

## UNANI MEDICINE: BRIDGING TRADITIONAL WISDOM WITH CONTEMPORARY SCIENTIFIC VALIDATION FOR MENTAL HEALTH AND OCCUPATIONAL WELL-BEING: A REVIEW

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### Abstract:

Unani medicine which derives from Greco-Arabic medical knowledge provides a complete system to study mental health through its three core concepts which include Mizāj (Temperament), Akhlāt (Humors) and Asbāb Sitta Darūriyya (Six Essential Factors). This comprehensive review examines how classical Unani psychiatric methods merge with contemporary scientific evidence which supports mental disorder treatments for Iztirāb-e-Nafsānī (Anxiety) and Mālānkhūliyā (Melancholia) to demonstrate their impact on workplace health. A dual-layered methodology encompassing systematic literature search across multiple databases and diagnostic framework analysis was employed. The review presents evidence from relevant studies which appeared between 2011 and 2026 alongside classical sources including Ibn Sīnā's *Al-Qānūn fī al-Ṭibb* and Al-Rāzī's works. Scientists have discovered neurobiological associations which link Unani medical principles of Tanqiya'-i-Dimāgh (Brain Cleansing) to present-day scientific knowledge about oxidative stress and neuroinflammation and HPA-axis dysregulation. The pharmacological evaluation of Muqawwī-i-Dimāgh (Cerebral Tonics) which includes Brāhmī (*Bacopa monnieri*) and Ustukhudūs (*Lavandula stoechas*) shows their potential to reduce anxiety and protect the nervous system. The Mizāj-based diagnostic system which uses Ajnās 'Ashara (ten identifying features of temperament) enables doctors to determine individual psychiatric risk levels. The application of Asbāb Sitta Darūriyya modifications in the prevention of burnout at the workplace is of practical significance. However, the limitations in methodology, such as the absence of standardized biomarker studies and the paucity of evidence from Randomized Control Trials (RCTs) in the current study, require rigorous future work to provide evidence-based integration of Unani psychiatry into the contemporary mental health care system.

**Keywords:** Unani medicine, Mizāj (Temperament), Mālānkhūliyā (Melancholia), Iztirāb-e-Nafsānī (Anxiety), occupational well-being, Tanqiya'-i-Dimāgh (Brain Cleansing), *Bacopa monnieri*, neurobiological validation.

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### Introduction:

The worldwide burden of mental health disorders has been increasing because more than 300 million people now suffer from anxiety and depressive disorders which result in substantial occupational disabilities and decreased life quality.<sup>1</sup> Contemporary psychiatric methods achieve results through their use of

biomedical models which tend to overlook the full range of mental health factors that affect personal wellness. Unani Medicine provides a complete framework which connects personal makeup with environmental conditions, mental states and lifestyle factors in understanding and managing mental health problems.<sup>2</sup>

Unani medicine which *Ibn Sīnā* (Avicenna, 980-1037 CE) and *Al-Rāzī* (Rhazes, 854-925 CE) developed as a system defines mental well-being through the combination of *Mizāj* (Temperament) with *Akhlāt-e-Arba'a* (Four Humors) and *Quwwat Nafsāniyya* (Psychic Faculty).<sup>3,4</sup> Unani psychiatry bases its treatment approach on the two core concepts which include *Iztirāb-e-Nafsānī* (Anxiety) and *Mālānkhūliyā* (Melancholia/Depression) which result from imbalanced body humors and disrupted mental functions.<sup>5,6</sup> The Unani preventive paradigm emphasizes *Asbāb Sitta Ḍarūriyya* (Six Essential Factors) *Al-Hawā' al-Mustanshaq* (inhaled air), *Ma'kūlāt-o-Mashrūbāt* (foods and drinks), *Al-Ḥaraka wa'l Sukūn al-Badanī* (bodily movement and repose), *Al-Ḥaraka wa'l Sukūn al-Nafsānī* (psychic movement and repose), *Al-Nawm wa'l Yaqza* (sleep and wakefulness), *Al-Iḥtibās Wa Al-Istifrāgh* (retention and evacuation) as modifiable determinants of mental health.<sup>7</sup>

Scientific validation of traditional medical knowledge has become more popular during the past several decades. Research findings show that Unani medical practices which include *Tanqiya'-i-Dimāgh* (Brain Cleansing/Detoxification) share neurobiological connections with current scientific knowledge about oxidative stress, neuroinflammation and HPA axis dysregulation.<sup>8,9</sup> The pharmacological research of *Muqawwī-i-Dimāgh* (Cerebral Tonics) which includes *Brāhmī* (*Bacopa monnieri*) and *Ustukhudūs* (*Lavandula stoechas*) has demonstrated their anxiolytic, antidepressant and neuroprotective properties in preclinical and clinical studies.<sup>10,11,12</sup>

Unani medicine provides solutions which address the medical requirements of contemporary occupational health challenges. The combination of workplace stress and burnout which produces emotional exhaustion, depersonalization and reduced personal accomplishment affects more than half of healthcare

workers and employees in other demanding fields.<sup>13</sup> The Unani framework of *Infi'ālāt Nafsāniyya* (Psychic Reactions) and temperament-based vulnerability assessment offers personalized preventive strategies that may complement contemporary occupational health interventions.<sup>14</sup>

This comprehensive review has four main objectives to achieve which include: (1) combining traditional Unani mental health theories with contemporary scientific findings; (2) assessing the neurobiological and pharmacological evidence which supports Unani mental health interventions; (3) assessing Unani preventive approaches for occupational well-being and (4) determining research voids and upcoming research paths which will support Unani psychiatric practice integration into current mental healthcare systems.

#### Methodology:

#### Search Strategy:

A comprehensive dual-layered literature review which identified research articles that studied Unani medical practices and their effects on mental health, neurobiological validation and occupational well-being. The search strategy aimed to find traditional Unani medical texts along with contemporary scientific validation research published between 2011 and 2026.

#### Database Selection and Search Terms:

The research involved a structured investigation of academic databases which included Google Scholar, PubMed/MEDLINE and ArXiv. The search strategy employed a combination of Unani-specific terminology and contemporary psychiatric/neurobiological terms to ensure comprehensive coverage. The primary search terms were “Unani Medicine, *Mizāj*, temperament, *Mālānkhūliyā*, melancholia, *Iztirāb-e-Nafsānī*, anxiety, *Akhlāt*, humors, *Asbāb Sitta Ḍarūriyya*, occupational stress, burnout, *Tanqiya'-i-Dimāgh*, neuroinflammation, oxidative stress, HPA axis, *Bacopa monnieri*, *Brāhmī*, *Lavandula stoechas*,

*Ustukhudūs, Muqawwī-i-Dimāgh, cerebral tonics, Ibn Sīnā, Avicenna, Al-Rāzī, Rhazes and Jurjānī.*"

### Search Process:

The search process through all databases resulted in discovering more than 930 academic papers. The search terms were combined through Boolean operators which included both AND and OR functions. The search query follows this structure: (“Unani medicine” OR “Mizāj” OR “temperament”) AND (“anxiety” OR “depression” OR “melancholia” OR “mental health”) AND (“validation” OR “clinical trial” OR “neurobiology” OR “mechanism”).

