus pneumoniae (20.3%), Streptococcus pyogenes (14.3%), Escherichia coli (10.3%) Staphylococcus aureus (10.3%). Pseudomonas aeruginosa (5.0%), fungi (1.1%), and Klebsiella (0.7%) were also found.

Conclusion: mobile phones can be heavily colonized by high quantities of pathogenic bacteria and thus potential sources of disease transmission requiring application of sound personal hygiene as preventive methods.

Keywords: *Bacteria , Contamination, Mobile phone , Students*

1. Introduction

Cell phones are common among undergraduate students, and can be used to communicate for social or academic purposes, according to the technological features of the device and Internet connection. Students related to health sciences majors use their cell phones while performing internships at hospitals or clinical laboratories, either to access information on their field of expertise, answer calls, text messages or take

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pictures during their practices. The use of this mobile communication technology in healthcare and higher education has increased and generated interest in evaluating their role as reservoir of pathogenic and opportunist bacteria, and as a source of contamination to our foods or ourselves, However, one of the most common concerns regarding heavy use of mobile devices is that they can act as a vehicle for transmitting pathogenic bacteria and other microorganisms [1].

Recent studies have revealed that mobile phones used by university students—especially those in medical and health-related fields—are frequently contaminated with pathogenic bacteria. A study at Basrah University found 137 bacterial isolates from 100 student phones, with Staphylococcus aureus, Staphylococcus epidermidis, and Pseudomonas aeruginosa being the most common. The findings emphasized that mobile phones can act as vectors for disease transmission and highlighted the need for hygiene protocols to prevent cross-contamination [2]. At Adekunle Ajasin University in Nigeria, researchers discovered bacterial growth on 50 out of 120 phones, with Staphylococcus aureus being the most prevalent. Notably, 80% of participants reported using their phones in toilets, suggesting poor hygiene practices. The study recommended frequent cleaning and personal hygiene to reduce bacterial load [3]. In Bangladesh, a cross-sectional study showed that smartphones used by students carried various microorganisms. Samples were cultured and incubated, confirming that mobile phones can serve as carriers for microbial transmission [4]. A study in Thailand among pharmacy students revealed that 98.11% of phones were contaminated, and 84.62% had dense bacterial colonies. The most common organisms were coagulase-negative staphylococci (CoNS), Bacillus species, and Staphylococcus aureus. The study stressed the importance of awareness and proper cleaning of personal medical instruments [5].

In Libya, research conducted at the University of Sirte found that 60.8% of student phones were contaminated, with 96% of the bacteria being Gram-positive. The dominant species included Staphylococcus epidermidis, Staphylococcus aureus, and Streptococcus agalactiae. The study concluded that mobile phones are significant vectors of infection in both community and healthcare settings, and recommended the use of disinfectants and hand hygiene to mitigate risks [6].

Mobile phones are recognized as potential carriers of various pathogens. Within academic environments, faculties and universities may serve as primary sources for the spread of these microorganisms.

The study aims to assess the prevalence of bacterial contamination on mobile phones used by Health Sciences students, identify the most common bacterial species involved, and raise awareness about proper phone hygiene. It also seeks to evaluate the extent of contamination within the Faculty of Health Sciences. Notably, this topic has not been previously investigated among students at Elmergib University.

2- Materials and Methodology:

The study was cross-sectional descriptive study

2.1 Research Material:

Blood agar, a nutrient-rich medium that supports the growth of diverse bacteria, was used in this study. This medium was obtained ready-made from Al-Khums Hospital and Al-Itqan Lab, and bacterial samples were cultured immediately after collection.

2.2 Research Tools:

The following tools were used in this study:

Sterile cotton swabs and sterile transport medium swabs: Used to collect samples from the surfaces of mobile phones, and the samples were cultured immediately after collection.

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Blood agar medium: Used to culture the samples and identify bacterial species.
Heat source: Used to sterilize the work surface at the sample collection site before beginning the procedure.
Incubator: Used to incubate the culture media at 37°C for 24–48 hours.
Refrigerator: Used to store the culture media under appropriate conditions before use

2.3. Scope of the research:

This research examines the prevalence of bacterial contamination on mobile phones and its associated factors among students of the College of Health Sciences. The study scope is limited to students only, excluding faculty members and administrative staff, to ensure sample homogeneity in terms of mobile device usage and the educational environment.

2.4 Time and place of the research:

This study was conducted at the faculty of health sciences at Elmergib University in Al-Khums, where data collection and sample analysis were conducted within the college's laboratory in the Department of Medical Laboratories. Samples were collected during the period from November 2024 to January 2025, according to the methodological procedures approved by the academic department.

2.5 Research design:

This study was conducted to analyze the prevalence of bacteria on students' mobile phones in the College of Health Sciences, focusing on the factors contributing to bacterial contamination. Data were collected through questionnaires to assess students' habits such as handwashing, phone cleaning, and the duration of phone use. Bacterial samples were also taken from students' phones using sterile swabs and cultured on growth media to identify the types of bacteria presents. The results were analyzed using statistical methods to determine the relationship between usage patterns and the level of bacterial contamination on mobile phones.

2.6 Study population and sampling size:

The study was conducted on students in the faculty of Health Sciences. The number of participants was 200 students, divided into 51 males and 149 females, from various disciplines within the college. The sample was determined based on the following criteria:
Participants were randomly selected to ensure representation of all disciplines.
Participants' ages ranged between 18 and 25 years old.
The sample size was determined based on the statistical requirements of the study to ensure accurate and generalizable results.

2.7 Research procedure:

To ensure the accuracy of the results and avoid any cross-contamination, strict preventive measures were followed before collecting samples. The researcher sterilized his hands using a rapid alcohol-based sanitizer and wore powder-free medical gloves. Samples were collected from the surfaces of mobile phones using sterile cotton swabs and sterile transfer media. These swabs were passed over all parts of the phone, including the screen, sides, and back, using regular circular motions to ensure the collection of the largest possible number of bacteria. The collection process was conducted within the college's laboratory in the Department of Medical Laboratories, and the samples were inoculated directly onto blood agar, which helped maintain bacterial viability and ensure the reliability of the results.

2.8 Principle of the tests:

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The laboratory testing principle was based on culturing samples on blood agar, and then incubating them in an incubator at 37°C for 24 hours. After the incubation period, the media were examined for bacterial growth. Samples that did not show any visible growth were excluded. The results were read under the supervision of a microbiologist to ensure accurate observation and interpretation.

2.9. Data collection:

Data were collected from 200 male and female students in the College of Health Sciences using a questionnaire containing closed and open-ended questions. The questionnaire included information on the participant's name and age, as well as the students' mobile phone usage practices, their awareness of personal hygiene, and the impact of this on student health. The questionnaires were randomly distributed to ensure representation across all academic year groups.

3. Ethical clearance:

Ethical approval ethical approval was obtained from the Faculty of Health Sciences Research Ethics Committee (HS: 13:2024) before data collection began. Participants were informed about the study's purpose and procedures, and an informed consent was obtained. Participants were also informed that participation was completely voluntary and that the data collected would be used for research purposes only.

The site file is saved and only researchers can reach the data inside, also the data has been saved in another out databank which also protected and no sign in can be done only by the researchers. All biosafety requirements were followed during the study,

4. Statistics analysis:

All statistical analyses were performed using IBM SPSS Statistics version (SPSS Inc., Chicago, IL, USA), Excel Office, and Chi-Square Test, Categorical data were presented as numbers and percentages, and the prevalence of bacteria was calculated and presented as a percentage.

5. Results:

The data obtained by the researcher from the faculty of health sciences, was used, where she obtained a sample of 200 male and female students. By studying this sample statistically, the researcher reached the following:

5.1 Distribution of the research sample by gender:

In the research sample, the total number of cases reached 200 participants, where the number of male students reached 51, representing 25.5%, while the number of female students reached 149 female students, representing 74.5%, as shown in Figure 1.

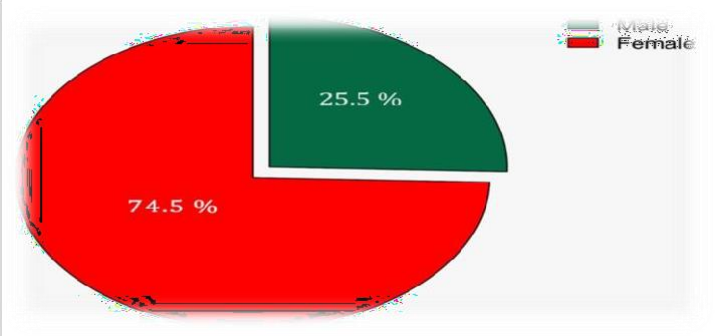

Figure 1: Distribution of the sample by gender

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5.2 Distribution of the research sample according to the academic stage:

The number of first-year students was 38, representing 19% of the respondents, of whom 5% were males and 14% were females, the number of second-year students was 36, representing 18% of the respondents, of whom 4% were males and 14% were females, the number of third-year students was 65, representing 32.5% of the respondents, of whom 8.5% were males and 24% were females, while the number of fourth-year students was 61, representing 30.5% of the respondents, of whom 8% were males and 22.5% were females, as shown in Figure 2

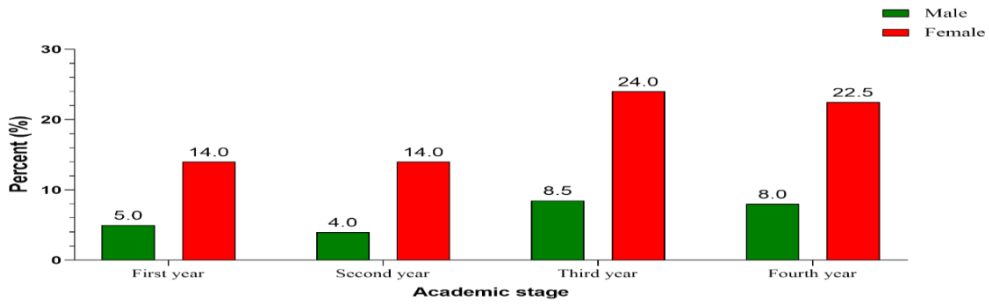

Figure 2: Distribution of the research sample according to Academic year and gender

5.3 Distribution of respondents' answers about the number of hours they spend using their phone daily:

When the study sample participants were asked about the number of hours they spend daily using their mobile phones: 14.5% of them answered (Less than 3 hours) which is the lowest percentage among the responses. The highest percentage (30%) was for those who reported using their phones for three to five hours daily. Additionally, 28% of them answered (6-8 Hours), while the remaining participants reported using their phones for More than 8 Hours, as shown in Figure 3

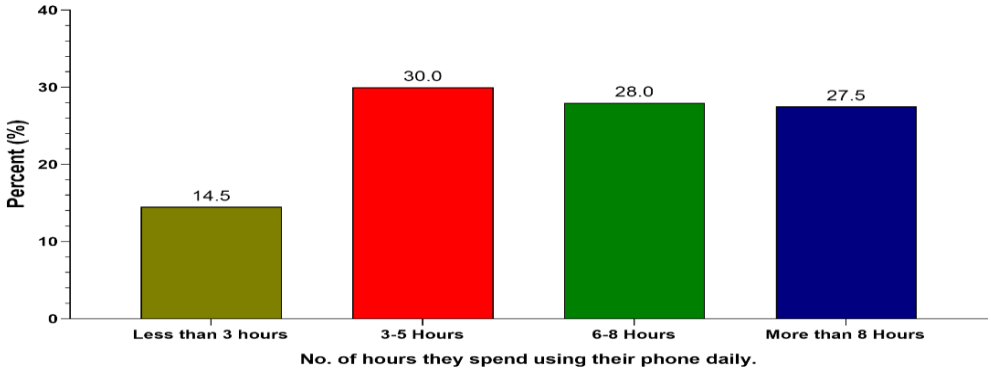

Figure 3: Distribution of respondents' answers about the number of hours they spend using their phone daily.

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5.4 Distribution of respondents' answers about using mobile phones while eating and drinking:

When the students representing the research sample were asked about using their mobile phones while eating or drinking, 14% of them answered (Yes, Regularly), which is the lowest percentage, while 44% answered (Sometimes), which is the highest percentage. Additionally, 26.5% reported using their phones (Rarely), and the remaining percentage answered (No, Never), as shown in Figure 4.

