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Contents

Review Article

The Unlikely Doctor: Leech Therapy's Role in Human Health

Abstract

Leech therapy is one of the components of traditional medicine practiced from ancient times in humans. Leeches are used when conventional therapies fail to correct human ailments. The medicinal properties of leeches have been explored focusing on their saliva which is rich in bioactive compounds including hirudin, calin, hyaluronidase, destabilase, eglins, bdellins, tryptase inhibitors, and complement inhibitors. These compounds exhibited interesting biological activities such as anti-inflammatory, anticoagulant, antitumor, vasodilatory, and antibacterial effects. In humans, medicinal leeches are used for the treatment of various medical conditions such as inflammatory reactions, venous congestions, cardiovascular diseases, hypertension, varicose veins, osteoarthritis, thrombosis, hematomas, ophthalmic, respiratory, and dental infections and also in plastic and reconstructive surgeries. There are some minor contraindications where leech therapy is not used including absolute hemophilia, anemia, leukemia, hypotonia, and pregnancy. This review will give better insights to medical professionals based on the medicinal use of leeches that will warrant further scientific exploration in this traditional medical practice.

Keywords: *Bioactive compounds, hirudotherapy, leeches, medicine*

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Introduction

Hirudotherapy or leech therapy involves applying medicinal leeches to treat different medical ailments in human patients. The word leech originates from the Anglo-Saxon word "laece," which means physician indicating the value of leeches in the field of medicine.[1] *Hirudo asiatica*, *Hirudo medicinalis*, *Hirudinaria manillensis*, *Hirudo nipponia*, *Hirudo orientalis*, *Hirudinaria granulosa*, and *Macrobdella decora* are the most widely used medicinal leeches in leech treatment.[2] The medicinal use of leeches' dates back to ancient Egyptians. It is currently practiced by different medical practitioners including dermatology, neurology, gynecology, and reconstructive surgery specialists.[3] The medicinal properties of leeches are attributed to their saliva which contains more than 100 bioactive substances with hirudin as the most common bioactive compound.[4] These bioactive compounds in leech saliva possess a plethora of therapeutic properties such as anti-inflammatory, thrombolytic, anticoagulant, antibacterial, antitumor, vasodilatory, and anesthetic activities.[5,6]

In humans, medicinal leeches are used for the treatment of various medical conditions such as inflammatory reactions, venous congestions, cardiovascular diseases, hypertension, varicose veins, osteoarthritis, thrombosis, hematomas, ophthalmic, respiratory, and dental infections and also in plastic and reconstructive surgeries.[7-13] Knowing the myriad benefits of hirudotherapy, it is now gaining a good position in veterinary practice.[14] For leech application, the site should be clean, free from any chemical, and they are applied directly by hand or using an open-end syringe followed by its removal.[15] The number of leeches applied depends on the area that has to be treated.[15]

There are some minor contraindications where leech therapy is not used including absolute hemophilia, anemia, leukemia, hypotonia, and pregnancy.[16] Therefore, it is imperative to evaluate the health status of patients before applying leech on the affected areas. Frequently, leech therapy is accepted when all the other methods fail. This safe and effective therapeutic intervention is expected to grow in human and veterinary medicine with stunning results. In 2004, the FDA approved hirudotherapy as a medical tool in plastic

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and reconstructive surgeries.[1] Based on the above facts, we compiled this review to reintroduce medicinal leeches and their applications in human patients. The accumulation, assimilation, and distribution of knowledge and skills in this novel therapy will persuade professionals to develop this ancient practice toward human well-being.

Historical Overview of Leech Therapy

Hirudotherapy or medicinal leech therapy dates to ancient civilizations. It was one of the important forms of treatment for various ailments. A complete chapter in the ancient text of *Sushruta Samhita* was devoted to hirudotherapy. Hirudotherapy or leech therapy has roots in every ancient civilization and the earliest evidence of leech therapy dates to the primeval Egyptian period.[1,11] Its therapeutic use was reported by Chinese, Greeks, Americans, and Indians, where it is mostly practiced by Unani and Ayurveda practitioners.[17,18] In veterinary medicine, the records revealed the use of leeches for bloodletting in ancient Egypt on felines and other domestic animals. The use of leeches as medical devices was also documented in the Sanskrit writings. Nicander of Colophon (200–130 BC) was perhaps the earliest medical expert to utilize medicinal leeches for medicinal purposes.[19] Leech therapy was one of the standard practices during the 17th and 18th centuries, to treat many illnesses from gout to headaches.[20] With the advent of antibiotics in the 20th century, the practice of leech therapy slowly lost its market in human and veterinary patients. After identifying the therapeutic component of leech saliva, leech therapy started again to gain popularity in modern medicine. Hirudin is one of the most outstanding biological components that was discovered in the leech saliva by John Berry Haycraft in 1884. It was isolated by Jacoby in 1904, was employed in a blood transfusion procedure in 1915, and was further characterized by Fritz Markwardt in the 1950s.[21-23] Based on its therapeutic potential, the FDA approved its use in plastic and reconstructive surgeries in 2004.[1] Hence, it is gaining attention in human and veterinary practices to treat various medical derangements with excellent results.[2]

Leech Biology

Leeches are creepy bloodsucking annelid worms that are hermaphrodites and fit in the order *Arhynchobdellida*, family *Hirudinidae. Ou*t of 650 species, only 15 species are classified as therapeutic leeches, such as *H. medicinalis, H. verbena, H. orientalis, H. granulosa,* and *H. manillensis.*[17,24] Leeches have two suckers, one anterior and posterior; the anterior sucker has three sharp jaws each having 100 teeth (total of 300 teeth) and salivary glands that secrete more than 100 bioactive substances with medicinal properties; the wound after bite resembles a Mercedes-Benz symbol.[12,17] Medicinal leeches use their posterior sucker for locomotion, attachment, and the body are cylindrical and dorsoventrally flattened with 33 or 34 segments measuring up to 20 cm in length; on the head, five pairs of eyes are present, but their olfactory system helps them to sense their host.[6] Leeches dwell in fresh, clean waters in the temperature range of 0°C–30°C. Rapid temperature changes kill leeches.[5] Oxygen is consumed either dissolved or as atmospheric through the general body surface, and it can survive in closed containers containing dechlorinated water.[5]

Stress conditions force leeches to secrete a mucous layer, thus acting as a stress indicator. The periodical shedding of skin is reported in leeches, and the juvenile leeches gnaw into the skin of small water animals, frogs, and fish to take their meals.[25] After taking a single blood meal that is 10 times their body weight, leeches can survive for 1 year without a blood meal.[26] For feeding, leeches frequently linger on their host for 30–45 min and get puffed up with blood, and they can imbibe about 5–15 ml of blood, but the blood continues to leak for 4–24 h requiring antiseptic dressing.[12] For practicing hirudotherapy in humans and animals, the primary factor is the procurement of medicinal leeches from commercial leech breeding farms where leeches are bred for medicinal purposes.[6] Leeches collected directly from ponds, rivers, and streams can pose a severe threat to human and animal patients because they may be infected with bacterial, viral, parasitic, and fungal infections.[6,27]

Procedures in Leech Therapy

After receiving the leeches from commercial leech breeding farms, the therapist must select only healthy leeches and keep them in closed containers (glass or ceramic) with or without perforation, and dechlorinated water is changed twice a week.[6] Leech therapy in humans demands an expert therapist who treats the patients either once or at different intervals depending on the dynamics of the disease.[6] Studies revealed a better effect of leech therapy during morning hours due to the freshness of leeches and non-agitated behavior in the morning.[28,29] Morning hours are recommended for leech therapy. The leeches used for all medical procedures should be only obtained from a certified bio farm. They should be maintained, cultured, transported, and stored under clean environmental conditions. It is essential to protect patients undergoing leech therapy from other microbial infections.[6] In human patients, Ibn Sina, the famous medieval Arabic physician, stated that patients are instructed to have a light semi-solid meal before therapy. The afflicted area is carefully cleaned with distilled water or a borax solution and massaged until redness emerges. If the leech is hesitant to attach, a little droplet of blood may be placed on the area to be treated before applying the leech. Typically, one or more leeches are administered to the afflicted region and kept in the affected area for 30 min. Once attached, the leech will most likely remain safely in place until fully satisfied, but it is critical to examine the location regularly to verify that

the leech has not detached. The leeches are then carefully removed by tugging them off or weakening their hold with table salt, borax, or heat, although occasionally leeches detach naturally. The leeches that have been utilized are then killed followed by their disposal.[30]

When the leeches bite the host skin, the patient remains quiet because the leech saliva contains an anesthetic-like substance that alleviates the pain.[31] After complete feeding, the leech drops off, and blood flow continues from the bite area, which is considered an element of the treatment procedure in both humans and animals. Once the bleeding stops, the hirudotherapist dresses the wound with an antiseptic solution with the help of suitable bandage material.[32] After completing the therapy procedures, the medicinal leeches are kept in a 70% alcohol container for 4–5 min which kills them. Finally, the leeches are disposed of as an infectious biological agent.[4]

Therapy's Medicinal Effects

In human medicine, leeching is practiced since the beginning of civilization, and the credit goes to their salivary glands producing a plethora of therapeutic compounds including hirudin, destabilase, eglins, bdellins, chloromycetin, hyaluronidase, histamine-like substances, and some neurotransmitters.[33-36] Eglin proteins are without cysteine residues; hirudin, tryptase inhibitors, bdellin-B3, and saratin are with six cysteine residues; carboxypeptidase inhibitors with eight cysteine residues; hirustatin with 10 cysteine residues, whereas destabilase are with 14 cysteine residues.[37] Hirudin is one of the most significant proteins recognized for its strong antithrombotic properties.[38] Hirudin also shows a synergistic effect with other isolated bioactive substances such as antistasin and ghilanten which are documented as potent inhibitors of blood coagulation factor Xa.[5] Recently, hirudin-HN, a new anti-thrombin protein in the saliva of a medicinal leech *H. nipponia* was identified and characterized.[39] In addition to the anticoagulant effect, leech saliva shows anti-inflammatory, antimicrobial, antioxidative, and analgesic properties.[2,40] Bdellin is the compound present in leech saliva that reduces the production of protease involved in the inflammatory processes.[6] The antibiotic activity of leech saliva is related to the enzyme hyaluronidase (capable of degrading hyaluronic acid), destabilase, and chloromycetin causing the obliteration of cellular components of bacteria.[2] There are reports related to the bacteriostatic effect of destabilase against *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*, but this information is narrow and needs further exploration.[41]

Studies showed that leech saliva also contains a cocktail of neurotransmitters such as serotonin, dopamine, acetylcholine, and enkephalin that help in alleviating pain and promote relaxation in patients.[6] A specific component responsible for the analgesic effect is yet to be identified. However, clinical evidence is ample in both human and veterinary medicine.[42] A study of the sialotranscriptome of a medicinal leech, *H. nipponia,* predicted that more than 21 genes were involved in the anti-inflammatory, anticoagulatory, antibacterial, antithrombotic, and antitumor processes which may be important for treating various diseases of humans and animals.[7] Efficient use of hirudotherapy requires better knowledge of the profiles of leech salivary secretions.[6,43] The therapeutic potential and efficiency can vary depending on the species of sucking leech used. Therefore, the high-throughput proteomic and transcriptomic analysis will help to determine the profiles of proteins present in the salivary secretions of medicinal leeches.[7,43] The extensive diversity of the bioactive molecules indicates the potential for future investigations and may even result in the development of novel pharmacological agents derived from salivary secretions. A liposome-based gel can be developed using leech saliva extract, and such formulations can be used as a supplementary treatment for managing the symptoms of osteoarthritis.[44,45] The nanoliposome base formulation can offer better therapeutic utility as it enhances skin absorption. Keeping in mind the gamut of therapeutic effects of leech saliva, the major biologically active compounds isolated from leeches along with their functions are described in Table 1.

Indications of Hirudotherapy

Leech application for curing various diseases in humans is practiced since times immemorial and the idea was laid down by the renowned physicians of the Unani System of Medicine such as Hippocrates (460–370 BC), Galen (129–200 AD), Avicenna (980–1037 AD), Razes (850–923 AD), Hakim Azam Khan (1920 AD), and Hakim Ajmal Khan (1927 AD).[46] They used leeches as an instrument to get rid of several body ailments painlessly. One medical condition known as frostbite is commonly reported in colder climatic zones of India like Kashmir and the use of leech therapy for its treatment proved to be a successful therapeutic option. Iqbal *et al*. reported the successful treatment of frostbite in 20 patients in Kashmir during the winter months with the help of leeches. The treatment suppressed local inflammation, edema, and itching in 6 weeks, thus validating the use of leeches against frostbite.[47] The varicose vein is one of the common medical conditions reported in all age groups from teenagers to elderly people. For this medical disease, leech therapy proved effective when combined with compression stocking and limb elevation techniques.[48] At our Regional Research Institute of Unani Medicine, Hazratbal, Srinagar, we have successfully used leech therapy in patients with gout [Figure 1], varicose veins [Figure 2], arthritis [Figure 3], and cervical pain [Figure 4] with good therapeutic outcomes.

In skin diseases, leech therapy proved very beneficial. A randomized open-phased clinical trial evaluating the anti-inflammatory effect of leech therapy in patients with

Table 1: Major bioactive compounds in leech saliva

Bioactive compound	Molecular weight (kDa)	Effect
Hirudin	7	Thrombin inhibitor[2,4-6]
Bdellins	8.1	Inhibitor of trypsin, plasmin, and acrosin with anti-inflammatory activity[2,5,6,29,41]
Calin	65	Obstruction of the Von Willebrand factor that binds to collagen hampers platelet aggregation interceded by collagen[2,5,6]
Destabilase	12.6–12.9	Glycosidase action, fibrin dissolving, and antimicrobial action[5,27]
Hyaluronidase	27.5	Degraded hyaluronic acid, antibiotic activity, and decreased the viscosity that increased tissue permeability to injected solutions, thereby enhancing its absorption rate[27,29]
Tryptase inhibitor	4.3–4.8	Anti-inflammatory, tryptase inhibitor of mast cells, also inhibited trypsin and chymotrypsin[2,4,27,29,42]
Eglin C	5–38	Anticoagulant effect, anti-inflammatory, inhibitor of α subtilisin, chymotrypsin chymase, elastase, and cathepsin G[2,4]
Carboxypeptidase inhibitor	7.2–7.3	Carboxypeptidase B inhibitor[2,27]
Saratin	12	Inhibitor of platelet aggregation and Von Willebrand factor to collagen[38]
Histamine like compound	11	Vasodilator[2,27,29]

