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Editorial

Unani System of Medicine is a comprehensive medical system, which provides promotive, preventive, curative and rehabilitative healthcare. The fundamentals, diagnosis and treatment modalities of the system are based on scientific principles and holistic concepts of health and healing. Its holistic approach considers individual in relation to his environment and stresses on health of body, mind and soul. Temperament (*Mizāj*) of a patient is given great importance in diagnosis and treatment of diseases with natural remedies. Unani Medicine has different modes of treatment, namely *'Ilāj bi'l-Dawā'* (Pharmacotherapy), *'Ilāj bi'l-Ghidhā'* (Dietotherapy), *'Ilāj bi'l-Yad* (Surgery) and *'Ilāj bi'l-Tadbīr* (Regimen Therapy). *'Ilāj bi'l-Dawā'* (Pharmacotherapy) in Unani Medicine is primarily based on herbal origin drugs. In the present era, such drugs have witnessed resurgence for management of various diseases due to their cost effectiveness and less associated side effects. Despite vast development in the field of modern medicine and surgery, there is a growing global interest in traditional systems of medicine. Unani Medicine in particular is presently practiced, with its different regional names, in India, Bangladesh, Pakistan, Sri Lanka, Nepal, China, Iran, Iraq, Malaysia, Indonesia, Central Asian and Middle Eastern countries and some African as well as European countries. In India, it has been developed and nurtured scientifically and integrated systematically in the healthcare delivery system over the years. With the government patronage, a wide network of quality educational institutions, state-of-the-art research organizations and well-developed healthcare facilities of Unani Medicine has been developed. The country has well-developed infrastructure and expertise in Unani System of Medicine. In view of all these facts, India is considered the world leader in Unani Medicine.

As the apex institution for research and development in Unani Medicine under the Government of India, the Central Council for Research in Unani Medicine (CCRUM) is making concerted efforts for globalization of Unani Medicine. Besides focusing on clinical research, drug standardization, survey and cultivation of medicinal plants and literary research at its own research institutes, the Council collaborates with various scientific and academic institutions at national and international levels. With a view to pave the way for global propagation of the system, the CCRUM has recently entered into international collaborations with Iran, Bangladesh and Tajikistan.

In an effort to propagate research outcomes, the CCRUM has been publishing various periodical and non-periodical publications which include Hippocratic Journal of Unani Medicine, a peer reviewed quarterly journal. In the recent past, a few of the issues of the journal could not be published in time due to compelling circumstances. In an effort to clear the backlog and maintain continuity of the journal, the current series is published to fill the gap.

The issue includes six papers. In the first paper, the authors have made an attempt to highlight anti-inflammatory and analgesic activities of *Maida Lakdi* (Stem Bark of *Litsea glutinosa* (Lour.) C.B.Rob.). Another paper discusses clinical safety and efficacy of Unani pharmocopoeial formulation of *Ḥabb-i Suranjān* and *Raughan-i Suranjān* in the treatment of *Waja' al-Mafāṣil* (joints pain). It is based on a study conducted at the Regional Research Institute of Unani Medicine, Patna. The third paper is based on clinical evaluation of Unani pharmacopoeial formulation *Sharbat Tūt Siyāh* in *Waram-i Ḥalaq* (Pharyngitis). The fourth one is a review paper which deals with several issues concerning the theory of *Akhlāṭ*. In the fifth paper, *Tukhm-i Kāhū*, a hypnotic, anaesthetic, hypoglycaemic, anti-dysentric and sedative Unani drug, has been reviewed, whereas the sixth paper is a review of *Kushta* (Calx), one of the drug dosage forms commonly used in Unani Medicine. The paper analyzes the published studies on Calx in three traditional systems of medicine viz. Unani Medicine, Ayurveda and Siddha.

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

New Delhi
January 23, 2019

Prof. Asim Ali Khan
Editor-in-Chief

Contents

A Study of Analgesic and Anti-inflammatory Activity of *Maida Lakdi* (Stem Bark of *Litsea glutinosa* (Lour.) *C.B. Rob.*) in Albino Rats

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Abstract

Maida Lakdi (ML); a well-known Unani drug; has been used for centuries to treat inflammatory disorders including rheumatoid arthritis, gouty joints, sprains and bruises. It was identified as stem bark of *Litsea glutinosa* (Lour.) C.B. Rob. of family Lauraceae. The present study was conducted to investigate its anti-inflammatory and analgesic activity in experimental albino rats. The coarsely powdered drug was extracted in ethanol and distilled water separately. The dried extract was used to study the anti-inflammatory and analgesic effects using carrageenan induced paw oedema test and analgesiometer test respectively. The low and high doses of aqueous (90 and 130 mg/kg) and alcoholic extracts of the test drug (100 and 140 mg/kg) were used. The animals were divided into six groups with six rats in each group and piroxicam 3 mg/kg body weight was given orally as standard drug. The data were expressed as Mean±SEM and analyzed by ANOVA followed by Dunnett's "t" test. The aqueous and alcoholic extracts of ML at high doses exhibited a significant ($P< 0.01$) anti-inflammatory activity in carrageenan model as compared to control group. The aqueous extract of the test drug at high dose and alcoholic extract in both the doses (low and high) exhibited a significant increase in the reaction time ($P< 0.01$) as compared to control group. The findings of the study revealed that ML consists of different compounds which are responsible for decreasing the oedema and nociceptive stimuli; hence, the test drug possesses anti-inflammatory and analgesic activities.

Keywords: Analgesic, Anti-inflammatory, Carrageenan, *Litsea glutinosa, Maida lakdi.*

Introduction

Maida lakdi (ML) is a Unani drug which consists of stem bark of *Litsea glutinosa* (Lour.) C.B. Rob. of family Lauraceae. In many works of Muslim scholars, the drug is briefly described under the name of Mogath-e-Hindi and Kilz. It is commonly used to treat inflammatory disorders like rheumatoid arthritis, gouty joints, sciatica, backache, joint stiffness and as emollient for sprains and bruises (Ibn Sina, 1927; Khan, 1987; Ghani, 1921; Singh, 1974; Kabeeruddin, 1955). It is used as resolvent, astringent and nervine tonic in paralysis (Dymock *et al*., 1890). *Litsea glutinosa* is an evergreen shrub or tree grows up to 25 m in height and 1.5 m in girth with a clean bole 6.0 m long. It is found throughout India, ascending up to an altitude of 1350 meter in the outer Himalayas, especially in Bengal and the hills of South India. Bark is brownish grey, fragile and readily powdered, section corky and composed of several layers of soft granular, when placed in water it affords a large quantity of bland mucilage, taste feebly balsamic, bitter and mucilaginous (Anonymous, 1962; Khory and Katrak, 1981; Nadkarni, 1989; Sattyawati and Gupta, 1987; Chatterjee and Pakrashi, 1991). Bhakuni *et. al* (1969) has reported that 50% ethanolic extract of *Litsea glutinosa* showed antispasmodic action on isolated guinea pig ileum. *Litsea glutinosa* bark extract was also tested for antifungal activity and found active against *Fusaricum solani,*

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Fusaricum moniliforme, Helminthosporium turicum, Helminthosporium oryzae, Pythium vexans, Rhizoctonia solani, Rhizoctonia bataticola and more active against *Colletotrichum capsici, Pryricularie setariae* and *Alternasia helianth* (Mishra *et al*., 1979). Menon *et al* (1970) has reported that the essential oil of *L. glutinosa* produces marked reduction in spontaneous motor activity with no concomitant muscle weakness and mild psychotic effect.

Despite the clinical use of ML in Unani medicine to alleviate various inflammatory disorders, there is no scientific report to support the claim except the work by Rauf *et al*., (2016) in which its analgesic and anti-inflammatory effect was investigated using formalin induced paw oedema test and tail flick model. It guided the investigators to explore the potential of drug on other parameters so as to further confirm its reported action and also the diversity of its age-old practice in a number of inflammatory disorders. Therefore, the present study was designed to undertake anti-inflammatory effect of ML on carrageenan induced rat paw oedema model because it is considered as a suitable test for evaluating anti-inflammatory drugs. The study conducted in the past had indicated a significant analgesic effect possessed by the test drug, probably of opioid type, therefore in the present study the analgesic effect of the drug was undertaken on tail clip model in order to confirm the findings of the study conducted in the past and also to know the other mechanism of action possessed by the test drug, if any.

Material and Methods

The study was undertaken during the year 2007-2008 at Hamdard University, New Delhi. ML was procured from Taj Trading Company, 6682, Kharibawli, Delhi, in July 2007. The drug was primarily identified on the basis of classical descriptions available in Unani reference books and subsequently it was authenticated by National Institute of Science Communication and Information Resources (NISCAIR), Council of Scientific and Industrial Research (CSIR), New Delhi. A voucher specimen (06/765/82) was deposited to the Advia Museum of the Department of Ilmul Advia, Hamdard University, New Delhi.

Fig 1: Stem Bark of *Litsea glutinosa* (Maida Lakdi)

Preparation of Alcoholic and Aqueous Extract

The dried powder of stem bark (400 gm) of *Litsea glutinosa* was extracted by refluxing with alcohol for 6 hours and filtrate was evaporated on a water bath to get viscous alcoholic extract (56.5gm /14%) whereas to get aqueous extract, the coarsely powdered drug (200gm) was boiled in 2000 ml of distilled water for one hour, then filtered and the filtrate decoction was evaporated on a water bath to get a mucilaginous viscous aqueous extract (26.5gm/13%).

Experimental Animals

Wistar albino rats weighing 150-200gm of 12 weeks of either sex, supplied by the Central Animal House Facility, Hamdard University, New Delhi and approved by the Institutional Animal Ethical Committee vide ethical clearance No. 366/ IAEC dated 09.08.2007 were used in this study. The animals were housed in six groups with six rats in each group in polyacrylic cages (38×23×10cm) and maintained under standard laboratory conditions. They were allowed free access to standard dry pellet diet and water. The experiments were performed in accordance with the guidelines laid down by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Social Justice and Empowerment, Government of India, for the care and use of laboratory animals.

Chemicals, Drugs and Instruments

Carrageenan (Central Drug House, New Delhi, India), Methanol (SD Fin chemicals Ltd. Bombay) and Piroxicam were used. The instruments used in the study were Plethysmometer (Ugo Basil 7140) and Hot plate (Ugo Basil Model-DS-37).

Test for Anti-inflammatory Activity

Carrageenan-induced Rat Paw Oedema Test

The test was carried out to determine the anti-inflammatory effect of test drug by the method of Winter *et al* (1962). The animals were divided into six groups with six rats in each group and treated orally. Animals in group I and II were given normal saline (1ml/rat) and Piroxicam (3mg/kg) and served as plain and standard control respectively. Groups III, IV, V and VI were treated with aqueous extract (90 and 130 mg/kg) and alcoholic extract (100 and 140 mg/kg) respectively. After an hour, 0.1ml of 1% Carrageenan solution was injected to all the animals in the sub planter aponeurosis of left hind paw to produce the inflammation and the paw volume was measured at an interval of one hour using plethysmometer 0, 1st, 2nd, 3rd, 4th, and 5th hour by the method of Winter *et al* (1962). The findings were expressed as Mean±SEM and analyzed by ANOVA followed by Dunnett's"t"test.

Test for Analgesic Activity

Tail Clip Test

To determine the analgesic activity of ML extract, the method described by Bianchi et. al, (1954) was used. Albino rats were divided into six groups of six rats each

and treated in a similar way as in previous test. After an hour, an artery clip/ bulldog clamp was applied to the base of the tail of every rat for 30 seconds and the reaction time of rat to biting the clip was recorded. It was repeated at 30, 60 and 90 minutes from the time the drug was given. The cut off time was kept at 10 seconds. A significant reduction in reaction time was considered as antinociceptive response.

Results

Anti-inflammatory Activity of Carrageenan-induced Rat Paw Oedema Test

The reduction in the volume of paw oedema was observed at different doses of aqueous and alcoholic extract of test drug. The alcoholic extract exhibited a significant ($P<0.01$) anti-inflammatory activity in both the doses (100mg/kg and 140 mg/kg) at 1st, 2nd, 3rd, 4th, & 5th hour but it was found slightly lower than the standard drug. In the group treated with low dose of alcoholic extract, maximum inhibition was found at 5th hour whereas in high dose of alcoholic extract, this inhibitory effect was exhibited at 2nd, 3rd, 4th and 5th hour. In case of aqueous extract, both the doses (90mg/kg and 130mg/kg) showed a significant ($P<0.01$) anti-inflammatory activity at 1st and 2nd hours whereas at 3rd, 4th and 5th hours, the drug did not inhibit the paw oedema significantly (Table 1).

Table 1: Effect of Aqueous and Alcoholic Extract of ML (*Litsea glutinosa*) on Carrageenan Induced Paw Oedema in Rats

Group	Treatment	Time after drug administration (Mean ± S.E.M.)					
		0 hr.	After 1 hr.	After 2 hrs.	After 3 hrs.	After 4 hrs.	After 5 hrs.
I	Control	0.88 ± 0.04	1.45±0.06	1.55±0.08	1.7±0.05	1.73±0.06	1.73±0.08
II	Standard (piroxicam) 3mg/kg body weight	0.83 ± 0.04	0.98±0.04** 32.41%	1.01±0.04** 34.83%	1.08±0.06** 36.47%	1.08±0.04** 37.57%	1.06±0.06** 38.72%
III	Test drug (Aq. Ext. Low Dose) 90mg/kg body weight	0.85 ± 0.05	1.15±0.07* 20.68%	1.25±0.06*# 19.35%	1.5±0.06## 11.76%	1.55±0.09## 10.4%	1.61±0.15## 6.93%
IV	Test drug (Aq. Ext. High Dose) 130mg/kg body weight	0.88 ± 0.03	1.15±0.07* 20.68%	1.26±0.06*# 18.7%	1.55±0.06## 8.82%	1.48±0.08## 14.45%	1.51±0.14# 12.71%
V	Test drug (Alc. Ext. Low Dose) 100mg/kg body weight	0.98 ± 0.07	1.16±0.09* 20%	1.21±0.08** 21.93%	1.35±0.04**## 20.5%	1.33±0.04** 23.12%	1.26±0.07** 27.16%
VI	Test drug (Alc. Ext. High Dose) 140mg/kg body weight	0.93 ± 0.07	1.13±0.06* 22.06%	1.13±0.05** 27.09%	1.25±0.02** 26.47%	1.23±0.03** 28.9%	1.2±0.04** 30.63%

*P<0.05 and **P<0.01 as compared to group I (control group)

#P<0.05 and ## P<0.01 as compared to group II (standard group)

One-way analysis of variance (ANOVA) followed by Dunnett's't' test.

Analgesic Activity of Tail Clip Test

The extract of ML at different doses induced a significant (P<0.01) increase in the tail clip latency when compared to control group. A significant increase in reaction time of tail clip latency was observed at 90 minutes at a high dose of aqueous extract whereas at low dose of aqueous extract, the drug did not increase the reaction time significantly during the study period. The significant result was exhibited at 60 and 90 minutes in both the doses of alcoholic extract, whereas it did not produce any significant result at 30 minutes in groups treated with low and high doses (Table 2).

Table 2: Effect of Aqueous and Alcoholic Extract of ML (*Litsea glutinosa*) on Tail Clip Test in Rats

Tail-clip latency in seconds (Mean±S.E.M.)				
Treatment	**Time after drug administration**			
	Pre-drug reaction time	**30 min.**	**60 min.**	**90 min.**
Control	9.40±0.59	9.59±0.96	11.48±0.77	11.18±0.46
Standard (piroxicam) 3mg/kg	8.30±0.24	8.63±0.52	10.23±0.33**	11.88±0.42**
Litsea glutinosa (Aq.Ext.90mg/kg)	11.35±0.51	11.88±0.42	11.83±0.42	11.45±0.41
Litsea glutinosa (Aq.Ext.130mg/kg)	10.17±0.18	10.36±0.42	11.62±0.62	12.77±0.67**
Litsea glutinosa (Alc.ext.100mg/kg)	10.38±0.45	11.27±0.75	12.73±0.55**	13.73±0.25**
Litsea glutinosa (Alc.ext.140mg/kg)	9.39±0.75	10.05±0.36	12.41±0.29**	13.66±0.36**

*P<0.05, **P<0.01 as compared to pre drug reaction time

One-way analysis of variance (ANOVA) followed by Dunnett's't' test.

Discussion

In the present study the alcoholic extract of stem bark of ML at high dose showed marked anti-inflammatory activity on carrageenan induced paw oedema in rats, however, this effect was found little lower than the standard drug Piroxicam. As the carrageenan induced inflammation is a significant predictive test for anti-inflammatory agents acting by inhibiting the mediators of acute inflammation, the result therefore indicated that the stem bark of *Litsea glutinosa* is effective in acute inflammatory disorders particularly at a higher dose. The drug may contain different alcohol soluble compounds which are responsible for reducing the

oedema in different phases of carrageenan induced inflammation. The low dose of alcoholic extract also produced significant anti-inflammatory effect but the higher degree of inhibition was observed at 5th hour indicating that anti-inflammatory effect of ML was mediated through its interposition with prostaglandins, whereas the inhibition observed at initial hours may be mediated through the inhibition of histamines, serotonins and kinin like substances which play a significant role in the causation of acute inflammation. The findings are in agreement with the earlier reports of anti-inflammatory and analgesic activity possessed by ML on formalin induced paw oedema and tail flick model respectively (Rauf *et al*., 2016). Further, the present study also demonstrated that the drug can be used in different stages of inflammatory conditions because the different models used in previous and present studies evolve different mechanism of action. The findings have provided a rational basis of its clinical use in different inflammatory diseases.