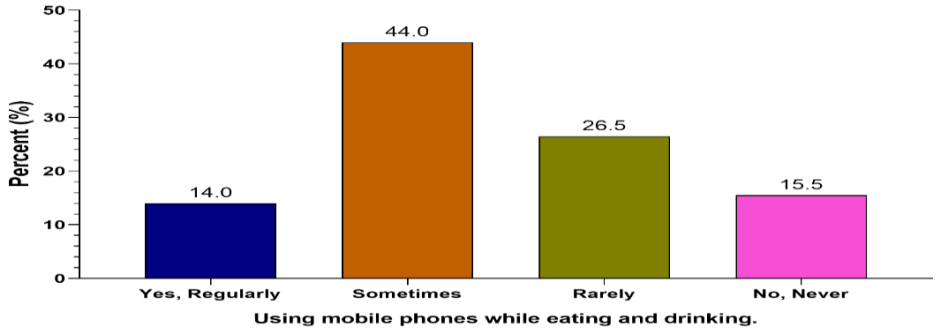

Figure 4: Distribution of respondents' answers about using mobile phones while eating and drinking

5.5 Distribution of respondents' answers about the times when the phone is used most:

When the students representing the research sample were asked about the times when the phone is used most: 2.5% indicated they use their phones most while commuting on public transportation. The majority, 61%, reported using their phones primarily at home, representing the highest percentage. Conversely, only 1% noted they use their phones most in college or university, the lowest percentage. The remaining participants selected "all of the above," as illustrated in Figure 5.

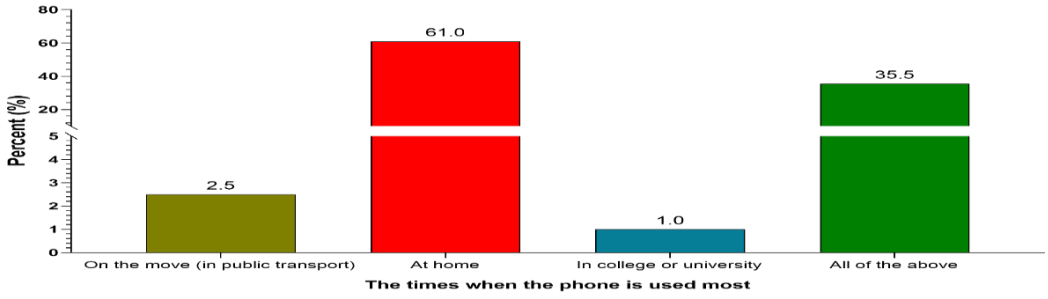

Figure 5: Distribution of respondents' answers about the times when the phone is used most

5.6 Distribution of respondents' answers about whether using a phone together with the family can affect personal hygiene:

When the students representing the research sample were asked whether using a phone jointly with family members could affect personal hygiene, only 13.5% responded "yes, significantly," representing the lowest percentage. The majority, 46.5%, answered "yes, to some extent," which is the highest percentage. The remaining participants indicated "no, it does not have much effect," as illustrated in Figure 6

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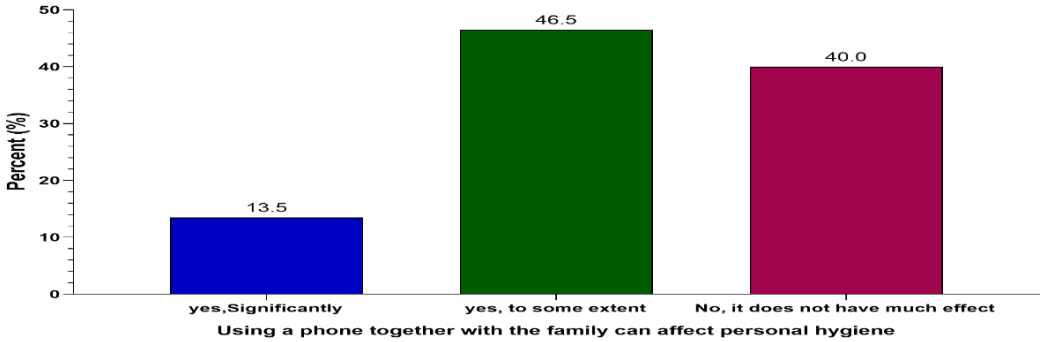

Figure 6: Distribution of respondents' answers about whether using a phone together with the family can affect personal hygiene

5.7 Distribution of respondents' answers regarding the fact that sharing:

When the students representing the research sample were asked whether sharing phones with family members can affect the health of children in the household, 47% of them answered (Yes, especially the little kids Yes) which represents the highest percentage, Meanwhile, 38.5% answered (yes, but to a limned), while the rest answered (No, I do not think it has an effect) which is the lowest percentage as illustrated in Figure 7

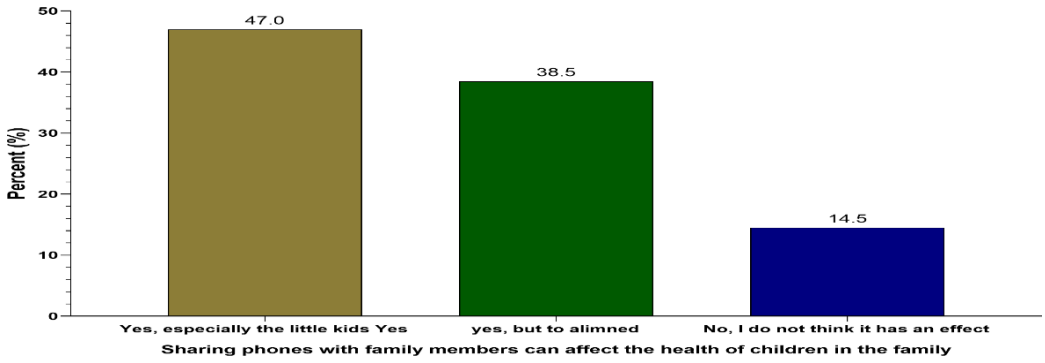

Figure 7: Distribution of respondents' answers regarding the fact that sharing phones with family members can affect the health of children in the family

5.8 Distribution of respondents' answers about sharing mobile phone with colleagues:

When the students representing the research sample were asked whether they share their mobile phones with colleagues,55% of them answered (Yes) which is the lowest percentage, while the remaining participants answered (No) which represents the highest percentage, as illustrated in Figure 8.

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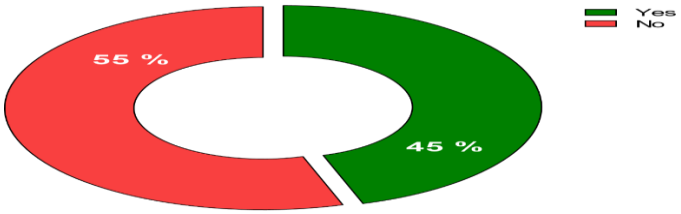

Figure 8: Distribution of respondents' answers about sharing mobile phone with colleagues

5.9 Distribution of respondents' answers about cleaning the mobile phone surface regularly:

When the students representing the research sample were asked about the frequency of cleaning their mobile phone surfaces, 31% of them answered (Yes, daily), 20.5% of them answered (Yes, weekly), 46% of them answered (Sometimes) which represents the highest percentage, while the rest answered (No, I never did that) which is the lowest percentage, as illustrated in Figure 9

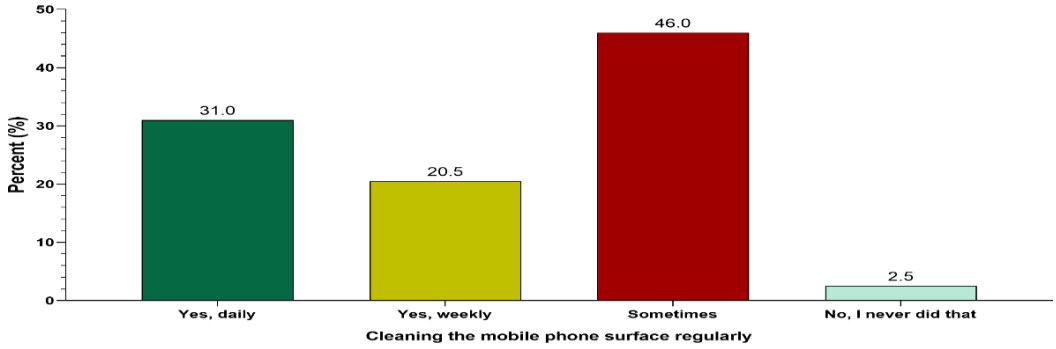

Figure 9: Distribution of respondents' answers about cleaning the mobile phone surface regularly

5.10 Distribution of respondents' answers about the methods:

When the students representing the research sample were asked about the methods they use to clean their phones, 45.5% of them answered (Sterile wipes), 52% of them answered (Peace of cloths) which represents the highest percentage. The remaining students indicated that they do not clean their phones, which constitutes the lowest percentage, as illustrated in Figure 10.

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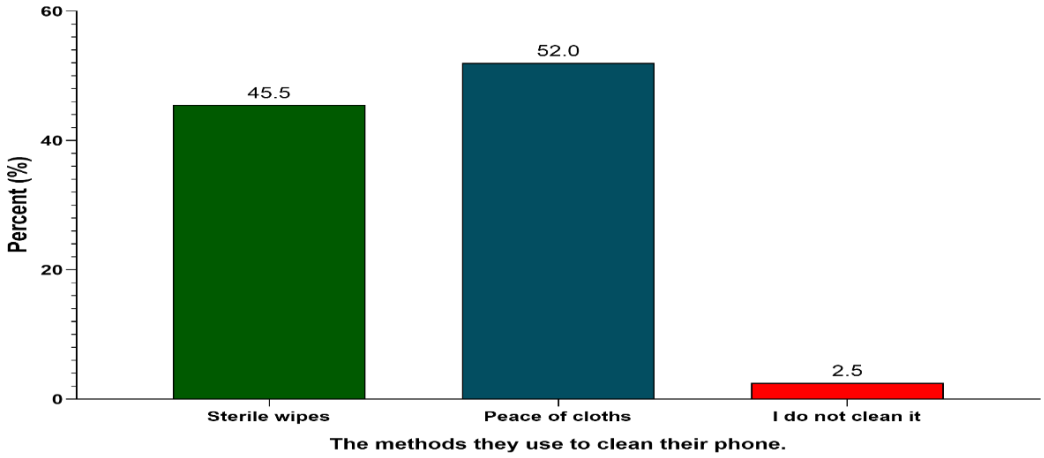

Figure 10: Distribution of respondents' answers about the methods they use to clean their phone.

5.11 Distribution of respondents' answers about hand cleaning before and after using a mobile phone:

When the students representing the research sample were asked How often they should clean their hands before and after using their mobile phones, 15.5% of them answered (Always), 36% of them answered (Mostly), 40% of them answered (Sometimes) which represents the highest percentage. The remaining students answered (No, never) which is the lowest percentage, as illustrated in Figure 11

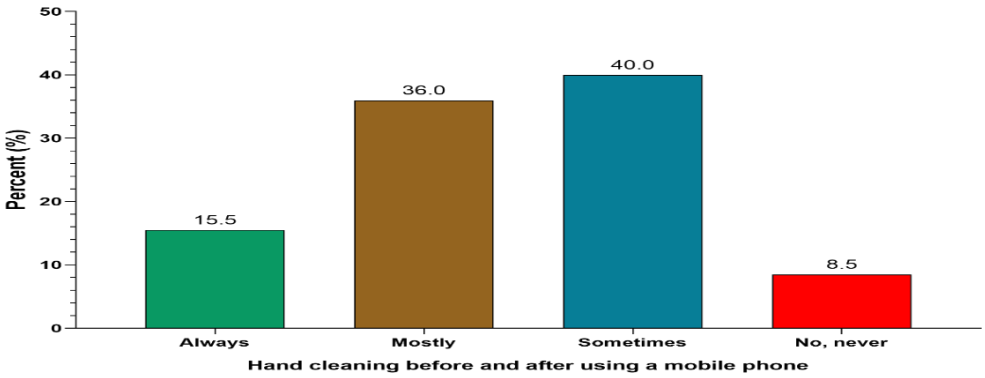

Figure 11: Distribution of respondents' answers about hand cleaning before and after using a mobile phone

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5.12 Distribution of respondents' answers about avoiding sharing a phone with a family member with an infectious disease:

When the students representing the research sample were asked whether they avoid sharing their phone with a family member who has a contagious illness (such as influenza) ,57.5% of them answered (Yes) which is the highest percentage, while the rest answered (No) which represents the lowest percentage, as shown in Figure 12

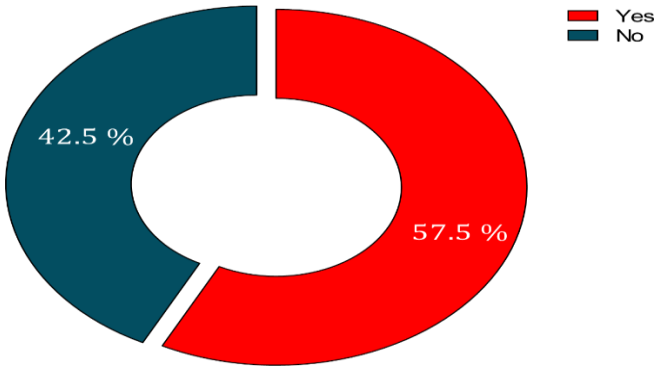

Figure12: Distribution of respondents' answers about avoiding sharing a phone with a family member with an infectious disease

5.13 Distribution of respondents' answers about mobile phone transmission of harmful bacteria:

When the students representing the research sample were asked whether they believe mobile phones can be a source of harmful bacteria transmission, 30% of them answered (Yes, Significantly), 40% of them answered (Yes, to a moderate degree) which is the highest percentage, 23% of them answered (Yes, but to a limited extent), while the rest answered (No, I do not think so) which represents the lowest percentage, as shown in Figure 13.

