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CENTRAL COUNCIL FOR RESEARCH IN UNANI MEDICINE
Ministry of AYUSH, Government of India
61-65, Institutional Area, Janakpuri, New Delhi - 110 058
Telephone: +91-11-28521981, 28525982
Email: unanimedicine@gmail.com
Website: www.ccrum.res.in

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Editorial

In the recent years, traditional systems of medicine have received renewed global attention for they open new vistas of research for treatment of many diseases having no satisfactory cure in modern medicine and offer remedies through medicines which are mostly derived from natural sources and generally free from side effects associated with modern medicines. This attention is driven by various factors including the intention of masses to avoid the adverse health effects of modern medicine. This shift has pressed the need for validation of safety and efficacy of traditional systems of medicine on scientific parameters to meet the expectations and address the concerns of the rationale-oriented human generation.

Unani Medicine is one of the oldest and time-tested traditional medical systems practiced in India and various other countries as a recognized system of medicine. The system has well-developed and largest infrastructure for practice, education and research in India. The Central Council for Research in Unani Medicine (CCRUM) as an apex organization of the country is entrusted with the responsibility of conducting research and development activities in Unani Medicine. Over the last four decades of its existence, the CCRUM has been busy in conducting scientific studies and generating evidences for validation of safety and efficacy of medicines which are in medical practice for centuries. The objective has been to explore the rationale behind the principles of treatment, therapeutics and philosophies adopted by the system and convince the modern scientific world in the contemporary rational language they are used to. Through its four key research programmes, namely literary research, survey and cultivation of medicinal plants, drug standardization and clinical research, the CCRUM has been making concerted efforts and contributing significantly to the cause of research and development in Unani Medicine. Vitiligo, sinusitis, filariasis, eczema, malaria, infective hepatitis and asthma are some of the conditions where Unani therapies have earned recognition due to the scientific studies conducted by the council. This has earned the CCRUM well-deserved recognition in the contemporary scientific fraternity and acceptability among diverse populations.

The Hippocratic Journal of Unani Medicine (HJUM) has played a crucial role in the propagation and dissemination of research in the system amongst the scientific fraternity. Along with studies on fundamental and applied aspects of Unani Medicine, the journal publishes recent advances in other related sciences and traditional medicines as well as different streams of medical sciences, which have bearing on validation and scientific interpretation of various concepts and strengths of Unani Medicine.

This issue of HJUM contains six papers. The first paper entitled 'Pharmacological and therapeutic profile of *Kāfūr* (*Cinnamomum camphora* (L.) J. Presl) - a review' covers morphology, pharmacology, ethno-medicinal uses, chemical constituents and proven pharmacological activities of camphor and various parts of the camphor plant. In the second paper, *Nisyān* (amnesia) has been elaborated along with details about its types, causes and treatment in Unani Medicine as well as conventional medicine. The third paper provides information on the management of *Fālij* (paralysis) in Unani Medicine and details the pharmacological basis of the treatment along with *Uṣūl-ī-'Ilāj* of various phases of treatment delineating the Unani mechanism of action. The fourth paper is based on an ethnobotonical study on floristic diversity of Unani medicinal plants in Kalakadu Mundanthurai Tiger Reserve Forest, Tirunelveli District, Tamil Nadu, India. The fifth paper presents phytochemical analysis of *Gymnema sylvestre* L. and identification of bio-inhibitors linked to diabetes and oxidative stress using HPTLC-MS bioautography, whereas the last paper presents data of a clinical study conducted to validate the safety and efficacy of Unani pharmacopoeial formulation *'Araq-i-'Ajīb* in *Sudā'* (headache).

While we present this issue, we extend our appreciation and acknowledgement to the authors and reviewers for their valuable contribution in bringing out this publication. We are sure that the support and contribution of scientific fraternity shall continue with us and together we will achieve the highest standard of quality for this journal.

Prof. Asim Ali Khan
Editor-in-Chief

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Pharmacological and Therapeutic Profile of *Kāfūr* (*Cinnamomum camphora* (L.) J. Presl) – A Review

*[1]Khurshid Alam,
[2]Mohammad Nawab
and
[3]Munawwar Husain Kazmi

[1]Postgraduate Research Scholar, Department of Moalajat (Medicine), Central Research Institute of Unani Medicine, Hyderabad

[2]Reader, Department of Moalajat (Medicine), Central Research Institute of Unani Medicine, Hyderabad

[3]Professor, Department of Ilmul Advia (Pharmacology), Central Research Institute of Unani Medicine, Hyderabad

Abstract

Kāfūr (camphor) has been in use as a remedy for various ailments since a long time. It is a natural product obtained through steam distillation and purification by sublimation of the wood of the tree *Cinnamomum camphora* (L.) J. Presl. It is used as *Dāfi'-i-Ta'affun* (antiseptic), *Musakkin-i-Alam* (analgesic), *Muḥammir* (rubefacient) and nasal decongestant. This review paper covers morphology, pharmacology, ethno-medicinal uses, chemical constituents and proven pharmacological activities of camphor and various parts of the camphor plant. The main aim of the present work is to provide an overview of therapeutic uses, mode of administration, dosage forms and toxicological aspect of camphor in order to assess its scope to treat different clinical symptoms in clinical practice. This paper includes all the information mentioned in Unani classical literature and scientific publications based on the outcomes of the studies carried out as experimental and clinical studies in the recent past. The studies demonstrated its activities as anthelmintic, antibacterial, anti-inflammatory, antifungal, anticancer and hepatoprotective efficacy in animal models. In this review, it is concluded that camphor as a medicinal product may be used in clinical practice as *Dāfi'-i-Ta'affun* (antiseptic), *Musakkin-i-Alam* (analgesic), *Muḥammir* (rubefacient), *Mukhrij-i-Janīn* (abortifacient) and *Muqawwi-i-Bāh* (aphrodisiac) to treat various clinical symptoms and diseases. This plant may be a resource material for the development of a newer drug and a viable option for the treatment of life threatening diseases.

Keywords: Analgesic, Camphor, *Cinnamomum camphora*, *Kāfūr*, Unani Medicine

Introduction

Kāfūr (camphor) has been used traditionally for many years as a remedy for relief of pain, inflammation and skin irritation. *Kāfūr* is a natural white crystalline substance obtained through steam distillation, purification and sublimation of wood, twigs and barks of *Cinnamomum camphora* (L.) J.Presl, a green tree with shiny alternate leaves mainly found in Japan and China and cultivated in India with a height of 50-60 feet (Khare, 2007). *Kāfūr* (camphor) has been used for various therapeutic purposes as analgesic, antiseptic, antispasmodic, antipruritic, anti-inflammatory, anti-infective, expectorant and nasal decongestant (Ghani, YNM; Baghdadi, 2005). It is used as one of the ingredients in many formulations such as balms, oils, liniments and creams. There are many scientific reports which have reported that camphor has anticancer, anthelmintic, antibacterial, antifungal, and hepatoprotective activities.

Medicinal plants are the main source of development of newer drugs. They are used in raw form in Indian traditional and alternative medicine as therapeutics

*Author for Correspondence; Email: khursheed6459@gmail.com

for treatment of diseases. Camphor, a plant-origin medicine, had attracted the attention of scientists, researchers and academicians in the past. There is a long list of scientific studies focused on its pharmacology and pharmacokinetics conducted on its different parts such as bark, wood, leaves, twigs, etc. The study of leave extract has shown protective effect against DNA damage as biochemical changes in mice. The leave extracts also showed anthelmintic, anti-cancer and anti-inflammatory activities in animal studies. This medicine has been used as an emergency medicine in allergic conditions (Ansari, YNM).

Unani classical literature describes identification, morphological characteristics, indications, dosage forms and side effects of camphor and parts of its plant. In this review, the main aim is to compile the information documented as empirical evidence in rich literature of Unani Medicine and to report the outcomes of experimental and clinical studies related to this medicine conducted in the recent past.

Taxonomy

Kingdom	Plantae
Order	Laurales
Family	Lauraceae
Genus	*Cinnamomum*
Species	*Camphora*
Common name	*Kapūr/ Kāfūr/ Camphor*

(Garg & Jain, 2017; Nadkarni, 2010)

Vernacular Names

Table 1: Vernacular Names of Camphor

English	Camphor tree (Khare, 2007)
Hindi	*Kapūr* (Nadkarni, 2010)
Urdu	*Kāfūr* (Nadkarni, 2010)
Arabic	*Kāfūr* (Tariq, 2010)
Sanskrit	*Karpoor* (Nadkarni, 2010)
Tamil	*Karpooram* (Garg & Jain, 2017)
Telugu	*Karpooram* (Chopra *et al.*, 2009)
Malayalam	*Karpooram* (Nadkarni, 2010)

Morphological Characteristics

Camphor tree is native to China, India, Mongolia, Taiwan and Japan. (Khare, 2007; Nadkarni, 2010). Camphor tree is an evergreen tree or shrub (Kirtikar & Basu, 2012). Its leaves are opposite or alternate usually 3-nerved, long petiolate, ovate or oblong, or lanceolate-oblong, 5-12.5 cm long, 2.5-5 cm broad. Its flowers are small, hermaphrodite or by abortion polygamy. The females are usually the largest and sometimes with fewer parts. Stamens are nine, perfect, or by abortion fewer. Ovary sessile, free from the perianth, narrowed into the style, stigma discoid or obscurely 3-lobed (Kirtikar & Basu, 2012). Fruit is a berry, resting on the spreading more or less enlarged perianth, the segments of which are wholly or partly deciduous, less often persistent. Seed found with thin testa (Kirtikar & Basu, 2012).

Parts Used as Therapeutics

In Unani classical literature, it is mentioned that various parts of camphor tree are used therapeutically in different dosage forms to treat various health problems. Natural camphor has been used internally in the treatment of hysteria, epilepsy and chorea. For external application, camphor is used as one of the constituents of oils, liniments, balms and ointments. Moreover, wood, leaves, barks and twigs are used medicinally in Indian systems of medicine. The essential oils which can be obtained by distillation of the chipped branches, trunk, leaves, twigs and wood of the tree are also used for therapeutic purposes (Singh & Jawaid, 2012).

Varieties of Camphor

The camphor is obtained naturally or synthesized artificially. The natural camphor is D-camphor (its dextrorotatory form) whereas the synthetic one is L-camphor (laevorotatory form) (Zuccarini, 2009). In traditional medicine, camphor is of the following three types:

1. Formosa camphor (Nadkarni, 2010)
2. Borneo or Barus camphor, known in India as Bhimseni Kapur (Nadkarni, 2010)
3. Blumea or Ngai camphor (Nadkarni, 2010)

Of them, Bhimseni camphor is considered the best (Nadkarni, 2010).

Mizāj (Temperament)

In Unani literature, temperament of camphor is mentioned as *Bārid 3° Yābis 3°* (cold *3°* and dry *3°*) (Baghdadi, 2005; Ansari YNM; Ghani YNM; Ibn Rushd, 1987).

Therapeutic Dosage

Natural camphor has been used in the dosage of 1 *ratti* (121.5 mg) to 6 *ratti* (729mg) for local application (Ghani, YNM). For internal use, it is recommended in the dosage of 3 grain (194.37 mg) (Ghani, YNM). Its essential oils are used for inhalation purpose in the dosage of 5 drops (Ghani, YNM). FDA (Food and Drug Administration, USA) has approved that the concentration of camphor should be in the range of 3% to 11% in any of its topical dosage forms (Garg & Jain, 2017; Hamidpour *et al.,* 2013).

Maḍarrāt (Adverse Effects)

Camphor is not suitable for persons having cold temperament, because its temperament is cold3^0 and dry3^0. As per literature, it adversely affects the functions of kidneys and urinary bladder and sexual desire in doses higher than those recommended (Baghdadi, 2005; Ghani, YNM; Hakim, 2002).

Muṣlih (Corrective)

To reduce the already known side effects of this drug, *Zaʿfrān* (*Crocus sativus* L.), *Mushk* (*Moschus)* and Elva (*Aloe vera* (L.) Burm.f.) may be added in the formulation to be used for therapeutic purposes (Ansari, YNM; Hakim, 2002).

Badal (Substitute)

In case camphor is not available, its alternative (substitute) may be used. Unani physicians have already identified the single drug *Ṭabāshīr* (*Bambusa arundinacea* Willd.) and *Ṣandal Safaid* (*Santalum album* L.) as substitutes for camphor (Ansari, YNM; Kabiruddin, 2000; Hakim, 2002).

Afʿāl (Pharmacological Actions)

Table 2: Pharmacological Actions of Different Parts of Camphor

S.No.	Part Used	Indications
1	Wood	Analgesic, antispasmodic, odontalgic, rubefacient and stimulant. Infusion is used as an inhalant in the treatment of common cold and diseases of the lungs (Singh & Jawaid, 2012)
2	Leaves	Analgesic, antispasmodic, odontalgic, rubefacient and stimulant. Infusion is used as an inhalant in the treatment of colds and diseases of the lungs (Singh & Jawaid, 2012).
3	Essential oil	Anthelmintic, antirheumatic, antispasmodic, cardiotonic, carminative, diaphoretic, sedative and tonic. It is used externally in liniments for treating joint and muscle pains, balms for chilblains, chapped lips, cold sores, skin diseases, etc., and as an inhalant for bronchial congestion. (Singh & Jawaid, 2012)

Pharmacological Actions of Camphor

Table 3: Pharmacological Actions of Camphor

S. No.	Actions	Mode of Administration	Ethno-botanical reference	Unani reference
1	*Mufarriḥ* (exhilarant)	Internal	-	[2][17]
2	*Ḥābis-i-Dam* (haemostyptic)	External & Internal	-	[2]
3	*Qābiḍ* (astringent)	Internal	-	[2][8][10]
4	*Mufarriḥ-i-Qalb-wa-Dimāgh* (exhilarant to heart and brain)	Internal	-	[2][3]8][10]
5	*Munawwim* (hypnotic)	External & Internal	[1][11]	[2]
6	*Muḥarrik-i-Jild-wa-Qalb* (stimulant of skin and cardiac stimulant)	External & Internal	[5][6][13]	-
7	*Musakkin-i-Alam* (analgesic)	External	[1][5][6] [13]	[7][8][10]
8	*Musakkin* (anodyne)	External	[7][11]	[8]
9	*Mukhrij-i-Janīn* (abortifacient)	Internal	[18][29]	-
10	*Qātil-i-Dīdān* (anthelmintic)	Internal	[5][18]	-
11	*Muqawwī-i-Bāh* (aphrodisiac) / *Qāṭi'-i-Bāh* (antiaphrodisiac)	Internal	[5][7][18]	[2][3][8] [15]
12	*Dāfi'-i-Jarāthīm* (antibacterial)	External	[1]	-
13	*Dāfi'-i-Ta'affun* (antiseptic)	External	[6][7][18]	[8][10][15]
14	Antirheumatic	External & Internal	[18]	-
15	*Dāfi'-i-Tashannuj* (antispasmodic)	Internal	[5][6][7] [18]	[10]
16	Antitussive	External & Internal	[13][18]	
17	*Muqawwī-i-Qalb* (cardiotonic)	Internal	[18]	-
18	*Kāsir-i-Riyāḥ* (carminative)	Internal	[7][18]	[10]
19	CNS-Depressant, CNS-Stimulant	Internal	[1][18]	-
20	Convulsant	External & Internal	[18]	-
21	*Dāfi'-i-Mukharrish* (counterirritant)	External	[5][6][13] [18]	[2]8][10] [17]
22	Decongestant	External	[6][18]	-

S. No.	Actions	Mode of Administration	Ethno-botanical reference	Unani reference
23	*Mu'arriq* (diaphoretic)	Internal	[6][7][18]	[8][10]
24	*Muqī* (emetic)	Internal	[18]	
25	*Munaffith-i-Balgham* (expectorant)	Internal	[1][7][18]	[8]
26	*Ṭilā'* (liniment)	External	[18]	-
27	Fungicide	External	[1][5][18]	
28	Respiratory stimulant	External & Internal	[5][6][13] [18]	-
29	*Muḥammir* (rubefacient)	External	[1][18]	[8][10]
30	*Musakkin-i-Dimāgh* (sedative)	Internal	[1][6][7] [18]	-
31	*Muḥarrik* (stimulant)	External & Internal	[1][7][18]	[8][10]
32	*Waja' al-Asnān* (odontalgic)	External	[6]	[8]
33	*Mukhaddir* (anaesthetic)	External	[5]	[2][8][10]
35	*Dāfi'-i-Ḥumma* (antipyretic), *Muqawwī-i-Mi'da* (stomachic)	Internal	[5]	[10]
36	*Tiryāq* (antidote)	Internal	[7]	[10]
38	Antipruritic	External	[6][13]	-

1- (Khare, 2007), 2- (Ghani, YNM), 3- (Baghdadi, 2005), 5- (Garg & Jain, 2017), 6- (Singh & Jawaid, 2012), 7- (Nadkarni, 2010), 8- (Kabiruddin, 2000), 10- (Tariq, 2010), 11- (Chopra *et al.*, 2009), 13- (Zuccarini, 2009), 15- (Ibn Rushd, 1987), 17- (Hakim, 2002), 18- (Duke *et al.*, 2002).

Therapeutic Uses of Camphor

Cinnamomum camphora is a plant that contains volatile oil comprising camphor, safrol, linalool, eugenol, etc. The oil has antimicrobial activity against many pathogens. It acts as reflex expectorant and is helpful in respiration as well as circulation. Topically, it is used as a rubefacient and mild analgesic (Singh & Jawaid, 2012; Maridass & Victor, 2008). In Ayurvedic medicine, it is used against a wide spectrum of diseases like bronchitis, cold, congestion, diarrhoea, dysentery, oedema, flu, gas, metabolic and heart strengthening, hiccups, indigestion, liver problems, menorrhagia, melancholy, muscle tension, nausea and vomiting. It assists uterine contractions during labour and menstrual pain from low metabolic function. For external applications, it is used for relieving headaches and pain. In Unani Medicine, it is used as a cephalic tonic and cardiac stimulant and for treatment of cough (Singh & Jawaid, 2012).

Table 4: Therapeutic Uses of Camphor

S. No.	Therapeutic Uses	Mode of Administration	Ethno-botanical References	Unani References
1.	*Ishāl Mi'wī Ṣafrāwī* (bilious enterorrhoea)	Internal	[1][5][6]	[2][3][8][15]
2.	*Tadarrun Ri'wī* (pulmonary tuberculosis)	Inhalation	-	[2][3]
3.	*Ru'āf* (epistaxis)	Inhalation	[5][6]	[3][8][10]
4.	*Waram-i-Jild wa Ābla* (inflammation of skin and vesicles)	External	-	[3]
5.	*Ṣudā' Ḥārr* (headache)	External & Internal	[6][7]	[3]
6.	*Āshob-i-Chashm* (acute conjunctivitis)	Internal	-	[2][3][8][10]
7.	*Ikhtilāj-i-Qalb* (fasciculation of heart), *Bakhr al-Fam*	Internal	-	[2]
8.	*Ikhtināq al-Raḥim* (hysteria)	Internal	[1]	[2]
9.	*Ḥummā* (fever)	Internal	[7]	[2][8]
10.	Sore throat	Internal	[5][7]	-
11.	*Dummal* (boils)	External	[7]	-
12.	Arrhythmia	Internal	[18]	-
13.	*Ḍīq al-Nafas* (asthma)	Internal	[18]	[2]
14.	*Raḍḍ* (bruises)	External	[6][18]	-
15.	*Ḥarq* (burn)	External	[18]	-
16.	*Saraṭan al-Kabid* (liver cancer), *Saraṭān al-Anf* (nose cancer), *Saraṭān al-Ṭiḥāl* (spleen cancer)	Internal	[5][18]	-
17.	Cardiopathy	Internal	[18]	-
18.	*Nazla–o-Zukām* (catarrh)	Inhalation	[5][18]	[8]
19.	*Intifākh al-Aṣābi'* (chilblain)	External	[18]	-
20.	*Hayḍa Wabā'ī* (cholera)	Internal	[18]	[8]
21.	Chorea	Internal	[1][18]	-
22.	*Su'āl-o-Surfa* (cough), *Fasād al-Haḍm* (dyspepsia)	Internal	[5][18]	[2][8]
23.	*Ṣar'* (epilepsy)	Internal	[1][18]	-

S. No.	Therapeutic Uses	Mode of Administration	Ethno-botanical References	Unani References
24.	*Niqris* (gout), *Bawāsīr* (hemorrhoids), *Namla* (herpes), *Ḍaght al-Dam Qawī* (high blood pressure), *'Ufūnat* (infection), Neuralgia, *Waja'* (pain), *Dhāt al-Ri'a* (pneumonia), *Rabw Rīḥī* (emphysema), *Ishāl* (diarrhea), *Hadhayān* (delirium), *Qūlanj* (colic)	External	[18]	[2]
25.	*Waram* (inflammation)	External	[5][18]	[2] [3][15]
26.	*Sahr* (insomnia), *Fālij* (paralysis), *Tashannuj* (convulsion), *Imtilā'* (congestion)	External & Internal	[18]	-
27.	*Ḥikka* (itch)	External	[6][13] [18]	[2]
28.	*Waja' al-Mafāṣil* (polyarthritis), *Waja' al-Asnān* (odontolgia / toothache)	External	[5]	[8][10]
29.	*Dhāt al-Janb* (pleurisy)	External	-	[2][8][10] [17]
30.	*Nafkh-i-Shikam* (flatulence)	Internal	[6]	[8]
31.	*Tap-i-Diq*	Internal	-	[2][8][17]

1- (Khare, 2007), 2- (Ghani, YNM), 3- (Baghdadi, 2005), 5- (Garg & Jain, 2017), 6- (Singh & Jawaid, 2012), 7- (Nadkarni, 2010), 8- (Kabiruddin, 2000), 10- (Tariq, 2010), 13- (Zuccarini, 2009), 15- (Ibn Rushd, 1987), 17- (Hakim, 2002), 18- (Duke *et al.*, 2002)

Chemical Compositions

Chemically, camphor is a cyclic monoterpene ketone. Its IUPAC name is 1, 7, 7-trimethylbicyclo (2. 2.1) heptan-2-one (camphor, 2019).

a. Leaf essential oil

A total of 68 compounds were identified from the hydro-distillated leaf oil. The main constituents were linalool (87.3%), β-caryophyllene (2.1%), camphene hydrate (1.5%), β-selinene (0.8%), camphor (0.7%) and hotrienol (0.7%) (Chen Hai Ping *et al.*, 2014; Rastogi & Mehrotra, 1999; Ho Chen-Lung *et al.*, 2009).

b. Flower essential oil

A total of 77 compounds were identified from the hydro-distillated flower oil. The main components were linalool (72.4%), β-caryophyllene (5.3%), β-selinene (2.9%), α-caryophyllene (1.8%), camphene hydrate (1.8%), camphor (1.7%), α-selinene (1.4%) and hotrienol (1.3%).%) (Chen Hai Ping *et al.*, 2014; Rastogi & Mehrotra, 1999; Ho Chen-Lung *et al.*, 2009).

c. Twig essential oil

Hydro-distillated essential oil of camphor tree twigs was composed of 83 compounds. Linalool (40.0%), camphor (33.5%), eugennol (3.6%), 1-8-cineole (3.0%), α-terpineol (2.1%), β-caryophyllene (1.5%), limonene (1.3%) and α-pinene (1.1%) were the main components (Chen Hai Ping *et al.,* 2014; Rastogi & Mehrotra, 1999; Ho Chen-Lung *et al.*, 2009).