The analgesic activity of stem bark of *Litsea glutinosa* extract was also assessed using sensitive tail clip model. The result indicated that both the aqueous and alcoholic extract of *Litsea glutinosa* produced significant analgesic effect. The alcoholic extract of test drug at two doses (100 mg/kg and 140mg/kg) showed a significant increase in reaction at 60 and 90 minutes ($P<0.01$) suggesting that the alcoholic extract of the test drug exerts the analgesic effect similar to the non-steroidal anti-inflammatory drugs and ML might possess centrally and peripherally mediated anti-nociceptive properties. In both the doses of alcoholic extract, the drug did not produce significant analgesic effects at 30 minutes but started in late phases. In case of aqueous extract the drug has shown a significant increase in reaction time at 90 minutes only in higher dose whereas the drug did not increase the latency time significantly at other doses, indicating that the constituents responsible to produce analgesia were not present in aqueous extract in sufficient quantity. Drugs effective against thermal and mechanical nociceptive stimuli are considered to possess opioid and aspirin-like analgesic activity, respectively. The findings of the present study are in agreement with the findings of previous studies and revealed that ML is effective against two different types of nociception and could be clinically used to produce opioid and aspirin-like analgesic activity. The findings of the study suggest that the detailed phytochemical studies including the characterization of active constituents must be analyzed to correlate these effects with the constituents present in the drug. The study validated its clinical use as an analgesic and anti-inflammatory agents to treat various inflammatory disorders.

Conclusion

On the basis of the findings, it can be concluded that ML produces significant analgesic and anti-inflammatory activity and it may be used therapeutically in various inflammatory disorders. As the high doses were found to produce more pronounced response, it is suggested that further studies may be conducted with higher doses in order to determine its optimal pharmacological response and also the dose response relationship.

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सारांश

एल्बिनो चूहों में *मैदा लकड़ी* (*लिट्सिया ग्लूटिनोसा* (लूर.) *सी.बी. रोब.* की तने की छाल) की एनाल्जेसिक और एंटी-इन्फ्लैमेटॉरी गतिविधि का एक अध्ययन

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मैदा लकड़ी (एम एल); एक जानी पहचानी यूनानी औषधि है जिसका उपयोग सदियों से संधिशोथ, जोड़ों के दर्द, मोच और चोट सहित इन्फ्लैमेटॉरी विकारों का उपचार करने के लिए किया जाता है। इसकी पहचान लौरासी परिवार के लिट्सिया ग्लूटिनोसा (लूर.) सी.बी. रोब. की तने की छाल के रूप में की गई। वर्तमान अध्ययन, प्रयोगात्मक एल्बिनों चूहों में इसकी एनाल्जेसिक और एंटी–इन्फ्लैमेटॉरी गतिविधि की जांच करने के लिए किया गया। दरदरी पिसी हुई औषधि को इथेनॉल और आसुत जल में अलग–अलग सत्त निकाला गया। सूखे सत्त का प्रयोग क्रमशः कैरेजेनन से उत्पन्न पॉ एडिमा परीक्षण और एनाल्जेसियोमीटर परीक्षण के उपयोग से एंटी–इन्फ्लैमेटॉरी और एनाल्जेसिक प्रभावों का अध्ययन करने के लिए किया गया। परीक्षित औषधि के जलीय सत्त की कम व अधिक खुराक (90 और 130 मि.ग्रा./कि.ग्रा.) और (100 और 140 मि.ग्रा./कि.ग्रा.) के एल्कोहलिक सत्त का उपयोग किया गया। प्रयोगात्मक चूहों को छः चूहों को छः समूहों में साथ विभाजित किया गया और पिरॉक्सिकैम 3 मि.ग्रा./कि.ग्रा. शरीर भार वालों को मौखिक रूप से मानक औषधि के रूप में दिया गया। डाटा को Mean±SEM के रूप में व्यक्त किया गया और एनोवा के साथ–साथ डनेट "टी" टैस्ट द्वारा विश्लेषण किया गया। उच्च खुराक पर एम एल के जलीय और एल्कोहलिक सत्त ने नियंत्रण समूह की तुलना में कैरेजेनन मॉडल में एक महत्वपूर्ण (P< 0.01) एंटी इन्फ्लैमटॉरी गतिविधि दिखाई। उच्च खुराक पर परीक्षण औषधि के जलीय सत्त और दोनों खुराक (कम और उच्च) में एल्कोहलिक सत्त ने नियंत्रण समूह की तुलना में प्रतिक्रिया समय में (P< 0.01) एक महत्वपूर्ण वृद्धि दिखाई। अध्ययन के निष्कर्षों से पता चला कि एम एल में विभिन्न यौगिक होते हैं जो एडिमा और नोसिसेप्टिव उत्तेजनाओं को कम करने के लिए जिम्मेदार होते हैं; इसलिए, परीक्षित औषधि में एंटी इन्फ्लैमटॉरी और एनाल्जेसिक गतिविधियां होती हैं।

शब्दकुंजीः एनाल्जेसिक, एंटी–इन्फ्लैमेटॉरी, कैरेजेनन, लिट्सिया ग्लूटिनोसा, *मैदा लकड़ी*

A Clinical Study of Safety and Efficacy of Unani Pharmocopoeial Formulations of Habb-e-Suranjan and Raughan-e-Suranjan as Anti-arthritic Effect in Waja-al-Mafasil (Joints Pain)

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Abstract

The clinical study was carried out to validate Unani pharmocopoeial compound formulation of Habb-e-Suranjan and Raughan-e-Suranjan for its safety and efficacy in the treatment of joints pain as these are well known Unani formulation for analgesic and anti-inflammatory effect in joints pain. For this study, based on the complaint of joint pain, 117 patients were selected under the protocol approved by the Institutional Ethics Committee, Regional Research Institute of Unani Medicine, Patna from General Outpatient Department and Mobile Clinical Research Unit of the institute. Only 97 patients completed the treatment. The treatment was given for 14 days and the clinical evaluation was done on seventh and fourteenth day of the treatment. At the end of fourteenth day intensity of individual parameters like joints pain, swelling, tenderness and restriction of movement showed statistically a significant improvement from the baseline ($p<0.001$). A comprehensive evaluation (clinical and laboratory) was done at the end of the study. The results revealed that out of 97 cases, 5 (5.15%) showed very good response (relief 60-89%), 62(63.92%) good response (partial relief 30-59%) and 30(30.93%) no response (<30%). The laboratory investigations also showed that the drugs used were neither hepato-toxic nor nephro-toxic. It can be concluded that Habb-e-Suranjan in combination with Raughan-e-Suranjan possesses anti- inflammatory and analgesic property and can be a better option for the patients of Arthritis.

Keywords: Arthritis, *Balgham*, Caustive factors, Joints pain, Temperament.

Introduction

The term Waja-al-Mafasil (Joints Pain) consists of two words, “Waja” means pain and “Mafasil” means joints, hence, Waja-al Mafasil means pain in joints. Waja-al-mafasil or polyarthritis includes many types of arthritis and autoimmune diseases that affect the bones and joints and other parts of the musculoskeletal (MSK) system causing morbidity and disability. Joints form the connection between bones which provide support and help to move. Any damage to the joints from disease or injury can interfere with the movement and cause a lot of pain. Many different conditions can lead to painful joints; including osteoarthritis, rheumatoid arthritis, bursitis, gout, strains, sprains and other injuries. Knee pain is the most common complaint followed by shoulder and hip but joints pain can affect any part of your body from your ankles to your shoulders (Richard et al,. 2010). Joints pain is one of the most leading public health problems globally (Halverson *et al.*, 1987). According to WHO statistics, it is estimated to be the 31st leading causes of non fatal burden in 0.8% of the world population and women are at two to three times greater risk of developing the disease (Barbour *et al.*, 2013). As per reports, Arthritis affects 15% of the total population in India. This prevalence is higher than many well known diseases such as diabetes, AIDS and cancer. And in case of Bihar 1821 females per lakh and 1250 males per lakh are suffering from Arthritis as per the Annual Health Survey (2010-2011).

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According to Unani scholars, it is a painful condition of joints irrespective of their size (Razi, 2002) and commonly caused by accumulation of viscid phlegm (balgham-e-lazij) in joints due to weakness of joints (Zoaf-e-Mafasil) (Majoosi, 1889; Khan, 1939). Ibn Sina (1995) described the main causative factors of joints pain as weakness of joints, impairment of temperament of whole body or affected joints. According to Unani theory, besides Soo-e-mizaj (Dyscrasia), there are several other factors causing the disease, for example; pain occurs in joints where there is Qillat-e-Hararat-e-Ghariziya which causes slow absorption of the morbid humours leading to accumulation of waste matter in the joints. Vigorous exercise or hard physical work associated with improper or poor nutrition is also a reason for such joints pains. Accordingly, it is stated that Hamiz-e- Labni is one of the root causes which is produced by the derangement of digestive process and accumulates in the blood and joints produce joints pain (Kabeeruddin, 1916). The causes of the pain can all be grouped together under sudden change of temperament and breach of continuity. The perception of such a contrary temperament is pain, thus pain by its nature is the appreciation of a contrary or deviated temperament (Alam *et al.*, 2013). Depending upon the materials affecting the joints, Balgham (phlegm) predominates Dum (Blood) and Safra (bile) are next to it and quite rarely Sawda (black bile) is involved. In some cases more than one khilt (Humours) are involved (Kabeeruddin, 2003) i.e., sue mizaj barid balghami and har balghami are the main causes (Tanwir *et al.*, 2013).

It is a very common problem of old age but may start at earlier stage of life specially when there is predominance of Balgham along with obesity, indigestion, prolonged breast-feeding, poverty, damp, exposure to cold and humid climates (Kabeeruddin, 2007). A detailed information regarding pain in low back, hip, knee and ankle joints has been given by the physicians of the unani system; including its line of treatment according to the causative factors. Besides, a lot of compounds have been prescribed as analgesic/anti-inflammatory for joints pain. Two such compounds namely; Habb-e-Suranjan and Raughan-e-Suranjan have Musakkin-e-alam (Analgesic) effect which are being used frequently by unani physician to relieve joints pain and selected for the study.

Methodology

117 patients suffering from joints pain were selected as per the protocol approved by the Institutional Ethics Committee, Reginoal Research Institute of Unani Medicine, Patna in 2013. The study was started in February, 2013 and completed by March, 2014. The cases were selected from General Outpatient Department and Mobile Clinical Research Unit of Regional Research Institute of Unani medicine, Patna.

Inclusion Criteria

Patients of either sex in the age group of 18-65 years presenting joints pain (single/multiple joints) with or without anyone of the symptoms/signs such as tenderness, swelling and restriction of movement were included in the study.

Exclusion Criteria

1. Patients having disorders requiring long term treatment: Diabetes Mellitus, Hypertension etc

2. H/O Addictions (Alcohol, drugs)

3. Pregnant and lactating women

4. Known cases of hepatic, renal or cardiac ailments

117 patients of varied age groups, after necessary ethical clearance and after getting written consent from them, were enrolled for treatment. Out of which 97 (Male-29 and Female-68) completed the study. The duration of the study was two weeks. All the cases were subjected to the investigations like CBC, Hb%, TLC, DLC, ESR, LFT (Serum Bilirubin, SGOT, SGPT, Serum Alkaline Phosphates) and KFT (Urea, Createnine). The investigations were repeated after the therapy with study drugs to assess their safety.

For assessment of the efficacy of drugs, joints pain, tenderness, joints swelling and restriction of movement were scored on the following grading from 1-4.

Joints pain: (1= barely perceptible; 2=mild: can carry out daily activities with some trouble; 3=moderate: cannot carry out daily activities easily; 4=severe: bed ridden)

Tenderness: (1= on palpation, patient says it is tender, when touched; 2= on palpation, patient says it is tender and winces; 3= on palpation, patient says it is tender, winces and pull back; 4=patient doesn't allow palpation)

Joints Swelling: (0= no swelling/effusion; 1= barely perceptible; 2=mild; 3=moderate; 4= severe)

Restriction of Movement: (1=painful movement; 2=partial restricted movement; 3=partial movement, when the joints moved by the examiner; 4= complete restricted movement)

Safety of the drugs was assessed by clinical and laboratory parameters.

Outcome Measures

Outcome measure was assessed on the following parameters:

(a) 60-89% improvement in the signs and symptoms of disease i.e. joints pain, tenderness, joints swelling and restriction of movement = Relieved

(b) 30-59% improvement in the signs and symptoms of disease i.e. joints pain, tenderness, joints swelling and restriction of movement = Partially Relieved

(c) < 30% improvement in the signs and symptoms of disease i.e. Joints pain, tenderness, joints swelling and restriction of movement = Not Relieved

Drug Dosage and Mode of Administration

1. Two tablets (500 mg each) of Habb-e-Suranjan were given thrice a day after meals or with milk for two weeks. Each tablet contained the powder of three herbs, Elwa/Sibr (*Aloe barbadensis*), Halela (*Terminalia chebula*), Suranjan (*Colchicum luteum*) in equal proportion (Kabeeruddin, 1977-1978)
2. Raughan–e-Suranjan (*Colchicum luteum*) - The patients were advised to apply lukewarm oil locally on affected joints in the morning and evening twice daily for two weeks (Anonymous, 2006).

Post Treatment Observation

The follow-up of all the cases was carried out at an interval of 7 days up to 14 days on the basis of clinical history and physical examinations. The investigations were repeated after the treatment. Statistical analysis was restricted to only those patients who completed the full duration of study and followed the protocol. Student's Paired t test was used to analyze the data. The confidence level was set to be $p<0.001$ for significance.

Safety Assessment

Safety of the drugs were assessed on the follow-ups by the complaints of the patients through biochemical investigations (LFT, KFT and Blood Glucose) and pathological investigations (CBC and Urine examination: Routine & Microscopic) done at baseline and end of the study.

Results

Habb-e-Suranjan and Raughan-e-Suranjan were used to treat joints pain in this study. For this 29 (29.9%) male and 68 (70.1%) females were registered which indicates more prevalence of disease among females. The highest incidence of disease was observed in the age group of 18-30 years i.e. total of 30 cases (30.93%), whereas 24(24.74%) cases were in the age group of 31-40 years. Only 2(2.06%) cases were above 60 years of age suggesting that younger generation is more prone to develop pain earlier in life due to their lifestyle changes. The highest number of patients treated were from phlegmatic temperament (Balghami Mizaj) i.e., 63(64.95%). (Table 3). This observation was in accordance with the etiology of joints pain described in Unani classical texts and it shows that the persons of balghami Mizaj are more prone to develop joints pain.

After completion of 14 days of treatment, there was a significant ($p< 0.001$) improvement in all the four parameters of disease (Table 1). Thus, the outcome of the treatment i.e. effectiveness of drug was found to be 39.45% in joints pain; 35.02% tenderness, 44.68% swelling and 22.52% restriction of movement. All the investigations done at the baseline and after completion of the study, i.e., CBC, Hb%, TLC, DLC, ESR and LFT (Serum Bilirubin, SGOT and SGPT, Serum

Alkaline Phosphates) and KFT (Urea and Createnine) to assess the safety of the drugs were found within the range and there was no significant difference in any of the above parameter readings after the use of the drugs.

Table 1: Effect of Drug on Clinical Parameters

Sr. No.	Clinical parameter	Mean ± S.E.M		Efficacy (%)
		Before treatment	After treatment	
1	Joints pain	2.64 ± 0.05	1.6 ± 0.05	39.45
2	Tenderness	2.24 ± 0.06	1.45 ± 0.05	35.02
3	Swelling	1.94 ± 0.07	1.07 ± 0.08	44.68
4	Restriction of movement	1.14 ± 0.07	0.89 ± 0.05	22.52

Students pair t test applied, SEM±SD at p<0.001

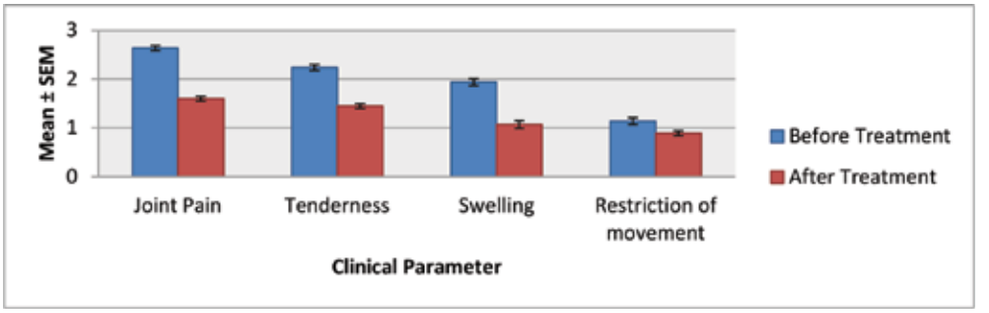

Fig. 1: Effect of Drugs on Clinical Parameters

Table 2: Outcome of the Treatment

S. No.	Outcome	No of patients
1.	Relieved	5.15%
2.	Partially Relieved	63.92%
3.	Not Relieved	30.93%

Table 3: Response in Relation to the Temperament of the Patients and the Treatment Outcome

Temperament	No. of cases	%	Relived (60-89%)	Partially relieved (30-59%)	Not relieved (<30%)
Damvi (sanguine)	17	17.53	1	9	7
Balgami (phlegmatic)	63	64.95	2	44	17
Safravi (bilous)	16	16.49	2	8	6
Saudavi (melancholic)	1	1.03	-	1	-
Total no of patients	97		5	62	30
Percentage/ GTR	100	-	5.15%	63.92%	30.93%

Discussion

Results clearly indicate that Habb-e- Suranjan and Raughan Suranjan have promising result in Joints Pain. It was found that the study drugs are more effective in less chronic cases as compared to more chronic cases. Data reveal that Joints Pain is higher among women, the non-vegetarian, people belonging to lower and middle income groups and among those residing in slum and congested areas. This finding is in agreement with the report of national health survey (Anonymous, 2008) which states that women are at higher risk of developing this disease. Pain is reported more in younger age group as compared to older age group which is similar to the finding observed in a study by Tanwir *et al.*, (2014). The shifting trend of pain towards younger age group could be that the sedentary lifestyle followed by them and their long working hours on computers.