### Inclusion Criteria:

- Research articles spanning from 2011 to 2026 together with classical sources for historical background.
- Peer-reviewed articles, systematic reviews, clinical trials, observational studies, theoretical reviews.
- Studies on Unani concepts of mental health, temperament, psychiatric disorders or related pharmacological treatments.
- Research that proves Unani concepts through neurobiology, pharmacology and clinical methods.
- All publications in Urdu, English and English versions of classical texts.

### Exclusion Criteria:

- Studies unrelated to mental health or psychiatric applications
- Duplicate publications
- Studies lacking methodological rigor or peer review
- Publications outside the specified timeframe (except classical sources).

### Filtering and Relevance Ranking:

In total, 288 research papers were identified after duplicates were removed from 930+ initially eligible papers. The chosen papers were ranked in relevance i.e. 1) direct relevance to Unani psychiatry and mental health; 2) applicability to temperament theory or

humoral concepts; 3) neurobiological or pharmacological validation; 4) clinical evidence for mental health outcomes; and 5) classical source citations. Papers were based on a 0-100 scale of relevance and consisted of only the best 30 ones with relevance scores  $\geq 35/100$  as included into the study before further detailed examination and the review. The relevance of the research papers were assessed with respect to these five criteria.

### Diagnostic Framework Analysis

At the next methodological layer, Unani’s clinical model of mental health assessment with *Mizāj* assessment and psychiatric vulnerability assessment was systematically analyzed.

### Classical Text Analysis:

The primary classical material used is *Ibn Sīnā's Al-Qānūn fī al-Ṭibb* (The Canon of Medicine), the *Kitāb al-Hāwī* (The Comprehensive Book) by *Al-Rāzī*, and the *Zakhīra-e-Khwārizm Shāhī* (Treasure of the Khwarizm Shah) by *Jurjānī*. The following sections were analyzed for terms of mental illnesses: (i) definitions and classifications of mental disorders, (ii) humoral and temperamental etiology, (iii) diagnostic parameters and assessment methods, (iv) therapeutic approaches such as *‘Ilāj bi’l Taghdhiya* (Dietotherapy), *‘Ilāj bi’l Tadbīr* (Regimenal therapy), *‘Ilāj bi’l Dawā’* (Pharmacotherapy) and *‘Ilāj Nafsānī* (Psychotherapy); as well as (v) preventive principles.

### Mizāj (Temperament) Assessment Framework:

The *Ajnās ‘Ashara* ((Ten identifying features of temperament)) for *Mizāj* determination were systematically documented from classical and contemporary Unani literature. These parameters include: (1) *Malmas* (Touch/ Feel of the body); (2) *Laham -o-Shaham* (Muscularity and adiposity); (3) *Sha’r* (Body hair); (4) *Lawn-o-Jild* (Skin color); (5) *Hayyat A’dā’* (Physique); (6) *Kayfiyat Infi’āl* (Receptivity of organs); (7) *Nawm-o-Yaqza* (Sleep & wakefulness); (8) *Af’āl A’dā’* (Functional state of

organs); (9) *Fuḍlāt Badan* (Body wastes); and (10) *Infi ‘ālāt Nafsāniyya* (Psychic reactions).<sup>15,16</sup>

### Psychiatric Vulnerability Mapping:

The most recent Unani research linking temperament and mental health presentation was reviewed for mapping temperament-specific vulnerabilities. The four main temperaments, *Damawī* (Sanguine, warm-moist), *Ṣafrāwī* (Choleric, warm-dry), *Balghamī* (Phlegmatic, cold-moist), and *Saudāwī* (Melancholic, cold-dry), were investigated for relationships with anxiety, depression, irritability and stress responses.<sup>17,18,19</sup>

### Validation Against Contemporary Scales:

Studies comparing the Unani diagnostic measures to standard psychiatric scales, such as Hamilton Depression Rating Scale (HDRS), Beck Anxiety Inventory (BAI) and Depression Anxiety Stress Scales (DASS), were identified to assess convergent validity of Unani diagnostic parameters.<sup>20</sup>

### Quality Assessment:

The methodological quality of included studies was assessed with relevant tools: PRISMA guidelines for systematic reviews, Cochrane Risk of Bias tool for randomized controlled trials and Newcastle-Ottawa Scale for observational studies. Due to the variety of study methods and inclusion of theoretical reviews and classical text analyses, a narrative synthesis rather than a meta-analysis approach was used.

### Literature Review:

#### Classical Foundations of Unani Psychiatry

The conceptual foundations of Unani psychiatry are based on Greco-Arabic physicians who combined the principles of Hippocratic and Galenic humoral theory with philosophies and medical science. Ibn Sīnā (Avicenna, 980-1037 CE) in *Al-Qānūn fī al-Ṭibb* (The Canon of Medicine), his major work, included detailed descriptions of conditions such as *Mālānkhūliyā* (Melancholia), *Junūn* (Mania) and various psychosomatic conditions.<sup>21,22</sup> Ibn Sīnā considered

mental disorders to be caused by humoral disturbances in *Dimāgh* (Brain) and *Quwwat Nafsāniyya* (psychic faculty) and emphasized the interaction of constitutional temperament, environmental factors, and psychological stressors.<sup>4</sup>

In *Kitāb al-Ḥāwī* (The Comprehensive Book) and other writings, *Al-Rāzī* (Rhazes, 854-925 CE) provided detailed clinical descriptions of melancholic and anxious states and their physical manifestations, suggesting therapies based on humoral correction.<sup>23</sup> *Al-Rāzī*'s empirical approach emphasized careful observation of symptoms and individualized treatment based on the patient's temperament and the quality of the disturbed humor.<sup>19</sup>

*Jurjānī* (*Sayyid Ismā'īl Jurjānī*, 1042-1136 CE), author of *Zakhīra-e-Khwārizm Shāhī*, described melancholia in detail, including subtypes according to humoral etiology and clinical presentation.<sup>24</sup> Contemporary analyses of *Jurjānī*'s work highlight his sophisticated understanding of the relationship between *Sawdā* (black bile) imbalance and depressive symptomatology.<sup>8</sup>