Safety and Toxicity of Camphor

In an animal study, the natural form of camphor was nontoxic at 100mg/kg body weight, but synthetic camphor showed different kinds of toxic and behavioral effects, such as body jerks and hunched postures, at the same dose (Zuccarini, 2009). In another study on rats, natural camphor showed signs of toxicity, such as convulsion and piloerection, at an oral dose of 64 mg/kg body weight. Camphor is safe and nontoxic in humans at the maximum recommended therapeutic dose. Adult lethal dose of camphor has been reported to be 5gm to 20gm (Khare, 2007). Camphor and its formulations are easily available in the market and widely used as a home remedy for adults as well as children, but due to lack of information regarding its dosage, camphor intoxication is frequent (Zuccarini, 2009).

Drug-Drug Interaction

Drug-drug interaction was already known to Unani physicians. In Unani classical literature, camphor has been used in many formulations as one of the ingredients. This indicates that camphor may have synergic action with other drugs present in the formulations (Singh & Jawaid, 2012). There are several formulations in Unani pharmacopoeia that have camphor as one of the ingredients such as:

1. *Ḥabb-i-Kattha* (Anonymous, 2016b)
2. *Qurṣ-i-Kāfūr Mumsik* (Anonymous, 2007)
3. *Ḥabb Qābiḍ* (Anonymous, 2007)
4. *Qurṣ-i-Saraṭān Kāfūrī* (Anonymous, 2007)

5. *Jawārish-i-Kāfūr* (Anonymous, 2007)
6. *Ḥalwā-i-Supāripāk* (Anonymous, 2007)
7. *Marham-i-Safeda Kāfūrī* (Anonymous, 2007)
8. *Qurṣ-i-Kāfūr* (Anonymous, 2008)
9. *Marham-i-Kāfūr* (Anonymous, 2008)
10. *Ḥabb-i-Pechish* (Anonymous, 2008)
11. *Rawghan-i-Benazīr* (Anonymous, 2011)
12. *Ṭilā' Nishāṭ Angez* (Anonymous, 2011)
13. *Sanūn Muqawwī-i-Dandān* (Anonymous, 2011)
14. *Zarūr Qulā'* (Anonymous, 2011)
15. *'Araq 'Ajīb* (Kabiruddin, 2000; Anonymous, 2009)
16. *Jawārish-i-Kāfūr* (Anonymous, 2016a)
17. *Qurṣ-i-Ṭabāshīr Kāfūrī* (Kabiruddin, 2000)
18. *Tiryāq A'zam* (*'Araq 'Ajīb*) (Kabiruddin, 2000)
19. *Qurṣ-i-Saraṭān Kāfūrī* (Kabiruddin, 2000)

In a study, administration of D-camphor combining with an extract from fresh crataegus berries demonstrated ameliorating cardiac performances. This signifies that camphor has synergistic actions with crataegus berries (Singh & Jawaid, 2012).

Pharmacological Studies / Scientific Reports

1. Anthelmintic Activity

Helmintic infestations are among the most common clinical conditions in humans. Unhygienic lifestyle, contaminated foods and water and poverty are responsible for the occurrence of this medical condition leading to the development of diseases like anaemia, eosinophilia and pneumonia. In Unani Medicine, natural camphor compound has been used therapeutically for treating worm infestation. In a study, aqueous extract of *Cinnamomum camphora* leaves exhibited anthelmintic activity in dose dependent manner showing max efficacy at 50 mg/ml concentration for 3 types of worms, i.e. earthworms (Pheretima posthuma), tapeworms (Raillietina spiralis) and roundworms (Ascaridia galli) (Singh & Jawaid, 2012; Haque *et al.*, 2011).

2. Antifertility Activity

In an in-vitro study, camphor treated samples showed a decrease in sperm motility and sperm viability which counts for decreasing effectiveness of fertilization. These results demonstrated that camphor may act as a contraceptive. The hypothesis behind this result explains that a decrease of sperm motility and sperm viability may be due to a decrease in fructose level or denaturation of protein and cholesterol which are the energy source for sperm motility (Singh & Jawaid, 2012; Jadhav *et al.*, 2010).

3. Abortifacient Activity

In an animal study conducted by Sabah A. Linjawi, the results showed that camphor had effects on the female rat reproductive system resulting in significant structural changes of the uterus of pregnant rats. It suggested that camphor has a negative influence on the reproductive health of animals which might cause abortion of rat on high dose of camphor. In the Unani literature, one of its actions has been described as abortifacient (Singh & Jawaid, 2012; Linjawi, 2009).

4. Cerebral Cortex Activity

Camphor essential oil induces seizure like activity and occasional clonic limb convulsions have been demonstrated in an animal study conducted by Grbic, *et al.* (2008). It is confirmed in this study that camphor essential oil has convulsant properties even in anaesthetic rats. This study suggests that camphor essential oil has a neurotoxic effect. There are several reports of severe pediatric toxicity resulting from exposure to a small amount of camphor containing products. It indicates that internal use of camphor should be given within the recommended dose (Singh & Jawaid, 2012; Grbic *et al.,* 2008).

5. Effects of Camphor on Sexual Behaviors

In Unani classical literature, camphor has been described for both sexual behavior attenuating and enhancing properties. In an animal study, the effect on sexual behaviors in male rats had been examined and the findings indicated that at a particular dose camphor had sexual desire and sexual performance enhancing properties which might be due to its effects on serum testosterone level or modulation of the sympathetic nervous system (Singh & Jawaid, 2012; Jamshidzadeh *et al.,* 2006).

6. Anti-inflammatory and Antioxidative Activity

In Unani Medicine, camphor has been prescribed for treatment of inflammatory diseases, such as rheumatism, sprain and muscle pain. Literature describes that

camphor is a good anti inflammatory agent. In an *in-vitro* study, leave extract of *Cinnamomum camphora* demonstrated anti-inflammatory and antioxidative activities (Singh & Jawaid, 2012; Lee *et al.*, 2005). Essential oils isolated from *Cinnamomum* species also demonstrated antimicrobial and anti-inflammatory activity. It was used for treating wounds, fever, intestinal worms, headache and menstrual problems (Maridass & Victor, 2008).

7. Immunoglobulin E-suppressing Activity

Immunoglobulin (IgE) has an important role in allergic diseases. In an *in-vitro* study, the methanolic extract of *Cinnamomum camphora* reduced the amount of IgE secreted by human myeloma U266 cells. The finding of this study suggested that the extract of *Cinnamomum camphora* has potential as an anti-allergic agent (Singh & Jawaid, 2012; Tanabe *et al.,* 2011).

8. Antifungal Activity

Ho Chen-Lung *et al.* conducted an *in-vitro* study which demonstrated that essential oil from the leaves, flowers and twigs of *Cinnamomum camphora* have antifungal activities. This study further showed that the leaf oil had the best antifungal activity (Ho Chen-Lung *et al.,* 2009).

9. Hepatoprotective Activity

Camphor has been used as a hepatoprotective agent in various liver disorders. In an animal study conducted by Johari *et al.* camphor has been demonstrated to have a stimulating effect on liver enzyme. The finding of this study suggested that using camphor in higher dosage leads to significant increase in concentration of liver enzyme (Johari *et al.,* 2015). Other scientific studies revealed that camphor oil possess mycostatic activity against Aspergillus flavus at 4000 ppm (Ray *et al.,* 2004; Mishra *et al.,* 1991).

Conclusion

Camphor has been widely used in Unani Medicine as a safe and effective medicine. It belongs to 3rd grade (3°) of the groups of drugs classified by Unani physicians and is considered as fast acting emergency medicine. Scientific studies demonstrated its activities as anthelmintic, anti-bacterial, anti-inflammatory, analgesic and anti-cancer. These findings have widened the scope of its application for therapeutic purposes in clinical practice. In the present health scenario, search for newer medicines is going on. The leads obtained from these studies may be helpful in the development of newer and better anti-cancer, anti-bacterial and hepatoprotective medicines. Rigorous experimental studies and clinical trials may be designed to generate evidences for human use. This review

may support and provide information to the researchers in the search for the development of a new drug. It is concluded from this study that camphor may be a viable option for the treatment of life threatening diseases.

Conflict of Interest

Authors have no conflict of interest in publication of this review paper.

Authors' Contribution

Dr. Khurshid Alam collected information from literature and drafted the manuscript, Dr. Mohammad Nawab edited the manuscript and Prof. Munawwar Husain Kazmi vetted it.

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सारांश

काफूर (*सिनमोमम कैम्फोरा* (एल.) जे. प्रेस्ल) की औषधीय एवं चिकित्सीय रूपरेखा – एक समीक्षा

***खुरशीद आलम, मोहम्मद नवाब, मुनव्वर हुसैन काज़मी**

काफूर (*कपूर*) लंबे समय से विभिन्न रोगों के उपचार में उपयोग किया जाता रहा है। यह एक प्राकृतिक उत्पाद है जिसे *सिनमोमम कैम्फोरा* (एल.) जे. प्रेस्ल के पेड़ की लकड़ी के उत्सादन द्वारा भाप आसवन और शुद्धिकरण के माध्यम से तैयार किया जाता है। इसका उपयोग *दाफ़े–ए–तअफ्फुन* (एंटीसेप्टिक), *मुसक्किन–ए–अलम* (एनाल्जेसिक), *मुहम्मिर* (रुबीफेसिएन्ट) और नाक की सर्दी–खांसी की दवा के रूप में किया जाता है। इस समीक्षा पत्र में *काफूर* के पौधे और उसके विभिन्न भागों के आकृति विज्ञान, भेषजगुण विज्ञान, मानवजाति–चिकित्सीय उपयोग, रासायनिक घटक और औषधीय गतिविधियों का उल्लेख किया गया है। इस कार्य का मुख्य उद्देश्य नैदानिक अभ्यास में विभिन्न नैदानिक लक्षणों का उपचार करने के लिए *काफूर* की सम्भावनाओं का आकलन करने हेतु इसके चिकित्सीय उपयोगों, औषधि देने की विधि, खुराक के रूप और विषैले पहलू का अवलोकन करना है। इस पत्र में यूनानी क्लासिकल साहित्य में मौजूद हाल के दिनों में प्रयोगात्मक और नैदानिक अध्ययन के रूप में किए गए अध्ययनों के परिणामों पर आधारित वैज्ञानिक प्रकाशनों में उल्लिखित सभी जानकारी सम्मिलित है। अध्ययनों में पशु मॉडल में एंटीहेल्मिंटिक, जीवाणुरोधी, एंटी–इन्फ्लामेटरी, फंगसरोधी, कैंसररोधी और हेपेटोप्रोटेक्टिव प्रभावकारिता के रूप में इसकी गतिविधियों को दर्शाया है। इस समीक्षा में यह निष्कर्ष निकाला गया है कि *काफूर* एक औषधीय उत्पाद के रूप में नैदानिक अभ्यास में विभिन्न नैदानिक लक्षणों और रोगों का उपचार करने के लिए *दाफ़े–ए–तअफ़्फुन* (एंटीसेप्टिक), *मुसक्किन–ए–अलम* (एनाल्जेसिक), *मुहम्मिर* (रुबीफेसिएन्ट), *मुख़रीज–ए–जनीन* (गर्भस्रावक) और *मुक़व्वी–ए–बाह* (कामोत्तेजक) के तौर पर उपयोग किया जा सकता है। यह पौधा नई औषधि के विकास के लिए एक संसाधन सामग्री हो सकता है और जानलेवा रोगों के उपचार हेतु एक व्यवहार्य विकल्प बन सकता है।

शब्दकुंजी: एनाल्जेसिक, कपूर, *सिनमोमम कैम्फोरा,* काफूर, यूनानी चिकित्सा

Nisyān (Amnesia): A Review

*[1]Anju,
[1]Rasikh Javaid
and
[2]Ghazala Javed

[1]Research Associate, Central Council for Research in Unani Medicine, New Delhi

[2]Research Officer (Unani) Scientist-IV, Central Council for Research in Unani Medicine, New Delhi

Abstract

Nisyān (amnesia) has become a major medical and social issue around the world. It is common in the ageing population. It is a state of forgetfulness or loss of memory. It can be defined as a special case of memory loss that is distinct from ordinary forgetting. According to Unani classical literature, *Nisyān* occurs due to disturbances in *Quwwat Ḥāfiza* (faculty of memory), *Quwwat-i-Fikr* (power of thinking) and *Quwwat-i-Takhayyul* (power of imagination) owing to *Sū'-i-Mizāj Bārid Raṭb* (cold and moist imbalanced temperament), *Sū'-i-Mizāj Bārid Yābis* (cold and dry imbalanced temperament) and *Sū'-i-Mizāj Ḥārr Yābis* (hot and dry imbalanced temperament) of brain. The types of *Nisyān* are *Nisyān Bārid Raṭb*, *Nisyān Bārid Yābis* and *Nisyān Ḥārr Yābis* as mentioned in the literature of Unani Medicine. The causative factors of *Nisyān* are head injury, brain trauma or brain surgery and it can be precipitated by alcohol consumption, drug use, or due to the effects of a stroke. Single as well as compound Unani formulations have been used to improve memory, attention, and related cognitive functions. In this review paper, *Nisyān* has been elaborated along with details about its types, causes and treatment in Unani Medicine and conventional medicine.

Keywords: Amnesia, Loss of memory, *Nisyān*, Unani Medicine

Introduction

Nisyān is defined a state of forgetfulness as per Unani classical literature and its possible English equivalent is amnesia (Anonymous, 2012). The word 'amnesia' comes from two Greek words (prefix 'a' meaning 'without' and 'mnemonic' meaning 'memory') which mean 'without memory'. It is a deficit in memory or loss of memory caused by brain damage, disease or psychological trauma (Gazzaniga *et al.*, 2009). Najibuddin Samarqandi, a renowned Unani physician, stated that *Nisyān* is a disorder which occurs due to disturbances among the three *Quwā* (faculties), viz. *Quwwat Ḥāfiza* (faculty of memory), *Quwwat-i-Fikr* (power of thinking) and *Quwwat-i-Takhayyul* (power of imagination).

The memory can be either wholly or partially lost according to the extent of brain damage. Amnesia can also be caused temporarily due to the use of various sedatives and hypnotic drugs (Lerner & Lerner, 2008).

Aetiology and Pathology of *Nisyān*

Nisyān is a disease which is caused by the loss of function in *Quwwat Ḥāfiza* (faculty of memory) and impairment of *Quwwat-i-Fikr* (power of thinking) as well as *Quwwat-i-Takhayyul* (power of imagination).

*Author for Correspondence; Email: 619ccrum@gmail.com

There are three types of *Quwā* (faculties) on which physical condition of the body depends totally, viz. *Quwwat Ḥaywāniyya*, *Quwwat Nafsāniyya* and *Quwwat Ṭabīʻiyya* (Masihi, 2008). *Quwwat Ṭabīʻiyya* is responsible for maintaining the balance of *Ruṭūbat Gharīziyya* and *Ḥarārat Gharīziyya* and production of *Akhlāṭ* (humours) in purest form. When *Quwwat Nafsāniyya* becomes weak, *Nisyān* (amnesia) and other neurological associated problems such as Alzheimer's disease and Parkinson's disease develop. *Quwwat Ḥaywāniyya* maintains blood circulation and helps in protecting body from free radicals which are responsible to initiate the process of ageing (Alam *et al.*, 2015) (Figure 1).

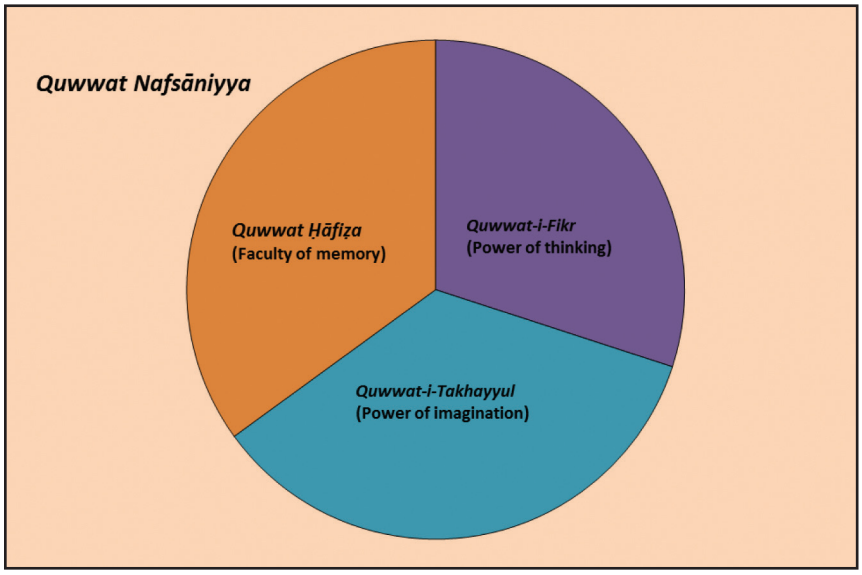

Fig. 1: Illustration of the Types of *Quwwat Nafsāniyya*

Predisposing Factors Responsible for *Nisyān*

The predisposing factors of *Nisyān* (amnesia) are excessive intake of *Balgham* (phlegm) producing substances (milk, vegetables, ice water, etc.), excessive use of sour food items (tamarind, pickles, curds, etc.), *Amrāḍ Muzmina* (chronic diseases), e.g. *Saraṭān* (*cancer*), *Sill-wa-Diqq* (tuberculosis), *Dhayābīṭus Sukkarī* (diabetes mellitus), *Amrāḍ-i-Aʻṣāb* (*Fālij* (paralysis), *Istirkhā'* (muscular dystrophy), *Ṣarʻ* (epilepsy), *Sarsām* (meningitis), malnourishment, hereditary causes, psychological causes, insufficient sleep, excessive consumption of alcohol, domination of implastic phlegm, *Ruṭūbat* in brain as well as *Bārid* temperament of whole body (Alam *et al.*, 2015; Arzani, YNM).

Types of *Nisyān* (Amnesia)

According to Unani classical literature, *Nisyān* is of three types: (1) *Nisyān Bārid Raṭb,* (2) *Nisyān Bārid Yābis,* (3) *Nisyān Ḥārr Yābis. Nisyān Bārid Raṭb* is caused due to predominance of *Burūdat* (coldness) or *Ruṭūbat* (moistness). *Nisyān Bārid*

Yābis is caused by the predominance of *Burūdat* (coldness) or *Yubūsat* (dryness) and *Nisyān Ḥārr Yābis* occurs due to predominance of *Ḥarārat* (hotness) and *Yubūsat* (dryness) in the brain tissues (Kabiruddin, 2009).