Both Habb-e-Suranjan and Raughan Suranjan have Suranjan as main ingredient where active principle is Colchicine. Colchicine is approved by USFDA for the treatment of gout and familial Mediterranean fever (Ishtiyaque *et al.*, 2014). Suranjan i.e. *Colchicum lutem* is found to possess anti-inflammatory and anti-granuloma (Nair *et al.*, 2012), anti-rheumatic (Jawed *et al.*, 2005) and disease modifying property (Nair *et al.*, 2011). Raughan Suranjan contains Raughan Zaitoon as the other ingredient which is reported to have anti-inflammatory effect (Fezai *et al.*, 2013).

Modern analgesics reduce the pain and inflammation but on long duration they cause severe side effects. Apart from this after continuous uses they tend to develop tolerance and then dose needs to be increased to marked level which would produce more harm. Contrary to this the study drugs showed no side effects or adverse effects during the treatment period. Further, follow-up of the cases showed good recovery and fine improvement in carrying out their daily activities. The patients were fully satisfied and had the sense of well being after treatment.

Conclusion

It can be concluded that Habb-e-Suranjan in combination with Raughan Suranjan possesses anti- inflammatory and analgesic property as described by Unani physicians (Ibn Baitar, 1291H; Abu quareshi, 1974) and can be a better option for the patients of arthritis.

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सारांश

वजा-उल-मफ़ासिल (जोड़ों में दर्द) में हबीब-ए-सुरंजान और रोग़न-ए-सुरंजान के यूनानी भेषजकोशीय मिश्रणों की सुरक्षा और एंटी-आर्थ्राइटिक प्रभाव के रूप में प्रभावकारिता का नैदानिक अध्ययन

[1]मोहम्मद इश्तियाक़ आलम, [2]तसलीम अहमद, [1]मोहम्मद वसीम अहमद, [1]आयशा परवीन, [1]हशमत इमाम, [3]निग़हत अंजुम और [3]नाहीद परवीन

हब्ब–ए–सुरंजान और रोग़न–ए–सुरंजान के यूनानी भेषजकोशीय मिश्रित यौगिक के वैधीकरण हेतु जोड़ो के दर्द के उपचार में नैदानिक अध्ययन किये गए जो इसकी सुरक्षा और प्रभावकारिता के लिए है। इसे जोड़ों के दर्द में एनाल्जेसिक और एंटी–इन्फ्लैमेटॉरी प्रभाव के लिए यूनानी मिश्रणों के रूप में जाना जाता है। इस अध्ययन के लिए, जोड़ों के दर्द की शिकायत के आधार पर, संस्थान के सामान्य बहिरंग रोगी विभाग और चल नैदानिक अनुसंधान एकक से संस्थान नीति समिति, क्षेत्रीय यूनानी चिकित्सा अनुसंधान संस्थान, पटना द्वारा अनुमोदित प्रोटोकॉल के अंतर्गत 117 रोगियों का चयन किया गया जिसमें मात्र 97 रोगियों ने उपचार पूरा किया। यह उपचार 14 दिनों के लिए दिया गया और उपचार का सांतवें और चौंदवें दिन नैदानिक मूल्यांकन किया गया। चौदवें दिन की समाप्ति पर व्यक्तिगत मापदण्डों की तीव्रता जैसे जोड़ों के दर्द, सूजन, दाबवेदना और गति में रुकावट ने बेसलाइन की तुलना में ($p<0.001$) संख्यिकीय रूप से एक सुधार दिखा। अध्ययन के अन्त में एक विस्तृत मूल्यांकन (नैदानिक और प्रयोगशाला) किया गया। परिणामों से पता चला कि 97 मामलों में से 5 (5.15%) ने बहुत अच्छी प्रतिक्रिया (60-89% राहत तक), 62(63.92%) ने अच्छी प्रतिक्रिया (30-59% आंशिक राहत तक) और 30(30.93%) ने कोई प्रतिक्रिया (<30%) नहीं दी। प्रयोगशाला की जांच से यह भी पता चला कि उपयोग की जाने वाली औषधियां न तो हेपेटोटॉक्सिक थीं और न ही नेफ्रोटॉक्सिक। इससे यह निष्कर्ष निकाला जा सकता है कि रोग़न–ए–सुरंजान के साथ हब्ब–ए–सुरंजान एंटी–इन्फ्लैमेटॉरी और एनाल्जेसिक प्रभाव रखती है और गठिया के रोगियों के लिए एक बेहतर विकल्प हो सकती है।

शब्दकुंजी – गठिया, *बलग़म*, उत्पादक कारक, जोड़ों का दर्द, मिज़ाज।

Clinical Evaluation of Unani Pharmacopoeial Formulation Sharbat Toot Siyah in Waram-i- Halaq (Pharyngitis)

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Abstract

Waram-i-Halaq is synonymously known as Pharyngitis. It is defined as the inflammation of Ghisha-e-mukhati (mucous membrane) of Halaq (Pharynx). According to the 2000 National Ambulatory Medical Care survey, the acute pharyngitis accounts for 1.1 percent of visits to the primary care settings and ranked in the top 20 reported primary diagnoses. There is a general perception that Unani treatment provides relief only in chronic diseases and has nothing to offer relief in acute diseases as compared to allopathic treatment. However, this is absolutely incorrect and there are certain Unani formulations which can provide instant symptomatic relief in acute diseases. Keeping this in view, the drug "*Sharbat Toot Siyah*" was selected for its clinical validation in *Waram-i-Halaq* (Pharyngitis).

Keywords: Humours, Inflammation, *Sharbat Toot Siyah,* Throat, Waram-i-Halaq

Introduction

Waram-i-Halaq is mentioned in classical Unani literature as "Pharyngitis". It is inflammation of *Ghisha e mukhati* (mucous membrane) of *Halaq* (Pharynx) (Kabeeruddin, 1956; Saunders, 2002). According to Unani system of medicine, *Waram-i-Halaq* (Pharyngitis) can be of four types on the basis of *Akhlat* (Humours): *Damwi, Sfrawi, Balghami* and *Sawdawi*. *Waram-i-Halaq Damwi* (Sanguneous Pharyngitis) is characterized by *Imtilaa-i-Uruq* (congestion of vein), *Shiddai-i-Zarban* (strong pulse) and flushing of face. There will be *Karb* (restlessness) and more *Hararat* (heat) in *Waram-i-Halaq Safrawi* (Bilious Pharyngitis). In *Waram-i-Halaq Balghami* (Phlegmatic Pharyngits), there will be the *Waram* (inflammation) and the *Istirkha* (paralysis) in the tongue and the taste of the tongue will be salty and spitting may be increased. The prevalence of *Waram-i-Halaq Sawdawi* (Melancholic Pharyngitis) is very rare (Rabban, 1994; Rhazi, 1996).

On the basis of severity of the conditions, there are two types of *Waram-i-Halaq* (Pharyngitis) as described below:

(i) ***Waram-i-Halaq Had* (Acute Pharyngitis):** It is mainly caused by *Nazla-o-Zukam* (Common Cold), *Waram al-Lawzatyn Raji* (recurrent tonsillitis), *Humma-i-Surkh* (scarlet fever), dusty atmosphere, entry of Jism Gharim (Foreign body) in the throat and *Tasammum Dam* (toxaemia) (Kabeeruddin, 1956). Clinical features of *Waram-i-Halaq Had* (Acute Pharyngitis) include *Humama Bul um* (Pharyngeal Erythema), *Suda* (headache), *Usr al-Bala* (Dysphagia), pain in throat, *Buhha al-Sawt* (Hoarseness of voice), Rhinorrhoea and fever with mild rigors (Davidson, 2010; Kabeeruddin, 1956; Khan, 1987; Kumar, *et al.*2004).

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(ii) ***Waram-i-Halaq Muzmin* (Chronic Pharyngitis):** It is caused by constant use of spicy food, chewing tobacco, alcohol, shouting and the people who use the throat beyond the limits like singing etc. *Sil* (Phthisis), *Niqris* (Gout), *Su al-hadm* (Dyspepsia) and *Hurqa al-Mi 'da* (Hyperacidity) can also lead to chronic Pharyngitis. But mostly chronic Pharyngitis is the later stage of the acute Pharyngitis. In *Waram-i-Halaq Muzmin* (Chronic Pharyngitis) *Surkhi* (redness) and *Tarashshuh* (dripping of fluids) in the pharynx will be lesser in comparison to acute Pharyngitis. Absence of fever, sputum comes after efforts, small round and superficial ulcers if caused by II stage of *Athsak* (Syphillis) (Kabeeruddin, 1956).

The objective of the study was to assess the safety and efficacy of Unani Pharmacopoeial formulation *Sharbat Toot Siyah* in case of *Waram-i-Halaq* (Pharyngitis).

Material and Methods

The study was designed as an open clinical trial to evaluate the efficacy of unani pharmacopoeial formulation on twenty nine patients of Waram-i-Halaq. The patients were treated for a period of one week with regular follow-up on 3rd day and 7th day of treatment at Regional Research Centre (Unani), Silchar. The duration of the protocol therapy was one week.

Treatment Details

Table 1: Study Drug Sharbat Toot Siyah

S. No.	Study Drug	Form	Rout of Administration	Doses & Frequency
1.	***Sharbat Toot Siyah***	Liquid	Oral	20ml Twice Daily

Table 2: Composition of Sharbat Toot Siyah

S. No.	Unani Name	Scientific Name	Weight
1.	Aab-e-Toot Siyah	*Morusnigra Linn.*	1 Litre
2.	Qand Safaid	*Honey or sugar*	1.5 kg

Dosage and Administration

All the patients were selected as per inclusion and exclusion criteria of Waram-i-Halaq (pharyngitis). Unani Pharmacopoeial Drug Sharbat Toot Siyah (Liquid) was given orally. No concomitant treatment was followed.

Place of Study

The present open level study was carried out after obtaining the approval of Institutional Ethics Committee of Regional Research Centre (Unani), Silchar, Assam in the patients attending the General Outpatient Department of the centre.

Selection of Patients

The patients were selected on the basis of inclusion and exclusion criteria as given below:

Inclusion criteria

1. Patients of either sex in the age group of 18-60 years.
2. Presence of all the following signs and symptoms of *Waram-i-Halaq* (Pharyngitis):
    1. *Buhha al-Sawt* (Hoarseness of Voice)
    2. *Surfa Yubsiyya* (Dry Cough)
    3. *Usr al-Bala* (Dysphagia)
    4. *Humama Bul um* (Pharyngeal Erythema)
    5. *Waja-e-halaq* (Pain in throat)
    6. *Khushuna al-Halaq* (Irritation in throat)

    (Davidson, 2010; Kabeeruddin, 1956; Khan, 1987; Martin, 2008).

Exclusion Criteria

Presence of any one of the following:

1. Patients with all four classical symptoms of Group A streptococcal pharyngitis:
    - Pharyngeal or Tonsillar exudates
    - Swollen anterior cervical nodes
    - History of fever more than 380C
    - Absence of cough.
2. Known cases of Renal/Hepatic/Cardiac ailments/Diabetes mellitus
3. Pregnant and lactating women
4. Oral candidiasis
5. Epiglottitis,
6. Herpes simplex
7. Mononucleosis
8. Gastro esophageal reflux

Safety Assessment

The safety was monitored on the basis of the laboratory investigations such as CBC (Hb%, TLC, DLC, ESR), Absolute Eosinophil Count (AEC), LFT (S. Bilirubin, SGOT, SGPT, S.Alkanine Phosphatase), KFT (S. Urea, S. Creatinine, Uric Acid)

and Urine R/M done at the baseline and end of the study. Blood Glucose (Fasting) was carried out only at the baseline.

The safety of the drug was also assessed clinically on the basis of adverse events as reported by the patients or observed clinically on the follow up. No adverse effect of the Unani Pharmacopoeial drug Sharbat Toot Siyah was observed during the course of the study and at the end of the study. The drug was found safe in the patients of Waram-i-Halaq.

Efficacy Assessment

The patients were assessed clinically on 3rd and 7th day of the treatment. The efficacy of the Unani Pharmacopoeial drug Sharbat Toot Siyah was evaluated on the basis of reduction in the sign and symptoms as mentioned in the Case Record Form. The severity of symptoms was recorded in numbers as per the Visual Analogue Scale (VAS).

Statistical Analysis

Clinical subjective parameters, pathological and biochemical parameters were statistically analyzed by using student's't' test and paired't' test. The results were expressed as Mean ± SEM. $P<0.05$ has been considered as statistically significant and $P<0.001$ considered as highly significant.

Results and Discussion

In the present study, the maximum number of patients belonged to the age group of 31-40 years (34.78%). It was also found that maximum number of patients 14 (61.00%) were male and 9 (39.00%) patients female (Tables 3 and 4).

Table 3: Age-wise Distribution of the Cases

S. No.	Age group (in years	No. of cases (N=29)	Percentage
1	18-30	4	17.39
2	31-40	8	34.78
3	41-50	6	26.09
4	51-60	5	21.74
Total		**23**	**100**

Table 4: Sex-wise Distribution of the Cases

Sl. No.	Sex	No. of Case (N=23)	Percentage
1	Male	14	61%
2	Female	9	39%
Total		**23**	**100**

In the study, maximum number of patients observed possess Damwi mizaj (52.17%), followed by Balghami (21.73%) and Safravi (21.73%). One patient of Saudavi mizaj (4.34%) was enrolled in the study (Table 5).

Table 5: Distribution of the Cases According to the Mizaj (Temperament)

Sl. No.	Temperament (Mizaj)	No. of Cases	Percentage (%)
1	Sanguine (Damwi)	12	52.17
2	Phlegmatic (Balghami)	5	21.73
3	Bilious (Safravi)	5	21.73
4	Melancholic (Saudavi)	1	4.34
Total		**23**	**100**

In the present study, efficacy of Sharbat Toot Siyah was evaluated over a period of seven days on the basis of symptom-wise improvement. The mean scores of hoarseness of voice, dry cough, dysphagia, pharyngeal erythema, pain in throat and irritation in throat before treatment were 5.74, 5.22, 4.52, 3.78, 4.61 and 4.35 respectively while after treatment they were 1.61, 1.57, 0.7, 0.43, 0.65 and 0.91 respectively. So the improvement in hoarseness of voice, dry cough, dysphagia, pharyngeal erythema, pain in throat and irritation in throat was 71.95%, 69.92%, 84.51%, 88.62%, 85.90% and 79.08% respectively which is statistically significant (Table 6 and Figure 1).

Table 6: Effect of Unani Pharmacopoeial Formulation, *Sharbat Toot Siyah* on Different Symptoms Associated with *Waram-i-Halaq* (Pharyngitis)

Sl. No.	Signs and Symptoms	Before Treatment	1st Follow Up	After Treatment	Improvement (%)
		Mean±SD	Mean±SD	Mean±SD	
1	Buha-al-Sawt (Hoarseness of Voice)	5.74±0.37	3.74±0.25	1.61±0.26*	71.95 %
2	Surfa Yubsiyya (Dry Cough)	5.22±0.37	3.52±0.32	1.57±0.16*	69.92 %
3	Usr-al-Bal (Dysphagia)	4.52±0.31	2.43±0.25	0.7±0.15*	84.51 %
4	Humama-Bull-um (Pharyngeal Erythema)	3.78±0.27	2.22±0.26	0.43±0.14*	88.62 %
5	Waja-e-halaq (Pain in throat)	4.61±0.39	2.61±0.35	0.65±0.20*	85.90 %
6	Khushuna-al-Halaq (Irritation in throat)	4.35±0.34	2.43±0.29	0.91±0.23*	79.08 %

* The mean values are significantly different (P<0.05)

Mean Values of Clinical Paramenters at Baseline, 1st Follow-up and after Treatment

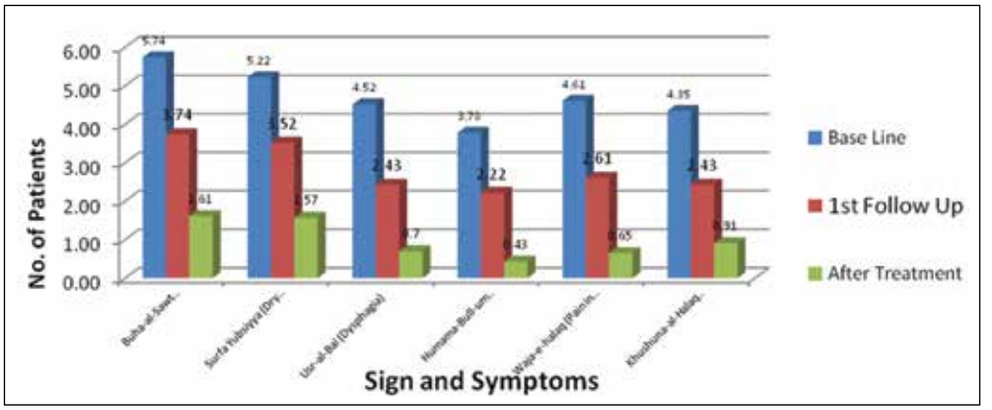

Fig. 1: Effect of Unani pharmacopoeial formulation, Sharbat Toot Siyah on different symptoms associated with Waram-i-Halaq (Pharyngitis).

