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Editorial

The Central Council for Research in Unani Medicine (CCRUM), as an apex research organization under the Ministry of AYUSH, Government of India, is making concerted efforts in the area of research and development in 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.

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 (HJUM). HJUM is a peer-reviewed scientific quarterly journal published since 2006. It covers papers on clinical research on single and compound Unani drugs, validation of regimen therapy, experimental pharmacological studies, standardization of single and compound drugs, development of standard operating procedures, ethnobotanical studies and development of agro-techniques thereof and literary research on classics of Unani Medicine. The journal is also open for studies on safety evaluation of Unani and other herbo-mineral drugs, nutraceuticals, cosmotherapeutics, aromatics, oral health, lifestyle disorders, sports medicine and such other newer areas which are the outcome of modern day living.

To curb the menace of increased incidence of compromised publication ethics and deteriorating academic integrity, a growing problem contaminating all domains of research, the University Grants Commission (UGC) recently took an initiative and established Consortium for Academic and Research Ethics (CARE) for creation and maintenance of 'UGC-CARE Reference List of Quality Journals' (UGC-CARE List) in January 2019. I am pleased to note that HJUM has been listed in the UGC-CARE List published online on June 14, 2019, which can be accessed from the UGC-CARE website https://ugccare.unipune.ac.in/site/website/index.aspx.

This issue of HJUM comprises six papers. The first paper is on the role of diet in the prevention and management of cancer (*Saraṭān*) in Unani Medicine. The second paper is review of pharmacological actions and therapeutic benefits of *Bābūnah* (*Matricaria chamomilla* L.). The third paper is a review paper on *Khabasul Hadeed* (Iron rust) and its importance in the management of hematopoietic disorders especially anaemia. The fourth paper discusses antimicrobial studies of *Ocimum basilicum* L. seeds against urinary tract infection causing organisms. The fifth paper is outcome of a preliminary study on effect of Unani pharmacopoeial formulation, *'Araq-i-'Ajīb* in cases of *Ṣudā'* (headache), while the last paper is based on a clinical study for validation of safety and efficacy of *Ḥabb-i-Shifā'* for symptomatic relief in *Nazla Ḥārr* (common cold) in Eastern India.

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

Prof. Asim Ali Khan
Editor-in-Chief

Contents

Role of Diet in the Prevention and Management of Cancer (*Saraṭān*) in Unani Medicine

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Abstract

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. Cancer is the second most common cause of death after heart diseases in the United States. According to Unani classical literature, cancer is a disease related to *Sawdā'* (black bile). The causes and development of cancer are multifactorial, i.e. excess production and abnormal changes that occur in *Sawdā'*. Cancer is a curable disease in most of the cases, if detected early. Unani physicians recommended *Uṣūl-i-'Ilāj* of cancer in successive steps, i.e. *Faṣd* (venesection), *Tanqiya-i-Mawād* (evacuation of morbid humor from the body with the help of *Mundijāt-i-Sawdā'* (concoction of black bile) and *Mushilāt-i- Sawdā'* (purgation of black bile), *'Ilāj bi'l-Ghidhā'* (dietotherapy), pain management and topical medication for cancer. In the management and prevention of cancer, the diet should be *Laṭīf* with *Jayyid al-Kaymūs* and should not produce *Sawdā'*. In this review paper, the role of diet in the management of cancer as mentioned in Unani classical literature will be discussed in detail.

Keywords: Cancer, Dietotherapy, *Saraṭān, Sawdā'*

Introduction

Cancer has emerged as a major public health problem worldwide as well as in developing countries (Manjul, 2015). It is defined as malignant growth characterized by the uninhibited proliferation of cells, often affecting healthy tissues locally or throughout the body (Venes, *et al.*, 2001). The most significant risk factor for cancer overall is age; two-thirds of all cases were found in those older than 65 years (Longu, *et al.,* 2012). Owing to its high incidence in nature, it is the second leading cause of death after cardiovascular etiology. Cancer is known as *Saraṭān* in Unani Medicine. *Saraṭān* is an Arabic word which means crab. According to Unani Medicine, cancer is a disease of black bile (*Sawdā'*), i.e. excessive production and collection of black bile. Galen (*Jālinūs*) was the first to deal with tumors, including cancer, in a systematic way and adopted Hippocrates' basic theory of cancer as an excess of black bile (Saad, *et al.,* 2008).

Types of Cancer

Based on tissue types, cancers may be classified into six major categories, *viz.* (a) carcinoma, (b) sarcoma, (c) myeloma, (d) leukemia, (e) lymphoma, and (f) mixed type (Manjul, 2015).

According to *Rāzī* (854-925), *Saraṭān* is a fatal disease, but if treated in early stage it does not increase and remains constant. According to Hippocrates'

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humoral theory, Galen extended Hippocrates' definition of cancer and classified tumours into three major types; (i) *Onkoi* (lumps or masses), (ii) *Karkinomas* (Non-ulcerating cancers), (iii) *Karkinos* (Ulcerating cancers) (Diamandopoulos, 1996; Weiss, 2000).

Etiology and Pathogenesis of *Saraṭān* in Unani Medicine

The eminent Unani physicians, notably *Jālinūs* (129-199AD), *Rāzī* (854-925), *Al-Zahrāwī* (936-1013) and *Ibn Sīnā* (980-1037) were well-acquainted with cancer. *Ibn Sīnā* and *Rāzī* described most types of cancers and suggested several treatments based on their belief. The cancer is a result of excess of burned black bile in the affected tissue. *Al-Zahrāwī* was the first to conduct classic removal of breast cancer. He recognized that in early stages cancer can be treated surgically, when its complete removal is possible (Saad *et al.*, 2008).

In Unani terminology, it is defined as *Waram Ṣalāba* (hard inflammation) with lesion and their tributaries filled by *Mādda Sawdāwiya* (morbid melancholic humour) (Maseehi, 1995). Usually, it is developed in those who are obese and flabby and high incidence of cancer is in females particularly in hollow organs where the causative substance *Mādda Sawdāwiya* accumulates easily, *viz.* breast, lungs, cervix, oral cavity, uterus, etc. (Maseehi, 1995; Ibn Rushd, 1980; Ibn Sīnā, 2010). The cause and development of cancer are multifactorial, i.e. excess production and abnormal changes occur in *Sawdā'*. There are five types of abnormal changes that occur in *Sawdā*'; (a) excess production of normal *Sawdā*', (b) burning of normal *Sawdā*' into abnormal *Sawdā*', (c) formation of *Sawdā*' due to burning of blood, (d) formation of *Sawdā*' due to burning of phlegm and (e) formation of *Sawdā*' due to burning of *Safrā*' (bile) (Arzani, 2002).

The altered *Sawdā'* being extremely hot in quality and *Akkāl* (irritative) in nature causes *Iḥtirāq* (combustion) in organs. Due to *Iḥtirāq*, the quantity and quality ratio of *Arkān* changes and *Mizāj* is also altered, as a result *Ṣūra Naw'iyya* and functions are changed. Thus, the altered *Sawdā'* erodes the tissues and produces malignant changes by altering their *Naw'iya* (structure) that is termed as *Saraṭān* (Ibn Rushd, 1980; Ibn Sīnā, 2010; Majusi, 2010; Ibn Nafis, 1987; Jalinus, 2008).

Mechanism of Cancer Therapy in Modern Medicine (Hanahan, 2000)

1. Inhibiting cancer cell proliferation directly by stimulating macrophage phagocytosis, enhancing natural killer cell activity.
2. Promoting apoptosis of cancer cells by increasing production of interferon, interleukin-2 immunoglobulin and complement in blood serum.
3. Enforcing the necrosis of tumor and inhibiting its translocation and spread by blocking the blood source of tumor tissue.

4. Enhancing the number of leukocytes and platelets by stimulating the hemopoietic function.
5. Promoting the reverse transformation from tumor cells into normal cells.
6. Promoting metabolism and preventing carcinogenesis of normal cells.
7. Stimulating appetite, improving quality of sleep, relieving pain, thus benefiting patient's health.

Characteristics of the Cancer Cell Phenotype that Result in Progressive Disease (Hanahan, 2000)

- Self-sufficiency in growth signals
- Insensitivity to antigrowth signals
- Evading apoptosis
- Limitless replicative potential
- Sustained angiogenesis
- Tissue invasion and metastasis

Side Effects of Cancer Treatment

The majority of patients receives little or no benefit from current chemotherapies mainly because most of the cancer cells are either intrinsically chemo-resistant or become resistant during therapy. Thus, the treatment success rates are very low; and the current standard therapeutic options for cancer are not adequate and still do not meet the criteria to cure patients suffering from this lethal disease. Radiotherapy / chemotherapy often causes side effects, such as nausea, mouth sores, taste changes and immunosuppression. These are the major side effects that may cause difficulty in eating and drinking.

The role of nutrition in the management of cancer is very broad. It has been estimated by the American Institute for Cancer Research and the World Cancer Research Fund that 30%–40% of all cancers can be prevented by appropriate diets, physical activity and maintenance of appropriate body weight (Anonymous, YNM).

Management of Cancer (*Saraṭān*) in Unani Medicine

In Unani Medicine, humoral balance is regained by giving *Mushilāt* (purgatives), *Mulayyin* (laxatives), *Faṣd* (bloodletting), *Muqī* (emetics), *Mudirr-i-Bawl* (diuretics) and *Huqna* (enemas). Preventive aspects are in the form of advice to take a balanced diet and perform adequate exercise. Unani physicians also recognize the natural healing process in achieving best possible health. The diseases heal naturally and physicians help nature to heal (Lioyd, 1989).

'Ilāj (Treatment)

In the classical Unani literature, treatment of *Saraṭān* is based on four modalities:

1. *'Ilāj bi'l-Ghidhā'* (Dietotherapy)
2. *'Ilāj bi'l-Tadbīr* (Regimenal therapy)
3. *'Ilāj bi'l-Dawā'* (Pharmacotherapy)
4. *'Ilāj bi'l-Yad* (Surgery)

1. *'Ilāj bi'l-Ghidhā'* (Dietotherapy): Most of the Unani physicians recommended diet according to *Mizāj* (temperament), *Quwwat-i-Badan* (body power) and disease state of a person. In the perspective of Unani *Uṣūl-i-'Ilāj*, *'Ilāj bi'l-Ghidhā'* works on the principle of *'Ilāj bi'l-Ḍidd* to restore the health or combat ailments. As per the nutritive value, diet is divided in three categories, i.e. *Ghidhā' Laṭīf* (light diet), *Ghidhā' Kathīf* (heavy diet) and *Ghidhā' Mu'tadil* (moderate diet). *Ghidhā' Laṭīf* decreases the viscosity of the blood. *Ghidhā' Kathīf* increases the viscosity of the blood. *Ghidhā' Mu'tadil* neither increases nor decreases the viscosity of the blood and is responsible for the moderate viscosity (Ibn Sīnā, YNM). For prevention and management of cancer, diet should be *Ghidhā' Laṭīf* with *Jayyid al-Kaymūs* and should not produce *Sawdā'*. In *Saraṭān,* generally use of *Ghidhā'* like *Kaddū* (*Cucurbita maxima* Duchesne), *Khurfa* (*Portulaca oleracea* L.), *Cholai* (*Amaranthus spinosus* L.), *Bathua* (*Chenopodium album* L.), *Kheera* (*Cucumis sativus* L.), *Qisa* (*Cucumis melo* L.), *Mā' al-Jubn (Whey), Mā' al-Sha'īr, Kashk al-Sha'īr, Taza Chhachh* (Butter Milk), *Roghan Badam* (*Prunus amygdalus* L.), *Moong* (*Vigna radiate* L.), *Palak* (*Spinacia oleracea* L.), *Gadhi ka Doodh (Donkey Milk), Bhed ka Doodh*, half boiled egg, etc. are recommended (Ibn Rushd, 1980).

2. *'Ilāj bi'l-Tadbīr* (Regimental therapy)

- *Faṣd* (Venesection) in *Warīd Akhall* (Median Cuboidal Vein) (Ibn Rushd, 1980; Razi, 1997).
- *Ishāl* (Purgation): Decoction of *Aftīmūn* (*Cuscuta reflexa*) with *Mā' al-Jubn* for few days or *Mā' al-'Asal*. Decoction of *Aftīmūn* (*Cuscuta reflexa*) with *Sikanjabīn* (compound formulation) and *Ayārij Kharbaq* can be used in strong built individuals.
- *Naṭūl* (Irrigation/pouring of medicated water) (Ibn Sīnā , YNM)
- *Ḥammām* (Bath) (Ibn Sīnā , YNM)
- *Ṭilā'* (application of liniment) and *Ḍimād* (external application of ointment) (Ibn Sīnā, YNM)

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

- *Tanqiya-i-Mawād* (evacuation of morbid humor) from the body with the help of *Munḍijat-i-Sawdā'* (concoctives of black bile) and *Mushilāt-i-Sawdā'* (purgatives of black bile).

Drugs Used as *Munḍijāt-i-Sawdā'*: *Bisfaij* (*Polypodium vulgare* L.), *Ustukhuddus* (*Lavendula stoechas* L.), *Parshiyonshan* (*Adiantum capillus-veneris* L.), *Gaozaban* (*Borago officinalis* L.), *Badranjboya* (*Melissa officinalis* L.), *Aslussus* (*Glycyrrhiza glabra* L.), *Badyan* (*Foeniculum vulgare* Mill), *Unnab* (*Ziziphus sativa* Gaertn), *Shahtara* (*Fumaria officinalis* L.) *Sapistan* (*Cordia latifolia* L.) (Ibn Sīnā , 2010; Razi, 1991).

Drugs Used as *Mushilāt-i-Sawdā'*: *Aftimoon* (*Cuscuta reflexa* L.), *Shaham Hanzal* (*Citrullus colocynthis* (L.) Schrad.), *Elva* (*Aloe barbadensis* (L.) Burm.f.), *Halela Siyah* (*Terminalia chebula* Retz.), *Turbud* (*Operculina turpethum* (L.) Silva Manso), *Badranjboya* (*Melissa officinalis* L.), *Barge Sana* (*Cassia angustifolia* Vahl), *Ghariqoon* (*Agaricus albus* L.) with *Sikanjabīn* and *Mā' al-'Asal* (honey water) (Ibn Rushd, 1980).

Pain Management: Pain in *Saraṭān* is controlled with oral administration of ash of *Tootiya* (Copper sulphate) mixed with milk (Ibn Sīnā, YNM).

Topical Medication for Cancer: As *Ibn Sīnā* described in his book *Al-Qānūn*, there are four purposes of such treatment; (i) total arrest of the cancer, (ii) preventing its progress, (iii) preventing ulceration, and (iv) treatment of ulceration. Unani physicians recommended various local applications such as an ointment made by mixing of *Safeda Kashgari*, *Tootiya Magsool, Gil Armani* and *Aab Kahu* with *Rowghan-i-Zaitoon* (olive oil) for local application (Ibn Sīnā , 2010).

4. *'Ilāj bi'l-Yad* **(Surgery)**: Those small cancers which are away from the vital organs can be excised surgically, but after *Tanqiya* of morbid *Akhlāṭ* from the body (Ibn Rushd, 1980; Qamri, 2008). Cancer situated deep inside the tissue cannot be surgically removed as surgeon is unable to cut its root resulting in severe complications, hence only analgesic drugs are advised (Ibn Sīnā, YNM).

Dietary recommendations made by Unani scholars have been validated scientifically for anticancer activity. So, the intake of theses diets may be helpful to prevent cancer in certain individuals. Anticancer activities of some Unani diets are as follows:

***Anār* (*Punica granatum* L.)**: Several *in-vitro* anticancer assays were carried out on prostate cell lines (DU-145, LNCaP, PC-3) using various pomegranate extracts (juice, seed oil and peel) and it was found that there was significant reduction in proliferation and invasiveness of cancer cells. Several effects were observed as disruption of cell cycle, induction of apoptosis, and ultimately inhibition of

tumor growth. Combination of *Punica granatum* extracts from various parts of fruit was found to be more effective than any single extract. The mechanism of anticancer activity was cleared as modulation of proteins regulating apoptosis. Pomegranate proved to be effective in prostate cancer, breast cancer, colon cancer, hepatocellular carcinoma, leukemia and chemotherapy induced toxicity (Jurjani, 2010; Manju *et al.,* 2014; Banerjee, *et al.,* 2011; Dahlawi, *et al.,* 2012; Cayir *et al.,* 2011).

Kheera (*Cucumis sativus* L.)

The MTT assay of the compound isolated from ethyl acetate fractions of *Cucumis sativus* L. flowers shows that all concentrations have anticancer activity. The sample concentrations of 1000µg/ml, 500 µg/ml, 250µg/ml, 125µg/ml and 62.5µg/ml show 82.15 µg/ml, 73.06 µg/ml, 69.74 µg/ml, 56.21 µg/ml and 49.83 µg/ml of CTC50 values against the human liver cancer HePG2 cell line respectively. These concentrations were able to induce apoptosis on human cancer cell lines and its anticancer activity was found to be precise (Muruganantham, *et al.,* 2016).

Cholai (*Amaranthus spinosus* L.)

The antitumor potential of *Amaranthus spinosus* L. was investigated against EAC bearing Swiss albino mice. The ethanol extract of its leaves was given orally to mice at the dose of 100 and 200 mg/kg body weight for 16 days. It exhibited decrease in tumor volume and viable cell count, while increase in mean survival time and non viable tumor cell count, when compared to the mice of the EAC control group. Restoration of hematological and biochemical parameters towards normal was also observed. The results suggest that the ethanol extract of *A. spinosus* leaves exhibits significant antitumor effects in EAC bearing mice (Joshua *et al.,* 2010).

Qisa (Kakri) (*Cucumis melo* L.)

Cucurbitacins are extremely oxygenated tetracyclic triterpenes, primarily establish in the cucurbitaceae family. Cucurbitacin B is an anticancer (oncogenic) agent naturally isolated from the stems of *C. melo*. In human leukemia cells, the anti-cancer activity of cucurbitacin B has been reported. Cucurbitacin B inhibits Raf/MEK/ERK and STAT 3 activation pathway in leukemia cell line K562. Cucurbitacin A along with cucurbitacin E also owns major anti-tumour activity (Chen, C. *et al.,* 2009).

Bathua (*Chenopodium album* L.)

The effects of *Chenopodium album* (leaves) was evaluated on the growth of estrogen dependent (MCF-7) and estrogen independent (MDA-MB-468)

human breast cancer cell lines. The different solvent extracts (petroleum ether, ethyl acetate and methanol) were assessed for their cytotoxicity using Trypan blue exclusion and MTT [3-(4, 5-dimethyl thiazol-2-yl)-2, 5-diphenyl tetrazolium] bioassay. Methanolic extract of *Chenopodium album* (leaves) exhibited maximum anti breast cancer activity having IC 50 value 27.31 mg/ml against MCF-7 cell line. Significant percent inhibition (94.06%) was recorded for MeOH extract of *Chenopodium album* (leaves) at 48 h of exposure and concentration 100 mg/ml ($p < 0.05$) against MCF-7 breast cancer cell line (Khoobchandani, *et al.,* 2009).

Kaddu (*Cucurbita maxima* Duchesne)

The MTT assay of the compound isolated from isolated ethyl acetate fraction of *Cucurbita maxima* flowers shows that all concentrations have anticancer activity. The sample concentration of 1000 µg/ml, 500µ/ml, 250µg/ml, 125µg/ml and 62.5µg/ml showed 72.05µg/ml, 68.94µg/ml, 54.22µg/ml, 43.19µg/ml and 37.80µg/ml of CTC50 (212µg/ml) value against the human cancer HePG2 cell line respectively (Murganathan, *et al.,* 2016).

Palak (*Spinacia oleracea* L.)

Ethanol extract of *S. oleracea* was evaluated for its anticancer activity against lung, cervix, bone, breast and liver cancer. The study has revealed that the ethanolic extract of *S. oleracea* has anti-cancer activity against lung and bone cancer (Murganatham *et al.,* 2016). Glycoglycerolipid fraction of *S. oleracea* can inhibit mammalian DNA polymerase activity, human cultured cancer cell growth, and *in-vivo* solid tumor proliferation with oral administration. This fraction could help to avoid cancer and be a functional food with anticancer activity (Maeda, *et al.,* 2008).

Khurfa (*Portulaca oleracea* L.)

Polysaccharides evidently scavenge the accumulation of free radicals and modulate immunity functions of rats with ovarian cancer (Chen, Y.G. *et al.,* 2009). Sulfated derivatives of POP, a water-soluble polysaccharide isolated from *Portulaca oleracea*, have a suppressive effect on the growth of HeLa and HepG2 cells in vitro, suggesting that the sulfation of POP increases the cytotoxicity in tumor cells (Chen, *et al.,* 2010).

Moong (*Vigna radiate* L.)

Moong beans have been found to exert antitumor effects through several different mechanisms. The recombinant plant nucleases R-TBN1 and R-HBN1, similar to nucleases derived from pine pollen and *Moong* beans, were found to be effective

against melanoma tumors and were about 10-times more potent than bovine seminal ribonuclease (RNase). Due to their relatively low cytotoxicity and high efficiency, these recombinant plant nucleases appear to be stable biochemical agents that can be targeted as potential antitumor cytostatics (Matousek, *et al.,* 2009). In addition, *Moong* beans have been found to exert antiproliferative effects, as examined by MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay using an *in-vitro* cell culture system. *Moong* beans exhibit dose-dependent antiproliferative effects against the tongue squamous cell carcinoma cell line CAL27 and several other cancer cell lines tested (i.e., DU145, SK-OV-3, MCF-7, and HL-60 cells) (Xu and Chang, 2012).

Gadhi ka Doodh (Donkey Milk)

Some donkey milk fractions are capable of stimulating the production of IL-2, IFN-g, IL-6, TNF-a and IL-1b cytokines. These cytokines are influential upon the anti-proliferation and differentiation of A549 tumour cells. Fraction-IV, a fraction of donkey whey protein of molecular mass higher than 10 kDa, exhibited strong anti-tumour activities against A 549 cells in a dose-dependent and time-dependent manner. It induced an accumulation of A549 cells in the G0/G1 and G2/M phases, indicating a potent cytotoxicity and causing cell death by apoptosis. Therefore, donkey milk whey protein, which possesses potent anti-proliferative activity, may have potential in the treatment of lung cancer (Xueying, 2009).

Mā' al-Jubn (Whey)

In a study, anti-proliferative activity of different milks, caseins and whey proteins was tested. Goat, cow, camel, sheep, mare and donkey milks and their casein and whey proteins were tested for cytotoxicity against MCF7 cells. All types of milk and the proteins were tested at different concentrations (0.5, 1 and 2 mg/ml). Mare, donkey, cow and camel milks showed dose-dependent cytotoxic activity against MCF7 cells while sheep and goat milks did not reveal any cytotoxic activity. The highest cytotoxic activity of the caseins was observed by mare milk casein followed by camel, donkey and cow. The results of whey proteins demonstrated that camel whey protein showed potent anticancer activity, while cow and donkey milks presented weak anticancer activity (Malihe, *et al.,* 2017).

Badam (*Prunus amygdalus* L.)

Protocatechuic acid is detected in nuts, such as almonds ordinary (*Prunus amygdalus* L.). Anticancer Activity: PCA seems to have chemopreventive potential because it inhibits the *in-vitro* chemical carcinogenesis and exerts

proapoptotic and antiproliferative effects in different tissues. The mechanism of the chemopreventive action of protocatechuic acid is mostly associated with antioxidant activity, including inhibition of generation as well as scavenging of free radicals and upregulating antioxidant enzymes. It influences phases 1 and 2 of the metabolism of certain carcinogens and perhaps directly blocks specific binding sites of ultimate carcinogens with DNA molecule, thus preventing adduct formation that may result in mutations and neoplastic transformation. Other biological aspects seem to have influence on the activity of inducible isoenzyme of cyclooxygenase and nitric oxide synthase, cell cycle regulating proteins, or inflammatory cytokines, which are involved in oncogenesis. Thus, PCA seems to have potential cancer chemopreventive properties (Sang *et al.,* 2002).

Conclusion

This review provides evidence-based scientific validation to some of the diet used for the prevention and management of cancer (*Saraṭān*). In classical Unani literature, cancer is a disease related to *Sawdā*' (black bile). The causes and development of cancer are multifactorial, i.e. excess production and abnormal changes that occur in *Sawdā*'. Cancer is a curable disease in most of the cases, if detected early. Unani physicians recommended *Uṣūl-i-'Ilāj* of cancer in successive steps, i.e. *Faṣd* (Venesection), *Tanqiya-i-Mawād* (Evacuation of morbid humor from the body with the help of *Munḍijāt-i-Sawdā*' (concoctives of black bile) and *Mushilāt-i-Sawdā*' (purgatives of black bile), *'Ilāj bi'l-Ghidhā*' (Dietotherapy), pain management and topical medication for cancer. The anti cancer activities of certain diets i.e. *Anar* (*Punica granatum* L.), *Kheera* (*Cucumis sativus* L.), *Cholai* (*Amaranthus spinosus* L.), *Kakri* (*Cucumis melo* L.), *Bathua* (*Chenopodium album* L.), *Palak* (*Spinacia oleracea* L.), *Qisa* (Kakri) (*Cucumis melo* L.), *Khurfa* (*Portulaca oleracea* L.), *Moong* (*Vigna radiate* L.), *Gadhi Ka Doodh* (Donkey milk), *Mā' al-Jubn* (Whey) and *Badam* (*Prunus amygdalus* L.) (Jurjani, 2010; Manju, *et al.,* 2014; Banerjee, *et al.,* 2011; Dahlawi, *et al.,* 2012; Cayır, *et al.,* 2011; Muruganantham, *et al.,* 2016; Chen, *et al.,* 2009; Khoobchandani, *et al.,* 2009; Chen, *et al.,* 2009; Matousek, *et al.,*2009; Xu and Chang, 2012; Xueying, 2009; Sang, *et al.,* 2002) have been validated scientifically and justify the claims as mentioned in classical Unani literature. It clearly reveals that diet plays an important role in the prevention and management of cancer. In view of this review article, further pre-clinical and clinical studies may be carried out for the development of new anticancer drugs with minimal toxic effects.

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सारांश

यूनानी चिकित्सा में कैंसर (सरतान) की रोकथाम और उपचार में आहार की भूमिका

***मुस्तेहसन, सोफ़िया नौशीन और माहे आलम**

कैंसर रोगों का एक समूह है जिसमें असामान्य कोशिका वृद्धि होती है जो शरीर के अन्य भागों में फैलने की क्षमता रखती है। संयुक्त राज्य अमेरिका में हृदय रोगों के बाद कैंसर मृत्यु का दूसरा सबसे आम कारण है। यूनानी क्लासिकी साहित्य के अनुसार कैंसर *सौदा* (काली पित्त) से संबंधित रोग है। कैंसर के कारण और वृद्धि बहु तथ्य हैं, अर्थात् अधिक उत्पत्ति और असामान्य परिवर्तन जो सौदा में होते हैं। यदि जल्दी पता चल जाए तो अधिकतर मामलों में कैंसर का उपचार संभव है। यूनानी चिकित्सकों ने अनुक्रमिक चरणों में कैंसर का *उसूल–ए–ईलाज* बताया है जो इस प्रकार हैः वेनिसेक्शन (फस्द), तनक़िया–ए–मवाद (मुन्ज़िजात–ए–सौदा और मुस्हिलात–ए–सौदा की सहायता से शरीर से रुग्ण ह्यूमर का निष्कासन), ईलाज बिल गिज़ा (आहार–चिकित्सा), पीड़ा उपचार और सामयिक दवाएं। कैंसर के उपचार और रोकथाम के लिए आहार जय्यिदुल कैमुस होने के साथ साथ लतीफ़ होना चाहिए तथा सौदा पैदा करने वाला नहीं होना चाहिए। इस समीक्षा पत्र में यूनानी क्लासिकल साहित्य में उल्लिखित कैंसर के उपचार में आहार की भूमिका पर विस्तार से चर्चा की जाएगी।

शब्दकुंजीः कैंसर, आहार–चिकित्सा, सरतान, सैदा

Pharmacological Actions and Therapeutic Benefits of *Bābūnah* (*Matricaria chamomilla* L.): A Review

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Abstract

Bābūnah (*Matricaria chamomilla* L.) is popularly known as chamomile in English, German and French languages. It is a well-known medicinal plant of Asteraceae family. Etymologically, the name of *Bābūnah* is derived from a place in Iraq where it was first discovered. There are many types of chamomile species out of which two varieties - German chamomile and Roman chamomile - are most commonly used. It has been preferred and much used medicinal plant in almost all the systems of medicine. Its multi-therapeutic, nutritional and cosmetic values have been established through years of traditional and scientific use and research. More than 120 constituents have been identified in chamomile flowers. In this paper, an attempt has been made to review the phytochemical studies, pharmacological actions, therapeutic uses and pharmacological studies for a comprehensive understanding of the importance of *Bābūnah* (*Matricaria chamomilla* L.).

Keywords: Anti-inflammatory, Analgesic, Aqueous extract, *Bābūnah,* Essential oil

Introduction

Bābūnah or chamomile (*Matricaria chamomilla L.*) is a well-known medicinal plant of the Asteraceae family and often referred to as the "star among medicinal species". It is grown in Iraq, Iran, Germany, Hungary, France, Russia and Brazil. It was introduced in India during the *Mughal* period. Now, it is grown in Delhi, Punjab, Uttar Pradesh, Maharashtra and Jammu and Kashmir. The plants can also be found in North Africa, Asia, North and South America, Australia, and New Zealand. Hungary is the main producer of the plant biomass. In Hungary, it also grows abundantly in poor soils and it is a source of income to the inhabitants of these areas. It often grows near roads, around landfills and in cultivated fields as a weed because the seeds require open soil to survive. In India, it is cultivated as a *Rabī'* season (winter) crop in plains and from April onwards in hills. It has been in use for medicinal purposes since long. It has *Muḥallil-i-Awrām* (Resolvent), *Dāfi'-i-Ta'affun* (Antiseptic), *Hāḍim* (Digestive), *Jādhib* (Absorbant), *Kāsir-i-Riyāḥ* (Carminative), *Muqawwī* (Tonic), *Muqawwī-i-Dimāgh* (Brain Tonic), *Muqawwī-*

Flower of *Bābūnah*

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i-Aʿṣāb (Nervine Tonic), *Muqawwī-i-Bāh* (Aphrodisiac), *Muqawwī-i-Baṣar* (Eye Tonic), *Mufattiḥ-i-Sudad* (Deobstruent), *Mufattit-i-Haṣāh* (Lithotriptic), *Muḥarrik* (Stimulant), *Muqawwi-i-Miʿda* (Stomachic), *Mudirr-i-Ḥayḍ* (Emmenogogue), *Mudirr-i-Bawl* (Diuretic), *Mudirr-i-Laban* (Galactogogue), *Mudirr-i-ʿAraq* (Diaphoratic), *Muqī* (Emetic) and *Musakkin-i-Alam* (Analgesic) properties.

It is used in *Ḥummā* (Fever), *Ḥudār* (Rheumatism), *ʿIrq al-Nasā* (Sciatica), *Ishāl* (Diarrhoea), *Mouch* (Sprain), *Niqris* (Gout), *Nazla wa Zukām* (Coryza and Catarrh), *Nuzūl al-Mā'* (Cataract), *Nafkh al-Shikam* (Flatulence), *Qulāʿ* (Stomatitis), *Jurūḥ* (Wound), *Qūlanj* (Colic), *Sūzāk* (Gonorrhea), *Suʿāl* (Cough), *ʿUsr-al-Ṭamth* (Dysmenorrhoe), *Waja' al-Mafāṣil* (Polyarthritis), *Waja' al-Zahr* (Backache), *Waram al-Khuṣyatayn* (Orchitis), *Waram al-Kabid* (Hepatitis), *Yaraqān* (Jaundice) and *Ḍīq al-Nafas* (Bronchial asthma) (Anonymous, 2007; Singh, *et al 2011*; Srivastava, *et al.*, 2010).

Vernacular Names

The plant is known by different names in different languages as given below:

Arabic	:	*Bābūnah, Zahr al-Malik*, *Bābūnj*
Catalan	:	Camamilla Comu, Camamilla De Ugel
English	:	German Chemomile, Persian Chemomile
French	:	Amarou, Chemomile, Chemomille Allemangne, Chemoimille Commune, Camomille Du Nord, Chamille, Malherbe, Mendiane
German	:	Feldkamille, Gelbermaiblume, Hearmelchen, Halmerl, Hameln, Hermligen, Hermuentzel, Hermmunel, Kamille, Karnille, Zauwith Kummerblume, Laugenblume, Magdblume, Mataronenkraut, Raimain, Remarian, Romein, Rome, Romey, Saekfit, Thamillen,
Gujrati	:	*Bābūnah*
Italian	:	Chamomilla Commune, Capomilla, Camamilla, Camomila
Maltese	:	Chamomille, Gowan, Camomilla, Camumilla
Naplese	:	Cambomilla
Norwegian	:	Kamille
Persian	:	*Bābūnah, Bābūnj*
Piedmontese	:	Amoreggiola, Camamia
Portuguese	:	Chemomillados Allemease

Basilicata	:	Cambomilla
Punjabi	:	*Bābūnah*, Suteigul
Romagnol	:	Camomilla, Crabumiglia
Sicilian	:	Clumidda
Spanish	:	Manzanilla Comun, Manzanillade Urgel
Swedish	:	Kamomil
Urdu	:	*Bābūnah*

(Ibn Baitar, 2006; Khan, 1273; Ghani, YNM; Kabiruddin, 2000; Hakeem, 2002; Kirtikar and Basu, 2005; Khare, 2007)

Description of the Plant as per Unani Classical Literature

Najmul Ghani in his book *Khazainul Advia* has mentioned three varieties of the plant as listed below:

i. White flowers with yellow in centre also known as *Karkāsh*

ii. Blue flowers

iii. Yellow flowers also known as *Rayḥān al-Thaʻālib*

On the basis of flowers of the plant, *Dioscorides* has also classified three types of chemomile plant.

Parts Used

Flowers and roots of the plant are mainly used for medicinal, cosmetic and nutritional purposes (Ghani, YNM; Kabiruddin, 2000; Hakeem, 2002; Kirtikar and Basu, 2005; Ibn Baitar, 2006; Khare, 2007).

Mizāj

Hot 1^0 and Dry 1^0	(Ghani, YNM - according to Ibn Sina)
Hot 2^0 and Dry 3^0	(Ghani, YNM - according to Jalinus)
Hot 2^0 and Dry 2^0	(Anonymous 2007; Kabiruddin, 2000)
Hot 2^0 and Dry 1^0	(Hakeem, 2002)
Hot 3^0 and Dry 3^0	(Ghulam, 2007)

Dose

Up to13 grams (Ghani, YNM)

1-3 grams (Kabiruddin, 2000)

5 grams (Anonymous, 2007)

Actions

Dāfi'-i-Ta'affun (Antiseptic)	Ghani, YNM
Hāḍim (Digestive)	Ghani, YNM; Kirtikar and Basu, 2005
Jādhib (Absorbant)	Ghani, YNM; Khan, 1273
Kāsir-i-Riyāḥ (Carminative)	Khan, 1273; Kirtikar and Basu, 2005; Kabiruddin, 2000; Ghani, YNM
Muḥallil-i-Awrām (Resolvent)	Hakeem, 2002; Ghani, YNM; Kabiruddin, 2000; Kirtikar and Basu, 2005; Jurjani, 1878; Khan, 1273; Khan, 1313
Mulaṭṭif (Demulcent)	Khan, 1273; Ghani, YNM; Ibn Baitar, 2006
Murkhī (Relaxant)	Ghani, YNM; Ibn Baitar, 2006
Musakhkhin (Calorific)	Ghani, YNM; Kabiruddin, 2000; Kirtikar and Basu, 2005; Nadkarni, 2007; Ibn Baitar, 2006
Muqawwī (Tonic)	Kirtikar and Basu, 2005
Muqawwī-i-Dimāgh (Brain Tonic)	Khan, 1273; Ghani, YNM; Kabiruddin, 2000; Hakeem, 2002; Kirtikar and Basu, 2005; Ibn Baitar, 2006
Muqawwī-i-A'ṣāb (Nervine Tonic)	Khan, 1273; Ghani, YNM; Hakeem, 2002; Nadkarni, 2007; Kabiruddin, 2000; Kirtikar and Basu, 2005; Ghulam, 2007
Muqawwī-i-Bāh (Aphrodisiac)	Khan,1273; Ghani, YNM; Kabiruddin, 2000; Kirtikar and Basu, 2005; Nadkarni, 2007; Ghulam, 2007
Muqawwī-i-Baṣar (Eye Tonic)	Ghani, YNM; Ghulam, 2007
Mufattiḥ-i-Sudad (Deobstruent)	Ghani, YNM; Hakeem, 2002
Mufattit-i-Ḥaṣāh (Lithotriptic)	Khan, 1273; Kabiruddin, 2000; Ghani, YNM
Muqawwī-i-Mi'da (Stomachic)	Ghani, YNM; Kirtikar and Basu, 2005
Mudirr-i-Ḥayḍ (Emmenogogue)	Khan, 1273; Ghani, YNM; Kabiruddin, 2000; Hakeem, 2002; Kirtikar and Basu, 2005; Ghulam, 2007
Mudirr-i-Laban (Galactogogue)	Hakeem, 2002; Ghulam, 2007
Mudirr-i-'Araq (Diaphoratic)	Khan, 1273; Hakeem, 2002; Ghulam, 2007
Muwallid-i-Laban (Galactopoietic)	Ghani, YNM; Ghulam, 2007

Mulayyin-i-Am'ā' (Laxative)	Khan, 1273; Ghani, YNM
Mudirr-i-Bawl (Diuretic)	Kabiruddin, 2000; Hakeem, 2002; Ghani, YNM; Kirtikar and Basu, 2005; Ghulam, 2007; Ibn Baitar, 2006
Munaqī-i-Badan	Ghani, YNM
Muqī (Emetic)	Ghani, YNM; Kabiruddin, 2000
Musakkin-i-Alam (Analgesic)	Kirtikar and Basu, 2005; Ghani, YNM; Kabiruddin, 2000; Ibn Baitar, 2006; Hussain, YNM
Muḥarrik (Stimulant)	Ghani, YNM; Kirtikar and Basu, 2005

Therapeutic Uses

Āshob-i-Chashm (Conjunctivitis)	Ibn Baitar, 2006; Khan,1273
Amrāḍ-i-Sar wa Dimāgh (Disease of head and brain)	Hakeem, 2002; Ghani, YNM; Kirtikar and Basu, 2005; Ibn Baitar, 2006
Waqr (Deafness)	Ghani, YNM; Ibn Baitar, 2006
Ṣudā' (Headache)	Khan, 1273; Ghani, YNM
Nār Fārsī (Eczema)	Nadkarni, 2007
Waja' al-Mi'da Riyāḥī (Gaseous Gastralgia)	Khan, 1273; Ghani, YNM
Ḥummā (Fever)	Khan, 1273; Ghani, YNM; Hakeem, 2002; Kirtikar and Basu, 2005
Ḥudār (Rheumatism)	Kirtikar and Basu, 2005; Nadarni,2007; Ghani, YNM
'Irq al-Nasā (Sciatica)	Ghani, YNM
Ishāl (Diarrhoea)	Ghani, YNM
Khārish (Itching)	Nadkarni, 2007
Mouch (Sprain)	Ghani, YNM
Niqris (Gout)	Ghani, YNM
Nazla wa Zukām (Coryza and Catarrh)	Khan,1273; Ghani, YNM
Nuzūl al-Mā' (Cataract)	Khan,1273; Ghulam, 2007; Ibn Baitar, 2006
Nafkh al-Shikam (Flatulence)	Khan, 1273; Ghani, YNM
Nāsūr (Fistula)	Nadkarni, 2007
Qulā' (Stomatitis)	Ghani, YNM; Hakeem, 2002

Qūlanj (Colic)	Khan,1273; Ibn Baitar, 2006; Ghani, YNM; Hakeem, 2002; Nadkarni, 2007
Sūzāk (Gonorrhea)	Kirtikar and Basu, 2005
Su'āl (Cough)	Ghani, YNM
'Usr al-Ṭamth (Dysmenorrhoe)	Nadkarni, 2007
Waja' al-Udhun (Otalgia)	Ghani,YNM; Hakeem,2002; Kirtikar and Basu,2005;Nadkarni,2007
Waja' al-Mafāṣil (Polyarthritis)	Ghani, YNM; Kabiruddin, 2000; Kirtikar and Basu, 2005; Kabiruddin, 2009
Waja' al-Zahr (Backache)	Ghani, YNM; Kirtikar and Basu, 2005
Waja' al-Mi'da (Gastralgia)	Kirtikar and Basu, 2005
Waram al-Khuṣyatayn (Orchitis)	Ghani, YNM
Waram al-Maq'ad (Proctitis)	Hakeem, 2002
Waram al-Kabid (Hepatitis)	Hakeem, 2002; Ghulam, 2007
Yaraqān (Jaundice)	Ghani, YNM; Kabiruddin, 2000; Nadkarni, 2007; Ghulam, 2007
Ḍīq al-Nafas (Bronchial asthma)	Ghulam, 2007
Jurūḥ (Wound)	Nadkarni, 2007

Botanical Description

Plant Description

Scientific Classification		
Kingdom	:	Plantae
Phylum	:	Antophyta
Order	:	Asterales
Family	:	Asteraceae
Genus	:	*Matricaria*
Species	:	*chamomilla*

True chamomile is an annual plant with thin spindle shaped roots only penetrating fitly into the soil. The branched stem is erect, heavily ramified. The long and narrow leaves are bi to tripinnate, fern like light green and feathery. The flowers, up to one inch across, have a hollow, cone-shaped receptacle, with tiny yellow disk flowers covering the cone. The cone is surrounded by 10 to 20 white, down-curving ray flowers, giving it the appearance of a miniature daisy. The dried flowers head are 3-5 mm in diameter; yellowish brown in color, pedencle is greenish, striated. The white strap shaped ligules are arranged in a single row on the periphery of the involucres of bracts. All the florets are borne on dark central conical receptacles (Sharafzadeh and Alizadeh, 2011; Anonymous, 2007; Kiritikar and Basu, 2005; Nadkarni, 2007).

Microscopic Examination

The receptacles in a longitudinal section show that it is hollow inside. The wall of the receptacle is quite thin and consists of elongated parenchymatous cells. The vascular strands run longitudinally, small cavities are observed at some places. Ligulate floret consists of an inferior appendage containing the ovary. The bracteole is thin papery, unevenly dissected into finger like projection at the ape. Androecium is absent. Gynoecium consists of an inferior, unilocular ovary containing a single basal ovule. The style is quite long and swollen near the base. The cells are thick walled in the swollen region. The stigma is bifid and protrudes out of the ligular tube. Two vascular strands run through the length of the style. The disc floret consists of separate inferior appendage containing ovary forming a neck. The stamens are born on corolla tube by curved filaments. The anthers are bilobed and terminate into conical structure. The structure of the gynoecium is same as in ligulate floret, except the swelling near the base which appears like a disc. Cross section of the peduncle shows a continuous band of 3-4 rows of chlorenchymatous cells. Vascular bundles are present below ridges portion. The epidermis is single layered followed by 2-3 layered hypodermis only in the ridge portions. No definite endodermis is distinguishable. The cells of the pith region are thin walled and large in size.

The powder is yellowish brown in colour. It is slightly bitter in taste and has its own characteristic aromatic odour. The powder under microscope shows an abundance of spherical pollen grains which show a spiny exine. The measure is 21-24.5 microns in diameter. Simple hairs and scales are seen amongst fragment of other floral appendages like corolla, stamens and style, etc. Isolated pitted xylem elements with reticulate thickenings are also seen (Sharafzadeh and Alizadeh, 2011; Anonymous, 2007).

Phytochemical Studies

Over 120 constituents have been identified in chamomile flowers. The main constituents of the oil include the terpenoids α-bisabolol and its oxides (≤ 78 %) and azulenes, including chamazulene (1-15 %). Chamazulene carboxylic acid and proazulenes occur in chamomile. Farnesene (12-28 %), spathulenol and spiroethers, including the cis/trans-en-yn-dicycloethers (8-20 %), are also present in the volatile oil. Eleven bioactive phenolic compounds (coumarins: herniarin, umbelliferone; phenylpropanoids: chlorogenic acid, caffeic acid; flavones: apigenin, apigenin- 7-O-glucoside, luteolin, luteolin-7-O-glucoside; flavonols: quercetin, rutin and flavanone: naringenin) are found in chamomile extract. The main constituents of the flowers include several phenolic compounds, primarily the flavonoids, apigenin, quercetin, patuletin, luteolin and their glucosides, coumarins and dicycloethers.

The principal components of the essential oil extracted from the flowers are the terpenoids alpha-bisabolol and its oxides and azulenes, including chamazulene. Chamomile (*Matricaria chamomilla*) in the above-ground organs synthesizes and accumulates (Z) - and (E)-2-beta-D:-glucopyranosyloxy-4-methoxy cinnamic acids (GMCA), the precursors of phytoanticipinherniarin (7-methoxycoumarin). The largest group of medically important compounds forming the essential oils are primarily chamazulene,(-)- alpha-bisabolol, bisabolol oxides, bisabolon oxide A, trans beta-farnesene, alpha-farnesene, spathulenol and the cis/trans-en-in-dicycloethers. Flavonoids, coumarins, mucilages, mono- and oligosaccharides also have pharmacological effects. Fractionation of the aqueous extract of this plant led to the detection of several fractions with significant affinity for the central benzodiazepine receptor and to the isolation and identification of 5, 7, 4'- trihydroxyflavone (apigenin) in one of them. The major flavonoids in the white florets of chamomile were rapidly purified using a combination of polyamide solid-phase extraction and preparative HPLC. From the combined LC/MS, LC/MS/MS, and NMR data the apigenin glucosides were identified as apigenin 7-Oglucoside (Ap-7-Glc), Ap-7-(6"-malonyl-Glc), Ap-7-(6"- acetyl-Glc), Ap-7-(6"-caffeoyl-Glc), Ap-7-(4"-acetyl-Glc), Ap-7-(4"-acetyl,6"-malonyl-Glc), and a partially characterized apigenin-7-(mono-acetyl/monomalonyl glucoside) isomer. (Yaguchi *et al.*,2009; Lis-Balchin *et al.*,1998; McKay *et al.*,2006; Schenck *et al.*,1956; Redaelli *et al.*,1981; Padula *et al.*,1976; Repcák *et al.*,2009; Ramadan *et al.*,2006; Mimica-Dukic *et al.*,1993; Pietta *et al.*,1987; Stanev *et al.*,1996; Pino *et al.*,2000; Schilcher *et al.*,1976).

Physicochemical Studies

Physical Constants	Values
Foreign matter	Not more than 2 %
Total Ash	Not more than 12 %
Acid-insoluble ash	Not more than 4 %
Alcohol-soluble extract	Not less than 64%
Water-soluble extract	Not less than 26 %

(Sharafzadeh and Alizadeh, 2011; Anonymous, 2007)

Pharmacological Studies

Anti-inflammatory Study

The flowers of chamomile contain 1–2% volatile oils including alpha-bisabolol, alpha bisabolol oxides A & B, and matricin (usually converted to chamazulene and other flavonoids which possess anti-inflammatory properties. A study in

human volunteers demonstrated that chamomile flavonoids and essential oils penetrate below the skin surface into the deeper skin layers. This is important for their use as topical anti-inflammatory agents. One of chamomile's anti-inflammatory activities involve the inhibition of LPS-induced prostaglandin E(2) release and attenuation of cyclooxygenase (COX-2) enzyme activity without affecting the constitutive form, COX-1 (Sakai, *et al.*, 2005; Pena, *et al.*, 2006; Merfort, *et al.*, 1994; Srivastava, *et al.*, 2009; Shipochliev, *et al.*, 1981).

The freeze-dried extract of chamomile was found to suppress both the inflammatory effect and the leukocyte infiltration. Chamomilla was assessed for its anti-inflammatory activity on intact rats by measuring the suppression of carrageenan induced paw edema produced by 1/10 of the intraperitoneal LD50 dose for 80% ethanol extract. Results showed that the plant possesses good anti-inflammatory activity (Shipochliev, *et al.*, 1981; Al-Hindawi, *et al.*, 1989).

Antimicrobial Study

Nogueira, *et al.* (2008) studied the essential oil of *Matricaria chamomilla* and found it active against 3 strains of *S. aureus* and Candida strains.

Acaricidal Study

Decoctions, infusions and macerates of dried flower heads of *Matricaria chamomilla* were tested *in vitro* against the mite *Psoroptes cuniculi Delafond* (Parasitiformes: Psoroptidae). This mite species is responsible for otoacariasis in domestic animals. Mites were exposed to the extracts for 24, 48 or 72 hours. All the extracts tested showed a highly significant acaricidal activity when compared to controls. Among them, a decoction of 10% was the only formulation which gave 100% activity at all the three observations (Macchioni, *et al.,* 2004)

Antihyperglycemic Study

Cemek, *et al.* (2008) studied that the ethanolic extract of *Matricaria chamomilla* protected the majority of the pancreatic islet cells with respect to the control group. As a result, *Matricaria chamomilla* ethanolic extract exhibited a significant antihyperglycemic effect and protected beta-cells in diabetic rats, in a dose-dependent manner and diminished the hyperglycemia-related oxidative stress.

Anticancerous Study

Most evaluations of tumor growth inhibition by chamomile involve studies with apigenin which is one of the bioactive constituents of chamomile. Studies on preclinical models of skin, prostate, breast and ovarian cancer have showed promising growth inhibitory effects (Way, *et al.*, 2004; Birt, *et al.*, 1997; Patel *et al.*, 2007; Gates, *et al.*, 2007). In a study by Srivastava, *et al.* (2007) chamomile

extracts showed to cause minimal growth inhibitory effects on normal cells, but showed significant reductions in cell viability in various human cancer cell lines. Chamomile exposure induced apoptosis in cancer cells but not in normal cells at similar doses.

Antihemorrhoids Study

Studies have suggested that chamomile ointment is beneficial in hemorrhoids. Tincture of chamomile was found effective for the management of hemorrhoids by Sitz bath. Tincture of chamomile also reduces inflammation associated with hemorrhoids (Misra, *et al.*, 2000).

Antianxiety and Seizure Study

Chamomile has been reported in the treatment of generalized anxiety disorder (GAD). But the reports seem contradictory as an earlier report suggests that German chamomile showed a significant inhibition of GAD activity (Awad, *et al.*, 2007). The recent results from the controlled clinical trial on chamomile extract for GAD suggest that it may have modest anxiolytic activity in patients with mild to moderate GAD (Amsterdam, *et al.*, 2009). Extracts of chamomile possess suitable effects on seizure induced by picrotoxin (Herdari, *et al.*, 2009). Furthermore, apigenin has shown to reduce the latency in the onset of picrotoxin-induced convulsions and reduction in locomotor activity but has not demonstrated any anxiolytic, myorelaxant or anticonvulsant activities (Herdari, *et al.*, 2009; Pinto, *et al.*, 2008).

Antidiabetic Study

Studies suggest that chamomile ameliorates hyperglycemia and diabetic complications by suppressing blood sugar levels, increasing liver glycogen storage and inhibition of sorbitol in the human erythrocytes (Kato, *et al.*, 2008).

The pharmacological activity of chamomile extract has shown to be independent of insulin secretion (Eddouks, *et al.*, 2005) and studies further reveal its protective effect on pancreatic beta cells in diminishing hyperglycemia-related oxidative stress (Cemek, *et al.*, 2008).

Anti-Sore Throat / Hoarseness Study

The efficacy of lubrication of the endo-tracheal tube cuff with chamomile before intubation on postoperative sore throat and hoarseness was determined in a randomized double-blind study. 161 patients as per American Society of Anesthesiologists (ASA) physical status was I or II, and undergoing elective surgical, orthopedic, gynecological or urological surgeries were divided in two groups. The study group received 10 puffs of chamomile extract (Kamillosan

M spray, total 370 mg of chamomile extract) at the site of the cuff of the endotracheal tube for lubrication while the control group did not receive any lubrication before intubation. Standard general anesthesia with tracheal intubations was given in both groups. 41 out of 81 patients (50.6%) in the chamomile group reported no postoperative sore throat in the post-anesthesia care unit as compared to 45 out of 80 patients (56.3%) in the control group (Kyokong, *et al.*, 2002).

Antipruritic Study

The single oral administration of the ethyl acetate extract or essential oil of German chamomile showed remarkable antipruritic effects in the compound 48/80-induced itch-scratching test in mice (Kobayashi, *et al.*, 2005).

Anti-Oral Mucositis Study

Methotrexate-induced oral mucositis in a patient with rheumatoid arthritis was successfully treated with chamomile mouthwashes and the result was significant (Mazokopakis, *et al.*, 2005).

Virucidal Study

Chamomile oil is used as virucidal agent for treatment of herpes genitalis (Nogueira, *et al.*, 2008).

Gastrointestinal Study

Chamomile is used traditionally for numerous gastrointestinal conditions, including digestive disorders, spasm or colic, flatulence (gas), ulcers and gastrointestinal irritation. Chamomile is especially helpful in dispelling gas, soothing the stomach and relaxing the muscles that move the food through the intestines (Khayyal, *et al.*, 2006; Kroll, *et al.*, 2006). Many Studies in preclinical models showed that chamomile inhibits *Helicobacter pylori,* the bacteria that can contribute to stomach ulcers. Chamomile is believed to be helpful in reducing smooth muscle spasms associated with various gastrointestinal inflammatory disorders (Wu, 2006; Weseler, *et al.*, 2005; Fugh, *et al.*, 2002).

Wound Healing Study

The efficacy of topical use of chamomile to enhance wound healing was evaluated in a double-blind trial on 14 patients who underwent derm abrasion of tattoos. The effects on drying and epithelialization were observed and chamomile was found statistically significant in producing wound drying and speeding epithelialization (Glowania, *et al.*, 1987). Antimicrobial activity of the extract against various microorganisms was also assessed. The test group, on

day 15, exhibited a greater reduction in the wound area when compared to the control. The increased rate of wound contraction, together with the increased wound-breaking strength, hydroxyproline content and histological observations support the use of *Matricaria recutita* in wound management (Nayak, *et al.*, 2007). Jarrahi, *et al* in 2008 suggested that chamomile caused complete wound healing faster than corticosteroids.

The chamomile extract in the form of rubbing oil had a good potential for acceleration of burn wound healing in rats. The extract of *Matricaria chamomilla* administered topically had wound healing potential in linear incisional wound model in rats. Animals treated with chamomile presented significantly faster wound healing effect as compared to those treated with corticosteroids (Izumi, *et al.*, 1999; Nayak, *et al.*, 2007; Jarrahi, *et al.*, 2008).

Conclusion

Ethanolic extract of *Matricaria chamomilla* exhibited a significant antihyperglycemic effect and protected beta-cells in diabetic rats in a dose-dependent manner and diminished the hyperglycemia-related oxidative stress. It also showed significant reductions in cell viability in various human cancer cell lines. Chamomile exposure induced apoptosis in cancer cells but not in normal cells at similar doses. Tincture of chamomile also reduces inflammation associated with hemorrhoids. And also, it may have modest anxiolytic activity in patients with mild to moderate generalized anxiety disorder. Besides, *Matricaria chamomilla* is beneficial for anti-sore throat, antipruritic, anti-oral mucositis, virucidal and wound healing.

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सारांश

बाबूना (मैट्रिकेरिया कैमोमिला एल.) के औषधीय कार्य और चिकित्सीय लाभ : एक समीक्षा

***शमीम, अमानुल्लाह और साद अहमद**

बाबूना (मैट्रिकेरिया कैमोमिला एल.) को अंग्रेजी, जर्मन और फ्रैंच भाषाओं में कैमोमाइल के नाम से जाना जाता है। यह एस्टरेसिया परिवार का एक प्रसिद्ध पौधा है। *बाबूना* का नाम ईराक के एक स्थान के नाम पर है जहां पहली बार इसकी खोज हुई थी। कैमोमाइल प्रजातियां कई प्रकार की हैं जिनमें से दो प्रजातियां अर्थात् जर्मन कैमोमाइल और रोमन कैमोमाइल सबसे अधिक उपयोग की जाती हैं। यह लगभग सभी चिकित्सा पद्धतियों में अधिक उपयोग किया जाने वाला औषधीय पादप है। इसके बहु–चिकित्सीय, पोषण और कॉस्मेटिक मूल्य वर्षों के पारंपरिक तथा वैज्ञानिक उपयोग और अनुसंधान से स्थापित हैं। कैमोमाइल के फूलों में 120 से अधिक घटकों की पहचान की गई है। इस शोध पत्र में *बाबूना* (मैट्रिकेरिया कैमोमिला एल.) के महत्व को व्यापक रूप से समझने के लिए फाइटोकेमिकल अध्ययन, औषधीय कार्य, चिकित्सीय उपयोग और औषधीय अध्ययन की समीक्षा करने का प्रयास किया गया है।

शब्दकुंजी: एंटी–इंन्फ्लामेट्री, एनाल्जेसिक, जलीय अर्क, *बाबूना*, गंध तेल

Khabasul Hadeed (Iron Rust): An Important Mineral Drug of Unani Medicine for the Management of Hematopoietic Disorders Especially Anaemia

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Abstract

Khabasul Hadeed (Iron rust) is a mineral drug used in different dosage forms in Unani Medicine and claimed to be effective in the management of hematopoietic disorders. This paper especially reviews the role of *Khabasul Hadeed* in the management of hematopoietic disorders (anaemia) as mentioned in Unani literature. The result of review reveals that *Khabasul Hadeed* as such and as an ingredient in various formulations has been used for the treatment of anaemia since ancient times by the practitioners of traditional medicine. Literature of Unani Medicine clearly indicates that *Khabasul Hadeed* and its different formulations are safe and have hematopoietic effect. Sufficient information in respect of morphological, physicochemical and ethnomedicinal properties of *Khabasul Hadeed* are available but a very few pharmacological and clinical studies have been conducted. Modern scientific reports, though scarce, also suggest the possibility of such hematological effects of this drug.

Keywords: Anaemia, Iron rust, *Khabasul Hadeed*, Mineral drug

Introduction

Unani Medicine uses three natural sources of drugs, i.e. plants, animal products and minerals, in different dosage forms. Individual natural drugs and their products have been comprehensively documented in traditional as well as scientific literature for their healing properties (Ahsan and Zafar, 2012; Makbul, *et al.*, 2017).

The use of metals in medicinal preparations is common in Unani Medicine. Minerals formed an important part of the Egyptian and Mesopotamian Materia Medica and acted as an active component in many effective remedies (Vohora and Athar, 2008). Some allopathic formulations also contain metals like cisplatin, carboplatin, colloidal gold, silver sulphadizine (Silvadane) and ferrous gluconate for different therapeutic purposes (Nagarajan, *et al.*, 2014). The medicinal use of mineral origin drugs, methods of their purification and the pharmacological properties have been mentioned by many eminent scholars in their books (Hafeez, 2010; Kabiruddin, 2011).

The survey of Unani literature shows that *Khabasul Hadeed* (Iron rust) has a long history of use as an important drug for the treatment of hematopoietic disorders including anaemia. Chemically, *Khabasul Hadeed* is Ferrosoferric oxide, commonly known as iron rust. It is also known as impure oxide of iron, magnetic iron oxide and magnetite. It consists of small particles of iron scattered round the blacksmith's anvil which on exposure to air becomes rusty (Anonymous, YNM and Nadkarni, 2010). In Unani Medicine, a particle

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which during beating of metals scatters as a forge scale is known as *Khabs* (rust). For iron, it is known as *Khabasul Hadeed*, which is driest of all rusts (Ibn Baitar, 1999; Hakim, 2002; Ghani, 2011). *Khabasul Hadeed* as a single drug in powder form or in combination with other drugs has been widely used in Unani Medicine for treating blood disorders, viz. anaemia. It is also an important ingredient of several formulations, viz. *Kushta Khabasul Hadeed, Habb-e- Khabasul Hadeed* (Said, 1997), *Majoon Fanjanoosh* (Kabiruddin, 2006), *Majoon Khabasul Hadeed* (Anonymous, 1986), *Majoon Bawaseer* (Usmani, 2008), *Majoon Murraweh-ul-Arwah* (Said, 1997), *Jawarish Khabasul Hadeed* (Kabiruddin, 2006), *Safuf Khabasul Hadeed*, *Safuf Fauladi, Sanoon Chob Chini* (Usmani, 2008), *Arq-e-Khabasul Hadeed* (Kareem, YNM) *Dolabi, Anushdaru* (Kabir, 2003), *Dawa-i-Atiya Allah* (Ibn Sina, 2006), *Habb-e Sandaroos* (Anonymous, 2007), *Itrifal Khabasul-Hadeed* (Anonymous, 2007), *Jawarish Khuzi* (Anonymous, 2006), *Majoon Muqawwi Mi'da* (Anonymous, 2008), *Qurs Salajit* (Anonymous, 2008), *Sufuf Khabasul-Hadeed Mujarrab* (Khan, 1996) and *Hamool Muqawwi Reham* (Anonymous, 2006). Since literature available on this important drug is very scant, therefore, in the present paper an attempt has been made to compile the available information on *Khabasul Hadeed* and its different formulations so as to bring to light the therapeutic potential of this lesser known drug.

Methodology

A review of literature on *Khabasul Hadeed* was done using the bibliographic database, viz. PubMed, Google Scholar, Science Direct, Scopus and other internet sources. The search was conducted using the terms '*Khabasul Hadeed*', 'Iron rust', 'Ferrosoferric oxide', 'impure oxide of iron', 'Magnetic iron oxide', 'Magnetite' 'Majoon *Khabasul Hadeed*', 'Arq-e-*Khabasul Hadeed* 'and '*Kushta Khabasul Hadeed*'. Further classical books published in Urdu and English were used to compile the information.

Description of *Khabasul Hadeed* in Ancient Literature

According to Hakim Muhammad Azam Khan, in Persian *Khabasul Hadeed* (Iron oxide) is known as *Noosh, Charak Aahan* and *Reem Aahan*. In *Sheeraji*, it is called as *Ramah* and in Hindi it is known as *lohe ka mail* (dust of iron) and *Keet*. The standard *Khabasul Hadeed* is the dust which is obtained from melted iron, consisting of purified, uniform in size, soft and fine particles. According to Sheikh, this *Khabasul Hadeed* is of the driest nature (Khan, 1996). *Khabasul Hadeed* is not used as drug in natural state; rather it is first detoxified and powdered or converted into *Kushta* (calx) before consumption. According to Hakim Karim Bakhsh, after detoxification, *Khabasul Hadeed* is also used in the preparation of certain *Majoon* viz. *Majoon Khabasul Hadeed*, also called *Majoon Fanjnosh*. It is used for debility of stomach, liver, anaemia, ascites and piles. It

is also recommended for aphrodisiac effect, bleeding disorders and incontinence of urine. *Khabasul Hadeed* is also called *Aab-e-Hayat*. *Khabasul Hadeed* can well substitute Faulad (iron) products in case of the latter's unavailability (Kareem, YNM).

Hakim Najmul Ghani and Hakim Karim Bakhsh mention that *Khabasul Hadeed* used for the preparation of *Kushta Khabasul Hadeed* should be *sadsala* (hundred years old) for best therapeutic uses (Ghani, 2011; Kareem, YNM)).

Ethnomedicinal Uses of *Khabasul Hadeed*

Khabasul Hadeed has been used as a haemopoetic agent and to treat anaemia and bleeding disorder, viz. dysmenorrhea, menorrhagia, piles, haemoptysis and melena (Ghani, 2011). Ibn Baitar (1197–1248 CE) wrote that Galen (129–200 CE) claimed it to be a tested (Mujarrab) drug in treating otorrhoea. Ibn Baitar (1197–1248 CE) also wrote that Ibn Sina claimed it to be a tested (Mujarrab) drug in treating menorrhagia, polyurea and for increasing the tone of rectal sphincter. *Khabasul Hadeed / Mandura* is especially useful in anaemia, amenorrhea, dysmenorrhea, menorrhagia, chlorosis, diarrhoea, chronic bowel complaints, dyspepsia, intestinal worms and nervous diseases, neuralgia of the 5^{th} nerve due to debility, kidney diseases, albuminuria, etc. (Nadkarni, 2010). The efficacy of *Khabasul Hadeed* in case of polyurea has also been proved and *Kohl* (*Surma*) of *Khabasul Hadeed* is useful in dryness of eyelids while ear drops prepared from *Khabasul Hadeed* is used for cleaning ear wax (Khan, 2013). The uses and indications of *Kushta Khabasul Hadeed* are mentioned in Hamdard Pharmacopoeia, National Formulary of Unani Medicine and other renowned Unani pharmacopoeias as stomachic and liver tonic, haematogogue, curative for debility of liver and stomach and for treating anaemia.

Properties of *Khabasul Hadeed* in Unani Medicine

a. Mizaj (Temperament)

Temperament of *Khabasul Hadeed* has been described to be *Har* and *Yabis* (Hot & Dry) in third degree (Khan, 2013). According to another statement, the temperament of *Khabasul Hadeed* has been described to be *Har* and *Yabis* (Hot in second degree and Dry in third degree) (Khan, 2013).

b. Pharmacological Actions

Mujaffif (Desiccant), *Habisuddam* (Styptic), *Muqawwi-e-Mi'da, Muqawwi-e-Jigar, Muqawwi-e-Tihaal, Muqawwi-e-Qalb* and *Muqawwi-e-Dimagh* (Ghani, 2011).

c. Therapeutic Uses

Khabasul Hadeed is used after making it *Maghsool* (washing) and *Mudabbar* (detoxified). It is used in *Zofe-Meda, Zofe-Jigar*, ascites, spleenomegaly and piles. *Khabasul Hadeed* is especially used in anaemia, dysmenorrhea, menorrhagia, chlorosis, dyspepsia, intestinal worms, kidney diseases and albuminuria (Ghani, 2011; Khan, 2013). Mamoon recommends its use as a tested (*Mujarrab)* drug for strengthening the functions of stomach, liver, heart and brain. *Khabasul Hadeed* with *Trikattu* is a household remedy, commonly used as an alternative tonic in the pregnant state (Jeelani, 2017).

d. Substitute

Abdal-e-Advia (substitution of drugs) is one of the important principles that governs the rules pertaining to drug substitution. In case of non-availability of a drug like *Khabasul Hadeed,* Unani scholars have suggested substitutes of this drug namely *Hurf* (*Lepidium sativum*) and other Unani scholars have suggested that substitute of *Maghsool Khabasul Hadeed* is *Itrifal Sagheer* (a Unani semisolid dosage form) (Khan, 2013).

e. Adverse Effects

Some of the drugs having pharmacological activity may also produce toxic effect by their inherent nature. In order to optimize their therapeutic effect, such agents are subjected to certain corrective measures (*Islah-e-Advia*) as described in Unani literature. Thus, the drug is partially modified through specific corrective procedures (*Amal-e-Tadbeer*) to reduce its toxicity. In case application of corrective measures on the drug is not possible, another drug which serves as a corrective agent (*Musleh*) is either admixed or used concomitantly with the first drug for minimizing its undesirable effects. Most of the Unani products are prepared with basic and adjuvant constituents; the adjuvant is meant to act as *Musleh* (corrective agent) of basic drug (Ghani, 2011). *Khabasul Hadeed* has been described as being harmful to lungs. *Kateera* (Tragacanth gum) and honey are used as corrective agents to reduce its harmful effect on lungs (Khan, 2013). The corrective agents are supposed to modify the *Mizaj* of *Khabasul Hadeed* to reduce its untoward effects on lungs. Since it possesses hot and dry temperament in third degree, therefore its desiccative property is reduced by combining it with honey or *Kateera.*

f. Dosage

In powder form (of crude drug), it is used in the dose of 1 gm (Khan, 2013), while in the form of *Kushta* (a fine powder form of a drug preparation

obtained by calcining the metals, minerals or drugs of animal origin), it is commonly used in the dose of 125mg twice a day with water (Anonymous, 2008).

g. Advantages of Compound Formulation of *Khabasul Hadeed*

A well-prepared *Kushta* from the drug offers many advantages over plant medicines due to its longer shelf life, lesser dose, easy storability and better palatability (Aziz, *et al.,* 2002; Khan, 1995).

Commonly Used Formulations of *Khabasul Hadeed* in Unani Medicine

Kushta (solid), *Majoon* (semi solid) and *Arq* (liquid) are three important formulations of *Khabasul Hadeed*. Since *Khabasul Hadeed* is a metalloid origin drug, therefore it is preferred to be used in calcined form. The *Kushta* (calx) is prepared by heating *Khabasul Hadeed* at a high temperature to oxidize it. The crude drug is however pretreated with some catalytic agents (particular herbal extract/juice) to make it more efficacious. *Kushta Khabasul Hadeed* possesses hematopoietic and styptic properties. It is used for the treatment of anaemia (Vohora and Athar, 2008).

The toxicity of the metallic constituents is removed by consecutive heat and cold cycles in oil, buttermilk, cow's urine and herbal decoctions, etc. (Nagarajan, *et al.,* 2014). *Kushta* is also prepared as a herbo-mineral preparation, and in this case different herbs or their extracts are mixed with minerals, before, during or after the process of calcination. These metals in combination with the constituents of medicinal herbs are said to form an effective combination useful in the management of diseases. The calcined form has certain advantages over non-calcined form. The dissolution rate of *Kushta* is high, therefore it is readily distributed in the body. It is more potent and quicker in action. Its magnitude of effect and the intensity of biological activities are greater than any other dosage forms used in Unani Medicine (Aziz, *et al.,* 2002).

Before making the *Kushta* form of *Khabasul Hadeed* (Table 1), it should be cleaned and purified. After this, the drug will be ground in pestle and mortar with the specified juices of the known drugs as mentioned in National Formulary of Unani Medicine (Anonymous, 2008) for a specified period of time. Then small cakes of varying sizes and thickness, depending on the nature of the drugs, are made. These are dried well in the shade and put in earthen bowel and then covered by a process known as *Gil-e-Hikmat* (application of specific semi solid materials all around the junction point of the brim of bowels to make it air proof), followed by drying the whole preparation. A particular size pit is dug in an open space to accommodate the vessel for preparation of the calx. Half the pit is filled with the cow dung cakes, then the *Boota* is placed in the pit and

Table 1: Ingredients of *Kushta Khabasul Hadeed*

Unani name	Botanical/Scientific name	Family	Parts used	Quantity (g/ml)
Khabasul Hadeed	*Iron oxide*	-	rust	250
Sirka desi	*Vinegar*	-		500
Triphala	*Emblica officinallis* Gaerth. *Terminalia belerica* Gaerth. *Terminalia chebula* Retz.	*Euphorbiaceae* *Combretaceae* *Combretaceae*	*Fruit* *Fruit* *Fruit*	250
Kakronda Booti	*Blumea balsamifera* (L) DC.	*Asteraceae*	*Booti*	250
Aabe Gheekwar	*Aloe barbadensis* Mill.	*Asphodelaceae*	*Juice*	250

heated by igniting the cakes. After the calcination is over, the pit is allowed to cool completely, the apparatus is removed and the contents are taken out. These contents thus obtained are again powdered with specified juices as many times as prescribed in the text, till the proper fineness and the quality is obtained.

Preparation of *Kushta Khabasul Hadeed*: Small cakes of iron oxide are placed on red hot coal. When they turn very hot, they are transferred with a pair of tongs in to a vessel containing vinegar. It is then separated from vinegar, ground and triturated in the *Triphala* water till all its water content dries up. Now, the iron oxide tablets weighing 10 gm each are dried in Pyrex flask or subjected to *Gil-e-Hikmat* and heated in a pit containing 10 kg of the cow dung cakes which are set on fire. The flask is taken out when all the cow dung cakes have completely burnt out. Then after triturating with *Blumea balsamifera*, it is made in to cakes and heated on 10 kg of the cow dung cakes. On cooling, the metallic oxide is taken out, triturated in the *Aloe barbadensis* juice and heated on 10 kg of the cow dung cakes. The *Kushta* when turns brick red in colour is sieved and preserved in a bottle (Anonymous, 2008; Said, 1997).

Majoon (Confection) is a semisolid preparation made by mixing *Safuf* (powder) of the drug ingredients in *Qiwam* (base, made of purified honey or sugar). The weight of sugar taken to make the *Qiwam* is two to three times of the total weight of powdered ingredients (Kabiruddin, 1938; Said, 1997).

For the preparation of *Majoon Khabasul Hadeed* (Table 2), the powder of Ferric oxide or iron rust is first heated on a cooker heated on burning coal and abruptly cooled in vinegar or in an infusion containing equal weights of *Emblica officinalis*, *Terminalia belerica*, and *Terminalia chebula* (*Aab-e-Triphala*) the procedure is repeated for seven days. The processed or treated iron oxide is added to the safuf of the dry ingredients obtained by grinding and then sieving through 80 no. mesh, after soaking the powder in ghee. The safuf is gradually

Table 2: Ingredients of *Majoon Khabasul Hadeed*

Unani name	Botanical/Scientific name	Family	Parts used	Quantity (g/ml)
Khabasul Hadeed Muddabar	*Proceesed ferric oxide*	-	*rust*	*50*
Balcharr	*Valeriana officinalis* Lin.	*Valerianaceae*	*Root*	*50*
Ab-e-Triphala	*Emblica officinallis* Gaerth.	*Euphorbiaceae*	*Fruit*	*50*
	Terminalia belerica Gaerth.	*Combretaceae*	*Fruit*	*50*
	Terminalia chebula Retz.	*Combretaceae*	*Fruit*	*50*
Pipal Kalan	*Piper longum* L.	*Piperaceae*	*Fruit*	*50*
Soya	*Anethum sowa* Roxb.	*Apiaceae*	*Seeds*	*20*
Gandana	*Nigella sativa* L.	*Ranunculaceae*	*Seeds*	*20*
Chita lakri	*Plumbago zeylanica* L.	*Plumbaginaceae*	*Woods*	*50*
Sonth	*Zingiber officinallis* Roscoe.	Zingiberaceae	Root	50
Sadkofi	*Cyperus scariosus* Roxb.	Cyperaceae	Root	50
Filfil-i-siyah	*Piper nigrum* L.	*Piperaceae*	Fruit	50
Ghee	-	-	-	50
White sugar	-	-	-	1000

added to a solution/base of sugar which has a specified viscosity. While adding, the solution is continuously stirred so as to mix the contents homogenously. The product is stored in a glass container. The dose of *Majoon Khabasul Hadeed* is 3-5g orally in the morning with 250 ml of yogurt. Its uses and indications are styptic for bleeding piles, stomachic, liver tonic, digestive and appetizing (Kabiruddin, 1938; Said, 1997).

Arq (aqua) is a distillate obtained from one or more medicinal ingredients with or without previous dilution with water. An aqua necessarily, however, postulates the condensations of vapours. *Arq* is a liquid dosage form of Unani system of medicine (Said, 1997). *Arq* of *Khabasul Hadeed* is made from old iron rust powder mixed with two parts of distilled vinegar. The mixture is poured into a clay pot which in turn stands on an iron pot dipped in sand up to a height of four fingers. After heating it on flame for 48 hours, the mixture is filtrated. This procedure is repeated three times in the same manner and the final filterate is known as *Arq-e-Khabasul Hadeed* (Kareem, YNM).

Morphological, Physicochemical and Clinical Studies on *Khabasul Hadeed*

Balasubramaniam, *et al.* (2003) carried out a study on characterization of rust on ancient Indian iron. Rust is a reddish-brown corrosion product of iron consisting of several different constituents. Hydrous ferrous oxide ($FeO.nH_2O$) or ferrous

hydroxide Fe $(OH)_2$ is the first diffusion-barrier layer formed on the surface. As the pH of saturated Fe $(OH)_2$ is about 9.5, the surface of such corroded iron is always alkaline. At the outer surface of the layer, access to dissolved oxygen converts ferrous oxide to hydrous ferric oxide or ferric hydroxide (Balasubramaniam, et al., 2016).

Rehman, et al. (2016) carried out a clinical study of *Qurse Kushta Khabsul Hadeed* and *Habbe Marvareed* in the management of *Sailan al-Rahim* (Leucorrhoea). Two important pharmacological compound drugs, viz. *Qurse Kushta Khabsal-Hadeed* and *Habbe Marvareed* have been described to be effective and used in the management of leucorrhoea since long time. A total of 58 cases of fertile age group (13-45 years) diagnosed to be afflicted with leucorrhoea were studied. It was found that out of 58 cases, 36 cases were relieved, 17 partially relieved, while no response was recorded in 05 cases. The drugs were found safe on biochemical and hematological parameters (Rehman et al., 2016).

Akhtar *et al.* (2013) studied the effect of *Majoon Khabsul Hadeed* on GI bleeding disorders. The constituents of this formulation are *Khabsul Hadeed Mudabbar*, *Oud*, *Saad Kufi, Zanjabeel, Filfil Siyah*, *Ajwain Desi*, *Izkhar*, *Halila Siyah* and *Halila Zard*. In combination, these constituents impart the drug haemopoietic, anti-ulcerative, ulcer healing, styptic, astringent, anthelmintic and laxative effects. These medicinal properties of *Majoon Khabsul Hadeed* make it useful not only in bleeding hemorrhoids but in all bleeding conditions of gastrointestinal tract (Akhtar et al., 2013).

Akhtar *et al.* (2011) carried out a study on efficacy of *Majoon Khabsul Hadeed in Faqruddam ba Sabab-e-Qillat-e-Faulad* (iron deficiency anaemia/ microcytic-hypochromic anaemia). Significant improvement in symptoms & signs and laboratory findings of the disorder was observed. The formulation was found effective in *Faqruddam ba Sabab-e-Qillat-e-Faulad*, especially improved PCV, MCV and serum iron.

In Unani System of Medicine, many formulations are prescribed for the management of anaemia, like *Majoon Khabsul Hadeed*, *Sharbat-e-Faulad, Kushta Faulad, Sayyal-e-Faulad*, etc. The researchers concluded that *Majoon Khabsul Hadeed* not only provides iron supplement, but also manages most of the etiologies of *Faqruddam ba Sabab-e-Qillat-e-Faulad* (iron deficiency/microcytic-hypochromic anaemia) (Akhtar et al., 2011).

Jeelani et al. (2017) carried out a study on efficacy of *Safuf Khabsul Hadeed* in iron deficiency anaemia during pregnancy. Results in both groups were highly significant ($p < 0.001$). Better improvement in peripheral smear was observed in control group than test group. No significant improvement in subjective parameters was observed in either group (Jeelani et al., 2017).

Pharmacological Studies on *Khabasul Hadeed*

Somani, *et al.* (2012) carried out a study on prokinetic effect of herbomineral Unani formulation *Dolabi* in diabetic rats. *Dolabi* exerts its prokinetic effect by reducing oxidative stress and therefore can be used as a drug for treating diabetic patients with gastrointestinal impairments. Mechanism underlying the action of *Dolabi* on impaired gastric motility may be neuronal dependent and its antioxidant activity may play an important role. Their data strongly revealed that *Dolabi* exerts a prokinetic action on gastric emptying and intestinal transit in diabetic rats. The study also suggests that antioxidant property of *Dolabi* may be responsible for halting progressive changes of chronic diabetes leading to gastric impairment (Somani, *et al., 2012)*.