Classical Unani texts describe *Mālānkhūliyā* (Melancholia) as primarily caused by *Sawdā Ghair Ṭabī'ī* (Abnormal black bile), which is either excessive or altered in quality, leading to disturbances in cognitive function, mood, and behavior.<sup>6,25</sup> It may result in *Gham* (Sadness), *Khauf Bilā Sabab* (Fear without an apparent cause), suspiciousness or social withdrawal and it manifests as somatic complaints.<sup>17</sup> *Iztirāb-e-Nafsānī* (Anxiety), which in classical texts was not always described as a distinct diagnostic category, is characterized by symptoms of *Fikr-e-Ziyāda* (Excessive worry), *Khafaqān* (Palpitation), *Bīqarārī* (Restlessness), and *Bīkhwābī* (Sleep disturbance).<sup>5</sup> Classical authorities explained anxiety states as disturbances of the psychic faculties, often said to be secondary to *Bukhārāt* (Vaporous humors) ascending to the brain or temperamental

predispositions.<sup>2</sup>

The therapeutic approach outlined in classical texts is structured as follows: (1) *'Ilāj bi'l Tadbīr* (Regimenal therapy), involving alteration of the six essential factors; (2) *Tanqīya* (Cleansing of morbid matter) to remove vitiated humors; (3) *'Ilāj bi'l Dawā'* (Pharmacotherapy) using *Mufarriḥāt* (Exhilarants) and *Muqawwiyāt-e-Dimāgh* (Cerebral Tonics); and (4) *'Ilāj Nafsānī* (Psychotherapy) incorporating both counselling and spiritual aid.<sup>26,27</sup>

### Temperament Theory and Psychiatric Vulnerability:

*Mizāj* (Temperament) is one of the fundamental of Unani medicine and is based on the assumption that people have distinct constitutional types affecting their physiological response, disease susceptibility, and psychological orientation.<sup>1,15</sup> The four primary temperaments *Damawī* (Sanguine), *Ṣafrāwī* (Choleric), *Balghamī* (Phlegmatic), and *Sawdāwī* (Melancholic) stem from the predominance of *Dam* (Blood), *Ṣafrā* (Yellow bile), *Balgham* (Phlegm), and *Sawdā* (Black bile) respectively, each having different thermal and moisture properties.<sup>3,28</sup>

Recent Unani studies have initiated systematic investigations of the link between temperament and psychiatric vulnerabilities. A thorough integrative review of the literature by Ahmad et al. merged traditional temperament theory with contemporary psychological trait science and showed conceptual similarities between Unani temperaments and contemporary personality-related traits.<sup>1</sup> The review pointed out that *Ṣafrāwī* (Choleric) people – characterized by warm-dry qualities – are more decisive, assertive, energetic, and prone to irritability and anger disorders.<sup>1,29</sup>

Recent empirical studies showed some validation for associations of temperament and psychopathology. Hashmi et al. performed an observational study of depression symptomatology in younger college

students experiencing COVID-19 lockdown, and observed significant relationships between temperament categories and depressive symptoms.<sup>30</sup> In line with classical Unani predictions, the students with *Sawdāwī* (Melancholic) temperament scored higher on depression scales.<sup>3</sup>

Fazil et al. conducted a clinical study evaluating the presence of irritability in patients with Type-2 diabetes and found that patients with a cold temperament (*Balghamī* or *Sawdāwī*) were significantly more likely to experience irritability, anxiety, and depressive symptoms than those with warm temperaments.<sup>31</sup> This observation supports the classical Unani claim that a cold-dry (*Sawdāwī*) temperament is a predisposing factor for melancholic states and emotional dysregulation.<sup>5</sup>

Ahmed et al. assessed both decision-making capacity and energy levels among the four temperamental constitutions, concluding that *Ṣafrāwī* individuals made decisions more quickly and had higher energy, while *Balghamī* individuals processed cognition more slowly and had low energy.<sup>32</sup> They suggest that temperament affects both emotional vulnerability and cognitive style and executive function, potentially impacting occupational performance and stress resilience.<sup>2</sup>

*Sawdāwī* (Melancholic) temperament has received particular attention in Unani psychiatric literature due to its strong association with depressive disorders. Classical descriptions are based on the fact that *Sawdāwī* individuals are cold-dry, with a reflective and cautious personality, concerned and pessimistic; moreover, their sensitivity to stress is unusually acute.<sup>4,17</sup> Current reviews by Usmani et al. and Ahmed et al. have expanded on the classical perspective of *Mālānkhūliyā*, relating the *Sawdāwī* constitutional type to an increased risk of persistent sadness, social withdrawal, and cognitive rumination.<sup>6,33</sup>

On the other hand, the *Damawī* (Sanguine) are warm-

moist characters who often do not struggle with depression and can remain sociable, positive, and flexible.<sup>1</sup> However, when in humoral imbalance, impulsivity or mood instability may also be present in them.<sup>1</sup> Cold-moist *Balghamī* (Phlegmatic), calm temperate with a low-reactive nature, may find the lack of motivation, apathy, and sluggish affect when imbalanced.<sup>34</sup>

### Diagnostic Parameters in Unani Mental Health Assessment:

The Unani framework to assess *Mizāj* is rooted in a methodological approach that is based on systematic review of *Ajnās ‘Ashara* ((Ten identifying features of temperament), which comprises constitutional, physiological, and behavioral measures.<sup>15,16</sup> This composite perspective provides a comprehensive alternative to symptom-focused psychiatric diagnostic assessment in which constitutional predisposition and individualized patterns of vulnerability are central to the evaluation.<sup>35</sup>

The ten parameters, as synthesized from classical texts and contemporary Unani practice, include:<sup>1,15</sup>

1. **Malmas (Touch/ Feel of the body):** Sensitivity to heat and cold, environmental preferences
2. **Laḥam -o-Shaḥam (Muscularity and adiposity):** Muscular, flabby, or lean.
3. **Sha’r (Body hair):** Hair thickness, color, texture, and growth pattern
4. **Lawn-o-Jild (Skin color):** Skin complexion, moisture, temperature, and texture
5. **Hayyat A’ḍā’ (Physique):** Constitutional body type, muscle tone, and overall physical structure
6. **Kayfiyat Infi’āl (Receptivity of organs):** response to *Kayfiyāt Arba’ā* (Physical qualities)
7. **Nawm-o-Yaqza (Sleep & wakefulness):** Sleep quality, duration, ease of falling asleep, depth of sleep, Daytime alertness, energy levels, and cognitive clarity

8. **Af’āl A’ḍā’ (Functional state of organs):** Appetite strength, food preferences, digestive capacity, metabolic rate, Pulse characteristics and overall vitality

9. **Fuḍlāt Badan (Body wastes):** Regularity and characteristics of excretory functions

10. **Infi’ālāt Nafsāniyya (Psychic reactions):** Emotional reactivity, cognitive style, and behavioral tendencies

Recent studies have been concentrated on defining structured tools for *Mizāj* assessment. Malik et al. performed an inter-rater reliability analysis for item selection in a questionnaire to ascertain *Mizāj-i-Insānī* (Human Temperament), suggesting acceptable reliability coefficients for most temperament domains.<sup>36</sup> Ansari et al. researched different temperament-determining instruments and stressed the importance of their clinical application in personalized diagnosis and treatment planning.<sup>37</sup>

Cross-sectional studies have utilized these diagnostic indicators in varied populations. Jameel et al. evaluated *Mizāj* in participants at an Ayurveda health fair and, based on the systematic application of the ten parameters, found consistent temperament classification.<sup>38</sup> Ahmad et al. clinically evaluated *Mizāj* in hypothyroidism patients, finding associations between a particular temperamental profile and thyroid dysfunction, with implications for psychosomatic interactions.<sup>39</sup>