In the present study, 86.95% of patients got relieved, 8.69% partially relieved and 4.34% no relief (Table 7 and Figure 2). No one got relieved completely

Table 7: General Therapeutic Response

Sl. No.		Cured (90-100)%	Relieved (60-89)%	Partially Relieved (30-59)%	Not Relieved (0-30)%	Total
1	No. of Cases	0	20	2	1	23
2	Percentage (%)	0%	86.95%	8.69%	4.34%	100%

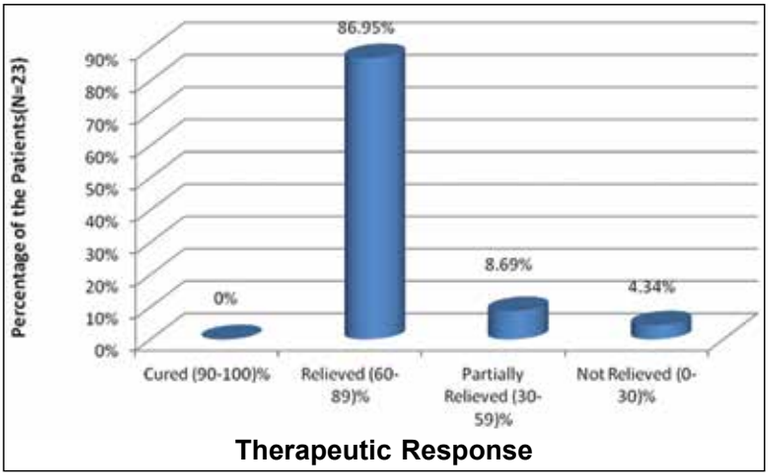

Fig. 2: General therapeutic response

There was no any change in TLC, DLC, Lymphocytes and Monocytes between the baseline and after the treatment. Results suggest that the Unani classical drug may be useful as a potent drug for the treatment of Waram-i-Halaq. ESR was significantly reduced after treatment with Unani classical drug ($P<0.05$). Results are shown in Tables 8 and 9.

Table 8: Hb, ESR and TLC at the Baseline and After Treatment

Sl. No.	Investigation		Base Line	After Treatment
			Mean±S.E.M	Mean±S.E.M
1	Hemoglobin (Hb) (gm%)		11.53±0.52	12.18±0.44*
2	Erythrocyte Sedimentation Rate (ESR) (mm/hr)	1st Hour	28.39±4.57	19.43±3.50**
3	Total Leucocyte Count (TLC) (cmm)		7252.17±195.42	7363.18±108.84*

* The mean values are not significantly different (P>0.05)

** The mean values are significantly different (P<0.05)

Table 9: DLC at the Baseline and After Treatment

Sl. No.	Investigation	Base Line	After Treatment
		Mean±S.E.M	Mean±S.E.M
1	Neutrophils (%)	57.96±1.66	66.43±1.05*
2	Lymphocytes (%)	37.57±1.51	36.35±1.03*
3	Eosinophils (%)	3.04±0.24	2.13±0.13**
4	Monocytes (%)	1.39±0.10	1.35±0.14*

* The mean values are not significantly different (P>0.05)

** The mean values are significantly different (P<0.05)

Conclusion

On the basis of the above observations, it can be concluded that Unani pharmacopoeial formulation Sharbat Toot Siyah is effective in the treatment of *Waram-i-Halaq* (Pharyngitis). Moreover, the drug is cheaper, easily available and well tolerated by the patients without having any side effect.

Acknowledgement

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सारांश

वरम-ए-हलक़ (ग्रसनी शोथ) में यूनानी भेषजकोशीय मिश्रण शर्बत तूत सियाह का नैदानिक मूल्यांकन

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वरम–ए–हलक़ को पर्यायवाची रूप से ग्रसनीशोथ के रूप में जाना जाता है। इसे हलक़ (ग्रसनी) के ग़िशा–ए–मुख़ाती (श्लेष्मा झिल्ली) की सूजन के रूप में परिभाषित किया जाता है। नेशनल एम्बुलेटरी मेडिकल केयर सर्वेक्षण–2000 के अनुसार प्राथमिक स्वास्थ्य सेवाओं में आने वाले रोगियों में 1.1 प्रतिशत रोगी तीव्र ग्रसनीशोथ के होते हैं और प्राथमिक निदान की जाने वाली सर्वोपरि 20 रोगों में ये रोग सम्मिलित हैं। एक आम धारणा है कि यूनानी उपचार केवल दीर्घकालीन रोगों में राहत देता है और एलोपैथिक उपचार की तुलना में तीव्र रोगों में राहत के लिए कुछ सुधार नहीं रखता। हालांकि यह बिल्कुल गलत है और कुछ यूनानी मिश्रण हैं जो तीव्र रोगों में तुंरत रोगनिवारक प्रभाव दर्शाते हैं। इसे ध्यान में रखते हुए औषधि "शर्बत तूत सियाह" को वरम–ए–हलक़ (ग्रसनी शोथ) में नैदानिक वैधीकरण के लिए चुना गया।

शब्दकुंजीः स्वभाव, सूजन, शर्बत तूत सियाह, गला और वरम–ए–हलक़।

Why Did the Theory of *Akhlāṭ* Put Forward?

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Abstract

Unani system of medicine deals with seven basic principles. These principles describe the basic knowledge required to understand the physiological system of human body. *Akhlāṭ* (Humour) is one of those seven principles. The concept of *Akhlāṭ* has occupied a central place in *unani tibb*. The fundamentals of humoral medical theory are found in the works of Hippocrates (c. 460–c. 370 BC) such as *The Nature of Man* where the four humours are named as blood, phlegm, yellow bile and black bile. It is always the task of medicine to trace the true causes as well as probable course of a disease so we can learn how to prevent the disease, if it is not possible, then how to control and cure it. Since ancient times various theories had been put forth regarding the causation of disease. One may ask, why did theory of *akhlāṭ* come? How do we know what is wrong within our bodies? We may be aware of symptoms like pains, nausea, vomiting etc. We are also aware of some of our bodily fluids like saliva, sweat, urine, menses or semen etc. In the past, with no way of seeing into the body, an entirely different approach grew up. It may be possible to have a comprehensive picture from the visible fluids of the body, seen as clues to the invisible fluids or internal disturbances. What were these fluids? This paper attempts to address various issues concering the theory of *Akhlāṭ*.

Keywords: *Akhlāṭ,* Causes of disease, Humoral theory, Treatment.

Introduction

Since ancient times various theories had been put forth regarding the causation of disease. In each era, the theories and concepts proposed by the earlier physicians and philosophers have been criticized by later physicians and philosophers and new ideas were proposed refuting the old one. They had given their own logical explanation and reason to support their theory and rejecting the earlier one. When Hippocrate proposed the theory of *akhlāṭ*, he also criticized and commented on the previous one. He gives justification to his theory by observation as well as by logical explanation. The Hippocratic humoral theory was later developed by Galen and Arab philosophers. They not only defined and classified these *akhlāṭ* into normal and abnormal but also systematized the theory on the basis of their keen observation. Though, it is quite difficult to state the reason for why the theory of *akhlāṭ* has been put forth. Hippocrates himself did not mention the reason for this theory specifically. Inferences can be drawn from Hippocratic

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corpus regarding this theory. He has criticized the earlier medical theory in his treatises *On Ancient Medicine* and *On the Nature of man*.

The word is nothing but a chain of cause and effect. Everything is bound by a cause for its existence. The world of medicine is no exception to this universal principle. Every disease has an underlying cause and the treatment depends upon identification and elimination of cause. In every medical system some factors are regarded as instrumental to create diseases. In Unani System of Medicine (USM) *mizāj* and *akhlāṭ* are of utmost importance as a cause of health and diseases.

According to USM, diseases are of two kinds; simple and compound. Simple disease belongs to either the category of the diseases of *Sū-ʾi-mizāj* or the category of the diseases of structure. Consequently, there are three groups of diseases; diseases which follow *Sū-ʾi-mizāj,* diseases which follow the disorders of structure and diseases which follow the loss of continuity. *Mizāj* is of two types; *motadil and ghayr motadil. Mizāj ghayr motadil* is also known as Sū-ʾi-mizāj which is due to deviation to a certain degree from moderation and the organ is unable to perform its functions normally. The *Sū-ʾi-mizāj* is either simple or compound. In simple *Sū-ʾi-mizāj,* the deviation is only in relation to one contrary quality i.e., hot or cold or moist or dry. In compound *Sū-ʾi-mizāj* the deviation is in relation to two contrary qualities at the same time e.g. hot and moist and hot and dry. Each of the above mentioned *Sū-ʾi-mizāj* must exist with or without matter (*madda*). When it is associated to matter then it is called *Sū-ʾi-mizāj māddi,* (Ibn Sina, YNM, Jurjani, 2010). On the basis of *Sū-ʾi-mizāj māddi,* most of the pathological condition (where the disturbance is in *akhlāṭ* or body fluids) is described, diagnosed and their line of treatment and selection of medicine are decided accordingly.

Why Did the Theory of Akhlāṭ Put Forward?

Several ideas in the theory of *akhlāṭ* have their origin in earlier Greek philosophy. The structural foundations for the humoral theory were abstracted from the works of the ancient Greek philosophers like Anaximander, Pythagoras and Alcmaeon. If we look at the works of Hippocratic treatises, we can trace various concepts and theories that preceded Hippocrates which form the basis for the theory of *akhlāṭ* such as principles of Pythagorean philosophy concerning harmony and balance, Empedocles theory of primary elements of the universe, Alcmaeon theory of *isonomia* of qualities like hot, cold, dry, moist, sweet and bitter to one's health etc. (Stelmack, Stalikas, 1991). It is believed that Alcmaeon was

the first to advance a rational account of disease causation in the fifth century BC. Alcmaeon's state of health is clearly defined by notions of balance, equality and blending of various opposing qualities (e.g. moist and dry, hot and cold) (Jonston, 2006). According to Alcmaeon the essential requirement for health is the *isonomia* of qualities i.e. moistness, dryness, coldness, bitterness, sweetness and the remainder, whereas what brings about disease is preponderance in them which he termed *monacrhi* (Jonston 2006).

While inquiring into the development of theory of *akhlāṭ,* one can get help from the Hippocratic treatise On *Ancient Medicine*. The Hippocratic treatise *On Ancient Medicine, On the Nature of Man and Galen's On the Natural Faculty* are the key texts to understand the basis for theory of *akhlāṭ*. Hippocrates holds over the observation and reasoning in the conceptualization of medicine. The pre Socratic philosopher employed a *priori method* and by means of pure hypothesis they came to their conclusion by deduction. Now, as a matter of fact, it is quite certain that as far as science is concerned this manner of reasoning is quite opposite to the general rule that every scientific theory should be based on the expression of facts and verified. Hippocrates revealed a method quite opposite, namely; the experimental method proceeding by induction based on the facts observed and terminating in general theories only by a posteriori reasoning. The analysis of his treatises *On Ancient Medicine* and *On the Nature of Man* shows this plainly in his work, Hippocrates raises his voice against physicians and philosophers who consider that life, disease and death come from a single cause. He opposes those who endeavor to explain facts by a single hypothesis. Hippocrates starts the chapter in *On Ancient Medicine* by attacking on pre-Socratic philosophers who attempted to systematize medicine by reducing it to the interaction of one or more of the opposite hot, cold, wet, and dry factors which had played an important role in much of early Greek natural philosophy (Shiefsky, 2005).

There are several factors which made Hippocrates to raise his voice against earlier theories of health and disease and to propose the humoral theory. The first one is observation of different bodily fluids as evident in various diseased conditions which are dissimilar in their appearance and qualities like moistness and dryness. The second one according to Hippocrates is that generation cannot be possible from a single substance. He asks the question that how could one thing generate another unless it copulated or combine with some other. The third reason given by Hippocrates is effect of some drug on body fluids (*akhlāṭ*). He mentioned that if a man is given a medicine which brings up phlegm or bile, he

will vomit phlegm or bile respectively i.e the vomit will be full of either phlegm or bile. Similarly, black bile can be eliminated by administrating a medicine which brings it up. The fourth one is observation of individuals that are affected by same diet in healthy and diseased condition as well as the effect of same diet on different individuals. These are the various factors which forced Hippocrates to propose the humoral theory (Jones, 1931 Coxe, 1846). Observing the reactions of different subjects to the same foods it draws distinctions between different constitutions which is the first step towards acquiring the ability to prescribe a beneficial diet to an individual or to a patient. Hippocrates gives a series of examples drawn from medical experience to support his humoral theory e.g. sick people who are too weak to digest barley gruels may suffer from serious effects after taking them. The author gives further evidence to support this by giving the example of imaginary situation of two peoples, one who is sick and eats some bread or meat, and another who is healthy and eats raw food such as raw barley or meat, the latter will suffer no less than the former. He mentioned that not only the quantity or quality of the food that is responsible for its harmful effects but also the fact that it is taken at the wrong time (Shiefsky, 2005). In Para 12 he begins by setting out two assumptions against the previous theory: first, that the cause of any disease is something hot, cold, wet or dry, and second, that the cure is the opposite of the cause. He then goes on to describe a situation in which a person with a relatively weak constitution ingests a diet of raw food e.g. raw wheat, raw meat etc. It is clear that such a person will experience some harmful effects as the raw food is not proper for him. He then asks what will be the treatment in such a condition. On the basis of previous assumptions, the cure for such a person must be something hot, cold, wet, or dry, since one of these factors is the cause of disease. But, he states that the obvious remedy in this condition is to substitute cooked food for raw and to give the person bread instead of raw wheat, boiled or cooked meat instead of raw meat. This change of diet definitely helps the person because the raw food harms the person and cooked food restores him to health (Shiefsky, 2005). It is well known that *akhlāṭ* are produced in the liver from the food ingested and the quality of *akhlāṭ* is very much depends upon the quality of the food. Hence by observing the effect of different food on an individual, Hippocrates concluded that not only the *dynamies* but also the food and constitution are responsible for diseases. It is here he insisted that the hot, cold, moist and dry are not substances; they are only *"dynamies"*, and, what is more, powers of secondary importance (Jones, 1923). Hippocrates continues to present the series of examples in support of

the claim that hot and cold are relatively of secondary importance as causes of disease. He takes it as a matter of common knowledge that a diet of raw foods would cause harmful effects and that the right remedy is to change back from raw to cooked food. In Para 14 there is a clear statement regarding the theory of *akhlāṭ*. According to the theory presented in section 14 of *'Ancient Medicine'*, the human body contains a mixture of a varied number of fluid substances or humors, each one of which is characterized by a particular smell or taste (sweet, bitter etc.) and each one of which has its own *dynamies* or capacity to cause a specific effect. When these *akhlāṭ* are well mixed and blended, none of them is manifested and the person is healthy. But when one of them separates from the mixture and stands apart on its own, it becomes manifest and causes pain (Shiefsky, 2005). The number of *chymoi* (*akhlāṭ*) is left indefinite in this section. In his treatise "On the Nature of Man" Hippocrates mentioned that *akhlāṭ* are four in number. According to Hippocrates, it is their harmony that produces a healthy body and their imbalances lead to disease (Jones, 1931).

Another reason for development of humoral theory apart from the reasons given by Hippocrates can be inferred from analysis of various Greco Arabic literature of medicine. As it is well known fact that human body is subjected to wear and tear due to movement and living processes and for this reason replenishment is unavoidable for sustenance of life. This replenishment is completed through nutrition. Digestion is a function by which the aliment is converted into the nutriment. No food can nourish until it is converted into a fluid analogous in composition to that part of the body in which it is assimilated. The conversion of the crude aliment into such a fluid is effected by a vital power peculiar to living thing. Nutrition is also common to plant. Plant can take up only liquid food through absorption. It never receives solid substance as aliment; it therefore needs no apparatus for the division, solution and fluidification of its food. But animals and human which live on vegetable and animal substance have to modify the food through digestion before it gets assimilated (Smith, 1851). Galen stated in his treatise 'On Natural Faculty' that (Arthur, YNM), Animal cannot naturally derive nourishment from any kind of food, and secondly, even in the case of those from which it can do so, it cannot do this at once. Therefore, by reason of this law, every animal needs several organs for altering the nutriment. For in order that the yellow may become red, and the red yellow, one simple process of alteration is required, but in order that the white may become black, and the black white, all the intermediate stages are needed. So also, a thing which is very soft cannot all

at once become very hard, nor vice versa; nor, similarly can anything which has a very bad smell suddenly become quite fragrant, nor again, can the converse happen. How could blood ever turn into bone, without having first become, as far as possible, thickened and white? And how could bread turn into blood without having gradually parted with its whiteness and gradually acquire redness?