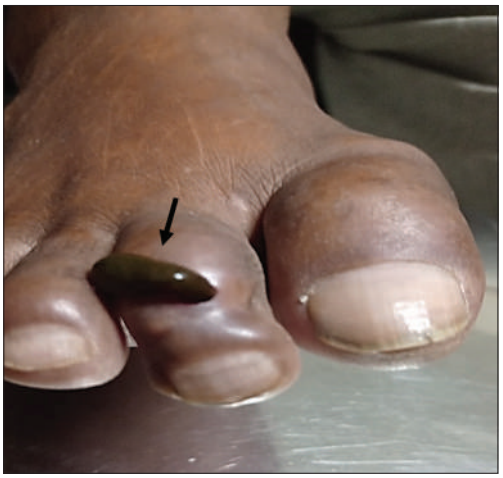

Figure 1: Use of leech in Gout

Figure 2: Leeching in frost bite patient

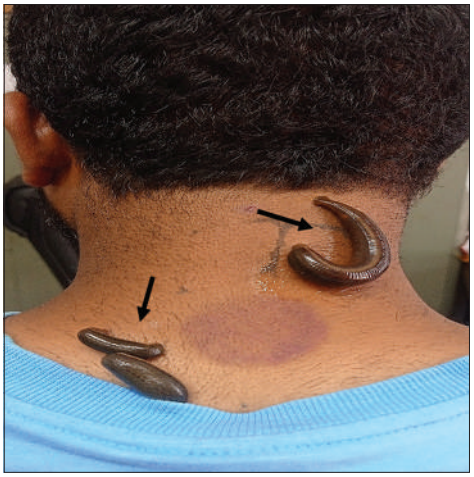

Figure 3: Leeching for cervical pain

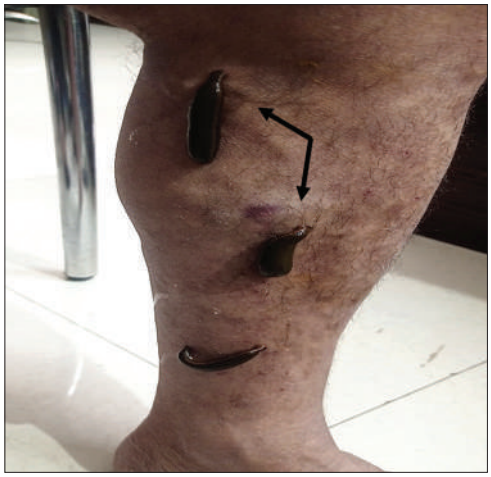

Figure 4: Leeching for varicosis

psoriasis was performed. The results indicated that leech therapy was significantly effective in treating psoriasis concerning the reduction in erythema, scaling, and induration of the lesion. Furthermore, the Auspitz sign, onion peel sign/candle grease sign, and erythema-squamous lesion were improved.[49] In the case of atopic eczema, leech therapy was found very effective. In one study, 27 patients with atopic eczema were subjected to medical leech

therapy once a week at least four times, and the effects were measured by eczema area and severity index (EASI) score, scoring of atopic dermatitis (SCORAD) index, and dermatology life quality index (DLQI). The results revealed a significant reduction of EASI (54.5%), SCORAD (55%), and DLQI (62.4%).[50] Leech therapy is currently practiced for the treatment of diabetic foot ulcers and venous leg ulcers in humans. It proved very effective in salvaging the leg in severe bad cases.[51-53] Leech therapy is also used for cancer pain management,[54] and osteoarthritis.[55,56] It is applied in lingual swelling secondary to blunt trauma.[57] The general list of indications of leech therapy in humans is summarized in Figure 5.[46]

Recently, one *in vivo* study in diabetic rats revealed the antihyperglycemic activity of leech saliva extract of *H. manillensis* that showed synergistic activity with insulin; therefore, it can help in plummeting the insulin dosage in diabetic animals (dogs and cats) and humans.[25] Hirudotherapy can be used in combination with antibiotics and anti-inflammatory drugs to obtain better results.

Leeching Contraindications

The obvious contraindications of leech therapy are bleeding disorders such as hemophilia, pregnancy, lactation, anemia, acute infections, immune-suppressive disorders, and cancerous skin conditions that need to be addressed before the application of leeches.[6] There is a risk of infection during leech therapy because of the presence of microbes such as *Aeromonas veronii* and *Aeromonas hydrophila* (Gram-negative) in the gut of medicinal leeches. Therefore, many clinicians recommend either dip the leech in 0.02% chlorhexidine hydrochloride solution for a few seconds or use a prophylactic dose of antibiotics to the animal before applying leeches on the wound.[4,6] However, cases related to the spread of antibiotic-resistant bacteria following leech therapy were proposed in humans with equal probability in animals.[58,59] Other complications were reported including allergy, infection, inflammation, prolonged bleeding, and fever.[46,60] After using the leech on humans, the reuse of the same leech on another patient must be avoided because there is a risk of transmission of diseases to other patients including plague, HIV, and hepatitis.[4,46] The possible medical benefits of these mysterious creatures with such minimal drawbacks support their wide-scale applications in treating disorders in humans and animals.

Conclusion and Future Directions

Hirudotherapy is one of the astounding medicinal therapies practiced in human medicine since the beginning of civilization. All credit goes to their salivary glands blessed with a cocktail of bioactive substances including hirudin, destabilase, eglins, bdellins, chloromycetin, hyaluronidase, and some neurotransmitters that play a very imperative role. To scientifically establish leech therapy, the primary factor for its success is the procurement of leeches from only a registered bio farm to avoid the risk of transmitting infections between patients. Furthermore, clinicians must have proper knowledge about the biology, maintenance, and care of medicinal leeches. While performing leeching, the hirudotherapist must avoid reusing the leeches on another patient because of the risk of infection transmission such as *Aeromonas hydrophilla*. It must be kept in mind that human health must be properly evaluated first before applying leech because there are some contraindications to leech therapy, including allergy, pregnancy, lactation, bleeding

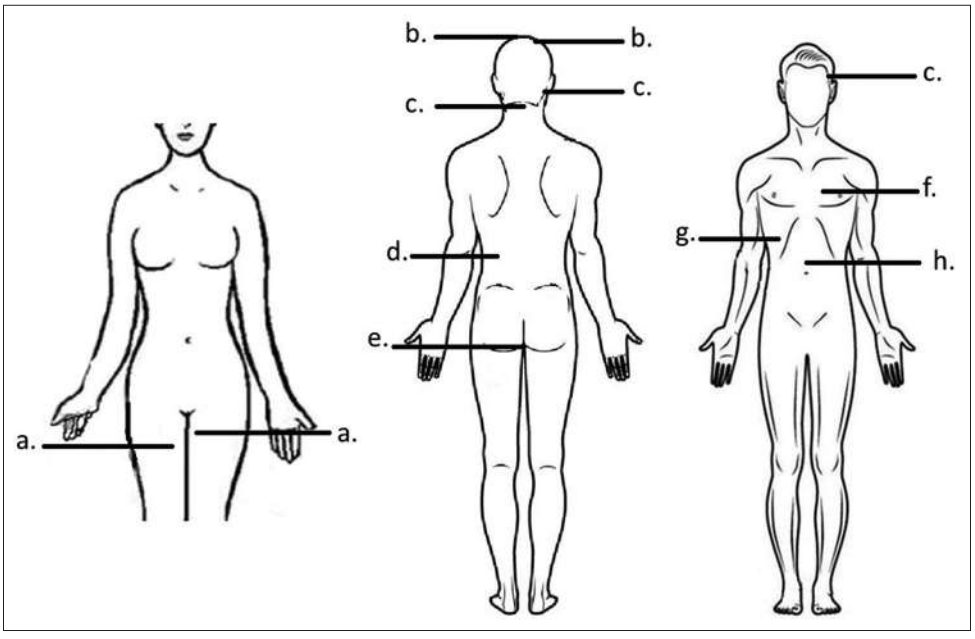

Figure 5: Indications of leech therapy in humans (a) Amenorrhea, dysmenorrhea, metritis; (b) Alopecia areata (on affected sites); (c) headache, migraine; (d) nephritis, renal atrophy, dysuria, retention of urine; (e) hemorrhoids; (f) pneumonia; (g) hepatitis; (h) gastritis[46]

disorders, immunosuppression, anemic state, and skin cancers. Describing the medical benefits of leeches from various clinical studies, it is imperative for medical and veterinary professionals to conveniently maintain medicinal leeches under laboratory conditions for therapeutics and research. Future scientific studies are warranted in human and veterinary leech therapy that will serve our human and animal patients on an immense magnitude.

Author's contribution

Each author agrees to be held accountable for the content of the manuscript and made substantial contributions to its concept, data compilation, proofreading, and approval.

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Review Article

Unveiling the Role of *Zingiber officinale* Roscoe in Combating Nonalcoholic Fatty Liver Disease: Mechanistic Insights and Clinical Perspectives

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Abstract

NonAlcoholic Fatty Liver Disease (NAFLD) is a rising global health concern, closely linked with metabolic disorders such as obesity, insulin resistance, and dyslipidemia. In Unani medicine, it is conceptually correlated with *Su'-i Mizāj Kabid Bārid* (cold derangement of liver temperament) and *Tashahhum al-Kabid* (fatty infiltration of the liver). *Zingiber officinale* Roscoe (ginger), known for its *Hār Yābis* (hot and dry) temperament, has been traditionally used for liver-related disorders. The objective of the study was to explore and elucidate the therapeutic potential of *Z. officinale* Roscoe in the management of NAFLD by analyzing mechanistic insights from contemporary scientific research and its traditional use in Unani medicine. This narrative review synthesizes data from classical Unani texts and modern scientific literature. Electronic databases such as PubMed, ScienceDirect, and Google Scholar were searched using keywords related to ginger and NAFLD. Peer-reviewed clinical trials, *in vivo* and *in vitro* studies, and pharmacological reports were included alongside references from authoritative Unani manuscripts. *Z. officinale* Roscoe demonstrates anti-inflammatory, antioxidant, hypolipidemic, insulin-sensitizing, digestive stimulant, and hepatoprotective activities. These pharmacological effects target key pathophysiological mechanisms of NAFLD, including hepatic fat accumulation, oxidative stress, and metabolic dysfunction. Clinical trials support its efficacy in reducing hepatic steatosis and improving inflammatory and metabolic markers without notable toxicity. Both classical Unani insights and modern evidence validate the role of *Z. officinale* Roscoe as a safe and effective adjunct in the management of NAFLD. Its multifaceted actions make it a promising candidate for integration into holistic treatment protocols, especially when combined with lifestyle and dietary modifications. Further large-scale trials are recommended to establish its therapeutic utility in broader clinical settings.

Keywords: *Ginger, nonalcoholic fatty liver disease, unani medicine, zanjabil, zingiber officinale*

Introduction

Nonalcoholic fatty liver disease (NAFLD) is a reversible condition of the liver, wherein large vacuoles of triglyceride fat accumulate within hepatocytes through the process of steatosis, despite the absence of significant alcohol consumption.[1,2] Initially considered clinically insignificant, fatty infiltration of the liver has now emerged as a major health concern, especially after it was established that NAFLD encompasses a spectrum ranging from simple steatosis to nonalcoholic steatohepatitis (NASH), with the potential to progress to cirrhosis.[2-4] Strongly associated with obesity, insulin resistance, dyslipidemia, and metabolic syndrome, NAFLD has become increasingly prevalent amid the global obesity epidemic.[2,4]

Unani Medicine is based on the theory of temperament (Mizāj), which reflects the unique combination of qualities – hot, cold, moist, and dry – present in every individual and organ. Health is believed to be the result of a balanced temperament, while disease arises from its disturbance (Su'-i Mizāj).[5,6] Diagnosis and treatment in Unani practice revolve around identifying and restoring the natural temperament through personalized regimens involving diet, lifestyle, and therapeutic interventions. From the Unani perspective, NAFLD may be correlated with *Su'-i Mizāj Kabid Bārid*, a condition characterized by the transformation of the liver's normal temperament, i.e., hot and moist, into a cold temperament due to inappropriate dietary habits and lifestyle factors.[5-8]

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This shift facilitates fat accumulation (*Tashahhum al-Kabid*), impairs hepatic function, and results in the formation of abnormal humors (*Akhlāṭ Raddiya*).[9] Classical Unani scholars have described fat as having a *Bārid Raṭab* (Cold and Moist) temperament, noting that its excess in organs leads to coldness and dysfunction, particularly in inherently hot organs like the liver.[10,11] Thus, the conceptual framework of Unani medicine offers valuable insights into the etiology and management of NAFLD.

Zingiber officinale Roscoe, commonly called as ginger, is a perennial rhizomatous horizontally growing herb, growing erect up to 60 cm height with several lateral rhizomes [Figure 1].[12] Unani physicians have described it as a slender rhizomatous perennial herb with leaves thin and about one hand long and sometimes used in syrups and soups. According to them it does not bear flower and fruits and its stem has a strong fragrance and taste. It is found abundantly in Yemen, Oman, India, and China. The part used as a drug is its rhizome. It has several varieties like mountainous ginger, wild ginger. Mountainous ginger is big in size with big plants and roots. The best ginger is the one that is fresh, whitish, heavy, without fibers, strong-smelling, pungent, and free from worms.[13-19]

Methodology

This narrative review was conducted by systematically analyzing both traditional Unani literature and contemporary scientific research to evaluate the therapeutic potential of *Z. officinale* Roscoe (ginger) in the management of NAFLD. Classical Unani sources such as *Al-Qānūn fī al-Ṭibb* by Ibn Sīnā, *Muheet-e-Azam* by Mohammad Azam Khan, and *Khazainul Advia* by Najmul Ghani, to name a few, were explored to understand the temperament, pharmacological actions, and indications of *Zanjabīl* (ginger) from a Unani perspective.

For modern scientific evidence, relevant literature was retrieved from electronic databases including PubMed, ScienceDirect, SpringerLink, and Google Scholar. The search terms included "*Zingiber officinale*," "ginger," "NAFLD," "nonalcoholic fatty liver disease," "anti-inflammatory," "hepatoprotective," and "lipid metabolism." Both *in vivo* and *in vitro* studies, systematic reviews, and clinical trials published in English were included, with preference given to peer-reviewed articles from journals with high indexing and impact factors. Data were synthesized to highlight the bioactive compounds of ginger and their role in modulating the pathophysiological mechanisms implicated in NAFLD.

Results

Binomial name

Z. officinale Roscoe Roscoe.[12,20-23]

Vernacular names

English:	Ginger[12-14]
Hindi:	Adrak[12-14,18]
Urdu:	Sonth[19-23]
Syrian:	Zangbil[12,13]
Persian:	Shangweez[12-14,18-21]
Kannada:	Shunthi, Ardaraka[22,23]
Malyalam:	Inci, Erukkilannu[23]
Sanskrit:	Ardrakam[22,23]
Tamil:	Inci[23]
Telugu:	Allamu, Ardrakamu[22,23]
Unani:	Fresh Rhizome: *Zanjabīl-i Raṭb, Al' Zanjabīl*[22]
Dried Rhizome:	*Zanjabīl i Yābis, Sonth.*[22]

Habitat

This herb is a native to southern Asia. It is cultivated over tropics and subtropics. Hot and moist climate with rich well-drained soil is favorable for its growth. Presently, it is primarily grown in Indonesia, Jamaica, Sri Lanka, and China. In India, it is cultivated in Kerala, Andhra Pradesh, Uttar Pradesh, West Bengal, and Maharashtra.[20-22]

Identifying features

Cochin ginger is light brown or yellowish grey in color, Calicut ginger is orange or reddish brown in color, and Kolkata ginger is greyish brown to greyish blue in color.[22] On physicochemical analysis, in pure ginger, foreign matter should not be more than 1%, total ash not more than 6%, water-soluble ash not more than 1.5% and it should be alcohol (90%) extractive not <3%, and water-soluble extractive not <10%.[23]

Organoleptic characteristics

Ginger flowers [Figure 2] have an aromatic odour while stems emit out only slight fragrance only when contused. The ginger rhizome [Figures 3 and 4] has an aromatic and penetrating odour, and spicy, pungent, hot and biting taste.[20-23]

Chemical constituents and active principles

Ginger (*Z. officinale* Roscoe) contains several bioactive compounds that can be beneficial in managing NAFLD. Among these, 6-gingerol is one of the primary constituents. It exhibits potent antioxidant and anti-inflammatory properties. 6-Gingerol enhances the activity of antioxidant enzymes, such as superoxide dismutase and catalase, which help reduce oxidative stress in liver tissues.[24] Additionally, it inhibits the nuclear factor kappa B (NF-κB) signaling pathway, leading to a decrease in the production of pro-inflammatory cytokines such as tumor necrosis factor-α and interleukin-6.[25] Furthermore, 6-gingerol modulates lipid metabolism by downregulating genes involved in

Figure 1: Zingiber officinale whole plant

Figure 2: Zingiber officinale flower

Figure 3: Fresh zingiber officinale rhizome

Figure 4: Dried zingiber officinale

lipogenesis and upregulating those responsible for fatty acid oxidation, ultimately reducing hepatic fat accumulation.[26]

Another key compound is 6-shogaol, which is formed during the drying process of ginger. Like 6-gingerol, 6-shogaol has strong anti-inflammatory effects, suppressing the activation of NF-κB and reducing the expression of inflammatory mediators. It also exhibits potent antioxidant activity by scavenging free radicals and protecting hepatocytes from oxidative damage.[24] Moreover, 6-shogaol has been shown to improve insulin sensitivity, which is crucial for managing NAFLD, particularly in the context of metabolic syndrome.[26]

Zingerone, another important component of ginger, also plays a role in NAFLD management. It has strong antioxidant properties, neutralizing reactive oxygen species and reducing oxidative stress in liver cells.[24] Zingerone further contributes to liver health by lowering serum triglycerides and cholesterol levels, which are often elevated in NAFLD patients.[26] In addition, it exhibits anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines, thus supporting the liver's normal function.

