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Editorial

Unani Medicine is one of the oldest healthcare systems. It originated in Greece (*Unan*) and travelled to many countries before it came to India and prospered enormously. It is one of the recognized systems of medicine in many countries that caters to healthcare needs of considerable population in rural as well as urban areas.

Although, Unani medicines have been in use for centuries and are known for their therapeutic efficacies, there is a need to scientifically establish their efficacy and safety in order to achieve global acceptance. Organized research work in this system was, therefore, a need of the hour. The Central Council for Research in Unani Medicine (CCRUM), through its research programmes namely clinical research, drug standardization, survey & cultivation of medicinal plants and literary research, is contributing significantly to this cause for the last four decades. Vitiligo, sinusitis, filariasis, eczema and malaria are some of the conditions where Unani therapies have earned recognition after scientific validation.

The CCRUM has been publishing the Hippocratic Journal of Unani Medicine (HJUM) mainly to propagate outcomes of research on fundamental and applied aspects of Unani Medicine. The journal also publishes recent advances in other related sciences and Traditional Medicine as well as different streams of medical sciences which have bearing on validation and scientific interpretation of various concepts and strength of Unani Medicine.

This issue of HJUM includes six original as well as review papers. In the first paper, review of literature on cancer prevention and treatment in Unani Medicine has been presented. In the second paper, the authors have presented information on phytochemical and pharmacological investigations on *Rummān* (*Punica granatum* L.). The third paper deliberates on elderly care in Unani Medicine. The fourth paper is based on a sub-acute oral toxicity study of *Kushta Qala'ī* (herbo-mineral Unani formulation) in Wistar rats, while the fifth paper presents data of a study on therapeutic response of Unani coded drugs in *Dā' al-Fīl* (lymphatic filariasis). The last paper is based on a clinical study conducted to evaluate the safety and efficacy of *Ma'jūn Muqawwī-i-Raḥim* in *Sayalān al-Raḥim* (leucorrhoea).

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

Prof. Asim Ali Khan
Editor-in-Chief

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Cancer Prevention and Treatment in Unani Medicine: A Literature Review

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Abstract

Unani Medicine, one of the traditional systems of medicines, relies on natural resources like herbs, shrubs, minerals, stones and animal and ocean products for drugs. It has been serving the humanity since long. It has been known by different names in different countries. The Unani system of medicine offers preventive as well as curative treatment for every disease. Cancer is a disease which has been described by *Buqrat* (Hippocrates) (460-377 B.C), *Anteelash, Boles, Jalinoos* (Galen 129-200 AD) and other physicians of Unani system of medicine such as Razi (Rhazez 850-923 AD), Abu Sahal Masihi (10th Centruy AD), Ali bin Rabban Tabari (770-850 AD), Ibn Sina (Avicenna 890-1037 AD), Ismail Jurjani (12 Century AD) and other prominent researchers and writers in detail. Almost all Unani physicians have stressed on internal causes based on imbalances in *Akhlat* (humours) in the human body. They have suggested preventive as well as curative methodology to fight against this disease which is causing large scale deaths, unbearable pain and unimaginable situation in the world. The details are discussed in this paper.

Keywords: *Akhlat,* Cancer, Disease, Pain

Introduction

Cancer (*Sartan*) is an age old disease well described in ancient classical literature of Unani Medicine. *Buqrat* (Hippocrates 460-377 B.C) has discussed the disease and its treatment. Similarly, *Jalinoos* (Galen 129-200 AD) has not only described the problem and its developing stages but recommended a good number of drugs and in some cases advocated surgery as well as cauterisation. He has discussed the prognosis in some cases and stated that these patients will definitely die and will not be saved by any treatment.

Galen has mentioned that *Sartan* is a round inflammation of soft tissues which has filled veins around than in deep. The pain in this condition is pinching and cutting. On palpation, the affected part will be hot; the area around it will be inflamed and swollen. This may be ulcerative cancer which will progress forward and very bad pus will flow. The superficial part will be reddish. Galen in his treatise "*Hilatul Bar'a*" has mentioned that if the cause of *Sartan* is *Khilt Suada,* then it is very difficult to diagnose in the early stages. He further emphasized that the use of *Advia Mushila* should be encouraged for the removal of *Khilt Sauda* (Razi, 2002). *Razi* (1991) in his book *Kitabul Mansoori* wrote that *Sartan* is a type of fatal disease but if it is diagnosed in the early stages and better *tabdabeer* are adopted, then its spread can be stopped, but if the spread continues then it is very unlikely to get treated. The condition gets worsen if the wound

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develops pus. In such cases, the disease is fatal.

According to modern system of medicine, cancer is a general term applied for a series of malignant diseases that may affect different parts of the body. These diseases are characterized by rapid and uncontrolled formation of abnormal cells which may be a tumour or proliferate throughout the body by the process of metastasis. The main forms of cancer treatment in humans are surgery, radiation and drugs (chemotherapeutic agents). They can often provide temporary relief of symptoms, prolongation of life and occasionally cures. Cancer continues to represent the largest cause of mortality in the world and claims over six million lives every year (Shettar, 2018).

It is considered as a chronic disease and a major cause of death world-wide. It is a serious public health problem. Studies have shown a tendency of exponential growth of this disease in the coming decades. The World Health Organization (WHO) estimates that by the year 2030, 75 million people will be affected by cancer, 27 million incidents of cancer and 17 million deaths by cancer in the world (Passos *et al.,* 2018). It is reported that 70% of cancer-related deaths are taking place in low-to-medium-income countries (Paul, 2017). The diagnosis of cancer can have a significant negative impact on the mind of individuals and their families. Safeguarding their mental health is the need of the hour. Verbal expression of these negative emotions and feelings may be difficult (Swasti, 2018)

Ibn Sina in his book *Al-Qanoon Fil Tib* described *Sartan* as a type of *waram e saudawi* which is produced due to incineration of that type of *sauda* which is produced due to combustion of safra. According to him the disease is more common in *Aaza Asabiya. Ibn al-Quff Maseehi* in his book *"Kitab al-Umda Fil Jarahat"* mentioned that *Sartan* is a type of warm which spreads to the nearby *urooq* and is more common in females (Maseehi, YNM). Yunus explains that *Sartan* is more common in females due to the fact that the body of women is soft which accepts *fuzlat* very easily. These *fuzlat* are hard and it is difficult to absorb in harder bodies i.e. males, that is why it is not much common in males (*Qumri,* 2008).

In his book *"Mukhtarat Fil Tib", Ibn Hubal Baghdadi* has described that if this disease is diagnosed in the early stages, its spread can be stopped. He also mentioned that *Sartan* is a type of *waram* with its roots penetrated inside deeply causing dryness and tension and as the disease increases pain also increases (Baghdadi, 2008).

Other Unani physicians have described cancer as a small inflammation which resembles *Baqilla* (legume) or *Chilgoza*. It shifts from one place to another and grow to a bigger one like *Akhrot* (walnut). Sometimes, it becomes so big that it cannot shift and reaches the deep. The colour is reddish, sometimes it is

yellow as it has burning and cutting pain to such extent that patient dislikes any medication, sometimes it bursts and blood flows out and affects healthy muscles, sometimes it ulcerates the body.

Aribasiyoos is another Greek physician who described cancer as having less heat and redness than *falgamoon*. Another ancient physician Doles has quoted as irregular inflammation with bad look, black in colour, painful and ulcerates and has veins around it. Another ancient physician Atnash has stated that cancer is a round inflammation but not much swollen. It creates unease during treatment; it is hot and heat can be felt on palpation. In case of ulceration, very bad pus comes out with very bad smell and affects deeper parts which creates spasm and has too much blood flow, its outer sides areas are hard and red.

Rhazes has defined cancer as round inflammation with roots compulsorily present in outer part of the organ. It has one big root with green veins around and feels hot on palpation. It has pinching pain gradually. Initially, it is small but later on, it becomes larger.

In "Ghina Muna", it has been mentioned that *Sartan*, if diagnosed in the early stages and proper *tadabeer* are followed which check the spread, then it can be treated, and if it starts ulcerating, then its prognosis becomes even worse (*Qumri*, 2008).

Nomenclature

According to *Ibn al Quff Maseehi,* the name *Sartan* is given due to the fact that the disease resembles the hunting of the animal *Sartan* as this creature captures its prey like the disease spreads to the adjacent organs. The second reason to mention is that this type of *waram* is larger in the centre having *urooq* joined to it from all sides resembling *Sartan* animal (Maseehi, YNM).

Cause

Galen wrote in his book *Jawamey* that the cause of cancer is *Saudawi* (Black bile) inflammation and because of this its blood is black and does not appear hot. On touch, the arteries are full and feel ulcerative and hot.

He also writes that the cause of all types of cancer is excessive heat or less heat, arteries are full and spread in hot inflammation, as the receding humour lacks viscosity so they are not white like *falghamooni* but green and black like the humour produced by it.

The ancient Unani physicians have identified three main causes for excess production of *Sauda* (Black bile) in the human body.

1. The liver is ultra-hot resulting in excess production of *Sauda*.

2. The spleen is not able to absorb humours.

3. There are diets which help in production of *Khilt Sauda* (Black Bile).

Galen and other Unani physicians have identified *Safra* (Yellow Bile) as a possible cause of cancer. He says further when pus is produced in the mouth of cancer patient; it is due to burnt *Khilt-e-Safra* (Yellow Bile).

All hard ulcers which are black or green kill the patient because this is the system that blood has changed to Black Bile and the soft ulcers which are hot and yellow fluid kills the affected parts and the parts of body wherever it falls. (Razi, 2002a).

Ibn Rushd (1124-1198 AD) has also described *Sartan* as *Waram e Sauda* which does not cause joint pain like *Balghami* inflammation but it is hard and has earth like colour. It has been named after the animal *Sartan* (Cancer) because of its shape. The veins around it are filled with putrefied and black blood whose shape is like cancer stages. *Ibn Rushd* (1987) has mentioned that *Sartan* is a type of disease born from *madda* which is *sard* and *khushk*.

Prevention

Unani Medicine advocates prevention of disease rather than treatment. The prevention has been divided into two types as mentioned below:

1. The method of prevention

2. To save healthy bodies from disease

Ibn Rushd says, diseases are caused mostly from the waste products of diets. *Ibn Sina* explains by dividing the prevention into three parts.

1. Up keep of weak bodies

2. Prevention from possible disease

3. Saving the healthy people's health

Ibn Sina presented the theory of body fluids and stated that these fluids when putrefied, create the condition of illness and death. In this connection, he has identified two important causes which reduce the power or strength of body then declared that if we are able to save the human body from self dissolution and putrefaction then the death may be avoided.

In the light of above observations, it can be said that prevention of any disease depends upon basic theory of *Asbab Sitta Zarooria* or Six Essentials (Factors) which maintain the fluids of body and they are as mentioned below:

1. Diet

2. Fluid intake
3. Sleep
4. Awaking
5. Retention
6. Expulsion

Hence the prevention of human body from Cancer is not possible unless we ensure the following:

1. To take such diet that provides all required calories and minerals.
2. Expulsion of waste products from the body.
3. Correction of Air. This requires protection of environment which is the root cause of all dreaded diseases.
4. To avoid tension and emotional damage, as it can alter the temperament from good to bad.
5. *Ibn Rushd* has quoted *Jalinoos* and *Ibn Zohr* repeatedly to prove his views. Today we are facing environmental changes to the extent that the climate of earth is highly polluted. The quality of food as well as water is so bad due to various types of pollutions and the stress resulting from modern lifestyle creating different types of cancers culminating in unimaginable and painful suffering as well as large number of deaths in every continent of the universe. This can be prevented only by preserving the Ecology and natural condition of the entire world as it has been described by ancient physician of Unani Medicine.

Treatment

Line of Treatment

The line of treatment in Unani Medicine for all diseases is based on *Akhlat* (Humour) theory and it is recognised as a reason for all elements. The *Khilt e Sauda* (Black bile) is the main cause of *Sartan* (Cancer) and *Khilt e Safra* (Yellow bile) has been recognised as the causative factor of mouth cancer. The line of treatment in *Sartan* is clearly stated by Buqrat (Hippocrates), *Jaalinoos* (Galen), Bols, Aratnashi, *Deesqooriodoos* (Diascorides), Abu Sahal Masihi, Ibn Rabban Tabari, Razi, Ibn Sina (Avicenna), Ismail Jurjani, Ibn Nafees, Ibn Rushd, Ibn Zohar and all other Unani physicians and philosophers as expulsion and evacuation (*Istifragh*) of causative factor (humour) that is *Sauda* (Black Bile), likewise evacuation of *Safra* is mandatory in case of mouth cancer. The dietary

restriction is equally important as it is necessary to stop the production of *Sauda* in liver and increase the absorbing power (*Quwwat e Jaaziba*) of spleen and increasing power of immunity and balancing body fluid is also an important part in fight against cancer, especially in patients of preliminary stage.

Surgery is the second option in the case of secondary stage where there is no choice but to remove completely the lesion and normal muscles around it in selected patients where the chance of survival is quite high than death. Then cauterisation (*Aml e Kayy*) is the last option as it has not been liked by the prophet due to involvement of fire and painful action of cauterisation but allowed to save the life of a person.

Ashleeman, a great physician of pre-Hippocratic period, has been quoted in *Al Hawi Fit Tib* to "give purgative (*Mushil*) to evacuate *Sauda* (Black bile) in Cancer and arrange healthy diets". Galen also wrote in his book that *Sartan* and *waram e raddi* can be cured with *advia mushila* (Razi, 2002). *Tiryaaq* as well as *Masrootidoos* are very useful. The milk of camel is very important in the treatment of cancer. Jalinoos (Galen) has recommended the evacuation of *Sauda* and suggested *Aftimoon*, honey water (*Maa ul Asl*) and barley water for the treatment of cancer. Hippocrates also advocates longer use of purgation. According to *Buqrat,* patients suffering from *Sartan* should be given *Advia Mushila* repeatedly. *Batini Sartan* is not treatable and Galen quotes that he has not seen anyone getting cured from the disease provided it is diagnosed in the early stages (*Qumri,* 2008). "Don't limit the use of purgatives for 3-4 days, instead repeat it many times and apply *Zangar* to create redness".

Razi and Ibn Sina also have supported his view and recorded their own parameters of treating Cancer patient with the same drugs. For purgation, Ibn Sina recommended that it is better to use *Aftimoon* along with *Maul Jubn* and *Maul Asl* and for people with *Mizaj-Qawi* it should be used with *Ayarij Khurbuk* (Ibn Sina, YNM)

Types of treatment are as follows:

1. *Ilaj bil Dawa* – (Pharmacotherapy)
2. *Ilaj bil Yad* – (Surgery)
3. *Ilaj bil Kayy* – (Cauterisation)

The pharmacotherapy has been given top priority in Unani Medicine. Diascordies, Galen, Ashleeman, Jorjas, Athursufas, Ahran, Bols, Artnash, Qusta, Arjanas, Ibn Sarabiyoon and Abu Juraih, all of them have recommended various drugs for the treatment of cancer.

Types of Cancer

There are so many types of cancer described in Unani Medicine:

1. *Sartan e Khafi* - Silent Cancer
2. *Sartan e Jali* - Open / Visible Cancer
3. *Sartan e Mutaqarreh* - Ulcerative Cancer
4. *Sartan e Ghair Mutaqarreh* – Non Ulcerative Caner
5. *Sartan e Mutakkil* – Destructive Cancer
6. *Sartan e Ghair Mutakkil* (Non Destructive Cancer)
7. *Sartan e Ibtidai* – (Primary Cancer)
8. *Sartan e Saanvi* (Secondary Cancer)
9. *Sartan e Mustahkam* (Stable Cancer)
10. *Sartan e Shadid* (Last Stage Cancer)
11. *Sartan e Damvi* – (Blood Cancer)
12. *Sartan e Muzmin* (Chronic Cancer)

Type of Drugs Used in Treatment of Cancer

According to morphology there are four types of drugs used in Unani Medicine as described below:

1. *Advia Nabatia* – Plant origin drugs
2. *Advia Haiwaniya* – Animal origin drugs
3. *Advia Madania* – Mineral origin drugs
4. *Advia Hajaria* – Stone origin drugs

There is another classification of drugs according to efficacy in the classical literature of Unani Medicine as given below:

1. *Advia Mushila* (Purgative)
2. *Advia Musakkina* (Sedative)
3. *Advia Mumsika* (Retentive)
4. *Advia Muhallila* (Anti-inflammatory)
5. *Advia Munqqia* (Detergent, cleaning)
6. *Advia Lazza'a* (Irritative)
7. *Advia Muharriqa* (Burning)
8. *Advia Mubarrida* (Febrifuge)
9. *Advia Murattiba* (Humectant)
10. *Advia Mutakkila* (Corrrosive)
11. *Advia Mudirra* (Diuretic)
12. *Advia Mulayyina* (Laxative)
13. *Advia Harrah* (Calorific)

The ancient Unani physicians have divided the drugs into two more types as given below:

1. *Advia Dakhilia* – Internal Medicine
2. *Advia Kharija* – External Medicine

Another classification of drugs has been described according to their use as mentioned below:

1. *Advia Mufrada* – Single drugs
2. *Advia Murakkaba* – Compound drugs

Internal Type of Drugs

Abu Bakr Mohammed Bin Zakaria Razi (Rhazes) has mentioned the following drugs for use as internal single drugs:

- Lead
- Snake Meat
- Common Salt
- *Sharab Rehani*
- *Cuscuta Reflexa*
- Whey
- Honey water
- *Helloborus niger*
- *Luffa acutangula*
- *Solanum nigrum*
- *Convolvulus scammonia*

External Type of Drugs

- *Blephris edulis*
- Carbonate of lead
- Water of *Cicorium intybus*
- Vinegar
- *Papever somniferum*
- Milk
- Copper sulphate
- Lead
- *Salix alba*
- *Cucumis sativa*
- *Malva sylvestris*
- *Juglaus regia*
- Stag's horn
- *Solanum nigrum*
- Rust

- *Curcuma longa*
- *Boswellia serrata*
- *Aloe barbadensis*
- *Armeninan bole*
- *Rosa damascene*
- Tin
- *Andropogon muricatus*
- Vinearosa
- Rhuscoriaria
- *Quercus infectoria*
- *Cassia lignea*
- *Cheiranthu scheiri*
- Honey
- *Plantago major*
- *Jasminum officinale*
- *Cyanara scolymus*
- *Linum usitatissimum*
- *Cicer arietinum*
- *Brassica oleracea*
- Crab
- Bismuth
- Wax
- Sealing clay

General Treatment

The local and oral applicant drugs in case of *Sartan Ghair Mutaqarreh* (non-ulcerative cancer) are given below:

1. *Luhoom e Afai, Namak*, *Sharab e Raihanani* boiled in water for oral intake
2. Milk with *Musakkin* and *Mumallis* drugs to relive pain

Ointment

1. *Asfidaj, Usrub, Abe Kasni, Afyoon* - all drugs in equal quantity
2. Powder *Salhafa Bahriyya* and mix in ghee then apply on the affected part
3. *Haldi, Asfidaj, Kundur, Sibr, Gile Armani* and *Alum* - mix these drugs in *Roghan-e-Gul* and apply on the affected part

Oral Drugs for Non Ulcerative Cancer

1. *Tiryaq*
2. *Masrudeetoos*

3. Decocotion of *Afteemoon*
4. Purgative drugs
5. *Fasad* (Venesection)
6. *Toodri*, Honey, water

Drugs for Local Application

1. Zaroor of *Zanjar*
2. *Barge Habs, Barge Suman*
3. Roots of *Karnab Nibti*, Fat
4. *Zimad* of *Bartang*
5. *Marham Rusul*

Sartan e Mutakkil

1. *Anjura*
2. *Zimad* e *Usrub*

Sartan e Ibtidai **(Primary Cancer)**

1. Purgative of *Sauda* drugs as decoction
2. Production of good blood
3. *Fasad* (Venesection) and *Marham Tootia* or *Ab-e-Inab us Salab*

Compound Drugs

1. *Itrifal Sagheer*
2. *Tiryaq e Farooq*
3. *Masrudeetoos*
4. *Tiryaq Arba*

Sartan-e-Shadeed **(Last Stage Cancer)**

1. *Sharab-e Qabiz, Semaq, Afis GhairMasqoob, Salikha*, each ¼ to be soaked for 4 days and boiled, after cooling use as ointment.