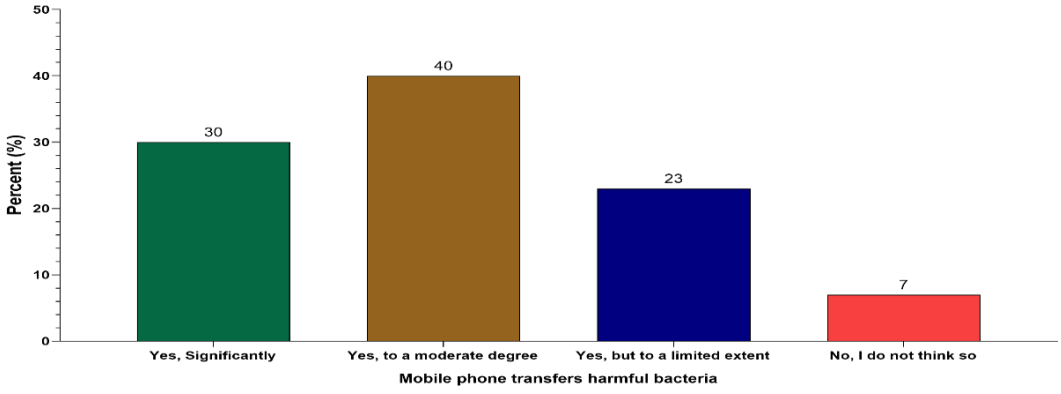

Figure 13: Distribution of respondents' answers about mobile phone transmission of harmful bacteria

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5.14 Distribution of respondents' answers regarding prior knowledge of studies or research indicating the presence of harmful bacteria on mobile phones:

When the students representing the research sample were asked whether they had prior knowledge of studies or research indicating the presence of harmful bacteria on mobile phones, only 8.5% responded with (Yes, I know her well) which represents the lowest percentage, 59.5% of them answered (I heard about it in general) which is the highest percentage, while the rest 32% answered (No, I have not heard of that before), as shown in Figure 14.

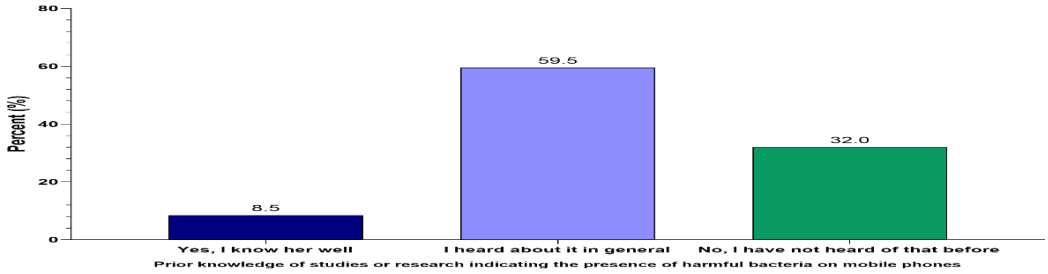

Figure 14: Distribution of respondents' answers regarding prior knowledge of studies or research indicating the presence of harmful bacteria on mobile phones

5.15 Relationship between academic stage and the transmission of harmful bacteria from mobile phones :

When students were asked about the transmission of harmful bacteria from mobile phones, 19% of the first-year students including 5%, answered (Yes, Significantly), 6% answered (yes, to a moderate degree), 5.5% answered (yes, but to a limited extent), while 2.5% of them answered (I don't think so). 18% of the second-year students, 32.5% of the third year students , while 30.5% of the fourth year students, as shown in figure 15, and we notice that there is no significant relationship between the academic stage and the transmission of harmful bacteria from mobile phones, where the correlation coefficient value was 0.011, indicating a very weak relationship, while the value of the Level of significance(P-value) was 0.881, which is greater than 5%, which confirms the absence of such a relationship.

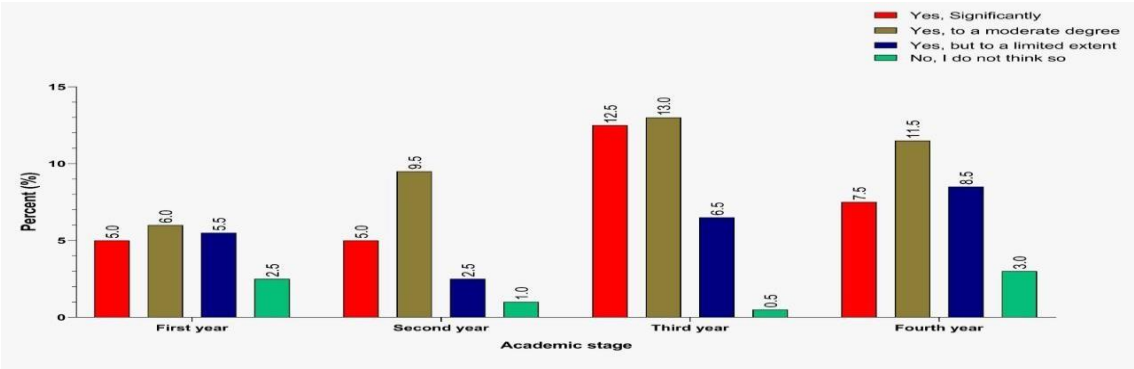

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Figure 15: Relationship between academic stage and the transmission of harmful bacteria from mobile phones.

5.16 Relationship between academic stage and the prior knowledge of studies or research indicating the presence of harmful bacteria on mobile phones:

When students were asked about their prior knowledge of studies or research indicating the presence of harmful bacteria on mobile phones, 19% of the first-year students including 2.5% answered (Yes, I know her well), 10% answered (I heard about it in general), while 6.5% of them answered (I don't think so). Among other academic levels, 18% of the second-year students, 32.5% of the third-year students, and 30.5% of the fourth-year students, as shown in figure 16. However, the data indicates no significant relationship between academic year and prior knowledge of such studies, where the correlation coefficient value was 0.015, which is very weak, while the value of the level of significance(P-value) was 0.828, which is greater than 5%, confirming that the relationship is not statistically significant.

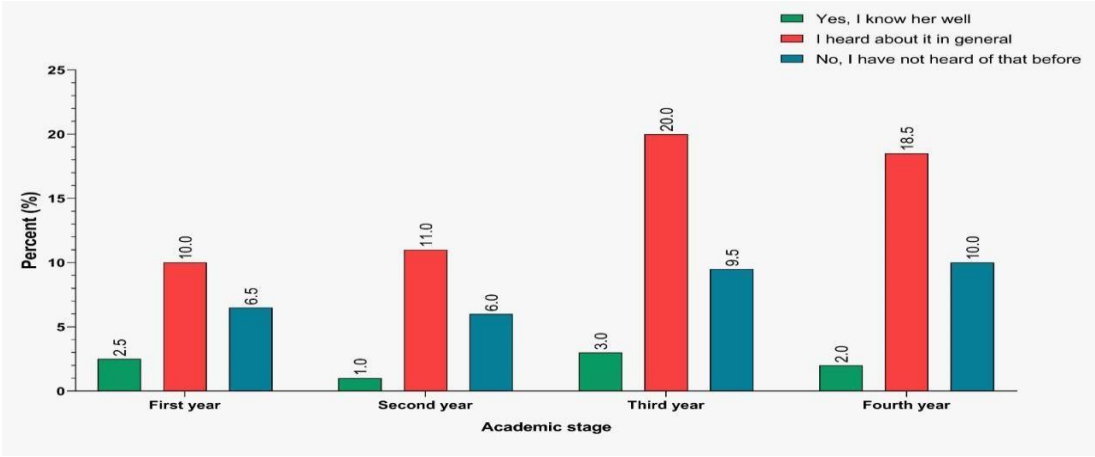

Figure 16: Relationship between academic stage and the prior knowledge of studies or research indicating the presence of harmful bacteria on mobile phones

5.17 Gender-Based Distribution of Microbes Presence:

This figure presents the distribution of bacterial species across male and female participants. The data illustrate potential gender-related variations in microbial prevalence.

Note: Samples showing no microbial growth were excluded from the main analysis, while fungal growth in mixed samples was ignored, focusing solely on bacterial growth. All samples were included in the results section to ensure accurate representation of the overall proportions.

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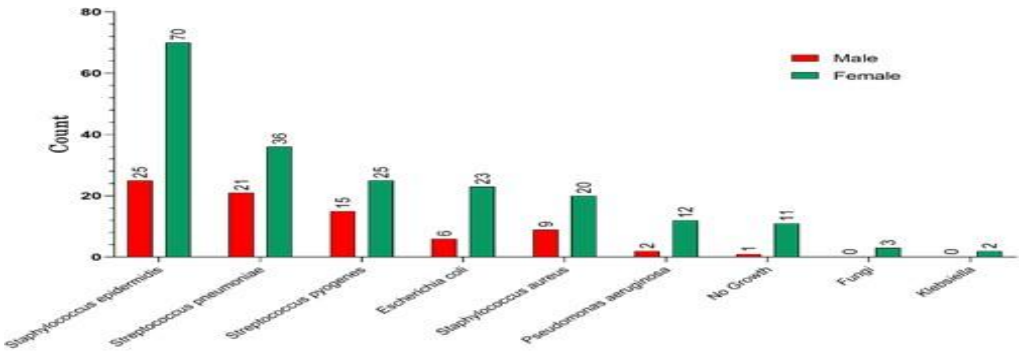

Figure 17: Gender-Based Distribution of Microorganisms Presence

5.18 Prevalence of Microorganisms in the Study Population:

The analysis of microorganism distribution within the study group revealed that Staphylococcus epidermidis was the most commonly detected bacterium, present in 33.8% of the samples, Streptococcus pneumoniae was found in 20.3%, followed by Streptococcus pyogenes in 14.2%. Both Escherichia coli and Staphylococcus aureus were identified in 10.3% of the samples, while Pseudomonas aeruginosa appeared in 5%. Additionally, 4.3% of the samples were excluded due to no bacterial growth, Fungal growth was excluded from 1.1%, and Klebsiella species were detected in only 0.7%. As illustrated in Figure 18, Staphylococcus epidermidis was the most prevalent bacterium, with other species occurring at comparatively lower rates.

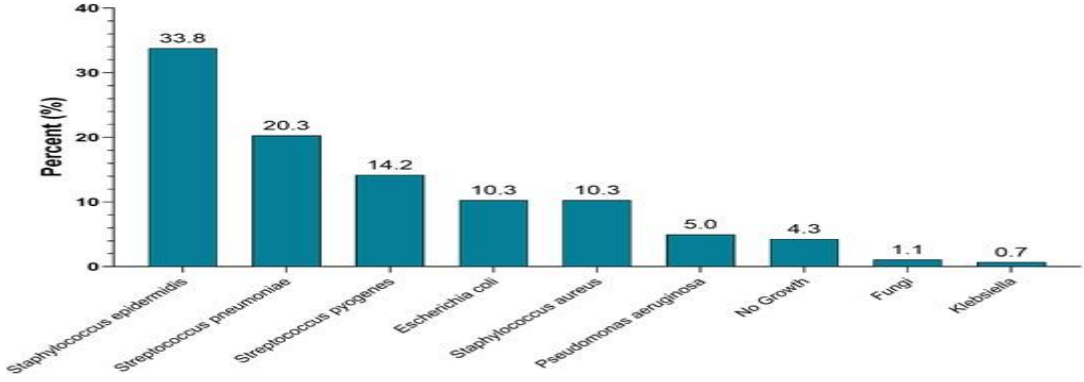

Figure 18: Prevalence of Microorganisms in the Study Population

5.19 Distribution of Microorganisms Presence Across Academic Years:

The distribution of bacterial species isolated from mobile phones of students in the College of Health Sciences was analysed based on academic year, ranging from first to fourth year. Out of a total of 200 isolates, 12 samples with no bacterial growth and 3 samples from which fungal growth was excluded, resulting in 188 valid samples for analysis Staphylococcus epidermidis was the most frequently isolated bacterium, identified with precent of (33.8%), with the highest incidence observed among third-year (31.6%) and fourth-year students

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(30.5%). Streptococcus pneumoniae followed, detected in 20.3% of the samples, most commonly among third-year students (38.6%). Streptococcus pyogenes accounted for 14.2% of cases, also peaking in the third year. Both Escherichia coli and Staphylococcus aureus were found in 10.3%, distributed relatively evenly across all years, with a slight increase in the second year (34.5%). Pseudomonas aeruginosa appeared in 5.0% of cases, most frequently in the third year (42.9%). Klebsiella was the least common, isolated in only two cases (0.7%), both from fourth-year students. Overall, the third-year students had the highest proportion of bacterial isolates (31.7%), followed by fourth-year (28.1%), first-year (20.6%), and second-year students (19.6%), as detailed in Figure 19.

