ISSN: 0974-1291

HIPPOCRATIC JOURNAL OF UNANI MEDICINE

Volume 15 • Number 2

April–June 2020

CENTRAL COUNCIL FOR RESEARCH IN UNANI MEDICINE

HIPPOCRATIC JOURNAL OF UNANI MEDICINE

Volume 15, Number 2, April - June 2020

Hippocratic J. Unani Med. 15(2): 1- 78, 2020

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

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

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 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

According to the World Health Organization, majority of the world population relies upon traditional remedies (mainly medicinal plants/herbs) for health care. Unani Medicine is one of the oldest systems of traditional medicine based on a strong foundation of principles and philosophies of medicine which is progressive and scientific in nature. This system based on its theories, philosophies of nature (*Ṭabī'at*) and temperament (*Mizāj*) and practices of medicine provides a holistic approach in promotion of health as well as prevention and management of diseases.

Immunity (*Quwwat-i-Mudāfa'at*) is a defence system within the body, assisted by natural healing power/ medicatrix naturae (*Quwwat Muddabira-i-Badan*), to protect an individual from invading pathogens, etc. In other words, it is the ability of the body to neutralize and eliminate the pathogenic micro-organisms and their toxic products, thus providing protection to the individual. In India, in the wake of COVID-19 pandemic, AYUSH systems of medicine have been roped in to boost immunity for possible protection against the disease. As the apex government organization engaged in research and development in Unani Medicine, we are creating awareness about preventive and prophylactic measures to boost immunity. We hope that the medical fraternity succeed in finding treatment of the disease and protecting the humans from this pandemic. We take this opportunity to call on the scientists and researchers to submit papers on different aspects of epidemic/pandemic diseases especially COVID-19 for publication in upcoming issues of this journal.

This issue of HJUM covers seven review and research papers. The first paper reviews therapeutic approach and management of *Qūbā* in the perspective of Unani Medicine. In the second paper, *Luk* (*Laccifer lacca*) has been discussed as a potent Unani drug for obesity and dyslipidemia. The third paper is based on the historical ethnopharmacological review of *Samm al-Fār* (arsenic trioxide), a Unani mineral drug. Authors in the fourth paper have presented etiopathogenesis of *Mālankhūliyā Marāqī* (a syndrome of depression and anxiety due to gastro-intestinal pathology). The fifth paper presents importance of *Quwwat Mudabbira-i-Badan* (medicatrix naturae) in the management of diseases. While the sixth paper is based on a preclinical study on prophylactic and curative potential of *Qurṣ-i-Ghāfis* against carbon tetrachloride induced hepatic injury in rats, the seventh and last paper presents outcome of a clinical study on efficacy and safety of Unani formulation *Ma'jūn Nisyān* in *Nisyān* (amnesia).

We hope that the papers would be helpful in furtherance of the cause of research and development in Unani Medicine. We sincerely acknowledge the contributions of authors and reviewers in bringing out this publication.

Prof. Asim Ali Khan
Editor-in-Chief

Contents

Therapeutic Approach and Management of *Qūbā* in the Perspective of Unani Medicine

*[1]Aaliya,
[2]Mohammad Nawab,
[3]Sana Ayyub
and
[4]M.H. Kazmi

[1]Postgraduate Scholar, Department of Moalajat, National Research Institute of Unani Medicine for Skin Disorders, Hyderabad

[2]Reader, Department of Moalajat, National Research Institute of Unani Medicine for Skin Disorders, Hyderabad

[3]Postgraduate Scholar, Department of Moalajat, National Research Institute of Unani Medicine for Skin Disorders, Hyderabad

[4]Prof. and Director Incharge, National Research Institute of Unani Medicine for Skin Disorders, Hyderabad

Abstract

Unani System of Medicine offers effective treatment for skin diseases. *Qūbā* (dermatophytosis) has been treated successfully since ancient time through herbo-mineral formulations. *Qūbā* is a superficial fungal infection of the skin. 20-25% individuals suffer from this dermatological problem worldwide. Intense itching is the main symptom which disrupts quality of life, causes sleeplessness and anxiety and hampers daily routine works. In Unani classical literature, treatment of *Qūbā* based on practical experiences is documented. Through this review paper, an attempt has been made to describe historical background, etiopathogenesis, diagnosis, therapeutic approach and management of *Qūbā*. The information available in the literature may help to develop a better understanding regarding the treatment of this stubborn disease. In Unani System of Medicine, there are a number of single and compound drugs which are recommended for its treatment. Therapeutic approach for its treatment also differs from allopathic system of medicine. Development of therapeutics for skin disorders is the potential area of research in Unani System of Medicine.

Keywords: Dermatophytosis, *Qūbā,* Unani

Introduction

Unani System of Medicine offers treatment for various health disorders. Unani pharmacopoeia contains a number of single drugs as well as compound formulations for therapeutic purpose of skin diseases and other disorders. Unani classical literature also describes various prescriptions and formulations effective in the treatment of *Qūbā*. *Qūbā* is one of the medical conditions known since ancient time and treated effectively in Unani System of Medicine through various modes of therapies such as *'Ilāj bi'l Ghidhā'* (dieto-therapy), *'Ilāj bi'l Dawā'* (pharmacotherapy) and *'Ilāj bi'l Tadbīr* (regimenal therapy).

Qūbā is defined as a superficial infection of keratinized skin. This infection invades hair, nails and skin. It is the most commonly occurring disease in India. As per a WHO estimate, 20-25% of world population suffer from this disease. This infection is designated particular name as per its site of infection like Tinea capitis (head), Tinea barbae (beard and moustache), Tinea corporis (whole body), Tinea cruris (groin), Tinea pedis (foot), Tinea mannum (hand), Tinea unguium (nails) and Tinea faciei (face). In India, Tinea corporis is reported highly prevalent. In this medical condition, typical lesions manifest on the trunk that are usually annular and circular in shape with erythematous border. Papules, vesicles and scales may be present in the lesion; margins of the lesions are usually raised and their central parts remain clear. Itching and

*Author for Correspondence; E-mail: aaliya.ansari974@gmail.com

sometimes oozing with yellowish crust may also be present. These symptoms are very troublesome for many patients. This disease has impact on the quality of life, sleep, personality, mood and behavior of the patients (Griffiths *et al.,* 2016; Siddappa *et al.,* 2016; Sehgal, 2011; Bhatia and Sharma 2014; Fitzpatrick *et al.* 2001).

Qūbā is a curable fungal disease. There are antifungal medicines available in the market that are claimed to be effective in this medical condition. But there are certain limitations such as recurrence of the disease, long term therapy, severe side effects, etc. Unani Medicine also offer its complete cure. The therapeutic approach in Unani System of Medicine for treatment is quite different from allopathic system of medicine. Unani System of Medicine adopts holistic approach which considerers mind, body and soul together to treat any medical condition. There are a number of classical prescriptions and pharmacopoeial formulations that are indicated for its therapeutic purposes. These formulations are documented as therapeutics for this medical condition after a long time of practice. In recent past, scientific studies had been conducted which demonstrated effectiveness of these formulations. Taking leads from these studies, a newer formulation having a better efficacy may be developed in future.

Historical background

Qūbā (dermatophytosis) is known to mankind since time memorial, but the first documented description of this disease is attributed to Aulus Cornelium Celsus, the Roman encyclopaedist, in the treatise De Re Medicina, written around 30 A.D. (Ali *et al.,* 2016). It was the Unani physician Jalinus (Galen 129-200 A.D.), who classified it into acute and chronic types (Tabari, 1997). Ibn Rabban Tabari (810-895 A.D.), the author of Firdaus ul Hikmat, further classified *Qūbā* into 3 types on the basis of humoral theory viz., *Qūbā Damwī* where *Fasād* and *Ruṭūbat-i-Fāsidā* are the causative factors, *Qūbā Ruṭūbī* which is caused by *Fāsid Ruṭūbat* and *'Ufūnat* (infection) and *Qūbā Sawdāwī* due to *Khilṭ Sawdā'* (Tabari, 1997). Muhammad ibn Zakariyya Razi (850-923 A.D.), the legend of Unani System of Medicine, provided another classification of *Qūbā* according to its morphology i.e. *Qūbā Raṭb* and *Qūbā Yābis*. Hasan Al-Qumri, Ali Ibn Abbas Majusi, Ibn Sina, Ahmad Al-Tabari, Ismail Jurjani, Akbar Arzani and Daud Antaki are the Unani physicians who contributed in the treatment of this disease. They added various Unani formulations as therapeutics as per causative factors to successfully treat this ailment (Ali *et al.,* 2016; Arzani, YNM; Ibn Sina, 1998; Tabari, 1997; Qumri, 2008; Majusi, 2010).

Etiopathogenesis

The fundamentals of Unani System of Medicine are based on humoral theory. Any change either in quality or in quantity of any of the four humours resulting

in the derangement of homeostasis of the body leads to the development of *Qūbā*. The great physician Ismail Jurjani hypothesized that the humour causing *Qūbā* is defined as *Khilṭ Bad* (morbid humour). He further divided this type of humour into two types *Khilṭ Tez* or *Raqīq* and *Khilṭ Ghalīz* or *Sawdāwī*. Moreover, he explained a faculty *Quwwat Ṭabī'iyya* which prevents vital organs to get diseased due to morbid humour by changing the direction of morbid humours towards the skin surface resulting in *Qūbā* (Jurjani, 2010). There is another philosophy explaining its etiopathogenesis where black bile (*Khilṭ Sawdāwī*) is the main causative factor of this problem. When black bile (*Khilṭ Sawdāwī*) is getting higher in proportion in the blood due to conversion of blood into black bile, it leads to the development of *Qūbā*. The viscid and thick black bile mixed with *Balgham Māliḥ* also causes this problem. Nowadays, *Qūbā* is a known infective disorder, the causative agent is a group of fungi known as dermatophytes belonging to *Microsporum, Trichophyton, Epidermophyton* (Griffiths *et al.,* 2016; Qumri, 2008; Majusi, 2010; Jurjani, 2010; Tabari, 2010; Ibn Hubal, 2007; Arora and Arora 2008; Pasricha and Gupta, 2006).

Classification

Qūbā has been classified depending on causative substances, clinical features, extension of the disease and disease pattern.

Classification I: This classification was given by *Muhammad ibn Zakariyya Razi* on the basis of humour causing this problem:

a. ***Qūbā Raṭb* (*Damwī*):** It manifests as reddish in color and some fluid ooze out on itching. This type is associated with blood (*Dam*) converted into *Sawdā',* and it is easily cured by treatment.

b. ***Qūbā Yābis* (*Sawdāwī*):** It manifests as whitish in color. This type is associated with saline phlegm (*Balgham Māliḥ*) which is burnt to be converted into *Sawdā'* (Razi, 1991).

Classification II: The great scholar Ibn Sina classified *Qūbā* into following 8 types according to causative factors, disease pattern and appearance of the disease (Ibn Sina, 1998):

a. ***Damwī* (*Raṭb*):** Some oozing on itching. It is easily curable.

b. ***Sawdāwī* (*Yābis*):** Due to *Sawdā'*, which is formed by the *Istiḥāla* (metabolism) of *Balgham Shor* and the *Iḥtirāq* (combustion) of *Balgham Māliḥ* (saline phlegm).

c. ***Mutaqashshir:*** This type resembles as *Baraṣ Aswad,* due to extreme dryness leading to scaling.

d. ***Ghayr Mutaqashshir***: It does not scale.

e. ***Sā'ī Khabīth***: This type is spreading in nature and not easily curable.

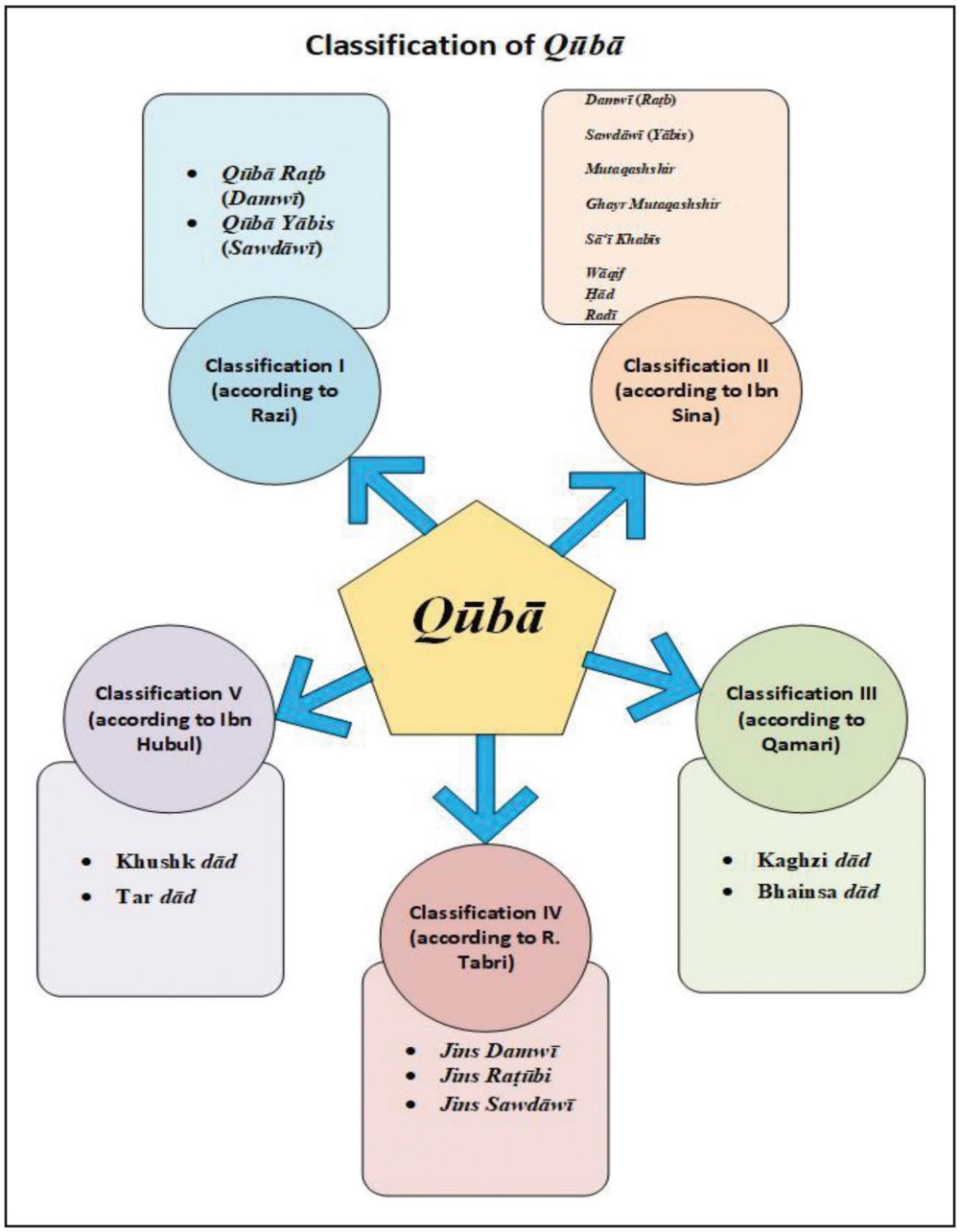
f. ***Wāqif***: This type is always localized.

g. ***Ḥād***: It is an acute in condition with short duration and easily curable.

h. ***Radī***: It has poor prognosis.

Classification III: The famous Unani classical book Ghina Muna describes *Qūbā* into 2 types on the basis of extension of the disease:

a. ***Kāghzī Dād***: Lesions are superficial.



b. ***Bhainsa Dād:*** Infection are invaded up to the deepest layer of the skin (up to muscle) (Qumri, 2008).

Classification IV: In the famous book *Al-Muʿālajāt al-Buqrāṭiya* written by Unani physician Ibn Rabban Tabari, *Qūbā* has been classified into three forms.

a. ***Jins Damwī:*** It appears due to *Fasād al-Dam* (abnormality in blood) and *Ruṭūbat Fāsida* (morbid fluid).

b. ***Jins Ruṭūbi*:** It occurs by the *'Ufūnat* (infection), heat and *Fāsid Ruṭūbat*

c. ***Jins Sawdāwī*:** It is produced by the *Khilṭ* which burnt and converted into *Sawdā'*.

Classification V: In *Kitāb al-Mukhtārāt fi'l-Ṭibb, Qūbā* has been classified into the following 2 types:

a. ***Khushk Dād:*** the causative agent is melancholic humour.

b. ***Tar Dād:*** It is produced when melancholic humour is mixed with blood which is red in colour (Ibn Hubal, 2007).

Clinical features

Qūbā is a superficial infection of the skin. The number of lesions may vary from one to many. The shape of the lesion is oval, circular or annular or irregular. Borders are erythematous and raised. The lesions may have papules, vesicles and scales. Central part of the lesions remains clear. The lesion is hypopigmented initially. Later on, it changes to hyperpigmented lesion. Itching, burning, pricking sensation and oozing are the chief complaints in *Qūbā* (Griffiths *et al.,* 2016; Siddappa *et al.,* 2016; Sehgal, 2011; Goldsmith *et al.,* 2012; James *et al.,* 2016; Kasper *et al.,* 2015; Munjal *et al.,* 2015; Weatherall *et al.,* 1996; Papadakis *et al.,* 2019; Mathew and Parveen, 2018).

Diagnosis

Qūbā is diagnosed clinically on the basis of the following clinical features:

a. Intense itching, burning and pricking sensation and sometimes oozing

b. Lesion is either hypopigmented or hyperpigmented

c. Shape of the lesion may be oval, circular or annular or irregular

d. Peripheral borders or margins are raised and erythematous

e. Papules, vesicles and scales may be present on the lesions

A clinically diagnosed patient is further confirmed by microscopic examination of skin scrapping of the lesion by KOH mount examination. This is further

confirmed by culture of skin scrapped from the lesion. There are several techniques to diagnose *Qūbā* such as polymerase chain reaction (PCR), wood's light, optical coherence tomography and confocal laser scan microscopy (Griffiths *et al.,* 2016; Bhatia and Sharma, 2014; Goldsmith *et al.,* 2012; James *et al.,* 2016; Grover and Ananta, 2012).

Therapeutic approach

Unani System of Medicine adopts holistic approach in the treatment of *Qūbā*. The causative factors have been identified. It is a humoral disorder and derangement in *Khilṭ Sawdā'* (melancholic humour) is main cause of *Qūbā*. The first recommended step is the removal of excessive *Sawdā'* from the body which is called *Tanqiya-i-Badan*. There are three steps for complete removal of excessive quantity of *Khilṭ Sawdā'* from the body: *Munḍij* therapy, *Mushil* therapy and *Tabrīd* therapy. The great scholar Ibn Sina recommended *Ta'līq al-'Alaq* (leeching) - A method of evacuation of bad humours from the body with the help of leeches – is the first step for treatment of *Qūbā* before application of any topical medicine. Razi recommended *Ḥammām* (bathing), *Faṣd* (venesection) and *Ḥijāmah bi'l-Sharṭ* (wet cupping) as per the type of *Qūbā*.

Management of *Qūbā*

Management of *Qūbā* differs according to disease severity, chronicity, involvement of humour and extension of the disease.

Qūbā Damwī: In this type of *Qūbā*, *Faṣd* (venesection) is the best option for its complete cure. *Faṣd* is done at nearest site of the lesion. Then *Ghassāl Adwia* (irrigator drugs) are applied in the form of *Ṭilā'* (liniment).

Prescription of *Ṭilā'*: The following four prescriptions are recommended to apply topically.

Prescription 1: *Kharpaza* (*Cucumis melo* L.), *Ushna* (*Usnea longissimia* Asch.), *Ārd Bāqlā* (*Vicia faba* L.) and *Ārd Nakhūd* (*Cicer arietinum* L.) in the form of paste is applied over the affected area.

Prescription 2: *Mazu* (*Quercus infectoria* Oliv.) and vinegar

Prescription 3: *Ṣamgh 'Arabī* (*Acacia arabica* Willd.), *Ṣamgh Fārsī, Ushaq* (*Dorema ammoniacum* D. Don.), vinegar, make a paste and apply over the affected area.

Prescription 4. *Rawghan-i-Gandum* (oil of *Triticum sativum* Lam.) (Tabari, 1997; Jurjani, 2010; Anonymous, 2006)

***Qūbā Ruṭūbi*:** Elimination of morbid humour is recommended as the first step of its therapy through *Ishāl* (purgative). *Maṭbūkh Aftīmūn* and *Ayārij Fīqra* are the best formulations for elimination of morbid humour.

Drugs for topical application: The recommended dosage form is *Ṭilā'*. There are several prescriptions for *Ṭilā'*.

Prescription 1: *Iqlīmīyā Dhahabī* and *Hartāl* (Arsenic) should be ground in *Gulnār* (*Punica granatum* L.) and *Gul Surkh* (*Rosa damascena* Mill.) mixed into vinegar.

Prescription 2: Ispand (*Peganum harmala*), *Kundush* and *Turbud* (*Operculina turpethum* L), ground and mixed with vinegar.

Prescription 3: Ground asafoetida root mixed with vinegar can be massaged over the affected area (Tabari, 1997).

Qūbā Sawdāwī: This type of *Qūbā* does not respond to treatment easily. In this case, elimination of *Khilṭ Sawdā*' is the first step through *Ishāl* with the help of formulation *Maṭbūkh Aftīmūn* (*Cuscuta epithymum* L.). Then topical application of *Ghassāl Adviya* (irrigator drugs) is advised.

Prescription for topical application: Wax, fats of duck, cocks and oil are applied topically in the form of *Ṭilā'*.

Qūbā Ḥād: Topical application of single as well as compound formulations are recommended such as: *Rawghan-i-Ālsī* (oil of *Linum usitatissimum* L.), *Rawghan-i-Gandum* (oil of *Triticum sativum* Lam.), *Rawghan-i-Bādām Talkh* (oil of *Prunus amygdalus* Batsch.), *Rawghan-i-Nārjīl* (oil of *Cocos nucifera* L.), ghee and butter.

***Qūbā Radī*:** In this type, pathology exists inside deeper into the skin. The first recommended step is leech therapy. Then the best prescription for topical application is given below:

Prescription: *Ushaq* (*Dorema ammoniacum* D. Don.) mixed with vinegar should be applied (Razi, 1991).

Some classical prescriptions for topical application

Prescription 1: Vinegar and *Ushaq* (*Dorema ammoniacum* D. Don.)/ Radish seeds/ *Rasaut* (*Berberis aristata* De.)/ *Ḥummāḍ* (*Rumex vesicarius* Linn.)/ *Zarāwand Mudaḥraj* (*Aristolochia rotunda* L.)/ *Rawghan-i-Bādām Talkh* (oil of *Prunus amygdalus* Batsch.) (Ali *et al.,* 2016).

Prescription 2: Vinegar, *Rawghan-i-Gandum* (oil of *Triticum sativum* Lam.), *Zarāwand* (*Aristolochia rotunda* L.), *Zarnīkh* (Arsenic), *Ushaq* (*Dorema ammoniacum* D. Don.), *Muqil* (*Commiphora mukul* Engl.), *Zāj* (Arzani, YNM).

Prescription 3: Vinegar, cinnamon, honey (*Apis mellifera* L.) (Ali *et al.,* 2016).

Prescription 4: Honey (*Apis mellifera* L.), *Sudāb* (*Ruta graveolens* L.)/ water/ garlic (*Allium sativum* L.)/ Chuqandar (Ali *et al.,* 2016).

Prescription 5: *Ushaq* (*Dorema ammoniacum* D. Don.), *Nakhchiknī* (*Centipeda minima* L.), *Ḥinā* (*Lawsonia inermis* L.) (Qumri, 2008).

Prescription 6: *Ushaq* (*Dorema ammoniacum* D. Don.), vinegar, lemon juice (Razi, 1991).

Prescription 7: Sulphur, *Kath Safaid* (*Acacia leucophloea* Willd.), sugar, *Afyūn* (*Papaver somniferum* L.) (Ali *et al.,* 2016).

Prescription 8: *Tukhm-i-Panwār* (*Cleome icosandra* L.), mercury (Ali *et al.,* 2016).

Pharmacopoeial formulations for topical application

Ḥabb-i-Qūbā, *Ḍimād-i-Dād, Ḥabb-i-Dād, Ḥabb-i-Ṭilā', Marham Khārish Jadīd* (Anonymous, 2008), *Marham-i-Dharārīḥ* (Qumri, 2008), *Marham-i-Qūbā* (Anonymous, 2008), *Marham-i-Dād* (Tabari, 2010), *Rawghan-i-Qūbā* (Anonymous, 1986).

