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Exploring the Therapeutic Potential of Ilāj-Bil-Ghizā (Dietotherapy) in Depression: A Systematic Review

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Abstract

Background: *Depression is a common mental health condition characterized by feelings of sadness, diminished interest in activities, and physical symptoms that disrupt daily activities functioning. Emerging research indicates that nutrition and dietary habits can significantly influence the management of depression. This review aims to explore the connection between diet and mental health, highlighting how nutritional approaches may complement traditional treatments for depression.* ***Objective:*** *This review aims to evaluate the relationship between diet and depression, focusing on dietary patterns, nutrient deficiencies, and evidence-based dietary interventions that may support mental health.* ***Methods:*** *An extensive review of peer-reviewed publications, clinical trials, and meta-analytical studies was undertaken to assess the influence of dietary factors on depression. Key areas examined included the effects of specific dietary patterns (e.g., Mediterranean diet, Western diet) and nutrients, such as omega-3 fatty acids, B vitamins, and antioxidants on depressive symptoms.* ***Discussion:*** *Evidence indicates that healthy dietary patterns are linked to lower risk and severity of depression, likely due to their anti-inflammatory and antioxidant effects. Essential nutrients, like omega-3 fatty acids, folate, vitamin D, and magnesium, play a crucial role in supporting mood regulation and cognitive function. Conversely, Western dietary patterns rich in processed foods, refined sugars, and trans fats have been linked to a higher risk of developing depression. Recent advance research also emphasizes the gut-brain axis as a vital pathway, with gut microbiota imbalances contributing to inflammation and depressive symptoms.* ***Conclusion:*** *Dietary interventions offer a promising adjunct to conventional treatments for depression. Encouraging a nutrient-dense diet may significantly improve mental health outcomes. Additional research is required to formulate personalized dietary interventions that consider individual nutritional requirements and cultural dietary practices.*

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INTRODUCTION

Depression is a prevalent mental health disorder and a leading cause of disability worldwide, contributing significantly to the global burden of disease and associated economic and social costs across both developed and developing nations [1]. Its prevalence varies across regions, ranging from 3.3% to 21.4%, influenced by factors, such as cultural perceptions, diagnostic criteria, and healthcare access [2]. Clinically, depression is marked by persistent sadness, low self-esteem, diminished concentration, anxiety, anhedonia, and

feelings of guilt. These psychological symptoms are often accompanied by physical complaints, including fatigue, sleep disturbances, and appetite changes, which further impair quality of life and functional capacity [3].

"In 2019, the World Health Organization reported that around 970 million individuals worldwide were affected by mental disorders, with depressive disorders representing a significant proportion" [1–4]. The pandemic of COVID-19 further exacerbated mental health issues globally, driven by increased stress, social isolation, and economic instability [5]. Consequently, there has been a rising interest in exploring the influence of diet on mental well-being. Nutritional psychiatry, an emerging field, explores the impact of dietary patterns and specific nutrients on brain health and emotional well-being, primarily through mechanisms, such as inflammation, oxidative stress, neuroplasticity, and modulation of the gut-brain axis [6, 7].

Standard approaches for treating mental disorders including depression typically involve the use of pharmacotherapy and psychotherapy. Antidepressant medications aim to correct neurochemical imbalances, while cognitive-behavioral therapy (CBT) helps patients address maladaptive thinking and behavior [8]. Though effective, these approaches may be complemented by dietary modifications, which recent studies suggest can support mood regulation and serve as adjunctive strategies in depression management [9, 10].

Unani physicians traditionally followed a four-tiered approach to treatment: i.e., Ilāj-bil-Ghizā (Dietotherapy), 'Ilāj-bi't-Tadbīr (regimenal therapy), Ilāj-bil-Dawā (Pharmacotherapy) and Ilāj-bil-Yad (Surgical or Manual Therapy). Ilāj-bil-Ghizā, or dietotherapy, is one of the foundational principles in Unani Tibb (Greco-Arabic medicine), emphasizing the role of food as medicine [11, 12]. The concept of Ilāj-bil-Ghizā originates from the teachings of Hippocrates, who famously said, "*Let food be thy medicine and medicine be thy food.*" [13, 14]. Ancient Greek physicians held that a balanced diet was essential for preserving the equilibrium of the four humors – blood, phlegm, yellow bile, and black bile—which were considered vital to maintaining health. This perspective underscores the importance they placed on diet as a primary form of treatment [15].

