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Editorial

The recent few decades have witnessed increased global interest in traditional systems of medicine, particularly herbal medicines. Global and national markets for medicinal herbs, associated products and services have been growing rapidly and significant economic gains are being realized. This positive change has put forward the challenge pertaining to issues of their quality, safety and efficacy before the scientists associated with researches in traditional drugs. In this context, the Central Council for Research in Unani Medicine (CCRU), through its research programmes, especially clinical research, drug research, literary research, and survey & cultivation of medicinal plants has been contributing significantly for about four decades and generating valuable scientific data.

To exchange the vital information pertaining to researches in Unani Medicine amongst academicians and researchers engaged in the scientific validation of traditional drugs, the CCRUM has been publishing *Hippocratic Journal of Unani Medicine* (HJUM), a peer-reviewed quarterly journal for about 15 years. The journal is listed on the portal of 'UGC-CARE Reference List of Quality Journals (UGC-CARE List)', an initiative of the University Grants Commission (UGC), Government of India to curb the menace of increased incidence of compromised publication ethics and deteriorating academic integrity.

This issue of HJUM is comprised of six papers. In the first paper, the authors have provided information on medicinal properties of *Filfil Darāz* (*Piper longum* L.) mentioned in Unani classical literature as well as those validated in the light of recent scientific studies supporting its potential as a promising health promoting herbal plant. The second paper provides a detailed survey of the literature on scientific researches of pharmacognostical characteristics, chemical composition and pharmacological activities of the seeds of *Kalonji* (*Nigella sativa*) with special reference to Unani Medicine. The third paper presents literature review of *Dawā'-i-Hiltīt* as an antipyretic drug of Unani Medicine. The fourth paper is a case report on the efficacy of a Unani regimen in the treatment of *Yaraqān* (jaundice) written with the objective of creating awareness about the effectiveness of Unani Medicine among academia, researchers, scientists and common people. While the fifth paper is based on a study conducted to determine physicochemical characters, standardization and quality control of *Sūranjān Shirīn*, an important drug of Unani Medicine commonly used in the management of *Waja' al-Mafāsil* (arthritis), the last paper is based on the outcome of a study on standardization and HPTLC fingerprinting of Unani formulation *Habb-i-Azarāqī* with contemporary analytical techniques.

We trust that the papers included in this issue would be of great use for the academicians and researchers of Unani Medicine and other traditional medical systems as well as entire medical science fraternity at large. We are thankful to our contributors and learned reviewers for their valuable contributions, time and efforts. As we are striving to attain higher standards for the HJUM and making it a leading journal of Unani Medicine and related sciences, we seek increased support and contributions from the quality-oriented authors and reviewers. We sincerely hope and trust that the mission can be accomplished with active partnership of quality-conscious individuals and institutions.



Prof. Asim Ali Khan
Editor-in-Chief

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Utility of *Filfil Darāz* (*Piper longum* L.) in Unani Medicine: An Evidence-Based Approach

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Abstract

Unani Medicine is one among the oldest systems and prevails till date with its efficient drugs derived from animal, plant and mineral resources. Thousands of plants have been used traditionally to treat various diseases. Among them, *Filfil Darāz* (*Piper longum* L.) (Piperaceae) is an important medicinal plant which finds uses in Unani as well as Ayurveda systems of medicine. It is most commonly used to treat bronchitis, asthma, respiratory infections, constipation, gonorrhea, paralysis of tongue, diarrhoea, cholera, chronic malaria, viral hepatitis, stomach ache, diseases of spleen, cough, and tumors. In this review, an effort has been made to provide information on medicinal properties of *Filfil Darāz* (*Piper longum* L.) mentioned in Unani classical literature as well as those which have been validated in the light of recent scientific studies and support the potential of *Filfil Darāz* as a promising health promoting herbal plant. Hence, more researches can be done to exploit the unexplored potentials of *Filfil Darāz* which have already been mentioned in Unani classical literature.

Keywords: Anti asthmatic, Anti-inflammatory, *Filfil Darāz*, Indian long pepper, *Piper longum* L., Unani Medicine

Introduction

The medicinal plants are being therapeutically used throughout the world for treating various ailments and it is the oldest and safest method to manage or cure illness. *Filfil Darāz* (*Piper longum*) is a flowering vine in the family Piperaceae cultivated for its fruit, which is usually dried and used as a spice. This plant is inexpensive, readily available, and effective for many diseases, including diarrhoea, cholera, chronic malaria, viral hepatitis, respiratory infections, and hepatotoxicity (Sumy *et al.*, 2000).

Synonyms

Arabic: *Dār Filfil*

Bengali: Piplamor

English: Indian long pepper, jaborandi pepper, long pepper

Gujarati: Pipli

Hindi: Pipar, piplamul

Kannada: Hippali, Lippali, Thippili

Malaya: Magadhi, Pippali, Thippili, Tippili

Marathi: Pimpli

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Tamil: Kandan lippilli, pippili, sirumulam, tippili, thippili

Telugu: Pippallu

Urdu: Pippal

(Anonymous, 2001; Rastogi and Mehrotra, 1993)

Ethno-Pharmacological Description

The plant is a native of North East India. It occurs in the hotter parts of India, from Central Himalayas to Assam, Khasi, the lower hills of West Bengal, and the evergreen forests of the Western Ghats from Konkan to Travancore. It has also been reported in the Car Nicobar Islands and is also cultivated there. Globally, the species is distributed in the Indo-Malaysian region and Sri Lanka.

Filfil Darāz is cultivated on large scale in limestone soil and in heavy rainfall areas where relative humidity is high (Sumy *et al.*, 2000; Sivarajan and Balachandran, 1994; Kirtikar and Basu, 1980; Kirtikar and Basu, 1987; Rastogi and Mehrotra, 1993).

Morphological Description

Filfil Darāz is a small shrub with a large woody root and numerous creeping, jointed stems that are thickened at the nodes. The leaves are alternate, spreading, without stipules and with blades varying greatly in size. The lowest leaves are 5–7 cm long, whereas, the uppermost are 2–3 cm long. Flowers grow in solitary spikes. The fruits, which grow in fleshy spikes 2.5–3.5 cm long and 5 mm thick, are oblong, blunt, and blackish-green. The mature spikes are collected and dried as the commercial form of pippali, and the root radix is known as pippalimula. There are three grades of pippalimul: grade I with thick roots and underground stems fetch a higher price than grade II or III, which consist of thin roots, stems, or broken fragments. The commercial drug consists almost entirely of transversely cut pieces (length, 5–25 mm; diameter 2–7 mm), which are cylindrical, straight, or slightly curved; some have distinct, swollen internodes exhibiting a number of leaf and rootlet scars. The surface is dirty



Fig. 1: *Filfil Darāz* Plant



Fig. 2: *Filfil Darāz* Fruit

light brown. *Filfil Darāz* has a peculiar odour and a pungent bitter taste that produces numbness on the tongue (Munshi *et al.*, 1977; Nadkarni, 1976; Rastogi and Mehrotra, 1993).

Microscopic Description

The roots are adventitious, up to 9 cm long; surface dark brown with few rootlet scars; fracture short and starchy. In T.S. the root shows thin walled and rectangular to slightly tangentially elongated cork cells. The cortical cells are large sized, thin walled and rounded to oblong with intercellular spaces. Most of the cortical cells contain spherical or oval starch grains. A few cortical cells contain minute prismatic crystals of calcium oxalate. Many few cortical cells are found scattered in the cortex (Rastogi and Mehrotra, 1993; Singh *et al.*, 2011; Nadkarni, 1976).

Scientific Classification

Kingdom:	Plantae
Division:	Magnoliophyta
Class:	Magnoliopsida
Order:	Piperales
Family:	Piperaceae
Genus:	<i>Piper</i>
Species:	<i>Longum</i>
Botanical name:	<i>Piper longum</i>

(Kirtikar and Basu, 1980)

Phytochemical Constituents

The fruits contain 1% volatile oil, resin, alkaloids, piperine and piperlonguminine, a waxy alkaloid N-isobutyl deca-trans-2-trans-4-dienamide and a terpenoid substance. The pungency of the fruits is mainly due to the piperidine alkaloid piperine. The fruits also contain calcium, 1230; phosphorous, 190; and iron, 62.1mg/100g. Roots contain piperine, piperlongumine or pipartine and dihydrostigmasterol (Khajuriya *et al.*, 1999; Neelam and Krishnaswamy, 2001).

Parts Used

Fruits and Roots (Anonymous, 1997).

Temperament

Hot 2° and Dry 2° (Anonymous, 2008; Ibn Sina, 2007).

Hot 3° and Dry 3° (Anonymous, 1997; Ibn Baitar, 2003; Ghani, YNM; Khan, 1892).

Dosage

500 mg to 1 g in powdered form (Ali, 2010).

Pharmacological Actions

- *Kāsir-i-Riyāḥ* (Carminative)
- *Mushil-i-Şafrā'* (Cholagogue)
- *Munaffith-i-Balgham* (Expectorant)
- *Muḥallil* (Resolvent)
- *Musakkin* (Sedative)
- *Mulattif* (Demulcent)
- *Qātil-i-Dīdān* (Anthelmintic)
- *Muqawwī 'Ām* (General tonic)
- *Muwallid-i-Dam* (Hematinic)
- *Mudirr-i-Ḥayḍ* (Emmenagogue)
- *Mukhrij-i-Janīn* (Abortifacient)
- *Hāḍim* (Digestive)

(Ali, 2010; Anonymous, 1969; Anonymous, 1997; Anonymous, 2008; Kirtikar and Basu, 1987)

Therapeutic Uses

- *Nafkh al-Mi'da* (Flatulence)
- *Ḍu'f al-Mi'da* (Weakness of stomach)
- *Iḥtibās al-Ṭamth* (Amenorrhoea)
- *Ḍīq al-Nafas* (Bronchial Asthma)
- *Surfa* (Bronchitis)
- *Su'āl* (Cough)
- *Şar'* (Epilepsy)
- *Niqris* (Gout)
- *Waram al-Kabid* (Hepatitis)
- *Tukhma* (Indigestion)

- *Sahr* (Insomnia)
- *Didān al-Am‘ā’* (Intestinal Worms)
- *Yaraqān* (Jaundice)
- *Ḍu‘f al-Ishtihā’* (Loss of Appetite)
- *Waram al-Ḥanjara* (Laryngitis)
- *Ghathayan* (Nausea)
- *Ḥudār* (Rheumatism)
- *‘Irq al-Nasā* (Sciatica)
- *Khushuna al-Ḥalaq* (Sore Throat)
- *Waja‘ al-Mi‘da* (Stomach ache)
- *Sūzāk* (Gonorrhoea)

(Anonymous, 1997; Anonymous, 2008; Ali, 2010; Ghani, YNM; Kirtikar and Basu, 1987; Ibn Sina, 2007)

Pharmacological Studies

Anti-Arthritic Activity

The aqueous extract of *Piper longum* shows anti-arthritic effect on CFA (Complete Freuds Adjuvant) induced arthritis in rats (Yende *et al.*, 2010).

Larvicidal Activity

Alakaloid A (Closely related to pellitorine) showed significant *in-vitro* anti-tubercular activity against *Mycobacterium tuberculosis*-H-37 Rv strain. It inhibited the growth of bacillus in 20µg/ml concentration. Alcoholic extract of dry fruits and aqueous extract of leaves showed activity against *Micrococcus pyogenes* var. aureus and *E. coli*. Ether extract of fruit showed larvicidal properties (Nadkarni, 1976).

Insecticidal Activity

In a study, piperlongumine - an alkaloid present in the root and stem-bark - showed insecticidal activity against *Musca domestica* (Rastogi and Mehrotra, 1993).

Antidepressant Activity

A bioassay guided isolation of ethanolic extract from the fruit yielded a piperine alkaloid and piperine having potent antidepressant like activity, which are mediated in part through the inhibition of MAO activity (Seon *et al.*, 2005).

Treatment with piperine (6.25-25mM) for 72h reversed the (corticosterone) induced reduction of BDNF mRNA expression in cultured hippocampal neurons (Song *et al.*, 2007). Therefore, the fruits of *Piper longum* represent a promising pharmaco therapeutic agent against depression (Lee *et al.*, 2008).

Anticancer Activity

The alcoholic extract of *P. longum* (10 mg/dose/animal) and piperine (1.14 mg/dose/animal) inhibit solid tumour development in mice induced with Dalton's lymphoma ascites cells and increase the life span of mice. Piperine was also found to be cytotoxic towards Dalton's lymphoma ascites and Ehrlich ascites carcinoma cells at 250 µg/mL. (Anuradha, 2004; Pradeep and Kuttan, 2002).

Anti-apoptosis and Antioxidant Activity

P. longum exhibits promising antioxidant potential against free radical-induced oxidative damage. Petroleum ether extract of the root and piperine from roots of *P. longum* L. decrease lipid peroxide levels and maintain glutathione content, demonstrating antioxidant activity (Natrajan *et al.*, 2006).

In another study, the hexane: ethanol (2:8) extract of *Piper longum* showed anti apoptosis and antioxidant activity through TUNEL ASSAY and Radical scavenger activity (DPPH Assay). The fruit extracts on GM-induced hair cell loss in basal, middle and apical regions in a neonatal cochlea cultures. The study accomplished that the fruit extract of *Piper longum* shows anti-apoptosis and antioxidant activity (Yadav *et al.*, 2014).

Hepato-protective Activity

In a study, *Piper longum* fruit extract was assessed in rodents for its hepato-protective action against carbon tetrachloride-induced acute, chronic reversible and irreversible damage using morphological, biochemical and histopathological parameters. The extract stimulates regeneration by restricting fibrosis, but offers no protection against acute damage or against cirrhosis. Piperine was found to protect against tertiary butyl hydroperoxide-induced and carbon tetrachloride-induced hepatotoxicity by reducing lipid peroxidation in vitro and in vivo (Koul and Kapil, 1993; Christina *et al.*, 2006).

In another study, Hepatogard - a preparation having *P. longum* as one of the ingredients - exhibited hepatoprotective activity in rats (650mg/kg, p.o.) and reversed biochemical and histopathological changes induced by CC14. The efficacy of Hepatogard was comparatively less when given to rats in which previously the liver damage was induced by CC1₄ (Koul and Kapil, 1993).

In another study, piperine exerted significant protection against tertiary butyl hydroperoxide and CCl₄ hepatotoxicity by reducing both *in-vitro* and *in-vivo* lipid peroxidation, enzymatic leakage of alanine aminotransferase and alkaline phosphate and by preventing the depletion of glutathione and total thiols in intoxicated mice. Piperine showed lower hepato protective potency than silymarin. *Piper longum* fruits have been tested for effect on aggregation of rat platelets (Jain, 1994).

Analgesic Activity

The *aqueous* extract of *Piper longum* root powder (200, 400, and 800/kg) was given orally to mice and rat to study its analgesic effects. In rat, the delay in reaction time to thermal stimulant was assessed. In mice, the amount of writhing to chemical stimulus was assessed. The effect of 400 and 800mg/kg doses of fruit were similar to that of NSAID drugs ($p < 0.0001$). Both ibuprofen (40mg/kg) and piper longum (800mg/kg) demonstrated 50% protection against writhing. The delay in reaction time to thermal stimulus was $< 6\%$ for different doses of fruit as compared with 100% for pentazocaine. The result shows that the plant and root extract of *Piper longum* produces a weak-opioid-type but potent non-steroidal anti-inflammatory drug type of analgesic (Vedhanayaki *et al.*, 2003).

Anti-inflammatory Activity

In the carrageenan-induced rat paw edema test of Brahmi Rasayana (which induced *P. longum* stalks as one of the ingredients) exhibited a dose dependent anti-inflammatory activity. It also inhibited nystatin-induced inflammation and castor oil-induced diarrhea in rats. The anti-inflammatory activity was comparable to that of indomethacin (Jain, 1994).

A marked anti-inflammatory activity of *P. longum* fruit decoction has been reported using carrageenan induced rat edema (Kumar *et al.*, 2005; Choudhary, 2006).

Immunomodulatory Activity

The specific and nonspecific immunostimulatory actions of *P. longum* fruits have been evaluated by hemagglutination titer (HA), macrophage migration index (MMI) and phagocytic index (PI) in mice. A well-known Ayurvedic preparation containing long pepper (pippali rasayana) was tested in mice infected with *Giardia lamblia* and found to activate macrophages, as shown by an increased macrophage migration index and phagocytic index, indicating immune stimulatory activity (Tripathi *et al.*, 1999).

Anti-asthmatic Activity

The *ethanolic* extract of *Piper longum* in milk reduced passive cutaneous anaphylaxis in rats and protected guinea pigs against antigen-induced bronchospasm (Kulshresta *et al.*, 1969; Kulshresta *et al.*, 1971).

Anti-diabetic Activity

The *aqueous extract* of *Piper longum* shows anti-hyperglycemic and anti-lipid peroxidative in streptozotocin induced diabetic rat (Nabi *et al.*, 2013). Oral administration of dried fruits of *Piper longum* has shown significant anti-hyperglycemic, anti-hyperlipidemic effects in diabetic rats compared to that of the standard reference during glibenclamide (Manoharan *et al.*, 2007).