Conclusion

Treatment of *Qūbā* has been mentioned in classical textbook of Unani System of Medicine. There are time-tested medicines which have been documented after a long time of clinical practice. Unani physicians have described procedures and formulations for complete cure of *Qūbā*. They found these procedures and formulations effective in all types of *Qūbā* according to chronicity, causative factors and extension of the disease. Although they were not aware that *Qūbā* was an infective disorder, but complete cure through these procedures and formulations indirectly proved that they were helpful in curbing infection in general and treating the ailment in particular. In the light of information available in classical literature with regard to the therapeutics recommended in the treatment of *Qūbā*, it can be said that these formulations and procedures should be implied in clinical practice to control and treat *Qūbā*. To generate evidences in the era of evidence-based medicine, the pharmacopoeial formulations may be used as study drugs in different clinical trials. Clinical studies to prove efficacy of these formulations are need of the hour. A quite large number of population have faith in Unani System of Medicine and opt it for therapeutic purpose as informed patients. The generation of evidence will help to build the image of Unani System of Medicine from traditional to conventional system of medicine.

References

1. Ali, A., Sultana, N., Firdaus, S. and Ali, F. (2016) "Dermatophytosis (Qooba) a Misnomer Infection and Its Management in Modern and Unani Perspective-A Comparative Review." Journal of Medicinal Plants Studies, (4): pp. 109.

2. Anonymous (1986) Qarabadeen Majeedi. All India Unani Tibbi Conference, Delhi.pp. 123-25.

3. Anonymous (2006) National Formulary of Unani Medicine Part - I. Central Council For Research In Unani Medicine, on behalf of Govt. of India, Ministry of health & F.W. (Deptt. of AYUSH).

4. Anonymous (2008) National Formulary of Unani Medicine CCRUM, Rakmo Press Pvt. Ltd, New Delhi. 1(5).

5. Arora, D.R. and Arora, B. (2008) Textbook of Microbiology. CBS Publishers & Distributors, Daryaganj, New Delhi. (3).

6. Arzani, H.A. (YNM): Tibb e Akbar (Urdu Translation by Husain M). Faisal Publications Jama Masjid Deoband.

7. Bhatia, V.K. and Sharma, P.C. (2014) "Epidemiological Studies on Dermatophytosis in Human Patients in Himachal Pradesh, India." https://doi.org/10.1186/2193-1801-3-134.

8. Fitzpatrick, T.B., Richard A.J., Klaus, W. and Dick, S. (2001) Color Atlas and Synopsis of Clinical Dermatology. 4th ed. McGraw-Hill Medical Publishing Division.

9. Goldsmith, Lowell A., Stephen, I., Katz, Barbara, A., Gilchrest, Amy, S.P., David, J.L. and Klaus, W. (2012) Fitzpatrick's Dermatology in General Medicine. 8th ed. McGraw-Hill Medical Publishing Division.

10. Griffiths, C., Jonathan, B., Tanya, B., Robert, C., and Daniel, C. (2016) Rooks Textbook of Dermatology Vol - 1. 9th ed. Wiley Blackwell.

11. Grover, C., and Ananta, K. (2012) "Onychomycosis: Newer Insights in Pathogenesis and Diagnosis." Indian Journal of Dermatology, Venereology, and Leprology 78 (3): 263.

12. Hubal, I. (2007): Kitabul Mukhtarat Fit Tib (Urdu Translation by CCRUM) Vol-4. CCRUM, Deptt of AYUSH, Ministry of health and family welfare, Government of India, New Delhi.

13. Ibn Sina (1998) Al Qanoon Vol -2. Idara Matbuaat Sulaimani, Urdu Bazaar, Lahore.

14. James, W.D., Timothy, G.B. and Dirk, M.E. (2016) Andrews Disease of the Skin. 12th ed. Elsevier.

15. Jurjani, I. (2010) Zakhira Khwarzam Shahi (Urdu Translation by Khan HH). Idara Kitab-UL- Shifa, Darya Ganj New Delhi.

16. Kasper, F., Hauser, C., Jameson and Coscalzo (2015) Harrison's Principles of Internal Medicine. McGraw Hill; 2(19);

17. Majusi, A.I.A. (2010) Kamilus Sana (Urdu Translation by Kantoori GH). Idara Kitab-UL- Shifa, Darya Ganj, New Delhi.

18. Mathew, K.G., and Praveen, A. (2018) Medicine Prep Manual for Undergraduates. 5th ed. Elsevier.

19. Munjal, Y.P., Agarwal, A.K., Gupta, P., Kamath, S.A., Nadkar, M.Y., Singal, R.K. and Sundar, S. (2015) API Textbook of Medicine Vol - 1. 10th ed. Jaypee Brothers Medical Publishers (P) Ltd.

20. Papadakis, Maxine, A., Stephen, J.M. and Micheal, W.R. (2019) Current Medical Diagnosis and Treatment. McGraw Hill Education. 58th ed.

21. Pasricha, J.S. and Gupta, R. (2006) Illustrated Textbook of Dermatology. 3rd ed. Jaypee Brothers Medical Publishers (P) LTD, New Delhi.

22. Qumri, H. (2008) Ghina Muna. CCRUM, Institutional Area, opp Block-D, Janakpuri, New Delhi.

23. Razi, A. (1991) Kitab Ul Mansoori (Urdu Translation by CCRUM). CCRUM, deptt of AYUSH, Ministry of health and family welfare, Government of India, New Delhi.

24. Sehgal, V.N. (2011) Textook of Clinical Dermatology. 5th ed. Jaypee Brothers Medical Publishers (P) Ltd.

25. Siddappa, K., Sacchidanand, S., Chetan, O. and Arun, C.I. (2016) IADVL Textbook of Dermatology Vol - 1. 4th ed. Bhalani publishing house.

26. Tabari, A.M. (1997) Moalajat-e-Buqrātiya, Translation by CCRUM Vol-2. CCRUM, deptt of AYUSH, Ministry of health and family welfare, Government of India, NEW DELHI.

27. Tabari, R. (2010) Firdaus Ul Hikmat. Idara Kitab-ul-Shifa, Darya Ganj New Delhi.

28. Weatherall, D.J., Ledingham, J.G. and Warrell, D.A. (1996) Oxford Textbook of Medicine Vol-1. 3rd ed. Oxford Medical Publications.

सारांश

यूनानी चिकित्सा पद्धति के परिप्रेक्ष्य में *कूबा* का चिकित्सीय दृष्टिकोण एवं उपचार

***आलिया, मोहम्मद नवाब, सना अय्यूब, एम.एच. काज़मी**

यूनानी चिकित्सा पद्धति में त्वचा रोगों का उपचार उपलब्ध है। प्राचीन काल से ही *कूबा* (डर्मेटोफाइटोसिस) का उपचार जड़ी बूटी–खनिज मिश्रणों के माध्यम से किया जाता रहा है। *कूबा* त्वचा का एक ऊपरी कवक संक्रमण होता है। दुनिया भर में 20–25% व्यक्ति इस त्वचा संबंधी समस्या से पीड़ित हैं। तीव्र खुजली इसका मुख्य लक्षण है जोकि जीवन की गुणवत्ता को बाधित करता है, अनिद्रा और चिंता का कारण बनता है और दैनिक कार्यों में बाधा डालता है। यूनानी क्लासिकल साहित्य में *कूबा* का उपचार व्यावहारिक अनुभवों के आधार पर प्रलेखित है। इस समीक्षा पेपर में *कूबा* के ऐतिहासिक पृष्ठभूमि, एटियोपैथेजेनेसिस, निदान, चिकित्सीय दृष्टिकोण और उपचार का वर्णन करने का प्रयास किया गया है। साहित्य में उपलब्ध सूचना इस रोग के उपचार के बारे में अच्छे से समझने में सहायता प्रदान कर सकती है। यूनानी चिकित्सा पद्धति में कई एकल और मिश्रित औषधियां हैं जो इसके उपचार के लिए अनुशंसित हैं। इसके उपचार के लिए चिकित्सीय दृष्टिकोण भी एलोपैथिक चिकित्सा पद्धति से भिन्न है। त्वचा विकारों के लिए चिकित्सीय विज्ञान का विकास यूनानी चिकित्सा पद्धति में अनुसंधान का संभावित क्षेत्र है।

शब्दकुंजी: डर्मेटोफाइटोसिस, *कूबा,* यूनानी चिकित्सा

Luk (*Laccifer lacca*): A Potent Unani Drug for Obesity and Dyslipidemia

[1]Qamar Alam Khan,
[2]Asim Ali Khan,
[3]Abdul Raheem
and
*[4]Shagufta Parveen

[1]Clinical Registrar, Majeedia Unani Hospital, Jamia Hamdard, New Delhi

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

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

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

Abstract

Luk (*Laccifer lacca*) is one of the most valuable gifts of nature to humanity. It is an animal origin drug with abundance of medicinal properties. Wide literature is available in Unani Medicine regarding its pharmacological actions and therapeutic uses. Beside classical literature, numerous studies have been conducted for anti-obesity, anti-hyperlipidemic effect and other pharmacological actions of the drug. Various Unani formulations having *luk* as a chief ingredient are available in the market and widely used in dyslipidemia and obesity. This paper presents literature review of *luk* and its medicinal uses along with pharmacological actions. The paper also demonstrates the geographical distribution of the drug across the world. The analysis shows that *luk* could be used as an effective medicine for various ailments especially obesity and dyslipidemia.

Keywords: Anti-obesity, *Laccifer lacca*, *Luk*, *Safūf Muhazzil,* Unani drug

Introduction

The word *luk* is derived from the Sanskrit word *lākshā*' which represents the number 100,000. It was used for both the *luk* insect (because of its enormous number) and the scarlet resinous secretion produced by it (Ulrich, 2007). Lac is the scarlet resinous secretion of a number of species of *luk* insects, of which the most commonly cultivated species is *Laccifer lacca*. Cultivation begins when a farmer gets a stick that contains eggs ready to hatch and ties it to the tree to be infested (Derry, 2014). Thousands of *luk* insects colonize the branches of the host trees and secrete the resinous pigment. The coated branches of the host trees are cut and harvested as stick lac. The harvested stick lac is crushed and sieved to remove impurities. The sieved material is then repeatedly washed to remove insect parts and other soluble material. The resulting product is known as seedlac. The prefix seed refers to its pellet shape. Seedlac which still contains 3–5% impurities is processed into shellac by heat treatment or solvent extraction.

Scientific classification of *luk* (*Laccifer lacca*)

Family : Lacciferidae

Order : Hemiptera

Genus : *Laccifer*

Species : *lacca*

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

Synonyms

Arabic	:	*Luk* (Hakeem, 1991)
Persian	:	Laak (Shirazi, 1874; Khan, 1892; Hussain, 1920; Hakeem, 1991)
Sanskrit	:	Lukhshah (Anonymous, 1992)
Hindi	:	Lakh (Anonymous, 1992)
Gujarati	:	Laak (Anonymous, 1992)
Tamil	:	Komorki (Anonymous, 1992)
Telugu	:	Komolkah (Anonymous, 1992)
Bengali	:	Gala (Anonymous, 1992)
Malayalam	:	Arkoo (Anonymous, 1992), Ambaloo (Nadkarni, 1982)
English	:	Lac (Anonymous, 1992)

Description

There is controversy in morphology of *luk*. The detailed description of *luk* in *Kitāb al-Ḥāwī al-Kabīr* by *Razi* is that *luk* is a gum like *Mur* and it smells good (Razi, 1846). *Ibn Sina* has described its name as *Qūlus* and described its morphology same as described by *Razi* (Ibn Sina, 1905). According to *Ibn Rushd,* it is a gum (Ibn Rushd, 1980)

Luk is a gum type secretion of *laccifer* (lac) insect which is found around the branches of many trees. These insects reside over the lactiferous trees and use this *laccifier* as their diet (Anonymous, 1992). When these insects suck large quantity of juice, they become lazy and sit and secret a substance which changes into a pale material. This chalky material is round around the female and oval around the male. The male comes out from this chalky material and female remains inside the chalky material which continues to thicken from its body's secretion. The female makes three holes in this chalky material for its respiration and delivers egg inside it. For the nourishment of its egg and larva, the female sucks the juice of tree till it swells and dies. After sometime, larva comes out from egg and then comes out of this chalky material by piercing it. The branches which contain this chalky material are plucked from the trees and dipped in the water turning it into red. This red water is boiled and precipitates separated. The precipitate is desiccated and melted over the heat. If this melted material falls down drop by drop over a type of bag, this type of *luk* is *chupra*. If we freeze this melted material, the luk is called *Gulāl*. If cotton is dried after dipping in this melted material, the luk is called *Maḥwar* or *Ultā* (Ghani, 1926).

Distribution

Since the *luk* insects thrive and feed on certain species of the tropical trees, it is found distributed in South-East Asian countries. It is currently produced

in India, Myanmar, Thailand, Malaya, Lao and Yuan provinces of China. India and Thailand are main areas in the world, while India has prime position in relation to *luk* production. Over 90% of Indian *luk* production comes from the states of Jharkhand, Bihar, West Bengal, Madhya Pradesh, Chattisgarh, Eastern Maharashtra and Northern Orissa. Some pockets of *luk* cultivation also exist in Andhra Pradesh, Punjab, Rajasthan, Mysore, Gujarat and few districts of Uttar Pradesh (Singh, 2012).

Temperament (*Mizāj*)

- Hot and Dry (Zaki, 1960; Safiuddin, 1986)
- Hot and Dry (2^{nd} degree) (Shirazi, 1874; Hussain, 1920; Antaki, 1930; Gosowami, 1977; Nadkarni, 1982; Hakeem, 1991)

Recommended dose in Unani Medicine

- 4 *Māsha* (Khan, 1892; Hussain, 1920; Hakeem, 1991)
- 3-4 *Māsha* (Zaki, 1960)
- 3½ *Māsha* (Ibn Sina, 1905)
- ½ -2 *Māsha* (Gosowami, 1977)

Substitute

- *Revand Chīnī* (Shirazi, 1874; Khan, 1892; Hussain, 1920)
- *Asārūn* (Shirazi, 1874; Khan, 1892; Hussain, 1920)
- *Ṭabāshīr* (Shirazi, 1874; Khan, 1892; Hussain, 1920)

Pharmacological action

- *Dāfi'-i-Siman Mufriṭ* (Antiobesity) (Razi, 1846; Shirazi, 1874; Antaki, 1930; Zaki, 1960; Gosowami, 1977; Hakeem, 1991)
- *Dāfi'-i-Khafaqān* (Antipalpitative) (Shirazi, 1874; Khan, 1892; Ibn Sina, 1905; Hakeem, 1991; Gosowami, 1977)
- *Dāfi'-i-Su'āl* (Expectorant) (Shirazi, 1874; Zaki, 1960; Gosowami, 1977; Hakeem, 1991)
- *Dāfi'-i-Ḍīq al-Nafas* (Antiasthmatic) (Shirazi, 1874; Safiuddin, 1986; Zaki, 1960; Gosowami, 1977; Hakeem, 1991)
- *Muqawwī-ī-Bāh* (Aphrodisiac) (Khan, 1892; Hussain, 1920)
- *Dāfi'-i-Fālij* (Anti-paralysis) (Shirazi, 1874; Khan, 1892; Antaki, 1930; Zaki, 1960)

- *Dāfi'-i-Iltīhāb* (Anti-inflammatory) (Shirazi, 1874; Khan, 1892; Antaki, 1930; Safiuddin, 1986; Gosowami, 1977; Hakeem, 1991)
- *Muqawwī-i-A'ṣāb* (Nervine tonic) (Shirazi, 1874; Khan, 1892; Hussain, 1920; Antaki, 1930; Zaki, 1960).
- *Muqawwī-i-Jigar* (Liver tonic) (Shirazi, 1874; Khan, 1892; Hussain, 1920; Gosowami, 1977; Safiuddin, 1986; Hakeem, 1991)
- *Ḥābis al-Dam* (Haemostatic) (Shirazi, 1874; Hussain, 1920; Gosowami, 1977; Safiuddin, 1986; Kabiruddin, 2007a&b)
- *Māni'-i-Ḥaml* (Contraceptive) (Maghrabi, 2007)
- *Dāfi'-i-Yaraqān* (Anti-bilious) (Suganthan and Santhakumari, 1979; Maghrabi, 2007)

Side effects

- It is harmful for spleen (Zaki, 1960)
- It is harmful for head (Khan, 1892; Hussain, 1920)
- *Luk* has no side effect (Hussain, 1920)

Corrective

- *Masṭagī* (Shirazi, 1874; Khan, 1892; Hussain, 1920; Zaki, 1960)
- *Kewṛa* and *Gulāb* (Hakeem, 1991)

Compound formulations

- *Safūf Muhazzil* (Kabiruddin, 1967)
- *Dawā' al-Luk* (Lavekar, 2008)
- *Dawā'-i-Zerishk* (Lavekar, 2008)
- *Qurṣ 'Ambar Bārid* (Anonymous, 2006)
- *Qurṣ Luk* (Khan, 1996)

Pharmacological studies

1. Anti-hyperlipidemic and anti-obesity activity of *luk*

- In a randomized standard controlled clinical study of *Safūf Muhazzil* (a compound formulation with *Laccifer lacca* as chief ingredient) in

hyperlipidemic patients, significant decrease in total cholesterol, TGs, LDL and VLDL were revealed. The test drug also increased HDL and was better than standard control Atorvastatin in relieving the associated clinical symptoms, hence enhancing the quality of life (Jahangir *et al.,* 2014).

- An open label randomized comparative clinical study of *Safūf Muhazzil* versus Atorvastatin in case of primary hyperlipidemia in 89 patients for 90 days denoted that the test drug (*Safūf Muhazzil*) is more effective than the control drug (Atorvastatin) for increment of HDLc, lowering BMI and WHR (Ahmed *et al.*, 2018).
- In a pre-clinical study conducted by Gupta, *et al.* on anti-obesity effect of *Safūf Muhazzil*, the Unani formulation significantly prevented the increase in body weight, lipid profile, insulin and leptin level as compared to standard pellet diet control after 14 weeks of intervention in rats (Gupta *et al.*, 2012).
- Inflammation and oxidative stress have been reported in obesity. Anti-inflammatory and anti-oxidative action of drug also advocates its efficacy in the management of obesity. Anti-inflammatory and anti-oxidative property of *Safūf Muhazzil* is proved on assessment of hepatic inflammatory markers in male Wistar rats after administration of Unani formulation for 14 days (Gupta *et al.,* 2015).

2. Besides antihyperlipidemic and anti-obesity activity, animal studies have been conducted on anti-fertility effect of *Laccifer lacca* (Perveen *et al.,* 2013).

Therapeutic uses

Luk is beneficial in ascites and opens the *Suddah* of liver, spleen and improves the function of stomach and liver (Shirazi, 1874; Khan, 1892; Hussain, 1920, Gosowami, 1977; Safiuddin, 1986; Hakeem, 1991). Powdered form of *luk* is advised as contraceptive by various Unani physicians since ages (Ibn Baitar, 1870; Khan, 1892). In Unani Medicine, luk is used for its anti-obesity effect since centuries. Its compound formulation *Safūf Muhazzil* is one of the most popular and acceptable drugs of Unani Medicine in Indian subcontinent, being prescribed in Unani OPDs for anti-obesity activity. *Luk* is not much evaluated in biological field, instead it is vastly studied for its industrial and other commercial purposes. An indigenous preparation having *Coccus lacca* as one of the ingredients in combination with *Saraca indica* L., *Areca catechu* L., gold and sugar has claimed to exhibit anti-implantation effect in rabbits (Suganthan and Santhakumari, 1979). It is already tested for its effects on diet induced hyperlipidemia in albino rats (Ghufran *et al.,* 2011).

Conclusion

Luk (*Laccifer lacca*) has been studied and tested vigorously, especially for its pharmacological actions, and has been proven for its uses in various systemic diseases. It is widely acceptable due to its anti-obesity, anti-inflammatory and antioxidant actions. This drug is used in Traditional Medicine since long and reference goes to *Ibn Sina*, *Tabari* and *Dioscorides*. This paper particularly provides pharmacological studies and uses of *Luk* which are mentioned in Unani Medicine and proven through various studies. Further studies on the drug are needed to explore its pharmacological action and proposed mechanism of action on scientific parameters.

Conflict of interest: None declared.

References

1. Ahmed, M.R., Rahman, M.N., Akhatar, J. and Farooqui, A.H. (2018) An Open label Randomized Comparative Clinical Study of Safoof-e-Mohazzil versus Atorvastatin in the Cases of Fart-e-Tadassum-Fid-Dam (Primary Hyperlipidemia), Research and Reviews: A Journal of Unani, Siddha and Homeopathy, 5(1): 6-12.
2. Anonymous (1992). Wealth of India, CSIR, New Delhi, Vol. III &VI, pp. 1-12, 67, 68.
3. Anonymous (2006). National Formulary of Unani Medicine, Part IV, Vol. I, Department of AYUSH, Ministry of Health & Family Welfare, Government of India, New Delhi, pp. 43-44.
4. Antaki, D. (1930) Tazkaratul Awlul-albab, Vol-I, Publisher Azharya Egypt, pp. 180-182, 260.
5. Derry, J. (2014) "Investigating Shellac: Documenting the Process, Defining the Product". Project-Based Master's Thesis, University of Oslo, pp. 27.
6. Ghani, M.N. (1926) Khazayanul Adviya (Unani Adviya Mufrada Encycolpedia) Naval Kishore, Lucknow, pp. 373-375.
7. Ghufran, A., Laique, A. and Khan N.A. (2011) The Effect of Luk Magsool (processed Lac) on diet induced Hyperlipidemia in Albino rats, *Hippocratic Journal of Unani Medicine,* 6(2): 155-165.
8. Gosowami, R.L. (1977) Bayanul Adviya, Vol-II Goswami Pharmacy, Delhi, pp. 168, 204.
9. Gupta, P., Mehla, J., Gupta, Y.K. (2012) Antiobesity effect of safoof Mohazzil, a polyherbal formulation in cafeteria diet induced obesity in rats, *Indian Journal of Experimental Biology,* 50(11): 776-84.

10. Gupta, P., Mehla, J., Siddique, K., Jamil, S. and Gupta, Y.K. (2015) Anti-oxidant and Anti-inflammatory activity of Safoof Mohazzil, a Polyherbal formulation for obesity, *Indian Journal of Traditional Knowledge,* 14(3): 461-465.

11. Hakeem, A. (1991) Bustanul Mufradat, Idara Taraqqi Urdu Publication, Lucknow, pp. 94, 188, 203.

12. Hussain, Z. (1920) Khazayenatul Advia, Vol-II, Naval Kishore, Lucknow. pp. 373-375, 574-575.

13. Ibn Rushd (1980) Kitabul Kulliyat (Urdu), Central Council for Research in Unani Medicine, New Delhi, pp. 46, 323,327.

14. Ibn Sina (1905) Al-Qanoon Fit Tibb (Urdu) Translation by Kantoori GH, Vol. IV, Nami press, Lucknow. pp.318.

15. Ibn Baitar (1870) Al-Jame-ul-Mufradat-Al-Advia-wal-Aghzia, Vol. III & IV, Publisher Azharya, Egypt. pp. 38-39,110.

16. Jahangir, U., Khan, A.A., Kapoor, P., Jalees, F. and Urooj, S. (2014) Evaluation of a Classical Unani Pharmacopeial formulation Safoof-e-Muhazzil in Hyperlipidemia: A Randomized, Standard Controlled Clinical Study, *Journal of Pharmacy and Bio-Allied Sciences,* 6(3): 167-179.

17. Kabiruddin, M. (1967) Bayaze Kabir, Vol II. Daftar al-Masih, Balli maran, Delhi pp. 101.

18. Kabiruddin, M. (2007a) Ilmul Advia Nafeesi ma Zameema, Aijaz Publishing House, New Delhi, pp. 331.

19. Kabiruddin, M. (2007b) Makhzanul Mufradat, Aijaz Publishing House, New Delhi, pp. 331, 365.

20. Khan, M.A. (1892) Muheet-e-Azam, Nizami Press, Kanpur, pp. 16-17, 64-65.

21. Khan, M.A. (1996) Makhzanul Mujarrabat (Urdu translation Qarabadeen Azam), Aijaz Publication House,New Delhi, pp-514.

22. Lavekar, G.S. (2008) Inventory of Animal Products used in Ayurveda, Siddha & Unani, Part II, CCRAS, New Delhi, pp.537.

23. Maghrabi, A.I. (2007) Kitab Al Fath Fi Al Tadawi (Urdu) Translation by Dept. of AYUSH), 1st ed., NCPC printers, New Delhi, pp. 42,138-39.

24. Nadkarni, K.M. (1982) Indain Materia Medica, 3rd edition, Vol.I & XI, Popular Parkashan, Bombay, pp. 148-150,1265.

25. Perveen, A., Jahan, N., Wadud, A. and Alam, T. (2013) Methods of processing of Lac (*Laccifer lacca* Kerr) described in Unani system of Medicine, *Research Journal of Pharmaceutical Sciences,* 2(8): 5-7.

26. Razi (1846) Kitabul Hawi Fit Tibb, Dairatul Maarif, Osmania, Hyderabad. Vol. 20 pp. 215-289.

27. Safiuddin (1986) Unani Adviya Mufradah, Taraqqi Urdu Bureau, New Delhi, pp. 289-290.

28. Shirazi (1874) Makhzanul Advia, Naval Kishore, Lucknow, pp. 358-359,566-567.

29. Singh, R. (2013) Applied zoology lac culture, Department of Zoology, Varanasi: Udai Pratap autonomous college, pp. 1-18.

