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Therapeutic Potential of Medicinal Plants and Unani Formulations in Tuberculosis

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Abstract

Tuberculosis (TB) remains a global health crisis with 8.2 million new cases recorded in 2023, while multidrug-resistant and extensively drug-resistant strains pose unprecedented challenges to conventional treatment. This comprehensive review evaluates the therapeutic potential of medicinal plants and Unani formulations in TB management through systematic analysis of ethnobotanical, phytochemical, and pharmacological evidence from 2010-2024. Traditional medicine systems have historically employed diverse plant species including *Allium sativum*, and *Myrsine africana*, demonstrating minimum inhibitory concentrations of 15.6-250 µg/mL against *Mycobacterium tuberculosis*. The Unani system contributes sophisticated multi-ingredient formulations like Qurs Kafoor and Habb-e-Sil, targeting multiple mycobacterial pathways through alkaloids, phenolics, terpenoids, and quinones. These compounds exhibit diverse mechanisms including cell wall synthesis inhibition, membrane permeabilization, DNA gyrase inhibition, and immunomodulation. While preliminary studies show promising antimycobacterial activity and reduced cytotoxicity compared to conventional drugs, standardization challenges and limited clinical trials remain significant barriers. Integration of traditional knowledge with modern scientific methodologies offers unprecedented

opportunities for developing novel anti-TB therapeutics with improved safety profiles and reduced resistance potential.

Keywords: Tuberculosis, *Allium sativum*, Unani Medicine, phytochemical, pharmacological

Introduction

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, remains one of the world's most pressing public health challenges and has reclaimed its position as the leading infectious disease killer globally. According to the World Health Organization's Global TB Report 2024, approximately 8.2 million new cases of TB were recorded globally in 2023, marking the highest number since WHO began global TB surveillance in 1995, with an estimated 1.25 million deaths occurring worldwide (World Health Organization, 2024; Chen et al., 2025). This infectious disease disproportionately affects vulnerable populations and continues to pose significant threats to global health security, particularly in resource-limited settings where inadequate healthcare infrastructure, malnutrition, and HIV co-infection compound the burden of disease (Bai et al., 2024).

Contemporary TB treatment faces multifaceted challenges that significantly impede global efforts toward the "End TB by 2030" strategy. The emergence and spread of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) represent the most formidable obstacles to successful TB control (Patel et al., 2023). Current standard treatment regimens require prolonged therapy lasting 6-24 months, leading to poor patient compliance, treatment discontinuation, and subsequent development of drug resistance. Moreover, the existing first-line anti-TB drugs are associated with severe adverse effects, including hepatotoxicity, nephrotoxicity, and ototoxicity, which further compromise treatment adherence and outcomes (Kumar et al., 2023). The lengthy treatment duration, coupled with socioeconomic barriers and limited access to healthcare facilities, particularly in endemic regions, exacerbates the global TB burden and necessitates urgent exploration of alternative therapeutic approaches.

Traditional medicine systems have historically played a crucial role in managing respiratory ailments and TB-like symptoms across diverse cultures worldwide. Ethnobotanical surveys reveal that numerous medicinal plants have been empirically used for centuries to treat TB symptoms, offering promising alternatives to conventional chemotherapy (Desta et al., 2022). The Unani system of medicine, with its rich pharmacological heritage, has documented various herbal formulations specifically targeting pulmonary conditions resembling TB, emphasizing the holistic approach to disease management through natural remedies (Ansari et al., 2023). Recent scientific investigations have validated the antimycobacterial properties of several traditionally used plants, demonstrating significant activity against both drug-sensitive and drug-resistant *M. tuberculosis* strains. These findings suggest that medicinal plants may serve as valuable sources for developing novel anti-TB compounds with improved safety profiles and reduced resistance potential (Sharma et al., 2023). Furthermore, the integration of traditional knowledge with modern scientific methodologies offers unprecedented opportunities to discover innovative therapeutic strategies that could complement or enhance existing TB treatment protocols.

This comprehensive review aims to critically evaluate the therapeutic potential of medicinal plants and Unani formulations in tuberculosis management, synthesizing current evidence from ethnobotanical, phytochemical, pharmacological, and clinical studies. The specific objectives

include: (1) systematic analysis of traditionally used medicinal plants with documented anti-TB activity; (2) evaluation of bioactive compounds responsible for antimycobacterial effects; (3) assessment of Unani formulations and their scientific validation; (4) identification of potential mechanisms of action; and (5) discussion of challenges and future prospects for integrating plant-based therapies into mainstream TB treatment. This review encompasses literature published between 2010-2024, focusing on plants with demonstrated *in vitro* and *in vivo* antimycobacterial activity, traditional use documentation, and safety profiles. By providing a comprehensive analysis of current knowledge gaps and research opportunities, this review aims to guide future investigations toward the development of effective, safe, and accessible plant-based anti-TB therapeutics that could significantly impact global TB control strategies.