From above passage two questions can be raised. How the food is transformed into incorporable substrate and how is it distributed to the other parts as alimentary canal is far away from peripheral organ. The idea of digestion is far from easy to follow. Apparently nutritive food is supposed to be converted into liquid form (*akhlāṭ*) and then to be carried to every part of the body, assimilating itself to bone, flesh and so on as it comes into contact with them. The aspect of nutrition which appeals most is the combination of unity and multiplicity which it exhibits. Food is one; yet it has the power of becoming many things. Similarly, the animal organism is one with many parts (organ) vitally connected with the whole. These organs differ from each other in *mizāj* and *qiwām*. Therefore, the nutriment for them should also be of different kinds. Unani philosophers considering these problems postulated the theory of *akhlāṭ,* which can be summarised as given below:

- Transformation of food into absorbable and incorporable chyle and chyme
- Distribution through blood vessels
- Incorporation into organs (badal ma yatahallal)

Besides the reason and argument in favour of the theory of *akhlāṭ* given by the ancient philosophers, another reason which can be concluded that the human body is consisted of three types of substances, Gaseous, liquid and solid. Liquid is intermediate in other two. i.e. in between gaseous and solid substances. Due to this the liquid part required only a step to convert into solid or gaseous. It can be easily converted into solid or gas as per need. But the Gaseous substance requires at least two stages to convert into solid, i.e. it first converts into liquid then into solid. Similarly, for the solid part which also requires two stages to convert into gaseous substance and also the transportation of solid substance to other part is not possible unless it is converted into liquid substance. In addition to this one more fluid has been described by Unani physicians. They called it *ruṭūbat gharīziya* (essential fluid) which maintains the integrity of organs. It is derived from the semen of parents (Ibn Sina, YNM). The essential fluid is lost gradually due to various desiccating factor like transition. The real need of *akhlāṭ* (*chymoi*)

is to conserve the essential fluid and to maintain the integrity of organ as long as possible through replenishment. Therefore *akhlāṭ* are the fluid substance of body which can be easily transported to other parts of the body and can provide replenishment.

Conclusion

Hippocratic humoral theory is one of the lasting contributions to the field of medicine. Ancient physicians created a novel system for explaining and curing disease and maintenance of health which is based upon the prevalent scientific and philosophical theories of their era. This system became known as the humoral theory of disease. Humoral theory adopted and incorporated the theories of ancient Greek philosophers in order to explain health and disease and also guidelines for cure. The humoural theory is based on direct and first-hand observation of natural phenomenon. Ancient Greco Arabic physicians including specially Hippocrates carefully observed the natural progression of disease in their patients and made inferences from these observations. The humoral pathogenesis of disease was the beginning of material causes of diseases. In short, mystical superstition has successfully been replaced by naturalistic theory. According to the theory of *akhlāṭ,* the cause of disease is the alteration in the quantity and quality of *akhlāṭ*. Variation in the quantity and quality of *akhlāṭ* is possible up to a certain limit from one individual to another at various stages of life and season of the year. Therefore, once it crosses a certain level the disease arises due to surplus or deficiency of any humour which disturbs the equilibrium.

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सारांश

अख़लात के सिद्धांत को आगे क्यों रखा गया?

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यूनानी चिकित्सा पद्धति सात मूल सिद्धांतों पर आधारित है। ये सिद्धांत मानव शारीरिक क्रिया को समझने के लिए आवश्यक मूल हैं। अख़लात (स्वभाव) उन सात सिद्धांतों में से एक है। यूनानी तिब्ब में अख़लात के सिद्धान्त का एक प्रमुख स्थान है। ह्यूमरल मेडिकल नियमों के मूल तत्व हिप्पोक्रेट्स (सी. 460 – सी. 370 ई. पू.) के कार्यों में पाए जाते हैं जैसे कि *दि नेचर ऑफ मैन* जहां चार ह्यूमर्स खून, बलग़म, सफरा और सौदा के रूप में नामित हैं। यह हमेशा चिकित्सा का कार्य होता है कि रोग का पता लगाए और साथ ही साथ एक रोग के उपचार हेतु संभावित कोर्स का भी पता लगाए ताकि हम सीख सकें कि कैसे रोग की रोकथाम करनी है। यदि यह संभव नहीं है तो इसे कैसे नियंत्रित और ठीक किया जा सकता है। प्राचीन काल से ही रोग के कारण ों के संबंध में विभिन्न सिद्धांत आगे रखे गए। कोई भी पूछ सकता है कि अख़लात का सिद्धांत क्यों आया? हमें कैसे पता चलेगा कि हमारे शरीर में क्या गलत है? हम दर्द, मतली, उल्टी आदि जैसे लक्षणों से अवगत हो सकते हैं। हम अपने कुछ शारीरिक तरल पदार्थों जैसे लार, पसीना, मूत्र, मासिक या वीर्य आदि के बारे में भी जानते हैं। भूतकाल में, शरीर में देखने का कोई तरीका नहीं था और पूर्णतः एक अलग दृष्टिकोण था। यह संभव हो सकता है कि शरीर के तरल पदार्थ के देखने से एक विस्तृत तस्वीर सामने आए जोकि आंतरिक तरल पदार्थ या विकृति की जानकारी दे सकते हैं। ये तरल पदार्थ क्या थे? यह पेपर अख़लात के सिद्धांत से संबंधित विभिन्न विषयों को हल करने का प्रयास है।

शब्दकुंजीः अख़लात, रोग के कारण, ह्यूमरल सिद्धांत, उपचार।

Pharmacological Action and Therapeutic Uses of *Tukhm-e-Kahu* (*Lactuca scariola* Linn.): A Review

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Abstract

Herbal origin of drugs has been playing an important role in the prevention and treatment of various diseases. Unani system of medicine has been popular since long and in the preset era it has become a centre of attraction for management of diseases due to its less associated side effects and cost effectiveness. Unani system is known for various effective drugs which are used for treatment of several disorders. One such drug is Tukhm-e -kahu (Lactuca scariola Linn.), belonging to the family Asteraceae. It is an important herbal medicine which has hypnotic, anaesthetic, hypoglycaemic, anti-dysenteric, sedative effects etc. It is recommended for various disorders like dribbling of urine, headache, insomnia, infectious fever, alopecia etc. Several pharmacological activities have been validated on scientific parameters which include sedative, hypoglycaemic, anti-inflammatory etc. Further, more potent antioxidant activity has also been reported, thus, making it as an important drug altogether. *Tukhm-e-Kahu* can potentially act as a strong traditional herbal drug due to its multiple pharmaceutical effects and is therefore generating interest among scholars in drug discovery and development of formulations. In the present review, an attempt has been made to cover the major pharmacological actions and therapeutic uses of *Tukhm-e-Kahu* as mentioned in the literature of Unani system of medicine as well as to cover the recent studies on the drug in human and animal models.

Keywords: Extracts, Herbal medicine, *Lactuca sativa* Linn., Test drug *Tukhm-e-kahu*

Introduction

The common name of Lettuce is derived from Latin word 'Lactus' (milk), because milky fluid flows, when stems broken or cut (Mur1983, Bunny 1992). *Tukhm-e-Kahu* are the seeds of *Lactuca scariola* Linn. and commonly known as "Wild Lettuce". In ancient Egypt period, Lettuce was first cultivated for the production of oil from its seed. Lactuca L. genus comprises 100 species, out of which 17 are European, 10 North American, 33 African and 40 Asian species (Ali *et al.* 2016). Although the composite is one of the largest families in the plant kingdom but includes relatively a few plants of economic and medicinal importance. *Lactuca sativa* is a common or garden variety which is cultivated in many parts of India as a cooking vegetable (Nadkarni 1954, Hayward 1967). Kahu plant and *Tukhm-e-Kahu* have been used for a long time and cultivated for more than 2000 years. Its medicinal properties were described by Hippocrates. The species were described by Theophrastus and Dioscorides. Galen gave the idea of its

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general use. Arabian Physicians have described it as an important drug (*Bazrul Khas*) in their books as Altabri in *"Firdausul Hikmat"*, Razi in *"Alhawi"*, Ibn-e-Sina in *"Alqanoon"* and Majoosi in *"Kamilal Sanaat"* (Sina YNM, Dioscoridies 1993).

Therefore, *Tukhm-e-Kahu* (*Lactuca scariola* Linn.) has occupied a special place for its medicinal value since centuries in the Middle East and Southeast Asia. It has been traditionally used in the treatment of a number of ailments related to respiratory, gastro-intestinal, hepatic, renal, circular system and general overall well-being.

Scientific Classification of *Tukm-e-Kahu* (*Lactuca scariola* Linn.)

Kingdom	:	Plantae – Plants
Subkingdom	:	Tracheobionta – Vascular plants
Super-division	:	Spermatophyta – Seed plants
Division	:	Magnoliophyta – Flowering plants
Class	:	Magnoliopsida – Dicotyledons
Subclass	:	Asteridae
Order	:	Asterales
Family	:	Asteraceae – Aster family
Genus	:	Lactuca L. – lettuce P
Species	:	Lactuca scariola Linn. (USD; Lactuca scariola)
Vernaculars		
Urdu	:	Tukhm-e-Kahu
Arabic	:	Bazrul khas
Hindi	:	Kahu kr binj
English	:	Prickly lettuce, Wild lettuce, Lactuca scariola seed
Persian	:	Tukhm-e-kahu
Greek	:	Thridox
Bengali	:	Kahu, Salad Beej
Danish	:	Laktuk
Dutch	:	Latuw
Hungarian	:	Kertisalata
Italian	:	Guado, Lattuga
Malta	:	Prickly lettuce, Lettuce, Lattuga, Hass, Salvagga
Punjabi	:	Kahu
Roumanian	:	Laptuc

Russian	:	Laktuk
Sind	:	Kahu
Spanish	:	Lactugalarga, Lechugaromana
Swedish	:	Laktuk
Tamil	:	Sallattu virai
Telugu	:	Kavu vittula

(Nadkarni 1954, Baitar 1985, Anonymous 1962, Agarwal 1986, Chopra and Nayer 1956, Kirtikar and Basu 1987, Perry 1895)

Morphology

Kahu (Lactuca scariola Linn.) basically has two varieties based on its occurrence (i) Bustaani (Baaghi). Lactuca sativa, “Garden lettuce” which is a cultivated variety; and (ii) Sahrai (Jungali), Lactuca scariola” wild Lettuce. Wild variety (Sahri) of *Lactuca scariola* has longer and thinner leaves than cultivated variety. The leaves are dark green and slightly bitter in taste. Cultivated variety could be further differentiated into two types. One is 1-1 ½ meter high, soft, smooth and sweetish stem with planate, wide leaves and white flowers along with small whitish seeds. Another is also a harvested variety which is again of two types. Amongst which, one is whitish green with smooth appearance as well as breakable and sweetish, violet colored leaves. Harvested Kahu is used as a vegetable (Salad). The latex is sometimes used as the substitute for opium which is not as potent as of Khash khash (Papaver somniferum) (Ghani 1996).

Habitat and Distribution

It is found as an erect glaucescent annual or biennial, leafy, 60-150 cm high. It is prickly plant found at the Western Himalaya from Marri to Kunawar, at an altitude of 6.000 to 11.000 feet. Also found in western Tibet, at altitudes of 9.000 to 12.000 feet and distributed to Siberia and westwards to the British islets and Canaries (Chopra and Nayer 1956, Kirtikar and Basu 1987, Dymock, Warden and Hoper 1890).

Description

Stem 3-10 cm. long, sparingly prickly bristly below, simple up to the inflorescence. Usually aculeate-setose below, Terete striate above stem leaves, capitula 8-15 mm long. On very short pedicles, in a cyme with spreading branches ligules pale yellow. Achenes 6-8 mm body elliptical setose at apex, 5-9 ribbed, sinuate beak as long as body. Leaves pinnatifide of lobed achenes light colored rarely sinuate, tending to turn edgewise into a vertical position. Flowers yellow achenes striate,

dark brown or grayish brown hispidulous near the top of the body. Seeds grey, oblong, 1.0 cm long and 1-2mm broad. Seeds are whitish, shiny, elongated and smaller in size. They are tasteless or have light bitter taste. According to some pharmacologists, the seeds are lighter and softer.

Parts Used

Different parts of *Tukhm-e-Kahu* used for medicinal purpose as per Unani literature are dried leaves, seeds oil and milky juice (Ghani 1996)

Temperament (Mizaj)

Cold and Dry in 2nd or 3rd degree (Ghani 1996, Haleeem, 1948)

Cold and Dry in 2nd degree (Hakeem 1953, Sadique 1927)

Chemical Constituent

Tannins, resin, alkaloid, lactocin, lectucin, lectopicrin, lactucic acid, oxalic acid, malic acid, citric acid, glycosides and steroids are the main constituents of the drug. *Lactuca sativa* contains other constituents like antioxidants, flavonol, quercetin and caffeic acid, ascorbic acid etc. alongwith trace amount of carotene, sodium, potassium, magnesium, iron, copper, chloride, sulphur, and phosphorus. Vitamin A, Vitamin B1, Vitamin B2, Nicotinic acid, Vitamin C, Vitamin E, Vitamin G, Vitamin K and Folic acid have also been reported to be present (Nadkarni 1954, Ali et al 2016, Anonymous 1962, Khory and katra 1985, Chopra and Nayer 1956).

Pharmacological / Clinical Studies

Some of the pharmacological studies of *Tukhm-e-Kahu* on animal models and clinical trial are listed as given below:

Sedative and Hypnotic Activity

- The seed oil of *L. sativa* showed sedative effect in locomotor activity test, potentiation of the hypnotic effect of barbiturates, analgesic effect in acetic acid-induced writhing test and anticonvulsant activity against pentylenetetrazole-induced convulsion. (Said, *et.al.*1986)
- In a pre-clinical study on motor activity and behavior of toads, *Bufo marinus*, A chemical agent with depressant effects was isolated from extracts of the stem of lettuce, *Lactuca sativa* L and administered. The DLS component depressed striated and smooth muscle contraction in nerve-muscle preparations and also decreased heart rate and ventricular

contraction in the normal heart or during tachycardia (Gunzalex-Lima *et.al.*, 1986).

Analgesic and Inflammatory Activity

- In a pre-clinical study, seeds and samples of stems from the two medicinal plants, *Lactuca scariola* and *Artemisia absinthium* respectively were extracted in absolute methanol to determine their analgesic and anti-inflammatory activity. The analgesic activity was assessed on intact mice by tail flick latency in tail immersion method. Results showed that Lactuca had potent analgesic activity and Artemisia had significant analgesic and anti-inflammatory activity (Ahmad, *et.al.*, 1992)
- In a preclinical study, anti-nociceptive and anti-inflammatory activities of a crude methanol/petroleum ether (70/30, v/v) extract of the seeds have been evaluated. The extract exhibited a time- and dose-dependent analgesic effect in formalin test and also a dose-dependent anti-inflammatory activity in a carrageenan model of inflammation. (Sayyah, *et.al*, 2004)
- Polyphenolic extracts from *Lactuca sativa* were able to reduce both the inflammatory and oxidative stress in LPS-stimulated J774A.1 murine monocyte macrophage cells by lowering the release of nitric oxide (NO) and reactive oxygen species (ROS). (Adesso et al 2015)

Anti-Anxiolytic Activity

- In a preclinical study conducted by Harsha et al (2013) extract of *Lactuca sativa* can afford significant protection against anxiolytic activity. The anxiolytic effects of hydro-alcoholic extract of leaves of *Lactuca sativa* was investigated on mice (Harsha and Kumar 2013).
- In another preclinical study anti-anxiolytic effect of the *Lactuca virosa* was reported by Gromek *et al.* 1992.

Anti-Oxidant Activity

- Methanolic leaf extract was investigated for in vitro inhibition of oxidative damage induced by UV-radiations to the salmonella typhi bacteria and in vivo effect on the production of body enzymes i.e. catalase and superoxide dismutase. The plant extract has shown significant antioxidant potential both in vitro and in vivo. (Garg *et al.*, 2004)
- The antioxidant activity of *Lactuca scariola* (Compositae) was investigated by measuring the radical scavenging effect on DPPH (1,1-diphenyl-2-picrylhydrazyl) radical. The methanolic extract of the

aerial parts of *Lactuca scariola* showed strong radical scavenging activity. (Kim, 2001)

Anti-Depressant Activity

- In a study, the MC (methanol and chloroform; 1:1) and aqueous extracts of seed and leaf of *Lactuca sativa* along with cell suspension exudate were prepared and explored for their analgesic, anti-inflammatory, antidepressant and anticoagulant effects. The extracts and the cell suspension exudate showed dual inhibition by reducing pain and inflammation (Ismail, *et.al.,* 2015).
- In a randomized placebo double blind study, the efficacy of seeds of *Lactuca scariola* Linn. on DSM IV defined mixed anxiety depressive disorder. Results showed that the test drug (*Lactuca scariola* Linn.) is comparably effective and superior to the placebo in reducing anxiety and depressive symptom (Javed *et.al.,* 2009).

Pharmacological Actions (*Afal-o-Khawas*)

Various pharmacological actions of the drug have been mentioned in classical literature and a few have already been proved on scientific parameters. List of the pharmacological actions of *Tukhm-e-Kahu* is as mentioned below:

- Expectorant (*Munaffis Balgham*) (Ghani 1996, Hakeem 1953, Sadique 1927, Kareem 1765, Razi 1967)
- Diuretic (*Mudir Baul*) (Nadkarni 1954, Anonymous 1962, Watt 1972, Khory and Katra 1985, Chopra and Nayer 1956, Ghani 1996, Said, *et.al.,* 1986, Stewart 1896, Griven and Leyel 1994)
- Sedative (*Musakkin*) (Bunny 1992, Nadkarni 1954, Dioscoridies 1993, Watt 1972, Chopra and Nayer 1956, Griven and Leyel 1994, Kareem 1765, Azam 1895, Hubal 1942, Kabiruddin 1951, Razi 1967)
- Hypnotic (*Munawwim*) (Nadkarni 1954, Sina YNM, Dioscoridies 1993, Bunny 1992, Watt 1972, Khory and Katra 1985, Anonymous 1962, Dymock, Warden and Hoper 1890, Hakim 1953, Said, *et.al.,* 1986, Azam 1895, Hubal 1942, Ansari 1885, Kritikar and Basu 1987)
- Refrigerant (*Mubarrid*) (Nadkarni 1954, Khory and Katra 1985, Dymock, *et.al.,* 1890, Griven and Leyel 1994)
- Anesthetic (*Mukhaddir*) (Ghani 1996, Haleem 1948, Hakeem 1953, Sadique 1927, Kareem 1765, Ansari 1885)
- Anti-inflammatory (*Mohallil*) (Sina YNM, Hubal 1942, Razi 1967)

- Appetizer (*Mushtahi*) (Sina YNM, Razi 1967)
- Antipyretic (*Dafye Humma*) (Anonymous 1962, Said, *et.al.,* 1986, Chopra and Nayer 1956, Agarwal 1986, Kritikar and Basu 1987, Kabiruddin 1951, Razi 1967)
- Blood Purifier (*Musaffi Khoon*) (Fazlullah YNM)
- Antispasmodic (*Dafae Tashannuj*) (Anonymous 1962, Nadkarni 1954, Sina YNM)
- Lactogauge (*Mowallide Laban*) (Nadkarni 1954, Chopra and Nayer 1956, Kritikar and Basu 1987)
- Desiccative (*Mujaffif*) (Nadkarni 1954, Chopra and Nayer 1956, Razi 1967)
- Resolvent (*Mohallile waram*) (Ghani 1996, Haleem 1948)

Therapeutic Uses (Istemal)

Tukhm-e-Kahu is used for various therapeutic purposes which have also been endorsed by Unani scholars.