30. Suganthan, D. and Santhakumari, G. (1979) Antifertility Activity of Indigenous Preparation Ayush-47, Indian J Med Res, 70(3): 504-516.

31. Ulrich, M.W. (2007) Polyurethanes: coatings, adhesives and sealants, Vincentz Network GmbH & Co KG, ISBN 978-3-87870-334-1.

32. Zaki, M.M. (1960) Jami-ul-Mufradat, Publication Anwar Mohhammadi, Lucknow, pp. 65, 160.

सारांश

लुक (लैसीफर लैका) : मोटापा और डिसलिपिडेमिया हेतु एक गुणकारी यूनानी औषधि

क़मर आलम ख़ान, आसिम अली ख़ान, अब्दुल रहीम, *शगुफ़्ता परवीन

लुक (*लैसीफर लैका*) मनुष्य के लिए प्रकृति के सबसे मूल्यवान उपहारों में से एक है। यह औषधीय गुणों से प्रचुर एक पशु मूल औषधि है। यूनानी साहित्य में इसकी औषधीय क्रियाओं और चिकित्सीय उपयोगों के बारे में व्यापक साहित्य उपलब्ध है। क्लासिकल साहित्य के अतिरिक्त इस औषधि के मोटापा रोधी, एंटी–हाइपरलिपिडेमिक प्रभाव और अन्य औषधीय क्रियाओं पर अनेक अध्ययन किए गए हैं। बाजार में ऐसे विभिन्न यूनानी मिश्रण उपलब्ध हैं जिनमें *लुक* एक मुख्य घटक के रूप में उपयोग होता है और व्यापक रूप से डिसलिपिडेमिया और मोटापे में उपयोग किए जाते हैं। यह पेपर *लुक* की साहित्य समीक्षा और औषधीय क्रियाओं के साथ इसके चिकित्सीय उपयोग को प्रस्तुत करता है। इस पेपर में दुनिया भर में इस औषधि के भौगोलिक वितरण को भी दर्शाया गया है। विश्लेषण से पता चलता है कि *लुक* को विभिन्न रोगों विशेष रूप से मोटापे और डिसलिपिडेमिया के लिए एक प्रभावी औषधि के रूप में उपयोग किया जा सकता है।

शब्दकुंजी: मोटापा रोधी, *लैसीफर लैका, लुक, सफ़ूफ़ मुहज़्ज़िल,* यूनानी औषधि

Historical Ethnopharmacological Review of a Unani Mineral Drug – *Samm al-Fār* (Arsenic Trioxide)

*[1]Mustehasan,
[2]Misbahuddin Azhar
and
[1]Sofia Naushin

[1]Central Council for Research in Unani Medicine, Janakpuri, New Delhi-110058

[2]Regional Research Institute of Unani Medicine, Shahjahan Manzil, Near AMU Riding Club, Aligarh-202002

Abstract

Minerals/heavy metals such as arsenic, mercury and lead are integral to various Unani compound formulations and have been used after detoxification for centuries. *Samm al-Fār* is a naturally occurring oduorless and tasteless element found in the ores of silver in the island and mountains of Khurasan. Chemically, *Samm al-Fār* is arsenic trioxide. Unani formulations of *Samm al-Fār* are used to treat nervine disorders, sexual disorders, skin disorders, anaemia, fevers, respiratory disorders and joints pain. In the present review, information related to history of medicinal use, occurrence, temperament, therapeutic actions & uses, importance for the human body, toxicity studies, pharmacological studies and use of arsenic trioxide in current scenario has been compiled.

Keywords: *Arsenic trioxide, Kushta Samm al-Fār, Samm al-Fār,* Unani Medicine, *Zarnīkh Abyaḍ*

Introduction

Unani Medicine is a comprehensive medical system based on Hippocrates' (460-377 BC) theory of humours. In 1976, the World Health Organization (WHO) framed a policy for promoting traditional medicine, since then Unani Medicine got considerable attention globally (Anonymous, 2016; Jabin, 2011; Mustehasan and Azhar, 2020). Eighty percent population of the developing countries uses traditional medicines as claimed by the WHO (Shaw, 1998). In Unani Medicine, metal / mineral origin drugs are used in the management of various ailments. Minerals/heavy metals such as arsenic, mercury and lead are integral to various Unani compound formulations and have been used for centuries. Metals used in Unani formulations are subjected to various purification processes to reduce their toxic effects before adding to formulations (Prakash, 1988). *Samm al-Fār* and its preparations are used in Unani Medicine to treat nervine disorders, sexual disorders, skin disorders, anaemia, fevers, respiratory disorders and joints pain since ancient times. The medicinal use of arsenic was reported by Hippocrates (460-370 BC), the father of medicine, who used an arsenic paste to treat ulcers and abscesses (Michael *et al.,* 2011). The great Unani scholar Dioscorides described arsenic as a poison in the court of the Roman Emperor Nero, then Nero used it to poison his step-brother to secure his position as Roman Emperor. The odourless, tasteless, crystalline white colour, soluble in water properties of *Samm al-Fār* make it an ideal poison. It can be readily made by heating arsenic ore. It is not easy to detect in food or drink, and even improves the taste of wine. *Samm al-Fār* poisoning is difficult to detect initially as symptoms mimic

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

food poisoning, but a single dose can produce severe diarrhoea and vomiting, paralysis and death. Because of its potency, it was known as 'the Poison of Kings and the King of Poisons' (Jolliffe, 1993).

Material and Method

In the present review, Unani classical literature was surveyed for its complete description, viz. temperament, actions, therapeutic and dosage uses, etc. For toxicological studies, pharmacological activities and clinical trials carried out to prove the importance of *Samm al-Fār,* computerized databases such as Medline, Pubmed, Ovid SP, Google Scholar and ScienceDirect were searched. All the information on *Samm al-Fār* available in Urdu, Persian and Arabic languages and studies were included.

Vernacular Names of *Samm al-Fār*

Arabic: *Samm al-Fār, Shak, Turāb al-Hālik, Turāb al-Fār, Rahj al-Fār*; English: Arsenic trioxide; Hindi: *Sankhiya, Somal Khar, Sanbul Khar, Sankhiya Zehar, Vish;* Latin: *Arsenicon;* Persian: *Marg-i-Mosh, Zahr-i-Ādam, Zarnīkh Abyaḍ;* Sanskrit: *Aakhu Pashan, Gauri Pashan* (Fazlullah, 1907; Ghani, 1921; Hakeem, 1948; Singh, 1949; Kabiruddin, 1951; Nadkarni, 1976; Rafiquddin, 1985; Ibn Baitar, 1999; Lubhaya, 2001; Ali, 2004; Tariq, 2004; Mustehasan and Ali, 2004; Khan, 2013).

Description

Arsenic is a naturally occurring odourless and tasteless transitional element or metalloid (mixture of metal and non-metal). Arsenic exists in three different valency states: elemental arsenic (zero oxidation state); trivalent; and pentavalent arsenic. The name 'arsenic' comes from the Greek word 'arsenikon' which means potent or strong or masculine because of its potent chemical properties (Jolliffe, 1993). It has organic and inorganic compounds. In Unani Medicine, only two inorganic compounds are used as medicine: (a) Arsenious oxide (Arsenic trioxide or white arsenic) which is white crystalline powder, slightly soluble in water and commonly known as *Samm al-Fār* or Sankhya; and (b) Arsenic trisulphide which is yellow arsenic or orpiment and commonly known as *Zarnīkh* or *Hartāl* (Bardale, 2011). In 1918, the US Army developed two organic arsenical compounds – Lewisite and Adamsite, vesicant and respiratory irritant agents, as chemical warfare weapons but did not use in the war (John, 2013). In the literature of Unani Medicine, *Samm al-Fār* and *Zarnīkh* have been described separately as their actions and therapeutic uses differ. After ingestion of *Samm al-Fār*, rats die immediately and for that reason it is called *Samm al-Fār* (*Samm* means poison and *Fār* means rat). According to some Unani physicians, it is

scum of silver, obtained from mines of silver. It is of two colours, white and yellow. White coloured is considered of superior quality. Its medicinal value is retained up-to 70 years (Ghani, 1921; Ibn Baitar, 1999; Tariq, 2004; Khan 2013).

History of the Use of *Samm al-Fār* in Humans

The initial medicinal use of arsenic was reported by Hippocrates (460-370 BC) who used an arsenic paste to treat ulcers and abscesses (Michael *et al.*, 2011). The great Unani scholar Dioscorides described arsenic as a poison. No nutritional role is known for arsenic in humans, while it has a function in animals to control disease and promote growth. In 1786, Thomas Fowler used a flavoured solution of *Samm al-Fār* for the cure of agues (fever with chill), remittent fevers, and periodic headaches. In 1781, Fowler along with Hughes identified *Samm al-Fār* as the major constituent of the 'ague drops' patented by a chemist Thomas Wilson. Fowler's solution (1% potassium arsenite, K AsO2) was used to treat anaemia, rheumatism, asthma, cholera, syphilis and skin disorders, such as psoriasis, eczematous eruptions and dermatitis herpetiformis. In 1865, Fowler's solution was identified as the first chemotherapeutic agent in the treatment of leukaemia which produced a transient improvement in leukemia. Forkner and Scott rediscovered Fowler's solution for the treatment of chronic myeloid leukaemia in 1931. The arsenicals and irradiation was the treatment of choice for leukemia until Busulphan was introduced in 1953 (John, 2013).

Occurrence

As per Unani literature, *Samm al-Fār* is found in the ores of silver of island and mountains of Khurasan (Ghani, 1921; Ibn Baitar, 1999; Tariq 2004; Khan, 2013). Arsenic occurs naturally in rocks, soil, ores of silver, lead, copper, nickel, antimony, cobalt and iron in combination with either inorganic or organic substances to form many different compounds. Inorganic arsenic compounds exist in soils, sediments, and groundwater, while organic arsenic compounds are found in seafood (fish and shellfish), and absorbed as arsenobetaine but rapidly excreted unchanged (Anonymous, 2000; McMahon and Chen, 2004, Anonymous, 2017). In 2017, China was the top producer of *Samm al-Fār* (white arsenic) followed by Morocco, Namibia and Russia (George, 2017).

Temperament

There is consensus among Unani scholars that its temperament is hot and dry in fourth degree (Ghani, 1921; Ibn Baitar, 1999; Tariq, 2004; Khan, 2013; Rafiquddin, 1985; Hakeem, 2011; Kabiruddin, 1951; Ali, 2004; Lubhaya, 2001; Singh, 1949; Mustehasan and Ali, 2004; Fazlullah, 1907).

Action

Unani scholars have mentioned its action as *Muqawwī ʻĀam* (general tonic), *Muqawwī-i-Aʻṣāb* (nervine tonic), *Muqawwī-ī-Bāh* (aphrodisiac), *Muqawwī-ī-Qalb* (cardiotonic) *Muqawwī-i-Miʻda* (stomachic), *Muqawwī-i-Dam* (hematinic), *Dāfiʻ-i-Amrāḍ Balghamī* (anti-phlegmatic diseases), *Dāfiʻ Wajaʻ al-Mafāṣil* (anti-arthritic), *Muṣaffī-i-Dam* (blood purifier), *Qātil-i-Jarāthīm* (antiseptic), *Akkāl* (corrosive), *Dāfi-i-Ḥummā* (antipyretic), *Mujaffif* (desiccant/ siccative) (Ghani, 1921; Ibn Baitar, 1999; Tariq, 2004; Khan, 2013; Rafiquddin, 1985; Hakeem, 2011; Kabiruddin, 1951; Ali, 2004; Lubhaya, 2001; Singh, 1949; Mustehasan and Ali, 2004; Fazlullah, 1907).

Therapeutic Uses

Unani scholars have recommended the use of *Samm al-Fār* in the following disease conditions considering its different actions: *Ḍuʻf-i-Badan* (debility), *Ḍuʻf-i-Miʻda* (weakness of the stomach), *Jarayān* (spermatorrhoea), *Surʻat-i-Inzāl* (premature ejaculation), *Ḍuʻf-i-Bāh* (sexual debility), *Surfa* (cough), *Ḍīq al-Nafas* (asthma), *Ḥummā Balghamiya* (phlegmatic fevers), *Ātshak* (syphilis), *Juzām* (leprosy), *Baraṣ* (leucoderma/vitiligo), *Bawāsīr* (hemorrhoids), *Laqwa* (facial paralysis), *Wajaʻ al-Mafāṣil* (arthralgia), *ʻIrq al-Nasā* (sciatica), *Faqr al-Dam* (anaemia) (Ghani, 1921; Ibn Baitar, 1999; Tariq, 2004; Khan, 2013; Rafiquddin, 1985; Hakeem, 2011; Kabiruddin, 1951; Ali, 2004; Lubhaya, 2001; Singh, 1949; Mustehasan and Ali, 2004; Fazlullah, 1907).

Samm al-Fār is used internally and externally in different diseases along with other drugs only after purification.

Potent Action

The potent action of *Samm al-Fār* is *Muqawwī-i-Bāh* (aphrodisiac) and *Dāfiʻ Wajaʻ al-Mafāṣil* (anti-arthritic) (Ghani, 1921; Ibn Baitar, 1999; Tariq, 2004; Khan, 2013; Rafiquddin, 1985; Hakeem, 2011; Kabiruddin, 1951; Ali, 2004; Lubhaya, 2001; Singh, 1949; Mustehasan and Ali, 2004; Fazlullah, 1907).

Dosage

Unani scholars have advocated for the use of its powder and calx. For powder from, its dose may be 1-5 mg (Ghani, 1921; Tariq, 2004; Khan, 2013; Rafiquddin, 1985; Hakeem, 2011; Kabiruddin, 1951; Ali, 2004; Lubhaya, 2001; Singh, 1949; Mustehasan and Ali, 2004; Fazlullah, 1907), while for calx it may be 10-15 mg (Mustehasan and Ali, 2004).

Lethal Dose

The great Unani scholar Mohammad Azam Khan has mentioned lethal dose of

Samm al-Fār as 1.75 gm (Khan, 2013). As per modern concept, the lethal dose of arsenic is 1-3mg/kg body weight (Vohra, 2007).

Adverse Action

According to Unani scholars, it should be taken carefully, especially in hot season and by patients of hot temperament. *Samm al-Fār* can be fatal if used in higher doses (Ghani, 1921; Tariq 2004; Khan, 2013; Rafiquddin, 1985; Hakeem, 2011; Kabiruddin, 1951; Ali, 2004; Lubhaya, 2001; Singh, 1949; Mustehasan and Ali, 2004).

Arsenic Toxicity and Guideline Values

People are exposed to arsenic through different sources, viz. drinking water, contaminated soil, foods and industrial sources. Exposure dose is cumulative to all routes. Arsenic can be absorbed by the human body through skin, inhalation or through GIT mucosa. However, the absorption is more through damaged skin (Bardale, 2011).

In case of acute *Samm al-Fār* poisoning, the patient may suffer from vomiting, abdominal pains, and diarrhea often accompanied by bleeding. Sub-lethal doses can cause cardiovascular problems, kidney and liver problems and abnormalities in the coagulation of the blood followed by white lines (Mees' lines) on the nails and hair loss. In case of 5 to 20 year exposure (arsenicosis) through drinking water, various disorders like skin cancer, cancers of the bladder, kidney and lung, and diseases of the blood vessels of the legs and feet, diabetes, hypertension and reproductive disorders may occur (Anonymous, YNM).

To avoid the health hazards of arsenic exposure to the public, the WHO, US Occupational Safety and Health Administration (OSHA) and USFDA have recommended certain limits of inorganic arsenic in drinking water, air and food.

The WHO recommends a limit of 0.01 mg/l of arsenic in drinking water (or 10 µg/L also expressed as 10 parts per billion (ppb). The limit of arsenic in water is 0.01 mg/liter and the permissible limit is 0.05 mg/liter according to the Bureau of Indian Standards (Anonymous, YNM).

The OSHA recommends a limit for arsenic not greater than 10 micrograms of inorganic arsenic per cubic meter of air, averaged over any 8 hour period for a 40 hour work week.

The USFDA-recommended permissible limits of inorganic arsenic range from 0.5 ppm in eggs and uncooked edible tissues of chickens and turkeys to 2 ppm in certain uncooked edible byproducts of swine (Anonymous, 2010). The permissible limit of arsenic in Unani formulations is 3ppm (Anonymous, 2010).

Correctives

Unani Medicine has a unique specialty of adding corrective drugs (*Muṣliḥ Adwiya*) to counter the toxicity of the main drug. In case of poisoning with *Samm al-Fār*, emesis is induced with hot water or saline. Afterwards, patients are advised to take plenty of milk. *Rawghan Zard* is the best corrective. *Kath Safed* is considered another corrective (Ghani, 1921; Ibn Baitar, 1999; Tariq, 2004; Khan, 2013).

Substitute

Unani scholars have mentioned that in case of non-availability of genuine medicine, a substitute may be used. *Zarnīkh/Hartāl* is the substitute of *Samm al-Fār* (Fazlullah, 1907; Ghani, 1921; Ibn Baitar, 1999; Tariq, 2004; Khan, 2013; Rafiquddin, 1985; Hakeem, 2011; Kabiruddin, 1951; Ali, 2004; Lubhaya, 2001; Singh, 1949; Mustehasan and Ali, 2004).

Important Formulations

Some important classical Unani formulations having *Samm al-Fār* as an ingredient are as follows: *Ḥabb Aḥmar*, *Ḥabb-i-Fālij*, *Jauhar-i-Munaqqā*, *Jauhar-i-Sīn*, *Kushta Samm al-Fār Ātshakī*, *Kushta Samm al-Fār Qawī*, *Ṭilā' Majlūq*, *Ṭilā' Surkh* (Anonymous, 2006), *Jauhar Kalān, Jauhar-i-Sīmāb* (Anonymous, 2007). *Ḥabb-i-Pān*, *Ḥabb Samm al-Fār*, *Ḥabb Samm al-Fār Musakkin* (Anonymous, 2001), *Ḥabb-i-Kalaf* (Anonymous, 2006). *Ḥabb-i-Sīn*, *Ṭilā' 'Ajīb* (Anonymous, 2008), *Nuqraī*, *Qurṣ Mubāhī Jadīd*, *Muqawwī Mumsik*, *Tilā' Aḥmār*, *Ṭilā' Nishāt Angez* (Anonymous, 2011).

Detoxification of *Samm al-Fār*

Unani scholars were aware of medicinal values as well as toxicity of *Samm al-Fār*. Therefore, they developed a detoxification method to get rid of its toxic effect before adding it to Unani formulations or prescribing to patients in any manner.

The method for detoxification of *Samm al-Fār* is to immerse fine powder of *Sankhiya* in sufficient quantity of fresh *Āb-i-Lemū* (lemon juice) and grind in a mortar of China clay or glass till the juice is completely absorbed. Repeat this process seven times to obtain *Samm al-Fār* or *Sankhya Mudabbar* (Anonymous, 2006).

Shamshi *et al.* (2010) conducted a study regarding comparative arsenic estimation before and after the detoxification process. The study results showed that the marker compound arsenic was decreased in case of detoxified *Samm al-Fār*. Similarly, the quantity of arsenic (µg / 100 mg) in the processed material was

found less in comparison to the unprocessed material. Arsenic depletion may be due to the treatment with *Āb-i-Lemū* (juice of *Citrus limon* (L.) Burm.f.) after reacting with hydrochloric acid and citric acid that may lead to the conversion of arsenious oxide into arsenic chloride and arsenic citrate. It may be possible that the chloride or citrate salt of arsenic is less toxic than its oxide form. That is why Unani scholars used lemon juice for detoxification of *Samm al-Fār*.

Arsenic and Human Body

The precise role/essentiality of arsenic for the human body is not known. However, it plays a structural role as a part of membrane phospholipids as suggested by some markers. It can activate or inhibit the activity of enzymes in vitro. The presence of arsenic has been observed in more than twenty five human tissues and body fluids including vital organs such as brain, heart, liver, kidney, lungs, pancreas and spleen. It can cross the blood brain barrier and placental barrier. Deficiency of arsenic in humans has not been reported, however low serum arsenic levels have been seen in hemodialysis and CNS disease patients. Inorganic arsenic primarily (70 to 80%) is excreted through urine, and remaining is excreted through feces, sweat, breath and milk. The organic arsenic is less toxic to the human body and readily excretes (Vohra, 2007).

Toxicological and Pharmacological Studies of *Kushta Samm al-Fār*

Chronic Toxicity of *Kushta Samm al-Fār*

Ansari, *et al.* conducted the dose dependent chronic toxicity of *Kushta Samm al-Fār*. The study drug was prepared by the method described in National Formulary of Unani Medicine. The study was conducted on healthy Wistar rats of either sex in four groups of 10 animals each. Group I served as control, while the rest three groups were served three dose levels of the test drug, i.e. low (8.75 mg–1 kg), medium (17.50 mg–1 kg) and higher (26.25 mg–1 kg) for three months. Chronic toxicity studies were evaluated on the basis of standard parameters. The study revealed dose dependent toxicity. In low dose (group II), *Kushta Samm al-Fār* did not produce remarkable toxic effects. In group III and IV, mild to moderate toxicity was seen (Ansari *et al.,* 2013).

Comparative Toxicity Studies on Various Dosage Forms of *Samm al-Fār*

Irshad, *et al.* conducted a comparative study on toxicity and elemental analysis of *Samm al-Fār Mudabbar*, *Kushta Samm al-Fār* prepared by classical method (KSCM) and *Kushta Samm al-Fār* prepared by muffle furnace (KSMF). The arsenic quantity of three forms was estimated by atomic absorption spectrometer and found as: *Samm al-Fār Mudabbar* - 386 ppm, KSCM - 6.388 ppm and KSMF

- 3.623. On analysis of acute and sub-acute toxicity studies, it was found that *Samm al-Fār Mudabbar* has more toxic effects than *Kushta* form. Further, it was also noticed that KSMF showed less toxicity in comparison to KSCM. It was also observed that the presence of arsenic in KSMF is close to the WHO permissible limit of arsenic in Unani formulations (Irshad *et al.,* 2011).

Analgesic, Anxiolytic and Proconvulsant Effect of *Kushta Samm al-Fār*

Siddiqui, *et al.* conducted analgesic, anxiolytic and proconvulsant activity on two varieties of *Kushta Samm al-Fār,* namely *Kushta Samm al-Fār Ātshakī* and *Kushta Samm al-Fār Qawī* in animals (rat and mice). It was found that both varieties of *Kushta* in the dose of 5 mg/kg/po has significant analgesic and anxiolytic activity. However, both varieties exhibited proconvulsant activity and it was concluded that these drugs have to be used by epileptic prone individuals with caution (Siddiqui *et al.,* 1999).

Use of Arsenic in Modern Medicine

Arsenic trioxide is an anticancer drug, sold under the brand name Trisenox and used to treat refractory or relapsed acute promyelocytic leukemia. It was approved for medical use in the United States in 2000. It is available for intravenous use only in the strength of 1 mg/mL (10 mg). It's mechanism of action is not fully understood. It is believed that it induces apoptosis (programmed cell death) of promyelocytic leukemia cells (Anonymous, 2019). It was included in the World Health Organization's 21st List of Essential Medicines published in 2019 as one of the safest and most effective medicines needed in a health system (Anonymous, 2019).

Conclusion

In Unani Medicine, *Samm al-Fār* has been described in *Darja Chahārum* (drugs having temperament of fourth degree). In the present review, all aspects related to the use of *Samm al-Fār* in humans have been covered. Studies have suggested that calx of *Samm al-Fār* prepared with modern method is quite safe for use as it was found to have arsenic element within the range permissible by the WHO for Unani formulations. Long term use of calx is to be avoided as it can cause harmful effects on the body. In a study, it was also observed that the quantity of element arsenic reduced after the detoxification process, a fact that validates the recommendation of Unani physicians for detoxification of *Samm al-Fār* before use. Only few pharmacological studies, e.g. analgesic, anxiolytic and proconvulsant activity have been conducted till date. This review will help researchers explore further studies relating to the therapeutic uses mentioned by Unani scholars.

