ISSN: 0974-1291

HIPPOCRATIC JOURNAL OF UNANI MEDICINE

Volume 14 • Number 1 January–March 2019

CENTRAL COUNCIL FOR RESEARCH IN UNANI MEDICINE

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Volume 14, Number 1, January - March 2019

Hippocratic J. Unani Med. 14(1): 1- 78, 2019

CENTRAL COUNCIL FOR RESEARCH IN UNANI MEDICINE

Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH)

Government of India

Hippocratic Journal of Unani Medicine

Editorial Office

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Annual Subscription: ₹ 300/- (India) US $ 100/- (Other Countries) **Single Issue:** ₹ 150/- (India) US$ 50/- (Other Countries)
Payments in respect of subscription may be sent in the form of bank draft drawn in favour of Director General, CCRUM, New Delhi.

Printed and published by Shri Devanand, Assistant Director (Admn.) on behalf of Central Council for Research in Unani Medicine
Ministry of AYUSH, Government of India
Printed at Rakmo Press Pvt. Ltd., C-59, Okhla Industrial Area (Phase I), New Delhi - 110020

Editorial

Herbal origin drugs have been playing an important role in the prevention and treatment of various diseases. Due to their cost effectiveness and less associated side effects, the Traditional Medicine which mainly relies on such drugs has witnessed resurgence and increased demand at global level in the recent past. Unani Medicine, which primarily depends upon such drugs, too got its share from the change in the patient's behavior of shifting towards the Traditional Medicine in spite of vast development in the field of modern medicine and surgery.

The contributions of the Central Council for Research in Unani Medicine in the area of research and drug development as well as its publicity through various publications have played significant role in increasing the acceptability of Unani Medicine. In particular, the Hippocratic Journal of Unani Medicine (HJUM) has been crucial in the propagation and dissemination of research in the system amongst the scientific fraternity. Since the beginning of its publication in 2006, we have been constantly striving to make HJUM a leading journal of Unani Medicine and related sciences.

This issue of HJUM includes six papers. The first paper entitled 'Polyherbal Pharmaceutical Preparations in Unani Medicine – A Rationale Approach' discusses the rationale approach adopted by Unani physicians in the preparation of polyherbal mixtures considering chemical constituents and properties of each ingredient. The second paper is review of *Rawghan Chahār Barg,* a classical Unani formulation having antiinflammatory, analgesic and antimicrobial activities. The third paper is review of pharmacological activities and clinical effects of *Suranjān Talkh* (*Colchicum luteum* Baker), an important Unani drug. In the fourth paper, the authors have discussed biochemical, immunological and pathological studies on the patients of *Waja' al-Mafāṣil* (rheumatoid arthritis) treated with Unani pharmacopoeial drugs *Ma'jūn Sūranjān, Safūf Sūranjān* and *Rawghan Sūranjān*. The fifth paper is based on macro and microscopical evaluation, HPTLC fingerprinting and quality control studies on fruits of *Mimusops elengi* L. The last paper discusses the result of a clinical study to validate analgesic effect and safety of Unani pharmacopoeial formulations in *Waja' al-Mafāṣil* (joint pain) in Eastern India.

I believe that the papers included in this issue would be of great help for the scientists and scholars. I sincerely appreciate the authors and reviewers for their scientific contribution and encourage all the scientists and scholars to submit their papers for publication in the upcoming issues.

Prof. Asim Ali Khan
Editor-in-Chief

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Polyherbal Pharmaceutical Preparations in Unani Medicine - A Rationale Approach

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Abstract

The use of polyherbo-mineral preparations is in vogue in Unani Medicine since centuries. The '*Ebers papyrus*' contains 875 prescriptions. The powder and ointment were introduced by Aristotle and Hippocrates respectively. But the credit goes to Galen who introduced several dosage forms and gave scientific logics to use of polyherbal mixtures. He is considered as the father of polyherbal pharmaceutical preparations. Many Arab physicians prepared several dosage forms and included chemistry in pharmacy. Unani physicians gave rationale to use of polyherbal mixtures for the treatment of diseases and now these have been scientifically proved. Certain drugs, such as *Acacia arabica, Pistacia lentiscus*, *Cochlospermum religiosum* and mucilage containing drugs, are added especially with irritant drugs to prevent mucosal injury in the gastrointestinal tract. Certain drugs are added to increase or decrease the potency of some other drugs in the formulations. Scientific studies have proved that piperine, curcumin, glycyrrhizine, etc. possess significant bioactive enhancing property justifying their inclusion in some other chemical molecules/ drugs. Honey possesses antibacterial, antiviral and antifungal properties due to presence of low pH, osmotic effect, high sugar concentration and presence of hydrogen peroxide. Honey and sugar are added as preservative in many semisolid and liquid dosage forms of Unani Medicine. Several isolated chemical constituents of plant drugs are added with allopathic drugs in conventional pharmacology to achieve many targets. Many scientific studies have revealed the beneficial effects of polyherbal mixtures, if they are judiciously mixed, in the treatment of various ailments. A concerted attempt has been made through this paper to deliberate the concept of polyherbal pharmaceutical formulations in Unani Medicine.

Keywords: Compound preparation, Polyherbal mixture, Polyherbal pharmaceutical formulations, Unani Medicine

Introduction

Historical Background

The prehistoric men did not use plant materials for treatment of diseases. They were mainly magical healers, used magical stones and other materials for treatment purposes. The use of medicinal plants and drug preparations begun from the earliest urban civilisation of the world, i.e. Mesopotamian civilisation (3000-539 BC). The pharmacists of Mesopotamia prepared wines, soap, vinegar, plant extract, ointments and volatile oils. The medical texts on clay tablets contain nearly 800 fragments which were the first recorded symptoms of illness,

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prescriptions and directions for compounding of drugs. The well-documented history pertaining to the use of compound drug is recorded from the Egyptian civilisation (3000-1200 BC) where empirical healers formulated and prepared several dosage forms, viz. decoction, infusion, pill, suppository, etc. They used wine, beer and honey as vehicles for the preparation of liquid dosage forms. They also used mortars and hand mills for grinding and powdering; sieve for sieving; and balance for weighing drugs. The ingredients of the recipes were given into a fixed ratio. The most important pharmaceutical record is the '*Ebers Papyrus*' which was written in 1500 BC. It contains 875 prescriptions including approximately 700 single drugs (Anonymous, YNM).

The Greek civilisation (1250-285 BC), amongst the most important civilisations in the history of medicine, introduced many dosage forms, viz. *Safūf* (powder) and *Tiryāq* (anti-dote) which were introduced by *Arasṭū* (Aristotle) and Magneeus Felsoof respectively; *Marham* (ointment) was first prepared by *Buqrāṭ* (Hippocrates); *Sharbat* (syrup) was invented by Pythagoras; *Shiyāf* (suppository), *Farzaja* (vaginal pessary) and *Fatīla* (bougie) were invented by *Bukhtishu*. Some potent polyherbal pharmaceutical formulations like *Ayārij Feeqra, Amroosiya* and *Basaliqoon* were prepared by Hippocrates. A large number of polyherbal pharmaceutical formulations emerged in the Roman civilisation (275 BC-476 AD) from the period of *Jālīnūs* (Galen) who proposed that the body would pull out of a complex prescription that needed to restore the humoral balance. His principles of preparing and compounding of drugs ruled the pharmaceutical industries of Western world for more than 1500 years. He introduced *La'ūq* (linctus), *Barsha'shā'* and a formula of cold cream. Hence, he is regarded as the father of polyherbal pharmaceutical preparations.

During 5th to 12th century AD, the Arab physicians immensely contributed to the fields of pharmacy and pharmaceutics. They introduced pharmaceutical chemistry including several equipment which are still used in pharmaceutics. They also prepared certain dosage forms such as '*Araq* (aqueous extract), *Kushta* (calx), paste, etc. (Ansari, *et al.*, 2016). The art of preparing, compounding and dispensing of drugs was categorised as separate science and recognized as '*Ṣaydala*' (pharmacy) in the 8th century AD. The professionals were designated as '*Ṣaydalānī*' (pharmacist). Drug stores were established in 754 AD in Baghdad. The licensing system for drug stores and preparation of drugs was first introduced during the reign of *Caliph Mamun al-Rashid* (d. 833 AD). *Sinān ibn Thābit* (d. 943 AD) was appointed as the founder administrator of licensing department. The druggists / pharmacists had to pass an examination in order to obtain a license for practice. *Jābir ibn Ḥayyān* (Geber) (d. 815 AD) considered as the father of chemistry discovered nearly 22 types of equipment including alembic and retort which are still used in pharmaceutics (Virk, YNM). *Ibn Rabban al-Ṭabarī* (d. 870 AD) introduced many methods for detoxification of toxic drugs

and recommended suitable vessels for storage of finished products. He stated that glass or ceramic vessels should be preferred for storage of liquid drugs, eye liquid salves should be stored into small jars and fatty substances should be kept in lead containers (Ṭabarī, 2010). *Al-Kindī* (Alkindus) (d. 873 AD) introduced 'posology', a separate branch of medicine concerned with dosage of drugs. He compiled '*Risāla fi ma'rifat quwā al-adwiya al-murakkaba*' which has been translated into Latin and named as '*De Medicinarum Compositarum Gradibus Investigandis Libellus*' (The Investigation of the Strength of Compound Medicine). This treatise has given mathematical formulas by which drugs can be formulated into a fixed ratio with the result that all patients would receive standardized doses. *Rāzī* (d. 925 AD) in his *Ṭibb al-Fuqarā'* (a short treatise on home remedies) discusses diets and drugs which can be easily available at apothecary shops, kitchen and in military camps (Virk, YNM). His largest encyclopaedia '*Kitāb al-Ḥāwī fi'l-Ṭibb*' covers all areas of medical knowledge including remedies tested in animals to evaluate their efficacy and safety (Al-Ghazal, 2003). *Ibn Sīnā* (d. 1048 AD) laid down certain rules for testing of new pharmacological agents (Ibn Sīnā, 2010; Ansari, *et al.*, 2018). *Al-Birūnī* (d. 1050 AD) compiled '*Kitāb al-Ṣaydana fi'l-Ṭibb*' (The Book on Pharmacy) which is in two volumes; the first volume is on pharmacology, toxicology and substitution of drugs. He stated that a physician should know the substitute of each drug and should also be aware about drug-drug interactions. The second volume is on *Materia Medica* which contains nearly 700 drugs.

Ibn Jazla (d. 1100 AD) wrote '*Al-Minhāj fi'l-Adwiya al-Murakkaba*' (Methodology on Compound Drugs) which has been translated by Jambolinus into Latin and named as '*Cibis et medicines simplicibus*'. *Abu Manṣūr Muwaffaq* (10th century AD) wrote '*Kitāb al-Abniya 'an Haqā'iq al-Adwiya* (The Foundations of the True Properties of Remedies) which deals with 585 remedies. The original manuscript is available in a library of Vienna. *Saeed ibn 'Abd Rabbihi* (d. 960 AD) wrote '*Kitāb al-Dukkān*' (The Pharmacy Shop) which contains 17 chapters on compound drugs. Abul Qasim ibn Abbas Zahrawi (Abulcasis) (d. 1013 AD) compiled '*Kitāb al-Taṣrīf*' (Magnum opus) whose 27th volume discusses preparing and compounding of complex mixtures (Virk, YNM). Ibn Bayṭār (d. 1248 AD) compiled a largest compendium '*Al-Jāmi' li-Mufradāt al-Adwiya wa'l-Aghdhiya*' which describes approximately 2300 drugs of botanical, animal and mineral origins (Ibn Baiṭār, 2003; Ansari, *et al.,* 2018). *Zain al-'Aṭṭār* wrote '*Miftāḥ al-Khazā'in*' in 1366 AD whose 3rd part discusses with compound drugs (Virk, YNM).

In India, the Unani physicians of *Mughal* period prepared '*Khamīra*' (fermented confection), a complex mixture which is used especially in the treatment of cardiac, cerebral and gastric disorders (Rehman, 1991). Noor Jahan, queen of Emperor Jahangir prepared '*Iṭr-ī-Jahāngīr*' (a perfume) for her husband (Virk,

YNM). Many noteworthy pharmacopoeias have been compiled by renowned Indian Hakims such as '*Qarābādīn-i-Qādrī*' by Arzānī, '*Qarābādīn-ī-A'zam*' by A'zam Khān', "*Ilaj al-Amrāḍ*' by Sharīf Khān, '*Qarābādīn-ī-Kabīr*' by Ḥusain Khān, *Qarābādīn-ī-Jadīd* by Abdul Hafeez, *Miftāḥ al-Khazā'in* by Kareem Baksh, *Ma'din al-Iksīr* by Firozuddin, *Makhzan al-Murakkabāt* by Ghulam Jilani, *Al-Qarābādīn* by Kabeeruddin and '*Bayāḍ-i-Kabīr*' by Kabīruddīn (Ansari, *et al.,* 2016). Hakim Ajmal Khan founded the '*Hindustani Dawakhana*' in Delhi, India to fulfil the demand of pharmacopoeial formulations on large scale (Anonymous, 2002).

Need for Compounding of Drugs

When the concept of polyherbal mixture emerged, many notable ancient Unani physicians had diverse opinion about the use of compound formulations. Rāzī mentioned that if possible, one single drug should be used than complex mixture for treatment purposes (Ansari, *et al.,* 2016). Ibn Sīnā wrote that tested drugs are always better than untested drugs and single drugs should be preferred to compound preparations especially for the treatment of simple (single) diseases. Ibn Sīnā further stated that those recipes whose ingredients and amounts are less should be preferred rather than those recipes whose ingredients and amounts are more (Ansari, *et al.,* 2016; Ibn Sīnā, 2006). But in certain circumstances, treatment of diseases is not possible by using single drugs only. Ali Ibn Abbas Majusi (Haly Abbas) stated that all diseases could not be cured only by using single drugs because of differences in the temperament and doses of the drugs, intensity of the pathology, and symptomatology of the diseases (Ibn Abbas, 2010). Therefore, most of the Unani physicians have opined that compound preparations may be preferred to achieve various objectives and to treat the body as a whole. Another opinion is that isolated active constituents of plant drugs might not be sufficient to attain desired therapeutic effects. Combining multiple herbs in a fixed ratio may give a better therapeutic effect and reduce the toxicity (Parasuraman, *et al.,* 2014).

Natural medicinal substances including plant origin drugs have been parts of the pharmacopoeias for thousands of years and offered a reliable source of medicine. Although, the medicinal uses of willow (Salix sp.) were known since 6000 years, the first synthetic drug, Aspirin, was formulated in 1897 AD from Salicylic acid extracted from willow barks. This discovery guided to the notion of mono-drug therapy for the treatment of complex diseases and synthetic drug development by the advent of structure activity-guided organic synthesis and high throughput screening (HTS) (Carmona and Pereira 2013).

The World Health Organization (WHO) has estimated that approximately 80% population of the world uses herbs for their health care issues. The Indian subcontinent is known to be one of the key biodiversity centres with approximately 45,000 plant species. Nearly 15,000 medicinal plants have been

recorded in India, of which 7,000-7,500 plants are used medicinally.

Single or compound mixtures are used for treatment of diseases in Ayurveda, Siddha and Unani Medicine since long. The concept of polyherbal formulation exists in Ayurvedic literature too, i.e. '*Sarangdhar Samhita*' which highlighted the greater therapeutic efficacy of polyherbal mixtures (Parasuraman, *et al.,* 2014).

Unani Medicine has given the following rationale to the use of polyherbal mixtures for the treatment of various bodily ailments:

(i) For Correction of Toxicities of Toxic Drugs

Certain Unani drugs are liable to produce moderate to severe adverse effects which can be minimized by adding some corrective drugs. *Saqmonia* (*Convolvulus scammonia* L.) and *Zangar* (verdigris) can produce gastroenteritis and mucosal injury in the gastrointestinal tract which may be prevented by adding *Samagh-e-Kateera* (*Cochlospermum religiosum* (L.) Alston.) or *Samagh-e-Arbi* (*Acacia arabica* Willd.var. indica Benth.) with them (Qureshi, 1995). Anyone of these aromatic drugs, viz. *Ilaichi Khurd* (*Elettaria cardamomum* Maton.), *Mastagi* (*Pistacia lentiscus* Linn.), *Darchini* (*Cinnamomum zeylanicum*), *Zanjabeel* (*Zingiber officinale* Rosc.), *Aslus Soos* (*Glycyrrhiza glabra* L.) and *Gul-e-Surkh* (*Rosa damascena* Mill.) (Said, 1997) is also added with *Saqmonia* to reduce its toxic effects (Ibn al-Quff, 1986). An isolated active constituent of *Convolvulus scammonia* is inert until it passes from the stomach to the duodenum, where it reacts with the bile, to produce a chemical reaction between it and the taurocholate and glycocholate of sodium, whereby it is converted into a powerful purgative agent (Al-Snafi, 2016)). Gum acacia and tragacanth gum make a layer over gastrointestinal mucosa and reduce the absorption of *Saqmonia* and *Zangar*. The taste of *Hilteet* (*Trigonella foenum-graecum* L.) is very unpleasant which is corrected by adding honey or sugar with it (Qureshi, 1995). The temperament of *Afiyun* (*Papaver somniferum* L.) is cold and dry in 4th degree which may decrease the innate heat of the body resulting in hypoesthesia/anaesthesia. This adverse effect can be minimized by adding another drug of hot temperament (Ibn al-Quff, 1986). Anyone of these drugs viz. *Filfil Siyah* (*Piper nigrum* L.), *Zafaran* (*Crocus sativus* L.), *Jaifal* (*Myristica fragrans* Houtt.), *Zanjabeel* (*Zingiber officinale* Rosc.), *Filfil Daraz* (*Piper longum* L.), *Zaranbad* (*Curcuma zedoaria* Rosc.) and *Darchini* (*Cinnamomum zeylanicum*) (Said, 1997) is added with opium. The dried bread is added in the recipe of '*Tiryaq-e-Farooq*' to soak the morbid fluids of snake flesh. Likewise, beeswax is added to verdigris in the preparation of an ointment to counteract its cauterizing action (Ibn al-Quff, 1986).

(ii) For Treatment of Complex Diseases

The principle cause of disease in Unani Medicine is either *Su-e-Mizaj Sada* (abnormal temperament without involvement of morbid humours) or *Su-e-Mizaj*

Maddi (abnormal temperament with involvement of morbid humours). All the diseases are categorized according to the involvement of *Su-e-Mizaj* (abnormal temperament), *Su-e-Tarkeeb* (disturbance in composition of the body) and/or *Tafarruq-e-Ittesal* (discontinuity of structure). When these three are combined in a disease, it is called '*Marz-e-Murakkab*' (complex disease) (Kabiruddin, 1935). Rāzī stated that a physician should prefer a preparation like *Tiryāq* (anti-dote) which is very much useful in the treatment of many complex diseases (Qureshi, 1995). Majusi stated that this was the major reason for the preparation of *Tiryaq-e-Farooq* (a pharmacopoeial compound preparation). He further stated that sometimes the temperament of two different diseases in a patient is quite different which needs more than one single drug for the treatment of such diseases (Ibn Abbas, 2010). An extract of *Ghafis* (*Gentiana kurroo* Royle.) is added in some pharmacopoeial formulations to evacuate the morbid humours from the liver. *Laung* (*Syzygium aromaticum* (L.) Merr. & Perry.) or *Javitri* (*Myristica fragrans* Houtt.) is added in some pharmacopoeial formulations to decrease the viscosity of viscid humours. *Ustukhuddūs* (*Lavandula stoechas* L.) is added in certain pharmacopoeial formulations to eliminate the morbid humours especially from the brain (Arzani, 1998) (Table 1 & 2).

Scientific studies on various isolated active compounds of plant drugs mentioned in Table 2 have confirmed the claims of Unani Medicine in terms of their activity. However, all the pharmacological actions and their mechanism could not be correlated because polyherbal mixtures have a different temperament which

Table 1: Compound Formulations with Ingredients and Therapeutic Uses

Compound Formulations	Ingredients	Therapeutic Uses
Ayariz-i-Feeqra (Khan, 2005)	*Balchad* (*Valeriana officinalis* L.), *Darchini* (*Cinnamomum zeylanicum*), *Ood-e-Balsan, Habb-e-Balsan* (*Balsamodendron opobalsamum* Kunth.), *Saleekha* (*Cinnamomum cassia*), *Mastagi* (*Pistacia lentiscus* L.), *Asaroon* (*Asarum europaeum* L.), *Zafaran* (*Crocus sativus* L.), *Sibr* (*Aloe barbadensis* Mill.) (Khan, 2005).	Headache, Paralysis, Arthritis (Khan, 2005).
Itrifal Ustukhuddus (Anonymous, (2006)	*Post-i-Halela Zard, Post-i-Halela Kabuli, Halela Siyah* (*Terminalia chebula* Retz.), *Post-i-Balela* (*Terminalia bellirica* Roxb.), *Aamla* (*Emblica officinalis* Gaertn.), *Gul-e-Surkh* (*Rosa damascena* Mill.), *Ustukhuddus* (*Lavandula stoechas* L.), *Bisfaij* (*Polypodium vulgare* L.), *Aftimoon* (*Cuscuta reflexa* Roxb.), *Kishmish* (*Vitis vinifera* L.), Almond oil or *Ghee,* sugar (Anonymous, (2006).	Headache, paralysis, epilepsy, chronic rhinitis (Anonymous, 2006), Dementia, tremor (Khan, 2005).