- Headache (*Suda*) (Baitar 1985, Kritikar and Basu 1987, Ghani 1996, Haleem 1948, Hakeem 1953, Kareem 1765, Antaki 1935, Ansari 1885)
- Palpitation (*Khafqan*) (Nadkarni 1954, Khory and Katra 1985)
- Insomnia (*Sahar*) (Nadkarni 1954, Baitar 1985, Anonymous 1962, Ghani 1996, Kareem 1765, Azam 1895, Razi 1967, Antaki 1935)
- Chest Pain (*Dard-e- Sadar*) (Dioscoridies 1993, Sadique 1927, Kareem `1765, Razi 1967)
- Delirium (*Ghonodgi*) (Nadkarni 1954)
- Dropsy (*Ozema*) (Griven and Leyel 1994, Murray 1983)
- Acute inflammation (*Iltehabe Had*) (Nadkarni 1954, Sina YNM, Khory and Katra 1985, Kritikar and Basu 1987, Hubal 1942, Razi 1967, Antaki 1935)
- Asthma (*Zeequn-nafas*) (Nadkarni 1954, Anonymous 1962, Chopra and Nayer 1956, Murray 1983)
- Burning Micturition (*Sozish-e-Baul*) (Ghani 1996, Kareem 1765, Ansari 1885)
- Dribbling of urine (*Taqtirul Baul*) (Hakeem 1953, Razi 1967)
- Chronic Bronchitis (*Warm Shoabe Muzmin*) (Nadkarni 1954, Watt 1972, Chopra and Nayer 1956, Kritikar and Basu 1987, Hubal 1942)

- Cold and Coryza (*Nazla Wa Zukam*) (Ghani 1996, Hakeem 1953, Sadique 1927, Kareem 1756, Razi 1967)
- Cough (*Sual*) (Nadkarni 1954, Said, *et.al.,* 1986, Hubal 1942)
- Fever (*Humma*) (Nadkarni 1954, Khory and Katra 1985, Said, *et.al.,* 1986, Kabiruddin 1951)
- Relief of excessive thirst (*Dafae Atash*) (Ghani 1996, Hakeem 1953, Azam 1895, Razi 1967)
- Sunstroke (*Zarbatus Shams*) (Griven and Leyel 1994, Antaki 1935).
- Malencholia (*Malenkholia*) (Ghani 1996, Kritikar and Basu 1987)
- Nightfall (*Kasrate ehtelam*) (Ghani 1996, Kritikar and Basu 1987)
- Dysentery (*Ishal*) (Nadkarni 1954, Kabiruddin 1951)

Substitute (*Badal*)

- *Khash khash* (Pappy seeds, Papaver somniferum) (Ghani 1996, Hakeem 1953, Fazlullah YNM, Hubal 1942)
- *Dammul Akhwain* (Dracaena cannabin) (Kareem 1765, Ansari 1885)

Dose (*Miqdare Khuraque*)

Therapeutic dosage of *Tukhm-e-Kahu* varies according to the part used for the medicinal purpose. Also different dosages are advised by different scholars in classical system of medicine.

- 6-12 gm (Ghani 1996, Hakeem 1953, Sadique 1927)
- 3-5 gm. (Kabiruddin 1951, Ansari 1885)

Side Effects (*Muzir*)

It has been mentioned in classical Unani literature that prolonged and excessive use of *Tukhm-e-Kahu* may have adverse effects like atony of body muscles, Dementia, Amnesia and Loss of vision (Ghani 1996, Hakeem 1953, Fazlullah YNM, Antaki 1935)

Correctives (*Musleh*)

Certain drugs have been recommended by Unani Scholars which may be used along with *Tukhm-e-Kahu* to reduce or prevent adverse effect. Mastagi (Pistecia lentiscus) and honey are correctives of *Tukhm-e-Kahu* (Hakeem 1953, Sadique 1927, Kareem 1756, Ansari 1885)

Conclusion

Tukhm-e-Kahu (*Lactuca scariola* Linn.) has been studied and tested vigorously especially for its pharmacological actions of the seeds and leaves and has been proved for its usage in various systemic diseases. *Tukhm-e-Kahu* (*Lactuca scariola* Linn.) is widely accepted due to its antibacterial activity, anti-inflammatory activity, antioxidant activity, analgesic activity, sedative effects, blood purifier, hepatoprotective activity and diuretic activity. This drug is used in traditional system of medicine since long time and reference goes to Hippocrates, Galen, Tabri and Dioscorides. Now it has been proved by various clinical and animal studies that it can be used in a number of diseases.

Conflicts of Interest: None declared.

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सारांश

तुख़्म-ए-काहु (लैक्टुका स्केरियोला लिन.) का औषध विज्ञानीय प्रभाव और चिकित्सीय उपयोग : एक समीक्षा

[1]क़मर आलम ख़ान, [2]आसिम अली ख़ान, [3]अज़हर ज़बीन और [*4] शगुफ़्ता परवीन

हर्बल उत्पत्ति वाली औषधियां विभिन्न रोगों की रोकथाम और उपचार में महत्वपूर्ण भूमिका निभा रही है। यूनानी चिकित्सा पद्धति लंबे समय से लोकप्रिय रही है और पूर्व–नियत युग से यह इसके कम दुष्प्रभावों और कम लागत के साथ–साथ प्रभावशीलता के कारण रोगों का उपचार करने के लिए आकर्षण का केन्द्र बन गई है। यूनानी पद्धति को कई प्रभावशील औषधियों के लिए जाना जाता है जिनका उपयोग विभिन्न विकारों के उपचार के लिए किया जाता है। ऐसी ही एक औषधि तुख़्म–ए–काहु (लैक्टुका स्केरियोला लिन.) है जोकि एस्टेरसी परिवार से संबंधित है। यह एक महत्वपूर्ण हर्बल औषधि है जिसमें हिप्नोटिक, एनेस्थेटिक, हाइपोग्लाइसेमिक, एंटीडिसंट्रिक, सिडेटिव प्रभाव इत्यादि शामिल हैं। यह विभिन्न विकारों जैसे मूत्र का बार–बार टपकना, सिर दर्द, अनिद्रा, संक्रामक ज्वर, ऐलोपेशिया इत्यादि के लिए बताई जाती है। इसके कई औषध–विज्ञानीय गतिविधियों का वैज्ञानिक मापदण्डों पर वैधीकरण किया गया है जिसमें सेडेटिव, हाइपोग्लाइसेमिक, एंटी इन्फ्लामेंटरी इत्यादि शामिल हैं। इसके अलावा अधिक प्रभावकारी एंटीऑक्सिडेंट गतिविधि भी बताई गई है। इस प्रकार, यह पूर्ण रूप से एक महत्वपूर्ण औषधि है। तुख़्म–ए–काहु अपने बहु औषधीय प्रभावों के कारण एक शक्तिशाली परंपरागत हर्बल औषधि के रूप में कार्य कर सकती है और इसीलिए यह स्कोलर्स में औषधि की खोज और मिश्रणों के विकास करने के लिए रुचि पैदा कर रहा है। वर्तमान समीक्षा में, तुख़्म–ए–काहु के प्रमुख औषधीय कार्यों और चिकित्सीय उपयोगों को सम्मिलित करने का प्रयास किया गया है जैसा कि यूनानी चिकित्सा पद्धति के साहित्य में उल्लेख किया गया है साथ ही मानव और जानवर के नमूनों में औषधि पर हाल के अध्ययनों को सम्मिलित किया गया है।

शब्दकुंजीः एक्सट्रेक्ट्स, हर्बल चिकित्सा, लैक्टुका *स्केरियोला लिन.*, परीक्षण औषधि, तुख़्म–ए–काहु

Review on *Kushta* (calx), a Unique Dosage Form of Traditional Systems of Medicine

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Abstract

Calx, known as *Kushta* in Unani medicine, *Bhasma* in Ayurveda and *Parpam* in Siddha, is a well-known dosage form of these systems. But, very often it is criticized for diverse issues like safety, adverse effects, methods of preparation, hypothetical explanation of efficacy, etc. Very few researchers have tried to explore, the mechanism of action of calx on scientific basis. The present study is collection and analysis of published studies on calx in three traditional systems of medicine viz. Unani medicine, Ayurveda and Siddha. Around 100 studies published in different standard journals have seen reviewed and categorized under Standardization, Toxicity Studies, Pharmacological and Clinical Studies and Pharmaceutical Studies. The study gave preliminary idea about the trend of research on calx.

Keywords: Ayurveda; *Kushta*; Siddha; Scientific studies, Unani medicine

Introduction

Most minerals intended for internal use are taken in calx forms. It is claimed that the process purifies metals/minerals and makes them safe (Bajaj and Vohora, 2000). In Unani medicine, the term *Kushta* is used for a dosage form used in small quantity (Hiremath *et al.*, 2010). Calcination removes undesirable part, toxic effect and increases potency (Ibn Sina, 1998). According to Ayurveda, *Bhasma* is a unique metal based drug obtained by calcinations which convert metals into mixed oxides (Shebina *et al.*, 2015). The advantage is its low dose (Hafeez, YNM).

There are a few studies that explain mechanism of action of calx. Hypothetical explanation is that constant heating of metals, vigorous wet grinding and underground heating encourage formation of pharmacologically active organo-metalic complex (Aziz *et al.*, 2002) which is yet debatable.

Classical methods of authentication of calx are outmoded in the present perspectives. Conventional methods for powdered drugs may be a beneficial step (Anonymous, 2006). Since most metallic drugs are lacking data with respect to amount of toxic substances, elemental contents and trace elements (Kapoor, 2010), latest analytical techniques are of utmost importance. Techniques like X-ray Diffraction (XRD), X-ray Fluorescence (XRF), Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES), Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES), Inductively Coupled Plasma Mass Spectrometry (ICP-MS),Atomic Absorption

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Spectroscopy(AAS), Flame Atomic Absorption Spectroscopy (FAAS),Graphite Furnace Atomic Absorption Spectroscopy (GFAAS), Scanning Electron Microscope (SEM), Transmission Electron microscopy (TEM), Electro Probe Micro analyzer/European Powder Metallurgy Association (EPMA), Electron Spectroscopy for Chemical Analysis (ESCA), Thermo gravimetric analysis/ Thermal Gravimetric analysis (TGA), Energy Dispersive X-Ray (EDX), Energy Dispersive Spectroscopy (EDS), Differential Scanning Calorimetry (DSC), Fourier Transform Infrared Spectroscopy (FTIR), Ion Chromatography (IC) etc. are being used in the studies of various aspects of traditional drugs like analysis of particle size, fuctional group, heavy metal, elemental composition, surface topography etc. These parameters are very much useful in pharmacological activities of Calx and other drugs.

Methodology

A bibliographic search was carried out to collect studies published in good quality journals. The studies were reviewed, analysed and categorized under standardization, toxicity studies, pharmacological and clinical studies and pharmaceutical studies. The studies were randomly selected irrespective of the systems of traditional medicine and this review does not contain all the studies carried out on calx heighterto.

Observations and Results

Purpose of this review paper is to explore the present status of the researches carried out on calx and, by no means; it is aimed at giving adverse comments on any study. It is to be noted that only some aspects of the study are taken up for review. In no case, any study has been reviewed completely and only important aspect was taken, therefore, there may be chances of omission of some points. Results and conclusion of the studies and safety and efficacy of the calx/ drug mentioned in this paper are not guaranted by the authors.

Studies on Standardization

The standardization of *Kushta* has been taken up from various dimensions. The process standardization and product standardization have been taken up for individual formulations of various *Kushta*.

Studies on Process Standardization are as described the below:

In a study conducted on 'Process Validation of *Kushtasazi* with reference to *Kushta-e- Sadaf',* an attempt was made to validate the process of purification. Trace elements and heavy metal analysis was carried out on raw and purified

Sadaf to observe changes after purification. Definite changes were observed which validated the purification (Mohammad *et al.*, 2017). In a study conducted on 'Standardization of *Kushta Sammul far* (Calx of Arsenic Trioxide) prepared by two different methods almost similar results were observed in the two samples with slight difference in the physicochemical properties. This study paved the way for alternate method of preparation by Muffle furnace (Ansari *et al.*, 2012). In a study conducted on 'Preparation of *Kushta Sammul far* by Muffle furnace using the temperature pattern extrapolated from the classical methods of its preparation using thermocouple 'concentration of elemental arsenic was found more in *kushta* prepared by classical method. This study revealed that muffle furnace is a safer option (Irshad *et al.*, 2011). In a study conducted on the 'preparation and characterization of *kushta* by SEM, TEM and EDAX, it was observed that *Kushta-e-Faulad* contained nano-particles of iron-oxide and metallic iron in the range of 06 to 49 nm. LD_{50} was 660 mg/kg b.w. in rats (Tajuddin *et al.*, 2015).

In a study conducted on use of furnace, *Kushta* made by furnace was evaluated on powder characterization parameters for preparation of various *Kushtajat* (Mohammad *et al.*, 2017). The study conducted on *'Rasasindoora* and *Rakta Parada Bhasma'* attempted to highlight the subtle differences between the method of preparation and characteristics of the final product with reference to XRD and XRF analysis and the researchers concluded that physical, chemical and therapeutic properties differed from one another (Rampratap *et al.*, 2017). The presence of heavy metals like Lead, Mercury, Arsenic and Cadmium in *Rajata Bhasma* was reported and found within the permissible limits. XRD revealed *Rajata Bhasma* as crystalline (Dalal, 2017). Study conducted on 'Role of Gallic acid in the preparation of an Iron–Based Indian Traditional Medicine-*Lauha Bhasma*' used the techniques such as UV-Vis spectroscopy, FTIR, TGA and SEM to characterize the gallic acid-metal complex. The thermal analysis showed that the complex was stable up to 850 ^{0}C and the complex formed was soluble in water. Thus Gallic acid present in *Kulatha* is responsible for removing Fe present in the raw material, thereby, reducing the toxicity of *Lauha bhasma* (Rajendran *et al.*, 2012). Physicochemical characterization of *Kushta Naushadar* on classical as well as on modern scientific parameters was performed to set up the standard quality control parameters in a study conducted on physicochemical characterization of *Kushta Naushadar* (Tariq *et al.*, 2013). The raw materials, intermediates and the final product were characterized using FTIR, XRPD and TGA in a study conducted on Quality Assessment of a Traditional Unani Medicine: *Kushta-e-Gaodanti*. Trace element analysis by ICP-OES revealed

the presence of arsenic, lead, chromium, cadmium, mercury, tin within the acceptable limits at therapeutic dose (Khan *et al.*, 2012). The FTIR spectra showed peaks attributed to calcium oxide, organic matter and several other substances in a study conducted on Quality Control of a Marine Origin Based Herbo-Mineral Unani Formulation. The study set up standard fingerprint of *Kushta Marjan* for the first time (Aslam *et al.*, 2015). The EDS showed almost 27% of Arsenic in the composition in a study conducted on Chemical and Structural Analysis of Ayurvedic Preparation: *Swarna Bhasma*. The researchers noted high antioxidant activity of the formulation. *Swarna bhasma* is nano particulate in nature and contains significant quantity of metallic gold, higher levels of Arsenic and traces of Fe, Si and Zn (Chittar and Pathade, 2017). The *bhasma* prepared was analysed by classical ayurvedic tests as well as by modern analytical techniques such as EDAX, SEM, XRD and FTIR in a study on Synthesis and Characterization of *Naga* (Lead) *Bhasma* focusing on the synthesis and characterization of the *Bhasma*. The study revealed *Naga bhasma* as a mixture of PbS, PbO, Pb_2O_5 Al, Ca, Fe and Si along with carbon (Kantak and Rajurkar, 2017). In a study conducted on Qualitative analysis of *Praval Bhasma* by *Namburi phased spot test,* the researchers concluded that Phased Spot Test for fineness of *bhasma* as helpful (Lata *et al.* 2017). Study was conducted on 'Particle Size Estimation and Elemental Analysis of *Lauha Bhasma* by AAS, EDAX, SEM and TEM'. SEM and TEM confirmed the formation of nanoparticles after 20th puta. AAS and EDAX showed incorporation of trace elements in the finally prepared *bhasma* (Singh and Reddy, 2011). Study was conducted on Validated Spectrophotometry Method for Estimation of Iron in Ayuvedic Preparation Containing *Lauha Bhasma*. Iron content was determined spectro-photometrically in the form of blood-red complex with ammonium thiocyanate (Joshi and Shankar, 2014). In a study conducted on 'Trace Metals Analysis in Selected Pharmaceutical Multi mineral Formulations', twelve pharmaceutical multi mineral formulations were analyzed for calcium, copper, iron, magnesium, manganese, potassium and zinc contents using AAS technique. Cu, Mn and Zn contents were low in most of the formulations (Choudhary *et al.*, 2005). In a study conducted on 'Characterization of Bio-Active Nanoparticles-Bhasma; an Indian Ayurvedic Drug', physicochemical analysis of various *bhasmas* showed the size as 1000nm (Arya, 2014). In a study conducted on 'Preparation and Characterization of *Vanga Bhasma*, a Tin-Based Herbo-Metallic Preparation', the temperature pattern observed over different *'puta'* cycles for the formation of particles of well-defined morphology and crystallinity were confirmed through SEM and XRD (Vishwakarma *et al.*, 2012). The study conducted on 'an Approach