Sartan **e** ***Mustahakam*** **or Stable Cancer**

1. Surgery
2. Cauterisation

Blood Cancer

1. Purgation of *Sauda*
2. Diet Control

***Sartan e Khafi* (Hidden Cancer)**

- Purgation of *Sauda*
- Buqrat, Jalinoos and other physicians have advised that *Sartan* e Khafi may be left untouched and surgery may be avoided.

Conclusion

A careful review of the literature reveals that the ancient Unani physicians were very well aware of cancer. They were also fully aware of the causes, pathogenesis, prognosis and diagnosis of the disease. They had developed a number of herbal treatments to fight against the disease. Cancer survivors can be encouraged to involve newly diagnosed cancer patients through creative writing workshops as a part of the support group endeavour. The developing world has not been spared of the effects of cancer which is a clear sign of migration in diets and social activities and possible effects of industrialization on clean environment. It is need of the hour to take *Asbab e Sitta Zaruria* into consideration to overcome these factors as soon as possible. It is also may be noted that the greats of Unani system of Medicine like *Ibn Sina, Zakarai Raazi, Jaalinoos* etc have worked on a on this disease extensively and their work is relevant today. The Unani physicians of this era and the modern researchers should take it forward in cooperation and begin a joint effort to stop this dreadful disease which will be a benchmark in the field of Medicine, a breakthrough possible with the help of time tested Unani literature.

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सारांश

यूनानी चिकित्सा में कैंसर की रोकथाम और उपचार - एक साहित्यिक समीक्षा

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यूनानी चिकित्सा पद्धति एक पारंपरिक चिकित्सा पद्धति है जो औषधियों के लिए प्राकृतिक संसाधनों जैसे जड़ी–बूटियों, झाड़ियों, खनिजों, पत्थरों, जानवरों और समुद्री उत्पादों पर निर्भर करती है। यह पद्धति लंबे समय से मानव सेवा कर रही है और दुनिया के लगभग सभी भागों में उपलब्ध रही है। इसे विभिन्न देशों में अलग–अलग नामों से जाना जाता है। यूनानी चिकित्सा पद्धति रोग के निवारण के साथ–साथ उपचार भी उपलब्ध कराती है। कैंसर एक ऐसा रोग है जिसका वर्णन बुक़रात (हिप्पोक्रेट्स) (460–377 ई.पू.), जालीनूस (गैलेन 129–200 ई.) और यूनानी चिकित्सा पद्धति के अन्य चिकित्सक जैसे राज़ी (850–923 ई.), अबू सहल मसीही (10वीं शताब्दी ई.), अली बिन रब्बन तबरी (770–850 ई.), इब्न ए सीना (ऐवेसिना 890–1037 ई.), इस्माइल जुरजानी (12 शताब्दी ई.) और अन्य प्रमुख शोधकर्त्ताओं और लेखकों ने विस्तार से किया है। लगभग सभी यूनानी चिकित्सकों ने मानव शरीर में अख़्लात (ह्यूमर्स) में असंतुलन के आधार पर आंतरिक कारणों पर ज़ोर दिया। उन्होनें इस रोग के निवारण के साथ–साथ उपचार का सुझाव भी दिया है जोकि दुनिया में बड़े पैमाने पर मृत्यु का कारण बन रही है तथा असहनीय पीड़ा और अकल्पनीय स्थिति पैदा कर रही है। इस पत्र में इस पर विस्तार से चर्चा की गई है।

शब्दकुंजी: अख़्लात, कैंसर, रोग, पीड़ा

Phytochemical and Pharmacological Investigations on *Rummān* (*Punica granatum* L.)

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Abstract

The use of medicinal plants for the prevention and treatment of various ailments has been in practice from the time immemorial. Pomegranate (*Punica granatum* L.) belonging to family Lythraceae has been reported to be effective against various disorders like gastrointestinal, haematological, renal or uro-genital disorders. The plant has been popularly known by the name of its fruit *Anār* or *Rummān*. Different parts of the plant, viz. flowers, fruits, rind of the fruit, seeds, dried bark of the stem and root are used as medicine among various ethnic and rural societies. *Gulnār* is the scarlet red flower of that pomegranate tree which cannot produce fruits. This flower is used for medicinal purpose exclusively in Unani Medicine. The parts of the plant are considered as astringent, anthelmintic, desiccant, stomachic, anti-diarrhoeal with good nutritional value in Unani Medicine. This communication is an attempt to compile and document information on different aspects of *Punica granatum* L. mentioned in classical Unani as well as modern literature. The plant has been suggested to be taken up for further scientific investigations so as to validate the medicinal claims presented herein and to utilize its maximum therapeutic potential.

Keywords: *Gulnār;* Lythraceae; *Punica granatum* L., Traditional; Unani Medicine

Introduction

Rummān (pomegranate) is an ancient, mystical, unique fruit borne on a small long-living tree of *Punica granatum* L. of the family Lythraceae, cultivated throughout India and distributed from Balkans to the Himalayas. Kandhar in Afghanistan is famous for its high quality pomegranates. Today, pomegranate is cultivated in most regions of the world, including Iran, Spain, Italy, Afghanistan, America, India, China, Russia, Uzbekistan, Morocco and Greece. *Gulnār* is the scarlet red flower of such pomegranate tree that does not produce fruits. Such flowers are used for medicinal purpose in Unani Medicine. The tree has both wild and garden varieties. In general, *Gulnār* refers to the wild type. The Egyptian and Iranian varieties are described as the best ones in Unani literature (Ibn Baitar, YNM, Ghani, 1921).

Common and Regional Names

Arabic: *Rummān, Shajarātur-Rummān;* Bengali: Dalimgachh; English: Pomegranate tree; Greek: Roia, Balusaitrn; Hindi: Anaar, Dhalim; Malayalam: Dadiman; Persian: Darakht-e-Anar, Gulnar, Anar; Punjabi: Anar, Daan, Danu; Sanskrit: Bijapura, Dadima, Shuka-dana, Kuchaphala; Urdu: Anar Mitha

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Taxonomy

Kingdom	Plantae - plants
Subkingdom	Viridaeplantae - green plants
Infrakingdom	Angiospermae - flowering plants
Division	Spermatophytina - seed plants
Subdivision	Tracheophyta - vascular plants
Infradivision	Streptophyta - land plants
Class	Magnoliopsida
Superorder	Rosanae
Order	Myrtales
Family	Lythraceae
Genus	*Punica*
Species	*Granatum* L.

Morphological Description

A large deciduous shrub or small tree, bark smooth, grey, thin; often armed with small axillary or terminal thorns. Leaves opposite, 2.6-6.3 cm long, oblong – lanceolate, oblong-elliptic or oblong-oblanceolate, glabrous, entire, minutely pellucid-punctate, shining above, bright green beneath, base narrowed into a very short petiole. Flowers scarlet red, 3.8-5cm long and as much across, mostly solitary, sometimes 2-4 together, terminating short shoots, sometimes apparently axillary, sessile or nearly so. Calyx-tube campanulate, adnate to and produced beyond the ovary, coriaceous, lobes 5-7, valvate. Petals 5-7, obovate, scarlet, wrinkled, inserted between the calyx-lobes. Stamens very numerous, inserted on the calyx below the petals at various levels; anthers elliptic, dehiscing longitudinally. Ovary inferior, many celled, cells arranged in 2 concentric circles; style long, bent; stigma capitate. Carples early coalescing and owing to unequal growth becoming arranged into 2 tiers, 3 in the lower and 5-9 in the upper. Fruit 3.8-7.5 cm diam., globose, tipped with the calyx limb, rind coriaceous, woody, the interior septate with the membranous walls of the carples each carple containing numerous seeds angular from mutual pressure. Seeds with a watery outer coat containing pink juice and a horney inner coat (Kirtikar and

Basu, 1988; Anonymous, 1994). Various parts viz. flowers, fruits, rind of the fruit, seeds, dried bark of the stem and roots are used for medicinal purposes.

Phytochemical Constituents

Bark and rind of the fruit contain tannin 22 to 25% and the **root bark** contains punico -tannic acid 20-25 %, mannitol, gallic acid, sugar gum pectin, ash 15%, an active liquid alkaloid "Pelletierine" and oil liquid "Isopelletierine" and two inactive alkaloids methyl pelletierine and pseudo-pelletierine. Different parts of pomegranate contain different phytochemicals like: **Seed oil** contains 95% punicic acid; ellagic acid; other fatty acids & sterols. **Pericarp** (Peel, rind) contains phenolic punicalagins; gallic acid and fatty acids; catechin; quercetin, rutin and other flavonols; flavones, flavonones; anthocyanidins. **Leaves** contain tannins (punicalin and punicafolin); and flavones glycosides, including luteolin and apgenin. **Flowers** contain gallic acid, ursolic acid; triterpenoids, including maslinic and asiatic acid. **Roots** and **bark** contain elligitannins including punicalin and punicalagin; numerous piperidine alkaloids. **Juice** contains anthocyanins, glucose, ascorbic acid, ellagic acid, gallic acid; caffeic acid; catechin, quercetin, rutin; numerous minerals, particularly iron and amino acids (Arun and Singh, 2012; Nadkarni, 1989; Chopra, *et al.,* 1956).

Temperament

Majority of Unani scholars described its temperament (*Mizaj*) as *Barid-Yabis* i.e. cold and dry in varying degrees as follows:

Cold in first and dry in second degree (Ibn Sina, 1998; Ghani, 1921); Cold and dry in second degree (Ibn Baitar, YNM; Nasir, 1886; Haleem, 1948); Cold and moist (Ali, 2010; Nigwami, 1985)

Ethnobotanical Uses

In addition to its ancient uses, pomegranate is used for a variety of ailments in Unani Medicine. Extract of flowers is astringent (*Qābiḍ-wa-Ḥābis)* thus checks haemorrhage from all internal organs (Ibn Baitar, YNM; Ghani, 1921; Haleem, 1948; Ali, 2010; Anonymous, 1994; Nadkarni, 1989). Its desiccant (*Mujaffif)* properties dry up *Ruṭūbat-e-Fāsida* i.e. morbid bodily secretions (Ibn Baitar, YNM; Haleem, 1948). Application of powder or its decoction is useful in *Qulā*' (Stomatitis) and also prevents various oro-dental disorders like bleeding gums, shaky teeth, bad odour, mouth ulcer, etc. Ointment is effective in wound healing because of its cicatrizant (*Mudammil-i-Jarāḥat*) properties (Ibn Baitar, YNM; Ghani, 1921; Haleem, 1948). It is also effective in treating *Saḥj* wa Qurūḥ *al-Am'ā*' (intestinal erosions or ulcers), *Ishāl* (diarrhoea) and Zaḥīr (dysentery). Sitz-bath in its decoction is useful in the treatment of *Bawāsīr* (piles), *Sayalān al-Raḥim*

(leucorrhoea) and abnormal uterine bleeding (Ghani, 1921). Flower extract is also beneficial in skin diseases like scabies (*Jarb*), irritation and pruritus (*Hikka*), etc. Moreover, the extract by virtue of its repellent (*Radi mādda*) properties is effective in protecting susceptible organs from morbid humours thereby enhancing the body-immunity (Ibn Baitar, YNM). Both root and stem bark, being anthelmintic (*Qātil-i-Dīdān*) in action expel the intestinal worms when administered in the form of decoction (Ali, 2010; Anonymous, 1994; Chopra, *et al.,* 1956; Nadkarni, 1989; Anonymous, 1982; Kirtikar and Basu, 1988; Wallis, 1985). Whole fruit is used as cardiac and liver tonic (*Muqawwī Qalb wa Jigar*) and aphrodisiac (*Muqawwī Bāh*) in sexual debility (Ali, 2010; Anonymous, 1994; Nigwami, 1985; Kirtikar and Basu, 1988). Fruit rind is effective in strengthening of teeth and gums (Ghani, 1921; Ali, 2010; Anonymous, 1994; Ibn Sina, 1998; Kirtikar and Basu, 1988). Seeds are anti-emetic (*Dāfi'-i-Qay'*) and diuretic (*Mudirr-i-Bawl*) in action (Ali, 2010; Anonymous, 1994).

Evidence based Pharmacological Activities: Several researches have reported different biological activities of *Punica granatum* L. in various *in-vitro* and *in-vivo* test models. Some of them with high translational value have been mentioned in detail:

Antioxidant Activity

An *in-vitro* assay using four separate testing methods demonstrated that pomegranate juice and seed extracts have 2-3 times the antioxidant capacity of either red wine or green tea (Gil, *et al.* 2000). Pomegranate extracts have been found to scavenge free radicals and decrease macrophage oxidative stress and lipid peroxidation in animals and increase plasma anti-oxidant capacity in elderly humans (Rosenblat, *et al.,* 2006; Guo, *et al.* 2008). Studies in rats and mice confirm the antioxidant properties of a pomegranate by-product (PBP) extract made from whole fruit minus the juice, showing 19% reduction in oxidative stress in mouse peritoneal macrophages (MPM), 42% decrease in cellular lipid peroxide content, and 53% increase in reduced glutathione levels (Rosenblat, *et al.,* 2006). *In-vitro* assay of fermented pomegranate juice (FPJ) extract and cold pressed seed oil (CPSO) extract found that antioxidant capacity of both are superior to red wine as well as green tea extract (Schubert, 1999). A separate study in rats with CCl_4 induced liver damage demonstrated that pre-treatment with a pomegranate peel extract (PPE) enhanced or maintained the free-radical scavenging activity of the hepatic-enzymes catalase, super oxide dismutase and peroxidase, and resulted in 54% reduction of lipid peroxidation values compared to controls (Chidambara, *et al.,* 2002). Research in humans has shown a juice made from pomegranate pulp (PPJ) has superior antioxidant capacity to apple juice. Using the FRAP assay (ferric reducing/antioxidant power), Guo *et al.* found that 250 mL PPJ given to healthy elderly subjects in the dose of 250

ml PPJ daily for four weeks increased plasma antioxidant capacity from 1.33 mmol to 1.46 mmol, while subjects consuming apple juice experienced no significant increase in antioxidant capacity. In addition, subjects consuming the PPJ exhibited significantly decreased plasma carbonyl content (a biomarker for oxidant/antioxidant barrier impairment in various inflammatory diseases) compared to subjects taking apple juice. Plasma vitamin E, ascorbic acid and reduced glutathione values did not differ significantly between groups, leading researchers to conclude that pomegranate phenolics may be responsible for the observed results (Guo, *et al.* 2008).

Anticarcinogenic Activity

In-vitro assays utilizing three prostate cancer cell lines (DU-145, LNCaP, and PC-3) demonstrated that various pomegranate extracts (juice, seed oil, peel) potently inhibit prostate cancer cell invasiveness and proliferation, cause cell cycle disruption, induce apoptosis and inhibit tumor growth. These studies also demonstrated that combinations of pomegranate extracts from different parts of the fruit were more effective than any single extract (Lansky, *et al.,* 2005; Albrecht, *et al.,* 2004). Several animal studies have elucidated pomegranate's potential anticancer mechanisms. Two studies in mice implanted with prostate cancer PC-3 cell line demonstrated that pomegranate fruit extract (PFE; edible parts of the fruit, excluding the peel) inhibits cell growth and induces apoptosis via modulation of proteins regulating apoptosis (Malik, *et al.,* 2006; Malik, *et al.,* 2005). In an open-label phase II clinical trial in 46 men with recurrent prostate cancer, 16 patients (35%) showed significant decrease in serum prostate specific antigen (PSA) levels (average=27%) during treatment with eight ounces of pomegranate juice. Corresponding *in-vitro* assays using patient plasma and serum demonstrated significant decrease in prostate cancer cell line proliferation and increased apoptosis. Nitric oxide preservation via ingestion of pomegranate polyphenols significantly correlated with lower PSA values. These results indicate pomegranate may affect prostate cancer because of anti-proliferative, apoptotic, antioxidant and possibly anti-inflammatory effects (Pantuck, *et al.,* 2006). Recent research also indicates pomegranate constituents inhibit angiogenesis via down regulation of vascular endothelial growth factor in MCF-7 breast cancer and human umbilical vein endothelial cell lines (Toi, *et al.,* 2003).

Anti-inflammatory Activity

Cold pressed pomegranate seed oil has been found to inhibit both cyclo-oxygenase and lipoxygenase enzymes *in vitro*. Cyclo-oxygenase, a key enzyme in the conversion of arachidonic acid to prostaglandins (important inflammatory mediators) was inhibited by 37 percent by a CPSO extract. Lipoxygenase, which catalyzes the conversion of arachidonic acid to leukotrienes, also a key

mediator of inflammation, was inhibited by 75 percent by a CPSO extract. By comparison, an FPJ extract resulted in 23.8% inhibition of lipoxygenase *in vitro* (Schubert, *et al.,* 1999). Another *in-vitro* study that may have far-reaching implications for those suffering from osteoarthritis (OA) demonstrated that PFE has a significant and broad inhibitory effect on matrix metalloproteinases (MMPs), a subgroup of collagenase enzymes expressed in high levels in arthritic joints and involved in the turnover, degradation and catabolism of extracellular joint matrix. In pre-treated human femoral OA chondrocytes, PFE inhibited IL-l beta induced destruction of proteoglycan, expression of MMPs at the cellular level and phosphorylation, and activation of mitogen-activated protein kinases (signal transduction molecules involved in MMP expression). The suppression of MMP expression in OA chondrocyte cultures by PFE suggests that pomegranate constituents prevent collagen degradation and may inhibit joint destruction in OA patients (Ahmed, *et al.,* 2005).

Hypoglycaemic Activity

Animal studies have revealed three possible hypoglycaemic mechanisms for *Punica granatum* extracts. Pomegranate flower extract (PFLE) improved insulin sensitivity and lowered glucose levels in rats as early as 30 minutes post-glucose loading. PFLE also inhibited alphaglucosidase *in-vitro*, thereby decreasing the conversion of sucrose to glucose (Huang, *et al.,* 2005). PPE demonstrates significant hypoglycaemic activity in diabetic rats, via enhanced insulin levels and regeneration of pancreatic beta cells (Khalil, 2004).

Anti Hyperlipidaemic and Anti-obesity Activity

A pilot study in type 2 diabetic patients with hyperlipidaemia found that concentrated PJ decreased cholesterol absorption, increased faecal excretion of cholesterol, had a beneficial effect on enzymes involved in cholesterol metabolism, significantly reduced total and LDL cholesterol, and improved total/HDL and LDL/HDL cholesterol ratios (Esmaillzadeh, *et al.,* 2006).

Antihypertensive Activity

Pomegranate juice consumption by hypertensive patients inhibits serum angiotensin converting enzyme (ACE; a catalyst for the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor) activity, thereby reducing systolic blood pressure (Aviram and Dornfeld 2001) and potentially protecting against cardiovascular disease.

Anti-atherosclerotic Activity

In early-stage atherosclerosis, elevated plasma cholesterol, increased oxidative stress and increased cholesterol esterification rates are factors contributing to

foam cell formation and development of atherosclerotic lesions (Ross, 1999; Tabas, 1995). Research in atherosclerotic apolipoprotein- E deficient (E°) mice by Aviram, *et al.* has suggested on the ability of pomegranate extracts to inhibit atherogenesis (Rosenblat, *et al.,* 2006; Aviram, *et al.,* 2000). Two months of PJ to E° mice with advanced atherosclerosis reduced MPM lipid peroxide content by 42 percent compared with placebo-treated mice; MPM lipid peroxide content in PJ-treated mice was 20% lower than in four-month-old control mice. In addition, MPM harvested from PJ-treated mice exhibited 80% lower rates of cholesterol esterification than placebo-treated mice. In PJ-treated mice atherosclerotic lesion size in the aorta was 17% smaller than in the age-matched placebo group. PJ and an isolated tannin fraction from PJ were also given to young E° mice prior to development of significant atherosclerosis. Researchers found 25% and 17% reductions in plasma lipid peroxide concentrations with the isolated tannin fraction and PJ, respectively (Kaplan, *et al.,* 2001).