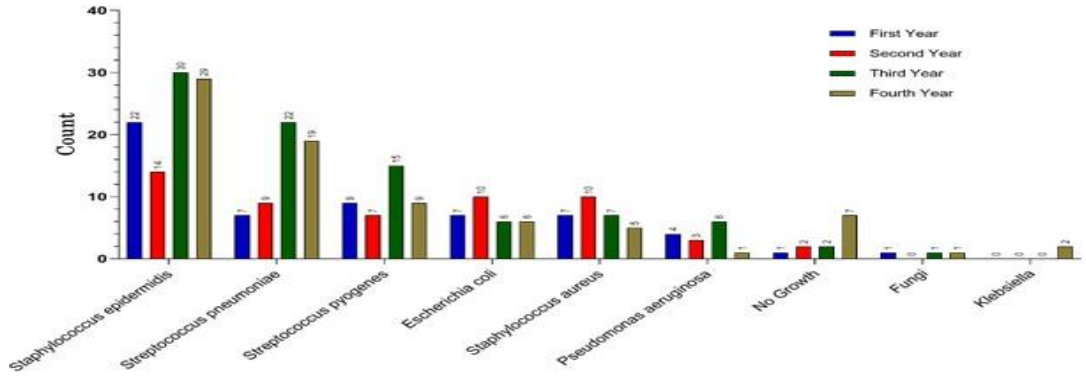

Figure 19: Distribution of Microorganisms Presence Across Academic Years

5.20 Distribution of Microorganisms Across Cleaning Methods and Chi-Square Test Results:

The figure below presents the distribution of microbes (both bacteria and fungi) isolated from mobile phones based on the cleaning method used—whether wiped with sterile wipes, cleaned with a cloth, or not cleaned at all. It also includes the results of the Pearson's Chi-Square test, which was conducted to assess whether there is a statistically significant relationship between the cleaning method and the type of microbe identified. The p-values indicate whether the observed differences among the groups are statistically significant, as illustrated in and Figure 20.

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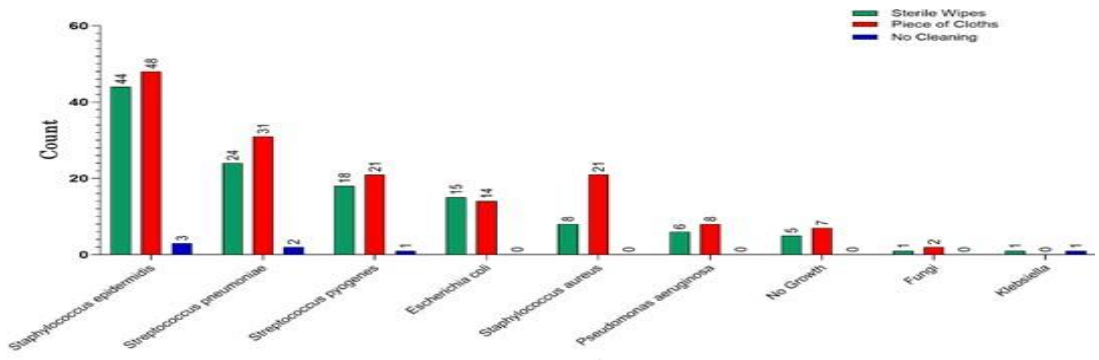

Figure 20: Distribution of Microorganisms Across Cleaning Methods and Chi-Square Test Results

6. Discussion:

The Pearson Chi-Square test results indicate no statistically significant association between cleaning methods and individual bacterial species (all p-values > 0.05). However, the overall Chi-Square test for all bacteria combined ($\chi^2 = 562$, $p < 0.001$) suggests a significant relationship between cleaning methods and bacterial presence.

Notably, the highest bacterial prevalence was observed in the "Piece of Cloths" cleaning method (54.1%), whereas sterile wipes had a slightly lower prevalence (43.4%), and no cleaning had the lowest bacterial detection (2.5%). This pattern suggests that the effectiveness of cleaning methods may vary, with piece of cloths potentially contributing to cross-contamination.

Certain bacteria, such as Staphylococcus aureus (72.4%) and Pseudomonas aeruginosa (57.1%), were predominantly found in the "Piece of Cloths" category, indicating that this cleaning method may be less effective in reducing bacterial load. Escherichia coli showed a nearly even distribution between "Sterile Wipes" (51.7%) and "Piece of Cloths" (48.3%), suggesting that both cleaning methods may have similar efficacy for this particular bacterium.

These results showed that the prevalence rate of microorganisms on students' mobile phones reached 95.7%. This rate is relatively close to the findings reported by Sribrapon et al. [5] in Thailand, where the prevalence was 98.11%. In contrast, the findings of Ya'aba et al. (2020) were lower, reporting a bacterial contamination rate of 56.3% among females and 43.7% among males [7].

These results suggest that mobile phones may serve as a favorable environment for the transmission and proliferation of bacterial pathogens, highlighting their potential role as a source of infection. When comparing the types of bacteria isolated, it was found that coagulase-negative Staphylococci were the most commonly isolated organisms in the study by Sribrapon et al. [5], accounting for 42.72%, compared to 33.8% in this study. Moreover, Staphylococcus aureus was detected at a rate of 20.39% in their study, while it was found at 10.3% in this study. Notably, Escherichia coli was not detected in the study by Sribrapon et al. [5], whereas it was identified in 10.3% of samples in this study. These results are consistent with the findings of Sribrapon et al [5]. regarding the predominance of coagulase-negative Staphylococci; however, the detection of Escherichia coli in this study may reflect differences in sources of contamination or variations in personal hygiene practices among the studied populations.

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When comparing these results with those of Ya'aba et al., it was found that the contamination rate of mobile phones with Staphylococci was 47.1% among males and 55.6% among females, compared to 28.65% and 71.35%, respectively, in this study. Additionally, Escherichia coli was detected in 38.2% of males and 41.7% of females in their study, compared to 20.7% of males and 79.3% of females in this study. Regarding Klebsiella spp., their study reported rates of 35.3% in males and 38.9% in females, while in this study, Klebsiella spp. was not detected among males and was found in 100.0% of females. As for Salmonella spp., Ya'aba et al. reported a prevalence of 47.1% in males and 55.6% in females, whereas no Salmonella spp. was detected in this study [7].

In general, these results are in agreement with previous studies in identifying coagulase-negative Staphylococci as the most common isolated bacteria. However, this study is distinguished by the absence of Salmonella spp. and the presence of Escherichia coli, which may be attributed to differences in environmental factors, sample characteristics, or hygiene practices among students. [8].

7. Conclusion:

A cross-sectional study was conducted, the results of this study revealed a high rate of bacterial contamination on mobile phones among health sciences students, highlighting their potential role as hidden carriers of infection in university environments characterized by intense human interaction. A wide range of microorganisms was identified, with Staphylococcus epidermidis being the most prevalent, followed by Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Klebsiella species and the students were known the role of immune blood cells against these bacterial agents

These findings suggest that mobile phones may represent a significant source of bacterial contamination, especially in the absence of adequate awareness regarding their potential to harbor pathogens. They also indicate that the transmission of infectious agents is not limited to healthcare settings but can also occur through everyday practices, emphasizing the need for greater attention to this issue within university life.

ETHICAL STATEMENT

Ethical approval was obtained from the Faculty of Health Sciences Research Ethics Committee.

AUTHORS' CONTRIBUTIONS

All authors contributed equally

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Antimycobacterial Effect of Naphthoquinone Natural Derivatives Identified in Henna leaves against Three Target Enzymes Computational Molecular Docking Study

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A B S T R A C T

Background:

Tuberculosis (TB) remains a major health threat, aggravated by rising drug resistance and treatment toxicity. Henna (*Lawsonia inermis*) is a plant commonly used in traditional medicine and folk cosmetics. The plant has topical anti-fungal effect, protect sunburn; topical analgesic and relief inflammation. However, their mechanism of action against *Mycobacterium tuberculosis* is not yet fully characterized.

Objective:

The present study aimed to evaluate the antimycobacterial effect of naphthoquinones natural derivatives from henna leaves extract against *M. tuberculosis* by computational approach targeting three essential *Mycobacterium* enzymes involved in bacterial growth and survival; and to identify the interactions between the derivatives and the target protein.

Methods:

The plant leaves were extracted by maceration in methanol and then subjected to GC-MS analysis and naphthoquinones derivatives were identified. Thereafter, the derivatives were investigated by molecular docking against mycobacterial target proteins including: Protein kinase G (PknG, PDB ID: 3CKQ), 4-diphosphocytidyl-2C-methyl-D-erythritol cytidyltransferase (IspD) and UDP-glucose-specific glycosyltransferase.

Results:

The docking results revealed that four Naphthoquinone compounds, 5-Hyroxy-1,4 Naphthoquinone, 2-Amino-3-chloro-1,4 Naphthoquinone and Coumarin-3-carboxylic acid exhibited binding affinities of −7.6, −8.2, −9.0, and −12.5 kcal mol^{-1} respectively, against protein kinase G, IspD and UDP-glucose-specific glycosyltransferase. Coumarin-3-carboxylic acid was a most promising candidate among the derivatives investigated achieved optimal binding stability and high inhibitory potential.

Conclusion:

The molecular docking analysis showed a significant antituberculosis potential of naphthoquinone derivatives found in henna leaves, particularly Coumarin-3-carboxylic acid as a promising lead for PknG inhibition. These findings provide a rationale for further biological validation and development of novel phytochemical-based therapeutics against drug-resistant TB. Further validating an *in vivo* activity of derivatives will be recommended.

Keywords: *Lawsonia inermis; GC-MS, Antimycobacterial, Naphthoquinone derivatives, Molecular Docking.*

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1. Introduction

Naphthoquinone derivatives found in *Lawsonia inermis* are recognized for their broad range of pharmacological properties, including potential applications in treating infectious and neoplastic diseases [1-2]. Naphthoquinones (NQs) represent a diverse class of phenolic compounds known for a spectrum of biological effects, such as antiviral, antibacterial, antiparasitic, anti-inflammatory, anticancer, and antifungal actions[3]. The antibacterial drug irrational use led to different microorganisms have emerged with enhanced resistance. Also, many of these drugs have shown potential adverse effects in humans. As global epidemic, *Mycobacterium tuberculosis* strains are emerged multi-drug-resistant threatening progress. *M. tuberculosis* is intrinsically resistant to many antibiotics, limiting the availability of effective treatment. Therefore, it has been a mounting in the efforts to discover or develop novel antimicrobial agents[4,5]. NQs unique chemical structure allows them to interact with biological molecules, and modifications can lead to more effective therapeutic agents. The continuing exploration of naphthoquinone derivatives for their biological and medicinal potential remains a vibrant area of research. Molecular docking serves as a computationally efficient approach for predicting how small molecules orient and interact within a protein's binding site, making it a valuable tool in structure-based drug discovery[6,7]. The *M. tuberculosis* PknG enzyme has been reported to mediate atypical ubiquitination processes that lead to the degradation of host signaling proteins such as TRAF2 and TAK1, consequently dampening innate immune defenses[8]. Therefore, targeting PknG is an important tool for development of a new effective drugs against *M. tuberculosis* resistant strains[9]. Given their diverse bioactivities, naphthoquinone derivatives represent promising structural templates for designing new agents effective against *Mycobacterium* species. This study aimed to evaluate antimycobacterial effect of naphthoquinone natural derivatives identified by GC-MS in Henna leaves against PknG enzyme by computational studies as anti-mycobacterium agents.

1. Methodology

2.1. Natural extract and chemicals:

L. inermis dried powdered leaves (50 g) were macerated with 500 mL methanol (1:10 w/v) for 72 h with occasional shaking and filtered. Extraction was repeated in triplicate and combined extracts were concentrated under reduced pressure to obtain a yield of 9.8% w/w. Lawsone (2-hydroxy-1,4-naphoquinone) and 5-hydroxy-1,4-naphthoquinone were purchased from Alfa Alesar (Ajaohnson Matthy company, USA). 2,3 dichloro-1,4-naphthoquinone, Squalene, 1,4 naphthoquinones were purchased from Sigma-Aldrich (product of Japan).