towards Standardization of *Swarna Makshik Bhasma*' tried to assure the quality of *bhasma and rasa shastra* quality control tests like *nischandratva, varitara, amla pariksha,* etc., were followed by using XRD and TGA which revealed the presence of Fe_2O_3, FeS_2, CuS and SiO_2 (Lagad *et al.*, 2011). A study was conducted on 'Synthesis, Characterization and Histopathological Study of a Lead-Based Indian Traditional Drug: *Naga Bhasma*.' The crude drug was purified as per classical method and analysed by XRD, FTIR, EDAX and XPS. The result showed that it contained lead in nano-crystalline (~60 nm) lead sulfide form (Pb^{2+}) and found safe in histopathology of skin, small intestine, pancreas, testis, brain, lung, kidney and liver at 6 mg/100 g/day in 40 day study (Singh *et al.*, 2010). In a study conducted on Analytical Assessment of *Rajata Bhasma'*, AESICP showed silver, sulphur and sulphide form of silver, iron, copper and platinum (Parikh *et al.*, 2012). In a study, FTIR peaks of Vengara parpam constituted some functional groups such as alcohol, phenols, alkyl, amines, aromatic, carboxylic acids, ether, fluroalkanes, chloroalkanes and iodoalkanes (Maduravani and Thiruthani, 2017). In a 'chemical Study of the Diamond Based Ayurvedic Drug *Hiraka Bhasma'*, chemical composition of *Hiraka bhasma* using EDX analysis and its structural aspects were elucidated through XRD, IR and UV spectroscopy (Kadam *et al.*, 2007). In 'Analytical study of raw *Swarna Makshika* (Chalcopyrite) and its *Bhasma* through TEM and EDAX', TEM and EDAX analysis revealed the presence of iron, copper and sulphur in the *Bhasma*. In addition, Potassium, Magnesium, Aluminum and Silicon in trace amount were also found (Mohapatra and Jha, 2013). In a study conducted on 'Characterization of *Tarakeshwara Rasa*: An Ayurvedic herbomineral formulation', the XRD studies indicated Fe_2O_3 in major phase and SnO_2, HgS, SiO_2, HgO as minor phases. SEM revealed the size of the majority of particles between 0.5 and 2 µm (Gupta *et al.*, 2014). Study conducted on 'Standard Manufacturing procedure of Lauha Bhasma using *Triphala* media and by employing Electric muffle furnace', it took 20 incineration cycles for obtaining the desired *bhasma* that fulfills the set standards of the classical literature (Virupaksha *et al.*, 2012). In a study on 'Comparative Pharmaceutico Characterization of *Kansya Bhasma* prepared by traditional *Puta* method and Electric Muffle Furnace Method', these two methods gave varied results (Neha and Pardeep, 2016). In a study on 'Physicochemical Characterization of *Kushta Kharmohra* (*Cyprea Moneta* Calx): An Advance towards Standardization', classical test showed quality of *kushta* that was in confirmation with the properties mentioned in classical text (Tariq *et al.*, 2013). In a study on 'Physicochemical Standardization of *Kushta Abrak Safaid*: A Herbo-Mineral Unani Formulation',

Kushta was evaluated on classical parameters. The physicochemical parameters evaluated in this study might be considered as standard parameters of *Kushta Abrak Safaid* (Tariq *et al.*, 2013). In a study on 'In-house preparation and quality control of a traditional Unani formulation of *Kushta Aqeeq', Aqeeq* was first purified as per classical Unani literature and then subjected to heat in furnace rather than cow dung cakes due to better temperature control. Finished product was evaluated for physicochemical characteristics including preliminary tests mentioned in classical literature. The findings obtained could be considered as the standard quality control parameters of *Kushta Aqeeq* for future references (Tariq *et al.*, 2014). The study conducted on 'Quality Control of *Kushta Shora Qalmi;* A Traditional Unani Formulation', set in quality control parameters of *kushta shora Qalmi* (Tariq *et al.*, 2013). A study on 'Preliminary physicochemical evaluation of *Kushta tutia*; a Unani Formulation' reported that finished product was evaluated for physicochemical characteristics by preliminary tests mentioned in classical literature and conventional methods. Findings may be considered as standard reference for quality (Tariq *et al.*, 2013). A study conducted on 'Quality Control of a Marine Origin Based Herbo-Mineral Unani Formulation' revealed that FTIR spectra showed peaks attributed to calcium oxide, organic matter and several other substances. Total weight loss during TGA was 30.09% and DSC curve showed peaks at 20°C, 65°C, 183°C and 261°C (Aslam *et al.*, 2015). Another study on 'Preparation and Physicochemical Evaluation of *Kushta Sang Jarahat'*, a Unani Formulation' reported that physico-chemical evaluation carried out on classical tests along with modern scientific analytic techniques may be considered as standard quality control parameters for *Kushta Sang Jarahat* (Aslam *et al.*, 2015). In a study conducted on 'Physico-Chemical analysis of *Nishchandra Abhraka Bhasma* prepared by traditional *Puta* method' revealed that *Abhraka Bhasma* when prepared by traditional *Puta* method of *Rasasara*, it took 18 *Puta* to complete the process of *Bhasma nirman*. SEM analysis showed particle size varying between 95 nm and 1.6 µm. XRF analysis of *Bhasma* revealed decreased % of Fe, Si, K, Al than raw *Abhraka* (Satvilkar *et al.*, 2017). Qualitative analysis indicated the presence of iron both in ferric and ferrous forms using spectrophotometric method in a study conducted on 'Standardization and Bioavailability of Ayurvedic Drug *Lauha Bhasma* Part I: physical and Chemical Evaluation' (Verma and Prasad, 2015). Final product was analyzed by PSD, SEM and ICP in a study conducted on 'Quality control parameters of *Tamra* (copper) *Bhasma*.' PSD analysis showed the volumetric mean diameter of 28.70 µm, 50% of the material was below 18.40 µm size. Particle size was

less than 2µm. Heavy metals like arsenic, lead and mercury were present in traces (Jagtap *et al.*, 2012). Samples for three different batches from the same manufacturer were procured and analyzed in a study conducted on 'Physico-Chemical Characterization of Lead Based Indian Traditional Medicine-*Naga Bhasma*.' Thermogravimetry analysis showed that *Naga bhasma* sample was thermally stable up to 900°C, indicating the absence of free organic molecules. The FTIR spectra revealed that all the samples contained organic moieties probably in the form of complexes. Particle size and surface area analysis indicated the presence of micron-sized particles. Elemental analysis indicated the presence of arsenic impurity in the samples. Electron microscopy studies revealed that *bhasma* contained particles in micron and sub-micron ranges. EDX analysis too showed the presence of arsenic along with Lead. XRD showed the lead oxide phase in all the three samples (Nagarajan *et al.*, 2012). The final product from the *Puta* was characterized by using XRD and XRF to understand the crystallographic form or forms of iron oxides and their composition at the end of each *Puta* in a study conducted on 'Identification studies of *Lauha Bhasma* by XRD and XRF.' The iron content at the end of repeated *Putas* showed decrease in case of *Teekshna* (Bhargava *et al.*, 2012). In an 'Analytical study of *Yashada Bhasma* with *Ayurvedic* and Modern Parameters', XRD identified the final product as Zinc oxide (ZnO). SEM revealed the amorphous nature of the *bhasma* with particle size range 5-20 micrometer. ICPAES showed the presence of Zinc in major portion (95.08ppm) and other elements like Sn (0.27), Pb (0.14), Fe (1.69), Ca (1.82), Mg (1.00), Cu, Co and Mn < 0.5 ppm in the final product (Santhosh *et al.*, 2013). The PXRD pattern in combination with the elemental analysis indicated a complex, heterogeneous and non-symmetric arrangement of atoms within the *bhasma* in a study conducted on 'Physico-chemical analysis of herbally prepared silver nanoparticles and its potential as a drug bio enhancer.' Interaction of these nanoparticles with different types of biological systems suggested that the *bhasma* is non-toxic to cells in contrast to pure silver nanoparticles (Mukkavalli *et al.*, 2017). In a study conducted on *'Pavalasilasathu parpam* (PSP) and analyzed by using FTIR and ICP-OES, SEM', the procedure *Suddhi* reduced the amount of sodium, iron, calcium, phosphorous, sulfur and magnesium in coral and selenite. Particle size ranged between 30 and 80 µm. Heavy metals like mercury, lead, arsenic and cadmium were below detectable level. FTIR showed the peaks for the presence of six organic compounds (Mekala *et al.*, 2015). The aim of the study on *'Poora Parpam'* was to determine the compound by qualitative and quantitative analysis by using ICP-MS, FTIR,

MS, SEM and TEM. The study revealed some specific compounds responsible for different pharmacological activity (Kabilan *et al.*, 2017).

Toxicity studies

Criteria for assessment of toxicity in a study of *Lauha Bhasma* (calcined iron) in albino rats, were ponderal changes, change in biochemical and hematological parameters. No sign of toxicity and mortality was observed up to 100 times of the therapeutic dose. However, alteration in some of the biochemical and haematological parameters along with histopathological findings were evident at the highest dose level (Joshi *et al.*, 2016). In 'Toxicity studies of Ayurvedic formulation-*Navratna rasa*', no mortality and behavioral changes were observed during the course of acute toxicity study. The chronic toxicity study revealed that the test drug has no serious toxicity potential to most of the important organs in therapeutics doses (Lavekar *et al.*, 2009). Percentage absorption of *bhasma(s)*, biochemical and hematological parameters were analyzed in a study conducted on 'Toxicity Profiles of *Abharak* and *Tamar Bhasma(s)* in different vehicles to assess the acute oral toxicity.' Simultaneously, an *in vitro* dissolution test was performed with both the *bhasma(s)* in artificial gastric fluid to study the dissolution rate at different time intervals. Single dose oral administration of *Abharak* and *Tamar bhasma(s)* with different vehicles did not show any systemic toxicity. The study concluded that selection of vehicle has a critical role in evaluating the toxicity of *bhasma(s)* (Srinivas *et al.*, 2010). In a study conducted on 'Acute and Sub-chronic Toxicity (90-Day) Study of *Swamala (SWA)* in Wistar Rats', it was found that after 90 days of oral administration of the drug it did not show any gross toxicological signs at a dose of 15 g/ Kg b. w. which is equivalent to five times of the therapeutic dose (Nilakash *et al.*, 2014). No significant toxicity was attributable to *Vanga bhasma* even in eight times higher dose than therapeutic dose, on exposure to the drug for ten days, obsereved in toxicity study on *Vanga bhasma* (Part I-with special reference to G. I. T, Liver and Pancreas)', for local irritation (Nagaraju *et al.*, 1984). An acute oral toxicity studies on the suspension of some Unani drugs *Azaraqi* (*Strychnos nux-vomica* Linn.) and *Sammulfar* (Arsenious oxide) were carried out on mice and compared to detoxified form. It was evident that the LD_{50} in detoxified form of both the test drugs were found higher than crude form (Shamsi *et al.*, 2011). A study on *'parpam* and *chendooram* in Indian system of medicine' focussed on analysis of heavy metals content in Siddha medicine *poora parpam* using ICP-OES (Rajmohan *et al.*, 2017). A study on acute and sub acute toxicity of Vedikara silasathu *parpam* (VSP)

and *Nerunjil kudineer* (NK), was carried out. The two Siddha formulations were given in combination for urinary tract infection which was evaluated in Wistar albino rats. VSP and NK were safe for the treatment of urinary tract infection at the dose of 500mg/kg/p.o (Akila and Manickavasakam, 2012). A study was conducted on 'Acute and sub chronic toxicity study of *Tamra Bhasma* (incinerated copper), prepared with and without *Amritikarana*.' The effects of both the drugs were assessed on ponderal changes, hematological, serum biochemical and histopathology of various organs. The results showed safety at therapeutic dose level (5.5 mg/kg) and therapeutic equivalent dose x 5 (27.5 mg/kg) while at higher dose of TED x 10 (55 mg/kg) showed mild toxicity in liver, kidney, heart and thymus on repeated administration for 28 days (Chaudhari *et al.*, 2016). *Swarna bhasma* in Wistar' was administered to three groups of rats at therapeutic dose, 5 times of therapeutic dose and 10 times of therapeutic dose levels in a 'Sub acute oral toxicity study. No mortality or sign of toxicity was observed during the study (Kumar *et al.*, 2017). *Kushta Qalai* in Wistar Rats' was administered at the limit dose of 1000 mg/kg and its sub fractions 500 and 250 mg/kg b.w. for 90 days in a 'Sub-Chronic Toxicity Study. No gross histopathological change in vital organs of rats, except the degeneration of liver and kidney tissues, was observed. The test drug showed impairment at 1000 mg/kg body weight while as the crude drug showed toxicity at all the dose levels (Showkat *et al.*, 2016). *Kushta Hajrul-Yahood* in Wistar Rats' showed elevation of liver enzymes at the dose level of 1000 mg/kg while in case of classically prepared unprocessed form there were a significant elevation of liver enzymes at all the three doses in another 'Sub-Chronic Oral Toxicity Study (Showkat *et al.*, 2016). 'Chronic Toxicity Study on *Tamra Bhasma* (A Generic Ayurvedic Mineral Formulation) in Laboratory Animals' was conducted. *Tamra Bhasma* was found relatively safe at the dose levels (Vahalia *et al.*, 2011). Ansari et al (2012) in a chronic toxicity of *Kushta Sammulfar* (KSF) in rats found dose dependent toxicity. Remarkable toxic effects were observed in KSF at higher doses. But in view of high risk, use of KSF in humanbeings was discouraged (Ansari *et al.*, 2013). In a study conducted on 'Biomarkers of oxidative stress for *in vivo* assessment of toxicological effects of iron oxide nanoparticles', the investigation of oxidative stress biomarkers demonstrated a significant increase in lipid per oxidation and decrease in reduced glutathione content in the liver, kidney and brain of the treated groups in a dose dependant manner. In conclusion accumulated IONPs and bulk in organs trigger free radical generation, leading to the induction of oxidative stress condition in rats. The results obtained highlight the importance of toxicity assessments

in evaluating the efficiency of IONPs for safe implementation in diversified applications (Utkarsh *et al.*, 2015). A comparative toxicity study of various dosages form of *Kushta Sammulfar* in mice was designed to evaluate acute and sub acute toxicity of *Sammul far*, prepared by different methods with an aim to prepare their safety profile and find the safest dosage form through their toxicity comparison. The study revealed that *Mudabbar* form was more toxic than the calcined form. Further, *kushta* prepared by furnace was safer than *Kushta* prepared by classical method (Irshad *et al.*, 2011).