Table 2: Main Active Constituents and Actions of the Ingredients of *Ayarij-i-Feeqra* and *Itrifal Ustukhuddus*

Plant Drugs	Main Active Constituents	Actions/ Possible Mechanism of Action/ Scientific Studies
Valeriana officinalis L. (Khare, 2007)	Valepotriates, Valeric acid (Khare, 2007)	Sedative. Valerenic acid inhibits breakdown of GABA, and hydroxylpinoresinol binds to benzodiazepine receptor (Khare, 2007)
Cinnamomum zeylanicum (Khare, 2007)	Cinnamaldehyde (Khare, (2007)	Inhibits cyclooxygenase and lipooxygenase enzymes of arachidonic acid metabolism (Khare, 2007).
Pistacia lentiscus Linn. (Khare, 2007)	Mastic acid, Isomastic acid (Khare, 2007)	Antisecretory and possibly cytoprotective effects (Khare, 2007).
Crocus sativus Linn. (Khare, 2007)	Crocin, Picrocrocin, Crocetin (Khare, 2007)	Crocetin may improve atherosclerosis by increasing plasma oxygen diffusion and decreasing cholesterol and triglyceride levels. Crocetin binds to albumin, potentially increasing oxygen diffusion and improving atherosclerosis (Khare, 2007).
Aloe barbadensis Mill. (Khare, 2007)	Aloin (Khare, 2007)	Aloin, in small doses, acts as a tonic to the digestive system, and at higher doses acts as a strong purgative and increases colonic secretions and peristaltic movement (Khare, 2007).
Terminalia chebula Retz. (Khare, 2007)	Phloroglucinol, Pyrogallol (Khare, 2007)	Antioxidant (Khare, 2007)
Terminalia belerica Roxb. (Khare, 2007)	Beta-sitosterol, Gallic acid, Ellagic acid, Chebulagic acid (Khare, 2007)	Alcoholic extract of the fruit showed negative chrono-inotropic and hypotensive effects of varying magnitude in a dose dependent manner on isolated rat, frog atria and rabbit heart (Khare, 2007).
Emblica officinalis Gaertn. (Khare, 2007)	Phyllembin (Khare, 2007)	Phyllembin exhibits CNS depressant and spasmolytic activity potentiates action of adrenaline and hypnotic action of Nembutal (Khare, 2007).

gets masked after interactions of many chemical constituents thereby exerting a holistic effect on the patient's health.

(iii) To Increase Potency of Drug

Sometimes, single drug is not adequately potent for curing diseases. Therefore, another single drug of same therapeutic property is added with such drug (Wadud, 2004). Ibn Sīnā stated that sometimes a physician wishes to prescribe a drug whose temperament should be hot in higher degree but the available drug has lower degree of hot temperament. In such circumstances, another drug having same intensity of temperament is added with the first drug to get the desired intensity of temperament (Ibn Baitar, 2003). Ibn Nafees stated that *Kaat Safed* (*Acacia catechu* (Linn. f.) Willd.) may be added with *Dammul Akhwain* (*Dracaena cinnabari*) in a formulation to achieve the desired astringent action (Qureshi, 1995). *Acacia catechu* (Khare, 2007) and *Dracaena cinnabari* (Altwair and Edrah 2005) both contain tannin (Khare, 2007) which produces astringent action. *Gul-e-Gaozaban* (*Borago officinalis* L.) is added to *Aslus Soos* (*Glycyrrhiza glabra* Linn.) to increase the antitussive, expectorant and demulcent potency of *Aslus Soos* (Qureshi, 1995). Some scientific studies have reported that *Gaozaban* (*Borago officinalis*) adjunctively increases the potency of other drugs used in the treatment of respiratory disorders, urinary disorders, arthritis and skin diseases (Pieszak, *et al.,* 2012). *Zanjabeel* (*Zingiber officinale* Rosc.) is sometimes added to *Turbud* (*Ipomea turpethum*) to increase the purgative effect of the latter (Qureshi, 1995).

(iv) To Decrease Potency of Drug

Sometimes, the potency of drug is reduced by adding another drug whose action may be opposite to the first drug. Such drug may antagonise the action of first drug and is considered to be an antagonist. An astringent drug is added with a strong purgative drug to reduce the purgative effect (Wadud, 2004). Sometimes a drug having cold temperament is added to a drug whose temperament is hot in higher degree to reduce the action of later one (Ibn Sīnā, 2006). *Mom* (wax) is added to *Zangar* (verdigris); *Acacia arabica* is added to *Farfiyun* (*Euphorbia resinifera*); white part of egg is added to *Noora* (lime) and sulphur to decrease the potency of drugs. Any of these drugs viz. *Uod* (*Aquilaria agallocha* Roxb.), *Tabasheer* (*Valeriana officinalis* L.), *Mastagi* (*Pistacia lentiscus* L.) is added to strong purgative drugs such as *Ghariqoon* (*Polyporus officinalis* Fries.) and *Saqmonia* (*Convolvulus scammonia* L.) to reduce their purgative action. Sometimes, a drug whose action is quite different to the main drug is added, viz. a diaphoretic drug is added to a diuretic drug to decrease the action of the latter one. Likewise, an emetic drug is added to purgative drug to reduce purgative action of the latter drug (Qureshi, 1995).

(v) To Enhance Absorption of Drug

Certain drugs are supplemented in the formulation to augment the absorption of another drug (Khan, 2005). Ibn Sīnā stated that *Zafaran* (*Crocus sativus* L.) is added in the formula of '*Qurs Kafoor*' to increase the absorption of other drugs of the formulation (Ibn Sīnā, 2006). Most of the semisolid and liquid dosage forms of Unani Medicine contain honey or sugar which may increase the absorption of other drugs (Kabīruddīn, 2010). Ibn Sīnā further stated that liver has a natural tendency of getting attracted towards sweet tasting foods. It means that the sweet item is metabolised in the liver very fast. *Sikanjabeen* (a dosage form) is prepared with vinegar and honey wherein honey increases the absorption of vinegar (Qureshi, 1995). A study was carried out to investigate the effect of Iranian honey, cinnamon and their combination against *Streptococcus mutans* bacteria. The combination of honey and cinnamon showed significant antibacterial effect and it was concluded that this effect might be due to synergistic effect of both drugs (Rezvani, *et al.,* 2017). Another study was carried out on synergistic effect of Trigona honey and Ampicillin on *Staphylococcus aureus* isolated from infected wound. The result showed significant antibacterial effect of the sample which had the combination of honey and Ampicillin compared to the honey or Ampicillin alone. The combination therapy also exhibited significant morphological alteration on *Staphylococcus aureus* in electron micrograph after 24 hours (Wen-Jie, *et al.,* 2017). These studies have given strength to the views of ancient Unani physicians who advised to mix honey in several compound preparations. Nugroho, *et al.* (2013) have evaluated the antidiabetic effects of *Andrographis paniculata* and *Centella asiatica* in diabetic animal model and found significant antidiabetic and antihyperlipidemic effects of *Andrographis paniculata* and *Centella asiatica* extracts in combination than that of single treatment of extract of either *Andrographis paniculata* or *Centella asiatica* (Nugroho, *et al.,* 2013). Mani, *et al.,* (2013) reported the antidiabetic and antihyperlipidemic effects of polyherbal formulation containing *Trigonella foenum-graceum*, *Momordica charantia*, *Aegle marmalos*. The results showed significant antidiabetic and antihyperlipidemic effects of polyherbal formulation compared to Glipizide in OGTT and streptozotocin induced animal model and also found significant result of combination therapy along with Glipizide (Mani, *et al.,* 2013).

Some scientific studies have revealed that certain isolated plant constituents such as piperine, quercetin, genistein, naringin, sinomenine, curcumin and glycyrrhizin possess significant potential to increase the bioavailability of several potent active pharmaceutical ingredients (Ajazuddin, *et al.,* 2014). The piperine is isolated from *Piper longum* L. and *Piper nigrum* L. (Khare, 2007), the bioavailability enhancing property of which first discovered in 1979 AD (Wadhwa, et al., 2014). A study revealed that combination of ethyl acetate fraction of *Crocus sativus* L. with chloroquine potentiated the antimalarial

property significantly more than on chloroquine or ethyl acetate fraction alone on chloroquine sensitive strain of *Plasmodium berghei* in mice. The outcome of combination therapy showed synergistic effect (Pestechian, *et al.,* 2015). It has also been found that the naturally occurring extract of *Crocus sativus* L. in combination of two synthetic compounds such as sodium selenite or sodium arsenite may have synergistic effect with *Crocus sativus* L. which may play an important role in prevention of carcinoma (Reddy, 2014). A study has reported that piperine 18, the chief constituent of *Piper longum* and *Piper nigrum* is being commonly added to allopathic drugs for synergistic effect (Houghton, YNM). Patwardhan, *et al.* (2017) has revealed that 2% n-hexane extract (NHE) of *Piper cubeba* possesses significant absorption enhancer activity as compared to that with synthetic enhancer. In Ayurveda, *Piper nigrum* L. and *Zingiber officinale* Rosc. are added with several pharmacopoeial compound preparations to increase the absorption of other drugs.

Several Unani pharmacopoeial preparations contain anyone of these drugs viz. *Filfil Daraz* (*Piper longum* L.), *Filfil Siyah* (*Piper nigrum* L.), *Zafaran* (*Crocus sativus* L.) and Aslus Soos (*Glycyrrhiza glabra* L.) which might be enhancing the bioavailability of other drugs (Table 3).

Table 3: Pharmacopoeial Preparations Containing *Piper longum* L., *Piper nigrum* L., *Crocus sativus* L. and *Glycyrrhiza glabra* L.

Pharmaco-poeial preparations containing *Piper longum* L. & *Piper nigrum* L.	Pharmaco-poeial preparations containing *Piper longum* L.	Pharmacopoeial preparations containing *Piper nigrum* L.	Pharmaco-poeial preparations containing *Crocus sativus* L.	Pharmaco-poeial preparations containing *Glycyrrhiza glabra* L.
Habb-e-Azaraqi, *Habb-e-Kibreet*, *Habb-e-Pachlona*, *Anqura-e-Kabir*, *Jawarish Fanjnosh*	*Jawarish Uod Shirin*, *Laooq Sagheer*, *Majun Salab*, *Majun Suranjan*	*Habb-e-Papita Desi*, *Habb-e-Papita Vilayti*, *Habb-e-Tinkar*, *Barsha'sha*, *Dawa-e-Luk*, *Jawarish Bisbasa*, *Jawarish Kamooni*, *Jawarish Safar Jali Qabiz*, *Jawarish Utraj*, *Majun Aqrab*, *Majun Jalali*, *Tiryaq-e-Samania*	*Habb-e-Hamal*, *Habb-e-Jadwar*, *Habb-e-Jawahar*, *Habb-e-Kabid Naushadri*, *Habb-e-Mudir*, *Qurs-e-Tabashir*, *Majun Dabeedul Ward*	*Qurs-e-Tabashir Qabiz*, *Qurs-e-Zarishk*

(Anonymous, 2006)

(vi) To Decrease Absorption of Drug

Sometimes, a drug is required for the treatment of some diseases where absorption should be slow from the oral route, but the available drug is absorbed very fast. In this condition, another drug is added with such drugs to decrease the absorption. Anyone of these drugs viz. *Gum acacia, Tragacanth gum, bee wax, Mastagi* (*Pistacea lentiscus*), *Bihidana* (*Cydonia oblonga* Mill.), etc. is added in several Unani pharmacopoeial formulations to decrease the absorption of other drugs (Qureshi, 1995). Mucilaginous drugs also reduce the absorption of other drugs (Qasmi, 2015). Ibn Sina stated that the seed of *Raphanus sativus* is added to decrease the absorption of other drugs. *Zarareeh*, an animal origin drug is added with diuretic and deobstruent drugs to decrease the absorption of them particularly in the treatment of renal diseases (Ibn Sina, 2006). *Acacia arabia*, *Cochlospermum religiosum*, *Althaea officinalis* and *Cydonia oblonga* contain large amount of tannins (Khare, 2007; Jafari and Jouyban, 2011) that may reduce the absorption of other drugs (Houghton, YNM).

(vii) For Preservation of Drug

Certain seasonal drugs used in Unani Medicine are not available throughout the year. Such drugs are mixed with sugar, honey or vinegar to preserve them for future use. Certain dosage forms such as *Murabba* and *Gulqand* are prepared in Unani Medicine for this purpose. *Murabba* of certain drugs such as *Embelica officinalis*, *Zingiber officinale*, *Cydonia oblonga*, *Terminalia chebula*, carrot, apple, pine-apple, *Belgiri* (*Aegle marmelos*), pear, etc. are prepared as pharmacopoeial preparations in Unani Medicine. Rose petals and petals of *Gul-e-Sewti* (*Chrysanthemum coronarium*) are mixed into *Qiwam* (syrup) of sugar or honey and prepared *Gulqand* (Said, 1997). Certain semisolid and liquid dosage forms such as *Majun* (confection), *Itrifal*, *Jawarish*, *Khameera* (fermented confection), *Sharbat* (syrup) are also prepared by adding sugar or honey (Kabiruddin, 2010) which also act as preservatives. Antibacterial activity of honey was first reported by Van Ketel in 1892. Sackett in 1919 reported that the antibacterial activity of honey was increased by limited dilution of honey but he couldn't give an explanation. Dold, *et al.* (1937) introduced a term 'inhibine' for the antimicrobial property of honey (Molan, YNM). Several studies have confirmed that honey has antibacterial, antifungal, antiviral and antimycobacterial properties which might be due to low pH, osmotic effect, high sugar concentration, presence of hydrogen peroxide, etc. (Israili, 2014). Honey is a super-saturated solution of sugar which contains 15-21% water content and 84% monosaccharides including fructose and glucose. These two compounds have tight bond among them and leave few of the water molecules available for the growth of microorganisms. The pH of honey is between 3.2 and 4.5 which are quite acidic in nature. The acidity is produced due to presence of gluconolactone/gluconic acid in honey.

The acidic reaction of honey does not permit for bacterial proliferation in honey. Adcock in 1962 revealed that an antimicrobial property of honey might be due to presence of hydrogen peroxide (Molan, YNM).

Conclusion

The combined effect of a polymixture compound preparation is due to pharmacodynamic and pharmacokinetic interactions amongst the various chemical constituents. Some scientific studies have revealed that plant extracts with combination of chemotherapeutic agents or in combination with some other molecular compounds such as antidiabetic or antibacterial agents possess more significant effects than single molecule. The concept of polyherbal mixture emerged in Unani Medicine in ancient times and now it has been proved that polyherbal mixture can give better results especially in the treatment of complex illnesses. The polyherbal preparation used in Unani Medicine is aimed to treat the body with a holistic approach.

Unani Medicine has given a scientific rationale to the use of polyherbal mixtures for the treatment of various bodily ailments. Whether correction of toxicities of toxic drugs, treatment of complex diseases, increase in potency of drug, decrease in potency of drug, enhancing the absorption of drug, delaying the absorption of drug or preservation of drugs, all these factors play an integral role in drug delivery system in Unani Medicine. Several isolated chemical constituents of plant drugs are added with conventional drugs in pharmacology to achieve many targets. Many scientific studies have revealed the beneficial effects of polyherbal mixtures, provided they are judiciously utilized, in the treatment of various ailments. The above discussion amply proves the fact that there is scientific rationale for the use of polyherbal pharmaceutical preparations, thus validating the principles of Unani Medicine.

Conflicts of Interest: The authors declare that they have no conflict of interest.

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सारांश

यूनानी चिकित्सा में पॉलीहर्बल फार्मास्यूटिकल मिश्रण - एक तर्कसंगत दृष्टिकोण

***अतहर परवेज़ अंसारी, एन ज़हीर अहमद, अब्दुल वदूद, मोहम्मद आरिफ़ और अब्दुल रहीम**

यूनानी चिकित्सा में एक से अधिक जड़ी बूटियों तथा खनिज से बने मिश्रणों का उपयोग सदियों से प्रचलन में है। *इबर्स पपाइरस* में लगभग 800 नुस्ख़े हैं। पाउडर और मरहम से क्रमशः अरस्तु और हिप्पोक्रेट्स ने परिचित कराया, लेकिन इसका श्रेय गैलेन को जाता है जिन्होंने कई खुराक़ रूपों को निर्मित किया और पॉलीहर्बल मिश्रणों के उपयोग के लिए वैज्ञानिक तर्क भी दिए। उन्हें पॉलीहर्बल फार्मास्यूटिकल मिश्रण का जनक माना जाता है। कई अरब चिकित्सकों ने कई खुराक रूपों को तैयार किया और फार्मेसी में रसायन सम्मिलित किया। यूनानी चिकित्सकों ने रोगों के उपचार के लिए पॉलीहर्बल मिश्रण के उपयोग को तर्कसंगत बताया और अब यह वैज्ञानिक रूप से सिद्ध हो चुका है। कुछ औषधियां जैसे *अकेसिया अरेबिका, पिस्ताशिया लेंटिस्कस, कोक्लोस्परमग रिलीजीयासम* और लसेदार औषधियां विशेषतः उत्तेजक औषधियों के साथ मिलाई जाती हैं ताकि जठरांत्र पथ में श्लेष्मली घाव को रोका जा सके। कुछ औषधियों को मिश्रणों में कुछ अन्य औषधियों की क्षमताओं को बढ़ाने या घटाने के लिए मिलाया जाता है। वैज्ञानिक अध्ययनों से साबित हुआ है कि पिपेरिन करक्यूमिन, ग्लाइसीराइजिन इत्यादि महत्वपूर्ण जैव सक्रिय गुण रखते हैं जोकि कुछ अन्य रासायनिक अणुओं औषधियों में इनके समावेश को सही ठहराते हैं। शहद में कम पीएच ओसमोटिक प्रभाव, उच्च शर्करा सांद्रता और हाइड्रोजन पेरोक्साइड की उपस्थिति के कारण जीवाणुरोधी एंटीवायरल और एंटी फंगल गुण होते हैं। शहद और चीनी को यूनानी चिकित्सा में कई अर्ध कठोर और तरल खुराक रूपों में परिरक्षक के रूप में मिलाया जाता है। पादप औषधियों के कई पृथक रासायनिक संघटकों को कई लक्ष्यों को प्राप्त करने के लिए पारंपरिक औषधि विज्ञान में एलोपैथिक औषधियों के साथ मिलाया जाता है। कई वैज्ञानिक अध्ययनों ने पॉलीहर्बल मिश्रणों के लाभकारी प्रभावों का खुलासा किया है यदि यह विभिन्न रोगों के उपचार में विवेकपूर्ण ढंग से मिश्रित होते हैं।

शब्दकुंजी: यौगिक मिश्रण, पॉलीहर्बल मिश्रण, पॉलीहर्बल फार्मास्यूटिकल मिश्रण, यूनानी चिकित्सा

Rawghan Chahār Barg - A Classical Unani Formulation Having Anti-inflammatory, Analgesic and Antimicrobial Activities: A Review

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Abstract

Topical drug administration is a localized drug delivery system anywhere in the body mainly through skin, partly from ophthalmic, rectal, and vaginal as topical routes. In Unani Medicine, analgesic and anti-inflammatory drugs are used in the form of single (*Mufrad*) drugs and compound (*Murakkab*) dosage forms. *Rawghan Chahār Barg* is one of the most potent topically used Unani formulations for the management of inflammatory conditions of joint disorders/diseases since long time as it has combination of anti-inflammatory and analgesic properties. All the four (4) ingredients, i.e. *Āk (Calotropis procera), Bed Anjīr (Ricinus communis), Dhatūrā (Datura stramonium)* and *Thuhar* (*Euphorbia neriifolia*) have been attributed to possess potent *Muḥallil-i-Awrām* (antiinflammatory) and *Musakkin* (analgesic) activities in almost all *Qarābādīn* (pharmacopoeias). In this paper, an attempt has been made to review anti-inflammatory, analgesic and antimicrobial activities for a comprehensive understanding of the importance of *Rawghan Chahār Barg.*

Keywords: Analgesic, Anti-inflammatory, *Murakkab, Qarābādīn, Rawghan Chahār Barg,* Topical

Introduction

Rawghan (medicated oil) is a medium which is used in different forms. It is used for making the medicine, as medicine itself, as one of the ingredients in a particular formula or as medicated oil by mixing with other drugs of plant, animal or mineral origin. It is mostly used as a base (as in the case of ointment) and generally obtained from plant sources. Oil can be extracted from different parts of the plant, viz. *Maghziyyāt* (kernels of the fruits), *Bīkh* (roots), *Barg* (leaves), *Gul* (flowers), *Tukhm* (seeds) and so on. On the basis of its use, method of extraction and preparation, it is broadly classified into two main categories: (1) Oil extracted from plant sources for use – Extracted oil; (2) Oil made out of mixing with other medicinal drugs (plant, animal or mineral) for use – Medicated oil. Extraction of oil from plant sources is generally done by the methods given in the Unani texts like *Jal Jantar, Patal Jantar,* etc. But because of the increasing demand and large scale preparation of Unani drugs, manufacturers are now extracting oil by adopting modern technologies. Nowadays, oil is mostly extracted and obtained by mechanical process, viz. (i) cold expelling process and (ii) steam distillation or solvent process. Oil from *Maghziyyāt* (kernels) and *Tukhm* (seeds) are mostly obtained by cold expelling process, while oils from cloves, cinnamon and anise fruits are obtained by steam distillation process. *Rawghaniyyāt* (extracted and medicated oils) should be preserved in clean and dry glass jar containers under hygienic conditions in cool and dry place and

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stored for one to two years. In Unani system of medicine, *Rawghaniyyāt* are used for medicinal purpose externally and internally but *Rawghan Chahār Barg* is used externally only for local application for the management of inflammatory conditions (Anonymous, 2011).

Rawghan Chahār Barg

As its name suggests, *Chahār Barg* means four leaves. The formulation consists of four leaves as main ingredient and therefore it is called *Rawghan Chahār Barg*. It has *Muḥallil-i-Awrām* (anti-inflammatory) and *Musakkin-i-Alam* (analgesic) properties. It is used in *Waja' al-Mafāṣil* (polyarthritis) and *Waram al-Mafāṣil* (arthritis), etc. It is used externally only.