Clinical Features of *Nisyān* (Amnesia)

The signs and symptoms of *Nisyān* are *Buṭlān-i-Takallum* (speech impairment), *Buṭlān-i-Taḥrīr* (writing impairment) and *Fasād-i-Fikr* (impaired thoughts) which gradually worsen over time (Anonymous, 2012; Kabiruddin, 2009). The other symptoms may include inability to describe dreams, headache, giddiness, discharge of fluids from the mouth and nose, excessive sleepiness and difficulty in speech (Khan, 2009).

Management of *Nisyān* (Amnesia) as per Unani Medicine

In Unani Medicine, the management of *Nisyān* is based on balancing the disturbance in the three powers of the brain, i.e. *Quwwat Ḥāfiza* (faculty of memory), *Quwwat-i-Fikr* (power of thinking) and *Quwwat-i-Takhayyul* (power of imagination). The modes of treatment or management are *'Ilāj bi'l-Ghidhā'* (dietotherapy), *'Ilāj bi'l-Dawā'* (pharmacothearapy), *'Ilāj bi'l-Tadābīr* (regimenal therapy) and *'Ilāj Nafsānī* (psychotherapy).

1. *'Ilāj bi'l-Ghidhā'* (Dietotherapy)

Ghidhā'-i-Laṭīf (easily digestible diet), *Kathīr al-Taghdhiya wa Jayyid al-Kaymūs* (attenuated highly nutritious and good chime forming), *Sarī' al-Nufūdh Aghdhiya* (fast penetrative diet) and *Muqawwī Aghdhiya* (nutritious diet) are recommended for the patients of *Nisyān*. Soup of mutton, chicken, semi-boiled eggs, *Mā' al-Jubn*, *Sirka*, *Ḥarīra*, partridge, *Mūng Dāl Ki Khichdi*, goat's brain, purslane, spinach, pumpkin and nuts like almond, hazelnut, coconut, walnut are advisable (Khan, 2009; Choopani *et al.,* 2014; Tabari, 1995).

2. *'Ilāj bi'l-Tadābīr* (Regimenal Therapy) and *'Ilāj Nafsānī* (Psychotherapy)

The therapy includes various regimes which are given to maintain the health of a person. Its working is based on several rules for improving physical as well as mental health. It helps in lifestyle modifications by creating changes in the obligatory causes of health, viz. *Asbāb Sitta Ḍarūriyya* (six essentials factors of health) on the principle of *'Ilāj bi'l-Ḍidd* (heteropathy) (Anonymous, 2012). These six essential factors are air, food and water, bodily movement and repose, mental movement and repose, sleep and wakefulness, and excretion and retention. There are various kinds of regimes which are beneficial in *Nisyān*

such as *Riyāḍat* (exercise), *Dalk* (massage), *Naṭūl* (pouring), *Ḥuqna* (enema) and *'Uṭās* (sneezing) (Razi, 1997; Arzani, YNM; Khan, 2009; Kabiruddin, 2009; Nasir *et al.,* 2014).

3. *'Ilāj bi'l-Dawā'* (Pharmacothearapy)

Mufradāt (single drugs) are preferred to *Murakkabāt* (compound formulations) for treatment of *Nisyān*. In the past, Unani physicians used to prescribe single drugs, but in the current scenario mostly compound formulations are used (Anonymous, 2008).

Mufradāt (Single Drugs) for *Nisyān*

Waj (*Acorus calamus*), *Kundur* (*Boswellia serrata*), *Zanjabīl* (*Gingiber officinalis*), *Khardal* (*Brassica nigra*), *Halela* (*Terminalia chebula*), *Barahmī* (*Bacopa monnieri*), *Balela* (*Terminalia bellerica*), *Āmla* (*Emblica officinalis*), *Haldī* (*Curcuma longa*), *Elva* (*Aloe vera*), *Qusṭ* (*Saussurea lappa*), *Sa'd Kūfī* (*Cyperus rotundus*), *Bālachar* (*Nardostachys jatamansi*), *Kabāb Chīnī* (*Piper cubeba*), *Filfil Darāz* (*Piper longum*), *'Āqarqarḥā* (*Anacyclus pyrethrum*), *Gilo* (*Tinospora cordifolia*), *Khūlanjān* (*Alpinia galanga*), *Asgand* (*Withania somnifera*), *Usṭūkhūdūs* (*Lavandula stoechas*), *Balādur* (*Semecarpus anacardium*), *Dārchīnī* (*Cinnamomum zeylanicum*), *'Ūd Ṣalīb* (*Paonea officinalis*), *Za'frān* (*Crocus sativus*), *Qaranful* (*Syzygium aromaticum*), *Pista* (*Pistacia vera*), *Raiḥān* (*Ocimum basilicum*), *Asārūn* (*Valerina wallichi*), *Chilghoza* (*Pinus gerardiana*) (Kunte and Kuna, 2013; Kirti, 2010).

Murakkabāt (Compound Formulations) for *Nisyān*

Ma'jūn Nisyān, Ma'jūn Bolas, Ma'jūn Kundur, Iṭrīfal Usṭūkhūdūs, Jawārish Jalīnūs, Rawghan Qusṭ, Rawghan Banafsha (Kabiruddin, 2006).

Conclusion

Ageing comes with certain disorders such as loss of memory, forgetfulness and confusion. The temperament of human body becomes *Bārid Yābis* (cold & dry) in old age. Accordingly, the temperament of brain becomes more *Bārid* and *Quwwat Nafsaniyya* of brain decreases. According to Unani Medicine, preventive measures like dietary modifications and lifestyle modifications are preferred for old age people. Unani principles of lifestyle modifications and management can be beneficial in the people suffering from *Nisyān* (amnesia).

Conflict of Interest

There is no conflict of interest.

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सारांश

निस्यान (विस्मरण) : एक समीक्षा

***अन्जु, रासिख़ जावेद, गज़ाला जावेद**

निस्यान (विस्मरण) विश्व भर में एक बड़ी चिकित्सीय एवं सामाजिक समस्या बन गया है। यह बढ़ती उम्र के लागों में आम है। यह विस्मृति या याददाश्त के कम होने की अवस्था होती है। इसे याददाश्त के कम होने की एक विशेष स्थिति के रूप में परिभाषित किया जा सकता है जोकि साधारण विस्मरण से अलग होती है। यूनानी क्लासिकल साहित्य के अनुसार *निस्यान* मस्तिष्क के *सू–ए–मिज़ाज बारिद रत्ब* (ठंडा और नम असंतुलित स्वभाव), *सू–ए–मिज़ाज बारिद याबिस* (ठंडा और सुखा असंतुलित स्वभाव) और *सू–ए–मिज़ाज हार्र याबिस* (गर्म और शुष्क असंतुलित स्वभाव) के कारण *कुव्वत हाफ़िज़ा* (स्मृति का स्वभाव), कुव्वत–ए–फ़िक्र (सोचने की शक्ति) और कुव्वत–ए–तख़य्युल (कल्पना की शक्ति) की अशांति के कारण होता है। जैसे कि यूनानी चिकित्सा के साहित्य में उल्लिखित है, *निस्यान बारिद रत्ब, निस्यान बारिद याबिस* और *निस्यान हार्र याबिस, निस्यान* के विभिन्न प्रकार हैं। *निस्यान* के प्रेरक कारक सिर की चोट, मस्तिष्क आघात या मस्तिष्क की सर्जरी हैं और यह शराब के सेवन, औषधि के उपयोग या स्ट्रॉक के प्रभाव के कारण हो सकता है। एकल के साथ–साथ यौगिक यूनानी मिश्रणों का उपयोग स्मृति, ध्यान और संबंधित ज्ञानात्मक कार्यों में सुधार करने के लिए किया जाता रहा है। इस समीक्षा पत्र में यूनानी चिकित्सा और पारंपरिक चिकित्सा के अनुसार *निस्यान,* इसके प्रकारों, कारणों और उपचार के बारे में विस्तार से बताया गया है।

शब्दकुंजी: विस्मरण, याददाश्त की कमी, *निस्यान,* यूनानी चिकित्सा

Management of *Fālij* (Paralysis) in Unani Medicine

*[1]Fouzia Bashir,
[2]Jamal Akhtar,
[2]Nighat Anjum,
[1]Shah Alam
and
[3]Asim Ali Khan

[1]Research Associate, Central Council for Research in Unani Medicine, New Delhi

[2]Research Officer (Unani) S-III, Central Council for Research in Unani Medicine, New Delhi

[3]Director General, Central Council for Research in Unani Medicine, New Delhi

Abstract

Fālij is a major topic in the literature of Unani Medicine since centuries. The aspects of diagnosis and treatment based on *Uṣūl-ī-'Ilāj* have remained a hallmark in the management of *Fālij*. The packaged treatment of *Fālij* includes various modalities of treatment – *'Ilāj bi'l-Ghidhā'*, *'Ilāj bi'l-Dawā'* and even surgical intervention. Unani Medicine has dealt the disease management in stepwise, rational manner. The treatment strategies vary during the course of treatment. Administration of *Mā' al-'Asal* in the initial days and *Munḍij* and *Mushil* therapy in the mid-course along with drugs for *Tabrīd* and *Taqwiyat* in the later days are regarded as the standard treatment guideline for *Fālij*. Along with this guideline, rules related to *Ayyām-i-Buḥrān* which depend on the *Mizāj* of the person and the deranged *Khilṭ* (humour) are taken into consideration for individualization of the treatment. Since the treatment of any disease needs to be dealt with keeping various features in view, framing of *Uṣūl-ī-'Ilāj* has got paramount importance. The paper details the pharmacological basis of the treatment along with *Uṣūl-ī-'Ilāj* of various phases of treatment delineating the Unani mechanism of action underlying all *Af'āl* (pharmacological actions) of Unani drugs.

Keywords: *Fālij*, Unani Medicine, *Uṣūl-ī-'Ilāj*

Introduction

The term *Fālij* is derived from Arabic word '*Falaja*' which means to divide into two symmetrical parts (Ibn Sina, 2010). Generally, the word *Fālij* is used for *Istirkhā'*. In particular, *Fālij* means *Istirkhā'* or paralysis of half body from head to toe longitudinally. It is of two types; one involves head and the other spares it (Ibn Sina, 2010; Baghdadi, 2004). Loss of movement, if developed in whole body, is called *Istirkhā'* and, if only one part is involved, is known as *Fālij* (Table 1). In modern medicine, the word equivalent to *Fālij* is *hemiplagia.* Ancient

Table 1: Types of *Fālij* (Tabari, 1994)

Fālij Niṣfī / *Fālij*	*Fālij Ma' Laqwa* (Hemiplegia with Facial Paralysis)	*Fālij 'Ām* (Quadriplegia)	*Fālij Aṭrāfī*/ *Fālij Asfal* (Paraplegia)	*Fālij Maqāmī*
When paralysis is longitudinally in half of the body	When paralysis occurs in whole longitudinal half of the body including head and face	When paralysis occurs in whole body except face	When paralysis occurs in lower part (lower limb) of the body	Paralysis of particular/ individual organ, e.g. hand, foot, tongue

*Author for Correspondence; Email: fouzia.ccrum@gmail.com

physicians of Unani Medicine considered *Fālij* as a disease in which one side of body is paralysed from head to foot. But according to *Majusi*, *Fālij* is known as a disease in which one side of body excluding head is paralysed (Kabiruddin, 2009). *Fālij* is sometimes referred as loss of both motor and sensory functions. The differentiation between these two functions is described by *Ibn Rushd*: 'Often if any one of these functions (*ḥiss* and *ḥarkat*) is lost, other is also lost, though it is not mandatory'. This is also mentioned by *Jalinus* (Ibn Rushd, 1987).

Causes of *Fālij*

- *Nazf Dimāghī* (brain hemorrhage)
- Obstruction of arteries of brain or clotting of blood
- Brain tumour
- *Ṣar'* (epilepsy)
- *Talayyun-i-Dimāgh* (softness of brain)
- Chorea
- *Ikhtināq al-Raḥim* (hysteria)

(Kabiruddin, 2009)

Pathology of *Fālij*

According to *Jalinus*, if posterior part of brain is injured, *Fālij Nisfī* (hemiplegia) will occur, and if whole brain is injured, *Sakta* (quadriplegia) will occur.

- If first part of *Mabda' al-Nukhā'* (origin of spinal cord) is affected, whole body will be paralyzed; if one side of spinal cord is affected, same side of body will be paralyzed.
- If both sides of brain near spinal cord is affected, *Sakta* (quadriplegia) occur; but if one side of brain is affected, *Fālij Nisfī* will occur (Kabiruddin, 2009).

The common cause of *Amrāḍ-i-A'ṣāb Mizājī* or temperamental neurological disease is *Burūdat*, either alone or associated with *Balgham*. *Sawdā'* is next to *Balgham* and *Ṣafrā'* hardly causes neurological disease due to its fast dissolving nature (Baghdadi, 2004).

The dominance of *Burūdat* and *Ruṭūbat* in any organ often interrupts the sensory and motor functions. *Burūdat* is opposite to *Mizāj* of *Rūḥ*. Therefore, it produces *Khadar* or decline of sense in *Rūḥ*. *Ruṭūbat* makes that organ blunt and insensitive (Ibn Sina, 2010). Besides dominance of *Burūdat* and *Ruṭūbat*, pathology in brain is also considered as a cause of movement disorders.

According to *Ibn Sina,* loss or diminution of movement anywhere in the body is often because of lesion in the brain (Ibn Sina, 2010). According to *Nafisi,* if

the *Jirm-i-'Urūq* (vessel wall) is *Ṣulb* or hard and blood is in excess quantity, rupture may occur in brain or heart vessels causing hemorrhage. It does not happen in other organs of body (Husain, 1906).

The cause of *Fālij* may be *Sudda* (any obstruction) in the course of nerves due to contamination of *Khilṭ Balghamī Ghalīz* in brain or neurons, compression or dislocation of spinal cord, injury to these structures and residual effects of acute diseases like meningitis (Majusi, 2010).

Initially, *Imtilā' Balghamī* occurs in the part of *Buṭūn-i-Dimāgh* (ventricles of brain), then it is suddenly dissolved from there and *Balgham* descends to either left or right side of the body, whichever side is weaker (Tabari, 1994).

Fālij usually occurs in elderly when their brains are occupied with *Khilṭ Bārid* (cold humours) and they come in sudden contact with either hot or cold temperature which melts this *Khilṭ*, carrying it up to the root of nerves. Mostly, this condition develops in persons with weakened nerves (Majusi, 2010).

Uṣū-i-'Ilāj (Line of Treatment) of *Fālij*

1. ***Betterment of Dimāgh Mu'akhkhar***: In all the diseases of nerves, betterment of *Dimāgh Mu'akhkhar* (rhombencephalon) is primarily focused (Ibn Sina, 2010).

2. ***Ta'dīl-i-Mizāj:*** *Ta'dīl* (normalization) of *Mizāj* if only *Kayfiyat* is altered.

3. ***Tanqiya:*** *Tanqiya* (elimination) of causative matter if there is excess *Khilṭ*. *Sū'-i-Mizāj Māddī* is relieved by two courses; *Istifrāgh-i-Mawād* (elimination of causative matter) and *Islāḥ-i-Mizāj* (correction of temperament). *Sū'-i-Mizāj Māddī* is alleviated by drugs having *Mulaṭṭif, Muqawwī*, *Mu'arriq, Mulayyin* and *Mudirr-i-Bawl* properties. For *Istifragh-i-Mawād,* two methods are used; first is *Faṣd* (venesection) while second includes use of *Mushil* (purgative drugs), *Muqī* (emetic drugs) and *Huqna Mushila* (Baghdadi, 2004).

   For *Tanqiya,* it is mandatory to use *Mulaṭṭif* drugs, e.g. *Anīsūn, Tukhm-i-Shibit, Ajwāyin, Tukhm-i-Karafs, Bīkh-i-Bādiyān, Bīkh-i-Karafs, Bīkh-i-Idhkhar, Aṣl al-Sūs*. A decoction made with *Anīsūn, Tukhm-i-Shibit,* and *Ajwāyin,* mixed with *Gulqand* may be taken daily morning. On 14th day, *Mushil* therapy may be given (Arzani, YNM).

4. ***Mushil* Regime:** While using *Mushilāt* (purgatives), following points should be kept in mind:

   - Addition of *Muqawwī-i-Qalb* drugs (heart tonic) to potentiate and stabilize *Rūḥ Ḥaywānī*.

- *Mudirrāt* (diuretics) not to be used in major quantity as they hinder the effect of *Mushilāt* (Jurjani, 2010).
- As the causative material is *Khilṭ Balgham, Munḍij-i-Balgham* drugs having *Talṭīf*, *Taqṭī'* and *Taḥlīl* properties should be used. Drugs like *Turbud* and *Usṭūkhūdūs* are added for effective elimination (Ibn Sina, 2010).

5. ***Taqwiyat:*** Following *Tanqiya,* potentiation is provided to nerves (Tabari, 1994) and body massage with *Ḥārr Mizāj* (hot temperament) oils having *Muḥallil* and *Muqawwī-i-A'ṣāb* actions is recommended to dissolve the causative matter and potentiate the nerves (Jurjani, 2010).

Drugs Used According to *Uṣūl-i-'Ilāj*

For *Ta'dīl-i-Mizāj*: Renowned Unani physician *Muhammad ibn Zakariyya Razi* (Rhazes) advocated a prescription based on the principles of treatment (*Uṣūl-i-'Ilāj*).

The treatment has to be started with *Ḥabb Muntin* (containing *Ayārij Fīqra* 3.5 g, *Shaḥm-i-Ḥanzal*, *Qanṭūriyūn Daqīq, 'Uṣāra Qiththā' al-Ḥimār*, 1.75 g each, *Farfiyūn, Jund Bedastar, Filfil, Hiltīt, Sakbīnaj, Jāoshīr, Shīṭraj Hindī, Khardal* 0.35 g each with *Āb-i-Sudāb* and any of *Ṣamghiyāt* for one day, followed by massage with *Rawghan-i-Qusṭ* and oral administration of *Mā' al-'Asal* with 7 gm of *Balāduri* (containing *Zanjabīl, 'Āqar Qarḥā, Shūnīz, Qusṭ, Filfil, Dār Filfil, Waj* 10 parts each, *Barg-i-Sudāb Khushk*, *Hiltīt, Juntiyānā, Zarāwand, Ḥabb al-Ghār, Jund Bedastar, Shīṭraj, Khardal* and *Balādur* 5 parts each fried with *Rawghan-i-Ākhrot* with *'Asal Khāliṣ* and *Ṣamghiyāt*) for three days to be used for *Ta'dīl-i-Mizāj* and this treatment cycle is to be given 10 times (Razi, 1991).

For Talṭīf-i-Mawād: In the first seven days, *Gulqand + Mā' al-Budhūr* or *Gulqand + Mā' al-Uṣūl* is preferred.

Mā' al-Budhūr: *Anīsūn, Soyā, Ajwāyin Desī, Tukhm-i-Karafs.*

Mā' al-Uṣūl: *Bīkh-i-Bādiyān, Bīkh-i-Karafs, Bīkh-i-Idhkar, Aṣl al-Sūs.*

For Tanqiya-i-Mawād: No *Mushil* should be given in initial stage of treatment, as Nafisi said '*Mawād* of *Fālij* are raw, *Mushil* drugs will not be able to excrete. If *Mushil* drug is given, these raw *Mawād* matters become active and may be dangerous'. Therefore, after *Talṭīf-i-Mawād* and *Nuḍj*, elimination of causative matter is done with *Mushil* (purgative) drugs like *Soyā, Marznajosh, Nākhūna, Methī, Tukhm-i-Arand, Anjīr, Aṣl al-Sūs, Shahd, Kānjī, Rowghan-i-Zaytūn, Tukhm-i-Ḥanzal* and some pills like *Ḥabb-i-Shīṭraj* and *Ḥabb-i-Muqil.*

For Taqwiyat-i-A'ṣāb: After *Tanqiya-i-Mawād,* potentiation of nerves should be focused on through application (massage) of *Mizāj Ḥārr* (hot temperament)

oils like *Rawghan-i-Arand, Rawghan-i-Zaytūn, Rawghan-i-Kakalānaj, Rawghan-i-Sumbul Rūmī, Rawghan-i-Qusṭ, Rawghan-i-Soyā,* etc. on vertebra and diseased part (Kabiruddin, 2009).

Ma'mūl-ī-Maṭab Nuskha

In the initial phase of treatment, nothing is given in the form of diet for first seven days except *Mā' al-'Asal*. Heavy, indigestible, flatulent foods, drinks and drugs of cold temperament should be avoided.

Preparation of *Mā' al-'Asal*

- 20 ml *'Asal Khāliṣ* boiled with water or *'Araq-i-Ga'uzabān* 20 ml.
- *Usṭūkhūdūs* and *Bādranjboya* are boiled in water, then *'Asal Khāliṣ* (20 ml) is mixed.