Anti-bacterial Activity

Numerous *in-vitro* studies (Voravuthikunchai and Limsuwan, 2006; Braga, *et al.,* 2005) and two human trials (Menezes, *et al.,* 2006; Vasconcelos, *et al.,* 2003) demonstrated the antimicrobial activity of pomegranate extracts. The growth of *Staphylococcus aureus, Streptococcus pyogenes, Diplococcus pneumoniae, Escherichia coli* O157:H7 and *Gandida albicaijs* was inhibited via direct bactericidal or fungicidal activity.

Adverse Effects and their Correction (Muzir and Musleh)

Prolonged and excessive use of pomegranate flowers may result in headache and obstruction which can be countered by using *Kateera* (*Sterculia urens*) or *Samagh-e-Arabi* (*Acacia arabica*) along with it (Ghani, 1921; Nasir, 1886; Haleem, 1948).

Substitute (Badal)

Extract of *Lahiyat-ut-tees* and *Juft Baloot* (*Quercus incana*) have been described as substitutes of pomegranate flowers and rind (Ghani, 1921; Ibn Baitar, YNM).

Compound Formulations (Murakkabat)

Qurs Gulnaar, Qurs Ziabetus, Qurs Tabasheer, Jawarish Anarain, Jawarish Pudina and *Sharbat Anaar* are some of the famous compound formulations of pomegranate used in Unani Medicine (Jeelani, 1995; Ali, 2010).

Conclusion

Punica granatum has been in use since ancient times to treat wide range of diseases in Unani system of medicine. In the present comprehensive review,

we referred primary and secondary data to compile the information based on taxonomy, distribution, morphological description, phyto-chemical constituents, ethnobotanical and pharmacological claims on *Punica granatum*. Though traditionally the plant is used widely for the treatment of various ailments, but scientifically only few of them were screened out. Thus more scientific studies must be conducted to investigate the unexploited potential of *Punica granatum* L.

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सारांश

रुम्मान (*पुनिका ग्रेनाटम एल.*) की पादप रासायनिक और औषधीय जांच

शाह आलम, निग़हत अन्जुम, जमाल अख़्तर, फौज़िया बशीर, आसिम अली और नाहीद परवीन

विभिन्न रोगों की रोकथाम और उपचार के लिए औषधीय पौधों का उपयोग प्राचीनकाल से ही चलन में है। लाइथ्रेसी प्रजाति से संबंधित रुम्मान/अनार (पुनिका ग्रेनटम एल.) को विभिन्न विकारों जैसे गैस्ट्रोइंटेस्टाइनल, हेमेटोलॉजिकल, रीनल या यूरो–जेनाइटल इत्यादि विकारों में प्रभावी बताया गया है। यह पौधा अपने फल अनार/रुम्मान के नाम से लोकप्रिय है। विभिन्न जातीय और ग्रामीण समूहों के बीच पौधे के विभिन्न भाग अर्थात् फूल, फल, फल के छिलके, बीज, तने की सूखी छाल और जड़ का उपयोग औषधि के रूप में किया जाता है। गुलनार उस अनार के पेड़ का सुर्ख लाल फूल है जो फल नहीं दे सकता। यूनानी चिकित्सा पद्धति में इस फूल का उपयोग औषधीय उद्देश्य के लिए किया जाता है। यूनानी चिकित्सा पद्धति में इस पौधे के कुछ भागों को पौष्टिक गुणों से युक्त होने के साथ स्तंभक, क मिनाशक, शुष्कक, आमाशायिक और दस्त निरोधक माना जाता है। यह लेखन क्लासिकी यूनानी के साथ–साथ आधुनिक साहित्य में पुनिका ग्रेनटम एल. के विभिन्न पहलुओं पर जानकारी संकलित और प्रलेखित करने का प्रयास है। पौधे को वैज्ञानिक जांच के लिए आगे ले जाने के लिए सुझाव दिया गया है ताकि यहां प्रस्तुत औषधीय दावों को मान्य किया जा सके और इसकी अधिकतम चिकित्सीय क्षमता का प्रयोग किया जा सके।

शब्दकुंजी: गुलनार, लियथ्रेसी, पुनिका ग्रेनटम एल., यूनानी

Elderly Care in Unani Medicine – A Review

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Abstract

Ageing is a normal, inevitable and universal phenomenon which is the result of progressive deterioration in the body. A person is said elderly or old when he reaches the age of 60 years. United Nations also defines a person elderly whose age is 60 years and above. We are living in an era of 'demographic transition', i.e. increased population of elderly. The number of people aged 60 years or above will rise from 900 million to 2 billion between 2015 and 2050 (moving from 12% to 22% of the total global population). This shows how population is changing in different countries around the world. More than two thousand years ago, the discussion about quality of life was started by Aristotle (384-322 BC): He said, "Good life is not only something to live for but also something to live by". Old age should not equate with ill-health; In fact, most of the health problems associated with ageing are preventable. Therefore, we need to study the factors which bring about ill-health with advancing age. The uniqueness of Unani Medicine is its holistic approach towards maintenance of physiological processes to delay ageing; hence, it has great potential in preventive geriatrics. With the gradual decline of *Hararat Ghariziya* and *Rutubat Ghariziya*, the *Mizaj* in old age gradually becomes *Barid* and *Yabis* (*Saudawi* or melancholic). The *Saudawi Mizaj* is responsible for many conditions and diseases which are caused by *Saudawi* humor. In this paper, an attempt has been made to compile information on how to improve quality of life of elderly with Unani Medicine and importance of *Tadābīr-i Mashāikh* (Elderly Healthcare).

Keywords: Dietotherapy; Elderly Healthcare; *Hararat-i Ghariziya*

Introduction

Elderly healthcare management is the process of planning and coordinating care of the elderly and others with physical and/or mental impairments to meet their long term care needs, improve their quality of life and maintain their independence for as long as possible. It entails working with persons of old age and their families in managing, rendering and referring various types of health and social care services. Geriatric care managers accomplish this by combining a working knowledge of health and psychology, human development, family dynamics, public and private resources and funding sources.

India is in a phase of demographic transition. As per the 1991 census, the population of the elderly in India was 57 million as compared with 20 million in 1951. There has been a sharp increase in the number of elderly persons between 1991 and 2001. According to Population Census 2011, there are nearly 104 million elderly persons (aged 60 years or above) in India; 53 million females

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and 51 million males. A report released by the United Nations Population Fund and Help Age India suggests that the number of elderly persons is expected to grow to 173 million by 2026 (Anonymous, YNM).

In Unani Medicine, the lifespan is divided into four stages:

- ***Sinn-e-Numu***: The stage of growth, which lasts upto the age of 30 years
- ***Sinn-e-Waquf***: The stage of stability, which lasts upto the age of 30-40 years
- ***Sinn-e-Kuhulat***: The stage when *quwa* start to decline, but some strength persists. This lasts upto the age of 60 years
- ***Sinn-e-Shaykhukhat***: The stage in which *inhetat* (decline) occurs, and ultimately leads to death (applies to people above 60 years of age)
- The people above 60 years of age are considered as *Mashāikh* (aged/ older people). It is the period of decline with the appearance of weakness in vigour

Health is maintained by equilibrium of *Akhlat-i Arbaʻa* i.e *Dam* (Sanguinous humour), *Balgham* (Phlegmatic humour), *Safra* (Bilious humour), *Sauda* (Atrabilious humour). As long as these humours remain in equilibrium, health is maintained and derangement in these either qualitatively or quantitatively leads to different diseases. Since the equilibrium mechanism becomes weak as the age advances due to decline in *Quwat wa Affʻal* (power and function), it leads to various age related diseases and lifestyle diseases in *Mashāikh* (old age).

Unani scholars were well aware about the ageing process and a very exhaustive description on this subject is mentioned in Unani classical literature under the heading of *Tadābīr-i Mashāikh*. The process of ageing is attributed to depletion of *Rutūbat-i Ghariziya* (moistness) and *Hararat-i Ghariziya* (innate heat) of the body. *Rutūbat-i Ghariziya* (moistness) is essential for maintaining health of vital organs of the body and its depletion marks the onset of senility. Healthy ageing can be secured by safeguarding innate moisture from too rapid dissipation and by maintaining it.

In Unani Medicine, management of ageing includes promotion and production of *Rutūbat-i Ghariziya* (moistness) and its preservation by following various regimens of *Ilaj bil Ghiza* (Dietotherapy), *Ilaj bil Tadbīr* (Regimenal Therapy) and *Ilaj bil Dawa* (Pharmacotherapy). Moreover, the unique Unani concept of organ-specific tonics and *Iksir i Badan Adviya* (elixir) is much relevant in elderly people than in any other age group. Good diets are necessary for good health of all ages. Due to deficiency of proper diet, chances of disease increase. Therefore we should try to provide proper diet to the *Mashāikh* because it is believed that

healthy diet has important influence on longevity (Majusi, 2010; Ahmed, 1980; Malik and Haque 2013; Rizwana, *et al.,* 2015; Anjum, 2017)

Tadābir-i Mashāikh (Regimen for Elderly)

Legendary Unani philosophers like Jalinus, Abu Sahal Masihi, Ibn Rushd, Ibn Rabban Tabari, Razi and Ibn Sina described *Tadābīr-i Mashāikh* (regimen for the elderly) in context of diet, bath, sleep, drink, exercise, defecation and urination.

The aims of *Tadābir-i Mashāikh* are:

- To protect *Rutūbat-i Gharizia* and *Harārat-i Gharizia* as long as possible.
- To prevent the conversion of *Mizaj* from *Har Ratab* to *Barid Yabis*.
- To check the production of *Rutūbat-i Ghariba.*
- To remove the waste from the body through natural methods and channels.
- To protect body from hazardous extrinsic factors.

Ilaj bil Ghiza (Dietotherapy)

Unani scholars have suggested principles about the diet of the elderly; it should be according to the *Mizaj* (temperament) of a person. They believed that different types of foods should be given to *Mashāikh*, but the quantity and quality of diet should be according to their digestive capacity. Frequent meal but small in quantity is recommended. Viscous, tenacious and flatulence yielding diet should be avoided.

- Beet root and spinach are specially advised.
- Meat of chicken or goat is recommended.
- Diet should be taken after *Hammam* (bath).
- Use of little amount of honey, rice and dates along with diet is also recommended.
- Milk is recommended for nutrition and *Tarteeb* (moistness).
- Use of fruits like *Anjeer, Akhrot, Badam, Angoor, Toot, Munaqqa, Alu Bukhara* is beneficial.
- Use of barley water is one of the best remedy for *Mashāikh.*
- Avoidance of hot condiment, *Muwallid-i Sauda* and *Balgham* diet (phlegm and black bile yielding diet).

- Drinking water immediately after and during meal should be avoided.
- *Mashāikh* are advised to take meal in small quantity at the time of hunger only.
- Sleeping on empty stomach should be avoided as it causes dryness in the body.
- For better sleep, moist diets are recommended. Massage of the scalp with aromatic oil is also recommended.
- For preservation of health of *Mashāikh,* good, nutritive and easily digestible diet should be given.
- Use of *Halelah*, *Zanjabeel* and *onion* is advised.
- *Ghaleez* diet which is not easily digestible like *Hareesa, red meat, Masoor,* etc. should be avoided.
- Vegetables like *Kasni, Kahu, Khubazi, Chuqandar* may be used. (Majusi, 2010; Ibn Sina, 1993; Ibn Rushd,1980; Shah, 2007; Ibn Sina, 2010)

Ilaj Bil Dawa (Drug Therapy)

Some Unani organ-specific tonics and *Iksir-i Badan Adwiya* (elixir drugs) used for prevention of geriatric diseases are as follows:

Drug	Botanical/ scientific name	Actions	Therapeutic / prophylactic uses
Amla	*Emblica officinalis*	*Mufarreh* (Exhilarant), *Muqawwi* (Tonic), *Muqawwi*-e-Qalb (Cardio protective), *Muqawwi-e-Dimagh* (Brain Tonic), *Musakkin* (Analgesic)	*Khafqan* (Palpitation), *Zo'f-e-Basr* (Asthenopia/ Amblyopia), *Zo'f-e-Dimagh* (*Cerebrasthenia*), *Nisyan* (Dementia). (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007a)
Zanjabeel	*Zingiber officinale*	*Muharrik* (Stimulant), *Mushtahi* (Appetizer), *Hazim* (Digestive), *Kasir-e-Riyah* (Carminative), *Munaffis-e-Blagham* (Expectorant)	*Zo'f-e-A'sab* (Nervine weakness like *Falij*, *Laqwa,* etc.), *Su-e-Hazm* (Indigestion), *Nafkh-e-Shikam* (Flatulence), Zof-e-Ishteha (Anorexia), *Waja-ul-Mafasil* (Polyarthritis), *Zeequn-Nafas* (Bronchial Asthma) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007a)

Drug	Botanical/ scientific name	Actions	Therapeutic / prophylactic uses
Asgandh	*Withania somnifera*	*Musakkin-e-A'sab* (Nervine Tonic), *Mudir* (Diuretic), *Mufatteh Sudad* (Deobstruent), *Muqawwi-e-Aam* (General Tonic), *Muqawwi-e-Meda* (Stomachich), *Muwallid*-e-Mani (Spermatogogue), *Munawwim* (Hypnotic)	*Waja-ul-Mafasil* (Polyarthritis), Asthenia, General Weakness, Psychological Stress, *Nisyan* (Dementia) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007a)
Sir	*Allium sativum*	*Dafa-e-Ta'ffun* (Anti-septic), *Muhallil* (Anti-inflammatory), *Dafa-e-Tashannuj* (Anti-spasmodic), *Muqawwi-e-Me'da* (Stomachic), *Muqawwi-e-A'sab* (Nervine Tonic)	*Hummma-e-Me'vi* (Typhoid Fever), *Nafkh-e-Shikam* (Flatuence), *Zo'f-e-Ishtiha* (Anorexia), *Ra'sha* (Tremors), *Waja-ul-Mafasil* (Polyarthritis), *Falij* (Paralysis) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007a)
Darchini	*Cinnamomum zeylanicum*	*Muqawwi-wa Muharrik-e-Qalb* (Cardiotonic and Stimulant), *Kasir-e-Riyah* (Carminative), *Dafa-e-Ta'ffun* (Antiseptic), *Mulattif* (Demulscent), *Munaffis-e-Balgham* (Expectorant), *Muqawwi-e-Meda* (Stomachic) *Mudirr-e-Baul* (Diuretic), *Mudirr-e-Haiz* (Emmenogogue)	Especially beneficial in cardiac diseases, also used in *Zo'f-e-Hazm* (Indigestion), *Zof-e-Bah* (Anaphrodisiab/loss of libido), *Zeequn-Nafas* (Bronchial Asthma) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007a)
Halela Zard	*Terminalia chebula*	*Muqawwi-e-Dimagh* (Brain Tonic), *Muqawwi-e-Me'da* (Stomachic), *Muqawwi-e-Basar* (Tonic for eye), *Musakkin* (Analgesic), *Musawwi-e-Shar*	*Nisyan* (Amnesia), *Zofe-e-Basarat* (Asthenopia/ Amblyopia), *Zo'f-e-Dimagh* (*Cerebrasthenia*), also used to prevent graying of hair (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007a)

Drug	Botanical/ scientific name	Actions	Therapeutic / prophylactic uses
Anjeer	*Ficus carica*	*Mulayyin* (Laxative), *Mulattif* (Demulscent), *Mughazzi* (Nutritive), *Musammin-e-Badan* (Enhances Body Weight), *Muhallil-e-Auram* (Resolvent)	*Qabz* (Constipation), *Zeequm-Nafas* (Bronchial Asthma), *Sara* (Epilepsy) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007b)
Mushk	*Moschus moschiferous*	*Mufarreh* (Exhilarant), *Muqawwi-e-Aza-e-Raisa* (Tonic to Vital Organs), *Mun'ish-e-Hararat-e-Gharizi* (Preserves Innate Heat), *Mufatteh Sudad* (Deobstruent)	*Zo'f-e-Qalb* (Cardiac weakness), *Khadar* (Numbness), *Ra'sha* (Tremors), *Nisyan* (Amnesia), Mental Confusion, General Weakness (Kabiruddin, 2000)
Sibr	*Aloe vera*	*Mushil* (Purgative), *Mudir* (Diuretic), *Muhallil* (Resolvent)	*Waja-ul-Mafasil* (Polyarthritis), *Qabz* (Constipation), *Ehtebas-e-Bawl* (Retention of urine), *Waram-e-Kabid* (Hepatitis) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007a)
Akhrot	*Juglans regia*	*Muqawwi A'sab wa Dimagh* (Cerebral and nervine tonic), *Mullaiyin* (Laxative), *Mulattif* (Demulscent)	*Suda-i-Asabi* (Headache with neurological involvement), *Zo'f-e-Hafiza* (Dementia) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007c)
Gaozaban	*Borago officinalis*	*Mulattif* (Demulscent), *Muqawwi-e-Dimagh* wa *Qalb* (Cardiac and Cerebral tonic)	*Zo'f-e-Qalb wa Dimagh* (Weakness of Heart and Brain), *Khafqan* (Palpitation), *Zat-al-Janab* (Pleurisy) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007b)
Gilo	*Tinospora cordifolia*	*Dafa-e-Humma* (Antipyretic), *Musaffi-e-Dam* (Blood purifier), *Mohallil-e-Auram* (Resolvent), *Mudir-e-Baul* (Diuretic)	*Humma* (Febrile illnesses), *Waja-ul-Mafasil* (Polyarthritis), *Ishal* (Diarrhea), *Zaheer* (Dysentery) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007a)

Drug	Botanical/ scientific name	Actions	Therapeutic / prophylactic uses
Anar	*Punica granatum*	***Anar Shireen***: *Muqawwi-e-Qalb* (Cardiac Tonic), *Muqawwi-e-Jigar* (Liver Tonic), *Musakkin Atash* (allays thirst), *Muwwalid-e-Dam* (Haematogenic), *Muddir-e-Baul* (Diuretic) ***Anar Tursh:*** *Qabiz* (Constipative), *Muqqawi-e-Qalb* (Cardiac Tonic), *Muqawwi-e-Jigar* (Liver Tonic), *Musakkin-e-Safra* (Bile Sedative), *Musakkine-e-Dam* (Blood Sedative), *Mudirre-e-Baul* (Diuretic), *Qat-e-Safra* (Antibilious)	***Anar Shireen***: *Atash-e-Mufrit* (Polydipsia), *Zof-e-Aam* (General Weakness), Faqruddam (Anaemia) ***Anar Tursh*** : *Sozish-e-Sadr* (Burning in the Chest), *Ghasiyan* (Nausea), *Qai* (Vomitting), *Yarqan* (Jaundice), *Atash-e-Mufrit* (Polydipsia) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007d)
Jadwar	*Delphinium denudatum*	*Muqawwi-e-Asab* (Nervine Tonic), *Muqawwi-e-Qalb* (Cardio Protective), *Tiryaq-e-Sumoom* (Antidote Poison), *Mufarreh* (Exhilarent), *Musakkin* (Analgesic), *Daf-e-Humma* (Antipyretic), *Mufatteh* (Deobstruent), *Mohallil* (Anti-Inflammatory)	*Nazla Muzmin* (Chronic Catarrh), *Iltehab Tajaweef-e-Anaf* (Sinusitis), *Sara* (Epilepsy), *Istirkha* (Paralysis), *Haiza* (Chlorea), *Yarqan* (Jaundice), *Zo'f-e-Meda* (Weakness Stomach), *Qulanj* (Colic) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2009)
Ajwain Khurasani	*Hyoscyamus niger*	*Mushtahi* (Appetizing), *Kasir-e-Riyah* (Carminative), *Dafa-e-Ta'fun* (Anti-Septic), *Dafa-e-Tashannuj* (Antispasmodic)	*Nafkh–e-Shikam* (Flatulence), *Zo'f-e-Hazm* (Indigestion), *Qulanj* (Colic), *Ishal* (Diarhhoea), *Waja-ul-Mafasil* (Polyarthritis), *Irq al-Nasā* (Sciatica), *Niqris* (Gout) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007d)

Drug	Botanical/ scientific name	Actions	Therapeutic / prophylactic uses
Zafran	*Crocus sativus*	*Daf-e-Ta'ffun* (Antiseptic), *Mohallil-e-Auram* (Anti-Inflammatory), *Muqawwi-e-Qalb* (Cardiac Tonic)	*Amraz-e-Qalb* (Cardiac Diseases), *Nazla* (Catarrh), *Zukam* (Coryza), *Zof-e-Basarat* (Asthenopia) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2009)
Kalonji	*Nigella sativa*	*Mohallil-e-Waram* (Resolvent), *Musakkin* (Analgesic), *Kasir-e-Riyah* (Carminative), *Muqawwi-e-A'sab* (Nervine Tonic), *Munaffis-e-Balgham* (Expectorant)	*Nisyan* (Amnesia), *Falij* (Paralysis), *Ra'sha* (Tremors), Zo'f-e-A'sab (Neurological Weakness), *Zeequn-Nafas*, Waja-*ul-Mafasil* (Polyarthritis) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007a)
Badranjboya	*Mellisa officinalis*	*Mufarreh* (Enhilarant), *Muqawwi-e-Qalb* (Cardiotonic)	*Zof-e-Qalb* (Cardiac insufficiency), *Khafqan* (Palpitation), *Sara* (Epilepsy), *Laqwa* (Facial Palsy), *Falij* (Paralysis), *Waja-ul-Mafasil* (Polyarthritis) (Ghani, YNM; Kabiruddin, 2000; Anonymous, 2007b)
Marjan	*Corallium rubrum*	*Mufarreh* (Enhilaratnt), *Muqawwi* (Tonic), *Habis* (Styptic)	*Wahshat* (Trepidation), *Khafqan* (Palpitation), *Waswasa* (Obsession), General Weakness (Kabiruddin, 2000)
Jal Brahmi	*Hydrocotyle asiatica/ Bacopa monnieri*	*Muqawwi-e-A'sab* (Nervine Tonic), *Muqawwi-e-Dimagh* (Brain Tonic), *Musakkin* (Alnalgesic), *Musaffi-e-Dam*, *Mudir-e-Baul,Waja-ul-Asab, Musakkin*	*Zo'f-e-Hafiza* (Amnesia), *Suda'* (Headache), *Zo'f-e-Basar* (Asthenopia), *Junoon* (Insanity) (Ghani, YNM; Kabiruddin, 2000; Anonymous, (2007c)

Some Compound Formulations Beneficial for the Elderly

- *Jawarish Jalinoos*
- *Majoon Falasfa*
- *Khamira Gaozaban*
- *Khamira Abresham*
- *Khamira Marwareed*
- *Majoon Azaraqi*
- *Sharbat Faulad*

Ilāj bil Tadbīr (Regimenal Therapy)

Riyazat (Exercise): Elderly people should perform *Motadil Riyazat* (moderate exercise) regularly because it produces a *Musakhkhin* (heating) effect in the body of elderly and it also expels harmful substances from the body (Majusi, 2010; Ibn Sina, 1993).

Dalak (Massage): For elderly people, moderate massage should be done specifically on weak parts of the body. The massage can be done with or without oil and the oil should be hot in temperament to provide *Taskhin* (heat) to the body (Majusi, 2010).

Nutool (Pouring)

Nutool therapy is one of the important components of various procedures of systematic purification techniques of *Ilāj bil Tadbīr*. *Insomnia* is a unique and complex problem in geriatric population. Oils having *murattib* (moisture) and *munawwim* (induces sleep) properties have been mentioned for *Nuthool* therapy of those suffering from insomnia. Ancient physicians had tried it with good results (Jahan, *et al.*, 2014).

Apart from the above regimens, *Hijama* (Cupping), *Irsal-i Alaq* (Leeching) and *Inkebaab* (Vaporisation) are also recommended in old age.

Lifestyle Modification for Elderly

As recommended by *Avicenna,* lifestyle modifications for the elderly are as follows:

- Aged persons should have adequate sleep
- Bowels should be kept soft
- They should continually use the diet having diuretic properties and phlegm should be evacuated from the body through bowels and bladder

- They should avoid heavy food which may produce phlegm and black bile.
- Avoid drinking of cold water as it produces heaviness in stomach and also lowers *Harārat-i Ghariziya* (Ibn Sina, 2010).

Conclusion

Ageing changes may be said to be a result of declining *Harārat-i Ghariziya* and *Rutūbat-i Ghariziya,* therefore the key to preventing ageing (not old age) lies in maintaining these two. In general, it is advisable that the *Tadābīr* for old people should be "*Murattib*" to compensate for the loss of *Rutūbat-i Ghariziya* and *Musakhkhin* to compensate for the loss of *Harārat-i Ghariziya,* meals should be short and frequent keeping in mind their *Quwa,* meals should constitute *Mulayyinat* (laxatives), *Ghaleez* (difficult to digest) *ghiza* should be avoided, especially which is *Moallid-e-Sauda* or *Moallid-e-Balgham*. Goat milk is preferred among others. *Ma-ul Asl* may be used in winters. *Roghan-e-Zaitoon* (Olive oil), carrots, *Chuqandar* (beetroot), *Karafs* (celery) etc are preferred as diet. Garlic should be taken in moderation as it may cause *yabusat*. *Anjeer* (Fig), *Aalu Bukhara* (Plum) and similar fruits may be used in summers. Old people should get more sleep than younger people. Moderate and gentle massage with oils is beneficial in old age. Type and extent of physical activity should be individualized depending on general health. Walking is preferred as a form of exercise. Specific *Riyazat* (exercise) may be advised for different organs if walking is not possible, for instance, breathing exercises. Regular massage should be done to strengthen the body. Massage should be done for short duration with moderate pressure. It may be repeated when necessary. *Mufatteh-Sudad* (deobstruent) measures should be taken regularly. *Hammam,* oil massage and diet such as barley, honey, *Zufa* (*Hyssopus officinalis*) and *Parsiyaoshan* (*Adiantum capillus-veneris*) are advisable for this purpose. Some single Unani drugs like Anti-oxidants *Amla, Sir, Zanjabeel and Elwa;* Immunomodulatory drugs like *Gilo, Zafran, Marjan* and *Badam* as well as compound *Unani* formulations like *Majoon Falasfa, Majoon Brahmi and Khamira Gaozaban Ambari,* etc. may be given for elderly care.

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सारांश

यूनानी चिकित्सा में बुजुर्गों की देखभाल - एक समीक्षा

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

प्रौढ़ावस्था एक सामान्य, अपरिहार्य और सार्वभौमिक तथ्य है जो शरीर में प्रगतिशील गिरावट का परिणाम है। किसी व्यक्ति को 60 वर्ष की आयु तक पहुंचने पर बुजुर्ग कहा जाता है। संयुक्त राष्ट्र भी ऐसे व्यक्ति को बुजुर्ग परिभाषित करता है जिसकी उम्र 60 वर्ष या इससे अधिक है। हम जनसांख्यिकीय संक्रमण के युग में जी रहे हैं अर्थात् बुजुर्गों की जनसंख्या में वृद्धि हुई है। 2015 से 2050 के बीच 60 से अधिक आयु वर्ग के लोगों की संख्या 900 मिलियन से 2 बिलियन (कुल वैश्विक जनसंख्या का 12% से 22%) हो जाएगी। दो हज़ार साल से भी ज्यादा पहले अरस्तू (384–322 ईसा पूर्व) ने जीवन की गुणवत्ता के बारे में चर्चा की थी। उन्होंने कहा, ''अच्छा जीवन केवल वह नहीं है जिसके लिए जिया जाए, बल्कि वह भी है जिसको जिया जाए''। वृद्धावस्था को अस्वस्थता के समान नहीं मानना चाहिए; वास्तव में, उम्र बढ़ने से जुड़ी अधिकांश स्वास्थ्य समस्याएं रोकी जा सकती हैं। इसलिए हमें उन तथ्यों पर अध्ययन करने की आवश्यकता है जो बढ़ती उम्र के साथ अस्वस्थता लाते हैं। यूनानी चिकित्सा की विशिष्टता बढ़ती उम्र को रोकने के लिए शारीरिक प्रक्रियाओं के संरक्षण के लिए इसका समग्र दृष्टिकोण है। हरारत–ए–ग़रीज़िया और रुतुबत–ए–ग़रीज़िया की गिरावट के साथ बुढ़ापे में मिज़ाज क्रमशः बारिद और याबिस (सौदावी या मेलनकोलिक) बन जाता है। सौदावी मिज़ाज कई स्थितियों और रोगों के लिए जिम्मेदार है जो सौदावी ह्युमर के कारण होते हैं। इस पेपर में यूनानी चिकित्सा के साथ बुजुर्गों के जीवन की गुणवत्ता में सुधार करने के तरीकों और तदाबीर–ए–मशएख (बुजुर्ग स्वास्थ्य देखभाल) के महत्व को संकलित करने का प्रयास किया गया है।

शब्दकुंजी: आहार–चिकित्सा, प्रौढ़ावस्था, हरारत–ए–ग़रीज़िया

Sub-Acute Oral Toxicity Study of *Kushta Qalai* (Herbo-mineral Unani Formulation) in Wistar Rats

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Abstract

Kushta Qalai is a herbo-mineral formulation of Unani System of Medicine which is used effectively for treatment of spermatorrhoea, premature ejaculation, nocturnal emission, impotency; it increases sex vigour and density of semen. The objective of this study was to investigate the sub-acute oral toxicity of *Kushta Qalai* drug as well as its crude material (its un-detoxified form) in young, healthy Albino rats (Wistar Strain) of both sexes in order to know their adverse effects, if any, and also to check the scientific validity of the detoxification method. A limit dose of 1000mg/kg and its sub fractions, 500mg and 250mg/kg body weight was administered to rats daily for 28 days. The animals were sacrificed on the 29th day. Blood sample was collected for haematological and biochemical investigations and the tissues for histopathological examination. There were no statistically significant changes in physiological, biochemical and haematological parameters at all the three dose levels, indicating NOAEL for *Kushta Qalai* drug and its crude material as 1000mg/kg body weight. The study concludes that *Kushta Qalai* drug is safe for oral administration at the therapeutic dose level.

Keywords: Haematological Parameters, Histopathology, *Kushta, Qalai,* Unani Medicine

Introduction

Kushta is the finest powder form of Unani medicinal preparation obtained by the calcinations of metal, mineral or animal origin drugs (Anonymous, 2008). These drugs, by special process, are calcinated in closed crucibles at a very high temperature and the oxide that we get (calcined form) is technically known as *Kushta* in Unani Medicine, *Bhasmas* in Ayurveda, and *Parpams* in Siddha. According to the traditional healers, these calcination techniques are specialized processes wherein herbal ingredients are incorporated during preparation of ash (Aziz, *et al.*, 2002). It is also claimed that these techniques increase the efficacy of drug and either remove the toxicity completely or downgrade it to the level where the drug can be safely used (Chopra, *et al.*, 1982; Kabiruddin and Wahid, 1992; Bajaj and Vohora, 2000). In the traditional system, *Kushta* is used for those dosage forms which are effective in small quantity and are prompt in action (Said, 1966). *Kushta* is quickly absorbed in the human body because of its nano particle size (Said, 1997; Anonymous, 2006).

In Unani System of Medicine, *Kushta Qalai* is used for the treatment of male sexual disorders like spermatorrhoea, excessive nocturnal emission, premature ejaculation and impotency. It increases sex vigour and density of semen (Said,

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1970; Sadananda, 1998; El-Eswed & Bassam, 2002; Hafeez, 2005; Kabiruddin, 2005; Qarabadeen, 2005).

The ingredients of *Kushta Qalai* are *Qalai*, *Aloe vera* and *Phitkari*. The *Qalai* (Tin) is one of the most popular metals known for its use since Vedic period (Jani *et al.,* 2009). *Qalai* is silver like metal, which is softer than the gold but harder than the lead, malleable and sparingly ductile with little elasticity (Nadkarni, 1976). It is used internally in the form of *Kushta*. It is known by diverse vernacular names like *Rasas* in Arabic, *Urziz* in Persian, *Rang* in Hindi, *Vanga* in Sanskrit and *Qalai* in Gujarati. There are two varieties of *Qalai-Khuraka* and *Mishraka*. Only the *Khuraka* is acceptable for therapeutic applications (Nadkarni, 1976). The *Qalai* was grinded with heavy duty wily mill to make its fine powder which was then used. Aloe vera (*Aloe bardadensis*) is an important component of *Vrihani gutika* which is considered the drug of highest potency useful in the treatment of sexual dysfunction (Charak & Shloka, 1998). *Phitkari (Alum)* is a mineral origin drug of Unani Medicine (Mariyam & Wajeeha, 2005). Table 1 shows the constituents of crude *Kushta Qalai*.

Table 1: Constituents of crude *Kushta Qalai*

Ingredient	English / Scientific Name	Amount
i. *Qalai*	Stannum (Tin)	250 gm
ii. *Aloe vera*	Aloe / Aloe vera	100 ml
iii. *Photkari*	Alum/ Potassium alum	125 gm

There is limited scientific data available about the difference in toxicity between the calcinated material and crude material. This study was done to determine the effectiveness of detoxification method adopted while preparation of *Kushta*. In this study, an effort has been made to scientifically validate these methods and also to intensify the adverse effects of the crude materials used in the preparation of *Kushta*.

Materials and Methods

Test Item (Drug and Crude Material)

The drug and crude ingredients of *Kushta Qalai* were procured from the registered Unani crude drug dealer M/s. Ellahi Dawakhana, Unani Ayurvedic Medicines, Habak, Naseem Bagh. The manufacturer of the drug of *Kushta Qalai* is Hamdard Laboratory India (P Certified) Mg. Lic No U-212/78. All the crude materials were identified by Dr. M.A. Wajid (Unani Pharmacologist), Ex. Deputy Director, RRIUM, Srinagar. The drug and crude material powder were mixed with RO water to make suspension for oral administration.

Experimental Animals and Maintenance

The experimental animals (young, healthy albino rats of Wistar strain) were procured from IIIM, Jammu. These rats were kept in the animal house and were observed during the quarantine and acclimatization period (Capdevila, *et al.*, 2007). A veterinary examination was conducted on the rats prior to and at the end of the acclimatization and quarantine period of 14 days. Five rats of same sex were housed per cage and the rats were housed under standard environmental condition in polypropylene cages at a temperature of 20 – 25°C with 12:12 hour dark and light cycle and had a free access to feed and water *ad libitum*. The rats were provided pelleted feed procured from Pranov Agro Industries, New Delhi and RO water. The use of animals in the study was approved by the Institutional Animal Ethics Committee (IAEC) of Regional Research Institute of Unani Medicine, Srinagar which is registered with the CPCSEA, India resting with registration No. 927/GO/C/06/CPCSEA.

Experimental Design

The sub-acute oral toxicity study was performed according to OECD guideline-407 (Organization of Economic Co-operation and Development) (OECD, 2008). The rats were randomly divided into 14 groups (7 male and 7 female groups) each consisting of 5 rats. The Group I and II being the male and female controls were orally given RO water (vehicle only). The Group III, IV & V being the experimental male rats and Group VI, VII, VIII, the experimental female rats were orally given *Kushta Qalai* drug at the dose of 1000mg, 500mg and 250mg/kg body weight respectively for 28 days daily. The Group IX, X & XI being the experimental male rats and group XII, XIII & XIV the experimental female rats were orally given crude material at the dose of 1000mg, 500mg and 250mg/kg body weight respectively for 28 days daily. All the animals were closely observed at 1 and 4 hours of dosing to examine any adverse toxic signs, behavioural changes, etc. The body weight of the rats was evaluated weekly. Feed and water consumption / rat / 24 hours was recorded before dosing and then weekly upto 4 weeks. On the 29th day, after over-night fasting, all the animals were sacrificed by withdrawing blood under Isoflurane anaesthesia. All the animals were dissected to check macroscopic morphology of the body organs. The organs such as liver, lung, kidney, adrenal gland, pancreas, spleen, brain, ovary/testes and heart were collected to determine the relative organ weight followed by grossing in which a small piece of tissue was collected and fixed in formalin for histopathological examination.

Dosage of *Kushta Qalai* in Humans: 125mg / day orally with water (Anonymous, 2008). This amounts to about 2mg/kg/day in human subjects. Table 2 shows the corresponding dose level in rats.

Table 2: Corresponding Dose Level in Rats

Particulars of Study	Sub-acute Toxicity Study
Dose Level	1000, 500 and 250mg/kg body weight (Corresponding to 70X, 35X and 17.5X the extrapolated dose in rats)
Dosing Schedule	Repeated daily dosing by oral route
Period of Observation	28 Days
Observation Parameters	See Text

Curry, *et al* has previously calculated interspecies dose conversion from rats weighing 100gm body weight to humans with 60kg body weight. The equivalent surface area dosage conversion factor from rat to humans was 1/7 (Curry, *et al.,* 2011).

Biochemistry Parameters

Biochemical parameters were studied in serum obtained after centrifugation of blood at 2000 RPM for 15 minutes on the day of sacrifice. Biochemical parameters were determined on fully automatic biochemistry analyzer (XL-600 TRANSASIA) using ERBA kits. Liver function tests - aspartate aminotransferase AST, alanine aminotransferase ALT, alkaline phosphatase ALP, Total bilirubin, total protein and albumin, and kidney function tests - blood urea, serum uric acid and serum creatinine were done. In addition to this, other metabolic function tests such as blood glucose, serum cholesterol and serum triglyceride were estimated.

Haematological Parameters

Haematological parameters were analyzed in freshly collected blood in blue top vacutainer containing EDTA anticoagulant. The blood was gently mixed with the EDTA anticoagulant coated on the tube walls. Haematological parameters were determined on fully automatic haematological analyzer (Sysmex XT-2000iV Sysmex Corporation Japan) having animal version software. Haematological parameters such as Haemoglobin Conc, WBC count, RBC count, haematocrit, Mean Corpuscular Volume, Mean Corpuscular Haemoglobin Concentration, Mean Corpuscular Haemoglobin, Platelet Count, differential leukocyte count – Neutrophil %, Lymphocyte %, Monocyte %, Eosinophil % and Basophil %, and Reticulocyte count were studied.

Histopathology

Tissue samples were collected from the organs of control rats as well as treated male / female rats. The tissue collected from the organs such as liver, lung,

kidney, adrenal gland, pancreas, spleen, brain, ovary/testes and heart ware numbered for individual identification and then transferred to tissue cassettes (SS) to enable fixation in 10% formalin for 3 to 5 days followed by the tissue processing which was carried out with the help of automatic tissue processor Model No. 1020 (LIECA make Germany). The tissue processing included dehydration in graded isopropyl alcohol, clearing in xylene I & II, impregnation in paraffin wax and finally tissue blocks were prepared on paraffin block making Model No. 1150 H+C (LIECA make Germany). Section cutting of tissue blocks was done using microtome (LIECA make Germany) to the thickness of 3 – 5 microns. The tissue sections were fixed on the slide by heat technique followed by Haematoxylin and Eosin staining. The staining was carried out with the help of automatic slide stainer (THERMO make Germany). After staining the tissue sections were mounted with DPX to prevent any damage to the stained tissue which was carried out on auto cover slipper Model No. CV5030 (LIECA make Germany). The stained tissue sections were examined under microscope 10x and 40x objective to check the adverse effects of drug on cell morphology as well as on the cell organelles.

Statistical Analysis

All results are expressed as mean ± standard deviation. Comparison of all results on body weight, feed & water consumption, haematological value, biochemical values was performed using one way analysis of variance (ANOVA) method using statistical software Graph Pad Prism version 6.07. Probability of 0.05 or small ($p \leq 0.05$) was used as the criterion of significance.

Results

Average Mean Body Weight

The rats treated with *Kushta Qalai* drug and crude material at the dose of 1000, 500 and 250mg/kg of body weight were found to grow and gain body weight normally and there was no treatment related changes found in the body weight gain of treated rats when compared with the respective control rats in both the sexes. Figure 1 shows the body weight of rats in sub-acute toxicity study.

The values are expressed as mean ± SD. n=5 in each group. *$*p<0.05$* as compared with the controls at the same time (one-way ANOVA)

Mean Feed and Water Consumption

The average feed and water consumption of both treated groups was found to be unaffected by the *Kushta Qalai* drug and crude material as there were no

significant changes in the average feed consumption and water consumption when compared with the respective controls as shown in Figure 2.

The values are expressed as mean ± SD. n=5 in each group. *$p<0.05$ as compared with the controls at the same time (one-way ANOVA)

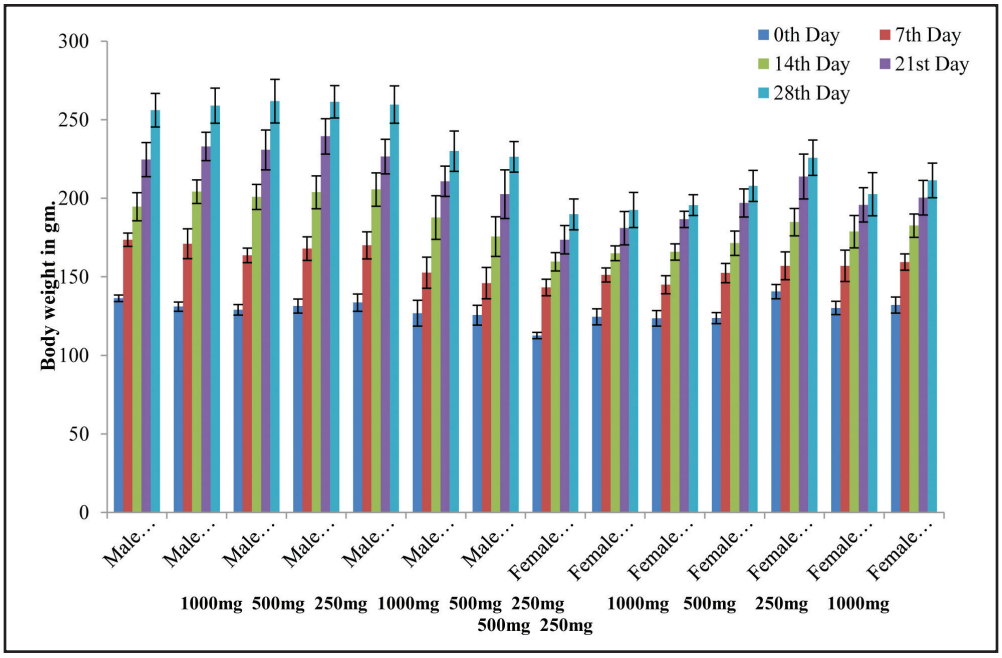

Fig. 1: Average Body Weight Gain of Male and Female Rats in Sub-acute Oral Toxicity Study of *Kushta Qalai* and its Crude Material

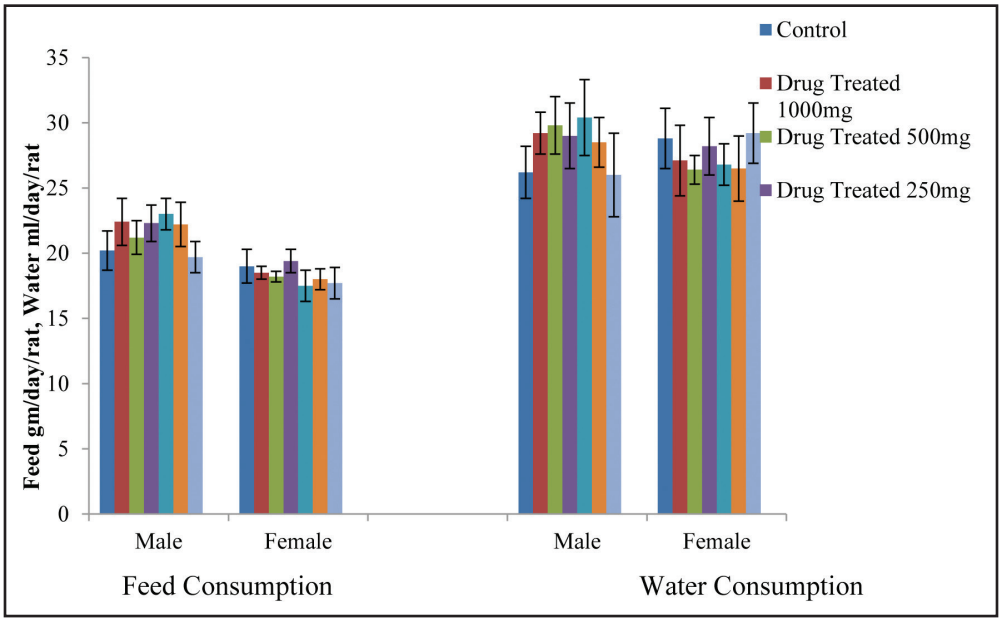

Fig. 2: Average Feed and Water Consumption of Male and Female Rats in Sub-acute Oral Toxicity Study of *Kushta Qalai* and its Crude Material

Relative Organ Weight of Male and Female Rats in Sub-acute Oral Toxicity Study of *Kushta Qalai* Drug and its Crude Material (Gram/100gram of Body Weight)

The relative organ weight of male and female rats in sub-acute oral toxicity study was found not altered by the administration of *Kushta Qalai* drug and its crude material when treated rats compared with their respective control rats as shown in table 3 and 4.

Table 3: Relative Organ Weight of Male Rats in Sub-acute Oral Toxicity Study of *Kushta Qalai* and its Crude Material

Organ	Male						
	Drug Treated				Crude Treated		
	Control	Treated 1000mg	500mg	250mg	Treated 1000mg	500mg	250mg
Brain (g)	0.700 ±0.10	0.703 ±0.11	0.787 ±0.14	0.695 ±0.11	0.687 ±0.10	0.673 ±0.11	0.742 ±0.12
Spleen (g)	0.462 ±0.12	0.443 ±0.14	0.453 ±0.11	0.499 ±0.11	0.383 ±0.10	0.429 ±0.08	0.398 ±0.12
Right adrenal (g)	0.010 ±0.005	0.011 ±0.006	0.009 ± 0.007	0.011 ±0.008	0.008 ±0.005	0.008 ±0.004	0.009 ±0.007
Left adrenal (g)	0.010 ±0.005	0.011 ±0.006	0.009 ± 0.007	0.011 ±0.008	0.008 ±0.005	0.008 ±0.004	0.009 ±0.007
Heart (g)	0.308 ±0.10	0.297 ±0.11	0.341 ±0.10	0.328 ±0.13	0.335 ±0.12	0.357 ±0.11	0.307 ±0.11
Lung(g)	0.674 ±0.18	0.602 ±0.19	0.597 ±0.20	0.726 ±0.21	0.643 ±0.22	0.655 ±0.19	0.721 ±0.16
Right kidney (g)	0.370 ±0.12	0.366 ±0.13	0.354 ±0.14	0.377 ±0.15	0.351 ±0.16	0.377 ±0.16	0.325 ± 0.13
Left kidney (g)	0.349 ±0.11	0.320 ±0.12	0.338 ±0.10	0.300 ±0.14	0.327 ±0.15	0.346 ±0.11	0.341 ± 0.12
Right testis (g)	0.489 ±0.15	0.445 ±0.17	0.462 ±0.17	0.434 ±0.18	0.464 ±0.16	0.567 ±0.20	0.501 ±0.20
Left testis (g)	0.482 ±0.15	0.447 ±0.16	0.639 ±0.17	0.443 ± 0.18	0.446 ±0.19	0.583 ±0.20	0.480 ±0.21
Liver (g)	3.913 ±0.55	3.216 ± 0.50	3.462 ±0.57	3.423 ±0.61	3.424 ±0.59	3.730 ±0.60	3.181 ±0.65
Pancreas (g)	0.251 ±0.10	0.220 ± 0.11	0.231 ±0.11	0.233 ±0.13	0.199 ±0.15	0.214 ±0.15	0.234 ±0.11

The values are expressed as mean ± SD. n=5 in each group. *$p<0.05$ as compared with the controls at the same time (one-way ANOVA)

Table 4: Relative Organ Weight of Female Rats in Sub-acute Oral Toxicity Study of *Kushta Qalai* and its Crude Material

Organ	Female						
	Drug Treated				Crude Treated		
	Control	Treated 1000mg	500mg	250mg	Treated 1000mg	500mg	250mg
Brain (g)	0.705 ±0.10	0.743 ±0.11	0.730 ±0.13	0.755 ±0.11	0.776 ±0.11	0.716 ±0.12	0.802 ±0.11
Spleen (g)	0.380 ±0.12	0.706 ±0.13	0.424 ±0.11	0.502 ±0.15	0.474 ±0.11	0.451 ±0.13	0.361 ±0.14
Right adrenal (g)	0.013 ±0.005	0.012 ± 0.006	0.012 ± 0.007	0.012 ±0.005	0.014 ±0.004	0.011 ±0.008	0.011 ± 0.006
Left adrenal (g)	0.013 ±0.005	0.012 ± 0.006	0.012 ± 0.007	0.012 ±0.005	0.014 ±0.004	0.011 ±0.008	0.011 ± 0.006
Heart (g)	0.301 ± 0.10	0.337 ± 0.11	0.355 ±0.10	0.312 ±0.13	0.344 ±0.11	0.319 ±0.15	0.350 ±0.13
Lung(g)	0.668 ±0.18	0.838 ± 0.19	0.869 ± 0.17	0.755 ± 0.13	0.776 ±0.15	0.750 ±0.23	0.738 ±0.20
Right kidney (g)	0.362 ± 0.12	0.392 ± 0.11	0.401 ± 0.14	0.336 ±0.10	0.355 ±0.16	0.306 ±0.12	0.355 ±0.11
Left kidney (g)	0.316 ±0.11	0.381 ±0.12	0.424 ± 0.10	0.322 ± 0.14	0.338 ±0.10	0.288 ±0.16	0.336 ±0.11
Right Ovary (g)	0.021 ± 0.005	0.031 ± 0.005	0.012 ±0.007	0.019 ± 0.006	0.028 ±0.004	0.023 ±0.006	0.035 ± 0.004
Left Ovary (g)	0.020 ±0.005	0.031 ±0.005	0.014 ± 0.007	0.020 ± 0.006	0.031 ±0.004	0.020 ±0.006	0.027 ± 0.005
Liver (g)	3.433 ± 0.55	4.116 ± 0.56	3.752 ± 0.57	3.772 ± 0.58	3.691 ±0.58	2.985 ±0.59	3.489 ±0.6
Pancreas (g)	0.216 ± 0.11	0.249 ±0.10	0.286 ± 0.13	0.216 ± 0.12	0.142 ±0.15	0.176 ±0.13	0.179 ± 0.11

The values are expressed as mean ± SD. n=5 in each group. *$p<0.05$ as compared with the controls at the same time (one-way ANOVA)

Biochemical Parameters

The results of biochemical parameters did not show any statistically significant variation between *Kushta Qalai* and its crude material treated rat groups and control rat groups as shown in Figure 3-5.

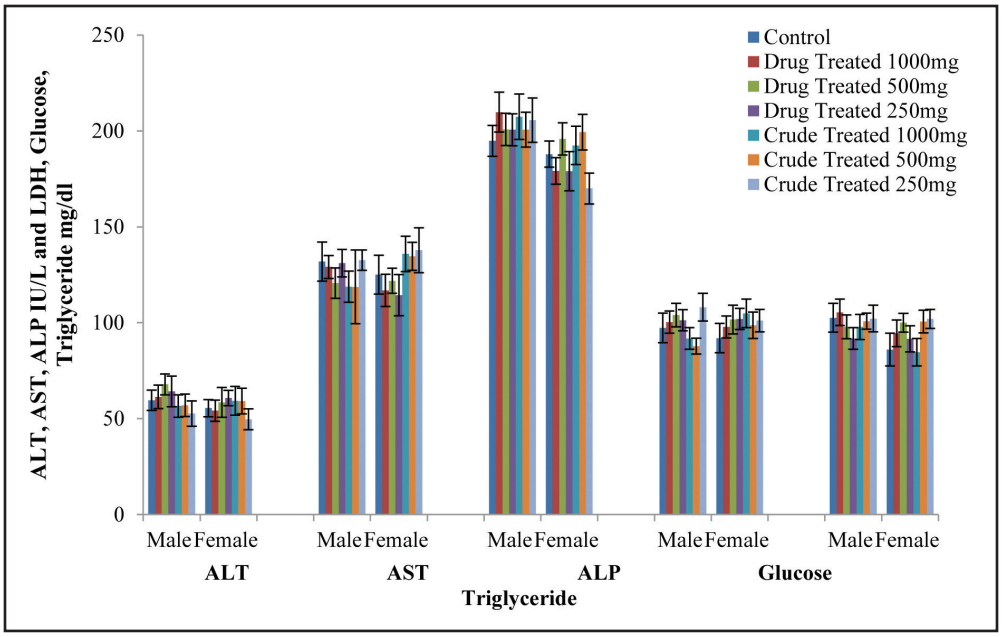

Fig. 3: Biochemistry Parameters ALT, AST, ALP, Glucose and Triglyceride of Male and Female Rats in Sub-acute Oral Toxicity Study of *Kushta Qalai* and its Crude Material

The values are expressed as mean ± SD. n=5 in each group. *$p<0.05$ as compared with the controls at the same time (one-way ANOVA)

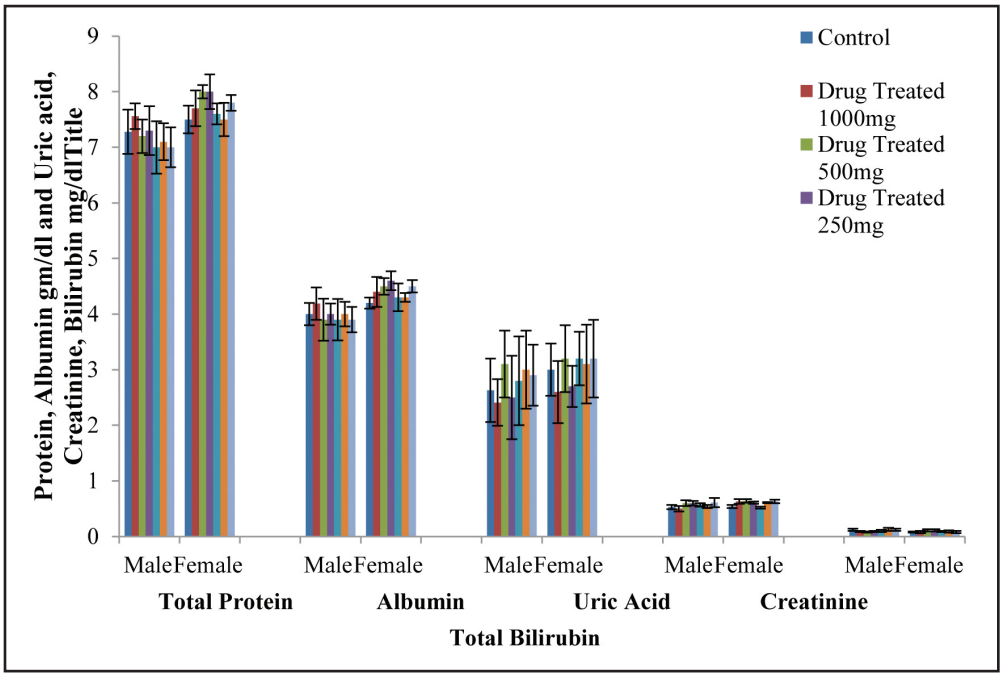

Fig. 4: Biochemistry Parameters Total Protein, Albumin, Uric Acid, Serum Creatinine and Total Bilirubin of Male and Female Rats in Sub-acute Oral Toxicity Study of *Kushta Qalai* and its Crude Material

The values are expressed as mean ± SD. n=5 in each group. *$p<0.05$ as compared with the controls at the same time (one-way ANOVA)

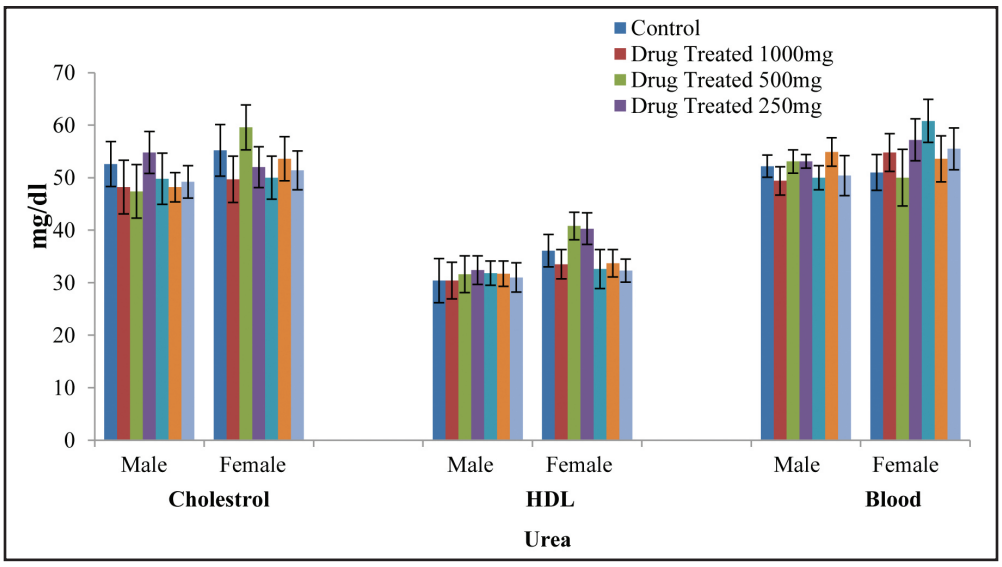

Fig. 5: Biochemistry Parameters Serum Cholestrol, HDL and Blood Urea of Male and Female Rats in Sub-acute Oral Toxicity Study of *Kushta Qalai* and its Crude Material

The values are expressed as mean ± SD. n=5 in each group. *$p<0.05$ as compared with the controls at the same time (one-way ANOVA)

Haematology Parameters

The results of haematological parameters of *Kushta Qalai* drug and crude material treated male and female rats did not show any statistically significant change in the values when treated rat groups compared with the respective control rat groups. Figure 6 - 8 shows the haematological parameters of rats.