2.2. GC-MS analysis

GC-MS analysis of the prepared sample of natural extract of was carried out using a GC/MS (GC/MS-QP2010-Ultra) instrument model from the Japanese Shimadzu Company (serial number: 020525101565SA) and a capillary column (Rtx-5 ms-30 m × 0.25 mm × 0 25 µm). The sample (1 mg) of the extract was dissolved in 1 mL methanol then 1 µL was injected using a split mode (10:1). The helium, a carrier gas, was passed at a flow rate of 1.61 ml/min, and the temperature program started from 60 ˚C at a rate of 10 ˚C/min to 300 ˚C as a last temperature degree with a holding time of 5 minutes, the temperature of injection channel was a 300 ˚C, an ion source temperature was a 200 ˚C and an interface temperature was 250 ˚C. Mass spectral analysis of the extract was performed using a scan mode with a mass to charge a range of 40–500 m/z. Component identification was achieved by comparing their retention index and mass fragmentation models with those available in the library of the National Institute of Standards and Technology (NIST) mass spectral database with (>89%) matching percentage, Kovats retention index comparison, and confirmation using analytical standards for lawsone and 5-hydroxy-1,4-naphthoquinone. Semi-quantitative analysis was conducted using normalized peak area %, and lawsone represented 20.1% of the total ion chromatographic area. The results were recorded.

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2.3. Molecular Docking

Preparation of ligand compounds and target protein

Depending on the GC-MS analysis of *L. inermis* extract, the three-dimensional assembly of the five naphthoquinones were collected from the chemical entities of biological interest CheBI online database[10]. Subsequently, the ligands set have been prepared through *LigPrep* module of Schrödinger to standardize their chemical properties[11]. Three of vital mycobacterial enzymes crystal structures for *M. tuberculosis* Protein kinase G (PknG; PDB: 2PZI, chain A, 2.00 Å resolution), IspD (2-C-methyl-D-erythritol cytidylyltransferase; PDB: 2XWL, chain A, 2.30 Å resolution), and UDP-glucose-dependent glycosyltransferase (PDB: 3CKQ, chain A, 2.40 Å resolution) were downloaded from protein data Bank (PDB) online database. Co-crystallized small molecules and non-essential water molecules were removed, while catalytically relevant ions and conserved water in the binding pocket were retained. Protein structures were prepared using Schrödinger Protein Preparation Wizard (Maestro v13.4; OPLS4 force field) including: assignment of protonation states at pH 7.0 ± 0.5 using Epik, optimization of hydrogen bonding networks, addition of missing side chains and restrained minimization to 0.3 Å RMSD.

Protein-ligand docking

Ligands were obtained from PubChem and ChEBI and processed using LigPrep (pH 7.0 ± 0.5), generating possible tautomers and protonation states. Docking was performed with Glide Extra Precision (XP) mode. Docking was performed with Glide Extra Precision (XP) mode. A receptor grid was generated around the co-crystallized ligand binding site with a 20 × 20 × 20 Å grid box centered at the binding pocket centroid. Default van der Waals scaling (0.80) was applied for nonpolar atoms. Up to 10 poses per ligand were generated and ranked by XP GlideScore. The top-ranked pose was further rescored using Prime MM-GBSA (VSGB solvation model) to refine binding energy estimates. All simulations were performed on a Windows 10 workstation, Intel Core i7, 16 GB RAM. Up to 32 stereoisomers per compound were retained for docking. The targeted proteins data set contained: Protein kinase G enzyme that maintains the existence of the mycobacterium inside the host through it is interference with the host lysosomal defence mechanism[12]. UDP-Glucose specific glycosyltransferase which is an essential enzyme that participates in biosynthetic machineries of oligosaccharide and glycoconjugate sequences production of the mycobacterial cell wall[13]. IspD enzyme that mediate the alternative mevalonate synthesis pathway, and it is descending derivatives[14]. For IspD enzyme the binding pocket was not clearly defined so it has been predicted using *site map* module of Schrödinger[11]. Naphthoquinone derivatives have been tested against the three proteins using the theory of inverse docking through *glide extreprescion docking (XP)* module in Schrödinger against these enzymes[15].

Docking Validation

Docking validation was performed by re-docking the native co-crystallized ligands into the binding pockets of PknG, IspD, and UDP-glucose glycosyltransferase using the same Glide XP protocol. RMSD values between docked and experimental poses were **1.**42 Å (2PZI), 1.96 Å (2XWL), and 1.71 Å (3CKQ), confirming reliability of the docking model (acceptable threshold <2.0 Å).

2. Results and Discussion

2.1. GC-MS analysis

The results of GC-MS analysis for *L. inermis* showed the presence of lawsone and its derivatives as shown in in Table 1. The major natural derivatives identified, more than 20%, were, squalene, lawsone and coumarin carboxylic acid derivatives. Minor constituents identified about 5% were a γ-sitosterol, α-tocopherol and phytol. This GC-MS results were confirmed with previous study that identified the presence of fifty-one natural constituents in such plant including the naphthoquinone derivatives[16,17]. Retention index (RI) validation was supported by reference databases and literature values. Lawsone GC-MS has been previously detected in henna treated samples[18].

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Table 1: GC–MS identified compounds in *L. inermis* methanolic extract.

No	IUPAC Name	Retention Time (Min)	Molecular Weight (g/mol)	Molecular Formula	Peak Area (%)
1	2-Hydroxy-1,4-naphthalenedione (Lawsone)	12.707	174	$C_{10}H_6O_3$	20.185
2	2H-1-Benzopyran-3-carboxylic acid, 2-oxo-, methyl ester **(Coumarin-3-carboxylic acid, methyl ester)**	14.647	204	$C_{11}H_8O_4$	5.131
3	3,7,11,15-Tetramethyl-2-hexadecen-1-ol **(Phytol)**	16.049	296	$C_{20}H_{40}O$	4.991
4	Coumarin-4-carboxylic acid, methyl ester	16.606	204	$C_{11}H_8O_4$	23.328
5	2,6,10,14,18,22-Tetracosahexaene, 2,6,10,15,19,23-hexamethyl-, (all-E)-(**Squalene)**	29.611	410	$C_{30}H_{50}$	34.433
6	**dl-α-Tocopherol**	33.592	430	$C_{29}H_{50}O_2$	5.985
7	**γ-Sitosterol**	35.922	414	$C_{29}H_{50}O$	5.947

2.2. Molecular Docking

Molecular docking is a key computational perspective for identifying the binding affinity of a ligand or compound and a target or receptor[19]. This method provides admired insights for derivatives interactions with a target and affect bacterial cellular processes. In this study, the antimycobacterial of naphthoquinone derivatives through molecular simulation has showed great perceptions for their chemical reactivity and stability. Naphthoquinone, 5-Hydroxy-1,4-naphthoquinone, 2-Amino-3-chloro-1,4-naphthoquinone and Coumarin-3-carboxylic acid have shown considerable interactions with Protein kinase G enzyme with docking scores less than (-6.0) as shown in Table 2. The three former compounds interact through H-bond formation with valine 235 residue of the binding pocket while Coumarin-3-carboxylic acid interact with residue Lys 181 and GLU 280 in the presence of water (Figure 1).

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Table 2: Docking scores and binding free energies of selected ligands.

	3CKQ	2XWL	2PZI
	Docking scores (kcal·mol^{-1})	*Docking scores (kcal·mol^{-1})*	*Docking scores (kcal·mol^{-1})*
Naphthoquinone	-4.468	-3.431	**-7.571**
2-Hydroxy-1,4-naphthalenedione (Lawsone)	-5.596	**-6.025**	-5.295
5-Hydroxy-1,4-naphthoquinone	-4.468	**-6.438**	**-8.224**
2-Amino-3-chloro-1,4-naphthoquinone	-4.514	-3.355	**-7.950**
Coumarin-3-carboxylic acid	**-6.278**	**-12.501**	-6.927

3CKQ: UDP-glucose-specific glycosyltransferase (UGT), 2XWL: IspD enzyme, 2PZI, Protein kinase G (PknG)

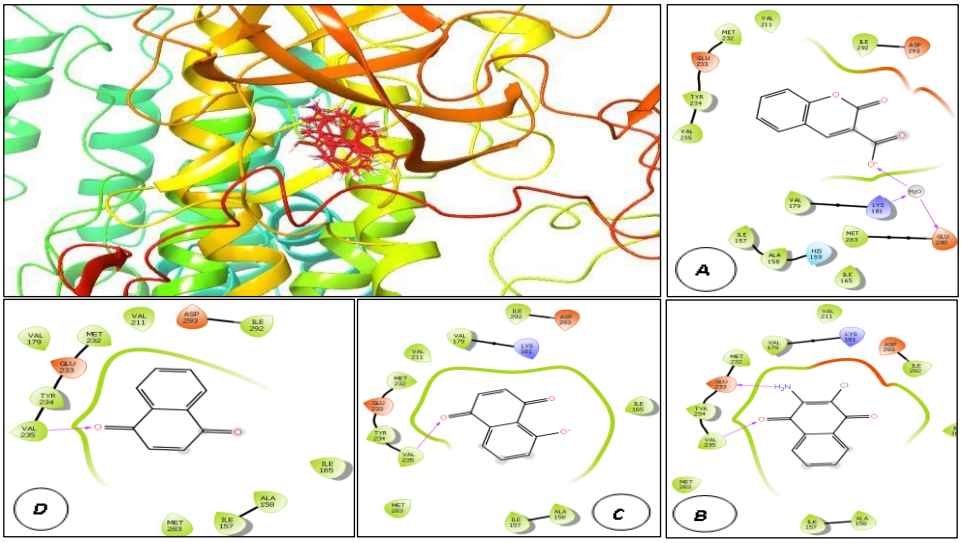

Figure 1: The interactions between naphthoquinones and Protein kinase G (pdb ID: 2PZI). A: Shows Coumarin-3-carboxylic acid interactions, B: represents 2-Amino-3-chloro-1,4 Naphthoquinone, C: 5-Hydroxy-1,4-naphthoquinone interaction, D: highlights the parent Naphthoquinone interaction with 2PZI.

Coumarin-3-carboxylic acid exerted the best interaction in comparison with the total set with docking score **-12.501** when tested against IspD enzyme**.** 2-Hydroxy-1,4-naphthalenedione and 5-Hydroxy-1,4-naphthoquinone also exhibited mild interaction with this target in their ionic state (Figure 2). Coumarin-3-carboxylic acid demonstrated a stronger predicted interaction with PknG (−12.5 kcal·mol^{-1}) than the positive reference inhibitor (−13.2 kcal·mol^{-1}), indicating potential inhibitory relevance within the validated scoring threshold.

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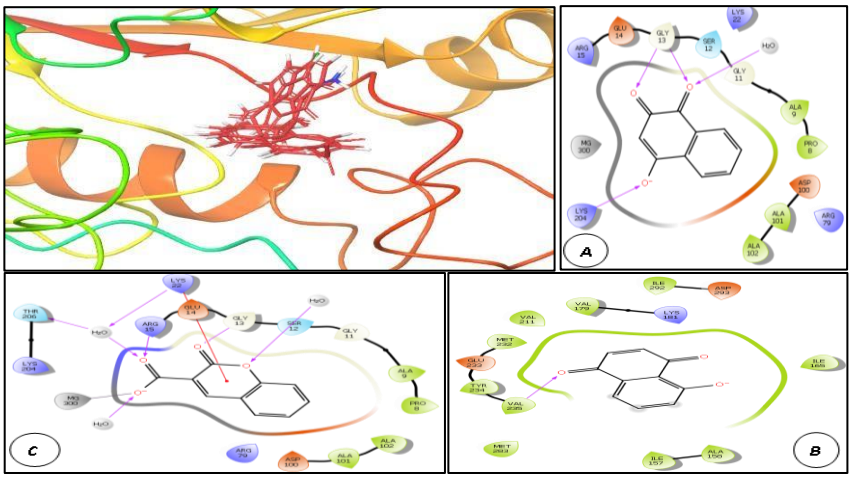

Figure 2*: The predicted interactions from XP docking of Naphthoquinones data set with IspD enzyme (pdb ID:2XWI). **A**: Interaction of 2-Hydroxy-1,4-naphthalenedione. B: Interaction of 5-Hydroxy-1,4-naphthoquinone. C: Shows the interactions Coumarin-3-carboxylic acid.*

In docking of naphthoquinone versus UDP-glucose-specific glycosyltransferase, coumarin-3-carboxylic acid showed better interaction with respect to the rest compounds as shown in Figure 3. These findings are in accordance with the results which were indicated that naphthoquinone derivatives have effects on many clinical drug resistant bacterial stains[20,21].