Finally, paradol, a pungent compound found in ginger, contributes to its therapeutic effects on NAFLD. Paradol has antioxidant properties, which protect liver cells from oxidative damage.[24] It also reduces inflammation by inhibiting the production of inflammatory cytokines, which are crucial in the pathogenesis of NAFLD.[26] Moreover, paradol helps regulate metabolic pathways, further supporting its potential in reducing hepatic fat accumulation.

Temperament (*Mizāj*)

Each drug in Unani medicine is believed to possess a specific temperament, which is derived from the qualities of the four basic elements – air (hot and moist), fire (hot and dry), water (cold and moist), and earth (cold and dry). The temperament of a drug is determined by the dominance of one or two of these qualities in the drug's nature. Thus Unani physicians classify the temperament of drugs into four types - Hot (*Hār*), Cold (*Bārid*), Moist (*Raṭb*), and Dry (*Yābis*).[11] These are further graded into four degrees to describe the intensity of their action.[11]

i. 1st degree: Mild effect; suitable for general use
ii. 2nd degree: Moderate effect; used under guidance
iii. 3rd degree: Stronger effect; may alter the temperament of the body
iv. 4th degree: Very potent; can be harmful or lethal if misused, but useful therapeutically in specific doses.

The temperament of ginger is Hot and Dry (*Hār Yābis*). According to renowned Unani scholar *Ibn Sina* ginger is

hot in 1st degree and dry in 2nd degree. According to some Unani physicians fresh ginger is dry in 1st degree while dry ginger is dry to 3rd degree. As ginger gets old it increases in dryness but its hotness does not reduce. Another renowned Unani scholar *Ibn Masuya* has said that ginger is hot in 3rd degree while wet in 1st degree. Ginger preserved in honey or sugar (*Murabbā*) is very hot and dry. It contains waste fluids less than fresh ginger as waste is reduced due to cooking in honey.[13-19]

Actions

Raw ginger is acrid, carminative, digestive, laxative, and thermogenic. The dry ginger is appetizer, anodyne, aphrodisiac, anti-helminthic, carminative, emollient, expectorant, laxative, rubefacient, stomachic, stimulant, and thermogenic.[21,22]

As described by Unani physicians it is a potent *Musakkhin* (Calorific), *Muqawwi meda wa jigar* (Stomachic and Heptatonic), *Mulayyan* (Laxative), *Mushtahi* (Appetizer), *Hazim* (Digestive), *Kasir-i-Riyah* (Carminative), *Muhallil-i-Riyah* (Gaseous resolvent), *Munaqqi-i-Balgham wa Ratubat-i-Meda* (clears vitiated humor from the stomach), *Musakkin* and *Dafa-i-Suale Balghami* (reduces phlegmatice cough), *Mufatteh Sudad* (Deobstruent).[13-19]

Indications

In Unani medicine, the principle of *Ilāj bil Ẓidd* (treatment by opposites) is a foundational therapeutic approach. It involves treating a disease by administering drugs or adopting measures that possess qualities opposite to those of the disease. Thus ginger, owing to its hot temperament, is very useful in people with diseases of cold temperament. It is useful in *Baroodat i Asab* (Coldness of nerves), *Falij* (Hemiplegia), *Laqwah* (Facial Palsy), *Khidr* (Numbness), *Jamood* (Catalepsy), *Tashannuj Ratab* (Repletive spasms), *Larzah* (Algor), *Irqunnisa* (Sciatica), *Nuqrus* (Gout), *Zof i Hafizah* (Loss of memory), *Iltehab i Ahsha* (Visceral inflammation), *Zof i Ishteha* (Loss of appetite), *Zof i Aam* (General weakness), *Amraz i Sadr, Uzn, Anf wa Halaq* (Disease of chest, ear, nose, and throat), *Bawaseer* (Haemorrhoids), *Istisqa* (Ascites), *Wajaul Mafasil* (Arthritis), etc.[13-18]

Compound formulations

Some important formulations are *Habbe Hilteet, Habbe Pachlona, Habbe Kabid Naushadri, Habbe Papita, Habbe Tursh Mushtahi, Jawarishe Bisbasa, Jawarishe Falafali, Jawarishe Fanjnosh, Jawarishe Jalinoos, Jawarishe Kamooni, Jawarishe Zanjbil, Majoone Lana, Majoone Nankhwah, Majoon Seer Alvi Khan, Majoone Zanjbil, Sufoofe hazim Kalan,* and *Sufoofe Qaranfal*.[12]

Pharmacological activities

Analgesic

From the studies conducted previously, it has been estimated that roughly 2 g/day of ginger supplementation for a minimum of 5 days reduces muscle pain from eccentric exercise and running.[27] A randomized clinical trial conducted by Shirvani *et al*. to study the effect of ginger on pain relief in primary dysmenorrhea suggested that ginger was equally effective as Mefenamic acid for pain relief in a dose of 250 mg every 6 h for 2 consecutive menstrual cycles.[28] The suggested mechanism of action behind the analgesic property of ginger may be the inhibition of cyclooxygenase and lipooxygenase pathways in prostaglandin and leukotriene synthesis.[29,30]

Anti-inflammatory

Anti-inflammatory property of ginger has been studied vastly in both *in vitro* and *in vivo* studies. In patients with symptomatic osteoarthritis and rheumatoid arthritis, the beneficial effect of ginger in mitigating arthritic knee pain has been evaluated in a few randomized and nonrandomized clinical trials.[31-33] Experimental studies have shown that ginger constituents inhibit a key pathway in the inflammatory process, i.e., arachidonic acid metabolism. Furthermore, it acts as an inhibitor of prostaglandins and leukotriene synthesis by suppressing cyclooxygenase and lipoxygenase pathways.[30,34,35] Zingerone, a bioactive component of ginger has been suggested to reduce lipopolysaccharide (LPS) induced inflammation in mice by inhibiting infiltration of inflammatory cells and suppressing LPS-induced NF-κβ activities in cells.[36] *In vitro* studies have been conducted on 6-, 8-, 10-gingerol, and 6-shogaol isolated from ginger rhizome.[37] The anti-inflammatory activity of ginger helps mitigate the chronic low-grade inflammation that drives the progression of NAFLD. By reducing hepatic inflammation and oxidative stress, ginger may slow the advancement from simple steatosis to NASH, thereby preserving liver function.

Anti-cholesterolemic

Ginger is known to reduce blood cholesterol levels. In a study conducted *in vivo* by Bhandari *et al*., it was reported that ethanolic ginger extract significantly reduced serum cholesterol, serum triglyceride, serum lipoproteins, and phospholipids in mice, which were given 1% cholesterol for 10 weeks, as tested against standard (gemfibrozil).[38] In rats which were fed 0.5% ginger oleoresin along with 1% cholesterol, it was reported that levels of serum and liver cholesterol were low and fecal cholesterol was high.[39] The mechanism of action behind this property of ginger, as suggested by Srinivasan *et al*. is that ginger stimulates the conversion of cholesterol to bile acids, thus facilitating the elimination of cholesterol from the body.[40,41] Thus by improving lipid metabolism and reducing hepatic lipid accumulation, ginger may prevent or reverse hepatic steatosis, a key feature of NAFLD. This lipid-lowering effect contributes to better liver function and reduces the risk of progression to more severe liver damage such as NASH or fibrosis.

Anti-atherosclerotic

In a study, Ethanol extract (50%) of ginger in quantity 500 mg/kg body weight was given to atherofed male rabbits for 60 days. It was observed that ginger extract feeding brought the cholesterol, triglyceride, and phospholipid content of the liver and aorta to near normal which was otherwise increased in atherofed rabbits. Simultaneously it was observed that the surface area of aortic walls that were covered with plaque was 32.7%–39.8% in atherofed rabbits while only 13.5% of aortic walls was covered by plaque after ginger treatment. The proposed mechanism behind this action was the inhibition of the influx of atherogenic lipoproteins and the conversion of cholesterol esters present in the plaque to free cholesterol which gets catabolized in the liver.[42] The anti-atherosclerotic activity of ginger, demonstrated by its ability to reduce hepatic and aortic lipid accumulation and significantly lower plaque formation, suggests a protective effect against lipid dysregulation and vascular inflammation – both of which are commonly associated with NAFLD. By inhibiting the influx of atherogenic lipoproteins and promoting hepatic catabolism of cholesterol, ginger supports improved lipid clearance and reduced hepatic steatosis. This will not only mitigate cardiovascular risk in NAFLD patients but will also help prevent progression to more advanced liver pathology.

Cholagogic

Wistar male rats weighing about 250 g were administered acetone and aqueous extracts of ginger (500 mg/kg) and the volume of bile excretion was measured at 0.5, 1, 1.5, 2, 3, 4, and 5 h after the drug administration. It was observed the acetone extract, which contains essential oils and pungent compounds, significantly increased bile secretion. It was proposed that the pungent principles 6-gingerol and 10-gingerol were responsible for the cholagogic properties of ginger.[43] This cholagogic activity of ginger stimulates bile secretion from the liver. Since bile is essential for breaking down and removing excess fats and cholesterol from the body, enhanced bile flow helps reduce fat buildup in liver cells. This action makes ginger beneficial in managing NAFLD by promoting fat metabolism, reducing hepatic steatosis, and supporting overall liver detoxification.

Antiemetic

The prophylactic use of 1 g powdered ginger root is reported to reduce the incidence of postoperative nausea and vomiting as effectively as metoclopramide 10 mg given orally 1 h before anesthesia.[44] 250 mg of powdered ginger given for 4 days was significantly found to reduce hyperemesis gravidarum,[45] also 65 women at or before 17 weeks of pregnancy were given 5 ginger biscuits per day for 4 days with 0.5 g of ginger, as fine powder, incorporated in each biscuit. The results showed a reduction in the severity of nausea and vomiting in the group receiving ginger biscuits as compared to the placebo.[46] Similarly, a systematic review of double-blind, randomized, placebo-controlled trials demonstrated the potential efficacy of ginger on nausea and vomiting of various origins.[47] Antiemesis through ginger could be explained by several mechanisms. 6-gingerol accelerates gastrointestinal transport; it also has been reported to exhibit anti-hydroxyl tryptamine activity in isolated guinea pig ileum.[48] This finding is annealed by the fact that 6-gingerol effectively prevented cyclophosphamide-induced vomiting in animal models.[46] Another constituent of ginger galanolactone is shown to be a competitive antagonist at ileal 5-HT3 receptors.[49] It can thus be concluded that the antiemetic potential of ginger may aid in the management of NAFLD by alleviating associated gastrointestinal symptoms such as nausea and vomiting, which can result from hepatic dysfunction. Additionally, its prokinetic effects and modulation of serotonin receptors may enhance digestive comfort and support better adherence to dietary and lifestyle interventions crucial for NAFLD management.

Anti-hepatotoxic

Ginger (1 g) orally combined with other herbs has been shown to reduce carbon tetrachloride-induced hepatic injury. A possible mechanism behind this action may be the protective activity of the drug in hepatocellular necrosis.[50] The anti-hepatotoxic potential of ginger suggests its role in mitigating hepatocellular necrosis and oxidative stress. In the context of NAFLD, this hepatoprotective effect may help prevent progression to steatohepatitis by improving liver cell integrity and reducing inflammation and lipid peroxidation.

Digestive stimulant

Ginger has been documented to possess sialagogue action, stimulating the production of saliva,[34] and is known to enhance bile acid production (cholagogue),[43] which has a key role in digestion and absorption of dietary fats. It also stimulates the secretion of lipase, amylase, and proteases (trypsin, chymotrypsin, and carboxypeptidase), which are the digestive enzymes of the pancreas[51] along with enzymes of the small intestinal mucosa.[52] It also lowers the gastrointestinal transit time owing to facilitated digestion.[34] By all these properties, ginger is proven to be a strong digestive stimulant. This property of ginger enhances the breakdown and absorption of dietary fats and nutrients, thereby reducing fat accumulation in the liver. By promoting efficient digestion and lowering gastrointestinal transit time, ginger may help prevent the metabolic imbalances that contribute to the development and progression of NAFLD.

Anti-hyperglycemic

Anti-hyperglycaemic effect of ginger has been demonstrated *in vitro*, *in vivo* as well as in clinical trials. Administration of ethanolic extract of ginger on diabetic rats has been reported to reduce fasting blood glucose levels.[53-55] In humans also ginger

is reported to possess hypoglycemic effect. 3 g of ginger powder daily for 3 months improved glycaemic indices in patients with type 2 diabetes mellitus.[56] The active ingredients of ginger namely gingerol and shogaol are responsible for hypoglycemic effect of ginger with the possible mechanism being insulin release and its sensitivity and reversal of altered carbohydrate and lipid metabolism.[34] The anti-hyperglycaemic effect of ginger improves insulin sensitivity and regulates carbohydrate and lipid metabolism – key factors implicated in the pathogenesis of NAFLD. By lowering blood glucose levels and mitigating insulin resistance, ginger may help reduce hepatic fat accumulation and prevent disease progression in NAFLD patients.

Weight gain inhibition

Ginger has been reported to bring about a significant reduction in weight in obese rats after 60 days of treatment with a 5% aqueous solution of the drug.[57] Since ginger stimulates digestion and absorption of dietary fats by enhancing bile production and increased activity of pancreatic lipase, it accounts for the suppressed accumulation of lipids in the body and hence helps in weight management.[34] This mechanism can be particularly beneficial in managing NAFLD, as it helps prevent excessive fat deposition in hepatic tissues, thereby improving liver function and mitigating disease progression.

Antioxidant

Ginger is reported to contain gingerol, hexahydro curcumin, eugenol, zingerone,[58-60] 6-gingerol, and 6-paradol,[34] all of which contain antioxidant properties. A possible mechanism by which ginger exhibits antioxidant action is by inhibiting lipid peroxidation, increasing glutathione content, and maintaining normal levels of antioxidant enzymes.[61] An interesting observation reported in some studies has been that even after boiling ginger at 100°C for 30 min, its antioxidant property is retained, indicating that it is resistant to thermal denaturation.[62] In the context of NAFLD, this antioxidant activity can protect hepatic cells from oxidative damage, a key contributor to liver inflammation and progression to steatohepatitis, thereby supporting liver health and disease management.

Discussion and Conclusion

The present review brings forth a consolidated understanding of the potential role of *Z. officinale* Roscoe (ginger) in the management of NAFLD, integrating insights from both Unani classical texts and contemporary scientific evidence. NAFLD, characterized by hepatic lipid accumulation independent of significant alcohol intake, has emerged as a global health burden closely associated with metabolic disorders such as obesity, insulin resistance, and dyslipidemia.[35,36,39] Within the Unani framework, this condition is conceptually aligned with *Su'-i Mizāj Kabid Bārid* and *Tashahhum al-Kabid*, wherein the liver's temperament becomes cold and moist, promoting fat deposition and functional impairment.[18,19,22,32]

From this perspective, ginger, owing to its *Hār Yābis* (hot and dry) temperament and its described actions is inherently suited to correct the underlying *Mizāj* imbalance contributing to NAFLD. This traditional rationale finds substantial support in modern studies which have demonstrated that ginger possesses significant anti-inflammatory, anti-hyperlipidemic, antioxidant, hepatoprotective, and digestive stimulant properties.[30,34,36,37,43,53]

Clinical investigations reinforce these findings. A randomized, placebo-controlled trial showed that 2 g/day ginger supplementation over 12 weeks significantly reduced hepatic steatosis in NAFLD patients, without adverse hepatic or renal outcomes.[63] Another clinical trial reported improvements in inflammatory markers and hemoglobin levels, suggesting systemic benefits and a reassuring safety profile.[64] Moreover, ginger's capacity to improve gastrointestinal motility,[47] reduce dyspeptic symptoms,[65] and alleviate nausea and vomiting[46-49] further enhances its suitability in NAFLD, where gastrointestinal discomfort and metabolic derangements commonly coexist.