Conclusion

Most of the available reports suggest that *Khabsul Hadeed* and its compound formulations possess haemopoietic, astringent and styptic property. Elemental analysis of *Khabsul Hadeed* demonstrated that iron oxide contains iron, which is responsible to maintain serum iron level, normalize the haemopoiesis in the bone marrow and maintain blood level in the body (Vohora, 1983). It is suggested that *Khabsul Hadeed* is very useful in anaemia as well as in bleeding disorders. Most of the studies conducted so far on the formulations are also suggestive of their haemopoietic potential. However, few studies have certain technical, methodological and design related issues. Therefore, before drawing definitive conclusions, it would be prudent to attempt further confirmatory experimental and clinical studies in order to ascertain the efficacy and safety of *Khabasul Hadeed* and its multidrug formulations.

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सारांश

ख़बसुल हदीद (आयरन रस्ट): रक्तोपादक विकारों विशेष रूप से एनीमिया के उपचार हेतु यूनानी चिकित्सा की एक महत्वपूर्ण खनिज औषधि

***हक़ीक़ अहमद, अब्दुल वदूद, ग़ुलामुद्दीन सोफ़ी और मुदस्सिर ख़ज़ीर**

ख़बसुल हदीद (आयरन रस्ट) एक खनिज औषधि है जिसका उपयोग यूनानी चिकित्सा पद्धति में विभिन्न खुराक रूपों में किया जाता है और जिसे रक्तोपादक विकारों के उपचार में प्रभावी बताया जाता है। यह पेपर विशेष रूप से यूनानी साहित्य में उल्लिखित रक्तोपादक विकारों (एनीमिया) के उपचार में ख़बसुल हदीद की भूमिका की समीक्षा करता है। समीक्षा के परिणाम से पता चलता है कि ख़बसुल हदीद का अलग से तथा विभिन्न मिश्रणों में एक घटक रूप में उपयोग पारंपरिक चिकित्सा के चिकित्सकों द्वारा प्राचीन काल से एनीमिया के उपचार के लिए किया जाता रहा है। यूनानी चिकित्सा का साहित्य स्पष्ट रूप से बताता है कि ख़बसुल हदीद और इसके विभिन्न मिश्रण सुरक्षित हैं और रक्तोपादक विकारों पर प्रभाव डालते हैं। ख़बसुल हदीद के मोरफोलोजिकल, फिज़ीकोकेमिकल और एथनोमेडिसिनल गुणों के संबंध में पर्याप्त जानकारी उपलब्ध है परन्तु औषधीय और नैदानिक अध्ययन बहुत कम किए गए हैं। आधुनिक वैज्ञानिक रिपोर्ट हालांकि दुर्लभ हैं, लेकिन इस औषधि के रक्तोपादक प्रभावों की संभावना का सुझाव देती हैं।

शब्दकुंजी: एनिमिया, आयरन रस्ट, ख़बसुल हदीद, खनिज औषधि

Antimicrobial Studies of *Ocimum Basilicum* L. Seeds against Urinary Tract Infection Causing Organisms

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Abstract

The genus *Ocimum* possesses several species of plants which are distributed throughout the tropical regions of Asia, Africa and South America. *Ocimum basilicum* L. is a popular culinary plant known as *Tiruniruppaccai, Tiruneetruppachcilai* in Tamil, Sweet basil in English, *Sabzah, Babuli, Jangli Tulsi* in Hindi and *Faranjmusk, Firanjmishk* in Urdu. The plant produces oval shaped black coloured seeds which swells up and produces a gelatinous mass when soaked in water. The seeds are used prevalently all over the world as flavouring agent in the preparation of soups, beverages (*Sharbat*), in making ice desserts like Falooda, etc. The seeds, apart from its culinary usage, have a long history of folklore claims, but their health effects have been tested in very few studies. Hence, the present study aimed to explore the antimicrobial property of the basil seeds against few pathogenic organisms that cause urinary tract infection (UTI) in human beings. The ethanol extract of *Ocimum basilicum* seeds was studied for its potency against certain UTI causing organisms namely *Escherichia coli, Staphylococcus* spp., *Klebsiella spp., Pseudomonas spp.*, *Proteus spp.* and the yeast *Candida albicans*. The obtained results revealed that the seeds of *Ocimum basilicum* have a significant effect on most of the organisms tested and could be concluded that the seeds can be taken as herbal drug at the time of UTI by people of all age groups. The study drug also validates the claims of ancient Unani physicians about its beneficial effects on symptoms of UTI, viz. micturition, dysuria, diuresis, etc.

Keywords: Antimicrobial Activity, *Firanjmishk*, *Ocimum basilicum* L., Urinary Tract Infection

Introduction

The genus *Ocimum* consists of 30 to 160 species and is distributed throughout the tropical regions of Asia, Africa, Central and South America (Amal, *et al.*, 2018). *Ocimum basilicum* L., also called great basil or Saint Joseph's wort, is a culinary herb of the family Lamiaceae (Simon, *et al.*, 1999). The seeds are black in colour with oval shape which swell up and produce gelatinous mass when soaked in water due to the presence of polysaccharide layer on its outer epidermis. The seeds are powerhouse of nutrition and are enriched with proteins, essential fats, fibres, minerals, magnesium, zinc, etc. (Mathews, *et al.,* 1993). In many parts of Asia, the seeds are used frequently in soups, meat products as a flavouring agent, in traditional beverages (*Sharbat*) and in making several varieties of ice desserts like *Falooda* (Masooma, *et al*, 2017). It is also used in Traditional Medicine in treatment of dyspepsia, ulcer, diarrhoea

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and other illnesses (Marwat, *et al.,* 2011). The seeds contain amazing medicinal properties like antioxidant, antimicrobial and mosquito repellent activities and radio productive effects (Alcicek, *et al.*, 2004). The seeds are enriched with various chemical constituents such as monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpene hydrocarbon, triterpene, flavonoids and aromatic compounds.

Urinary tract infection (UTI) is an infection in any part of the urinary system, i.e. kidney, ureters, bladder and urethra. Most infections involve the lower urinary tract, the bladder and the urethra (Ranganathan, 2014). Each type of UTI may result in specific signs and symptoms, depending on which part of urinary tract is infected (Werner, 2017). Women are at the greater risk and are more prone to develop UTI frequently than men. The infection is usually caused due to bacteria. Among the bacterial species, *Escherichia coli* accounts for nearly 80% to 85% followed by *Staphylococcus* species for 10% to 15%. In addition, bacterial species like *Klebsiella, Pseudomonas*, *Proteus* species and the yeast *Candida albicans* also play a minor role in causing infection (Sangwan, 2008; Batra, 2018; Friedrich, 2018). The present study aimed to explore the antimicrobial property of the basil seeds against few pathogenic organisms that cause UTI in human beings.

Materials and Methods

(A) *Ocimum basilicum* Vernacular and Regional Names

Arabic	:	*Raihan, Tukhm-i-Raihan*
English	:	*Basil, Common Basil, Sweet Basil*
Hindi	:	*Sabzah, Babuli, Jangli Tulsi*
Kannada	:	*Sabja Gida, Sajjebiya*
Malayalam	:	*Pach-cha Pushpam*
Marathi	:	*Bhumy Tulas, Sabja, Sabji*
Sanskrit	:	*Ajagandhika, Ajaka, Surabhi*
Tamil	:	*Tiruniruppaccai, Tiruneetruppachcilai*
Telugu	:	*Bhoo Tulsi, Sabja, Vipoodipathri*
Urdu	:	*Faranjmusk, Firanjmishk*

(B) Collection of *Ocimum basilicum* Seeds

Fresh seeds of *Ocimum basilicum* were purchased from local market of Chennai, Tamil Nadu. The collected seeds were authenticated at the Drug Standardization

Research Unit (DSRU) (Pharmacognosy Section) and the voucher specimens were deposited in the raw drug museum at DSRU, RRIUM Chennai.

(C) Collection of Urine Test Samples and UTI Isolates

During the month of Dec 2018 to Jan 2019, 50 urine samples were collected from Public Health Centre, Chennai with prior need for isolation of urinary tract infection causing organism such as *Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Pseudomonas aeruginosa, Proteus vulgaris* and the yeast *Candida albicans*.

All the above organisms were isolated from the urine samples and confirmed using staining techniques and specific biochemical test at DSRU (Microbiology Section) (Mackie & MacCartney, 1996).

(D) Extraction of *Ocimum basilicum* Seeds

For the performance of antibacterial activity studies, the ethanol extract of *Ocimum basilicum* was utilized. The extraction work and other related chemistry parameters were performed at DSRU (Chemistry Section).

The dried commercially purchased seeds of *Ocimum basilicum* (10g) were coarsely powdered, soaked in the aspirated bottle with ethanol (100 ml) by cold percolation method for 48h (AOAC, 2005). The filtrate were collected and evaporated for complete dryness. The required quantity of extract was then dissolved in required quantity of dimethyl sulphoxide (DMSO) for further antimicrobial studies.

(E) Antimicrobial Assay and Detection of Minimum Inhibitory Concentration

The *in-vitro* antimicrobial activity test and MIC of ethanol extract of *Ocimum basilicum* seeds were performed by cup plate method as per standard methods (IP, 1996).

The required amount of Muller Hinton agar plates were prepared and swabbed with different isolates of lag phase cultures of UTI organisms isolated from urine samples of patients having UTI. The plates were allowed to stand for few minutes. Required number of 6 mm diameter wells was made over the plates at an equidistant position. Each well was loaded with 60 µl of drug (*Ocimum basilicum* - seeds - ethanol extract) at an increasing concentration ranging from 250 mg/ml, 125 mg/ml, 62.5 mg/ml, 31.25 mg/ml, 15.62 mg/ml, 7.8 mg/ml, 3.9 mg/ml, 1.9 mg/ml, 0.97 mg/ml, 0.48 mg/ml, 0.2 mg/ml, 0.12 mg/ml, 0.06 mg/ml and 0.03 mg/ml. The ampicillin disc (10mcg) was used as standard for comparison. The plates were all kept at 37° C for 24 hours. The zone of inhibition was measured. The MIC was also determined to find the

lowest concentration of the drug required to completely inhibit the growth of the organisms (Mackie & MacCartney, 1996).

Results and Discussions

1. Collection of *Ocimum basilicum* Seeds

The fresh seeds of *Ocimum basilicum* were purchased from local market, Chennai, Tamil Nadu. The voucher specimen number obtained is S042. Fig. 1

Fig. 1: *Ocimum basilicum* Seeeds

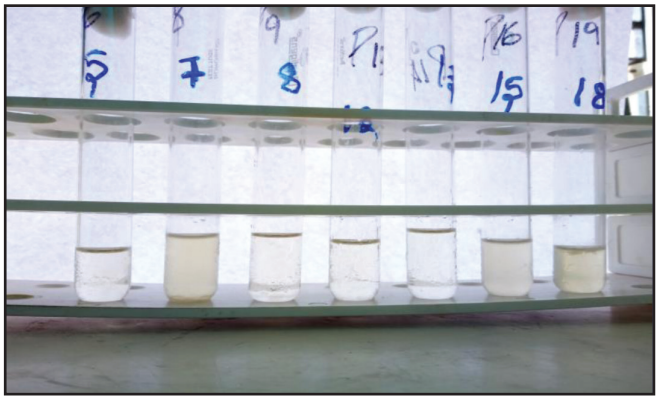
2. Collection of Urine Test Samples and UTI Isolates

The list of various UTI organisms isolated from randomly selected urine samples were tabulated (Table 1, Fig. 2). The organisms were confirmed using the staining techniques and biochemical reactions.

3. Extraction of *Ocimum basilicum* Seeds

The yield obtained for ethanol extract is 1.73 grams.

Fig. 2: Urine Sample



Growth of UTI Test Organisms in Nutrient Broth

Table 1: List of Various UTI Organisms Isolated

S.No.	Samples Collected From	Organisms Isolated
1.	Public Health Centre, Chennai	*Escherichia coli* – I
2.		*Escherichia coli* – II
3.		*Klebsiella pneumonia* – I
4.		*Staphylococcus aureus* – I
5.		*Staphylococcus aureus* – II
6.		*Pseudomonas aerugonisa* – I
7.		*Pseudomonas aeruginosa* – II
8.		*Proteus vulgaris* – I
9.		*Proteus vulgaris* – II
10.		*Candida albicans* – I
11.		*Candida albicans* – II

4. Antimicrobial Assay and Detection of Minimum Inhibitory Concentration

The results obtained is tabulated in Table 2, Fig. 3. The antimicrobial activity of ethanol extracts of *Ocimum basilicum* seeds against urinary tract infection causing organisms namely *Escherichia coli* I and II, *Klebsiella pneumonia* I, *Staphylococcus aureus* I and II, *Pseudomonas aerugonisa* I and II, *Proteus vulgaris* I and II and the yeast *Candida albicans* I and II were tested. Each well was loaded with 60 µl of increasing concentration ranging from 250mg/ml, 125mg/ml, 62.5mg/ml, 31.25mg/ml, 15.62mg/ml, 7.8mg/ml, 3.9mg/ml, 1.9mg/ml, 0.97mg/ml, 0.48mg/ml, 0.2mg/ml, 0.12mg/ml, 0.06mg/ml and 0.03mg/ml.

The results revealed that the ethanol extract of *Ocimum basilicum* seeds had a significant effect on most of the organisms tested. The diameter of zone ranged from 8mm to 25mm. The maximum sensitivity was exhibited by *Klebsiella pneumonia organisms, Escherichia coli* and *Candida albicans*. With respect to *Escherichia coli,* different strains exhibited different types of sensitivity pattern. Minimum inhibition was seen against all the tested organisms of *Pseudomonas aeruginosa* and *Proteus vulgaris*. Most of the tested strains of *Candida albicans* and *Klebsiella pneumonia* exhibited good zone of inhibition. Therefore, in this study, it is clear that the chemical composition of the *Ocimum basilicum* seeds has good antimicrobial effect on organisms causing urinary tract infection.

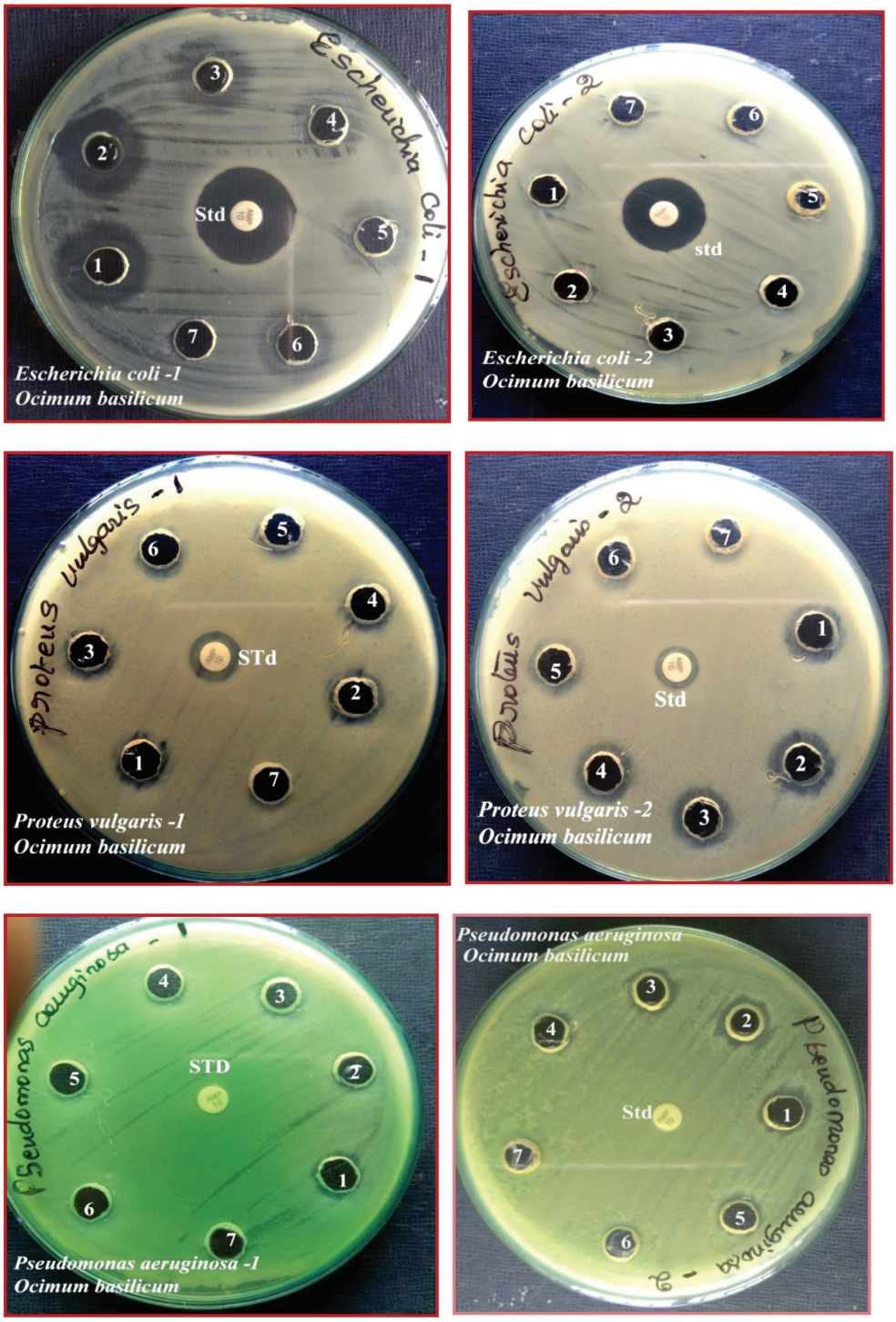
Drug Concentration

250mg/ml, 125mg/ml, 62.5mg/ml, 31.25mg/ml, 15.62mg/ml, 7.8mg/ml, 3.9mg/ml, 1.9mg/ml, 0.97mg/ml, 0.48mg/ml, 0.2mg/ml, 0.12mg/ml, 0.06mg/ml and 0.03mg/ml.