Hypocholesterolaemic Activity

Piper analogue isolated from *Piper longum* significantly inhibited the elevation of total serum cholesterol and total serum cholesterol to HDL-cholesterol ratio in rats fed with a high cholesterol diet (Wang *et al.*, 1993). The unsaponifiable fraction of the oil of *Piper longum* also significantly decreased total serum cholesterol and hepatic cholesterol in hypercholesterolaemic mice (Wu and Bao, 1992).

Antimicrobial Activity

Petroleum ether and ethyl acetate extracts of *P. longum* were found to exert antimicrobial effects against various microorganisms (Ali *et al.*, 2007).

Anti-hyperlipidemic Activity

The *ethanol extract* of *P. longum* L. fruit yields piperlonguminine, piperine and pipernonaline as the main antihyperlipidemic constituents. They exhibit appreciable anti-hyperlipidemic activity in vivo, which was comparable to that of the commercial antihyperlipidemic drug simvastatin (Jin *et al.*, 2009).

In a study, panchcole extract which included a combination of *P. longum* root and seed as one of the ingredients was shown to lower the lipid content of liver and ventricular heart muscles when administered to cholesterol fed rats. The treatment resulted in regression of atheroma and inhibition of plaque formation (Kaur, 1991).

Antileishmenial Activity

A study which tested extracts of several plants including *P. longum* for antileishmenial activity asserted that the drug might prove useful as it was cheap and easily available as compared with pentavalent antimonials (Rao *et al.*, 1993).

Antidepressant Activity

Ethanol extraction of *P. longum* fruits yields a known piperidine and piperine alkaloid, as a monoamine oxidase inhibitor. Thus *Piper longum* fruits represent a promising pharmaco-therapeutic agent against depression (Lee *et al.*, 2008).

A bioassay guided isolation of *ethanolic* extract from the fruit yielded a piperine alkaloid and piperine having potent antidepressant like activity, which is mediated in part through the inhibition of MAO activity (Seon *et al.*, 2005).

Anti-amoebic Activity

The *methanolic* extract of *Piper longum* fruits were tested for their efficacy against *Entamoeba histolytica in vitro* and against experimental *cecal amebiasis in vivo*. The ethanol extract and isolated piperine improved *cecal amebiasis* by 90% and 40%, respectively, in rats (Ghoshal *et al.*; 1996; Ghoshal and Lakshmi, 2002; Sawangjaroen *et al.*, 2004).

Anti-fertility Activity

The crude extract, various fractions, and the purified compound isolated from the active fraction of the powdered fruits of *P. longum* were studied for antifertility effects in female rats. The crude extract and its hexane fraction exhibited 100% and 86% efficacy, respectively (day 1–7 post coitum). On the other hand, the 1-butanol soluble, 1-butanol insoluble, and chloroform fractions were inactive. The *benzene* extract of *P. longum* L. fruit along with the *methanol* extract of the *Embelia ribes* berries inhibited pregnancy by 80% when administered to female rats (Lakshmi *et al.*, 2006).

In a study, fruit extract of *P. longum* showed marked antifertility effect in rats. The waxy alkaloid from petroleum *ether* extract of *P. longum* showed maximum activity amongst natural amides and semi-synthetic analogues from *Piper* species (D'- Cruz *et al.*, 1980).

In another study, essential oils obtained from dried fruits of *Piper longum* paralysed nerve muscle preparation of *Ascaris lumbricoides* quicker than piperazine but slower than tetramisole (Atal *et al.*, 1981).

Pharmacological studies showed that *P. longum* was capable of increasing the bioavailability of certain drugs in test animals when administered orally (Prakash, 1986).

Extract from *Piper longum* showed anti-implantation activity in female rats (Shoji *et al.*, 1986).

Dehydropipernonaline - an amide possessing coronary vasodilatory activity was isolated from *P. longum* fruits (Das *et al.*, 1987).

A preparation, which included extract of *P. longum* fruits, reduced fertility in rats over 3 oestrus cycle (Sharma *et al.*, 1990).

Anti-obesity activity

Pharmacological inhibition of acyl CoA diacylglycerol acyltransferase has emerged as a potential therapy for the treatment of obesity. Compounds containing piperidine groups are considered potential acyl CoA diacylglycerol acyltransferase inhibitors (Lee *et al.*, 2005).

Adulticidal activity

The dose dependent adulticidal effect of *ethanolic* extract of fruits was observed against *Stegomyi aegypti*, a main vector of dengue and dengue hemorrhagic fever. The various *extracts* of *Piper longum* demonstrated impressive adulticidal activity when tested on female mosquitoes by topical application (Choochote *et al.*, 2006).

Antifungal activity

Fungicidal activity of *P. longum* L. fruit-derived materials towards six phytopathogenic fungi, *Pyricularia oryzae*, *Rhizoctonia solani*, *Botrytis cinerea*, *Phytophthora infestans*, *Puccinia recondita*, and *Erysiphe graminis* was tested using a whole plant method *in vivo*. This treatment was compared with synthetic fungicides (chlorothalonil, dichlofluanid, and mancozeb) and four commercially available compounds (eugenol, piperine, piperlongumine, and piperettine) (Lee, *et al.*, 2001).

Antibacterial activity

Piper longum oil showed antibacterial activity against Gram+ve and Gram-ve bacteria (Rastogi and Mehrotra, 1993). Piperine is also isolated from *P. longum*. Piperine from *P. nigrum* inhibited the development of larva of *Drosophila* (Rastogi and Mehrotra, 1995).

Coronary Vasodilation

The amide dehydropiperonaline analogue isolated from the fruit of *Piper longum* demonstrated the ability to induce coronary vasodilation (Shoji *et al.*, 1986).

Anti-stress Activity

The *aqueous extract* of *Piper longum* was evaluated for anti-stress activity in stress rat models. With this result stress induced memory loss aqueous extract of *Piper longum* decreased the latent period indicating extract-produced no atropic activity (Srikanth and Venkatesh, 2012).

Protective Myocardial Activity

Piperaldehyde, one of the main active constituents of *Piper longum*, shows significant DPPH scavenging activity and exerts protective effect in the myocardial narcotic rats. Therefore, it can be concluded that the *extract* and piperaldehyde are useful in exerting protective activity against myocardial ischemia treated animals (Mishra, 2010).

Radioprotective Activity

The *ethanolic extract* of *Piper longum* showed radioprotective activity in Swiss mice. The fruit *extract* attenuated the elevated levels of glutathione pyruvate transferase, alkaline phosphatase and lipid peroxidation in the liver and serum of radiation treated animals and also restored glutathione production to offer radio-protection (Sunila and Kuttan 2005).

Anti-platelet Activity

The inhibitory effects of the four acid amides-piperine, piperonaline, piperoctadecalidine and piperlongumine, isolated from the fruits of *Piper longum* L. were evaluated on washed rabbit platelet aggregation. These four tested acid amides dose-dependently inhibited washed platelet aggregation induced by collagen, arachidonic acid and platelet-activating factor, but not that induced by thrombin (Das *et al.*, 1998).

Anti-Snake Venom Activity

The *ethanolic extract* of *Piper longum* L. (piperaceae) and piperine showed the anti-snake venom activities against Russell's viper venom in embryonated fertile chicken eggs, mice and rats by using various models. They found that administration of *P. longum extract* (PLE) and piperine significantly ($p < 0.01$) inhibited venom induced lethality, haemorrhage, necrosis, defibrinogenation and inflammatory paw edema in mice in a dose dependent manner. PLE possesses good anti-snake venom properties and piperine is one of the compounds responsible for the effective venom neutralizing ability of the plant (Shenoy *et al.*, 2013).

Bioavailability Enhancers

Piperine, the main active constituent of *Piper longum*, showed to enhance the bioavailability of structurally and therapeutically diverse drugs, possibly by modulating membrane dynamics due to its easy partitioning and increase in permeability of other drugs such as vasicine, indomethacin, diclofenac sodium, etc. (Atal *et al.*, 1981; Khajuria *et al.*, 1998; Zaveri *et al.*, 2010). Piperine also

has been reported to enhance the oral bioavailability of phenytoin in humans (Pattanaik *et al.*, 2006; Singh *et al.*, 2005; Khajuria *et al.*, 2002).

Safety Profile of *Filfil Darāz* (*Piper longum*)

Since it is widely used in cooking and traditional medicine, it is generally assumed to be safe in moderate doses. As the fruits are reported to have contraceptive activity in experimental models, therefore its use during pregnancy and lactation should be avoided. *Filfil Darāz* (long pepper) at a dose of 1gm/kg body weight was found to be an effective contraceptive agent without toxic or teratogenic effects (Das *et al.*, 1987).

Acute and chronic oral toxicity studies on the *ethanolic* extracts of common spice bark and *P. longum* fruits were carried out in mice and showed no significant acute or chronic mortality compared to the control during this study (Shah *et al.*, 1998).

The *ethanolic* extract of *Piper longum* showed radio protective property and reduced the elevated levels of glutathione pyruvate transaminase (GPT), alkaline phosphatase (ALP), and lipid peroxidation (LPO) in liver and serum of radiation treated mice. The extract administration also increased the reduced glutathione (GSH) production to offer the radioprotection (Sunila and Kuttan, 2005).

Piperine may interfere with enzymatic drug bio transformations resulting in the inhibition of hepatic aryl hydrocarbon hydroxylase (AHH) and UDP-glucuronyltransferase and altered the pharmacokinetic parameters of barbiturates and phenytoin (Shah *et al.*, 1998; Dhar *et al.*, 1968; Atal *et al.*, 1984).

Conclusion

This review reveals that the plant has potent pharmacological activities. The plant was found to have promising anti-asthmatic, anti-inflammatory, anti-diabetic, hepato protective, anxiolytic and antioxidant, etc. activities. The plant is traditionally claimed to be useful in the treatment of various disorders such as bronchitis, asthma, respiratory infections, constipation, gonorrhea, diarrhoea, cholera, hepatitis, stomach ache, etc. Moreover, it is economically cheap and easily available. Further investigations are needed to isolate the various phyto constituents present to get a clear idea of the mechanism of action of the plant and utility of *Filfil Darāz* in clinical practice.

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सारांश

यूनानी चिकित्सा में *फिल्फ़िल दराज़* (*पाइपर लॉंगम* एल.) की उपयोगिता : एक साक्ष्य-आधारित दृष्टिकोण

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यूनानी चिकित्सा सबसे प्राचीन चिकित्सा पद्धतियों में से एक है जो पशु, पौधों और खनिज संसाधनों से प्राप्त अपनी कुशल औषधियों के साथ आज तक प्रचलित है। विभिन्न रोगों के उपचार के लिए हजारों पौधों का उपयोग पारंपरिक रूप से किया जाता है। इनमें से *फिल्फ़िल दराज़* (*पाइपर लॉंगम* एल.) (पेपेरेसीई) एक महत्वपूर्ण औषधीय पौधा है जो यूनानी के साथ-साथ आयुर्वेद चिकित्सा पद्धति में भी उपयोग किया जाता है। यह आमतौर पर ब्रोंकाइटिस, अस्थमा, श्वसन संक्रमण, कब्ज़, सूज़ाक, जीभ का लकवा, अतिसार, हैज़ा, दीर्घकालीन मलेरिया, वायरल हेपेटाइटिस, पेट दर्द, तिल्ली के रोग, खांसी और ट्यूमर के उपचार के लिए उपयोग किया जाता है। इस समीक्षा में यूनानी क्लासिकल साहित्य में उल्लिखित *फिल्फ़िल दराज़* (*पाइपर लॉंगम* एल.) के औषधीय गुणों के साथ-साथ हाल के वैज्ञानिक अध्ययनों की रौशनी में वैध किए गए और स्वास्थ्यवर्धक महत्वपूर्ण औषधीय पौधे के रूप में *फिल्फ़िल दराज़* की क्षमता को स्थापित करने वाले गुणों के बारे में जानकारी प्रदान करने का प्रयास किया गया है। अतः *फिल्फ़िल दराज़* की अनन्वेषित क्षमता का लाभ उठाने के लिए और अधिक शोध किए जा सकते हैं।

शब्दकुंजी: अस्थमारोधी, एंटी-इनफ़्लामेटरी, *फिल्फ़िल दराज़*, *पाइपर लॉंगम* एल., यूनानी चिकित्सा



A Review on *Kalonji* (*Nigella Sativa*) with Special Reference to Unani Medicine

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Abstract

Nigella sativa L. (*Kalonji*) belonging to the family Ranunculaceae is a widely used medicinal plant throughout the world. It is very popular in Unani Medicine. The seeds of *N. sativa* have been widely used in the treatment of different diseases and ailments. In Islamic literature, it is considered as one of the greatest forms of healing medicine. It has been recommended for using on regular basis in *Tibb Nabwī* (Prophetic Medicine). It has been widely used as antihypertensive, liver tonic, diuretic, digestive, anti-diarrheal, appetite stimulant, analgesic, anti-bacterial and in skin disorders. Extensive studies on *N. sativa* have been carried out by various researchers and a wide spectrum of its pharmacological actions have been explored which may include antidiabetic, anticancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepato-protective, renal protective, gastro-protective, antioxidant properties, etc. It is revealed that most of the therapeutic properties of this plant are due to the presence of thymoquinone which is a major bioactive component of the essential oil. The present review is an effort to provide a detailed survey of the literature on scientific researches of pharmacognostical characteristics, chemical composition and pharmacological activities of the seeds of this plant.

Keywords: *Kalonji*, *Nigella sativa*, Unani Medicine

Introduction

Kalonji is a famous plant drug used in a number of pathological conditions in Unani Medicine. The drug *Kalonji* consists of seeds of *Nigella sativa* L. of Ranunculaceae family. The drug yielding plant is a small herb, 45-60 cm high. In India, it is mostly cultivated in Punjab, Himachal Pradesh, Bihar and Assam (Anonymous, 2007). In Islam, it is regarded as one of the greatest forms of healing medicine available. Ibn Sina refers to *Kalonji* as the seed that stimulates the body's energy and helps recover from fatigue. In Unani Medicine, the plant is regarded a valuable remedy for a number of diseases. It has been extensively studied for its biological activities and therapeutic potential and has shown to possess wide spectrum of activities, such as diuretic, antihypertensive, antidiabetic, anticancer, immunomodulatory, analgesic, antimicrobial, anthelmintic, analgesic, anti-inflammatory, spasmolytic, bronchodilator, gastroprotective, hepatoprotective, renal protective and antioxidant properties. The seeds of *N. sativa* are widely used in the treatment of various diseases like bronchitis, asthma, diarrhoea, rheumatism and skin disorders. It is also used as liver tonic, digestive, anti-diarrheal, appetite stimulant, emmenagogue, to increase milk production in

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nursing mothers to fight parasitic infections and to support immune system (Goreja, 2003; Khaled, 2009; Abdel-Zaher, 2011; Abel-Salam, 2012).

Vernacular Names

Arabic	: <i>Ḥabbat al Sawdā'</i> , Kabodan, <i>Kamūn Aswad</i> , <i>Shunīz</i>
Persian	: <i>Shunīz</i> , <i>Siyāh Dānā</i>
Urdu	: <i>Kalonjī</i>
Hindi	: <i>Kalonjī</i> , <i>Kālā Zīra</i> , <i>Mangrailā</i>
English	: Small Funnel, Black Cumin
Bengali	: <i>Kālā Zīra</i> , Mangrela Gujrati, Kalaunji Jirum, Kadujeeroo
Kannada	: Karijirige
Kashmiri	: Tukhme Gandana
Marathi	: Kalaunji-jire, Kalerjire
Malyalam	: Karinchirakam
Panjabi	: Kavanji
Tamil	: Karunjarakam, Karunjiragam
Telgu	: Peeajila Kara, Nallajilakara
Sanskrit	: Susavi, Krishna jiraka, Upakuncika, Karvi, Sthula Jiraka
Sindhi	: Kalodi
Unani	: Sino, Sheenon, Kamaazaruus

(Anonymous, 2007)

Taxonomical Classification

Kingdom	: Plantae
Division	: Magnoliophyta
Order	: Ranunculales
Family	: Ranunculaceae
Genus	: <i>Nigella</i>
Species	: <i>sativa</i>

(Abdulrazzaq *et al.*, 2016)

Distribution

Nigella sativa is native to Southern Europe, North Africa and Southwest Asia and cultivated in many countries like South Europe, India, Pakistan, Syria, Turkey, Saudi Arabia and Middle Eastern Mediterranean region.

Botanical Description

Morphology of the Plant: *Nigella sativa* is an annual flowering plant which grows to 20-90 cm tall, with finely divided leaves, the leaf segments narrowly linear to threadlike. The flowers are delicate, and usually colored white, yellow, pink, pale blue or pale purple, with 5-10 petals. The fruit is a large and inflated capsule composed of 3-7 united follicles, each containing numerous seeds (Goreja, 2003; Warriar *et al.*, 2004).

Characteristics of the Seeds and Powder

Macroscopically, seeds are small dicotyledonous, trigonus, angular, rugulose-tubercular, 2-3.5mm×1-2 mm, black externally and white inside, odour slightly aromatic and taste bitter.

Microscopic Characteristics

Transverse section of seed shows single layer of epidermis consisting of elliptical, thick-walled cells covered externally by a papillose cuticle filled with reddish-brown content. Epidermis is followed by 2-3 layers of thick-walled, tangentially elongated parenchymatous cells, followed by a reddish brown pigmented layer composed of thick walled, rectangular elongated cells. Inner to the pigment layer is present a layer composed of thick walled rectangular elongated or nearly columnar, elongated cells. Endosperm consists of moderately thick-walled rectangular to polygonal cells, a few filled with oil globules, embryo embedded in endosperm (Khare, 2007; Warriar *et al.*, 2004).