In conditions, such as *Mālankhūliyā* (melancholia), obesity, and gastrointestinal disturbances, dietary regulation often formed the cornerstone of therapy. This focus underscores the high value placed on lifestyle and nutritional modifications as frontline interventions in Unani practice [16].

This review aims to examine the role of diet in the prevention and treatment of depression. By synthesizing current scientific literature, it offers insight into the potential mechanisms linking nutrition and mood disorders and provides practical dietary recommendations to support mental health [6, 7].

METHODOLOGY

This study utilized a mixed-methods approach, integrating traditional Unani medical knowledge with contemporary scientific research to investigate the impact of diet (Ilāj bil Ghizā) on depression. A thorough examination of classical Unani texts was conducted, drawing on key sources, such as *Al-Qānūn fī al-Ṭibb* (Ibn Sīnā), *Kāmil al-Ṣanāʿa al-Ṭibbiyya* (Al-Zahrāwī), *Kitāb al-Hawī* (Al-Rāzī), and other established works. In parallel, an extensive literature review was performed, focusing on peer-reviewed articles, clinical trials, randomized controlled trials (RCTs), cohort studies, and meta-analyses primarily published over the past 20 years. Databases, such as PubMed, Scopus, Google Scholar, and ScienceDirect were systematically searched using keyword combinations including diet, depression, Mediterranean diet, mental health, omega-3 fatty acids, B vitamins, mood disorders, and gut-brain axis.

DISCUSSION

This review underscores the growing evidence linking diet to the onset, progression, and management of depression. Healthy eating patterns, such as the Mediterranean diet which are abundant in fruits, vegetables, whole grains, lean proteins, and beneficial fats have been consistently linked to a reduced

risk of depression. Nutrients including omega-3 fatty acids, B vitamins, vitamin D, and antioxidants are crucial for brain health, supporting neurotransmitter production and reducing inflammation, all essential for regulating mood. In contrast, the Western diet, characterized by excessive consumption of processed foods, sugars, and unhealthy fats, is associated with heightened inflammation, imbalances in gut microbiota, and nutrient deficiencies, which may contribute to depressive symptoms. The gut-brain axis has gained recognition as a significant pathway through which diet affects mental health, emphasizing the role of gut microbiota in mood regulation. While current evidence indicates that dietary approaches hold promise for managing depression, several limitations exist. Many investigations are observational, limiting the ability to determine causality. Moreover, individual responses to dietary changes can differ due to genetic, lifestyle, and environmental influences. Therefore, further rigorous randomized controlled trials are essential to establish stronger causal relationships.

The Link Between Diet and Depression

Recent research has increasingly highlighted the significant relationship between dietary habits and mental health, especially concerning depression. Western-style diets, which are high in processed foods, sugars, and unhealthy fats, have been consistently associated with an elevated risk of experiencing depressive symptoms [6, 17]. Conversely, dietary patterns abundant in fruits, vegetables, whole grains, lean proteins, and healthy fats, such as the Mediterranean and anti-inflammatory diets are linked to a reduced prevalence of depression and enhanced mental well-being. Evidence from large-scale studies, systematic reviews, and expert institutions, like the National Academies of Sciences, Engineering, and Medicine, underscores the positive impact of dietary improvements on mental health [7, 18]. The relationship between diet and depression is mediated by several interrelated biological pathways. Among the most studied are inflammation, the gut-brain axis, and neurotransmitter synthesis. Each of these mechanisms illustrates how nutritional factors can influence mental health and mood regulation [19].

INFLAMMATION

Chronic inflammation has been progressively recognized as a critical factor in the pathophysiology and progression of depression. Studies report that patients with depression exhibit elevated levels of inflammatory biomarkers, including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) [20]. Although inflammation is a natural defence mechanism against injury, infection, or oxidative stress, persistent or excessive inflammation can lead to tissue damage and has been linked to several neuropsychiatric disorders, including depression. Diet significantly influences inflammatory processes. Diets high in refined sugars, saturated fats, and heavily processed foods tend to promote inflammation, potentially worsening cognitive and emotional health [21]. Conversely, dietary patterns that prioritize anti-inflammatory foods – such as fruits, vegetables, whole grains, legumes, and omega-3 fatty acids – have been found to lower inflammatory markers and alleviate depressive symptoms [17]. Neuroinflammation, or inflammation within the brain, poses particular concern due to its association with increased risks of cognitive decline, dementia, and cardiovascular issues, such as stroke [22]. Therefore, addressing chronic inflammation through targeted nutritional strategies offers a promising approach to reducing the incidence and severity of depression and its related health complications.