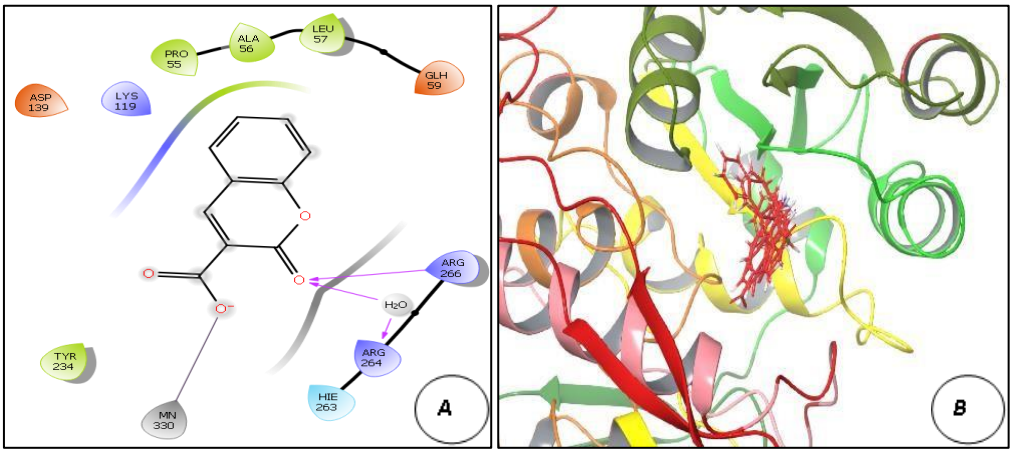

Figure 3: *A: Illustration of the interaction between Coumarin-3-carboxylic acid and UDP-glucose-specific glycosyltransferase (pdb ID:3CKQ). B: shows the different docking poses for naphthoquinone library with UDP-glucose-specific glycosyltransferase enzyme.*

3. Conclusion

This study concluded that computational study of natural naphthoquinone derivatives identified in *L. inermis* was recognised their medicinal value as antibacterial agents, emphasizing on their interactions with mycobacterium protein kinase G enzyme. The molecular docking study revealed a significant binding affinity of five naphthoquinone derivatives target protein. This underscores Coumarin-3-carboxylic acid exerted the most power interaction. All derivatives suit considerable drug-basis interaction, exhibiting antituberculosis via computational assessments. This study predicts favourable binding interactions between naphthoquinone derivatives identified from *L.*

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inermis and key *M. tuberculosis* target enzymes. These findings provide a hypothesis-generating basis for future experimental evaluation. Further in vitro and in vivo validation is required to confirm their potential antimycobacterial effects.

Abbreviations and Acronyms

NQs: Naphthoquinones.

PDB: Protein data Bank.

PknG or 2PZI: Protein kinase G.

TRAF2: Tumor necrosis factor receptor-associated factor 2.

TAK1: TGF-β-activated kinase 1.

GC-MS: Gas Chromatography–Mass Spectrometry.

NIST: National Institute of Standards and Technology.

CheBI: Chemical Entities of Biological Interest.

IspD or 2XWL: 2-C-Methyl-D-erythritol-4-phosphate cytidyltransferase.

XP: glide extreprescion docking.

3CKQ: UDP-Glucose specific glycosyltransferase.

RI: Retention index

ETHICAL STATEMENT

Not Applicable

CONFLICT OF INTEREST

No conflict of interest.

AUTHORS' CONTRIBUTIONS

All authors contributed equally, Anwar M. Abdelrahman carried out extraction and compound identification; Mohammed A. Almogaddam performed the molecular docking, Abdelgadir A. Abdelgadir carried out data analysis and wrote the manuscript draft. All authors approved the final version.

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Fresh Frozen Plasma Quality Control at the Al Marj Central Blood Bank, Libya

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A B S T R A C T

Background:

Fresh frozen plasma (FFP) is a vital blood component used to treat coagulation disorders, and ensuring its quality is essential to prevent transfusion-related complications.

Objectives:

This study aimed to evaluate the quality of FFP prepared at the Al Marj Central Blood Bank, Libya, and to compare the findings with the international standards established by the American Association of Blood Banks (AABB).

Methods:

A cross-sectional study was conducted on 100 FFP bags. Each unit was analyzed for volume, pH, prothrombin time (PT), partial thromboplastin time (PTT), and residual cell counts after thawing, according to AABB procedures.

Results:

The mean FFP volume (193 ± 28 ml) was significantly below the AABB standard of 200–400 ml ($p < 0.001$). The mean pH (6.9 ± 0.45) and PT (13.7 ± 1.43 s) were within acceptable limits, while the mean PTT (35.6 ± 2.04 s) was slightly above the upper limit of the standard range (25–35 s), suggesting borderline prolongation. Importantly, the mean platelet count (31.1 ± 38.4 $\times 10^9$/L) exceeded the AABB limit (<5$\times 10^9$/L).

Conclusion:

Although most parameters met AABB standards, the FFP units demonstrated reduced volume and elevated platelet counts, indicating possible inefficiencies in centrifugation and plasma separation processes. Optimization of preparation procedures is recommended to enhance FFP quality and ensure compliance with international standards.

Keywords: *Fresh Frozen Plasma, AABB standards, Quality control, Platelet residues, Libya, Blood component quality.*

1. Introduction

Ensuring the safety and quality of blood products is a fundamental objective of transfusion medicine. The primary goal of blood transfusion services is to maintain an adequate supply of high-quality blood components that provide maximum therapeutic benefit with minimal risk to patients and donors. A failure in the quality of collected or screened blood units can lead to catastrophic and potentially fatal outcomes. Therefore, a comprehensive quality management system must integrate good manufacturing, medical, and laboratory practices, all of which are interrelated and essential to guarantee patient safety and product reliability **[1, 7]**.

FFP is a blood component obtained from whole blood by high-speed centrifugation and rapidly frozen to preserve labile coagulation factors. It is typically prepared from triple or quadruple plastic blood bags and stored at –25 °C or lower to maintain stability. FFP contains all coagulation factors (except platelets), including both labile and stable factors, as well as albumin, fibrinogen, antithrombin, protein C, protein S, tissue factor pathway inhibitor, fibrinolytic and complement proteins **[2, 3]**. Clinically, FFP is widely used to treat coagulation factor deficiencies, liver disease, disseminated intravascular coagulation (DIC), and to reverse the effects of vitamin K antagonists **[4]**.

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The quality of FFP is critical for ensuring patient safety and effective transfusion outcomes. According to international quality principles, FFP should remain free from contamination by other blood elements, including red blood cells (RBCs) and white blood cells (WBCs), and should not show any leakage, clot formation, or discoloration **[5]**. The presence of residual cellular elements, particularly RBCs, may lead to alloimmunization, while elevated residual platelet counts—a frequent issue in FFP production—may increase the risk of transfusion-related acute lung injury (TRALI) and allergic or inflammatory reactions in recipients. These potential hazards underscore the importance of strict adherence to quality standards during plasma processing.

To address these risks, the American Association of Blood Banks (AABB) has established international standards defining acceptable ranges for FFP characteristics, including volume, pH, prothrombin time (PT), partial thromboplastin time (PTT), and residual cellular content. These parameters are used globally to monitor production consistency and ensure that each plasma unit meets clinical safety requirements **[6]**.

While these international standards and best practices are well established, local data on FFP quality in Libya remain limited. Published studies assessing the compliance of locally prepared plasma with AABB quality benchmarks are scarce, leaving a gap in regional transfusion quality monitoring.

Accordingly, the aim of the current study was to assess the quality of FFP produced at the Al Marj Central Blood Bank, Libya, and to compare the results with the international quality standards set by the AABB.

2. Materials and methods

A cross-sectional study was conducted on 100 FFP units collected at the Al Marj Central Blood Bank, Libya. Each FFP unit was prepared from fresh whole blood (450 ± 50 ml) collected in triple bags containing 63 ml of *Citrate Phosphate Dextrose Adenine-1 (CPDA-1)* anticoagulant. All collected units were screened and confirmed negative for Hepatitis B virus (HBV), Hepatitis C virus (HCV), and Human Immunodeficiency Virus (HIV) prior to processing.

Plasma Separation

Plasma was separated by centrifugation for 14 minutes at approximately 2900 × g (equivalent to 4158 rpm), producing PPP. The separated plasma was immediately frozen at –22°C or lower to preserve the stability of coagulation factors.

FFP Thawing Procedure

In accordance with the AABB guidelines, all FFP units were thawed before testing using the following standardized procedure:

1. Verify the unit identity against the transfusion request.
2. Confirm proper storage conditions, including temperature and expiration date.
3. Submerge the FFP bag in a water bath maintained between 30°C and 37°C for 15–30 minutes.
4. Ensure complete thawing and gentle mixing of the plasma within the bag.
5. Visually inspect the plasma for acceptable color and odor prior to testing.

Testing and Analysis

All quality control tests were performed on samples taken after the FFP units were fully thawed.

The volume of each FFP unit was measured directly.

From each unit, 5 ml of plasma was collected and divided into two plain containers:

One portion was used for counting residual cells (RBCs, WBCs, and platelets) using a *Nihon Kohden hematology analyzer*.

The second portion was used to determine PT and PTT using the *Technoclon (TC) kit* and a *Dia Lab Coagulometer Analyzer™*.

The pH of each plasma unit was measured using a calibrated pH meter.

Data Analysis

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All data were analyzed using SPSS software (version 27). Results were compared with AABB international reference standards using a one-sample t-test with 95% confidence intervals (CI). Statistical significance was set at $p < 0.05$.

3. Results

A total of 100 FFP units collected from the Al Marj Central Blood Bank, Libya, were analyzed. The evaluated parameters included total plasma volume, pH, PT, PTT, and residual cell counts (RBCs, WBCs, and platelets) to assess compliance with AABB quality standards.

1. Volume and pH

The mean FFP volume (193 ± 28 ml) was significantly lower than the AABB reference range (200–400 ml, $p < 0.001$). The mean pH (6.9 ± 0.45) showed no statistically significant difference from the acceptable range (7.0–7.4, $p = 0.123$).

These results indicate a notable reduction in plasma volume, while pH levels remained within acceptable limits.

(Table 1)

Table 1. Volume and pH levels of fresh frozen plasma units compared with AABB standards

Parameter	AABB Reference Range*	Measured Values (Mean ± SD)	Range	p-value
Volume (ml)	200–400	193 ± 28	135–208	< 0.001
pH	7.0–7.4	6.9 ± 0.45	6.0–7.5	0.123

* According to AABB guidelines.

2. Coagulation Profiles (PT and PTT)

The mean PT (13.7 ± 1.43 s) was within the acceptable range (11–15 s, $p = 0.46$).

Although PTT (35.6 ± 2.04 s) showed no statistically significant difference ($p = 0.67$), its mean value was slightly above the upper limit (25–35 s), suggesting a potential borderline prolongation that may be clinically relevant.

(Table 2)

Table 2. Coagulation profiles of fresh frozen plasma units compared with AABB standards

Parameter	AABB Reference Range*	Measured Values (Mean ± SD)	Range	p-value
PT (s)	11–15	13.7 ± 1.43	12–16	0.46
PTT (s)	25–35	35.6 ± 2.04	30–40	0.67

* According to AABB guidelines.

3. Residual Cellular Content

The mean RBC and WBC counts were within AABB standards and showed no statistically significant difference ($p > 0.05$).

However, the platelet count was markedly elevated compared with the AABB limit, indicating incomplete removal of platelets during centrifugation.

Given that WBC and platelet counts displayed non-normal distributions (with large variability and skewed data), results for these parameters were reanalyzed using median and interquartile range (IQR), and the Wilcoxon signed-rank test was applied instead of the *t*-test.

Table 3. Residual cellular content of fresh frozen plasma units compared with AABB standards (median and IQR used for non-normal data)

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Cell Type	AABB Reference Range*	Measured Values	Range	Statistical Test	p-value
RBCs (×10⁶/unit)	< 0.1	0.006 (0.00–0.02)	0.00–0.20	One-sample *t*-test	0.778
WBCs (×10⁶/unit)	< 0.1	0.05 (0.01–0.32) †	0.01–29	Wilcoxon signed-rank	0.212
Platelets (×10⁹/unit)	< 5	18.0 (6.0–52.0) †	0.00–175	Wilcoxon signed-rank	< 0.001

* According to AABB guidelines.
† Reported as median (IQR) due to non-normal data distribution.

4. Discussion

The present study evaluated the quality of FFP produced at the Al Marj Central Blood Bank, Libya, by comparing key physical and biochemical parameters with the international quality standards established by the American Association of Blood Banks (AABB). The findings revealed that while most parameters—including pH, PT, RBCs, and WBCs—were within the acceptable range, the mean plasma volume (193 ± 28 ml) was significantly lower than the AABB reference (200–400 ml). The mean PTT (35.6 ± 2.04 s) was slightly above the upper limit of the standard range, indicating a borderline prolongation, whereas the median platelet count (18 × 10⁹/unit) was markedly elevated compared with the AABB threshold (<5 × 10⁹/unit).