After seven days, *Nuskha-i-Munḍij* is given for 12 days.

Nuskha-i-Munḍij

Bādiyān, Bīkh-i-Bādiyān, Bīkhi-Idhkhar, Bīkh-i-Kabar 7 g each, *Parsiyāoshān, Aṣl al-Sūs Muqasshar, Ga'uzabān, Usṭūkhūdūs* 5 g each, *Anjīr Zard* (3 in number), *Mawīz Munaqqā* (9) soaked overnight in warm water, filtered in the morning and mixed with *Khamīra Banafsha* 40 ml. After 12 days, *Mushil* (purgatives) drugs are added with *Munḍijāt*.

Mushilāt* (Purgatives)*: *Sanā Makkī, Turbud Safed* 7 g each, *Maghz-i-Amaltās, Shīr-i-Khisht* 40 ml each, *Turanjabīn, Shakar Surkh* 40 ml each, *Maghz-i-Bādām Shīrīn* 5 each with *Gulqand* 40 g. After 12 days when *Tanqiya* is completed, *Taqwiyat-i-A'ṣāb* (potentiation of nerves) is focused with administration of *Kushta-i-Gaudantī* 2 mg, *Ma'jūn-i-Sīr* or *Ma'jūn Azarāqī* or *Ma'jūn Jograj Gūgal* 5 g with *'Araq-i-Ga'uzabān* 120 ml in the morning and *Khamīra Ābresham Ḥakīm Arshad Wālā, Dawā' al-Misk Ḥārr Jawāhar Wālī* with *'Aarq-i-Ga'uzabān* 20 ml in evening.

Local Application: After *Tanqiya,* massage with *Rawghan-i-Qusṭ* or *Rawghan Surkh* on paralysed organ is done (Kabiruddin, 2009).

Compound Drugs

The following compound drugs have beneficial effects in the treatment of *Fālij:*

1. ***Khamīra Ga'uzabān 'Ambarī Jadwār 'Ūd Ṣalīb Wālā:*** Nervine and brain tonic, used in epilepsy and convulsions. It is a unique preparation which acts as psychotropic as well as neurotropic agent.

Table 2: Single Drugs Used in the Treatment of *Fālij*

Name of Drug	*Mizāj* (Temperament)	*Afʿāl* (Actions)
Aṣl al-Sūs (*Glycyrrhiza glabra*)	Hot[2] Dry[1] (Ghani, YNM)	*Mulaṭṭif, Jālī* (Maghribi, 2007), *Muqawwī-i-Aʿṣāb*, excretes *Ruṭūbat* through motion, normalizes *Akhlāṭ*, cleanses the vessels of body, *Mudirr-i-Bawl, Mudirr-i-Ḥayḍ* (Ghani, YNM)
Barg-i-Bādiyān (*Foeniculum vulgare*)	Hot[2] Dry[1] (Ghani, YNM; Ibn Baitar, 1985)	*Mufattiḥ, Mulaṭṭif, Mudirr-i-Bawl,* eliminates viscid humours from stomach (Ghani, YNM; Ibn Baitar, 1985)
Usṭūkhūdūs (*Lavendula stoechos*)	Hot[1] Dry[2] (Maghribi, 2007)	*Mulaṭṭif, Muqawwī-i-Aʿṣāb, Mufattiḥ-i-Sudad,* induces *Nuḍj* in *Balgham* and *Sawdā'* and removes through bowel (Maghribi, 2007)
Bīkh-i-Bādiyān (*Foeniculum vulgare*)	Hot[2] Dry[2] (Ghani, YNM)	Along with *Mā' al-ʿAsal* produces *Nuḍj* in *Balgham* (Ghani, YNM)
Anīsūn (*Pimpinella anisum*)	Hot[2] Dry[3] (Ghani, YNM)	*Mulaṭṭif, Jālī, Mufattiḥ, Kāsir-i-Riyāḥ, Mudirr-i-Bawl*, effective in *Fālij* when used with *Gulqand Aṣlī* (Ghani, YNM; Maghribi, 2007)
Tukhm-i-Karafs (*Apium graveolens*)	Hot[2] Dry[2] (Ghani, YNM)	*Muḥallil, Muʿarriq, Mudirr-i-Bawl,* useful in *Bārid Balghamī Amrāḍ*, enhances the effect of *Mushil* drugs (Maghribi, 2007; Ibn Baitar, 1985)
ʿŪd Ṣalīb (*Paenia emodi*)	Hot[2] Dry[2] (Ghani, YNM)	*Muqawwi-i-Aʿṣāb, Mufarriḥ, Mufattiḥ-i-Sudad, Mulaṭṭif* and *Mujaffif* properties (Ghani, YNM; Ibn Baitar, 1985)
Bīkh-i-Idhkhar (*Andropogan jwarancusa*)	Hot[1] Dry[2] (Ghani, YNM)	*Mufattiḥ, Mulayyin, Mulaṭṭif,* eliminates *Ghalīz Akhlāṭ* after producing *Nuḍj*, removes waste from brain (Maghribi, 2007; Ibn Baitar, 1985)
Barg-i-Ga'uzabān (*Borage officinalis*)	Hot[1] Wet[1] (Ghani, YNM)	*Mufarriḥ,* potentiates *Rūḥ, Ḥarārat Gharīziyya* and *Aʿḍā' Ra'īsa, Mulayyin, Mulaṭṭif-i-Sawdā',* excretes *Akhlāṭ Muḥtariqa* (Ghani, YNM; Maghribi, 2007)
Gulqand Aṣlī	Hot[1] Dry[1] (Ghani, YNM)	Induces *Nuḍj* and *Talṭīf, Muqawwi-i-Dimagh, Miʿda wa Jigar,* improves digestion, effective in *Fālij,* facial palsy (Ghani, YNM)
Barg-i-Sanā (*Cassia angustifolia*)	Hot[1] Dry[1] (Kabiruddin, 2009)	*Mushil* for *Mirra Ṣafrā'* and *Balgham* (Ibn Baitar, 1985)

Name of Drug	*Mizāj* (Temperament)	*Afʿāl* (Actions)
Turbud (*Ipomia turpethum*)	Hot[3] Dry[3] (Ibn Baitar, 1985)	*Mushil,* eliminates *Balgham Lazij* from brain through purgation, beneficial for *Fālij,* convulsion and other neurological disorders (Kabiruddin, 2009; Ibn Baitar, 1985)
Maghz-i-Flūs (*Khayār Shambar*) (*Cassia fistula*)	Hot[1] Wet[1] (Ghani, YNM)	*Mushil, Mulayyin*, purifies nerves; along with *Turbud* it purges *Balgham* (Ghani, YNM; Maghribi, 2007; Ibn Baitar, 1985)
Rawghan Zard (ghee)	Hot[1] Wet[1] (Ibn Baitar, 1985)	*Muḥallil, Munḍij, Mulayyin, Musakkin,* normalizes consistency of causative matter, helps to remove blockage and potentiates brain (Ghani, YNM; Ibn Baitar, 1985)
Rawghan-i-Mālkangnī (*Celastrus paniculatus*)	Hot[1] Wet[1] (Ghani, YNM)	*Muqawwī-i-Aʿṣāb,* used in *Fālij, Laqwa, Waja' al-Mafāṣil, Niqris, Khadar* and *Ḍuʿf al-Aʿṣāb* (Ghani, YNM)

2. ***Maʿjūn Azarāqī:*** Neurotonic, used in neurological disorders, paralysis and arthritis.

3. ***Jawārish Jālīnūs:*** Specific medicine for phlegmatic derangement and used as nervine tonic and stomachic.

4. ***Maʿjūn Falāsifa:*** Nervine tonic, used in neurological disorders.

5. ***Kushta Nuqra:*** Neurotonic with analgesic, anxiolytic and anticataleptic properties.

6. ***Kushta Marajān:*** Very potent neurotonic. It improves immunological status of individual.

Research Studies Related to Drugs Used in *Fālij*

Aṣl al-Sūs: Roots and rhizomes of *Glycyrrhiza glabra* have been studied; study suggested that the aqueous extract of roots 250 and 500mg/kg possess a cerebro protective effect in sodium. Nitrite induced hypotoxic rat which may be mediated by its anti-oxidant effect (Murlidharan *et al.*, 2009).

Bīkh-i-Bādiyān: *In-vivo*, both essential oil and anethole (the main component of oil) orally administered in a sub-acute treatment to mice (30 mg/kg per day for 5 days) showed significant anti-thrombotic activity preventing the paralysis induced by collagen-epinephrine i.v. injection (70-83%) protection respectively (Tognolini *et al.*, 2007).

Usṭūkhūdūs: *Lavendula stoechus* flowers were studied for their possible anti-convulsant and anti-spasmodic activities. It increased the latency of convulsions induced by pentylene tetrazole. Lavender from *Lavendula angustifolia* also decreases the tone in the skeletal muscle preparation of phrenic nerve-diaphragm of rats (Balchin and Hart, 1999).

Anīsūn: Neuro protective effect of anise oil was observed (Karimzadeh *et al.*, 2010).

Tukhm-i-Karafs: Apigenin was studied on the contraction of rat thoracic aorta, and it was concluded that Apigenin relaxes rat thoracic aorta mainly by suppressing the calcium influx through both voltage receptor oriented calcium channels (Ko *et al.*, 1999).

'Ūd Ṣalīb: In a study, sedative and anti-inflammatory activities were assessed and it was found that *'Ūd Ṣalīb* has blocking effect on neuromuscular junction (Riaz *et al.*, 2004).

Barg-i-Ga'uzabān: Leaves were tested for flavonoids, coumarins, sterols and tannin, produced a contraction-dependent relaxation of spontaneous and k+ (80mM) induced contraction in isolated rabbit jejunum preparation, suggestive of calcium antagonist effect (Gilani *et al.*, 2007).

Barg-i-Sanā: *Cassia angustifolia* contains anthraquinone, carbohydrates, flavonoids, glycosides. *Sanā* is a potent laxative and its use in chronic constipation patient has been assessed (Picon *et al.*, 2010).

Turbud: Anti-secretory, ulcer protective, anti-inflammatory, hepato protective, anti-bacterial and anti-oxidant activity was confirmed (Kohli *et al.*, 2010).

Rawghan Mālkangnī: In a study, it was proved that extract of *Celastrus paniculatus* seeds exerts powerful myogenic and L-type calcium dependent relaxing effect in the isolated rat and the human ileum is sensitive to the inhibitory effect of its extract (Borrelli *et al.*, 2009).

Conclusion

Unani Medicine has the potential to treat *Fālij* through single drugs as well as compound formulations. Through this paper, an effort has been made to focus on adopting the measures in common practice so that individuals who have compromised their daily activities due to disability caused by this disease can overcome it by various Unani regimes.

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सारांश

यूनानी चिकित्सा पद्धति में *फ़ालिज* (लक़वा) का उपचार

***फौज़िया बशीर, जमाल अख़्तर, निग़हत अन्जुम, शाह आलम, आसिम अली ख़ान**

फ़ालिज सदियों से यूनानी चिकित्सा के साहित्य का एक बड़ा विषय है। *फ़ालिज* के उपचार में *उसूल–ए–इलाज* पर आधारित रोग–निदान एवं उपचार के पहलूओं को प्रमाणिकता हासिल है। *फ़ालिज* के उपचार के लिए उपचार के विभिन्न प्रकार हैं जैसे– *इलाज बिल ग़िज़ा, इलाज बिल–दवा* और यहां तक कि सर्जिकल हस्तक्षेप। यूनानी चिकित्सा ने इस रोग का उपचार चरणबद्ध और तर्कसंगत तरीके से किया है। उपचार की रणनीतियां उपचार के दौरान भिन्न होती हैं। प्रारंभिक दिनों में *मआ अल–असल* का सेवन और बाद के दिनों में *तबरीद* और *तक़वियत* की औषधियों के साथ–साथ मध्य समय में *मुन्ज़िज* और *मुस्हिल* थेरेपी को *फ़ालिज* के लिए मानक उपचार दिशानिर्देश माना जाता है। इस दिशानिर्देश के साथ–साथ *अय्याम–ए–बुहरान* जो व्यक्ति के मिज़ाज पर निर्भर करता है से संबंधित नियम और विक्षिप्त *ख़िल्त* (ह्यूमर) को उपचार के व्यक्तिगतकरण के लिए ध्यान में रखा जाता है। चूंकि किसी भी रोग का उपचार करने के लिए विभिन्न विशेषताओं को ध्यान में रखने की आवश्यकता होती है इसलिए *उसूल–ए–इलाज* को सर्वोपरि महत्व प्राप्त है। यह पेपर फार्माकॉलोजिकल आधार के साथ–साथ उपचार के विभिन्न चरणों के *उसूल–ए–इलाज* और यूनानी औषधियों के सभी *अफ़'आल* (फार्माकॉलोजिक कार्य) के साथ–साथ यूनानी कार्य विधि का विस्तृत वर्णन करता हैं।

शब्दकुंजी: *फ़ालिज,* यूनानी चिकित्सा, *उसूल–ए–इलाज*

Floristic Diversity of Unani Medicinal Plants in Kalakadu Mundanthurai Tiger Reserve Forest, Tirunelveli District, Tamil Nadu, India

*[1]K. Venkatesan,
[2]Mokhtar Alam,
[3]R. Murugeswarn
and
[4]N. Zaheer Ahmed

[1]Regional Research Institute of Unani Medicine, 1, West Mada Church Road, Royapuram, Chennai, Tamil Nadu

[2]Central Council for Research in Unani Medicine, Janakpuri, New Delhi

[3]National Medicinal Plant Board, New Delhi

[4]Regional Research Institute of Unani Medicine, 1, West Mada Church Road, Royapuram, Chennai, Tamil Nadu

Abstract

Floral diversity refers to the diversity of plants occurring in a specific region during a particular season. It generally refers to the diversity of naturally occurring indigenous or native plants. Floristic inventory and diversity assessment is necessary to understand the present diversity status and conservation of forest biodiversity. Unani Medicine is an elaborate medical science which largely depends on plants for drugs. A survey was carried out in the Kalakadu Mundanthurai Tiger Reserve, Tirunelveli district, Tamil Nadu, India. Tamil Nadu is the southernmost state of the country and covers an area of 1,30,060 sq. km which is 3.96% of the geographical area of the country. In the present study, 300 medicinal plants from Kalakadu Mundanthurai Tiger Reserve, Tirunelveli District have been collected and identified. Among them are 104 Unani medicinal plant species (Table 1) belonging to 53 families and 95 genus. Their diversity status has been analysed and it has been found that 62 species are common, 18 are rare, 15 are sporadic and 9 species are common/cultivated.

Keywords: Biodiversity, KMTR Tirunelveli, Unani medicinal plants

Introduction

Floral diversity refers to the diversity of plants occurring in a specific region during a particular era. It generally refers to the diversity of naturally occurring indigenous or native plants. India is known for its rich biodiversity and cultural values. It is estimated that around 46,000 plant species including higher plants such as angiosperms, gymnosperms and lower groups, viz. pteridophytes, bryophytes, fungi, lichens and algae are known to occur in India. Of them, 19,395 taxa, including infra-specific level, are angiosperms. About 8,000 flowering plant species have been recorded in different codified and non codified systems of medicine practised by 4,635 ethnic communities. These medicinal plants are distributed across different bio-geographic zones, forest types, altitudinal gradations, soil types and rainfall regions. These medicinal plants occur in different life forms ranging from prostrate herbs to lofty trees.

In India, there are about 7,000 species of angiosperms reported to be in medicinal use (Singh *et al.,* 2001). However, All India Coordinated Research Project on Ethnobiology (AICRPE) sponsored by the Ministry of Environment & Forest, New Delhi has reported 8,000 plant species in medicinal use by different ethnic communities across the country. Medicinal plants have been the subject of humankind's curiosity since time immemorial. Almost every civilization has a history of medicinal plant use (Ensminger *et al.,* 1983). Approximately 80% people in the world's developing countries rely on traditional medicines for their

*Author for Correspondence; Email: venkat050373@gmail.com

primary health care and about 85% of traditional medicine involves the use of plant extracts (Vieira and Skorupa, 1993).

A total of 560 plant species of India have been included in the International Union for Conservation of Nature and Natural Resources (IUCN) Red List of Threatened Species, out of which 247 species are in the threatened category. The IUCN has estimated that about 12.5% of the world's vascular plants, totalling about 34,000 species are under varying degrees of threat (Phartyal *et al.,* 2002). The IUCN recognises the following categories: extinct, extinct in the wild, critically endangered, endangered, vulnerable, near threatened, least concern, data deficient and not evaluated. Species with small population that are not at present endangered or vulnerable but are at risk are called rare (Singh *et al.,* 2006). Many of them are facing extinction. In the past few decades, there has been an ever-increasing global inclination towards herbal medicine, followed by a belated growth in international awareness about the dwindling supply of the world's medicinal plants (Bodeker, 2002). The plants used in the phytopharmaceutical preparations are obtained mainly from the naturally growing areas. The genetic diversity of medicinal plants in the world is getting endangered at alarming rate because of ruinous harvesting practices and over-harvesting for production of medicines, with little or no regard to the future. Also, extensive destruction of the plant-rich habitat as a result of forest degradation, agricultural encroachment, urbanization, etc. is another factor challenging their existence (Gupta *et al.,* 1998).

In India where about 90% plant materials are collected from wild sources, many of the plants have become rare, threatened, endangered or vulnerable due to the destructive harvesting. About 427 ethnic communities and folk healers use around 8000 species of medicinal plants in different parts of India (Savarimuthu *et al.,* 2006; Sukumran and Raj, 2010). India is endowed with rich wealth of medicinal plants which are widely used by all sections of people either directly as folk remedies or different indigenous system of medicine or indirectly in the pharmaceutical preparations of modern medicine (Alagesaboopathy, 2011).

Unani Medicine originated in Greece and was developed by Arabs into an elaborate medical science based on the framework of teaching of *Buqrāṭ* (Hippocrates) and *Jālīnūs* (Galen). Since that time, Unani Medicine has been known as Greco-Arab Medicine. The World Health Organization (WHO) has recognized Unani Medicine as an alternative system to cater the health care needs of human population. The principal sources of drugs in Unani Medicine are plants, animals and minerals. Treatment with crude drugs when used one at a time is called *'Ilāj bi'l- Mufrrad* (treatment by single drug), when two or more than two drugs are combined together it is called *'Ilāj bi'l-Murakkabāt* (treatment by compound drugs). Various drug formulations are used in Unani Medicine for different ailments (Husain *et al.,* 2010).

The Central Council for Research in Unani Medicine, New Delhi is continuously involved in ethno-botanical surveys through Survey and Cultivation of Medicinal Plants Programme by its regional research institutes throughout India particularly in tribal dominated areas of Andhra Pradesh, Tamil Nadu, Bihar, Jammu & Kashmir, Madhya Pradesh, Karnataka and Uttar Pradesh. Accordingly, the Southern Western Ghats region of Coimbatore district, Tamil Nadu was surveyed to study the diversity and status of Unani medicinal plants and to carry out the research activities in the clinical research and drug standardization research.

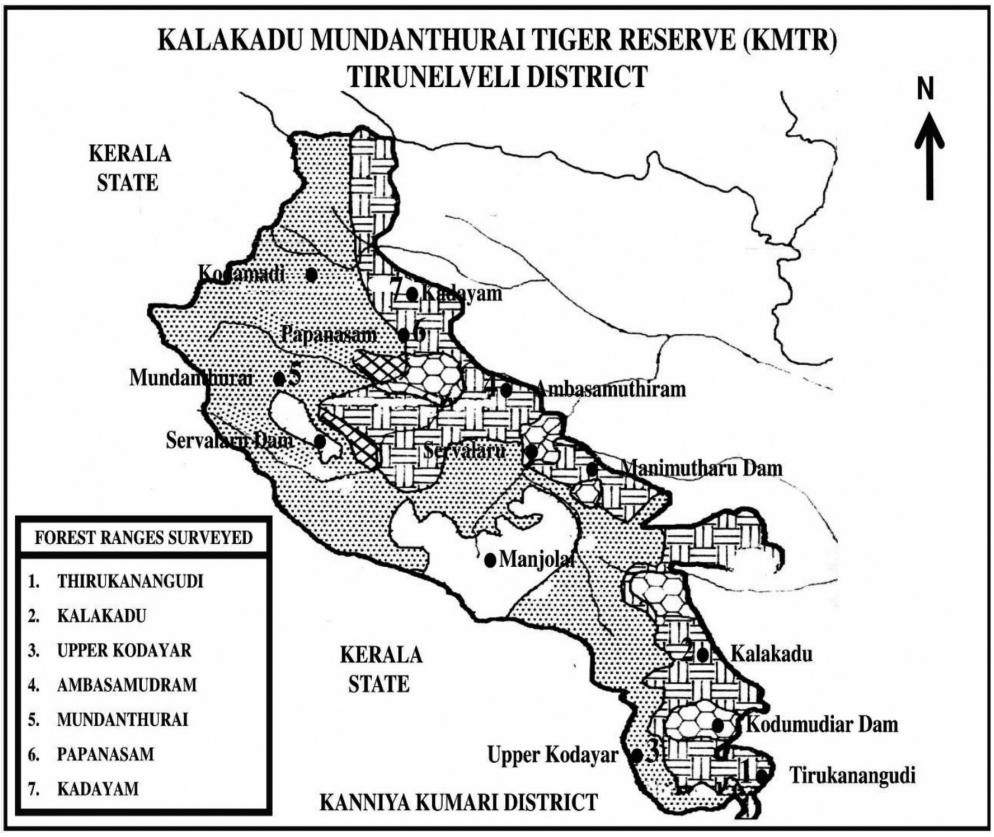
Present Knowledge on Diversity of Medicinal Plants

The Southern Western Ghats is one of the major tropical evergreen-forest regions in India and possesses enormous plant diversity. The richness of floristic diversity of the region has been brought out by Gamble, 1915-1936; Nair and Daniel, 1986; Rao, 1984, Matthew, 1981, 1982, 1983 & 1999). Diversity of medicinal plants has been documented from various parts of Indian sub-continent (Pascal., 1991; Sharma and Thokchom, 2014; Venkatesan *et al.,* 2018; Vijayashalini and Abirami 2018). A perusal of the research literature reveals that several diversity of medicinal plant studies in various forest areas have been reported from the various districts of this state except diversity of Unani medicinal plants in Kalakadu Mundanthurai Tiger Reserve at Tirunelveli district, which has not yet been studied from the perspective of diversity of medicinal plants.