References

1. Ali, S.S. (2004) Unani Advia Mufrada, 10th ed., National Council for Promotion of Urdu Language, New Delhi, pp. 306-308.
2. Anonymous (2000) Arsenic: Chapter 6.1, Air Quality Guidelines, 2nd ed., WHO Regional Office for Europe Copenhagen, Denmark.
3. Anonymous (2001) National Formulary of Unani Medicine, part-III, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH), Ministry of Health & Family Welfare, Government of India, pp. 33, 37, 38.
4. Anonymous (2006) National Formulary of Unani Medicine, part-I, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH), Ministry of Health & Family Welfare, Government of India, pp. 9, 13, 53, 76, 202, 204.
5. Anonymous (2006) National Formulary of Unani Medicine, part-IV, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH), Ministry of Health & Family Welfare, Government of India, p. 16.
6. Anonymous (2007) National Formulary of Unani Medicine, part-II, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH), Ministry of Health & Family Welfare, Government of India, pp. 41, 43.
7. Anonymous (2008) National Formulary of Unani Medicine, part-V, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH), Ministry of Health & Family Welfare, Government of India, pp. 16, 37, 58, 128.
8. Anonymous (2010) Arsenic Toxicity: What Are the Standards and Regulation for Arsenic Exposure, accessed from https://www.atsdr.cdc.gov/csem/csem.asp?csem=1&po=8 on July 07, 2020.
9. Anonymous (2010) The Unani Pharmacopoeia of India, part-II, vol.-II, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH), Ministry of Health & Family Welfare, Government of India, p. A-31.
10. Anonymous (2011) National Formulary of Unani Medicine, part-VI, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH), Ministry of Health & Family Welfare, Government of India, pp. 16, 24, 66, 91, 93.
11. Anonymous (2016) Unani System of Medicine – The Science of Health and Healing, Ministry of AYUSH, Government of India.

12. Anonymous (2017) Arsenic Factsheet, accessed from https://www.cdc.gov/biomonitoring/Arsenic_FactSheet.html on July 07, 2020.

13. Anonymous (2019) Arsenic Trioxide Monograph for Professionals, Accessed from https://www.drugs.com/monograph/arsenic-trioxide.html on July 07, 2020.

14. Anonymous (2019) World Health Organization model list of essential medicines: 21st list 2019, World Health Organization, Geneva

15. Anonymous (2020) Arsenicosis, accessed from https://www.lenntech.com/library/diseases/arsenicosis/arsenicosis on July 07, 2020.

16. Anonymous (YNM) Detection, Prevention and Management of Arsenicosis in India - A Field Guide, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India.

17. Ansari, A.P., Wadud, A., Jahan, N., Nagaraj, R.B., Irshad, S. and Iqbal, S.M.F. (2013) Evaluation of chronic toxicity of Kushta *Samm al-Fār* (calx of Arsenic trioxide), *Journal of Xenobiotics*, 3(1): 14-18.

18. Bardale, R., (2011) Principles of forensic Medicine and Toxicology, Jaypee Brothers Medical Publishers (P) Ltd, Delhi, pp. 451-452.

19. Fazlullah, M. (1907) Makhzanul Mufradat maroof ba Jami-ul-advia, Matba Swatantra, Lucknow, p. 250.

20. George, M.W. (2017) United States Geological Survey Minerals Year Book, Arsenic- 2017 (Advance Release)

21. Ghani, M.N. (1921) Khazaain-al-Advia, Idara Kitaabul Shifa, New Delhi, pp. 840-844.

22. Hakeem, M.A. (2011) Bustan-ul-Mufradat, Aijaz Publishing House, Delhi, p. 346.

23. Ibn Baitar, Z.U. (1999) Kitab al-Jami li-Mufradat al-Adviya wal-Aghzia, vol. III (Urdu translation), CCRUM, New Delhi, p. 146.

24. Irshad, S., Wadud, A., Najeeb, J., Sofi, G. and Ghufran, A. (2011) Comparative toxicity study of various forms of *Sam-mul-far* (Arsenic trioxide) in mice, *Indian Journal of Traditional Knowledge*, 10(4): 721-726.

25. Jabin, F. (2011) A guiding tool in Unani Tibb for maintenance and preservation of health: A review study, *Afr. J. Tradit. Complement. Altern. Med.*, 8(5 Suppl): 140-143.

26. John, F. (2013) Arsenic - the "Poison of Kings" and the "Saviour of Syphilis", *Journal of Military and Veterans Health*, 21(4): 11-17.

27. Jolliffe, D.M.A. (1993) History of the use of arsenicals in man, *Journal of the Royal Society of Medicine*, 86(5): 287-289.

28. Kabiruddin, M. (1951) Makhzan-ul-Mufradat, National Fine Printing Press, Hyderabad, pp. 351-352.

29. Khan, M.A. (2013) Muheet-e-Azam, vol. 3, Central Council for Research in Unani Medicine, New Delhi, pp. 143-144.

30. Lubhaya, R. (2001) Bayanul Advia, vol. I, Idara Matbul Sulemani, Lahore, pp. 291-292.

31. McMahon, T.F. and Chen, J. (2001) Hazard Identification and Toxicology Endpoint Selection for Inorganic Arsenic and Inorganic Chromium, FIFRA Scientific Advisory Panel Background Document, pp. 1-36.

32. Michael, F., Hughes, Barbara, D., Beck, Yu Chen, Ari, S., Lewis, David and Thomas, J. (2011) Arsenic Exposure and Toxicology: A Historical Perspective, *Toxicol Sci.*, 123(2): 305-332.

33. Mustehasan and Ali, A. (2004) Advia Madania, Aijaz Publishing House, Delhi, pp. 47-48.

34. Mustehasan and Azhar, M.U. (2020) Hajar ul Yahood (Jew's Stone) Anti-Urolithiatic Unani Mineral Drug-Review, *World Journal of Pharmaceutical Research*, 9(6): 1127-1133.

35. Nadkarni, K.M. (1976) Indian Materia Medica, 3rd ed. vol. II, Popular Prakashan Private Limited, Mumbai, pp. 15-19.

36. Prakash, V.B. (1998) Importance of metallic micronutrients in Ayurveda, Conference On Health & Environment, pp. 1-8.

37. Rafiquddin, M. (1985) Kanzul Advia Mufrada, University Publication Unit, AMU, Aligarh, pp. 425-426.

38. Shamsi, S., Tajuddin and Afaq, S.H. (2010) Comparative analysis of arsenic estimation in crude and processed arsenious oxide (*Sam-mul-far*), *International Journal of Pharma. Research & Development*, 2(4): 005.

39. Shaw, D. (1998) Risks or remedies? Safety aspects of herbal remedies in the UK, *J. R. Soc Med.,* 91(6): 294-296.

40. Siddiqui, R., Vohra, D. and Vohra, S.B. (1999) Proconvulsant effects of calcined arsenic preparations used in Unani Medicine, *Indian Journal of Pharmacology*, 31(2): 150-152.

41. Singh, D. (1949) Unani Daravyagun Vigyan, Nirnay Sagar Press, Mumbai, pp. 466-467.

42. Tariq, N.A. (2004) Taj-ul-Mufradat (Khawas-ul-Advia), Idara Kitaab-ul-Shifa, New Delhi, pp. 465-466.

43. Vohra, S.B. (2007) Encyclopedia of Medical Elementology, New Age International (P) Limited Publishers, New Delhi, pp. 18-28.

सारांश

यूनानी खनिज औषधि *सम्म अल–फ़ार* (आर्सेनिक ट्राइऑक्साइड) की ऐतिहासिक मानवजातीय–भेषजगुण विज्ञानीय समीक्षा

***मुस्तेहसन, मिस्बाहुद्दीन अज़हर, सोफ़िया नौशीन**

खनिज/भारी धातुएं जैसे आर्सेनिक, पारा और सीसा विभिन्न यूनानी यौगिक मिश्रणों के अभिन्न अंग हैं और सदियों से विषहरण के लिए इनका उपयोग किया जाता रहा है। *सम्म अल–फ़ार* खुरासान के द्वीप और पहाड़ों में चांदी के अयस्कों में प्राकृतिक रूप से पाया जाने वाला एक गंधहीन और बेस्वाद तत्व है। रासायनिक रूप से *सम्म अल–फ़ार* आर्सेनिक ट्राइऑक्साइड है। *सम्म अल–फ़ार* पर आधारित यूनानी औषधीय मिश्रण तंत्रिका, यौन, त्वचा, श्वसन संबंधी विकारों, रक्तहीनता, ज्वर और जोड़ो के दर्द के उपचार में उपयोग किये जाते हैं। वर्तमान समीक्षा में औषधीय उपयोग का इतिहास, उपस्थिति, स्वभाव, चिकित्सीय कार्य एवं उपयोग, मानव शरीर हेतु महत्व, विषाक्तता अध्ययन, भेषजगुण विज्ञानीय अध्ययन और वर्तमान परिदृश्य में आर्सेनिक ट्राइऑक्साइड के उपयोग से संबंधित जानकारी संकलित की गई है।

शब्दकुंजी: *आर्सेनिक ट्राइऑक्साइड, कुश्ता सम्म अल–फ़ार, सम्म अल–फ़ार,* यूनानी चिकित्सा, *ज़रनीख़ अब्यज़*

Etiopathogenesis of *Mālankhūliyā Marāqī* (A Syndrome of Depression and Anxiety due to Gastro-Intestinal Pathology)

*[1]Mohammed Yasir,
[1]Ataullah Fahad,
[2]Irfan Ahmad
and
[3]Mohammad Fazil

[1]Assistant Professor, Department of Ilmul Amraz, Ajmal Khan Tibbiya College, AMU, Aligarh, UP

[2]Research Officer (Unani), Regional Research Institute of Unani Medicine, Mumbai

[3]Research Officer (Unani) Scientist-IV and Incharge, HAK Institute for Literary and Historical Research in Unani Medicine, New Delhi

Abstract

Mālankhūliyā Marāqī is a syndrome characterised by depression, anxiety, disturbed mental functions, along with belching, abdominal bloating, burning and pain. It is considered as a secondary disease of mental functions caused due to gastro-intestinal, hepatic or other abdominal pathology as described in Unani medical literature. The description of cases of *Mālankhūliyā Marāqī* in classical Unani books and that of hypochondriasis in old medical books of allopathy is similar in clinical presentation and line of treatment. With evolutionary changes in the understanding of pathology, the concept of hypochondriasis transformed to purely mental disorder. But the gut brain theory comes out to support existing clinical manifestations having mixed symptoms of gastro-intestinal tract and mind. Irritable Bowel Syndrome (IBS) has been explained with different theories proposed till date including gut-brain axis theory. An attempt has been made in this paper to analyse the symptoms and presentation of *Mālankhūliyā Marāqī* in correlation with hypochondriasis and IBS. Possible scientific etiopathogenesis behind this syndrome too has been reviewed and summarised. This effort may be helpful in future for holistic management of such treatment resistant disorders.

Keywords: Gut-Brain Axis, Hypochondriasis, Irritable Bowel Syndrome, *Mālankhūliyā Marāqī*, Unani Pathology

Introduction

Unani Medicine has description of mood disorders, including depression, under an umbrella term *Mālankhūliyā* (melancholia). Apart from depression, *Mālankhūliyā* encompasses other psychiatric disorders, such as schizophrenia, anxiety, obsessive compulsive disorders, etc. *Mālankhūliyā* is defined as disturbance in the intellect characterised with fear, sadness and suspicion (Majusi, 2010). Unani scholars consider abnormal *Sawdā'* (black bile) as the main cause and basis of this disease (Tabari, 1994). It is stated that a type of *Mālankhūliyā* called *Mālankhūliyā Marāqī* is developed due to ascend of vapours of abnormal humour *Sawdā'* from abdomen (i.e. areas below ribs, in stomach, intestine and pelvic region) to brain (Majusi, 2010). According to Qumri, the primary site of pathology is *Marāq* which is external covering of intestine (Qumri, 2008). Generally, *Marāq* is a term used for the soft part of the abdomen below the ribs (Luwis, YNM). It includes skin of abdomen, fascia and (according to some authors) muscular layer (Ibn Sina, 2010; Jeelani, 1998). Most justifiable reason to call this disease *Marāqī* is to differentiate it from other types and indicating its origin with soft abdomen. *Marāq* in Unani literature roughly corresponds

*Author for Correspondence; Email: yasirm7@gmail.com

to the word hypochondrium in conventional medicine. *Mālankhūliyā Marāqī* is also named as *Mālankhūliyā Nāfikh* or *Nafkh Marāqiyya*. These are derivatives of word *Nafkh* meaning flatulence, a common symptom in this disease (Luwis, YNM).

Hypochondriasis is the term used for this disease in the past. Hypochondriasis is a Greek word meaning "below the cartilage". The ancient Greeks derived the concept of hypochondriasis from humoral theories of disease and considered it a special form of melancholia resulting from an excess of black bile (Gerog *et al.*, 1998). In his Anatomy of Melancholy, Robert Burton (1621) associated "windy, hypochondriacal melancholy" with "sharp belching, fulsome crudities, wind and rumbling in the guts", the patient feeling "fearful, sad, anxious (and) discontent" (Bound, 2006).

Conceptual Transformation of Hypochondriasis

The description of hypochondirasis changed over a period of time from a spectrum of disturbance in mood, suspicion, intellect having physical basis to only a narrow phenomenon of pure mental aspect. In the seventeenth century, Thomas Sydenham, an English physician, argued that hypochondriasis occurred only in men and was equivalent to hysteria occurring in females. Also, around this period, Descartes proposed that the mind and body were separate entities, and there could be no causal relation between the two (Gerog *et al.*, 1998). In the 18th century, hypochondria retained a material basis, although nerve theory shifted its emphasis from the body's fluids and humours to its solids and fibres. Robert Whytt's Observations on the Nature, Causes, and Cure of those Disorders which have been commonly called Nervous Hypochondriac, or Hysteric, suggested hypochondria derived from "too great delicacy of the nervous system together with some morbid matter in the blood". This focus on nervous debility continued to the next century with the idea of neurasthenia encompassing many symptoms traditionally associated with hypochondria, now redefined as a mental affliction. In the 1880s, the American neurologist George Beard confined the term hypochondriasis to cases with a definite delusion of physical disease, originating in exhaustion or abuse to the brain, stomach, and genitalia. Similarly, psychoanalytic accounts emphasised organic basis of hypochondria. Sigmund Freud included the term in the "actual" as opposed to "psycho" neuroses in his Sexuality in the Aetiology of the Neuroses (1898). Today, hypochondriasis is regarded as a mental health issue associated with chronic anxiety about one's health, and linked to anxiety and depression. Rather than being viewed as a disease in its own right, it is usually regarded as a somatoform complaint that has physical effects unattributable to any other known psychological or physical cause. Whether any cases of hypochondriasis will be redefined in the future with changes in diagnostic practice is uncertain; in the 19th century many sufferers

of multiple sclerosis were regarded as hypochondriacal (Bound, 2006). Although the psychiatric theories put forward have multi dimensions and varied aspects we will discuss here only its physical and mental inter relationship. The cycle of theoretical understanding in mind body relationship is still revolving. Previously, it was discarded, then again being accepted with slight change of terminologies. Now observation of association of psychiatric disorders with physical diseases lead the scientist search for biological and molecular changes appearing in brain & blood. Even the relation between gut and brain was previously discarded, this again considered in pathogenesis of diseases like IBS, ulcerative colitis, etc. Dictionaries still retain the term "hypochondrium" as an anatomical term but now we define "hypochondria" as a person's recurrent fear that he has a serious disease or is about to get one. It's different from "malingering", which is pretending to be sick (Beeling and Francis, 2012). Presently, the understanding of this disease is limited. Somatic symptom disorder also known as hypochondriasis is characterized by high levels of anxiety and persistent worry about somatic signs and symptoms that are misinterpreted as having a known medical disorder (Sadock *et al.,* 2015).

Relation with Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a gastrointestinal (GI) disorder characterized by altered bowel habits in association with abdominal discomfort or pain in the absence of detectable structural and biochemical abnormalities. Across the IBS subtypes, the presentation of symptoms may vary among patients and change over time. Patients report the most distressing symptoms to be abdominal pain, straining, myalgias, urgency, bloating and feelings of serious illness (Saha, 2014). Seven case-control studies evaluating IBS and three evaluating ulcerative colitis (UC) were included. All IBS and UC studies reported excess prevalence and severity of depression as well as anxiety, relative to healthy controls. The prevalence of depression in excess of healthy controls was 39% in UC case-control trials and 33% in IBS studies, and excess anxiety was present in UC (42%) and IBS (19%) case-control trials as well. Anxiety and depression scores were higher (representing more severe symptoms) in both UC and IBS patients compared to healthy controls. Visceral hyperalgesia is a common finding in IBS subjects, and brain imaging, suggests altered responses in IBS compared to controls (Shah *et al.,* 2014). The presentation of IBS has clinical similarities with that of *Mālankhūliyā Marāqī*.

Epidemiology

In general medical clinic population, the reported 6-month prevalence of hypochondriasis is 4 to 6 percent, but it may be as high as 15 percent. Although the onset of symptoms can occur at any age, the disorder most commonly appears

in the persons aged 20 to 30 years. Some evidences indicate that this diagnosis is more common among blacks than whites (Sadock *et al.,* 2015). Patients with hypochondriasis are three times more likely than the general population to have personality disorders, the prognosis is believed to be more promising for patients without personality disorders (Suzanne *et al.,* 2003). Throughout the world, about 10–20% of adults and adolescents have symptoms consistent with IBS (Longo, *et al.,* 2012). According to Unani literature, emotionally weaker persons are prone to develop such psychiatric diseases. These patients are unable to bear usual psychological trauma or have low threshold for it. Occurrence of this disease is common in *Sawdāwī* temperaments (Majusi, 2010).

Clinical Features

According to Unani medical literature, patients with *Mālankhūliyā Marāqī* present clinically with complaints of fear, sadness, doubt, belching, excessive salivation, burning sensation in abdomen, bloating and pain between shoulders (probably due to flatulence). Sometimes, food may not absorb at all and vomited out as it is. This type of *Mālankhūliyā* is comparatively easy to treat (Qumri, 2008; Razi, 2008).

In conventional literature, there are five elements that define the hypochondrisis and fear is one of them. Others are doubt (he doubts the doctor), embodiment (his body contains diseases he can't see), information (he's informed) and narrative (every suspicion of disease is a story) (Beeling and Francis, 2012). Patients with somatic symptom disorder believe that they have a serious disease that has not yet been detected and they cannot be persuaded to the contrary. They may maintain a belief that they have a particular disease or, as time progresses, they may transfer their belief to another disease. Their convictions persist despite negative laboratory results, the benign course of the alleged disease over time, and appropriate reassurances from physicians. Yet, their beliefs are not sufficiently fixed to be delusions. Somatic symptom disorder is often accompanied by symptoms of depression and anxiety and commonly coexists with a depressive or anxiety disorder (Sadock *et al.,* 2015). Nearly one-half of patients with hypochondriasis also have dysthymia (45%) or major depression (43%). Other comorbidities include phobias (38%), somatization disorder (21%), panic disorder (17%) and obsessive-compulsive disorder (8%) (Suzanne, 2003). Hypochondriasis is so commonly observed in cases of depressive disorders that it is considered an important aspect of measuring depression severity in a universally accepted valid scale of depression known as Hamilton depression rating scale (Reynolds and Kobak, 1995).

In the second volume of Annesley's work on Indian Diseases that zealous observer has made some remarks on the influence of morbid secretions in the bowels upon the mental faculties. Few clinical cases of hypochondriasis with effective

treatment outcome were discussed as supporting evidence of old concept of *Mālankhūliyā Marāqī* (Annesley, 1892).

In IBS, about 50% patients referred to hospital meet the criteria for a psychiatric diagnosis. A range of disturbances are identified, including anxiety, depression, somatisation and neurosis. Panic attacks are also common (Colledge *et al.,* 2010). Perceived symptoms of IBS consist of abdominal pain or discomfort, bloating, diarrhoea and constipation. Other than gastrointestinal symptoms, fatigue is very common (Saha, 2014). Between 25 and 50% of patients with IBS complain of dyspepsia, heartburn, nausea and vomiting. Patients with IBS frequently complain of abdominal distention and increased belching or flatulence, all of which they attribute to increased gas. In addition, patients with IBS tend to reflux gas from the distal to the more proximal intestine, which may explain the belching

Table 1: Comparative analysis of *Mālankhūliya Marāqī,* Hypochondriasis and IBS

Attributes	*Mālankhūliya Marāqī*	Hypochondriasis	Irritable Bowel Syndrome
Nomen-clature	Psychiatric symptoms related to soft abdomen	Somatic symptom disorder historically related to hypochondrium	Disorder of intestinal movements due to disruption of communication between gut and brain
Epide-miology	Occurs in emotionally weaker persons and having *Sawdāwī* temperament	Common in persons of 20-30 years age. More in black that whites	young women affected 2 to 3 times more than men
Psychiatric symptoms	Fear, depression, doubt	Fear, depression, anxiety, doubt, embodiment, delusion	anxiety, depression, somatisation and neurosis
Somatic symptoms	Belching, excessive salivation, burning sensation in abdomen, bloating and pain	Multiple somatic symptoms like pain, fatigue and other motor or sensory symptoms	abdominal pain or discomfort, bloating, belching or flatulence, diarrhoea, and constipation, dyspepsia, heartburn, nausea, vomiting, fatigue
Site of pathology	Abdomen and brain	Brain	Gut & brain
Effect of psychiatric treatment	Responds well to anti-inflammatory, carminative, laxative and antipsychotic Unani medicines	Antidepressants, placebo and Cognitive and behavioural treatment help	Symptomatic, Antidepressants, antibiotics, probiotics and psychotherapies are effective

(Longo *et al.*, 2011). These symptoms are attributed in Unani Medicine to abnormal humour *Sawdā*' and resemble that of *Mālankhūliyā Marāqī*.

Etiopathogenesis

In Unani literature, inflammations related to liver, intestine or any abdominal structure are considered as the cause of this disease. Obstruction in mesenteric channels or intense heat in the vessels (supplying blood to liver) are also supposed as the etiology (Ibn Sina, 2010; Razi, 2008). These abnormalities cause accumulation of abnormal *Sawdā*' in abdomen. Humours and vapours from here ascend to the brain causing disturbance in its functions. Unani physicians have observed some characteristics of this disease and tried to establish the holistic pathogenesis of *Mālankhūliyā*. According to them, emotions like fear and grief, thoughts, suspicion and unreality are related to excess *Sawdā,* and decreased function of *Rūḥ*. The *Mizāj* (temperament) of humour *Sawdā*' is *Bārid Yābis* (cold and dry) which is exactly opposite to the *Mizāj* of *Rūḥ-i-Dimāgh* or *Rūḥ Nafsānī* (responsible for active mental functioning), thus excess *Sawdā*' deteriorates the functions of *Rūḥ* (Ibn Sina, 2010; Ibn Rushd, 1987). This disease is caused by *Sawdā*' having properties like darkness and black colour. Such properties of *Sawdā*' disturb thought process similar to what we observe in real darkness, e.g. we feel fear in the darkness. *Sawdā*' vapours induce darkness and blackness in *Rūḥ Nafsānī* and produces sadness (*Gham*), rumination of thought (*Fikr*) and fear (*Khawf*) (Razi, 2008).

In the historical literature of hypochondriasis, it is mentioned that since hypochondriasis originated in the blood and humours, factors such as excessive study or an inappropriate diet could allow "gross, melancholy humours" to rise up from the abdomen and corrupt the brain (Bound, 2006).

Present understanding of hypochondriasis explains that persons with this disorder augment and amplify their somatic sensations; they have low thresholds for, and low tolerance of, physical discomfort. For example, what persons normally perceive as abdominal pressure, persons with somatic symptom disorder experience as abdominal pain. They may focus on bodily sensations, misinterpret them, and become alarmed by them because of a faulty cognitive scheme. The sick role offers an escape that allows a patient to avoid noxious obligations, to postpone unwelcome challenges, and to be excused from usual duties and obligations. Somatic symptom disorder is sometimes a variant form of other mental disorders, among which depressive disorders and anxiety disorders are most frequently included. An estimated 80 percent of patients with this disorder may have coexisting depressive or anxiety disorders. The patients who meet the diagnostic criteria for somatic symptom disorder may be somatizing subtypes of these other disorders. The psychodynamic school of thought holds that aggressive and hostile wishes towards others are transferred (through

repression and displacement) into physical complaints. The anger of patients with this disorder originates in past disappointments, rejections and losses, but the patients express their anger in the present by soliciting the help and concern of other persons and then rejecting them as ineffective. This disorder is also viewed as a defence against guilt, a sense of innate badness, an expression of low self-esteem, and a sign of excessive self-concern. Pain and somatic suffering thus become means of atonement and expiation (undoing) and can be experienced as deserved punishment for past wrongdoing (either real or imaginary) and for a person's sense of wickedness and sinfulness (Sadock *et al.,* 2015).

The IBS encompasses a wide range of symptoms and a single cause is unlikely. It is generally believed that most patients develop symptoms in response to psychosocial factors, altered gastrointestinal motility, altered visceral sensation or luminal factors (Colledge *et al.,* 2010). In a population study, a strong relationship was found between gastrointestinal symptoms, anxiety disorders and depression (Haug *et al.,* 2002). Altered gastrointestinal motility, visceral hypersensitivity, post infectious reactivity, brain-gut interactions, alteration in fecal micro flora, bacterial overgrowth, food sensitivity, carbohydrate malabsorption, and intestinal inflammation all have been implicated in the pathogenesis of IBS. Serotonin is largely present in the enterochromaffin cells in the gut and is a major regulator of the peristaltic reflex and sensory relays in the gut. There are two lines of evidence supporting the view that serotonin regulation is abnormal in IBS. The release of serotonin in plasma appears to be reduced in those with constipation-predominant IBS (IBS-C) and increased in diarrhea-predominant IBS (IBS-D). A defect in serotonin signalling was noted in both IBS and ulcerative colitis, with a reduction in normal mucosal serotonin and serotonin transporter immunoreactivity in both diseases (Saha, 2014).

Irritable bowel syndrome has clinical similarities with *Mālankhūliyā Marāqī*. Hence the mechanism underlying IBS may be supposed to be the possible pathogenesis behind *Mālankhūliyā Marāqī*. The similarities of hypochondriasis and IBS with *Mālankhūliyā Marāqī* is shown comparatively in Table 1.

Evidence indicates that microbiota communication with the brain involves the vagus nerve, which transmits information from the luminal environment to CNS. In fact, neurochemical and behavioral effects were not present in vagotomized mice, identifying the vagus as the major modulatory constitutive communication pathway between microbiota and the brain (Carabotti *et al.,* 2015).

Conclusion

Mālankhūliyā Marāqī has many evidences of its prevalence in present human population and is not an imaginary concept. The exact correlation of this disease with any conventional disease entity is difficult but symptoms and

clinical presentations are related with diseases like IBS, depressive and anxiety disorders and hypochondriasis. Being holistic in nature, proven age old, time-tested effective Unani regimes may help better control this emotional burden on the patient and society. Further clinical observations should be made on large scale with proper study design to assess the nature, etiology, pathogenesis and prognosis of this disease.

References

1. Annesley, J. (1829) Remarks on Hypochondriasis, Melancholia, and Insanity, *Med Chir Rev*, 11(22): 510–512.
2. Beeling and Francis, C. (2012) A Condition of Doubt: The Meanings of Hypochondria, Oxford University Press, New York, p. 1-90.
3. Bound, F. (2006) Historical keyword Hypochondria, *The Lancet,* 367(9505): 105.
4. Carabotti, M., *et al.* (2015) The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems, *Ann Gastroenterol*, 28(2): 203-209.
5. Colledge, N.R., *et al.* (2010) Davidson's Principles and of Practice of Medicine, 21st Edition, Churchill Livingstone, Edinburgh, pp. 904-906.
6. Gerog, H., *et al.* (1998) Comprehensive Clinical Psychology, Somatoform Disorders. Elsevier, pp. 546-560.
7. Haug, T.T., *et al.* (2002) Are anxiety and depression related to gastrointestinal symptoms in the general population? *Scand J Gastroenterol,* 37(3): 294-298.
8. Ibn Rushd, A.W.M. (1987) Kitabul Kulliyat, 1st Edition, CCRUM, New Delhi, pp. 139-140.
9. Ibn Sina A.A.H. (2010) Al Qanoon Fit Tibb, Vol. 4, Idara Kitabush Shifa, New Delhi, pp. 553-558.
10. Jeelani, G. (1998) Makhzanul Jawahar, Ejaz Publishing House, New Delhi, pp.781.
11. Longo, D., *et al.* (2011) Harrison's principles of Internal Medicine. 18th Edition, McGraw-Hill Companies, New York, pp. 1016-1017.
12. Luwis, M. (YNM) Al-Munjid Arabi-Urdu (Urdu translation by Abdul Hafeez Balyawi), Afzal Shareef Printers, Lahor, pp.305.
13. Majoosi, A.I.A. (2010) Kaamilus Sana'ah, Vol. 1, CCRUM, New Delhi, pp. 462-464.
14. Qamri, A.M.H. (2008) Ghina Muna, CCRUM, New Delhi, pp. 20-24.
15. Razi, A.M.Z. (2008) Kitabul Fakhir Fit Tibb. Vol.1. Part.1, CCRUM, New Delhi, pp. 96-113.

16. Reynolds, W.M. and Kobak, K.A. (1995) Reliability and Validity of the Hamilton Depression Inventory: A Paper-and-Pencil Version of the Hamilton Depression Rating Scale Clinical Interview, *Psychological Assessment*, 7(4): 472-483.

17. Sadock, B.J., *et al.* (2015) Kaplan & Sadock's synopsis of psychiatry, Wolters Kluwer, Philadelphia, pp. 347-349.

18. Saha, L. (2014) Irritable bowel syndrome: Pathogenesis, diagnosis, treatment, and evidence-based medicine. *World J Gastroenterol,* 20(22): 6759–6773.

19. Shah, E., *et al.* (2014) Psychological disorders in gastrointestinal disease: epiphenomenon, cause or consequence, *Annals of Gastroenterology*, 27:224-230.

20. Suzanne, B., *et al.* (2003) Don't be fooled by hypochondria, *Current Psychiatry*, 2(9):27-39

21. Tabri, A.M. (1994) Al Mualajatul Buqratiya, Vol.1, CCRUM, New Delhi, pp. 374-376.

सारांश

मालन्खूलिया मराक़ी (जठरांत्र विकृति के कारण अवसाद और चिंता का एक सिंड्रोम) का इटियोपैथोजेनेसिस

***मोहम्मद यासिर, अताउल्लाह फ़हद, इरफ़ान अहमद, मोहम्मद फ़ाज़िल**

मालन्खूलिया मराक़ी एक सिंड्रोम है जिसमें डकार, पेट फूलना, जलन और दर्द के साथ–साथ अवसाद, चिंता, अशांत मानसिक क्रियाओं की समस्याएं होती हैं। यूनानी चिकित्सा साहित्य में इसे जठरांत्र, यकृत या पेट की अन्य विकृति के कारण मानसिक क्रियाओं के द्वितीयक रोग के रूप में जाना जाता है। क्लासिकल यूनानी पुस्तकों में *मालन्खूलिया मराक़ी* के रोगियों का वर्णन और एलोपैथी की पुरानी चिकित्सा पुस्तकों में हाइपोकॉन्ड्रियासिस का वर्णन नैदानिक प्रस्तुति और उपचार में एक समान है। विकृति के समझ में विकासवादी परिवर्तन के साथ हाइपोकॉन्ड्रियासिस की अवधारणा विशुद्ध रूप से मानसिक विकार में बदल गई। लेकिन आंत मस्तिष्क सिद्धांत जठरांत्र पथ और मस्तिष्क के मिश्रित लक्षणों वाले मौजूदा नैदानिक स्वरूप के पक्ष में है। उद्दीप्य आंत्र सहलक्षण को अब तक के विभिन्न सिद्धांतों के साथ समझाया गया है जिसमें आंत मस्तिष्क अक्ष सिद्धांत शामिल है। इस पेपर में *मालन्खूलिया मराक़ी* के लक्षणों और प्रस्तुति का हाइपोकॉन्ड्रियासिस और उद्दीप्य आंत्र सहलक्षण के सहसंबंध में विश्लेषण करने का प्रयास किया गया है। इस सिंड्रोम के पीछे संभावित वैज्ञानिक एटियोपैथोजेनेसिस की समीक्षा की गई और इसे संक्षेप में प्रस्तुत किया गया है। भविष्य में यह प्रयास ऐसे उपचार प्रतिरोधी विकारों के समग्र उपचार के लिए सहायक हो सकता है।

शब्दकुंजी: आंत मस्तिष्क अक्ष, हाइपोकॉन्ड्रियासिस, उद्दीप्य आंत्र सहलक्षण, *मालन्खूलिया मराक़ी,* यूनानी विकृति

Importance of *Quwwat Mudabbira-i-Badan* (Medicatrix Naturae) in the Management of Diseases

[1]**Ansari Izhar Ahmad,**
[*2]**Masroor Ali Qureshi,**
[3]**Jaleel Ahmad**
and
[4]**B.S. Usmani**

[1]Lecturer, EMS Deptartment, Alghad International Applied Medical Science College, Nejran, Saudi Arabia

[2]Research Officer (Unani) Scientist-IV, Regional Research Institute of Unani Medicine, CCRUM, Ministry of AYUSH, Government of India), J.J. Hospital Compound, Byculla, Mumbai

[3]Professor, Department of Kulliyat, Z.V.M. Unani Medical College and Hospital, Pune

[4]Professor, Department of Kulliyat, Dr. M.I.J. Tibbia Unani Medical College, Mumbai

Abstract

Quwwat Mudabbira-i-Badan (Medicatrix Naturae) has prime importance in Unani Medicine. It has been mentioned as a very important factor in diagnosis, disease and treatment. According to the philosophy of Unani Medicine, there are two main conditions of the body, i.e. health and disease. Having complete knowledge of the health condition is more important than the knowledge of the diseased condition of the body. The reason behind this is that we can treat the pathological conditions only when we know the normal condition of the human body. According to Unani theory, there are seven major determinants of human health, which are known as *Umūr Ṭabī'iyya* (determinants) that control all the physiological functions of the body. The faculty that controls *Umūr Ṭabī'iyya* is known as *Quwwat Mudabbira-i-Badan* (QMB). The health is thus controlled by the QMB (Medicatrix Naturae). Medicatrix Naturae is responsible for the improvement and process of bio-transformation in the human body. If any disturbance emerges in the QMB, the health of the body will be disturbed and the diseased condition will emerge. The QMB will be fighting with the disease to remove it from the body and bring the body in healthy condition. In this review, outcome of literary survey concerning the QMB covering all the important books of Unani Medicine has been presented to highlight its importance.

Keywords: Medicatrix Naturae, *Quwwat Mudabbira-i-Badan, Umūr Ṭabī'iyya,* Unani Medicine

Introduction

According to the philosophy of Unani Medicine, there are two main conditions of the body – health and disease (Ahmed, 1980; Ahmed, 1992; Aqsarai, 1907; Ibn Sina, 1932; Nafisi, 1935a, 1935b, 1954; Tabari, 1981). Having complete knowledge of the health condition is more important than the knowledge of the diseased condition of the body. The reason behind this is that we can treat the pathological conditions only when we know the normal condition of the human body.

According to the theory of Unani Medicine, there are seven major determinants of human health known as *Umūr Ṭabī'iyya* that control all the physiological functions of the body (Ahmed, 1980, Ahmed, 1992; Azmi, 1991; Azmi, 1995; Hamdani, 1980; Ibn Rushd, 1980; Ibn Sina, 1927; Ibn Sina, 1930a; Ibn Sina, 1930b; Ibn Sina, 1932; Ibn Sina, 1945; Ibn Sina, 1998; Ibn Sina, 1999; Kabiruddin, 1916; Kabiruddin, 1952; Khan, 2000; Nafisi, 1935a; Nafisi, 1935b; Nafisi, 1954). The faculty that controls all these seven *Umūr* is known as *Quwwat Mudabbira-i-Badan* (QMB). The health is thus controlled by *Quwwat Mudabbira-*

*Author for Correspondence; E-mail: doctormasroorali@gmail.com

i-Badan. The *Quwwat Mudabbira-i-Badan* is responsible for the improvement and process of bio-transformation in the human body (Ibn Sina, 1998, 1999). If any disturbance emerges in the QMB, the health of the body will be disturbed resulting in diseased condition.

Methodology

The authors conducted literature survey of the relevant classical literature and books available in the Versova Tibbia College Library, Aligarh Muslim University Library, Aligarh and Khuda Baksh Library, Patna. Over fifty important Unan textbooks were reviewed. *Al-Qānīīn fi'l-Ṭibb* (The Canon of Medicine) of Ibn Sina (980-1035 CE), *Iksīr al-Qulūb* of Akbar Arzani (1722), *Kitāb al-Kulliyāt* of Ibn Rushd (1126 – 1198), *Dhakhīra Khawārizm Shāhī* of Ismail ibn Husayn Jurjani (1040–1136), *Kāmil al-Ṣanā'a al-Ṭibbiyya* of Ali ibn Abbas Majusi (925-994) were some of the important books that were comprehensively reviewed.

Importance of *Quwwat Mudabbira-i-Badan* (QMB) in Unani Medicine

In Unani Medicine, *Quwwat Mudabbira-i-Badan* (QMB) has prime importance. It has been mentioned as a very important factor in diagnosis, disease and treatment (Nafisi, 1935a). Unani physicians believe that it is *Quwwat Mudabbira-i-Badan* (QMB) which is the curator of diseases, not the physician. Physicians only help the QMB to cure the disease. The role of medicines is to strengthen the QMB and help it in curing the diseases. Physicians are known as *Ṭabī'ī*, which is derived from *Ṭabī'at* (Ibn Rushd, 1980; Ibn Sina, 1927, 1930a, 1930b, 1932, 1945, 1998, 1999; Kabiruddin, 1916, 1952; Nafisi, 1935a, 1935b, 1954).'Physis' is the synonym of the QMB or *Ṭabī'at*. Physiology is also derived from this word. In Unani Medicine, the word *Umūr Ṭabī'iyya* is used instead of physiology. Therefore, the physis also controls *Umūr Ṭabī'iyya*. Nature, *Ṭabī'at*, physis, vis medicatrix naturae and *Quwwat Mudabbira-i-Badan* (QMB) are all synonyms.

We can say that many diseases are cured by the QMB with its administrative regimen and curative power without the help of physicians and drugs. This is usually seen in the people residing in villages or rural areas, whose *Ṭabī'at* is very powerful.

In the external environment, the way the decomposed matters are destroyed and disappeared, the functions of the internal environment are not escaped from nature's rules and regulations. Initial abnormal changes and concealed disease effects are not easily felt. After some time, the bad effects emerge out. Less appetite, mental and physical tiredness are bearable till the QMB is able to control the disease matter in the body. Once the natural struggle between the QMB and disease matter takes place, diseases can be felt and symptoms are clearly shown. Thereafter, the QMB starts its function to cure the disease.

In the human body, the QMB helps to maintain the balance of the human body system and to keep the temperament of the body normal. If anything makes the body temperament abnormal or disturbs it, the QMB immediately controls it and brings it to normal and thus the health is maintained and also the *Ḥarārat Gharīziyya* (innate heat or body energy) is regained to normal state (Azmi, 1995; Hamdani, 1980; Ibn Rushd, 1980; Ibn Sina, 1927; Jamiee, 1963; Jurjani, 1878; Masihi, 1963; Nafisi, 1935a).

Ḥarārat Gharīziyya is the instrument of the QMB. With the help of this instrument, the QMB serves the faculties (natural, vital, and psychic), fulfils their administration of functions and maintains the body health. If *Akhlāṭ* (humours) are imbalanced, the temperament becomes abnormal and *Ḥarārat Gharīziyya* is weakened. As a result of it, the faculties become unable to fulfil their functions (Ahmed, 1992).

Relation of *Quwwat Mudabbira-i-Badan* with Disease

It is the object of all trained physicians and surgeons to combine scientific methods with human ingenuity and sympathetic insight in the struggle against disease. Every endeavour is made to build up constructive and defensive mechanisms by indicating the laws of life, growth and health. All known causes are dealt with, either by neutralizing or removing the cause from the patient, or removing the patient from the cause. Such management is usually considered under three factors relating to environment, nourishment and hindrances. Firstly, there must be, for instance, such conditions as rest, warmth, brightness and oxygen in the environment. Secondly, calculated supplies of necessary food, vitamins and water must be given for nourishment. Thirdly, the conditions that hinder recovery, comfort or health are considered and changed, if possible. Such states as pain, strain, stress and undue movement are brought under control. Poisons and all hostile influences are removed. Poorly functioning organs are assisted. Bowels, kidney and skin are encouraged towards normal removal of wastes. Venous and arterial circulation of blood is supported, or, if necessary, increased in the affected area. Medicines may be given to make desirable changes in the body. Surgical procedures may be required for the same purpose.

But none of the above-mentioned items really heals the patient. Cough medicines and digestive powders do not heal. Castor oil never healed anyone. Foments do not heal. Penicillin and antibiotics do not heal - they only discourage the germs. Surgery does not heal; it involves further wounding of the body. These all create conditions in which we expect healing to occur. In other words, we have faith that the result will follow if we do these things. But healing is really given by a power more ultimate than the body or mind and is not under direct human control. It is God who heals.

Theories of health and disease have always followed the pattern of the current philosophy of the age. In early history, ideas of magic were common, gods and spirits were blamed for diseases, and healing was associated with priests and temples. The early Unani philosophers spoke of the importance of four elements - air, water, fire and earth. Hence the concept of four temperaments - sanguine, phlegmatic, choleric, and melancholic - ruled all thinking about disease (Qadir, 2016).

Following the later materialistic philosophies, the methods of observation and experiment opened up new worlds of thought regarding the disease, its causes and effects. The first classification was made in terms of changes in organs. The next was based on changes in cells and made possible by the invention of the microscope. The discovery of bacteria followed and brought the most productive lines of inquiry into the habits and effects of numerous external agents which invade the body (Arzani, 1987; Gazroni, 1911; Ibn Sina, 1927; Jamiee, 1963, Jurjani, 1878; Kabiruddin, 1916; Kabiruddin, 1952; Majusi, 1889a; Majusi, 1889b; Masihi, 1963; Qurrah, 1987). Other causes were then found such as nutritional deficiency, hereditary and constitutional factors. Due to consideration of all these viewpoints, the causation of disease was shown to be very complex. To add to the difficulties it was found that in ill health the whole personality, the body, mind, and spirit are involved, and results differ from person to person. This demonstrated the vital importance of the reaction to the impact of the complex causes. An apparently similar situation may mean for one person a trivial illness but for another a long course of serious disease (Ahmed, 1980).

Before we discuss treatment methods or strategy to care illness, it is necessary to understand that *Ṭibb* perceives the process of illness in two ways - by means of a sudden/temporary cause or a progressive/prolonged cause. The sudden/temporary cause is a result of a sudden change; motional, dietary or environmental excess, e.g. shock, overheating foods, extreme changes in weather and excessive awakening. This condition will result in symptoms that will arise almost immediately and can impair functions of the body. Changing these causative factors or counteracting them will enable the QMB to overcome this temporary condition and restore health. If these influencing factors are not eliminated, this condition can lead to more serious illnesses (Bhikha & Haq, 2003).

The second or long-term category of illnesses progresses in three stages. The beginning stage occurs at a vascular level in the humours of the body, resulting in a humoural imbalance. This occurs when the quality or quantity of humours is altered as a result of the influence of the six factors. If this condition is not reversed, over a period, the humoural imbalance will progress to the next stage, which is a functional imbalance, whereby the functions of the body will be affected (the functions of the circulatory, digestive systems, etc.). Finally,

when the imbalanced humour invades tissue/organs, it will result in structural damage. This structural imbalance is the final stage and associated with serious disease conditions (Hamdani, 1980).

Now that we have spoken about stages of illnesses, let us discuss how *Ṭibb* views microorganisms as the cause of infections and illnesses. The Greco-Arabic physicians had theorized many external influences that invade the body. As they did not have the technology to identify bacteria and viruses, they did not name them and were unable to study them. Contemporary *Ṭibb* practice understands the existence of microorganisms and regards them as important components in any ecosystem.

Ṭibb believes that a change at the humoural level provides a medium for micro-organisms to cause infections. Whilst the micro-organism such as mycobacterium tuberculosis is responsible for the diseased condition of tuberculosis and the micro-organism pneumococci is responsible for the condition of pneumonia, it is, in fact, the six factors (*Asbāb Sitta Ḍarūriyya*) that actually determine whether this micro-organism can lead to the diseased state (Bhikha & Haq, 2003).

According to *Ṭibb* philosophy, infections from micro-organisms are possible only when an imbalance occurs at the humoural level, which provides the environment for the micro-organism to thrive. This is evident from the above explanation of the three stages of illness and explains why some people are susceptible to bacterial infection and others are not. An infection will only take place in persons whose humours are not in the state of balance.

According to *Ṭibb*, many viral infections are actually an imbalance at the humoural level. During the infection period, the QMB helps in restoring this imbalance at humoural level. It is common knowledge that the 'viral' symptoms of cold are overcome with rest and heating foods. The implementation of the six factors (*Asbāb Sitta Ḍarūriyya*) needed to assist the QMB in restoring balance in the humours will overcome most 'viral' conditions within a few days.

Relation of *Quwwat Mudabbira-i-Badan* with Treatment

As we consist of the same primary matter and qualities as the rest of the universe and disease processes also require these primary matters and qualities, we have a lot in common with them. It also means that our bodies can control the environment in which micro-organisms or disease processes try to take hold. A major advantage that *Ṭibb* has over modern medicine is for the fact that modern medicine believes that many illnesses such as hypertension, arthritis, etc., are incurable as the causes are unknown. At best, modern medicine focuses on the 'management' of this illness.

Inspired by the prophetic tradition, which teaches: 'for every illness, there is a cure' (Azmi, 1985), Unani physicians have always aspired to find cures. In

the practice of *Ṭibb*, any illness that is acquired after birth can be completely reversed depending on the extent of tissue or organ damage, age of the patient, compliance to treatment and the six factors (*Asbāb Sitta Ḍaruriyya*). Modern medicine aims at controlling symptoms and managing the illness, whereas *Ṭibb* aims at curing illnesses and managing health (Bhikha & Haq, 2003).

By using the insights of *Ṭibb*, you not only maintain your health but also intervene and thus avoid serious functional and structural damages. The holistic approach of *Ṭibb* is once again highlighted in the way the treatment of illnesses is applied. While signs and symptoms are used to diagnose an illness, treatment can only be effective if the fundamental causes of the illnesses are dealt with. The treatment must include the six factors to ensure that not only are the symptoms treated but the causes of the illnesses are also addressed.

The advice given in 'The Treatment of Illness' lays emphasis on the causes of these illnesses, for example whether it is hot and moist, hot and dry, etc. Implementing the advice of the six factors, even in conjunction with other medications, will enhance the healing process, restoring health more effectively and permanently. The simple herbal recipes can prove beneficial in addressing the conditions and balancing the temperament (Bhikha & Haq, 2003).

Ṭabī'at plays a very important role in the treatment of diseases as discussed in the forgoing pages. The following points should always be kept in mind by a physician while treating a patient:

i. *Ṭabī'at* is the real healer

ii. The physician is only a helper of *Ṭabī'at*

iii. Physicians should not interfere with *Ṭabī'at* in the initial stage of the disease. Only energizing dietary measures may be taken.

iv. When the physician feels that *Ṭabī'at* is unable to over-power disease-causing agent, he should start treatment promptly by administering suitable drugs to the patient, so that *Ṭabī'at* can control the disease in due course (Azmi, 1995).

The principles of treatments in Unani Medicine are more rational in comparison with modern medicine (allopathic). Drugs are administered in modern medicine as soon as disease manifest, hampering natural effort of the defence mechanism of the body and sometimes causing unnecessary harm to various faculties of the body.

Unani Medicine's approach in dealing with diseases is quite different. "Drugs are not prescribed in the beginning and the full opportunity is given to *Ṭabī'at* to control the disease. The only help given from outside are certain dietary measures and nothing else. The drug is the last resort and it is given when it appears that *Ṭabī'at* has failed to check the disease" (Azmi, 1995).

The only correct procedure is to dig, nourish and weed the earth, see that water and sunlight and all necessary elements are supplied, and discourage pests and all hostile influences. This allows the normal laws of growth to apply, the natural sap and force of life to flow and apples to grow. The active agent is the same *Quwwat Mudabbira-i-Badan* namely the creative action of God. It is only through the existence of the factors of equilibrium, homeostasis, and the QMB that medicine can help to correct an undesirable bodily condition.

Conclusion

It is concluded on the basis of a detailed review of the literature that the QMB (*Quwwat Mudabbira-i-Badan*) is responsible for the improvement and process of bio-transformation in the human body. If any disturbance emerges in the QMB, the health of the body will be disturbed and the diseased condition will emerge. The QMB fights with the disease to remove it from the body and bring the body in healthy condition.

Acknowledgements

Authors are grateful to the principal and management of Anjuman-i-Islam and Dr. M.I.J. Tibbia Unani Medical College, Versova, Mumbai for kind guidance and moral support.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Reference

1. Ahmed, S.I. (1980) Introduction to *Al-Umūr Ṭabīʿiyya*, Saini Printers, Delhi, pp. 34, 206-210.
2. Ahmed, T. (1992) *Kulliyyāt-i-Umūr Ṭabīʿiyya*, Nizami Press, Victoria Street, India, pp. 116-117.
3. Aqsarai, J. (1907) *Sharḥ Mūjiz,* Urdu translation by Ayyub Ahmad Israili, Munshi Nawal Kishore, Lucknow, p. 11.
4. Arzani, M.A. (1987) *Iksīr al-Qulūb*, Tarjuma *Mufarriḥ al-Qulūb*, Urdu translation by Hakim Sayyad Baquir, Munshi Nawal Kishore, Lucknow, pp. 7-9.
5. Azmi, A.A. (1991) *Mabādiyāt-i-Ṭibb*, Taraqqi Urdu Bureau, New Delhi, pp. 130-31.

6. Azmi, A.A. (1995) Basic Concepts of Unani Medicine, Department of History of Medicine, Jamia Hamdard, New Delhi, pp. 128-29.

7. Azmi, A.R. (1985) *Ṭibb-i-Nabvī*, Al-Darulsalfiya, India, pp.168-171.

8. Bhikha, R., Haq, M.A. (2003) *Ṭibb* - Routes to Health, Mountain of Light, South Africa, pp. 103-5.

9. Gazroni, S. (1911) *Kulliyyāt Sadīdī*, Urdu translation by Sayyad Abid Husain, Munshi Nawal Kishore, Lucknow, p. 8.

10. Hamdani, S.M.K.H. (1980) *Uṣūl-i-Ṭibb*, Litho Colour Printers, Aligarh, p. 15.

11. Ibn Rushd, A.M. (1980) *Kitāb al-Kulliyyāt*, Urdu translation by Central Council for Research in Unani Medicine, Printo Experts, Delhi, pp. 89-91.

12. Ibn Sina (1927) *Al-Qānīīn fi'l-Ṭibb,* Urdu translation by Ghulam Husnain Kanturi, Munshi Nawal Kishore, Lucknow, vol. I, pp. 76-77.

13. Ibn Sina (1930a) *Tarjama-o-Sharḥ Kulliyyāt-i-Qānūn,* Urdu translation by Mohammed Kabiruddin, Barqi Press, Delhi, vol. I, p. 140.

14. Ibn Sina (1930b) *Al-Qānīīn fi'l-Ṭibb,* English translation by O. Cameron Gruner, Luzac and Co, London, pp. 19-20.

15. Ibn Sina (1932) *Tarjama-o-Sharḥ Kulliyyāt-i-Qānūn,* Urdu Translation by Mohammed Kabiruddin, Barqi Press, Delhi, vol. II, pp. 659, 660, 664.

16. Ibn Sina (1998) *Al-Qānīīn fi'l Ṭibb,* English translation by Mazhar H. Shaha T, Naveed Clinic, Karachi, pp. 127-28.

17. Ibn Sina (1999) *Al-Qānīīn fi'l Ṭibb,* English translation by Laleh Bakhtiar (ed. Seyyed Hossein Nasr), Great Books of the Islamic Inc., United State of America, p. xvii.

18. Ibn Sina (1945) *Tarjama-o-Sharḥ Kulliyyāt-i-Qānūn,* Urdu translation by Khawaja Rizwan Ahmed, Daftarut Talif, Karol Bagh, Delhi, pp. 231-254.

19. Jamiee, M.S. (1963) *Muḥīṭ al-Amrāḍ*, Sayyad Imtiyaz Ali Taj, Nazim Majlis Taraqqi Adab, Lahore, p. 360.

20. Jurjani, A.H. (1878) *Dhakhīra Khawārizm Shāhī*, Urdu translation by Hadi Husain Khan, Munshi Nawal Kishore, Luckonw, pp. 234-237.

21. Kabiruddin, M. (1916) *Sharḥ*-i-*Asbāb,* (Tarjuma Kabir), Hikmat Book Depot, Hydrabad, Vol IV, pp. 83-89.

22. Kabiruddin, M. (1952) *Risala Jarasim aur Ṭabī'at,* Daftarul Masih, Hyderabad, pp. 6, 7, 15, 32, 33, 44-48, 51.

23. Khan, K.Z. (2000) *Kulliyāt-i-Ṭibb,* Aejaz Pub. House, Delhi, p. 90.

24. Majusi, A.A. (1889a) *Kāmil al-Ṣanā'a al-Ṭibbiyya,* Urdu translation by Gulam Husnain Kuntoori, Matbah Nawal Kishor, Lucknow, vol.1, pp. 15, 172, 228, 294, 340, 595.

25. Majusi, A.A. (1889b) *Kāmil al-Ṣanā'a al-Ṭibbiyya,* Urdu translation by Gulam Husnain Kuntoori, Matbah Nawal Kishor, Lucknow, vol. 2, p. 39.

26. Masihi, A.S.I. (1963) *Kitāb al-Mi'a,* (ed. S G House Mohiuddin Qaqdri Sharfi), Islamic Publication Society, Hyderabad, p. 89.

27. Nafisi, B. (1935a) *Tarjama-o-Sharḥ Kulliyāt-i-Nafīsī,* Urdu translation by Mohammed Kabiruddin, Shoukat Printing Press, Lahore, vol. 1, pp.15, 61, 63, 132-33,144-45, 164-68, 175, 179, 203, 280.

28. Nafisi, B. (1935b) *Tarjama-o-Sharḥ Kulliyāt-i-Nafīsī*, Urdu Translation by Mohammed Kabiruddin, Shoukat Printing Press Lahore, Pakistan, vol. 1, pp. 429, 527, 531.

29. Nafisi, B. (1954) *Tarjama-o-Sharḥ Kulliyāt-i-Nafīsī*, Urdu Translation by Mohammed Kaabiruddin, Daftar-ul-Masih, Noor-ul-Umrah, Hydrabad, vol. I, pp. 383, 385, 429, 527, 531-33, 660, 708, 709.

30. Qadir, A. (2016) *Tārīkh-i-Ṭibb-o-Akhlāqyyāt,* 6th ed., Adab Publishing House, New Delhi, pp. 34-35.

31. Qarshi, A. (1947) *Sharaḥ Mūjiz al-Qānūn Ifāda-i-Kabīr,* Urdu translation by Mohammed Kabiruddin, Matba Islami Bazar, Hydrabad, pp. 14, 26, 27, 143, 166, 188-91, 193, 203.

32. Qurrah, S.B. (1987) *Tarjama Ḍakhīra Thābit ibn Qurrah,* Urdu translation by Sayyad Ayyub Ali, Litho Colour Printers, Aligarh, p. 2.

33. Razi, M. (1961) *Kitāb al-Murshid,* Urdu translation by Raziul Islam Nadvi, Taraqqi Urdu Bureau, Delhi, pp. 100-2.

34. Tabari, A.R. (1981) *Firdaws al-Ḥikma fi'l-Ṭibb*, Urdu translation by Rashid Ashraf Nadvi, Matba Naved Printing Press, Nizamabad, Karachi, pp. 68, 203, 235, 259, 279, 285, 762.

सारांश

रोगों के उपचार में *कुव्वत मुदब्बिरा–ए–बदन* (मेडिकेट्रिक्स नेचुराइ) का महत्व

अन्सारी इज़हार अहमद, *मसरूर अली कुरैशी, जलील अहमद, बी.एस. उस्मानी

यूनानी चिकित्सा में *कुव्वत मुदब्बिरा–ए–बदन* (मेडिकेट्रिक्स नेचुराइ) का बहुत महत्व है। निदान, रोग और उपचार में एक बहुत ही महत्वपूर्ण तत्व के रूप में इसका उल्लेख किया गया है। यूनानी चिकित्सा के दर्शनशास्त्र के अनुसार शरीर की दो मुख्य स्थितियां हैः– स्वास्थ्य और रोग। शरीर की रोगग्रस्त स्थिति के ज्ञान की तुलना में स्वास्थ्य स्थिति का पूर्ण ज्ञान होना अधिक महत्वपूर्ण है। इसके पीछे कारण यह है कि हम पैथेलॉजिकल स्थितियों का उपचार तभी कर सकते हैं जब हम मानव शरीर की सामान्य स्थिति के बारे में जानते हों। यूनानी सिद्धांत के अनुसार मानव स्वास्थ्य के सात प्रमुख निर्धारक हैं जिन्हें *उमूर तबीईया* (निर्धारक) के रूप में जाना जाता है जो शरीर के सभी शारीरिक कार्यों को नियंत्रित करते हैं। जो शक्ति *उमूर तबीईया* को नियंत्रित करती है उसे *कुव्वत मुदब्बिरा–ए–बदन* के रूप में जाना जाता है। इस प्रकार *कुव्वत मुदब्बिरा–ए–बदन* (मेडिकेट्रिक्स नेचुराइ) द्वारा स्वास्थ्य नियंत्रित किया जाता है। मेडिकेट्रिक्स नेचुराइ मानव शरीर में जैव–परिर्वतन के सुधार और प्रक्रिया के लिए जिम्मेदार होता है। यदि *कुव्वत मुदब्बिरा–ए–बदन* में कोई समस्या आती है तो शरीर के स्वास्थ्य में समस्या होगी और रोगग्रस्त स्थिति सामने आएगी। *कुव्वत मुदब्बिरा–ए–बदन* शरीर से समस्या को दूर करने और शरीर को स्वस्थ स्थिति में लाने के लिए रोग से लड़ रहा होगा। इस समीक्षा में यूनानी चिकित्सा की सभी महत्वपूर्ण पुस्तकों को आच्छादित करते हुए *कुव्वत मुदब्बिरा–ए–बदन* से संबंधित साहित्यिक सर्वेक्षण के परिणाम इसके महत्व को उजागर करने के लिए प्रस्तुत किए गए हैं।

शब्दकुंजीः मेडिकेट्रिक्स नेचुराइ, *कुव्वत मुदब्बिरा–ए–बदन, उमूर तबीईया,* यूनानी चिकित्सा

Prophylactic and Curative Potential of *Qurṣ-i-Ghāfis* Against Carbon Tetrachloride Induced Hepatic Injury in Rats

*[1]Shamshad Alam and [2]Naeem A. Khan

[1]Department of Ilmul Advia, A.K. Tibbiya College, AMU, Aligarh, Uttar Pradesh - 202002

[2]Department of Ilmul Advia, A.K. Tibbiya College, AMU, Aligarh, Uttar Pradesh - 202002

Abstract

The present study was undertaken to evaluate anti-hepatotoxic effect of *Qurṣ-i-Ghāfis,* a pharmacopoeial compound preparation against CCl_4 induced liver toxicity in rats. Albino rats were used for the experiment and divided into 2 major groups – prophylactic (protective) and curative groups. Each group was further subdivided into 5 test groups consisting of 6 animals in each group. Group I served as healthy control. Group II received CCl_4 (2 ml/kg ip), group III, IV and V received silymarin (100mg/kg B.W.) and test drug in crude (700 mg/Kg) as well as in extract form (330 mg/ kg) respectively by oral route for 7 days. On day 6, all the animals in each group except group I were administered CCl_4 (2 ml/kg IP) and after 48 hours of CCl_4 administration, these rats were subjected for protective effect evaluation. Similarly, the animals in all the curative groups received a single dose of CCl_4 (2 ml/kg IP) on day 2 followed by the respective drug treatment as in protective group for 7 days to evaluate the curative effect of the test drug. The blood was collected and anti-hepatotoxic potential was assessed by the estimation of biochemical markers, viz. SGPT and SGOT. In addition, MDA levels and histopathological examination were studied to confirm the biochemical changes.

The study showed significant ($p<0.01$) rise in enzymes and histological changes in CCl_4 administered animals, while the treatment with the test drug crude and extract exhibited the ability to counteract the CCl_4 induced hepatotoxicity by decreasing serum enzyme levels and maintained the disintegration of liver structure when compared to the control in protective and curative studies. Extract showed enhanced protective and curative effect in hepatotoxicity induced in rats than crude form. It could be suggested on the basis of observations of the study that the test drug in its both forms has hepatoprotective as well as curative activity but extract is slightly better than the crude form comparable with standard drug silymarin.

Keywords: Anti-Hepatotoxic, Pharmacopoeial compound, Protective and Curative effect, *Qurṣ-i-Ghāfis,* Silymarin

Introduction

Liver is one of the most important multifunctional organs of the body, as it maintains body's metabolic homoeostasis and regulates the internal chemical environment efficiently, but it is more susceptible to be affected by a wide variety of diseases, including acute and chronic hepatitis, fatty liver, cirrhosis and hepatic carcinoma (Kumar *et al.,* 2003). There are alarmingly increasing number of hepatic patients worldwide and about 20,000 deaths occur every year

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

in India due to the liver problems (Sharma *et al.*, 2000). Hepatotoxicity is defined as any injury to the liver that is associated with impaired liver function caused by exposure to a drug or another non-infectious agent (Bahirwani & Reddy, 2014). The intensity of hepatic damage is generally accessed by measuring the activities of hepatic cytoplasmic enzymes [serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), serum alkaline phosphatase (ALP)], serum bilirubin concentration and histological studies (Ravikumar *et al.*, 2005). Hence, we determined the levels of enzymes in the serum such as SGPT and SGOT. Chemical toxins including carbon tetrachloride (CCl_4), acetaminophen, galactosamine and thioacetamide are often used as the model substance causing experimental hepatocyte injury in both *in-vivo* and *in-vitro* conditions (Kim *et al.*, 2014). CCl_4, producing reactive free radicals when metabolized, a widely used hepatotoxic agent induces toxicity in rat liver which closely resembles human cirrhosis via the generation of tricholoromethyl (CCl_3) free radical (El-Saeed *et al.*, 2015). Moreover, CCl_4 increases lipid peroxidation in hepatic cells and induces liver damage and necrosis (Weber *et al.*, 2003). That's why CCl_4 induced liver damage is generally used as experimental model for screening of hepatoprotective and hepatocurative drugs. In spite of tremendous scientific advancement in the field of hepatology in recent years, treatment options for common liver diseases are too limited, and therapy with modern medicine may lack in efficacy. In addition, numerous side effects are associated with synthetic drugs used in treating hepatic disorders (Palanivel *et al.*, 2008). So, the study of the liver ailments and development of drugs for various liver diseases is one of the priority areas of research. Unani Medicine and other traditional medicinal plants have gained popularity over the past decades owing to their safety and efficacy. There are numerous single as well as compound drugs in Unani Medicine that are highly effective and safe for the management of hepatic disorders. Some compound formulations, such as *Jigrīn* (Abul *et al.,* 2004), Icterene (Fatima, 1993), *Majūn Dabīd al-Ward* (Khan *et al.,* 1990), Hepatogard, Biliarin, Livol (Khan, 2001) and Livergen (Qadri, 2003) have been proven scientifically for their activities against the liver injury. However, only a small portion of the hepatoprotective plants as well as formulations used in traditional medicine are pharmacologically evaluated for their efficacy and a number of drugs particularly compound drugs have still not been scientifically investigated for their described effects (Handa & Sharma, 1990). *Qurṣ-i-Ghāfis* (QG) is one such widely used compound preparation for the treatment of various liver ailments such as inflammation of liver, jaundice and fever (Khan, 1921) and prescribed commonly by Unani physicians which has not been investigated so far for its effect in hepatic diseases. *Gul-i-Ghāfis* is the chief ingredient of *Qurṣ-i-Ghāfis* and has been mentioned as liver tonic (*Muqawwī-i-Jigar*), anti-inflammatory (*Muḥallil-i-Awrām*) in Unani classical literature and frequently used in several liver diseases such as inflammation of liver and spleen, jaundice,

hepatic and splenic obstruction, ascites and fever (Kareem, 1880; Ghani, 1921, Khan, 1313H; Ibn Sina, 1906). It is also reported and scientifically evaluated for anti-inflammatory activity (Gupta & Neeraj, 2004), antioxidant (Venskutonis *et al*., 2007) and free radical scavenging activity (Copland *et al*., 2003). The other ingredients of QG i.e. *Blachad* (*Nordostachys jatamansi*) and *Ṭabāshīr* (*Bambusa arundinaea*) are added for their general tonic properties known traditionally to cure the liver disorders and reported as having high antioxidant activity (Joshi & Parle, 2006). There is a relation between antioxidant and hepatoprotective mechanisms that has aroused the present study. However, comparative studies on prophylactic (protective) and curative potential of the test drug on CCl_4 damaged rat liver has not been investigated so far. Thus, the current study aims to determine potential impact of QG in combating liver dysfunction induced by carbon tetrachloride in rats by measuring liver function tests, TBARS test as well as histopathological examination of liver.

Materials and Methods

Ingredients of *Qurṣ-i-Ghāfis* (Khan, 1921)

1.	*Gul-i-Ghāfis*	(*Agremonia eupatoria*) 60 gm
2.	*Balchad*	(*Nordostachys jatamansi*) 30 gm
3.	*Tabāshīr Safaid*	(*Bambusa arundinacea*) 14 gm

Preparation and Dosing of Test Drug

The ingredients of *Qurṣ-i-Ghāfis* were purchased from the herbal market in Aligarh and New Delhi and identified and authenticated at the Department of Ilmul Advia, Aligarh Muslim University, Aligarh. All the crude drugs of QG were dried to make a powder and homogenized in water for crude administration in aqueous medium. A 50% ethanol extraction was also made through Soxhlets Apparatus (Anonymous, 1968; Anonymous, 1987) and dissolved/suspended in water for oral administration to the animals. Both the forms of the compound drug collectively were used for screening the protective and curative effects against CCl_4 induced liver damage. The doses for animals were determined by extrapolating the Unani human dose range by multiplying it by conversion factor of 7 (Dhawan, 1982). The doses of *Qurṣ-i-Ghāfis* thus calculated for albino rats as 700 mg/kg, and 330 mg/kg crude and extract forms respectively.

Chemicals

CCl_4, n-butanol, acetic acid were purchased from Thomas Baker Pvt. Limtd. Mumbai, sodium dodecyle sulphate, thiobarbituric acid were purchased from Otto

Kemi Mumbai, 1, 1, 3, 3-tetraethoxypropane (Sigma USA), Silymarin (Sigma-Aldrich, Germany), Folin's reagent (CDH, Mumbai), AST, ALT, estimation kits (Span Diagnostic Ltd, Surat), Olive oil, Formalin were purchased from SD Fine Chemicals, Chennai and all other reagents were of analytical grade.

Animals

Albino rats of either sex weighing 125-175 gm were used for the experiment. The rats were randomly selected and divided into five groups with six animals in each group for both protective as well as curative study. So, total 60 animals were utilized for both (protective and curative study). They were housed in clean polypropylene cages and the room temperature was maintained at 25 ± 1^0 C with 12 hour light and dark cycle. All the animals received standard diet (Amruta Labs, Pune) and water *ad libitum*. The animals were deprived of food for 12 hours before the treatment. The study protocol was approved by the Institutional Animal Ethics Committee (IAEC) before commencement of the experiment.

Experimental Design

The animals were divided into 5 groups, each comprising six animals. Except normal control, all other groups (CCl_4 treated, standard, test drug crude and extract treated) received carbon tetrachloride (CCl_4) 50% v/v in olive oil (2 ml/kg of body wt.) intraperitoneally on 6^{th} day (for protective study) and on 2^{nd} day (for curative study) to induce hepatotoxicity along with their routine treatment. The normal control group received normal saline orally in equal volume of the test drug. The standard group received Silymarin 100 mg/kg orally for 7 days. The animals kept in group IV & V received treatment of QG crude and extract suspended in vehicle at doses of 700 mg/kg and 330 mg/Kg orally. On the 8^{th} day, all the rats were sacrificed under ether anesthesia and blood was collected from each animal for serum analysis and liver was removed and fixed in 10% formalin for histopathological studies of the liver to determine the degree of hepatic damage (Devaraj *et al.*, 2011).

Preparations of Samples for Biochemical Studies

The blood and liver were collected after sacrificing the animals. The blood was kept for 30 minutes without disturbing and centrifuged for 15-20 minutes at 5000 rpm to separate the sera and stored at 4^0C. The serum of each animal of all groups were estimated for ALT, AST (Reitman and Frankel 1957). In addition, Malonaldialdehyde (MDA) as a lipid peroxidation parameter was measured in serum based on the reaction of thiobarbituric acid (TBARS) with MDA (Okhawa *et al.,* 1979) which is an index of lipid peroxides (Lowry *et al.,* 1951).

Histopathological Observations

For the histopathological study, the livers of rats were immediately removed and the tissues were fixed in 10% formalin for a period of at least 24 hours. Care was taken to keep the volume of the fixative (Mukherjee, 1988). The tissue was processed and sections were cut. Thereafter, the sections were stained with H&E (haematoxylin and eosin) dye and observed the histopathological changes by a photomicroscope under various magnifications.

Statistical Analysis

Data was presented as mean ± standard error and analyzed using one way ANNOVA test, followed by pair-wise comparison of various groups by LSD. The analysis was carried out by using the software of the https://analyse-it.com/. $P<0.05$ was considered significant.

Results

CCl_4 in the dose of 2ml/kg of body weight i.p. produced acute hepatic damage in the negative control group (carbon tetrachloride treated) when compared with the normal control. There was significant rise in levels of enzymes (biochemical parameters) SGOT, SGPT, and TBARS as compared to the normal control. The level of Malondialdehyde (MDA), SGOT and SGPT in CCl_4 treated animals in the protective group were found to be 4.92 ±0.45 (η mole of MDA / mg of protein), 111.7 ± 3.60 (U/ml) and 97 ± 6.61(U/ml), whereas, the concentration of MDA, SGOT and SGPT in the plain control animals of protective group were found to be 1.18± 0.095 (η mole), 26.3 ± 2.94 (U/ml) and 27.7± 3.40 (U/ml) respectively that is much lesser than that in the CCl_4 group ($P<0.001$). The standard Silymarin showed significant reduction in all parameters when compared to CCl_4 treated group. Treatment with the test drug in crude and extract forms with CCl_4 intoxication showed decrease in the levels of enzymes SGOT, SGPT, and TBARS. The values for SGOT, SGPT are near normal in extract. This pattern was also followed in the curative group animals ($P<0.001$). The greater concentration of MDA and higher level of SGOT and SGPT in CCl_4 treated animals of both protective and curative groups exhibited the role of wide spread hepatic damage of CCl_4. The rise in MDA, SGOT & SGPT in the test groups (IV & V) which were administered QG in crude or extract form was not found in both protective and curative studies, showing protection against CCl_4 liver damage. Result is summarised in (Table A and B) with their respective graphs.

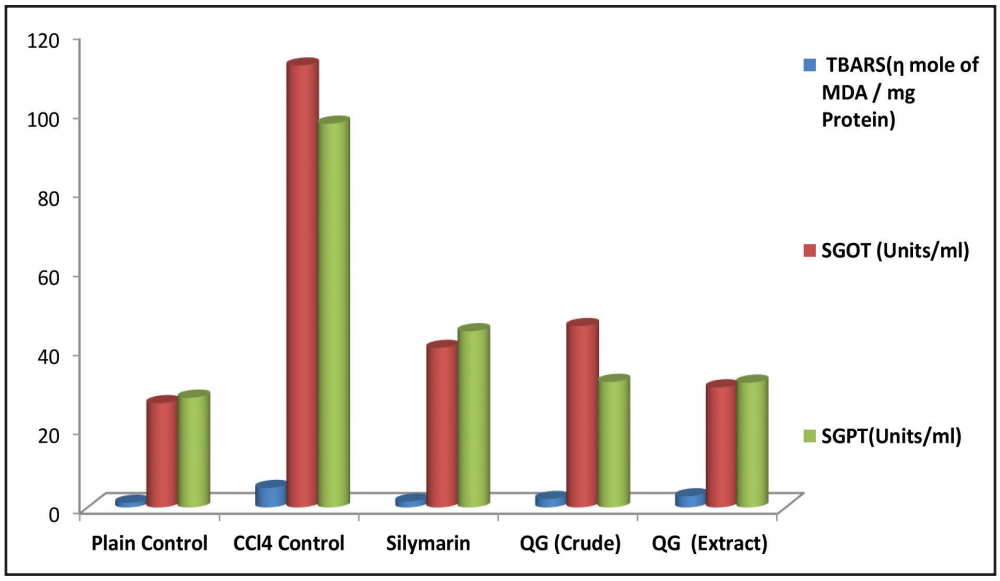
Histopathology

The histopathological studies of the liver showed centrilobular necrosis and vascular congestion with mononuclear cell infiltration in CCl_4 control rats. CCl_4

Table A: Protective effect of *Qurṣ-i-Ghāfis* in CCl_4 mediated hepatic damage

Groups	TBARS (η mole of MDA / mg Protein)	SGOT (Units/ml)	SGPT (Units/ml)
Plain Control	1.18 ± 0.095	26.3 ± 2.94	27.7 ± 3.40
CCl4 (2ml/kg)	4.92 ± 0.45	111.7 ± 3.60	97 ± 6.61
Silymarin (100mg/kg)	1.48 ± 0.05	40.3 ± 3.40	44.5 ± 2.06
QG (Crude) (700mg/kg)	2.12 ± 0.10 a^3	45.8 ± 4.17 a^3	31.7 ± 3.25 a^3 c^2
QG (Extract) (330mg/kg)	2.81 ± 0.20 a^3	30.3 ± 2.64 a^3 c^3	31.5 ± 2 a^3 c^2

(n=6); 1 = P<0.05; 2 = P<0.01; 3 = P<0.001; a = against CCl_4; b = against plain control; c = against Silymarin

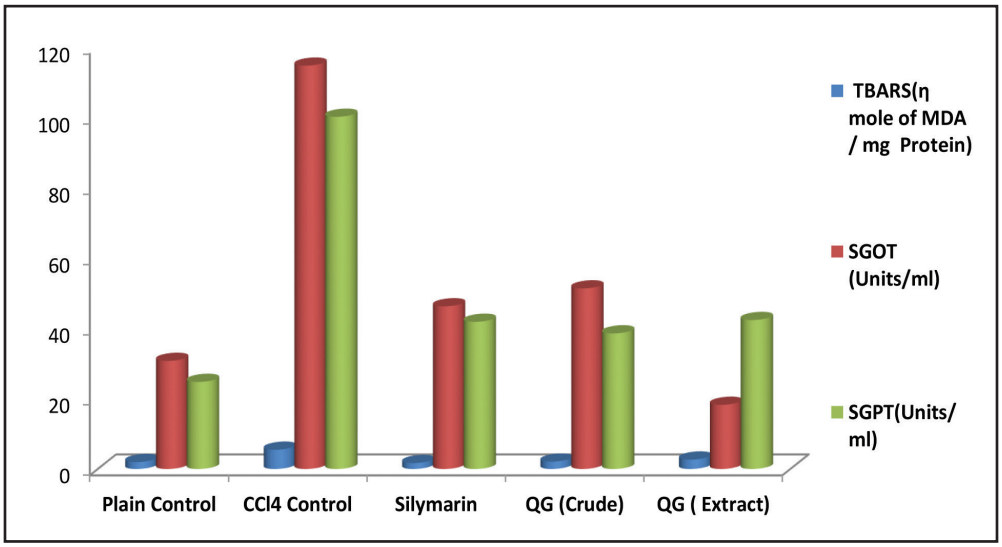


treatment caused marked congestion of central vein and portal triads, indicating fibrosis (Figure 2) in comparison with the normal control where central blood vessels and radiating cords of hepatocytes as well as the vascular sinusoids were observed with no evidence of fatty changes, necrosis or inflammation (Figure 1). The animals treated with Silymarin showed almost normalization of fatty accumulation and necrosis (Figure 3). The animals administered with crude form

Table B: Curative effect of *Qurṣ-i-Ghāfis* in CCl_4 mediated hepatic damage

Groups	TBARS (η mole of MDA / mg Protein)	SGOT (Units/ml)	SGPT (Units/ml)
Plain Control	1.96 ± 0.13	30.7 ± 2.40	24.7 ± 2.58
CCl_4 (2ml/Kg)	5.46 ± 0.45	114.8 ± 3.43	100.2 ± 4.05
Silymarin (100mg/Kg)	1.68 ± 0.10	46.2 ± 2.10	41.8 ± 2.74
QG (Crude) (700mg/Kg)	2.08 ± 0.08 a^3	51.3 ± 4.46 a^3	38.5 ± 4.58 a^3
QG (Extract) (330mg/Kg)	2.67 ± 0.28 a^3	18.2 ± 2.04 a^3 c^3	42.3 ± 7.74 a^3

(n=6); 1 = P<0.05; 2 = P<0.01; 3 = P<0.001; a = against CCl_4, b = against plain control, c = against Silymarin



exhibited intact hepatocytes, some congestion in portal triad. The group received extract form of the test drug showed minimal degree of edema normalization of fatty changes as well as normalization of necrosis of the liver. The maximum protection against hepatic damage was achieved by the both forms of the test drug (Figure 4 and Figure 5). Both the doses forms prevented CCl_4-induced changes in liver. The Silymarin and test drug treated groups showed excellent protection and cure to liver architecture.