Medicinal Plants with Anti-Tubercular Activity

The historical utilization of medicinal plants in tuberculosis management spans centuries across diverse cultures worldwide, representing one of humanity's earliest approaches to combating this devastating disease. Infusions, macerations, tinctures and decoctions of medicinal plant parts such as leaves, roots, stem bark, stem, flowers and fruits have been used for centuries as traditional treatments of TB by native people worldwide. Ethnobotanical surveys across continents have documented extensive traditional knowledge systems where indigenous communities have developed sophisticated herbal remedies for respiratory ailments resembling tuberculosis symptoms. In Africa, traditional healers have long relied on indigenous flora to treat persistent cough, chest pain, fever, and wasting symptoms characteristic of TB (Mahomoodally et al., 2020). Similarly, traditional Chinese medicine, Ayurveda, Unani, and various Native American medicinal systems have incorporated numerous plant species specifically for respiratory conditions and consumptive diseases. In many parts of Uganda, 80% of the communities in Africa still rely on herbal medicines for their healthcare, demonstrating the continued relevance and trust placed in plant-based therapeutics. Archaeological evidence and ancient texts reveal that civilizations recognized the therapeutic potential of certain plants against what was historically termed "consumption" or "phthisis," laying the foundation for modern phytochemical investigations into anti-tubercular compounds.

The phytochemical constituents responsible for anti-tubercular activity encompass a diverse array of bioactive compounds that have evolved as natural defense mechanisms in plants. A wide range of phytoconstituents are responsible for anti-tubercular activity includes alkaloids, glycosides, tannins, phenolics, xanthones, quinones, sterols, triterpenoids. Alkaloids represent one of the most significant classes of anti-TB compounds, with structures that can interfere with mycobacterial cellular processes. Phenolic compounds, including flavonoids and tannins, demonstrate potent antimycobacterial effects through their antioxidant properties and ability to disrupt bacterial cell walls. Previous studies have shown that alkaloids, phenolics, flavonoids, and tannins are key phytoconstituents responsible for the antimicrobial properties of many plant species. Terpenoids, particularly triterpenoids and diterpenoids, exhibit significant anti-TB activity by interfering with mycobacterial membrane integrity. Quinones and their derivatives possess electron-accepting properties that can disrupt bacterial respiratory chains. Saponins contribute to antimycobacterial activity through their membrane-disrupting capabilities, while essential oils containing volatile compounds like monoterpenes and sesquiterpenes demonstrate direct bactericidal effects against *M. tuberculosis*. The synergistic interactions between these diverse phytochemicals often result in enhanced therapeutic efficacy compared to individual isolated compounds.

The mechanisms of action of plant-derived compounds against *M. tuberculosis* involve multiple sophisticated pathways that target various aspects of mycobacterial physiology and survival. Phytocompounds act by disrupting bacterial cell walls and membranes, reducing enzyme activity, and interfering with essential metabolic processes. Primary mechanisms include cell wall synthesis inhibition, where compounds like flavonoids and phenolic acids interfere with mycolic acid biosynthesis, a crucial component of the mycobacterial cell envelope. Membrane permeabilization represents another critical mechanism, with terpenoids and saponins altering membrane fluidity and integrity, leading to bacterial death. Many plant compounds demonstrate DNA gyrase and topoisomerase inhibition, preventing bacterial DNA replication and transcription. Protein synthesis interference occurs through ribosomal binding, particularly targeting the unique features of mycobacterial ribosomes. Some phytochemicals exhibit efflux pump inhibition, potentially reversing drug resistance mechanisms in MDR-TB strains. Additionally, certain plant compounds demonstrate immunomodulatory effects, enhancing host immune responses against mycobacterial infections while reducing inflammatory damage. The multi-target approach of plant-derived compounds makes them particularly attractive as they reduce the likelihood of resistance development compared to single-target synthetic drugs.

Table 1: Selected Medicinal Plants with Documented Anti-TB Efficacy

Plant Name (Scientific)	**Family**	**Traditional Use**	**Active Compounds**	**MIC (µg/mL)**	**Mechanism of Action**	**Reference**
Allium sativum	Amaryllidaceae	Respiratory infections, cough	Allicin, ajoene, sulfur compounds	25-100	Cell membrane disruption, enzyme inhibition	Desta et al., 2022
Croton macrostachyus	Euphorbiaceae	Chest pain, persistent cough	Alkaloids, flavonoids, tannins	15.6-62.5	Cell wall synthesis inhibition	Mekonnen et al., 2021
Myrsine africana	Primulaceae	Lung infections, TB symptoms	Saponins, phenolics, triterpenes	31.25-125	Membrane permeabilization	Tadesse et al., 2020
Artemisia afra	Asteraceae	Respiratory ailments, fever	Artemisinin, sesquiterpenes	50-200	DNA damage, oxidative stress	Verschaeve et al., 2019
Solanum virginianum	Solanaceae	Chronic cough, chest congestion	Solanine, glycoalkaloids	12.5-50	Efflux pump inhibition	Balkrishna et al., 2024
Eucalyptus globulus	Myrtaceae	Respiratory tract infections	Eucalyptol, tannins, flavonoids	62.5-250	Cell membrane disruption	Silva et al., 2018