Powder: Black, oily to touch; under microscope shows groups of parenchyma, endosperm cells and oil globules (Anonymous, 2007).

Parts used: Dried fruit, seed & oil (Khare, 2007; Ghani, 2010).

Temperament

- Hot² and Dry² (Kabiruddin, 2007; Ghani, 2010)
- Hot³ and Dry³ (Ibn Baitar, 1991; Ibn Sina, 1992)

Dose

- 1 to 2 g (Anonymous, 2007)
- 3-5 gm (Rafiquddin, 1985; Khare, 2007)

Side Effects: *Kalonji* leads to diphtheria and unconsciousness when used in a high dose. It has adverse effect on kidney, organs of urinary system, lungs, liver and causes headache (Ghani, 2010).

Correctives

- *Katīra / Bansalochan / Kāsnī / Tukhm-i-Khayār* are used as corrective.
- It may also be corrected by mixing it with vinegar or water of *Kāsnī / Khurfa* (Ghani, 2010)

Compound Formulations

- *Ma'jūn Kalkalānaj*
- *Ma'jūn Fanjnosh*
- *Ma'jūn Kundur* (Anonymous, 2007)

Chemical Constituents

Essential oil, volatile oil, fixed oil, steroid, saponin, melanthin, mucilage, resins, sugars, alkaloids, tannins, linoleic acid, palmitic acid, stearic acid, palmitoleic acid and oleic acid, nigellidine, nigellicine, dithymoquinone, iron, copper, zinc, phosphorus, calcium (Dymock, 2005; Nadkarni, 2005; Anonymous, 2006; Khare, 2007).

Pharmacological Actions

- *Munaffith-i-Balgham* (Expectorant)
- *Muqawwi-i-Mi'da* (Stomachic)
- *Qātil-i-Dīdān-ī-Am'ā'* (Antihelminthic)
- *Mudirr-i-Ḥayḍ* (Emmenagogue)
- *Musakkin-i-Alam* (Analgesic)
- *Muḥallil-i-Waram* (Anti-inflammatory)
- *Mudirr-i-Laban* (Galactagogue)
- *Mudirr-i-Bawl* (Diuretic)
- *Mufattiḥ-i-Sudad* (Deobstruent)
- *Mukhrij-i-Janīn* (Abortifacient)
- *Mulayyin* (Laxative)
- *Muḥallil-i-Riyāḥ* (Carminative)
- *Dāfi'-i-Siman Mufrit* (Anti obesity)
- *Dāfi'-i-Dhayābītus* (Anti diabetic)
- *Dāfi'-i-Ḥummā* (Anti pyretic)
- *Dāfi'-i-Su'āl* (Anti tussive)

- *Mufattit-i-Hāṣāt* (Lithotriptic)
- *Dāfi'-i-Dīq al-Nafas*

(Ibn Baitar, 1991; Ibn Sina, 1992; Hakeem, 2002; Baghdadi, 2005; Anonymous, 2007; Kabiruddin, 2007; Haleem, 2009)

Therapeutic Uses

- *Baraṣ* (Leucoderma / Vitiligo)
- *Qūbā* (Ring worm / Dermatophytosis)
- *Shaqīqa* (Migraine)
- *Dīq al-Nafas* (Bronchial asthma)
- *Ḍu'f al-Mi'da* (Gastric debility)
- *Bahaq* (Pityriasis alba / nigra)
- *Nafkh al-Mi'da* (Flatulence)
- *Yaraqān* (Jaundice)
- *Waja' al-Mafāṣil* (Polyarthritis)
- *Fālij* (Paralysis)
- *Laqwa* (Facial palsy)
- *Dhayābītus* (Diabetes)
- *Saraṭān* (Cancer)
- *Ḥaṣāt al-Kulya* (Nephrolithiasis)
- *Siman Mufriṭ* (Obesity)
- *Iḥtibās al-Ṭamth* (Amenorrhea)
- *Dīdān al-Am'ā'* (Worm infestation)
- *Nisyān* (Amnesia)
- *Ḍu'f-i-Bāh*
- *Ḥummā* (Fever)
- *Ḍu'f al-Ishtihā'* (Anorexia)
- *Bawāsīr* (Hemorrhoids)

(Ibn Sina, 1992; Hakeem, 2002; Duke, 2003; Anonymous, 2006; Anonymous, 2007; Kabiruddin, 2007; Ghani, 2010; Perveen *et al.*, 2013)

Pharmacological Studies

- Abortifacient (Paarakh, 2010; Ansari *et al.*, 2016; Hussain & Hussain, 2016)
- Antibacterial Activity (Ahmad *et al.*, 2013; Hussain & Hussain, 2016)

- Antidiabetic Activity (Najmi *et al.*, 2008; Huseini *et al.*, 2010; Ansari *et al.*, 2016)
- Antispasmodic Activity (Huseini *et al.*, 2010; Hussain & Hussain, 2016)
- Antitumour activity (Hussain & Hussain, 2016)
- Anticarcinogenic and mutagenic Activity (Huseini *et al.*, 2010; Ansari *et al.*, 2016; Hussain & Hussain, 2016)
- Antihypertensive (Ansari *et al.*, 2016)
- Anticonvulsant (Ahmad *et al.*, 2013; Hussain & Hussain, 2016)
- Anxiolytic (Paarakh, 2010)
- Hepatoprotective Activity (Hussain & Hussain, 2016)
- Nephroprotective (Hussain & Hussain, 2016)
- Antihyperlipidemic Activity (Ali & Blunden, 2003; Najmi *et al.*, 2008; Haseena *et al.*, 2015)
- Antioxidant Activity (Huseini *et al.*, 2010; Ansari *et al.*, 2016)
- Analgesic Activity (Ali & Blunden, 2003)
- Antifertility (Yaheya & Ismail, 2009)
- Anti-inflammatory (Ansari *et al.*, 2016)
- Anti-microbial (Huseini *et al.*, 2010)
- Antifungal Activity (Huseini *et al.*, 2010)
- Bronchodilator (Huseini *et al.*, 2010)
- Contraceptive (Ahmad *et al.*, 2013)
- Cardioprotective Activity (Hussain & Hussain, 2016)
- Diuretic Activity (Hussain & Hussain, 2016)
- Gastroprotective (Hussain & Hussain, 2016)
- Neuroprotective Activity (Hussain & Hussain, 2016)

Conclusion

Nigella sativa L. (*Kalonji*) has been in use since time immemorial to treat wide range of indications. Experimental studies have demonstrated its abortifacient, analgesic, anti-inflammatory, anthelmintic, anti-asthmatic, anticancer, anticonvulsant, antiepileptic, antifungal, antihypertensive, antimicrobial, antinociceptive, antioxidant, antioxytotic, anti-rheumatoid arthritis, antispasmodic, anxiolytic, bronchodilator, CNS depressant,

contraceptive, diuretic, galactagogue, gastroprotective, hepatoprotective, human neutrophil elastase inhibitor, hypoglycemic, hypolipidemic, immunomodulatory, nephroprotective, wound healing and diabetic embryopathy protective effects. The scientific studies have proved most of the claims of traditional medicine. However, further detailed clinical research appears worthwhile to explore the full therapeutic potential of this plant in order to establish it as a standard drug.

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सारांश

यूनानी चिकित्सा के संदर्भ में कलौंजी (नाइजेला सटाइवा) पर समीक्षा

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नाइजेला सटाइवा (कलौंजी) रैनमकुलासी जाति से संबंध रखने वाला औषधीय पौधा है जिसका उपयोग दुनिया भर में व्यापक रूप से किया जाता है। यह यूनानी चिकित्सा में बहुत लोकप्रिय है। एन. सटाइवा बीजों का उपयोग व्यापक रूप से विभिन्न रोगों के उपचार में किया जाता है। इस्लामी साहित्य में इसे उपचार औषधि के सबसे महत्वपूर्ण रूपों में से एक माना जाता है। तिब्ब नबवी (पैगम्बरी चिकित्सा) में बराबर इसका उपयोग करने के लिए कहा गया है। इसका उपयोग व्यापक रूप से एंटीहाइपरटेन्सिव, यकृत स्वास्थ्य वर्धक, मूत्रवर्धक, पाचक, अतिसाररोधी, भूख उत्तेजक, एनाल्जेसिक, रोगाणुरोधी और त्वचा विकारों में किया जाता है। एन. सटाइवा पर विभिन्न शोधकर्त्ताओं द्वारा विस्तृत अध्ययन किये गए हैं और इसके औषधीय कार्यों की एक विस्तृत श्रृंखला का पता लगाया गया है जिनमें मधुमेहरोधी, कैंसररोधी, इम्युनोमोड्यूलेटर, एनाल्जेसिक, सूक्ष्मजीवीरोधी, एंटी-इन्फ्लामेटरी, स्पैस्मोलीटिक, श्वासनलिकासारकयंत्र, हेपाटो-प्रोटेक्टिव, वृक्क रक्षक, गैस्ट्रो रक्षक, ऑक्सीकरणरोधी गुण इत्यादि शामिल हैं। यह पाया गया कि इस पौधे के अधिकांश चिकित्सीय गुण थाइमोकिनोन, जोकि आवश्यक तेल का एक प्रमुख जैव सक्रिय घटक है, की उपस्थिति के कारण है। वर्तमान अध्ययन इस पौधे के बीजों की फॉर्मोकोग्नोस्टिक विशेषताओं, रासायनिक संरचना और औषधीय गतिविधियों के वैज्ञानिक अनुसंधानों पर साहित्य का एक विस्तृत सर्वेक्षण प्रदान करने का एक प्रयास है।

शब्दकुंजी: कलौंजी, नाइजेला सटाइवा, यूनानी चिकित्सा



Dawā'-i-Hiltīt: As an Antipyretic Drug of Unani Medicine

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Abstract

Elevated core body temperature above the normal range (>38 °C) is considered as fever. According to Unani Medicine, *Ḥummā* (fever) is a transient state that initiates at first in the heart and spreads along with *Rūḥ* and *Dam* (blood) of vessels across the body leading to the malfunctioning of normal body function. In this condition, body temperature is higher than that of exercise and anger. It is caused by *Ḥarārat Gharība Ajnabiyya*. There are a number of single drugs and compound formulations which are used in fever in Unani Medicine. *Dawā'-i-Hiltīt* is described in various Unani classical books. It is basically indicated in *Ḥummā al-Rib'*. *Ḥummā al-Rib'* is a type of *Ḥummā 'Ufūnī*. There are four ingredients in this formulation: *Hiltīt* (Gum of *Ferula foetida* Regel.), *Mur Makkī* (Gum of *Commiphora myrrha* Nees), *Filfil Siyāh* (Fruits of *Piper nigrum* L.) and *Sudāb* (Leaves of *Ruta graveolens* L.). In the compound formulation *Dawā'-i-Hiltīt*, all the four ingredients are *Dāfi'-i-Ḥummā* and *Dāfi'-i-'Ufūnat*.

Keywords: *Dawā'-i-Hiltīt*, *Ḥarārat Gharība*, *Ḥummā*, *'Ufūnat*, Unani Medicine

Introduction

Unani Medicine is based on the teachings of Hippocrates (*Buqrat*), Rhazes (Mohammad ibn Zakariya Razi), Avicenna (Ibn Sina) and Galen (Jalinus). The system provides cure as well preventive measures. The concept of health and disease is based on *Akhlāt* (humors) and *Mizāj* (temperament) (Majusi, 2010; Ibn Rushd, 2017). Any disturbance in *Akhlāt* and *Mizāj* causes disease. For the maintenance of health, they should remain in normal state both in consistency and composition (qualitative and quantitative measures). Disturbance at any level, such as in formation of *Akhlāt*, in *Ta'dīl-i-Akhlāt* by *Arwāḥ* or any *Ta'diya* (infection) can disturb or change the quality of *Akhlāt* leading to diseases.

Akhlāt (humours) are related to some *Kayfiyāt* – blood (*Khilt Dam*): hot and wet; phlegm (*Khilt Balgham*): cold and wet; yellow bile (*Khilt Şafrā'*): hot and dry; and black bile (*Khilt Sawdā'*): cold and dry (Nafees, 1954). Any disturbance of their *Mizāj* also becomes a cause of disease. As the disease is referred in terms of disturbance in *Akhlāt*, the treatment is also based on normalising *Akhlāt*. *Ḥummā 'Ufūnī* is one of the diseases which are related to humours. According to Ibn Sina, *Ḥummā* (fever) is a transient state that initiates at first in the heart and spreads along with *Rūḥ* and *Dam* (blood) of vessels all over the body leading to the malfunctioning of normal body function. In this condition, body temperature is higher than that of exercise and anger. It is caused by *Ḥarārat Gharība Ajnabiyya* (Majusi, 2010; Kabiruddin, 2009). According to Jalinus, main cause of fever is

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Waram (inflammation) or '*Ufūnat* (infection). According to Unani Medicine, *Ḥummā 'Ufūniyya* is caused by derangement in the quality of humour. '*Ufūnat* in humour is caused by several factors – disturbance in metabolism of food, intake of infectious food material, polluted water and air and any obstruction (Majusi, 2010). In other words, fever is a diseased condition caused by *Sū'-i-Mizāj*. *Sū'-i-Mizāj* is produced when external heat affects the normal physiological condition of heart. Heart is the main source of *Ḥarārat Gharīziyya*, it provides energy to whole body by blood circulation. In the same manner, *Ḥarārat Gharība* also produces effect on whole body by heart. It is the cause of fever (Razi, 2005).

According to the recent theories, fever is described as a state in which core temperature increases. It is defensive mechanism of host cells in response to the invasion of micro-organism or innate matter which is recognised by host as pathogenic or foreign body (Mackowiak, 1998).

All the metabolic process in human depends on temperature. Sweating, shivering and vasoregulation regulate the temperature at the peripheral level. At the central level, temperature is regulated by hypothalamus. Body temperature is increased by some exogenous and endogenous stimuli. These stimuli increase $TNF\alpha$, interleukin 1 & 6, and cytokines synthesis. All these act on pre optic region of hypothalamus and activate phospholipase A. This phospholipase A liberates plasma membrane arachidonic acid as substrate for cyclo oxygenase pathway. All these processes activate/synthesize prostaglandin E2 which acts on thermo sensitive neuron in the thermoregulatory centre and increases normal body temperature (Davidson, 2006).

There are a number of single drugs and compound formulations in Unani Medicine which are used in fever. Some reduce the excessive body temperature by the mechanism of sweating, diuresis and some act on *Akhlāt Radī'a* and *Mādda Ufūniyya*. *Dawā'-i-Hiltīt* is one of the formulations described in Unani Medicine.

Dawā'-i-Hiltīt

It has been described in various Unani classical books. It has been indicated basically in *Ḥummā al-Rib'*. Other indications include antidote in snake bite and scorpion bite. Its dosage form as described in various classical books varies. As in some books, its dosage form is mentioned as *Ma'jūn* and in some other as *Ḥabb* (pill) (Shareef, 2006; Arzani, 2009; Kabiruddin, 2006; Qumri, 2008).

Ḥummā al-Rib' is a type of *Ḥummā 'Ufūniyya*. *Ḥummā 'Ufūniyya* possesses some particular conditions such as fever with chills, periodic in nature, along with other related ailments like headache and dyspepsia. Sweating is not present in the starting of fever. Treatment of *Ḥummā 'Ufūniyya* is based on general treatment guidelines of fever along with the treatment of main causative factor (Razi, 2005). *Ḥummā 'Ufūniyya* treatment guidelines are based on three points

– Treatment of *Sū' Mizāj*, *Istifrāgh-i-Mādda* (evacuation of morbid matter) and removal of the factors responsible for '*Ufūnat* (Ibn Rushd, 2017). *Hummā al-Rib'* has two days between two episodes; its longevity depends upon the consistency of *Khilṭ*. Any leniency in its treatment may cause prolongation. If the duration of this fever increases, it affects mainly liver and spleen (Baghdadi, 2007). In the treatment of *Hummā al-Rib'*, the drugs mainly used are *Mufattiḥ*, *Muqatti'* and *Mulattiṭif* in nature. It is a favourable condition if these *Mufattiḥ* and *Mulattiṭif* drugs are effective in splenomegaly, because '*Ufūnat-i-Sawdā'* mainly occurs in spleen and causes fever (Ibn Rushd, 2017).

Ingredients of *Dawā'-i-Hiltīt* and their Reported Activities

There are four ingredients in this formulation: *Hiltīt* (Gum of *Ferula foetida* Regel.), *Mur Makkī* (Gum of *Commiphora myrrha* Nees), *Filfil Sīyāh* (Fruits of *Piper nigrum* L.) and *Sudāb* (Leaves of *Ruta graveolens* L.) (Shareef, 2006; Arzani, 2009; Kabiruddin, 2006; Qumri, 2008). The ingredients used in the preparation of *Dawā'-i-Hiltīt* have peculiar activities. These ingredients are used not only in normalising the *Akhlāt* but also to maintain body temperature by different mechanisms.