GUT-BRAIN AXIS

The gut-brain axis represents a complex bidirectional signaling network between the gastrointestinal tract and the central nervous system. This interplay is mediated by neural, endocrine, and immune pathways and is significantly modulated by the gut microbiota which is the diverse population of microorganisms colonizing the gastrointestinal lumen [19]. Nutritional intake directly influences the composition and functional diversity of the gut microbiome, which subsequently affects central nervous system function and neuropsychiatric outcomes. Diets high in fermentable fiber promote the growth of commensal bacteria that produce short-chain fatty acids (SCFAs) and neuroactive compounds, such as serotonin and gamma-aminobutyric acid (GABA), both critical modulators of mood and behavior [23]. Conversely, dysbiosis (microbial imbalance) has been associated with increased intestinal permeability, systemic inflammation, and the development of depressive symptomatology [24].

NEUROTRANSMITTER SYNTHESIS

Neurotransmitters function as critical chemical mediators facilitating synaptic transmission between neurons, with their biosynthesis dependent on the availability of specific nutrients. For example, tryptophan, an essential amino acid found in protein-rich sources, acts as the biochemical precursor for serotonin synthesis, whereas tyrosine is a key substrate required to produce catecholamines, such as dopamine and norepinephrine. B vitamins, particularly B6, B9 (folate), and B12, play crucial roles as cofactors in these biochemical processes. Additionally, minerals, like magnesium and zinc, along with omega-3 fatty acids, are important for maintaining healthy brain function and emotional balance [25, 26]. A diet rich in nutrient-dense foods, such as vegetables, fruits, whole grains, legumes, nuts, seeds, and healthy fats helps ensure a consistent supply of these key nutrients. This dietary pattern supports efficient neurotransmitter function, promotes stable mood regulation, and lowers the likelihood of developing depression [27].

Nutrients and Their Role in Mental Health

Nutrients are essential for supporting mental health, as they help regulate brain function, neurotransmitter synthesis, and cognitive performance. Adequate intake of important vitamins, minerals, and amino acids is crucial for maintaining mood stability, managing stress, and preventing mental health conditions like depression and anxiety. Understanding how specific nutrients contribute to brain chemistry and emotional balance is essential for developing effective dietary strategies to promote psychological wellness.

Omega-3 Fatty Acids

Omega-3 polyunsaturated fatty acids, predominantly present in marine sources, such as salmon, mackerel, and sardines, as well as in plant-derived sources including flaxseed, chia seeds, walnuts, and pharmaceutical-grade fish oil supplements, have been extensively investigated for their neuroprotective and psychotropic effects in mental health. A substantial body of evidence from randomized controlled trials and meta-analyses indicates that omega-3 supplementation, particularly with eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), can significantly alleviate symptoms of depression, especially in individuals with major depressive disorder [28, 29]. The therapeutic effects of omega-3s are attributed to their anti-inflammatory properties, their ability to modulate cytokine production, and their role in maintaining the fluidity of brain cell membranes. These actions contribute to enhanced functioning of neurotransmitter systems, notably serotonin and dopamine, which are vital for mood regulation and emotional stability [30].

B Vitamins

B vitamins, which are abundant in whole grains, leafy vegetables, legumes, nuts, eggs, dairy, and meat, are crucial for maintaining brain function and regulating mood. Vitamin B12 (cobalamin) is essential for proper neurological activity and DNA synthesis, with its deficiency linked to symptoms, such as fatigue, irritability, and depression [31]. Vitamin B6 (pyridoxine) is involved in the synthesis of key neurotransmitters like serotonin, dopamine, and gamma-aminobutyric acid (GABA). Folate (vitamin B9) plays a critical role in one-carbon metabolism and methylation processes necessary for neurotransmitter production and gene regulation. Several cohort studies and clinical trials have shown that low levels of B vitamins, especially B12 and folate, are correlated with an increased risk of depression [32].

Vitamin D

Vitamin D, obtained through sunlight exposure, fortified dairy and plant-based milk, fatty fish, like salmon and tuna, egg yolks, and supplements, plays a significant role in mental health. Epidemiological research shows that individuals with depression often have lower levels of serum vitamin D. Interventional studies further indicate that vitamin D supplementation can improve mood, especially in those with clinically deficient levels [33, 34]. This vitamin influences brain function as its receptors are found in key areas involved in mood regulation, such as the hippocampus. Additionally, vitamin D

helps regulate serotonin production by affecting the gene expression of tryptophan hydroxylase, an enzyme critical for serotonin synthesis [35].