Table 2: Antimicrobial Assay and Detection of Minimum Inhibitory Concentration

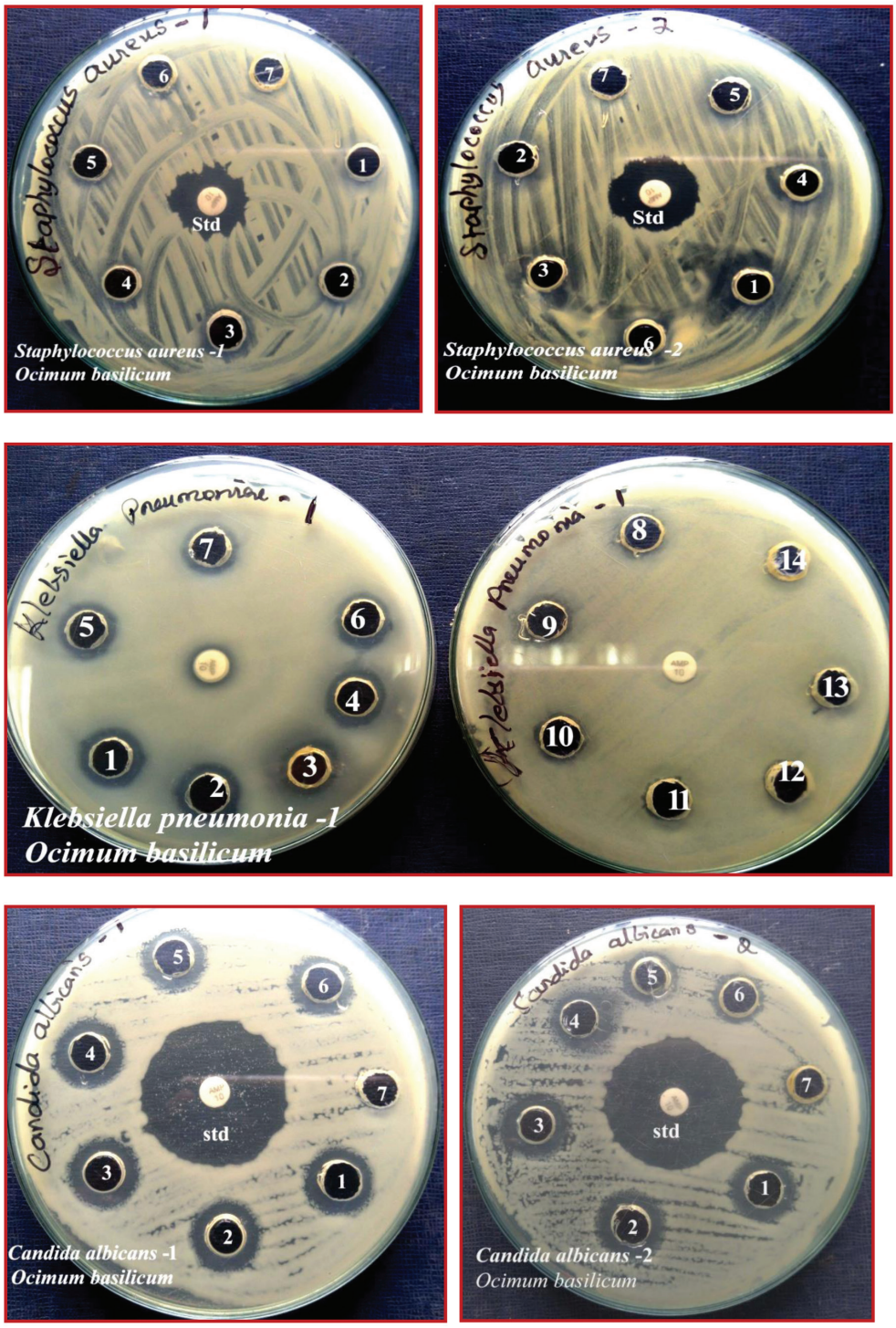
S.No.	Organism	Zone Diameter in MM														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	S
1.	*Escherichia coli – I*	25	23	20	13	12	11	-	-	-	-	-	-	-	-	+
2.	*Escherichia coli – II*	-	-	--	-	-	-	-	-	-	-	-	-	-	-	+
3.	*Klebsiella pneumonia – I*	19	18	17	15	14	12	11	-	-	-	-	-	-	-	-
4.	*Staphylococcus aureus – I*	13	12	11	9	7	-	-	-	-	-	-	-	-	-	+
5.	*Staphylococcus aureus – II*	17	15	13	12	12	8	-	-	-	-	-	-	-	-	+
6.	*Pseudomonas aerugonisa – I*	11	10	8	-	-	-	-	-	-	-	-	-	-	-	-
7.	*Pseudomonas aeruginosa – II*	15	13	12	9	-	-	-	-	-	-	-	-	-	-	-
8.	*Proteus vulgaris – I*	13	12	11	9	-	-	-	-	-	-	-	-	-	-	-
9.	*Proteus vulgaris – II*	15	14	13	9	7	-	-	-	-	-	-	-	-	-	-
10.	*Candida albicans – I*	22	21	20	15	13	12	-	-	-	-	-	-	-	-	+
11.	*Candida albicans – II*	20	19	18	15	13	11	-	-	-	-	-	-	-	-	+
S - Ampicillin Standard 10mcg/disc Well Concentration 60µl																

Fig. 3: Antimicrobial Activity of *Ocimum basilicum* Against UTI Organisms



Conclusion

The seeds of *Ocimum basilicum,* the culinary herb, are widely used as a beverage during summer season as a refrigerant and exhilarant. The study revealed that the drug possesses antimicrobial property in assessing the growth of organisms



that most frequently cause UTI. It is observed that the seeds are particularly effective in combating acute infections caused due to *Klebsiella pneumoniae* and *Candida albicans*, while in case of other suspected organisms it may be used as adjuvant along with other conventional drugs for desired results. The study drug also validates the claims of ancient Unani physicians as to its beneficial effects on symptoms of UTI.

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सारांश

यूरिनरी ट्रेक्ट इन्फेक्शन (मूत्र पथ संक्रमण) कारक जीवों के विरुद्ध *ओसीमम बेसिलिकम* एल. के बीज का सूक्ष्मजीवीरोधी अध्ययन

***पी मीरा देवी श्री, रामप्रताप मीणा, एस मागेश्वरी, मुर्गेश्वरन आर और एन ज़हीर अहमद**

ओसीमम जाति में पौधों की कई प्रजातियां हैं जो एशिया, अफ्रीका और दक्षिण अमेरिका के उष्णकटिबंधीय क्षेत्रों में पाये जाते हैं। *ऑसीमम बेसिलिकम* एल. एक लोकप्रिय रसोई पौधा है जिसे तमिल में तिरूनिपाकाई और तिरुणीतृप्पच्किलाई, अंग्रेज़ी में स्वीट बासिल, हिन्दी में सब्ज़ा, बाबूली, जंगली तुलसी और उर्दू में फरंजमुस्क, फ़िरंजमिश्क कहा जाता है। यह पौधा अंडाकार के काले रंग के बीज पैदा करता है जो पानी में भिगोने से फूल जाता है और एक जिलेटिन द्रव्यमान बन जाता है। इस के बीज दुनिया भर में सूप, पेय पदार्थ (शरबत) और फालूदा आदि बनाने में स्वाद देने वाले पदार्थ के रूप में उपयोग किये जाते हैं। रसोई में उपयोग के अलावा इस के बीज के लोक दावों का एक लंबा इतिहास है लेकिन इनके स्वास्थ्य प्रभावों का बहुत कम अध्ययनों में परीक्षण किया गया है। इसलिए कुछ रोगजनक जीवों के विरुद्ध जो मानव में मूत्र पथ के संक्रमण का कारण बनते हैं, तुलसी के बीज के रोगाणुरोधी गुण का पता लगाने के लिए वर्तमान अध्य्यन किया गया। प्राप्त परिणामों से तुलसी के बीजों का परीक्षण किए गए अधिकांश जीवों पर महत्पूर्ण प्रभाव का पता लगा जिस से यह निष्कर्ष निकाला जा सकता है कि सभी आयु वर्ग के लोग मूत्र पथ संक्रमण में हर्बल औषधि के रूप में तुलसी के बीज का सेवन कर सकते हैं। यह अध्ययन मूत्र पथ संक्रमण के लक्षण अर्थात् पेशाब का बारबार आना, पेशाब में जलन, अधिक पेशाब होना पर इसके लाभकारी प्रभावों के बारे में प्राचीन यूनानी चिकित्सकों के दावे को भी मान्य ठहराता है।

शब्दकुंजी: रोगाणुरोधी गतिविधि, फरंजमूस्क, *ओसीमम बेसिलिकम* एल., मूत्र पथ संक्रमण

Effect of Unani Pharmacopoeial Formulation *'Araq-i-'Ajīb* in Cases of *Ṣudā'* (Headache): A Preliminary Study

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Abstract

'Araq-i-'Ajīb is a Unani pharmacopoeial drug used frequently in Unani Medicine to treat many ailments. It has three ingredients; *Kāfūr*, *Jauhar-i-Pudīna* and *Jauhar-i-Ajwāyin*. The present study was carried out to evaluate the safety and efficacy of *'Araq-i-'Ajīb* in the patients of *Ṣudā'* (headache). In this study, *'Araq-i-'Ajīb* (liquid) was applied locally in quantity sufficient twice a day for seven days. The safety was assessed clinically on day 3 and 7 of the treatment. No adverse effect was recorded in the CRF and laboratory (biochemical and pathological) parameters done at the baseline and end of the study. The efficacy was assessed by measuring the reduction in the signs and symptoms associated with headache. *'Araq-i-'Ajīb* significantly reduced the associated symptoms of headache like headache (52.01%,), disturbed concentration (39.45%), irritability (47.32%), difficulty in falling asleep and staying asleep (35.14%). Severity of the disease was evaluated with the visual analogue scale (VAS). The present study advocates that *'Araq-i-'Ajīb* is a safe drug in the given dosage level and has a potency to treat headache. It is also useful in alleviating sign and symptoms associated with headache.

Keywords: Analgesic, *'Araq-i-'Ajīb*, Headache, Unani Medicine

Introduction

Ṣudā' (headache) is defined as a pain arising from the head or upper neck of the body. Frequent headaches can affect relationships and employment. There is also an increased risk of depression in those with severe headaches (Samarqandi, *et al.*, 2009). The pain originates from the tissues and structures that surround the brain because the brain itself has no nerves that give rise to the sensation of pain (pain fibres). The periosteum that surrounds bones; muscles that encase the skull, sinuses, eyes and ears; meninges that cover the surface of the brain and spinal cord, arteries, veins and nerves; all can become inflamed or irritated to cause the headache. This pain may be a dull ache, sharp, throbbing, constant, mild, or intense (Bennett and Plum, 1996; Edlow *et al.*, 2008).

Based upon the aetiology of the disease, headache has been classified into primary and secondary headache. Primary headaches include migraine, tension and cluster headaches as well as a variety of other less common types of headaches. Primary headaches account for more than 90% of all headache complaints, and of these, episodic tension-type headache is most common (Davidson, 1999; Kumar and Clark, 1998; Bennett and Plum, 1996; David and Daniel, 2003).

Tension headaches are the most common type of primary headache. Tension headaches occur more commonly among women than men. According to the

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World Health Organization, 1 in 20 people in the developed world suffers from a daily tension headache. Associated symptoms of tension headaches include headache upon awakening, difficulty in falling asleep and staying asleep, chronic fatigue, irritability, disturbed concentration, mild sensitivity to light or noise, and general muscle aching (Davidson, 1999; Kumar and Clark, 1998; Bennett and Plum, 1996; David and Daniel, 2003).

Chronic tension headaches (occur more than 15 days per month): Pain may vary in intensity throughout the day, but the pain is almost always present. Pain affects the front, top or sides of the head. Pain comes and goes over a prolonged period of time. There may be general muscle aching (Davidson, 1999; Kumar and Clark, 1998; Bennett and Plum, 1996; David and Daniel, 2003).

Cluster headache is an intense one-sided pain described as having a burning or piercing quality that is throbbing or constant. Pain is located behind one eye or in the eye region, without changing sides. Pain lasts a short time, generally 30 to 90 minutes (but can last for three hours); the headache disappears only to recur later that day (most sufferers get one to three headaches per day during a cluster period). Headaches occur very regularly, generally at the same time each day, and they often awakens the person at the same time during the night (Davidson, 1999; Kumar and Clark, 1998; Bennett and Plum, 1996; David and Daniel, 2003).

Sinus headache is characterized by deep and constant pain in the cheekbones, forehead or bridge of the nose. The pain usually intensifies with sudden head movement or straining and usually occurs with other sinus symptoms, such as nasal discharge, feeling of fullness in the ears, fever, and facial swelling. There may be mild to severe pain in head or head and neck but no neck stiffness and recurrent headache (Davidson, 1999; Kumar and Clark, 1998; Bennett and Plum, 1996; David and Daniel, 2003).

Migraine headaches are the second most common type of primary headache. It is estimated that women are three times more prone than men to suffer from migraines. Also, the prevalence of this particular type of headache seems to vary depending on the specific area of the world where one lives. However, migraines appear to be experienced by 12% to 18% of the population. Migraine headaches affect children as well as adults. Before puberty, boys and girls are affected equally by migraine headaches, but after puberty, more women than men are affected. It is estimated that 6% of men and up to 18% of women will experience a migraine headache in their lifetime. The symptoms of migraine headaches can occur in various combinations and include moderate to severe pain (often described as pounding, throbbing pain) that can affect the whole head, or can shift from one side of the head to the other, sensitivity to light, noise or odours, blurred vision, nausea or vomiting, stomach upset, abdominal

pain, loss of appetite, sensations of being very warm or cold, paleness, fatigue, dizziness, fever (rare), headache with aura, bright flashing dots or lights, blind spots, and wavy or jagged lines (aura) (Davidson, 1999; Kumar and Clark, 1998; Bennett and Plum, 1996; David and Daniel, 2003; Khan, 2011).

According to the literature of Unani Medicine, *Ṣudā'* (headache) is the pain felt in the structure of head up to neck (Samarqandi, *et al.*, 2009; Azam, *et al.*, 2015). As per patho-physiology and aetiology of the disease, *Ṣudā'* (headache) has been divided into *Ṣudā' Sādhij* (primary headache) where simple change in the temperament of the organ leads to *Ṣudā'* (headache), whereas in case of *Ṣudā' Māddī*, there is quantitative or qualitative change in the *Akhlāṭ* (humours) of the organ leading to *Ṣudā'* (headache). According to the types of predominant *Kayfiyāt* (qualities) and *Akhlāṭ*, *Ṣudā'* (headache) has been further divided into several types. Similarly, according to the origin of the cause of *Ṣudā'* (headache), it has been further divided into *Ṣudā' Aṣlī* (when aetiology lies within the parts of head / pathology originates from the parts of head) and *Ṣudā' Shirkī* (secondary headache) wherein *Ṣudā'* (headache) arises due to pathologies of other organs (Khan, 2002; Azam, *et al.*, 2015). Another classification of *Ṣudā'* (headache) is based on the site and extent of pain. Accordingly, *Ṣudā'* (headache) is named *Bayḍa-o-Khūdha* when the pain involves whole head, while if the pain is localised in either halves of the head, it is named as *Shaqīqa* (migraine) (Khan, 2002; Tabari, 1995; Qumri, 2008; Azam, *et al.*, 2015). In case of *Ṣudā'* (headache), pain may lead to certain other symptoms which include disturbed concentration, irritability, decreased appetite, fatigue, difficulty in falling asleep and staying asleep, and mild sensitivity to light / noise (Khan, 2011; Arzani, YNM; Azam, *et al.*, 2015).

In cases of *Ṣudā' Sādhij* (primary headache), as there is no involvement of *Akhlāṭ*, the disease may be managed by applying principles of *Ta'dīl-i-Mizāj* and *Taskīn* either under regimenal therapy or pharmacotherapy. The principles of treatment of *Ṣudā' Māddī* (headache due to involvement of *Akhlāṭ* (humours) include *Nuḍj* and *Tanqīya* (concoction and evacuation). Similarly, in case of *Ṣudā' Shirkī* (secondary headache), removal of the cause will relieve the *Ṣudā'* (headache) (Qumri, 2008; Arzani, YNM; Mujeeb, *et al.*, 2015; Kabiruddin, 1925; Rahman, *et al.*, 2015).

Study Objectives

1. To assess the safety of Unani pharmacopoeial formulation *'Araq-i-'Ajīb* for symptomatic relief the in patients of *Ṣudā'* (headache)
2. To assess the efficacy of Unani pharmacopoeial formulation *'Araq-i-'Ajīb* for symptomatic relief in patients of *Ṣudā'* (headache)

Methodology

The study drug *'Araq-i-'Ajīb* was procured from the Central Research Institute of Unani Medicine, Hyderabad. Composition of *'Araq-i-'Ajīb* is given in Table 1. It was an open-label clinical preliminary study conducted at Regional Research Institute of Unani Medicine (RRIUM), Patna.

Table 1: Formulation of *'Araq-i-'Ajīb* (Anonymous, 2006).

S.No.	Unani Name	Botanical Name	Weight
1.	*Kafūr*	*Cinnamomumcamphora* Nees & Eberm.	20 g
2.	*Jauhar-i-Pudīna*	*Mentha arvensis* L.	20 g
3.	*Jauhar-i-Ajwāyin*	*Trachyspermumammi* (L.) Sprague	10 g

Place of Study

The present open label study was carried out at RRIUM, Patna. The Institutional Ethics Committee of RRIUM Patna granted ethical clearance to the study in its meeting held on March 10, 2014.

Patient Selection

Patients from the GOPD at RRIUM, Patna were screened for the study and selected on the basis of inclusion and exclusion criteria given below:

Inclusion Criteria

1. Patients of either sex in the age group of 18-65 years
2. Patient presenting with onset of *Ṣudā'* (headache) with or without any of the symptoms like disturbed concentration, irritability, *Ḍu'f al-Ishtihā'* (decreased appetite), *I'yā'* (fatigue), difficulty in falling asleep and staying asleep, mild sensitivity to light / noise

Exclusion Criteria

1. Patients of headache not responded to standard therapy
2. Headache accompanied by impaired neurological functions (loss of balance, weakness, numbness, or speech disturbances), double vision, seizures, mental disturbances, and loss of consciousness
3. Headache accompanied by persistent nausea, vomiting, fever and stiff neck
4. History of recent head injury
5. Known cases of any other acute illness

6. Known cases of severe renal / hepatic / cardiac ailments

7. Pregnant and lactating women

Diagnostic Criteria

Each case was diagnosed on the basis of sign and symptoms and with the help of history in respect of selected patients, i.e. previous similar episode, physical and systemic examinations.

Dosage Schedule and Mode of Administration

All the patients were selected as per inclusion and exclusion criteria of *Ṣudā'* (headache). Unani pharmacopoeial Drug *'Araq-i-'Ajīb* (liquid) was applied locally twice a day in quantity sufficient on the forehead for seven consecutive days. No concomitant treatment was given.

Safety Assessment

The safety was monitored on the basis of the laboratory investigations CBC (Hb%, TLC, DLC, ESR), LFT (S. Bilirubin, SGOT, SGPT, S. Alkaline Phosphatase), KFT (S. Urea, S. Creatinine, Uric acid) and Urine R/M done at baseline and at the end of the study. 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 effects of the Unani pharmacopoeial drug *'Araq-i-'Ajīb* were observed during the course of study and at the end of the study. The drug was found safe in the patients of *Ṣudā'*.

Efficacy Assessment

The patients were assessed clinically on day 3 and 7 of the treatment and the efficacy of the Unani pharmacopoeial drug *'Araq-i-'Ajīb* was evaluated on the basis of reduction in the sign and symptoms as mentioned in the CRF. 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 analysed using Friedman post-hoc test and Student's paired 't' test. Results were expressed as the Mean ± SEM. $P<0.05$ has been considered as statistically significant and $p<0.001$ has been considered as statistically highly significant.

Result and Discussion

In the present study, it was found that maximum incidence 45.45% of the disease was in the age group of 18-30 years and they all were females. The incidence of the disease was also high (31.82%) in the age group of 31-40 years. In this age group, only two (4.54%) patients were male. It was also found that out of 44 patients, 05 (11.36%) patients were male while 39 (88.64%) patients were female (Results are depicted in Table 2).

The prevalence of the disease *Ṣudā'* (headache) was found more (54.55%) in the *Balghamī Mizāj* patients than *Damwī* (38.64%) and *Ṣafrāwī* (6.82%). No patient of *Sawdāwī Mizāj* was found in the study (Results are depicted in Table 3).

In the present study, 6.82% of the patients showed very good response and 61.36% showed good response, while 31.82% patients showed poor response. No patient showed excellent response to the drug (Results are depicted in Table 4).

In the present study, the efficacy of *'Araq-i-'Ajīb* was evaluated over a period of seven days on the basis of improvement in subjective parameters. Significant improvement was reported in headache (52.01%,), disturbed concentration

Table 2: Distribution of Patients According to Age and Sex

Age Group (Years)	Sex		Total
	Male	Female	
	Number & Percentage of Males	Number & Percentage of Females	Total (Percentage)
18-30	-	20 (45.45)	20 (45.45)
31-40	2 (4.54)	12 (27.28)	14 (31.82)
41-50	1 (2.27)	4 (9.09)	5 (11.36)
51-60	2 (4.54)	3 (6.82)	5 (11.36)
Total (Percentage)	**5 (11.36 %)**	**39 (88.64 %)**	**44 (100)**
Mean±S.E.M	**47.2 ± 5.31**	**32.05 ± 1.73**	**33.77 ± 1.78**

Table 3: Distribution of Patients According to Temperament

Temperament	Number of Cases	Percentage (%)
Damwī (Sanguine)	17	38.64
Balghamī (Phlegmatic)	24	54.55
Ṣafrawī (Bilious)	3	6.82
Sawdāwī (Melancholic)	-	-
Total	**44**	**100**

(39.45%), irritability (47.32%), difficulty in falling asleep and staying asleep (35.14%), while decreased appetite, fatigue, and mild sensitivity to light / noise were not improved significantly as the sample size was small (Results are depicted in Table 5 and Fig. 1 and 2).