Study Area

Tirunelveli district is southernmost district of Tamil Nadu state located between 8°05' and 9°30' north latitude and 77°05' and 78°25' east longitude. During the rule of the Pandyan dynasty, the district was known as Thenpandiyanadu followed by the period of Chola dynasty when the district was named as Mudikonda Cholamandalam. During the period of the British East India Company in 1879, it was called Tinnevelly district. The district is bounded by Virudhunagar district to the north, by Thiruvananthapuram, Kollam and Pathanamtheta districts in the west, by Kannyakumari district in the south and Thoothukudi district in the east. It covers about 6823 square kilometres land area. The district is covered with mountains (Western Ghats) and lowland plains, including sandy soil and fertile alluvium which make it rich in flora and fauna diversity. Tirunelveli district is said to be the only district of Tamil Nadu to have all the five types of ecological zones as described in the ancient Tamil literature i.e. Kurunji (Hilly areas), Mullai (Forest areas), Marutham (Flat fertile land areas), Neithal (Forming the seashore areas) and Palai (Dry desert lands areas). The district receives annual rainfall and benefits through both the northeast and southwest monsoons.

Map-1: Tirunelveli District



Kalakadu Mundanthurai Tiger Reserve

The Kalakkad Mundanthurai Tiger Reserve (KMTR) was established in 1988 and covers 900 square kilometres land area. The reserve located at 8°39'N and 77°23'E is about 45 km west of Tirunelveli district. The tribal community Kani or Kaniyakaran is inhabited in the forest areas of Periyamayilaru and Servalaru Kanikudil in Mundanthurai Range. The tribal and rural communities of this district are basically farmers. They are hard workers and economically belong to backward status. The ethnobotanical survey was conducted in Nambi Koil, Kodumudiyaru, Karungalkasam and Kozhikal Odai forest areas in Thirukanangudi Range; Muththalaru, Vadakarai, Pachaiaru Dam, Sengaltheri View point and Padmaneri forest areas in Kalakadu Range; Chinnakutriyar dam, Vinchipoint, Vazhukku parai, Vattaparai forest areas in Upper Kodayar Range; Manjolai lower slope, Kakachi, Nalumukku, Voothu, Kuthiraivetti, Vandalodai, Arival theeti, Manimutharu forest areas in Ambasamudram Range; Kodamadi, Nathalaiodai, Fathermalai, Karaiyaru, Kavuthalaiyaru, Vazhukkaru forest areas in Mundanthurai Range; S.M. Koil, Kottaimadam, Kundaru forest areas in Papanasam Range; and Kadananathi dam, Kallaru, Ramanathi forest areas in Kadayam Range. The vegetation of KMTR is predominantly evergreen,

deciduous, wet evergreen, shola and scrub jungles. All the forest ranges are mostly covered with deciduous, ever green and scrub jungle vegetation. The KMTR forest areas are mainly occupied by rural inhabitant but Mundanthurai range of Periyamaiyalaru Kanikudil and Servallaru Kanikudil forest areas are occupied by Kani or Kaniyakaran tribal community. The main occupation in this district is agriculture.

Methodology

The study was conducted during 2016 (25 days) and in 2019 (20 days) by the research team of Survey of Medicinal Plants Unit, Regional Research Institute of Unani Medicine, Chennai under the Central Council for Research in Unani Medicine (Ministry of AYUSH), New Delhi to collect information on diversity and status of Unani medicinal plants in the southern Western Ghats of the KMTR, Tirunelveli district, Tamil Nadu (Map-1). The collected wild Unani medicinal plant species were identified taxonomically using the Flora of Presidency of Madras (Gamble and Fischer, 1936) and the Flora of Tamil Nadu Carnatic (Matthew, 1983) and Unani names were crosschecked with the existing Unani literature (Anonymous, 1981, 1987, 1992, 1997). The identified plant specimens were then confirmed through referral tour programme with herbaria of Botanical Survey of India, Coimbatore. The specimens were deposited in the herbarium of Survey of Medicinal Plant Unit, Regional Research Institute of Unani Medicine, Chennai. During the survey, about 36 forest areas belonging to 7 forest ranges were covered. During the field study, about 300 species of plant specimens were collected and identified. Among them, 104 species of Unani medicinal plants were identified and documented. The botanical identity of all the plant species was established through modern floras. The plants are arranged alphabetically according to their botanical names with collection number, followed by family, Unani name, habit and their status based on their occurrence in the nature (Table I).

Result and Discussion

In the present study, 300 medicinal plants from Kalakadu Mundanthurai Tiger Reserve, Tirunelveli District have been collected and identified. Among them are 104 Unani medicinal plants species (Table 1) belonging to 53 families, 95 genus. Of them, 62 species are common, 18 species are rare, 15 species are sporadic and 9 species are common/cultivated (Fig. 1).

The species like *Cajanus cajan* (L.) Millsp., *Camelia sinensis* (L.) Kuntze, *Hibiscus esculentus* L., *Lablab purpureus* (L.) Sweet., *Manilkara zapota* (L.) P.Royen, *Piper nigrum* L., *Raphanus sativus* L. and *Tamarindus indica* L. are found in cultivation activities in some parts of the study area. In the family level, Fabaceae and

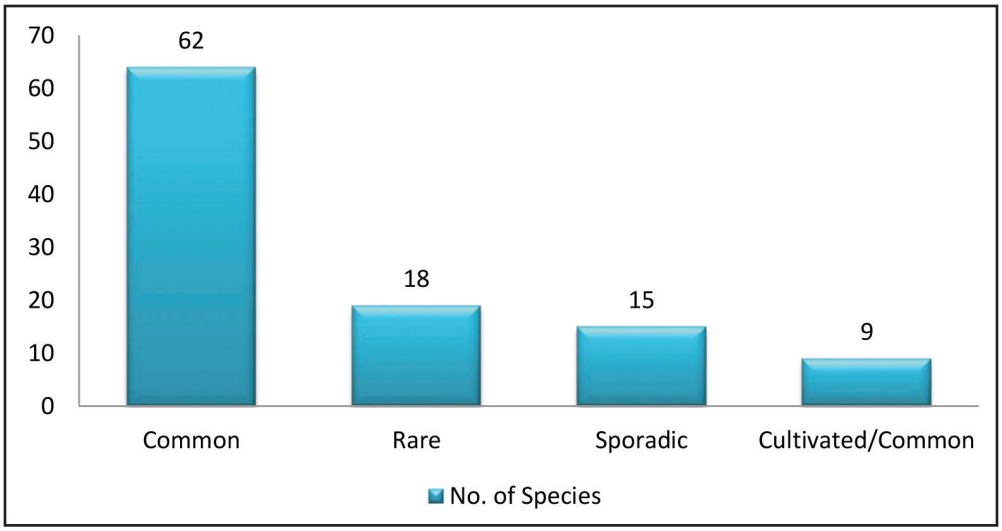


Fig. 1: Analysis of Unani medicinal plant diversity status

Table 1: List of Unani medicinal plants identified in Kalakadu Mundanthurai Tiger Reserve, Tirunelveli District, Tamil Nadu

S. No.	Botanical Identification/ Family/Voucher Specimen No.	Unani Name	Local Name	Habit	Status
1.	*Abrus precatorius* L. Fabaceae RRIUM CH: 12329, 13157	Ghunghchi	Kundumani	Shrub	C
2.	*Abutilon indicum* (L.) Sweet Malvaceae RRIUM CH: 12351	Kanghi	Thuthi	Shrub	C
3.	*Acacia leucophloea* (Roxb.) Willd. Mimosaceae RRIUM CH: 13323	Kath	Velvalam	Tree	C
4.	*Acacia nilotica* (L.) Willd. ex Del Mimosaceae RRIUM CH: 13179, 13321	Kikar	Karuvelai	Tree	C
5.	*Achyranthes aspera* L. Amaranthaceae RRIUM CH: 12493	Chirchita	Nayuruvi	Shrub	C
6.	*Justicia adhatoda* L. Acanthaceae RRIUM CH: 13361	Arusa	Adathodai	Shrub	C
7.	*Aegle marmelos* (L.) Corr. Rutaceae RRIUM CH: 12300, 13153	Belgiri	Vilvam	Tree	S

S. No.	Botanical Identification/ Family/Voucher Specimen No.	Unani Name	Local Name	Habit	Status
8.	*Aerva lanata* (L.) Juss. Amaranthaceae RRIUM CH: 12342, 13183	Bisheributi	Sirupoolai	Herb	C
9.	*Alangium salvifolium* (L.f.) Wangerin Alangiaceae RRIUM CH: 13201	Ankol	Alingil	Tree	S
10.	*Albizia lebbeck* (L.) Benth. Mimosaceae RRIUM CH: 12485	Siras	Vagai	Tree	C
11.	*Alstonia scholaris* R. Br. Apocynaceae RRIUM CH: 12489	Kasim	Ealilaipalai	Tree	S
12.	*Amaranthus spinosus* L. Amaranthaceae RRIUM CH: 12421, 13182	Chaulai Kharda	Mullukerai	Herb	C
13.	*Anacardium occidentale* L. Anacardiaceae RRIUM CH: 12304, 13381	Kaju	Mundhari	Tree	C
14.	*Andrographis paniculata* (Burm.f.) Nees Acanthaceae RRIUM CH: 12451, 13382	Kalmegh	Nilavembu	Herb	C
15.	*Annona squamosa* L. Annonaceae RRIUM CH: 12492, 13368	Sharifa	Seethamaram	Tree	C
16.	*Anogeissus latifolia* (Roxb.ex DC.) Wall. ex Guill. & Perr. Combretaceae RRIUM CH: 12335, 13229	Dhawa	Vekkali	Tree	C
17.	*Argemone mexicana* L. Papaveraceae RRIUM CH: 13176	Satyanasi	Pramathandu	Herb	C
18.	*Aristolochia indica* L. Aristolochiaceae RRIUM CH: 12465	Zarawand	Isvaramuli	Shrub	R
19.	*Bauhinia racemosa* Lam. Caesalpiniaceae RRIUM CH: 13186, 13327	Kachnal	Mandarai	Tree	C
20.	*Boerhavia diffusa* L. Nyctaginaceae RRIUM CH: 13184	Handakaku	Mookiratai	Herb	C

S. No.	Botanical Identification/ Family/Voucher Specimen No.	Unani Name	Local Name	Habit	Status
21.	*Brassica juncea* (L.) Czern. & Coss. Brassicaceae RRIUM CH: 12349	Rai	Kadugu	Herb	C/C
22.	*Caesalpinia crista* L. Caesalpiniaceae RRIUM CH: 12524	Karanjawa	Kalachikai	Shrub	S
23.	*Cajanus cajan* (L.) Millsp. Fabaceae RRIUM CH: 13394	Arhar	Thuvaram	Shrub	C/C
24.	*Calotropis gigantea* (L.) Dryand. Asclepiadaceae RRIUM CH: 12319, 13399	Madar	Eruku	Shrub	C
25.	*Camelia sinensis* (L.) Kuntze Theaceae RRIUM CH: 13312	Chai	Tea leaf	Shrub	C/C
26.	*Cardiospermum halicacabum* L. Sapindaceae RRIUM CH: 12471, 13200	Habb-ul-Qil Qil	Mudakathan	Herb	C
27.	*Careya arborea* Roxb. Lecythidaceae RRIUM CH: 13213	Baikhumbi	Pelaimaram	Tree	S
28.	*Carissa carandas* L. Apocynaceae RRIUM CH: 12513	Karandas	Kalakai	Shrub	C
29.	*Chamaecrista absus* (L.) H.S.Irwin & Barneby Syn. *Cassia absus* L. Fabaceae RRIUM CH: 12301	Chaksu	Nilaavarai	Herb	R
30.	*Cassia fistula* L. Fabaceae RRIUM CH: 12293, 13197	Amaltas	Sarakonnai	Tree	C
31.	*Senna occidentalis* L. Fabaceae RRIUM CH: 12362, 13168	Kasondi	-	Herb	C
32.	*Senna tora* (L.) Roxb. Fabaceae RRIUM CH: 12315, 13190, 13370	Panwar	Oosithagarai/ Seemaiagathi/ Thagarai	Herb	C
33.	*Catharanthus roseus* (L.) G. Don. Apocynaceae RRIUM CH: 12436, 13340	Sadabahar	Nithiyakalyani	Herb	C

S. No.	Botanical Identification/ Family/Voucher Specimen No.	Unani Name	Local Name	Habit	Status
34.	*Catunaregam spinosa* (Thunb.) Tiruv. Rubiaceae RRIUM CH: 12504, 13202	Mayeenphal	Karai	Shrub	C
35.	*Centella asiatica* (L.) Urban Apiaceae RRIUM CH: 13316	Brahmi	Vallarai	Herb	S
36.	*Cinnamomum zeylanicum* Bl. Lauraceae RRIUM CH: 13227	Darchini	Lavanga pattai	Tree	R
37.	*Citrullus colocynthis* (L.) Schrad Cucurbitaceae RRIUM CH: 12314, 13193	Indrain	Athuthumbati	Herb	S
38.	*Cleome viscosa* L. Cleomaceae RRIUM CH: 13174	Bantakalan	Naikadugu	Herb	C
39.	*Clitoria ternatea* L. Fabaceae RRIUM CH: 12280	Mazaryoon	Sangupoo	Herb	C
40.	*Coccinia grandis* (L.) Voigt. Cucurbitaceae RRIUM CH: 12348, 13374	Kanduri	Kovai	Climbing Shrub	C
41.	*Curculigo orchioides* Gaertn. Hypoxidaceae RRIUM CH: 12456	Musli Siyah	Nilappanai	Herb	R
42.	*Cuscuta reflexa* Roxb. Convolvulaceae RRIUM CH: 12520, 13397	Kasoos	Ottuchedi	Herb	C
43.	*Dalbergia sissoo* DC. Fabaceae RRIUM CH: 13226	Shisham	Nukkam	Tree	S
44.	*Datura alba* L. Solanaceae RRIUM CH: 13178	Dhatura siyah	Oomathai	Herb	C
45.	*Datura fastuosa* L. Solanaceae RRIUM CH: 12320	Dhatura Siyah	Oomathai	Herb	C
46.	*Diospyros ebenum* J.Koenig Ebenaceae RRIUM CH: 13337	Aabnoos	Karungali	Tree	R
47.	*Euphorbia hirta* L. Euphorbiaceae RRIUM CH: 12496	Dudhikalan	Ammanpachai	Herb	C

S. No.	Botanical Identification/ Family/Voucher Specimen No.	Unani Name	Local Name	Habit	Status
48.	*Ficus benghalensis* L. Moraceae RRIUM CH: 13206, 13329	Bargad	Alamaram	Tree	C
49.	*Ficus hispida* L.f. Moraceae RRIUM CH: 12455	Anjeer Dashti	Kattuaathi	Tree	C
50.	*Ficus racemosa* L. Moraceae RRIUM CH: 12509, 13195	Gular	Aathi	Tree	C
51.	*Gloriosa superba* L. Liliaceae RRIUM CH: 12508	Muleem	Senganthal	Herb	S
52.	*Gmelina asiatica* L. Verbenaceae RRIUM CH: 13155	Badhaara	Kumil	Shrub	S
53.	*Helicteres isora* L. Sterculiaceae RRIUM CH: 12288, 13330	Marorphali	Edampuri Valampuri	Tree	R
54.	*Hibiscus esculentus* L. Malvaceae RRIUM CH: 13400	Barg-e-Bhindi	Vendaikai	Herb	C/C
55.	*Holarrhena pubescens* Wall.ex G.Don Apocynaceae RRIUM CH: 12395	Inderjo Talkh	Kudasappaalai	Tree	R
56.	*Hygrophila auriculata* (Schum.) Heine Acanthaceae RRIUM CH: 12523, 13402	Talmakhana	Neermulli	Herb	C
57.	*Indigofera tinctoria* L. Fabaceae RRIUM CH: 12307	Neel	-	Herb	C
58.	*Jatropha curcas* L. Euphorbiaceae RRIUM CH: 12454, 13375	Buniyoon Hindi	Aadhalai	Shrub	C
59.	*Lablab purpureus* (L.) Sweet Fabaceae RRIUM CH: 12519	Lablab	Avarai	Shrub	C/C
60.	*Lawsonia inermis* L. Lytheraceae RRIUM CH: 13377	Hina	Maruthani	Shrub	C
61.	*Leucas linifolia* Spreng. Lamiaceae RRIUM CH: 12311	Thumba	Thumbai	Herb	C

S. No.	Botanical Identification/ Family/Voucher Specimen No.	Unani Name	Local Name	Habit	Status
62.	*Mallotus philippensis* (Lam.) Muell. – Arg. Euphorbiaceae RRIUM CH: 12337, 12412, 12435, 13334	Kamila	Senthuram	Tree	R
63.	*Manilkara zapota* (L.) P.Royen Sapotaceae RRIUM CH: 12514, 13387	Cheeku	Sapota	Tree	C/C
64.	*Martynia annua* L. Martyniaceae RRIUM CH: 13396	Kalabi-chhuwa	Pancha-narayanan	Herb	S
65.	*Mimosa pudica* L. Mimosaceae RRIUM CH: 12482	Lajwanti	Thottalvadi	Herb	C
66.	*Mirabilis jalapa* L. Nyctaginaceae RRIUM CH: 12469	Gul-e-Abbas	-	Herb	C
67.	*Morinda tinctoria* Roxb. Rubiaceae RRIUM CH: 13189, 12506	Aal	Nuna	Tree	C
68.	*Morus alba* L. Moraceae RRIUM CH: 12452	Toot siyah	Mulberrg	Tree	R
69.	*Mucuna pruriens* (L.) DC. Fabaceae RRIUM CH: 12336, 13223	Konch	Poonaikali	Shrub	R
70.	*Nelumbo nucifera* Gaertn. Nelumbonaceae RRIUM CH: 13392	Nilofer	Thamarai	Herb	C
71.	*Nerium indicum* Mill. Apocynaceae RRIUM CH: 12521, 13188	Kaner	Arali	Shrub	C
72.	*Ocimum americanum* L. Lamiaceae RRIUM CH: 12306	Kali Tulsi	Naitulasi	Herb	C
73.	*Ocimum tenuiflorum* L. Lamiaceae RRIUM CH: 13215	Raihan	Nalla Thulasi	Herb	C
74.	*Pavonia odorata* Willd. Malvaceae RRIUM CH: 13181	Java	Paramutti	Herb	R
75.	*Phoenix sylvestris* (L.) Roxb. Arecaceae RRIUM CH: 13230	Khajur	Eacham	Tree	S