The composition of *Rawghan Chahār Barg* is as follows:

S.No.	Name	Botanical name	Part Used	Quantity
1.	*Barg-i-Dhatūrā*	*Datura stramonium*	*Barg*	25gm
2.	*Barg-i-Āk*	*Calotropis procera*	*Barg*	25gm
3.	*Barg-i-Bed Anjīr*	*Ricinus communis*	*Barg*	25gm
4.	*Barg-i-Thuhar*	*Euphorbia neriifolia*	*Barg*	25gm
5.	*Kunjad*	*Sesamum indicum*	Seeds'oil	800 gm

Method of Application: *Rawghan Chahār Barg* is applied luke warm and massaged on the affected part (Anonymous, 2006; Anonymous, 1988).

Rawghan Chahār Barg is one of the most potent topically used Unani formulations for the management of inflammatory conditions of joint disorders/diseases since long time as it has combination of anti-inflammatory and analgesic properties.

Table: *Muḥallil-i-Aawrām* (anti-inflammatory) and *Musakkin-i-Alam* (analgesic)

S. No.	Drug Name	References for *Muḥallil-i-Aawrām* (Anti-inflammatory) and *Musakkin-i-Alam* (Analgesic) Activities of *Rawghan Chahār Barg* Ingredients from Classical Unani Books
1.	*Dhatūrā* (*Datura stramonium*)	Ibn Baitar, 2006; Anonymous, 2007b; Ghani, YNM; Kirtikar and Basu, 2005b; Nabi, 2007; Hakeem, 2002; Kabiruddin, 2000; Anonymous, 2005a; Ghani, 2010; Anonymous, 2006; Khan, 2006a; Khan, 1273; Khan, 1313c.
2.	*Āk* (*Calotropis procera*)	Anonymous, 2007a; Anonymous, 2006; Khan, 1313a; Hakeem, 2002; Ghani, YNM; Nabi, 2007; Anonymous, 1992; Kabiruddin, 2000; Kirtikar and Basu, 2005b; Anonymous, 2005a; Khare, 2007; Khan, 1273; Ibn Baitar, 1999; Jurjani, 1878; Ghani, 2010; Khan, 2006a.

3.	*Bed Anjīr (Ricinus communis)*	Khan, 1313a; Anonymous, 2005a; Hakeem, 2002; Ghani, YNM; Nabi, 2007; Anonymous, 2005b; Kirtikar and Basu, 2005b; Nadkarni, 2007; Sharma et al., 2005; Arzani, 2009; Ghani, 2010; Anonymous, 2006; Khan, 2006a, Anonymous, 2007d.
4.	*Thūhar (Euphorbia Neriifolia)*	Nabi, 2007; Hakeem, 2002; Kabiruddin, 2000; Khan, 1273; Khan, 1313b; Anonymous, 2007c; Kirtikar and Basu, 2005b; Anonymous, 2006; Jurjani, 1878; Anonymous, 2005a; Ghani, 2010; Khan, 2006a.
5.	*Kunjad (Sesamum indicum)*	Hakeem, 2002; Ghani, YNM; Nabi, 2007; Kabiruddin, 2000; Kirtikar and Basu, 2005a; Ibn Baitar, 1999; Masihi, 2008; Anonymous, 2005a; Arzani, 2009; Ghani, 2010; Anonymous, 2006; Khan, 2006b; Anonymous, 2007b.

Scientific Research on Ingredients of *Rawghan Chahār Barg*

1. *Dhatūrā* (*Datura stramonium)*

Anti-inflammatory Study

Sonika, *et al.* (2010) found that the ethanolic extract of *Datura stramonium* leaves has significant anti-inflammatory activity against carrageenan induced paw edema in rats. In one experiment, 39.43% inhibition of the edema was observed after 3 hour of oral administration of 200 mg/kg extract. Maximum activity was observed when the extract was administered in doses of 3-hour intervals. Since the extract of *Datura stramonium* inhibited the carrageenan-induced edema that involves the release of histamine and serotonin in the first phase, the inhibitory effect of the extract could be partly due to inhibition of mast cell mediator release.

Antimicrobial Studies

Iranbakhsh, *et al.* (2010) studied the effects of methanolic extract from root, stem and leaf of *Datura stramonium* on the vegetative and generative phases of the growth process of four bacterial strains (Escherichia coli, Pseudomonas aeruginosa, Staphylococcus epidermidis and Bacillus subtilis) and four fungi strains (Fusarium semithectum, Fusarium colmorum, Ceratocystisulmi and Rhizoctoinasolani). The result showed that the methanol extract from green leaf explant callus had inhibitory effects on the growth of B. subtilis and S. epidermidis with inhibition zones of 22 and 23mm, respectively.

A study carried out by Shagal, *et al.* (2012) found that ethanol extract has the highest inhibitory activity against Klebsiella pneumonia followed by

Staphylococcus aureus, with the least activity against Salmonella typhi. The aqueous extract showed activity on S. aureus only, while Neisseria gonorrhea was resistant to both extracts.

Sharma, *et al.* (2009) found that *Datura stramonium* was very effective as vibriocidal against various strains of Vibrio cholera and Vibrio parahaemolyticus. The minimum inhibitory concentration (MIC) value of acetone extracts of *Datura stramonium* was in the range of 2.5 to 15 mg/ml serving as broad-spectrum vibriocidal agents.

2. *Āk* (*Calotropis procera*)

Anti-inflammatory and Analgesic Studies

Saba, *et al.* (2011) studied ethanolic extract of the leaves of *Calotropis procera* for its anti-inflammatory and analgesic activities. The results showed that ethanolic extract of the leaves of *Calotropis procera* had potent anti-inflammatory and analgesic activities.

The methanolic extract of plant *Calotropis procera* has been reported to exhibit potent anti-inflammatory activity against carrageenan induced paw oedema and cotton pellet induced granuloma in albino Wistar rats (Basu and Chaudhury, 1991; Dewan, *et al.*, 2000).

The ethanolic extract of root bark of *Calotropis procera* was investigated for its anti-inflammatory activity at different doses in different animal models. The experimental paradigms used were Complete Freunds Adjuvant (CFA) induced arthritis (chronic inflammation), acetic acid induced vascular permeability model in mice for anti-inflammatory activity. The study result showed that ethanolic extract of root bark of *Calotropis procera* has potent anti-inflammatory activity (Parihar, *et al.,* 2011).

A study carried out with the chloroform fraction of *Calotropis procera* root showed that this structure has potent anti-inflammatory activity against the exudative and proliferative phases of inflammation, and presents potential analgesic properties through tests assessing changes induced by acetic acid in rats (Parihar, *et al.,* 2011).

Wound Healing Study

In a study carried out by Sharma, *et al.* (2014), *Calotropis procera* was selected for evaluation of its wound healing potential in guinea pigs. For this purpose, four full thickness excision wounds of 8.0 mm diameter were inflicted on the back of guinea pigs. Topical application of 20 µl of 1.0% sterile solution of the latex of the plant twice daily was followed for 7 days. The latex significantly

augmented the healing process by markedly increasing collagen, DNA and protein synthesis and epithelization leading to reduction in wound area. Thus the result provided a scientific rationale for the traditional use of this plant in the management of wound healing.

Antimicrobial Study

Mann and Abalaka (1997) showed *in-vitro* antibacterial activity of methanol extract of the leaves against gram negative bacteria such as Salmonella typhi, Pseudomonas fluorescens, Pseudomonas aeruginosa and Escherichia coli. The methanol extract of the leaves showed potent antibacterial activities against gram negative bacteria.

Mainasara, *et al.* (2011) conducted a study on antibacterial activity of *Calotropis procera* using water, methanol and ethanol extracts of fruit and bark against gram positive and gram negative bacteria. The result showed that the drug has antibacterial activity against both gram positive and gram negative bacteria.

The antimicrobial activities of water, methanol and ethanol extracts were determined by using disc diffusion method. The study shows that plant extracts crude and aqueous, methanolic and ethanolic with antibiotics, provide evidence that *Calotropis procera* extracts has the similar antibacterial activity as these antibiotics against test pathogens i.e. Salmonella Typhi, E. Coli (Muzammal, 2014; Kawo, *et al.,* 2009; Nenaah and Ahmed 2011).

3. *Bed Anjīr (Ricinus communis)*

Anti-inflammatory Studies

Jena and Gupta (2012) studied anti-inflammatory activities of the leaves and root extract in Wistar albino rats in acute and chronic inflammatory models. The study indicated the paw edema formation due to sub plantar administration of carrageenan, characterizing the cellular events of acute inflammation. The 250 and 500 mg/kg dose of *Ricinus communis* methanolic leaves extract possess protective effect in prevention of cellular events during edema formation and in all the stages of acute inflammation. The anti-inflammatory activity of *Ricinus communis* methanolic extract was due to the presence of flavonoids because the flavonoids have the protective effect against carrageenan-induced paw edema in rats.

In a study by Ladda and Kamthane (2014), the effect of petroleum ether extract of root of *Ricinus communis* (150 mg/kg p.o.) was investigated against Carrageenan, 5-Hydroxytryptamin, Dextran, Bradykinin and Prostaglandin E induced rat's hind paw edema. The result exhibited significant anti-inflammatory activity.

Wound Healing Study

Jena and Gupta (2012) found that *Ricinus communis* possesses wound healing activity due to the active constituent of castor oil which produces antioxidant activity and inhibits lipid peroxidation. The agents inhibiting lipid peroxidation are believed to increase the viability of collagen fibrils by increasing the strength of collagen fibers, increasing the circulation, preventing the cell damage and promoting the DNA synthesis.

Antimicrobial Study

Poonam and Pratap (2012) found that the methanolic and aqueous extracts of *Ricinus communis* have antimicrobial activity against four clinical bacterial stain; Escherichia coli, Bacillus subtilis, Bacillus cereus and Staphylococcus aureus, and two fungal strains; Candida albicans and Candida galabrata with standard drug tetracycline (10 mg /ml).

Sharma, *et al*. (2013) reported that *Ricinus communis* showed good activity against P. aeruginosa, S. aureus, K. Pneumonia and Proteus vulgaris. The antimicrobial assay revealed that the methanol and ethyl acetate extracts of leaves of *Ricinus communis* possess good zone of inhibition whereas petroleum ether extract has antimicrobial activity only on higher concentration.

In a study carried out by Verma, *et al*. (2011), the antimicrobial activity of various extracts of roots (200mg/ml) of *Ricinus communis* was investigated against pathogenic microorganisms such as Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhimurium, Proteus vulgaris, Bacillus subtilis, Candida albicans and Aspergillus niger using well diffusion method. The result showed that *Ricinus communis* has potent antimicrobial activity.

4. *Thūhar* (*Euphorbia neriifolia*)

Anti-inflammatory and Analgesic Study

Kalpesh, *et al.* (2009) observed the anti-inflammatory and analgesic activity of 70% v/v hydro-alcoholic extract of dried leaves of *Euphorbia neriifolia* by oral administration at the dose of 400 mg/kg/day of body weight to healthy albino rats. The hydro-alcoholic extract was also evaluated for analgesic activity using Eddy's hot plate method and tail-flick method in albino rats. It showed significant ($P<0.05$) reduction in the carrageenan-induced paw edema in rats and analgesic activity evidenced by increase in the reaction time by Eddy's hot plate method and tail-flick method in albino rats. The hydro-alcoholic extract also showed greater anti-inflammatory and analgesic effect when compared with the standard drugs, Indomethacin and Diclofenac sodium, respectively. The observation indicated significant ($P<0.001$) activity of the hydro-alcoholic

extract of *Euphorbia neriifolia* in the treatment of inflammation and pain.

Wound Healing Study

The wound healing effect of aqueous extract of latex was evaluated in guinea pig. The 0.5% and 1% sterile aqueous solution of extract facilitated the healing process as evidenced by increase in tensile strength, DNA content, epithelization and angiogenesis. The aqueous extract of the latex shows potent wound healing activity (Rasik, *et al.* 1996).

5. Kunjad (*Sesamum indicum*)

Anti-inflammatory Study

The anti-inflammatory activity was assessed on the basis of paw edema inhibition induced by the injection of carrageenan (an edematogenic agent) into the subplantar region of the right hind paw of the rat. The results showed that the sesame oil and *sesamin* inhibited the formation of pleural exudates and the leucocyte migration confirming the anti-inflammatory activity (Monteiro, *et al.* 2014).

Wound Healing Study

Free radicals are generated at the site of injury, which are known to impair the healing process by causing damage to cellular membranes, nucleotides, proteins and lipids. In this context, several antioxidants, such as curcumin, vitamin E, have been reported to give protection against oxidative damage to tissues. The use of antioxidants has been found to promote wound healing. Sesame oil extract has potential antioxidant activity which helps to prevent oxidative damage and promote the healing process. *Sesamum indicum* seeds and oil both promote wound healing in experimentally induced rats. Gel containing seeds or oil applied topically or administration of seeds or oil orally significantly promoted the breaking strength, wound contraction and period of epithelialization in incision, excision and burn wound models (Fukuda, *et al.*, 1986; Kiran and Asad, 2008).

Antimicrobial Study

Sesame is naturally antibacterial for common skin pathogens such as Staphylococcus and Streptococcus, as well as common skin fungi such as athlete's foot fungus. As a throat gargle, it kills Streptococcus and other common cold bacteria. It helps sufferers of psoriasis and dry skin ailments. It is a useful natural ultraviolet protector. In a study, the results revealed that minimum inhibitory concentration (MIC) of sesame oil against Salmonella typhi is 10 µl/ml. However, for other organism, the MIC values were in the range of 350-

500 µl/ml. The sesame oil shows best antimicrobial activity and equates with standard drug Kanamycin. It also shows highest zone of inhibition against S. typhi. It reported that sesame oil is found to have antibacterial activity against Streptococcus mutans, Lactobacilli acidophilus and total bacteria (Anand, *et al.* 2008).

Conclusion

After reviewing *Rawghan Chahār Barg* and its ingredients in the classical and modern texts, it may be said that it has *Muḥallil-i-Aawrām* (resolvent), *Musakkin-i-Alam* (analgesic) and wound healing properties. Scientific studies also validate that the ingredients of *Rawghan Chahār Barg* i.e. *Āk (Calotropis procera), Bed Anjīr (Ricinus communis), Dhatūrā (Datura stramonium) and Thūhar* (*Euphorbia neriifolia*) possess potent *Muḥallil-i-Aawrām* (anti-inflammatory) and *Musakkin* (analgesic) properties. Apart from above, *Rawghan Chahār Barg* may also be found beneficial for management of inflammatory conditions of joint disorders/diseases like *Waja' al-Mafāṣil* (polyarthritis). Nowadays, when joint disorders/diseases increase day by day, it may be one of the best topically used Unani formulations as a drug of choice for the management of inflammatory conditions of joint disorders/diseases.

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सारांश

रोग़न-ए-चहार बर्ग - एंटीइनफ्लामेटरी, एनाल्जेसिक और एंटीमाइक्रोबियल गतिविधियों वाला एक क्लासिकी यूनानी मिश्रण : एक समीक्षा

***शमीम, आसिम अली खान, अमानुल्लाह और साद अहमद**

टोपिकल ड्रग एडमिनिस्ट्रेशन एक स्थानीय औषधि वितरण प्रणाली है जो शरीर पर कहीं भी मुख्य रूप से त्वचा, आंशिक रूप से नेत्र, मलाशय और योनि के माध्यम से दी जाती है। यूनानी चिकित्सा पद्धति में एनाल्जेसिक और एंटीइनफ्लामेटरी औषधियां एकल (मुफरद) औषधियों और यौगिक (मुरक्कब) खुराक रूपों में उपयोग की जाती हैं। *रोगन–ए–चहार बर्ग* लंबे समय से जोड़ों के दर्द संबंधी विकारों की इनफ्लामेटरी स्थितियों के उपचार के लिए सबसे अधिक उपयोग की जाने वाली गुणकारी औषधियों में से एक है। इस मिश्रण की चारों औषधियां अर्थात् *आक* (*कैलोट्रोपिस प्रोसेरा*), *बैद अंजीर* (*रिसिनस कम्युनिस*), *धतूरा* (*दतूरा स्ट्रैमोनियम*) और *थूहर* (*युफोरबिया नेरीफोलिया*) लगभग सभी कराबादीन (फार्माकोपिया) में गुणकारी मुहल्लिल–ए–अवराम (एंटीइनफ्लामेटरी) और मुसक्किन (एनाल्जेसिक) गतिविधियों से युक्त बताई गई हैं। इस पेपर में *रोगन–ए–चहार बर्ग* के महत्व को व्यापक रूप से समझने के लिए इसकी एंटीइनफ्लामेटरी, एनाल्जेसिक और एंटीमाइक्रोबियल गतिविधियों की समीक्षा करने का प्रयास किया गया है।

शब्दकुंजी: एनाल्जेसिक, एंटीइनफ्लामेटरी, *मुरक्कब, कराबादीन, रोग़न–ए–चहार बर्ग,* टोपिकल

Sūranjān Talkh (*Colchicum luteum* Baker): A Review of Pharmacological Activities and Clinical Effects

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Abstract

Sūranjān Talkh is one of the important Unani drugs mentioned by great Unani physicians for the treatment of arthritis and other joint diseases. It is a medicine of great repute in Afghanistan, Turkey and Northern India. In Unani System of Medicine, it is used as *Muḥallil-i-Awrām* (anti-inflammatory), *Mushil* (purgative), *Musakkin-i-Alam* (analgesic), *Mulaiyyin* (laxative), *Mufattih-i-Sudad* (deobstruent), etc. Keeping in view its high medicinal importance, a comprehensive review based on Unani, ethnobotanical, phytochemical and pharmacological literature has been done with an aim to explore new frontiers for the research of *Sūranjān Talkh*.

Keywords: *Colchicum luteum, Muḥallil-i-Awrām, Musakkin-i-Alam, Mushil, Sūranjān,* Unani Medicine

Introduction

Sūranjān Talkh (*Colchicum luteum* Baker) is a well-known drug described in Unani Pharmacopoeia (Anonymous, 2001). It is an annual herb also known as Indian Colchicum which belongs to the family Liliaceae. It is mainly used as *Muḥallil-i-Awrām* (anti-inflammatory) (Ghani, 2005; Hakim, 2002). It is found in hilly and valley areas in Western Temperate Himalayas extending from Murree hills (Pakistan) to Kashmir and Chamba (India) from 700-3000 meter in height (Chopra, *et al.,* 1958). This drug was recommended and authenticated by Ibn Sīnā (980-1037 CE) (Ghani, 2005; Khan, 1305). According to him, it consists of two opposite actions; purgative and constipative (*Mushil wa Qābiḍ*), simultaneously. When there is action of *Ḥarārat Gharīzyya* and *Quwwat Tabī'iyya* in the body, the purgative (*Mushil*) part gets separated, resolved and expelled out, later on constipative part acts on the joints and helps in retaining the healthy condition of joints and strengthens them (Ibn Baitar, 1999; Ghazruni, 1311). Plants occur from December to March, flowering takes place from June to July and corms are collected during this season, after which the leaves fall down (Anonymous, 1987). There are two varieties commonly sold in the Indian market, one is sweet (*Sūranjān Shīrīn*) and the other bitter (*Sūranjān Talkh*). The dark brown dry extract of bitter *Sūranjān* is known as *Haran-tutiya* (Golden collyrium). The bitter variety is *Colchicum luteum* which contains alkaloid colchicine in fairly large proportion. The sweet or tasteless variety is *Colchicum autumnale* which comes from Persia and resembles bitter colchicum, also contains traces of alkaloid but has been found to be physiologically inactive. *Sūranjān Talkh* (*Colchicum luteum*) is distinguished from the sweet variety *Sūranjān Shīrīn* (*Colchicum autumnale*) by its bitter taste, smaller size, darker colour and by having a reticulated appearance of the corms (Chopra, *et al.,* 1958).

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Botanical Name

Colchicum luteum (Chopra, *et al.,* 1958; Nadkarni, 2000; Kirtikar and Basu, 1996)

Family

Liliaceae (Nadkarni, 2000; Dymock, 1893)

Vernacular Names

Arabic	–	Qalb al-Arḍ, Akba, Al-Halah
English	–	Colchicum, Golden Collyrium, Kashmir Hermodactyls
Hindi	–	Hirantutiya, Sūranjān Karwa, Jangli Singhara
Indian Bazaar	–	Haran-tutiya
Kasmiri	–	Virkum, Bitter Hermodactyl
Persian	–	Haqeer, Surangan
Sanskrit	–	Hirnayatutha, Tutham, Tutthanjana
Unani	–	Flahqin, Aqimaroon, Balboosa
Urdu	–	Sūranjān Talkh

(Anonymous, 2001; Ghani, 2005; Chopra, *et al.,* 1958; Ibn Baitar, 1999; Anonymous, 1987; Nadkarni, 2000; Kirtikar and Basu, 1996; Khan, 1305; Attar, 1888; Hakim, 1862)

Botanical Description

It is a root (corm) of small size plant (herb); leaves are narrow and long originated from the same joints. The plant can be propagated through seeds or corms. The seeds are sown under cover in beds or boxes from May onwards and lightly covered with soil. It is just like onion plant in appearance. Plants with white flower are treated as best quality. Leaves are shed off on the appearance of flower. Leaves are few in number, lorate, linear-oblong or oblanceolate, obtuse, appearing with flowers, short at flowering time, at fruiting 15-30 cm (Anonymous, 1987). In August–September, 2-6 flowers bloom which are identical to saffron and have liliac or pale purple colour. Flowers are 2.5-3.8 cm in diameter when expanded, perianth golden yellow, tube 7.5 cm (3-4inch) stamens shorter than the perianth, filaments very much shorter than the long yellow anthers (Kirtikar, 1996; Hooker, 1894).

