

ROLE OF IMMUNOMODULATOR UNANI DRUGS IN PREVENTION OF COVID-19**Reesha Ahmed*, Mohd. Wasim Ahmed, Asma Sattar Khan and Shoeb Ahmed Ansari**

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ABSTRACT

Unani is a traditional system of medicine developed during the medieval period, which employs natural drugs of herbal, animal and mineral origin for treatment. Basically, it is based on the humoral theory postulated by Hippocrates, according to him the state of body health and disease are regulated by qualitative and quantitative equilibrium of four humours i.e. Blood, Phlegm, Yellow bile and Black bile. Amraz-e-Waba (epidemic diseases) is an umbrella term which is used in Unani medicine for all types of epidemics (smallpox, measles, plague, influenza etc.) mostly fatal in nature. The coronavirus disease 2019 (COVID-19) is a severe acute respiratory infection, and the pathogenesis and clinical features resemble with those of Nazla-e-Wabaiya (influenza) and Zatul Riya (pneumonia) which were well described many years ago in Unani text such as high-grade fever, headache, nausea and vomiting, running nose, dry cough, respiratory distress, alternate and small pulse, asthenia, foul smell from breath, insomnia, frothy stool, syncope, coldness in both upper and lower extremities, etc. The pathogenesis and clinical manifestations of COVID-19 is close to Amraz-e-Wabai (epidemic diseases) which was described by Hippocrates, Galen, Aristotle, Razes, Haly Abbas, Avicenna, Jurjani etc. The present study focuses on some Unani drugs used in prevention, and management of COVID-19 in the light of Amraz-e-Waba (epidemic diseases) and Nazla-e-Wabaiya (epidemic influenza).

KEYWORDS: Unani system, Amraz-e-Waba, COVID-19 and Humours.**INTRODUCTION**

At the end of 2019, a series of pneumonia cases by unknown causal agent was emerged in Wuhan (Hubei, China).^[1] A few weeks later, in January 2020, deep sequencing analysis from lower respiratory tract samples identified a novel virus severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) as causative agent for that observed pneumonia cluster.^[2] Thereafter, this disease was declared a pandemic by the World Health Organization (WHO). The causative agent of Covid-19 was temporarily named as 2019 nCoV (2019 novel coronavirus) by WHO Later, it was officially named as SARSCoV-2 (severe acute respiratory syndrome coronavirus 2) by the International Committee on Taxonomy of Viruses.^[3] The nCoV are enveloped non-segmented positive-sense RNA viruses which belong to the family Corona viridae, order Nidovirales and distributed among humans and other mammals.^[2] Clinical features and risk factors are highly variable, making the clinical severity range from asymptomatic to fatal. Coronaviruses causes mainly illness ranging from the common cold to more severe infections such as middle-east respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus

(SARS-CoV). Common symptoms of infection include respiratory symptoms, fever, and cough, shortness of breath, and breathing difficulties. In more severe cases, this infection results in pneumonia, severe acute respiratory syndrome (SARS), kidney failure, and death.^[4] Transmission of this virus is through droplet infection or fomites, but other modes such as airborne transmission and oro-fecal transmission are also speculated.

Besides this, the present control strategies of the disease include the reduction of secondary infections by early diagnosis and isolation of cases, providing optimal care to infected patients along with many vaccines as suggested by WHO. However, traditional systems of medicine are being explored for providing preventive, supportive and rehabilitative care to patients. Unani medicine is one of the officially recognized traditional system of medicine in India. It has a detailed description of many drugs that are utilized in large number of infectious diseases, including respiratory diseases. The present study explores an overview of some Unani drugs which have specific antiviral as well as immunomodulatory activities.

Unani Concept

The Unani medicine is considered as one of the oldest and time tested systems of medicine practiced for more than 2500 years. According to Unani theory, when the quality or quantity of anyone or admixture of humours is compromised, the pathological condition is developed. *Tabiyaat* (physis-nature) or *tabiyat al-insaniyah* (human nature) or *tabiyat al-mudabbira-ibadan* is considered as supreme planner and healer of the body. *Ibn Sina* (980–1037 AD) states that *tabiyat* would aim at reasons for health and illness far deeper than those given by the microbic and cognate theories. The homeostasis of each cell, tissue, organ and system is maintained by the *tabiyat* through various mechanisms mainly *Quwat-i-tabiyah* (natural faculties), *Quwat-i-haywaniyah* (vital faculties) and *Quwat-i-nafsaniyah* (mental faculties).^[5] These faculties control, regulate and restore the normal functions of each organ and system, and also assists in modulating the immune system of the body, and produces resistance against diseases.

Concept of Amraz-i-Wabai (Epidemic diseases) in Unani medicine

According to Unani theory, sometimes contamination or putrefaction occurs in the air resulting in waba which is the standardized term for epidemic.^[6] *Ibn Sina* (980–1037 AD) advocates that the fever may occur in masses due to contamination of water and air with *ajsam khabisa* (pathogenic organisms).^[7] *Ibn Khatima* (1369 AD) says the human body is surrounded by minute bodies which when entered in the human body may cause disease. *Hippocrates* (460–370 BC) depicts the symptomatology of certain contagious diseases which are currently referred as influenza, mumps, diphtheria, tuberculosis, malaria etc. *Galen* (129–200 AD) has given miasma theory of transmission of infectious diseases. First time, the complete clinical picture of small pox and measles was described by an Unani physician, *Zakaria Razi* (854–925 AD).^[8] He has also affirmed that the infectious diseases may be more prevalent when the person moves from non-contaminated to contaminated zone. *Ibn Zohar* (1126–1198 AD) has asserted that he observed few patients who died in spite of having mild fever and concurrently some recovered completely when their place of stay and diets were modified. During epidemics, the severity of the disease is assessed by respiratory distress and foul smell of breath.^[9] Unani literature has also described certain specific diseases which have been categorized as epidemic in earlier days such as measles (*hasba*), small pox (*judariyya*), leprosy (*juzamām*) etc, nevertheless ancient Unani scientists were completely cognisant about the existence of microbial organisms in the environment.^[6,7,10]

Nazla-i-Wabai (Influenza) in Unani medicine

In unani medicine, two terminologies i.e. *zukam* and *nazla* are being used for common cold and influenza like conditions.^[7,10] *Nazla va Zukam* may be associated with pharyngitis, sore throat, conjunctivitis, headache, hoarseness of voice, cough, fever, gastric pain, diarrhoea

etc. According to Unani medicine, the etiological factors of this disease are abrupt change of weather, toxic substances, excessive hot or cold climate, excessive bathing with cold water, extreme physical exertion, stress, *su-i-mizaj* (deranged temperament) etc. *Hakim Ajmal Khan* (1868–1927 AD) Stated that *nazla* and *zukam* also transmits epidemically. He termed these conditions as *nazla va zukam-i-wabai* and correlated it with influenza. *Najeebuddin Samarqandi*, has mentioned the cardinal features of *nazla-i-wabaiya* viz. sneezing, nasal irritation, sore throat, fever and malaise. The patients may also complain of cough, diarrhoea and delirium, and when the condition is worsened, they may have pneumonia and pleurisy as sequel. Some patients may also suffer from hoarseness of voice, throat pain, difficulty in breathing, loss of appetite, nausea and vomiting, headache etc. which closely resembles to influenza like illness and COVID-19 like infections.^[11]

Treatment

In general, four modes of treatment viz. regimenal therapy (Ilaj bil Tadbeer), dieto-therapy (Ilaj bil Ghiza), pharmacotherapy (Ilaj bil Dawa) and surgery (Ilaj bil Yad) are applied for the management of any disease. Conventionally, plant drugs are being commonly used by different traditional systems of medicine such as Unani medicine, Ayurveda, Chinese medicine etc. for treatment purposes. The pathogenesis and clinical manifestations of COVID-19 is close to *Amraz-e-Wabai* (epidemic diseases) which was described by Unani scholars.