Plasma Volume and Coagulation Parameters

The reduced FFP volume observed in this study contradicts findings from previous reports by Uwamungu et al. (2014) [10] and Gunjan Bala et al. (2019) [11], where FFP volumes were consistent with international standards. Several operational factors may account for this discrepancy. The collection volume of whole blood (450 ± 50 ml) may not have been precisely standardized, or the expression of plasma into the satellite bag may have been incomplete, leading to suboptimal plasma yield. Additionally, minor evaporation losses or improper sealing during freezing could contribute to the reduced volume.

The measured pH values (6.9 ± 0.45) were consistent with AABB recommendations and with earlier studies (Uwamungu et al., 2014 [10]; Pták et al., 2000 [12]), confirming the adequacy of storage and freezing conditions. The mean PT (13.7 ± 1.43 s) was within the expected range, reflecting proper preservation of stable coagulation factors [6]. However, the PTT (35.6 ± 2.04 s), although not statistically different from AABB standards, exceeded the upper limit clinically, suggesting a possible borderline prolongation. This mild prolongation could indicate partial loss or instability of labile coagulation factors, particularly Factor VIII, during freezing or thawing, which may slightly reduce the hemostatic efficacy of transfused plasma.

Platelet Contamination and Centrifugation Efficiency

The most critical finding in this study was the significantly elevated residual platelet count, with a median value of 18 × 10⁹/unit, well above the AABB standard of <5 × 10⁹/unit. This clearly indicates a methodological issue in plasma preparation. The current centrifugation protocol approximately 2900 × g for 14 minutes appears insufficient to produce platelet-poor plasma (PPP) as required by AABB specifications [13]. Incomplete platelet removal during centrifugation can lead to higher residual counts in the plasma fraction.

From a clinical perspective, such elevated platelet levels in transfused FFP may increase the risk of transfusion-related acute lung injury (TRALI), allergic reactions, and inflammatory complications. These findings underscore the need for a review and optimization of the centrifugation process, possibly by increasing the relative centrifugal force or extending centrifugation time to ensure more efficient separation of plasma from platelets.

Limitations

This study has several limitations. It was conducted at a single blood bank, which may limit the generalizability of the results. The sample size (n=100), while adequate for initial evaluation, may not fully capture inter-batch variability in FFP production. In addition, some parameters—such as PT and PTT—showed wide variability that could mask subtle differences due to the use of parametric statistical tests.

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Future studies should include larger sample sizes and biochemical analyses of specific coagulation factors (e.g., Factor VIII and fibrinogen) to provide a more comprehensive assessment of plasma quality.

5. Conclusion

This study assessed the quality of FFP prepared at the Al Marj Central Blood Bank, Libya, in comparison with international standards set by the AABB. The findings demonstrated that most parameters—pH, PT, RBCs, and WBCs—were within the acceptable limits, reflecting satisfactory control of basic production and storage conditions.

However, two significant quality deviations were identified:

The mean plasma volume (193 ± 28 ml) was significantly below the AABB standard (200–400 ml).

The median residual platelet count (18 × 10^9/unit) was markedly higher than the recommended limit (<5 × 10^9/unit).

Additionally, the PTT value (35.6 ± 2.04 s) was slightly above the upper reference range, indicating a possible borderline prolongation that may be linked to minor degradation of labile coagulation factors during processing.

These results indicate that, although the overall FFP quality is acceptable, the centrifugation and plasma separation procedures require optimization to meet international standards consistently and ensure patient safety.

Practical Recommendations

Optimize Centrifugation Protocol:

Increase the relative centrifugal force (RCF) and/or extend centrifugation time beyond 14 minutes to achieve more effective platelet separation and ensure the production of platelet-poor plasma (PPP).

Standardize Blood Collection Volume:

Ensure that all whole blood donations consistently meet the target volume (450 ± 50 ml) to maintain adequate FFP yield.

Enhance Staff Training:

Provide periodic technical training for laboratory and transfusion staff on plasma preparation, separation, and freezing procedures according to AABB guidelines.

Implement Continuous Quality Control:

Conduct routine internal audits and quality checks for FFP units, focusing on volume, platelet contamination, and coagulation parameters to detect process deviations early.

Review Equipment Calibration and Maintenance:

Regularly verify the calibration of centrifuges, coagulometers, and pH meters to ensure consistent accuracy in analytical and preparation steps.

Future Research:

Future studies should include multi-center evaluations across Libyan blood banks and incorporate biochemical assays of coagulation factors (e.g., Factor VIII, fibrinogen) to provide a more comprehensive understanding of FFP quality.

ETHICAL STATEMENT

Not Applicable

CONFLICT OF INTEREST

No conflict of interest.

AUTHORS' CONTRIBUTIONS

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Assessment of prescription pattern and prescription errors at primary healthcare centres in Alkhoms city, northwestern Libya

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ABSTRACT

Background: The medical prescription is a handwritten or electronically computerised legal document. It must include all the required information and adhere to the prescription writing guidelines to be considered valid. In Libya, many of the previous studies reported that the majority of prescriptions are handwritten and contain medication errors that arise due to the high omission of legal or procedural requirements in the medical prescriptions by the majority of physicians. Consequently, the present study is designed to help in understanding the medical prescription practices and errors, which will lead to developing the healthcare system in Libya.

Objectives: This study aimed to evaluate the prescription patterns and prescription errors in outpatient prescriptions issued by physicians working in primary healthcare centres in Alkhoms city, northwestern Libya

Methods: A comprehensive analytical study was carried out to evaluate the outpatient prescription patterns and errors. A total of 405 outpatient prescriptions issued by physicians and specialists working in various primary healthcare centres in Alkhoms city and its suburbs in northwestern Libya were collected from several pharmacies and assessed. The study lasted three months.

Results: A total of 405 prescriptions containing 1852 drugs were reviewed in this study. The handwritten percentage prescriptions and computer-typed percentage prescriptions were 98.52% and 1.48%, respectively. The average number of drugs per prescription was 4.57. Most of the physicians prescribed drugs using their brand names (96.06%). The name of the patient was not mentioned on 5.18% of the prescriptions, whereas the prescriber's name was not found on 80.25% of the total prescriptions. The outcomes of the present study also displayed that the information related to the patient was usually available; in contrast, some important information related to the drugs was ignored in most of the prescriptions, including the route of drug administration (71.12%). Half of the examined prescriptions were approximately lacked information about the diagnosis (48.40%), and 29.62% of the prescriptions lacked the date of the prescription.

Conclusions: The present study shows a low level of commitment to World Health Organization (WHO) guidelines related to prescribing indicators and high prescription errors. Moreover, according to the findings of this study, we recommend introducing the use of electronic prescriptions throughout the healthcare system in Libya. This will lead to updating the prescription form to include all the elements recommended by the WHO in the prescription guidelines.

Keywords: *Prescription patterns; pharmacists; Prescription errors; Primary healthcare, Libya; WHO prescribing indicators*

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1. Introduction

Improving drug therapy is an essential part of the health care system to optimize a patient's quality of life. Drugs play a vital role in the enhancement of a good health status for patients. Generally, prescribing a medication is a complex process, and thus, the drug should be prescribed carefully and used in the right way. The complexity of the process lies in the knowledge of drug indications, determining the appropriate dose and its frequency, defining the suitable route of drug administration and dosage form for use, educating the patient about expected side effects, and monitoring for effectiveness and toxicity. In addition, selecting the drug of choice, avoiding the drug-drug interactions, and finally, considering the background of the cost and availability of drugs in pharmacies [1]. Incorrect use of medicine in addition to its direct impact on patient life and safety, it wastes resources and reduces the quality of patient care. Most of the drugs in the essential medicines list are safe, efficacious, and affordable, and thus the access and rational use of these drugs is the best way to improve the level of primary health care in communities [2].

The prescription is a handwritten or electronically computerised legal document, comprising instructions for medication authorization from a qualified healthcare provider licensed to the pharmacist, such as a physician or dentist. The medical prescription must include specific vital components to be considered valid. These components include registration number, the date of issue, the patient's name, date of birth, sex, and address; moreover, it should be contained on the specific treatments prescribed involving the drug's name, strength, dosage form, and route of administration, and finally, the name and signature of the prescriber [1,3]. Prescription errors are a failure in the prescription writing process, leading to incorrect descriptions about the formulation, dosage form, therapeutic dose, frequency of the dose, route, and duration of administration of the described drug, as well as the identity of the recipient. Therefore, a prescribing fault can arise due to the high missing of legal or procedural requirements in the medical prescriptions, such as the choice of the wrong drug, wrong strength of the dose, wrong dosage form, wrong route of administration, and drug-drug interactions which outcomes in several drug related problems, such as, insufficient dose, over-dose, drug interactions, drug allergy, and non-compliance [4]. In contrast, poor legibility of handwriting prescriptions, which is represented in the use of abbreviations or incomplete writing of prescriptions, can also lead to misinterpretation by healthcare personnel, and this can result in errors in drug dispensing and administration [5]. Consequently, the present study is designed to help in understanding the medical prescription practices and errors, which will lead to developing the healthcare system in Libya.

2. Methods

Study design and data collection, and analysis

The present study was designed to evaluate the outpatient prescription patterns and prescription errors, which were issued by various healthcare centres in Alkhoms city, northwestern Libya. The study was conducted over three months and used the random sampling method, in which outpatient prescriptions were included, whereas the prescriptions of discharged patients and admitted patients were excluded. In this work, 405 official prescriptions were collected and analyzed. The information from these prescriptions was recorded separately for each prescription, and then analysed using Microsoft Office Excel 2013. The results of this study were expressed in the form of numbers, average, and percentage according to prescribing indicators adopted from previous studies (3,6-8), which were based on the WHO guidelines. These indicators with their optimal values include; the average number of drugs prescribed per prescription (1.6–1.8), the percentage of drugs prescribed by generic name (100%), the percentage of prescription where an injection was the route of administration (13.4– 24.1%), the percentage of prescriptions compromising an antibiotic (20.0– 26.8%), and the percentage of drugs prescribed from the Essential Drugs List (EDL) (100%). Furthermore, the prescription errors are mainly classified as omission errors related to drugs (including drug dosage form,

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dose, frequency, and route of administration) and omission errors related to the prescriber (including patient name, age, and gender, prescriber name, and signature).

3. Results

A total of 405 prescriptions containing 1852 drugs were evaluated in this study. The resulting data corresponding to the prescribing indicators is summarized in Table 1.

Table 1. Prescribing indicators (n= 405 prescriptions with 1852 drugs)

Prescribing indicator assessed	Total drugs/prescriptions	Average/ percentage
The percentage of handwritten prescriptions	399	98.52%
The percentage of computer-typed prescriptions	6	1.48%
The number of drugs per prescription	1852	4.57
Percentage of drugs prescribed by generic name	73	3.95%
Percentage of drugs prescribed by brand name	1779	96.05%
The percentage of prescriptions with antibiotics	132	32.59%
The percentage of prescriptions with injection	45	11.11%

Additionally, the results of the current study displayed a variety of prescribing errors related to prescriber, patient, and drug due to missing optimum prescription details specified in the WHO guidelines, as shown in Table 2.

