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An Insight on Wabāi Amrād (Epidemic Diseases) and COVID-19 Like Conditions – Unani Perspective

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ABSTRACT

Background and Objective: The World Health Organization has declared the COVID-19 as global pandemic on March 11, 2020. Hippocrates the father of medicine was supposedly the first ancient Unani physician to document the infectious diseases with their conspicuous clinical features which are today named as malaria, tuberculosis, influenza, mumps diphtheria etc. In Unani medicine, the epidemic diseases are referred to as *Amrād-i-Wabāi*. The present review has been embarked on to explore the Unani perspective into the scientific insight on epidemic diseases with the focus to unearth tangible information and solution to control the COVID-19 pandemic.

Methodology: A total of 89 citations comprising classical Unani texts and published papers in various reputed indexed journals from 2005 to 2020 were reviewed about prevention and management of epidemic/ pandemic diseases; antiviral, antipyretic, antitussive, immunomodulators activities of Unani drugs etc.

Results: Various measures such as isolation, social distancing; spray and fumigation treatment with Unani drugs for sanitization of the environment; modified diets such as barley water, *murabba-i-turanj*, *sikanjbeen*, vinegar etc to augment the immune system of the body; and pharmacotherapy such as *Tiryaq-i-Afayee*, *QursKafoor, Sharbat-i-Khaksi, Khameera Marwareed, Cydonia oblonga*, *Ziziphus jujuba* etc have been mentioned by Unani physicians for prevention and management of epidemic diseases and COVID like conditions.

Discussion: Certain scientific studies have reported that the individual ingredients of *Tiryaq-i-Afayee*(a pharmacopoeial preparation) such as *Aloe vera* and *Crocus sativus* possess significant antiviral effect, and the whole preparation exhibited an immunomodulatory effect. *Sharbat-i-Khaksi* and *Khameera Marwareed* (pharmacopoeial preparations) revealed potent antipyretic and immune system potentiating effects, respectively. *Cydonia oblonga* and *Ziziphus jujuba* possesses antiviral, antiinfluenza, antitussive, antipyretic and immunomodulator activities.

Conclusion: The aforesaid Unani classical and contemporary material surveyed has yielded substantial key information and practical solutions in the prevention and control of epidemic diseases and COVID like conditions.

Key Words: *Amrād-i-Wabāi*, COVID-19, Epidemic diseases, *Tiryaq-i-Afayee*, Unani medicine

INTRODUCTION

The outbreak of coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV- 2) was first reported on 31st December 2019, in the Wuhan city of China.[1] Earlier, this virus was named as a 2019-novel coronavirus (2019-to, but now it has been labelled as SARS CoV-2. It is a member of the Coronaviridae family which has large single-stranded RNA genomes. The SARS CoV-2 is found in both avian and mammals such as a bat, camels, dogs, masked palm civets etc. The first time, this virus has produced severe acute respiratory syndrome (SARS CoV) in late 2002. In 2012, the same virus produced Middle-East Respiratory Syndrome (MERS-CoV) and leftovers in camel.[2] The present outbreak of COVID-19 is believed to be originated from animals in China.[3] The World Health Organization (WHO) declared an outbreak of COVID-19 as Public Health Emergency of International Concern (PHEIC) on 30 January 2020 and a pandemic on 11 March 2020. According to the Coronavirus disease 2019 (COVID-19) Situation Report published by the WHO, till 5 Au-

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gust 2020 CE, 18354342 patients of COVID-19 have been confirmed and 696147 deaths have been reported due to it in the whole world[4] and more than 227 countries and territories, and 26 cruise and naval ships are affected.[5] In India, as of 6 August 2020, 08:00 IST (GMT+5:30), 1923837 cases have been confirmed and 40699 patients have been died because of COVID-19.[6] The mortality rate due to COVID-19 is different in various countries, and as of 6 August 2020 CE, the death rate in the United Kingdom, Italy, France, Belgium, Spain, United States and India is 15.12%, 14.14%, 13.95%, 13.86%, 9.32%, 3.29%, 2.07%, respectively.[7]

The Unani system of medicine is one of the officially recognized traditional systems of medicine practised in India under the patronage of Ministry of AYUSH (Ayurveda, Yoga andNaturopathy, Unani, Siddha and Homeopathy), Government of India.[3] This is an age-old system of medicine which was originated in Greece and propounded by Hippocrates (460–370 BC).[8] The system has also been recognized as an alternative traditional system of medicine by the World Health Organization to cater to the health care needs of the population.[9] In Unani medicine, the *wabā'* is referred as an epidemic and is defined as putrefied changes in the air, water, soil or environment which lead to alteration in the homeostasis of humour thus conducive to putrefaction of humour in the body in a large population at a very short period. The outbreak of an infectious disease in a wide geographic area of the world is called *wabā' 'umūmī*, which is synonymous to the pandemic. The disease is termed as *marād* and *amrād-i-wabāi* is referred to as epidemic diseases.[10] Hippocrates is considered as the first epidemiologist of the world. He was the first scholar who has defined epidemic and endemic nature of diseases. According to Roman physician Galen (130–210 CE), diseases are caused by three factors viz. predisposing, exciting and environmental factors.[11] Razi (Rhazes) (865–925 CE), the great Unani scholar, physician and epidemiologist, has written a small renowned masterpiece treatise entitled '*Kitab fi al-Jadariva-al-Hasbah* (*De Variolis et Morbiliis/* