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Review Article

Therapeutic Values of Frequently Used Unani Drug *Turbud* (*Operculina turpethum* (L.)) Silva Manso: A Comprehensive Review

Abstract

Plants are always considered for their multidimensional approach from livelihood to medicinal use. Traditional Systems of Medicine including the Unani System of Medicine (USM) have a treasure of important Medicinal plants. Turbud is one of the important Medicinal plants of the USM. The root powder of the drug is used for the treatment of rheumatism, flatulence, paralysis, scorpion sting, snakebite, and skin disorders (such as Vitiligo, eczema, abscesses, acne, scabies, and warts). It is used frequently for *Mushil* (i.e., therapeutic purgation) in USM. The rhizomes/roots are phlegm-purgative and used for the treatment of phlegmatic and nervous diseases, such as *Waj'al Mafāsil* (Arthritis), *Irqun Nisa (Sciatica) Niqras* (Gout), *Fālij (Paralysis) Laqwa (facial palsy)*, *Ḍīq al-Nafas* (bronchial asthma), and *Su'al* (cough). The present review comprehensively integrates the pharmacognosy, therapeutic uses, and pharmacology and some evidence-based scientific studies of *O. Turpethum* related to its efficacy like anti-inflammatory, anticancer, cytotoxic, antisecretory, ulcer protective, hepatoprotective, and antibacterial activities also incorporated.

Keywords: *Operculina turpethum (Turbud), therapeutic, Unani System of Medicine*

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Introduction

A vast population in developing countries adopted the traditional system of medicine to solve their healthcare-related problems. However, the use of synthetic medicine is continuing but in the present scenario, traditional systems of medicine including Ayurveda, Unani, and Siddha are becoming popular due to their minimal side effects. The Unani system of medicine (USM) is the oldest system of medicine which has a holistic approach to treating various kinds of disease and most of the time the drugs mentioned in this system have tremendous effects on chronic disease. The ingredients of these drugs are derived from plants, minerals, and animals, whereas the majority of drugs are obtained from plants.[1-4]

Turbud is well-known Unani drug and used for its medicinal properties for a long. It is botanically known as *Operculina turpethum* (L.) Silva Manso. It is also known as Silva Manso, and belongs to the family Convolvulaceae, it is the oldest medicinal plant and is used in various traditional systems of medicine. *Turbud* possesses the following pharmacological actions such as *Mushil-i-Balgham wa Ratūbat-i-Raqiqa* (Phlegmagogue), *Mushil-i-Safrā* (cholagogue), *Mohallil-e-Waram* (Anti-inflammatory), *Mus'hil* (Purgative), *Dāfi'-i-Waj'al Mafāsil* (anti-arthritic), hepatoprotective, and antibacterial activities.[5-7]

In the USM, *turbud* has been frequently used for centuries in the treatment of *Waj'al Mafāsil* (Arthritis), *Ḍīq al-Nafas* (bronchial asthma), *Su'al* (cough), *Niqris* (Gout), *Irqun Nisā* (Sciatica), *Fālij (Paralysis), Laqwa (facial palsy), Waja' al warik* (low back pain), etc. The drug also reported its antimicrobial, antioxidant, anticoagulant, antiallergic, expectorant, antiulcer, anxiolytic properties, and some other pharmacological actions.[8,9]

Botanical Descriptions

Turbud consists of the dried root of *Operculina turpethum* (L.) Silva Manso, family Convolvulaceae. It is a perennial twiner and climber, milky juice, slender, fleshy branched root, and the stem is long twisted, very hard, and brown stem. It is grown throughout India at an altitude of 900–1000 m. It is grown in the garden, the root occurs in cylindrical or spirally twisted pieces, and the outer surface is

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grayish-brown along with longitudinal wrinkles. Fracture is irregular, short in bark, and fibrous in wood. The flowers are tubular-campanulate, white, and in a few flower cymes. Fruit globose capsule, enclosed in woody calyx. Leaves variable in shape, ovate-cordate, propagated by seed. Turbud is in two varieties: (i) white and (ii) black, the black turbud is a powerful irritant, and drastic purgation causes vomiting, fainting, and giddiness, so it is not used in medicine, only White Turbud is commonly used as purgative and laxative.[6,10,11]

Synonyms:
- *Ipomoea turpethum* (L.) R.Br.
- *Merremia turpethum* (L.) Rendle
- *Convolvulus turpethum* L.[6,9]

Vernacular name:
- English: Indian Jalap, turpeth
- Hindi: Nisoth, Nisotar, Pitohri
- Unani: Turbud, Nishoth
- Arabic: Turbud
- Urdu: Turbud, Nishoth
- Persian: Turbud
- Ayurvedic: Trivrta, Tribhandi, Triputaa, Saralaa, Suvahaa, Rechani, Nishotra, Kumbha, Kaalaa, Shyaama
- Malayalam: Chivaka, Trikolpakonna, Rochani, Tribhandi
- Bengal: Dudhkalmi, Tohri
- Gujarat: Nashotar, Nahotara
- Orissa: Dudholoma
- Tamil: Shaddai, Kumbam, Karunchivadai
- Telegu: Talladega
- Punjab: Nisoth
- Marathi: Nisottar, Phutkari.[6,9,10,12,13]

Organoleptic Characters of *Turbud* Root

Medicinally used part of the drug is roots. It is available in cylindrical or longitudinal pieces.
- Color: Reddish-gray to brown longitudinal wrinkles, transversely cut surface show thick, whitish bark and light-yellow center
- Shape: Cylindrical elongated
- Size: Length 1.5–15 cm, diameter 1–5 cm
- Taste: Bland at first, slightly acrid, and nauseating
- Odor: Distinct but unpleasant or musty
- Fracture: Short in bark fibrous in wood.[11]

Microscopic Characters of Turbud

Histological diagnostic characters of *Turbud* (Root) are thin cork, 3–5 rows of brown cell secondary cortex 4–6 layers; xylem shows 3–5 radiating arms, small patches of intraaxillary phloem frequently formed, xylem vessels in singles or 2–3 in groups, having simple pits on their walls; calcium oxalate crystals as prisms and rosettes found scattered in the cortex; phloem parenchyma, xylem parenchyma, and medullary ray cells contain starch grains, both simple and compound, simple ones elliptical to spherical with central cleft hilum, compound grains consisting of 2–4 components, the size vary from 5 to 44 μ in diameter, found scattered in the cortex, phloem parenchyma, xylem parenchyma and medullary ray cells.[6]

Powder

The powder of root is grayish to light brown in color consisting of parenchymatous cells, and cellulosic fibers have pointed tips. The vessels consist of simple pits. Simple and compound starch grains elliptical to spherical with a central cleft, measuring 5–44 μ in diameter having 2–4 components, rosette, and prismatic crystals of calcium oxalate.[6]

Chemical constituents

Turbud contains various types of chemical constituents the active principle of the plant is glycoside resin up to 10%, concentrated mostly in root bark, resin is brownish yellow, odorless, and bitter pungent taste. It is soluble in alcohol and partially soluble in ether (WOI). Five glycosidic acids have been isolated from the alcoholic soluble resin of turbud. The turpethinic acids are (i) 11-Hydroxyhexadecanoic acid, (ii) 3,12 dihydroxy pentadecanoic acid (operculonic acid), (iii) 3,12 dihydroxy palmitic acid, (iv) 4,12 dihydroxy pentadecanoic acid, and (v) 4,12 dihydroxy palmitic acid.[11] It contains an ether-insoluble glycoside, turpethin, which constitutes about half of resin and two ether-soluble glycoside, α-turpethein 8% and β-turpethein 0.6%. Various secondary metabolites including saponins, flavonoids, phenolics, and small amount of volatile oil, albumin, glucose, fructose, salt, lignin, ferric oxide, and yellow coloring matter are also present in the chemical composition of the drug.[13]

Mizāj (temperament)

Hār (Hot) in 3°, Yābis (Dry) in 3°.[8,13]

Muḍir (adverse effects)

For the stomach, and *Am'ā'* (Intestine) it produces dryness.[7,8,14]

Muṣliḥ (correctives)

Mastagi (Gum resins of *Pistacia lentiscus*), Roghan-i-Badam (Seed oil of *Prunus amygdalus*), *Kateera* (Gum of *Sterculia urens*).[7,8,15]

Badal (substitute)

Ghariqoon (*Polyporus officinalis*), Hab-ul-nil (*Ipomoea nil*).[7,14]

Dose

5–10 g.[7,8,15]

Dosage forms

The powdered root is used alone or it may be used as *Joshānda* (decoction) with other drug ingredients.[8]

Afʿāl (action)

Turbud has the following pharmacological actions:

- *Mus'hil* (Purgative)
- *Mulayyin* (Laxative)
- *Da'fa-i-Amraz-i-Balgham-wa-Sauda* (removes morbific matters of phlegmatic and biliary diseases) actions
- *Mus'hil-i-Balgham*, (Phlegmagogue)
- *Qāta-i-Balgham-i-Ghaliz* (Expectorant)
- *Munaqqi-i-Dimāg*
- *Muqawwī-i-Dimāgh* (Brain tonic)
- *Munaqqi-i-Meda* (Gastric depurative)
- *Mujaffi-i-Badan* (desiccative)
- *Istifiragh-i-Rutubat* (Excretory)
- *Mus'hil* (Laxative)
- *Mukhrij-i-Didānwa Hiyyāt* (Vermifuge)
- *Mus'hil-i-Safra* (Cholagogue)
- *Mohallil-e-Waram* (Anti-inflammatory)
- *Da'fa-i-Humma* (Antipyretic).[7,12,16-19]

Isteʿmāl (therapeutic uses)

In the USM, there are two types of turbud white and black, white is commonly used in purgative and laxative, white turbud commonly used in *Waj'al Mafāsil* (Arthritis), *Ḍīq al-Nafas* (bronchial asthma), *Su'al* (cough), *Niqris* (Gout), *Irq'al Nasa* (Sciatica), *Falij* (Hemiplegia), *Laqwa* (facial palsy), *Wajul warik* (Ischialgia), *Istisqa* (Ascites), *Junoon* (Insanity), *Sara* (Epilepsy). *Malenkholia* (Melancholia), leprosy, splenomegaly, abdominal troubles, anemia, fevers, constipation, piles, erysipelas, tumors, and jaundice. Turbud has anti-inflammatory properties so it can be used in paralysis, rheumatic fever, and edema hepatic and hemophilic diseases. White *Turbud* is known for moderate-to-mild purgative effect, so also used in acute constipation, fever, chronic constipation, ascites due to cirrhosis of the liver, and splenomegaly. It can be mixed with *Halela Kabli* (*Terminalia chebula*) and used in *Junoon* (Insanity), *Sara* (Epilepsy), and *Malenkholia* (Melancholia). It is also given with *Roghan-e-Badam and Katan* in *Su'āl Kohna* (Chronic Cough) and *Waj'ul-Sadr* (Chest pain).[7-9,12-16,18-20]

Mashhūr Murakkabāt (important unani formulations)

Itrifal Ustu-khud'dus, Itrifal Zamani, Jawarish-i-Oode-Mulayyin, Itrifal Mulayyin, Habb-i-Istisqa, Habb-i-Ayarij, Habb-i-Muqil, Habb-i-Suranjan, Sharbat Mus'hil, Majoon-i-Suranjan, Majoon-e-Najah. Qurs-i-Mulayyin.[6,15,19,21]

Evidence-based Scientific Studies

Laxative effect

In an experimental study in mice, an extract of the dried leaves of *O. turpethum* plant in hexane, chloroform, and methanol showed a laxative effect at low doses (200 and 400 mg/kg). The castor oil was used as positive control in this study. The test drug produced various degrees of wet feces.[22]

Anti-inflammatory effect

In an experimental study, the anti-inflammatory activity of three different extracts (ethanolic, aqueous, and ethereal) of *O. turpethum* has been reported in carrageenan-induced paw edema, cotton pellet-induced granuloma, and formalin-induced arthritis animal model of rats. The aqueous extract was reported more potent fraction in all three animal models.[23] In another experimental study, the anti-inflammatory activity of O. *turpethum* root powder was reported in formalin-induced edema in rats. Root powder of the drug and its Ayurvedic polyherbal formulation (Avipattikar Churna) were administered orally in rats at a dose of 100 mg/kg dose. The drug was found to reduce the formalin-induced edema.[24]

Antimicrobial effect

An experimental study of the ether and ethanol extracts from leaves of *O. turpethum* showed the potent antimicrobial activity against numerous pathogenic bacteria with a minimum inhibitory concentration (MIC) extract range from 0.13 to 0.75 mg/ml. In general, ethanol extracts show higher activity than petroleum ether extracts and produced inhibition zones ranging from 9 to 14 mm in diameter at a concentration of 5.0 mg/ml. The MIC values of active extracts were determined by the broth dilution method. Ethanol extracts had lower MIC values comparable with petroleum ether extract against the tested strains.[25] In another laboratory study, the antimicrobial effect of resin-rich methanolic extracts of *O. turpethum* has shown antimicrobial activity against Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*, *Micrococcus luteus*, and *Escherichia coli*) and Gram-negative bacterial strains (*Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Shigella dysenteriae, and Shigella sonnei*).[26]

Antiarthritic activity

In an *in vitro* study, the ethanolic extracts of *O. turpethum* root showed inhibition of protein denaturation to find the antiarthritic activity, while acetylsalicylic acid was used as a standard. The ethanolic root extracts in various concentrations with bovine serum albumin were measured for potency. A significant inhibition, i.e., 70%, was observed in the case of acetylsalicylic acid, whereas 67.22% with the ethanolic extract of a drug.[27]

Anticancer activity

In an experimental study, the methanolic extract of *O. turpethum* stem (MEOTS) at the dose of 100 mg/kg body weight showed regained level of antioxidant enzymes such as Superoxide Dismutase, Catalase, Glutathione Peroxidase (GPx) and nonenzymic antioxidants such as glutathione (GSH), ascorbic acid (Vitamin C),

alpha-tocopherol (Vitamin E) and inhibited the levels of lipid peroxidation on 7,12 dimethylbenzo anthracene (DMBA) induced breast cancer in female Sprague–Dawley rats. Moreover, a significant reduction in tumor weight was observed in *O. turpethum*-treated groups compared to the nontreated group. This study revealed that the *O. turpethum* possess antioxidant activity and may play a protective role against DMBA-induced breast cancer.[28] Another study in male mice showed ameliorating effects of *O. turpethum* and its isolated Stigma-5,22 dien-3-o-ß-D-glucopyranoside on hematological parameters exposed to a potent carcinogen N-nitrosodimethylamine (NDMA).[29]

Cytotoxic activity

In an experimental study, the aqueous extract of *O. turpethum* exhibited a significant cytotoxic potential with moderate brine shrimp lethality, and LC_{50} value was found to be 81. In another experiment, it was observed that the stem extract of *O. turpethum* has anticancer effects of in DMBA-induced breast tumor in a female rat model. For monitoring their antioxidant efficacy, the ethanolic extracts of stem bark were given orally at 100 mg/kg dose, and also DMBA (as an inducer) was used at a dose of 20 mg for 45 days. In this study, reduction in lipid peroxidation was noted; similarly, increased antioxidant levels with decreased breast tumor weight were also observed.[28]

Antiulcer activity

In an animal experimental study, the methanolic extract and hydroalcoholic extract of the stem of *O. turpethum* were assessed for antiulcer activity in aspirin and pyloric ligation-induced ulcers. Both the extracts of the drug ware showed significant antiulcer activity, whereas it was observed that the hydroalcoholic extract of the drug revealed better results as compared to the methanolic extract (Bhande *et al.,* 2006).[29] In another study in the rats model, it was found that the antiulcer activity of *O. turpethum* and its polyherbal formulation showed a reduction in hyperacidity, gastric ulcers, and gastrointestinal tract-related problems.[30]

Antidiabetic effect

In an experimental study, the anti-diabetic effect of the MEOTS and methanolic extract of *O. turpethum* root (MEOTR) was observed. The MEOTS and MEOTR were evaluated in the streptozotocin-induced type 2 diabetic models. The MEOTS and MEOTR were administered in the dose of 100 mg/kg to normal, glucose-loaded, and experimental diabetic rats for 21 days. The study shows a significant ($P < 0.05$) reduction in fasting blood glucose levels observed in the normal rats at 3 h as well as in the treated diabetic animals at 21 days.[31] In an experimental study, the methanolic extract of the stem and root of *O. turpethum* was found to significantly reduce fasting blood glucose levels in streptozotocin-induced diabetic rats at a dose of 100 mg/kg of body weight. The Glipalamide was used as a standard drug.[32]

Hepatoprotective effect

Methanolic extract of the root of *O. turpethum* showed hepatoprotective, antifibrotic, and anticlastogenic effects by decreasing collagen contents, restoring SMA skeleton, overcoming chromosomal breakage, and sera enzyme markers of the liver injury toward normal levels against NDMA-induced toxic liver injury rats.[3,33] In another study, the ethanolic extract of *O. turpethum* exhibited hepatoprotective effect in paracetamol-induced hepatotoxicity in a rat animal model. In this study, administration of *O. turpethum* in a dose-dependent manner (100–00 mg/kg body weight) showed a significant reduction in the serum levels of serum glutamic oxaloacetic transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase and Bilirubin when compared to the nontreated rats.[34]

Cardioprotective and antidyslipidemia effect

In an experimental study, the ethanolic root extract of *O. turpethum* showed a protective effect on serum lipid profile in male albino mice intoxicated with N-Nitrosodimethylamine. Adult male albino mice, treated with NDMA at a concentration of 10 mg/kg body weight received root extract orally in doses of 300 and 400 mg/kg body weight at 5 h after the administration of NDMA. NDMA-treated mice showed a significant decrease in the levels of LDL in the serum of mice received extract at a concentration of 300 mg/kg body weight, further, an increase in the level of high-density lipoprotein in the serum of mice reported, who received extract at a concentration 400 mg/kg body weight after intoxication with NDMA. It shows that administration of ethanolic extract at a dose of 300 mg/kg body weight significantly attenuated the alterations caused by the intoxication of NDMA when compared with the standard and restored the levels of triglycerides in the serum of mice.[35]

Antinephrotoxic activity

In an experimental study on male mice, the antinephrotoxic effect of steroidal glycoside isolated from ethanolic root bark extract at a dose level of 50 mg/kg in NDMA-induced renal carcinogenesis was observed. A significant reduction in nephrotoxicity biochemical parameters was observed in this study.[35]

Analgesic and antioxidant effects

In an experimental study, the methanolic extract of leaves of *O. turpethum* has shown analgesic and antioxidant effects using acetic acid-induced abdominal writhing reflex and tail flick methods in mice. The antioxidant activity was assessed using photometric 2, 2-diphenyl-1-picrylhydrazyl free radical scavenging assay method.[36]

Conclusion

In this review with an extensive literature survey, it is concluded that Turbud has been used therapeutically as an

important Unani medicine for the treatment of a wide range of disease conditions and also has a diverse pharmacological action. It is also noted that the scientific interest in the drug plant *O. turpenthum* has increased greatly; therefore, the review will help in the further scientific exploration of this valuable medicinal plant.

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Conflicts of interest

There are no conflicts of interest

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Review Article

Hypolipidemic Activity of Medicinal Plants: An Overview

Abstract

Dyslipidemia, characterized by abnormal lipid levels in the bloodstream, is a significant risk factor for cardiovascular diseases and metabolic disorders. In recent years, there has been growing interest in harnessing the therapeutic potential of medicinal plants to mitigate dyslipidemia and its associated health risks. Numerous studies have explored the potential of medicinal plants such as guggul (*Commiphora wightii* (Arn.) Bhandari), fenugreek (*Trigonella foenum-graecum* L.), garlic (*Allium sativum* L.), turmeric (*Curcuma longa* L.), and green tea (*Camellia sinensis* (L.) Kuntze in managing dyslipidemia. These plants contain bioactive compounds such as guggul sterones, trigonelline, allicin, curcumin, and catechins, which have shown promising lipid-lowering properties. The mechanisms underlying the antidyslipidemic effects of these medicinal plants involve the modulation of lipid metabolism pathways. They can reduce total cholesterol, low-density lipoprotein cholesterol, and triglyceride levels while increasing high-density lipoprotein cholesterol concentrations. Moreover, they may exert antioxidant and anti-inflammatory effects, contributing to their overall cardioprotective properties. Medicinal plants have demonstrated significant antidyslipidemic potential, offering a natural and complementary approach to managing dyslipidemia. Further research is warranted to elucidate the specific mechanisms of action, optimal dosages, and long-term safety of these herbal interventions. Integrating medicinal plants into a balanced diet and lifestyle may hold promise for individuals seeking alternative strategies to improve lipid profiles and reduce the risk of cardiovascular diseases and related metabolic disorders. This article provides an overview of the antidyslipidemic effects of various medicinal plants and their bioactive compounds.

Keywords: *Dyslipidemia, hypolidemic activity, medicinal plants, traditional medicine*

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Introduction

Dyslipidemia, a prevalent and increasingly recognized health concern worldwide, represents a complex disturbance in the balance of lipids, or fats, within the bloodstream.[1] This condition manifests as elevated levels of cholesterol, triglycerides, or both, often predisposing individuals to a heightened risk of cardiovascular diseases, including heart disease and stroke.[2] Consuming a diet high in saturated fats, trans fats, and cholesterol can significantly contribute to dyslipidemia.[3] Lack of regular physical activity can lead to higher levels of low-density lipoprotein (LDL) cholesterol and lower levels of high-density lipoprotein (HDL) cholesterol, contributing to dyslipidemia.[4] Genetic factors can influence how the body metabolizes lipids. A family history of dyslipidemia or early onset of cardiovascular disease can increase an individual's risk.[5] Being overweight or obese is often associated with dyslipidemia, particularly elevated triglyceride levels and low HDL cholesterol levels.[6] Conditions such as diabetes, metabolic syndrome, and hypothyroidism can disrupt lipid metabolism and contribute to dyslipidemia.[7] Excessive alcohol intake can increase triglyceride levels and lead to dyslipidemia.[8] Smoking tobacco and exposure to secondhand smoke can lower HDL cholesterol and raise triglyceride levels.[9] Some medications, such as certain antipsychotics, corticosteroids, diuretics, and some HIV medications, can cause dyslipidemia.[10-12] Dyslipidemia typically does not cause noticeable symptoms, making it often referred to as a "silent" condition. The only way to diagnose dyslipidemia is through a blood test (lipid panel).[13] Chest pain or discomfort due to reduced blood flow to the heart muscles, which may be a sign of underlying heart disease.[14] Difficulty in breathing, particularly during physical exertion, can be a symptom of heart disease associated with dyslipidemia.[15] Peripheral artery disease caused by dyslipidemia can lead

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to tingling, numbness, or weakness in the legs or arms.[16] Dyslipidemia can contribute to headaches or migraines in some individuals.[17] Fatty deposits under the skin, particularly around the eyes, elbows, knees, or hands.[18] Dyslipidemia significantly increases the risk of developing heart disease, atherosclerosis (hardening of the arteries), heart attack, stroke, and other cardiovascular events.[19] Dyslipidemia can lead to the narrowing and hardening of arteries in the legs and lower extremities, causing reduced blood flow and potentially leading to pain and nonhealing ulcers.[20] Extremely high levels of triglycerides can cause pancreatitis, a painful inflammation of the pancreas.[21] Dyslipidemia, especially high levels of cholesterol, can increase the risk of developing gallstones.[22] Dyslipidemia is associated with the accumulation of fat in the liver, which can lead to liver inflammation and scarring.[23] If left unmanaged, dyslipidemia can significantly reduce life expectancy and overall quality of life due to the increased risk of severe health conditions.[24] As a result, the management of dyslipidemia has become a paramount aspect of preventive medicine and public health.[25] While conventional pharmacological interventions have proven effective in treating dyslipidemia, there is a growing interest in exploring complementary and alternative approaches to its management, particularly those rooted in traditional medicinal practices.[26]

Medicinal plants, a cornerstone of many traditional healing systems across the globe, offer a vast repository of bioactive compounds that may hold the key to addressing dyslipidemia naturally and holistically.[27] The integration of medicinal plants into the management of dyslipidemia embodies the convergence of modern scientific inquiry and age-old botanical wisdom.[28] Traditional herbal remedies passed down through generations have been employed in diverse cultures for their potential to promote cardiovascular health and regulate lipid profiles.[29] These botanical solutions often harness the therapeutic potential of various plant parts, including leaves, roots, seeds, and fruits, each harboring a unique constellation of bioactive compounds with the capacity to modulate lipid metabolism.[30] This exploration into the realm of dyslipidemia and medicinal plants aims to unravel the intricate relationship between nature's pharmacopoeia and human health.[31] It delves into the scientific underpinnings of traditional herbal knowledge, investigating the efficacy, safety, and mechanisms of action of specific plant-derived compounds in managing dyslipidemia.[32] Furthermore, this inquiry extends beyond individual plant species, encompassing a diverse array of ethnobotanical practices from around the world that have contributed to our understanding of how nature's bounty can play a pivotal role in fostering cardiovascular wellness.[33] In this comprehensive exploration, we navigate the synergy between ancient traditions and contemporary science, shedding light on the potential of medicinal plants to offer holistic solutions for dyslipidemia.[34] By bridging the gap between traditional wisdom and modern medicine, we embark on a journey to unearth nature's treasures, examining their promise in the pursuit of optimal lipid profiles and a healthier, heartier existence.[35,36]

Pharmacological Actions of Medicinal Plants as Antidyslipidemic Effect

Medicinal plants exhibit various pharmacological actions that contribute to their antidyslipidemic effects.[37] These actions target different aspects of lipid metabolism, including cholesterol synthesis, absorption, and elimination.[27] HMG-CoA reductase is a key enzyme involved in cholesterol synthesis.[38] Medicinal plants such as red yeast rice (containing lovastatin-like compounds) and garlic contain bioactive compounds (allicin) that inhibit this enzyme, reducing cholesterol synthesis.[39,40] Some medicinal plants, including red yeast rice and green tea, can increase the activity of LDL receptors in the liver cells. This action helps in the clearance of LDL cholesterol from the bloodstream.[41] Certain plants, such as fenugreek and psyllium, increase the excretion of bile acids in the feces. Bile acids are made from cholesterol in the liver, and their excretion helps reduce cholesterol levels by stimulating the conversion of cholesterol to bile acids.[42] Plant sterols and stanols found in various plants such as soybeans, nuts, and seeds can inhibit the absorption of dietary cholesterol in the intestines, thereby reducing cholesterol levels in the blood.[43] Many medicinal plants possess antioxidant properties due to the presence of compounds like polyphenols (e.g., in green tea and cinnamon).[44,45] Antioxidants help prevent oxidative damage to lipids, including LDL cholesterol, which is a key step in atherosclerosis.[46] Certain plants, such as turmeric and holy basil, have anti-inflammatory properties that help reduce inflammation in blood vessels.[47] Chronic inflammation is associated with dyslipidemia and cardiovascular diseases.[48] Medicinal plants can influence enzymes involved in lipid metabolism. For example, garlic can modulate enzymes that regulate lipid synthesis and degradation.[49] Some plants, like fenugreek, can enhance lipoprotein lipase activity, an enzyme that breaks down triglycerides in the blood, resulting in reduced triglyceride levels.[50] Certain medicinal plants, such as guggul, can reduce the production of very LDL (VLDL), which is a precursor to LDL cholesterol.[51] Medicinal plants can regulate proteins involved in lipid transport, such as apolipoproteins.[52] For instance, amla has been shown to modulate ApoB levels, impacting LDL metabolism.[53] Understanding these pharmacological actions is essential for leveraging the potential of medicinal plants in managing dyslipidemia effectively. However, it is crucial to consult with a healthcare professional before using any medicinal plants for their antidyslipidemic effects, especially if patients are on medication or have underlying health conditions.

Hypolipidemic Activity of *Commiphora wightii* (Arn.) Bhandari

Commiphora wightii (Arn.) Bhandari, commonly known as guggul or guggul gum, is a resinous plant resin that has been used for centuries in traditional Indian (Ayurvedic, Unani) medicine for various health conditions, including its potential to lower lipid levels.[54] The hypolipidemic (cholesterol and lipid-lowering) activity of guggul is attributed to its bioactive components, primarily guggul sterones.[55] Guggulsterones, the active compounds found in guggul, have been shown to reduce total cholesterol, LDL cholesterol (often referred to as "bad" cholesterol), and triglyceride levels in the blood.[55] Guggul has been reported to increase the levels of HDL cholesterol (often referred to as "good" cholesterol), which is beneficial for cardiovascular health.[56] Guggulsterones have been found to inhibit HMG-CoA reductase, an enzyme involved in cholesterol synthesis. By inhibiting this enzyme, guggul helps reduce the production of cholesterol in the liver.[57] Guggulsterones can increase the activity of LDL receptors in the liver. This action helps in the clearance of LDL cholesterol from the bloodstream by promoting its uptake by liver cells.[58] Guggul possesses anti-inflammatory properties that contribute to its lipid-lowering effects. Chronic inflammation is often associated with dyslipidemia, and by reducing inflammation, guggul may help improve lipid profiles.[59] Guggul exhibits antioxidant activity, which can help prevent oxidative damage to lipids, including LDL cholesterol. This antioxidative effect is beneficial in managing dyslipidemia.[60] Guggul has been reported to influence adipose tissue metabolism, promoting the breakdown of fats stored in adipocytes and improving lipid profiles.[61] Guggul may enhance the metabolism of lipoproteins, such as VLDL, thereby indirectly impacting LDL cholesterol levels.[62]

Hypolipidemic Activity of Fenugreek (*Trigonella foenum-graecum* L.)

Fenugreek (*Trigonella foenum-graecum* L.) is a well-known medicinal plant with various health benefits, including potential hypolipidemic activity.[63] The seeds of fenugreek, in particular, are commonly used in traditional medicine and culinary practices.[64] Fenugreek seeds have been found to lower total cholesterol, LDL (LDL) cholesterol ("bad" cholesterol), and triglyceride levels in the blood.[65] Fenugreek has been reported to increase the levels of HDL cholesterol ("good" cholesterol), which is beneficial for heart health.[66] Fenugreek contains soluble fiber and compounds like saponins that can inhibit the absorption of cholesterol in the intestines, leading to reduced levels of LDL cholesterol.[67] Fenugreek seeds can enhance lipid metabolism by promoting the breakdown of fats and reducing their accumulation in the body.[68] Fenugreek has been shown to modulate key enzymes involved in lipid metabolism, including lipoprotein lipase, 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase), and acyl-CoA: cholesterol acyltransferase (ACAT).[68] Fenugreek seeds are rich in antioxidants that help prevent oxidative stress and lipid peroxidation, which are linked to dyslipidemia and cardiovascular diseases.[50] Fenugreek possesses anti-inflammatory properties that contribute to its lipid-lowering effects. Inflammation is closely associated with dyslipidemia and its complications.[69] Fenugreek may regulate adipose tissue and reduce fat accumulation, influencing lipid levels in the body.[70] Fenugreek has been reported to modulate apolipoprotein levels, which are crucial for the structure and function of lipoproteins and lipid metabolism.[63] Fenugreek consumption may alter the composition of bile acids, affecting cholesterol metabolism and reducing cholesterol levels.[71]

Hypolipidemic Activity of Garlic (*Allium sativum* L.)

Garlic (*Allium sativum* L.) has been studied for its potential hypolipidemic (cholesterol-lowering) activity for many years. It is believed to have a range of beneficial effects on lipid metabolism, which can contribute to reducing cholesterol levels in the blood.[72] Allicin is a sulfur-containing compound found in garlic that is responsible for its characteristic odor and taste. It has been associated with cholesterol-lowering effects. Allicin may inhibit the enzyme HMG-CoA reductase, which is involved in cholesterol synthesis.[73] Garlic contains various sulfur compounds, including diallyl disulfide, diallyl trisulfide, and others. These compounds have been shown to have lipid-lowering effects, including reducing total cholesterol and LDL cholesterol levels.[74] Saponins found in garlic have been reported to possess hypolipidemic properties. They may help reduce cholesterol absorption in the gut and lower blood cholesterol levels.[72] Garlic contains polysulfides, which can have beneficial effects on lipid metabolism. They may help lower cholesterol levels by inhibiting cholesterol synthesis and increasing its excretion.[75] Garlic contains phytosterols and plant compounds with a structure similar to cholesterol. Phytosterols can compete with cholesterol for absorption in the digestive tract, potentially leading to reduced cholesterol levels in the blood.[76] Garlic possesses antioxidant properties due to its organosulfur compounds. Antioxidants may help prevent oxidative damage to lipids (lipid peroxidation) and contribute to overall cardiovascular health.[77]

Hypolipidemic activity of turmeric (*Curcuma longa* L.)

Turmeric (*Curcuma longa* L.) is a popular spice and medicinal herb that has been traditionally used in various cultures for its potential health benefits.[78] One of the potential health benefits attributed to turmeric is its hypolipidemic activity, meaning it may help lower levels of

lipids (fats) in the blood.[79] Turmeric has been studied for its potential to lower levels of LDL cholesterol (LDL-C), commonly referred to as "bad" cholesterol.[80] Curcumin, a bioactive compound found in turmeric, is believed to be the primary component responsible for this effect.[81] Studies have demonstrated that curcumin may help reduce LDL-C levels and increase HDL cholesterol (HDL-C) levels, which is considered beneficial for heart health.[82] Elevated levels of triglycerides in the blood can increase the risk of heart disease. Some research suggests that curcumin may help lower triglyceride levels, contributing to an overall improvement in lipid profiles.[83] Turmeric and its active compound, curcumin, possess antioxidant and anti-inflammatory properties. These properties may help protect cells from oxidative stress and reduce inflammation, which is associated with the development of cardiovascular diseases and dyslipidemia.[84] Curcumin may influence enzymes and pathways involved in lipid metabolism. It has been shown to modulate the activity of enzymes related to cholesterol synthesis and metabolism, potentially contributing to its lipid-lowering effects.[85] Studies suggest that curcumin may help reduce the progression of atherosclerosis (hardening and narrowing of the arteries) by inhibiting plaque formation and improving endothelial function. Improved vascular health can contribute to better lipid profiles and reduced cardiovascular risk.[86] Turmeric may work synergistically with other natural compounds or medications used for managing lipid levels. Combining turmeric with a healthy diet and lifestyle modifications could enhance its hypolipidemic effects.[87]

Conclusion

Medicinal plants have exhibited promising hypolipidemic activity, showcasing their potential as natural alternatives in managing lipid levels and mitigating associated health risks. Among these, turmeric (*C. longa*) stands out as a notable candidate, primarily due to its bioactive component, curcumin. Research indicates that curcumin, the principal bioactive compound in turmeric, contributes to its hypolipidemic effects by positively influencing cholesterol and triglyceride levels. Curcumin's ability to lower LDL-C, elevate HDL-C, and regulate lipid metabolism demonstrates its potential in reducing cardiovascular risk factors. Moreover, the antioxidant and anti-inflammatory properties of curcumin are essential in reducing oxidative stress and inflammation associated with dyslipidemia and atherosclerosis. These effects further contribute to the overall improvement of lipid profiles and vascular health. However, it is essential to acknowledge that while there is a growing body of evidence supporting the hypolipidemic activity of turmeric, further well-designed clinical trials are imperative to establish its efficacy, optimal dosages, and long-term safety. In addition, understanding potential synergies with other medicinal plants and conventional lipid-lowering therapies will provide a comprehensive approach for enhancing hypolipidemic effects. Incorporating medicinal plants like turmeric into a balanced diet and a healthy lifestyle may hold promise in managing lipid levels and promoting cardiovascular well-being. Collaborative efforts involving healthcare professionals, researchers, and the community will be vital in advancing our understanding of the potential hypolipidemic benefits offered by various medicinal plants.

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Conflicts of interest

There are no conflicts of interest.

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Review Article

Fasd (Venesection) in Traditional Unani Medicine

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Abstract

Unani medicine also referred to as Greco-Arab medicine is a traditional system of medicine which originated in ancient Greece. According to Unani medicine, there are six essential factors which are responsible for the maintenance of health and any disruption in them may lead to disease. *Ilāj bit Tadbīr* (regimental therapy) encompasses regimes that attempt to correct this disruption and help the body to restore itself. *Faṣd* (venesection) is a part of *Ilāj bit Tadbīr* which involves blood-letting by placing an incision in specified veins. It is prescribed as a minor excretory procedure which has both preventive and therapeutic benefits. *Faṣd* has manifold benefits including *istifrāgh* (excretion) of wastes, removal of *imtila* (plethora), and reduction of viscosity of blood. Hence, if carried out according to the guidelines, it serves as an effective treatment modality for many local and systemic disorders. The historical background of *Faṣd*, timing, duration, its types and importance, recent scientific reports, and the disorders in which it can be used will be discussed in this paper.

Keywords: *Faṣd, Ilāj bit Tadbīr, therapy, Unani*

Introduction

In Unani medicine, humoral theory believes the presence of four humors, namely *Dam* (blood), *Balgham* (phlegm), *Safrā* (yellow bile), and *Saudā* (black bile) in the body. An alteration in the quality and/or quantity of these humors produces morbid material, which results in various diseased conditions. Hence, evacuation (*Istafragh*) of this morbid material from the body becomes essential to regain homeostasis of humors. Moreover, the Unani system of medicine includes three therapeutic modalities, namely *Ilāj bit Tadbīr* (regimenal therapy) including *Ilāj bil Ghiza* (dieto therapy); *Ilāj bil Dawa* (pharmaco-therapy), and *Ilāj bil Yad* (surgery). *Ilāj bit Tadbīr* is an ideal and simple way of treating a disease as well as the means to preserve health. It comprises of *Hijamah* (cupping), *Faṣd* (venesection), *Ta'līq* (leeching), *Kaiyy* (cauterization), *Riyāḍat* (exercise), *Dalk* (massage), *Takmeed* (fomentation), *Naṭūl* (pouring of medicated liquid on affected part), *Zimaad-wa-tila* (ointment and liniment), *Ta'reeq* (sweating), *Idrare-boul* (diuresis), *Ḥammām* (bath), *Ishāl* (purgation), *Qay'* (emesis), *Ḥuqna* (enema), and *Imāla* (diversion of morbid material).[1-3]

Out of these, *Faṣd* (venesection/ bloodletting) enjoys great importance in the management of various diseases. It is a procedure in which an incision is given to any of the superficial vessels and blood containing *madda-e-fasidah* (morbid material) is allowed to flow.[4-7] The purpose is the evacuation of the morbid material. This removes either excess humors in the same proportion as present in the blood vessels or abnormal humors or both. According to *Ibn Hubal Baghdadi* (1121–1213 AD), *Faṣd* excretes completely all harmful matter lurking in the blood.[1] That is why *Faṣd* is given extreme importance in the Unani system of medicine for the prevention of disease and restoration of health.[8] It is most effective when the disease-causing matter is uniformly distributed in the whole body.[9]

Historical Background

The first records concerning venesection by cutting a vein, or *Faṣd* were found in the Hippocratic collection in the 5th century BC. The popularity of *Faṣd* in Greece was reinforced by the ideas of *Galen*, after he discovered the veins and arteries were filled with blood, not air as was commonly believed at that time. In Greece, *Faṣd* was in use around the time of *Hippocrates*. *Erasistratus*, however, theorized that many diseases were caused by plethora, or overabundance, in the blood. *Archagathus*, one of the first Greek physicians to practice

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in Rome, practiced *Faṣd* extensively and gained a most sanguinary reputation. *Galen* believed that blood was the dominant humor and the one in most need of control. In order to balance the humor, a physician would either remove "excess" blood (plethora) from the patient or give them any other treatment for evacuation.

Importance of *Faṣd*

(a) To normalize the overabundance of blood in persons prone to sanguineous disorders
(b) To excrete morbid matters out of the blood in particular and the body in general
(c) To prevent the accumulation of toxins and other morbid matters inside the body
(d) To maintain the normal physis (*Tabiyat*)
(e) To stimulate metabolic functions.[5]

Indications of *Faṣd*

- Venesection (*Faṣd*) is carried out when there is an excess of *Dam* (blood) in the body
- It is also carried out when the patient is either exposed to the risk of developing a disease or has actually developed one.

In both cases, the idea is to remove the general excess of humor or the abnormal humor or both.

- General excess (plethora) of blood predisposes to:
  1. Sanguineous sciatica, gout and rheumatism
  2. Recurrent hemoptysis
  3. Convulsions, coma, and melancholia
  4. Swelling of the throat and internal organs
  5. Inflammatory type of conjunctivitis, bleeding piles, and amenorrhea
  6. Excessive heat or weakness in the internal organs
  7. It is recommended in wounds and contusions as a prophylactic against inflammation
  8. It is carried out when an abscess is threatening to rupture before maturation, even though there is no other indication and no excess of humor
  9. Sometimes venesection is carried out in fevers for no other reason than to reduce the excess of morbid matter
  10. Venesection is sometimes carried out to stop hemorrhage, as in epistaxis, hemoptysis, menorrhagia, and bleeding piles. In such cases, the objective is to divert the blood to the opposite side (*Imala mawad*), this is often quite useful and effective.[2]

Contraindications

Faṣd/venesection is carried out freely as long as the disease has not yet developed, but once it has appeared the idea of venesection should be given up because it would then make the humours thin and disperse them into the normal blood stream. *Faṣd* is not allowed when: (1) Age: Not before 14, or after 70 years of age. (2) Physique: Those who are very emaciated, corpulent, flabby muscles, white or yellow coloured and those who have often been ill. (3) Physiological states: (a) Stomach full of food (b) bowels still loaded with faeces or chronic constipation (c) a state of nauseative satiety (d) a state of sensitiveness of the pylorus, or weakness of the sphincter and colitis (4) Miscellaneous: A resolving bath should not have been taken shortly before *Faṣd*; cold temperament, cold climate etc. (a) A state of fasting (b) pregnancy (c) menstruation (d) after coitus (e) in acute (infective) fevers, and on the days of paroxysms.[5]

Guidelines and Procedure

Suitable time for *Faṣd*

Faṣd should be carried out ideally during the spring season in the middle of the lunar calendar.[2,5]

Amount of blood to be let out

This varies from case to case. Some people can stand blood loss of even more than five or six pounds, while others seemingly fit and healthy are unable to bear even a fraction of this loss.[2,5]

Preoperative Treatment

The stomach requires to be previously fortified. If the stomach is weak and sensitive, give pieces of bread soaked in rob made with vinegar of good odor. If the person is also of cold temperament, the bread should be dipped in sugar water with aromatics or a syrup of spearmint perfumed with musk.

Instrument

Several scalpels, a ball of silk or thread, an instrument to excite vomiting such as rabbit-hair, Lozenges of musk.

Make the Veins Stand Out

A band is tied out for this purpose to prominent the vein.

Position

Venesection should be carried out in the supine position. This conserves strength and prevents fainting.[4]

Incision

The incision in the vein should be longitudinal to render clotting less likely.

Size of Incision

A small incision is generally the best during the summer. A large wide incision is recommended when *Faṣd* is being applied as prophylaxis, preferably in the winter.[3]

Postvenesection Recommendations

(a) The food at first should be light and then gradually made normal, (b) The same applies to exercise, (c) rest in a supine position, (d) resolving baths are not recommended, (e) if the puncture gets inflamed, a

Table 1: Therapeutic applications

Veins	Indications
Warīd-e-Qīfāl (cephalic vein)	Diseases of the head and neck like meningitis, conjunctivitis, and pain in the ear
Warīd-e-Akḥal (median cubital vein)	Diseases of the head and neck such as melancholia and headache
Warīd-e-Bāsalīq A'la (basilic vein)	Pleurisy, pain in the stomach and liver, splenomegaly, piles, proctitis, and endometritis
Warīd-e-Ḥabl-uz-Zarā' (accessory cephalic vein)	Similar to those of the cephalic vein
Warīd-e-Usailum (third dorsal metacarpal vein)	Right third dorsal metacarpal-liver disorders. Left third dorsal metacarpal-cardiac and splenic disorders
Warīd-e-Ibti (axillary vein)	Chest pain, similar to those of the basilic vein
Warīd-e-Ṣāfin (external saphenous vein)	Sciatic pain, gout, varicose vein, elephantiasis amenorrhea, and orchitis
Warīd-e-Ṣāfin (internal saphenous vein)	Obstructed bleeding piles and menstruation
Warīd-e-Mābiz-ur-Rakba (popliteal vein)	Obstructed bleeding piles and menstruation
Warīd-e-Musht-e-Qadam (vein over the heel)	Similar to those of saphenous vein
'Irq-ul-Jabha (frontal vein)	The heaviness of the head and eyes, chronic headaches
Warīd-e-Maiqain (veins at the inner canthus of the eye)	Headache, migraine, chronic conjunctivitis, ectropion, leucoma, trachoma, styes, and night blindness
Widāj Zāhir (jugular vein)	Early stages of leprosy, serious throat angina, asthma, bronchitis, pneumonia, hoarseness of voice, and dyspnea
Warīd Aranba (nasal branches of facial vein)	Chloasma, discoloration of face, piles, boils, and itching of nose
Irq e Khalf-al Uzn (parotid veins)	Dizziness, tinnitus
Warīd-e-Shafa (labial vein)	Ulcers of the mouth, stomatitis, thrush, bleeding gums, and foul breath
Warīd Tahtul-lisān (inferior lingual vein)	Diphtheria and tonsillitis

small bloodletting should be carried out from the other extremity,[3] and (f) *Faṣd* should be carried out through a narrow rather than a wide opening and repeated on alternate days. Repeated sessions of bloodletting are preferred rather than a large let-out in a single sitting.[4] The details of therapeutic applications are given in Table 1.[2,5,6,8,9]

Conclusion

The popularity of *Faṣd* in Greece was reinforced by the ideas of Galen after he discovered the veins and arteries were filled with blood. In Greece, *Faṣd* was in use around the time of Hippocrates. *Faṣd* is mostly used in people who are prone to *Amraze damwia* (diseases due to blood impairment) where there occurs plethora in the body preferably in spring or summer is recommended in the person of sanguineous temperament. *Erasistratus*, however, theorized that many diseases were caused by plethora, or overabundance, in the blood. Plethora is basically the increased quantity of blood in the whole body. This increased quantity leads to the rupture of vessels. If the quality of blood is altered, then the normal physis of the body will not function with it which leads to the generation of *hārarat-e-ghāriba* (Morbid Heat), which causes sepsis of humors. Hence, to maintain all the qualities and quantities of normal blood (humors), we can transfuse blood and apply venesection for the preservation of health. For the prevention of different diseases and maintenance of humors, *Faṣd* is found to be a very effective therapy.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Clinical Study for Validation of Safety and Efficacy of *Sharbat Zufa Murakkab in Su'āl-i-Ratb* (Productive Cough) in Eastern India

Abstract

Background: Cough is the most common symptom of respiratory tract disease. It is caused by the mechanical or chemical stimulation of the cough receptors in the epithelium of the pharynx, larynx, trachea, and bronchi. It is an explosive expiration that provides a normal protective mechanism for clearing the tracheobronchial tree of secretions and foreign material. Cough can be initiated by a variety of irritant triggers either from an exogenous source (smoke, dust, fumes foreign bodies, etc.) or from an endogenous origin (upper airway secretions and/or gastric contents). **Aims and Objectives:** The present clinical study was performed to validate the safety and efficacy of Unani Pharmacopoeial formulation "*Sharbat Zufa Murakkab*" on scientific parameters, in patients of *Su'āl-i-Ratb* (productive cough). **Material and Method:** This study was carried out at the Regional Research Institute of Unani Medicine, Bhadrak (Odisha) during the year 2013–2015. A total of 67 patients completed the study out of all registered cases. The treatment duration was of 15 days and the patients of either sex in the age group of 18–65 years were selected for the study with the complaints of cough for more than 3 days associated with expectoration, *Khushūna al-Halaq* (sore throat), *Buhha al-Sawt* (hoarseness of voice), and chest tightness. **Result:** Nearly 91% of cases have shown more than 60% relief in signs and symptoms of the disease as compared to baseline. The variations in the values of liver function tests and kidney function tests before and after treatment were found within normal limits. **Conclusion:** The test drug has shown very good results. It was found well tolerated and no adverse effects were observed during the study. The study is asserting the safety and efficacy of "*Sharbat Zufa Murakkab*" in the treatment of *Su'āl-i-Ratb* (productive cough).

Keywords: *Buhha al-Sawt, chest tightness, hoarseness of voice, Khushūna al-Halaq, Sharbat Zufa Murakkab, sore throat, Su'āl-i-Ratb*

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Introduction

The prevalence of cough in Europe and the USA has been reported in about 9%–33% of the population, including young children.[1,2] In the USA, cough is one of the most frequent reasons for consultation in outpatient departments (OPDs). Patients with chronic cough probably account for about 10%–38% of respiratory OPD practice in the USA.[3,4] There is no doubt that chronic cough is a major cause of morbidity being reported by 3%–40% of the population. A European Respiratory Society-supported survey reported that nocturnal cough occurs in 30%, productive cough in 10%, and nonproductive cough in 10%.[5] Several studies have shown that the reporting of cough is more prevalent in females than males, possibly due to an increased sensitivity of cough reflex in women.[6]

Cough is the most common symptom of respiratory tract disease. It is caused by the mechanical or chemical stimulation of the cough receptors in the epithelium of the pharynx, larynx, trachea, and bronchi.[7-9] Cough is an explosive expiration that provides a normal protective mechanism for clearing the tracheobronchial tree of secretions and foreign material. Approximately 100 ml of mucus is produced daily in a healthy, nonsmoking individual. This flows at a regular pace up the airways, through the larynx, and is then swallowed. Excess mucus is expelled as sputum.[8]

Cough receptors exist in the epithelium of the upper and lower respiratory tracts, pericardium, stomach, esophagus, and diaphragm. Afferent receptors are located within the sensory distribution of the trigeminal, glossopharyngeal, superior

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laryngeal, and vagus nerves. Efferent receptors located in the recurrent laryngeal and spinal nerves respond to signals from a cough center in the medulla. Irritation of the cough receptors by smoke, dust, or fumes leads to stimulation of a complex reflex arc once stimulated, an impulse is sent to the cough center. After a series of muscle contractions, an increased intrathoracic pressure develops, which leads to an increased airflow through the trachea. These shearing forces help to eliminate mucus and foreign materials.[9-11]

Cough can be initiated by a variety of irritant triggers either from an exogenous source (smoke, dust, fumes foreign bodies, etc.) or from an endogenous origin (upper airway secretions and/or gastric contents). These stimuli may affect receptors in the upper airway (especially the pharynx and larynx) or the lower respiratory tract, following access to the tracheobronchial tree by inhalation or aspiration. Any disorder resulting in inflammation, constriction, infiltration, or compression of airways can be associated with a cough. Inflammation commonly results from airway infections, ranging from viral or bacterial including postnasal drip (due to perennial or allergic rhinitis, vasomotor rhinitis, or chronic sinusitis). Acute viral upper respiratory tract infection affecting the pharynx, larynx, or postnasal space is the most common cause of short-lived cough at all ages. The parenchymal lung disease potentially producing cough include interstitial lung disease, pneumonia, lung abscess, bronchitis, asthma, bronchial carcinoma, tuberculosis, bronchiectasis, and pulmonary edema.[9,11,12]

Ibn Sīnā (Avicenna) (980–1037 AD) defined the causes of *Su'āl* (cough) as *Asbāb Bādiya* (external causes), *Asbāb* Wasila (internal causes), and *Asbāb* Sabiqa (internal causes are related to adjacent organs).[13] *Asbāb Bādiya* (external causes) includes external cold, which causes extra cold to the lung and musculature of the lung, for example, extremely cold air and water, besides these, dust and smoke are also included in the study. *Asbāb Wāsila* (internal causes) is related to *Su'-i-Mizāj Ri'a* (impaired temperament of the lung), either *Su'-i-Mizāj Sāda* (abnormal temperament) or *Su'-i-Mizāj Māddī* (abnormal substantial temperament) such as *Damwī*, *Balghamī*, *Safrāwī,* and *Sawdāwī*. *Asbāb Sābiqa* is a cause which is related to an adjacent organ which affects the lungs indirectly, i.e., inflammation of the liver, stomach, diaphragm, and esophagus; fever is also included in *Asbāb Sābiqa*.[13]

Hakīm Muhammad Akbar Arzānī (d. 1721 AD) defines the causes of *Su'āl* (cough) in four groups, i.e., (1) *Su'-i-Mizāj Sāda* (abnormal temperament) or *Su'-i-Mizāj Māddī* (abnormal substantial temperament), (2) *Qurūh wa Buthūr al-Ri'a* (ulcers or boils of lungs), (3) any external stimuli reach to the lung through inspiration, and (4) disease of adjacent organ.[14] *Su'-i-Mizāj Māddī* (abnormal substantial temperament) is specifically associated with *Su'āl-i-Ratb*.[15] Nazlawī Rutūbat (catarrhal fluids), *Awrām* (inflammations), *Qurūh wa Buthūr al-Ri'a* (ulcers or boils of lungs), injury or macular lesions of the lungs,[15,16] and *Dhātī* Rutūbat of *Ri'a* (excess secretion of lungs) are the main causes of *Su'āl-i-Ratb* (productive cough).[17,18]

Materials and Methods

The present study was conducted at the Regional Research Institute of Unani Medicine, Bhadrak, in the year 2013–2015. Data presented in this paper were compiled on 67 patients of *Su'āl-i-Ratb* (productive cough). The patients of *Su'āl-i-Ratb* were selected from the OPD of the institute. The patients of either sex in the age group of 18–65 years were selected for the study with the complaints of cough for more than 3 *day*s associated with expectoration, *Khushūna al-Halaq* (sore throat), *Buhha al-Sawt* (hoarseness of voice), and chest tightness.

The patients below 18 *year*s and above 65 years of age, cases of nonproductive cough, known cases of respiratory diseases needed concomitant therapy such as pneumonia, bronchiectasis, bronchial asthma, pulmonary tuberculosis, and lung carcinoma, known cases of renal/hepatic/cardiac impairment or the ailments needing long-term therapy, and pregnant or lactating women were excluded from the study. The clinical study protocol was approved by the Institutional Ethics Committee of the Institute on March 15, 2013, and the trial has been registered with Clinical Trials Registry India (CTRI) with registration number CTRI/2013/11/004171. After obtaining written informed consent, patients were enrolled in the study and they were subjected to the hematological and biochemical investigations. Hematological investigations included hemogram (hemoglobin, erythrocyte sedimentation rate, total leukocyte count, and differential leukocyte count [neutrophils, eosinophils, basophils, lymphocytes, and monocytes]), urine examination (routine and microscopic). Biochemical investigations included, liver function tests (LFTs) comprising serum bilirubin, serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, and alkaline phosphatase, kidney function tests (KFTs) comprising serum creatinine, blood urea, and serum uric acid and blood sugar.

The parameters for assessment of the efficacy of the formulation were frequency, intensity, and quantity of *Su'āl-i-Ratb* (productive cough), *Khushūna al-Halaq* (sore throat), Buhha al-Sawt (hoarseness of voice), and chest tightness. These parameters were graded accordingly, in case of (1) frequency of *Su'āl-i-Ratb* 1 = Mild/Occasional, 2 = Moderate/several times (>5 *time*s) throughout the day, and 3 = Severe/constantly; any time throughout the day; in case of (2) intensity of *Su'āl-i-Ratb* 1 = Mild/no troublesome, 2 = Moderate/affecting usual works, noticed by every visitor, 3 = Severe/makes the things worst and patient has to stop everything for few movements; in case of quantity of sputum in *Su'āl-i-Ratb* 1 = Mild/scanty (1–2 Teaspoonful [TSF]/day), 2 = Moderate/moderate (3 TSF to half cup/day), and 3 = Severe/copious (half cup to full

cup/day); in case of *Khushuna al-Halaq* (sore throat), *Buhha al-Sawt* (hoarseness of voice), and chest tightness 0 = Absent, 1 = Mild/(+), 2 = Moderate/(++), and 3 = Severe/(+++).

Procedure

The overall assessment of efficacy and relief in symptoms and signs were calculated and patients were divided into four groups on the basis of the relief they have got. If a patient got 90%–100% relief in symptoms and signs, he/she was placed as cured, if gets 60%–89% relief in symptoms and signs, then he/she was labeled as relived, if gets 30%–59% relief in symptoms and signs, then marked as partial relived, and if a patient got <30% relief he/she was placed as not relieved.

The clinical follow-up of all the cases was carried out at regular intervals of 1 week for 2 weeks. The hematological and biochemical investigations were conducted at baseline and the end of the study. The safety of trial drugs was evaluated by biochemical investigations and clinically by monitoring adverse effects which were carefully sought at each follow-up. The *Mizāj* (temperament) of the patients was assessed as per the parameters described in Unani classical literature. The clinical and laboratory findings observed in every case were recorded on a separate case record form designed, especially for clinical study on *Su'āl-i-Ratb* (productive cough). The duration of treatment was 2 *week*s and no concomitant medication was allowed during the study. Baseline and follow-up values of hematological and biochemical investigations were statistically analyzed using Student's paired *t*-test. The significance level of $P < 0.05$ was used in this study.

Study drug, dosage schedule, and mode of administration

The test drug "*Sharbat Zufa Murakkab*" (SZM) a Unani Pharmacopoeial formulation was prepared and supplied by the Pharmacy section of the Central Research Institute of Unani Medicine, Hyderabad. SZM was given at the dose of 10 ml orally, thrice daily with lukewarm water. The composition of the SZM is given in Table 1.[19]

Table 1: Composition of study drug *Sharbat Zufa Murakka*

Constituents	Latin name	Part used	Quantity
Anjeer	*Ficus carica L.*	Fruit	10 pieces
Tukhm-e-Khatmi	*Althaea officinalis L.*	Seed	10 g
Aslus-soos	*Glycyrrhiza glabra L.*	Root	10 g
Irsa	*Iris ensata Thunb.*	Root	10 g
Badiyan	*Foeniculum vulgare L.*	Seed	15 g
Tukhm-e-Karafs	*Apium graveolens L.*	Seed	15 g
Parsioshan	*Adiantum capillus-veneris L.*	Whole plant	20 g
Zufa Khushk	*Hyssopus officinalis L.*	Whole plant	20 g
Mavez Munaqqa	*Vitis vinifera L.*	Fruit	90 g

Results

After completion of 14 days of treatment, the SZM exhibited significant improvement in symptoms and signs of *Su'āl-i-Ratb* (productive cough). Nearly 91% of the patients get more than 60% relief in their symptoms and signs as compared to baseline. Out of 67 *patient*s of *Su'āl-i-Ratb* who have completed the study, 4 *(*5.97%) patients were cured (90%–100% relief in symptoms and sign), 57 *(*85.07%) patients were relieved (60%–89% relief in symptoms and sign), and 6 *(*8.96%) patients were partially relieved (30%–59% relief in symptoms and sign). The general therapeutic response of the formulation and the mean values of clinical parameters at baseline, 1st follow-up, and after treatment are shown in Tables 2, 3 and Figures 1, 2, respectively. The mean values of hematological and biochemical parameters at baseline and after 14 days of treatment are shown in Tables 4 and 5. The variations in the values of LFTs and KFTs before and after treatment were found within normal limits revealing the safety of study drugs. The study drug was found well-tolerated and no adverse effects were observed.

Discussion

There are several drugs in allopathic medicines which are used as an antitussive. Their modes of action are different, such as bronchodilators, sedatives, H1-receptor antagonists, and secretolytics.[20] H1-receptor antagonists such as chlorpheniramine, loratadine, and diphenhydramine are used as antitussive drugs but they have shown several side effects such as central nervous system depression, sedation, drowsiness, gastrointestinal disturbance, anorexia, epigastric pain, blurring of vision, hypotension,

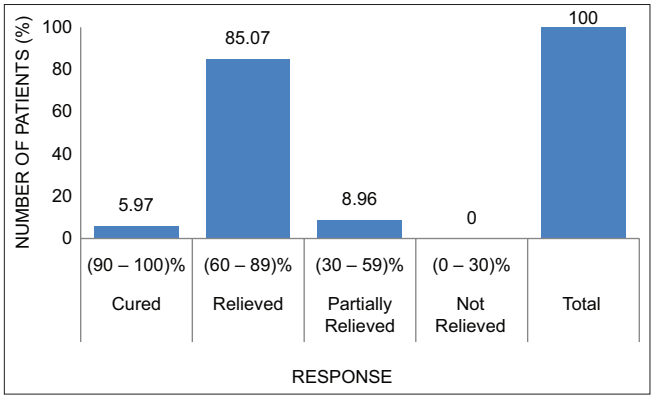

Figure 1: General therapeutic response

Table 2: General therapeutic responses

Response	Cured (90%–100%)	Relieved (60%–89%)	Partially relieved (30%–59%)	Not relieved (0%–29%)
Number of cases (%)	4 (5.97)	57 (85.07)	6 (8.96)	-

Table 3: Mean values of clinical parameters at baseline, first follow-up, and after treatment

Signs and symptoms	Baseline, mean±SD	1st follow-up, mean±SD	After treatment, mean±SD
Su'āl-i-Ratb (productive cough)			
Frequency	2.49±0.07	1.58±0.07	1.01±0.04*
Intensity	2.48±0.07	1.33±0.06	0.91±0.05*
Quantity	2.34±0.08	1.31±0.08	0.67±0.06*
Khushūna al-Halaq (sore throat)	1.97±0.10	1.00±0.07	0.27±0.05*
Buhha al-Sawt (hoarseness of voice)	1.40±0.12	0.78±0.08	0.24±0.05*
Chest tightness	1.67±0.12	0.93±0.08	0.36±0.06*

*The mean values are significantly different at $P<0.05$. SD: Standard deviation

Table 4: Mean values of pathological parameters at baseline and after treatment

Pathological investigations	Period	Mean±SD	*P*
Hb (g%)	BT	12.30±0.15	>0.05
	AT	12.23±0.14	
ESR (mm/h)			
1st h	BT	25.72±2.86	<0.05
	AT	21.22±2.48	
2nd h	BT	50.39±4.86	<0.05
	AT	41.21±3.94	
TLC (cm)	BT	6811.94±165.78	>0.05
	AT	6763.43±140.81	
DLC			
Neutrophils	BT	61.28±0.62	>0.05
	AT	61.88±0.50	
Lymphocytes	BT	28.61±0.58	>0.05
	AT	28.75±0.49	
Eosinophils	BT	9.58±0.41	>0.05
	AT	8.75±0.28	
Monocytes	BT	0.52±0.07	>0.05
	AT	0.63±0.07	

BT: Before treatment, AT: After treatment, DLC: Differential leukocyte count, TLC: Total leukocytes count, ESR: Erythrocyte sedimentation rate, Hb: Hemoglobin, SD: Standard deviation

Table 5: Mean values of biochemical parameters at baseline and after treatment

Biochemical investigations	Period	Mean±SD	*P*
SGOT (Units/mL)	BT	32.46±1.35	>0.05
	AT	32.51±1.42	
SGPT (Units/mL)	BT	29.20±1.19	>0.05
	AT	32.46±1.97	
ALP (K and A Units/100 mL)	BT	102.90±5.74	>0.05
	AT	99.78±4.80	
Serum bilirubin (mg %)	BT	0.57±0.03	>0.05
	AT	0.60±0.04	
Serum creatinine (mg %)	BT	1.17±0.03	>0.05
	AT	1.19±0.03	
Serum urea (mg %)	BT	27.73±1.39	>0.05
	AT	26.16±1.23	

BT: Before treatment, AT: After treatment, SD: Standard deviation, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic-pyruvic transaminase, ALP: Alkaline phosphatase

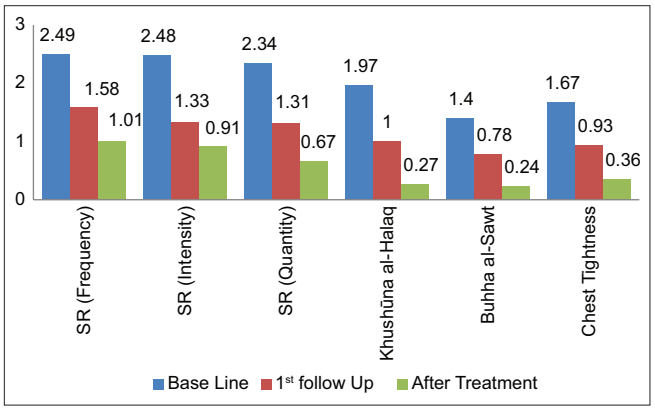

Figure 2: Mean values of clinical parameters at baseline, first follow-up, and after treatment

headache, and tightness of chest.[21] Dextromethorphan hydrobromide (dextromethorphan) was first reported in 1953 as a treatment for cough without the undesirable side effects of codeine but have other side effects such as dizziness and gastrointestinal disturbance. Opiates such as codeine and morphine have adverse effects such as dependence, withdrawal symptoms, nausea, vomiting, constipation, dizziness, sweating, headache, vertigo, bradycardia, tachycardia, and palpitation.[21,22]

Bromhexine and its metabolite ambroxol are widely used as secretolytics, but according to Hamilton *et al*., it decreases sputum viscosity significantly in bronchitis patients but it also produces side effects such as gastrointestinal disturbance, headache, dizziness, sweating, and skin rashes.[21,23,24] β2-agonists such as salbutamol have shown bronchodilator effects and other respiratory effects including antitussive action but have shown side effects such as tachycardia, muscle tremors, palpitation, muscle cramps, headache, urticaria, and hypotension.[21,25,26]

Guaifenesin is the only Food and Drug Administration-approved expectorant for children and adults. The mechanism of action of guaifenesin is not clear, but it is thought to influence the cholinergic innervations of airway mucous glands. It has side effects such as headache, nausea, dizziness, vomiting, gastrointestinal discomfort, and urticaria.[21] Theophylline is a drug commonly used as a bronchodilator and demonstrated anti-inflammatory activity in patients with asthma or chronic obstructive pulmonary

disease but has side effects such as headache, nausea, dizziness, vomiting, insomnia, anxiety, restlessness, tremor, convulsion, cardiac arrhythmias, and hypotension (Sullivan *et al*., 1994; and Anonymous, 2012).[21,27]

SZM did not produce any abovementioned side effects in enrolled cases of the study, thus confirming its superiority against modern management of different types of cough. It is proved by the abovementioned results that SZM is an excellent drug of choice for productive cough. This drug was found well-tolerated and the values of LFTs and KFTs after treatment showed the safety of study drugs. The study is affirmative of the safety and efficacy of Unani Pharmacopoeial formulations in the treatment of *Su'āl-i-Ratb* (productive cough).

Conclusion

It is clearly evident that SZM produced significant improvement in frequency, intensity, and quantity of cough. It also reduced the severity of sore throat, hoarseness of voice, and chest tightness significantly. The test drug SZM was also found well-tolerated without any known side effects clinically. It can be concluded that SZM is a safe and effective regimen in the management of productive cough.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Long-term Safety of Coded Unani Formulation and PUVASOL in Patients with Vitiligo - A Randomized Comparative Controlled Clinical Trial

Abstract

Background: Vitiligo, a skin disorder is viewed as a multifactorial process characterized by the acquired loss of constitutional pigmentation manifesting as white macules and patches. The Unani system of medicine offers many formulations including the ones designed by the Central Council for Research in Unani Medicine for the successful treatment of vitiligo. **Aims and Objectives:** Herein, we evaluated the comparative long-term safety (9 months) of test Unani formulation (UNIM 001 and UNIM 003) with controlled allopathic therapy (PUVASOL: Psoralen and UVA obtained by solar light) in terms of blood parameters. **Materials and Methods:** In this clinical study, 39 vitiligo patients in the test group and 33 vitiligo patients in the control group were assessed for blood parameters viz., aspartate aminotransferase, alanine aminotransferase, bilirubin, urea, creatinine, hemoglobin, red blood cells, white blood cell, and Platelet before, during, and after the treatment period. **Results:** All the blood parameters were in the normal biological reference range in the test and control group at the baseline, during the treatment, and at the end of the study. These results indicate that at a given dose of the UNIM-001 and UNIM 004, there is no effect on the liver, kidney, and other hematological blood parameters in the patients with vitiligo and are comparable with PUVASOL therapy. **Conclusion:** A combination of Unani formulation i.e., UNIM 001 as oral and UNIM 003 as topical application may be considered an effective and safe treatment alternative to patients with vitiligo.

Keywords: *Blood parameters, Unani medicine, UNIM-001, UNIM-003, vitiligo*

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Introduction

Vitiligo is a skin disorder characterized by the acquired loss of constitutional pigmentation manifesting as white macules and patches caused by a loss of functioning epidermal melanocytes. Vitiligo affects 1% of the world's population,[1] but the prevalence has been reported as high as 3%–4% of the Indian population[2] and in Kashmir Valley about 2.3%.[3] Clinically, treatment modalities for vitiligo require extended treatment plans that may last many months to years and may still result in disappointing outcomes.[4] At present, various treatment options including medical therapeutics, surgical interventions, and adjunctive treatments are available in vitiligo for restoring normal color to the white patches of the skin.[5] The treatment measures include topical applications, antioxidants, laser therapy, and photochemotherapy, although effective but less than satisfactory and can be prohibitively expensive. Thus, the current vitiligo treatment options are considered to be suboptimal, and attention is being diverted to complementary and alternative medicine, especially the Unani system of treatment due to their versatile role in the treatment of this disease. The Unani system of medicine has a rich treasure of therapeutically active products and extensive patient-beneficial clinical experience on vitiligo. In the Unani system of medicine, vitiligo is known as bars and has been defined by ancient physicians in the classics along with its line of treatment.[6-8] Thus, it is of great interest to know whether these preparations used in the Unani system of medicine have activities that might be useful in modern formulations as an adjuvant therapy. Many Unani formulations both single as well as compound formulations have been used to treat vitiligo for a long time,[6-8] and some formulations as designed by CCRUM, Ministry of AYUSH,[9] are also in use to treat vitiligo. However, there is a paucity of published studies which have systematically evaluated their efficacy and safety. Herein,

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we have reported for the first time the comparative long-term safety (9 months) of Unani formulation (UNIM-001 and UNIM-003) with controlled allopathic therapy (PUVASOL: Psoralen and UVA obtained by solar light) in terms of blood parameters represented by the liver, renal function, and other hematological profile in vitiligo patients of our population.

Materials and Methods

Study population

Self-reporting vitiligo patients attending the Outpatient Department of Regional Research Institute of Unani Medicine (RRIUM), Srinagar, from November 2013 to September 2017 with clinically diagnosed segmental and nondermatomal vitiligo with various chronicities and of either sex with age 13–60 years and willing to give written consent were included in the study. After getting approval from the Institute's Ethical Committee, the trial was registered in the Clinical Trials Registry of India with CTRI no. CTR/2013/12/004215 registered on 13/12/2013. Two hundred and eight patients were screened, and 59 patients were recruited in the test group and 49 patients in the control group in which 39 patients in the test group and 33 patients in the control group completed the trial [Figure 1]. It was ensured that no patient had received either topical or systemic antivitiligo therapy for 4 weeks before the entry into the trial. Pregnant mothers, patients with cardiopulmonary, hepatorenal malfunctions, noncooperative patients, patients with a history of drug or alcohol abuse, chronic smokers not willing to abstain from smoking during the study period, patients with known allergies with any Unani preparations, and patients with a history of malignancy or uncontrolled infection were excluded from the study. Detailed demographic data including history concerning age, age of onset, chronicity of diseases, site, extension and distribution of lesions, and family history of all the patients were recorded on the Case Record Form. Written informed consent was signed by the patients after explaining to them the study trial and its possible outcome.

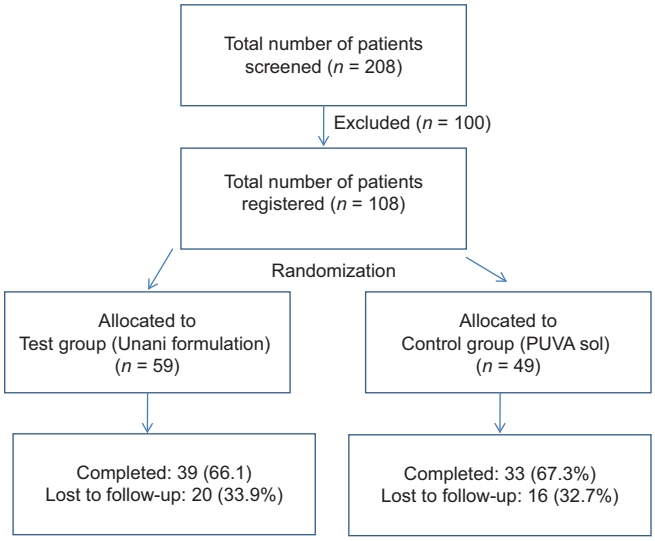

Figure 1: Flowchart of participants through the trial

Treatment

Patients were allotted the treatment by prerandomization schedule (block randomization technique was used to allocate the treatment schedule to the patients) as test group, i.e., Unani formulation, and control group, i.e., PUVA sol. No placebo was used in the trial, and both treatment groups received drugs with active ingredients. Both the drugs (test and control) were kept in coded form as UNIM-001 as oral and UNIM-003 as topical to avoid bias.

Test group (Unani formulation)

A total of 39 patients received the test drug, i.e. Unani-coded formulation in two forms UNIM-001 and UNIM-003 for 9 months. Patients were instructed to apply oil once a day in the morning to the depigmented area of the skin and to expose the affected part to sunlight which ranges from 3 to 30 min. The exposure time was adjusted as per the skin sensitivity of an individual.

Control group (psoralen plus ultraviolet A sol)

A total of 33 patients received the control drug, i.e., PUVA sol, with the same coded names UNIM-001 and UNIM-003 for 9 months. UNIM-001 was psoralen which was in tablet form of 500 mg. Patients were instructed to take 1 tablet (500 mg) twice a day. Whereas, UNIM-003 was the oil form of psoralen. Patients were instructed to apply oil once a day in the morning to the depigmented area of the skin and to expose the affected part to sunlight which ranges from 3 to 30 min. The exposure time was adjusted as per the skin sensitivity of an individual.

Evaluation of blood parameters

The primary outcome measure for this study was the safety of the test drug in comparison to the control drug by assessment of blood, liver, renal function, and hematological parameters in vitiligo patients. For hematological and biochemical assessment, a fasting blood sample (8.0 mL) was taken from each participant four times; at baseline, after 3 months, after 6 months, and at the end of the treatment, i.e., after 9 months. Isolated serum was utilized for the assessment of the markers of liver function (serum glutamate pyruvate transaminase, glutamate oxaloacetate transaminase, and bilirubin), renal function (urea, creatinine, and uric acid) during the trial using the kits of ERBA make on clinical chemistry analyzer (Accurex, India). The assay was performed as per the kit manufacturers manual provided with the kits. For evaluation of hemoglobin (Hb), red blood cells (RBCs), white blood cells (WBCs), and platelets, the whole blood was used and the tests were performed on Heamatology analyzer (Sinduri make, India).

Statistical analysis

The results were analyzed using a one-way analysis of variance on GraphPad Prism 5, and $P < 0.05$ was considered to be statistically significant.

Results

A total of 72 patients completed the trial, wherein the test group had 39 patients and the control group had 33 patients. The characteristics of patients of the test and control group are given in Table 1. The mean age of patients studied in both the groups was quite young. The 17.9% and 15.1% of patients, respectively, of the test and control groups have a family history of vitiligo. As a part of safety evaluation, the blood, liver, and renal function parameters represented by aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, urea, and creatinine were evaluated at baseline, after 3 months, after 6 months, and after 9 months of treatment in both the test and control groups. In the test group (Unani formulation), there was no significant difference ($P > 0.05$) among these values at baseline and all follow-ups, and all the values were well within the biological reference range [Table 2]. In the control group (PUVA sol), there was no significant difference ($P > 0.05$) among the values of AST, ALT, bilirubin, and creatinine at all follow-ups, and all the values were well within the biological reference range [Table 3]. However, in the control group, there was a statistically significant difference ($P < 0.05$) in the value of urea within baseline and after 9 months of treatment. The values were well within the biological reference range [Table 3]. Further, the hematological profile of patients as analyzed by evaluating Hb, RBC count, WBC count, and platelet count were evaluated at baseline, after 3 months, after 6 months, and after 9 months of treatment in both the test and control groups. In the test group (Unani formulation), there was no significant difference ($P > 0.05$) among these values at baseline and all follow-ups, and all the values were well within the biological reference range [Table 4]. Similarly, in the control group (PUVA sol), there was no significant difference ($P > 0.05$) among these values at all follow-ups, and all the values were well within the biological reference range [Table 5]. The total number of patients who developed clinical side effects (Gastrointestinal effects such as nausea and abdominal cramps) was higher in the control group (PUVA sol) as compared to the test group (Unani formulation) among the completed cases [Table 6].

Discussion

The increasing demand for safe and effective alternative drugs for the treatment of vitiligo can be addressed by identifying promising formulations from alternative and complementary forms of medicine including the Unani system of medicine. Many Unani formulations both single

Table 1: Characteristics of patients of the test and control groups

Groups	Age (years)	Gender	Family history, *n* (%)
Test (Unani formulation) (*n*=39)	26.02±9.75 (13–45)	20 female, 19 male	7 (17.9)
Control (PUVA sol) (*n*=33)	24.60±11.04 (13–48)	20 female, 13 male	5 (15.1)

Values are means±SD (range). SD: Standard deviation, PUVA: Psoralen plus ultraviolet A

Table 2: Effect of test drug (Unani formulation) on blood, liver, and renal function parameters of patients with vitiligo (*n*=39)

Parameters	Baseline	After 3 months	After 6 months	After 9 months
AST (IU/L)	25.76±10.07	26.62±9.717	26.79±12.17	26.95±11.87
ALT (IU/L)	25.39±13.00	26.29±8.52	25.79±6.45	26.25±7.85
Bilirubin (mg/dL)	0.76±0.28	0.87±0.34	0.81±0.27	0.77±0.20
Urea (mg/dL)	28.27±6.87	26.81±8.19	25.45±9.90	25.19±5.40
Creatinine (mg/dL)	0.84±0.11	0.84±0.28	0.82±0.12	0.79±0.11

Values were presented as mean±SD. No significant difference (ANOVA, $P>0.05$) within each parameter. *n*: Number of patients, AST: Aspartate transaminase, ALT: Alanine aminotransferase, SD: Standard deviation

Table 3: Effect of control drug (PUVASOL) on blood, liver, and renal function parameters of patients with vitiligo (*n*=33)

Parameters	Baseline	After 3 months	After 6 months	After 9 months
AST (IU/L)	25.90±7.06^{Aa}	24.52±6.84^{a}	24.46±6.86^{a}	25.80±6.21^{a}
ALT (IU/L)	26.94±11.86^{a}	26.43±10.69^{a}	26.37±10.71^{a}	24.01±7.19^{a}
Bilirubin (mg/dL)	0.72±0.16^{a}	0.73±0.13^{a}	0.74±0.13^{a}	0.73±0.15^{a}
Urea (mg/dL)	27.01±6.20^{a}	24.14±8.20^{a,b}	24.21±8.10^{a,b}	23.10±7.30^{b}
Creatinine (mg/dL)	0.78±0.12^{a}	0.71±0.20^{a}	0.70±0.20^{a}	0.72±0.17^{a}

Values were presented as mean±SD; Values with different superscripts (a, b) within each parameter are significantly different (ANOVA, $P<0.05$). *n*: Number of patients, AST: Aspartate transaminase, ALT: Alanine aminotransferase, SD: Standard deviation

Table 4: Effect of test drug (Unani formulation) on hematological parameters of patients with vitiligo (*n*=39)

Parameters	Baseline	After 3 months	After 6 months	After 9 months
Hb (g/dL)	13.37±1.80	12.68±1.68	12.94±1.82	12.61±1.80
RBC count×10^6 cells/μL	4.52±0.54	4.86±1.41	4.61±0.83	4.78±0.55
WBC count×10^3 cells/μL	6.85±1.64	7.02±1.82	7.09±1.81	6.40±1.62
Platelet count×10^9 cells/L	233.38±78.54	253.72±74.18	253.18±79.23	262.49±70.68

Values were presented as mean±SD. No significant difference (ANOVA, P>0.05) within each parameter. *n*: Number of patients, Hb: Hemoglobin, RBC: Red blood cell, WBC: White blood cell, SD: Standard deviation

Table 5: Effect of control drug (PUVASOL) on hematological parameters of patients with vitiligo (*n*=33)

Parameters	Baseline	After 3 months	After 6 months	After 9 months
Hb (g/dL)	13.41±1.51	13.12±1.80	13.12±1.80	12.24±1.70
RBC count×10^6 cells/μL	4.57±0.65	4.69±0.78	4.72±0.76	4.85±0.99
WBC count×10^3 cells/μL	7.30±1.99	7.64±2.06	7.58±2.11	6.89±1.86
Platelet count×10^9 cells/L	258.08±91.60	259.91±81.29	255.58±79.57	249.15±80.59

Values were presented as mean±SD. No significant difference (ANOVA, P>0.05) within each parameter. *n*: Number of patients, Hb: Hemoglobin, RBC: Red blood cell, WBC: White blood cell

Table 6: Clinical side effects in the test group (Unani formulation) and the control group (PUVASOL)

	Test group (Unani formulation) (*n*=39)	Control group (PUVA sol) (*n*=33)
Total clinical side effects	1 (2.5)	3 (9)

Values in parentheses are percentages. PUVA: Psoralen plus ultraviolet A

as well as compound formulations have been used to treat vitiligo for centuries.[6-9] Herein, we evaluate the safety in terms of blood parameters of the given Unani formulation in comparison to an allopathic control drug for 9 months of treatment. A total of 72 patients completed the trial, wherein the test group had 39 patients and the control group had 33 patients. The percentage of dropouts was higher in both the groups due to the devastating floods of 2016 in the state of Jammu and Kashmir. The maximum number of patients in both the groups were quite young (<30); a probable reason for the younger age group can be because of social stigma in the community, as young people tend to seek medical attention earlier due to anxiety. As age advances, the chances of diseases fade due to a decrease in stress in the later stages of life as observed in earlier studies also.[10,11] Among the patients studied, we have found a positive family history in some cases (17.9% in the test group and 15.1% in the control group) which was reported elsewhere also.[11]

The primary outcome measure for this study was the safety of the Unani formulation in comparison to PUVA sol. To ensure that Unani formulation does not cause adverse effects, we monitor the patients for the emergence of liver, renal, and hematological adverse effects. In addition, a regular clinical examination was performed for each patient to report any deleterious effects due to the test and control drugs. No major adverse effects were recorded, and this result may be considered additional evidence that supports the safety and tolerability of Unani formulation at the given dose and is comparable with PUVA sol treatment for 9 months. The outcomes of this study will help determine the efficacy of long-term treatment with given Unani formulation in patients with vitiligo. The results also provide an extension and confirmation to the previous clinical observations of Unani physicians that assessed the safety and efficacy of Unani formulations in vitiligo patients.[9] Our study was designed to evaluate the noninferiority of Unani formulation with PUVA sol in patients with vitiligo for 9 months of treatment in terms of its safety. Clinical side effects of psoralen-based therapies are frequent which have been reported in many skin diseases including vitiligo.[12-14] However, the present study revealed that Unani formulation and PUVA sol did not negatively impact the liver function, renal function, and other hematological functions and thus defines Unani formulation as a safe supplement with negligible harmful effects. The study encountered the limitation related to a small sample size in both the groups; meanwhile, the strong point of this study is that it is a double-blind randomized allopathic-controlled study, where the safety of Unani formulation has been compared with PUVA sol in patients with vitiligo for the first time.

Conclusion

A combination of Unani formulation, i.e. UNIM-001 as oral and UNIM-003 as a topical application, may be an effective and safe treatment alternative for patients with vitiligo.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Physicochemical Characterization of *Kushta Hajrul yahood* (Calx of *Lapis judaicus*) Commonly Used for the Management of Urolithiasis

Abstract

Aims and Objective: To standardize and characterize the *Kushta Hajrul yahood* for its various physico-chemical parameters. **Materials and Methods:** The preparation of *Kushta* requires heat treatment with herbal constituents and calcination steps aimed at converting the raw material to a suitable therapeutic form. *Kushta Hajrul yahood* was prepared by standard method as mentioned in Unani literature. It was subjected to different physico-chemical tests (pH, ash value, bulk density, tapped density etc.) to establish that final product is upto the mark. Further it was tested for its purity, quality and characterization by using XRD, FTIR, and SEM-EDAX. **Results:** *Kushta Hajrul yahood* was found to be khaki in colour with no odour and taste, smooth and lustreless with alkaline pH. The chemical analysis showed the presence of Cao, MgO, SiO_2, Al_2O_3, Fe_2O_3, P, Zn. The morphology of *kushta* by XRD showed crystalline form with strongest peak of calcium as final product. The absence of organic compound authenticated that Kushta is successfully prepared. Heavy metals were found within permissible limits. **Conclusion:** Results from this study may be used as a future reference for standardization and characterization of herbo-mineral formulation.

Keywords: *Hajrul yahood, Kushta, Lapis judaicus, Unani system of medicine, urolithiasis*

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Introduction

Unani system of medicine uses plant, animal, and mineral-origin drugs in different dosage forms. Herbs and minerals are integral parts of traditional systems of medicine in many countries. Metals have been used in disease treatment since time immemorial. Gold in medicine was mentioned by the Roman physician Pliny and Greek philosopher Dioscorides. Hippocrates, the father of modern medicine, explained the beneficial healing and anti-disease properties of silver.[1] The medicinal use of mineral-origin drugs, methods of their purification, and their pharmacological properties have been mentioned by many eminent scholars in their books.[2] Herbo-mineral medicinal preparations called *Kushta* are unique to the Ayurvedic, Unani, and Siddha systems of medicine. These preparations have been used for a long and are claimed to be very effective and potent dosage forms.[3] Metals, minerals, and many plant drugs are known for their toxic effect which is why they are not used as such because of their ability to induce toxic effects even at therapeutic dose levels. Therefore, they are subjected to various detoxification processes in order to remove or reduce the level of the elements of toxicity. Some of the drugs are incinerated at a high temperature so as to ascertain the plausibility of their safe use. The incinerated material is technically known as *Kushta* (calx) – a Persian word meaning killed, containing carbonate or oxide in finely divided form. The product has a high dissolution rate and the ability to get absorbed in the body in a very short period; therefore, a small amount of *Kushta* induces a quick onset of action and a high magnitude of effect.[4]

The survey of Unani literature revealed that *Hajrul yahood* (*Lapis judaicus*) has a long history of use as an important drug for the treatment of urinary disorders including urolithiasis. *Hajrul yahood* as a single drug in powder form or combination with other drugs has been widely used in Unani medicine for dissolving kidney stones. It is also an important ingredient in several formulations. Metals and minerals in particular are converted either into carbonate or oxide by the process of *Taklees* (calcination) to make them

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consumable. The product obtained by this process is known as *Kushta* (calx). It is a herbo-metallic ash in which the metal is calcined along with various herbal ingredients to form organometallic complexes. These complexes should neither contain free metal nor contain free organic constituents, whose presence in *Kushta* indicates improper calcination.[2,5-8]

The toxicity of the metallic constituents is believed to be removed by consecutive heat and cold cycles in oil, buttermilk, cow's urine and herbal decoctions, etc.[9] *Kushta* is also prepared as a herbal-mineral preparation, as in this case different herbs or their extracts are mixed with minerals, before, during, or after the process of calcination. These metals in combination with the constituents of medicinal herbs are said to form an effective combination useful in the management of diseases. The calcined form has certain advantages over the noncalcined form. The dissolution rate of *Kushta* is high; therefore, it is readily distributed in the body. Its onset of action is quick, and a comparatively low dose is required for therapeutic effect. Its magnitude of effect and the intensity of biological activities are greater than any other dosage forms used in Unani medicine.[10]

Although this Unani herbo-mineral formulation enjoys a very good reputation for treating several ailments efficiently, still no scientific study has been carried out regarding physicochemical evaluation of *Kushta Hajrul yahood*. In this study *Kushta Hajrul yahhod* is prepared as per the procedure mentioned in classical literature. It is standardized by using classical and modern parameters to establish the quality of *Kushta Hajrul yahood*.

Materials and Methods

Raw materials

The ingredients of *Kushta Hajrul yahood,* namely *Lapis judaicus*, *Raphanus sativus* L., and potassium carbonate, were purchased from an authentic herb supplier in the local market of Bengaluru, India. They were identified at Trans-Disciplinary University, Bengaluru, by Dr. S. Noorunnisa Begum, Associate Professor (FRLHT Acc. No. 5042, 5043, 5044, and 5045). *Hajrul yahood* (*Lapis judaicus*) was characterized by the Regional Ore Dressing Laboratory, Bengaluru, the Indian Bureau of Mines (IBM), Ministry of Mines Government of India, (Report investigation no.: K-24011/2016-17/BNG-OD). A voucher specimen (Ref. no. 58/IA/Res/2019) was deposited in the department of Ilmul Advia, National Institute of Unani Medicine (NIUM), Bengaluru, for future reference.

Physicochemical parameters

The prepared *Kushta Hajrul yahood* was evaluated for classical parameters of *kamil Kushta* (ideal *Kushta*). Modern scientific parameters, such as bulk density, tapped density, Hausner's ratio, and Carr's compressibility index, were evaluated in a density tester (Lab India, tap density tester, TD1025). pH in 1 and 10% solution was observed by digital pH meter (digital pH meter 7007, Digisun Electronics, Hyderabad).[10-14]

Classical tests

1. Floating test: A small quantity of *Kushta* was sprinkled on the water's surface to see whether it floated on the surface or not
2. Grain floating test: A small amount of *Kushta* was placed on the floating grain and it was observed whether the *Kushta* was floating or not on the floating grain
3. Fineness test: A small quantity of the *Kushta* was rubbed between the fingers and observed whether it pierced into the lines and creases of the fingers
4. Loss of metallic luster: The *Kushta* was examined visually preferably in the presence of sunlight for any metallic luster
5. Wall stick test: A little amount of *Kushta* was thrown on the wall and observed for its stickiness on the wall).[10-14]

Determination of loss on ignition

5.0 g *Kushta* was taken in a silica crucible and heated to constant weight at 950°C for 2 h and then allowed to cool. Loss of weight on ignition was calculated by the following equation:

$$LOI\% = \frac{[(W3 - W2) \times 100]}{W2 - W1}$$

where W1 = weight of empty crucible, W2 = weight of crucible + sample, and W3 = weight of crucible + sample after ignition.

Physico-chemical characterization

Chemical analysis of *Kushta Hajrul yahood* for Cao, MgO, SiO_2, Al_2O_3, $F_{e2}O_3$, loss on ignition, P, and Zn was done from IBM, Regional Mineral Processing Laboratory and PP, Goraguntepalaya, Bengaluru.

Estimation of heavy metals

Kushta 0.5 g (wet weighed) was taken into a vessel in which 10 ml of Conc. HNO_3 was added and then the sample was to predigest by standing open for 15 min before sealing the vessel. The vessel was placed in a microwave digester after digestion allowed the vessel to cool. Samples were filtered and made up to 25 ml with water. The above solution was aspirated into inductively coupled plasma-optical emission spectrometry (ICP-OES), Teledyne Leeman Labs, Hudson, USA; model: Prodigy 7; instrument condition: spectrophotometer temperature: 35°C, axial time: 30 s; and nebulizer: 37 PSI1, Azyme Biosciences Laboratory, Bengaluru.

Fourier transform infrared spectroscopy

Fourier transform infrared spectroscopy (FTIR) is the preferred method of infrared spectroscopy; it is an important and more advanced technique. It is used to identify the functional group, determine the quality and consistency of the sample material, and determine the amount of compounds present in the sample. In the

present study FTIR, infrared was passed through a sample *(Kusht*a *Hajrul yahoo*d). This infrared was absorbed by the sample according to the chemical properties and some were transmitted. The spectrum that appeared denotes the molecular absorption and transmission. In this way, it formed the molecular fingerprint of the *Kushta Hajrul yahood*. Like the fingerprint, there were no two unique molecular structures producing the same infrared spectrum. It was recorded as the wavelength and the peaks seen in the spectrum indicate the amount of material present. FTIR was performed in the spectroscopy analytical test facility, Society for Innovation and Development (SID), IISc, Bengaluru. Thermo Fisher Scientific, model: Nicolet 6700 FTIR. Source: IR, beam splitter: XT-KBr. Detector: DTGS KBr. Scan range: 4000 cm^{-1}–400 cm^{-1}, no of scans: 64, resolution: 4, sample gain: 8, optical velocity: 0.4747, aperture: 80, sample preparation: KBr pellet method. Goniometer = PW3050/60 (theta/theta); minimum step size 2Theta:0.001; minimum step size omega: 0.001. Sample stage = PW3071/xx Bracket Diffractometer system = XPERT-PRO. Measurement program = A general user program.

X-ray diffraction measurement (XRD)

Powder method of diffraction has been adopted in this study. Instrument PAN analytical Inc, Netherlands, X'Pert Pro was used.

Goniometer=PW3050/60 (Theta/Theta); Minimum step size 2Theta:0.001; Minimum step size Omega:0.001

Sample stage=PW3071/xx Bracket

Diffractometer system=XPERT-PRO

Raw Data Origin XRD measurement (*.XRDML)
- Scan axis Gonio
- Start position (°2Th.) 6.0087
- End position (°2Th.) 89.9937
- Step size (°2Th.) 0.0330
- Scan step time (s) 221.9647
- Scan type Continuous
- PSD mode Scanning
- PSD length (°2Th.) 2.12
- Offset (°2Th.) 0.0000
- Divergence slit type Fixed
- Divergence slit size (°) 0.4354
- Specimen length (mm) 10.00
- Measurement temperature (°C) 25.00
- Anode material Cu
- K-alpha1 [Å] 1.54060
- K-alpha2 (Å) 1.54443
- K-beta (Å) 1.39225
- K-A2/K-A1 ratio 0.50000
- Generator settings 30 mA, 40 kV
- Diffractometer type 0000000011021228
- Diffractometer number 0
- Goniometer radius (mm) 240.00
- Dist. Focus-Diverg. Slit (mm) 100.00
- Spinning No.

Scanning electron microscopy

In scanning electron microscopy (SEM), a high-energy electron beam was focused through a probe towards the sample. A variety of signals was produced in interaction with the surface of the sample. This results in the emission of electrons or photons, and it is collected by an appropriate detector. This gave information about the sample including external morphology, texture, crystalline structure, and chemical composition.

Results

Traditional medicines use considerable amounts of heavy metals such as lead, mercury, and arsenic, which according to modern toxicology principles are extremely poisonous even in small doses. However, traditional medical practitioners claim that these preparations are made nontoxic by several detoxification processes.[9] The role of these herb-mineral preparations for curing skin diseases such as psoriasis, eczema, alopecia, diabetic ulcer, warts, vitiligo, and leprosy is well studied. Most medicines are a mixture of compounds, and because of their synergistic action, toxicity is being diminished, thereby increasing bioavailability through the cells of the body. Treating the minerals with herbal juices may lead to a reduction (trituration) in particulate size even up to nano levels (<100 nm) enabling to increase in their potency. These drugs are known to be effective even in low concentrations.[1] The use of a particular media and particular sequence is notable. The probable concept behind using such variation may be the removal of impurities from the drug in a particular acidic or alkaline media and also a reduction in the particle size of a drug.[6] Reduction in particle size facilitates absorption and assimilation of the *Kushta* in the system.[15] The method of *Kushta* preparation varies for each mineral and metal such that final products of different colors are produced. Unani system of medicine provides a list of tests to detect the completeness *Kushta* process. The tests are essentially qualitative and ensure that the resulting drug is fulfilling all the standards of a *kamil Kushta* (ideal calx) on classical parameters. However, these qualitative tests do not provide any quantitative information about the composition and structure of the final drug.[10,11,16]

Physicochemical analysis is an important characteristic to evaluate the quality, standardization, and safety of Unani drugs and provide information about correct identification and authentication of the crude drugs and formulations and may help in preventing adulteration.[17] In the present study, the prepared *Kushta Hajrul yahood* was found to be khaki in color, devoid of any odor and taste, smooth to touch, and lusterless.

Bulk density is measured as the mass per unit volume. It is an important factor in the process development of solid dosage forms. The tapped density indicates the random

dense packing of the substance. The mean values of bulk and tapped density were found to be 0.6663 ± 0.0003 and 1.0341 ± 0.0003, respectively. The mean values of Hausner's ratio and compressibility index were 1.5516 ± 6.6667 and 35.5203% ±0.03517%, respectively [Table 1]. These are the indicators of the tendency of powder to consolidate.[11] For poorly flowing substances, there are larger inter-particle interactions, which consequences in lower bulk density and a larger difference between bulk and tapped densities. These differences are reflected in the compressibility index.[12]

The moisture content of the drug is determined by the Wensar Moisture Analyzer (ACZET Series Moisture Analyzer Sl. No.:72521) and found to be 0.26% lower value of loss on drying indicating the absence of moisture in the drug. Here, the percentage denotes the higher stability of the *Kushta Hajrul yahood*.[6,18] However, all these are highly empirical and hardly provide any information on the composition and structural properties of these mixed metal oxides. Therefore, it is highly desirable that these drugs should be characterized with the help of modern instruments, such as X-ray diffraction (XRD), SEM-energy-dispersive X-ray, and FTIR.[14] *Kushta Hajrul yahood* is used effectively in the treatment of urolithiasis. After its chemical analysis, it was found that it contains Cao, MgO, SiO_2, Al_2O_3, Fe_2O_3, P, and Zn. The pH of *Kushta Hajrul yahood* at 1% and 10% solution was 11.0233 ± 0.0167 and 11.0133 ± 0.0176, respectively. It is slightly alkaline in nature. The alkaline medium enhances the mineral storage to buffer, reduces the aging process, and increases the utilization of oxygen levels in the body.[18] *Kushta Hajrul yahood* contains magnesium, which is a protective agent in calcium oxalate crystal growth. Magnesium (Mg) can form complexes with oxalate and decreases supersaturation. Moreover, its basic pH nature could be another inhibitor for stone production. Furthermore, the *Kushta* contains silica (SiO_2) which has the ability to convert calcium oxalate monohydrate to calcium oxalate dihydrate, which is more soluble and easily excreted through urine.[19,20] Pyrophosphate and diphosphate have been shown to inhibit the precipitation of CaP, whereas diphosphates also inhibit the growth of apatite crystals.[20] Mg powerfully inhibits the crystallization of calcium oxalate *in vitro*, forms a complex with oxalate to form a soluble complex, and reduces the supersaturation of calcium oxalate. As a consequence, it reduces the growth and nucleation rate. Mg inhibits oxalate absorption and excretion and thus prevents its supersaturation. Several studies demonstrate that a low level of magnesium in urine is a risk factor for lithogenesis.[21-25] On the other hand, the excretion of citrate in urine has been reported to be elevated after administration of magnesium and its basic pH could be another inhibitor of stone formation.[20,26] The chemical analysis of *Kushta Hajrul yahood* is given in Table 2.

Table 1: Physicochemical tests of *Kushta Hajrul yahood* (*n*=3)

Parameters	Mean±SEM
Bulk density (g/mL)	0.6663±0.0003
Tapped density (g/mL)	1.0341±0.0003
HR	1.5516±6.6667
Compressibility index (%)	35.5203±0.03517
pH (1%)	11.0233±0.0167
pH (10%)	11.0133±0.0176

HR: Hausner's ratio, SEM: Standard error of mean

Discussion

XRD is done to confirm the exact molecular structure of crystalline products, their arrangement, phase equilibria, and particle size measurement. It is comparatively easy and detects crystalline structures rapidly and accurately. It was performed in IISc, Bengaluru, and results are summarized in Figure 1 and Table 3. The strongest peak identified in the final product was Calcium. The high intensity of XRD lines in the XRD pattern suggests that the drug is present as a crystalline material.[14]

FTIR spectra of the drug sample showed that they do not contain organic compounds. The absence of organic matter is further proof of proper incineration during the preparation of the *Kushta Hajrul yahood* and the absence of any external organic contamination.[1] In general, the

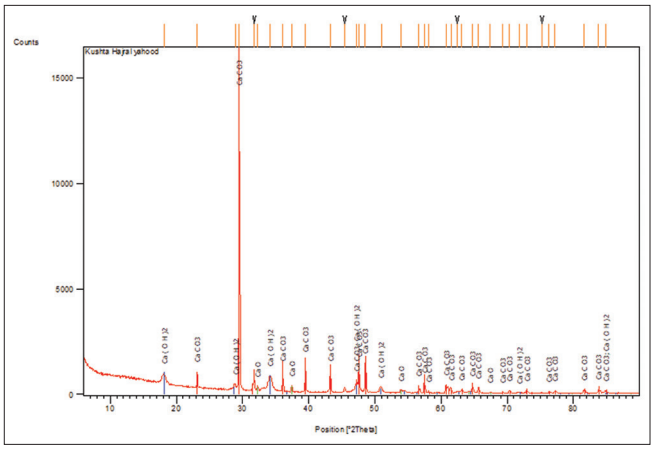

Figure 1: X-ray diffraction pattern of *Kushta Hajrul yahood*

Table 2: Chemical analysis of *Kushta Hajrul yahood*

Sample name	Values in percentage							
	SiO_2	Fe_2O_3	Al_2O_3	CaO	MgO	*P*	Zn (ppm)	LOI
Kushta Hajrul yahood	0.35	1.01	0.25	53.10	1.86	Traces	144	43.30

LOI: Loss on ignition

Table 3: X-ray diffraction of *Kushta Hajrul yahood*

Position (°2Th.)	Height (cts)	FWHM (°2Th.)	d-spacing (Å)	Relative intensity (%)	Area (cts*°2Th.)
18.1728	469.88	0.5196	4.88170	3.36	240.82
23.1660	761.49	0.1299	3.83957	5.44	97.57
28.8853	242.04	0.2273	3.09103	1.73	54.27
29.5271	13991.10	0.1299	3.02529	100.00	1792.65
31.7567	898.23	0.1299	2.81780	6.42	115.09
32.3098	151.95	0.1624	2.77081	1.09	24.34
34.1618	673.99	0.2273	2.62472	4.82	151.13
36.0807	980.44	0.1624	2.48941	7.01	157.03
37.4392	311.80	0.1948	2.40214	2.23	59.93
39.5011	1443.65	0.1948	2.28138	10.32	277.46
43.2459	1042.34	0.1624	2.09211	7.45	166.94
45.4500	239.45	0.2273	1.99565	1.71	53.69
47.1935	477.79	0.1624	1.92591	3.41	76.52
47.5729	1199.88	0.1624	1.91143	8.58	192.17
48.5806	1362.68	0.1624	1.87412	9.74	218.25
50.9595	243.60	0.3247	1.79207	1.74	78.03
53.9182	128.35	0.1948	1.70052	0.92	24.67
56.6550	323.53	0.0974	1.62470	2.31	31.09
57.4841	533.29	0.1188	1.60190	3.81	84.47
58.1981	62.38	0.2376	1.58393	0.45	19.76
60.7510	387.48	0.1188	1.52334	2.77	61.38
61.5253	155.19	0.3168	1.50601	1.11	65.55
62.4393	59.08	0.4752	1.48615	0.42	37.43
63.1025	130.07	0.1188	1.47211	0.93	20.60
64.7390	329.07	0.1584	1.43880	2.35	69.50
65.6717	234.43	0.1584	1.42060	1.68	49.51
67.4287	43.86	0.4752	1.38779	0.31	27.79
69.2834	50.96	0.3168	1.35510	0.36	21.53
70.2932	111.06	0.1584	1.33809	0.79	23.46
71.9222	19.69	0.6336	1.31174	0.14	16.64
72.9616	127.03	0.1584	1.29559	0.91	26.83
75.2388	29.01	0.4752	1.26193	0.21	18.38
76.3424	88.94	0.1188	1.24641	0.64	14.09
77.2265	122.46	0.1584	1.23433	0.88	25.86
81.5925	166.43	0.1584	1.17896	1.19	35.15
83.8210	188.30	0.1584	1.15320	1.35	39.77
84.8683	126.46	0.1188	1.14162	0.90	20.03

Pattern list

Reference Code	Score	Compound Name	Displacement (°2θ)	Scale factor	Chemical formula
01-085-1108	63	Calcium carbonate	0.000	0.613	$CaCO_3$
01-072-0156	48	Portlandite, syn	0.000	0.043	Ca(OH)2
01-077-2010	42	Calcium oxide	0.000	0.017	CaO

peak appears around 400–1400 region are of C–C, C–N, and C–O. The broad peak above 3000 is of the –OH group; whereas the sharp peak around 3300 was of NH stretching. The peak around 2550 is C triple bond C. The peak around 400–below 1000 may be due to some halogen attached to the carbon. FTIR spectrum of the present study the peak around 874 may be due to some halogen attached to carbon. The peak at 1416 may be due to C–C, C–N, and –C–O which depend on the molecule. The peak around 2512 is of carbon triple bond carbon, and the peak around 2983 is of OH bond, whereas the sharp peak around 3644 may be of NH stretching. OH group has a higher potential for inhibitory activity against microorganisms.[18] Agglomeration of the particles is due to repeated cycles of calculations involved in preparation. The size and shape of the particles determine the mode of their entry into a cell and thus in turn influence the intracellular compartment to which the particle is directed. Consequently, its molecular targets and its biological effects are altered.[9,15] The FTIR pattern of *Kushta Hajrul yahood* is shown in Figure 2.

SEM and Energy Dispersive X-ray Analysis (EDAX) provide good estimates of the concentration of main elements in the sample in a significantly faster way compared to the ICP-OES method. Moreover, it also gives information on the distribution of the elements forming the sample and their possible chemical form.[1] The elemental composition of the drug sample analyzed by EDAX is presented in Table 4. EDAX analysis shows the presence of 13 elements (C, N, O, Mg, Al, Si, Sr, S, K, Ca, Fe, Cu, and Zn) in the *Kushta Hajrul yahood*, where Ca (47.28 wt %) is present as major element followed by oxygen (27.55 wt %). SEM images of *Kushta Hajrul yahood* are shown in Figure 3 while the SEM-EDAX pattern of *Kushta Hajrul yahood* is shown in Figure 4. The large amount of carbon was due to repeated cycles of calcination in the presence of plant juices.[14] Heavy metals such as cadmium and mercury were found to be below the detectable limit while lead and arsenic were within permissible limits as per WHO and FDA limits and were analyzed by ICP-OES.[2,27] Hence, the safety of the drug *Kushta Hajrul yahood* is ensured.

Table 4: *Kushta Hajrul yahood*. EDAX ZAF quantification (standard less), element normalized

Element	Wt %	At %	*K*-ratio	*Z*	*A*	*F*
C K	19.76	34.56	0.0819	1.0482	0.3949	1.0008
N K	1.54	2.31	0.0013	1.0389	0.0818	1.0004
O K	27.55	36.18	0.0331	1.0305	0.1167	1.0001
MgK	0.69	0.60	0.0031	0.9885	0.4573	1.0021
AlK	0.37	0.29	0.0021	0.9594	0.5999	1.0041
SiK	0.49	0.36	0.0035	0.9873	0.7267	1.0077
SrL	0.23	0.06	0.0018	0.8102	0.9582	1.0092
S K	0.16	0.11	0.0015	0.9750	0.8932	1.0271
K K	0.34	0.18	0.0036	0.9378	0.9949	1.1358
CaK	47.28	24.78	0.4567	0.9598	1.0059	1.0006
FeK	1.01	0.38	0.0085	0.8727	0.9613	1.0009
CuK	0.30	0.10	0.0025	0.8432	0.9857	1.0000
ZnK	0.29	0.09	0.0024	0.8432	0.9905	1.0001
Total	100.00	100.00				

Element	Net Inte.	Bkgd Inte.	Inte. error	P/B
C K	74.62	4.34	1.73	17.19
N K	1.52	4.34	29.71	0.35
O K	79.80	4.96	1.68	16.09
MgK	10.98	9.36	7.02	1.17
AlK	7.38	12.40	10.87	0.60
SiK	11.35	14.94	8.00	0.76
SrL	2.68	16.60	31.61	0.16
S K	4.10	17.62	21.63	0.23
K K	7.96	12.46	10.19	0.64
CaK	919.68	10.46	0.47	87.92
FeK	7.82	5.82	7.98	1.34
CuK	1.36	5.12	35.42	0.27
ZnK	1.06	4.80	43.56	0.22

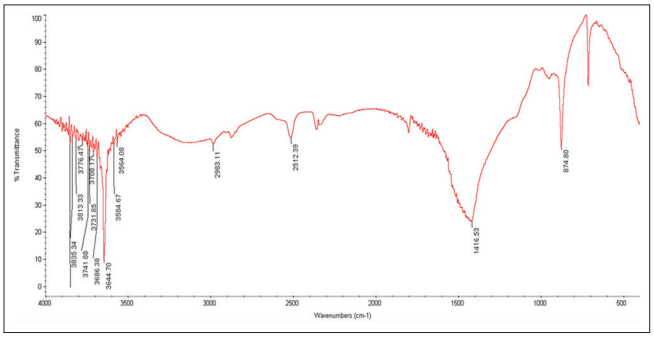

Figure 2: Fourier transform infrared spectroscopy pattern of *Kushta Hajrul yahood*

Conclusion

Kushta Hajrul yahood is one of the important drugs used in the treatment of urolithiasis. The present study is the first attempt to characterize it for chemical composition, morphology, etc., by various methods. Hence, the inferences laid down in this study may be utilized for future reference. The results demonstrated that the formulation contains magnesium, zinc, and silica which act as inhibitors in the stone formation; moreover, its basic pH further aids in the prevention of urolithiasis.

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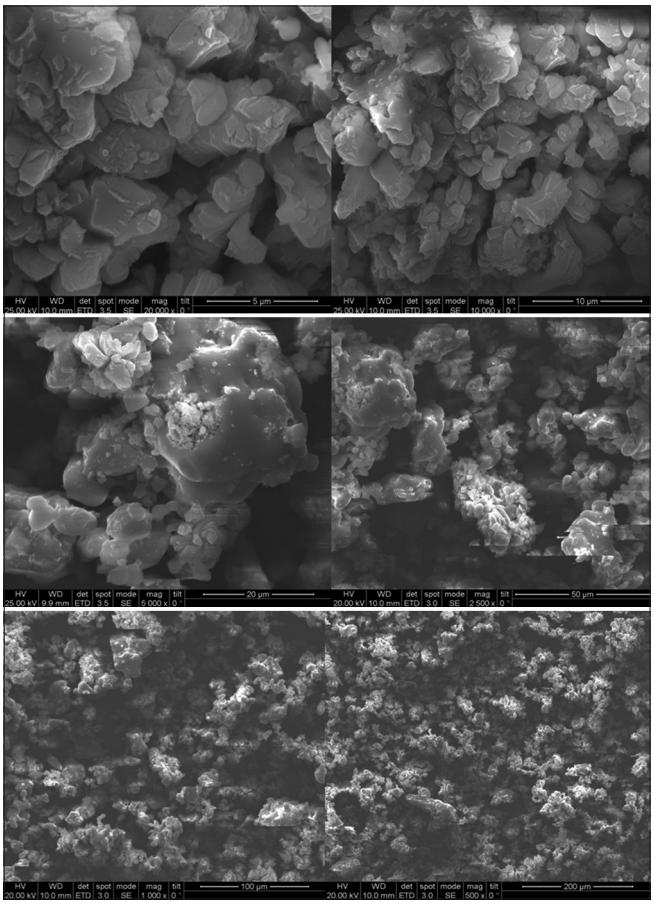

Figure 3: Scanning electron microscopy images of *Kushta Hajrul Yahood*

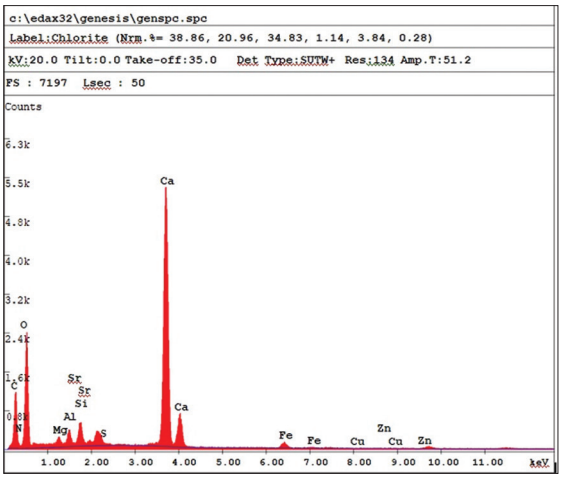

Figure 4: *Kushta Hajrul Yahood* scanning electron microscopy-EDAX pattern

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Conflicts of interest

There are no conflicts of interest.

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