The whole corms are 2.5-5 cm long and 1.5-2.5cm broad. They are translucent or opaque and gibbously ovoid with tapering apex and prominent longitudinal groove on one side. Corms are odorless and have a bitter and acrid taste (Anonymous, 1987). Collection of corms may start when the plants are two

years old. The corms are collected during June–July in the Kashmir valley and in the hill ranges of Uri, Domel, Kishtwar and Badharwah (Anonymous, 2001; *Chopra, et al.,* 1958; Ghazruni, 1311; Antaki, 1343). There are two varieties; one is Egyptian which is hard in texture, white in colour, treated as best quality, while other is Non-Egyptian which is not better (Harawi, 1312). European physicians in India who have tried the drug consider that the sweet variety is inert or nearly so, and the other has the properties similar to colchicum (Dymock, 1893). Plant is one feet long and the corm is ovate cordate, one inch in length, three forth (3/4) inch broad and one forth (1/4) in thickness, grooved on one side and convex on the other side, brownish-yellow in colour (Dymock, 1893; Khan, 1305). Colour of flower is like saffron or jasmine, leaves like onion plant, releases sticky material. The potency of this drug lasts up to three years (Khan, 1305; Momin, 1272).

Parts Used

The medicinal part used of *Sūranjān Talkh* is dried corm (Rhizome) (Ghani, 2005; Ibn Baitar, 1999; Ghazruni, 1311; Anonymous, 1987).

Mizāj (Temperament)

Unani physicians described the *Mizāj* (temperament) of *Sūranjān Talkh* (*Colchicum luteum*) as:

- Hot 3º and Dry 2º (Ghani, 2005; Ibn Baitar, 1999; Hakim, 1862)
- Hot 3º and Dry 3º (Hakim, 2002; Anonymous, 1987)
- Hot 2º and Dry 2º (Ghazruni, 1311; Avicenna, 1998)
- Hot 2º and Dry 3º (Khan, 1305)

Dose

Corm (Rhizome) powder: 3.5 to 4.5 gm (Ghazruni, 1311; Attar, 1888; Kantoori, 1889)

Decoction: 30 to 50 g (Ghazruni, 1311; Harawi, 1312)

Extract: 4 to 16 mg (Nadkarni, 2000; Khory and Kartak, 1985).

Substitute

Sūranjān Shīrīn (Anonymous, 1987; Nadkarni, 2000; Antaki, 1343)

Ḥinā (Khan, 1305; Attar, 1888; Avicenna, 1998)

Muqil (Khan, 1305; Avicenna, 1998)

Adverse Effects

Irritant to stomach (Hakim, 2002; Ibn Baitar, 1999; Ghazruni, 1311; Antaki, 1343)

Detrimental to liver (Hakim, 2002; Antaki, 1343)

Corrective

Kateera (Khan, 1305; Antaki, 1343)

Samagh-i-'Arabi (Anonymous, 1987)

Mirch Siyāh (Hakim, 2002; Ibn Baitar, 1999; Khan, 1305)

Action

The following different pharmacological actions of *Sūranjān Talkh* (*Colchicum luteum*) have been described in Unani literature:

Muḥallil-i-Awrām (anti-inflammatory), (Anonymous, 2001; Ghani, 2005), *Musakkin-i-Alam* (analgesic) (Ibn Baitar, 1999; Momin, 1272), *Mushil* (purgative) (Chopra, *et al.,* 1958; Nadkarni, 2000; Avicenna, 1998), *Dāfi'-i-Andrūnī Bawāsīr* (internal hemorrhoids) (Ghani, 2005; Hakim, 2002), alterative (Chopra, *et al.,* 1958; Nadkarni, 2000), *Jādhib-i-Akhlāṭ Lazij* (Ghazruni, 1311; Antaki, 1343), *Mulayyin* (laxative) (Anonymous, 1987; Kirtikar, 1996), *Kāsir-i-Riyāḥ* (carminative) (Hakim, 2002), *Mubahhī* (aphrodisiac) (Khan, 1305; Momin, 1272), *Mudammil-i-Qurūḥ* (cicatrizant) (Chopra, *et al.,* 1958; Ibn Baitar, 1999), *Mudirr-i-Bawl* (diuretic) (Anonymous, 1987; Attar, 1888), *Mufattiḥ-i-Sudad* (deobstruent) (Khan, 1305; Momin, 1272), *Mujaffif* (desiccant) (Khan, 1305; Momin, 1272), *Mulaṭṭif* (demulscent) (Khan, 1305), *Mushil* and *Qābiḍ* (purgative and constipative) (Ghazruni, 1311; Harawi, 1312), *Mushil-i-Balgham* (phlemogogue) (Ibn Baitar, 1999; Attar, 1888), *Mushil-i-Ṣafrā'* (cholagogue) (Ghani, 2005), *Tiryāq* for *Waja' al-Mafāṣil* (anti-dote for arthritis) (Ghani, 2005), *Qātil-i-Dīdān* (vermicidal), (Khan, 1305) and antipyretic (Anonymous, 2001).

Uses

Sūranjān Talkh (*Colchicum luteum*) has been described to be useful in various diseases such as *Waja' al-Mafāṣil* (rheumatoid arthritis) (Ghani, 2005; Chopra, *et al.,* 1958; Avicenna, 1998), *Niqris* (gout) (Ghani, 2005; Nadkarni, 2000; Avicenna, 1998) and *'Irq al-Nasā* (sciatica) (Ibn Baitar, 1999; Kantoori, 1889). It is also useful in *Andrūnī Bawāsīr* (internal piles) (Ghani, 2005; Ibn Baitar, 1999) and *Yaraqān* (jaundice) (Nadkarni, 2000; Antaki, 1343). It acts as laxative relieving constipation (Ghani, 2005; Harawi, 1312). It is beneficial in *Awrām Balghamī* (Khan, 1305), liver and spleen diseases (Kirtikar, 1996), *Khurūj-i-Kabid* (liver abscess) (Khan, 1305), wound healing (Nadkarni, 2000), Mediterranean

fever, Falciparum malaria (Anonymous, 2001) and headache (Kirtikar, 1996). It is also used in cataract (Ibn Baitar, 1999) and *Khadar* (numbness) (Ibn Baitar, 1999; Khan, 1305).

Phytochemistry

Indian colchicum corm contains alkaloids, glycosides, proteins, carbohydrates, resins, steroids/triterpenes, sodium, calcium, iron, potassium, sulphate, phosphate and chloride (Anonymous, 1987). From the colchicum, thirty-one different alkaloids have been isolated. The corms of *Colchicum luteum* contain alkaloid, chiefly colchicine, to the extent of about 0.25% (Bharathi, *et al.*, 2006).

It contains about 0.21 to 0.25 percent of colchicines and abundance of starch (Wallis, 1985; Hamayun, *et al.,* 2006). The major phenolic compounds obtained from the genus, colchicum, are 4-hydroxy-3-methoxybenzaldehyde (vanillin), 4-hydroxybenzoic acid (vanillic acid), 3-(3-hydroxyphenyl)-2-propanoic acid (coumaric acid), 3-(3, 4-dihydroxyphenyl)-2-propanoic acid (caffecic acid) and 3, 4, 5, 7tetrahydroxyflavone (luteolin) (Ahmad, 2010).

The alkaloid was later identified as a tricyclic alkaloid, and its pain-relieving and anti-inflammatory effects for curing gout were linked to its ability to bind with tubulin, one of the main constituents of microtubules (Gupta, 2005; "Colchicine", 2019).

Chemical analysis shows that *C. luteum* contains a large amount of starch, a small quantity of oily resinous matter and a bitter alkaloid. Following the assay method, the percentage of the alkaloid in the *C. luteum* (rhizome) was found to be from 0.21 to 0.25 and in the seeds from 0.41 to 0.43 % (Chopra, *et al.,* 1958; Nadkarni, 2000). Demecolcine, also a constituent of colchicum spp., is a more immediate precursor of colchicines (Evans, 2009). Luteidine isolated and characterized structure of luteicine elucidated, luteine isolated and structure assigned. β and γ-lumicolchicines, N-formyldesacetyl colchicines and 3-demethyl-N-desacetylformylcolchicine and 3-demethyl-colchicine isolated from corms.

Corms and aerial parts contained total alkaloids (0.94% and 0.70%) and colchicines (0.40% and 0.20%) respectively (Rastogi and Mehrotra, 1999). Total synthesis of colchicine new alkaloid –2-demethylcolchicine, colchamine, cornigerine, and β-lumicolchicine (Rastogi and Mehrotra, 1998). Collutine N-oxide-isolated and characterized, structure of luteidine revised by X-ray analysis (Rastogi and Mehrotra, 1995).

Powder Study of Corm

The powder is creamy white to light yellow colored, with yellow to brown

specks, it shows the presence of epidermis cell, ground tissue and numerous starch grains.

Table 1: Identification and Purity Parameters of *Colchicum luteum*

Name of Parameter	Value of Test
Total Ash Value	Not more than 2.75%
Acid Insoluble Ash	Not more than 18.20%
Water Soluble Ash	Not more than 43.60%
Alcohol Soluble Extractive	Not more than 1.50%
Water Soluble Extractive	Not more than 9.00%

Pharmacological Studies

- The antiarthritic activity of hydroalcoholic extract of *Colchicum luteum* was due to its modulatory effect on the expression of pro-inflammatory cytokine in the synovium. It produced a significant inhibition of joint swelling in both formaldehyde and CFA (Complete Freund's adjuvant) induced arthritis. Serum TNF-α level was also reduced significantly (Nair, *et al.,* 2011).
- An experimental study of Unani pharmacopoeial formulation *Qurṣ Mafāṣil Jadīd* containing *Colchicum luteum* as a main constituent on albino rats shows potent anti-inflammatory effect (Ansari and Khan, 2014).
- A preclinical study carried out at the Department of Pharmacology, AIIMS, New Delhi on a polyherbal formulation *Ma'jūn Sūranjān* containing *Sūranjān Talkh* as a main constituent showed potent anti-inflammatory and anti-arthritic effect in dose dependent manner (Singh, *et al.,* 2011).
- The colchicum preparations have a specific clinical effect in the treatment of acute gout. It acts against the inflammatory response to the urate crystals and has no effect on the concentration of uric acid in blood or on uric acid excretion. Colchicine also inhibits the deposition of uric acid (urate) crystals. Since the formation of such crystals is enhanced by a low pH in the tissues, it is surmised that colchicine raises the tissue pH by inhibiting the oxidation of glucose, thereby reducing the production of lactic acid in leukocytes. The inhibition of uric acid crystals is a vital aspect of the mechanism of gout treatment.
- Colchicine has a specific effect in gouty arthritis and can be used both to prevent and to relieve acute attacks. It prevents migration of neutrophils in to the joint, apparently by binding to tubulin, resulting in the depolymerisation of the microtubules and reduced cell motility. Colchicine inhibits neutrophil motility and activity, leading to a net anti-inflammatory effect.

- The crude drug and colchicine exhibited a highly significant lowering effect on total lipids and cholesterol. A decrease in serum uric acid level was also observed (Anonymous, 2001).
- Colchicine inhibited delayed type hypersensitivity response of mice to sheep red blood cells, it also inhibited production of leukocyte migration inhibitory factor from spleen cells as well as migration of normal chicken peripheral lymphocytes (Rastogi and Mehrotra, 1995).
- The effect of orally administered ethanolic extract of crude drugs *C. luteum* and colchicine on biochemical parameters of rabbits showed a transitory hypoglycemic effect, significant lowering effect on total lipids and cholesterol, serum uric acid and a significant increase in the activity of LDH, SGOT and alkaline phosphatase but these changes are transitory. It reduces or minimizes the effect of signs /symptoms of the ailments (Chaudhry, *et al.,* 1993).
- Colchicine was found to be effective in generalized pustular psoriasis and palmoplantar pustulosis. Improvement with a daily dose of 1.5 mg colchicine was found in Sweet's syndrome.
- Colchicine is also effective in several bullous diseases (Bulla-a large blister containing serous fluid), dermatitis herpetiformis, Epidermolysis bullosa acquisita, chronic bullous dermatosis of childhood with G6PD deficiency, urticarial vasculitis associated with hypocomplementemia, systemic scleroderma (Konda and Rao, 2010).
- It prevents attacks of familial Mediterranean fever and also useful in falciparum malaria (Dholwani, *et al.,* 2008).
- It produces a significant clinical improvement in liver cirrhosis patients and is also effective in treatment of Mollaret's meningitis.
- It is also used for antipyretic action in Hodgkin's disease. In large doses, it may cause profuse diarrhoea, gastro-intestinal haemorrhage, muscle weakness, skin rashes and irritation.
- Chronic cutaneous vasculitis in a C3-deficient patient was successfully treated with colchicine.
- Colchicine inhibits microtubule polymerization by binding to tubulin, one of the main constituents of microtubules. Availability of tubulin is essential to mitosis, and therefore colchicine effectively functions as a "mitotic poison" or spindle poison. Since one of the defining characteristics of cancer cells is a significantly increased rate of mitosis, this means that cancer cells are significantly more vulnerable to colchicine poisoning than normal cells.

However, the therapeutic value of colchicine against cancer is limited by its toxicity against normal cells.

- The mitosis inhibiting function of colchicine has been of great use in the study of cellular genetics. To see the chromosomes of a cell under a light microscope, it is important that they may be viewed near the point in the cell cycle in which they are most dense. This occurs near the middle of mitosis, so mitosis must be stopped before it completes. Adding colchicine to a culture during mitosis is part of the standard procedure for doing karyotype studies ("Colchicine", 2019).
- The study also reveals that the drug has no effect on blood pressure, pulse, respiration and weight of patients.
- Colchicine is given orally, is well absorbed, and reaches peak concentration in about an hour. It is excreted partly in gastrointestinal tract and partly in urine.
- During study gastric upsets and sometimes loose motion were observed as the side effects of drug (Siddiqui, *et al.,* 2002; Javed, *et al.,* 2005).
- The acute unwanted effects of colchicine are largely gastrointestinal: nausea, vomiting and abdominal pain. Severe diarrhoea may be a problem, and with large doses may be associated with gastrointestinal haemorrhage and kidney damage. Prolong treatment can rarely cause blood dyscrasias, rashes or peripheral neuropathy (Rang *et al.,* 2008). Some time it is known to cause neuropathy and myopathy. Alopecia, peripheral neuritis and bone marrow depression with agranulocytosis and aplastic anaemia may occur after prolong treatment.
- Its use for long term is not recommended owing to its depressant action upon the central nervous system.
- Amyloidosis is most common renal complication of Familial Mediterranean fever that can be prevented with colchicine treatment (Hatem, 2003).
- Its use is contra-indicated during pregnancy.
- The fatal dose varies, 7 mg of colchicines has caused death but recovery has also been reported after using much larger dose. In acute poisoning the stomach should be emptied by aspiration and lavage. A purgative such as sodium sulphate (12%) should be given and demulcent drinks may be given freely. Morphine sulphate (10mg) intramuscularly can be given to relieve severe abdominal cramps, atropine can also be given. The use of hyoscyamus or belladonna with calcium removes the tendency to intestinal irritation, because colchicine excites the vagal nerve endings in the gut and effect of this are antagonized by atropine.

- Colchicine should be given with care to old and feeble patients and to those with cardiac, renal, hepatic, or gastro-intestinal diseases.

Conclusion

Herbal drugs are preferred in comparison to synthetic ones due to their unwanted health effects. In modern medicine, joint diseases like arthritis, gout and other ailments are treated mainly by NSAIDS and steroids which produce many side effects, so herbal medicines are presenting best alternative to allopathic drugs in joint diseases. *Sūranjān Talkh* is one of the important medicinal plants used in Unani Medicine. In classical literature, it has been described to be widely used in arthritis and other joint ailments in single or in compound formulation as a first line drug and its efficacy has been proved by many preclinical and clinical studies conducted at leading institutes of India. Phytochemistry of the said drug shows many constituents which have potential anti-inflammatory, antiarthritic and analgesic activities. Many research studies have also demonstrated its importance in hyperlipidemia, uricemia, falciparum malaria, familial mediterranean fever, amyloidosis, generalized pustular psoriasis, palmoplantar pustulosis, sweet's syndrome, etc.

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सारांश

सुरंजान तल्ख़ (कोलचिकम ल्यूटियम बेकर): औशधीय गतिविधियों और नैदानिक प्रभावों की समीक्षा

***मो. मसीहुज़्ज़मा अंसारी, अज़ीजुर रहमान, अख़्तर हुसैन जमाली**

सुरंजान गठिया और जोड़ों से संबंधी अन्य रोगों के उपचार के लिए महान् यूनानी चिकित्सकों द्वारा उल्लिखित महत्वपूर्ण यूनानी औषधियों में से एक है। यह अफगानिस्तान, तुर्की और उत्तरी भारत की एक प्रसिद्ध औषधि है। यूनानी चिकित्सा पद्धति में *मोहल्लिल–ए–अवराम* (एंटी–इन्फ्लामेटॉरी), *मुस्हिल* (पर्गेटिव), *मुसक्किन–ए–अलम* (एनाल्जेसिक), *मुलय्यिन* (लैक्सेटिव), *मुफत्तेह–ए–सुदद* (डीओब्स्ट्रयूएन्ट) इत्यादि के रूप में इसका उपयोग किया जाता है। इसके अत्यधिक औषधीय महत्व को ध्यान में रखते हुए सुरंजान तल्ख़ के अनुसंधान के लिए नई सीमाओं का पता लगाने के उद्देश्य से यूनानी, एथनोबोटेनिकल, फाइटोकेमिकल और औषधीय साहित्य पर आधारित एक व्यापक समीक्षा की गई है।

शब्दकुंजी: *कोलचिकम ल्यूटियम, मोहल्लिल–ए–अवराम, मुसक्किन–ए–अलम, मुस्हिल, सुरंजान तल्ख़,* यूनानी चिकित्सा

Biochemical, Immunological and Pathological Studies on the Patients of *Waja' al-Mafāṣil* (Rheumatoid Arthritis) Simultaneously Treated with Unani Pharmacopoeial Drugs *Ma'jūn Sūranjān*, *Safūf Sūranjān* and *Rawghan Sūranjān*

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Abstract

Waja' al-Mafāṣil (Rheumatoid arthritis/RA) is an inflammatory disorder associated with pain in multiple joints which affects the quality of life. Several drugs including nonsteroidal anti-inflammatory drugs (NSAID) and steroids are available in allopathic system of medicine to treat RA but they have serious side effects such as hepatotoxicity, nephrotoxicity and gastric ulcer. In the present study, the effect of Unani formulations *Ma'jūn Sūranjān*, *Safūf Sūranjān* and *Rawghan Sūranjān* on certain biochemical, pathological and immunological parameters in the cases of *Waja' al-Mafāṣil* (RA) is studied. These classical Unani drugs were found effective with reference to SGOT ($P<0.001$), SGPT ($P<0.01$), ALP ($p<0.05$), creatinine ($p<0.001$) and uric acid ($p<0.001$) and not effective with reference to bilirubin and urea. All the safety parameters were within the normal limits at the baseline and remained normal after the treatment. ESR was found high at the baseline which reduced significantly ($p<0.001$) after the treatment. In immunological parameter, significant reduction was found in RA factor ($p<0.001$) and CRP ($p<0.001$) after the treatment. Out of 84 patients, 35 patients showed very good response, 43 patients showed good response and six patients showed poor response to the drugs. No adverse effect was observed during the entire study period.

Keywords: *Balgham,* Inflammation, Joints, Rheumatoid arthritis

Introduction

Rheumatoid arthritis is a systematic, inflammatory autoimmune disorder of unknown aetiology that affects about 1% of the world population. It is a disease of joints characterized by the inflammation of the synovial membrane, infiltration by blood-derived cells; chiefly memory T cell, macrophages and plasma cells mediated by the cytokine induction of destructive enzymes which resulted in progressive destruction of cartilage and bone (Distler, *et. al*, 2005). In Unani context, arthritis is termed as *Waja' al-Mafāṣil* which in broader terms means pain in joints. In *Waja' al-Mafāṣil,* pain occurs in joints of hand, feet, knees and ankle. It is also seen in temporo-mandibular joints and vertebrae (Munshi, *et al.,* 2013). According to Unani physicians, *Balgham-i-Lazij* (viscid phlegm) accumulates in the joints due to its weakness and causes *Waja' al-Mafāṣil.* Also, due to weakness of joints, the viscid phlegm is retained in joint itself and the nutrients reaching the joints are not utilized but converted into harmful products (morbid matter) which induce inflammatory process (Alam, *et. al*, 2014). According to Ibn Sīnā, the causative organism of the disease is *Ajsām Khabītha* (foul bodies), while another group says that *Ḥāmiḍ Labanī*

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is the root cause which is produced by the derangement of digestive process and accumulates in the blood and joints and causes *Waja' al-Mafāṣil. Balgham* (phlegm) is the predominate in *Waja' al-Mafāṣil,* followed by *Dam* (blood) and *Ṣafrā'* (bile), while *Sawdā'* (black bile) is rarely involved (Majusi, 1889; Jurjani, 1903).

C-reactive protein (CRP), rheumatoid arthritis factor and erythrocyte sedimentation rate (ESR) are commonly used as measures of inflammation in RA. Liver function test and kidney function test are used as safety markers in clinical trials. There are several single and compound drugs available in Unani Medicine for management of the disease but scientific data to prove their safety and efficacy are lacking. However, two clinical studies on *Ma'jūn Sūranjān, Safūf Sūranjān* and *Rawghan Sāranjān* have been done with and without cupping therapy and found to be effective (Alam, *et al.,* 2014; Alam, *et al.,* 2018). Preclinical studies have been done on *Ma'jūn Sūranjān* and found effective and safe (Singh, *et al.,* 2011). *Colchicum luteum* is the main ingredient of these test formulations which has well-known anti-arthritic property in experimental and clinical trial (Nair, *et al.,* 2012; Javed, *et al.,* 2005). Keeping this background in view, this study was planned to evaluate the effect of *Ma'jūn Sūranjān, Safūf Sūranjān* and *Rawghan Sāranjān* on certain biochemical, pathological and immunological parameters in the cases of *Waja' al-Mafāṣil* (RA).

Materials and Methods

Study Drugs

Ma'jūn Sūranjān, Safūf Sūranjān and *Rawghan Sāranjān* (compositions are given in Table 1, 2 and 3) were prepared and procured from GMP certified pharmacy of Central Research Institute of Unani Medicine, Hyderabad.