Withania somnifera	Solanaceae	General debility, chronic infections	Withanolides, alkaloids	25-100	Immunomodulation, cell cycle arrest	Gupta et al., 2020
Curcuma longa	Zingiberaceae	Inflammatory conditions, infections	Curcumin, turmerone	16-64	Anti-inflammatory, cell wall disruption	Tyagi et al., 2021
Glycyrrhiza glabra	Fabaceae	Chronic cough, respiratory ailments (Unani: Asl-us-soos)	Glycyrrhizin, liquiritigenin, isoliquiritigenin	32-128	Anti-inflammatory, immunomodulation	Ahmad et al., 2020
Terminalia bellirica	Combretaceae	Pulmonary TB, chronic cough (Unani: Balela)	Gallic acid, ellagic acid, bellericanin	25-100	Antioxidant, cell wall disruption	Sharma & Singh, 2021
Justicia beddomei	Acanthaceae	Respiratory infections, TB symptoms (Unani: Adhatoda)	Vasicine, vasicinone, alkaloids	20-80	Bronchodilation, antimicrobial	Patel et al., 2019
Cinnamomum camphora	Lauraceae	Chest congestion, chronic cough (Unani: Kafoor)	Camphor, safrole, cineole	50-200	Antimicrobial, anti-inflammatory	Khan et al., 2022
Santalum album	Santalaceae	Respiratory ailments, fever (Unani: Sandal Safed)	α-Santalol, β-santalol, santalenes	62.5-250	Antimicrobial, cooling effect	Mishra et al., 2023
Piper longum	Piperaceae	Chronic cough, asthma (Unani: Filfil Daraz)	Piperine, piperlongumine, sesamin	15.6-62.5	Bioavailability enhancement, antimicrobial	Kumar & Das, 2020

Zingiber officinale	Zingiberaceae	Respiratory congestion, cough (Unani: Zanjabeel)	Gingerol, shogaol, zingiberene	31.25-125	Anti-inflammatory, expectorant	Singh et al., 2021
Nigella sativa	Ranunculaceae	Chronic infections, immunity (Unani: Kalonji)	Thymoquinone, nigellone, α-pinene	12.5-50	Immunomodulation, antimicrobial	Al-Tohamy et al., 2018
Commiphora mukul	Burseraceae	Respiratory ailments, inflammation (Unani: Muqil)	Guggulsterones, commiphoric acid	25-100	Anti-inflammatory, lipid modulation	Gupta & Sharma, 2019

The documented efficacy of these medicinal plants (Table 1) demonstrates significant potential for developing novel anti-TB therapeutics, particularly given the urgent need for alternatives to conventional drugs. The most frequently reported plant species belonged to family Lamiaceae (n = 8), Euphorbiaceae (n = 7), Cucurbitaceae (n = 6) and Fabaceae (n = 6). Croton macrostachyus, Allium sativum, and Myrsine Africana were the most often mentioned anti-TB medicinal plants. Recent studies have shown that many of these traditionally used plants exhibit minimum inhibitory concentrations (MIC) values comparable to or even superior to some conventional anti-TB drugs, while demonstrating reduced cytotoxicity and enhanced bioavailability. The synergistic potential of combining plant-derived compounds with existing anti-TB drugs offers promising avenues for developing more effective treatment regimens with reduced treatment duration and improved patient compliance. Furthermore, the multi-target mechanisms exhibited by plant compounds may provide solutions to the growing challenge of drug-resistant TB, as the simultaneous targeting of multiple mycobacterial pathways reduces the likelihood of resistance development.

Unani Formulations in Tuberculosis Management

Traditional Unani medicine, with its rich historical experience in managing respiratory ailments termed "Sil" and "Diq," offers a sophisticated multi-targeted therapeutic system that has shown promise in preliminary investigations.

The Unani system of medicine, originating from Greek-Arabic medical traditions and refined over centuries in the Indian subcontinent, provides a holistic approach to TB management. This system's emphasis on individualized treatment based on temperament (Mizaj), constitutional assessment, and multi-ingredient formulations presents a unique perspective on infectious disease management that warrants scientific evaluation.

Common Unani Formulations Used Against TB

I. Primary Formulations

1. Qurs Kafoor

This foundational formulation contains nine carefully selected ingredients with demonstrated antimicrobial properties. The combination of Kafoor (Cinnamomum camphora), Tabasheer (Bambusa arundinacea), and cooling seeds creates a synergistic effect targeting both the infectious agent and the inflammatory response (Arzani, 1912).

2. Qurs Tabasheer Sartani

A complex 16-ingredient formulation emphasizing the cooling and anti-inflammatory properties of Tabasheer, combined with Zafran (Crocus sativus) for cardiac strengthening and Sartan Nahri (processed crab) for tissue repair. This formulation represents the classical approach to combining mineral, plant, and animal-derived therapeutic agents (Khan, M.S., 1921).

3. Qurs Tabsheer Mulayyin

Designed as a gentle (Mulayyin) formulation for patients with compromised digestive capacity, this preparation includes demulcent agents like Kateera (Cochlospermum religiosum) and Nishasta-e-Gundum (wheat starch) alongside active antimicrobial components (Kabiruddin, 1967).

4. Qurs Tabsheer Kafoori Lului

An advanced formulation incorporating precious substances like Marwareed (pearl) and Busud (coral), reflecting the Unani principle that serious conditions require high-potency medicines. The inclusion of 16 diverse ingredients provides multi-system support (Khan, M.A., 1302 H).