Unlike pharmacological agents that often target isolated pathways, *Z. officinale* Roscoe offers a multifaceted therapeutic approach by modulating inflammation, improving digestion, promoting lipid clearance, and supporting metabolic health. This multimodal mechanism positions ginger not merely as a symptomatic reliever but as a potential disease-modifying adjunct in NAFLD management.

In conclusion, the traditional wisdom of Unani medicine finds strong corroboration in modern biomedical research with regard to the efficacy of ginger in liver ailments. Its integration into therapeutic protocols for NAFLD, alongside dietary regulation and lifestyle modifications, could offer a safe, accessible, and evidence-informed intervention. However, larger, long-term randomized controlled trials are warranted to confirm these findings and to determine the optimal dosage and formulations suitable for clinical application.

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There are no conflicts of interest.

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Review Article

Exploring the Role of Pomegranate (*Punica granatum* L.) in Unani Medicine for Managing Metabolic Syndrome: A Comprehensive Review

Abstract

Metabolic syndrome (MetS) is a complex disorder marked by central obesity, hypertension, dyslipidemia, and insulin resistance, which collectively heighten the risk of cardiovascular disease and type 2 diabetes. Unani medicine, a traditional healing system, emphasizes holistic management through medicinal plants, among which pomegranate (*Punica granatum* L.), known as *Rummān*, holds a prominent place. This review explores its role in managing MetS by drawing on classical Unani manuscripts, modern pharmacological research, and peer-reviewed studies. Pomegranate is rich in bioactive compounds such as polyphenols, flavonoids, anthocyanins, and tannins, which contribute to its antioxidant, anti-inflammatory, antihypertensive, lipid-lowering, and hypoglycemic activities. Its fruit, seeds, and peel have been shown to reduce oxidative stress, improve lipid profiles, enhance insulin sensitivity, and support endothelial health. Traditional Unani formulations incorporating pomegranate correspond closely with these pharmacological effects, reinforcing its value for cardiovascular and metabolic wellness. The integration of pomegranate into diets and therapeutic regimens presents a promising natural approach for the prevention and management of MetS, though further rigorous clinical trials are essential to confirm its efficacy and refine its use in modern healthcare.

Keywords: *Metabolic syndrome, Pomegranate, Punica granatum, Rummān, traditional remedies, Unani medicine*

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Introduction

Metabolic syndrome (MetS) has become a major global health concern due to its significant association with increased risks of cardiovascular diseases, type 2 diabetes, and all-cause mortality.[1] MetS is a complex medical condition characterized by a combination of interrelated risk factors, including obesity, hypertension, dyslipidemia, and insulin resistance.[2] Given its multifaceted nature, an integrated and holistic approach is vital for its prevention and management.[3] In recent years, there has been growing interest in natural dietary interventions to combat MetS and its related complications.[4] *Punica granatum* L., commonly known as pomegranate, *Anār*, and flower is known as *Gulnār*, belongs to Lythraceae, which has gained recognition for its potential therapeutic properties and bioactive constituents, making it a subject of considerable interest in the realm of MetS management.[4] This article aims to provide an overview of the potential role of *P. granatum* in mitigating the components of MetS, focusing on its bioactive compounds and their plausible mechanisms of action.[5] In addition, it sets the stage for an in-depth exploration of current research and evidence on the use of *P. granatum* in the context of MetS.[6] Understanding the potential impact of *P. granatum* in mitigating MetS holds promise for future dietary strategies and integrative healthcare approaches to tackle this burgeoning health challenge.[7] The active phenolic components of pomegranate are punicalagin, ellagic acid, and gallic acid.[8]

Methodology

This review employs a systematic approach to explore the role of Pomegranate (*P. granatum*) in Unani medicine for managing MetS. The methodology involves three key stages: Literature collection, analysis, and synthesis. (1) A comprehensive search of scientific databases, including PubMed, Scopus, and Google Scholar, was conducted. Keywords such as "*Punica granatum*," "pomegranate," "Unani medicine," and

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"metabolic syndrome" were used to identify relevant studies. Both original research articles and review papers published in English were considered, with a preference for peer-reviewed journals. To ensure a thorough review, additional references were obtained from the bibliographies of selected articles. (2) The identified literature was screened for relevance and quality. Studies focusing on the biochemical properties of pomegranate, its therapeutic applications in Unani medicine, and its effects on MetS parameters such as obesity, diabetes, hypertension, and dyslipidemia were prioritized. Articles unrelated to the topic or lacking scientific rigor were excluded. (3) The data from the selected studies were categorized and analyzed. Special attention was given to the pharmacological properties of pomegranate, including its antioxidant, anti-inflammatory, and lipid-lowering effects, as described in both modern and Unani medicine frameworks. The findings were then synthesized to provide a holistic understanding of the subject. By combining insights from traditional Unani texts and contemporary scientific research, this review aims to bridge the gap between ancient knowledge and modern healthcare practices in addressing MetS.

Causes of metabolic syndrome

MetS is a complex health condition that arises from a combination of various risk factors, including genetic, lifestyle, and environmental factors.[8] The precise cause of MetS is not fully understood, but a range of interrelated factors contribute to its development.[9] Genetic predisposition plays a significant role in the development of MetS.[10] Individuals with a family history of diabetes, hypertension, or early heart disease are at a higher risk of developing MetS. Genetic factors can influence how the body processes and stores fats, regulates blood sugar, and manages cholesterol levels.[11] Central obesity, particularly excess fat around the abdomen and visceral adiposity, is a primary component of MetS.[12] An inactive lifestyle and consuming a diet high in calories, unhealthy fats, sugars, and refined carbohydrates can lead to weight gain and obesity.[13] Adipose tissue, especially in the abdomen, can trigger inflammation and insulin resistance.[14] Insulin resistance is a key feature of MetS. It occurs when cells in the body do not respond effectively to insulin, a hormone that helps regulate blood sugar levels.[15] Insulin resistance leads to elevated blood glucose levels, increased insulin production, and subsequent metabolic abnormalities.[16] Dyslipidemia involves abnormal levels of lipids (fats) in the blood, such as elevated triglycerides, low high-density lipoprotein (HDL) cholesterol, and high levels of low-density lipoprotein (LDL) cholesterol.[17] Poor dietary habits and a sedentary lifestyle contribute to dyslipidemia, a critical component of MetS.[18] High blood pressure, or hypertension, is a significant factor in MetS.[19] Lifestyle factors such as excess salt intake, obesity, insulin resistance, and a diet high in sodium contribute to high blood pressure.[12,19] Hypertension is a risk factor for various cardiovascular diseases associated with MetS.[20] Lack of regular physical activity is a major contributor to MetS.[21] Physical inactivity can lead to obesity, insulin resistance, and impaired glucose metabolism, all of which are fundamental components of MetS.[22] Aging is associated with changes in metabolism, muscle mass reduction, and alterations in hormone levels, particularly in women after menopause.[23] These changes can contribute to the development of MetS.[24] Chronic low-grade inflammation is often present in individuals with MetS.[25] Inflammatory processes, whether triggered by obesity or other factors, can interfere with insulin signaling and contribute to insulin resistance.[26] Poor quality or insufficient sleep and chronic stress can disrupt hormonal balance, including insulin and cortisol levels, which may contribute to the development and worsening of MetS.[27] Environmental influences such as exposure to endocrine-disrupting chemicals, urbanization, and certain socioeconomic factors can contribute to the development of MetS.[28] Understanding these causes is essential for the prevention, early detection, and effective management of MetS.[29] Lifestyle modifications, including a balanced diet, regular physical activity, maintaining a healthy weight, and managing stress, are critical in mitigating these risk factors and reducing the risk of MetS.[30]

Clinical features of metabolic syndrome

MetS is diagnosed when an individual exhibits a cluster of specific clinical features or risk factors.[31] The presence of these features increases the risk of developing cardiovascular diseases and type 2 diabetes.[32] Central obesity is a hallmark feature of MetS. It is characterized by excess fat accumulation around the abdomen, often measured using waist circumference.[33] Men with a waist circumference of 40 inches (102 cm) or more and women with a waist circumference of 35 inches (88 cm) or more are considered to have central obesity.[34] Elevated blood pressure is a key component of MetS. A blood pressure reading of 130/85 mmHg or higher is generally indicative of hypertension.[35] High blood pressure increases the risk of heart disease, stroke, and other complications associated with MetS.[36] Dyslipidemia involves abnormal levels of lipids (fats) in the blood.[36] MetS is associated with high levels of triglycerides, low levels of HDL cholesterol (below 40 mg/dL for men and below 50 mg/dL for women), and elevated levels of LDL cholesterol.[37] Elevated fasting blood glucose levels or impaired glucose tolerance are indicative of insulin resistance and impaired glucose metabolism.[38] A fasting blood glucose level of 100 mg/dL or higher suggests impaired glucose metabolism, while a diagnosis of diabetes is confirmed with a fasting blood glucose level of 126 mg/dL or higher.[39] Insulin resistance occurs when cells in the body do not respond efficiently to insulin.[40] It leads to elevated blood glucose levels and increased insulin production, both of which are associated with MetS.[41] Chronic low-grade inflammation and an increased tendency

for blood clotting (prothrombotic state) are common in MetS.[42] Elevated levels of certain inflammatory markers, such as C-reactive protein (CRP), are often observed in individuals with MetS.[43] Microalbuminuria involves the presence of small amounts of albumin (a protein) in the urine, indicating early kidney damage.[44] It is associated with MetS and signifies a risk of kidney dysfunction and cardiovascular disease.[45] In women, the presence of polycystic ovary syndrome (PCOS), characterized by irregular menstrual periods, excess facial and body hair, and polycystic ovaries, is associated with MetS. It often manifests due to insulin resistance.[46] *Acanthosis nigricans* is a skin condition characterized by dark, thickened patches of skin, often appearing in body folds and creases.[47] It can be a visible sign of insulin resistance and is associated with MetS.[48] Recognizing and diagnosing these clinical features is essential for identifying individuals at risk of MetS.[49] Timely intervention through lifestyle modifications, including a healthy diet, appropriate regimes, regular physical activity, and medical management, is crucial in reducing the risk of cardiovascular diseases and diabetes associated with MetS.[50]

Complications of metabolic syndrome

MetS is a cluster of interrelated metabolic abnormalities that significantly elevate the risk of various health complications.[51] The presence of MetS can lead to several potentially serious complications, including: Individuals with MetS face a markedly increased risk of developing cardiovascular diseases such as coronary artery disease, heart attack (myocardial infarction), stroke, and peripheral arterial disease.[52] The combination of hypertension, dyslipidemia, and insulin resistance contributes to atherosclerosis, a condition characterized by the accumulation of plaques in the arteries, restricting blood flow and increasing the risk of heart-related events.[53] Insulin resistance, a central component of MetS, often precedes the onset of type 2 diabetes.[54] The impaired ability of cells to respond to insulin results in elevated blood glucose levels.[55] Over time, the pancreas may struggle to produce enough insulin, leading to the development of type 2 diabetes.[56] MetS is closely associated with Nonalcoholic fatty liver (NAFLD), a condition characterized by an accumulation of fat in the liver, which may progress to nonalcoholic steatohepatitis and, eventually, liver cirrhosis or liver failure.[57] Hypertension, a critical component of MetS, increases the risk of various complications, including heart disease, stroke, kidney disease, and vision loss due to retinopathy.[58] MetS is a risk factor for the development and progression of chronic kidney disease.[59] The cluster of metabolic abnormalities, particularly hypertension and insulin resistance, can impair kidney function over time.[60] MetS is strongly associated with Obstructive sleep apnea (OSA), a condition characterized by pauses in breathing during sleep.[61] OSA can lead to daytime fatigue, increased risk of accidents, and cardiovascular complications.[62] Some research suggests that individuals with MetS have a higher risk of certain cancers, including colorectal, breast, and prostate cancers.[63] The chronic low-grade inflammation associated with MetS may play a role in the development and progression of cancer.[64] MetS is linked to an increased risk of developing cognitive impairments, dementia, and Alzheimer's disease.[65] Insulin resistance and inflammation may contribute to these neurological complications.[66] MetS can affect reproductive health, leading to complications such as PCOS in women and erectile dysfunction in men.[67] Individuals with MetS may experience higher rates of depression, anxiety, and overall reduced quality of life due to the physical health challenges and associated lifestyle modifications.[68] Managing and preventing MetS through lifestyle modifications, including a healthy diet, regular physical activity, weight management, and medical interventions such as blood pressure and cholesterol control, is crucial to reduce the risk of these serious complications and enhance overall well-being.[69]

Management of metabolic syndrome

Managing MetS involves a multifaceted approach aimed at addressing its various components and reducing the risk of associated complications.[70] The main goals of management are to improve lifestyle factors, control individual risk factors (e.g. high blood pressure, high blood sugar, abnormal lipid levels), and prevent cardiovascular diseases and type 2 diabetes.[71] Here are the key components of managing MetS.

Lifestyle modifications

Lifestyle modifications encompass a range of changes that individuals can make to their daily habits, behaviors, and choices to improve their overall well-being, health, and quality of life.[3] These modifications can have a significant impact on preventing or managing various health conditions, including MetS, cardiovascular diseases, diabetes, obesity, and more.[4] It can be managed by various ways, for example.

Healthy diet

Adopt a balanced diet rich in fruits, vegetables, whole grains, lean proteins, and healthy fats.[72] Limit intake of processed foods, sugary beverages, and high-fat, high-sugar items.[73]

Regular physical activity

Engage in regular aerobic exercises (e.g. brisk walking, cycling) and strength training exercises to improve insulin sensitivity, manage weight, and reduce blood pressure.[74]

Weight management

Achieve and maintain a healthy weight through a combination of a healthy diet and regular physical activity.[75] Weight loss can improve insulin resistance and reduce the risk of MetS.[76]

Smoking cessation and limit alcohol consumption

Quit smoking, as it exacerbates cardiovascular risks. If consuming alcohol, do so in moderation, as excessive intake can increase blood pressure and triglyceride levels.[77]

Stress management and adequate sleep

Practice stress-reduction techniques such as yoga, meditation, or deep breathing. Aim for 7–9 hours of quality sleep per night to help manage stress and maintain overall health.[78]

Medical management

Blood pressure control

Monitor blood pressure regularly and work with a healthcare provider to maintain it within the recommended range through lifestyle changes and, if necessary, prescribed medications.[79]

Blood glucose control

Regular monitoring and maintaining blood glucose levels within the target range are vital. Lifestyle changes and medication (if needed) can help achieve this goal.[80]

Lipid management

Maintain healthy lipid levels through diet, exercise, and possibly medications, such as statins, to control cholesterol levels and reduce the risk of cardiovascular disease.[81]

Medications

Depending on individual risk factors and health conditions, a healthcare provider may prescribe medications to manage blood pressure, blood sugar, or cholesterol levels.[82]

Regular monitoring and check-ups

Schedule regular check-ups with a healthcare provider to monitor progress, adjust medications if needed, and undergo necessary tests (e.g. lipid panel, blood glucose tests) to assess the state of the condition.[83]

Education and support

Educate yourself about MetS and its management. Seek support from healthcare professionals, dietitians, and support groups to stay motivated and on track with your management plan.[84]

Multidisciplinary approach

Engage a team of healthcare professionals, including a primary care physician, dietitian, exercise physiologist, and mental health professional, to coordinate care and tailor a comprehensive management plan suited to individual needs.[85] Effective management of MetS involves a proactive approach in making healthy lifestyle choices and working closely with healthcare professionals to monitor and control risk factors.[86] It is important to have a personalized management plan that aligns with individual health status and risk factors.[87]

Pharmacological actions of *Punica granatum* in metabolic syndrome

P. granatum, commonly known as pomegranate, has gained attention for its potential role in preventing and managing MetS due to its rich nutritional profile and various bioactive compounds.[88] While research is ongoing, studies suggest several ways in which pomegranate may contribute to preventing MetS.[89]

Antioxidant properties

Pomegranates are rich in antioxidants, including flavonoids, polyphenols, and Vitamin C.[90] These antioxidants combat oxidative stress, which is implicated in the development and progression of MetS.[91]

Anti-inflammatory effects

Pomegranate has anti-inflammatory properties that may help mitigate the chronic low-grade inflammation associated with MetS.[92] Inflammation is a key factor in the development of insulin resistance and other metabolic abnormalities.[93]

Blood pressure regulation

Studies suggest that pomegranate consumption may help lower blood pressure.[94] Compounds in pomegranate, such as polyphenols and potassium, contribute to improved cardiovascular health, a crucial aspect of MetS prevention.[95]

Lipid profile improvement

Pomegranate has been shown to positively influence lipid profiles by reducing levels of LDL cholesterol and triglycerides while increasing levels of HDL cholesterol, thus aiding in lipid management associated with MetS.[96]

Blood glucose regulation

Research suggests that pomegranate may help regulate blood glucose levels.[97] Certain compounds in pomegranate, such as ellagic acid and punicalagins, may contribute to better glycemic control.[98]

Weight management

Pomegranate consumption may support weight management, which is a fundamental aspect of preventing MetS.[99] The fiber content in pomegranate can promote satiety, potentially aiding in weight control.[100]

Improving insulin sensitivity

Studies indicate that pomegranate may enhance insulin sensitivity, contributing to better glucose metabolism.[101] This can be crucial in preventing insulin resistance, a central component of MetS.[102]

Modulation of gut microbiota

Pomegranate may positively influence gut health by modulating the gut microbiota.[103] A healthy gut

microbiome is associated with improved metabolic health and may contribute to preventing MetS.[104]

Antiatherosclerotic effects

Pomegranate has potential anti-atherosclerotic effects, helping to prevent the buildup of plaques in arteries, which is significant in reducing the risk of cardiovascular complications associated with MetS.[105]

Potential antidiabetic effects

Some studies suggest that pomegranate may have anti-diabetic effects by improving insulin sensitivity and reducing insulin resistance, which is crucial in preventing and managing MetS.[106,107] Incorporating pomegranate into a balanced diet, along with a healthy lifestyle that includes regular physical activity and a well-rounded nutrition plan, may contribute to the prevention of MetS.[108,109] However, it is essential to consult a healthcare professional before making significant dietary changes or starting any new supplementation.

Conclusion

P. granatum (pomegranate) shows substantial potential as a natural therapeutic agent in managing MetS. Rich in antioxidants, polyphenols, and flavonoids, it targets multiple pathological aspects of MetS, including oxidative stress, inflammation, dyslipidemia, hypertension, insulin resistance, and obesity. Its antioxidant and anti-inflammatory activities help counteract chronic inflammation and oxidative damage, while its effects on lipid regulation, blood pressure control, and insulin sensitivity contribute to improved metabolic health. Evidence also suggests antidiabetic benefits and favorable modulation of gut microbiota, further enhancing its relevance. These multifaceted properties position pomegranate as a valuable adjunct in integrated management strategies for MetS. Nonetheless, robust clinical trials and mechanistic studies are essential to determine optimal dosing, treatment duration, and synergistic potential with conventional therapies. A deeper understanding of its pharmacological role may support its incorporation into modern healthcare, offering a holistic approach to reducing MetS-related risks and improving patient quality of life.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Evaluation of Nephroprotective Activity of *Maghz-e-Pambadāna* (Kernel of *Gossypium herbaceum* L.) in Gentamicin-induced Nephrotoxicity

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Abstract

Background: Gentamicin (GM) a widely used aminoglycoside antibiotic, was discovered in 1963 and from 1970s it is used parenterally. It is used to treat Gram-negative infections. The subsequent systemic use causes nephrotoxicity. GM alters the mitochondrial functions, enhancing the production of reactive oxygen species causing oxidative stress in the renal cortex. It also has been found that renal cortical lipid peroxidation,In vivo renal H2 O2 generation and in vivo mitochondria H2 O2 generation are increased in GM-treated rats. **Aims:** To investigate the nephroprotective effects of Maghze-Pambadāna. **Objectives:** To evaluate the nephroprotective effect of aqueous methanolic extract (AME) of crushed Maghze-Pambadāna in rats, in gentamicin (GM) induced nephrotoxicity. **Materials and Methods:** The aqueous methanolic extract (AME) of Maghz-e-Pambadāna, i.e., the kernel of Gossypium herbaceum L. (family: Malvaceae) was investigated for possible nephroprotective effect in rats in gentamicin (GM) induced nephrotoxicity. AME of the kernel of G. herbaceum (560 mg/kg, 840 mg/kg, 1400 mg/kg) was administered orally to rats 4 days before GM treatment, and thereafter, concomitantly with GM (80 mg/kg/day) for another 6 days. **Results:** The results suggested dose-related amelioration in the indices of nephroprotective activity with all the three doses of extract given. The extract at the three doses used, had no significant adverse effect on the body weight of treated rats or on the measured renal functions in serum. However, the two higher doses, significantly and dose-dependently increased SOD activity and GSH concentration, and decreased that of lipid peroxides in the kidney cortex **Conclusion:** AME of Maghz-e-Pambadāna, i.e., the kernel of G. herbaceum L. may contain compounds that could potentially ameliorate GM-induced nephrotoxicity in rats.

Keywords: *Gentamicin-induced nephrotoxicity, kernel of Gossypium herbaceum, Maghz-e-pambadāna, nephroprotective activity*

Introduction

Maghz-e-Pambadāna (kernel of *Gossypium herbaceum* L.) is indigenous to India, Pakistan, the USA, Middle East countries, central Asia, and Africa. Eastern Physicians consider all parts of the *G. herbaceum* plant to be hot and moist and usable as medicine. The plant has been in use from ancient periods. In Unani literature, it is described as *Musammin-e-Badan* (Anabolic), *Muqavvi-e-badan* (Aphrodisiac), *Moallid-e-mani* (Spermatogenic), *Moallid-e-sheer* (Galactagogue), *Zouf-e-kulliya* (Weakness of kidney) and *Baul-e-zulali* (Albuminuria) etc.[1-3] Therefore, it was of interest to determine the renal effects of this drug. In the present study, the effect of aqueous methanolic extract (AME) of crushed *Maghz-e-Pambadāna* is investigated on gentamicin (GM) induced renal toxicity in rats.

GM, a widely used aminoglycoside antibiotic, was discovered in 1963 and from 1970s it is used parenterally. It is used to treat Gram-negative infections such as infection due to *Klebsiella pneumoniae*, *Escherichia coli*, *Citrobacter* species, *Enterobacteriaceae* species, *Pseudomonas* species, *Staphylococcus* species; bacterial meningitis and sepsis, eye infection, bone infection, skin and/or subcutaneous tissue infection, gastrointestinal tract infections; respiratory tract infections; and urinary tract infections.[4] It accumulates in the proximal tubular cells of the kidney leading to mild proteinuria and decreased glomerular filtration rate.[5] The subsequent systemic use causes nephrotoxicity. GM alters the mitochondrial functions, enhancing the production of reactive oxygen species causing oxidative stress in the renal cortex.[6] It also has been found that renal cortical lipid peroxidation,[7] *In vivo*

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renal H_2O_2 generation[8] and *in vivo* mitochondria H_2O_2 generation[9] are increased in GM-treated rats. Moreover, hydroxyl radical scavengers and chelators have been found to lessen the GM-induced functional and histological tubular damage.[10] Therefore, in the present work, we attempted to test the possible protective action of the kernel of *G. herbaceum* on GM-induced nephrotoxicity in rats.

Nephrotoxicity is the adverse effect on renal function caused directly or indirectly by substances which include molds, fungi, anticancer drugs like cisplatin, antibiotics like aminoglycosides, metals such as mercury, arsenic, and lead, and drugs of abuse like cocaine. The common clinical presentations of nephrotoxicity are acute renal failure, tubulopathies, and glomerulopathies.[11]

Materials and Methods

Chemicals

Gentamicin (GM) (Wockhardt Ltd.) Was purchased from Bhagirath Place, Delhi (India). The other chemicals utilized in the present study were provided by JAMIA Hamdard, New Delhi, India.

Plant material

The dried kernels of seeds of *Maghz-e-Pambadāna (G. herbaceum* L.) were purchased from M/S Mohammad Hussain and Ajmal Hussain, Khari Bawli, Delhi - 110 006. The identity of the purchased drug was established as the kernel of the seed of *G. herbaceum* by the scientist at National Institute of Science Communication and Information Resources, Dr. K. S. Krishnan Marg, Pusa Gate, New Delhi 110 012.

Preparation of extract

The crushed dried kernels of the seeds of *G. herbaceum* were extracted with aqueous methanol using Soxhlet's Apparatus (25 cycles). Methanol was recovered by distillation method under reduced pressure. The dark brown residue left after the removal of the solvent was coded as AME. The yield of AME was 15.7% w/w in terms of starting material.

Animals and environmental conditions

The animals used for the study were obtained from Central Animal House, Jamia Hamdard, New Delhi (Registration No. 173/CPCSEA). The experiments were performed in accordance with the guidelines for the care and use of laboratory animals, laid down by the Committee for the Purpose of Control and Supervision of Experiments in Animals, Ministry of Social Justice and Empowerment, Government of India, January 2000. All animals were housed in groups in polypropylene cages and maintained on a standard pellet diet supplied by Amrut Laboratory Rat and Mice Feed, New Maharashtra Chakan Oil Mills Ltd. Mumbai. Water was allowed *ad libitum*. Animals were maintained under standard environmental conditions (22°C ± 5°C with 12 h of light/dark cycle).

Experimental design for gentamicin-induced nephrotoxicity

The experiment was conducted on Albino Wistar rats of either sex weighing about 180–260 g were considered for the investigation and were acclimatized for 3 days before the initiation of the study. In the experiment, 1% Carboxymethyl cellulose (CMC) in water was used as a vehicle and given in volume of 10 mL/kg. All the treatments were given in the form of a suspension in the vehicle and given in a volume of 10 mL/kg. The rats were assigned randomly to 10 groups as follows:

- Group 1: Treated orally for 10 days with normal saline (1 mL/kg), during the last 6 days of treatment also injected intramuscularly (i.m.) with 0.9% normal saline at a dose of 1 mL/kg/day
- Group 2: Treated as in Group 1 except that the normal saline was replaced with GM at a dose of 80 mg/kg/day
- Group 3, 4 and 5: Treated orally with kernel of *G. herbaceum* extract at doses of 560 mg/kg/day (low dose [LD]), 840 mg/kg/day (medium dose [MD]), 1400 mg/kg/day (high dose [HD]), respectively for 10 days, and during the last 6 days of treatment also injected i.m. GM at a dose of 80 mg/kg/day
- Group 6 and 10: Treated orally for 10 days with Vitamin E 400 mg/kg/day, except that for Group 6, during the last 6 days of treatment also injected i.m. GM at a dose of 80 mg/kg/day
- Group 7, 8, and 9: Treated orally only with the kernel of *G. herbaceum* extract at doses of 560 mg/kg/day (LD), 840 mg/kg/day (MD), 1400 mg/kg/day (HD), respectively, for 10 days.

Twenty-four hours after the last treatment, the animals were anesthetized with diethyl ether, and 2–3 mL of blood samples were collected in sterile centrifuge tubes and covered with parafilm and left undisturbed at 37°C for 1 h after which they were subjected to cooling in a refrigerator for 3 h. The clot formed was then removed and the serum samples were then decanted out. These serum samples were then centrifuged at 3000 rpm for 15 min. These supernatants after centrifugation were the serum samples used for analysis. The serum obtained was stored at −20°C pending measurements of creatinine and urea concentrations. Only nonhemolysed serum was used. The kidneys were removed quickly, rinsed in ice-cold saline, dried on filter paper, and weighed; one kidney was placed in formaldehyde for subsequent histological processing, and the other one for biochemical estimations.

Estimation of biochemical parameters

In plasma, creatinine, and urea were measured using freshly prepared reagents. Glutathione (GSH) level, superoxide dismutase (SOD) activity, and lipid peroxidation in the cortex of the right kidney were measured spectrophotometrically by the methods described.[12-15] Lipid peroxidation product, thiobarbituric acid reactive substances (TBARS) was taken as an index of the degree of lipid peroxidation.

Histopathological studies

Small pieces of the cortex of the left kidney were fixed in 10% neutral buffered formalin, dehydrated in graded alcohol and embedded in paraffin wax, sectioned at 5 mm thickness, and stained with hematoxylin and eosin for light microscopic examination.

Statistical analysis

Statistical analysis was carried out using Graphpad Prism 3.0 (Graphpad software San Diego, CA, USA). All results are expressed as mean ± standard error of mean Groups of data were compared with the analysis of variance followed by Dunnett's *t*-test. Values were considered statistically significant when $P < 0.05$. Values were considered extremely significant when $P < 0.01$. Values were considered nonsignificant, when $P > 0.05$.

Results

As shown in Table 1 below, GM treatment significantly increased the concentrations of urea and creatinine in plasma. The generation of oxygen-free radicals in the kidney cortex plays an important role in the pathogenesis of GM nephrotoxicity. Therefore, in the present work, we aimed at testing, in this species, the possible protective effect of AME of *Maghz-E-Pambadāna* on GM nephrotoxicity. AME of *G. herbaceum* seed kernels (560, 840, 1400 mg/kg) was given orally to rats 4 days before GM treatment, and thereafter, concomitantly with GM (80 mg/kg/day) for another 6 days. Nephrotoxicity was evaluated histopathologically by light microscopy, and biochemically by measuring the concentrations of urea and creatinine in serum, reduced GSH, lipid peroxidation, and SOD activity in the kidney cortex. The results suggested that a dose-related amelioration in the indices of toxicity was noted when AME doses were given. The AME at the three doses used, had no significant adverse effects on the body weight of treated rats or on the measured renal functions in serum. However, these three doses significantly and dose-dependently increased SOD activity and GSH concentration and decreased that of lipid peroxides in the kidney cortex.

Discussion

The doses of the AME of *G. Herbaceum* seed kernels were given for a total period of 10 days. The dose and duration of treatment with GM used here, produces in rats, a moderate degree of nephrotoxicity.

In this study, the effect of AME of *Maghz-e-Pambadāna* was examined in GM-induced nephrotoxicity model. The administration of GM at 80 mg/kg for 6 days caused renal dysfunctions in the rats as induced by the increase in blood urea and serum creatinine compared with control. Co-administration of AME prevented the rise in blood urea and serum creatinine significantly.

In this study, the effect of AME of *Maghz-e-Pambadāna* at three different doses (560 mg/kg body wt./day, 840 mg/kg body wt./day, and 1400 mg/kg body wt./day) and of Vitamin E on renal functions was examined in GM-induced nephrotoxicity rat model. Nephrotoxicity was induced by daily subcutaneous (in the neck region) administration of GM at 80 mg/kg for 6 days. Results confirmed that GM produced significant nephrotoxicity as evidenced by significant changes in blood urea, serum creatinine, GSH, TBARS, SOD, and histopathology. In other words, the nephroprotective effects of *Maghz-e-Pambadāna* at all three doses and of Vitamin E are significantly effective.