Photomicrographs of Histological Studies (Protective and Curative)

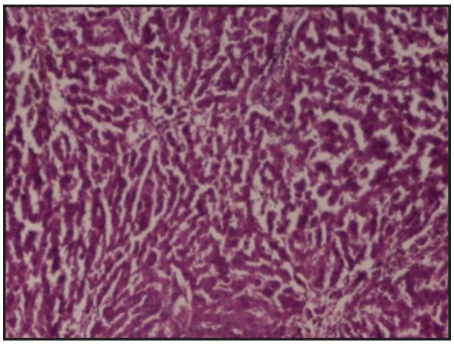


Fig. 1: Plain control (Water only)

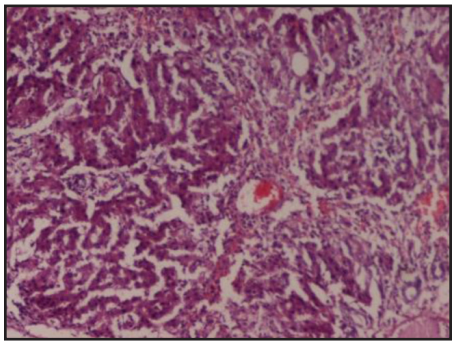


Fig. 2: Negative Control (CCl_4 only)

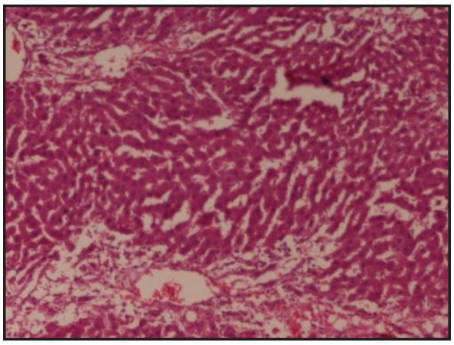


Fig. 3: Standard (Silymarin) + CCl_4

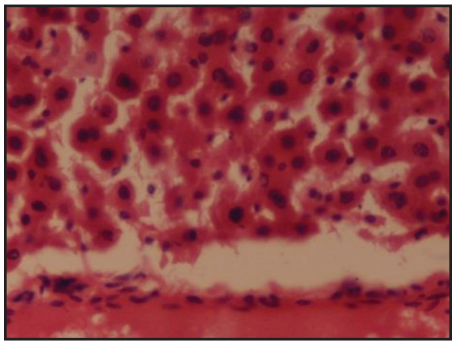


Fig. 4: (Protective) *Qurṣ-i-Ghāfis* (Crude) +CCl_4

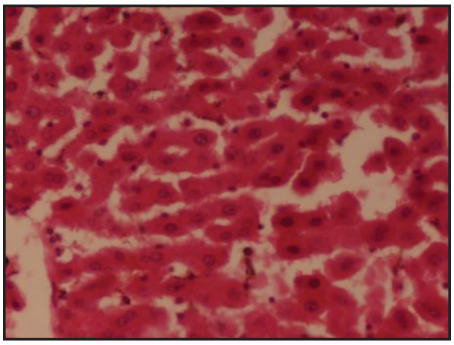


Fig. 5: (Protective) *Qurṣ-i-Ghāfis* (Extract) +CCl_4

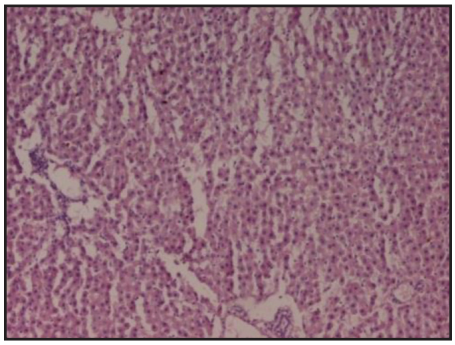


Fig. 6: (Curative) *Qurṣ-i-Ghāfis* (Crude) + CCl_4

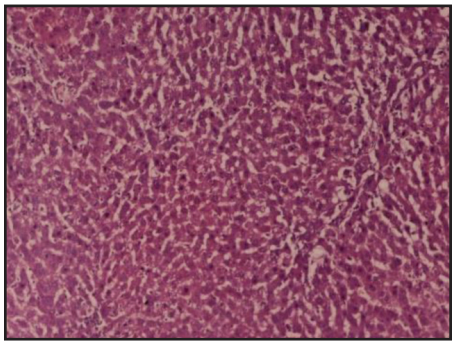


Fig. 7: (Curative) *Qurṣ-i-Ghāfis* (Extract) + CCl_4

Fig. 1: Photomicrograph of the liver of a normal rat shows central blood vessels and radiating cords of hepatocytes as well as the vascular sinusoids with no evidence of fatty changes, necrosis or inflammation.

Fig. 2: Photomicrograph of the liver of a negative control shows centrilobular (acidophilic) necrosis and vascular congestion

Fig. 3: Standard drug (Silymarin) shows mild vascular congestion and peri-vascular infiltrate of mono nuclear cells and fibroblast. No fatty changes.

Fig. 4: The Photomicrograph of *Qurṣ-i-Ghāfis* crude (protective studies) reports less edema, and fewer inflammatory cell.

Fig. 5: In Photomicrograph of *Qurṣ-i-Ghāfis* extract (protective studies) there is intact hepatocytes, edema and kupffer cell noted

Fig. 6: Photomicrograph of the liver of *Qurṣ-i-Ghāfis* crude (curative study) shows intact hepatocytes and no inflammatory cell

Fig. 7: Photomicrograph of the liver of *Qurṣ-i-Ghāfis* extract (curative study) shows congested portal triad some inflammatory cells and no cholestasis

Discussion

The aim of the present evaluation was to study the prophylactic (protective) and curative effects of *Qurse Ghafis* on CCl_4 poisoned liver damage in rats. Several plants and their preparations have shown hepatoprotective property and have been reported for their efficacy in controlling the CCl_4 induced hepatic damage (Luper, 1998). According to the literature available, the compound Unani formulation *Qurṣ-i-Ghāfis* has anti-inflammatory and liver tonic property and frequently used by Unani physicians in various diseases but extensive scientific study was not done on this compound drug. So, in the present study, this formulation was selected to prove its hepatoprotective and curative activity scientifically by using experimental animal models. CCl_4 can cause damage to many tissues in the body. However, the most important primary target organ for CCl_4 induced toxicity in many species is the liver. Therefore, CCl_4 induced hepatic injury is the most common model used for hepatoprotective drug screening (Recknagel, 1983). The signs of hepatoprotective effects of a biological agent are to maintain the normal physiological function of hepatocytes and reduce the damage of intercellular structures from exposure to the toxic agent (Mehdi *et al.*, 2015). The extent of hepatic damage is assessed by the elevated level of biochemical parameters which is attributed to the generation of trichloromethyl free radical which in turn causes peroxidation of lipids of cellular membrane (Mumoli *et al.* 2006). Hepatocellular necrosis leads to very high level of aspartate transaminase and alanine transaminase released from

liver to blood. Between the two, alanine transaminase is a better index of liver injury, as its activity represents 90% of total enzyme present in the body. The decrease in serum transaminase concentration indicates the stabilization of plasma membrane and protection of hepatocytes against the damage caused by CCl_4 (Maheshwara Rao *et al.*, 2014). The data shown in Table A and B reveal the decreased level of serum transaminase in animals treated with crude as well as extract forms of QG indicating the stabilization of plasma membrane and hepatoprotection against the effect of CCl_4 and decreased SGPT concentration evidences the normal functioning of hepatic cells. Further, in the present investigation, MDA was also measured which is an end product of lipid peroxidation which is known as a marker of oxidative stress (Pramod *et al.*, 2008). In this study, CCl_4 increased MDA level in group II which is in agreement with other studies and treatment with Silymarin and QG decreased significantly the levels of MDA in groups III to V. Histological studies of the liver also showed severe damage to the hepatocytes and necrosis is quite prominent in rats in CCl_4 treated group of both hepatoprotective as well as hepatocurative groups (Figure 2) as compared to the control group (Figure 1). Whereas less damage was observed in the test drug treated groups as compared to the CCl_4 treated group (Figures 4 and 5 protective - Figures 6 & 7 curative). Therefore, on the basis of above observations it could be suggested that the test drug in its both forms has hepatoprotective as well as curative activity but extract is slightly better than the crude form and comparable with the standard drug Silymarin. The reason for the variation in the potency of the drug may be due to the presence of phytoconstituents like alkaloids and flavonoids in more concentrated form in the extract. The present finding provides scientific evidence to the therapeutic value of this frequently used compound drug in treating hepatitis and other hepatic disorders.

Conclusion

The findings of the present study suggest that Unani compound formulation QG possesses equally potent prophylactic and curative effect against CCl_4 rendered liver injury in rats. Further studies with individual drugs and their active phytochemicals are needed to understand the exact mechanism of action.

Acknowledgements

The authors wish to thank Prof. Nafees Ahmad Farooqi, Department of Anatomy and Prof. Shaista Vasenwala, Department of Pathology, J.N.M.C., AMU, Aligarh for extending their generous support in conducting the histopathological studies.

References

1. Abul, K.N., Pillai, K.K., Pal, S.N., Aqil, M. (2004) Free radical scavenging and Hepatoprotective activity of Jigrine against Galactosamine induced hepatopathy in rats, *Journal of Ethanopharmacology*, 97(3):521-525.

2. Anonymous (1968) British Pharmacopoeia, General Medical Council, Pharmaceutical Press, London, pp. 1276-77, 1285-88.

3. Anonymous (1987) Physico-chemical Standards of Unani Formulations, Central Council for Research in Unani Medicine, New Delhi, part II, pp. 274, 277.

4. Bahirwani, R., Reddy, K.R. (2014) Drug-induced liver injury due to cancer chemotherapeutic agents, *Seminars in Liver Disease*, 34: 162-171.

5. Copland, A., Nahar, L., Tomlinson, C.T.M., Hamilton, V., Middleton, M., Kumarasamy, Y., Sarker, S.D. (2003) Antibacterial and free radical scavenging activity of seeds of Agrimonia eupatoria, *Fitoterapia,* 74(1-2): 133-135.

6. Devaraj, V.C., Gopala, K.B., Viswanatha, G.L., Jagadish, K.V., Kumar, S. (2011) Hepatoprotective activity of Hepax- A polyherbal formulation, *Asian Pacific Journal of Tropical Biomedicine,* 142-146.

7. Dhawan, B.N. (1982) Organization of Biological Screening of Medicinal Plants with special reference to C.D.R.I programs, Appendix-1, Lectures UNESCO-CDRI workshop on the use of Pharmacological Techniques for Evaluation of Natural Products, CDRI, Lucknow, 61.

8. El-Sayed, E.M., Fouda, E.E., Mansour, A.M., Elazab, A.H. (2015) Protective effect of lycopene against carbon tetrachloride-induced hepatic damage in rats, *International Journal of Pharma Sciences*, 5(1): 875-881.

9. Fatima, N. (1993) Hepatoprotective activity of Icterene, *Hamdard Medicus,* XXXVI (3): 56-62

10. Ghani, N. (1921) Khazainul-Advia, vol. I-V, Idara Kitabul-Shifa, New Delhi pp. 959-60.

11. Gupta. A.K., Neeraj, T. (2004) Reviews on Indian Medicinal Plants, Indian Council of Medical Research, New Delhi, vol. 2, pp. 399-401.

12. Handa, S.S., Sharma, A. (1990) Hepatoprotective activity of andrographolide from Andrographis paniculata against carbontetrachloride, *Indian Journal of Medical Research*, 92:276-83.

13. Ibn Sina (1906) Al-Qanoon fil-Tibb, Mataba Nami, Lucknow, vol. II, pp.195.

14. Joshi, H., Parle, M. (2006) Nardostachys jatamansi improves learning and memory in mice, *Journal of Medicinal Food*, 9(1): 113-18.

15. Kareem, N. (1880) Makhzan-ul-Advia, Matba Munshi Nawal Kishore, Kanpur, vol. II pp. 77-78.

16. Khan, M.A. (1313H) Muheet-e-Azam, Mataba Nizami, Kanpur, vol. III, pp. 241-42.

17. Khan, M.T.H. (2001) Traditional Medicines and Plant Drugs in Hepatic Diseases, *Hamdard Medicus*, XLIV (1): 14-16.

18. Khan, N.A., Rahman, S.Z., Amin, K.M.Y. (1990) Majoon Dabeedul Ward: A compressive study of its protective effect in experimental liver damage, International Seminar on Ilmul Advia, Faculty of Unani Medicine, Aligarh Muslim University, Aligarh, 4-5.

19. Khan, S. (1921) Ilaj-ul-Amraz, Matba Munshi Naval Kishor, Lucknow, pp. 223-24

20. Kim, Y., You, Y., Yoon, H.G., Lee, Y.H., Kim, K., Lee, J., Kim, M.S., Kim, J.C., Jun, W. (2014) Hepatoprotective effects of fermented Curcuma longa L. on carbon tetrachloride-induced oxidative stress in rats, *Food Chemistry*, 151:148-153.

21. Kumar, V., Cortan, R.S., Robbins, S.L. (2003) Robin's Basic Pathology, 7th ed., Pennysylvania Saunders, pp.11, 600.

22. Lowry, O.H., Rosenbrough, N.J., Farr, A.L., Randall, R.J. (1951) Protein measurement with Folin phenol reagent, *Journal of Biological Chemistry*, 193:265-275.

23. Luper, S. (1998) A Review of plants used in the treatment of liver disease, part I, *Alternative Medicine Review*, 3 (6):410-21.

24. Maheshwara Rao, K.U., Reddy, R.R., Vangoori, Y., Sundharam, J.M. (2014) Evaluation of hepatoprotectiv (preventive & curative) activity of leaves extract of *Rosa centifolia* on experimental animal models, *Asian Journal of Pharmaceutical and Clinical Research*, 7(1): 105-107.

25. Mehdi, A.T., Behzad, J., Heibatollah, S., Hussein, S. (2015) Hepatoprotective activity of aerial parts of *Otostegia persica* against CCl4-induced liver damage in rats, *Avicenna Journal of Phytomedicine,* 5(3): 238–246.

26. Mukherjee, K.L. (1988) Medical Laboratory Technology, Tata McGraw Hill, Publishing Company, vol. 3, pp. 1111-1124.

27. Mumoli, N., Cei, M., Cosimi, A. (2006) Drug-related hepatotoxicity, *N Engl J Med*, 354 (20): 2191-2193.

28. Ohkawa, H., Ohishi, N., Yagi, K. (1979) Assay for Lipid Peroxides in animal tissues by Thiobarbituric Acid Reaction, *Analytical Biochemistry*, 95:351-358.

29. Palanivel, M.G., Rajkapoor, B., Kumar, R.S., Einstein, J.W., Kumar, E.P., Kumar, M.R., Kavitha, K., Kumar, M.P., Jayakar, B. (2008) Hepatoprotective and antioxidant effect of Pisonia aculeata L. against CCl4-induced hepatic damage in rats, *Scientica Pharmaceutica*, 76:203-215.

30. Pramod, K., Deval Rao G., Lakshmayya, S., Ramachandra, S.S. (2008) Antioxidant and hepatoprotective activity of tubers of Momordica tuberosa Cogn against CCl4 induced liver injury in rats, *Indian Journal of Experimental Biology*, 46:510–513.

31. Qadri, N.M., Qureshi, S., Zakir-Ur-Rehman, Yaqeen, Z. (2003) Studies on Beneficial Role and Subchronic Toxicity of Livergen - A Polyherbal Hepatoprotective Drug, *Hamdard Medicus,* XLVI (2): 127-140.

32. Ravikumar, V., Shivashangari, K.S., Devaki, T. (2005) Hepatoprotective activity of Tridax procumbens against d-galactosamine/lipopolysaccharide-induced hepatitis in rats, *Journal of Ethnopharmacology,* 101:55-60

33. Recknagel, R.O. (1983) Carbon tetrachloride hepatotoxicity, status quo and future prospects, *Trends Pharmacol Sci*, 4:129.

34. Reitman, S., Frankel, S. (1957) A colorimetric method for determination of serum glutamic oxaloacetic acid glutamic pyruvate transaminases, *American Journal of Clinical Pathology*, 28:56-63.

35. Sharma, S.K., Ali, M., Ansari, S.H., Gupta, J. (2000) Evaluation of Indian herbal Hepatoprotective drugs, *Hamdard Medicus*, XLIII (2), 39-58.

36. Venskutonis, P.R., Skemaite, M., Ragazinskiene, O. (2007) Radical scavenging capacity of Agrimonia eupatoria and Agrimonia procera, *Fitoterapia*, 78(2): 166-168.

37. Weber, L.W.D., Boll, M., Stampf, L.A. (2003) Hepatotoxicity and mechanism of action of halo alkanes: carbon tetrachloride as a toxicological model, *Critical Reviews in Toxicology*, 33: 105-136.

सारांश

चूहों में कार्बन टेट्राक्लोराइड प्रेरित हेपेटिक घाव में *कुर्स–ए–गाफ़िस* की रोगनिरोधी और उपचारात्मक क्षमता

***शमशाद आलम, नईम. ए. ख़ान**

वर्तमान अध्ययन चूहों में CCl_4 प्रेरित यकृत विषाक्तता के विपरीत फार्माकोपियल मिश्रण *कुर्स–ए–गाफ़िस* की एंटी–हेपेटोटॉक्सिक प्रभाव का मूल्यांकन करने के लिए किया गया। परीक्षण के लिए श्वेत चूहों का उपयोग किया गया और उन्हें दो प्रमुख समूहों – रोगनिरोधी (सुरक्षात्मक) और उपचारात्मक में बांटा गया। फिर प्रत्येक समूह का पांच परीक्षण समूहों में उप–विभाजन किया गया जिसमें प्रत्येक समूह में 6 जीव थे। प्रथम समूह ने स्वस्थ नियंत्रण के रूप में कार्य किया। द्वितीय समूह को CCl_4 (2 मि.ली./कि.ग्रा. आई.पी.) और तृतीय, चतुर्थ तथा पंचम समूह को क्रमशः सिलीमरीन (100 मि.ग्रा./कि.ग्रा. शरीर भार) और अध्ययन औषधि क्रूड (700 मि.ग्रा./कि.ग्रा.) तथा सत्त (330 मि.ग्रा./कि.ग्रा.) 7 दिनों तक मौखिक रूप से दिया गया। छठे दिन प्रथम समूह को छोड़कर प्रत्येक समूह के सभी जीवों को CCl_4 (2 मि.ली./कि.ग्रा./आई.पी.) दी गई और CCl_4 देने के 48 घंटों के बाद इन चूहों को सुरक्षात्मक प्रभाव मूल्यांकन के अधीन किया गया। इसी प्रकार सभी उपचारात्मक समूहों के जीवों को परीक्षण औषधि के उपचारात्मक प्रभाव का मूल्यांकन करने हेतु 7 दिनों के लिए सुरक्षात्मक समूह की तरह संबंधित औषधि उपचार के बाद दूसरे दिन CCl_4 (2 मि.ली./कि.ग्रा. आई.पी.) की एकल खुराक दी गई। रक्त एकत्र किया गया और जैव–रासायनिक मार्करों अर्थात् एसजीपीटी और एसजीओटी के अनुमान द्वारा एंटी–हेपेटोटॉक्सिक क्षमता का आकलन किया गया। इसके अलावा जैव रासायनिक परिवर्तनों की पुष्टि करने के लिए एमडीए स्तर परीक्षण और हिस्टोपैथोलॉजिकल अध्ययन किया गया।

अध्ययन ने जीवों को CCl_4 देने पर एंजाइमों में महत्वपूर्ण ($p<0.01$) वृद्धि और हिस्टोलॉजिकल परिवर्तन दिखाया जबकि परीक्षण औषधि क्रूड और सत्त के साथ उपचार ने सीरम एंजाइम के स्तर को कम करके CCl_4 प्रेरित हैपेटोटॉक्सिसिटी को रोकने में सामर्थ्य दिखाया और सुरक्षात्मक तथा उपचारात्मक अध्ययनों में नियंत्रण की तुलना में यकृत के आकार के विघटन को बनाए रखा। सत्त ने क्रूड की तुलना में चूहों में हैपेटोटॉक्सिसिटी प्रेरित में बढ़ा हुआ सुरक्षात्मक और उपचारात्मक प्रभाव दिखाया। अध्ययन के अवलोकनों के आधार पर यह सुझाव दिया जा सकता है कि परीक्षण औषधि के दोनों रूपों में हेपेटोप्रोटेक्टिव के साथ–साथ उपचारात्मक सक्रियता है परन्तु सत्त मानक औषधि सिलीमरीन के साथ तुलना में क्रूड से थोड़ी बेहतर है।

शब्दकुंजी: एंटी–हेपेटोटॉक्सिक, फार्माकोपियल मिश्रण, सुरक्षात्मक और उपचारात्मक प्रभाव, *कुर्स–ए–गाफ़िस,* सिलीमरीन

Efficacy and Safety Study on Unani Formulation *Ma'jūn Nisyān* in *Nisyān* (Amnesia)

[1]Munawwar Hussain Kazmi,
[2]T. Shahida Begum,
[2]Hafiz. C. Md. Aslam,
[3]Ghazala Javed,
[4]Nighat Anjum,
*[5]Anju
and
[5]Rasikh Javaid

[1]Deputy Director Incharge, Central Research Institute of Unani Medicine, Hyderabad

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

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

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

[5]Research Associate (Unani), Central Council for Research in Unani Medicine, New Delhi

Abstract

The study was carried out to evaluate the efficacy and safety of Unani formulation *Ma'jūn Nisyān* in *Nisyān* (amnesia). *Ma'jūn Nisyān* was administered orally to the patients in the dose of 7gm once a day for 12 weeks. A total of 235 patients completed the study. The results suggest that the study drug is effective in *Nisyān* (amnesia) as significant increase in MMSE score and reduction in severity score of clinical signs and symptoms have been found. The study drug has no adverse effects, as no statistically significant changes have been observed in the values of pathological and biochemical parameters after 12 weeks of treatment. Therefore, it can be concluded that the study drug *Ma'jūn Nisyān* is safe and effective in the treatment of *Nisyān* (amnesia).