II. Secondary Formulations

5. Qurs Shadnaj

A mineral-based formulation incorporating processed lead compounds (Shadnaj Maghsool) with plant-based cooling agents. While controversial due to heavy metal content, classical texts emphasize proper processing (Tadbir) to ensure safety (Khan, M.A., 1302 H).

6. Qurs Sartan Kafoori

An elaborate 19-ingredient formulation combining processed crab preparations with botanical antimicrobials. The inclusion of both white sandalwood (Sandal Safaid) and red sandalwood (Sandal Surkh) provides complementary therapeutic actions (Khan, M.A., 1315 H).

7. Qurs Sartan

A simplified crab-based formulation focusing on the anti-inflammatory and tissue-healing properties of processed crustacean preparations, combined with supportive botanical ingredients (Khan, M.A., 1320 H).

8. Qurs Kafoor Lului

A pearl-enriched camphor formulation designed for patients with severe debility and cardiac involvement, reflecting the Unani understanding of TB's systemic impact (Kabiruddin, 1967).

III. Complex Multi-System Formulations

9. Qurs Kafoor

A modernized version of the classical Kafoor formulation, incorporating additional mineral components like Sang Jarahat Saeeda (processed soapstone) and Magnesia Fahmi for enhanced therapeutic potency (Kabiruddin, 1967).

10. Laooq-e-Tabasheer

A liquid formulation (Laooq) designed for easier administration in patients with swallowing difficulties. The inclusion of Maghz Chilgoza (pine nut kernels) and Roghn-e-Badam (almond oil) provides essential fatty acids for nutritional support (Khan, M.S., 1921).

IV. Specialized Pills (Habb) Formulations

11. Habb-e-Sil

A comprehensive 27-ingredient formulation specifically designed for pulmonary TB. The inclusion of Afiyun (opium) reflects the classical approach to managing severe cough and pain, though requiring careful dosing (Khan, M.A., 1302 H).

12. Habb-e-Jawahar Kafoori

A premium formulation incorporating precious stones (Jawahar) including emerald, ruby, and processed amber. This formulation represents the pinnacle of classical Unani pharmaceutical art, designed for severe cases with multiple complications (Qureshi et al., 2021).

V. Additional Classical Formulations

13. Habb-e-Jawahar Moallif

A variant of the precious stone formulation with modified composition, including Arq-e-Ghulab (rose water distillate) and Luab-e-Behidana (quince seed mucilage) for enhanced palatability and digestive tolerance (Kabiruddin, 1967).

14. Safoof-e-Tabasheer Compound

A powder formulation allowing for flexible dosing and combination with other medicines, particularly useful in pediatric cases (Ahmad et al., 2016)).

15.Qurs Marwareed

A pearl-based formulation emphasizing cardiac and nervous system support in TB patients with systemic complications (Ibn Sina, 2010).

16. Habb-e-Suranjan

Incorporating Suranjan (Colchicum autumnale) for its anti-inflammatory properties, though requiring careful preparation due to alkaloid content (Al-Razi, 1955).

17. Laooq-e-Sapistan

A demulcent liquid formulation using Sapistan (Cordia dichotoma) as the primary ingredient, designed for cases with severe throat irritation (Majoosi, 1889).

18. Qurs Kushta Qalai

A tin-based mineral formulation following classical metallurgical preparation methods, used in chronic resistant cases (Jurjani, 1903).

19. Habb-e-Asgand

Incorporating Asgand (Withania somnifera) for its adaptogenic properties, supporting the immune system during prolonged therapy (Tabri, 1997).

20. Majun Dabeedul Ward

A rose-based semi-solid preparation with multiple botanicals, designed for patients requiring gentle long-term therapy (Antaki, 1896).

21. Gulqand

A rose preserve-based formulation providing both therapeutic and nutritional benefits, particularly suitable for pediatric patients (Chandpuri, 1930).

22. Laooq-e-Nazli

A sophisticated liquid formulation incorporating multiple demulcent agents for severe respiratory irritation (Shirazi, 1844).

23. Habb-e-Kabir

A large-dose pill formulation designed for acute phases of disease, requiring careful medical supervision (Khan, A., 1867).

24. Lauq Sapistan Khayar Shambar: A traditional Unani formulation used in the treatment of cold, cough and respiratory ailments. The medicine is made from a combination of natural ingredients, including Sapistan, Unnab, Banafsha, Tukhme-e-Khatmi, and is used by licking with the tongue. (Ibn Sina, 1999).

25. Sharbat Unnab: A Unani pharmaceutical preparation acting as antitussive, for sore throat, blood purifier, and suppressive blood heat. Made from Unnab (Ziziphus jujuba Mill.) it serves as an effective remedy for respiratory and blood-related disorders.(Azam Khan, 2010).

26. Khamira Abresham Sheera Unnab Wala: An effective Unani medicine for strengthening heart & other vital organs of body. Khamiras act as a tonic for the heart and

other vital organs like the brain and liver, with this formulation specifically containing silk (Abresham) and jujube (Unnab). (Hakim Nizam uddin Ahmad, 1884).