Mizāj of *Dawā'-i-Hiltīt*

Compound formulations are prepared with an aim to cure a specific disease, therefore major literature of *Murakkabāt* does not mention their *Mizāj*. Several authors of Unani Medicine like Al-Kindi, Ibn Rushd, Sharif Khan and Najmul Ghani have stated that the compound preparations inherit *Mizāj* of their ingredients. They developed a rule to assess *Mizāj* of a *Murakkab* drug. Following the same, *Mizāj* of *Dawā'-i-Hiltīt* is as follows (Table 1):

$$\begin{aligned} \text{Darjāt and Kayfiyāt Fā'ila} &= \{\sum DH \times dH - \sum DB \times dB\} / \sum DH - \sum DB \\ &= 39/12=3.25 \end{aligned}$$

$$\begin{aligned} \text{Darjāt and Kayfiyāt Munfa'ila} &= \{\sum DR \times dR - \sum DY \times Dy\} / \sum DR - \sum DY \\ &= 36/12=3 \end{aligned}$$

Therefore, *Mizāj* of *Dawā'-i-Hiltīt* is *Hārr Yābis* of degree 3 and can be administered 3 to 5 grams. Actual dose quoted from the literature is 3½-6 masha (3½-6g) (Ibn Sina, 2010; Jurjani, 2010).

Reported Activities of Ingredients of *Dawā'-i-Hiltīt*

Sudāb is effective in fever with chills and rigor. Along with this, it is used in poisoning and inflammatory conditions. Oil of *Sudāb* is effective in fever and aches (Ghani, 2011; Ibn Baitar, 1999; Khan, 2014; Baghdadi, 2005). Several recent

Table 1: Mizāj Assessment of *Dawā'-i-Hiltīt*

S. No.	Ingredients	<i>Darjāt-i-Mizāj</i>	Dosage as Mufrad Drug <i>Hārr</i>	Dosage as Mufrad Drug <i>Yābis</i>	Product of <i>Hārr</i> Drugs and Dosage	Product of <i>Yābis</i> Drugs and Dosage
1	<i>Hiltīt</i> (Gum of <i>Ferula foetida</i> Regel)	Hot 4° and Dry 2°	3g	3g	12g	6g
2	<i>Mur Makkī</i> (Gum of <i>Commiphora myrrha</i> Nees)	Hot 3 ° and Dry 4°	3g	3g	9g	12g
3	<i>Filfil Siyāh</i> (Fruit of <i>Piper nigrum</i> L)	Hot 3° and Dry 3°	2g	2g	6g	6g
4	<i>Sudāb</i> (Leaves of <i>Ruta graveolens</i> L)	Hot 3° and Dry 3°	4g	4g	12g	12g
Calculations			ΣDH=12g ΣDB=nil	ΣDY=12g ΣDR=nil	ΣDH ×dH=39 ΣDB ×dB=nil	ΣDY ×dY=36 ΣDR ×dR=nil

studies reveal that *Ruta graveolens* has antimicrobial, antioxidant and anticancer activities (Cunha *et al.*, 2015). *Piper nigrum* has activity against poisoning of scorpion. Along with *Rawghanīyāt*, it is effective in fever. It is effective in periodic fever (Ghani, 2011; Ibn Baitar, 1999; Khan, 2014; Baghdadi, 2005; Khan, 2018). Its activity as antimicrobial is proved (Rani *et al.*, 2013). Piperine is the active constituent in *Piper nigrum*. It was studied in a previous study by introducing 20-30mg/kg piperine in mice reduced fever wherein Indomethacin 10mg/kg was used as standard (Sabina *et al.*, 2013). Suspension of *Piper nigrum* and *Nyctanthus arboristis* was effective clinically in the patients suffering from malaria. It is effective as by improving the feeling of chills, subsided nausea, vomiting and smear becomes negative at the end of the treatment in three weeks (Ghiwarei *et al.*, 2007).

Asafoetida is mentioned as anti-flatulent drug. Its action as an antipyretic is also described in classical books. It is specifically used in *Ḥummā al-Rib'* (Ghani, 2011; Khan, 2014; Ibn Baitar, 2000; Khan, 2013). It is reported for its anti-nociceptive, anti-inflammatory and anti-microbial activity (Bagheri *et al.*, 2014; Upadhyay *et al.*, 2017; Sooud *et al.*, 2014). In Unani Medicine, diuretics are used

in fever according to *Usūl-i-ʿIlāj* of *Ḥummā*. Asafoetida has diuretic activity; it was given 25-50mg/kg intraperitoneally and significant results obtained (Bagheri *et al.*, 2016). *Commiphora myrrha* has anti-infective (*Dāfi'-i-Ta'affun*) and antidote property. It is effective in scorpion sting (Ghani, 2011; Khan, 2014; Khan, 2018; Ibn Baitar, 2004). In pyrexia, it is used with *Filfil Siyāh*. There are several scientific studies both *in-vitro* and *in-vivo* that validate its antibacterial, antifungal, anti-inflammatory, anti-oxidant and anti-malarial activities. These activities of myrrh are due to the presence of secondary metabolites such as Furanodene 6-one and Methoxy Furanoguaia 9-ene-8-one (Su *et al.*, 2011; Germane *et al.*, 2017; Sabri *et al.*, 2014; Almekhalifi *et al.*, 2014).

Scope of *Dawā'-i-Hiltīt* in *Usūl-i-ʿIlāj* of *Ḥummā* (Pyrexia)

In *Ḥummīyāt 'Ufūniya*, treatment should be started with the drugs having property as *Dāfi'-i-'Ufūnat* and the drugs which have both antipyretic and *Dāfi'-i-'Ufūnat* are considered as the drug of first choice (Razi, 2005). In the compound formulation *Dawā'-i-Hiltīt*, all the four ingredients are *Dāfi'-i-Ḥummā* and *Dāfi'-i-'Ufūnat*. *Dawā'-i-Hiltīt* can be used as antipyretic. The medicinal value of each ingredient as antimicrobial is proved, but preclinical and clinical study of this formulation is a necessary part.

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सारांश

दवा-ए-हिल्लीत : यूनानी चिकित्सा की एक ज्वरनाशक औषधि

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सामान्य सीमा ($>38^{\circ}\text{C}$) से ऊपर उच्च कोर शरीर का तापमान ज्वर माना जाता है। यूनानी चिकित्सा के अनुसार हुम्मा (ज्वर) एक क्षणिक अवस्था है जो सबसे पहले हृदय से शुरू होती है और रूह तथा दम (रक्त) के साथ पूरे शरीर में फैल जाती है जिससे सामान्य शारीरिक क्रिया में खराबी आती है। यह व्यायाम और क्रोध की तुलना में और अधिक होता है। यह हरारत गरीबा अजनबिया के कारण होता है। कई एकल औषधियाँ और यौगिक मिश्रण हैं जिनका यूनानी चिकित्सा में ज्वर के लिए उपयोग किया जाता है। विभिन्न क्लासिकल पुस्तकों में दवा-ए-हिल्लीत के बारे में वर्णन किया गया है। इसे हुम्मा अल-रिब में बताया गया है। हुम्मा अल-रिब हुम्मा उफूनी का एक प्रकार है। इस मिश्रण में चार घटक हैं – हिल्लीत (फेरुला फोइटीडा रीगल. का गोंद), मुर मक्की (कॉफीफोरा मीरा नीस का गोंद), फिल्फिल सियाह (पाइपर निगरम एल. का फल) और सुदाब (रूटा ग्रेवीओलेन्स एल. की पत्तियाँ)। यौगिक मिश्रण दवा-ए-हिल्लीत में सभी चार घटक दाफे-ए-हुम्मा और दाफे-ए-उफूनीत हैं।

शब्दकुंजी: दवा-ए-हिल्लीत, हरारत गरीबा, हुम्मा, उफूनीत, यूनानी चिकित्सा



Efficacy of a Unani Regimen in the Treatment of *Yaraqān* (Jaundice): A Case Report

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Abstract

25-year-old male presented with itching, yellowish discolouration of urine, nausea, vomiting, disturbed sleep for one week and pain in abdomen for last two days. On physical examination, there was remarkable scleral icterus and mild tenderness on palpation in the right upper quadrant of the abdomen. The liver was palpable and enlarged (2 fingers), margin was smooth and regular. The investigations revealed marked hyperbilirubinemia, raised serum transaminases and serum HbsAg was negative. The patient was diagnosed as suffering from *Yaraqān* (jaundice) and prescribed Unani regimen comprising 'Araq-i-Mako (distillate of *Solanum nigrum*) and 'Araq-i-Kāsnī (distillate of *Cichorium intybus*) 60 mL each twice a day and *Ma'jūn Dabīd al-Ward* 5 gm twice daily for 21 days. After 21 days, the patient showed good response to the given Unani regimen. Clinically, his condition improved and the raised total serum bilirubin, SGOT, SGPT profile were within normal range on the last day of the treatment. The main aim of this case report is to highlight the effectiveness of Unani regimen in the treatment of jaundice. This case report may create awareness about the effectiveness of Unani Medicine among academia, researchers, scientists and common people.

Keywords: 'Araq-i-Mako, 'Araq-i-Kāsnī, *Ma'jūn Dabīd al-Ward*, *Yaraqān*, Unani Medicine

Introduction

The word 'jaundice' is derived from an old French word 'jalnice' followed by 'jaunice' which means 'yellowness' (Tewari *et al.*, 2017). In Unani Medicine, *Yaraqān* (jaundice) is defined as visible yellow or black discolouration of conjunctiva and skin due to diffusion of yellow or black bile in blood towards skin with or without infection (Ansari *et al.*, 2015; Arzani, YNM; Kabiruddin, 2003; Ibn Sina, 1992; Baghdadi, 2004). It is of two types; *Yaraqān Aşfar* (yellow discoloration) and *Yaraqān Aswad* (blackish discoloration) (Kabiruddin, YNM). Jaundice can also be classified into three types; viz. Pre-hepatic Jaundice, Hepatic Jaundice, Post-hepatic Jaundice according to the site of pathology (Briggs *et al.*, 2007). Its main causes are *Sū'i-Mizāj Hārr* (altered hot temperament) (Anonymous, 1992), toxicity due to insect bites (Tabari, 1997), *Sudda-i-Majrā-i-Marāra* (biliary duct obstruction), *Takassur al-Dam* (haemolysis), (Anonymous, 2016a), acute hepatitis, abnormal function of gall bladder and liver, consumption of poisonous food, *Buḥrān* (crisis and lysis), *Harārat-i-Kabid* and *Marāra* (altered temperament of liver and gall bladder), (Ibn Sina, 1992) and weakness of gall bladder (Tabari, 1997). Clinical features of jaundice include abdominal pain, anorexia, general

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weakness, pruritus, soft hepatic enlargement, hard hepatic enlargement, acute constipation, severe nausea, vomiting, diarrhoea, anaemia, oedema, weight-loss, excessive thirst and severe pain in hepatic region (Kabiruddin, YNM; Ibn Sina, 1992; Tabari, 1997; Jurjani, 2010). The colour of urine varies from light to dark yellow and froth may be present on the surface of urine. The faeces become dry (Kabiruddin, YNM; Anonymous, 1992). In the treatment of non-obstructive hepatic jaundice, anti-inflammatory, diuretics and purgatives of *Khilt-i-Şafrā'* (yellow bile) are used as mentioned in Unani classical literature (Anonymous, 1992). In Unani Medicine, several steps for the treatment of jaundice are described, viz. evacuation of causative matter through *Ishāl* (purgation), *Qay'* (emesis), *Idrār* (diuretic), correction of hepatic temperament and resolution of hepatic inflammation (Ibn Sina, 1992; Anonymous, 2016a). Many single and compound Unani drugs are recommended for the treatment of jaundice, viz. '*Uşāra-i-Afsantīn* (extract of *Artemesia absinthium* L.), '*Aarq-i-Kāsnī*, *Sharbat-i-Afsantīn*, *Ma'jūn Dabīd al-Ward*, *Sharbat-i-Nilofer*, *Sharbat-i-Revand* and decoction of *Masūr* (*Lens esculenta* Moench) (Anonymous, 2016a). *Yaraqān* (jaundice) is diagnosed on the basis of raised total serum bilirubin level, i.e. (>03 mg/dL) (Munjal, 2015; Longo, *et al.*, 2012; Kundu, 2010). Persistent jaundice leads to complications like kernicterus, coma or even death (Mathew, 2015).

Case Information

A 25 years old male presented with itching, yellowish discolouration of urine, nausea, vomiting, disturbed sleep, mild grade fever (off and on) for one week and pain in abdomen for last two days at GOPD, Central Research Institute of Unani Medicine (CRIUM), Hyderabad. The patient was admitted with these complaints in the IPD of CRIUM, Hyderabad on 1st April 2019. The OPD registration no. of the patient was 19921 and IP No. was 02/GOPD/19-20. The patient was an unmarried student belonging to lower middle class family. According to the statement of the patient, he was completely healthy seven days ago. He felt nausea and vomiting and the same complaint continued till his visit to the GOPD of CRIUM, Hyderabad. The patient suffered from typhoid and jaundice eight years ago. He has been smoker for last two years. In his family, mother was diabetic. On physical examination, there were remarkable scleral icterus and mild tenderness on palpation in the right upper quadrant. There was no guarding or rigidity, but liver was palpable and enlarged, its margin was regular and smooth. His temperament was bilious. The blood pressure, temperature, pulse rate and respiratory rate of the patient were 120/80mmHg, 98.6°F, 72bpm, 18/minute respectively at the time of admission. On examination of the patient, all other systemic organs were found normal. Written informed consent was taken from the patient before starting of the treatment.

Investigations

At the time of admission, the patient was investigated for liver function test (Total S. bilirubin, SGOT, SGPT, ALP), ESR, complete urine examination, complete blood picture and USG whole abdomen. The lab investigations revealed hyperbilirubinemia and raised serum transaminases; total bilirubin was 11.4 mg/dl; serum alanine amino transaminase (ALT)860 IU/L, serum aspartate aminotransferase (AST)1550 IU/L, serum alkaline phosphatase (ALP)208IU/L. The Australia antigen (HbsAg) was negative in serum. The abdominal ultrasound showed mild hepatomegaly. The parameters in complete blood picture of the report are listed in Table 1. Physical, chemical and microscopic examinations of urine showed normal report except dark yellow colour.

Table 1: Effect of Unani Regimen on Complete Blood Picture

Parameters	Hb (gm%)	RBC (million/ Cumm)	WBC (Cells/ mm3)	P	N %	L %	B %	M %	E %
Baseline	14.5	5.3	3800	1.4	38	56	04	02	00
After Treatment	14.8	5.4	37900	1.5	40	55	03	02	00

P=Platelets (Cells/mm3); N=Neutrophils; L=Lymphocytes; E=Eosinophil; M=Monocytes; B=Basophils

Differential Diagnosis

Hepatitis B was differentiated in this case, as Australia antigen was negative in serum.

Drug Dosage and Mode of Administration

The following Unani pharmacopoeial formulations were given in combination as a regimen.

1. 'Araq-i-Mako (Distillate of *Solanum nigrum*) 60 ml
2. 'Araq-i-Kāsnī (Distillate of *Cichorium intybus*) 60 ml
3. Ma'jūn Dabīd al-Ward 5 gm

This regimen was advised twice a day in the given dose orally after meals.

Duration of Treatment

After diagnosis, the patient was given the regimen for 21 days. The dietary restrictions included avoidance of fatty foods.

Observations, Outcome and Follow-up

The patient was followed up every day for 21 days. On day 4, blood sample of the patient for liver function test was taken. The lab investigations revealed reduction in total serum bilirubin to 8.0 mg/dL from 11.4 mg/dL and serum aspartate aminotransferase (AST) to 325 IU/L from 1550 IU/L. The same treatment continued with restriction of diet for further eight days. On day 12, blood sample for liver function test (Total serum bilirubin, SGOT, SGPT and ALP) was taken. The lab investigations revealed further reduction in hyperbilirubinemia and high transaminases level; total bilirubin was reduced to 2.5 mg/dl; serum alanine amino transaminase (ALT) reduced to 223 IU/L and serum aspartate aminotransferase (AST) 78 IU/L. On day 21, blood sample for the liver function test revealed all the parameters were within normal range, i.e. total bilirubin was 1.8 mg/dl, (indirect bilirubin 1.4mg/dl and direct bilirubin 0.4), serum alanine amino transaminase (ALT) 53 IU/L, serum aspartate aminotransferase (AST) 38 IU/L and serum alkaline phosphatase 208IU/L (Table 2). After completion of the treatment, an abdominal ultrasound was done that yielded a normal report. The patient improved symptomatically, too. The formulations used in the therapy were prepared by Indian Medicines Pharmaceutical Corporation Limited (IMPCL).