Hippocrates, *Galen*, *Rhazes*, and *Avicenna* had described four etiological factors for *Amraz-e-Waba* viz., change in quality of air, water, Earth, and celestial bodies, accordingly mentioned various preventive measures to be adopted during epidemics such as restriction of movement, isolation or "quarantena", and fumigation with *Styrax benzoin* (*loban*), *Santalum album* (*sandalwood*), *Crocus sativus* (*Zafran*) and antidotes (*Tiryaaq*) as prophylaxis, and avoiding consumption of milk, oil, sweet, meat, and alcohol.^[12] Some unani drug used as systematic treatment of patients with COVID-19, as they has shown to possess antiviral, antioxidant, anti-inflammatory, immunomodulatory, bronchodilatory, antipyretic, antihistaminic, antitussive, antipyretic and analgesic activities.

DRUGS

Filfil Siyah (*Piper nigrum*)

Piper nigrum L. is the source of one of the world's most widely and frequently used spices. Botanically, it belongs to the family of Piperaceae. Black pepper is very commonly used remedy in the traditional system of medicine. They are most frequently used as an appetizer and to treat problems associated with the digestive system. It has been used in Unani System of medicine since the time immemorial. Great ancient physicians such as *Galen*, *Dioscorides*, and *Ibn-e-Baitar* have mentioned it for the treatment of various diseases.^[13]

Vernacular name

Arabic	Filfil aswad, babary
English	Black pepper, pepper
Hindi	Habush, Kali mirch
Persian	Filfil-e-aswad, Filfil-e-gard
Sanskrit	Dharmapattana, Katuka
Tamil	Aguttam, Arisu, Kari
Urdu	Kalimirch

Pharmacological action

Piper nigrum and its active constituent 'Piperine' exhibits diverse pharmacological activities like antiperiodic, alterative, alexipharmic, abortifacient, aphrodisiac, antacid, absorbent, antidote, aromatic, cardiac stimulant, detergent, deobstruent, digestive, antihypertensive, antiplatelet, antioxidant, antitumor, anti-asthmatics, analgesic, anti-inflammatory, anti-diarrheal, antispasmodic, antidepressants, immunomodulatory, anticonvulsant, anti-thyroids, antibacterial, antifungal, hepato-protective, insecticidal and larvicidal activities.^[14,15]

Therapeutic uses

In the classical literature, many Unani scholars have mentioned various medicinal uses of black pepper. It is also used in case of sore throat, cholera, dyspepsia, flatulence, diarrhea, and other gastrointestinal ailments, alopecia, skin disorders, and piles.^[15]

**Gilo (*Tinospora cordifolia*)**

Tinospora cordifolia commonly known, as "Amrita" or Guduchi" is an important drug of Indian System of Medicine and used as an ingredient in various traditional compound formulations from times immemorial. It is a climbing shrub belongs to family Menispermaceae.^[16] In china, Greece, Egypt and India the medicinal plants are considered as part of oldest sciences and commonly used as disinfectants, spices and aromatic agents. The usage of Gilo has been found in the treatment of number of diseases and recommended for improving the immunity of human beings as it increases the body resistance.^[17]

Vernacular names

Sanskrit	Guduchi, amrita, somavall
Hindi	Gurcha, giloe, gulanha
Tamil	Seendal

Gujarati	Galo
Telugu	Teppatige
Urdu	Gilo
Kashmiri	Amrita, Gilo

Pharmacological Action

Tinospora cordifolia L., the versatile herbal drug is the distinctive source of constituents which is having antidiabetic, antimicrobial and anticancer activity.^[18] The extract of different parts of this plant have shown anti-aging, anti-inflammatory and immunomodulatory characteristics.^[17] It shows Antipyretic and cytotoxic action.^[19] And the roots are employed for their powerful emetic, antistress, antioxidant, antiulcer, and hypoglycemic properties.^[20]

Therapeutic uses

It is used to treat several disorders including common cold and fever. Dried fruits are used to treat jaundice and rheumatism, whereas the leaves are used to treat diabetes.^[21] The roots are employed for the treatment of visceral obstructions.^[20]