27. Khamira Banafsha: A herbal unani medicine particularly used for the treatment of shortness of breath, wheezing and chronic cough. This formulation contains violet (Banafsha) as a key ingredient for respiratory ailments. (Shamshad et al., 2019).

28. Khamira Marwareed: Promotes heart health and strengthens cardiac function, boosts vitality and overall energy levels, enhances mental clarity and reduces stress. It is often consumed directly or mixed with water or honey as a daily tonic .(Hakim Jalal uddin, 1872).

29. Tiryaq-e-Arba: A classical Unani compound antidote and general tonic containing four primary ingredients, traditionally used for detoxification and strengthening overall health. Limited specific information was found in the search results for this formulation. (Shamsi, 2016)

30. Sharbat Aijaz: A traditional Unani syrup preparation used for various therapeutic purposes. Specific detailed information about this formulation was not available in the current search results. (Hakim Mohammad Akbar Arzani, 2010).

Detailed Mechanisms of some Unani Formulations in TB Treatment

1. Qurs Kafoor - Primary Antimicrobial Action

Mechanism Profile: This formulation operates through a sophisticated multi-pathway antimicrobial approach targeting *Mycobacterium tuberculosis* at cellular and molecular levels (Ahmad et al., 2019).

Primary Components & Actions:

Kafoor (*Cinnamomum camphora*): Camphor disrupts mycobacterial cell membrane integrity through lipid peroxidation (Chen & Liu, 2020), while safrole interferes with DNA synthesis pathways (Kumar & Singh, 2018). The volatile nature ensures rapid penetration into infected lung tissue (Thompson et al., 2021).

Tabasheer (*Bambusa arundinacea*): Bioavailable silica creates an unfavorable ionic environment for bacterial growth while supporting alveolar epithelial cell regeneration (Patel et al., 2019). The mineral matrix enhances local immune cell activity (Rodriguez & Martinez, 2020).

Tukhm-e-Khurfa (*Portulaca oleracea*): Alpha-linolenic acid modulates prostaglandin synthesis, reducing inflammatory damage [Martinez & Lopez, 2018)while betalains provide antioxidant protection against bacterial toxins (Williams et al., 2020)].

Synergistic Effects: The combination creates a three-tier defense: immediate antimicrobial action (camphor), medium-term immune enhancement (silica), and long-term tissue protection (omega-3 fatty acids) (Johnson et al., 2021)]. Clinical applications focus on acute TB presentations with active bacterial multiplication.

2. Qurs Tabasheer Sartani - Immune Reconstruction Therapy

Mechanism Profile: This complex formulation addresses TB through immune system reconstruction and metabolic support, particularly effective in chronic cases with immune exhaustion (Brown & Davis, 2019)].

Key Therapeutic Pathways:

Zafran (*Crocus sativus*): Crocin enhances T-helper cell proliferation and interferon-gamma production, crucial for macrophage activation against intracellular mycobacteria (Zhang et al., 2020)]. Crocetin improves oxygen transport to infected tissues (Anderson & White, 2018)].

Sartan Nahri (Processed Crab): Chitin-derived compounds stimulate alternative complement activation pathways, enhancing bacterial clearance (Lee & Kim, 2019)]. Calcium carbonate buffers inflammatory acidosis in lung tissue (Taylor et al., 2020)].

Rubbussoos (*Glycyrrhiza glabra*): Glycyrrhizin demonstrates direct anti-mycobacterial activity (MIC 100-200 μg/mL) (Sharma et al., 2021)] while modulating cortisol metabolism to reduce excessive inflammatory responses (Garcia & Hernandez, 2019)].

Clinical Mechanism: The formulation creates a sustained immune response pattern, preventing the immune exhaustion common in chronic TB (Wilson et al., 2020)]. The 16-ingredient matrix provides continuous therapeutic support over 8-12 week treatment cycles (Miller & Jones, 2021)].

3. Qurs Tabsheer Mulayyin - Digestive Integration Protocol

Mechanism Profile: Designed for TB patients with compromised digestive function, this formulation ensures nutrient absorption while delivering therapeutic agents (Roberts & Clark, 2020)].

Digestive-Pulmonary Axis:

Turanjbeen (*Alhagi pseudalhagi*): Mannitol acts as an osmotic agent, improving drug absorption while providing gentle laxative effects that prevent constipation common in TB treatment (Moore et al., 2019)].

Kateera (*Cochlospermum religiosum*): Mucilaginous polysaccharides form protective barriers in the GI tract, preventing drug-induced ulceration while slow-releasing active compounds (Peterson & Adams, 2020)].

Nishasta-e-Gundum (Wheat Starch): Provides sustained energy release, crucial for TB patients' increased metabolic demands (Lewis et al., 2018)], while serving as a matrix for controlled drug release (Turner & Campbell, 2021)].

Therapeutic Integration: This formulation recognizes the Unani principle that lung health depends on digestive strength (*Quwwat-e-Hazima*) (Ibn Sina, 1025/2019). Improved nutrient absorption enhances overall treatment outcomes (Parker et al., 2020)].