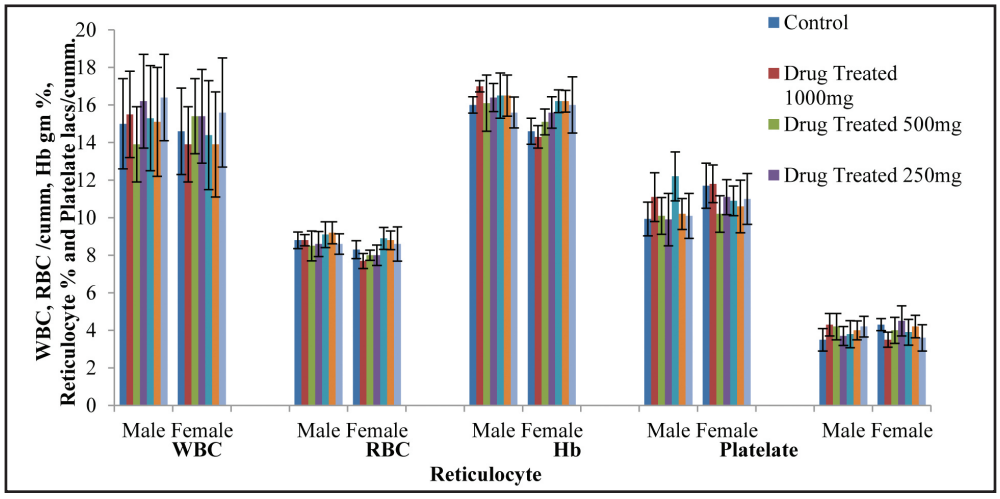

Fig. 6: Haematological parameters WBC Count, RBC Count, Haemoglobin, Reticulocyte and Platelet Count of Male and Female Rats in Sub-acute Oral Toxicity Study of *Kushta Qalai* and its Crude Material

The values are expressed as mean ± SD. n=5 in each group. *$p<0.05$ as compared with the controls at the same time (one-way ANOVA)

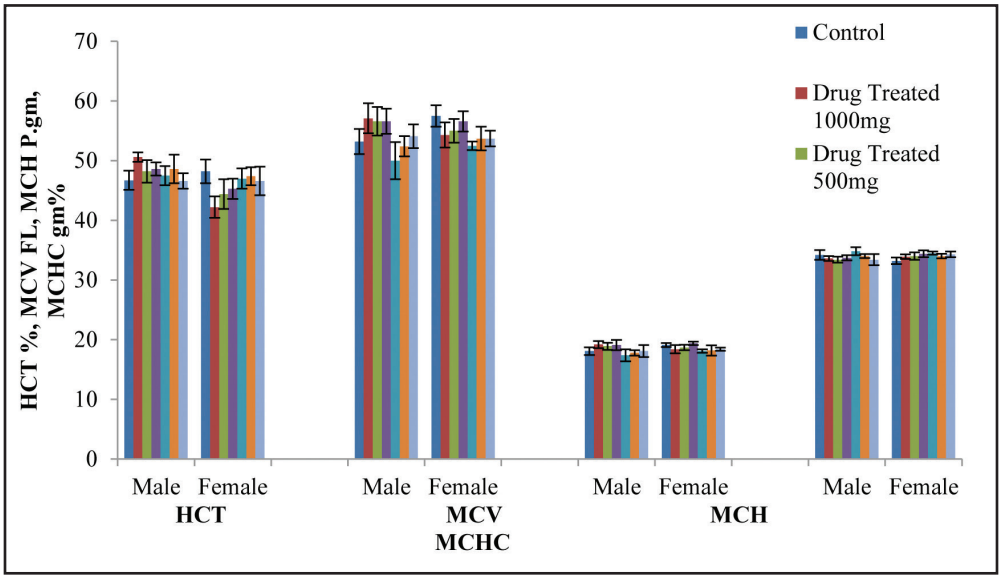

Fig. 7: Haematological parameters HCT, MCV, MCH and MCHC of Male and Female Rats in Sub-acute Oral Toxicity Study of *Kushta Qalai* and its Crude Material

The values are expressed as mean ± SD. n=5 in each group. *$p<0.05$ as compared with the controls at the same time (one-way ANOVA)

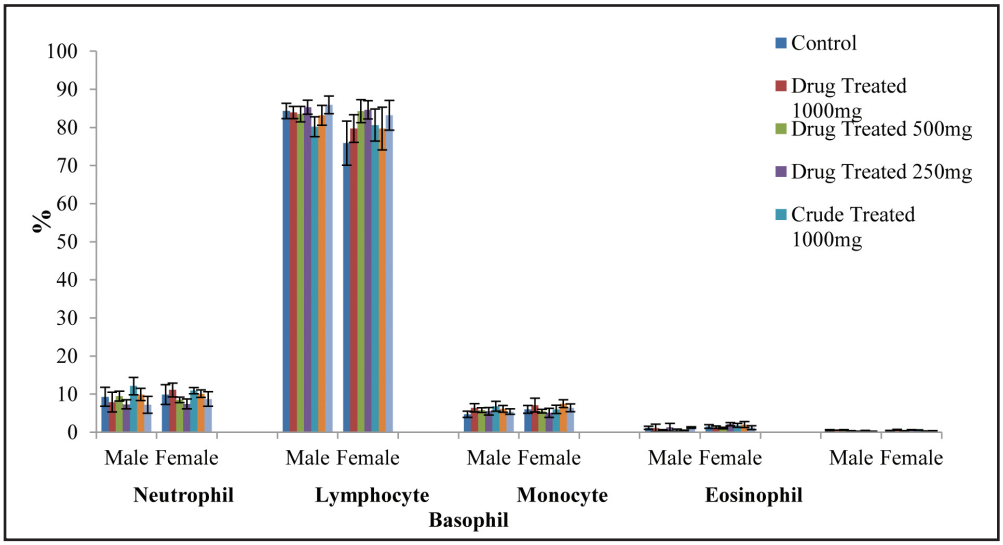

Fig. 8: Haematological parameter DLC – Neutrophil, Lymphocyte, Monocyte, Eosinophil and Basophil Percentage of Male and Female Rats in Sub-acute Oral Toxicity Study of *Kushta Qalai* and its Crude Material

The values are expressed as mean ± SD. n=5 in each group. *$p<0.05$ as compared with the controls at the same time (one-way ANOVA)

Histopathological Examination

The interpretation of the histopathological slides was carried by the Veterinary Pathologist of SKUAST-K Shuhama Srinagar. The histopathological examination of vital organs showed normal structure, cytoarchitecture and absence of any

pathological lesion in the tissues of both male and female rats as shown in Figure 9 -17, except that liver tissues showed increased Kupffer cell proliferation, vascular congestion and hepatocellular swelling as shown in Fig. 9.

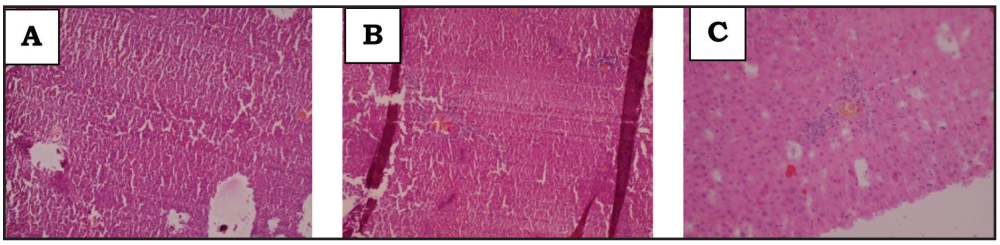

Fig. 9: Photomicrographs of Liver: [40X10X4] except (A) and (B) i.e. 10X10X4].

(A) Control - Showing normal hepatocytes. (B) Drug treated 1000mg/kg body Wt. – Showing Kupffer's cell proliferation, vascular congestion and hepatocellular swelling. (C) Crude treated 1000mg/kg body Wt. – Showing normal hepatocytes with perivascular Kupffer's cell proliferation.

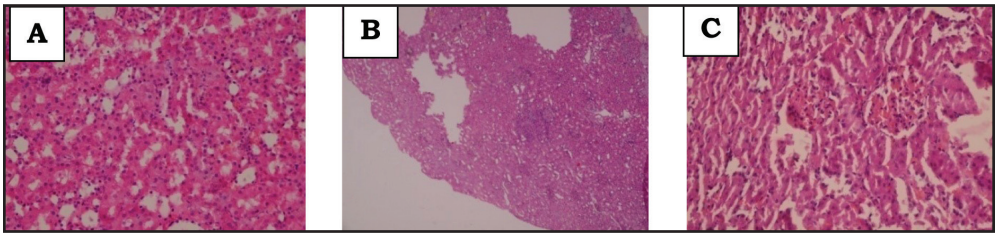

Fig. 10: Photomicrographs of Kidney: [40X10X4] except (B) i.e. 10X10X4]

(A) Control – Showing normal tubules and glomeruli (B) Drug treated 1000mg/kg body Wt. – Showing normal convoluted tubules, frequently glomeruli were enlarged with mildly congested. (C) Crude treated 1000mg/kg body Wt. – Showing normal epithelium with glomerular congestion.

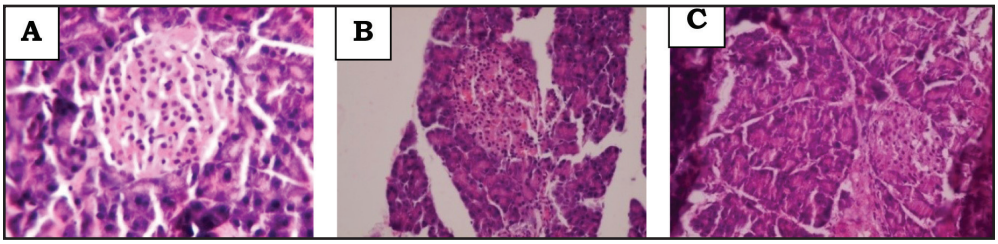

Fig. 11: Photomicrographs of Pancreas: [40X10X4]

(A) Control - Showing exocrine gland and islets of Langerhans. (B) Drug treated 1000mg/kg body Wt. – Showing normal exocrine gland and islets. (C) Crude treated 1000mg/kg body Wt. – Showing normal exocrine gland and mild degeneration of cells in islets.

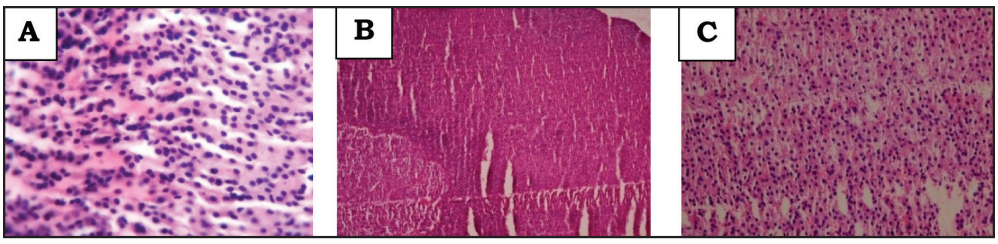

Fig. 12: Photomicrographs of Adrenal gland: [40X10X4 except (B) i.e. 10X10X4]

(A) Control - Showing adrenal cortex. (B) Drug treated 1000mg/kg body Wt. – Showing normal adrenal cells. (C) Crude treated 1000mg/kg body Wt. – Showing normal adrenal cortex.

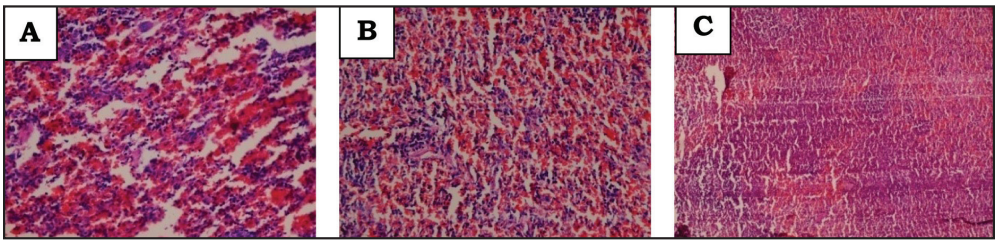

Fig. 13: Photomicrographs of Spleen: [40X10X4] except (C) i.e. 10X10X4]

(A) Control – Showing normal splenic corpuscles. (B) Drug treated 1000mg/kg body Wt. – Showing normal morphology of spleen cells. (C) Crude treated 1000mg/kg body Wt. – Showing normal splenic corpuscles.

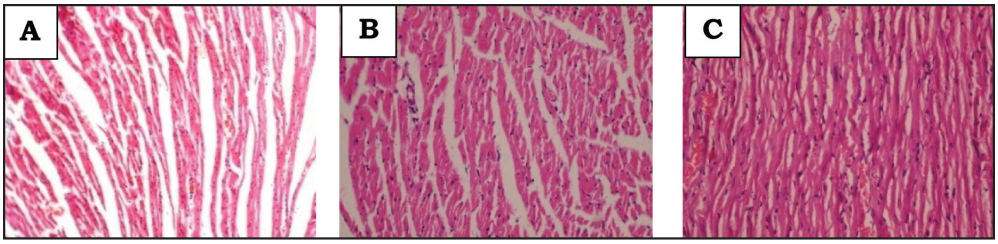

Fig. 14: Photomicrographs of Heart: [40X10X4].

(A) Control - Showing normal myocardium. (B) Drug treated 1000mg/kg body Wt. – Showing normal cardio-myocytes (C) Crude treated 1000mg/kg body Wt. – Showing normal morphology of cardiac muscle.

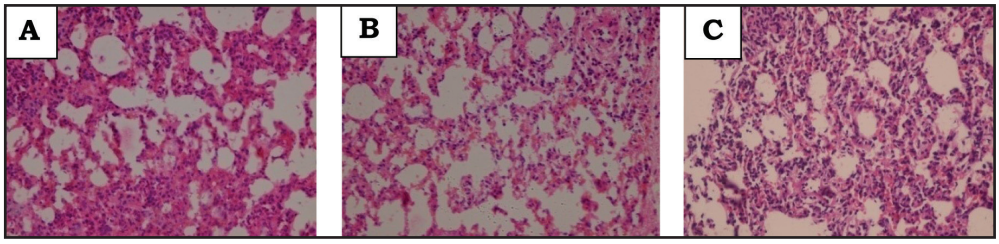

Fig. 15: Photomicrographs of Lung: [40X10X4].

(A) Control - Showing normal lung alveoli. (B) Drug treated 1000mg/kg body Wt. – Showing normal alveoli. (C) Crude treated 1000mg/kg body Wt. – Showing normal alveoli with micro vascular congestion.

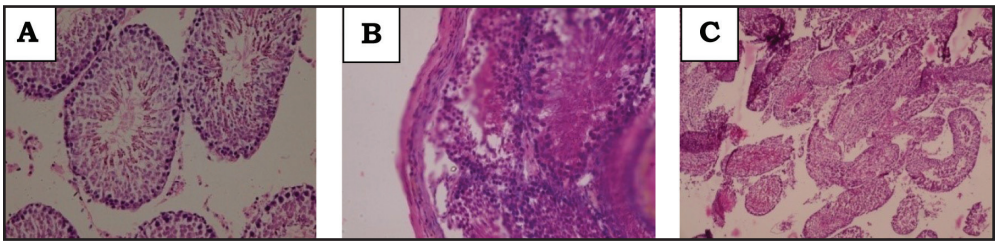

Fig. 16: Photomicrographs of Testes: [40X10X4 except (C) i.e. 10X10X4]

(A) Control - Showing normal seminiferous tubules with spermatozoa. (B) Drug treated 1000mg/kg body Wt. – Showing normal spermatozoa in seminiferous tubules. (C) Crude treated 1000mg/kg body Wt. – Showing normal seminiferous tubules.

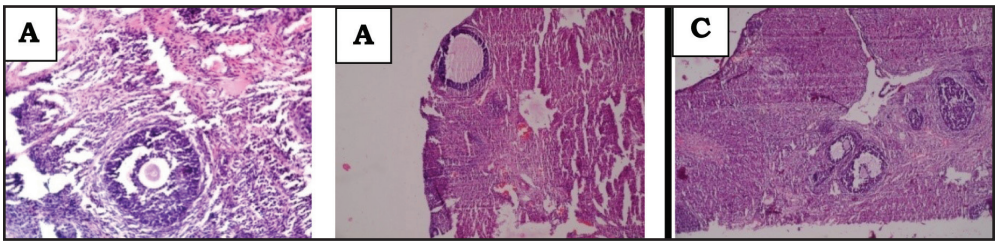

Fig. 17: Photomicrographs of Ovary: [40X10X4].

(A) Control - Showing normal ovarian tissue, follicle and ovum. (B) Drug Treated 1000mg/kg body Wt. – Showing normal ovarian follicles. (C) Crude treated 1000mg/kg body Wt. – Showing follicles normal with mild focal haemorrhages.

Discussion

World Health Organization survey indicates that about 70-80% of the world's population rely on non-conventional medicine mainly of herbal source in their primary healthcare (Hariharan *et al.,* 2012). The growing number of herbal drug users around the globe and lack of scientific data on the safety profile of herbal products make it necessary to conduct toxicity study of herbal products (Saad *et al.,* 2006). The strategy for establishment of safety of a test item depends on demonstration of its adverse effects (toxicity) or no adverse effects (no toxicity) under the conditions of exposure to its high doses to the test animals rodents or non-rodents. Initially, these studies for demonstration of toxicity are conducted in rodents, using the limit doses which are based on the technical feasibility as well as scientific utility of the highest single or repeated (or daily) doses of the test item that can be given to the animals.

The Organization for Economic Cooperation and Development (OECD) sets guidelines for conducting various toxicity studies. The first study aimed at demonstrating the toxicity of "repeated daily dosing" of a test item is called Sub-acute Toxicity Study, and as per the internationally accepted OECD Test

Guidelines, it employs the daily exposure to daily oral dosing of 1.0g/kg b.wt. with two sub fractions of test item in the rodent species for a period of 28 days. This sub-acute toxicity study involves the determination of long term effects of the test item upon repeated administration.

Repeated oral administration of *Kushta Qalai* drug and crude material at the dose level of 1000mg/kg body weight for 28 days did not cause lethality or any significant sign of toxic effect in male and female rats. After exposure to a few possible toxic substances, there will be changes in the body weight gain as well as internal organ weight which indicate the first sign of toxicity (Teo *et al.,* 2002). The body weight change is considered as the marker of adverse effects of drugs and if the body weight change is more than 10% of the initial body weight, it is considered as statistically significant (Teo *et al.,* 2002; Raza *et al.,* 2002). There were no statistically significant differences in body weight gain between *Kushta Qalai* and crude material treated rats and control rats during the study period. The organ weight is also an important indicator of physiological and pathological status of experimental animals. The relative organ weight is fundamental to confirm whether the organ was exposed to injury or not. The vital organs such as liver, kidney, pancreas, spleen, lung, adrenal gland, testes/ovaries, brain and heart are the primary organs affected by metabolic reaction caused by toxicant (Dybing *et al.,* 2002). There was no statistically significant difference in organ weight, in all the treated groups of both sexes when compared with the respective control rat groups. The feed and water consumption is also an important parameter of the safety study, as proper intake of feed and water is necessary to the physiological status of the animals and to achieve a better response to the test substance under investigation (Steven & Mylecrdfaine, 1994; Iversen & Nicolaysen, 2003). The feed and water consumption were also not affected by the administration of *Khusta Qalai* and crude material to the rats. The changes in the haematological parameters have a great indicative value for human toxicity, when the data are converted from the animal studies (Olson *et al.,* 2000). The haematological parameters did not show any statistically significant changes in the *Kushta Qalai* drug and crude material treated rats when compared with the control rats which indicates that *Kushta Qalai* and crude material did not affect the blood cellular components or their production. Biochemical parameters such as liver enzymes are known indicators of liver function and are used as biomarkers to conclude the probable toxicity of drugs (Rehman *et al.,* 2000). Any damage to the liver parenchymal cells will result in an increase in the level of SGOT and SGPT enzymes in the blood plasma (Wolf *et al.,* 1972). There were no statistically significant changes in the SGOT, SGPT and ALP levels, which reveals that the *Kushta Qalai* drug and crude material did not affect the liver function. The total bilirubin and protein/ albumin were also not affected by the test substance in both male and female rats when compared with the respective control rats. The kidney function parameters

such as blood urea, serum creatinine and serum uric acid were also not affected by the test substance indicating thereby that the *Kushta Qalai* drug and crude material did not cause any damage to the kidney tissues. The histopathological examination of the vital organs (liver, kidney, pancreas, spleen, adrenal gland, heart, lung and testes/ovaries) of the drug treated and crude treated rats did not show any significant difference except in liver tissues. The drug treated rats at the dose level of 1000mg/kg body weight and crude material treated rats at all the three dose levels showed increased Kupffer cell proliferation, vascular congestion and hepatocellular swelling. This Kupffer cell proliferation is because the liver plays a central role in the detoxification of drugs (Aashish *et al.,* 2012). The liver and kidney regulate the level of blood chemicals and the main role of these organs is the elimination of waste products and toxic substances. The proliferation of these Kupffer cells was seen because there was overloading of drug detoxification in the liver as this Kupffer cell proliferation was seen at 1000mg/kg body weight only (70X, X is the extrapolated therapeutic dose in rats) in case of drug material treated rats and at all the three dose levels in case of its crude material treated rats, since it was undetoxified form that is why it was found on all the three dose levels.

Conclusion

The results therefore suggest that *Kushta Qalai* drug is safe for oral consumption at the therapeutic dose level, however the increased Kupffer cell proliferation was seen only at high limit dose in drug treated rats and at all the three dose levels in crude material treated rats. The study indicates that the method of detoxification adopted by Unani System of Medicine reduces the signs of toxicity.

It may be noted that *Kushta Qalai* drug is orally administered in human subjects at a dose level of 125mg/kg body weight per day for a period of 30 days.

Conflict of Interest Statement

The authors declare that there is no conflict of interest.

Acknowledgement

The authors thank the Director General, Central Council for Research in Unani Medicine, New Delhi for his interest in the study, guidance and administrative support. The authors also thank Department of Science and Technology, Govt. of India, New Delhi for funding and establishing a standard research facility at RRIUM, Srinagar.