**Rehan (*Ocimum sanctum*)**

Tulsi belongs to plant family Lamiaceae, known in English as Holy Basil and botanically called *Ocimum sanctum* L., Tulsi has been described as of two types-wild and cultivated. Although having identical usage, the former has darker leaves. *Ocimum sanctum* has two varieties i.e. black (Krishna Tulsi) and green (Rama Tulsi), their chemical constituents are similar. Both the varieties also have common medicinal properties.^[22] It helps to mobilize mucus in bronchitis and asthma. Chewing Tulsi leaves relieves cold and flu. A decoction of the leaves, with honey and ginger is an effective remedy for bronchitis, asthma, influenza, cough and cold.^[23] The phytochemical constituents such as alkaloids, steroids, flavanoids, tannins, phenols and several other aromatic compounds of plants serve a defense mechanism against predation by many microorganisms, insects and other herbivore.^[24]

Vernacular names

Sanskrit	Surasa, Krishna tulasi, Bana Tulasi
Assamese	Tulasii
Bengali	Tulasai
English	Holy Basil
Hindi	Tulasii
Punjabi	Tulsi
Tamil	Tulaesi, Thulasii, Theiru Theezaei
Urdu	Raihana, Tulss

Pharmacological Action

Tannins have anti-diarrheal and haemostasis properties.^[25] Flavanoids are responsible for antioxidant and immunostimulatory properties. It possess Antipyretic, Antimicrobial, Immunomodulatory, Anticancer, Hepatoprotective, Anti-inflammatory, Adaptogenic, Antidiabetic, Anticoagulant and Antiarthritic activity.^[23] Extract of fresh leaves and stem contains some antioxidant property.^[26]

Therapeutic uses

Healing power, fever & common cold, coughs, sore throat, respiratory disorder, stress, mouth Infections and Insect Bites.^[26]

**Zanjabeel (*Zingiber officinale*)**

Zanjabeel (Ginger) is a rhizome, botanically named as *Zingiber officinale* L., it is a member of Zingiberaceae family. It is one of the most common spices and used as an important drug in Unani system of medicine as well as in other non-conventional systems of medicine.^[27] *Zingiber officinale* individually or as a combination with other herbs is effective in both infective and non-communicable diseases.^[28] It is being medicinally used from pre-historic period and its diverse medicinal actions have been described in a number of Unani pharmacopoeias.

Fresh rhizome has been proven with an antiviral effect against Human Respiratory Syncytial Virus (HRSV) infection via decreasing HRSV induced plaque formation in respiratory mucosal cell lines.^[29] This effect is much beneficial in the management of common cold and fever associated with mucous secretions and management of complications due to cough and asthmatic conditions.^[30]

Vernacular Names

Arabic	Zanjabeel
Persian	Shangwez
Greek	Hotiyoon
Sanskrit	Adrakam
Hindi	Adrak, Sonth
English	Ginger
Urdu	Zanjabeel
Bengali	Ada
Assamese	Ada
Gujrati	Sunth

Pharmacology Action

The primary activities include anti-inflammatory, analgesic, anti-proliferative and hepatoprotective, Antibacterial, Antidiabetic, Antiemetic. The plant is reported for antimicrobial, anticancer, antioxidant, nephroprotective, larvicidal, analgesic and immunomodulatory activities.^[31]

Therapeutic uses

Zingiber officinale has been used in cold, cough and digestive disorders, headache and rheumatism.^[28] Maintaining proper circulation, nervous conduction, heart functions and balancing digestive and absorptive disorders through enhancing appetite is beneficial in enhancement of the immunity of the body.^[32]

**Kalonji (*Nigella sativa*)**

Nigella sativa L. is an annual herb that belongs to the family Ranunculaceae and is most extensively investigated for its therapeutic purposes.^[33] Ibn-e-sina revealed historical importance of *Nigella sativa* as seeds that stimulates the body's energy and help recovery from fatigue and dispiritedness. The immunomodulatory action may be due to its main constituent's thymoquinone, nigellone and d-limonene through their antioxidant and anti-inflammatory activities.^[34]

Vernacular name

English	Black cumin, Love-in-a-mist, Fennel flower, Nutmeg flower
Arabic	Habatut Barakah; Shuneez; Habbat-us-sauda

Persian	Siyadanah; Hindi: Kalonji, Kalajira
Sanskrit	Upakunchika, Kaalajaajee, Sushavee, Ajaji, Kalvanjika, Kalika
Bengali	Mungrela
Malyalam	Karun shiragani
Tamil	Karun shiragam
Talugu	Nillajila;