Sample Size and Duration of Study

In all, 84 patients suffering from RA were enrolled in the study as per the protocol provided by the Central Council for Research in Unani Medicine (CCRUM), New Delhi. The Duration of the study was 84 days. The study protocol was approved by the Institutional Ethical Committee (IEC) of Regional Research Institute of Unani Medicine, Patna. This study was open label and only one group was treated with Unani pharmacopoeial drugs. This study was conducted during 2012–2015.

Follow-up

The patients were assessed clinically every fortnight. Blood for biochemical, pathological and immunological study was collected at the time of enrolment and after completion of the study.

Selection of Patients

Patients who fulfilled the inclusion criteria proposed by American College of Rheumatology 1987 criteria were considered for the study (Arnett, *et al.*, 1988).

The patients were treated with Unani pharmacopoeial formulations for a period of 84 days with regular follow-ups at the interval of fourteen days at Regional Research Institute of Unani Medicine, Patna.

Inclusion Criteria

- Patients of either sex in the age group of 18-65 years
- Patients who fulfilled the inclusion criteria of American College of Rheumatology 1987 (revised criteria), i.e. morning stiffness, symmetrical arthritis, three or more than three joints involved, duration of the disease for six weeks or more, rheumatoid nodules, radiological changes
- Normal ECG, normal x-ray of chest
- Patients complaining of joint pain (single/multiple joints) with or without anyone of the following symptoms/signs such as tenderness, swelling and restriction of movement

Exclusion Criteria

- Patients below 18 years of age
- Patients having complicated RA associated with deformity, surgery of affected joint, disorder requiring long term treatment, drug addicts (alcohols, drugs)
- Overweight subjects – BMI>35
- Patients having gout or associated with deformity
- Patients showing abnormality in any investigations done at the baseline like SGOT, SGPT and ALP, Sr. Creatinine, B. Urea (would be considered abnormal if raised> 2 ½ times the normal value)
- Pregnant and lactating women
- Patients with concurrent physical illness like uncontrolled hypertension and diabetes.

Treatment Details

Dose Schedule and Mode of Administration

1. ***Ma'jūn Sūranjān***

Dose: Trial drug *Ma'jūn Sūranjān* (semi-solid form 7gm) was given orally with water twice a day after meals.

Table 1 : Ingredients and Composition of *Ma'jūn Sāranjān*

Name of Ingredient	Botanical Name	Quantity
Sūranjān Shīrīn	*Colchicum luteum*	500 GM
Sanā	*Cassia angustifolia*	250GM
Zanjabīl	*Zingiber officinale*	100 GM
Zīra Siyāh	*Carum carvi*	100 GM
Filfil Darāz	*Piper longum*	100 GM
Asārūn	*Asarum europaeum*	100 GM
Qand Safaid	*Saccharum officinarum*	3.5 KGS

2. *Safūf Sūranjān*

Dose: *Safūf Sūranjān* (powder form 6gm) was given orally twice a day with water after meals.

Table 2: Ingredients and Composition of *Safūf Sūranjān*

Name of Ingredient	Botanical Name	Qty
Sūranjān Shīrīn	*Colchicum luteum*	25 GM
Buzidān	*Pyrethrum indium*	25 GM
Post-i-Halela Zard	*Terminalia chebula*	25 GM
Maghz-i-Tukhm-i-Tarbūz	*Citrullus vulgaris*	25 GM
Maghz-i-Bādām	*Prunus amygdalus*	25 GM
Maghz-i-Tukhm-i-Bādranjboyā	*Nepeta hindostana*	25 gm
Maghz-i-Tukhm-i-Kheyār Darāz	*Cucumis sativus*	25 gm
Kishnīz Khushk	*Coriandrum sativum*	25 gm
Tukhm-i-Khaskhāsh	*Papaver somniferum*	25 gm
Qand Safaid	*Saccharum officinarum*	225gm

3. *Rawghan Sūranjān*

Dose: *Rawghan Sūranjān* (oil form) was applied locally on the affected joints with gentle massage till it absorbed twice a day in the morning and at bed time.

Laboratory Investigations

The pathological, biochemical and radiological investigations were carried out before the treatment (at the baseline) and after the treatment.

Collection of Blood Sample

Blood sample was collected for biochemical and pathological study on day 0 and after completion of the study. Serum was separated for biochemical study by centrifuging the clotted blood at 3000 rpm for 10 minutes.

Table 3: Ingredients and Composition of *Rawghan Sūranjān*

Name of Ingredient	Botanical Name	Qty
Sūranjān Talkh	*Colchicum luteum*	50 gm
Āb-i-Karafs	*Apium graveolens*	50 gm
Chirā'ita	*Swertia chirata*	25 gm
Rawghan-i-Zaitūn	*Olea europea*	150 gm

Biochemical Study

Diagnostic reagents kits from Span Diagnostic Pvt. Ltd. were used for biochemical tests which included SGOT and SGPT, bilirubin, alkaline phosphatase, blood urea, serum creatinine and uric acid. All the parameters were estimated by using spectrophotometer from Systronic Pvt. Ltd. India.

Serological Test (RA Factor and C-reactive Protein)

RA factor and CRP were also carried out by haemagglutination methods by kits from Span Diagnostic Pvt. Ltd. RA factor and CRP were categorized by scoring system which were 0, 1 and 2. Score 0 was for negative test result, 1 for weak positive and 2 for strong positive.

Pathological Study

TLC (Total leukocyte count), DLC (Differential leukocytes count), haemoglobin% and ESR (Erythrocyte sedimentation rate) were done before and after treatment using standard methods of estimation.

Statistical Analysis

Baseline and follow-up values of pathological, biochemical and immunological parameters (RA factor and CRP) were statistically analysed using Student's paired 't' test and Paired wilcoxon signed test. The result was expressed as the Mean ± SEM. $P<0.05$ has been considered as statistically significant.

Results

In biochemical parameters, SGOT (***$p<0.001$), SGPT (***$p<0.001$), ALP (***$p<0.05$), creatinine (***$p<0.001$) and uric acid (***$p<0.001$) were significantly reduced. Bilirubin and urea were non-significantly reduced after treatment, although all parameters were within normal limits at the baseline and remained normal after the treatment with Unani pharmacopoeial formulations (Results depicted in Table 4).

In pathological parameters, ESR was significantly (***$p<0.001$) reduced and TLC was also significantly (**$p<0.001$) reduced. DLC were measured before

Table 4: Effect of Test Drugs on Biochemical Parameters

Parameter	Mean ± S.E.M	
	Before Treatment	After Treatment
S. Bilirubin (mg/100 ml)	0.72 ± 0.03	0.74 ± 0.03^{ns}
SGOT (IU/L)	18.19 ± 0.61	16 ± 0.37 ***
SGPT (IU/L)	24.93 ± 1.3	22.49 ± 0.65**
S. ALP (KA)	6.1 ± 0.16	5.8 ± 0.11*
S. Creatinine (mg/100 ml)	0.85 ± 0.02	0.78 ± 0.01***
Urea (mg/100 ml)	21.2 ± 0.53	21 ± 0.37 ^{ns}
Uric Acid	4.7 ± 0.11	4.4 ± 0.08***

***P<0.001, **p<0.01, *p<0.05 and ns = non-significant as compared to baseline

and after treatment in which neutrophil, lymphocytes, monocytes and basophils were within normal limits and remained normal after treatment with the test drugs although they were significantly altered after treatment with Unani test formulations (Results depicted in Table 5).

Table 5: Effect of Test Drugs on ESR, TLC and DLC

Parameter		Mean ± S.E.M	
		Before Treatment	After Treatment
ESR (mm/hr)		22.56 ± 1.55	11.56 ± 0.74***
Total Leukocyte Count(1000/cu.mm)		6451 ± 130	6148 ± 72 **
DLC	N (%)	60 ± 0.68	58 ± 0.36**
	L (%)	33 ± 0.69	35 ± 0.43**
	E (%)	4.3 ± 0.25	3.5 ± 0.21***
	M (%)	1.45 ± 0.07	1.73 ± 0.06**
	B (%)	0 ± 0	0 ± 0

***P<0.001, **p<0.01, *p<0.05 and ns=nonsignificant as compared to baseline

RA factor and CRP was significantly (***p<0.001) inhibited after treatment. RA factor was 98.41% inhibited and CRP was 88.09% inhibited after treatment with Unani formulations (Results depicted in Table 6).

Table 6: Effect of Test Drugs on RA Factor & CRP

Clinical Parameter	Mean ± SEM		(% Inhibition) Before Treatment – After Treatment / Before Treatment X 100	P-Value
	Before Treatment	After Treatment		
RA	0.63± 0.1	0.01± 0.01	0.63- 0.01/0.63 X 100 = (98.41%)	<0.001
CRP	0.42± 0.1	0.05± 0.03	0.42-0.05/ 0.42 X 100 = (88.09%)	<0.001

Grading: Negative=0; Weak Positive=1; Positive=2

Total 42% patients showed very good response, 43% patients showed good response and 7% patients showed poor response (Table 7).

Table 7: Response of Test Drugs

No. of Patients (n)	Excellent (90-100%)	Very Good (60-89%)	Good (30-59%)	Poor (<30%)
84	-	35 (42%)	43 (51%)	6 (7%)

Discussion

Treatment decisions in rheumatoid arthritis are individualized and depend largely on the intensity of the disease. Many drugs are clinically used in modern medicine for the treatment of rheumatoid arthritis but therapeutic effects are restricted due to their side effects such as bone marrow suppression leading to leucopoenia and thrombocytopenia, gastrointestinal dysfunction, skin rash, allergic reaction, loss of body weight, and reversible baldness (Zhou, *et al.,* 2002; Ye and Sun, 2000).

In the present study, the changes of biochemical, pathological and immunological parameters were studied after the treatment of RA patients with *Ma'jūn Sūranjān, Safūf Sūranjān* and *Rawghan Sāranjān*. All biochemical parameters such as SGOT, SGPT, ALP, bilirubin, urea, createnine and uric acid were in normal limits at the baseline and remained within normal limits after the treatment with the Unani pharmacopoeial formulations. It was demonstrated that the test formulations did not alter hepatic function and renal functions, and indicated that these drugs were safe.

In Unani Medicine, many herbal formulations are claimed to possess anti-arthritic activity and this system is being increasingly recognized as an alternative and effective approach for the management of RA. Many formulations have been used since a long time in Unani Medicine for the management of RA (Alam, *et al.,* 2014).

The present study reports that Unani pharmacopoeial formulations are effective as there was significant reduction in some inflammatory markers such as ESR, CRP and RA factor.

The erythrocyte sedimentation rate (ESR) has been the most widely used marker of inflammation in RA. It indirectly measured inflammation in the body which reflects the tendency of RBCs to settle more rapidly in the face of some disease states, usually because of increase in plasma fibrinogen, immunoglobulins and other acute-phase reaction proteins (Ahmad, *et al.,* 2015). ESR levels respond slowly to inflammatory stimulation thus to the changes in disease activity (Siemons, *et al.,* 2014). In this study, significant reduction was observed after treatment with the test formulations. TLC and DLC were in normal limits and

remained normal after treatment with the Unani test formulations.

The C-reactive protein (CRP) is an acute-phase protein produced from liver. It serves as a pattern-recognition molecule in the innate immune system. It is a marker of inflammation with or without playing a direct role in the inflammatory process and may play a pro-inflammatory role in activating monocyte chemotactic protein (Du Clos, 2000; Yeh, 2004). Present study reports significant reduction of CRP after treatment.

The presence of auto antibodies which react with antigenic determinants on the Fc part of IgG (rheumatoid factors (RFs) is a common feature of RA. In the early stages of the disease, the measurement of rheumatoid factor may give valuable information on the severity of RA and the prognosis. This information may prove to be useful for the optimum clinical management of the disease (Zeben, *et al.,* 1992). In this study, significant reduction was observed in RA factor after treatment with the Unani pharmacopoeial formulations.

In the present study, these classical Unani drugs were found to be safe and effective with reference to biochemical, pathological and immunological parameters. These results suggest that the Unani pharmacopoeial formulations are safe and might exert their effect by ameliorating inflammation.

Conclusion

This study concludes that these Unani pharmacopoeial formulations are safe and effective in reducing rheumatoid factor, C-reactive protein and ESR in the cases of RA at the given dosage. No change was found in hepatic function test and renal function test after the treatment. However, as this study was limited to only 84 patients for a shorter duration in Bihar, a State of North India, the authors suggest that study with a larger number of patients may be carried out to substantiate the findings of this study. These Unani pharmacopoeial formulations are low cost and can be advocated for the management of RA.

Acknowledgement

Authors are thankful to the Director General, Central Council for Research in Unani Medicine, New Delhi for providing necessary facilities and financial support to conduct the study at Regional Research Institute of Unani Medicine, Patna.

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सारांश

यूनानी भेषजकोशीय औषधियों माजून सुरंजान सफ़ूफ़ सुरंजान और रोग़न सुरंजान से उपचारित वजा-उल-मफ़ासिल के रोगियों पर जैव रासायनिक, प्रतिरक्षात्मक और रोगविज्ञानीय अध्ययन

तसलीम अहमद, मो. इश्तियाक़ आलम, अनीर्बन गोस्वामी, पवन कुमार यादव और मुनव्वर हुसैन क़ाज़मी

वजा–उल–मफ़ासिल (गठिया) विभिन्न प्रकार के जोड़ों के दर्द से जुड़ा इनफ्लामेटरी विकार है जो जीवन की गुणवत्ता को प्रभावित करता है। गठिया के उपचार के लिए एलोपैथिक पद्धति में नॉनस्टेरॉइडल एंटी–इनफ्लामेटरी ड्रग्स (एनएसएआईडी) और स्टेरॉयड सहित कई औषधियां उपलब्ध है लेकिन इनके हेपेटोटॉक्सिसिटी, नेफ्रोटॉक्सिसिटी और गैस्ट्रिक अल्सर जैसे गंभीर दुष्प्रभाव है। वर्तमान अध्ययन में वजा–उल–मफ़ासिल (गठिया) के रोगियों में कुछ जैव रासायनिक रोगविज्ञानीय और प्रतिरक्षात्मक मापंदडों पर यूनानी मिश्रणों अर्थात माजून सुरंजान, सफ़ूफ़ सुरंजान और रोगन सुरंजान के प्रभाव का अध्ययन किया गया। ये क्लासिकी यूनानी औषधियां एसजीओटी ($p<0.001$), एसजीपीटी ($p<0.01$), एएलपी ($p<0.05$), क्रिएटिनिन ($p<0.001$) और यूरिक एसिड ($p<0.001$) के संदर्भ में प्रभावी पाई गई और बिलरुबिन और यूरिया के संदर्भ में प्रभावी नहीं पाई गईं। सभी सुरक्षा मापदंड आधार–रेखा पर सामान्य सीमा के भीतर थे और उपचार के बाद सामान्य बने रहे। ईएसआर आधार–रेखा पर अधिक पाया गया जो उपचार के काफी कम ($p<0.001$) हो गया। प्रतिरक्षात्मक मापदंडों में उपचार के बाद गठिया कारक ($p<0.001$) और सीआरपी ($p<0.001$) में महत्वपूर्ण कमी पाई गई। कुल 84 रोगियों में से 35 रोगियों ने बहुत अच्छी प्रतिक्रिया दिखाई, 43 रोगियों ने अच्छी प्रतिक्रिया दिखाई और छः रोगियों ने औषधियों के प्रति ख़राब प्रतिक्रिया दिखाई। संपूर्ण अध्ययन अवधि के दौरान कोई प्रतिकूल प्रभाव नहीं देखा गया।

शब्दकुंजी: बलग़म, सूजन, जोड़, रुग्ण पदार्थ, संधिशोथ

Macro and Microscopical Evaluation, HPTLC Fingerprinting and Quality Control Studies on *Mimusops elengi* L. Fruits

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Abstract

Mimusops elengi L., which belongs to Sapotaceae family, is a tree native to the Western Ghat region of the peninsular India. The plant possesses several medicinal properties such as astringent, tonic, febrifuge, purgative, diuretic, aphrodisiac and spermicidal as well as properties against chronic dysentery, diabetes, hydrophobia, piles and gonorrhea. In view of high traditional use of the plant, the present investigation was undertaken for research and development of pharmacopoeial standards. Despite the modern techniques, identification of plant drug by pharmacognostic study is more reliable. The present investigation deals with the macro and microscopical evaluation and pharmacopoeial studies for the fruit of *Mimusops elengi* L. Microscopical studies show the presence of epidermal cells, mesocarpic parenchyma cells, sclereids, endosperm cells, cotyledonary parenchyma cells, T shaped trichomes and calcium oxalate crystals. The HPTLC fingerprinting studies on chloroform and alcohol extract using toluene: ethyl acetate: formic acid solvent system and in VS reagent show 11 and 10 spots respectively. The quality control parameters such as microbial load and heavy metals were found within the permissible limits and other parameters like aflatoxins and pesticidial residues were not detected from the seeds of the drug. This information can be used as an important parameter for future pharmacological and therapeutical investigations and also for ensuring quality formulations.

Keywords: HPTLC Fingerprinting, Macro and Microscopical Studies, *Mimuspos elengi* L., Quality Control

Introduction

Mimusops elengi L. (Family - Sapotaceae) is a large glabrous evergreen tree of 12 to 15m of height distributed in Western and Eastern Ghats. The plant is cultivated throughout the tropical parts of India, Deccan Peninsula in particular and often planted on road sides. *M. elengi* L. is a short, dark, very rough trunk and wide spreading, the ends of which tend to rise and form a thick globular head to the tree. The tree attains large dimensions in the moist evergreen forests of Western Ghats; while in the Eastern Ghats it is found in dry areas, often on laterite and is comparatively small in size.

M. elengi L. plant is known as Bakulah in Sanskrit, Magilam and Vagulam in Tamil and Mulsari in Urdu and Persian. The plant blooms flowers from March to May and it is very fragrant in nature. It starts bearing fruits from May to June. The fruit is ovoid, berry, yellow when ripe, size upto 2.5cm long and encloses one seed.

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The various parts of the plant has some therapeutic uses: Fruit - astringent; Ripe fruit - chronic dysentery (Kritikar and Basu, 1998); Seeds – purgative and suppository for children in case of constipation; Flowers - astringent and powder used as snuff to remove headache; Flowers & Fruits - lotion for wounds and ulcers; Bark - astringent, tonic, febrifuge, increases fertility in women; Infusion or decoction is used as a gargle in disease of gums and teeth (Chatterjee and Pakrashi, 1995). *M. elengi* L. seed is used traditionally for curing piles, headache, constipation, spermicidal, etc. (Gopalkrishnan and Shimpi, 2010).

The fruit contains large proportion of sugars and saponins (Nadkarni, 1976). The chemical constituents present in the fruits and seeds are quercitol, quercetin, α-spinasterol, β sitosterol, lupeol, ursolic acid and glucose. Other constituents like arachidic, behenic, capric, lauric, linoleic, oleic, myristic, palmitic and stearic acids, polysaccharide composed of L-arabinose, D-galactose, D-glucose, D-glucuronic acid, L-rhamnose & D-glucose, dihydro quercetine, quercetine, β-d glycosides of mimusopic acid, mimusopsic acid, mimusopane, mimusopgenone, mimugenone, mimusopin, mimusopsin, mimusin, Mi-saponin A, 16 alpha-hydroxy Mi-saponin A were also reported from seeds and fruits (Chatterjee and Pakrashi, 1995; Shivatare, *et al.*, 2013).

The nutritional values of the fruit viz. protein (1.29%), fat (2.76K Cal), reducing sugar (8.9%), non-reducing sugar (6.3%), total sugar (15.2%), fiber (1.13%), vitamin C (3.27mg/100gm), mineral content (0.32%), iron (0.59 mg/100gm), sodium (5.16 mg/100gm), potassium (98.54mg/100 gm) are also reported (Nazarudeen, 2010).

As the fruit of the plant *M. elengi* L. is used in various ailments and contains various organic and inorganic compounds, the fruit sample was undertaken to authenticate and to study the macro and microscopical, HPTLC fingerprinting and quality control studies to lay down the standards for future references.

Materials and Methods

Pharmacognostical Study

Collection of Sample: Fresh fruits of *M. elengi* L. were collected in the month of March from Regional Research Institute of Unani Medicine (RRIUM), Chennai. The plant was identified and authenticated by Flora of Presidency of Madras (Gamble, 1921). The morphological authenticity of the plant was referred and compared with the herbarium specimen in the Survey of Medicinal Plants Unit (SMPU), RRIUM, Chennai.

The macroscopical, microscopical and powder microscopy were carried out using standard methods (Johansen, 1940). The free hand sections of the seed were taken, stained with safranin and fast green and mounted in glycerine. The powder

of the drug was treated with various chemical reagents like phloroglucinol + HCl and Jeffrey's reagent for clearing the tissues to study the various elements. Photomicrographs were made using the digital SLR camera attached with the microscope.

Extract Preparation: The collected fruit samples were shade dried and coarsely powdered. These coarse powdered samples were used for TLC, HPTLC analysis, and quality control parameters.

TLC/ HPTLC Fingerprint Analysis

The TLC/HPTLC analysis was performed for chloroform and alcohol extract of the fruit of *M. elengi* L. 2gm of drug sample was extracted in 20 ml of chloroform and alcohol separately by refluxing on a water bath for 30 min. The extract was filtered and concentrated to 5ml and thin layer chromatography was carried out. The extracts (8µl each) were applied on pre-coated silica gel 60 F_{254} TLC plate (E Merck) and developed the plate using Toluene: Ethyl acetate: Formic acid (8.8: 1.2: 0.1 for chloroform and 8.8: 0.5: 0.1 for alcohol) solvent systems as mobile phase. The developed plates were scanned densitometrically at 254nm, 366nm and derivatized using spray reagent Vanillin sulphuric acid. The Retention factor (Rf) values, peak area and peak height were determined (Wagner, *et al.,* 1984; Sethi, 1996).