Notably, several parameters have been studied for their diagnostic value. Nasir examined the analysis of temperament as a function of hair thickness and color, and found correlations between these morphological features and overall *Mizāj* classification, which is in accordance with classical Unani claims.<sup>40</sup> Such studies suggest that even individual parameters may present easily accessible screening instruments for temperament assessment in low-resource settings.<sup>41</sup>

The integration of *Mizāj* assessment with modern

psychiatric evaluation has been explored in several studies. Saifi et al. performed a qualitative approach to mental health in apparently healthy individuals and assessed lifestyle changes according to different *Mizāj* categories.<sup>42,43</sup> This study found that temperament-tailored lifestyle interventions were perceived as acceptable and potentially beneficial for mental health maintenance.<sup>20</sup>

Ansari et al. explored the correlation between *Mizāj* and diseases in adult samples identifying that certain traits correlated significantly with disease manifestations, which supports the clinical validity of temperament-based diagnosis.<sup>44</sup> Such concordance indicates that *Mizāj* assessment can be a useful complementary tool for detection of psychiatric vulnerability and for directing preventive interventions.<sup>16</sup>

### Results:

#### Clinical Spectrum of Unani Mental Health Disorders:

In Unani medicine, the clinical characterization of mental health disorders revolves around two main psychological illnesses: *Iztirāb-e-Nafsānī* (Anxiety) and *Mālānkhūliyā* (Melancholia/Depression), understood as disturbances of psychic faculties arising from humoral derangement and abnormal psychic reactions.<sup>2,5</sup>

#### Clinical Presentation of *Iztirāb-e-Nafsānī* (Anxiety):

Clinical presentation of *Iztirāb-e-Nafsānī* (Anxiety): Contemporary Unani literature describes *Iztirāb-e-Nafsānī* as characterized by autonomic and cognitive features including *Khafaqān* (Palpitations), *Khauf-e-Ziyāda* (Excessive fear), *Ghuṣṣa* (Irritability), *Bīkhwābī* (Insomnia), *Za'f-e-Ḥāfīza* (Poor concentration) and *Bīqarārī* (Restlessness).<sup>5</sup> This is due to perturbations of *Infi'ālāt Nafsāniyya* (Psychic reactions) and temperament imbalance, frequently provoked by environmental stressors or lifestyle alterations.<sup>2</sup>

In their extensive review of Unani approaches to *Amrād-i-Nafsāniyya* (Psychological Disorders), Iqbal et al. argued that anxiety states may be caused by both humoral excess and qualitative changes; vaporous humors ascending to the brain are a main component of acute anxiety presentations.<sup>2</sup> The review underlined the need to treat underlying temperamental vulnerabilities via regiminal modifications.<sup>2</sup>

#### Clinical Presentation of *Mālānkhūliyā* (Melancholia/Depression):

*Mālānkhūliyā* (Melancholia) is characterized by persistent sadness, loss of interest in things, social withdrawal, and features similar to *Sawdā* (Black bile) dyscrasia, with symptoms such as dark thoughts, suspiciousness, and somatic complaints.<sup>6,17</sup> Classical Unani nosology distinguishes several subtypes of Melancholia based on the location and quality of the disturbed humor.<sup>4,25</sup>

Usmani et al. provided detailed insights into the classical perspective of Melancholia, noting that the condition can manifest with either *Raṭb* (Moist) or *Bārid Ghair Ṭabī'ī* (abnormal cold) temperamental qualities, each requiring distinct therapeutic approaches.<sup>6</sup> Ahmed et al. elaborated on the Unani perspective of melancholia, emphasizing similarities and differences with contemporary depression diagnosis, noting that Unani classification incorporates constitutional, humoral, and psychic dimensions not captured in DSM-based diagnosis.<sup>33</sup>

Rajabnejad et al. examined *Ismā'il Jurjānī's* perspectives on melancholia, highlighting his nuanced understanding of the connection between black bile imbalance and depressive symptoms, including descriptions of cognitive impairment and emotional dullness in severe melancholic states.<sup>8</sup>

#### Etiopathogenesis:

The Unani etiopathogenesis of mental disorders involves several elements of causation, namely: (1) *Mizāj-e-Aṣlī* (Constitutional temperament); (2) *Sū'-e-*

*Mizāj* (Humoral imbalance); (3) *Asbāb Sitta Ḍarūriyya* (Six essential causes); (4) *Arāz-e-Nafsānī* (Psychic reactions); and (5) organ-specific pathology, with particular attention to the *Dimāgh* (Brain) and *Qalb* (Heart).<sup>2,43</sup>

Javed et al. examined in detail the perspective of psychiatric disorders within the Unani system, noting that depression and melancholia are inherent to an imbalance of *Mizāj*, with the *Sawdāwī* temperament being the most prominent constitutional vulnerability.<sup>44</sup> The review highlighted the fact that chronic stress and unhelpful psychogenic responses, neglected through measures such as regimenal therapy or prompt evacuation of vitiated humors, can lead to persistent melancholic symptoms.<sup>2</sup>

#### Preventive Framework:

Unani preventive strategy focuses on *Asbāb Sitta Ḍarūriyya* (Six essential causes)—the regimen and environment of modulating temperament and reducing vulnerability to psychic disorders.<sup>1,7</sup> Recent Unani reviews suggest optimizing these domains (sleep, diet, physical activity, environmental quality, retention and evacuation, and cognitive/emotional balance) for workplace stress and maladaptive psychic reactions.<sup>2</sup>

Iqbal et al. emphasized that regular exercise improves both physical and mental health and is an essential part of regimenal therapy for maintaining mental health with these characteristics.<sup>2</sup> The focus on lifestyle-first initiatives is consistent with modern preventive psychiatry approaches that emphasize sleep hygiene, high-quality food and activity.<sup>7</sup>

#### Therapeutic Sequence:

Classical Unani therapeutic protocols are sequential: (1) lifestyle and dietary changes, (2) *Tanqiya* (Cleansing of morbid matter) of vitiated humors via the appropriate therapies (purgation, venesection, cupping), (3) the administration of *Mufarriḥāt* (Exhilarants) to enhance mood and cognition; (4) *Muqawwiyāt-e-Dimāgh* (Cerebral Tonics) for the

stimulation of psychic faculties.<sup>26,27</sup>

#### Neurobiological Validation of Unani Concepts:

Recent research has focused on the neurobiology of the concepts of Unani, with an emphasis on *Tanqiya'-i-Dimāgh* (Cleansing of morbid matter from brain) and its contribution towards oxidative stress, neuroinflammation, and neuroendocrine regulation.<sup>8,9</sup>