Table 2: Effect of Unani Regimen on Liver Function Parameters

Parameters	Baseline	1st Follow-up	2nd Follow-up	3rd Follow-up
Total Serum Bilirubin (mg/dL)	11.4	8.0	2.5	1.8
AST (SGPT) (IU/L)	1550	325	78	38
ALT(SGOT) (IU/L)	860	950	223	53
ALP(IU/L)	208	244	146	208

Probable Mechanism of Action of Drugs

The actions of 'Araq-i-Kāsnī (distillate of *Cichorium intybus*) are refrigerant, demulcent, anti-inflammatory, deobstruent and diuretic (Azmi, 2010; Anonymous, 2009), appetizer, stomachic, cholagogue and cardio-tonic (Mathur and Mathur, 2016). It is also indicated in obstructive jaundice (Mathur and Mathur, 2016), chronic fever, hepatitis (Anonymous, 2009), liver disorders, vomiting, loose motion, fever and pleurisy (Bhalla *et al.*, YNM) and reduces *Ḥarārat of Khūn* (intensity of blood) and *Khilt-i-Ṣafrā* (yellow bile) in blood (Azmi, 2010). The actions of 'Araq-i-Mako (distillate of *Solanum nigrum*) are mentioned as antiphlogistic, anti-inflammatory, deobstruent, diuretic and analgesic (Azmi, 2010; Anonymous, 1987). In a study, the effect of *Cichorium intybus* was much pronounced as compared to the effect of *Solanum nigrum*. This study suggested that the hepatoprotective effect of this crude plant extract

may be due to its ability to suppress the oxidative degradation of DNA in the tissue debris (Sultana *et al.*, 1995). Another study conducted by Subash *et al.* suggested that the distillate of *Solanum nigrum* and *Cichorium intybus* showed significant hepatoprotective activity in albino rats with CCl₄ liver injury. *Cichorium intybus* showed significantly better hepatoprotective response than *Solanum nigrum* (Subash *et al.*, 2011). The action of *Ma'jūn Dabīd al-Ward* is diuretic, anti-inflammatory and it is indicated in diseases like hepatitis, gastritis, uteritis, weakness of liver, weakness of stomach and hepatotonic (Anonymous, 2016; Arzani, 2009). The ingredients of *Ma'jūn Dabīd al-Ward* (Anonymous, 2016) are listed in Table 3. In this regimen, 'Araq-i-Mako (distillate of *Solanum nigrum*), 'Araq-i-Kāsnī (distillate of *Cichorium intybus*) and *Ma'jūn Dabīd al-Ward* might have acted synergistically to reduce inflammation of the liver and thereby causing reduction in raised serum bilirubin level.

Table 3: Composition of *Ma'jūn Dabīd al-Ward*

Unani Name	Botanical / English Name	Part Used	Weight (gram)
Idhkhar Makkī	<i>Cymbopogon jwarancusa</i> (Jones) Schult	Whole plant	20 g
Agar ('ūd)	<i>Aquilaria agallocha</i> Roxb	Heart wood	20 g
Balchar	<i>Nardostachys jatamansi</i> DC	Rhizome	20 g
Banslochan	<i>Bambusa bambos</i> (L.) Voss.	Concretion	20 g
Tukhm-i-Kāsnī	<i>Cichorium intybus</i> L.	Fruit	20g
Tukhm-i-Kasūs	<i>Cuscuta reflexa</i> Roxb.	Seed	20g
Tukhm-i-Karāfs	<i>Apium graveolens</i> L.	Seed	20g
Tāj Qalamī	<i>Cinnamomum cassia</i> Blume	Stem bark	20g
Dārchīnī	<i>Cinnamomum zeylanicum</i> Blume	Stem bark	20g
Zarawand Mudahraj	<i>Aristolochia rotunda</i> L	Tuber	20g
Qusṭ Shīrīn	<i>Saussurea lappa</i> C.B. Clarke	Root	20g
Gul-i-Surkh	<i>Rosa damascene</i> Mill.	Petals	300g
Gul-i-Ghāfis	<i>Gentiana olivieri</i> Griseb.	Flower	20g
Lūk Maghsūl	Lac, Appendix	Resin	20g
Majīth	<i>Rubia cordifolia</i> L.	Stem	20g
Qiwām-i-Shakar	Sugar syrup	Crystal	2.4 Kilogram
Za'frān	<i>Crocus sativus</i> L.	Style & Stigma	2.9 g
'Araq-i-Ga'ozabān	<i>Borago officinalis</i> L.	Distillate	30 millilitre
Maṣṭagī	<i>Pistacia lentiscus</i> L.	Resin	20 g
Ghī	Rawghan Zard		5g

(Anonymous, 2016b)

Discussion

It was observed that Unani regimen comprising 'Araq-i-Mako (distillate of *Solanum nigrum*), 'Araq-i-Kāsnī (distillate of *Cichorium intybus*) and Ma'jūn Dabīd al-Ward is hepatoprotective and anti-inflammatory reducing the symptoms of jaundice. The objective parameters such as total serum bilirubin, AST (SGPT), ALT (SGOP) and ALP were normalized. The patient was found completely healthy after 21 days of the treatment. The constituents of this Unani regimen are recommended pharmacopoeial formulations for *Waram al-Kabid* (hepatitis) and *Yaraqān* (jaundice). They contain many diuretic, anti-inflammatory, hepatoprotective and bioactive compounds which might be responsible for the therapeutic effect in this case.

Conclusion

This Unani regimen comprising 'Araq-i-Mako (distillate of *Solanum nigrum*), 'Araq-i-Kāsnī (distillate of *Cichorium intybus*) and Ma'jūn Dabīd al-Ward is widely used for the treatment of hepatobiliary disorders and *Yaraqān* (jaundice) in Unani Medicine. These are pharmacopoeial formulations and generally used in combination as a regimen. In this case, it was found that this regimen reduced the highly raised serum bilirubin and serum transaminases and the patient improved symptomatically. This case report is a documented evidence which reveals that this regimen is effective in the treatment of jaundice. This is an era of evidence based medicine and this evidence may highlight the potential of Unani Medicine in general and this regimen in particular. More and more evidences are required to be generated in documented form in clinical practice which may help in mainstreaming of this system of medicine.

Conflict of Interest: Authors have no conflict of interest in publication of this research paper.

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सारांश

यरक़ान (पीलिया) के उपचार में यूनानी चिकित्सा की प्रभावकारिता: एक केस रिपोर्ट

नदीम अहमद, मोहम्मद नवाब, एम. हुसैन काज़मी

एक 25 वर्षीय पुरुष उपचार के लिए लिया गया जिसे खुजली, मूत्र में पीलापन, मतली, उल्टी, एक सप्ताह से नींद में गड़बड़ी और पिछले दो दिन से पेट में दर्द की समस्या थी। शारीरिक परीक्षण में पेट के दाहिने ऊपरी भाग को छुने पर कोमलता और उल्लेखनीय स्केरल आइकटरस पाई गई। लीवर फूला और बड़ा (2 उंगल तक) था, मार्जिन चिकना और ठीक था। जांच से पता चला कि हाइपरबिलीरुबिनेमिया उल्लेखनीय, सीरम ट्रांसएमिनेस बढ़ा हुआ और सीरम एचबीएसएजी नकारात्मक है। रोगी को यरक़ान (पीलिया) से पीड़ित पाया गया और उसे यूनानी चिकित्सा अर्थात् अर्क-ए-मको (*सोलेनम नाइग्रम का सत्त*) और अर्क-ए-कासनी (*सिचोरियम इंटीबस* का सत्त) 60 मि.ली. की मात्रा में और माजून दबीद उल-वर्द 5 ग्रा. की मात्रा में 21 दिनों तक दिन में दो बार दिया। 21 दिनों के बाद रोगी ने यूनानी चिकित्सा की अच्छी प्रतिक्रिया दिखाई। नैदानिक रूप से रोगी की स्थिति में सुधार हुआ और उपचार के अंतिम दिन कुल सीरम बिलरुबिन, एसजीओटी, एसजीपीटी प्रोफाइल सामान्य सीमा के भीतर पाए गए। इस केस रिपोर्ट का मुख्य उद्देश्य पीलिया के उपचार में यूनानी चिकित्सा की प्रभावकारिता को उजागर करना है। यह केस रिपोर्ट शिक्षाविदों, शोधकर्त्ताओं, वैज्ञानिकों और आम लोगों के बीच यूनानी चिकित्सा के प्रभाव के बारे में जागरूकता पैदा कर सकती है।

शब्दकुंजी: अर्क-ए-मको, अर्क-ए-कासनी, माजून दबीद उल-वर्द, यूनानी चिकित्सा



Organoleptic and Physicochemical Characterization of *Sūranjān Shīrīn* (*Colchicum autumnale*), An Anti-Arthritic Unani Drug

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Abstract

Sūranjān Shīrīn (*Colchicum autumnale*) is an important drug of Unani Medicine commonly used in the management of *Waja' al-Mafāṣil* (arthritis). In Unani Medicine, a large number of drugs are confounded with each other due to resemblance in their physicochemical characteristics. *Sūranjān Shīrīn* (*Colchicum autumnale*) is commonly confounded with its other species such as *Colchicum luteum*, *Merendra persica* and *Colchicum speciosum*. Further, a number of natural products have significantly different biological activity and varied clinical efficacy due to natural variations. Therefore, it becomes imperative to standardize the herbal drugs to ensure their identity, quality and purity so as to ascertain their therapeutic efficacy. In the present study, an attempt has been made to determine the physicochemical characters helpful in identification, standardization and quality control of *Sūranjān Shīrīn*. It includes the parameters used in Unani Pharmacopoeia of India, i.e. ash values (Total ash, acid insoluble ash, water soluble ash), successive extractive values, loss on drying, pH at 1% & 10%, bulk density and moisture content. Qualitative analysis and chromatographic study (TLC) were also performed.

Keywords: *Colchicum autumnale*, Standardization, *Sūranjān Shīrīn*, TLC

Introduction

Sūranjān believed to be derived from species of *Colchicum* had long been known under the names of 'colchicum', 'hermodactyl', '*Sūranjān*' and 'ephemeron', etc. It was subsequently identified as *Colchicum autumnale*. *Colchicum* extracts were first described as a treatment for gout in *De Materia Medica* by Dioscorides in the first century AD (Trease & Evans, 2009). *Colchicum* corm is the contracted subterranean stem of the meadow saffron, *Colchicum autumnale*. The meadow saffron produces in the autumn a conspicuous reddish purple flower springing from the side of a contracted and enlarged stem (corm) situated several inches below the surface of the ground (Greenish, 1999). The corms and seeds of *Colchicum autumnale* are official in the British Pharmacopoeia and are used extensively in western medicine as a sovereign remedy for gout. Attempts have frequently been made to introduce this species into India but with very little success. Though *C. autumnale* does not grow in India, a very good substitute in the form of *C. luteum* Baker is available (Chopra *et al.*, 1958). It is perennial herb up to 30 cm tall, distributed in the Netherland, Denmark, England, Ireland, Poland, Spain, Italy, and North Africa. It is commercially grown in Italy and Yugoslavia (Bhattacharjee, 2004). John Lindley in his book '*Flora Medica*' described that the best time for collection of the corm of *Colchicum autumnale* is just after withering of leaves and should be used without loss of

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time (Lindley, 1981). The medicinal properties of this plant were well-known to the Arabs and still used by the physicians of traditional medicines especially Unani Medicine as alterative and aperient, especially in gout, rheumatism and diseases of the liver and spleen. The drug was recommended in Arabian writings for use in gout but it was little employed in either classical or medieval times owing to the wholesome fear inspired by its poisonous nature. *Colchicum corm* appeared in London Pharmacopoeias of 1618, 1627, 1632, 1639. It was then deleted but reappeared in the edition of 1788 (Trease & Evans, 2009). The corms of *Colchicum autumnale* is chiefly used to relieve the pain and inflammation and shorten the duration of acute gout and certain gouty infections, but is liable to cause intestinal pain accompanied by vomiting and purging (Greenish, 1999). The decoction (10 percent w/w) of the corm caused *in vitro* activation of an enzyme trypsin (Anonymous, 2008). According to Najmul Ghani, the efficacy of the drug remains for three years (Ghani, 2010). In Al-Mansuri, it has been mentioned for aphrodisiac activity (Ibn Baitar, 1999). On treating the drug with 60-70% sulphuric acid or with concentrated hydrochloric acid gives yellow colour due to colchicine. It contains alkaloids colchicein, colchicoresin, demecolcine including colchicine. Dried colchicum corm contains about 0.6 % of the alkaloid colchicine. It also contains abundance of starch and yields 2.2 to 2.4 % of ash (Wallis, 1985).

Sūranjān Shīrīn, *Sūranjān Talkh* and few drugs of other species are mutually confused with each other due to their morphological resemblance and used in place of each other without knowing the difference in their efficacy and toxicity. So after standardizing both the species and evaluating their pharmacological efficacy, we may be able to use them in the management of different types of arthritis. Present study has been designed to study *Sūranjān Shīrīn* (*C. autumnale*) on certain physicochemical parameters in order to set the standards of its quality and purity.

Material and Methods

Sūranjān Shīrīn (*Colchicum autumnale*) was procured from the local market of Aligarh. Professor S. H. Afaq, Pharmacognosy Section, Department of Ilmul Advia, A. K. Tibbiya College, Aligarh Muslim University, Aligarh identified the drug sample. It was further authenticated by the National Institute of Science Communication and Information Resources (NISCAIR), New Delhi (NISCAIR/RHMD/Consult/2015/2844/37-2). The sample of the test drug was submitted to *Mawālīd Thalātha* Museum of the department for future reference with voucher No. SC-0171/15.

The corms of *Sūranjān Shīrīn* were ground to get coarse powder. The powder was then subjected to physicochemical and phytochemical studies to determine various constants.

Determination of Organoleptic Characteristics

Organoleptic evaluation refers to evaluation of the drug by its appearance, colour, odour, taste and texture (Table 1).

Physicochemical Study

The physicochemical study included the determination of extractive values of the test drug in different solvents, moisture content, ash values, loss of weight on drying, bulk density and pH values (Table 2).

Ash Values

Total Ash

About 2 to 3 gm accurately weighed powdered drug was incinerated in silica dish at a temperature not exceeding 450 °C, until free from carbon. It was then cooled and weighed. The percentage of ash was calculated with reference to air dried drug (Anonymous, 2007).

Water Soluble Ash

The ash was boiled for 5 minutes with 25 ml of water. The insoluble matter was collected on an ash less filter paper, washed with hot water, and ignited for 15 minutes at a temperature not exceeding 450 °C. The weight of the insoluble matter was subtracted from the weight of the ash; the difference in weight represented the water soluble ash. The percentage of water soluble ash was calculated with reference to air dried drug (Anonymous, 2007).

Acid Insoluble Ash

The ash was boiled for 5 minutes with 25 ml of dilute hydrochloric acid. The insoluble matter was collected on ash less filter paper, washed with hot water and ignited to constant weight. The percentage of acid insoluble ash was calculated with reference to the air dried drug (Anonymous, 2007).

Moisture Content

The drug was kept in a flask along with sufficient quantity of toluene. The level of toluene was kept above the level of drug to allow the latter to get submerged. Then it was distilled for sufficient time. The distillate was collected in a measuring receiver along with the toluene, and a separated upper layer was measured in the receiver (Afaq *et al.*, 1994).

Loss of Weight on Drying

The known weight of the test drug was taken, spread uniformly and thin layered in a shallow Petri dish. It was heated at a regulated temperature of 105 °C,

cooled in a desiccator and weighed. The process was repeated many times till two consecutive weights were found constant. The percentage of loss in weight was calculated with respect to initial weight (Jenkins, 2008).

pH Value

Determination of pH was carried out by a synchronic digital pH meter (model no. 335) equipped with a combined electrode. The instrument was standardized by using buffer solution of 4.0, 7.0, and 9.20 to ascertain the accuracy of the instrument prior to the experiment. The pH value of 1% and 10% aqueous solution of powdered drug was measured (Anonymous, 2007).

Bulk Density

It was measured by digital bulk densitometer. A clean, dry and previously washed bottle of 250 ml capacity was filled with 100 gm of powdered test drug. It was allowed to tap till the time when no further decrease in the level of the drug was observed. It was calculated by the formulae -

Tapped bulk density = Mass of powdered drug/Volume (tapped) of test drug.

Qualitative Analysis

The qualitative analysis of the different chemical constituents present in the test drug was carried out according to the scheme proposed by Bhattacharjee and Das (1969). The powder of the test drug was extracted with petroleum ether (BP.60-80 °C). The petroleum ether extract (I) was tested for free phenols, alkaloids and sterols/terpenes. A part of this extract was saponified and this portion (II) was tested for fatty acids, whereas, unsaponified portion (III) was tested again for phenols, and sterols/terpenes for confirmation. The defatted marc was divided into two portions. One portion was extracted with hot water and the other with ethanol (70%). The aqueous (IV) and alcoholic (V) extracts were tested for alkaloids, flavonoids, saponins, sugars and tannins. Aqueous extract was extracted with ether and ether soluble portion (VI) was tested again for alkaloids, sterols/terpenes, whereas water-soluble portion (VII) was tested for glycosides. The water-soluble portion was again hydrolyzed with 5% hydrochloric acid and extracted with chloroform. The aglycone portion (VIII) was tested for insoluble hydrochloride of alkaloid. Chloroform soluble portion (IX) was tested for alkaloids and sterols/terpenes, whereas water-soluble fraction (X) was tested for alkaloids. One part of this water-soluble portion was basified with alkali (ammonia) and extracted with immiscible solvent (ether). The solvent soluble part (XI) was again tested for alkaloids (Afaq, *et al.*, 1994) (Table 3).

Test for Alkaloids

A drop of Dragendorff's reagent was added in the extract. The brown precipitate showed the presence of alkaloids.

Test for Carbohydrate/Sugars

Fehling's Test

In the aqueous extract, a mixture of equal parts of Fehling's solution A and B previously mixed was added and heated. A brick red precipitate of cuprous oxide indicates the presence of reducing sugars.

Molisch Test

In an aqueous extract, α -naphthol was added. Afterwards, concentrated sulphuric acid was gently poured. A brown colour ring at the junction of the two solutions indicates the presence of the sugar.