A relationship between oxidative stress and nephrotoxicity of GM has been well documented in many experimental animal models. Administration of SOD provides a marked protection against GM-induced impairment of renal function.[16] Co-administration of antioxidant, Vitamin E, and selenium is protective against GM-induced nephrotoxicity.[17] Based on this evidence,

Table 1: The effect of kernel of *Gossypium herbaceum* extract on biochemical parameters in gentamicin-induced nephrotoxicity in plasma and renal cortex of rats

Groups	Urea	Creatinine	GSH	TBARS	SOD
Group 1: Saline + Saline	36.87±0.85	1.93±0.18	2.3±0.2	116.5±11.7	2547±40
Group 2: Saline + GM	55.04±3.86	3.54±0.25	1.44±0.02	233.9±16.1	1719±45
Group 3: LD + GM	36.97±2.23	2.38±0.20	1.22±0.02	205.5±17.1	1647±45
Group 4: MD + GM	29.10±4.31	2.40±0.25	2.0±0.3	120.5±12.9	2332±47
Group 5: HD + GM	35.19±3.78	1.94±0.15	2.2±0.2	122.5±12.5	2402±49
Group 6: Vitamin E + GM	36.69±1.66	3.44±0.18	1.91±0.04	231.8±16.5	1841±49
Group 7: LD	27.18±2.12	2.21±0.14	2.0±0.02	109.4±10.8	2339±57
Group 8: MD	29.85±2.39	2.41±0.14	2.2±0.2	105.4±10.1	2387±49
Group 9: HD	26.18±1.23	2.38±0.30	2.4±0.2	95.4±10.6	2484±42
Group 10: Vitamin E	23.58±1.28	2.76±0.27	2.6±0.2	115.4±11.6	2527±40

Values are means±SEM (n=6) GM (80 mg/kg/day for 6 days) was injected i.m., and AME of the kernel of *Gossypium herbaceum* given concomitantly at oral doses of LD (560 mg/kg), MD (840 mg/kg), HD (1400 mg/kg). Urea and creatinine were expressed as mg/dL. GSH refers to reduced glutathione (mmol SH/100 g). TBARS (nmol/g). SOD is expressed as units/g kidney cortex. AME: Aqueous methanolic extract, GM: Gentamicin, TBARS: Thiobarbituric acid reactive substances, SOD: Superoxide dismutase, GSH: Glutathione, SEM: Standard error of the mean, LD: Low dose, MD: Medium dose, HD: High dose, SH: Sulfhydryl groups, i.m.: Intramuscularly

it may be concluded that *Maghz-e-Pambadāna* showed nephroprotective action against GM-induced nephrotoxicity possibly through the antioxidant action of its AME, but it needs further exploration. Since the nephroprotective effect of *Maghz-e-Pambadāna* at a higher dose is weaker than that of *Maghz-e-Pambadāna* at a lower dose. It is advised not to use this drug in higher amounts.

The present results indicated that AME of *Maghz-e-Pambadāna*, particularly at the highest dose used, was effective in ameliorating the studied biochemical and histological effects of GM-induced nephrotoxicity. The mechanism (s) of the nephroprotective effect of AME of *Maghz-e-Pambadāna* is not certain but may be related to the scavenging of free radicals (oxygen metabolites) that are generated from GM-induced nephrotoxicity.[18] It has been shown that GM-induced nephrotoxicity is associated with a significant decrease in GSH levels, and catalase and SOD activities[19-22] and agents with antioxidant actions may be effective in ameliorating the nephrotoxic signs of GM. These include some Vitamins (*e.g.,* Vitamins E and C) and natural products (e.g*.,* melatonin, garlic, and *Ginkgo biloba*).

Conclusion

The results suggest that all the three doses along with Vitamin E have nephroprotective effect in GM-induced nephrotoxicity in rat model possibly through their antioxidant actions and may contain compounds that could potentially ameliorate GM nephrotoxicity in rats.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Physicochemical Characteristics and High-performance Thin-layer Chromatography Fingerprinting of Unani Pharmacopeial Formulation *Habb-e-Tabashīr*

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Abstract

Background: The standardization and evaluation of Unani formulations are essential for ensuring their quality, safety, and efficacy. *Habb-e-Tabashīr* is a classical Unani herbal–mineral formulation with therapeutic applications, particularly in fever, hyperacidity, and excessive thirst. This study aims to establish a scientific basis for the formulation through organoleptic, physicochemical, phytochemical, and chromatographic evaluations. **Materials and Methods:** The raw ingredients of *Habb-e-Tabashīr* were authenticated and processed as per the National Formulary of Unani Medicine guidelines. The formulation underwent standardization through organoleptic evaluation (color, odor, texture, and taste), physicochemical tests (moisture content, ash values, pH, and extractive values), and phytochemical screening for active constituents. High-performance thin-layer chromatography (HPTLC) fingerprinting was conducted to establish a qualitative profile of its constituents. **Results:** The physicochemical analysis revealed a total ash value of 6.616%, acid-insoluble ash of 5.08%, and a moisture content of 9.5%. The pH was recorded at 7.30. Successive solvent extraction showed extractive values of 0.92% (petroleum ether), 3.14% (chloroform), 5.22% (methanol), and 3.38% (aqueous). HPTLC analysis demonstrated distinct chromatographic fingerprints under ultraviolet light at 254 nm and 366 nm, confirming the presence of bioactive compounds. **Conclusion:** The comprehensive standardization of *Habb-e-Tabashīr* ensures its quality, safety, and reproducibility in Unani medicine. The findings provide scientific validation of its formulation and therapeutic claims, supporting its continued use in traditional medicine. Further studies, including pharmacological and clinical evaluations, are recommended to substantiate its efficacy and expand its potential applications.

Keywords: *Habb-e-Tabashīr, high-performance thin-layer chromatography fingerprinting, physicochemical evaluation, phytochemical screening, standardization, Unani medicine*

Introduction

The standardization and evaluation of Unani formulations are crucial for ensuring these traditional medicine's quality, safety, and efficacy. *Habb-e-Tabashīr* is a classical Unani Pharmacopeial formulation with a herbal–mineral origin, widely utilized for its diverse therapeutic benefits. It is known for its *Mufarreh* (exhilarant), *Daf-e-Tap* (antipyretic), *Daf-e-Humuzzat* (antacid), and *Musakkin* (sedative) pharmacological actions. Traditionally, it is prescribed for conditions such as *Ḥummiyāt* (fevers), *Atash-e-Mufrit* (excessive thirst), and *Hummuzat-e-Meda* (hyperacidity).[1,2] In addition, due to its bioactive constituents, it is valued for its antidote, anti-inflammatory, antioxidant, antiviral, and immunomodulatory properties.[3,14]

The formulation derives its name from its principal ingredient, "*Tabashīr*" (bamboo silica), which is believed to possess potent antioxidant, anti-inflammatory, and immunomodulatory properties. Along with *Tabashīr*, the composition of *Habb-e-Tabashīr* includes other herbal and mineral ingredients such as Zahar Mohra (serpentine stone) and several pharmacologically active substances [Table 1]. These ingredients are carefully processed following classical Unani pharmacopeial guidelines to enhance their therapeutic potential, safety, and efficacy.

To ensure the consistency and quality of *Habb-e-Tabashīr*, standardization techniques, including high-performance thin layer chromatography (HPTLC) fingerprinting,

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are employed. This scientific approach helps validate the formulation, providing a robust foundation for its therapeutic claims and ensuring compliance with global quality standards for traditional medicine.

Materials and Methods

Procurement and authentication

The raw ingredients for *Habb-e-Tabashīr* were sourced from Nadeem Dawakhana, Delhi, and authenticated by experts from SUMER and SCLS, Jamia Hamdard, ensuring compliance with Unani pharmacopeial standards.

Formulation preparation

The formulation was prepared following the *National Formulary of Unani Medicine* guidelines:

Table 1: Ingredients of *Habb-e-Tabashīr*[1]

Unani name	Scientific/botanical name	Quantity (g)
Tabashīr	*Bambusa arundinaceae* Retz.	90
Tukhm-e-Gaozaban	*Borago officinalis* L.	60
Satt-e-Gilo	*Tinospora cordifolia*	60
Dana Heel Khurd	*Elettaria cardamomum*	60
Zahar-Mohra	Serpentine/borage stone	40

Granulation

- Ingredients were powdered, sieved (80-mesh), and mixed in specified ratios
- A wet mass was prepared by adding water, passed through a 10-mesh sieve (granule size: 0.2–4.0 mm), and dried in the shade for 3–4 days.

Tablet formation

Dried granules were compressed into uniform tablets using a tablet compression machine in the Department of Ilmul Advia, SUMER, Jamia Hamdard.

Packaging and storage

- Tablets were packed in airtight PET containers with silica gauze to prevent moisture
- Containers were labeled with information regarding dosage details: *Habb-e-Tabashīr* (500 mg, twice daily).

Standardization

The formulation underwent organoleptic, physicochemical, and phytochemical evaluations to ensure quality and safety Tables 2-15:

- Organoleptic properties: Assessed for color, odor, texture, and taste

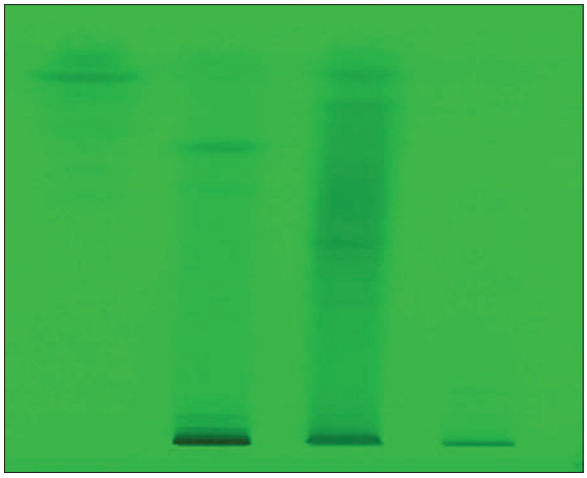

Figure 1: Under ultraviolet light of 254 nm

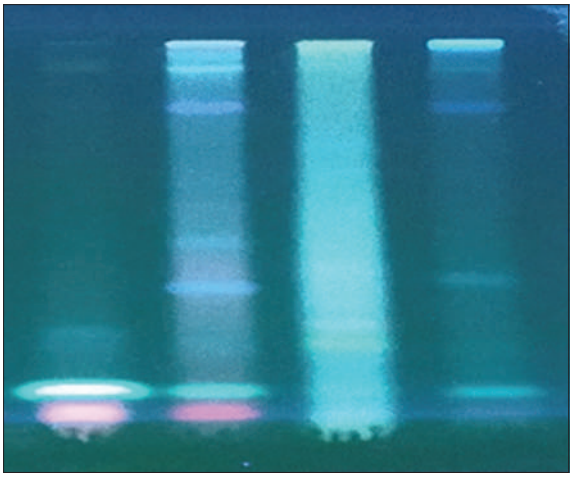

Figure 2: Under ultraviolet light of 366 nm

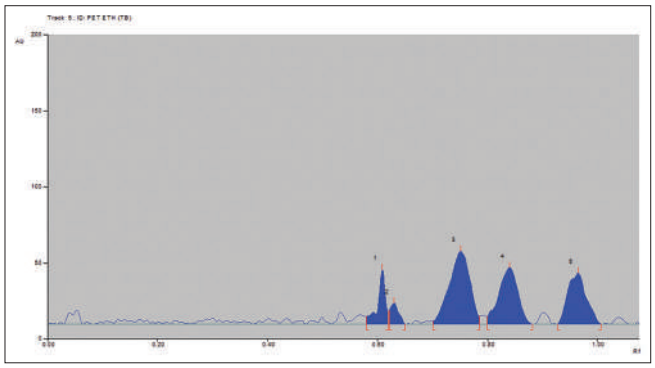

Figure 3: Chromatogram of *Habb-e-Tabashīr* 254 nm (Track-1)

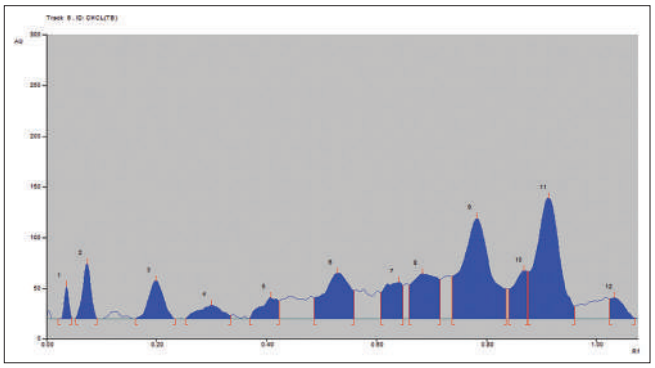

Figure 4: Chromatogram of *Habb-e-Tabashīr* 254 nm (Track-2)

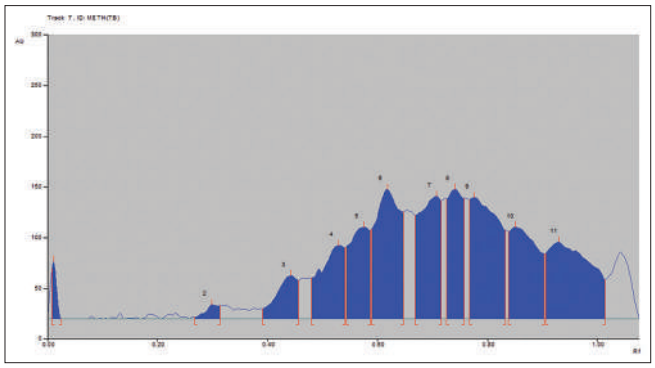

Figure 5: Chromatogram of *Habb-e-Tabashīr* 254 nm (Track-3)

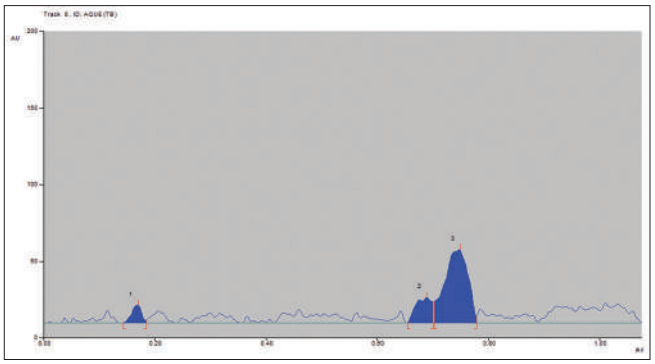

Figure 6: Chromatogram of *Habb-e-Tabashīr* 254 nm (Track-4)

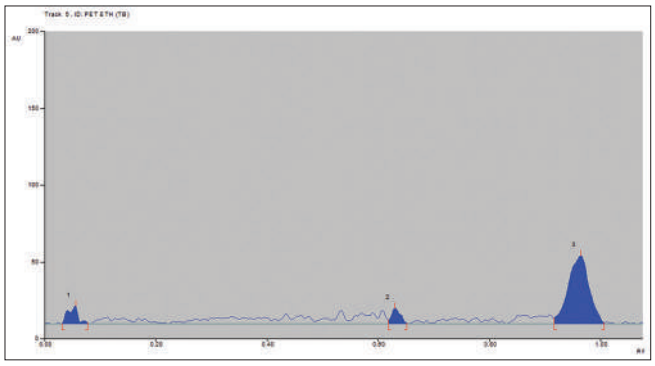

Figure 7: Chromatogram of *Habb-e-Tabashīr* 366 nm (Track-1)

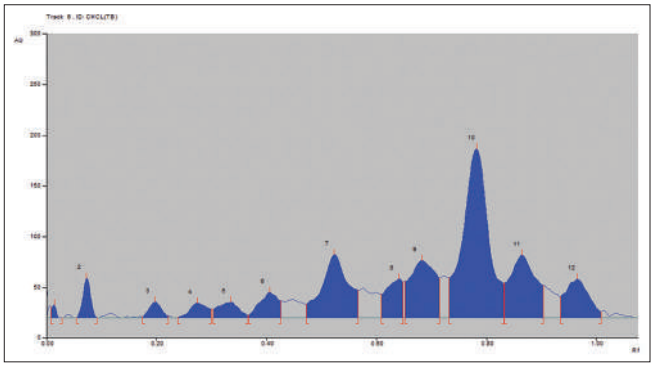

Figure 8: Chromatogram of *Habb-e-Tabashīr* 366 nm (Track-2)

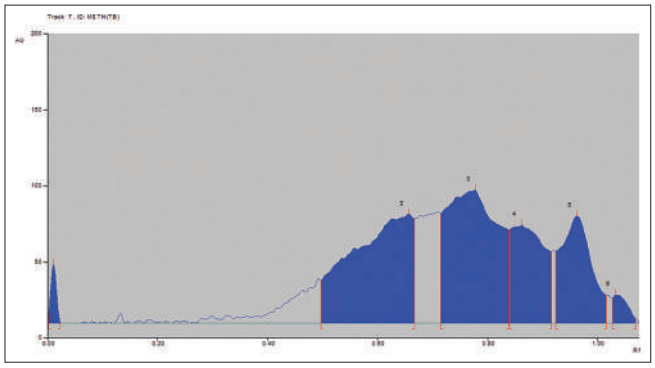

Figure 9: Chromatogram of *Habb-e-Tabashīr* 366 nm (Track-3)

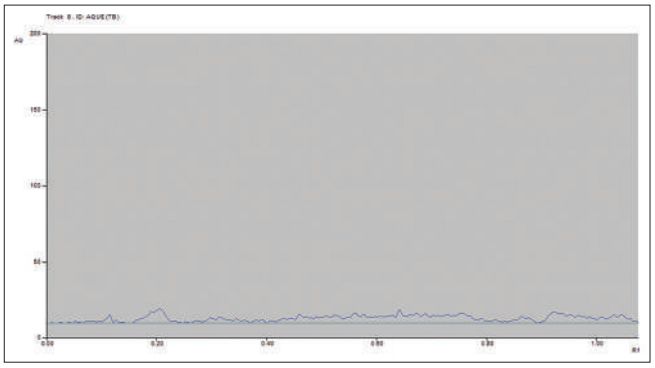

Figure 10: Chromatogram of *Habb-e-Tabashīr* 366 nm (Track-4)

- Physicochemical tests: Moisture content, pH, ash values, and extractive values were determined
- Phytochemical screening: Alkaloids, glycosides, tannins, and flavonoids were qualitatively analyzed.

Determination of ash value

Determination of ash value for Habb-e-Tabashīr

To determine the ash value of *Habb-e-Tabashīr*, 6 g of powdered drug were placed in a silica crucible and incinerated at 450°C for 6 h. After the incineration process, the crucible was allowed to cool at room temperature. The remaining ash content was then measured to calculate the total ash value. The percentage of total ash value was calculated using the following formula:

%Total ash value = (Weight of drug taken) ÷ (Weight of total ash) × 100

Acid insoluble ash for Habb-e-Tabashīr

To determine the acid-insoluble ash content of *Habb-e-Tabashīr*, 6 g of the powdered drug was initially incinerated as described in the total ash value determination. After this, the remaining ash was mixed with 10 ml of hydrochloric acid (HCl) and 90 ml of water, ensuring no sample adhered to the sides of the container. The mixture was boiled in a water bath for 10 min.

The insoluble matter collected on ashless filter paper was thoroughly washed with hot water to remove any soluble components. After washing, the insoluble matter was ignited at 450°C for 6 h in a furnace.

The percentage of acid-insoluble ash was calculated using the formula:

%Acid insoluble ash = (Weight of acid insoluble ash) ÷ (Weight of drug taken) × 100

Water soluble ash

The water-soluble ash content of *Habb-e-Tabashīr* was determined by dissolving the total ash in distilled water. The insoluble portion was filtered, washed, and ignited at 450°C. The soluble ash was calculated by subtracting the weight of the insoluble portion from the total ash.

Loss on drying

The moisture content of *Habb-e-Tabashīr* was determined by placing a 2.0 g powdered sample on a tarred evaporating plate, which was then dried at 105°C for 6–8 h. The drying process continued until two consecutive weight readings were consistent.

Determination of pH

The pH of *Habb-e-Tabashīr* was determined by preparing a 1% solution of the drug. For *Habb-e-Tabashīr*, 1.0 g of the drug was dissolved in 100 mL of distilled water, followed by filtration. The pH was measured using a standard glass electrode submerged in the filtered solution.

Table 2: Comparison of physical properties of *Habb-e-Tabashīr* with the standards of Unani formulary characteristics

Physicochemical properties	Standard as per Unani formulary[2]	Test drug: Formulated
Appearance	Tablet	Tablet
Color	Clay	Clay
Smell	Agreeable	Agreeable
Taste	Clay like	Elaichi flavor

Table 3: Physicochemical analysis of *Habb-e-Tabashīr*

Physicochemical standards	Percentage
Loss of weight on drying at 105°C (%)	9.5
Ash value	
Total ash	6.616
Acid insoluble ash	5.08
Water soluble ash	0.4
pH value	7.30
Extractive values in different organic solvent	
Pet ether	0.92
Chloroform	3.14
Methanol	5.22
Aqueous	3.38

Determination of extracting value

Successive extraction

The extracting values of *Habb-e-Tabashīr* were determined using successive extraction. In this process, 50 g of powdered drug was subjected to extraction in a Soxhlet apparatus with different solvents: petroleum ether, chloroform, methanol, and water. The extracts were then evaporated to dryness using a water bath, and the constant extractive weights were recorded. The percentage of successive soluble extractives was calculated using the formula:

% Successive soluble extractive = (Weight of extract × 100)/Weight of drug taken

High-performance thin-layer chromatography fingerprinting

HPTLC was performed to establish a fingerprint profile:

- Sample preparation: Hydroalcoholic extracts of tablets were used
- Chromatographic conditions:
  - Stationary phase: Silica gel 60 F254 plates
  - Mobile phase: Optimized solvent system for active constituents
  - Detection: Ultraviolet (UV) light visualization at 254 nm and 366 nm.
- Data analysis: Rf values and chromatogram peaks were documented for quality control and reproducibility.

This comprehensive process ensured adherence to Unani standards and guaranteed the formulation's safety, efficacy, and consistency.

Results

Physicochemical standardization of test drug

The test drug was assessed and fingerprinting was done using the following parameters:

Chromatographic analysis

Thin layer chromatography (TLC) fingerprinting profiles were developed for the aqueous, petroleum ether, chloroform, and methanol extracts of *Habb-e-Tabashīr* to establish a qualitative profile of the constituents.

TLC is a widely used, contemporary, and automated technique for separating components to generate reference

Table 4: Extract values of *Habb-e-Tabashīr*

Extracts	Weight of drug (g)	Weight of empty beaker (g)	Weight of beaker with extraction	Weight of extract (g)	Weight of extractive matter (%)
Pet-ether	50	33.68	34.14	0.0092	0.92
Chloroform	50	32.73	34.30	0.0314	3.14
Methanol	50	32.69	35.30	0.0522	5.22
Aqueous	50	31.30	32.99	0.0338	3.38

Table 5: Thin-layer chromatography-*Habb-e-Tabashīr*

Solvent	Short wavelength (254 nm) spot	Long wavelength - (366 nm) spot
Petroleum ether	1	1
Chloroform	3	5
Methanol	2	1
Aqueous	0	0

Table 6: Rf values of *Habb-e-Tabashīr* at 254 nm (Track-1)

Peak	Rf value	Maximum height (AU)	Maximum (%)	Area (%)
1	0.58	36.3	21.43	9.94
2	0.62	13.9	8.20	4.37
3	0.70	48.1	28.40	36.57
4	0.80	37.4	22.07	26.06
5	0.93	33.7	19.90	23.06

Table 7: Rf values of *Habb-e-Tabashīr* at 254 nm (Track-2)

Peak	Rf value	Maximum height (AU)	Maximum (%)	Area (%)
1	0.02	31.9	5.59	1.22
2	0.05	54.5	9.56	3.94
3	0.16	37.6	6.60	4.85
4	0.25	13.4	2.36	2.83
5	0.37	20.7	3.64	3.19
6	0.49	45.0	7.90	10.45
7	0.61	36.1	6.33	5.99
8	0.66	44.5	7.80	10.02
9	0.74	99.0	17.38	24.78
10	0.84	47.4	8.32	5.86
11	0.88	119.0	20.88	24.26
12	1.02	20.8	3.66	2.62

Table 8: Rf values of *Habb-e-Tabashīr* at 254 nm (Track-3)

Peak	Rf value	Maximum height (AU)	Maximum (%)	Area (%)
1	0.01	56.5	6.02	1.15
2	0.27	13.9	1.48	0.89
3	0.39	42.6	4.53	4.15
4	0.48	72.4	7.71	7.89
5	0.54	90.7	9.67	8.33
6	0.59	127.7	13.60	14.37
7	0.67	120.9	12.89	11.95
8	0.73	127.7	13.61	8.98
9	0.77	119.5	12.73	15.66
10	0.84	90.7	9.67	11.72
11	0.91	75.9	8.09	14.91

fingerprints for herbs. These fingerprints serve as benchmarks to assess the raw materials and assay in the final product for consistency and quality.

Table 9: Rf values of *Habb-e-Tabashīr* at 254 nm (Track-4)

Peak	Rf value	Maximum height	Maximum (%)	Area (%)
1	0.14	11.8	15.42	7.77
2	0.66	16.6	21.70	17.75
3	0.70	48.0	62.88	74.48

Table 10: Rf values of *Habb-e-Tabashīr* at 366 nm (Track-1)

Peak	Rf value	Maximum height (AU)	Maximum (%)	Area (%)
1	0.03	11.5	17.42	10.41
2	0.62	10.3	15.56	8.10
3	0.92	44.4	67.02	81.50

Table 11: Rf values of *Habb-e-Tabashīr* at 366 nm (Track-2)

Peak	Rf value	Maximum height (AU)	Maximum (%)	Area (%)
1	0.01	12.6	2.31	0.49
2	0.05	39.2	7.15	2.51
3	0.17	15.7	2.87	1.63
4	0.24	14.6	2.67	2.13
5	0.30	15.5	2.83	2.71
6	0.37	25.3	4.62	3.88
7	0.47	62.3	11.38	13.62
8	0.61	38.6	7.06	5.30
9	0.65	56.7	10.36	12.01
10	0.73	166.9	30.49	35.15
11	0.83	61.8	11.29	13.09
12	0.94	38.2	6.98	7.47

Table 12: Rf values of *Habb-e-Tabashīr* at 366 nm (Track-3)

Peak	Rf value	Maximum height (AU)	Maximum (%)	Area (%)
1	0.00	39.1	11.11	1.62
2	0.50	71.7	20.38	31.81
3	0.72	87.6	24.88	33.27
4	0.84	64.5	18.33	15.55
5	0.92	70.4	20.00	15.68
6	1.03	18.6	5.29	2.07

This method ensures that the extract's composition adheres to the expected standards, providing a reliable tool for quality control.

Sample preparation for thin-layer chromatography

The powdered drug sample (50 g) of *Habb-e-Tabashīr* was placed in a round-bottom flask, and 500 mL of the respective solvent (petroleum ether, chloroform, methanol, or water) was added to extract the active constituents. The extraction was performed using a Soxhlet apparatus for 6 h. The resulting solution was

Table 13: Rf values of *Habb-e-Tabashīr* at 366 nm (Track-4)

Peak	Rf value	Maximum height (AU)	Maximum (%)	Area (%)
1	0.00	39.1	11.11	1.62
2	0.50	71.7	20.38	31.81
3	0.72	87.6	24.88	33.27
4	0.84	64.5	18.33	15.55
5	0.92	70.4	20.00	15.68
6	1.03	18.6	5.29	2.07

Table 14: *Habb-e-Tabashīr* at 254 nm wavelength

Extract	Number of peaks	Rf values	Area (%)
Petroleum ether	5	0.58–0.93	9.94–23.06
chloroform	12	0.02–1.02	1.22–2.62
Methanol	11	0.01–0.91	1.15–14.91
Aqueous	3	0.14–0.70	7.77–-74.4

Table 15: *Habb-e-Tabashīr* at 366 nm wavelength

Extract	Number of peaks	Rf values	Area (%)
Petroleum ether	3	0.03–0.92	10.41–81.50
chloroform	12	0.01–0.94	0.49–7.47
Methanol	6	0.00–1.03	1.62–2.07
Aqueous	6	0.00–1.03	1.62–2.07

filtered, and the filtrate was evaporated to dryness on a water bath and weighed.

For TLC fingerprinting, 30 mg of each extract was dissolved in 1.0 mL of the corresponding solvent. Aqueous extracts were dissolved in methanol. All solutions were filtered through a 0.45 μm syringe filter, yielding extract solutions with a concentration of 20 mg/mL.

Thin-layer chromatography analysis procedure

Sample application

4 μL of each filtered extract solution was applied to 10 cm × 10 cm silica gel 60 F254 precoated TLC plates using a CAMAG Linomat-V applicator, with a bandwidth of 6.0 mm and a sample flow rate of 150 nL/s.

Development

The plates were eluted to a distance of 8.5 cm in a solvent system of toluene:ethyl acetate:formic acid (5:4:1, v/v/v) within a CAMAG twin-trough glass tank presaturated with the mobile phase for 30 min at room temperature.

Visualization

Developed plates were air-dried and photographed under short-wave UV light (254 nm) and long-wave UV light (366 nm).

Scanning

The plates were scanned using a CAMAG TLC densitometry scanner III controlled by WinCATS software. The scanning parameters included:

- Radiation source: Tungsten lamp
- Slit dimensions: 6.0 mm × 0.3 mm
- Scanning speed: 10 mm/s.

This detailed procedure allowed for the qualitative evaluation of chemical constituents and the creation of reliable TLC fingerprints for quality control and comparative analysis of the extracts.

Chromatograms of extracts of *Habb-e-Tabashīr*

Figures 1-10.

Discussion

The present study aimed to standardize and evaluate the quality of the Unani formulation *Habb-e-Tabashīr* through comprehensive physicochemical, phytochemical, and chromatographic analyses. Standardization is critical in ensuring the safety, efficacy, and reproducibility of traditional medicine formulations, which often face challenges due to variable raw material quality, preparation methods, and environmental factors.[15]

Organoleptic and physicochemical properties

Organoleptic parameters (e.g., color, odor, texture) were consistent with the standards outlined in the Unani Pharmacopeia, ensuring proper formulation. Physicochemical evaluations provided a detailed assessment of the quality of the drug. For instance, the pH value (7.30) specified a slightly alkaline rather neutral pH which is almost similar to that of the human body,[16] and hence suitable for its pharmacological actions and therapeutic applications.[1-14,17-20]

The low moisture content (9.5%) ensures stability and reduces susceptibility to microbial contamination, while the ash value (total ash 6.616%, acid-insoluble ash 5.08%, and water-soluble ash 0.4%) reflects the appropriate balance of mineral components in the formulation. These values align with pharmacopeial limits, ensuring consistency in mineral composition and quality.[1,2]

Phytochemical screening

The qualitative analysis indicated the presence of bioactive compounds such as alkaloids, glycosides, flavonoids, and tannins. These phytochemicals are well-known for their therapeutic roles, including anti-inflammatory, immunomodulatory, and antioxidant properties. The most prominent health benefits of phenolic compounds are antioxidant activity, anti-inflammatory properties, antifungal activity, antimicrobial activity, antibacterial properties, anticoronavirus activities, neuroprotective potential, appropriate for skin health, suitable for wound healing, and anticancer activities while flavonoids possess several medicinal benefits, including anticancer, antioxidant, anti-inflammatory, and antiviral properties. They also have neuroprotective and cardio-protective effects.[14,21,22] The

presence of these compounds supports the traditional claims of *Habb-e-Tabashīr*'s efficacy in managing conditions such as fever, excessive hyperacidity, and thirst.[1,2]

Successive extraction and solvent analysis

The extraction process revealed varying solubility profiles of active compounds in different solvents. The Methanolic extract showed the highest extraction yield (12.648%). Methanol is considered a relatively polar solvent, which means it can effectively extract polar compounds such as phenolic acids, flavonoids, and other bioactive molecules often found in plants.[23] Chloroform and aqueous extract also exhibited moderate extractive values (3.14% and 3.38%, respectively). Aqueous extract had the lowest extractive value (0.92%).