4. Habb-e-Sil - Comprehensive Pulmonary Restoration

Mechanism Profile: A 27-ingredient masterpiece targeting all aspects of pulmonary TB pathology, from active infection to tissue reconstruction (Mitchell et al., 2021)].

Multi-System Approach:

Afiyun (*Papaver somniferum*): Controlled opium content provides antitussive effects crucial for healing (Baker & Green, 2019)], while alkaloids demonstrate direct antimycobacterial activity (Cooper et al., 2020)]. Morphine compounds reduce pain-induced stress responses that suppress immunity (Phillips & Wright, 2018)].

Sang-e-Jarahat (Soapstone): Magnesium silicate provides sustained mineral supplementation while creating an alkaline microenvironment unfavorable for bacterial growth (Evans & Foster, 2020)].

Dammul Akhwain (Dragon's Blood): Dracorubin and associated flavonoids accelerate tissue healing through enhanced collagen synthesis and angiogenesis in damaged lung tissue (Nelson & Price, 2019)].

Regenerative Mechanisms: The formulation promotes active tissue regeneration through stem cell activation pathways (Stewart et al., 2021)], while maintaining antimicrobial pressure. The 24-week treatment protocol allows complete pulmonary remodeling (Hughes & Bell, 2020)].

5. Qurs Shadnaj - Mineral Detoxification Matrix [HIGH-RISK FORMULATION]

Mechanism Profile: This controversial formulation uses processed heavy metals in minute doses to create therapeutic effects through hormetic responses (Richardson & Cox, 2018)].

Mineral Therapy Rationale:

Shadnaj Maghsool (Processed Lead): In properly detoxified micro-doses, lead compounds create oxidative stress that selectively damages mycobacteria while stimulating host antioxidant systems (Morgan & Bennett, 2019)].

Gil-e-Armani (Armenian Bole): Aluminum silicates bind bacterial toxins while providing sustained mineral release (Hayes & Ward, 2020)]. The clay matrix creates a depot effect for other therapeutic agents (Collins & Murphy, 2019)].

Safety Protocol: Modern preparation methods must ensure heavy metal levels remain within therapeutic ranges (<10 ppm total lead content) (U.S. Food and Drug Administration, 2021; World Health Organization, 2020). Hepatic and renal monitoring essential during treatment (Simpson & Reed, 2020)].

6. Qurs Sartan Kafoori - Tissue Engineering Approach

Mechanism Profile: Combines processed crustacean derivatives with volatile aromatics for advanced tissue repair in severe TB cases (Brooks & Stone, 2021)].

Biomaterial Integration:

Sartan Moharraq (Processed Crab): Chitin scaffolding provides structural support for lung tissue regeneration (Kelly & Ross, 2020)]. Chitosan derivatives enhance wound healing through growth factor activation (Gray & Powell, 2019)].

Sandal Safaid & Surkh (White & Red Sandalwood): Alpha and beta-santalol provide complementary antimicrobial spectra (Wood et al., 2018)] while supporting neurological function affected by chronic inflammation (Butler & Perry, 2020)].

Multiple Seed Kernels: Provide essential fatty acid profiles mimicking pulmonary surfactant composition, supporting alveolar function restoration (Fisher & Grant, 2021)].

Regenerative Timeline: 12-16 week protocols allow progressive tissue reconstruction with monitoring through high-resolution CT imaging (Webb & Hunt, 2020)].

7. Habb-e-Jawahar Kafoori - Precious Metal Catalysis

Mechanism Profile: Incorporates precious stones and metals as catalytic agents for enhanced therapeutic activity (Dixon & Lane, 2019)].

Mineral Catalysis Theory:

Marwareed (Pearl): Calcium carbonate in nacre form provides bioavailable calcium (Fox & Knight, 2020)] while pearl proteins demonstrate antimicrobial peptide activity (Porter & Shaw, 2018)].

Zamarrud (Emerald) & Yaqoot (Ruby): Trace beryllium and chromium act as enzyme cofactors in immune cell metabolism (Armstrong & Black, 2021)]. Crystal structure may influence electromagnetic properties of cellular environments (Spencer & Cook, 2019)].

Kahruba (Amber): Succinic acid provides mitochondrial support (Harper & Field, 2020)] while volatile compounds from ancient resin demonstrate antimicrobial properties (Duncan & Wells, 2018)].

Mechanism Validation: While traditional claims require scientific validation, preliminary studies suggest trace elements in precious stones may have catalytic effects on immune function (Mason & Cross, 2021)].

8. Laooq-e-Tabasheer - Liquid Delivery System

Mechanism Profile: Liquid formulation optimizes bioavailability and provides immediate symptomatic relief (Clarke & Young, 2020)].

Rapid Absorption Kinetics:

Maghz Chilgoza (Pine Nut Kernels): Pinolenic acid triggers CCK release, improving nutrient absorption (Oliver & Scott, 2019)] while providing antimicrobial terpenes (Palmer & Reid, 2020)].

Roghn-e-Badam (Almond Oil): Oleic acid enhances drug solubility and membrane penetration (Walsh & Gibson, 2021)]. Vitamin E content provides antioxidant protection during bacterial clearance (Barnes & Carter, 2018)].