Test for Flavonoids

A piece of magnesium ribbon was added to alcoholic extract of the drug followed by drop wise addition of concentrated HCl. Colour ranging from orange pink to red is a confirmatory test for flavonoids.

Test for Glycosides

The test solution was filtered and sugar was removed by fermentation with baker's yeast. The acid was removed by precipitation with magnesium oxide. The remaining alcoholic extract that contained the glycosides was subsequently detected by the following method:

The hydrolysis of the solution was done with concentrated sulphuric acid and after the hydrolysis sugar was determined with the help of Fehling's solutions.

Test for Tannin

Ferric chloride solution was added in the aqueous extract of the drug. A bluish-black colour, which disappeared on addition of dilute sulphuric acid followed by a yellowish brown precipitate, shows the presence of tannin.

Test for Proteins

Xanthoproteinic Reaction

In the test solution, concentrated nitric acid was added. A yellow precipitate appeared. Strong solution of ammonia was added to it. Appearance of yellow colour shows the presence of proteins.

Biurette's Reaction

In the hot test solution, 1 ml concentrated sodium hydroxide was added, followed by one drop of copper sulphate solution. A violet or red colour indicates the presence of proteins.

Test for Starch

0.015 gm of iodine and 0.015 gm of potassium iodide was added in 5 ml of distilled water; 2 ml of iodine solution formed was added to 2 ml of aqueous test solution, the presence of blue colour indicates the presence of starch.

Test for Phenol

5-8 drops of 1% aqueous solution of lead acetate was added to aqueous or alcoholic test solution. The presence of yellow coloured precipitate indicates the presence of phenols.

Test for Sterol/Terpenes

Salkowski Reaction

In the test solution of chloroform, 2 ml sulphuric acid (concentrated) was mixed from the side of the test tube. The colour of the ring at the junction of the two layers was observed. A red colour ring indicates the presence of the sterols/terpenes.

Test for Amino Acids

The alcoholic extract was mixed with ninhydrin solution (0.1% in acetone). After heating gently on water bath for few minutes, it gives a blue to red-violet colour that indicates the presence of amino acids.

Test for Resin

The test solution was gently heated and acetic anhydride was added to it. After cooling, one drop of sulphuric acid was mixed. A purplish red colour that rapidly changed to violet indicates the presence of the resins.

Thin Layer Chromatography

Thin layer chromatography of petroleum ether extract of the drug was carried out on aluminium plates precoated with Silica gel-G (Layer thickness 0.20-0.25 mm) for all extracts in various phases later sprayed by different spraying reagents. The R_f value of spots was calculated by the following formulae (Anonymous, 2007).

R_f Value – Distance travelled by the spot / Distance travelled by the solvent

Observations and Results

The organoleptic evaluation carried out has been given below in Table 1:

Table 1: Organoleptic Characters

S. No.	Organoleptic Characters	Observations
1.	Appearance	Solid and ovoid
2.	Colour	White to brown
3.	Odour	Inodorous
4.	Texture	Firm and smooth
5.	Taste	Tasteless or sweet

Table 2: Physicochemical Parameters

The amount of total ash, water soluble ash and acid insoluble ash of *Sūranjān Shīrīn* (*Colchicum autumnale*) were found to be 2.926 ± 0.2513 , 2.0368 ± 0.0498 and 0.783 ± 0.6516 , respectively. Percentage of loss of weight on drying, moisture content and bulk density were found to be 0.79 ± 0.2082 , 0.68 ± 0.01642 and 0.853 ± 0.01421 for *Sūranjān Shīrīn*. pH of *Sūranjān Shīrīn* was found to be 7.32 ± 0.1049 in 1% solution and 7.36 ± 0.3606 in 10% solution. The percentage of extractive values of *Sūranjān Shīrīn* (*Colchicum autumnale*) by successive extraction with different solvents was found to be 0.055 ± 0.515 in petroleum ether, 0.023 ± 0.397 in chloroform, 0.190 ± 0.548 in acetone, 0.719 ± 0.849 in alcohol and 6.318 ± 0.787 in distilled water.

S. No.	Parameters	Results
1.	Ash value	Total ash: 2.926 ± 0.2513 Water soluble: 2.0368 ± 0.0498 Acid insoluble ash: 0.783 ± 0.6516
2.	Moisture content	0.68 ± 0.01642
3.	Bulk density	0.853 ± 0.01421
4.	Loss on drying at 105 °C	0.79 ± 0.2082
5.	pH values	1 % pH- 7.32 ± 0.1049 10 % pH- 7.36 ± 0.3606
6.	Extractive values	Petroleum ether 0.055 ± 0.515 Chloroform 0.023 ± 0.397 Acetone 0.190 ± 0.548 Alcohol 0.719 ± 0.849 Distilled water 6.318 ± 0.787

Table 3: Qualitative Analysis

The qualitative test for chemical constituents demonstrated that alkaloids, glycosides, proteins, amino acids, tannins, resins, steroids and saponins were present in *Sūranjān Shīrīn* (*Colchicum autumnale*).

S. No.	Chemical Constituents	Tests/Reagent	Inference
1.	Alkaloid	Dragendroff's reagent Hager's test Mayer's reagent	+ve +ve +ve
2.	Carbohydrate	Molisch's Test Fehling's test	-ve -ve
3.	Glycoside	NaOH Test	+ve
4.	Flavanoids	Mg ribbon and Dil. Hcl	-ve
5.	Tannin	Ferric chloride test	+ve
6.	Protein	Xanthoproteinic test Biurette's test	+ve -ve
7.	Steroid	Salkowski reaction	+ve
8.	Amino acid	Ninhydrin solution	+ve
9.	Resins	Acetic Anhydride Test	+ve
10.	Phenol	Lead acetate Test	-ve
11.	Saponin	Frothing with NaHCO_3	+ve

Table 4: TLC Profile of *Sūranjān Shīrīn* (*Colchicum autumnale*)

Extract	Solvent System	Treatment	Number of Spots	Rf Value
Aqueous	n-butanol:acetic acid:distilled water (4:1:5)	UV Long UV Short Iodine vapour	2 2 2	0.26, 0.53
Chloroform	Chloroform: Methanol (4:1)	UV Long UV Short Iodine vapour	1 1 1	0.90

Discussion

Standardisation is an essential tool to ensure identity, purity and quality of herbal drugs. Pharmacognostical studies are the first step of standardisation which helps in identification, characterization and distinguishing the drug from confounding varieties. Since the therapeutic efficacy of a drug mainly depends upon its physicochemical characteristics, therefore, the determination

Fig 1: TLC of aqueous extract of *Sūranjān Shīrīn* (*Colchicum autumnale*)

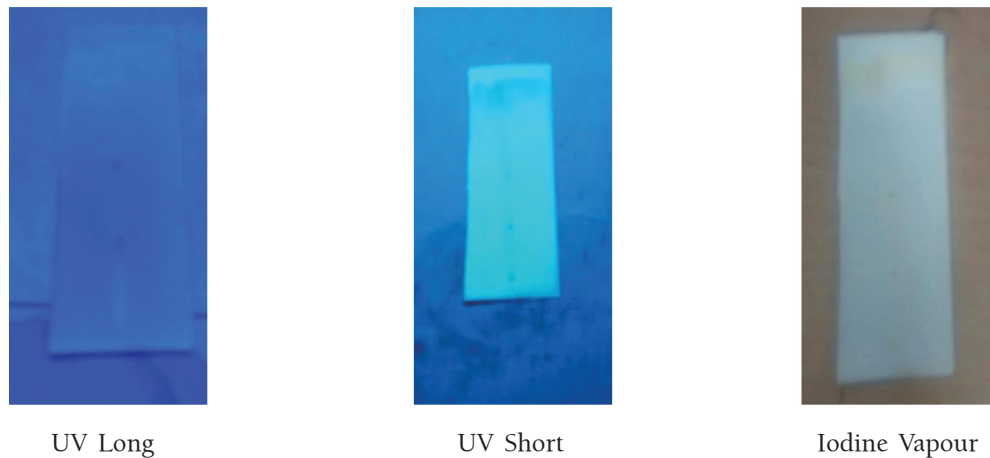


Fig 2: TLC of chloroform extract of *Sūranjān Shīrīn* (*Colchicum autumnale*)



of physicochemical characters for the authenticity of a drug is imperative before studying it for pharmacological activity. Physicochemical study helps in characterization of constituents or groups of constituents which interact at molecular level in human being. It must be appreciated that Unani drugs produce effects mostly due to their *Mizāj* as they modify the deranged *Mizāj* and *Kayfiyāt* of the human body and bring them back to normal level. Since specific temperament (*Mizāj*) develops because of the unique configuration of the constituents that a drug possesses, therefore, a little change in physicochemical characters may modify the temperament of the drug compromising its ability to deal with the pathological condition.

Standardization of *Sūranjān Shīrīn* (*Colchicum autumnale*) which is an effective anti-arthritic drug will ensure its proper identification, purity and quality and thereby its therapeutic efficacy. The findings of the present study will also help in distinguishing it from confounding varieties, mainly *Colchicum luteum*

and *Marendra persica* which possess few common characters and stimulating pharmacological effect. The former is considered as the best Indian substitute of *Colchicum autumnale*. Some Unani physicians have described *Colchicum luteum* to be more toxic than *Colchicum autumnale*. So, the standardization of *Colchicum autumnale* and its comparison with *Colchicum luteum* would explore the claim of Unani physicians on the basis of physicochemical constant. However, since both have different physicochemical and phytochemical characters, therefore, their pharmacological effect and the degree of effect may vary. Therefore, their characters must be defined. Standardization is also mandatory because qualitative or quantitative deviation of the constituents of a plant drug may alter its efficacy and safety, therefore, standardization is considered mandatory. The present study determines a comprehensive range of physicochemical characters of the drug according to the parameters used in National Formulary of Unani Medicine. Therefore, these findings may be used as the standards for ensuring the purity and quality and thereby the predictable efficacy and safety of *Sūranjān Shīrīn* (*Colchicum autumnale*).

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सारांश

गठियारोधी यूनानी औषधि सुरंजान शीरी (कोल्चिकम औटमनेल) का इन्द्रियाग्राही और भौतिक रासायनिक विशेषीकरण

***मोहम्मद ज़ाकिर सिद्दीकी, गुफरान अहमद, कुवंर मोहम्मद यूसुफ अमीन, सुम्बुल रहमान, सदा अख्तर**

सुरंजान शीरी (कोल्चिकम औटमनेल) यूनानी चिकित्सा की एक महत्वपूर्ण औषधि है जो आमतौर पर वज-उल-मफ़ासिल (गठिया) के उपचार में उपयोग की जाती है। यूनानी चिकित्सा में बड़ी संख्या में औषधियों को उनके भौतिक रासायनिक विशेषताओं में समानता के कारण पहचानने में गड़बड़ी हो जाती है। सुरंजान शीरी (कोल्चिकम औटमनेल) को सामान्यतः इसकी अन्य प्रजातियों जैसे कोल्चिकम ल्यूटियम, मेरेंद्रा परसिका और कोल्चिकम स्पेसियोसम के साथ गड़मड़ कर दिया जाता है। इसके अलावा प्राकृतिक विविधताओं के कारण प्राकृतिक उत्पादों में महत्वपूर्ण रूप से विभिन्न जैविक गतिविधि और विविध नैदानिक प्रभावकारिता होती है। इसलिए इनकी पहचान, गुणवत्ता और शुद्धता सुनिश्चित करने के लिए हर्बल औषधियों का मानकीकरण करना अनिवार्य है ताकि इनकी चिकित्सीय प्रभावकारिता का पता लगाया जा सके। वर्तमान अध्ययन में सुरंजान शीरी की पहचान, मानकीकरण और गुणवत्ता में नियंत्रण करने वाले भौतिक रासायनिक विशेषताओं को निर्धारित करने का प्रयास किया गया है। इसमें भारतीय यूनानी फार्माकोपिया में उपयोग किए गए मापदंड अर्थात् राख मान (कुल राख, एसिड में अघुलनशील राख, पानी में घुलनशील राख), क्रमिक प्राप्त मान, सुखाने पर नुकसान, 1% और 10% पर पीएच, स्थूल घनत्व और नमी अवयव शामिल हैं। गुणात्मक विश्लेषण और वर्णलेखी अध्ययन (टीएलसी) भी किए गए हैं।

शब्दकुंजी: कोल्चिकम औटमनेल, मानकीकरण, सुरंजान शीरी, टीएलसी



Standardization and HPTLC Fingerprinting of Unani Formulation *Habb-i-Azarāqī* with Contemporary Analytical Techniques

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Abstract

Habb-i-Azarāqī (HA), a highly potent compound Unani formulation (Tablet form), is in clinical use for last several decades for various ailments like *Fālīj* (Paralysis), *Laqwa* (Facial palsy or Bell's palsy), *Niqris* (Gout) and *Waja' al-Mafāṣil* (Arthritis). The present study aims at standardization and development of HPTLC fingerprinting of HA by modern analytical techniques to comprehend its quality. HA in its three different batches was evaluated for organoleptic parameters, microscopic studies, physicochemical parameters, phytochemical screening, TLC and HPTLC profile, aflatoxin, microbial load and heavy metal analysis. HA was successfully standardized with all the parameters such as total ash, acid insoluble ash, water and alcohol soluble matter and loss of weight on drying. Further, TLC and HPTLC fingerprinting profile of HA was developed and detected under various detection systems, viz. UV 366nm, UV 254nm, exposure to iodine vapours and anisaldehyde sulphuric acid. The present study ensured authenticity of the formulation and furnished referential facts for its identification and purity thereby substantiating into a validated scientific data.

Keywords: *Habb-i-Azarāqī*, HPTLC, Standardization, Unani

Introduction

The current scenario unveils the importance of Traditional Medicine which not only imparts health but social as well as economic benefits too. Toxicity, side effects and cost of allopathic drugs are another reason for the popularity of Traditional Medicine. WHO Traditional Medicine Strategy 2014-2023 aims to strengthen the role of Traditional Medicine by keeping population healthy and prioritizing health services. The Hellenistic origin of Unani Medicine that comes under Traditional Medicine is based on the four humours; Phlegm, Blood, Yellow bile and Black bile. In accordance with its principle roots, Unani Medicine uses macroscopic parameters rather than microscopic parameters for diagnosis, and therefore it is highly economical and independent of technological paraphernalia (Anonymous, 2016). The strength of Unani Medicine is its holistic approach and temperament-based treatment which emphasizes and targets the underlying cause of a disease. The way a large number of people still rely on Unani treatment proves its effectiveness and credibility. One of the tenets of herbal medicine is that the maximum effectiveness of the drug derives from the whole drug or its crude extract rather than from isolated components. In cases where an assay is lacking, it is important that the crude drug is properly authenticated, its general quality verified and all formulations of it prepared in accordance with good manufacturing practices (Evans, 2009). According to WHO, standardization and

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quality control of herbal drug is involved with physicochemical evaluation of crude drug such as selection and handling of crude material, safety, efficacy and stability assessment of finished product (Folashade *et al.*, 2012). A huge amount of work is done in the field of chemical analysis of plants, but mere chemical analysis is not standardization, it should aim at giving a reproducible pattern with known biological activity. It has now become evident that there is a need for a holistic approach to health care and utilize the untapped potential of Traditional Medicine in a proper way (Dhiman *et al.*, 2016).

Ḥabb-i-Azarāqī (HA) is one of the important polyherbal Unani formulations that need attention in context of standardization. Though a few scattered reports on standardization of *Ḥabb-i-Azarāqī* are available which reveal only some pharmacopoeial parameters like total ash, acid insoluble ash, alcohol soluble and water soluble matter, thin layer chromatography (TLC), and thus it has been taken for standardization on account with modern analytical parameters.

HA possesses *Muqawwī-i-A'ṣāb* (Nervine tonic) and *Muḥarrik-i-A'ṣāb* (Nervine stimulant) properties (Hakim, 2002; Anonymous, 2006b; Kabiruddin, 2007). It is generally used for various ailments like *Fālij* (Paralysis), *Laqwa* (Facial palsy or Bell's palsy), *Niqris* (Gout) and *Waja' al-Mafāṣil* (Arthritis) (Azmi, 2011). HA contains four ingredients, namely *Azarāqī Mudabbar* (*Strychnos nux-vomica* L., detoxified), *Filfil Siyāh* (*Piper nigrum* L.), *Filfil Darāz* (*Piper longum* L.) and *'Araq-i-Ajwāyin* (*Trachyspermum ammi* L.) which are endowed with properties like *Musakkin* (Analgesic), *Muqawwī-i-A'ṣāb* (Nervine tonic), *Muḥarrik* (Stimulant) and *Muḥallil* (Resolvent) (Neetu *et al.*, 2013). The chief ingredient of the formulation is *Azarāqī/Kuchla* (*Strychnos nux-vomica* L.), belonging to the family Loganiaceae which is considered to be toxic in nature, having strychnine and brucine as major alkaloids and was used originally as a nervine tonic and to treat rheumatic pain (Ghani, 2011). The present paper describes the standardization profile with modern analytical analysis such as HPTLC fingerprinting and moreover subjected to analysis for organoleptic parameters, physico-chemical parameters, phytochemical screening, microscopical studies, aflatoxin, microbial load, and heavy metal analysis. The study established and created authentic data enriching Unani Medicine which ultimately contributes to the health benefit of the ailing masses of the society.