#### Oxidative Stress and *Iḥtirāq* (Pathological Combustion):

However, current reviews in Unani pharmacology suggest that the classical notion of *Iḥtirāq* (pathological combustion or excess heat) in humoral theory may be consistent with modern knowledge of oxidative stress and free radical-related cellular damage.<sup>9</sup> Although Unani's objective of alleviating *Iḥtirāq* via cooling and detoxifying modalities is consistent with antioxidant methods currently used in neuropharmacology, direct biomarker studies linking Unani detoxification processes to markers of oxidative stress (e.g., malondialdehyde, superoxide dismutase, glutathione peroxidase) have not been performed in the reviewed literature, and preclinical studies on individual Unani herbs have shown antioxidant roles that may lead to neuroprotection.<sup>9</sup>

#### Neuroinflammation and Humoral Evacuation:

Unani *Tanqiya* treatments and detoxifying protocols have been suggested to attenuate proinflammatory systems that affect brain function.<sup>9</sup> Current knowledge on the gut-brain axis, systemic inflammation, and neuropsychiatric conditions provides a possible mechanistic framework to clarify the potential central nervous system effects of Unani evacuation procedures.<sup>9</sup>

However, the reviewed literature does not contain clinical trials directly measuring peripheral inflammatory biomarkers (e.g., C-reactive protein, interleukin-6, tumor necrosis factor-alpha) before and after classical Unani detoxification procedures, representing a significant evidence gap.<sup>9</sup>

### HPA Axis and Temperamental Regulation:

For example, Unani medicine proposed that temperamental correction based on regiminal modifications has been conceptually aligned with hypothalamic-pituitary-adrenal (HPA) axis regulatory modulation, a key mechanism in stress response and mood disorders.<sup>9</sup> The *Asbāb Sitta Darūriyya* framework is focused on known modulators of HPA axis function, especially in the areas of sleep regulation, dietary quality, and stress management.<sup>7</sup> However, despite these conceptual parallels, the reviewed literature lacks clinical studies measuring cortisol, adrenocorticotrophic hormone (ACTH), or other HPA axis biomarkers in response to Unani regiminal interventions, limiting definitive conclusions about neurobiological mechanisms.<sup>9</sup>

### Neurotrophic and Neurotransmitter Effects:

Current Unani pharmacology reports suggest that *Muqawwiyyāt-e-Dimāgh* (Cerebral Tonics) may exert immunomodulatory and neurotrophic effects compatible with the restoration of neuronal homeostasis in the wake of humoral imbalance.<sup>9</sup> Preclinical studies show there appear to be preclinical correlations of Unani cerebral tonics with neuronal control and central neurotransmission (e.g., on neurotrophic signaling [e.g., brain-derived neurotrophic factor] and central neurotransmission [serotonin, dopamine, acetylcholine]), thus serving as possible bridges between the restoration of *Rūḥ* (Pneuma) function of Unani and modern neurobiology.<sup>9</sup>

### Evidence Gaps:

The evidence base reviewed in the review demonstrates major limitations that Unani ideas could not be directly validated as neurobiological research topics in direct neurobiological studies. Noteworthy findings are: (1) clinical investigation of oxidative stress biomarkers before and after detoxification using Unani treatments; (2) neuroimaging studies examining brain changes with Unani interventions; (3) HPA axis biomarker studies; (4) recordings of neurotransmitter or neurotrophic factors in populations receiving Unani treatments; and (5) mechanist studies that correlate specific humoral dysregulatory effects to measurable neurobiological indices.<sup>9</sup>

### Pharmacological Evidence for Cerebral Tonics

*Adwiya-e-Muqawwi-e-Dimāgh* (Cerebral Tonics/Nootropics) represent a major therapeutic category in Unani psychiatry, attributed with sedative, exhilarant, immunomodulatory, and neurotrophic properties.<sup>9,27</sup> Contemporary pharmacological research has focused particularly on *Brāhmī* (*Bacopa monnieri*) and, to a lesser extent, *Ustukhudūs* (*Lavandula stoechas*).

### Evidence for *Brāhmī* (*Bacopa monnieri*):

*Bacopa monnieri* represents one of the most extensively studied Unani cerebral tonics, with substantial preclinical and clinical evidence supporting its cognitive-enhancing and anxiolytic properties.<sup>10,11,12</sup> Table 1 summarizes key studies on *Bacopa monnieri* from the reviewed literature:

**Table 1: Key Studies on *Bacopa monnieri* (2011-2026)**

Study	Year	Design	Population/Model	Key Findings
Dhawan BN <sup>10</sup>	2014	Experimental and clinical review	Animal models; human clinical trials	Bacosides identified as active constituents; extracts improve learning, memory, and show anxiolytic effects; clinical trials report improved information processing and safety
Mathur D et al. <sup>45</sup>	2016	Narrative review	Preclinical and clinical literature	Discusses synaptic plasticity basis for memory effects; outlines therapeutic potentials across CNS disorders
Banerjee S et al. <sup>46</sup>	2021	Pharmacological review	Preclinical models of neurological disorders	Summarizes signaling pathways modulated by bacosides; neuroprotective actions across in vitro and animal studies
Fatima U et al. <sup>11</sup>	2022	Review	Clinical and preclinical literature	Reviews clinical manifestations, mechanisms (antioxidant, acetylcholinesterase modulation), safety, and standardized extracts used in trials
Valotto Neto LJ et al. <sup>12</sup>	2024	Systematic review	Human clinical trials and preclinical studies	Reports anti-inflammatory, antioxidant, anti-apoptotic mechanisms; summarized 22 clinical trials showing improvements in cognition and emotional measures

### Active Constituents and Mechanisms:

The main active constituents of *Bacopa monnieri* are bacosides A and B, along with bacopasaponins and other secondary phytochemicals.<sup>10,11,46</sup> Mechanisms of action are proposed as follows:<sup>10,11,12,45,46</sup>

- Enhancement of synaptic plasticity and memory consolidation
- Modulation of neurotransmitters (acetylcholine, dopamine, serotonin)
- Antioxidant and anti-inflammatory effects
- Mitochondrial protection and anti-apoptotic activity
- Inhibition of acetylcholinesterase
- Restoration of neuroprotective signaling pathways

### Clinical Evidence:

In selected populations, evidence of better information processing, learning, memory consolidation, and reductions in anxiety and sleep disturbances have been reported in double-blind placebo-controlled and other

clinical trials.<sup>10,11,12</sup> Valotto Neto et al.'s systematic review of 22 clinical trials documented consistent benefits for cognition and emotion, with chronic administration reported as safe and tolerable.<sup>12</sup>

### Dosage and Standardization:

Although overall clinical efficacy was documented in the literature reviewed, the precise recommended dosage and standardization of constituents based on studies differ. Standardized extracts containing 20-55% bacosides with daily doses ranging from 300-600 mg, administered for 8-12 weeks, were widely used by clinical trials.<sup>11,12</sup> The corpus reviewed does not mention any Unani dosing protocols or formulations as stated in the original corpus.<sup>10</sup>

### Evidence for *Ustukhudūs (Lavandula stoechas)*:

Despite classical Unani texts describing *Ustukhudūs* as *Jarūb-e-Dimāgh* (Broom of the Brain) with purported anxiolytic and mood-enhancing properties, the

reviewed literature contains limited contemporary scientific evidence for this specific species.<sup>47</sup>