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सारांश

विस्टार चूहों में *कुश्ता क़लई* (हर्बल-खनिज यूनानी मिश्रण) का उप तीव्र मौखिक विषाक्तता अध्ययन

शौक़त ए. डार, *सीमा अक़बर, शौक़त ए. गनी, ख़ालिद ग़ज़नफ़र, मारिया हमदानी, ताज़ीन नाज़िर, अक़बर मसूद और मसूद एस. मीर

कुश्ता क़लई यूनानी चिकित्सा पद्धति का एक हर्बल–खनिज यूनानी मिश्रण है जो स्पर्मेटोरिया, प्री–मेच्योर इजेकुलेशन, नॉक्टेर्नल एमिशन, नपुंसकता के उपचार के लिए प्रभावी रूप से उपयोग किया जाता है; यह सेक्स शक्ति और वीर्य सघनता को बढ़ाता है। इस अध्ययन का उद्देश्य *कुश्ता क़लई* औषधि और इसके अपक्व पदार्थ (अन–डिटॉक्सिफाइड फॉर्म) के प्रतिकूल प्रभाव और विषहरण विधि की वैज्ञानिक वैधता जांचने के लिए दोनों लिंगों के अल्पायु, स्वस्थ श्वेत चूहों (विस्टार स्ट्रेन) में उप तीव्र मौखिक विषाक्तता का पता लगाना था। 1000 मि.ग्रा./कि.ग्रा. की सीमित खुराक और इसके उप अंश, 500 मि.ग्रा. और 250 मि.ग्रा./कि.ग्रा. शरीर भार की मात्रा में 28 दिनों के लिए प्रतिदिन चूहों को दी गई। 29वें दिन चूहों को बलि कर दिया गया। हेमैटोलॉजिकल और बायोकेमिकल जांच के लिए रक्त के नमूने और हिस्टोपैथेलॉजिकल जांच के लिए ऊतकों को एकत्र किया गया। तीनों खुराक स्तरों पर शारीरिक, जैव रासायनिक और रुधिरविज्ञान मापदंडों में कोई महत्वपूर्ण परिवर्तन नहीं हुआ जो *कुश्ता क़लई* औषधि और इसके अपक्व पदार्थ के लिए एनओएईएल को 1000 मि.ग्रा./कि.ग्रा. शरीर भार के रूप में दर्शाता है। अध्ययन से निष्कर्ष निकलता है कि चिकित्सीय खुराक स्तर पर मौखिक रूप से देने के लिए *कुश्ता कुलई* औषधि सुरक्षित है।

शब्दकुंजी: रुधिरविज्ञान संबंधी मापदंड, हिस्टोपैथेलॉजिकल, *कुश्ता क़लई,* यूनानी चिकित्सा

Therapeutic Response of Unani Coded Drugs in Lymphatic Filariasis *(Daul-Feel)*

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Abstract

Lymphatic filariasis is a mosquito-borne parasitic disease which is endemic in many tropical countries including India. The objective of the present study was to assess the therapeutic response of Unani coded drugs in lymphatic filariasis (*Daul-Feel*), which is mainly swelling of feet and calf in which the affected leg becomes hugely swollen in advanced stage. A total of 163 patients of either sex were divided into two groups to assess the therapeutic response of the Unani coded drugs, with and without *Munzij-Mushil* therapy (MM therapy). It was observed that associated symptoms of the disease including lower limb volume in grade-3 lymphedema cases were subsided after the treatment. Comparatively better response was observed when Unani coded drugs UNIM 268, UNIM 270, UNIM 271 and UNIM 272 were used with *Munzij-Mushil* therapy. No adverse effect was reported by any patient during the study. The variations in liver function test and kidney function test parameters were found within normal range after the treatment. The Unani coded drugs have given encouraging response to subside the oedema volume even in grade-2 and grade-3 cases of disease, which are rarely reversible.

Keywords: Lymphatic Filariasis, Lymphedema, UNIM, *Daul-Feel*

Introduction

Lymphatic filariasis is a mosquito-borne neglected tropical disease which is caused by thread-like parasitic filarial worms named *Wuchereria bancrofti* responsible for 90% cases; Brugia Malayi and B. Timori for rest of 10% cases in the world (Das, *et al.,* 2002; Fauci, *et al.,* 2008; Park, 2009). The disease is endemic in many countries in Africa, South Asia, the Pacific Islands and Americas. Worldwide, an estimated 120 million people are affected by the lymphatic filariasis (Michael and Bundy, 1997). India alone accounts for about 40% of the global burden followed by Sub-Sahara Africa that accounts for about 37% of global burden (Ramaiah, *et al.,* 2000). Nine Indian states (Andhra Pradesh, Bihar, Gujarat, Kerala, Maharastra, Orissa, Tamil Nadu, Utter Pradesh and West Bengal) contribute about 95% of the total burden (Michael, *et al.,* 1996) with the highest incidence rate in Bihar (over 17%) followed by Kerala (15.7%) and Uttar Pradesh (14.6%).

In Unani System of Medicine, lymphatic filariasis is known as *Daul-Feel* and defined as swelling of feet and calf muscle up to the knee, which appears like a leg of elephant (Kabiruddin, 2007). According to Abu Baker Mohammad Bin Zakariya Razi and Ibn al-Quff Masihi, the disease is caused by the black bile (*Sauda*) (Razi, 1962; Masihi, 1356H), while *Nuh Qumri* has mentioned the

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abnormal flow of the thick matters towards the legs as causative factor of the disease (Qumri, 2008). According to some Unani physicians, the disease is due to the abnormality of phlegm (*Balgham*) and black bile (*Sauda*) (Antaki, 2009). Unani scholars Avicenna and Allama Samarquandi have described *Daul-Feel* in *Al-Qanoon fit-Tib* and *Sharh-i Asbab-wa-Alamat* respectively. According to them, it is due to accumulation of *Balgham-e-Ghaleez* in the affected part which gets converted into *Sauda*.

The World Health Assembly resolved in 1997 to eliminate lymphatic filariasis as a public health problem. The goal of World Health Organization's (WHO's) 'Global Programme to Eliminate Lymphatic Filariasis (GPELF) is to eliminate the disease as a public health problem by 2020 (Anonymous, 1997).

Diethylcarbamazine (DEC) is the only drug available in modern medicine for therapeutic control of filariasis (Park, 2009), which has variable efficacy and serious allergic reactions, while Unani Medicine offers safe and effective drugs. Therefore, it is need of time to use Unani drugs which have least or no side effect on human body.

Unani physicians had used single and compound drugs in the management of lymphatic filariasis since ancient times but the clinical data to show the therapeutic response of Unani drugs in the management of disease is not available, therefore present study was conducted with an aim to assess the therapeutic response of Unani coded drugs in the treatment of lymphatic filariasis.

Materials and Methods

Study Drugs

Unani coded drugs UNIM 268, UNIM 270, UNIM 271 and UNIM 272 with and without *Munzij-Mushil* therapy (MM therapy)

Study Design

Double blind clinical trial

Selection of Cases

Patients registered at Regional Research Institute of Unani Medicine, Patna who had lower limb swelling with present or past history of limb redness were screened for the clinical evidences of disease. A total of 163 patients with confirmed clinical diagnosis, who met the inclusion/exclusion criteria, were enrolled for study between April 2008 and March 2014.

Clinical Examination

After obtaining informed consent, all human subjects of study were asked for their age, occupation, dietary habit, duration of disease, symptoms suggesting disease, frequency and duration. After that, they were subjected to clinical examination for filarial lesions as lower limb lymphedema and elephantiasis.

Diagnosis of each case was made with the help of detailed history of the patient i.e. allergic history, physical and clinical examinations as well as laboratory investigations.

Inclusion Criteria

- Patients of either sex in the age group ranging from 11 to 65 years
- Patients having lower limb lymphedema
- Patients presenting symptoms of lymphatic filariasis
- Patients willing to sign informed consent form to participate in the study

Exclusion Criteria

- Patients suffering from other chronic diseases
- Patients with Hb% (hemoglobin percentage) less than 50%
- Pregnant or lactating women

Treatment of Patients

Patients were divided into Group-A (84 patients) and Group-B (79 patients). They were treated with Unani coded drugs. The coded drugs were used with and without *Munzij-Mushil* therapy.

(I) Group A patients (Treatment without *Munzij-Mushil* therapy)

UNIM 268, two tablets of 500 mg, twice daily on empty stomach for 90 days

UNIM 270, five grams powder

UNIM 272, 20 ml liquid

UNIM 270 and UNIM 272 were mixed together and applied on the affected part at night for 90 days

UNIM 271, 20 grams of coarse powder boiled in one litre of water was slowly dropped on the affected part daily for 10-15 minutes before applying the paste at night

(II) Group-B patients (Treatment with *Munzij-Mushil* therapy)

(i) UNIM-MUNB (*Munzij*)

Decoction of UNIM – MUNB (35 gm of coded drug) in the dose of 125 ml was given orally, once a day on empty stomach daily in the morning for 10 to 15 days according to chronicity of disease or till the appearance of *Nuzj* in the urine.

(ii) UNIM-MUSB (*Mushil*)

35 gm of UNIM-MUSB was added to 15 gm UNIM-MUNB recipe. Decoction of UNIM-MUSB in the dose of 125 ml was given orally at night on alternate days for 5 days. The treatment with UNIM-MUSB was started after treatment with UNIM-MUNB.

(iii) UNIM-TAB (Tabreed) (coded drug)

Decoction of UNIM-TAB (crude drugs) in the dose of 50 ml was given orally on empty stomach on alternate days to UNIM-MUSB (*Mushil*) administration for 5 days.

After *Munzij-Mushil* therapy, Group-B patients were given same treatment as was given to Group-A patients.

Treatment Duration

Treatment duration for Group-A patients was 90 days and for Group-B patients, it was 90 days in addition to number of days of *Munzij-Mushil* therapy.

Followup Method

Patients were clinically examined at baseline, after *Munzij-Mushil* therapy, at regular interval of 30 days and at the end of treatment. All patients were asked about the improvement or deterioration in their symptoms during the course of study. Finding of clinical and laboratory investigations were recorded.

Assessment Criteria

After treatment, therapeutic responses of Unani coded drugs were recorded in terms of percentage improvement in disease as compared to baseline. Percentage improvements were categorized into 4 groups:

(i) 90% to 100% (Excellent Response)

(ii) 60% to 89% (Very Good Response)

(iii) 30% to 59% (Good Response)

(iv) Below 30% (Poor Response)

Grades of Lymphedema

The lower limb lymphedema was graded as follows to assess the therapeutic effect of the study drugs.

(i) No edema (No swelling of limbs= 0): This stage may exist for months upto years before edema becomes evident.

(ii) Grade -1 (mild edema=1): The excessive accumulation of watery fluids in tissue that subsides with limb elevation. The edema may be pitting at this stage.

(iii) Grade-2 (moderate edema=2): Pitting or non-pitting edema. Affected limb elevation alone rarely reduces swelling. There are no skin changes.

(iv) Grade-3 (severe edema=3): The tissue is hard and pitting is absent. Skin changes such as thickening, hyper-pigmentation and fat-deposit are seen.

Patients were clinically examined at the baseline, after MM therapy, at regular interval of 30 days and at the end of treatment.

Safety Assessment

The safety was assessed by monitoring adverse events either volunteered by patients or elicited by investigator by clinical as well as laboratory investigations at the baseline, after MM therapy, at regular interval of 30 days. The laboratory tests included heamogram, liver function test and kidney function test.

Observations and Results

The therapeutic response of the study drugs was observed in 163 patients of either sex ranging in age from 11 to 65 years. Mean age was 38.13 years.

General therapeutic response in Group-A patients was 60-89% in 35 cases, 30-59% in 43 cases and below 30% in 6 cases. General therapeutic response in 79 cases of Group-B patients was noted as 60-89% in 29 cases, 30-59% in 48 cases and below 30% in 2 cases (Table 1).

Table 1: General Therapeutic Responses of Unani Coded Drugs

Group	No. of Patients	Response			
		90-100%	60-89%	30-59%	<30%
A	84 (51.53%)	-	35 (21.47%)	43 (26.38%)	6 (3.68%)
B	79 (48.47%)	-	29 (17.80%)	48 (29.45%)	2 (1.22%)
Total	163 (100%)	-	64 (39.27%)	91(55.83%)	8 (4.90%)

The highest incidence (33.75%) of the disease was observed in age-group of 31-40 years. Out of 55 cases in age-group 31-40 years, response was 60-89% in 25 cases, 30-59% in 28 cases and below 30% in 2 cases. Out of total 163 cases, 64 cases got 60-89% response, 91 cases 30-59% response and below 30% response in 8 cases (Table 2).

Table 2: Age-wise Response

Age Group (Years)	Number of Patients	Response			
		90-100%	60-89%	30-59%)	<30%
10-20	17 (10.43%)	-	6 (3.68%)	11 (6.75%)	-
21-30	32 (19.63%)	-	17 (10.43%)	14 (8.59%)	1 (0.61%)
31-40	55 (33.75%)	-	25 (15.34%)	28 (17.18%)	2 (1.23%)
41-50	23 (14.12%)	-	8 (4.91%)	13 (7.98%)	2 (1.23%)
51-60	35 (21.46%)	-	8 (4.91%)	24 (14.72%)	3 (1.83%)
Above 60	1 (0.61%)	-	-	1 (0.61%)	-
Total	163 (100%)	-	64 (39.27%)	91(55.83%)	8 (4.90%)

The maximum incidence (60.12%) of disease was seen in female. Out of 98 cases of female, 39 cases got 60-89% response, 56 cases got 30-59% response and 3 cases got no response. Out of 65 cases of male, 25 cases got 60-89% response, 35 cases 21.47% response and 5 cases got below 30% response (Table 3).

Table 3: Gender-wise Response

Gender	Number of Patients	Response			
		90-100%	60-89%	30-59%	<30%
Male	65 (39.88%)	-	25 (15.34%)	35 (21.47%)	5 (3.07%)
Female	98 (60.12%)	-	39 (23.93%)	56 (34.36%)	3 (1.83%)
Total	163 (100%)	-	64 (39.27%)	91(55.83%)	8 (4.90%)

The prevalence of disease was highest (78.53%) among the people of phlegmatic (*Balghami*) temperament and least in people of sanguine (*Damawi*) temperament. Out of 128 cases of phlegmatic temperament, 57 cases got 60-89% response, 67 cases 30-59% response and 4 cases below 30% response. In the 5 people of sanguine temperament, 4 got 30-59% response and 1 got below 30% response (Table 4).

Table 4: Temperaments-wise Response

Tempera-ment	No. of Patients	Response			
		90-100%	60-89%	30-59%)	<30%
Damwi (Sanguine)	5 (3.07%)	-	-	4 (2.46%)	1 (0.61%)
Balghami (Phlegmatic)	128 (78.53%)	-	57 (34.98%)	67 (41.10%)	4 (2.45%)
Safrawi (Bilious)	21 (12.88%)	-	7 (4.29%)	12 (7.36%)	2 (1.23%)
Saudawi (Melancholic)	9 (5.52%)	-	-	8 (4.91%)	1 (0.61%)
Total	163 (100%)	-	64 (39.27%)	91(55.83%)	8 (4.90%)

The incidence of the disease was seen maximum (80.37%) in non-vegetarian people. It was observed that out of 131 cases of non-vegetarian dietary habits, response was 60-89% in 54 cases, 30-59% in 69 cases and below 30% in 8 cases (Table 5).

Table 5: Dietary Habits-wise Response

Dietary Habits	Number of Patients	Response			
		90-100%	60-89%	30-59%)	<30%)
Vegetarian	32 (19.63%)	-	10 (6.13%)	22 (13.50%)	-
Non-vegetarian	131 (80.37%)	-	54 (33.14%)	69 (42.33%)	8 (4.90%)
Total	163 (100%)	-	64 (39.27%)	91(55.83%)	8 (4.90%)

It was observed that maximum patients had chronicity of the disease above two years. Out of 60 cases of chronicity more than 2 years, 19 cases got 60-89% response, 37 cases 30-59% response and 4 cases below 30% response (Table 6).

Table 6: Chronicity-wise Response

Chronicity of Disease	Number of Patients	Reponse			
		90-100%	60-89%	30-59%	<30%
Upto 1 year	61 (37.42%)	-	29 (17.79%)	30 (18.40%)	2 (1.23%)
1-2 year	42 (25.77%)	-	16 (9.82%)	24 (14.72%)	2 (1.23%)
Above 2 years	60 (36.81%)	-	19 (11.66%)	37 (22.71%)	4 (2.44%)
Total	163 (100%)	-	64 (39.27%)	91(55.83%)	8 (4.90%)

A total of 89 patients (54.6%) who had earlier taken some treatment in other system of medicine, came for treatment by Unani System of Medicine. It was noted that out of 89 known cases, 33 cases got 60-89% response, 51 cases got 30-59% response and 5 cases got below 30% response (Table 7).

Table 7: New/Known Status-wise Response

Status	No. of Patients	Response			
		90-100%	60-89%	30-59%	<30%
New Status	74 (45.40%)	-	31 (19.02%)	40 (24.54%)	3 (1.84%)
Known Status	89 (54.60%)	-	33 (20.25%)	51 (31.29%)	5 (3.06%)
Total	163 (100%)	-	64 (39.27%)	91(55.83%)	8 (4.90%)

It was found that Grade-2 lymphedema cases were maximum. Responses in 87 cases of grade-2 lymphedema were 60-89% in 40 cases, 30-59% in 41 cases and poor response in 6 cases. Responses in 11 cases of grade-1 lymphedema were 60-89% in 3 cases, 30-59% in 7 cases and poor response in one case. In 65 lymphedema cases of grade-3, responses were 60-89% in 21 cases, 30-59% in 43 cases and poor response in one case (Table 8).

Table 8: Filarial Edema Grades-wise Response

Filarial Edema (Grades)	Number of Patients	Reponse			
		90-100%	60-89%	30-59%	<30%
Grade-1	11 (6.75%)	-	3 (1.85%)	7 (4.29%)	1 (0.61%)
Grade-2	87 (53.37%)	-	40 (24.54%)	41 (25.15%)	6 (3.68%)
Grade-3	65 (39.88%)	-	21 (12.88%)	43 (26.39%)	1 (0.61%)
Total	163 (100%)	-	64 (39.27%)	91(55.83%)	8 (4.90%)

Discussion

Analysis of the results has revealed some interesting facts which have been discussed as below:

- The present study has exhibited that UNIM 268, UNIM 270, UNIM 271 and UNIM 272 used with and without *Munzij-Mushil* therapy were effective in lymphatic filariasis. Therapeutic responses of drugs in Group-B patients were better than Group-A patients. This finding advocates that decrease in

volume of affected leg can be achieved through purgation as described by Razi (Razi, 1962) (Table 1).

- The study shows that the patients of all age-groups got relief after the treatment. The study also shows that incidence of disease is maximum in age group 31-40, which is in consonance with the finding that filarial infection is maximum in young age-group between 30 to 40 years (Steel *et al.*, 2001) (Table 2).
- The present study has disclosed that incidence of the disease was highest (78.53%) among the people of phlegmatic temperament, which is in consonance with the observation of Antaki (Antaki, 2009). The study has further disclosed that patients of all temperaments got relief but study drugs were found more effective in patients of phlegmatic temperament (Table 4).
- The study reveals that highest number of chronic cases were more than 2 years old. It may be due to lack of awareness of the disease in most of the people. The study has revealed that study drugs were more effective in chronic cases of less than one year (Table 6).
- The study has disclosed that 54.6% patients of known status not getting relief in other system of medicine came for treatment of disease through Unani medicines. As much as 84 out of 89 patients of known status got relief after the treatment (Table 7).
- The study has disclosed and exhibited that after treatment edema volume was reduced in patients of Grade-1, Grade-2 and Grade-3 lymphedema cases. Responses in out of 65 Grade-3 edema cases were 60-89% in 21 cases and 30-59% in 43 cases. The patients with Grade-3 edema cases, whose limb tissue was hard and skin was thick with fat-deposit got relief after the treatment. Grade-3 edema volume, which was supposed to be non-reversible, was reversed with reduction in edema volume and patients got relief (Table 8). The study reveals that the UNIM-268 combination has potential to achieve the goal of the WHO's GPELF to eliminate the disease as a public health problem by 2020.
- No adverse effect was reported by the patients during the course of study. No adverse effect of study drug was detected by clinical examination and laboratory tests during the course of the study. Hematological parameters, liver function test and kidney function test, as assessed by laboratory investigation, were found within normal range.