Methodology

Collection of Material

All the ingredients of HA were procured from the pharmacy of National Research Institute of Unani Medicine for Skin Disorders, Hyderabad and local market of Hyderabad (herbal dealers), authenticated and identified by botanist and their voucher specimen numbers were provided as SMPU/CRI-Hyd viz. *Azarāqī*-13552,

Filfil Darāz-13553, *Filfil Siyāh* -13554 and *Ajwāyin* -13555. All the chemicals and solvents used were of analytical grade and calibrated analytical instruments were used in the study.

Preparation of Formulation

HA was prepared at the pharmacy (GMP certified) of National Research Institute of Unani Medicine for Skin Disorders (NRIUMSD), Hyderabad according to the composition of the formulation given in National Formulary of Unani Medicine.

Composition of *Habb-i-Azarāqī*

S. No.	Name of drug	Botanical name	Family	Part used	Quantity
1.	<i>Azarāqī Mudabbar</i> (Detoxified)	<i>Strychnos nux-vomica</i> L.	Loganiaceae	Seed	20 gm
2.	<i>Filfil Siyāh</i>	<i>Piper nigrum</i> L.	Piperaceae	Fruit	10 gm
3.	<i>Filfil Darāz</i>	<i>Piper longum</i> L.	Piperaceae	Fruit	10 gm
4.	<i>'Araq-i-Ajwāyin</i>	<i>Trachyspermum ammi</i> L.	Apiaceae	Seed distillate	10 gm

(Anonymous, 1981)

Method of Preparation

Habb-i-Azarāqī was prepared according to the following steps:

- Procurement, authentication and identification of ingredients
- Processing of raw materials
- Preparation of tablet (*Habb*)

Procurement, Authentication and Identification of Ingredients

The raw materials were procured from the pharmacy of National Research Institute of Unani Medicine for Skin Disorders (NRIUMSD) and local market / herbal dealer of Hyderabad, which were authenticated and identified with the help of a botanist at the institute.

Processing of Raw Materials

All the raw materials were cleaned separately for removal of any foreign matter. The chief ingredient *Azarāqī* was detoxified as per National Formulary of Unani Medicine to make *Azarāqī Mudabbar*. *Azarāqī* was buried in yellow clay for ten days watering it thrice per day. After ten days, the outer covering (testa) peeled

off and the cotyledons of *Azarāqī* were separated after removing the embryo part (pitta). It was washed with hot water and tied in a clean cloth bag, immersed in a vessel containing milk which was boiled till it evaporated. Thereafter, *Azarāqī* was removed from the bag and washed with normal water to obtain *Azarāqī Mudabbar* (detoxified *Strychnos nux-vomica* L.) (Anonymous, 2007a).

Coarse powder of cleaned and dried *Ajwāyin*, which was further soaked in purified water in the quantity 12 times of the drug for 24 hrs, was taken and transferred (soaked powdered *Ajwāyin*) to the distillation plant along with the purified water to collect '*Araq-i-Ajwāyin*. *Filfil Siyāh* and *Filfil Darāz* were powdered in a grinder and filtered with sieve number 80 to obtain fine powder. The fine powder of *Filfil Siyāh*, *Filfil Darāz*, *Azarāqī Mudabbar* and '*Araq-i-Ajwāyin* were mixed uniformly to yield wet mass. Further, the wet mass (whole content) was made into granules with the help of granulator and dried at room temperature.

Preparation of Tablet (*Habb*)

The granules were subjected to make HA tablets of 500 mg each by using automatic tablet making machine. In the same manner, three different batches of HA were prepared to use for further study.

Methodology for Standardization of *Habb-i-Azarāqī*

For standardization, HA was subjected to various parameters including organoleptic evaluation, macroscopic and microscopic study. Physicochemical parameters such as extractive value, total ash, acid insoluble ash, pH (of 1% and 10% aqueous solution), loss of weight on drying at 105 °C, disintegration time, friability test, uniformity of weight, thin layer chromatography (TLC) & HPTLC were also evaluated along with microbial load, aflatoxin and heavy metal analysis. The phytochemical screening for the nature of compounds was carried out as per the methods described in The Unani Pharmacopoeia of India (Anonymous, 2006b).

Organoleptic Evaluation

Morphological or macroscopical characteristics of HA were recorded under naked eye in three different batches that include colour, shape, size, odour, taste, etc. The powder form of HA was examined under microscope for epidermal cells, cork cells, starch, phloem fibers, xylem fibers, sclereids, parenchymatous cells, tracheids, calcium oxalate crystals and stone cells. The phytochemical screening was carried out to detect nature of phyto-constituents that vary in their content depending upon various atmospheric factors, storage and drying conditions. The class of compounds was found to be alkaloids, carbohydrates,

glycosides, phenols, resins, saponins, proteins, starch, sterols/terpenes, tannins and flavonoids (Anonymous, 1987; Afaq *et al.*, 1994).

Physicochemical Evaluation

In physicochemical parameters, pH value fundamentally represents the value of hydrogen ion activity in solutions that influences the concentrations of anions, cations, and undissociated molecules. Digital pH meter was used to calculate pH value of 1% and 10% aqueous solution. Loss of weight on drying at 105 °C, disintegration test by disintegration testing apparatus, tablet friability by friability testing apparatus, uniformity of weight, bulk density and TLC & HPTLC were carried out as per the pharmacopoeial standards (Anonymous, 2006b; Anonymous, 2007b; Gilbert *et al.*, 1987; Cid & Jaminet, 1971; Manjula *et al.*, 2012; Rubinstein & Price, 1977; Caramella *et al.*, 1978).

TLC and HPTLC Evaluation

TLC and HPTLC studies were done by the alcoholic extract of HA, for which 5 g of powdered HA was taken and refluxed with 200 ml of alcohol using Soxhlet apparatus on a water bath for 30 min. The extract was then filtered and concentrated to 5 ml and further used for thin layer chromatography. The alcoholic extract was applied on TLC plate and spotted on silica gel “G” plate and developed with Toluene: Ethyl Acetate: (8:2, v/v) as mobile phase. The HPTLC fingerprinting profile of HA was studied on three different batches and detected under four detection systems and R_f values of the spots were calculated (Anonymous, 2006a). The developed TLC plates were dried completely and detected under four detection systems like UV cabinet system for detection of spots at 366nm, 254nm, under iodine vapours and after derivatizing with anisaldehyde sulphuric acid reagent. Further, it was scanned with the densitometer CD60 of DESAGA Sarstedt Gruppe system that showed typical densitogram, in which peaks appeared for the corresponding spots being detected in the densitometer. The peak areas of each component after separation correspond to the concentration of the component in HA and R_f values were recorded through the software.

Determination of Microbial Load

For the determination of microbial load, one gram each of the three samples of HA was taken separately for carrying out the study and soya bean casein digest agar media, sabouraud dextrose agar with chloramphenicol media, Hi Crome™ E. coli agar media and Hi Crome Raj Hans medium, modified (Salmonella Agar, Modified) media were used. After inoculation and incubation, the petri plate was counted at 24-48 hours for soya bean casein digest agar media, Hi Crome

E. Coli agar media and modified salmonella agar media and at 48-72 hours for sabouraud dextrose agar media (WHO, 2018).

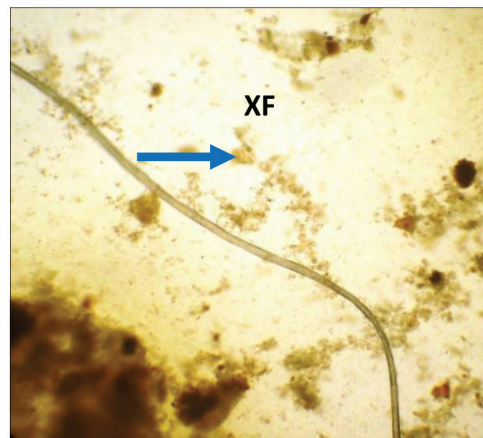
Determination of Aflatoxin

HA was analyzed for the presence of aflatoxin B1, B2, G1 and G2 by using thin-layer chromatography method (Anonymous, 2010; Liu & Wu, 2010; WHO, 2000).

Determination of Heavy Metals

Heavy metals detection of HA was done by the instrument Atomic absorption spectrophotometer (AAS) at DSRI, Ghaziabad. Flame atomization technique was followed for the detection of lead (Pb), cadmium (Cd) and hydride generator was used for the detection of the arsenic (As) and mercury (Hg) elements.

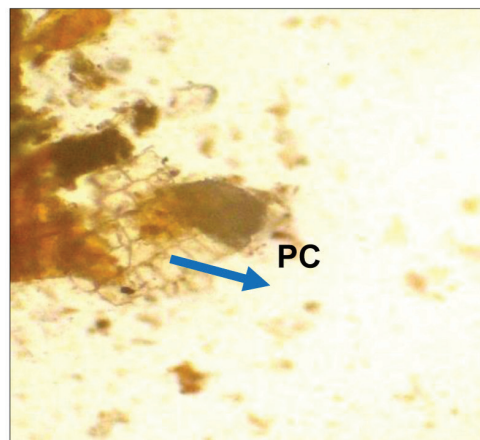
Microscopical Study of *Habb-i-Azarāqī*



Xylem fibres



Sclereids



Parenchymatous cells



Tracheids

PC

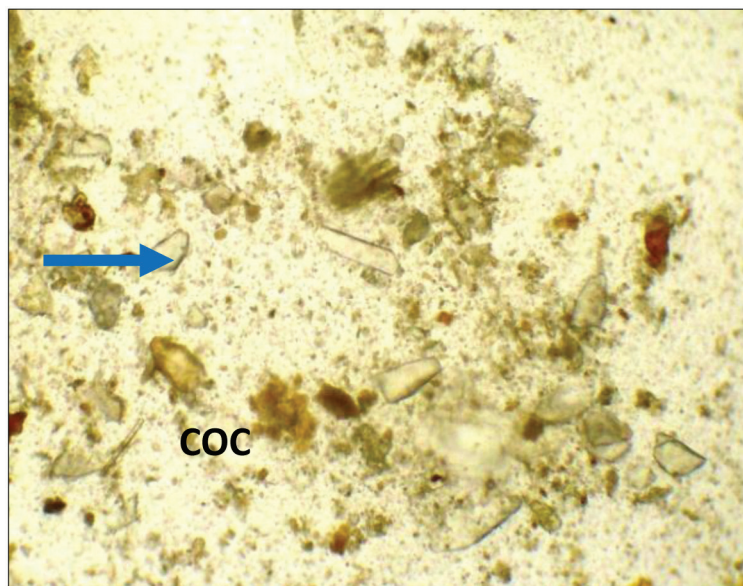
Result and Discussion

On naked eye examination, it was confirmed that HA was free from any foreign materials and other adulteration. Organoleptic properties which serve a number of functions, such as, colour can be used as a means of rapid identification of drug, the presence of the odour could be characteristic of the drug which ultimately helps to judge the quality of drugs. Organoleptic parameters in three different batches of HA were found to be round shape tablet, greyish brown in colour, hard in texture, having disagreeable odour and bitter in taste (Table 1).

The uniformity of weight of HA tablet for the randomly selected twenty tablets was checked and the mean value was found to be $522.5 \text{ mg} \pm 6.8$. Friability of HA revealed that the tablet was not deviating more than 5% of actual weight in all three batches (Figure 7). The mean value of bulk density

Table 1: Identity, Purity and Strength (Physico-chemical Parameters)

Parameters	Batch 1	Batch 2	Batch 3
Form	Tablet	Tablet	Tablet
Texture	Hard	Hard	Hard
Colour	Greyish Brown	Greyish Brown	Greyish Brown
Odour	Disagreeable	Disagreeable	Disagreeable
Taste	Bitter	Bitter	Bitter
Total ash (% w/w) (Mean \pm SD)	9.99 ± 0.44	10.09 ± 0.44	10.05 ± 0.25
Acid insoluble ash (% w/w) (Mean \pm SD)	4.97 ± 0.16	4.69 ± 0.29	4.83 ± 0.41
Alcohol soluble matter (% w/w) (Mean \pm SD)	11.90 ± 0.48	11.68 ± 0.08	10.85 ± 0.44
Water soluble matter (% w/w) (Mean \pm SD)	38.49 ± 0.31	38.77 ± 0.74	37.09 ± 1.81
Friability Test (Mean)	0.05	0.05	0.05
Uniformity of weight (Mean \pm SD)	5.23 ± 6.8	5.23 ± 6.8	5.23 ± 6.8
pH 1% aqueous solution (Mean \pm SD)	5.94 ± 0.01	5.98 ± 0.03	5.91 ± 0.03
pH 10% aqueous solution (Mean \pm SD)	5.71 ± 0.03	5.71 ± 0.02	5.73 ± 0.02
Bulk Density	0.81 ± 0.01	0.82 ± 0.01	0.81 ± 0.02
Loss of wt. on drying at 105°C (% w/w) (Mean \pm SD)	5.96 ± 0.03	5.95 ± 0.02	5.96 ± 0.02
Disintegration time /Aqueous Media (minutes)	19	20	23



Calcium Oxalate Crystals

Figure 1: Powder Microscopy of HA

of HA was found to be 0.80. pH of 1% and 10% aqueous solution was found in the range of 5.91 to 5.98 and 5.71 to 5.73 respectively in three different batches. The mean percentage of HA for the loss of weight on drying at 105°C in three different batches was found in the range of 5.95 to 5.96% w/w. The ash value represents the inorganic content and the high ash value indicates the contamination, substitution, adulteration in preparing the formulation from the crude ingredients. The mean percentage values of total ash and acid insoluble ash in three different batches were found in the range of 9.99 to 10.09 and 4.69 to 4.83% w/w respectively (Table 1, Figure 4).

The determination of alcohol and water soluble matter has an important role in evaluation of crude drug. Less extractive value indicates addition of exhausted material, adulteration or incorrect process during drying, storage or formulating. The mean percentage of water and alcohol soluble matter was found to be in the range of 37.09 to 38.77 and 10.85 to 11.90% w/w in three different batches respectively (Table 1, Figure 5–6). The disintegration time of HA in three different batches was found around 19–23 minutes. These physicochemical results are presented in Table 1. Microscopic parameters exhibited characteristic features for the xylem fibres, sclereids, elongated parenchymatous cells, tracheids with spiral thickenings and calcium oxalate crystals are as shown in Figure 1. The phytochemical screening analysis of HA was carried out using qualitative tests and the nature of phyto-constituents such as alkaloids, flavonoids, carbohydrates, tannins, etc. was observed to be present and tabulated in Table 2.

The TLC and HPTLC studies hold a distinct importance in the qualitative as well as quantitative analysis assuring the purity of a compound or a drug. The

Table 2: Phytochemical Screening for the Nature of Compounds Present

Chemical Constituents	Test / Reagents	Inference
Alkaloids	Dragendroff's reagent	Positive
	Hager's test	Positive
	Wagner's reagent	Positive
	Tannic acid test	Positive
	Mayer's reagent	Positive
Carbohydrates	Fehling's test	Positive
	Molish's test	Positive
	Barfoed's test	Positive
	Benedict's test	Positive
Flavonoids	Shinoda test	Positive
	Zinc hydrochloride test	Positive
	Alkaline reagent test	Positive
Tannins	Ferric chloride test	Positive
	Gelatin test	Positive
	Lead acetate test	Positive
Proteins	Warming test	Positive
	Biuret test	Positive
Steroids	Salkowski test	Positive
	Sulphur powder test	Positive
	Hosse's reaction	Positive
	Moleschott's reaction	Positive
Glycosides	NaOH Test	Positive
Saponins	Frothing with NaHCO ₃	Positive
Fats and fixed oils	Copper sulphate / Sodium hydroxide	Positive

alcoholic extract of HA was developed using toluene: ethyl acetate: (8:2, v/v) as mobile phase (Figure 2 and 3) and detected under four detection systems. Under UV 366nm, it showed eight major spots at R_f values 0.14 (blue), 0.28 (blue), 0.35 (blue), 0.42 (yellow), 0.50 (light blue), 0.64 (light blue), 0.71 (light blue), 0.85 (light blue), under UV 254nm it showed three spots at R_f values 0.35, 0.42, 0.57 (All black), under iodine vapours it showed one spot at R_f value 0.32 (brown) and under anisaldehyde sulphuric acid on heating at 105 °C it showed three spots at R_f values 0.47 (dark blue), 0.50 (light blue), 0.57 (light blue). The TLC plate under densitometer scanning provided the typical densitogram having corresponding peaks for the separated components which are recorded and presented in Figure 3 and their corresponding R_f values by the HPTLC software was tabulated in Table 3, 4, 5 and 6.