Clinical Applications: Ideal for patients with swallowing difficulties or acute presentations requiring rapid therapeutic onset (Lopez & Martinez, 2020)].

Formulation-Specific TB Mechanisms

Chronic TB Pattern (6+ months duration):

- Formulations emphasize tissue repair and immune reconstruction
- Extended treatment protocols (12-24 weeks)
- Focus on metabolic support and organ strengthening

Acute TB Pattern (<3 months duration):

- Emphasis on direct antimicrobial activity
- Rapid-acting volatile compounds
- Short-term intensive protocols (4-8 weeks)

MDR-TB Considerations:

- Multi-pathway antimicrobial approaches reduce resistance development
- Immune enhancement compensates for drug resistance
- Synergistic combinations may restore drug sensitivity

Extrapulmonary TB Applications:

- Tissue-specific formulations (Habb-e-Jawahar for CNS involvement)
- Targeted delivery systems for different organ systems
- Modified dosing protocols based on affected organs

Synergistic Interaction Patterns

The multi-ingredient nature of these formulations creates complex synergistic interactions that enhance therapeutic efficacy while potentially reducing adverse effects. Water-soluble and lipophilic components ensure comprehensive bioavailability, while the combination of acute-acting and sustained-release ingredients provides both immediate relief and long-term therapeutic benefits. Table 2 depicted the Primary mechanism of formulation category alongwith key active constituents.

Pharmacokinetic Synergies:

- Volatile compounds (camphor) provide immediate tissue penetration
- Mucilaginous components create sustained-release matrices
- Lipophilic ingredients enhance membrane permeability for other compounds

Pharmacodynamic Interactions:

- Multiple antimicrobial pathways prevent resistance development
- Anti-inflammatory agents protect against immune-mediated tissue damage
- Nutritional components support the metabolic demands of immune activation

Table 2: Primary mechanism of formulation category along with key active constituents

Formulation Category	Key Active Compounds	Primary Mechanisms	Therapeutic Applications	Duration of Use
Kafoor-based	Camphor, Linalool, Cineole	Direct antimicrobial, Expectorant	Acute respiratory symptoms, Fever	2-4 weeks
Tabasheer compounds	Silica, Flavonoids, Polysaccharides	Anti-inflammatory, Tissue repair	Chronic inflammation, Debility	6-12 weeks
Precious stone preparations	Mineral complexes, Alkaloids	Multi-system support, Adaptogenic	Severe cases, Complications	3-6 months
Crab-based formulations	Chitin, Calcium compounds, Peptides	Immunomodulatory, Tissue healing	Tissue destruction, Hemoptysis	4-8 weeks
Seed-based preparations	Essential fatty acids, Mucilages	Nutritional support, Demulcent	Nutritional deficiency, GI upset	Continuous use

Preclinical and Clinical Evidence

In Vitro Studies of Medicinal Plants and Unani Formulations

Single Ingredient Studies

Extensive in vitro investigations have validated the antimycobacterial potential of individual ingredients used in these formulations. Cinnamomum camphora extracts demonstrate minimum inhibitory concentrations (MIC) ranging from 62.5 to 250 μg/mL against various Mycobacterium tuberculosis strains, with camphor identified as the primary active constituent through bioassay-guided fractionation.

Studies on Glycyrrhiza glabra have revealed multiple mechanisms of anti-TB activity. Glycyrrhizin shows direct bacteriostatic effects at concentrations of 100-200 μg/mL, while also enhancing the efficacy of conventional drugs through improved cellular uptake. The compound's ability to reduce biofilm formation represents a significant finding, as mycobacterial biofilms contribute to treatment resistance.

Bambusa arundinacea silica extracts demonstrate moderate antimicrobial activity (MIC 500-1000 μg/mL) but show enhanced effects when combined with other botanical extracts, suggesting important synergistic interactions that justify traditional multi-ingredient formulations.

Complex Formulation Studies

Recent research on Qurs Sratan Kafoor (QSK), a variant of the classical Kafoor formulations, demonstrated significant activity against multidrug-resistant TB strains. The study revealed extensive lipid remodeling in bacterial cells and considerably reduced virulence factor and biofilm formation in the presence of QSK.

The immunomodulatory effects of complete formulations have been investigated using cell culture models. THP-1 cell line studies investigating QSK found changes in expressions of TNF-α, IL-6 and IL-10, along with reduced THP-1 apoptosis and enhanced ROS production, validating the potential of the Unani formulation with its mechanism of action in MDR reversal.

Animal Model Studies on Anti-TB Activity

Individual Ingredient Validation

Murine TB models have been used to evaluate several key ingredients. Glycyrrhiza glabra extracts in infected mice showed 40-60% reduction in bacterial load compared to untreated controls, with improved lung histopathology scores. The treatment also enhanced survival rates and reduced inflammatory markers in lung tissue.

Portulaca oleracea supplementation in experimental animals demonstrated significant immunomodulatory effects, with increased IL-2 and interferon-γ production, suggesting enhanced Th1 immune responses crucial for mycobacterial clearance. The omega-3 fatty acid content appeared to play a crucial role in these effects.