Keywords: Amnesia, *Ma'jūn Nisyān*, *Nisyān,* Unani Medicine

Introduction

Nisyān has become a major medical and social issue around the world. It is very common in the ageing population. It is a state of forgetfulness and termed as amnesia. *Nisyān* (amnesia) can be defined as a special case of memory loss which is distinct from ordinary forgetting (Anonymous, 2012). A French psychologist named Theodule-Armand Ribot first discovered amnesia. It is a dissociative psychological disorder manifested by total or partial loss of memory and can be attributable to various diseases including Alzheimer's disease (AD) and other dementias. It is often caused by head injury, brain trauma or brain surgery and can also be precipitated by alcohol consumption, drug use or due to the effects of a stroke.

Najibuddin Samarqandi, an eminent Unani physician, had described *Nisyān* as a disease in which *Quwwat Ḥāfiza* (faculty of memory), *Quwwat-i-Fikr* (power of thinking) and *Quwwat-i-Takhayyul* (power of imagination) are disturbed. It is caused by *Sū'-i-Mizāj Bārid Raṭb* (predominance of cold and moist temperament) and *Sū'-i-Mizāj Bārid Yābis* (predominance of cold and dry temperament) of brain. *Nisyān* is mostly caused by *Ḍu'f al-Dimāgh* (cerebro-asthenia) and predominance of *Balghamī Mādda* (phlegmatic matter) (Kabiruddin, 2009). *Ḍu'f al-Dimāgh* (cerebro-asthenia) is the main cause of *Nisyān* (amnesia) (Kabiruddin, 2009; Arzani, 2003). Other causes may include predominance of *Yubūsat* (dryness) in the brain, *Sal'a al-Dimāgh* (brain tumor), *Nazla-o-Zukām Muzmin* (chronic cold and catarrh), *Tashannujāt* (convulsions), *Fālij* (paralysis), *Kathrat-i-Sharāb Noshī* (alcoholism), use of narcotics, *Kathrat-i-Jimā'* (excessive coitus), frequent and prolonged exposure to sunlight and extreme heat and *Infi'ālāt Nafsāniyya* (psychological factors), e.g. stress, anxiety, depression, and extreme anger.

*Author for Correspondence; Email: dranju28@gmail.com

The clinical findings of *Nisyān* (amnesia) are excessive sleepiness, heaviness in backside of head and discharge of fluids from the head, insomnia, dryness of fluids from the nose and *Buṭlān-i-Takallum* (speech impairment), *Buṭlān-i-Taḥrīr* (writing impairment), *Fasād-i-Fikr* (impaired thoughts), *Ḍu'f al-Haḍm* (delayed digestion), inability to remember dreams and *Sadr* (giddiness) (Kabiruddin, 2009; Khan, 2009).

Treatment of *Nisyān* (amnesia) depends on its root cause. It may be prevented by avoiding or minimizing the brain injury. Brain infections should be treated swiftly and aggressively to minimize the damage due to swelling. However, there is no effective medicine available for the treatment of amnesia. Conventional drugs are used to treat *Nisyān* (amnesia) and other cognitive declines but their effects are not satisfactory. Therefore, the development of a novel remedy for amnesia is the need of the hour. In Unani classical literature, *Ma'jūn Nisyān* has been mentioned for the treatment of *Nisyān* (amnesia), to improve memory, attention and related cognitive functions (Anonymous, 1986), but there is the need of clinical data to prove its efficacy and safety. Therefore, the present study was designed to evaluate the safety and efficacy of *Ma'jūn Nisyān* in the patients suffering from mild to moderate *Nisyān* (amnesia).

Material and Method

The study drug was *Ma'jūn Nisyān*. The composition is given in Table 1. The drug was manufactured by the Central Research Institute of Unani Medicine, Hyderabad and standardized for quality control on various parameters by the said institute.

The study was designed as open-label, single arm, multicentre trial carried out at three peripheral centers of the Central Council for Research in Unani Medicine, namely Central Research Institute of Unani Medicine, Hyderabad, Regional Research Institute of Unani Medicine, Chennai and Regional Research Institute of Unani Medicine, Mumbai. Patients were screened in accordance with the inclusion and exclusion criteria mentioned in the protocol.

A total of 268 patients fulfilling the selection criteria were recruited in the study after obtaining their written informed consent. Out of them, 235 patients completed the study. The laboratory tests including haematological test (Hb.%, TLC, DLC), liver function test (Serum bilirubin, SGOT, SGPT, Alkaline phosphatase), kidney function test (Blood urea, Serum creatinine) and blood sugar fasting were done at the baseline and at the end of the protocol therapy. The screened patients were given *Ma'jūn Nisyān* 7gm with water in morning before meal; one tablet of the drug once daily for a period of 12 weeks. No concomitant treatment was given.

The efficacy of Unani formulation *Ma'jūn Nisyān* was assessed on clinical parameters of *Nisyān* (amnesia), viz. short term memory loss, past memory

Table 1: Composition of *Ma'jūn Nisyān*

S. No.	Ingredients (Unani Name)	Botanical Name	Part Used	Quantity
1.	*Asārūn* (Tagar)	*Valeriana wallichii* DC.	Rhizomes & Roots	20 g
2.	*Bādranjboyā*	*Melissa parviflora* Benth.	Herb	20 g
3.	*Irsā*	*Iris ensata* Thunb.	Root	20 g
4.	*Sumbul al-Ṭibb*	*Nardostachys jatamansi* DC.	Root	20 g
5.	*Waj*	*Acorus calamus* L.	Rhizome	20 g
6.	*Behman Surkh*	*Salvia haematodes* L.	Root	40 g
7.	*Post Halela Zard*	*Terminalia chebula* Retz.		
	Pericarp of mature fruit	40 g		
8.	*Pīpal Kalān*	*Piper longum* L.	Fruit	10 g
9.	*Tāj Qalmī*	*Cinnamomum cassia* (L.) J. Presl	Bark	20 g
10.	*Dārchīnī*	*Cinnamomum zeylanicum* Blume	Bark	20 g
11.	*Darūnaj 'Aqrabī*	*Doronicum hookeri* C. B. Clarke ex Hook. f.	Root	20 g
12.	*Zanjabīl*	*Zingiber officinale* Roscoe	Rhizome	10 g
13.	*Sa'd Kūfī*	*Cyperus scariosus* R.Br.	Rhizome	20 g
14.	*'Ūd Ṣalīb*	*Paeonia emodi* Royle	Root	20 g
15.	*Filfil Safed*	*Piper nigrum* L.	Fruit without seed coat	10 g
16.	*Kabābchīni*	*Piper cubeba* L. f.	Fruit	20 g
17.	*Kundur*	*Boswellia serrata* Roxb. ex Colebr.	Gum	20 g
18.	*Maghz Chironjī*	*Buchanania lanzan* Spreng.	Kernel	30 g
19.	*Maghz Nārjīl*	*Cocos nucifera* L.	Fruit	40 g
20.	*Ābresham Muqarraz*	*Bombyx mori* (Silkworm)	Cocoon	20 g
21.	*Mawīz Munaqqā*	*Vitis vinifera* L.	Dried Fruits	250 g
22.	*Za'frān*	*Crocus sativus* L.	Stigma and Style	1.8 g
23.	*'Araq-i-Ga'uzabāṉ*	*Borago officinalis* L.	Distillate	20 ml
24.	*Maṣṭagī Rūmī*	*Pistacia lentiscus* L.	Gum	20 g
25.	*Rawghan Zard*	Pure Ghee	-	5 g
26.	*Qiwām-i-Shakar*	Sugar Solution	-	1 kg 300 g

loss, present and past memory loss, and cognitive dysfunction. The results of the study were assessed on the basis of improvement in the Mini Mental State Examination (MMSE) score along with signs and symptoms and recorded as good response, fair response and poor response. The patients were followed-up after 12 weeks. The results of the study were analysed by using SPSS V20.0. Baseline and follow-up values of clinical subjective parameters, pathological and biochemical parameters were statistically analysed using Friedman post-hoc test, Mann-Whitney U test and Student's paired 't' test. The result was expressed as the Mean ± SEM. $P<0.05$ has been considered as statistically significant and $p<0.01$ and $p<0.001$ as statistically highly significant. The safety was assessed by monitoring adverse events reported by the patients or elicited by the investigator by clinical as well as laboratory investigations at the baseline and after the treatment. The laboratory tests included haematological test (Hb.%, TLC, DLC), liver function test (Serum bilirubin, SGOT, SGPT, Alkaline phosphatase), kidney function test (Blood urea, Serum creatinine) and blood sugar fasting.

Results and Discussion

The present study was designed to evaluate the efficacy of a Unani classical formulation – *Ma'jūn Nisyān* in the patients with *Nisyān* (amnesia). A total of 268 patients were enrolled in this study, out of which 33 patients dropped out of the study. A total of 235 patients completed the study and were treated with *Ma'jūn Nisyān*. Composition of *Ma'jūn Nisyān* is shown in Table 1. Their age ranged between 18 and 72 years with mean age 45.57 ± 14.26 (SD) years. The chronicity of disease ranged between 01 month and 15 years with mean chronicity 4.1 ± 3.9 years (Table 2).

Male patients (69%) dominated female patients and maximum (30%) patients were in the age group of 40-50 years. Minimum (12%) patients were in the age group of 18-28 years (Table 3).

Table 2: Gender and Age of Patients and Chronicity of Disease (Mean ± SD, Range)

S. No.	Characteristics	Number of Cases
1.	Male	162 (69%)
	Female	73 (31%)
	Total cases	235
2.	Age (Mean ± SD)	45.57 ± 14.26 years
	Age (Range)	18 to 72 years
3.	Chronicity (Mean ± SD)	4.1 ± 3.9 years
	Chronicity (Range)	One month to 15 years

Table 3: Age and Sex-wise Distribution of Patients

Age (in yrs)	Gender		Total	Percentage
	Male	Female		
18-28	23	6	29	12%
29-39	38	16	54	23%
40-50	43	28	71	30%
51-60	21	13	34	14%
≥61	37	10	47	20%
Total	**162**	**73**	**235**	**100**

All the patients were grouped according to the chronicity of the disease ranging from less than 01 to 10 years. The maximum number of patients, i.e. 156 (66%) were in the chronicity range of 1-4 years followed by 43 (18%) who had chronocity of less than 01 year (Table 4).

Table 4: Chronicity-wise Distribution of Patients

Duration of Disease	Male	Female	Total	Percentage
< 1 year	23	20	43	18%
1 - 4 years	111	45	156	66%
5 - 9 years	22	7	29	13%
≥10 years	6	1	7	3%
Total	**162**	**73**	**235**	**100**

All the patients were assessed for their *Mizāj* (temperament) according to classical Unani parameters. The maximum number of patients, i.e. 124 (53%) were having *Balghamī* (Phlegmatic) temperament followed by 87 (37%) *Damwī* (Sanguine), 17 (7%) *Ṣafrāwī* (Bilious) and 7 (3%) *Sawdāwī* (Melancholic) temperament (Table 5).

Table 5: *Mizāj* (Temperament)-wise Distribution of Patients

Mizāj (Temperament)	Male	Female	Total	Percentage
Damwī (Sanguine)	62	25	87	37%
Balghamī (Phlegmatic)	81	43	124	53%
Ṣafrāwī (Bilious)	12	5	17	7%
Sawdāwī (Melancholic)	7	0	7	3%
Total	**162**	**73**	**235**	**100**

The maximum number of patients, i.e. 188 (80%) belonged to middle income group (MIG), whereas 44 (19%) and 3 (1%) patients belonged to low income group (LIG) and high-income group (HIG), respectively (Table 6).

Table 6: Distribution of Patients According to Socio-economic Status

Income Group	Male	Female	Total	Percentage
Low	29	15	44	19%
Middle	131	57	188	80%
High	2	1	3	1%
Total	**162**	**73**	**235**	**100**

All the patients were evaluated for their therapeutic response in relation to their gender. Out of 235 patients, 80 (34%) patients got good response, 87 (37%) patients fair response and 68 (29%) patients poor response. Good response was obtained in 46.6% female and 28.4% male patients, whereas fair response was obtained in 39.7% female and 35.8% male patients, and poor response in 13.7% female and 35.8% male patients (Table 7).

Table 7: General Therapeutic Response in Relation to Sex of the Patients

S. No.	Response	Male	Female	Total	Percentage
1.	Good Response	46	34	80	34%
2.	Fair Response	58	29	87	37%
3.	Poor Response	58	10	68	29%
	Total	**162**	**73**	**235**	**100**

Clinical findings, including short-term memory loss, past memory loss, present and past memory loss, and cognitive dysfunction present at the baseline were significantly reduced ($p<0.001$) after the treatment (Table 8, Figure 1).

Table 8: Therapeutic Response in Relation to Clinical Parameters

Presenting Symptoms	Severity Score (Mean ± SEM)		'p' value
	Baseline	After treatment	
Short-term Memory Loss	3.46 ± 0.14	1.10 ± 0.17	<0.001[S]
Past Memory Loss	02.86 ± 0.20	0.90 ± 0.14	<0.001[S]
Present and Past Memory Loss	02.77 ± 0.19	0.72 ± 0.14	<0.001[S]
Cognitive Dysfunction	0.41 ± 0.11	0.24 ± 0.10	<0.001[S]

*$p<0.001$ Significant

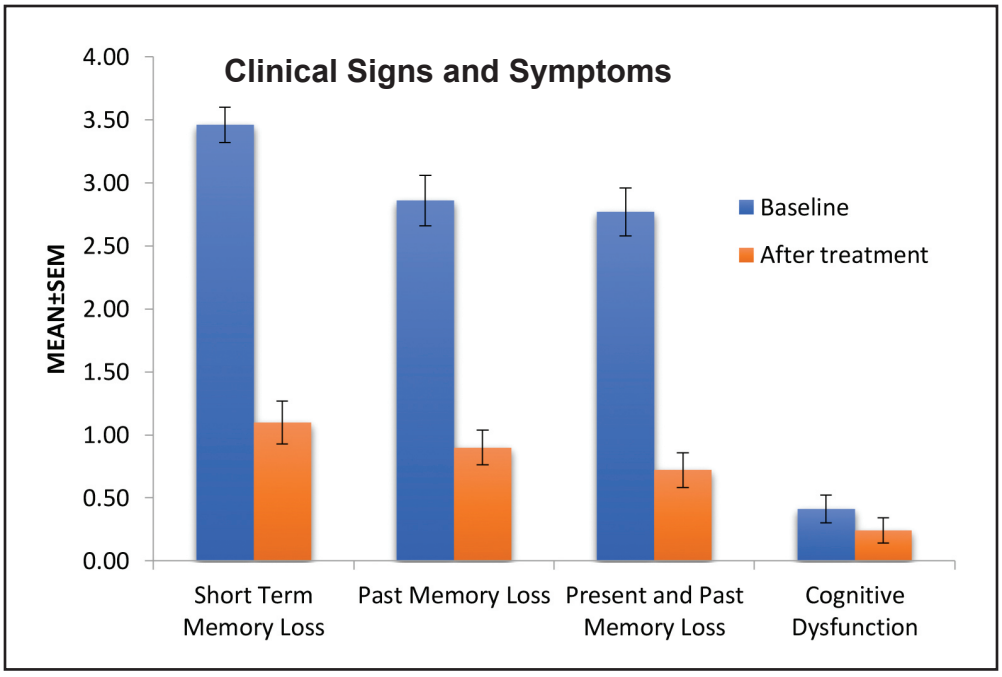


Figure 1: Therapeutic Response in Relation to Clinical Parameters

Effect of *Ma'jūn Nisyān* after 12 weeks of the treatment on cognitive function in patients with *Nisyān* (amnesia) was assessed using the Mini Mental State Examination (MMSE) score which was significantly improved ($p<0.001$) after the treatment when compared to the baseline (Table 9).

Table 9: Effect of *Ma'jūn Nisyān* on MMSE Score

Parameter	Range		Baseline (Mean ± SEM)	After treatment (Mean ± SEM)	'p' value
	Min.	Max.			
MMSE Scoring	6	30	17.93 ± 0.301	23.31 ± 0.208	<0.001[S]

*p<0.001 Significant

Pathological and biochemical laboratory findings at the baseline and after the treatment are shown in Table 10 and 11. The results indicated that the drug had no effect on the laboratory findings, including Hb, RBC, TLC, DLC, Platelet Count, S. Bilirubin, SGOT, SGPT, Serum Alkaline Phosphatase, Serum Creatinine, Serum Urea and Fasting Blood Sugar. No adverse effects of the study drug were reported by any of the patients over the treatment period and no statistically significant changes were observed in the values of pathological and biochemical parameters at the end of the treatment ($p>0.05$), which suggested that the study drug has no adverse effects.

Table 10: Pathological Parameters at Baseline and After Treatment

Laboratory Parameter			Mean ± SEM		Paired 't' test	
			Baseline	After Treatment	Statistical value	P-value
HAEMOGRAM	Hb (gm/dL)		13.64 ± 0.1026	13.48 ± 0.098	2.134	0.52
	RBC		3.67 ± 0.06	3.69 ± 0.06	-0.497	0.62
	Platelet Count		2.81 ± 0.096	2.64 ± 0.065	2.679	0.09
	TLC		8072.05±190.085	8030.33±191.419	-0.206	0.84
	DLC	N (%)	56.06 ± 0.658	56.22 ± 0.709	-0.246	0.81
		L (%)	34.57 ± 0.589	33.62 ± 0.584	1.793	0.07
		E (%)	7.31± 0.318	7.24 ± 0.296	0.276	0.78
		M (%)	1.72 ± 0.094	1.72 ± 0.105	-0.090	0.93

*p<0.001 Significant

Table 11: Biochemical Parameters at Baseline and After Treatment

Laboratory Parameter		Mean ± SEM		Paired 't' test	
		Baseline	After Treatment	Statistical value	P-value
LFTs	S. Bilirubin (mg/dL)	0.68 ± 0.042	0.615 ± 0.0457	1.110	0.27
	SGOT (IU/L)	20.92 ± 0.379	21.663 ± 0.715	-1.173	0.25
	SGPT (IU/L)	23.574 ± 0.633	23.76 ± 0.648	-0.306	0.76
	S. Alkaline Phosphatase (IU/L)	11.07 ± 1.424	13.98 ± 1.953	-2.040	0.04
KFTs	S. Creatinine (mg/dL)	1.36 ± 0.361	1.02 ± 0.031	1.057	0.34
	S. Urea (mg/dL)	23.32 ± 1.225	21.93 ± 0.519	1.042	0.30
Blood Sugar (F)		81.90 ± 2.982	85.82 ± 3.919	-0.990	0.33

*p<0.001 Significant

Conclusion

On the basis of the above observations, it can be concluded that the Unani formulation *Ma'jūn Nisyān* is clinically effective and safe in the treatment of *Nisyān* (amnesia) and hence it can be prescribed to the patients for treatment of *Nisyān*. This Unani formulation can be easily tolerated by the patients without any adverse effect on them.

Acknowledgement

The authors are indebted to the Director General, Central Council for Research in Unani Medicine, New Delhi for sponsoring the study drug for conducting this study. The authors are also thankful to all officers of the three centres for providing necessary facilities to conduct this study. The team members of the study deserve appreciation for their active cooperation and support throughout the study.

References

1. Anonymous (1986). *Qarābādīn-i-Majīdi*. 9th ed., Daftar Jamia Tibbiyya, Delhi, pp. 397-98.
2. Anonymous (2012). Standard Unani Medical Terminology, CCRUM, New Delhi, p. 184.
3. Arzani, M.A. (2003). *Tibb-i-Akbar*, Urdu translation by Hakīm Muhammad Husayn, Faisal Publications, Deoband (U.P.), pp. 40-45.
4. Kabiruddin, M. (2009). *Sharh al-Asbāb* (*Tarjama al-Kabīr*), vol. I, 1st ed., Idāra Kitāb al-Shifa, New Delhi, pp. 80-83.
5. Khan, A. (2009). *Ḥādhiq*, Bīswīn Sadi Publication Pvt. Ltd., New Delhi, pp. 43-46.

सारांश

निस्यान (विस्मरण) में यूनानी मिश्रण *माजून निस्यान* पर प्रभावकारिता और सुरक्षा अध्ययन

मुनव्वर हुसैन काज़मी, टी. शाहिदा बेग़म, हाफ़िज़ सी.मो. असलम, ग़ज़ाला जावेद, निगहत अन्जुम, *अन्जु, रासिख़ जावेद

यह अध्ययन *निस्यान* (विस्मरण) में यूनानी मिश्रण *माजून निस्यान* की प्रभावकारिता और सुरक्षा का मूल्यांकन करने के लिए किया गया। *माजून निस्यान* रोगियों को 12 सप्ताह तक 7 ग्रा. की मात्रा में मौखिक रूप से दिन में एक बार दिया गया। कुल 235 रोगियों ने अध्ययन पूरा किया। परिणामों से पता चला कि अध्ययन औषधि *निस्यान* के उपचार में प्रभावकारी है क्योंकि रोग के नैदानिक संकेतों तथा लक्षणों के गंभीरता स्कोर में महत्वपूर्ण कमी और एमएमएसई स्कोर में महत्वपूर्ण वृद्धि देखी गई। अध्ययन औषधि का कोई प्रतिकूल प्रभाव नहीं है क्योंकि 12 सप्ताह के उपचार के बाद रोगात्मक और जैव रासायनिक मापदंडों के मान में कोई महत्वपर्ण परिवर्तन नहीं देखा गया। अतः यह निष्कर्ष निकाला जा सकता है कि *निस्यान* (विस्मरण) के उपचार में अध्ययन औषधि *माजून निस्यान* सुरक्षित और प्रभावकारी है।

शब्दकुंजी: *निस्यान,* विस्मरण, *माजून निस्यान,* यूनानी चिकित्सा

HIPPOCRATIC JOURNAL OF UNANI MEDICINE

Instructions to Contributors

1. The paper(s) should be submitted through email at rop.ccrum@gmail.com or in CD/DVD. Submission of a paper will be taken to imply that it is unpublished and is not being considered for publication elsewhere.

2. Papers should be written in English language and typed with double spacing on one side of A-4 size paper leaving top and left hand margin at least 1" (One inch) wide. Length of the paper should normally not exceed 12 pages.

3. Papers should be headed by a **title**, the initial(s) and surname(s) of author(s) followed by address.

4. Each paper should bear **abstract,** 2 to 5 **keywords, introduction, methodology, observations, results and discussion** followed by **acknowledgements and references.**

5. In all studies of plants or animals, proper identification should be made as to the materials used.

6. While submitting the paper(s) for publication, author(s) should decode the drugs specially in case of clinical studies.

7. Bibliographical references should be listed in alphabetical order of the author at the end of the paper. Authors should be cited in the text only by their surname(s) but their initial(s) should be shown in the bibliography.

8. References to periodicals should include the name(s) and initial(s) of author(s), year of publication, title of the book, periodical, title of the article, volume number (Arabic numerals), issue number where appropriate, first and last page number. Reference to books should include name(s) and initial(s) of the author(s), year of publication, exact title, name(s) of publisher, place of publication, page number.

9. Reference should be cited in the text in parentheses by the name(s) of author(s) followed by the year of publication, e.g. "(Jain,1991)" except when the author's name is part of the sentence, e.g. "Jain (1991) has reported that." If there are more than two authors it is in order to put "..... *et al*." after the first name, e.g., Khan *et al.*, 1981.

10. Each table should be typed on a separate sheet of paper. Tables should be numbered consequently in Arabic numerals e.g. “Table 1, Table 2” etc., and attached to the end of the text. Tables should be provided with headings and kept as simple as possible and should be referred to in the text as “Table 1” etc.

11. Figures (including photographic prints, line drawings on strong white or transparent paper, and maps) should be numbered consequently in Arabic numerals, e.g. “Fig. 1”, etc. and attached to the text behind the tables. Graphs and diagrams should be large enough to permit reduction to a required size, legends for figures should be listed consequently on a separate sheet of paper. Photographs should be on glossy printing paper.

12. The editors reserve the right to refuse any manuscript submitted, whether on invitation or otherwise, and to make suggestions and modifications before publication.

13. Paper accepted by the editorial board will become the property of the CCRUM. No article or any part thereof may be reproduced in whatever form, without the written permission of the Editor-in-Chief.

14. The editors and publisher are not responsible for the scientific contents and statements of the authors of accepted papers.

Address for submission of papers: Director General, Central Council for Research in Unani Medicine, 61-65 Institutional Area, Janakpuri, New Delhi-110058.

R.N.I. Registration No. DELENG/2006/18866

HIPPOCRATIC JOURNAL OF UNANI MEDICINE

This is a peer-reviewed publication and included in the abstracting and indexing of Medicinal and Aromatic Plants Abstracts (MAPA); Biological Abstracts; Chemical Abstracts; Contemporary Researches in Traditional Drugs & Medicinal Plants: Unani Medicine Abstracts, etc.

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