Response of *'Araq-i-'Ajīb* by reducing symptoms associated with headache can be attributed to presence of its ingredients. A possible explanation for response of *'Araq-i-'Ajīb* against headache can be provided by quick survey of the ingredients of *'Araq-i-'Ajīb*.

Table 4: General Therapeutic Response

	Total	Complete Relieved (90-100 %)	Relieved (60-89 %)	Partially Relieved (30-59 %)	Not Relieved (< 30 %)
No. of Patients	44	-	3	27	14
Percentage (%)	100	-	6.82	61.36	31.82

Table 5: Effect of *'Araq-i-'Ajīb* on Different Symptoms Associated with *Ṣudā'* (Headache)

Clinical Symptoms	Base Line	1st Follow-up		2nd Follow-up	
	Mean ± S.E.M	Mean ± S.E.M	Efficacy (%)	Mean ± S.E.M	Efficacy (%)
Ṣudā' (Headache)	6.73 ± 0.15	5.05 ± 0.19 ***	24.96	3.23 ± 0.2 ***	52.01
Disturbed Concentration	2.18 ± 0.34	1.73 ± 0.29 ns	20.64	1.32 ± 0.27 *	39.45
Irritability	3.36 ± 0.24	2.77 ± 0.24 ns	17.56	1.77 ± 0.23 ***	47.32
Ḍu'f al-Ishtihā' (Decreased appetite)	0.55 ± 0.19	0.5 ± 0.17 ns	9.09	0.41 ± 0.15 ns	25.45
I'yā' (Fatigue)	0.82 ± 0.21	0.77 ± 0.2 ns	6.10	0.64 ± 0.17 ns	21.95
Difficulty in falling asleep and staying asleep	2.59 ± 0.29	2.23 ± 0.25 ns	13.90	1.68 ± 0.22 *	35.14
Mild sensitivity to light/ noise	0.68 ± 0.21	0.64 ± 0.19 ns	5.88	0.55 ± 0.18 ns	19.12

***p<0.001, **p<0.01,*p<0.05, ns=non significant when compared to the baseline

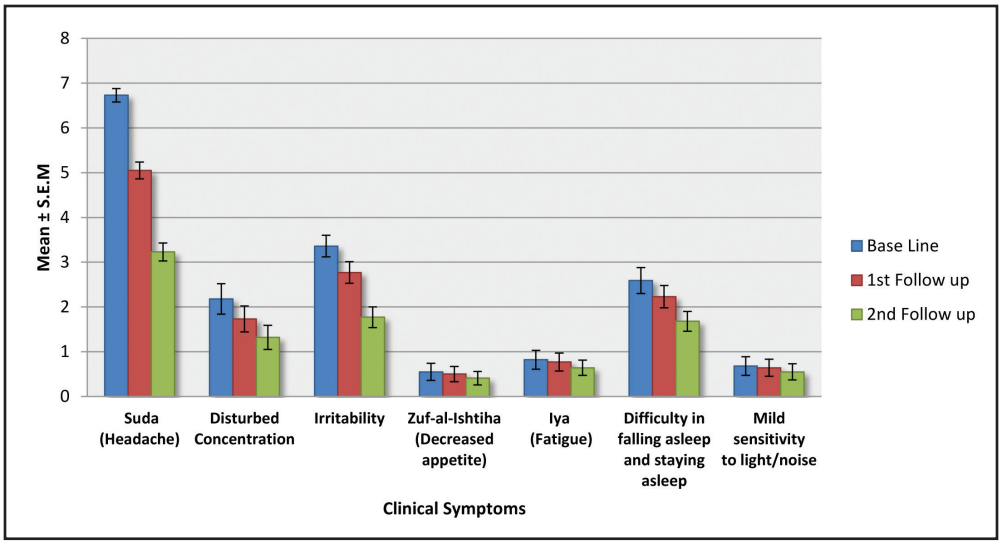

Fig. 1: Effect of *'Araq-i-'Ajīb* on Different Symptoms Associated with *Ṣudā'* (Headache)

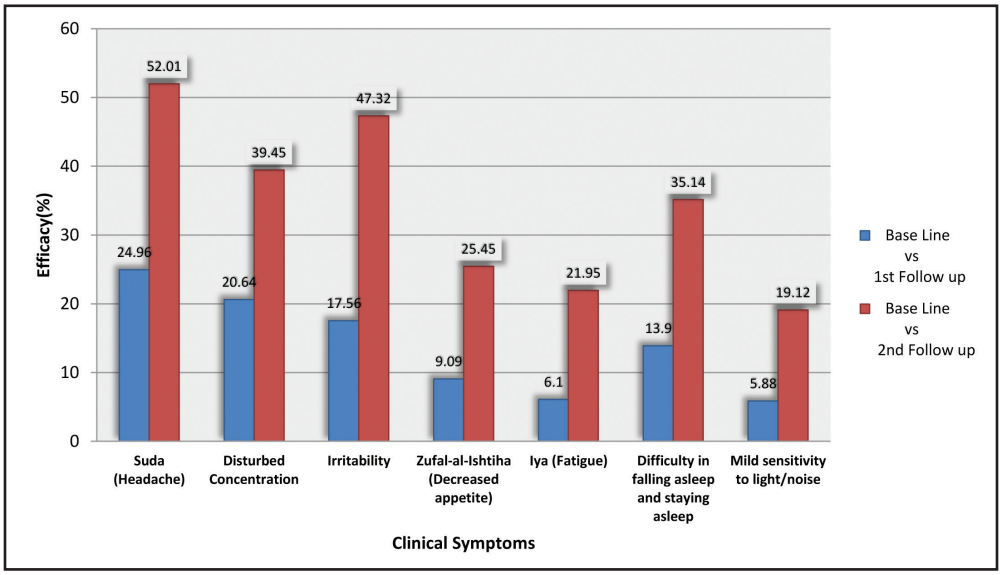

Fig. 2: Efficacy of *'Araq-i-'Ajīb* on Different Symptoms Associated with *Ṣudā'* (Headache)

The present study supports the claims of Traditional Medicine showing that *T. ammi* extract possesses a clear-cut analgesic effect as the test drug contains *T. ammi*. This effect may be due to its parasympathomimetic action on descending pain modulating pathways (Asif, *et al.*, 2014; Mohammad, *et al.*, 2014).

In a recent study, presence of glycosides, fixed oils, steroids, terpenes is reported in *T. ammi* and the molecules may be responsible for its antispasmodic and analgesic properties which are also in consonance to the present study as the results revealed (Kamini and Kiran, 2012; Kumar, *et al.*, 2011; Yadav, *et al.*, 2011; Wadnap, *et al.*, 2006).

Mentha arvensis L. is also one of its constituents and phytochemically it exhibited alkaloids, glycosides, steroids and sugars and is used as a contraceptive, carminative, antispasmodic, antipeptic ulcer agent, and used to treat indigestion, skin diseases, coughs and colds in folk medicine and it may have played an important role in the results of this study (Sandeep, *et al.,* 2010).

'Araq-i-'Ajīb has *Kafūr* (*Cinnamomum camphora* Nees & Eberm.) in its ingredients which is proven analgesic (Wadnap, *et al.,* 2006), which may have helped in relieving the symptoms of *Ṣudā'* (headache) as *Cinnamomum camphora* has a long history of use as antiseptic, analgesic, antipruritic, counterirritant and rubefacient. Its success and wide medical use, especially in topical preparations, is connected to its mild local anesthetizing effect. Camphor is today mostly used in the form of inhalants and of camphorated oil, a preparation of 19% or 20% camphor in a carrier oil, for the home treatment of colds and as a major active ingredient of liniments and balms used as topical analgesics (Zuccarini, 2009; Hamidpour, *et al.,* 2013).

The present study is also in agreement with a study by Akram M, who has reported that *'Araq-i-'Ajīb* has significant analgesic effect (Akram, *et al.,* 2014).

As there was no undesired results reported in the pathological and biochemical parameters done at the baseline and at the end of the study and no adverse / side effects were noticed during the study, the drug was found safe at the given dosage schedule.

Conclusion

On the basis of above observations, it can be concluded that Unani pharmacopoeial formulation *'Araq-i-'Ajīb* is effective in the management of *Ṣudā'* (headache). The drug is affordable, easily available and well-tolerated by the patients without having any side effect.

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सारांश

सुदा (सिरदर्द) के रोगियों पर यूनानी भेषजकोशीय मिश्रण 'अर्क़-ए-अजीब' का प्रभाव : एक प्राथमिक अध्ययन

***मोहम्मद वसीम अहमद, तसलीम अहमद, अनीर्बन गोस्वामी, नजमुस सेहर, मो. हशमत ईमाम और मो. इश्तियाक़ आलम**

'अर्क़–ए–अजीब' एक यूनानी भेषजकोशीय औषधि है जिसका उपयोग यूनानी चिकित्सा पद्धति में विभिन्न रोगों के उपचार के लिए आम तौर से किया जाता है। इसमें तीन संघटक होते हैं – कपूर, जौहर–ए–पुदिना और जौहर–ए–अजवाइन। वर्तमान अध्ययन सुदा (सिरदर्द) के रोगियों में अर्क़–ए–अजीब की सुरक्षा और प्रभावकारिता का मूल्यांकन करने के लिए किया गया। इस अध्ययन में सात दिनों तक अर्क़–ए–अजीब (तरल) का स्थानीय रूप से दिन में दो बार सेवन कराया गया। उपचार के तीसरे और सांतवे दिन सुरक्षा का मूल्यांकन किया गया। अध्ययन के पहले और अंत में किए गए प्रयोगशाला (जैव रासायनिक और रोगविज्ञान) मापदंडों और सी.आर.एफ. में कोई प्रतिकूल प्रभाव दर्ज नहीं किया गया। सिरदर्द से जुड़े संकेतों और लक्षणों में कमी को आंकते हुए प्रभावकारिता का आकलन किया गया। अर्क़–ए–अजीब के सेवन से सिरदर्द से जुड़े लक्षणों जैसे सिर दर्द में 52.01%, वितरित एकाग्रता में 39.45%, चिड़चिड़ापन में 47.32%, सोने में परेशानी और सोते रहने की समस्या में 35.14% सुधार हुआ। विजुअल एनालॉग स्केल (वी.ए.एस.) से रोग की तीव्रता का मूल्यांकन किया गया। यह अध्ययन दर्शाता है कि अर्क़–ए–अजीब दी गई खुराक स्तरों में एक सुरक्षित औषधि है और सिरदर्द का उपचार करने की क्षमता रखती है।

शब्दकुंजी: एनाल्जेसिक, अर्क़–ए–अजीब, सिरदर्द, यूनानी चिकित्सा

Clinical Study for Validation of Safety and Efficacy of *Ḥabb-i-Shifā'* for Symptomatic Relief in *Nazla Ḥārr* (Common Cold) in Eastern India

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Abstract

A clinical study was carried out to scientifically validate the safety and efficacy of Unani pharmacopoeial formulation *Ḥabb-i-Shifā'* for symptomatic relief in patients of *Nazla Ḥārr* (common cold) at Regional Research Institute of Unani Medicine (RRIUM), Bhadrak (Odisha) during 2013-2014. Out of all the cases registered for the study, 94 patients completed the trial. After 7 days of treatment, the symptoms of the disease, including *Khushūnat al-Ḥalaq* (sore throat), *Buḥḥat al-Ṣawt* (hoarseness of voice), *'Uṭās* (sneezing/nasal irritation), runny nose, *Ṣudā'* (headache), *Su'āl* (cough), *I'yā'* (malaise), flushing of face and low grade fever (<102 ^{0}F) were found decreased by 49.74%, 44.89%, 49.04%, 52.15%, 41.14%, 39.44%, 45.12%, 78.49% and 100% respectively as compared to the baseline. The variations in the values of liver function tests (LFTs) and kidney function tests (KFTs) before and after the treatment were found within normal limits. The study drug was found well-tolerated and no adverse effects were observed during the study. The study findings confirm the safety and efficacy of *Ḥabb-i-Shifā'* in the treatment of *Nazla Ḥārr* (common cold).

Keywords: Common cold, *Ḥabb-i-Shifā'*, *Nazla Ḥārr*

Introduction

The common cold, also known as nasopharyngitis, acute viral rhinopharyngitis, acute coryza, or cold, is a viral infectious disease of the upper respiratory system, caused primarily by rhinoviruses and corona viruses (Heikkinen, *et al.,* 2003). It is extremely common condition world-wide which mostly affects children younger than one year 6-10 times in a year and 3-4 episodes per year in adulthood (Gwaltney, *et al.,* 1977). There are more than 200 types of cold virus. Each one affects every person differently. Colds are the most frequent illness in modern society (Eccles, 2002; Eccles, 2005; Kalra, *et al.,* 2011). Over 50 percent of cold is caused by rhinoviruses, corona viruses account for 10-20 percent, followed by influenza viruses (10-15%) and adenoviruses (5%) (Durand, M., 2001; Gwaltney, 1995). There are three primary modes of viral transmission involving the shedding of respiratory particles: droplet, contact, and airborne (Brankston, *et al.,* 2007). As per a WHO report, the most prevalent form of influenza virus in India is B strain. Viruses enter the body through the respiratory tract and attach to cells lining the nose, throat and bronchial tubes. Exposure to cold, damp, wind and rapid temperature change can make us more susceptible. During cold, virus particles penetrate the mucous layer of the nose and throat and attach themselves to cells there. The viruses punch holes in the

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cell membranes, allowing viral genetic material to enter the cells. Within a short time, the virus takes over and forces the cells to produce thousands of new virus particles (Zambon, 2001; Jefferson, *et al.,* 2009). The symptoms experienced as cold are actually the body's natural immune response. Colds manifest slowly with cough, nasal congestion and sore throat, usually without fever. Flu comes on more suddenly with fever, sore muscles, fatigue and cough. These ailments can last from a few days to about a week, but can progress into bronchitis, strep throat or asthma if not properly treated. Fever causes the body to heat up and destroy infection (Mario, 2007; Zambon, 2001).

According to literature of Unani Medicine, *Nazla-o-Zukām* is defined as the flow of catarrhal fluids from the brain towards nose and throat. Some physicians have differentiated them by saying that while the flow of these fluids towards nose is known as *Zukām,* the flow towards throat is known as *Nazla*. If the symptoms are intense, then it is known as *Nazla-o-Zukam Ḥārr* (acute). If these are of low intensity, then it is known as *Nazla-o-Zukam Bārid* (chronic) (Arzani, 2010; Khan, 1987; Khan, 2003; Kabiruddin, 1935; Qumri, 2008; Kabiruddin, 1916).

Nazla Ḥārr is common in children and caused by excessive *Ruṭūbat* (moisture/ wetness) and *Ḍu'f-i-Dimāgh* (weakness of brain). The causes of *Nazla-o-Zukām* have been divided broadly into two; *Nazla Ḥārr* due to predominance of *Ḥarārat*, either intrinsic or extrinsic and *Nazla Bārid* due to predominance of *Burūdat*, either intrinsic or extrinsic. In case of *Nazla Ḥārr,* symptoms of disease are usually higher in intensity and include flushing and burning sensation of face, burning sensation in nose and throat, watery eye, increased body temperature, nasal discharge of thin yellow fluid and malaise. In case of *Nazla Bārid,* symptoms are mild and include nasal discharge of thick yellow fluid, malaise and nasal blockage. Third type of *Nazla-o-Zukām* is defined as *Nazla Wabā'ī* by some Unani physicians. In this type of disease, the symptoms resemble those of *Nazla Ḥārr* but are more intense.

Nazla Ḥārr (common cold) may spread as epidemic and patient feels severe body ache, irritation in nose and throat and redness of eyes. In this condition, patient feels very weak. A detailed treatment of *Nazla Ḥārr* (common cold) has been mentioned by physicians of the system including its line of treatment according to the causative factors. *Uṣūl-i-'Ilāj* (principle of treatment) of *Nazla Ḥārr* includes *Nuḍj-i-Mādda* (concoction of morbid material), *Tanqiya-i-Mādda* (elimination of morbid material from the body), *Man'-i-Tabkhir* (antiflatulent), *Muqawwī-i Dimāgh* (brain tonic) and *Muqawwī-i-Mi'da* (tonic for stomach, stomachic). Diet play an important role in this condition and therefore, meat, *Mubakhkhira* (flatulent) food, wine and oily food should be avoided. Easily digested food and lots of fluid should be taken. *Behīdānā, 'Unnāb, Sapistān, Tukhm-i-Khatmī* and *Gaozabān* are some commonly used single drugs to treat this condition. *Kalonjī Biryān, Anīsūn* and *Qust* may be placed in cotton cloth

and smelled frequently or these drugs may be used as *Lakhlakha* (inhalation of the vapour from drugs kept in a wide mouthed bottle) for instant relief from the symptoms (Tabari, 2010; Qumri, 2008; Khan, 1987; Arzani, 2010; Khan, 2003; Kabiruddin, 1916).

Material and Method

The present study was conducted at Regional Research Institute of Unani Medicine (RRIUM), Bhadrak (Odisha) on 94 patients of *Nazla Ḥārr* (common cold) selected from those who visited the OPD of the institute for treatment of cold during 2013-2014. The patients of either sex in the age group of 18 to 65 years were included in the study. Inclusion criteria were *Khushūnat al-Ḥalaq* (sore throat), *Buḥḥat al-Ṣawt* (hoarseness of voice), *'Uṭās* (sneezing/ nasal irritation), runny nose, *Ṣudā'* (headache), *Su'āl* (cough), *I'yā'* (malaise), flushing of face and low grade fever (<102 ^{0}F). The patients below 18 years and above 65 years of age, patients of acute or chronic lower respiratory tract infection like pneumonia, bronchitis, asthma and bronchiectasis, fever > 102^{o}F, known cases of any other acute illness, pregnant and lactating women and known cases of hepatic, renal or cardiac ailments or the ailment requiring long term therapy were excluded from the study.

The clinical study protocol was approved by the Institutional Ethics Committee (IEC) of the institute on March 15, 2013 and the trial was registered with CTRI bearing registration number CTRI/2013/12/004257. After obtaining written informed consent from the patients, they were enrolled for the study and then subjected to the pathological and bio-chemical investigations. Pathological investigations included Haemogram [Haemoglobin (Hb), Erythrocyte sedimentation rate (ESR), Total leukocyte count (TLC) and Differential leukocyte count (DLC: Neutrophils, Eosinophils, Basophils, Lymphocytes, Monocytes)], Urine examination (routine and microscopic). Bio-chemical investigations included liver function tests (LFTs) comprising serum bilirubin, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and alkaline phosphatase (ALP) and kidney function tests (KFTs) comprising serum creatinine and serum urea.

The parameters for assessment of efficacy of the formulation were *Khushūnat al-Ḥalaq* (sore throat), *Buḥḥat al-Ṣawt* (hoarseness of voice), *'Uṭās* (sneezing/ nasal irritation), runny nose, *Ṣudā'* (headache), *Su'āl* (cough), *I'yā'* (malaise), flushing of face and low grade fever (<102 ^{0}F). These parameters were graded according to visual analogue scale (VAS) score.

The clinical follow-up of all the cases was carried out on 3rd and 7th day of the treatment. The pathological and bio-chemical investigations were conducted at the baseline and end of the study. The safety of trial drugs was evaluated by

bio-chemical investigations and clinically by monitoring adverse effects carefully at each follow-up. The *Mizāj* (temperament) of the patients was assessed as per the parameters described in Unani classical literature. The clinical and laboratory findings observed in every case were recorded on a separate case record form (CRF) designed especially for clinical study on *Nazla Ḥārr* (common cold). The duration of treatment was 7 days. No concomitant treatment was allowed during the study. Baseline and follow-up values of bio-chemical and pathological investigations were statistically analyzed using Student's paired 't' test.