Quality Control Parameters

The quality control parameters like estimation of microbial load and analysis of aflatoxins were carried out as per WHO guidelines (WHO, 2007). Heavy metals analysis was done by atomic absorption spectrophotometer (AOAC, 2005). Pesticidal residues were analyzed using GC-MS agilent instrument equipped with mass selective detector as per the methods of AOAC (**AOAC**, 2005).

Results

Pharmacognostical Studies

Macroscopic features: Fruit berry, pedunculate, 3.0cm long and upto 1.5cm mid-width (Fig. 1), ovoid with single seed; young fruits light green to yellow; pinkish brown or orange when ripe; often with a thin leathery to bony outer surface; mesocarp fleshy and endocarp stony; seeds with fleshy endosperm, obliquely ovate and slightly compressed; testa shining; odour slightly aromatic; taste sweet and acrid.

Microscopic Features

Pedicel – T. S. of pedicel shows circular in outline; epidermis consisting of single layer of rectangular to squarish, thick walled parenchyma cells with thick

cuticle; unicellular thick walled trichome present (2 armed); cortex consisting of several layers of thin walled, oval to round, loosely arranged parenchyma cells with intercellular spaces; cells in outer region smaller and gradually becomes larger towards the centre; sclereids or groups of stone cells present in the cortex; sclerenchyma patches (pericycle) present below the cortical region; vascular bundle in the centre with continuous ring of xylem elements surrounded by few layers of phloem cells; pith in the centre consisting of thin walled polygonal parenchyma cells; druses of calcium oxalate crystals present in secondary cortex, phloem and pith parenchyma cells (Fig. 1).

Fruit – T. S. of fruit pericarp shows epidermis consisting of single layer of thick walled parenchyma cells with a thick cuticle; mesocarp consisting of several layers of thin walled, oval to round, loosely arranged parenchyma cells with intercellular spaces; sclereids or groups of stone cells present in the cortex; latex cells present in 5 to 6 layers of cells in the mesocarp; few vascular strands present in the mesocarp (Fig. 1).

Seed – T. S. of fruit (endocarp) shows the testa consisting of 5 concentric regions; outer most composed of 12 to 13 layers of thick walled polygonal isodiametric, sclerenchymatous cells; second and third regions consisting of thin walled parenchyma cells; deep reddish contents comprise the fourth region, vascular strand present; fifth region composed of few layers of round to oval cells, devoid of cellular contents; endosperm consisting of few layers of thin walled, polygonal parenchyma cells filled with oil globules and aleurone grains; cotyledons consisting of small compactly arranged thin walled polygonal parenchyma cells filled with aleurone grains and oil globules (Fig. 1).

Powder Features: Light brown; odour slightly aromatic; taste sweet and acrid; epidermal cells in surface view with compactly arranged parenchyma cells; mesocarpic parenchyma cells with laticiferous cells; T shaped unicellular trichomes; sclereids of various shapes and size upto 250µ; spiral vessels upto 15µ; latex cells; fragments of endosperm cells with aleurone grains and oil globules; cotyledonary parenchyma cells with aleurone grains and oil globules; fibres thin walled of length upto 500µ and breadth upto 15µ; fibres tracheids of length upto 500µ and breadth upto 20µ; prism of calcium oxalate crystals upto 20µ, druses of calcium oxalate crystals upto 50µ (Fig. 2).

TLC/ HPTLC Fingerprint Studies

The TLC/HPTLC profile of chloroform and alcohol extracts of the fruit samples is shown in Fig. 3 and 7. The R_f values of both chloroform and alcohol extracts were noted separately in 254nm, 366nm and after derivatization with plates in vanillin-sulphuric acid reagent followed by heating till the spots appeared bright coloured under visible light (Table 1 and 2).

Fig. 1

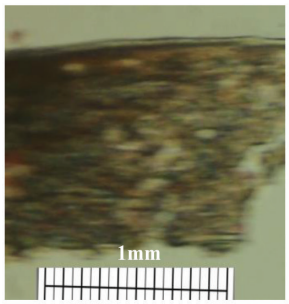
Mimusops elengi L. - Fruit

T. S. of Pedicel

Fruit - Surface View

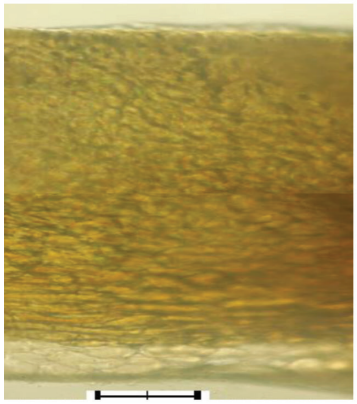
A Diagrammatic Sketch

T.S. of Fruit (Pericarp)

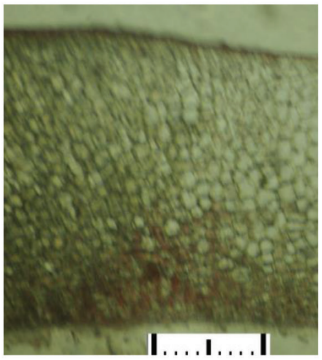


T. S. of Fruit (Endocarp)

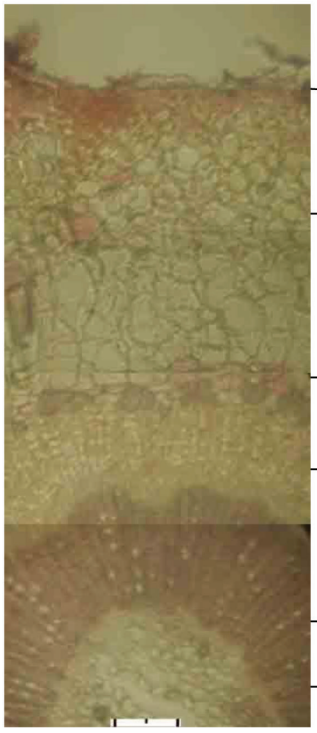
T. S. of Fruit (Cotyledons)

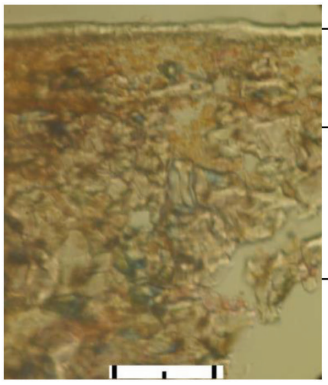


T. S. of Pedicel



T. S. of Fruit (Pericarp)





T. S. of Fruit (Pericarp)

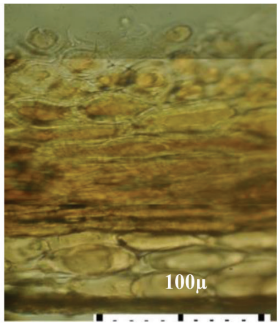
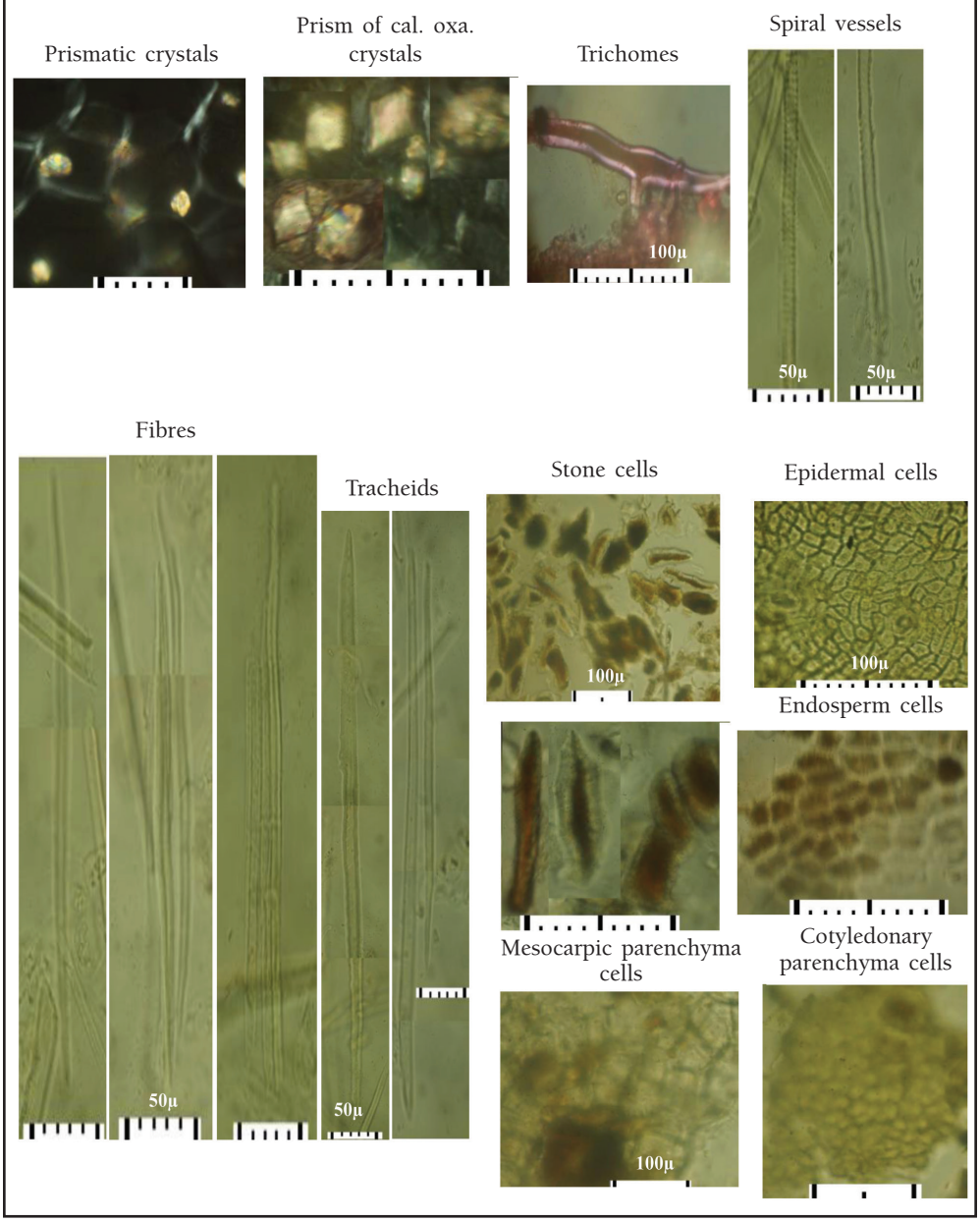


Fig. 2

Powder

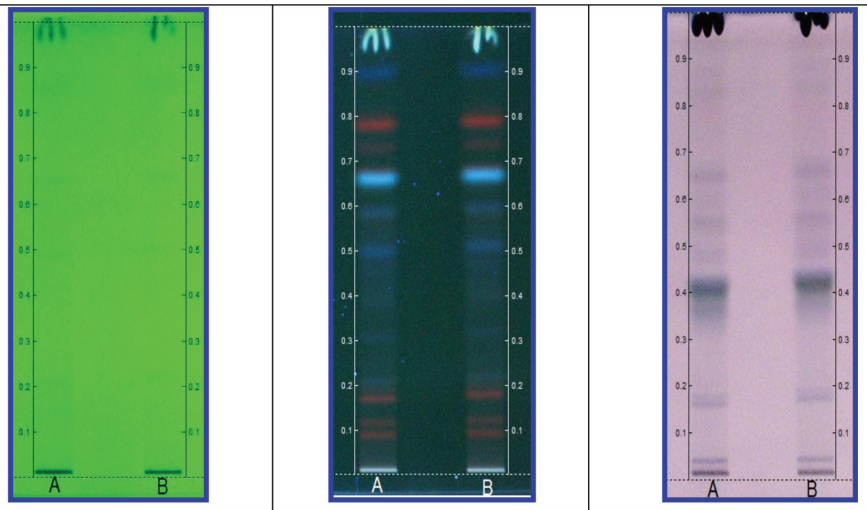


HPTLC fingerprinting profile of chloroform extract showed 7 peaks at 254nm, 2 peaks at 366nm (absorbance mode) and 11 peaks at 366nm (fluorescence mode) (Fig. 4, 5 and 6), of which one major peak at Rf value 0.67 was seen in 366nm (fluorescence mode).

HPTLC fingerprinting profile of alcohol extract showed 7 peaks at 254nm, 3 peaks at 366nm (absorbance mode) and 10 peaks at 366nm (fluorescence mode) (Fig. 8, 9 and 10), of which one major peak at Rf value 0.71 was seen in 366nm (fluorescence mode).

Fig. 3

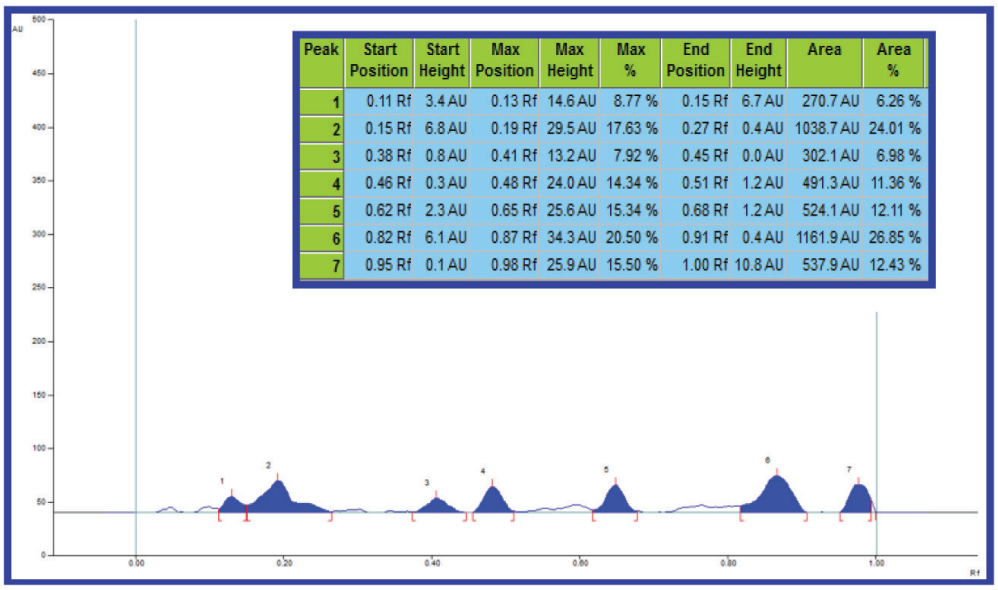
Thin Layer Chromatography
Chloroform extracts



UV – 254 nm	UV – 366 nm	V - S Reagent
Solvent System: Toluene : Ethyl acetate : Formic acid (8.8: 1.2: 0.1) 8 µl Track 1. Batch - I; Track 2. Batch - II		

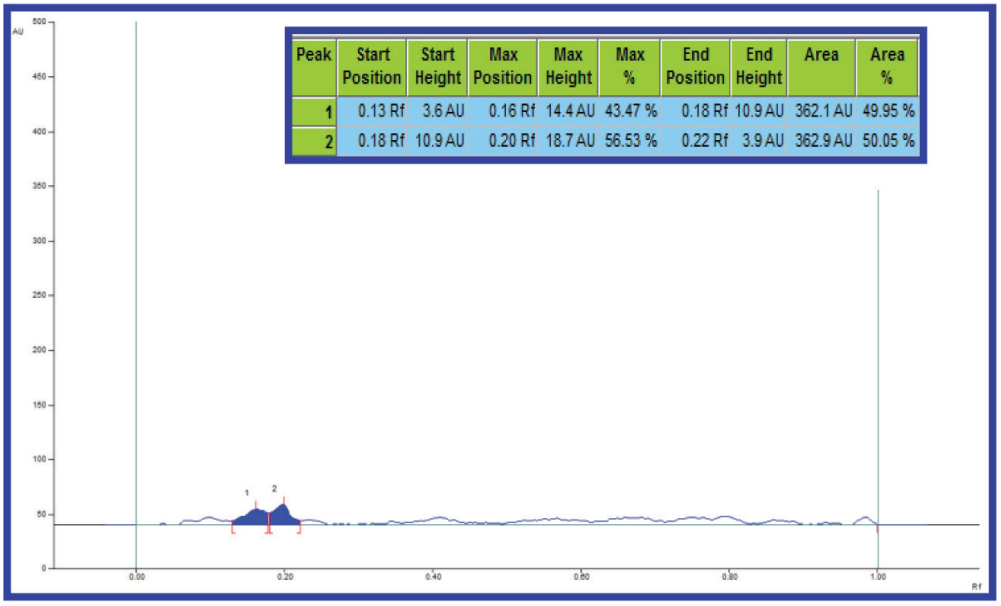
Table 1: TLC data of the *M. elengi* L. (Fruit) in Chloroform extract

Solvent system	R_f Values		
	UV 254 nm (5 spots)	UV 366 nm (13 spots)	V. S. Reagent (11 spots)
Toluene : Ethyl acetate : Formic acid (8.8 : 1.2 : 0.1)	0.98 Green	0.98 Blue	0.98 Dark grey
	0.85 Green	0.90 Blue	0.91 Grey
	0.65 Green	0.79 Red	0.81 Grey
	0.48 Green	0.73 Light red	0.64 Grey
	0.20 Green	0.67 Fluorescent blue	0.59 Grey
		0.59 Blue	0.55 Grey
		0.50 Blue	0.48 Grey
		0.39 Blue	0.42 Dark grey
		0.31 Blue	0.36 Grey
		0.22 Blue	0.19 Grey
		0.17 Red	0.04 Grey
		0.12 Red	
		0.08 Red	



Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	0.11 Rf	3.4 AU	0.13 Rf	14.6 AU	8.77 %	0.15 Rf	6.7 AU	270.7 AU	6.26 %
2	0.15 Rf	6.8 AU	0.19 Rf	29.5 AU	17.63 %	0.27 Rf	0.4 AU	1038.7 AU	24.01 %
3	0.38 Rf	0.8 AU	0.41 Rf	13.2 AU	7.92 %	0.45 Rf	0.0 AU	302.1 AU	6.98 %
4	0.46 Rf	0.3 AU	0.48 Rf	24.0 AU	14.34 %	0.51 Rf	1.2 AU	491.3 AU	11.36 %
5	0.62 Rf	2.3 AU	0.65 Rf	25.6 AU	15.34 %	0.68 Rf	1.2 AU	524.1 AU	12.11 %
6	0.82 Rf	6.1 AU	0.87 Rf	34.3 AU	20.50 %	0.91 Rf	0.4 AU	1161.9 AU	26.85 %
7	0.95 Rf	0.1 AU	0.98 Rf	25.9 AU	15.50 %	1.00 Rf	10.8 AU	537.9 AU	12.43 %

Fig. - 4 : HPTLC fingerprint and Rf values of *M. elengi* L. (Fruit) in Chloroform extract at 254nm (Absorbance mode)



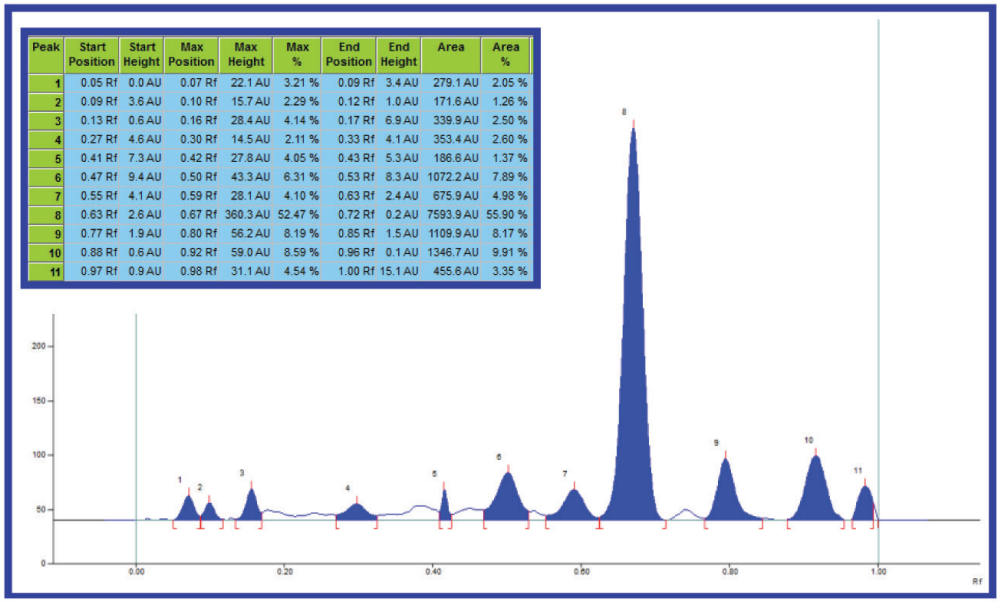
Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	0.13 Rf	3.6 AU	0.16 Rf	14.4 AU	43.47 %	0.18 Rf	10.9 AU	362.1 AU	49.95 %
2	0.18 Rf	10.9 AU	0.20 Rf	18.7 AU	56.53 %	0.22 Rf	3.9 AU	362.9 AU	50.05 %

Fig. - 5 : HPTLC fingerprint and Rf values of *M. elengi* L. (Fruit) in Chloroform extract at 366nm Absorbance mode)

Quality Control Parameters

Analysis of Microbial Load

The total bacterial count and total fungal count were 7 x 10^2 and less than 10 CFU respectively (Table 3). The detection of the microbial load was found below the permissible limits of WHO (1998). At the same time, the bacteria