S. No.	Botanical Identification/ Family/Voucher Specimen No.	Unani Name	Local Name	Habit	Status
76.	*Phyllanthus amarus* Schum. & Thonn. Euphorbiaceae RRIUM CH: 12292, 13166	Bhuiamla	Kezhanelli	Herb	C
77.	*Phyllanthus emblica* L. Euphorbiaceae RRIUM CH: 12334	Amla	Nellimaram	Tree	C
78.	*Piper nigrum* L. Piperaceae RRIUM CH: 13313, 13376	Fil Fil siyah	Milagu	Climbing Shrub	C/C
79.	*Plantago ovata* Forssk. Plantaginaceae RRIUM CH: 13307	Isapghol	Isapgul	Herb	R
80.	*Plumbago zeylanica* L. Plumbaginaceae RRIUM CH: 12324, 12473	Sheetraj Hindi	Kodivelli / Sithiramoolam	Shrub	R
81.	*Plumeria rubra* L. Apocynaceae RRIUM CH: 13192	Gulchin	Sampangi	Tree	C
82.	*Pongamia pinnata* (L.) Pierre Fabaceae RRIUM CH: 12460, 13203	Karanj	Pungan	Tree	C
83.	*Pterocarpus marsupium* Roxb. Fabaceae RRIUM CH: 13231, 13389	Bijasar	Vengai	Tree	S
84.	*Raphanus sativus* L. Brassicaceae RRIUM CH: 12420	Turb	Mullangi	Herb	C/C
85.	*Ricinus communis* L. Euphorbiaceae RRIUM CH: 12516, 13208	Arand	Amanaku	Shrub	C
86.	*Santalum album* L. Santalaceae RRIUM CH: 12323	Sandal Safaid	Sandha-namaram	Tree	R
87.	*Sida rhomboidea* Roxb. Malvaceae RRIUM CH: 13196	Bariyala	Kurunthotti	Herb	C
88.	*Smilax zeylanica* L. Smilacaceae RRIUM CH: 13266	Jungli Ushbaa	Malai-thamarai	Climbing Shrub	R
89.	*Solanum virginianum* L. Solanaceae RRIUM CH: 12341, 13300, 13212	Katai khurd	Kandankathiri	Herb Shrub	C

S. No.	Botanical Identification/ Family/Voucher Specimen No.	Unani Name	Local Name	Habit	Status
90.	*Sphaeranthus indicus* L. Asteraceae RRIUM CH: 12505, 13187	Mundi	Vizhana karanthai / Vishnukaranthai	Herb	C
91.	*Strychnos nux-vomica* L. Loganiaceae RRIUM CH: 13221	Azaraqi	Eatti	Tree	R
92.	*Strychnox potatorum* L.f. Loganiaceae RRIUM CH: 13325	Nirmali	Eatti	Tree	R
93.	*Symplocos racemosa* Roxb. Symplocaceae RRIUM CH: 12375, 13233	Lodh Pathani	Vellilithi	Tree	R
94.	*Syzygium cumini* (L.) Skeels Myrtaceae RRIUM CH: 13170	Jamun	Narinaval	Tree	C
95.	*Tamarindus indica* L. Caesalpiniaceae RRIUM CH: 13151	Tamar-e-Hindi	Puliyamaram	Tree	C/C
96.	*Tephrosia purpurea* (L.) Pers. Fabaceae RRIUM CH: 13194, 13173	Sarphuka	Kolingi	Herb	C
97.	*Terminalia arjuna* (Roxb. ex DC.) Wt. & Arn. Combretaceae RRIUM CH: 13191	Arjun	Neermaruthu	Tree	C
98.	*Terminalia bellerica* (Gaertn.) Roxb. Combretaceae RRIUM CH: 13348	Balela	Thandri	Tree	S
99.	*Terminalia chebula* (Gaertn.) Retz. Combretaceae RRIUM CH:12333, 13228	Halela	Kadukai	Tree	S
100.	*Toddalia asiatica* (L.) Lam. Rutaceae RRIUM CH: 12458	Duhan Daz	Milagaranai	Shrub	C
101.	*Tribulus terrestris* L. Zygophyllaceae RRIUM CH: 13199	Khar-e-khasak khurd	Nerungil	Herb	C
102.	*Vitex negundo* L. Verbenaceae RRIUM CH: 13199	Sambhalu	Nochi	Shrub	C

S. No.	Botanical Identification/ Family/Voucher Specimen No.	Unani Name	Local Name	Habit	Status
103.	*Wrightia tinctoria* R. Br. Apocynaceae RRIUM CH: 13224, 13393	Inderjo Shireen	Veppalai	Tree	C
104.	*Ziziphus mauritiana* Lam. Rhamnaceae RRIUM CH: 12357, 13218, 13326	Ber	Elanthai	Tree	C

Common = C; S = Sporadic; R = Rare; C/C = Common Cultivated

Caesalpiniaceae are the largest ones with 8 species each, followed by 7 species in Apocynaceae, 6 species in Euphorbiaceae, 5 species in Moraceae, 4 species in Combretaceae, Malvaceae and Mimosaceae, 3 species in Amaranthaceae, Lamiaceae, Solanaceae and Verbenaceae, 2 species in Acanthaceae, Brassicaceae, Cucurbitaceae, Loganiaceae, Nyctaginaceae, Rubiaceae and Rutaceae, and other families each with 1 species respectively. The life forms of the identified Unani medicinal plants were analyzed and a total of 40 trees, 40 herbs (including 1 parasitic herb), 24 shrubs including climbers and twiners were documented (Fig. 2).

The Unani medicinal plants used in the treatment of various ailments like arthritis, vitiligo, boils, bleeding haemorrhoids, diarrhoea, dysentery, gastric ulcer, headache, inflammation, piles, sex related disorders, skin diseases, stomach disorders and urinary diseases, etc. fall under vulnerable, rare and sporadic categories due to various external factors. These wild medicinal plant species which are available in the natural sources are recommended for the germplasm

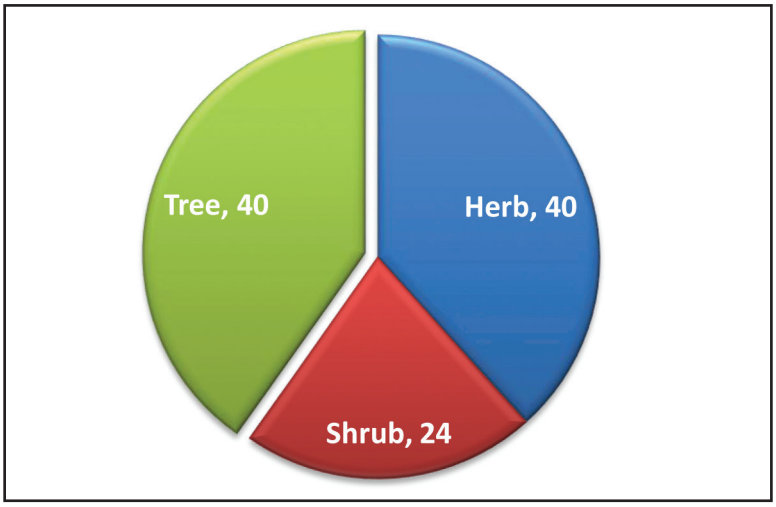


Fig. 2: Analysis of Unani medicinal plants habit/life forms with respect to number of species in the study area

collection to take up conservation and propagation activities seriously as many of the valuable plant species are under threat to became rare, endangered and some are on the verge of extinction due to various external factors. Around 1000 plant species are under threat in different bio-geographic regions of the country. It is concluded that these wild plant species should be conserved seriously and encouraged for large scale cultivation and herbal gardens for medicinal plants be developed in the suitable areas adopting the modern agronomical techniques.

The AYUSH systems of medicine which comprise the traditional medicinal systems rely upon plants and their derivatives for the production of medicines. In the developing countries, usage of medicinal plants in health care practices is relatively high. India exhibits remarkable outlook in modern medicines that are based on natural products besides traditional system of medicines. According to Hamilton, India has about 44% of flora which is used medicinally (Hamilton, 2008). India with its enormous natural flora is considered as the "herbarium of world" and is one of the 12-mega biodiversity countries harbouring three unique "biodiversity hotspots" in the world. India and world market demands for medicinal plants and their raw materials are increasing over the years and income obtained from cultivating these crops give higher income to the farmers and employment opportunity to the people throughout the year. There is an urgent need to popularize, create awareness and familiarity with plant products through press reports, advertising, education and scientific reports. As a precaution to conserve its population and to maintain the gene pool of these medicinal plants, for our future generations, the tribal communities should be educated about the importance and significance of these medicinal plants. Even though there is need of several regulations and policies for the conservation of medicinal plants, no actions are being taken for most of the endangered ones. It's time to take effective steps for the conservation of these highly demanded threatened plants by drafting effective policies on aspects like conservation, cultivation, education, capacity building, research, regulations and trade.

The importance of traditional medicine is also recognized by the World Health Organization (WHO) which has created strategies, guidelines and standards for botanical medicines. For the cultivation, processing of medicinal plants and manufacture of herbal medicines, agro-industrial technologies need to be applied (WHO, 1993). Medicinal plants are resources of new drugs and many of the modern medicines are produced indirectly from plants.

Conclusion

Medicinal plants are always considered as a very important source of medicines especially for the traditional systems of medicine. As depicted above, the status of the medicinal plants is highly alarming and in near future they may get extinct. If there is no sustainable availabilities of these crude drugs, the classical Unani

formulations and medications used for the treatment of a large number of diseases including lifestyle diseases like diabetes, heart problems, obesity, hypertension and bronchial asthma will be lost forever. Only by the strict compliance to the laws for conservation, we can make sure these valuable medicinal plants are protected and remain an unending genuine natural source for the crude drugs which forms the firm base of the traditional systems comprising AYUSH.

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सारांश

कालकाडु मंडनथुराई टाइगर रिज़र्व वन, तिरुनेलवेली ज़िला, तमिलनाडु, भारत में यूनानी औषधीय पौधों की वानस्पतिक विविधता

***के. वेंकटेसन, मोख़्तार आलम, आर. मुर्गेसवरन, एन. ज़हीर अहमद**

वनस्पति की विविधता एक विशेष मौसम के दौरान एक विशिष्ट क्षेत्र में होने वाले पौधों की विविधता से संबंध रखती है। यह सामान्यतः स्वदेशी या देशी पौधों की स्वाभाविक रूप से होने वाली विविधता के बारे में बताता है। वर्तमान विविधता की स्थिति और वन जैव विविधता संरक्षण को समझने के लिए वनस्पति की सूची और विविधता का आकलन आवश्यक है। यूनानी चिकित्सा एक विस्तृत चिकित्सा विज्ञान है जो व्यापक रूप से औषधियों के लिए पौधों पर निर्भर करती है। कालकाडु मंडनथुराई टाइगर रिज़र्व वन, तिरुनेलवेली ज़िला, तमिलनाडु, भारत में एक सर्वेक्षण किया गया। तमिलनाडु देश का दक्षिणी राज्य है और यह 1,30,060 वर्ग किलोमीटर में फैला हुआ है जो देश के भौगोलिक क्षेत्र का 3.96% है। वर्तमान अध्ययन में कालकाडु मंडनथुराई टाइगर रिज़र्व वन, तिरुनेलवेली ज़िले से 300 औषधीय पौधे एकत्रित तथा शिनाख़्त किए गए। इनमें 104 यूनानी औषधीय पौधों की प्रजातियां (तालिक 1) है जो 53 परिवारों और 95 जीनस से संबंधित हैं। इनकी विविधता की स्थिति का विश्लेषण किया गया और यह पाया गया कि 62 प्रजातियां सामान्य, 18 दुर्लभ, 15 छिटपुट और 9 प्रजातियां सामान्य/कृषि योग्य हैं।

शब्दकुंजी: जैव विविधता, केएमटीआर तिरुनेलवेली, यूनानी चिकित्सीय पौधे

Phytochemical Analysis of *Gymnema sylvestre* L. and Identification of Bio-Inhibitors linked to Diabetes and Oxidative Stress Using HPTLC-MS Bioautography

[1]Anisur Rahman,
[2]Javed Inam Siddiqui,
[3]Sayeed Ahmad
and
*[4]Shafeeque Ahmed Ansari

[1]Department of Biotechnology, Jamia Millia Islamia, New Delhi

[2]Department of Ilmul Advia (Pharmacology), Central Research Institute of Unani Medicine, Hyderabad, Telangana

[3]Bioactive Natural Product Laboratory, School of Pharmaceutical Education and Research, Jamia Hamdard, New Delhi

[4]Center for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, New Delhi

Abstract

Gymnema sylvestre, known as *Gurmār*, is broadly used in Unani Medicine for diabetes, abdominal diseases, liver ailments and cardiac disorders. The present study was designed to investigate the bioactive metabolites in aqueous extract of *Gurmār*. Complete metabolomics study was performed by TLC, LCMS and HPTLC-MS. Anti-oxidant activity was tested against DPPH which showed IC50 value is 66.28±1.0 µg/ml. Hypoglycemic potential of extract was checked by α-amylase and α-glucosidase inhibitory activity. IC50 values of α-amylase and α-glucosidase were found 68.41±0.7 µg/ml and 33.22±0.29 µg/ml respectively. Quality control examination of extract was carried out by HPTLC fingerprint which showed that there were 12 and 15 metabolites detected at 254 and 366 nm respectively, whereas 26 metabolites were detected in LCMS screening. HPTLC-MS bioautographic results revealed total eight bioactive compounds. Out of eight compounds gymnemagenin, quercetin and catechine possess DPPH, amylase and glucosidase inhibition potential.

Keywords: Bioautography, Chromatography, G. sylvestre., α-amylase, α-glucosidase

Introduction

Diabetes mellitus (DM) is one of the oldest known chronic diseases affecting millions of people around the globe. According to a WHO report, 425 million people have diabetes and by 2035 this will rise upto 592 million (Anonymous, 2016). A major diabetic complication is occurring due to metabolic dysregulation including carbohydrate, lipid and protein metabolisms which increase blood glucose level (Ullah, 2016; Huizinga and Rothman, 2006).

Many synthetic drugs are used for diabetes mellitus (DM) that act either by enhancing insulin secretion or by improving insulin sensitivity to cells. These drugs are found effective, but frequently cause toxicity. Furthermore, synthetic drugs in low and middle-income countries are often inaccessible or too expensive. Hence for low cost, better safety and potential therapeutic value, the search for novel molecules has been extended to plant-based drugs that offer better protection with greater safety profile (Atanasov *et al.*, 2015).

Gymnema sylvestre L. (Apocynaceae), commonly called *Gurmār*, is highly reputed medicinal plant used in Unani Medicine. It possesses high therapeutic value for the management of different diseases. For centuries, it has been used to control cholesterol levels, liver diseases and cardiac disorders (Reddy *et al.*, 2017; Grover *et al.*, 2002; Ankit *et al.*, 2010).

*Author for Correspondence; Email: saansari@jmi.ac.in

Previous studies suggested that *G. sylvester* extensively used in the therapy of hyperglycemia has direct insulinotropic activities on β cells and isolated islets of human *in vitro* (Aghajanyan *et al.,* 2018; Joshi *et al.*, 2011; Chopra *et al.*, 1958).

We have detected the metabolites present in bioactive extract of *G. sylvestre* using advanced analytical technique LCMS and evaluated its *in-vitro* antidiabetic and antioxidant potential, respectively. Further, HPTLC bioautography coupled with mass spectrometry (HPTLC-MS bioautography) was performed to identify bio-inhibiters present in *G. sylvestre* linked to diabetes and oxidative stress.

Material and Method

Collection and preparation of extract

Seeds of *G. sylvestre* were collected and authentication was done as per protocol. The seeds in the quantity of 100 gm were coarsely powdered and extracted through maceration using distilled water. Thereafter, extract was filtered and subjected to lyophilization and stored in suitable container at 4 °C until its use.

Estimation of total phenolic and flavonoid content

Total phenolic and flavonoid content in the aqueous extract of *G. sylvestre* was determined according to described procedure (Parveen *et al.,* 2019). Gallic acid and rutin were used to quantify total phenol and flavonoid content in sample. All the experiments were performed in triplicate.

In-vitro antioxidant activity

The DPPH assay was used to evaluate antioxidant activity of *R. vesicariu* (Parveen *et al.,* 2019). Briefly, 200 ml of different concentration of sample (100-500 mg/ml) were mixed with 3.8 mL of DPPH solution and kept in dark place. After an hour, absorbance was recorded at 517 nm. Ascorbic acid was used as a positive control (Khan *et al.,* 2017).

In-vitro alpha-amylase and alpha-glucosidase inhibition assay

α-amylase and α-glucosidase activities were carried out as per described method (Chukwuma & Islam, 2015). For α-amylase, 1.0 ml of sample and 1.0 ml α-amylase were mixed and incubated for 30 min at 37 °C. Starch solution was added in incubated mixture and again incubated for an hour at 37 °C. Further, 100µL of supernatant was taken out and glucose concentration was measured by glucose reagent. Whereas for α-glucosidase inhibition activity, 120 µL of sample and 20 µL of α-glucosidase in potassium phosphate buffer were incubated for 15 minutes at 37 °C. The reaction was carried out by adding 20 µL of para-

nitrophenyl-α-D-glucopyranoside and final solution was further incubated for 15 minutes. The reaction was terminated by adding 80 µL of sodium carbonate. Absorbance was measured at 545 and 405 nm for α-amylase and glucosidase, respectively.

TLC fingerprinting of extract

5µl aqueous extract of *G. sylvestre* was applied on TLC-plates. After application, TLC plates were transferred in development chamber in mobile phase such as n-butanol: acetic acid: water (4:1:5,% v/v/v). The developed plates were dried in air and scanned at 254 and 366 nm respectively for fingerprint analysis.

Liquid chromatography-mass spectrometry analysis of extract

The extract was chromatographically separated in mobile phase consisting of 0.5% v/v formic acid in water (A) and acetonitrile (B) in gradient elution mode. Water's ACQUITY BEH C18 column was used and flow rate of mobile phase was 0.5 ml/min. About 05 µL of sample was injected with the split mode of 5:1 with the help of autoinjector and the pressure of the system was set to 15000 psi. The separated metabolites were detected by MS detector. Both LC and MS were operated by using Mass Lynx V 4.1 software incorporated with the instrument. The separated compounds were identified based on their m/z value through literature survey (Singh *et al.*, 2015).

Bioautography screening for anti-diabetic activity

Bioautographic evaluation for identification of alpha-amylase and alpha glucosidase inhibitors were performed as per standard protocol with slight modification (Simoes-pires *et al.,* 2009). All the solutions were freshly prepared in suitable solvents.

Alpha-amylase

Developed TLC plates were sprayed with enzyme solution and incubated in desiccator for 1.5 hour. Thereafter, starch solution was poured and kept for another 15 minutes and finally dipped in iodine solution. The α-amylase activity was visible on the TLC plate by the appearance of white-yellow spot against dark brown background. A subsequent co-TLC was also performed for each sample for isolation of respective bioautograms from active plates.

Alpha-glucosidase

Developed TLC plates were dipped in enzyme solution and kept in desiccator for 2 hours. Thereafter, TLC plates were removed and dipped in substrate solution (*p*-NPG: fast blue, 1:1). Further, glucosidase inhibitions were clearly visible on

the TLC plates by the appearance of white spot against purple/violet background within 5-10 minutes. A subsequent co-TLC was also performed for each sample for isolation of respective bioautograms from active plates.

Mass spectrometry analysis of bioactive metabolites isolated from bioautography

Areas corresponding to the DPPH, alpha amylase and alpha glucosidase inhibition zones on a TLC plate were marked on co-TLC and scraped with specially designed scrapper and dissolved in methanol. In the present study, MS analysis was performed using flow rate of 10 µL/min at optimum temperature. The flow rate of the nebulizer gas was set to 500 L/h, for cone gas it was set to 50 L/h and the source temperature was fixed to 100 °C. For collision, argon was employed at a pressure of 5.3 x 10-5 Torr. Separated metabolites present in different samples were tentatively identified based on their m/z value from mass data bank or literature.

Result and Discussion

Estimation of total phenolic and flavonoid content

Total phenolic and flavonoid content was determined from the calibration curve of gallic acid (r^2= 0.9969) and quercetin (r^2= 0.9921). The total phenolic and flavonoid content were found to be 60.46±0.10 and 84.46±0.20 mg equivalents per gram of gallic acid and rutin, respectively. Our results revealed that *G. sylvestre* extract is enriched with phenolic and flavonoids.

DPPH radical scavenging assay

The capability of electron donation by natural products can be measured by DPPH. This method is based on scavenging of DPPH by addition of antioxidant that decolorizes the DPPH solution. The degree of colour change directly represents the potency of the antioxidants. In the present study, DPPH screening G. sylvestre had clearly shown the dose dependent antioxidant activity. IC50 value of *G. sylvestre* extract (84.52±0.30 µg/ml) possesses excellent inhibition potential as compared to standard ascorbic acid (44.82±0.17 µg/ml). Results of this study suggested that the plant extract contain phenols and flavonoids that are capable of donating hydrogen to a free radical to scavenge the potential damage (Saeed *et al.,* 2012).

In-vitro alpha amylase and alpha glucosidase inhibition activity

The ability of α-amylase and α-glucosidase inhibition of *G. sylvestre* was found in dose dependent manner. In case of α-amylase, the IC50 value was found 68.41±0.7 µg/ml for extract and 22.65±0.09 µg/ml for acarbose whereas in

case of α-glucosidase, the IC50 value was found 33.22±0.29 µg/ml for extract and 15.07±0.17 µg/ml for acarbose. IC50 value clearly shows that *G. sylvestre* possesses better glucosidase activity as compared to amylase. Our results revealed that *G. sylvestre* may delay the carbohydrates digestion and reduce the blood glucose level. Inhibition of the key hydrolyzing enzymes of carbohydrate digestion like α-amylase and α-glucosidase is an excellent approach for the management of diabetes and is especially suited for carbohydrate rich diet (Nazir *et al.,* 2017).