Table 2. Prescribing errors: omission errors related to prescriber, patient, and drug (*n*= 405)

Types of information	Missing (*n*)	Missing (%)
Prescriber information		
The name of the prescriber	325	80.25%
The communication way with the prescriber	405	100%
The signature of the prescriber	81	20%
Patient information		
Name	21	5.19%
Age	69	17.04%
Gender	53	13.09%
Address	405	100%
Drug information		
Dosage form	38	8.64%
Therapeutic dose	32	7.90%
Frequency of dose	24	5.92%
Route of drug administration	288	71.12%
Others		
Diagnosis	196	48.40%
Prescription date	120	29.63%

4. Discussion

A total of 405 drug prescriptions were collected and reviewed in this study. On the basis of WHO guidelines, none of these prescriptions contained all the requirements of the typical prescription. Only six prescriptions were computer-typed. The percentage of handwritten prescriptions and computer-typed prescriptions was 98.52% and 1.48%, respectively. These prescriptions comprise a total of 1852 drugs. The average number of drugs per prescription was 4.57. This value is higher than the WHO-recommended optimum level of (1.6-1.8); however, it's similar to the reported value in the previous study conducted in Libya by (*Ahmed Atia, et al, 2022*) (8). The percentage of drugs prescribed by generic name was very low (3.95%), since most doctors prefer to use the brand name when prescribing medications. Nevertheless, these findings are compatible with *Emira Bousoik et al (2023)* previous study. Out of 405 prescriptions were reviewed, 132 of

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them had at least one antibiotic prescription (Table 1), resulting in an overall percentage of prescriptions with antibiotics of 32.59%; however, the finding was close to the WHO recommendation and similar to outcomes of the previous study conducted in Libya by (*Ahmed Atia, et al, 2022*) (12). Moreover, a percentage of 11.11% of prescriptions contain injections. This percentage value is consistent with the WHO guidelines and slightly lower than the previously reported value in Libya (*El Yamani M.A., et al, 2021*) (9), and also in Nepal (Shrestha and Prajapati, 2019) (3). Additionally, the results of the current study also displayed a variety of prescribing errors related to prescriber, patient, and drug, as shown in Table 2. This is a significant variation arising from missing the optimum prescription details specified in the WHO guidelines. The prescriber's name was mentioned on 19.75% of the prescriptions, and in contrast, only 20% of doctors did not sign their prescriptions. Notably, all of the prescriptions lacked communication with the prescriber. These results were almost identical to the results of previous studies (Shrestha and Prajapati, 2019; Emira Bousoik, 2023) (3,10). In the present study, although some of the patients' names were not fully written in the reviewed prescriptions, 94.82% of prescriptions contained the patient's name. The age of the patient was presented in 82.96% of the prescriptions. According to the WHO guidelines, the patient's address is an essential element that should exist in prescriptions. Remarkably, in this study, all of the prescriptions lacked the patient's address. This finding is similar to most of the previous studies (10). Finally, writing down the diagnosis is an essential element of the prescription, as it may help pharmacists to understand the correct drug when the handwriting is not clearly readable. The outcomes of the current study indicate that half of the prescriptions fail to specify the diagnosis. Furthermore, the date of prescription is a very important part as it helps patients know the start and end dates of treatment and also when to follow up with the doctor. In the present study, the date was absent only in 29.63% of the prescriptions, and these results were better than the results obtained by *Alhmmali Abdalla et al (2024)* (11), who found that the date error was 53%.

5. Conclusion and recommendation

The study shows a low level of commitment to WHO guidelines related to prescribing indicators and high prescription errors. Prescribing using handwritten, brand names, and a high number of drugs per prescription was a major problem. The study found that major errors in the prescriber were the name of the prescriber and the communication method with them.

In the present study, researchers recommend introducing the use of electronic prescriptions throughout the healthcare system in Libya, and updating the prescription form to include all requirements by the WHO.

ETHICS STATEMENT

Not Applicable

AUTHORS' CONTRIBUTIONS

MA: Conceptualization; study design; lead investigator; data curation; supervision of fieldwork; writing — original draft; corresponding author and guarantor.

ME: Methodology; data collection and verification; formal analysis; preparation of tables; writing, review, and editing.

NB: Resources support, critical revision for important intellectual content, supervision and mentoring, and final manuscript approval.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Effect of Crude Ethanolic Extract of Mangosteen Pericarp (*Garcinia mangostana Linn.*): A Comprehensive Narrative Review

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ABSTRACT

Objective: This comprehensive narrative review aims to consolidate and critically evaluate the existing scientific literature on the biological effects and pharmacological potential of the crude ethanolic extract of mangosteen pericarp (CEMP). **Methods:** A systematic literature search was conducted in PubMed, Scopus, and Google Scholar for articles published from database inception to March 31, 2024. Search terms included "*Garcinia mangostana*", mangosteen, pericarp, "crude extract", "ethanolic extract", and key pharmacological activities. **Results:** The findings reveal that CEMP is rich in bioactive xanthones, particularly α-mangostin, and exhibits a wide spectrum of potent pharmacological activities. These include antioxidant, anti-inflammatory, antimicrobial, anticancer, antidiabetic, and neuroprotective effects, primarily demonstrated in *in vitro* and *in vivo* studies. The mechanisms are largely attributed to the modulation of key signaling pathways, such as NF-κB and MAPK. **Conclusion:** Preclinical evidence strongly supports the multifaceted bioactivity of CEMP. However, clinical research is scarce. Translation to human therapeutics requires standardized extracts, detailed pharmacokinetic and drug interaction studies, and robust clinical trials to establish safety and efficacy.

Keywords: *Garcinia mangostana*, Xanthones, alpha-mangostin, Ethnopharmacology, Biological Activities, Natural Products.

1. Introduction

The search for novel therapeutic agents from natural products has gained immense momentum in recent decades, driven by their historical efficacy, structural diversity, and often favorable toxicity profiles compared to synthetic drugs [1]. Among these, *Garcinia mangostana* Linn. (Family Clusiaceae), commonly referred to as the mangosteen, has emerged as a subject of significant scientific interest. Traditionally dubbed the "queen of fruits," its dark purple pericarp (rind) has been a cornerstone in Southeast Asian folk medicine for centuries, used to treat skin infections, wounds, diarrhea, and various inflammatory conditions [2]. The crude ethanolic extract of mangosteen pericarp (CEMP) is particularly valued as it effectively solubilizes a wide range of both polar and non-polar bioactive compounds, primarily xanthones. α-Mangostin, a prenylated xanthone, is the most abundant and studied compound within CEMP, often serving as a marker for standardization

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[3]. Modern pharmacological investigations have unveiled a plethora of biological activities associated with CEMP, positioning it as a promising candidate for drug development. However, the existing literature is vast yet fragmented. Therefore, this comprehensive narrative review aims to systematically compile, summarize, and critically appraise the current knowledge on the extraction, phytochemistry, pharmacological effects, and toxicological profile of CEMP, thereby identifying research gaps and future directions for its potential application in modern medicine.

2. Review Methodology

This review was conducted as a comprehensive narrative synthesis. A systematic literature search was performed to identify all relevant English-language studies on the biological effects of CEMP. Electronic databases, including PubMed, Scopus, and Google Scholar, were searched from their inception until March 31, 2024.

The search strategy utilized a combination of keywords and Boolean operators: ("Garcinia mangostana" OR mangosteen) AND (pericarp OR rind) AND ("crude extract" OR "ethanolic extract") AND (pharmacology OR "biological activity" OR antioxidant OR anti-inflammatory OR antimicrobial OR anticancer OR antidiabetic OR neuroprotective).

Articles were included if they were original research studies or reviews published in English that focused on the crude or ethanolic extract of mangosteen pericarp. Studies focusing solely on isolated compounds (e.g., pure α-mangostin) without reference to the crude extract, or those not available in English, were excluded. The reference lists of retrieved articles were also screened for additional relevant publications. The data from selected studies were extracted and synthesized thematically to provide a comprehensive overview of CEMP's pharmacological profile.

Limitations of the methodology: This review may be subject to publication bias, as it relied primarily on published literature in English. Grey literature and non-English publications were not systematically searched.

3. Phytochemistry and Extraction

3.1. Bioactive Compounds

The mangosteen pericarp is a rich reservoir of secondary metabolites. The most therapeutically relevant compounds are xanthones, with over 50 different types identified. The crude extract predominantly contains α-mangostin, γ-mangostin, garcinone C, garcinone D, and gartanin [4]. Besides xanthones, CEMP also contains other beneficial compounds like flavonoids, tannins, anthocyanins, and phenolic acids, which contribute synergistically to its overall antioxidant capacity [5].

3.2. Extraction Efficiency

The ethanolic extraction method is preferred for preparing CEMP due to ethanol's efficiency in extracting a broad spectrum of xanthones and its status as a generally recognized as safe (GRAS) solvent. Studies have optimized extraction variables—including ethanol concentration, extraction time, temperature, and solvent-to-material ratio—to maximize the yield of total phenolics, flavonoids, and specifically α-mangostin [6]. Maceration and Soxhlet extraction are commonly used, though advanced techniques like ultrasound-assisted extraction have been shown to improve yield and reduce extraction time significantly.

3. Pharmacological Activities

Table 1 summarizes Key Pharmacological Activities of Crude Ethanolic Mangosteen Pericarp Extract (CEMP).

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Table 1: Summary of Key Pharmacological Activities of Crude Ethanolic Mangosteen Pericarp Extract (CEMP)

Activity	Key Findings	Proposed Mechanisms	References
Antioxidant	Potent free radical scavenging in DPPH, ABTS, and FRAP assays.	High phenolic/xanthone content donates hydrogen atoms to neutralize free radicals.	[5, 7]
Anti-Inflammatory	Inhibits production of NO, PGE2, TNF-α, IL-6, and COX-2.	Suppression of NF-κB and MAPK signaling pathways.	[8]
Antimicrobial	Effective against Gram-positive and Gram-negative bacteria, fungi, and viruses.	Disruption of microbial cell membranes; inhibition of energy metabolism.	[9]
Anticancer	Induces apoptosis and cell cycle arrest; inhibits proliferation and metastasis in various cancer cell lines.	Modulation of apoptosis-related proteins (e.g., Bcl-2, Bax, caspases).	[11]
Antidiabetic	Reduces blood glucose; enhances insulin sensitivity in diabetic rat models.	Inhibition of α-glucosidase enzyme; improvement of insulin signaling.	[12]
Neuroprotective	Demonstrates protective effects in models of neuronal damage.	Antioxidant and anti-inflammatory actions; reduction of oxidative stress in neural tissues.	[13]

4.1. Antioxidant Activity

CEMP demonstrates potent free radical scavenging activity in various assays (e.g., DPPH, ABTS, FRAP). This activity is directly correlated with its high phenolic and xanthone content, which donate hydrogen atoms to stabilize free radicals, thereby mitigating oxidative stress, a key contributor to chronic diseases and aging [5, 7].

4.2. Anti-Inflammatory Effects

The anti-inflammatory properties of CEMP are among its most well-documented effects. In vitro and in vivo studies show that CEMP, primarily through α-mangostin, inhibits the production of pro-inflammatory mediators such as nitric oxide (NO), prostaglandin E2 (PGE2), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and cyclooxygenase-2 (COX-2) [8]. This suppression is mediated via the inhibition of the NF-κB and MAPK signaling pathways.

4.3. Antimicrobial and Antiparasitic Properties

CEMP exhibits broad-spectrum antimicrobial activity against Gram-positive bacteria (**e.g., *Staphylococcus aureus*, *Bacillus subtilis***), Gram-negative bacteria (**e.g., *Salmonella* Typhimurium, *Escherichia coli***), fungi, and viruses [9]. Its mechanism involves disrupting microbial cell membranes and inhibiting energy metabolism. It also shows efficacy against parasites like *Plasmodium falciparum* and *Leishmania* species [10].

4.4. Anticancer Potential

Numerous studies have investigated the anticancer potential of CEMP against various cancer cell lines, including breast, colon, and liver cancer. It induces apoptosis (programmed cell death) and cell cycle arrest, inhibits cancer cell proliferation, and suppresses metastasis [11]. These effects are mediated through the modulation of multiple apoptosis-related proteins and signaling pathways.

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4.5. Other Activities

Research also supports other beneficial effects of CEMP, such as antidiabetic (by enhancing insulin sensitivity and inhibiting α-glucosidase), anti-obesity, cardioprotective, and neuroprotective activities, primarily in animal models [12, 13].

4.6 Toxicological and Safety Profile

CEMP demonstrates high efficacy, but its safety profile is crucial for therapeutic use. Acute and sub-chronic toxicity studies conducted on rodents show that CEMP has a relatively high safety margin, with no observed adverse effect levels (NOAEL) reported in multiple studies[14]. However, high doses may cause mild lethargy or gastrointestinal discomfort. Additionally, certain xanthones have been found to inhibit cytochrome P450 enzymes, indicating a potential for herb-drug interactions that require further investigation before CEMP can be widely used in clinical settings [15].

5. Conclusion and Future Perspectives

This review confirms that the crude ethanolic extract of mangosteen pericarp (CEMP) is a pharmacologically rich natural product with multifaceted therapeutic benefits, as demonstrated consistently in preclinical studies. The primary advantage of CEMP lies in its multi-target mechanism of action, driven by a complex mixture of bioactive xanthones.

However, significant limitations exist. The lack of standardized extracts with defined xanthone content and the scarcity of well-designed human clinical trials represent the major hurdles for its translation into evidence-based medicine. Preclinical evidence indicates that crude ethanolic mangosteen pericarp extract exhibits multiple promising biological activities, but translation to clinical use requires standardization of extracts, detailed pharmacokinetic and interaction studies, early-phase human safety trials, and robust randomized controlled trials before therapeutic recommendations can be made.

Future research should focus on:

1. Standardizing extraction protocols to ensure batch-to-batch consistency.
2. Conducting detailed pharmacokinetic and pharmacodynamic studies in humans.
3. Rigorously investigating potential drug interactions in clinical settings.
4. Designing robust randomized controlled trials to validate efficacy for specific human health conditions.

With concerted and rigorous research efforts, CEMP holds potential for development as an adjunct therapy or a preventive nutraceutical, but its journey to the clinic is still at an early stage.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Adell Abubakeer: Conceptualization, Writing – Original Draft, Writing – Review & Editing.
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