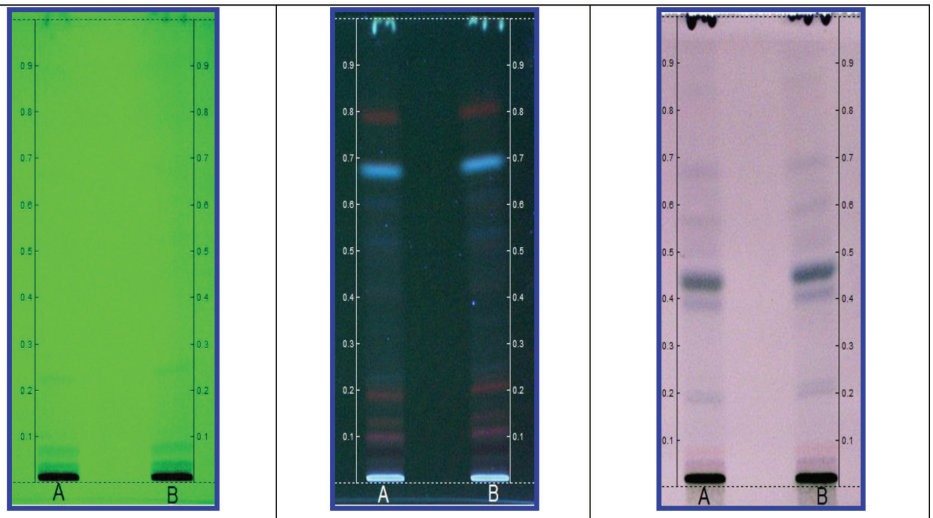


Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	0.05 Rf	0.0 AU	0.07 Rf	22.1 AU	3.21 %	0.09 Rf	3.4 AU	279.1 AU	2.05 %
2	0.09 Rf	3.6 AU	0.10 Rf	15.7 AU	2.29 %	0.12 Rf	1.0 AU	171.6 AU	1.26 %
3	0.13 Rf	0.6 AU	0.16 Rf	28.4 AU	4.14 %	0.17 Rf	6.9 AU	339.9 AU	2.50 %
4	0.27 Rf	4.6 AU	0.30 Rf	14.5 AU	2.11 %	0.33 Rf	4.1 AU	353.4 AU	2.60 %
5	0.41 Rf	7.3 AU	0.42 Rf	27.8 AU	4.05 %	0.43 Rf	5.3 AU	186.6 AU	1.37 %
6	0.47 Rf	9.4 AU	0.50 Rf	43.3 AU	6.31 %	0.53 Rf	8.3 AU	1072.2 AU	7.89 %
7	0.55 Rf	4.1 AU	0.59 Rf	28.1 AU	4.10 %	0.63 Rf	2.4 AU	675.9 AU	4.98 %
8	0.63 Rf	2.6 AU	0.67 Rf	360.3 AU	52.47 %	0.72 Rf	0.2 AU	7593.9 AU	55.90 %
9	0.77 Rf	1.9 AU	0.80 Rf	56.2 AU	8.19 %	0.85 Rf	1.5 AU	1109.9 AU	8.17 %
10	0.88 Rf	0.6 AU	0.92 Rf	59.0 AU	8.59 %	0.96 Rf	0.1 AU	1346.7 AU	9.91 %
11	0.97 Rf	0.9 AU	0.98 Rf	31.1 AU	4.54 %	1.00 Rf	15.1 AU	455.6 AU	3.35 %

Fig. - 6 : HPTLC finger print and Rf values of M. elengi L. (Fruit) in Chloroform extract at 366nm (Fluorescence mode)

Fig. - 7

Thin Layer Chromatography
Alcohol extracts



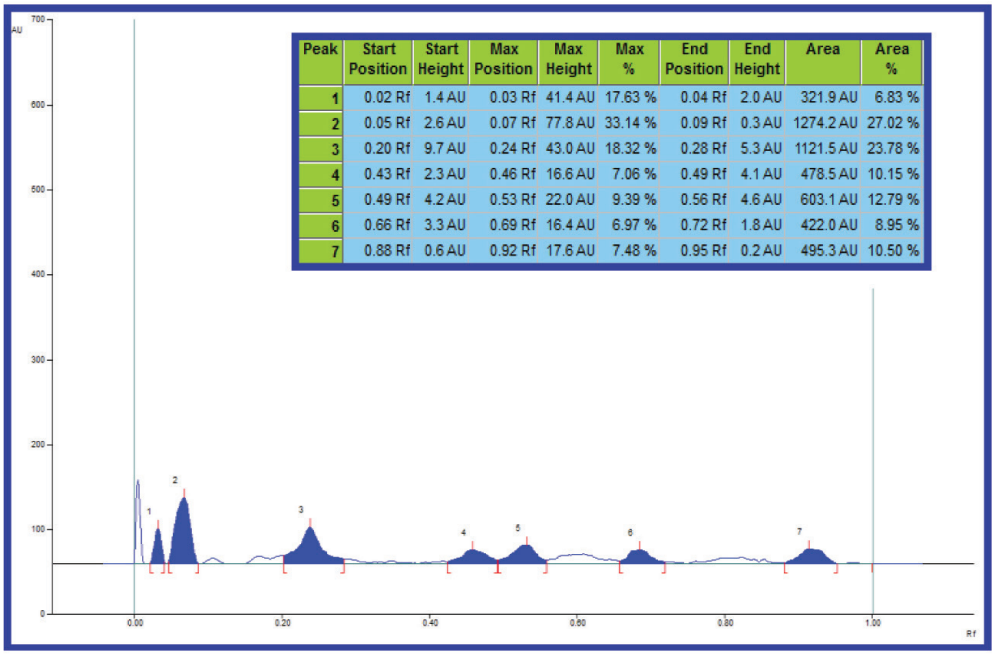
UV – 254 nm	UV – 366 nm	V - S Reagent

Solvent System: Toluene : Ethyl acetate : Formic acid (8.8: 0.5: 0.1) 8 µl
Track 1. Batch - I; Track 2. Batch - II

Enterobacteriaceae, *Salmonella* spp, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas* spp were found to be absent in the plant materials which indicated that the plant is not the carrier of these microorganisms.

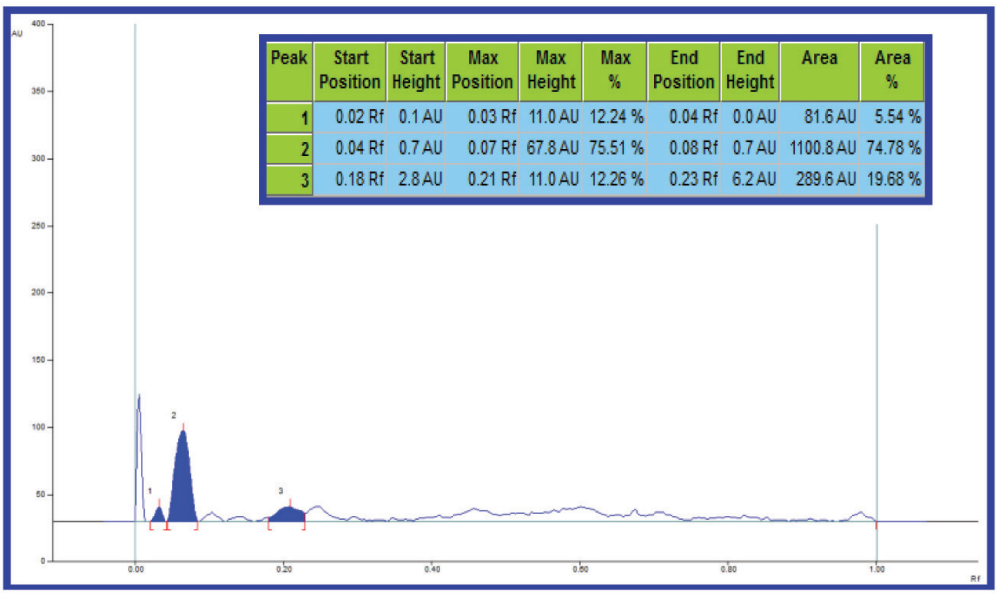
Table - 2. TLC data of the *M. elengi* L. (Fruit) in Alcohol extract

Solvent system	Rf Values		
	UV 254 nm (4 spots)	UV 366 nm (11 spots)	V. S. Reagent (10 spots)
Toluene : Ethyl acetate : Formic acid (8.8 : 1.2 : 0.1)	0.89 Green	0.79 Red	0.95 Grey
	0.67 Green	0.68 Fluorescent blue	0.84 Grey
	0.23 Green	0.61 Blue	0.68 Grey
	0.08 Green	0.52 Blue	0.58 Grey
		0.41 Blue	0.49 Grey
		0.32 Grey	0.45 Dark grey
		0.22 Grey	0.39 Grey
		0.19 Red	0.20 Grey
		0.13 Red	0.19 Grey
		0.10 Pink	0.07 Orange
		0.05 Brown	



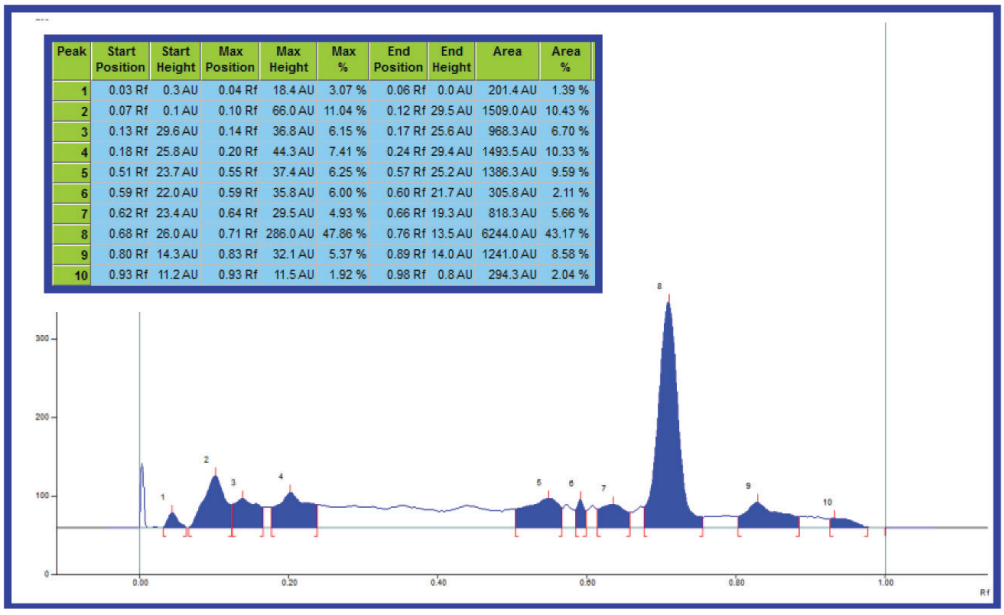
Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	0.02 Rf	1.4 AU	0.03 Rf	41.4 AU	17.63 %	0.04 Rf	2.0 AU	321.9 AU	6.83 %
2	0.05 Rf	2.6 AU	0.07 Rf	77.8 AU	33.14 %	0.09 Rf	0.3 AU	1274.2 AU	27.02 %
3	0.20 Rf	9.7 AU	0.24 Rf	43.0 AU	18.32 %	0.28 Rf	5.3 AU	1121.5 AU	23.78 %
4	0.43 Rf	2.3 AU	0.46 Rf	16.6 AU	7.06 %	0.49 Rf	4.1 AU	478.5 AU	10.15 %
5	0.49 Rf	4.2 AU	0.53 Rf	22.0 AU	9.39 %	0.56 Rf	4.6 AU	603.1 AU	12.79 %
6	0.66 Rf	3.3 AU	0.69 Rf	16.4 AU	6.97 %	0.72 Rf	1.8 AU	422.0 AU	8.95 %
7	0.88 Rf	0.6 AU	0.92 Rf	17.6 AU	7.48 %	0.95 Rf	0.2 AU	495.3 AU	10.50 %

Fig. - 8 : HPTLC fingerprint and Rf values of *M. elengi* L. (Fruit) in Alcohol extract at 254nm (Absorbance mode)



Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	0.02 Rf	0.1 AU	0.03 Rf	11.0 AU	12.24 %	0.04 Rf	0.0 AU	81.6 AU	5.54 %
2	0.04 Rf	0.7 AU	0.07 Rf	67.8 AU	75.51 %	0.08 Rf	0.7 AU	1100.8 AU	74.78 %
3	0.18 Rf	2.8 AU	0.21 Rf	11.0 AU	12.26 %	0.23 Rf	6.2 AU	289.6 AU	19.68 %

Fig. - 9 : HPTLC fingerprint and Rf values of *M. elengi* L. (Fruit) in Alcohol extract at 366nm (Absorbance mode)



Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	0.03 Rf	0.3 AU	0.04 Rf	18.4 AU	3.07 %	0.06 Rf	0.0 AU	201.4 AU	1.39 %
2	0.07 Rf	0.1 AU	0.10 Rf	66.0 AU	11.04 %	0.12 Rf	29.5 AU	1509.0 AU	10.43 %
3	0.13 Rf	29.6 AU	0.14 Rf	36.8 AU	6.15 %	0.17 Rf	25.6 AU	968.3 AU	6.70 %
4	0.18 Rf	25.8 AU	0.20 Rf	44.3 AU	7.41 %	0.24 Rf	29.4 AU	1493.5 AU	10.33 %
5	0.51 Rf	23.7 AU	0.55 Rf	37.4 AU	6.25 %	0.57 Rf	25.2 AU	1386.3 AU	9.59 %
6	0.59 Rf	22.0 AU	0.59 Rf	35.8 AU	6.00 %	0.60 Rf	21.7 AU	305.8 AU	2.11 %
7	0.62 Rf	23.4 AU	0.64 Rf	29.5 AU	4.93 %	0.66 Rf	19.3 AU	818.3 AU	5.66 %
8	0.68 Rf	26.0 AU	0.71 Rf	286.0 AU	47.86 %	0.76 Rf	13.5 AU	6244.0 AU	43.17 %
9	0.80 Rf	14.3 AU	0.83 Rf	32.1 AU	5.37 %	0.89 Rf	14.0 AU	1241.0 AU	8.58 %
10	0.93 Rf	11.2 AU	0.93 Rf	11.5 AU	1.92 %	0.98 Rf	0.8 AU	294.3 AU	2.04 %

Fig. - 10 : HPTLC fingerprint and Rf values of *M. elengi* L. (Fruit) in Alcohol extract at 366nm (Fluorescence mode)

Analysis of Heavy Metal

The heavy metal contents viz. of lead, cadmium, mercury and arsenic were within the permissible limits viz. 10, 0.3, 1 and 3 ppm respectively (Table 4).

Analysis of Aflatoxins

The aflatoxins B_1, B_2, G_1 and G_2 were found below the detecting limit and hence the present study shows non-toxic effect of the plant (Table 5).

Analysis of Pesticide Residues

The various pesticidal residues HCH (all isomers), DDT (all isomers), DDE (all isomers), Endosulphan (all isomers), etc. were tested in the plant but were not detected (Table 6).

Discussion

The microscopical studies reveal the compactly epidermal cells, parenchyma cells with laticiferous cells, T shaped unicellular trichomes and sclereids of

Table – 3. Quality Control Studies on Microbial Load Analysis

S.No.	Parameters Analysed		Results	WHO Limits
1.	**Total Microbial Plate Count**	-	$7x10^2$cfu/gram	10^5cfu/gram
2.	Total Yeast & Mould Count	-	Less than 10 cfu/gram	10^3cfu/gram
3.	Specified Microorganisms	-		
	Escherichia coli	-	Absent	Absent
	Salmonella species	-	Absent	Absent
	Pseudomonas aeruginosa	-	Absent	Absent
	Staphylococcus aureus	-	Absent	Absent

Table – 4. Quality Control Studies on Heavy Metal Analysis

S.No.	Parameter Analysed	Results	Limits
1	Lead	Nil	10 ppm
2	Arsenic	Nil	3 ppm
3	Cadmium	Nil	0.3 ppm
4	Mercury	Nil	1 ppm

Table – 5. Quality Control Studies on Aflatoxins

S.No.	Aflatoxins	Results
1	B_1	Not detected
2	B_2	Not detected
3	G_1	Not detected
4	G_2	Not detected

Table – 6. Quality Control Studies on Pesticide Residue Analysis

S.No.	Pesticide Residues	Results
1	**Organo Chlorine Group**	ND
2	**Organo Phosphorus Group**	ND
3	Acephate	ND
4	Chlordane	ND
5	Dimethoate	ND
6	Endosulphan	ND
7	Endosulfan	ND
8	Endosulfon	ND
9	Ethion	ND
10	Endosufon sulphate	ND
11	Fenthion	ND
12	Lindane	ND
13	Methoxychlor	ND
14	Phorate sulfoxide	ND
15	Phorate sulfone	ND
	ND – Not detected	

various shapes and size, prism type and druses of calcium oxalate crystals are some of the important characters.

The present investigations are also similar to Metalfe and Chalk (1957) in which longitudinal arranged rows of laticiferous sacs generally situated in cortex, phloem, pith; Two armed hairs of somewhat varied types of trichomes; Crystals either solitary, clustered or in the form of crystal sand in nature and distribution are some of the most important characteristic features for most members of the family Sapotaceae. Shivatare, *et al.* (2013) reported the powdered fruits and seeds possess fragments of fibres, sclereids, stone cells, and masses of rubber like bodies, parenchyma cells, spiral and scalariform vessels, in which the microscopic characters are similar to our investigations. In the same plant *M. elengi,* the pharmacognostical and phytochemical studies of stem bark were reported by Kadam, *et al.* (2012), bark and seeds by Gopalkrishnan and Shimpi (2010) and Bharat Gami and Parabia (2010).

The elemental analysis of bark and seeds has been reported by Bharat Gami and Parabia (2010). Calcium is found to be highest as well as some other elements, like potassium, manganese, iron, copper and strontium are present in greater percentage in *M. elengi* seeds.

The HPTLC fingerprinting and quality control parameters are the new findings for these investigations. The HPTLC fingerprinting chromatogram is also helpful

in the identification of various phyto-constituents and quality evaluation of the plant samples.

Conclusion

The pharmacognostic studies, TLC/HPTLC fingerprint analysis and quality control studies on fruits of *M. elengi* have been carried out which could serve as a basis toll for the identification and authentication of the sample in dry and powdered form. These evaluated data may help in laying down the pharmacopoeial standards of the drug.

Acknowledgement

The authors are deeply indebted to the Director General, CCRUM, New Delhi for providing necessary research facilities and encouragement.

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सारांश

मिमुसोप्स एलेंगी एल. फलों पर मैक्रो और माइक्रोस्कोपिकल मूल्यांकन, एच.पी.टी.एल.सी. फिंगरप्रिंटिंग और गुणवत्ता नियंत्रण अध्ययन

***मागेश्वरी एस, रामप्रताप मीणा, मीरा देवी, मुर्गेश्वरन आर, जैकलीन रैज़ा और ज़हीर अहमद एन**

मिमुसोप्स एलेंगी एल. जोकि सैपोटेसी प्रजाति से सम्बन्धित है प्रायद्वीपीय भारत के पश्चिमी घाट का एक मूल वृक्ष है। इस पौधे में कई औषधीय गुण होते हैं जैसे कि स्तंभक, टॉनिक, ज्वरनाशक, शोधक, मूत्रवर्धक, कामोद्दीपक, शुक्रनाशक तथा दीर्घकालीन पेचिश, मधुमेह, जलभीति, बवासीर और गोनॉरिया विरोधी गुण। वर्तमान अध्ययन इस पौधे के उच्च पारंपरिक उपयोग को देखते हुए इसके भेषजकोशीय मानकों के अनुसंधान और विकास के लिए किया गया। आधुनिक तकनीकों के बावजूद औषधीय अध्ययन द्वारा पादप औषधि की पहचान अधिक विश्वसनीय है। वर्तमान अध्ययन *मिमुसोप्स एलेंगी* एल. के फल के लिए मैक्रो और माइक्रोस्कोपिकल मूल्यांकन और भेषकोशीय अध्ययन से संबंधित है। माइक्रोस्कोपिकल अध्ययन एपिडर्मल कोशिकाओं, मेसोकोपिक पैरेनकिमा कोशिकाओं, स्केलेरिड्स, एंडोस्पर्म कोशिकाओं, कोटिलेडोनरी पैरेनकिमा कोशिकाओं, टी आकृति ट्राइकोम और कैल्शियम ऑक्सालेट क्रिस्टल की उपस्थिति को दर्शाता है। एच.पी.टी.एल.सी. फिंगरप्रिंटिंग अध्ययन ने टोल्यूनिः एथिल एसीटेटः फॉर्मिक एसिड सोलवेन्ट सिस्टम और वीएस रीऐजन्ट में उपयोग के माध्यम से क्लोरोफॉर्म और एल्कोहल सत्त पर क्रमशः 11 और 10 स्पोट्स दिखाए। गुणवत्ता नियंत्रण मापदंड जैसे कि माइक्रोबियल लोड और भारी धातुएं उचित सीमा के भीतर पाई गईं और अन्य मापदंड जैसे एफ्लाटॉक्सिन और कीटनाशक अवशेष औषधि के बीजों में नहीं पाए गए। इस सूचना को भविष्य में औषधीय और चिकित्सीय जांच के लिए एक महत्वपूर्ण मापदंड के रूप में और गुणवत्ता मिश्रणों को सुनिश्चित करने के लिए उपयोग किया जा सकता है।

शब्दकुंजीः एच.पी.टी.एल.सी. फिंगरप्रिंटिंग; मैक्रो और माइक्रोस्कोपिकल अध्ययन; *मिमुसोप्स एलेंगी* एल.; गुणवत्ता नियंत्रण

Clinical Study to Validate Analgesic Effect and Safety of Unani Pharmacopoeial Formulations in *Waja' al-Mafāṣil* (Joint Pain) in Eastern India

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Abstract

A clinical study was carried out to scientifically validate the analgesic effect and safety of Unani pharmacopoeial formulations *Ḥabb-i-Sūranjān* and *Rawghan-i-Sūranjān* in the patients of *Waja' al-Mafāṣil* (Joint Pain) at Regional Research Institute of Unani Medicine (RRIUM), Bhadrak (Odisha) during 2013-2014. All the cases (49) registered for the study completed the trial. After 14 days of treatment, the symptoms of the disease, like joint pain, tenderness, swelling and restriction of movements were found decreased by 64.70%, 47.83%, 50% and 50% respectively as compared to the baseline. The variations in the values of liver function tests and kidney function tests before and after the treatment were found within normal limits. The study drugs were found well-tolerated and no adverse reaction was observed during the study. The study findings confirm the safety and efficacy of Unani pharmacopoeial formulations in the treatment of *Waja' al-Mafāṣil* (Joint Pain).