Kalam et al. reviewed *Ustukhudūs* (*Lavandula stoechas* L.) as a potential intervention for neuropsychiatric disorders from a Unani perspective, mentioning temperament basics and some contemporary comparisons.<sup>47</sup> Nonetheless, its review did not include in-depth pharmacological findings, evidence from clinical testing, and mechanistic investigations for *Lavandula stoechas* in mental health use.<sup>47</sup>

There are no original studies described in the reviewed corpus as to active constituents (i.e., linalool, linalyl acetate), mechanisms (i.e., GABAergic modulation, neuroprotection), or efficacy in *Ustukhudūs* in anxiety or depressive disorders, indicating a major evidence deficit.<sup>47</sup>

#### Evidence for Polyherbal Unani Formulations:

While limited single-herb evidence is available for some traditional remedies, clinical trials for compound Unani formulations are more promising. Contemporary Unani practice often uses polyherbal preparations involving more than one *Mufarriḥāt* (Exhilarants) and *Muqawwiyāt* (Tonics).<sup>27</sup>

Symptomatic improvement in melancholia and mixed anxiety-depressive presentations have been reported in clinical trials of compound Unani formulations, although the reviewed literature does not provide detailed trial data for specific formulations.<sup>27</sup> The effectiveness of such formulations was associated with combined antioxidant, anti-inflammatory, and central nervous system modulatory actions of their constituent plants, but the constituent-level pharmacokinetic and dose-response data are not available in the reviewed corpus.<sup>9,27</sup>

#### 4.4 Occupational Well-being and Six Essential Causes

The use of Unani principles in the prevention of occupational health and burnout is an emerging area of research, albeit direct empirical evidence remains

limited in the reviewed literature.<sup>2,7</sup>

#### Conceptual Framework:

Work-related chronic stress and burnout are described in Unani medicine as long-term and harmful *Arāz-e-Nafsānī* (Psychic Reactions) that, unless corrected with proper practice and prompt removal of vitiated humors, progress to fixed melancholic states.<sup>2</sup> The Unani preventive emphasis on routine, sleep hygiene, dietary regulation, and mental therapies is positioned as workplace mental health prevention.<sup>2,7</sup>

#### Modifications of *Asbāb Sitta Ḍarūriyya* for Occupational Settings:

Unani literature advises specific measures of the *Asbāb Sitta Ḍarūriyya* concerning occupational stress management:<sup>1,2,7</sup>

1. ***Al-Hawā' al-Mustanshaq* (Inhaled air):** Improve ventilation, lighting, and ambient conditions of the workplace to limit physiological stress.<sup>1</sup>
2. ***Al-Ma'kūlāt wa'l Mashrūbāt* (Foods and drinks):** Modification of diet to help with energy and mood stability; emphasis on moderate or balanced diet customized for the individual *Mizāj*.<sup>1</sup>
3. ***Al-Ḥaraka wa'l Sukūn al-Badanī* (Bodily movement and repose):** Moderate exercise is prescribed for mood improvement and anxiety symptom reduction.<sup>2,7</sup>
4. ***Al-Ḥaraka wa'l Sukūn al-Nafsānī* (Psychic movement and repose):** Interventions to reduce worry, encourage relaxation, and promote social balance tailored to individual *Mizāj*.<sup>1,2</sup>
5. ***Al-Nawm wa'l Yaqza* (Sleep and wakefulness):** Structured sleep hygiene and regular schedules to overcome occupational fatigue.<sup>7</sup>
6. ***Al-Iḥtibās wa'l Istifrāgh* (Retention and evacuation):** Emphasis on bowel and metabolic regularity as contributors to mental well-being.<sup>1</sup>

#### Evidence Base:

Iqbal et al. emphasized that exercise and lifestyle modification had beneficial effects on psychological

outcomes, thus supporting the importance of regimenal interventions for mental health.<sup>2</sup> Saifi et al. also found in his qualitative study that temperament-tailored lifestyle interventions were perceived as acceptable and potentially beneficial for mental health maintenance in apparently healthy individuals.<sup>42,43</sup>

However, based on the literature reviewed, there are no high-quality randomized controlled trials that specifically measure *Asbāb Sitta Darūriyya* interventions for occupational burnout or workplace stress.<sup>2,7</sup> According to literature, research on its possible application from *Bacopa monnieri* trials suggesting anxiolytic and cognitive benefits to structured Unani regimenal routines for occupational burnout is not recorded in the literature reviewed.<sup>10,11,12</sup>

### Temperament-Based Vulnerability and Occupational Stress:

*Mizāj* frameworks provide a structure that can help identify individuals at high risk for occupational burnout. Individuals with a *Ṣafrāwī* (Choleric) temperament, characterized by irritability and dysregulation, are likely to be identified within this framework and will require specific interventions for anger management and work-life balance in response to these factors.<sup>1,29</sup> Since *Sawdāwī* (Melancholic) individuals are at high risk for depressive symptoms, they might benefit from enhanced social support and cognitive interventions.<sup>4,5,6</sup>

Ahmed et al.'s findings on decision-making and energy levels across temperaments indicate that *Balghamī* (Phlegmatic) individuals, who have slower cognitive processing and lower energy, may be particularly vulnerable to occupational fatigue and require accommodations for pacing or recovery.<sup>32</sup>

### Discussion:

#### Integration of Traditional and Contemporary Frameworks:

This review identifies promising convergences and major gaps between classical Unani psychiatry and

current scientific validation. The Unani framework represents a comprehensive patient-driven perspective of mental health that incorporates constitutional, environmental, lifestyle, and psychological aspects—an approach increasingly perceived as of benefit in modern integrative and preventive psychiatry.<sup>1,2</sup>

#### Conceptual Convergences:

Among the Unani concepts, some of them have a conceptual alignment with contemporary notions:

- 1. Temperament and Psychiatric Vulnerability:**  
 The *Mizāj* typology of psychiatric vulnerability based on constitutional type has partial backing provided by recent research in personality traits, stress reactivity, and psychopathology risk.<sup>1,3</sup> The correlation between *Sawdāwī* (Melancholic) temperament and depressive vulnerability that appears frequently in Unani clinical studies is consistent with modern studies linking neuroticism and negative affectivity to depression risk.<sup>6,30,31</sup>
- 2. Lifestyle Factors and Mental Health:** The *Asbāb Sitta Darūriyya* framework on sleep, diet, physical activity, and quality of environment as mental health determinants strongly corresponds with the current preventive psychiatry and lifestyle medicine perspective.<sup>2,7</sup> There is now considerable evidence to support exercise, sleep hygiene, and dietary treatments that can help to improve mental health in mainstream psychiatry, which reinforces the Unani concept of regimenal therapy.<sup>2</sup>
- 3. Oxidative Stress and Neuroinflammation:** Given the growing understanding of oxidative stress and inflammation in psychiatric disorders, the conceptual parallels suggested between pathways such as *Ihtirāq* (pathological combustion) and oxidative stress, and between humoral evacuation and anti-inflammatory effects, present conceptual possibilities.<sup>9</sup> However, direct empirical validation through studies using biomarker results is lacking.<sup>9</sup>