Pharmacological and Clinical Studies

A study on '*Kushta Just* suspension formulation' was evaluated for sedimentation volume, viscosity, pour ability and redispersibility. When orally administered to hyperglycemic Rabbits, blood glucose levels were found decreased and the plasma zinc levels were significantly increased (Agarwal *et al.*, 1998). A study was conducted on 'Experimental Appraisal of Nephro-Protective Activity of *Varunadi Loha*'. It is a known fact that Iron is nephro toxic. But in *Ayurveda*, after subjecting to various processing Loha in *bhasma* form in numerous formulations is used to treat urinary diseases. *Varunadi loha* described in *Bhaishjyaratnavali* was studied for its nephro protective activity. Significant decrease in serum creatinine and serum urea in curative group was suggestive of the fact that Varunadi *loha* was delivering its best to improve the lost kidney function (Hitesh *et al.*, 2016). A study on Neuropsycho behavioral effects of Silver preparations, *Raupya Bhasma, Kushta Nuqra* and *Chandi Warq* used in Indian Systems of Medicine was carried out by Nadeem *et al.* (1999). The preparations were subjected to a battery of 30 tests for general neuropsychopharmacological effects, cognitive functions, antidepressant, anxiolytic, neuroleptic and serenic activities, effects on growth, body weight, endurance and fatigue, at 50 mg/kg b. w., p.o) caused a significant reduction in haloperidol-induced catalepsy in rats (Nadeem *et al.*, 1999). In study on Anti-cataleptic, anti-anxiety and anti-depressant activity of gold preparations, *Swarna Bhasma* used in Ayurveda, *Kushta Tila Kalan* of Unani medicine and *Auranofin* of conventional medicine were studied by Bajaj *et al.* (2000). The Wistar rat and Swiss mice were tested for anxiolytic activity, behavioral despair and learned helplessness tests for antidepressant activity, haloperidol-induced catalepsy tests for neuroleptic activity and maximum tolerated dose, gross behavioral observations and hematological parameters for safety evaluation in rats and mice. The maximum tolerated doses were found to be more than 80 times of the effective doses and no weight loss or untoward effect was observed

on gross behaviour and hematological parameters. The drugs exhibited anxiolytic, antidepressant and anticataleptic actions with wide margin of safety (Bajaj *et al.*, 2000). In a study conducted on 'Relative efficacy of *Shankha bhasma* with *Sootshekhar rasa* in *garavishjanit amlapitta'*, significant results were noted in *Avipak, Klam, Utklesh, Tikta- amlaudgar, Gaurav, Hrud kanthadah, Aruchi* in both the groups. The study confirmed that *Sootshekhar ras* is relatively more effective than *Shankha bhasma* in *Garavishajanit amlapitta* (Bhati *et al.*, 2017). In a study conducted on 'Evidence for safety of Ayurvedic herbal, herbo-metallic and *Bhasma* preparations on neurobehavioral activity and oxidative stress in rats', results showed that there was no significant change in cognitive function, motor coordination, MDA and GSH levels as compared to normal control group at all the doses of Calcury tablet, Energic-31 capsule and *Basant Kusumkar Rasa* (Kumar and Gupta, 2014). In a study conducted on 'Screening antibacterial activity of some *bhasma* (metal-based herbal medicines) against enteric pathogens', antibacterial potential of Ayurvedic preparations such as *Mandura bhasma, Tamra bhasma, Lauha bhasma* and *Kashis bhasma* against enteric bacterial pathogens such as *Escherichia coli, Staphylococcus aureus, Enterobacter aerogenes, Pseudomonas aeruginosa, Bacillus subtilis, Klebsiella pneumoniae, Salmonella typhi, Staphylococcus epidermidis, Salmonella typhimurium* and *Proteus vulgaris* revealed that *Tamra bhasma*h as strongest antibacterial activity while *Lauha bhasma* and *Mandura bhasma* showed significant antibacterial activity (Tambekar *et al.*, 2010). In 'anti-microbial Study of Calcined Sliver (*Rajata Bhasma*)', *Rajata Bhasma* (RB) was prepared by *Kajjali* (Black Sulphide of Mercury) as a media and subjecting to *Laghu Puta* (Incineration cycle with Max temp 550 ^{0}C). Seven repeated Calcination cycles were followed to achieve Chief Desired Characteristics (CDC). Alcoholic extract of *RB* was found to be very effective against all the bacterial strains studied i.e. *Escherichia coli, Pseudomonas aeuruginosa* and *Staphylococcus aureus* with the diameter of zone of inhibition being 16, 22 and 22 mm respectively. RB showed moderate antibacterial activity by following disc diffusion method (Hebbar *et al.*, 2016). Study conducted on 'Clinical effect of *Kukkutanda Twak Bhasma* in the management of *Swetapradara', Kukkutanda twak bhasma* showed significant improvement in white discharge, backache, itching, anemia, weakness and urinary tract infection (Panda *et al.*, 2014). 'In Vitro Evaluation for Antimicrobial activity of *Tuttha Bhasma* in Comparison to Gentamicin and Amphoterecin B'was carried out. Antibacterial activity of *Tuttha bhasma* at 20 mg was equivalent to the inhibition shown by 1 mg of Gentamicin and antifungal activity was equivalent

to standard drug Amphotericin B at 1 mg (Anita *et al.*, 2013). Antioxidant and antimicrobial activities of aqueous extract of *Muthuchippi parpam* by using reducing power/FRAP (Ferric reducing antioxidant potential assay), Inhibition of DPPH radical, ABTS radical cation decolorisation assay, total phenolic content (TPC), and *In vitro* anti-lipid peroxidation assay using TBARS was carried out. The MIC values of the various concentrations of aqueous extract of *Muthuchippi parpam* against different strains of fungi showed promising effect (Ganesan *et al.*, 2016). A study conducted on *Pavala Parpam* (PP)' showed the property of haemostatic action. *In vitro* studies on PP has shown anti microbial activity at the dilution of 25 microlitre/disc against the bacterial strains such as *S. mutans, S. aureus, E. coli, K. pneumoniae* and *P. aeruginosa* (Thanigavelan *et al.*, 2011). In a study conducted on 'Clinical study of *Qurse Kushta Khabsal-Hadeed* and *Habbe Marvareed* in the management of *Sayalan al-Raham* (Leucorrhoea)', the drugs were found effective and safe on biochemical and hematological parameters. However, the study had no control group for comparison (Rehman *et al.*, 2016). Kumar *et al.* (2014) conducted a study on Rationality of Swarna Prashan in Pediatric Practice. Study showed that by classical *bhasmikaran* process there is reduction in the particle size of gold to dimension of about 56-57 nm. Toxicity study showed that chronic administration of *Swarna Bhasma* is non toxic as judged by various laboratory and histological parameters. However, scientific evidences regarding the safety and efficacy of *Swarna prashan* in pediatric practice is lacking (Kumar *et al.*, 2013). In a study conducted on 'Clinical evaluation of Ayurvedic iron (*Lauha*) containing preparation in Iron deficiency anemia', the results revealed that all the three iron containing preparations were found effective in the correction of anemia (Joshi *et al.*, 2015). A study was conducted on 'Haematinic Evaluation of *Lauha Bhasma* and *Mandura Bhasma* on $HgCl_2$-Induced Anemia in Rats'. In Charles Foster strain rats of either sex, anemia was induced by administering mercuric chloride (9 mg/kg). *Lauha bhasma* and *Mandura bhasma* (11 mg/kg) were possessing haematinic and cytoprotective activity (Sarkar *et al.*, 2007). In a study conducted on 'Velvanga parpam (VP) for styptic activity against the standard drug Adrenochrome in Wister albino rats', the investigation showed a significant reduction in the bleeding time, clotting time, prothrombin time and fibrinogen time. The values of the trial drug VP treated animals were compared with standard drug Adrenochrome 10mg/animal i.p single dose. Good Styptic activity response of trial drugs was explored (Parthibhan *et al.*, 2015). In a study conducted on 'Anti diabetic activity of Palingu Abraga Parpam (PAB) validated the anti diabetic activity of PAB on patients with

Type II diabetes mellitus' (Anbu *et al.*, 2012). A study was conducted on 'Hypoglycemic property of *Shilajeet* and *Yashada bhasma*'. Result was determined in normoglycemic and alloxanized rats. A significant activity was observed in the treated groups (Bharati *et al.*, 2017). In a study conducted on *'Sangu Parpam* and *Silasathu Parpam'*, the results revealed that *Sangu Parpam* and *Silasathu Parpam* have good antiulcer effect on albino rats (Thirupathi *et al.*, 2002). A study conducted on 'Antiulcer Activity of a Traditional Pearl Preparation: *Mukta Bhasma* for antiulcer activity in experimental animals by cold restraint stress induced ulcer model and Diclofenac induced ulcer model', suggested that this preparation possesses a significant gastro protective and antiulcer activity in lower doses of therapeutic range and its effect is not dose dependent (Dubey *et al.*, 2009). A study reported on *'Nillavari Choornam* (NC) and *Thamarai Parpam* (TP) for anti-ulcer activity' and toxicological effects in rats at dose levels of 200mg/kg and 250 mg/kg , respectively by pylorus ligation induced ulcer model, aspirin induced ulcer model and gastric lesions induced by stress in rats. Both, NC and TP were found to possess significant anti-ulcer activity in all the above models (Manjunath *et al.*, 2011). In a study on 'Pharmacological Evaluation of Wound Healing Potential of *Jasad Bhasma* (JB) using Wistar Rats: A Mechanistic Approach for its wound healing activity', it was observed that JB exhibited an excellent wound healing activity by both excision wound model and *resutured* incision wound model (Shah *et al.*, 2009). A study was conducted on 'Gastric Antisecretory, Antiulcer and Cytoprotective Properties of *Tamira Parpam* (bio-copper) from earthworm.' The anti-ulcer properties of *Tamira Parpam* (bio-copper) from earthworm against Aspirin plus pylorus ligation induced gastric ulcer in rats, HCl-Ethanol induced ulcer in mice and water immersion stress induced ulcer in rats indicated *Tamira Parpam* a potential anti-ulcer drug in animal models (Krishnaveni *et al.*, 2012). In a study conducted on '*Swarna Bhasma* in cancer: A prospective clinical study', it was observed that the response was best in rectal cancer group 70% (7/10). Nearly 41.02% patients survived for 1 year after treatment but after 5 years this came down to 15.38% (Das *et al.*, 2013). Samraj *et al.* (2013) conducted a study on *Velvanga parpam* (VP) for anti-tumor activity against Swiss albino mice. The VP was administrated at the doses of 1.5 and 3 mg /kg / per day for 9 days. VP caused a significant decrease in tumor volume and it prolonged the life span of DAL-tumor bearing mice. In a study, it was noted that '*Abhraka Bhasma* treatment ameliorates proliferation of germinal epithelium after heat exposure in rats.' The test drug can correct heat induced male infertility and it can be used for treatment of human heat induced

oligozoospermia and azoospermia (Bhatia *et al.*, 2012). A study was conducted on 'The Vrsya Property (Testicular Regenerative Potential) of *Vanga Bhasma*'. The drug has testicular regenerative potential on cadmium induced testicular degeneration in albino rats (Nagaraju *et al.*, 1985). A study on 'the safety and anti-arthritic efficacy of herbomineral formulation *kanthaga parpam* (KP) in animal models' was conducted. The anti-arthritic activity of KP (in doses of 25 mg/kg and 50 mg/kg of body wt.) using the complete Freund's adjuvant induced arthritis models, with standard drug Diclofenac sodium (45 mg/kg body wt.) significantly inhibited the progression of the arthritis in animal models (Parthiban *et al.*, 2013). The study conducted on '*Seenakara parpam* (SKP) and its effect on Urolithiasis' revealed that treatment with SKP and cystone significantly reduced the excretion of calcium and the volume of urine output increased in treatment group when compared to that of the disc implanted group rats. The results of the study reflect that treatment with SKP at the dose of 200 and 400 mg/kg and standard drug cystone 500 mg/kg indicated a significant decrease in the weight of calculi from 113.5 mg to 10.5 mg (Mariappan *et al.*, 2016). A study was conducted on 'Physico-chemical properties and antimicrobial activity of *Shukti Marit Haratal bhasma* in Vitro'. XRD analysis of *Shukti bhasma* matched with the match of Calcite ($CaCO_3$) with rhombohedral structure. $CaCO_3$ percentage in gravimetric analysis was 96.80%. *Shukti Marit S. M. Haratal bhasma* has significant activity on Gram positive bacteria (*S. aureus*) (Swati *et al.*, 2017).

Pharmaceutical Studies

Hitesh *et al.* (2015) and Singh *et al.* (2016) reported a study on Pharmaceutical Study of *Loha Bhasma*. Pharmaceutical and analytical studies were conducted during the process of preparation of the *Loha bhasma* to know the changes in the temperature pattern at various *putas*. Namburi Phased Spot Test was done to prove the fineness of the *bhasma* (Hitesh *et al.*, 2015; Singh *et al.*, 2016). In a study conducted on 'A Green approach for the synthesis of nano-sized iron oxide, by Indian *Ayurvedic* modified *bhasmikaran* method', XRD was used to monitor phase transformation from α - to γ- phase and characterizations were done using TG analysis, TEM, FTIR (Pavani *et al.*, 2013). A study was conducted on '*Bhasma* and Nano Medicine'. The *Bhasma* particles when analyzed microscopically through SEM and TEM fall under the range of Nanoparticles of contemporary science. In this study researchers explained the basic principle of change of properties of substances at their Nano level. It is an attempt to understand and apply basics of Nano technology in Ayurvedic Pharmaceutics (Santosh Kulkarni, 2013). Zargar, *et al.* (2011)

conducted a study on green synthesis and antibacterial effect of Silver Nanoparticles using *Vitex Negundo* L. extract and its antimicrobial properties have been reported. The resulting silver particles were characterized by using TEM, XRD and UV-Vis spectroscopic techniques. The TEM study showed the formation of silver nanoparticles in the 10–30 nm range and average 18.2 nm in size. The XRD study showed that the particles are crystalline in nature with a face centered cubic structure. The silver nanoparticles showed the antimicrobial activity against Gram positive and Gram negative bacteria (Zargar *et al.*, 2011). In a study conducted on 'Green synthesis of gold nanoparticles by using *Cinnamomum verum, Syzygium aromaticum* and *Piper nigrum* extract', the UV-visible spectrum of Au NPs showed a broad band in the region 543-546 nm corresponding to the surface plasmon resonance band (SPR) of Au NPs. Furthermore, the rate of formation of nanoparticles using different spice extracts as reducing agent give an indication towards the concentration of active components present in them. FESEM confirmed the size range, polydispersity and existence of nanoparticles as separated particles. DLS confirmed their polydispersity and size in the range between 2.9 and 3.6 nm (Sharma *et al.*, 2017).

Miscellaneous Studies

In a study conducted on 'Evaluation of cytotoxic activity of platinum nanoparticles against normal and cancer cells and its anticancer potential through induction of apoptosis', the researchers have found that ptNPs exerted cytotoxic effect on cancer cell lines whereas no cytotoxic effect was observed at the highest dose on normal cells. The results showed that ptNPs had potent anticancer activities against ovarian teratocarcinoma (PA-1) cell line via induction of apoptosis and cell cycle arrest. These findings have proved that biosynthesized ptNPs could be potent anti-ovarian cancer drugs (Bendale *et al.*, 2017). A study was conducted on 'Structural and Optical Properties of Pure Iron and Iron Oxide Nanoparticles Prepared via Pulsed Nd: YAG Laser Ablation'. Particle size and morphology, crystal structure and optical properties of the nanoparticles were characterized by SEM, XRD and UV-visible spectroscopy respectively. The results provide a flexible and fast method for synthesis of pure iron and iron oxide nanoparticles especially for biological applications (Dadashi *et al.*, 2015). Study was conducted on 'Synthesis of Iron Oxide Nanoparticles coated sand by biological method and chemical method'. The synthesized particles were characterized by using EDS, SEM, and PXRD. From ED's analysis, the highest percentage coating of iron on the sand surface was

obtained for the iron oxide nanoparticles coated sand synthesized using chitosan templates. The PXRD analysis revealed the crystallite size of the synthesized particles as 42.8 nm. The SEM image showed the presence of almost spherical shaped particles on the sand surface and the coating was discontinuous (Rasheed and Meera, 2016).

Discussion

The review has highlighted certain facts about the studies carried out on calx. Almost all the papers have been published in the journals having International Standard Serial Number. Some of the studies have been published in journals claimed to be indexed with impact factor. Out of 23 studies carried out in Unani Medicine, 15 were on standardization followed by five toxicity studies and three pharmacological studies. Out of 44 studies carried out in Ayurvedic sciences, 26 were on standardization followed by nine toxicity studies and nine pharmacological studies. Out of 15 studies carried out in Siddha, three were on standardization, two on toxicity and 10 on Pharmacology. Three miscellaneous and five pharmaceutical studies have also been reviewed. Based on the review, it is obvious that most of the studies have focused on standardization only.

Studies on standardization were mainly based on X-RD, SEM, TEM, FTIR, TGA, UV-S, EDX, AAS, etc. It means that the authors have focused their attention on particle size determination, determination of elemental contents, crystal structure, determination of traces elements, thermal decomposition etc. Most of the studies on standardization have used XRD followed by SEM, TEM, and FTIR. With the emergence of technology, new methods are being introduced in traditional systems of medicine. Analytical techniques like X-RD, SEM, ICP-MS, FTIR, AAS, energy dispersive X-ray analysis which have favored the scientific studies and are now used for characterization of calx.

A very few studies have been carried out on efficacy and mechanism of action of calx in any system of medicine. It seems that there is a tendency to work on set type of studies rather than new areas of research. Some studies have been carried out on nano aspect of the calx by chemists. The types of journals, except some, are not very standard. Most preferred journal for publication of studies in Ayurveda is Ancient Science of Life followed by AYU Journals in which Unani and Siddha studies have also been published but not of standard. This shows that world's best medical journals don't have

interest in publishing such studies probably because of lack of intrest in this doasage form. This review has highlighted the quantum of researches done on calx. However, there is still much to do to improve the quality of research in healthcare instead of research on set topics.

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सारांश

कुश्ता (कैलेक्स), पारंपरिक चिकित्सा पद्धति की एक विशेष खुराक प्रारूप

*हकीक़ अहमद, अब्दुल वदूद, गुलामुद्दीन सोफ़ी और नसरीन जहां

कैलेक्स जिसको यूनानी चिकित्सा में कुश्ता, आयुर्वेद में भस्मा और सिद्ध में परपम के रूप में पाया जाता है और इन पद्धतियों की एक जानी–पहचानी औषधि है। लेकिन कई बार इसकी सुरक्षा, प्रतिकूल प्रभाव, तैयारी के तरीके, प्रभावकारिता के काल्पनिक विवरण आदि जैसे विभिन्न मामलों के लिए आलोचना की जाती है। बहुत कम शोधकर्ताओं ने वैज्ञानिक आधार पर कैलेक्स के प्रभाव का पता लगाने की कोशिश की। वर्तमान अध्ययन, चिकित्सा की तीन पारंपरिक पद्धतियों अर्थात् यूनानी चिकित्सा, आयुर्वेद और सिद्ध में कैलक्स पर प्रकाशित अध्ययनों का संग्रह और विश्लेषण है। विभिन्न मानक जरनल्स में प्रकाशित लगभग 100 अध्ययनों की समीक्षा की जा चुकी है और मानकीकरण, विषाक्तता अध्ययन, फार्माकोलॉजीकल एवं नैदानिक अध्ययन और फार्मास्युटीकल अध्ययन के अन्तर्गत वर्गीकृत किया गया। अध्ययन ने कैलक्स पर अनुसंधान की प्रवृत्ति के बारे में प्रारंभिक विचार प्रस्तुत किया।

शब्दकुंजी: आयुर्वेद; *कुश्ता*; सिद्ध; वैज्ञानिक अध्ययन, यूनानी चिकित्सा

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