Antioxidants

Antioxidant-rich foods, such as colorful fruits and vegetables (including berries, spinach, and kale), nuts, seeds, dark chocolate, and green tea play an important role in mental health. It also play a crucial role in scavenging reactive oxygen species, thereby mitigating oxidative stress that can cause cellular and neuronal damage. Chronic oxidative stress has been implicated in the pathogenesis of depression [36]. Epidemiological studies have demonstrated that diets rich in antioxidant compounds correlate with reduced incidence of depressive disorders and enhanced cognitive performance. Bioactive substances, such as flavonoids and polyphenols, abundant in foods, like berries and dark chocolate, exhibit anti-inflammatory properties within the central nervous system and may contribute to mood stabilization [37].

Amino Acids

Protein-rich dietary sources (including meat, eggs, dairy products, legumes, soy, and nuts) provide tryptophan, an essential amino acid and precursor for serotonin biosynthesis. Tryptophan is notably present in foods, such as turkey, chicken, dairy, and seeds. Sufficient dietary intake of tryptophan is critical for maintaining adequate serotonin synthesis, a neurotransmitter integral to mood regulation. Clinical and experimental studies have shown that tryptophan deficiency or depletion can precipitate depressive symptomatology, particularly in vulnerable populations [38].

Dietary Patterns and Mental Health

The relationship between diet and depression is well-established, with certain dietary patterns showing protective effects while others increase risk. The Mediterranean diet, rich in plant-based foods, healthy fats, and omega-3s, has been consistently linked to reduced depression risk due to its anti-inflammatory and antioxidant properties, support for gut health, and essential nutrient content [17, 23, 27]. In contrast, the Western diet – high in processed foods, sugars, and unhealthy fats – contributes to chronic inflammation, oxidative stress, and nutrient deficiencies associated with depressive symptoms [21–39]. Plant-based diets may lower depression risk due to antioxidants and fiber but can lead to nutrient deficiencies like B12 and omega-3s if not balanced [40, 41]. Anti-inflammatory diets, which emphasize whole foods and restrict processed items, are also associated with better mood and reduced neuroinflammation [21–42].

Dietary Recommendations for Managing Depression

A balanced, nutrient-rich diet emphasizing whole and minimally processed foods is essential for promoting mental well-being and mitigating symptoms of depression. Regular, proportionate meals contribute to stable blood-glucose levels, which are important for mood regulation and consistent energy. Diets rich in fruits, vegetables, whole grains, lean proteins, and healthy fats – particularly omega-3 fatty acids from sources, such as fatty fish, flaxseeds, and walnuts supply essential nutrients including antioxidants, fiber, vitamins, and fatty acids that reduce inflammation, support neurotransmitter activity, and enhance the gut-brain axis. These mechanisms are critical in managing depression. In contrast, consumption of ultra-processed foods high in refined carbohydrates, added sugars, and trans fats has been consistently linked to increased depression risk due to their roles in systemic inflammation, oxidative stress, and insulin resistance [21–27]. High sugar intake may also trigger glucose fluctuations, causing fatigue and mood instability. Additionally, excessive caffeine, though it may temporarily improve alertness, can disrupt sleep and increase anxiety, while alcohol, a central nervous system depressant, interferes with neurotransmitter balance, sleep, and the efficacy of antidepressants [43, 44]. Although dietary intake is the preferred method for obtaining essential nutrients, supplementation may be beneficial in instances of nutritional deficiencies or insufficient dietary intake. Omega-3 fatty acids, particularly EPA-dominant formulations, have been found effective in reducing depressive symptoms and complementing standard treatments in major depressive disorder [45, 46]. Similarly, B vitamins, such as folate (B9), B6, and B12 (important for neurotransmitter

synthesis and methylation) have shown benefits in improving mood and enhancing antidepressant response when supplemented in deficient individuals [38]. Moreover, low vitamin D levels are commonly observed in people with depression, particularly in those with limited sunlight exposure; supplementation may improve mood in such individuals, though further research is needed to establish optimal dosing and long-term outcomes [45].