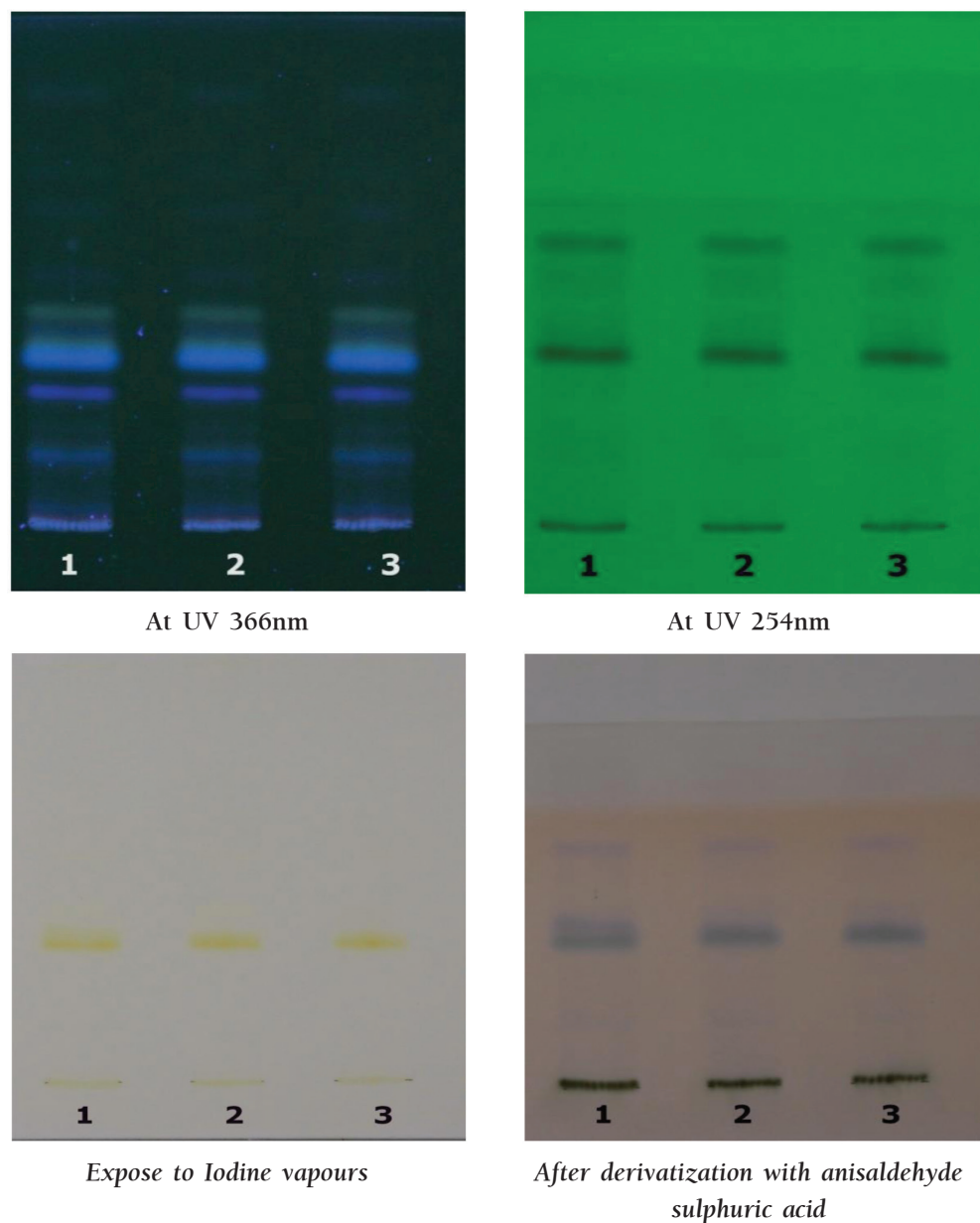


Figure 2: TLC of Alcoholic Extracts of HA in Various Detection Systems

Table 3: Peak List of Alcoholic Extract of *Habb-i-Azarāqī* at UV 366nm

Peak No	Y-Pos	Area	Area %	Height	R _f value
1	9.5	409.60	9.98	239.99	0.01
2	19.4	259.00	6.31	101.42	0.14
3	23.1	22.22	0.54	15.45	0.20
4	28.5	37.41	0.91	18.64	0.27
5	33.1	2745.32	66.92	719.33	0.33
6	39.1	551.65	13.45	230.19	0.42
7	49.0	32.81	0.80	18.84	0.56
8	70.2	44.49	1.08	17.70	0.85

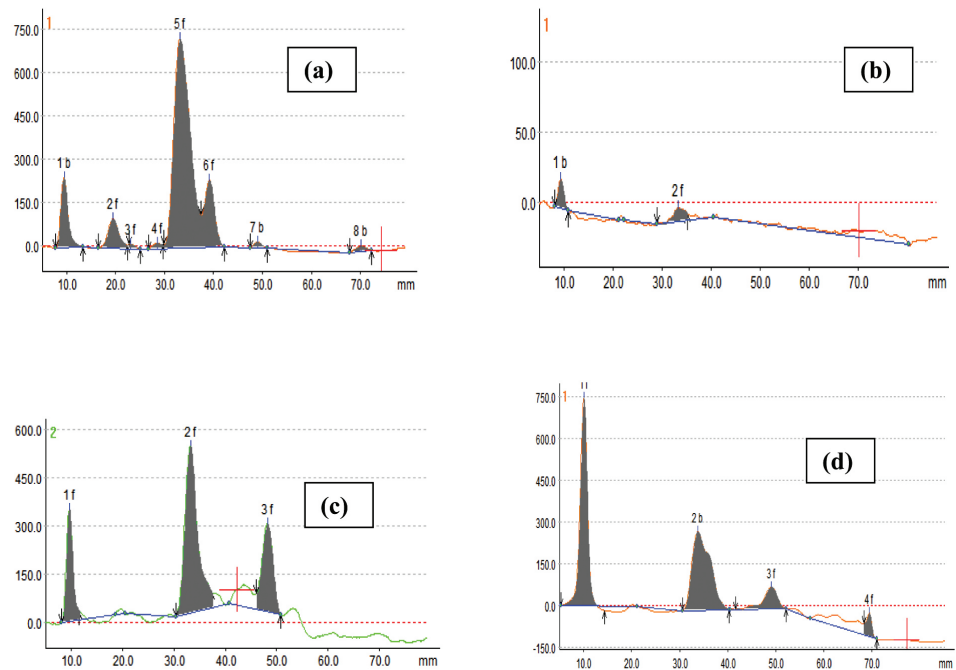


Figure 3: Densitogram of Alcoholic Extract of *Habb-i-Azarāqī* a) at UV 366nm b) at UV 254 nm c) expose to Iodine vapours d) upon derivatization with Anisaldehyde sulphuric acid.

Table 4: Peak List of Alcoholic Extract of *Habb-i-Azarāqī* at UV 254nm

Peak No	Y-Pos	Area	Area %	Height	R _f value
1	9.6	493.88	18.79	340.57	0.01
2	33.2	1472.21	56.00	508.65	0.34
3	48.2	662.94	25.22	268.83	0.54

Table 5: Peak List of Alcoholic Extract of *Habb-i-Azarāqī* upon Exposure to Iodine Vapour

Peak No.	Y-Pos	Area	Area %	Height	R _f value
1	9.4	27.20	50.22	20.13	0.01
2	33.4	26.96	49.78	9.47	0.34

Table 6: Peak List of Alcoholic Extract of *Habb-i-Azarāqī* upon derivatization with anisaldehyde sulphuric acid at 580nm.

Peak No	Y-Pos	Area	Area %	Height	R _f value
1	10.1	1312.51	44.68	735.30	0.02
2	33.8	1236.95	42.10	278.56	0.34
3	49.1	272.76	9.28	78.52	0.56
4	69.4	115.68	3.94	84.48	0.84

The total bacterial load of HA in the three samples varied from 45×10^2 to 78×10^2 (not more than $10^5/\text{g}$), which was found to be below permissible limits while *Salmonella Spp.*, *Escherichia coli* and total fungal count were found to be absent indicating HA may be used for medicinal purpose (Table 7). The aflatoxin

Table 7: Microbial Load Contamination

S. No.	Parameter Analyzed	Results			Permissible Limits as per WHO/UPI
		Sample-I	Sample-II	Sample-III	
1.	Total Bacterial Load	45×10^2	78×10^2	66×10^2	Not more than $10^5/\text{g}$
2.	<i>Salmonella Spp.</i>	Nil	Nil	Nil	Nil
3.	<i>Escherichia. Coli</i>	Nil	Nil	Nil	Nil
4.	Total Fungal count	Nil	Nil	Nil	Not more than $10^3/\text{g}$

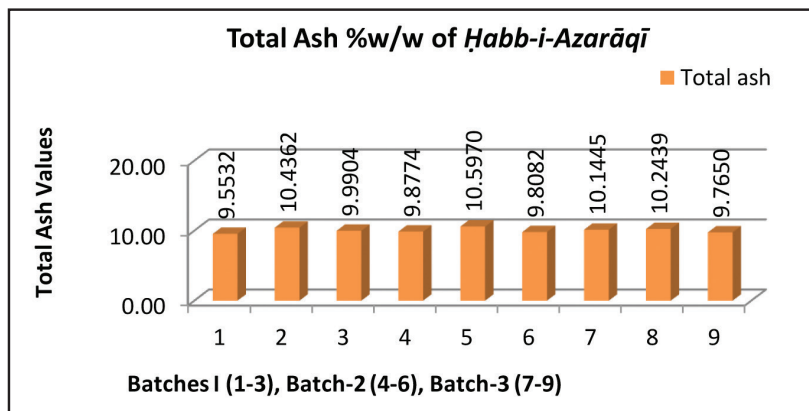


Figure 4: Total Ash of HA

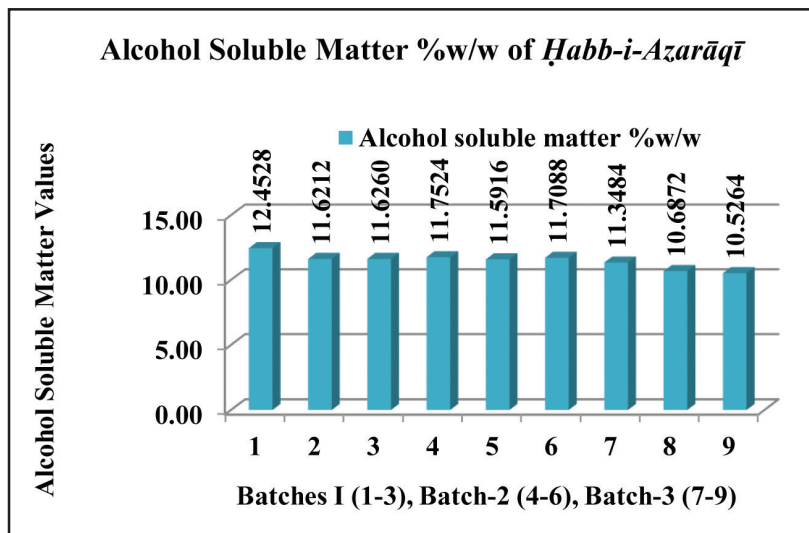


Figure 5: Alcohol Soluble Matter of HA

B1, B2 and G1, G2 was found to be absent (Table 8), thus HA can be safely consumed. Contamination of medicinal plant materials with heavy metals can be attributed to many causes including environmental pollution and traces of pesticides. Heavy metal analysis revealed no traces of lead (Pb), cadmium (Cd), arsenic (As) and mercury (Hg) in HA (Table 9).

Table 8: Aflatoxin Contamination

S. No.	Parameter Analyzed	Results			Permissible Limits as per UPI
		Sample-I	Sample-II	Sample-III	
1.	B1	Nil	Nil	Nil	Not more than 0.50 ppm
2.	B2	Nil	Nil	Nil	Not more than 0.10 ppm
3.	G1	Nil	Nil	Nil	Not more than 0.50 ppm
4.	G2	Nil	Nil	Nil	Not more than 0.10 ppm

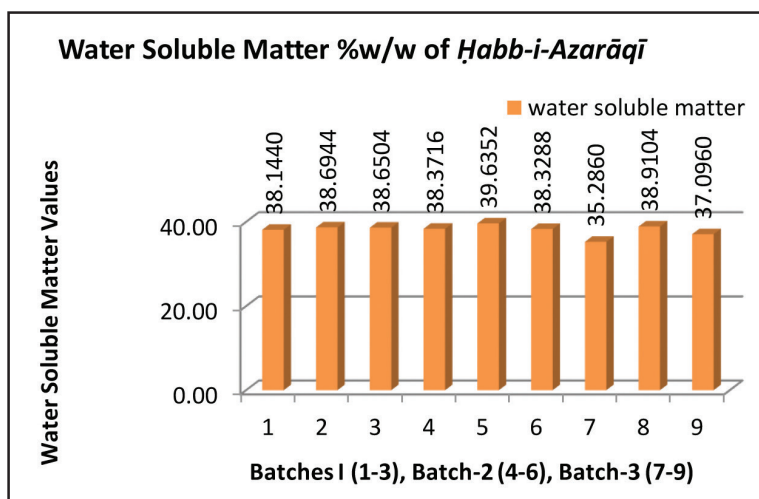


Figure 6: Water Soluble Matter of HA

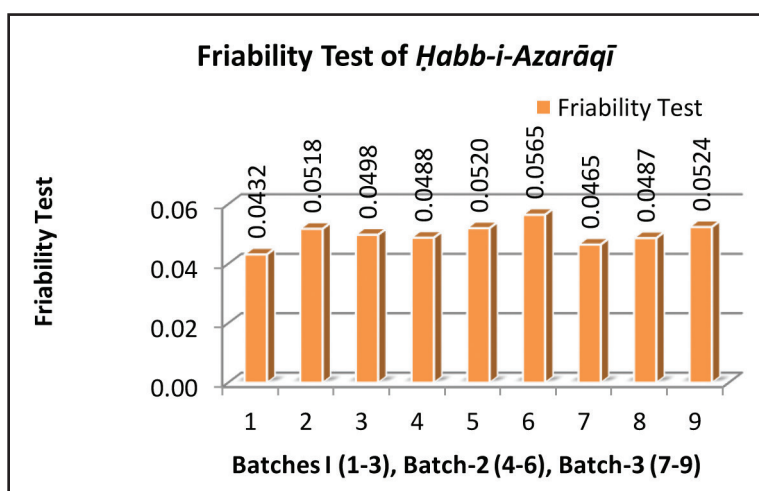


Figure 7: Friability Test of HA

Table 9: Heavy Metal Estimation

S.No.	Parameter	Result	Permissible Limits as per UPI
1.	Lead (Pb)	Not detected	10 ppm
2.	Cadmium(Cd)	Not detected	0.3 ppm
3.	Arsenic (As)	Not detected	3.0 ppm
4.	Mercury (Hg)	Not detected	1.0 ppm

Conclusion

The present study explored an integrated approach in respect of HA that limits the irrational use of the formulation, ceasing quality breach, thereby contributing a step further in validation and authenticity of herbal drugs. *Habb-i-Azarāqī* was studied utilizing modern techniques for ascertaining its quality standard that proved its identity, purity and can be used as standards for future evaluation and reference. The approach of the authors incorporates the use of genuine products and setting an example of proper understanding of standardization and quality control.

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सारांश

समकालीन विश्लेषणात्मक तकनीकों के साथ यूनानी मिश्रण हब्ब-ए-अज़राकी का मानकीकरण और एचपीटीएलसी फिंगरप्रिंटिंग

शबनम अन्जुम आरा, *उज़मा विकार, मोहम्मद जाकिर, मोहम्मद अब्दुल रशीद नाइकोडी,
मुनव्वर हुसैन काज़मी, ताज मोहम्मद

हब्ब-ए-अज़राकी (एचए) एक अत्यधिक गुणकारी यौगिक मिश्रण (टैबलेट रूप में) है जिसका उपयोग पिछले कई दशकों से विभिन्न रोगों जैसे फ़ालिज, (पैरालिसिस), लकवा (चेहरे पर फ़ालिज या बेल्स फ़ालिज), निकरिस (गाउट), वज़-उल-मफ़ासिल (गठिया) के लिए किया जाता है। वर्तमान अध्ययन का उद्देश्य इसकी गुणवत्ता को समझने के लिए आधुनिक विश्लेषणात्मक तकनीकों द्वारा इस औषधि की एचपीटीएलसी फिंगरप्रिंटिंग का मानकीकरण और विकास करना है। तीन अलग-अलग बैचों में इसके इन्द्रियाग्राही मापदंडों, सूक्ष्म अध्ययनों, भौतिक रासायनिक मापदंडों, फीटोकेमिकल जांच, टीएलसी और एचपीटीएलसी प्रोफ़ाइल, एपलाटॉक्सिन, माइक्रोबियल भार और भारी धातु विश्लेषण के लिए मूल्यांकन किया गया। एचए सफलतापूर्वक सभी मापदंडों जैसे कुल राख, एसिड अघुलनशील राख, जल और शराब घुलनशील पदार्थ और सुखाने पर वज़न में कमी के साथ मानकीकृत किया गया। इसके अलावा एचए के टीएलसी और एचपीटीएलसी फिंगरप्रिंटिंग प्रोफ़ाइल का विभिन्न अनुसंधान प्रणाली अर्थात् यूवी 366एनएम, यूवी 254एनएम, आयोडीन वाष्प और एसेल्लिडहाइड सल्फ़यूरिक एसिड के अनावरण के अंतर्गत विकास किया गया और पता लगाया गया। वर्तमान अध्ययन ने इस मिश्रण की प्रमाणिकता सुनिश्चित की और इसकी पहचान और शुद्धता के लिए संदर्भात्मक तथ्यों को प्रस्तुत किया जिससे एक मान्य वैज्ञानिक डेटा में पुष्टि होती है।

शब्दकुंजी: हब्ब-ए-अज़राकी, एचपीटीएलसी, मानकीकरण, यूनानी



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