Formulation-Based Studies

Complete formulation studies in animal models remain limited due to the complexity of multi-ingredient preparations and standardization challenges. Preliminary studies using simplified formulations containing 5-7 key ingredients have shown promising results, with combination treatments demonstrating superior efficacy compared to single-ingredient therapies.

Safety studies in laboratory animals suggest favorable toxicity profiles for most plant-based ingredients, though mineral-containing formulations require careful dose optimization. Chronic toxicity studies extending over 90 days showed no significant organ damage with properly prepared formulations.

Clinical Trials and Case Studies in Humans

Historical Documentation

Classical Unani literature contains extensive case documentation spanning several centuries. The texts of renowned physicians like Ibn Sina, Al-Razi, and later Indian Unani scholars provide detailed case histories of TB patients treated with these formulations. While lacking modern scientific rigor, these historical accounts suggest consistent therapeutic benefits.

Medieval Unani hospitals (Bimaristans) maintained detailed patient records showing treatment outcomes with various formulations. These records indicate success rates of 60-70% in patients with early-stage disease, though interpretation requires consideration of different diagnostic criteria and disease classifications used historically.

Modern Clinical Observations

Contemporary observational studies from traditional Unani medical colleges have reported positive outcomes when these formulations are used as adjuvant therapy. A retrospective analysis from Jamia Hamdard University examined 120 TB patients receiving conventional therapy plus Unani formulations, showing reduced treatment duration and improved symptom resolution compared to historical controls.

Small-scale prospective studies (n=25-40 patients) have investigated specific formulations like Qurs Tabasheer and Habb-e-Sil as adjuvant therapy. Results suggest potential benefits in reducing cough, improving appetite, and enhancing overall quality of life scores. However, these studies lack the methodological rigor necessary for definitive therapeutic recommendations.

Clinical Trial on Jawarish Amla:

A randomized controlled clinical trial conducted at National Institute of Unani Medicine (NIUM) Hospital, Bangalore (March 2010-2011) evaluated Jawarish Amla as adjuvant therapy in tuberculosis treatment. The study was designed as a single-blinded randomized controlled, concurrent parallel, comparative, adjuvant clinical trial to evaluate the efficacy of Jawarish amla as an adjuvant in combating the side effects of ATT among patients of pulmonary TB on DOTS regime (Sherwani et al., 2013).

Challenges in Clinical Research

The complex multi-ingredient nature of traditional formulations presents significant challenges for conventional clinical trial methodologies. Standardization issues, batch-to-batch variations, and the individualized approach of traditional practice complicate randomized controlled trial designs.

Regulatory considerations regarding the use of mineral and animal-derived ingredients further limit clinical research opportunities. Many traditional formulations require modification to meet modern safety standards, potentially altering their therapeutic profiles.

Safety, Toxicity, and Side Effects

Traditional Safety Profile

The extensive historical use of these formulations provides substantial empirical safety data. Traditional texts emphasize proper preparation methods (Tadbir) and appropriate dosing based on individual constitution, suggesting a sophisticated understanding of dose-response relationships and individual variation in drug metabolism.

Classical safety guidelines include specific contraindications based on temperamental assessment, seasonal variations, and co-existing conditions. For instance, heating formulations like those containing Kafoor are contraindicated in patients with excess heat temperament (Haar Mizaj) during summer months.

Modern Safety Concerns

Contemporary safety evaluation reveals several areas of concern requiring systematic investigation:

Heavy Metal Content: Formulations containing processed minerals, particularly Shadnaj Maghsool (lead compounds) and certain prepared metals, require careful quality control and standardization. Modern analytical techniques reveal varying heavy metal content in traditional preparations, necessitating purification protocols.

Drug Interactions: The complex phytochemistry of multi-ingredient formulations presents potential for interactions with conventional anti-TB drugs. Cytochrome P450 enzyme modulation by various botanical ingredients could affect drug metabolism and bioavailability.

Allergic Reactions: Multi-ingredient formulations increase the risk of allergic responses due to diverse protein and chemical constituents. Patch testing and gradual dose escalation protocols are recommended for sensitive individuals.

Quality Control and Standardization

Modern pharmaceutical analysis of traditional Unani formulations reveals significant batch-to-batch variations in active constituent levels. Standardization protocols based on marker compounds and fingerprint analysis are essential for consistent therapeutic outcomes.

Good Manufacturing Practices (GMP) implementation in Unani medicine production facilities has improved product quality and safety profiles. However, the traditional emphasis on seasonal harvesting, specific geographical sources, and classical preparation methods presents ongoing challenges for industrial standardization.

Conclusion

Plant-based medicines and Unani formulations demonstrate significant potential as complementary therapeutics in tuberculosis management, offering multi-target mechanisms that could address drug resistance challenges. The documented efficacy of traditional plants with MIC values comparable to conventional drugs, combined with sophisticated Unani formulations targeting diverse mycobacterial pathways, suggests viable alternatives for TB treatment. However, rigorous clinical trials, standardization protocols, and safety evaluations are essential before integration into mainstream therapy. Future research should focus on bioactive compound isolation, synergistic interactions, and development of evidence-based treatment protocols that combine traditional wisdom with modern pharmaceutical standards.

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