Study Drugs, Dosage Schedule and Mode of Administration

Unani pharmacopoeial formulation *Ḥabb-i-Shifā*' used in the study was supplied by the Central Research Institute of Unani Medicine (CRIUM), Hyderabad. It was prepared according to the *National Formulary of Unani Medicine*, Part-I at pharmacy unit of CRIUM, Hyderabad. *Ḥabb-i-Shifā*' was given in the dose of 1 pill orally twice a day with water if patient's weight was less than 50 kg and 2 pills twice a day if patient's weight was more than 50 kg. *Ḥabb-i-Shifā*' is made up of four ingredients in different proportion (Table-1) (Anonymous, 2006).

Results

In this study, 58.51% (55) patients were male and 41.49% (39) female. Besides, 55.32% (52) patients were of *Damwī* (Sanguine), 26.60% (25) patients of *Balghamī* (Phlegmatic), 12.77% (12) patients of *Ṣafravī* (Bilious) and 5.32% (5) patients of *Sawdawī* (Melancholic) *Mizāj*. Out of 94 patients included in the trial, the highest incidence (47.87%) was observed in the age group of 18-30 years and the least incidence (8.51%) was seen in the age group of 41-50 years. 27.65% incidence was seen in the age group of 31-40 years. As far as chronicity of the symptoms is concerned, 42.55% patients had symptoms for less than one month and 43.62% patients had symptoms for 1-12 months, only 12.77% patients had symptoms for more than 24 months.

Visual analogue scale (VAS) score was calculated in all the patients before and after the treatment. The mean value of VAS score for *Khushūnat al-Ḥalaq* (sore throat), *Buḥḥat al-Ṣawt* (hoarseness of voice), *'Uṭās* (sneezing/ nasal irritation),

Table 1: Composition of *Ḥabb-i-Shifā*'

S.No.	Unani Name	Scientific Name	Quantity
1	*Tukhm-i-Jauzmasil*	*Datura metel* L.	6 parts
2	*Rewand Chīnī*	*Rheum emodi* Wall.	4 parts
3	*Zanjabīl*	*Zingiber officinale* Rosc.	2 parts
4	*Samag-i-'Arabī*	*Acacia Arabica* Willd.	2 parts

Anonymous, 2006

runny nose, *Ṣudā'* (headache), *Su'āl* (cough), *I'yā'* (malaise), flushing of face and low grade fever (<102 ^{0}F) were 1.95, 1.76, 2.08, 2.09, 1.75, 1.80, 1.64, 0.93 and 0.29 respectively before the treatment. At the end of study, these scores were 0.98, 0.97, 1.06, 1.00, 1.03, 1.09, 0.90, 0.20 and 0.00 respectively.

Out of nine parameters studied, 49.74% improvement in case of *Khushūnat al-Ḥalaq* (sore throat), 44.89% in *Buḥḥat al-Ṣawt* (hoarseness of voice), 49.04% in *'Uṭās* (sneezing/ nasal irritation), 52.15% in runny nose, 41.14% in *Ṣudā'* (headache), 39.44% in *Su'āl* (cough), 45.12% in *I'yā'* (malaise), 78.49% in flushing of face and 100% in low grade fever (<102 ^{0}F). The overall improvement was good (Table 4, Figure 1).

Ḥabb-i-Shifā' demonstrated significant improvement in symptoms and signs of *Nazla Ḥārr* (common cold). Out of 94 patients, 80 (85.11%) patients showed 60-89% relief in overall symptoms and signs, 11 (11.70%) patients showed 30-59% relief in overall symptoms and signs, 01 (1.06%) patient showed more than 90% relief in overall symptoms and signs, and 02 (2.13%) patients showed less than 30% relief in overall symptoms and signs of *Nazla Ḥārr* (common cold) (Table 5, Figure 2).

The mean values of haematological and bio-chemical parameters at the baseline and after the treatment are given in Table 2 and 3 respectively. The values of safety parameters [Haemoglobin ESR, TLC, DLC, LFTs and KFTs] remained

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

Pathological Investigations		Period	Mean ± SD	P value
Haemoglobin (gm%)		BT	12.56±0.13	P > 0.05
		AT	13.80±1.26	
ESR (mm/hr)	1st Hour	BT	20.53±2.26	P > 0.05
		AT	19.80±1.85	
	2nd Hour	BT	40.11±3.37	P > 0.05
		AT	38.23±2.88	
Total Leucocytes Count (cmm)		BT	6722.87±141.83	P > 0.05
		AT	7227.13±648.42	
DLC	Neutrophils	BT	62.49±0.54	P > 0.05
		AT	61.99±0.52	
	Lymphocytes	BT	27.62±0.51	P > 0.05
		AT	28.35±0.46	
	Eosinophils	BT	9.45±0.40	P > 0.05
		AT	8.87±0.34	
	Monocytes	BT	0.40±0.06	P < 0.01
		AT	0.64±0.07	

BT= Before Treatment; AT= After Treatment

Table 3: Mean Values of Biochemical Investigations at Baseline and After Treatment

Biochemical Investigations	Period	Mean ± SD	P value
SGOT (Units/ml)	BT	34.27±1.60	P > 0.05
	AT	32.08±0.95	
SGPT (Units/ml)	BT	32.12±1.96	P > 0.05
	AT	29.37±1.54	
ALP (K&A Units/100ml)	BT	101.17±4.63	P > 0.05
	AT	100.74±5.00	
Serum Bilirubin (mg %)	BT	0.72±0.06	P > 0.05
	AT	0.63±0.03	
Serum Creatinine (mg %)	BT	1.47±0.18	P > 0.05
	AT	1.41±0.14	
Serum Urea (mg %)	BT	28.59±1.34	P > 0.05
	AT	28.84±1.19	

BT= Before Treatment; AT= After Treatment

Table 4: Mean Values of Clinical Parameters at the Baseline and After the Treatment

S.No.	Signs and Symptoms	Base Line	After Treatment	% Decrease
1	*Khushūnat al-Ḥalaq* (Sore throat)	1.95	0.98	49.74 %
2	*Buḥḥat al-Ṣawt* (Hoarseness of Voice)	1.76	0.97	44.89 %
3	*'Uṭās* (Sneezing/ Nasal irritation)	2.08	1.06	49.04 %
4	Runny nose	2.09	1.00	52.15 %
5	*Ṣudā'* (Headache)	1.75	1.03	41.14 %
6	*Su'āl* (Cough)	1.80	1.09	39.44 %
7	*I'yā'* (Malaise)	1.64	0.90	45.12 %
8	Flushing of Face	0.93	0.20	78.49 %
9	Low grade fever (<102 ^{0}F)	0.29	0.0	100 %

Table 5: Therapeutic Response

Response	Cured (90-100 %)	Relieved (60-89%)	Partially Relieved (30-59%)	Not Relieved (0–29%)
No. of Patients	01	80	11	02
Percentage (%)	1.06 %	85.11 %	11.70 %	2.13 %

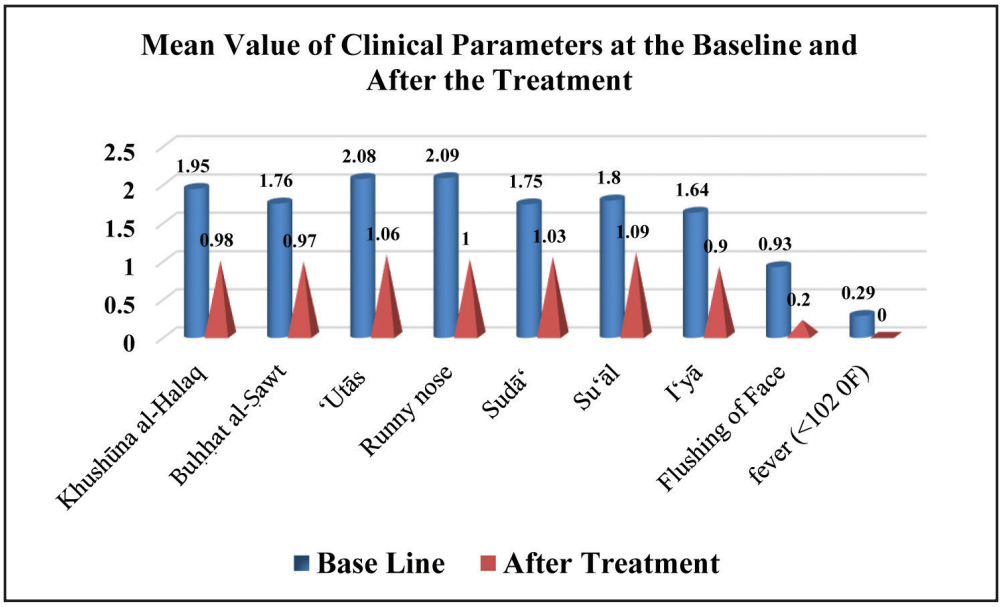

Fig. 1: Mean Values of Clinical Parameters at the Baseline and After the Treatment

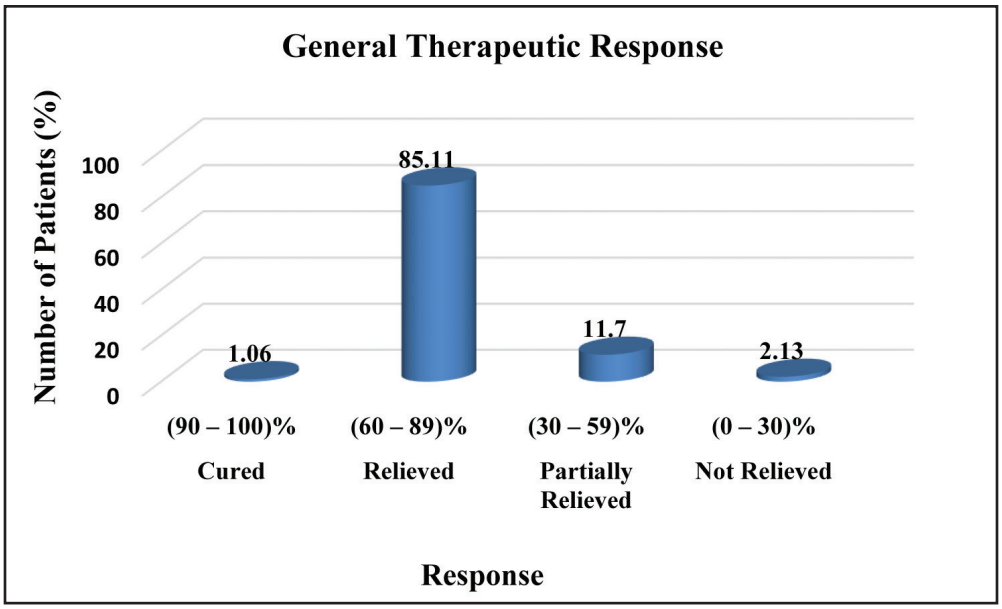

Fig. 2: General Therapeutic Response

within normal limits after the treatment. There was no significant change in serum level of SGOT, SGPT, ALP, bilirubin, urea and creatinine after treatment as compared to the baseline. Likewise, no significant change in value of Haemoglobin, ESR, TLC and DLC was seen after the treatment as compared to the baseline. The study drug was found well-tolerated and no unbearable adverse effects were reported clinically during or after the treatment.

The results of the present study are in agreement with several studies on herbal treatment of common cold. A multiherbal formula with vitamin C and zinc

(Immumax) had helped to improve cold symptoms of 60% of the participants (Mostafa Yakoot, *et al.,* 2011). A herbal solution containing *Pelargonium sidoides* was found to reduce the duration and severity of 10 different cold symptoms in a randomized controlled trial (Lizogub, *et al.,* 2007). Another randomized controlled trial demonstrated the benefit of *Andrographis paniculata* (Kalmcold) in improving symptom scores (Saxena, *et al.*, 2010). A systematic review also indicated that *Andrographis paniculata* alone or in combination with *Acanthopanax senticosus* may be more effective for symptom relief than placebo (Poolsup, *et al.,* 2004). Early use of *Echinacea purpurea* shortens duration and decreases severity of cold symptoms; preparations with the aerial parts versus the flowering parts are most effective (Linde, *et al.,* 2006). Buckwheat honey is the superior to placebo for reducing frequency of cough, reducing bothersome cough and improving the quality of sleep for the child (Paul, *et al.,* 2004).

Discussion

The improvement in various clinical parameters of *Nazla Ḥārr* (common cold) might be due to alteration of temperament (*Ta'dīl-o-Tabdīl-i-Mizāj*), or by evacuation of vitiated or morbid matter in case of *Sū'-i-Mizāj Māddī* (impaired temperament due to abnormal humour). *Ḥabb-i-Shifā'* has four ingredients; *Tukhm-i-Jauzmasil, Rewand Chīnī, Zanjabīl* and *Samag-i-'Arabī. Tukhm-i-Jauzmasil* has dual property; it acts as *Muḥarrik-i-Dimāgh* (brain stimulants, enhances the function of brain) followed by *Musakkin* and *Mukhaddir* (anaesthetic) action. It also acts as *Dāfi'-i-Tashannuj* (antispasmodic/anticonvulsant), *Dāfi'-i-Ḥummayāt Balghamiyya* (antipyretic) and *Dāfi'-i-Su'āl Balghamī,* (anti cough/bronchitis). *Rewand Chīnī* is known for its *Muqawwi-i-Badan* (general tonic), *Muqawwi-i-Jigar* (hepatotonic), *Muḥarrik-i-Jigar* (enhances the function of liver), *Muqawwi-i-Mi'da wa Am'ā'* (strengthens the stomach and intestines and improves their functions) and *Mukhrij-i-Balgham* (expectorant) activities. *Zanjabīl* is *Hāḍim* (digestive) and *Kāsir-i-Riyāḥ* (carminative), while *Samag-i-'Arabī* acts as *Dāfi'-i-Su'āl* (antitussive), *Mugharrī* (mucilaginous) and *Mujaffif* (desiccant). The combination of all the drugs makes *Ḥabb-i-Shifā'* a special drug which has several properties described in the *Uṣūl-i-'Ilāj* (principle of treatment) of *Nazla Ḥārr* (common cold). It provides comprehensive protection from the virus by strengthening body defense system. It improves brain as well as liver functions. At the same time, it corrects the digestive system and expectorates the phlegm, if present.

As far as the management of common cold in the modern system of medicine is concerned, several studies have been done to validate the effective and safe management by the existing/new medications, but a comprehensive effective and safe drug for common cold could not be figured out. The existing drugs which are used in cold do not help to reduce the symptoms as shown by

the following studies. Antibiotics have no role in common cold (Arroll, *et al.,* 2013). Carbocysteine is no more effective than placebo (Chalumeau, *et al.,* 2013). Dextromethorphan and Diphenhydramine (Benadryl) are not superior to placebo in nocturnal cough or sleep quality in patients (Paul, *et al.,* 2004). Low-dose inhaled corticosteroids have not shown any decrease in the number of episodes, the frequency of wheezing, or duration of episodes (McKean, *et al.,* 2000). In preschool children with mild-to-moderate wheezing associated with a viral infection, oral prednisolone was not superior to placebo (Panickar, 2009). Antihistamines, decongestant, antitussives and bronchodilator found no more effective than placebo for cough and cold symptoms (Smith, *et al.,* 2008). Vitamin C was found no more effective than placebo for reducing duration or severity of cold symptoms (Douglas, *et al.,* 2007). Antihistamine monotherapy (sedating and non-sedating) was found no more effective than placebo (Sutter, *et al.,* 2003). Codeine was found no more effective than placebo for cough (Bolser, *et al.,* 2006). Intra-nasal corticosteroid was found no more effective than placebo (Puhakka, *et al.,* 1998; Qvarnberg, *et al.,* 2001). Hypertonic saline does not improve nasal symptoms or illness duration in patients with the common cold or rhinosinusitis (Adam, *et al.*, 1998).

In the light of the above observations, it is obvious that medications used for the management of common cold in the modern system of medicine do not exhibit any significant improvement in the symptoms and signs of common cold and have side effects in varying degree. On the contrary, study drug i.e. *Ḥabb-i-Shifā*' has shown a significant improvement in symptoms and signs of *Nazla Ḥārr* without any known side effect. The study proves efficacy as well as safety of *Ḥabb-i-Shifā*' in the treatment of *Nazla Ḥārr* (common cold).

Conclusion

It is clear that *Ḥabb-i-Shifā*' produced significant improvement in various symptoms and signs including *Khushūnat al-Ḥalaq* (sore throat), *Buḥḥat al-Ṣawt,* (hoarseness of voice), *'Uṭās* (sneezing/nasal irritation), *Ṣudā'* (headache), *Su'āl* (cough), runny nose, *I'yā*' (malaise), flushing of face and low grade fever (<102 ^{0}F). Likewise, the therapy was found to be safe and well-tolerated as the safety parameters (Hb%, ESR, TLC, DLC, LFT and KFT) remained within the normal limits after the treatment. No unbearable side effects were seen and overall compliance to the trial drug was good. Thus, it may be concluded that *Ḥabb-i-Shifā*' is an effective and safe regimen in the symptomatic management of *Nazla Ḥārr* (common cold).

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सारांश

पूर्वी भारत में नज़ला-ए-ह़ार्र (सामान्य सर्दी) में लक्षणात्मक राहत के लिए हब्ब-ए-शिफ़ा की सुरक्षा और प्रभावकारिता के वैधीकरण का नैदानिक अध्ययन

अख़्तर हुसैन जमाली, *मौहम्मद ज़ाकिर, ज़ियाउल हक़ सिद्दीक़ी, किशोर कुमार, चंद्रपाल, नरेन्द्र सिंह, हकीमुद्दीन ख़ान और मुनव्वर हुसैन काज़मी

क्षेत्रीय यूनानी चिकित्सा अनुसंधान संस्थान (क्षे.यू.चि.अ.सं.), भद्रक (ओडिशा) में 2013–2014 के दौरान नज़ला–ए–ह़ार्र (सामान्य सर्दी) के रोगियों में लक्षणात्मक राहत के लिए यूनानी भेषजकोशीय मिश्रण हब्ब–ए–शिफ़ा की सुरक्षा और प्रभावकारिता का वैज्ञानिक वैधीकरण करने के लिए एक नैदानिक अध्ययन किया गया। अध्ययन के लिए पंजीकृत रोगियों में से 94 रोगियों ने परीक्षण पूरा किया। सात दिनों के उपचार के बाद रोग के लक्षणों जैसे ख़ुशूनत अल–हलक़ (गले में ख़राश), बुह्हत अल–सौत (गला बैठना), उतास (छींक/नाक में जलन), बहती नाक, सुदा (सिरदर्द), सुआल (खांसी), इया (बैचेनी), चेहरे पर लालिमा और निम्न स्तर का ज्वर (<102°F) आदि में आधार–रेखा की तुलना में क्रमशः 49.74%, 44.89%, 49.04%, 52.15%, 41.14%, 39.44%, 45.12%, 78.49% और 100% तक कमी पाई गई। उपचार से पहले और बाद में लीवर फंक्शन टेस्ट (एलएफटी) और किडनी फंक्शन टेस्ट (केएफटी) के परिणामों में भिन्नता सामान्य स्तर के भीतर पाई गई। अध्ययन में औषधि को सहनशील पाया गया और अध्ययन के दौरान कोई प्रतिकूल प्रभाव नहीं देखा गया। अध्ययन ने नज़ला–ए–ह़ार्र (सामान्य सर्दी) के उपचार में हब्ब–ए–शिफ़ा की सुरक्षा और प्रभावकारिता की पुष्टि की।

शब्दकुंजी: सामान्य सर्दी, हब्ब–ए–शिफ़ा, नज़ला–ए–ह़ार्र

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