Keywords: Joint Pain, *Ḥabb-i-Sūranjān, Rawghan-i-Sūranjān, Waja' al-Mafāṣil*

Introduction

Arthritis does not refer to a single disease but a term used to describe more than 100 different conditions of which the most common is osteoarthritis (Barbour, *et al.,* 2017). In Unani Medicine, *Waja' al-Mafāṣil* is defined as the pain in the joints of the organs. If the pain is not associated with particular joint and affects joints of hands and legs uniformly, it is called *Waja' al-Mafāṣil*. If it affects some specific joints of the body, then it is named according to the joint involved, i.e. *Waja' al-Warik* (pain in hip joints), *Waja' al-Rukba* (pain of knee joints), *Niqris* (pain in ankle joint and toes), etc. *Waja'-al-Mafāṣil* has been classified according to underlying causes, e.g. *Waja' al-Mafāṣil Sāda, Waja' al-Mafāṣil Damwī, Waja' al-Mafāṣil Balghamī, Waja' al-Mafāṣil Sawdāwī, Waja' al-Mafāṣil Ṣafrāwī* and *Waja' al-Mafāṣil Rīḥī*. The main cause of *Waja'-al-Mafāṣil* is *Sū'-i-Mizāj Ḥārr Multahib* (dyscrasia/immoderate temperament/impaired temperament due to heat), *Sū'-i-Mizāj Bārid* (dyscrasia/immoderate temperament/impaired temperament due to cold) or *Sū'-i-Mizāj Yābis* (dyscrasia/immoderate temperament/impaired temperament due to dryness). This *Sū'-i-Mizāj* is present either in whole body, in *A'ḍā' Ra'īsa* (vital organs) or in specific organ; it is either *Sāda* (without involvement of humour) or *Māddī* (due to abnormal humour/morbid humour); *Mufrad* (simple abnormal temperament) or *Murakkab* (compound abnormal temperament). *Sūranjān* has specific role in the treatment of *Waja' al-Mafāṣil* and considered as drug of choice, therefore, it is recommended to add it in compound drugs for joint pain. *Asārūn* is also an important drug in the management of joint pain.

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Rāzī clarifies that *Riyāḥ* (flatus) has a role in the development of joint pain, so it is advised to add some drugs in the compound formulation to deal with it. Vomiting is also useful in joint pain. Excessive eating, sedentary lifestyle, use of unhealthy diet (junk food) and addiction to narcotics predispose the joint pain and should be avoided. Vomiting, diuresis and exercise may be used to treat joint pain.

According to *Shaikh,* the treatment of joint pain should be started as early as possible, because if it becomes stable then treatment would not be easy. In case of *Sū'-i-Mizāj Sāda* (dyscrasia/immoderate temperament/impaired temperament without involvement of any humour), treatment is easy and can be achieved by only *Ta'dīl-o-Tabdīl-i-Mizāj* (temperamental equilibrium/alteration) and *Tanqiya* of *Ṣafrā'* and *Dam* (elimination of morbid material from the body, i.e. bile and blood), but in case of *Sū'-i-Mizāj Māddī* (impaired temperament due to abnormal humour/morbid humour), treatment is not easy. *Istifrāgh* (evacuation, expulsion of humours from the body) needs to be done to treat the disease (Kabiruddin, 1916; Kabiruddin, 1935; Khan, 2003; Khan, 1987; Majusi, 2010).

Materials and Methods

The present study was conducted at Regional Research Institute of Unani Medicine (RRIUM), Bhadrak (Odisha) on 49 patients of *Waja' al-Mafāṣil* (joint pain) selected from GOPD of the institute during 2013-2014. The patients of either sex in the age group of 18 to 65 years were included in the study. Inclusion criteria were joint pain (single/multiple joints) with or without tenderness, swelling or restriction of movement. Patients below 18 years and above 65 years of age, patients with other long-term diseases like diabetes mellitus, hypertension, etc., pregnant women and lactating mothers, known cases of hepatic, renal or cardiac ailments and persons with history of addiction were excluded from the study.

The clinical study protocol was approved by the Institutional Ethics Committee (IEC) of the institute on March 15, 2013 and the trial was registered with CTRI bearing registration number CTRI/2013/12/004197. Patients were enrolled for the study after obtaining written informed consent from them and they were subjected to pathological and bio-chemical investigations. Pathological investigations included haemogram [haemoglobin (Hb), erythrocyte sedimentation rate (ESR), total leukocyte count (TLC) and differential leukocyte count (DLC: neutrophils, eosinophils, basophils, lymphocytes, monocytes)], urine examination (routine and microscopic) and blood sugar (random). Bio-chemical investigations included 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 and blood urea.

The parameters for assessment of efficacy of the formulations were joint pain, tenderness, joint swelling and restriction of movement. These parameters were graded accordingly. In case of joint pain graded as: Barely perceptible = 1; Mild - can carry out daily activities with some trouble = 2; Moderate - cannot carry out daily activities easily = 3; and Severe - bed ridden = 4.

In case of tenderness as on palpation - patient says it is tender when touched = 1; on palpation, patient says it is tender and winces = 2; on palpation, patient says it is tender, winces and pulls back = 3; and patient does not allow palpation = 4.

In case of joint swelling as: No swelling/effusion = 0; Barely perceptible = 1; Mild = 2; and Moderate = 3.

In case of restriction of movement: Painful movement = 1; Partially restricted movement = 2; Partial movement, when the joint is moved by the examiner = 3; and Complete restricted movement = 4.

The clinical follow-up of all the cases was carried out on 7th and 14th day of the treatment. The pathological and bio-chemical investigations were conducted at the baseline and end of the study. The safety of trial drugs was evaluated by biochemical investigations and clinically by monitoring the 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 *Waja' al-Mafāṣil* (joint pain). The duration of treatment was 14 days. No concomitant treatment was allowed during the study. Baseline and follow-up values of bio-chemical and pathological investigations were statistically analyzed using Student's paired 't' test.

Study Drugs, Dosage Schedule and Mode of Administration

The following Unani pharmacopoeial formulations used in the study were obtained from GMP certified pharmacy of Central Research Institute of Unani Medicine (CRIUM), Hyderabad.

1. *Ḥabb-i-Sūranjān* was given in the dose of 2 pills orally thrice daily with water.
2. *Rawghan-i-Sūranjān* (oil) was advised to apply locally twice daily.

Composition of Study Drugs

Ḥabb-i-Sūranjān contained five ingredients (Table 1) and *Rawghan-i-Sūranjān* contained four ingredients (Table 2).

Table 1: Composition of *Ḥabb-i-Sūranjān*

S.No.	Unani Name	Scientific Name	Quantity
1	*Sūranjān*	*Colchicum luteum* Baker	1 part
2	*Post-i-Halela Zard*	*Terminalia chebula* Retz.	1 part
3	*Shaḥm-i-Ḥanzal*	*Citrullus colocynthis* (L.) Schrad.	1 part
4	*Muqil*	*Commiphora mukul* Hook. ex Stocks	1 part
5	*Turbud*	*Ipomoea turpethum* R. Br.	1 part

(Anonymous, 2006)

Table 2: Composition of *Rawghan-i-Sūranjān*

S.No.	Unani Name	Scientific Name	Quantity
1	*Sūranjān*	*Colchicum luteum* Baker	50 gm
2	*Āb-i-Karafs*	*Apium graveolens* L.	50 gm
3	*Chirā'ita*	*Swertia chirata* Ham.	25 gm
4	*Rowghan-i-Zaytūn*	*Olea europaea* L.	150 gm

(Anonymous, 2006)

Results

In this study, 51% (25/49) patients were male while 49% (24/49) patients were female. Besides, 42.86% (21/49) patients were of *Balghamī* (phlegmatic), 28.57% (14/49) patients of *Damwī* (sanguine), 22.45% (11/49) patients of *Ṣafrāwī* (bilious) and 6.12% (3/49) patients of *Sawdāwī* (melancholic) *Mizāj*. Out of 49 patients included in the trial, the highest incidence (30.61%) was observed in the age group of 31-40 years while the least incidence of 8.16% each was seen in the age group of 21-30 years and 61-65 years. Similarly, 26.53% incidence was seen in the age group of 41-50 years and 50-60 years respectively.

The clinical parameters for assessment of efficacy were calculated in all the patients before and after the treatment. The mean value of these parameters for joint pain, tenderness, swelling and restriction of movement were 5.1, 2.3, 2.0 and 2.2 respectively before the treatment. At the end of study, these scores were 1.8, 1.2, 1.0 and 1.1 respectively. Out of four parameters studied, improvement in case of joint pain was eminent; the pain was decreased by 64.70% indicating that both drugs in combination have significant analgesic effect. Tenderness was decreased by 47.83% and swelling and restrictions of movement were decreased by 50% each. The overall improvement is very good (Table 5; Figure 1).

Ḥabb-i-Sūranjān and *Rawghan-i-Sūranjān* exhibited significant improvement in symptoms and signs of *Waja' al-Mafāṣil*. Out of 49 patients, 04 (8%) patients showed more than 90% relief in overall symptoms and signs, 24 (49%) patients

showed 60-89% relief in the overall symptoms and signs, 19 (39%) showed 30-59% relief in the overall symptoms and signs and 02 (4%) patients showed less than 30% relief in overall symptoms and signs of *Waja'-al-Mafāṣil* (Table 6; Figure 2).

The mean values of haematological and bio-chemical parameters at the baseline and after the treatment are given in Table 3 and Table 4 respectively. The values of safety parameters [Haemoglobin ESR, TLC, DLC, LFT and KFTs] remained within normal limits after the treatment. There was no significant change in serum level of SGOT, SGPT, ALP, bilirubin, urea and creatinine after treatment as compared to the baseline. Likewise, no significant change in value of haemoglobin, ESR, TLC and DLC was seen after the treatment as compared to the baseline. The study drugs were found well-tolerated and no unbearable adverse effects were observed clinically during or after the treatment.

The results of the present study are in agreement with several studies on Unani treatment for joint pain (Nayab, 2007; Arshid, 2013; Sheeraz, 2013). The results are also supported by animal study on *Maūjūn Sūranjān*, a Unani pharmacopoeial formulation (Surender, 2011).

Table 3: Mean Values of Pathological Investigations at Baseline and after Treatment

Pathological Investigations			Mean ± SD	P Value
Haemoglobin (gm%)		BT	12.45±0.18	P > 0.05
		AT	12.38±0.17	
ESR (mm/hr)	1st Hour	BT	27.31±3.24	P > 0.05
		AT	26.37±3.16	
	2nd Hour	BT	51.10±4.43	P > 0.05
		AT	48.69±4.21	
Total Leucocytes Count (cmm)	BT		7046.94±234.19	P > 0.05
	AT		6544.90±149.01	
DLC	Neutrophils	BT	61.41±0.81	P > 0.05
		AT	61.00±0.71	
	Lymphocytes	BT	28.71±0.76	P > 0.05
		AT	28.73±0.63	
	Eosinophils	BT	9.41±0.43	P > 0.05
		AT	9.67±0.52	
	Monocytes	BT	0.47±0.08	P > 0.05
		AT	0.59±0.10	

BT= Before Treatment; AT= After Treatment

Table 4: Mean Values of Biochemical Investigations at Baseline and After Treatment

Biochemical Investigations		Mean ± SD	P Value
SGOT (Units/ml)	BT	31.61±1.46	P > 0.05
	AT	32.86±1.96	
SGPT (Units/ml)	BT	28.50±1.25	P > 0.05
	AT	27.61±2.12	
ALP (K&A Units/100ml)	BT	112.15±4.96	P > 0.05
	AT	112.03±5.09	
Serum Bilirubin (mg %)	BT	0.59±0.03	P > 0.05
	AT	0.58±0.04	
Serum Creatinine (mg %)	BT	1.34±0.04	P > 0.05
	AT	1.38±0.06	
Serum Urea (mg %)	BT	27.87±1.56	P > 0.05
	AT	27.88±1.76	

BT= Before Treatment; AT= After Treatment

Table 5: Mean Values of Clinical Parameters at Baseline and After Treatment

S.No.	Signs and Symptoms	Baseline	After Treatment	% Decrease
1	Joint Pain	5.1	1.8	64.70 %
2	Tenderness	2.3	1.2	47.83 %
3	Joint Swelling	2.0	1.0	50 %
4	Restriction of Movement	2.2	1.1	50 %

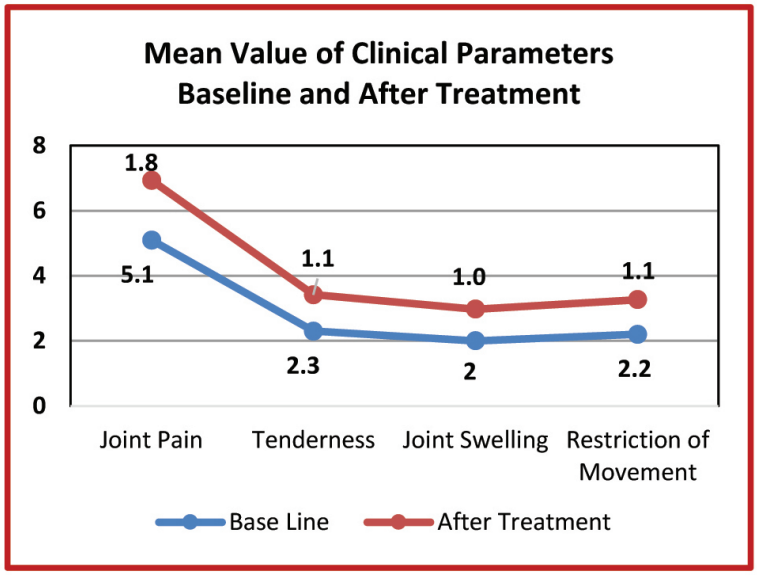

Fig. 1: Mean values of clinical parameters at baseline and after treatment

Table 6: Therapeutic Response

	Not Relieved (0 – 29%)	Partially Relieved (30 – 59%)	Relieved (60 – 89%)	Cured (90 – 100%)
No. of Patients	02	19	24	04
Percentage (%)	4 %	39 %	49 %	8 %

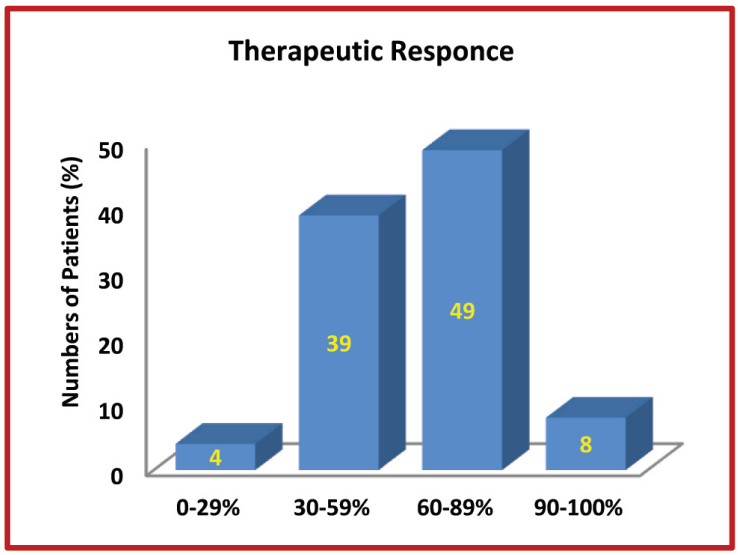

Fig. 2: Therapeutic response

Discussion

The test drugs *Ḥabb-i-Sūranjān* and *Rawghan-i-Sūranjān* have *Sūranjān* (*Colchicum luteum* Baker) as the chief ingredient which is a drug of choice for management of joint pain as mentioned in Unani literature. The improvement in clinical parameters might be due to correction of *Mizāj* in case of *Sū'-i-Mizāj Sāda* (impaired temperament without any humour/substance) or it may be due to correction and evacuation of morbid substance/humour in case of *Sū'-i-Mizāj Māddī* (abnormal substantial temperament). *Sūranjān* exhibits *Musakkin* (neutralizing), *Muḥallil* (resolvent) and *Mufattiḥ-i-Sudad* (deobstruent) activities. *Post-i-Halela Zard* has *Mushil-i-Ṣafrā'* (cholagogue) activity; *Shaḥm-i-Ḥanzal* acts as *Mushil-i-Balgham* (phlegmagogue) and *Mushil-i-Sawdā'* (melanogogue). *Muqil* has *Munḍij* (concoctive) and *Mushil-i-Balgham* (phlegmagogue) property in addition to *Muḥallil* (resolvent) action. *Turbud* works as *Mushil-i-Balgham* (phlegmagogue). The combination of the above ingredients makes *Ḥabb-i-Sūranjān* an all-inclusive and effective drug in accordance with *Uṣūl-i-'Ilāj* (line of management) for *Waja' al-Mafāṣil* (joint pain).

In the modern system of medicine, opioids are generally used for severe pain. For moderate to severe pain, nonsteroidal anti-inflammatory drugs (NSAIDs)

or cyclo-oxygenase-2 (COX-2) inhibitors are commonly used. For management of mild pain, acetaminophen is generally used (Stovitz and Johnson 2003). Several groups (American College of Rheumatology, American Pain Society and American Geriatrics Society) recommend increasing or changing medications to gain adequate control of symptoms in case of chronic pain (Anonymous, 2000; Anonymous, 2002). Acetaminophen at higher doses may produce nephropathy in the form of papillary necrosis and interstitial nephritis as well as an increased risk of gastrointestinal bleeding (Fauci, *et al.,* 2008), acetaminophen is contraindicated in patient with active hepatitis. NSAIDs and COX-2–selective inhibitors have gastrointestinal adverse events. The gastrointestinal side effects of opioids are also well-known. Often, opioids may only provide a reduction in pain of 15% - 20% (Noble, *et al.*, 2000). Topical medications are very useful but potential side effects including burning, stinging and erythema may be present (Whitefield, *et al.,* 2002).

In the light of above observations, it is apparent that all the medicines used for pain management in the modern system of medicine exhibit side effects in varying degrees. In contrast, study drugs i.e. *Ḥabb-i-Sūranjān* and *Rawghan-i-Sūranjān* have shown a significant analgesic effect without any known side effect. The study findings confirm the safety of *Ḥabb-i-Sūranjān* and *Rawghan-i-Sūranjān* in the treatment of *Waja' al-Mafāṣil* (joint pain).

Conclusion

It is clear that *Ḥabb-i-Sūranjān* and *Rawghan-i-Sūranjān* produce significant improvement on various symptoms and signs including joint pain, tenderness, swelling and restriction of movement. Besides, the therapy was found to be safe and well-tolerated as the safety parameters (Hb%, ESR, TLC, DLC, LFT and KFT) remained within the normal limits after the treatment. No intolerable side effects were seen and overall compliance to the trial drugs was very good. Thus, it may be concluded that *Ḥabb-i-Sūranjān* and *Rawghan-i-Sūranjān* in combination are effective and safe regimen in the symptomatic management of *Waja' al-Mafāṣil* (joint pain).

Acknowledgement

Authors sincerely acknowledge the financial support and the facilities provided by the Director General, Central Council for Research in Unani Medicine (CCRUM), New Delhi to carry out this research work. Authors also wish to express their gratitude to all the staff of the Regional Research Institute of Unani Medicine (RRIUM), Bhadrak for their valuable help and co-operation during the course of study.

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सारांश

पूर्वी भारत में वजा-उल-मफ़ासिल (जोड़ों का दर्द) में यूनानी भेषजकोशीय मिश्रणों के एनाल्जेसिक प्रभाव और सुरक्षा का वैधीकरण करने के लिए नैदानिक अध्ययन

***मोहम्मद ज़ाकिर, अख़्तर हुसैन जमाली, क़मरूद्दीन, चन्द्रपाल, किशोर कुमार, नरेन्द्र सिंह, हकीमुद्दीन ख़ान और मुनव्वर हुसैन काज़मी**

यह नैदानिक अध्ययन क्षेत्रीय यूनानी चिकित्सा अनुसंधान संस्थान (क्षे.यू.चि.अ.सं.), भद्रक (ओडिशा) में 2013–2014 के दौरान वजा–उल–मफ़ासिल (जोड़ों का दर्द) के रोगियों में यूनानी भेषजकोशीय मिश्रण *हब्ब–ए–सुरंजान* और *रोग़न–ए–सुरंजान* के एनाल्जेसिक प्रभाव और सुरक्षा का वैज्ञानिक वैधीकरण करने के लिए किया गया। अध्ययन के लिए पंजीकृत सभी रोगियों (49) ने परीक्षण पूरा किया। आधार–रेखा की तुलना में उपचार के 14 दिनों के बाद रोग के लक्षणों जैसे जोड़ों के दर्द, टेंडरनेस, गतिविधि में बाधा और सूजन में क्रमशः 64.70%, 47.83%, 50% और 50% की कमी पाई गई। उपचार से पहले और बाद में लीवर फंक्शन टेस्ट और किडनी फंक्शन टेस्ट के परिणामों में भिन्नता सामान्य सीमा के भीतर पाई गई। अध्ययन औषधियों को सहनीय पाया गया और अध्ययन के दौरान कोई प्रतिकूल प्रतिक्रिया नहीं देखी गई। अध्ययन के निष्कर्ष वजा–उल–मफ़ासिल (जोड़ों का दर्द) के उपचार में यूनानी भेषजकोशीय मिश्रणों की सुरक्षा और प्रभावकारिता की पुष्टि करते हैं।

शब्दकुंजी: जोड़ों का दर्द, *हब्ब–ए–सुरंजान, रोग़न–ए–सुरंजान, वजा–उल–मफ़ासिल*

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