Role of Ilāj-bil-Ghizā (Dieto Therapy)

In Unani medicine, *Ilāj-bil-Ghizā* (dieto-therapy) plays a crucial role in managing *Mālankhūliyā* (melancholia), which is characterized by a predominance of cold and dry temperament due to an excess of *Sawdā'* (black bile). Dietary recommendations emphasize the elimination of foods believed to exacerbate this imbalance, such as excessively salty, spicy, or sour items, as well as foods that stimulate black bile production. These include beef, lentils, cabbage, eggplant, raw garlic and onions, beans, dry cheese, and whole grain bread [15, 47–49]. Instead, Unani physicians advocate for a light diet of low nutritive value (*Ghidhā' Laṭīf Qalīl al-Ghidhā'*) to support weak digestion and produce healthy, thin-consistency blood and humors [50–52]. Suitable dietary items include barley water (*Ma'ul Sha'eer*), light soups, cooked vegetables, like squash and spinach, pomegranate juice in moderation, soft-boiled eggs, and diluted milk if tolerated. Moreover, foods classified as *Muraṭṭibāt* (moisturizing agents) are recommended to counter the dryness associated with *Sawdā'*, particularly for nourishing the brain (*Dimāgh*) and restoring emotional balance. Moisturizing foods include barley water, milk, pumpkin, cucumber, spinach, lettuce, and purslane. Recommended fruits for *Mālankhūliyā* encompass a variety of sweet and moist items, such as cucumber, serpent cucumber, sweet pomegranate (alone or with rosewater), prunes, sweet apricots, sweet apples and pears, sweet melon, figs, grapes, sweet berries, fresh coconut, bananas, sweet quince, well-cooked sweet cherries, almonds, hazelnuts, pistachios, dates, and sweet watermelon with rosewater. These foods are believed to soothe the temperament, nourish the body, and support emotional and psychological well-being [15, 41, 48–49].

Lifestyle Factors Complementing Dietary Management

Regular engagement in physical exercise has been demonstrated to enhance mood and mitigate depressive symptoms, thereby serving as an effective adjunct to nutritional interventions [53]. Adequate sleep hygiene is also essential for optimal mental health, and dietary modifications, such as limiting caffeine intake can facilitate improved sleep quality [54]. Incorporating stress reduction strategies, including mindfulness, meditation, and relaxation techniques, can augment the benefits of dietary changes by alleviating stress and promoting overall psychological well-being [55]. Furthermore, robust social support networks are critical in fostering adherence to dietary modifications, ultimately contributing to better mental health outcomes and emotional stability [56].

Removal of Predisposing Causes

To manage the condition effectively, it is essential to address and eliminate underlying contributors, such as chronic fear, stress, overexertion, alcohol use, and social isolation. This can be supported through various strategies, including engaging the patient in uplifting activities like poetry and music to promote joy, ensuring a restful sleep environment, and maintaining a clean, well-ventilated, pleasantly scented living space. It is also important to treat any associated liver and spleen disorders, avoid detrimental habits, such as smoking and alcohol consumption, and limit excessive sexual activity [57]. Reducing physical overexertion, steering clear of crowded or unsanitary environments, and avoiding exposure to extreme heat are also recommended. Special attention should be given to heart health, using *Muqawwi-e-qalb* (cardiotonic) and *Mufarrih-e-qalb* (mood-lifting) remedies when necessary [58].

CONCLUSIONS

Diet plays a crucial role in managing depression, with increasing research highlighting the positive effects of certain nutrients and dietary patterns – such as the Mediterranean and plant-based diets – on mood and cognitive health. Nutrients, like omega-3 fatty acids, B vitamins, and antioxidants, are particularly linked to improved emotional well-being. Adopting a nutrient-dense, balanced diet in

combination with lifestyle changes provides a comprehensive and sustainable strategy for alleviating depressive symptoms.

In the context of Unani medicine, *Ilāj bil Ghizā* (dietotherapy) is a core therapeutic approach aimed at restoring harmony among the body's humors and temperament. This is especially relevant in the treatment of *Mālankhūliyā* (melancholia), which is thought to result from an excess of *Sawdā'* (black bile). Foods with warm and moist qualities, along with regimens that counteract dryness and restore equilibrium, are central to this healing process. Unani medicine also stresses the importance of tailoring nutrition to an individual's unique temperament (*Mizāj*), reinforcing diet's role in long-term mental health support.

Future research should continue to bridge traditional and modern nutritional sciences, enabling the development of targeted, culturally sensitive dietary interventions for depression that combine both evidence-based medicine and time-tested traditional wisdom.

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