4. **Phytopharmacology:** The strong evidence for the cognitive-boosting and anxiolytic actions of *Bacopa monnieri* supports the classical use of *Brāhmī* in Unani medicine as a cerebral tonic.<sup>10,11,12</sup> The mechanistic aspects of this (neurotransmitter modulation, antioxidant effects, neuroprotection) provide biological support to traditional therapeutics.<sup>45,46</sup>

#### Divergences and Challenges:

Direct integration is complicated by a number of challenges:

1. **Epistemological Differences:** The humoral model in Unani medicine and contemporary biomedicine's molecular-cellular framework reflect two radically different explanatory models. Although conceptual links can be laid out for understanding, it is difficult to draw a straight line of equivalence between the two systems and hence can lead to oversimplification.<sup>3,28</sup>
2. **Diagnostic Validity:** Internal consistency of *Mizāj* assessment is present within Unani practice; however, convergent validity with standardized psychiatric instruments requires more rigorous investigation.<sup>36,37</sup> The *Ajnās 'Ashara* ((Ten identifying features of temperament) need psychometric validation against contemporary personality and psychopathology measures.<sup>15,16</sup>
3. **Mechanistic Gaps:** Although similar in concept, the direct mechanistic connection between Unani interventions and neurobiological endpoints is currently speculative. The absence of biomarker studies, neuroimaging research, and mechanistic clinical trials limits definitive conclusions about how Unani therapies exert their effects.<sup>9</sup>
4. **Standardization Challenges:** Unani practice is complex, with highly individualized, multi-component interventions that are challenging to standardize for rigorous clinical trials. Polyherbal formulations, while potentially

effective, pose challenges for identifying active constituents and mechanisms.<sup>27</sup>

#### Clinical Implications for Mental Healthcare:

In this review, although evidence remains lacking, some clinical relevance is observed, namely:

##### Personalized Risk Assessment:

The *Mizāj* framework enables customized, personalized assessment of psychiatric risk, possibly providing an added layer to recent tools. With the *Ajnās 'Ashara* ((Ten identifying features of temperament) in use, a systematic examination of temperament could find people at risk for particular forms of mental health problems, allowing such efforts to be targeted in prevention.<sup>15,16,36</sup> For example, identifying *Sawdāwī* temperament in occupational health screening might prompt enhanced monitoring and early intervention for depressive symptoms.<sup>6,30,31</sup>

##### Lifestyle-First Interventions:

Unani medicine focus on regimenal therapy supports the recent trend to use a lifestyle approach as first-line or adjunctive treatment for mild-to-moderate mental health problems.<sup>2,7</sup> The framework of *Asbāb Sitta Ḍarūriyya* offers a broad, culturally based approach to lifestyle counseling that might increase patient engagement with such counseling – especially in populations familiar with traditional medicine concepts.<sup>1,42,43</sup>

##### Integrative Pharmacotherapy:

*Bacopa monnieri*, which has extensive evidence of cognitive and anxiolytic effects, can provide a potential integrative path for patients in need of adjunctive interventions or those with adverse effects from traditional psychotropics.<sup>10,11,12</sup> But clinical use should be performed in standardized extracts containing known bacoside content, and patients shall observe for potential herb-drug interactions.<sup>11</sup>

##### Occupational Health Applications:

The temperament-based vulnerability assessment and *Asbāb Sitta Ḍarūriyya* modification framework

provide a structured approach to occupational mental wellness which may be piloted in workplace wellness programs.<sup>1,2,7</sup> Temperament-mediated stress management interventions could offer a better effect than blanket solutions.<sup>32</sup>

### **Cultural Competence:**

Providers of healthcare who work with populations of members of the traditional medicine background may have opportunities to use culturally competent and therapeutic allied work through learning about Unani. The inclusion of Unani terminology and concepts in patient education & shared decision-making, may help increasing treatment adherence as well as outcome.<sup>2,43</sup>

### 5.3 Methodological Considerations

The evidence base highlighted in this review identifies several methodological limitations that should be addressed:

#### **Study Design Limitations:**

The studies included in this article are majority observational, cross-sectional or narrative reviews and not randomized controlled trials.<sup>1,2,3,6</sup> Although these designs yield useful descriptive and correlational data, they cannot establish causality or definitively demonstrate treatment efficacy. The few clinical trials described lack detailed methodological data in their abstracts.<sup>27</sup>

#### **Sample Size and Generalizability:**

Most studies rely on small, convenience samples from single institutions, resulting in limited generalizability.<sup>30,31,32</sup> More extensive, multi-center studies in diverse populations are necessary to validate temperament–psychopathology relationships and treatment effects.<sup>36</sup>

#### **Measurement Standardization:**

There are no standardized, validated *Mizāj* assessment instruments to compare across studies and to perform a rigorous psychometric evaluation.<sup>36,37</sup> The development and validation of standardized instruments for assessing temperament with

established reliability and validity is a research priority.<sup>15,16</sup>

#### **Biomarker Studies:**

The lack of any biomarker studies directly associating Unani concepts and interventions with quantifiable neurobiological factors represents a critical gap.<sup>9</sup> Open lines of inquiry would require further investigation of oxidative stress markers, inflammatory cytokines, HPA axis hormones, neurotransmitter metabolites, and neuroimaging to investigate the mechanisms.<sup>9</sup>

#### **Publication Bias:**

The literature can be biased toward publication with positive findings being far more common than null results. Systematic reviews with comprehensive search strategies and inclusion of grey literature are needed to address this limitation.<sup>12</sup>

#### **Herb-Specific Evidence:**

With the body of evidence for *Bacopa monnieri*, it is well established, but there is a lack of rigorous scientific evaluation by clinical trials of many other Unani cerebral tonics, such as *Ustukhudūs*.<sup>47</sup> Systematic pharmacological and clinical research on the full range of Unani psychotropic herbs is needed.<sup>27</sup>

#### **Conclusion:**

This thorough review illustrates that Unani medicine presents an in-depth approach for understanding mental health through a lens of a holistic framework including constitutional, humoral, lifestyle, as well as psychological dimensions. Classical Unani psychiatry, conceptualized by *Ibn Sīnā*, *Al-Rāzī*, and *Jurjānī*, gives in-depth nosology, etiopathogenesis, and treatment of anxiety and melancholic conditions that remain clinically relevant.<sup>4,8,21,22,23,24</sup>

Recent researches have begun to confirm essential concepts in Unani through scientific methodologies. The *Mizāj* (Temperament) framework shows predictive validity for psychiatric vulnerability; *Sawdāwī* (Melancholic) temperament was linked to depressive symptoms with reliable effect from multiple

studies.<sup>1,3,6,30,31</sup> Finally, *Ajnās ‘Ashara* ((Ten identifying features of temperament) offers an organized, multi-dimensional framework for personalized risk appraisal and merits additional psychometric validation.<sup>15,16,36</sup>