TLC fingerprinting analysis

Quality control analysis is of prime importance in establishing the identity, quality and efficacy of natural products. TLC fingerprinting analysis is usually used to establish the pattern of metabolites so that we can identify the sample in future. If any sample has the same TLC pattern, it must show the same biological activity. In this context, we have developed the TLC method and analyzed our extract. The developed method was reproducible, and we have identified total 12 and 15 metabolites at 254 and 366 nm, respectively (Figure 1 and Table 1). This TLC fingerprint can be used for its identity, quality control analysis and regulatory bodies to assure its quality and safety.

Table 1: Data pertaining to HPTLC fingerprint of aqueous extract of *G. sylvester* at 254 and 366 nm.

Metabolites	R_f	Area (%) at 254 nm	Area (%) at 366 nm
M1	0.06	6.25	3.62
M2	0.09	-	2.51
M3	0.15	4.57	13.14
M4	0.20	7.31	9.56
M5	0.27	7.34	2.42
M6	0.31	4.37	7.05
M7	0.33	3.55	2.96
M8	0.39	6.46	3.43
M9	0.43	4.88	6.00
M10	0.48	8.09	7.94
M11	0.51	-	2.05
M12	0.56	15.29	16.33
M13	0.65	-	0.34
M14	0.59	5.82	-
M15	0.70	4.21	0.53
M16	0.75	-	0.46
Total Metabolites		12	15

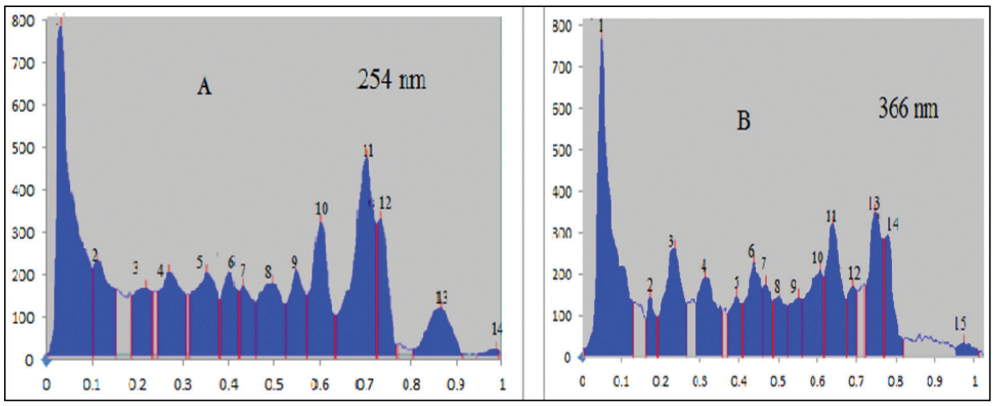

Figure 1: TLC photography and chromatogram of aqueous extract of *G. sylvestre* at 254 and 366 nm.

LCMS analysis

Therapeutic effectiveness of the natural products depends upon their chemical constituents. Further, to identify the chemical constituents present in the extract, we performed LCMS analysis. LCMS is the most powerful tool for the identification of polar and nonpolar metabolites. In our experiment, we performed LCMS for their complete metabolic profiling and identification of diversity of metabolites based on their mass (Table 2). Total of 26 metabolites were separated and tentatively identified through m/z value (Figure 2-4) respectively.

HPTLC-MS bioautography assay

MS-bioautography is also a beneficial tool for separation and detection of the active antidiabetic and antioxidant compounds in a mixture. The HTLC-MS

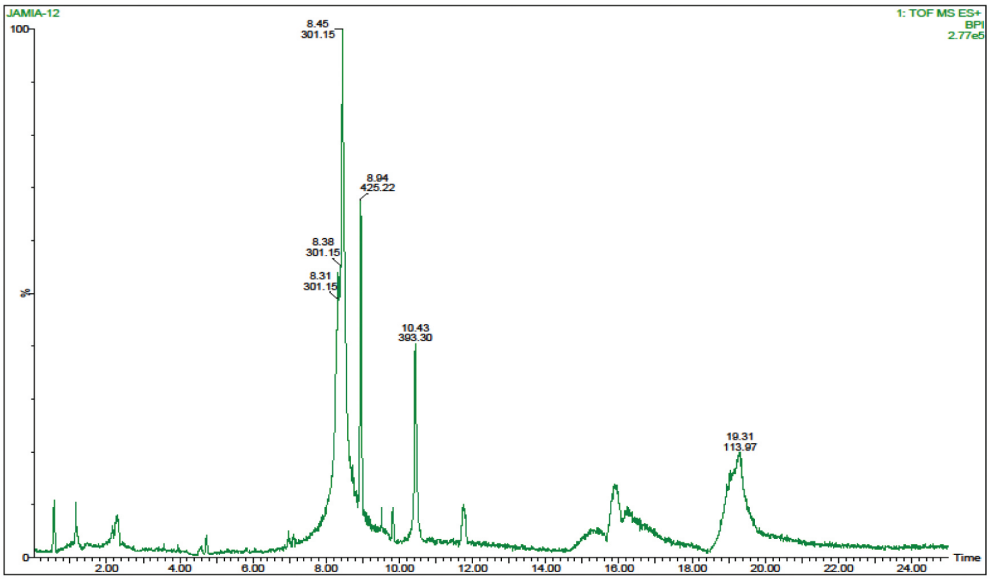

Figure 2: A typical LCMS chromatogram of metabolites present in *G. sylvestre*

Table 2: LCMS (metabolites of *gymnema sylvestre*)

Meta-bolites	Compound Name	Tentative Mass	Exact Mass	Formula	Mass ID.	Class
M1	Anthranilic acid	137.04	137.04	C7H7NO2	PR100494	Aminoacid
M2	Methionine	149.02	149.05	C5H11NO2S	PB000443	Aminoacid
M3	DL-Hexanoyl-carnitine	261.04	260.18	[C13H26NO4	MT000135	Fatty Acid
M4	Quercetin	301.15	302.04	[C16H13O6]+	PR040050	Flavonoid Flavonoid
M5	Berberin	335.12	335.24	C20H18NO4+	RO008886	Isoquinoline alkaloid
M6	D-Pinitol	193.00	194.18	C7H14O6	Pubchem CID:164619	Triterpinoid
M7	4-Methyl-alpha-pyrrolidino-propiophenone	217.15	217.14	C14H19NO	AU169906	Amino Acid
M8	Quercitol	163.04	164.15	C6H12	Pubchem CID: 441437	Flavonoid
M9	N-Acetyl-DL-glutamic acid	189.03	189.06	C7H11NO5	PR100420	Amino Acid
M10	Hematoxilin	301.14	301.16	C16H14O6	BML18375	Neoflavonoid
M11	O-Phospho-L-Serine	185.08	185.00	C3H8NO6P	PR100594	Amino Acid
M12	Purpurin	256.26	256.03	C14H8O5	SM837253	Anthraqui-none glycoside
M13	Capillarisin	315.16	316.05	C16H12O7	TY000038.	Sesquiterp-noid
M14	Isopentenyl-Adenin 7-glucoside	365.11	365.16	CE000239	C16H23N5O5	Pyridine alkaloid
M15	Hispidulin acetate	425.22	426.09	. C22H18O9	TY000233	Flaonoid
M16	Catechine	295.19	294.32	C15H67O8	TY000543	
M17	Lupeol	426.22	426.72	C30H50O	Pubchem CID:259846	Triterpinoid
M18	Gymnemic Acid X	723.65	724.88	C38H60O13	Pubchem CID: 15674686	Triterpinoid Saponin
M19	Tricin	329.17	330.07	C17H14O7	FlO00742	Flavonoid
M20	Hesperetin	302.15	302.07	C16H14O6	BML81380	Flavonoid
M21	Methionine	150.03	149.05	C5H11NO2S	MT000102	Amino Acid
M22	Linoliec acid	282.22	280.24	C18H32O2	EQ331601	Unsaturated fatty acid
M23	Triamcinolone	393.30	394.17	$C_{21}H_{27}FO_6$	SM873501	Steroid
M24	Gymne-magenin	505.34	506.45	C30H50O6	Pubchem CID:10051937	Saponin
M25	9-KODE	295.19	294.21	$C_{18}H_{30}O_3$	UT000279	Fatty Acid
M26	Myricetin	315.17	318.03	C15H10O8	TY000149	Flavonoid

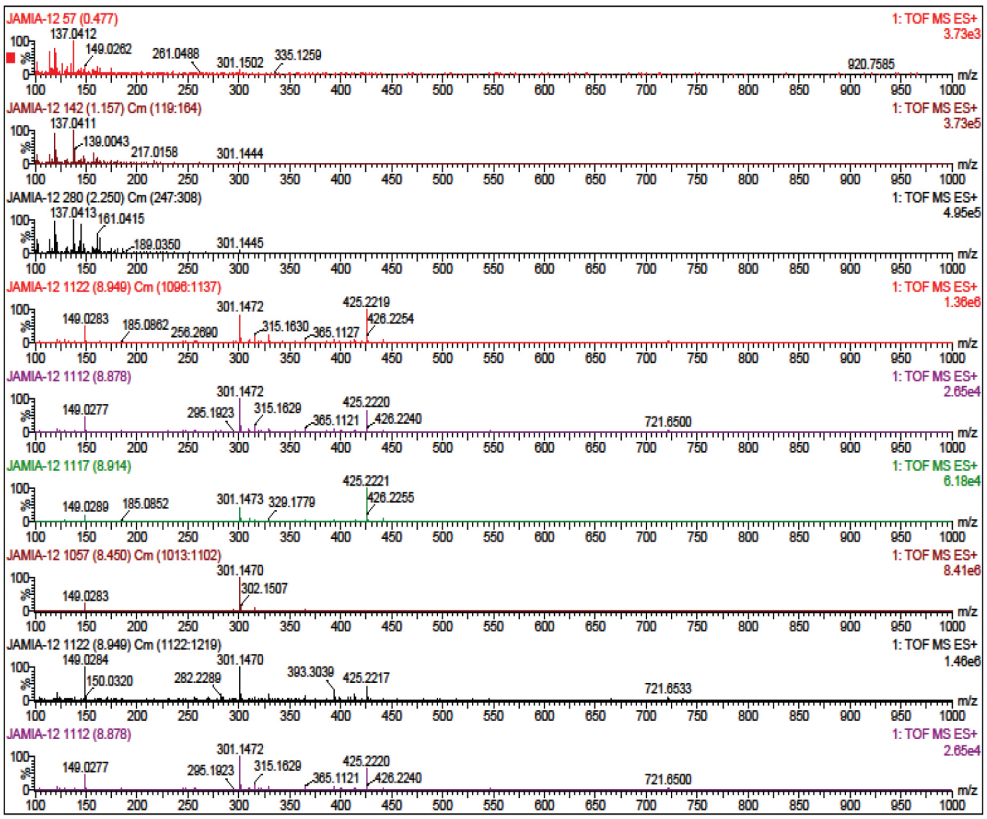

Figure 3: A typical extracted MS chromatogram of major metabolites present in *G. sylvestre*

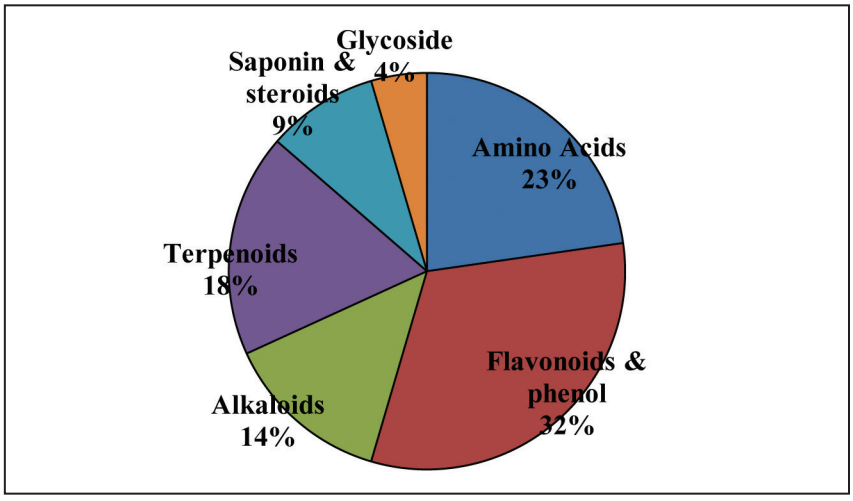

Figure 4: Major groups of metabolites present in *G. sylvestre* detected by LCMS.

bioautography assay is the method of choice in the screening of antidiabetic and antioxidant compounds due to advantages such as its simplicity, flexibility and high throughput (Belaqziz *et al.,* 2017). In order to find a suitable method to detect DPPH, α-amylase and α-glucosidase activity on TLC plates, different parameters were tested, such as type and concentration of substrates,

temperature and time of incubation, as well as the pH of the buffer solution. For DPPH bioautographic assay, a bright yellowish or cream colour band was observed against purple background. For α-amylase assay, a white-yellow spot was observed against dark brown background, while in case of α-glucosidase appearance of white spot was observed on purple/violet background.

Many bioactive compounds were identified as antidiabetic and antioxidant by comparing experimental data for mass-to-charge ratio (m/z) of molecular ion peak and with those of the literature reports. To identify the antioxidant and antidiabetic compounds in aqueous extract of *G. sylvestre* with a direct HPTLC-MS bioassay couples with DPPH, α-amylase and α-glucosidase.

There were four bioactive bands observed in case of amylase, while two were observed for glucosidase. Simultaneously, active bands were scrapped from co-TLC, dissolved in methanol and analyzed using mass spectrometry by their m/z value and found gymnemagenin, quercetin, N-feruloyl serotonin, solasodin, as amylase inhibitors and Cis-zeatin-9-glucosidase, catechine glucosidase inhibitors, respectively (Table 3).

Table 3: TLC-bioautography-MS analysis of isolated bioactive compounds from different extract of *G. sylvestre*.

TLC (Rf Value)	Name of Compounds	Exact Mass	Tentative Mass	Molicular Formula	Mass ID	Class	Positive Activities
0.4	Citramalic acid	148.03	149.02	C5H8O5	PR100770	Amino acid	DPPH
0.4	Catechin	294.27	295.19	$C_{15}H_{14}O_6$	Pubchem CID:9064	Phenol	DPPH, α-Amylase & Glucosidase
0.54	Quercitin	302.23	301.14	C15H10O7	PubChem CID: 5280343	Flavo-noid	Anti-Oxidant & α-amylase inhibition
0.5	4-Couma-roylquinic acid	338.31	339.13	$C_{16}H_{18}O_8$	PM000310	Steroid	α-gluco-sidase
0.5	N-Feruloyl Serotonin	352.39	353.27	C20H20N2O4	PubChem CID: 5969616	Fatty acid	DPPH, & α-amylase
0.5	Cis-Zeatin-9-glucosidase	381.16	381.30	C16H23N5O6	CE000607	glyco-side	DPPH α-Gluco-sidase
0.5	Solasodin	413.32	413.27	C27H43NO2	BML00913	Alka-loid	α-Amylase
	Gymne-magenin	506.7	506.9	$C_{30}H_{50}O_6$	10051937	Triter-peniod	DPPH, & α-amylase

Conclusion

The aqueous extract of *G. sylvestre* showed the hypoglycaemic activity by scavenging DPPH, and by inhibiting α-amylase and α-glucosidase. Metabolomic profiling of aqueous extract reveals the metabolites present in the plant by using the LCMS. The HPTLC-MS bioautography showed that the extract enriched with gymnemagenin and quercitin which played beneficial role for prevention of highperglycemic condition and oxidative stress.

Conflict of Interest

Authors declare that there is no conflict of interest associated with this manuscript.

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सारांश

जिमनेमा सिल्वेस्ट्रे एल. का फाइटोकेमिकल विश्लेषण और एचपीटीएलसी–एमएस बायोआटोग्राफी के माध्यम से मधुमेह और ऑक्सीकरण तनाव से जुड़े जैवरोधकों की पहचान

अनीसुर रहमान, जावेद इनाम सिद्दीक़ी, सईद अहमद, *शफ़ीक़ अहमद अन्सारी

जिमनेमा सिल्वेस्ट्रे, जिसे *गुरमार* के नाम से जाना जाता है, का उपयोग यूनानी चिकित्सा में मधुमेह, पेट के रोगों, यकृत रोगों और हृदय संबंधी विकारों के लिए बड़े पैमाने पर किया जाता है। वर्तमान अध्ययन *गुरमार* के जलीय सत्त में जैवसक्रिय चयापचयों की जांच करने के लिए किया गया। पूर्ण मेटाबॉलोमिक्स (चयापचयी) अध्ययन टीएलसी, एलसीएमएस और एचपीटीएलसी–एमएस के द्वारा किया गया। डीपीपीएच के प्रतिकूल एंटी–ऑक्सीडेंट गतिविधि का परीक्षण किया गया जिसने IC50 का मान 66.28±1.0 µg/ml दिखाया। सत्त की हाइपोग्लाइसेमिक क्षमता α–एमिलेज और α– ग्लूकोसाइडेज अवरोधक गतिविधि द्वारा जांच की गई। α–एमिलेज और α–ग्लुकोजीडेस का IC50 मान क्रमशः 68.41±0.7 µg/ml और 33.22±0.29 µg/ml पाया गया। सत्त की गुणवत्ता नियंत्रण जांच एचपीटीएलसी फिंगरप्रिंट द्वारा की गई जिसमें क्रमशः 254 और 366 एनएम पर 12 और 15 चयापचयों का पता चला जबकि एलसीएमएस स्क्रीनिंग में 26 चयापचयों का पता चला। एचपीटीएलसी–एमएस बायोआटोग्राफ़िक परिणामों से कुल आठ जैवसक्रिय यौगिकों का पता चला। आठ यौगिकों में से जिम्नेमेजेनिन, क्वेरसेटिन और कैटेचिन में डीपीपीएच, एमीलेज और ग्लूकोसाइडेज अवरोधक क्षमता होती है।

शब्दकुंजी: बायोआटोग्राफी, क्रोमैटोग्राफी, *जी. सिल्वेस्ट्रे,* α–एमिलेज, α–ग्लुकोजीडेस

Clinical Study to Validate the Safety and Efficacy of Unani Pharmacopoeial Formulation *'Araq-i-'Ajīb* in *Ṣudā'* (Headache)

*[1]Mohammad Zakir, [2]Hakimuddin Khan, [3]Chander Pal, [4]Kishore Kumar and [5]Narendra Singh

[1]Research Officer (Unani), Central Research Institute of Unani Medicine, Hyderabad

[2]Research Officer Incharge, Regional Research Institute of Unani Medicine, Bhadrak

[3]Research Officer (Pathology) Scientist-IV, Clinical Research Unit of Unani Medicine, Meerut

[4]Research Officer (Biochemistry), Regional Research Institute of Unani Medicine, Bhadrak

[5]Investigator (Statistics), Regional Research Institute of Unani Medicine, Bhadrak

Abstract

A clinical study was carried out to scientifically validate the safety and efficacy of Unani pharmacopoeial formulation *'Araq-i-'Ajīb* for symptomatic relief in the patients of *Ṣudā'* (headache) at Regional Research Institute of Unani Medicine (RRIUM), Bhadrak (Odisha) during 2014-2016. Out of 127 cases registered, 97 cases completed the study strictly as per protocol. Of the completed cases, 22 showed more than 90% relief, 67 showed 60 to 89% relief, 06 showed 30-59% relief, while 02 cases showed less than 30% relief in the signs and symptoms of *Ṣudā'* (headache). After seven days of treatment, the symptoms of the disease, including *Ṣudā'* (headache), disturbed concentration, irritability, *Ḍu'f al-Ishtihā'* (decreased appetite), *I'yā'*, difficulty in falling asleep and staying asleep, and mild sensitivity to light / noise were found decreased by 94.19%, 80.51%, 81.06%, 51.03%, 58.46%, 72.86% and 83.84% respectively as compared to the baseline. The variations in the values of Hb, ESR, TLC and DLC tests before and after the treatment were found within normal limits. The study drug was found well-tolerated and no adverse effects were observed during the study. The study is affirmative of the safety and efficacy of Unani pharmacopoeial formulation for symptomatic relief in the patients of *Ṣudā'* (headache).

Keywords: *'Araq-i-'Ajīb,* headache, *Ṣudā'*, Unani Medicine

Introduction

Ṣudā' (headache) is defined as a pain arising from the head or upper neck of the body. The pain originates from the tissues and structures that surround the brain, because the brain itself has no nerves that give rise to the sensation of pain (pain fibers). The periosteum that surrounds bones; muscles that encase the skull, sinuses, eyes and ears; meninges that cover the surface of the brain, spinal cord, arteries, veins and nerves, all can become inflamed or irritated to cause the headache. This pain may be dull, sharp, throbbing, constant, mild or intense.