Conclusion

In the light of above discussion, it can be concluded that Unani coded drugs UNIM 268, UNIM 270, UNIM 271 and UNIM 272 combination can be used

to reduce the edema volume in the patients of Grade-3 lymphedema cases, which was supposed to be non-reversible. Therapeutic response of Unani coded drugs used with MM therapy was better than the Unani coded drugs combination used without MM therapy. The Unani coded drugs UNIM 268, UNIM 270, UNIM 271 and UNIM 272 combination is effective in the treatment of lymphatic filariasis.

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सारांश

लिम्फेटिक फाइलेरियासिस (*दऊल-फील*) में यूनानी कोडित औषधियों की चिकित्सीय प्रतिक्रिया

***नजमुस सेहर, महबूब-उस-सलाम, तसलीम अहमद, अनीर्बन गोस्वामी और एम.आई. आलम**

लिम्फेटिक फाइलेरियासिस एक मच्छर जनित परजीवी रोग है जो भारत सहित कई उष्णकटिबंधीय देशों में स्थानिक रोग है। वर्तमान अध्ययन का उद्देश्य लिम्फेटिक फाइलेरियासिस में यूनानी कोडित औषधियों की चिकित्सीय प्रतिक्रिया का आकलन करना था। यह मुख्य रूप से पैरों और पिंडली की सूजन है जिसमें प्रभावित पैर विकसित चरण में बहुत सूज जाते हैं। *मुन्ज़िज–मुस्हिल* थेरेपी (एम.एम.थेरेपी) के साथ और इसके बिना यूनानी औषधियों की चिकित्सीय प्रतिक्रिया का आकलन करने के लिए 163 चयनित रोगियों को दो समूहों में विभाजित किया गया। यह देखा गया कि ग्रेड–3 लिम्फेडेमा रोगियों में निचले अंग सहित रोगों से जुड़े लक्षण कम हो गये। जब यूनानी कोडित औषधियां यूनिम 268, यूनिम 270, यूनिम 271 और यूनिम 272 का उपयोग *मुन्ज़िज–मुस्हिल* थेरेपी के साथ किया गया तब तुलनात्मक रूप से बेहतर प्रतिक्रिया देखी गई। अध्ययन के दौरान किसी भी रोगी ने कोई प्रतिकूल प्रभाव नहीं दिखाया। उपचार के बाद लीवर फंक्शन टेस्ट ओर किडनी फंक्शन टेस्ट मापदंडों में भिन्नता सामान्य सीमा के भीतर पाई गई। यूनानी कोडित औषधियों ने ग्रेड–2 और ग्रेड–3 के रोगों में भी एडिमा की मात्रा कम करने के लिए उत्साहजनक प्रतिक्रिया दी है जो शायद ही कभी उलटने योग्य है।

शब्दकुंजी: लिम्फेटिक फाइलेरियासिस, लिम्फेडेमा, यूनिम

Clinical Validation of Unani Pharmacopoeial Formulation *Ma'jūn Muqawwī-i-Raḥim* in *Sayalān al-Raḥim* (Leucorrhoea)

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Abstract

Sayalān al-Raḥim (leucorrhoea) is one of the major problems encountered in gynaecological practice. Most women in the reproductive age group complain about white discharge. *Ma'jūn Muqawwī-i-Raḥim* is a drug which is used in Unani Medicine for the management of *Sayalān al-Raḥim*. The present study was designed to evaluate the safety and efficacy of *Ma'jūn Muqawwī-i-Raḥim* in *Sayalān al-Raḥim*.

A total of 118 cases in the age group of 13-45 years suffering from *Sayalān al-Raḥim* were selected for the study after obtaining their informed written consent. Of them, 102 cases completed the study. Out of the completed cases, 10 showed excellent improvement, 26 marked improvement, 50 moderate improvement, 13 minimal improvement and 3 showed no change. The drug had no effect on hematological and biochemical parameters. Thus, it can be concluded that *Ma'jūn Muqawwi-i-Raḥim* is a safe and effective drug in the management of *Sayalān al-Raḥim*.

Keywords: *Ma'jūn Muqawwī-i-Raḥim, Sayalān al-Raḥim,* Leucorrhoea

Introduction

The term 'leucorrhoea' is defined as running of white substance (Kumar and Malhotra, 2008) and the term should be restricted to mean an excessive normal vaginal discharge (Guntoory *et al.*, 2017; Eram, 2017). Secretions from the endometrial glands, cervical glands and vagina contribute to this discharge (Guntoory *et al.*, 2017). It may be physiological or pathological (Guntoory *et al.*, 2017; Gul *et al.*, 2013). Vaginal discharge or leucorrhoea is a common gynaecological problem faced by women (Mitchell, 2004; Gupta *et al.*, 2016; Devi, 2013). The physiological discharge may be due to sexual arousal, pre-menstrual, or during pregnancy, while pathological discharge may be further categorized as infectious (occurring due to one or multiple infections) or non-infectious (bearing due to detergents, foreign bodies, or due to some cancers) (Kaur and Kapoor, 2014). Studies have shown that of women seeking care in the primary and secondary health care setting, 11% to 38.4% in India, and 34% in Ethiopia were availing care for vaginal discharge (Zemouri *et al.*, 2016; Toppo *et al.*, 2018). In India, the symptoms of vaginal discharge are also associated with psycho-social factors of non-infectious etiology. It is considered that changes in the vaginal epithelium; changes in the normal bacterial flora and pH of the vaginal secretion predispose to leucorrhoea (Abid *et al.*, 2016). Pathological vaginal discharge may be of vaginal or cervical origin. Discharge of vaginal origin may be associated with bacterial vaginosis (BV), and infection with *Candida*

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spp. and *Trichomonas vaginalis* (TV). Discharge of cervical origin is usually due to infection with *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), and *Mycoplasma genitalium* (MG); primary genital herpes simplex cervicitis can also manifest as vaginal discharge (Zemouri *et al.*, 2016). Vulvovaginal candidiasis is a common infective cause of vaginal discharge that affects about 75% of women at some time during their reproductive life (Mitchell, 2004).

Sayalān al-Raḥim is very well described in Unani literature. Ibn Sina (YNM) and Jurjani (2010) mentioned the poor *Quwwat Hāḍima* (digestive faculty) of uterine vessels as the cause of *Sayalān al-Raḥim* while Khan (2011) and Arzani (YNM) described weakness of *Quwwat Ghādhiya* as the causative factor. Majusi (2010) stated that it occurs due to the weakness of *Quwwat Jādhiba* while some added infection of accumulated morbid humour in the uterine vessels as the cause. However, almost all the physicians stated general debility as one of the important predisposing factors for this disease (Khan, 2011).

There are so many single as well as compound Unani formulations which are safe and effective in the treatment of *Sayalān al-Raḥim*. *Maʻjūn Muqawwī-i-Raḥim* is used to treat disorders like *Sayalān al-Raḥim* (leucorrhoea) since long by eminent Unani physicians (Anonymous, 2006) but scientific data on their safety and efficacy are lacking. Therefore, this study was designed to validate the safety and efficacy of the said drug in the treatment of *Sayalān al-Raḥim* (leucorrhoea) and results are presented.

Materials and Methods

It was an open-label clinical study with sample size of 100 patients of *Sayalān al-Rahim* conducted at Regional Research Institute of Unani Medicine (RRIUM), Aligarh during March 2016–July 2017 after ethical clearance from Institutional Ethical Committee. The study was registered with CTRI vide CTRI/2018/10/016191. The test drug *Maʻjūn Muqawwī-i-Raḥim* (MMR) was supplied by the Central Research Institute of Unani Medicine, Hyderabad. Female patients having excessive white discharge with or without backache and general weakness in the age group of 13-45 years were included in the study. Patients having acute / acute on chronic / chronic PIDs, or those having any abnormal condition on p/s examination (in case of married women), taking hormonal therapy, patients on long-term medications, patients on oral contraceptives/ IUDs, pregnant and lactating women were excluded from the study. Patients fulfilling the inclusion criteria were asked to sign the written informed consent form. The duration of study was 2 years. The duration of treatment was 2 weeks. *Maʻjūn Muqawwī-i-Raḥim* 5 gm was given orally twice a day after meal for 2 weeks and the patients were evaluated weekly. No concomitant medication was allowed during the treatment. A total of 118 patients who visited the OPD of

RRIUM, Aligarh during March 2016–July 2017 were selected for the study on the basis of their fulfillment of inclusion and exclusion criteria. Complete blood count (CBC), urine examination (routine and microscopic), VDRL (at the time of screening) and biochemical investigations (random blood glucose at the time of screening only), LFT and KFT were carried out before starting and at the end of treatment for each and every case.

A 10-point visual analog scale (VAS) was applied and improvement in the symptoms on this scale was checked for the assessment of efficacy of the study drug. The results were interpreted in terms of percentage efficacy. Percentage of efficacy was calculated by reduction in VAS score from baseline findings which was calculated through the following formula:

$$\text{Percentage efficacy} = \frac{\text{Maximum score - Minimum score}}{\text{Maximum score}} \times 100$$

Assessment was done in the following manner:

71-100% – Excellent Improvement
51-70% – Marked Improvement
31-50% – Moderate Improvement
11-30% – Minimal Improvement
0-10% – No Change

Data obtained from hematological and biochemical parameters were analyzed statistically by one-way analysis of variance (ANOVA) followed by Dennett's test. The values were considered significant when the p-value was less than 0.01.

The details of ingredients of the formulation *Maʿjūn Muqawwī-i-Raḥim* are as under:

S.No.	Ingredients	Quantity
1.	*Mochras*	10 g
2.	*Fofil*	10 g
3.	*Tabasheer*	10 g
4.	*Nishasta e Gandum*	10 g
5.	*Gil e Makhtoom*	10 g
6.	*Gul e Surkh*	10 g
7.	*Mazu*	10 g
8.	*Hab ul Aas*	10 g
9.	*Post Halela Zard*	10 g
10.	*Balela*	10 g
11.	*Aamla*	10 g
12.	*Musli Siyah*	10 g

S.No.	Ingredients	Quantity
13.	*Musli Safaid*	10 g
14.	*Post e Anar*	15g
15.	*Aab e Behi Taza*	50 ml
16.	*Aab e Anar Tursh*	50ml
17.	*Nabat Safaid*	210 g
18.	*Asal or Qand Safaid*	210 g

(Anonymous, 2006)

Observations and Results

Total 121 patients were screened and 118 were enrolled in the study of which 102 subjects completed the trial.

It was observed that mean age (years) of the patients was 23.64 yrs and mean duration of disease (in months) was 35.20. (Table 1)

According to temperament, 50 patients (49.02%) belonged to *Ṣafrāwī* (Bilious) temperament, 42 (41.18%) to *Damwī* (Sanguine) temperament and 10 (9.8%) to *Balghamī* (Phlegmatic) temperament, while none of the patients belonged to the *Sawdāwī* (Melancholic) temperament (Table 1). According to marital status, 55 (53.92%) were married, and 47 (46.08%) were unmarried (Table 1).

Most of the patients (75 i.e. 73.53%) belonged to lower socio-economic group and 27 (26.47%) patients to middle socio-economic group while no case was recorded in upper socio-economic group (Table 1).

Assessment of efficacy of the test drug was done in terms of percentage efficacy. Total 10 patients (9.8%) showed excellent improvement, 26 (25.49%) showed

Table 1: Demographic Data

S.No.	Demographic Data	Mean ± S.D.	
1	Age (in years)	23.64±6.83	
2	Duration of disease (in months)	35.20 ± 32.88	
3	*Mizāj* (Temperment)	*Balghamī* (Phlegmatic)	10 (9.8%)
		Damwī (Sanguine)	42 (41.18%)
		Ṣafrāwī (Bilious)	50 (49.02%)
		Sawdāwī (Melancholic)	0
4	Marital status	Married	55 (53.92%)
		Unmarried	47 (46.08%)
5	Socio-economic status	Upper	0
		Middle	27 (26.47%)
		Lower	75 (73.53%)

marked improvement, 50 (49.02%) showed moderate improvement, and 13 (12.75%) showed minimal improvement while no change was seen in 3 (2.94%) cases (Table 2).

For the assessment of safety of drug, haematological and biochemical parameters were conducted before and after the study and no adverse effect was noted (Table 3 and 4).

Table 2: Effect of Treatment

Response	No. of cases (%)
Excellent Improvement (71-100%)	10 (9.8%)
Marked Improvement (51-70%)	26 (25.49%)
Moderate Improvement (31-50%)	50 (49.02%)
Minimal Improvement (11-30%)	13 (12.75%)
No Change (0-10%)	3 (2.94%)

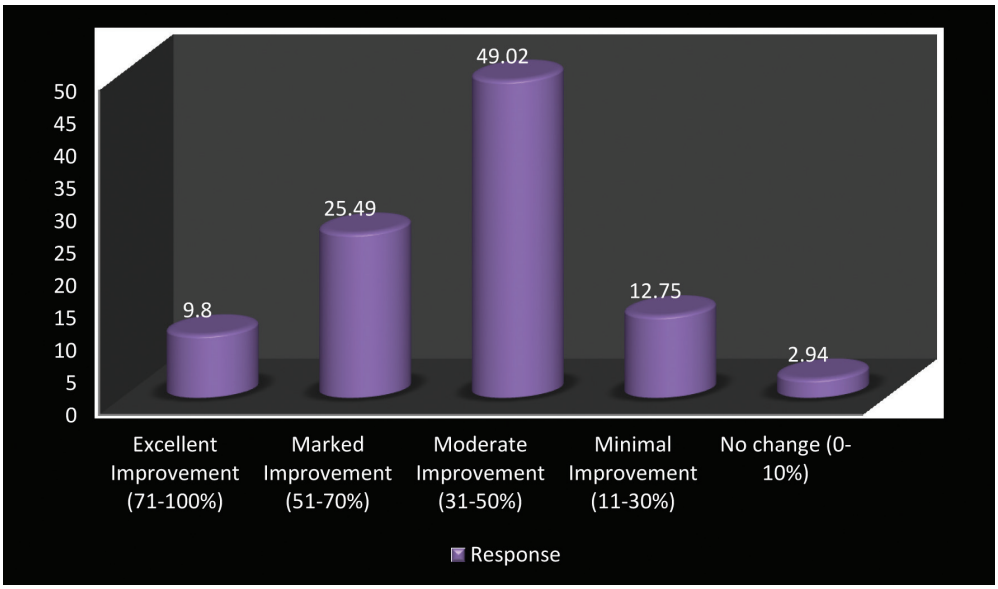

Table 3: Effect of *Maʿjūn Muqawwī-i-Raḥim* on CBC

Parameter → Group ↓	Haemoglobin (gm %)	R.B.C. (10^6/mm^3)	T.L.C. (10^3/mm^3)	E.S.R.(mm/hr)		Polymorphs (%)	Lymphocyte (%)	Eosinophil (%)
				1 Hour	2 Hour			
(Baseline-treatment)	11.43 ±1.26	3.94 ±0.64	7.25 ±2.11	38.0 ±11.39	47.0 ±9.67	64.0 ±9.49	32.0 ±9.28	04 ±2.34
End follow-up (14th day)	11.25 ±1.23▪	3.83 ±0.42	6.92 ±1.92▪	38.0 ±10.35▪	48.0 ±8.96▪	64.0 ±9.36▪	31.0 ±9.38▪	05 ±2.12▪

▪P is not significant

Table 4: Effect of *Ma'jūn Muqawwī-i-Raḥim* on Liver and Kidney Function

Parameter → Group ↓	SGPT (IU/L)	SGOT (IU/L)	Alkaline Phosphatase (IU/L)	Bilirubin	Blood Urea (mg %)	Serum Creatinine (mg %)
(Baseline-Treatment)	33.04 ± 13.8	20.83 ± 7.10	73.46 ±23.85	0.71 ±0.53	19.85 ±6.41	1.09 ±2.36
End Follow-Up (14^{th}-days)	18.79 ± 10.37	22.43 ± 7.89▪	76.36 ±31.35▪	0.71 ±0.25▪	20.55 ±5.8▪	1.05 ±1.98▪

▪P is not significant

Discussion

The study was carried out at Regional Research Institute of Unani Medicine (RRIUM), Aligarh. Total 75 patients (73.53%) belonged to lower socio-economic group and 27 (26.47%) to middle socio-economic group while no case was recorded in upper socio-economic group. It is similar to the finding of previous study that was done at our institute (Rehman *et al.*, 2017). Assessment of efficacy of test drug was done in terms of percentage efficacy. Ten (9.8%) patients showed excellent improvement, 26 (25.49%) showed marked improvement, 50 (49.02%) showed moderate improvement and 13 (12.75%) showed minimal improvement while no change was seen in three (2.94%) cases. In Unani classics, *Ma'jūn Muqawwī-i-Raḥim* is indicated for treatment of leucorrhoea and other uterine disorders (Anonymous, 2006). It is described as having *Muqawwī-i-Raḥim* (uterine tonic) and *Muwallid-i-Dam* (hematopoietic) action. For safety assessment of the drug, haematological and biochemical parameters were conducted before and after the study and no adverse effect was noted. The drug was found to be safe for use.

There was found no clinical study on *Ma'jūn Muqawwī-i-Raḥim* (MMR) in this condition to corroborate. However, classics of Unani Medicine recommend this formulation for the treatment of leucorrhoea (Anonymous, 2006). Hence, it is justified to use it. The fact that ingredients of the formulation possess *Muqawwī* (tonic), retentive and astringent properties on the female genital tract (Ghani, YNM) also justifies it as the scholars of Unani Medicine mentioned weakness of *Quwa* (faculties) viz. *Quwwat Hāḍima*, *Quwwat Ghādhiya* and *Quwwat Māsika* of uterus as the basic cause of the disease.

Majority of the cases (49.02%) were found belonging to *Ṣafrāwī* temperament, followed by *Damwī* (41.18%) and *Balghamī* (9.8%) temperament. No case was found having *Sawdāwī* temperament. This finding is in line with the general tendency of the occurrence of *Mizāj* in the society as the least number of subjects are found having *Sawdāwī Mizāj* in the society. The response of the drug was found significant as more than 80% of the cases got relieved.

As no significant changes were found in hematological and biochemical parameters at baseline and after the study, it was observed that the formulation was safe.

Conclusion

It may be concluded that the test drug *Maʿjūn Muqawwī-i-Raḥim* (MMR) is safe and effective in ameliorating the signs and symptoms of *Sayalān al-Rahim*.

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सारांश

सैलान अल-रहिम (ल्यूकोरिया) में यूनानी भेषकोशीय मिश्रण *माजून मुक़व्वी-ए-रहिम* का नैदानिक वैधीकरण

***शगुफ़्ता रहमान, निदा सुल्ताना, आर.एस. वर्मा, जमाल अख़्तर और सरफ़राज़ अहमद**

सैलान अल–रहिम (ल्यूकोरिया) स्त्री संबंधी प्रमुख समस्याओं में से एक है। प्रजनन आयु वर्ग में अधिकांश महिलाओं को सफ़ेद स्राव की शिकायत होती है। *माजून मुक़व्वी–ए–रहिम* एक औषधि है जिसका उपयोग यूनानी चिकित्सा में *सैलान अल–रहिम* के उपचार के लिए किया जाता है। यह अध्ययन *सैलान अल–रहिम* में *माजून मुक़व्वी–ए–रहिम* की सुरक्षा और प्रभावकारिता का मूल्यांकन करने के उद्देश्य से किया गया है।

अध्ययन के लिए 13–45 वर्ष की आयु के *सैलान अल–रहिम* से पीड़ित कुल 118 रोगियों को उनकी लिखित सहमति के बाद चुना गया। कुल 102 रोगियों ने अध्ययन पूरा किया जिनमें से 10 ने उत्कृष्ट सुधार, 26 ने उल्लेखनीय सुधार, 50 ने मध्यम सुधार और 13 ने न्यूनतम सुधार दिखाया जबकि 3 में कोई बदलाव नहीं था। हेमेटोलॉजिकल और जैव रासायनिक मापदंडों पर औषधि का कोई प्रभाव नहीं था। इस प्रकार यह निष्कर्ष निकाला जा सकता है कि माजून *मुक़व्वी–ए–रहिम, सैलान अल–रहिम* के उपचार में एक सुरक्षित और प्रभावी औषधि है।

शब्दकुंजी: *माजून मुक़व्वी–ए–रहिम, सैलान अल–रहिम,* ल्यूकोरिया

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