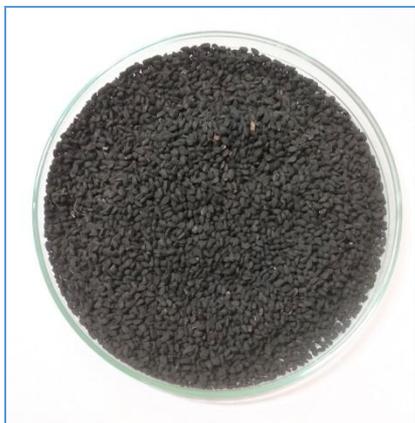
Pharmacological Action

It possess pulmonary-protective, anti-asthmatic, anti-flatulence, antipyretic, antibacterial, antifungal, antioxidant, immunomodulatory, anticancer, anti-inflammatory and analgesic activities.^[35] Also possess diuretic and emmenagogue, abortifacient, expectorant and phlegmatic diseases.^[36,37]

Therapeutic uses

Use in asthma, pleural effusion, cold and cough, chest pain and Tertian Fever.^[35]

Externally: Coryza - snuffing of roast seed or as nasal drop by mixing its powder with olive oil. Jaundice, migraine and chronic headache - used as nasal drop (sauoot) by mixing paste of kalonji in vinegar, haemorrhoids.^[36,37,38]



Haldi (*Curcuma longa*)

Turmeric is a golden spice, rhizome of the *Curcuma longa* L. plant, which belongs to the Zingiberaceae family. Its rhizomes are oblong, ovate, pyriform, often short-branched.^[39] Research suggests that curcumin is a good antioxidant can help in the management of oxidative and inflammatory conditions, metabolic syndrome, anti inflammatory, anxiety, and anti diabetic and hyperlipidemia^[40] Curcumin is a chemopreventive agents and responsible for the Anti-inflammatory effects.^[41]

Vernacular Names

Arabi	Kurkum, Urukesabghain, urukesabra, Ureka sufra, Zarsud
Persian	Darzardi; Dardachobah
Japanese	Ukon
Bengali	Haldi, Pitras
English	Indian saffron, Turmeric

Hindi	Haldi
Gujrati	Halada; MahrastraHalad
Chinene	Jianghuang
Kannad	Arsina
Punjabi	Halдар, Halja; TamilManjal
Telgu	Pampi, Pasupu

Pharmacological Action

Turmeric extract shown hepato and cardioprotective, Hypoglycemic, anti-amyloidogenic, antifungal, parasiticidal, antioxidant, antimicrobial. It is used as stimulant, aspirant, carminative, emenagogue, astringent, detergent and diuretic.^[42]

Therapeutic uses

It is used in the treatment of gastric, hepatic, gynecological and infectious diseases, also rheumatism and sinusitis.^[43]



CONCLUSION

Unani is a traditional system of medicine developed during the middle ages, which employs natural drugs of herbal, animal and mineral origin for the alleviation of ailment. It is well recognized fact that there is high incidence of drug related unexpected side effects in allopathic medicine for immunomodulation. It is where the role of Unani medicine come into play. Concepts of sanitation, isolation, air purification and immunomodulation described in Unani medicine remain the basic tenets of infection containment in the contemporary preventive medicine. Immune response is essential to eliminate virus and to preclude disease progression to severe stages. Therefore, boost immune response are certainly important.

Unani classical literature does not mention epidemics and pandemics as separate entities. Instead of it, they used a common term 'waba' for those diseases which affects the large population. The cardinal features COVID-19 are closely resembles to Amraz-e-Wabai (epidemic diseases) which was described in many unani classical books. During epidemic situation renowned unani scholars recommended to stay at home, and fumigate the shelters with aromatics herbs. Above mentioned unani drugs may be used for the management of such epidemic or pandemic situation. Such drugs are claimed as antioxidant, immunomodulatory, antipyretic, antiviral,

anti-inflammatory, bronchodilatory, antihistaminic, antitussive, analgesic and general tonic.

Conflict of Interest: None.

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