Neurobiological studies indicate potential mechanistic connections of Unani concepts to present-day knowledge of oxidative stress, neuroinflammation, and neuroendocrine modulation, although direct biomarker validation remains limited.<sup>9</sup> Pharmacological evidence is compelling for using *Brāhmī* (*Bacopa monnieri*) as a cognitive enhancer and anxiolytic, which has been verified in several clinical trials as effective and safe.<sup>10,11,12</sup> Still, evidence for other traditional remedies like *Ustukhudūs* (*Lavandula stoechas*) is inadequate.<sup>47</sup>

In this respect, the *Asbāb Sitta Darūriyya* (Six Essential Causes) framework also closely resembles that of modern lifestyle medicine and preventive psychiatry, providing a culturally-based framework that frames a holistic approach to promoting mental well-being.<sup>1,2,7</sup> On workplace well-being, application is promising, however, there is a need for specific data to determine effectiveness of workplace stress & burnout reduction therapies.<sup>2,7</sup>

Utilization of Unani psychiatry in modern mental healthcare has great potential to strengthen individualized systems, whole body models, and cultural sensitivity. However, such integration needs to be grounded in evidence, and recognition of the virtue of traditional wisdom along with the limits of what science has previously confirmed as true. We need to ensure a sound research approach using contemporary methods, whilst also protecting the epistemological values of the Unani system.

### Study Limitations and Future Scope:

#### Study Limitations:

This review is subject to several important limitations:

1. **Literature Search Constraints:** Despite a thorough search, only four main databases were

included, and all major publications are in English. Studies in Arabic, Persian, Urdu, or other languages may have been overlooked. Classical Unani texts were accessed through secondary sources, not original manuscripts.<sup>21,22,23,24</sup>

2. **Heterogeneity of Evidence:** The studies included in this review vary in design (reviews, observational studies, clinical trials, theoretical papers) and methodological quality, preventing meta-analysis and limiting the strength of conclusions.<sup>1,2,3</sup>
3. **Limited RCT Evidence:** Few high-quality randomized controlled trials specifically assessing Unani mental health interventions were found; the evidence is predominantly in observational reports and reviews.<sup>27</sup>
4. **Biomarker Validation Gap:** Without studies measuring neurobiological biomarkers directly following Unani interventions, no results are available, so there is no conclusion on whether suggested neurobiological correlates are mechanistically valid.<sup>9</sup>
5. **Standardization Issues:** Since both the *Mizāj* assessment tools and Unani formulation specifications are not standardized, differences in studies and clinical applicability are limited.<sup>36,37</sup>
6. **Single-Herb Evidence Gaps:** *Bacopa monnieri* has substantial scientific evidence, but many other Unani psychotropic herbs were not adequately investigated to allow for a comprehensive assessment of the Unani pharmacopeia.<sup>47</sup>
7. **Occupational Health Evidence:** There is little to no direct evidence for Unani interventions in occupational settings (i.e., recommendations are largely extrapolated from general mental health literature).<sup>2,7</sup>
8. **Cultural and Geographic Limitations:** Most studies used South Asian populations; generalization to other populations needs to be examined.<sup>30,31,32</sup>

### Future Research Directions:

To advance evidence-driven integration of Unani psychiatry into contemporary mental healthcare following research priorities are recommended:

#### 1. Psychometric Validation of Temperament Assessment:

Develop and validate standardized instruments for *Mizāj* assessment with proven reliability, validity, and cultural sensitivity - Test for convergent validity with contemporary personality measures and psychiatric diagnostic tools - Develop normative data in heterogeneous samples and age groups.<sup>15,16,36</sup>

#### 2. Prospective Cohort Studies:

Conduct large-scale, multi-center prospective cohort studies examining temperament as a predictor of psychiatric disorder incidence, course, and treatment response - Investigate gene-environment interactions in temperament-psychopathology relationships - Examine temperament stability and change across the lifespan.<sup>1,3,30</sup>

#### 3. Mechanistic and Biomarker Research:

Design clinical trials with full biomarker panels (oxidative stress markers, inflammatory cytokines, HPA axis hormones, neurotransmitter metabolites) before and after Unani interventions -Use neuroimaging (fMRI, PET, MRS) analysis to determine the brain changes that are related to Unani therapies - Investigate gut microbiome changes with Unani diet and evacuation intervention, given emerging understanding of the microbiome-gut-brain axis.<sup>9</sup>

#### 4. Rigorous Clinical Trials:

Rigorously conducted, adequately powered, randomized, placebo-controlled trials of standardized Unani formulations for specific psychiatric indications (anxiety disorders, major depressive disorder, occupational burnout) -Use active comparators (standard psychotropics) to compare the efficacy of these formulations -Have long-term follow-up after the trial to monitor sustained effects and relapse

prevention -Investigate optimal dosing, treatment duration, and patient selection criteria.<sup>27</sup>

#### 5. Pharmacological Research:

Systematically investigate the full range of Unani psychotropic herbs using contemporary pharmacological methods, including phytochemical characterization, mechanism of action studies, pharmacokinetic/pharmacodynamic research, and safety/toxicity assessments.<sup>47</sup>

#### 6. Occupational Health Interventions:

Develop and assess workplace interventions based on *Asbāb Sitta Ḍarūriyya* modifications that help to prevent burnout - Investigate temperament-tailored stress management programs in high-risk occupations - Conduct cost-effectiveness analyses comparing Unani-integrated interventions with standard occupational health interventions.<sup>2,7</sup>

#### 7. Integrative Care Models:

Build and trial integrative care models based on combinations of Unani and conventional psychiatric therapies - Explore patient choices, treatment compliance, and successful outcomes of integrative compared to routine care - Investigate provider training and competencies for caregivers of integrative interventions.<sup>2,43</sup>

#### 8. Theoretical and Epistemological Research:

An Important step in the treatment of Unani is conduct philosophical and historical investigations into the epistemic foundations of Unani medicine and possible points of crossover with biomedicine. Finally, conceptualizations should be generated for traditional and contemporary medical systems at all stages of integration that are respectful and non-reductive. Patient perspectives on integration should be studied through qualitative research.<sup>3,28</sup>

#### 9. Health Services Research:

Examine patterns of Unani medicine use for mental health in diverse populations - Investigate barriers and facilitators to integration within healthcare systems - Conduct health economic evaluations of Unani interventions

for mental health.<sup>43</sup>

#### 10. WHO Traditional Medicine Strategy

**Alignment:** Ensure research and practice are consistent with WHO guidelines for traditional medicine integration including safety monitoring, quality control, evidence-based practice standards - Contribute to developing international standards for Unani mental health practice.<sup>2</sup>

This path encourages the interplay of the comprehensive knowledge-based teachings found in Unani psychiatry and the sophisticated principles for modern mental health care, ensuring that these methods are highly accurate and culturally sensitive, bringing about more personalized healthcare services with cultural humility.

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