Ṣudā' (headache) is a painful and common symptom. Primary headache disorders are of various types which include tension-type headache (TTH), migraine, cluster headache (CH) and medication-overuse headache (MOH). Overall, these disorders account for approximately 95% of all headache complaints (Brust, 2007). Headache also occurs as a typical symptom of a range of other health conditions, the so-called secondary headaches like chronic daily headache (CDH) (Anonymous, 2004). Primary headache disorders are a significant, largely unaddressed burden of ill health and disability everywhere (Anonymous, 2006b). Primary headache disorders have a lifetime prevalence of 90% (Steiner, 2004).

*Author for Correspondence; Email: urzakir@rediffmail.com

Migraine on its own ranks among the top 20 causes of years of life lived with disability (YLD) (Anonymous, 2001). Tension-type headache afflicts 80% of women and two-thirds of men living in the developed countries (Anonymous, 2006b).

Tension-type headache is bilateral and often located in the occipital region and the pain feels like being pressed or tightened up. The headache is not paroxysmal but persistent, accompanied by stiff shoulders and a sense of dizziness, but without vomiting or hypersensitivity to light and sound. In actual clinical practice, however, it is sometimes difficult to differentiate between episodic tension-type headache (ETTH) and chronic tension-type headache (CTTH), the latter of which lasts longer than 15 days a month (Sakuta, 2001). The mechanism of tension-type headache is poorly understood, though it has long been regarded as a headache with muscular origins. It may be stress related or associated with musculoskeletal problems in the neck, shoulders and head (Kellgren, 1938).

Migraine is characterized by intense throbbing head pain, blurred vision with shimmering light speck. It has a paroxysmal onset at an interval of several days or weeks, but lasts only a few days; there is nausea, vomiting, and hypersensitivity to light and sound during attacks; and pain is caused by release from stress, hunger, crowdedness, excessive sleep, being in direct hot sunlight, drinking, exercise, etc. (Young and Siberstein, 2006). It almost certainly has a genetic basis (Ferrari, 1998), but environmental factors play a significant role in how the disorder affects those who suffer from it. Patho-physiologically, it defines that activation of a mechanism deep in the brain causes release of pain-producing inflammatory substances around the nerves and blood vessels of the head (Stovner *et al.,* 2007).

Cluster headache is one of a group of primary headache disorders (trigeminal autonomic cephalalgia) of uncertain mechanism that are characterized by frequently recurring, short-lasting but extremely severe headache (Anonymous, 1998). It is so called because it occurs in clusters, daily, almost at a set time, for one to two months, in many cases. The cluster period, in which a severe headache behind the eyes is accompanied by lacrimation from the eyes and a stuffed nostril, can occur once or twice a year, or once in several years. The pain usually involves one side of the head and spreads around the eye. Cluster headaches start suddenly and generally last about an hour. It is one of the most excruciating pains people experience, similar to trigeminal neuralgia (Koichi, 2004).

Medication-overuse headache is caused by chronic excessive use of medication to treat headache (Diener *et al.,* 1989). Medication-overuse headache is oppressive, persistent and often at its worst on awakening in the morning (Anonymous,

2006b). All medications for the acute or symptomatic treatment of headache, in overuse, are associated with this problem, but what constitutes overuse is not clear in individual cases. Suggested limits are the regular intake of simple analgesics for 15 or more days per month or of codeine or barbiturate containing combination analgesics, ergotamine or triptans for more than 10 days a month (Anonymous, 1998).

Secondary headache disorders are caused by an underlying illness or condition that affects the brain. Secondary headaches are usually diagnosed based on other symptoms that occur concurrently and the characteristics of the headaches. Some of the more serious causes of secondary headache include brain tumour, disorders of blood vessels in the brain, including stroke, hemorrhagic stroke, ischemic stroke, exposure to a substance or its withdrawal (like alcohol), increased intracranial pressure, head injury, inflammation from meningitis, encephalitis, and other infections, seizures, spinal fluid leak, structural abnormalities of the head, neck and spine, trigeminal neuralgia (Anonymous, 2009; Anonymous, 1999).

According to the literature of Unani Medicine, *Ṣudā‘* (headache) is the pain felt in the structure of head up to neck. As per pathophysiology and aetiology of the disease, *Ṣudā‘* (headache) has been divided into *Ṣudā‘ Sādhij* (primary headache) where simply change in the temperament of the organ leads to *Ṣudā‘* (headache), whereas in case of *Ṣudā‘ Māddī*, there is quantitative or qualitative change in the *Akhlāṭ* (humours) of the organ leading to *Ṣudā‘* (headache). According to the types of predominant *Kayfiyāt* (qualities) and *Akhlāṭ*, *Ṣudā‘* (headache) has been further divided into several types. Similarly, according to the origin of the cause of *Ṣudā‘* (headache), it has been further divided into *Ṣudā‘ Aṣlī*, when aetiology lies within the parts of head (pathology originates from the parts of head) and *Ṣudā‘ Shirkī* (secondary headache) where *Ṣudā‘* (headache) arises due to pathologies of other organs. Another classification of *Ṣudā‘* (headache) is based on the site and extent of pain. Accordingly, *Ṣudā‘* (headache) is named as *Bayḍa-o-Khūdha* when the pain involves whole head, and *Shaqīqa* (migraine) when the pain is localised in either half of the head.

In case of *Ṣudā‘ Sādhij* (primary headache), as there is no involvement of *Akhlāṭ*, the disease may be managed by applying principles of *Ta‘dīl-o-Tabdīl-i-Mīzaj* (temperamental equilibrium / alteration) and *Taskīn* either under regimen therapy or pharmacotherapy. The principles of treatment of *Ṣudā‘ Māddī* (headache due to involvement of *Akhlāṭ*) include *Nuḍj* and *Tanqiya* (concoction and elimination of morbid matter from the body). Similarly, in case of *Ṣudā‘ Shirkī* (secondary headache), removal of the cause will relieve *Ṣudā‘* (headache). In case of *Ṣudā‘* (headache), pain may lead to certain other symptoms which include disturbed concentration, irritability, decreased appetite, fatigue, difficulty in falling asleep and staying asleep, and mild sensitivity to light / noise (Arzani, 1924; Kinturi,

1906; Majusi, 2010; Tabari, 1995; Ibn al-Zuhr, 1986; Samarqandi, 1916; Kabiruddin, 1935; Khan, 1987; Khan, 2003).

Materials and Methods

The present study was a multi-centric study conducted simultaneously in seven centers including Bhadrak. Total sample size was 540 completed cases. The sample size for RRIUM, Bhadrak was 90 completed cases. The data presented in this study belongs to RRIUM, Bhadrak only. Final study with complete sample size may be published later on.

The study was conducted at Regional Research Institute of Unani Medicine (RRIUM), Bhadrak (Odisha) on 97 patients of *Ṣudā'* (headache) selected from the OPD of the institute during 2014-2016. The patients of either sex in the age group of 18 to 65 years were included in the study. Inclusion criteria were cases having *Ṣudā'* (headache) with or without disturbed concentration, irritability, *Ḍu'f al-Ishtihā'* (decreased appetite), *I'yā'* (fatigue), difficulty in falling asleep and staying asleep, and mild sensitivity to light / noise. The patients below 18 years and above 65 years of age, patients of headache not responding to standard therapy, headache accompanied by impaired neurological functions (loss of balance, weakness, numbness, or speech disturbances), double vision, seizures, mental disturbances and loss of consciousness, headache accompanied by persistent nausea, vomiting, fever and stiff neck, history of recent head injury, known cases of any other acute illness, known cases of severe renal / hepatic / cardiac ailments, pregnant and lactating women were excluded from the study.

The clinical study protocol was approved by the Institutional Ethics Committee (IEC) of the Institute on March 20, 2014 and the trial was registered with CTRI vide registration number CTRI/2015/03/005608. After obtaining written informed consent, patients were enrolled for the study and subjected to the haematological and biochemical investigations. Haematological investigations including haemogram [haemoglobin (Hb), erythrocyte sedimentation rate (ESR), total leukocyte count (TLC) and differential leukocyte count (DLC: neutrophils, eosinophils, basophils, lymphocytes, monocytes) were conducted at the baseline and after the treatment, while urine examination (routine and microscopic) was conducted only at the baseline. Biochemical investigations including liver function tests (LFTs) comprising serum bilirubin, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and alkaline phosphatase (ALP), and kidney function tests (KFTs) comprising serum creatinine, blood urea, and serum uric acid were conducted only at the baseline.

The parameters for the assessment of efficacy of the formulation were *Ṣudā'* (headache), disturbed concentration, irritability, *Ḍu'f al-Ishtihā'* (decreased

appetite), *I'yā'* (fatigue), difficulty in falling asleep and staying asleep and mild sensitivity to light / noise. These parameters were graded according to VAS score.

For overall assessment of efficacy, relief in signs and symptoms were calculated and patients were divided into four groups on the basis of relief they got. Patients getting 90-100% relief in signs and symptoms were marked cured, patients getting 60-89% relief relived, and those getting 30-59% relief were marked partially relived, whereas patients getting less than 30 percent relief were marked not relieved.

The clinical follow-ups of all the cases were carried out on day 3 (1st follow-up) and day 7 (2nd follow-up) of the treatment. The safety of the trial drug was evaluated by pathological investigations and clinically by monitoring adverse effects which were carefully sought at each follow-up. The *Mizāj* (temperament) of the patients was assessed as per the parameters described in Unani classical literature. The clinical and laboratory findings observed in every case were recorded on a separate case record form (CRF) designed especially for clinical study on *Ṣudā'* (headache). No concomitant treatment was allowed during the study. Baseline and follow-up values of pathological investigations were statistically analyzed using Student's paired 't' test. The significance level of $P < 0.05$ was used in this study.

Study Drug, Dosage Schedule and Mode of Administration

The topical Unani pharmacopoeial formulation *'Araq-i-'Ajīb* used in the study was obtained from the Central Research Institute of Unani Medicine (CRIUM), Hyderabad. *'Araq-i-'Ajīb* was applied locally at forehead twice daily.

Composition of Study Drug

'Araq-i-'Ajīb contained three ingredients as shown in Table 1 (Anonymous, 2006a).

Results

After completion of the treatment, *'Araq-i-'Ajīb* exhibited significant improvement in the signs and symptoms of *Ṣudā'* (headache). *Ṣudā'* (headache), disturbed

Table 1: Composition of *'Araq-i-'Ajīb*

S.No.	Unani Name	Scientific Name	Quantity
1.	*Kāfūr*	*Cinnamomum camphora* Nees & Eberm.	2 part
2.	*Jawhar-i-Pūdīna*	*Mentha arvensis* L.	2 part
3.	*Jawhar-i-Ajwāyin*	*Trachyspermum ammi* L.	1 part

(Anonymous, 2006a)

concentration, irritability, *Ḍu'f al-Ishtihā'* (decreased appetite), *I'yā'* (fatigue), difficulty in falling asleep and staying asleep, and mild sensitivity to light / noise were decreased by 94.19%, 80.51%, 81.06%, 51.03%, 58.46%, 72.86% and 83.84% respectively as compared to the baseline (Figure 1).

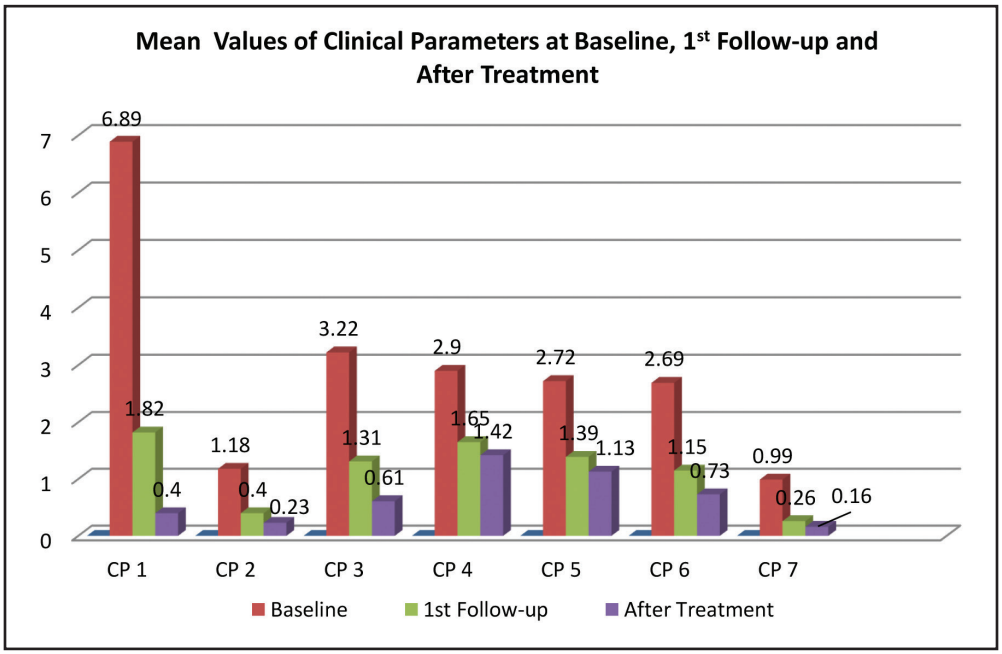

Figure 1: Mean Values of Clinical Parameters at Baseline, 1st Follow-up and After Treatment

CP 1 = *Ṣudā'* (headache); CP 2 = Disturbed concentration; CP 3 = Irritability; CP 4 = *Ḍu'f al-Ishtihā'* (decreased appetite); CP 5 = *I'yā* (fatigue); CP 6 = Difficulty in falling asleep and staying asleep; CP 7 = Mild sensitivity to light/ noise

Out of 97 cases who completed the study, 22 (22.68%) cases were cured, 67 (69.07%) cases were relieved, 06 (6.19%) cases were partially relieved, whereas only 02 cases (2.06%) were not relieved (Figure 2).

The mean values of haematological parameters at the baseline and after completion of the treatment are shown in Table 2. The variations in the values of Hb, ESR, TLC, and DLC before and after the treatment were found within normal limits revealing safety of the study drug. The study drug was found well-tolerated and no adverse effects were observed.

Discussion

Unani pharmacopoeial formulation used in this study was found effective in providing symptomatic relief in the treatment of *Ṣudā'* (headache). The signs and symptoms of *Ṣudā'* (headache) were significantly reduced. After seven days of treatment, the improvement recorded was 94.19% for *Ṣudā'* (headache), 80.51%

Table 2: Mean Values of Pathological Investigations at Baseline and After Treatment

Pathological Investigation		Period	Mean ± SD	P value
Haemoglobin (gm%)		BT	12.21±0.12	P < 0.05
		AT	12.11±0.11	
ESR (mm/hr)	1st Hour	BT	13.61±1.16	P > 0.05
		AT	15.17±1.29	
	2nd Hour	BT	31.13±2.39	P > 0.05
		AT	32.39±2.32	
Total Leucocytes Count (cmm)		BT	6943.81±100.29	P > 0.05
		AT	6710.31±96.40	
DLC	Neutrophils	BT	61.05±0.40	P > 0.05
		AT	61.22±0.37	
	Lymphocytes	BT	28.26±0.41	P > 0.05
		AT	28.99±0.35	
	Eosinophils	BT	10.11±0.27	P < 0.05
		AT	9.15±0.20	
	Monocytes	BT	0.56±0.07	P > 0.05
		AT	0.64±0.05	

BT = Before Treatment; AT = After Treatment

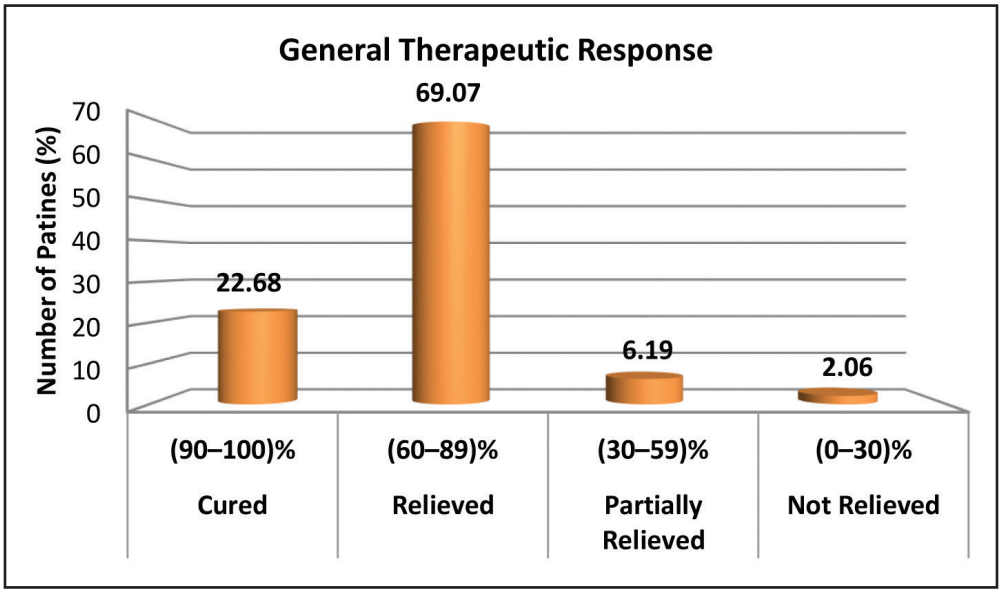

Figure 2: General Therapeutic Response

for disturbed concentration, 81.06% for irritability, 51.03% for *Ḍu'f al-Ishtihā'* (decreased appetite), 58.46% for *I'yā'* (fatigue), 72.86% for difficulty in falling asleep and staying asleep and 83.84% for mild sensitivity to light / noise. The test

drug was found well-tolerated and no adverse effects were observed during the study. The values of pathological investigations before and after the treatment showed safety of the study drug. The study is affirmative of safety and efficacy of Unani pharmacopoeial formulation *'Araq-i-'Ajīb* in the treatment of *Ṣudā'* (headache).

Conclusion

On the basis of the above findings, it can be concluded that Unani pharmacopoeial formulation *'Araq-i-'Ajīb* is safe and effective in the treatment of *Ṣudā'* (headache).

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सारांश

सुदा (सिरदर्द) के रोगियों पर यूनानी भेषजकोशीय मिश्रण *'अर्क़–ए–अजीब'* की सुरक्षा और प्रभावकारिता का वैधीकरण करने के लिए नैदानिक अध्ययन

***मोहम्मद ज़ाकिर, हकीमुद्दीन ख़ान, चन्द्र पाल, किशोर कुमार, नरेंद्र सिंह**

सुदा (सिरदर्द) के रोगियों में लाक्षणिक राहत के लिए यूनानी भेषजकोशीय मिश्रण *'अर्क़–ए–अजीब'* की सुरक्षा और प्रभावकारिता का वैज्ञानिक रूप से वैधीकरण करने के लिए 2014–2016 के दौरान क्षेत्रीय यूनानी चिकित्सा अनुसंधान संस्थान (क्षे.यू.चि.अ.सं.), भद्रक (ओडिशा) में एक नैदानिक अध्ययन किया गया। पंजीकृत 127 रोगियों में से 97 रोगियों ने प्रोटोकॉल के अनुसार दृढ़ता से अध्ययन पूरा किया। अध्ययन पूर्ण रोगियों में से 22 रोगियों ने *सुदा* (सिरदर्द) के संकेतों और लक्षणों में 90% से अधिक राहत, 67 रोगियों ने 60–89% राहत, छः रोगियों ने 30–59% राहत जबकि दो रोगियों ने 30% से कम राहत दिखाई। उपचार के सात दिनों के बाद रोग के लक्षणों अर्थात् *सुदा* (सिरदर्द), अशांत एकाग्रता, चिड़चिड़ापन, *ज़ोफ अल–इश्तिहा* (भूख कम होना), *ईया,* नींद आने और सोते रहने में कठिनाई तथा प्रकाश/शोर के प्रति हल्की संवेदनशीलता में आधार रेखा की तुलना में क्रमशः 94.19%, 80.51%, 81.06%, 51.03%, 58.46%, 72.86% और 83.84% तक कमी पाई गई। उपचार से पहले और बाद में एचबी, ईएसआर, टीएलसी और डीएलसी परीक्षणों के मान में भिन्नता सामान्य सीमा के भीतर पाई गई। अध्ययन औषधि सहनशील पाई गई और अध्ययन के दौरान कोई प्रतिकूल प्रभाव नहीं देखा गया। यह अध्ययन *सुदा* (सिरदर्द) के रोगियों में लाक्षणिक राहत के लिए यूनानी भेषजकोशीय मिश्रण *'अर्क़–ए–अजीब'* की सुरक्षा और प्रभावकारिता की पुष्टि करता है।

शब्दकुंजी: *अर्क़–ए–अजीब,* सिरदर्द, *सुदा,* यूनानी चिकित्सा

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CENTRAL COUNCIL FOR RESEARCH IN UNANI MEDICINE
Ministry of Ayurveda, Yoga & Naturopathy, Unani,
Siddha and Homoeopathy (AYUSH), Government of India
61-65, Institutional Area, Janakpuri, New Delhi - 110 058
Telephone: +91-11-28521981, 28525982
Email: unanimedicine@gmail.com
Website: http://ccrum.res.in