High-performance thin-layer chromatography fingerprinting

HPTLC fingerprinting established a robust chromatographic profile for *Habb-e-Tabashīr*. Chromatograms obtained under UV light at 254 nm and 366 nm identified distinct peaks corresponding to various active constituents.

Petroleum ether extract

The extract displayed 5 peaks at 254 nm and 3 peaks at 366 nm. The major compounds were observed at Rf values between 0.58 and 0.93 (Area%: 9.94–23.06 at 254 nm). These peaks correspond to lipophilic constituents.

Chloroform extract

The chloroform extract revealed 12 peaks at 254 nm and 12 peaks at 366 nm. The significant peaks at 254 nm ranged from Rf 0.02–1.02 (Area %: 1.22–2.62), indicating the presence of semi-polar compounds such as alkaloids and glycosides.

Methanol extract

This extract demonstrated 11 peaks at 254 nm and 6 peaks at 366 nm. The major constituents at 254 nm appeared between Rf 0.01 and 0.91 (area %: 1.15–14.91). Methanol extracts primarily polar and semipolar compounds, including flavonoids and tannins.

Aqueous extract

The aqueous extract showed 3 peaks at 254 nm and 6 peaks at 366 nm. The major constituents at 254 nm appeared between Rf 0.14 and 0.70 (area %: 7.77–74.4). This suggests a high concentration of hydrophilic constituents, including polysaccharides and phenolics.

Comparative analysis

The diversity in peak profiles across different solvents highlights the complexity of the formulation. Aqueous and methanolic extracts showed prominent peaks, reflecting their role as primary carriers of the bioactive compounds in the formulation. The chromatographic profiles can serve as a reference for future quality control, ensuring consistency across batches.

Therapeutic implications

The presence of bioactive phytochemicals corroborates the traditional use of *Habb-e-Tabāshīr* in treating *Ḥummiyāt* (fevers), *Atash-e-Mufrit* (excessive thirst), and *Hummuzat-e-Meda* (hyperacidity).[1,2] Furthermore, the anti-inflammatory and immunomodulatory potential of the identified constituents aligns with its traditional use as an antidote and in other therapeutic applications.[14,19,24]

Limitations and future directions

While the study established a fingerprint profile and assessed physicochemical properties, further *in vitro* and *in vivo* studies are required to validate the pharmacological claims and mechanisms of action. Advanced techniques such as LC-MS/MS and NMR spectroscopy could also be employed to identify and quantify the active constituents more precisely.

Conclusion

The study successfully standardized *Habb-e-Tabashīr* using a combination of traditional and modern analytical techniques. The findings validate the quality and efficacy of the formulation, supporting its therapeutic claims in Unani medicine. The HPTLC fingerprinting profiles provide a robust framework for quality control and can aid in regulatory compliance, ensuring safety and efficacy.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

Clinical Improvement in a Morbidly Obese Patient of Sciatica/lumbosacral Radiculopathy with *Ilaj bit Tadbeer*

Abstract

'Irq al-Nasā (Sciatica) is one of the most common manifestations of *Waja' al-Ẓahr* (backache), a type of *Waja' al-Mafāṣil* (arthritis/ arthralgia). In Unani medicine, *Waja' al-Mafāṣil* is one of the most common disorders caused prevalent in general population and increases with advancing age. As per Unani classical text, arthralgia is mostly caused due to *Balgham* (phlegm), followed by *Dam* (blood) and *Ṣafrā'* (bile), whereas *Sawdā'* (black bile) is rarely involved. The management is based on the elimination of the *māddī asbāb* (causative matters) and rectification of *sū'-i-mizāj* (impaired temperament), which can be attained by *tanqiya māwad* (evacuation of morbid matter) and *Ta'dīl* (restoration). We present the case of a 55-year-old female patient suffering from lumbar radiculopathy manifesting as sciatica, besides morbid obesity (Grade II). She was treated with multiple sessions of *Ḥijāma bi'l Sharṭ* (cupping with scarification), *ḥijāma mutaḥarrika* (gliding cupping), *inkibāb* (steam therapy), and *riyāḍat* (exercises). Over a period of nearly 8 months, the patient gradually started having improved mobility, feeling of lightness in the body, reduced pain, and flexibility in joints. *Ḥijāma* and *inkibāb* can be safely and effectively utilized in the management of sciatica and lumbar radiculopathy, without the use of pharmacological or surgical treatment.

Keywords: *Arthralgia, ḥijāma, inkibāb, radiculopathy, sciatica*

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Introduction

Lumbosacral radiculopathy is a clinical term that encompasses a diverse range of symptoms secondary to several mechanical, degenerative, or inflammatory causes that affect at least one of the lumbosacral nerve roots. Although the exact prevalence is not determined, an estimated 60%–90% of the population suffers from backache at least once during their lifetime, of which 5%–10% suffer from radiculopathy. Globally, it is also estimated that about 5 million people suffer from disabling backache.[1] Patients are mostly affected in their midlife – most male patients describe the first occurrence of symptoms in their 40s, while women are generally affected during 50s–60s. However, physically demanding work like military service, diseases, or conditions that promote degenerative changes may cause earlier onset of radiculopathy.[2] Sciatica is the most common presenting symptom of lumbosacral radiculopathy which is characterized by pain in the back radiating to the leg and is distributed in the dermatome of sciatic nerve.[3]

Unani medicine is one of the traditional medicine systems which are included among the Indian Systems of Medicine and also recognized by the World Health Organization. It is currently practiced in more than 20 countries over the world.[4] In Unani medicine, the treatment of a disease is aimed toward restoration of natural equilibrium of the body in a holistic manner, hence promoting natural healing.[5] In Unani literature, the broad term *Waja' al-Mafāṣil* (arthritis/arthralgia) encompasses all kinds of pain, inflammation, and degenerative changes due to a variety of causes.[6] The term *Waja' al-Ẓahr* refers to backache which may be caused by any reason, while *'Irq al-Nasā* refers to sciatica. According to Unani concepts, backache may originate from any part of the back, but mostly, the lumbar or lumbosacral region is affected by the disease, mostly due to *balghamī* (phlegmatic) accumulation.[7,8] It has also been found in a previous study that sciatica is more prevalent in patients with *balghamī* temperament.[9] It is known that the sciatic nerve originates from the lumbosacral region and is one of the most common manifestations of lumbar radiculopathy.

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Quick Response Code:

Recent researches have also elucidated that obesity is likely to be a major risk factor for the development of sciatica.[10]

The management of backache and its related manifestations in Unani medicine is based on *Tanqiya-i-mawād* (evacuation of morbid matter), *imāla* (diversion of morbid matter), and providing relief to the patient. The treatment may be done by "*Ilāj bi'l Ghidhā*" (diet therapy), *'Ilāj bi'l Tadbīr* regimenal therapy, "*Ilāj bi'l Dawā*" (pharmacotherapy), or *'Ilāj bi'l Yad* (surgical intervention) in severe cases. Among the regimenal therapies, *ḥijāma bilā sharṭ* (cupping without scarification), *ḥijāma bi'l sharṭ* (cupping with scarification), and *inkibāb* (medicated steam) are safe and effective therapies for evacuation of morbid matter and also provide palliative relief to the patient.[11] *Ḥijāma bi'l sharṭ* helps to eliminate accumulated morbid matter from the body, while *ḥijāma bilā sharṭ* is effective in diverting the morbid matter from the disease site. In this way, the obstructions get relieved, the flow of blood is stimulated, and healing is promoted.[12] *Inkibāb* involves the application of medicated steam to various parts of the body. The prescribed herbal drugs are boiled in water in a specialized apparatus and the steam is applied on the body surface from a safe distance. It helps in relieving inflammation, relaxing body tissues, and is an effective analgesic.[13]

Case Report

Presenting symptoms

A 55-year-old female patient presented in January 2024 to Ilaj bit Tadbeer Outpatient Department, Majeedia Unani Hospital, Jamia Hamdard with the complaint of backache radiating to legs, and pain in both knees for approximately 5 years. The pain was felt more in the right leg as compared to the left. The onset of the pain was insidious, and the pain was continuous, although it increased when the patient tried to walk or did any kind of exertion and a sharp pain sensation was felt occasionally from the back to the legs. The patient had been unable to walk for the past 1 year, partly due to pain and also due to obesity. She could only walk a few steps with support, otherwise she was carried on a wheelchair. Besides, she was suffering from hypertension for 10 years and hypothyroidism for nearly 5–6 years for which she was already taking allopathic medicines. She had had menopause at 47 years of age. There was no history of diabetes mellitus, hyperlipidemia, surgery, any other chronic disorder, or long-term medication. She had a normal appetite and bowel habits, but sleep was decreased. The patient reported that she could sleep for only 3–4 h a night and remained restless during that period also.

On examination, the patient was conscious, well-oriented, having normal pulse rate, temperature, and respiratory rate; while blood pressure was 140/90 mmHg. Her weight was 98 kg and her calculated BMI was 37 (Obese Class II). The *mizāj* (temperament) of the patient was found to be *balghamī* (phlegmatic) after assessment of *Adilla'-i-Mizāj'* (*Ajnās 'Ashara*, the ten identifying features of temperament). There was mild pitting oedema on feet; while pallor and icterus were absent. Chest examination and cardiac sounds were normal. Abdominal examination revealed no significant findings. On local examination, spinal curvature was maintained, there was no tenderness or altered temperature at the spine. There was also no neurological deficit, muscular weakness, or loss of sensation. The Lasègue test (straight leg-raising test) was positive at 40° in the left leg and 30° in the right leg indicating lumbosacral involvement. On investigation, the biochemical and hematological tests were normal [Table 1]. Magnetic resonance imaging of lumbosacral spine revealed disc bulge and indentation in the lumbar and sacral vertebra.

Management plan

As per standard practice, it was decided to initiate the treatment with conservative management. There were no symptoms which indicated the need for surgery or any kind of emergency management.[14] The patient was generally cooperative and positive in behavior and willing to undergo required therapies and do regular exercises. The treatment was initiated with alternate-day sessions of *ḥijāma mutaḥarrika* (gliding cupping) and *inkibāb* (medicated steam) therapy on all the affected areas to promote relaxation and decrease pain. For *inkibāb*, the drugs *Bābuna* (*Matricaria chamomilla* L. flowers), *Nākhūna* (*Trigonella glabra* subsp. *uncata* [Boiss. and Noë] Lassen seed pods), and *Gul-i-Tesū* (*Butea monosperma* [Lam.] Kuntze flowers) were boiled in water in a steam apparatus. The medicated steam was first applied for 10–12 min on all affected areas, then gliding cupping was done for 5–7 min followed by *ḥijāma bilā sharṭ* (dry cupping) till the signs of *imāla* (diversion) were visible on the skin. After

Table 1: Relevant laboratory investigations of the patient

Tests	Results
Blood sugar fasting (70–100 mg/dL)	86.76
HbA1c (%)	5.8
Bleeding time (1–5 min)	1:30
Clotting time (5–10 min)	6:20
HbsAg	Negative
HCV	Negative
Hemoglobin (12–16 g/dL)	12.9
Serum calcium (8.4–10.2 mg/dL)	9.4
Blood urea (21–51 mg/dL)	22
Total cholesterol (<200 mg/dL)	154
Serum sodium (135–145 mEq/L)	142
Serum potassium (3.5–5.0 mEql/L)	4.6
Vitamin D3 (30–75 ng/dL)	35
IPTH (10–65 pg/mL)	52.16
Free T3 (2.0–4.4 pg/mL)	3.04
Free T4 (0.8–2.0 ng/dL)	1.53
TSH (0.5–4.8 μIU/mL)	4.36

that, the patient was allowed to rest for 15–20 min and then return on the 3rd day.[15] *Roghan Surkh* was used for lubrication during *ḥijāma mutaḥarrika*.[11,16] Besides, the patient was prescribed *Ma'jūn Chobchīnī*, *Ma'jūn Jograj Gogul*, and *Ma'jūn Sūranjān* orally, and *Roghan Qusṭ* for local application, as per the prescribed dosage. After 5–6 sessions, the patient felt relaxed and able to walk a few steps unassisted. Then, we carried out one session of *Ḥijāma bi'l Sharṭ* (cupping with blood-letting) for *istifrāgh* (expulsion of morbid matter). After 7 days of *Ḥijāma bi'l Sharṭ*, the previous treatment was continued along with *riyāḍat* (exercises) to improve movements and *taqlīl-i-ghidhā'* (reduction in diet/ low-calorie diet) to enable some loss of weight. Further sessions of *Ḥijāma bi'l Sharṭ* were carried out after every 45 days, while *ḥijāma mutaḥarrika*, *inkibāb*, and *riyāḍat* were continued in between (after healing of *Ḥijāma bi'l Sharṭ* wounds). The oral medicines were stopped after 3 months, and further management was done with *'Ilāj bi'l Tadbīr* only.

Progress and outcome

For the initial 15–20 days, we did not notice much change in the patient, except that she reported some feeling of relaxation. However, after some days of carrying out the first session of *Ḥijāma bi'l Sharṭ*, the patient had an improvement in her walking ability. After regular sessions of *ḥijāma mutaḥarrika* (gliding cupping) and *inkibāb* (medicated steam) therapy, she gradually started having a feeling of lightness in the body and found it easier to move about, although assistance was still required. With continuous therapies and *istifrāgh* by *Ḥijāma bi'l Sharṭ*, the patient started having gradual improvement in movements and feeling positive about her progress. At present, the patient is able to walk around her house unassisted, her pain is much decreased, and she feels easier during movements. She has been advised to continue taking *ḥijāma mutaḥarrika* (gliding cupping) and *inkibāb* (medicated steam) therapy at least once a week and a session of *Ḥijāma bi'l Sharṭ* once in 2 or 3 months and to continue prescribed exercises and diet to sustain the results.

Conclusion and Future Directions

In the present study, we have reported a case of lumbar radiculopathy who presented with predominant symptoms of sciatica. The patient was morbidly obese and unable to walk even a few steps. The sedentary lifestyle and obesity worsened her symptoms and probably aggravated the disease progression also. Hence, we initiated the treatment with such therapies which would improve mobility and promote relaxation, along with increasing the flow of morbid humors, so that they could be expelled later by *ḥijāma bi'l sharṭ* (cupping with scarification/blood-letting). We observed that the patient had improved movements with gliding cupping and medicated steam therapy which reduced her pain. Over the period of nearly 8 months, during which she has had 6 sessions of *ḥijāma bi'l sharṭ*, her symptoms have reduced, and she has been able to walk for some distance without any support. Similar results have been reported in few recent studies also. In a recent case series study, gliding cupping with *Roghan Surkh* was found to be effective in reducing backache in three patients over 14 days, without causing any adverse effects.[11] In another clinical study, *ḥijāma bi'l sharṭ* was found to be effective in reducing the signs and symptoms of sciatica.[17] Similarly, *Ḥijāma bi'l sharṭ* (wet cupping), *Dalk* (massage), and *Inkibāb* (medicated steam) were found to be effective in reducing the symptoms of low back pain in 97% of patients (n = 31 total) over 14 days.[16] *Dalk*, *Inkibāb*, and pharmacotherapy have also shown positive results in a case study on knee osteoarthritis.[18] Hence, it is evident that *Ḥijāma bilā sharṭ* and *inkibāb* can be effectively utilized in the management of lumbar radiculopathy symptoms.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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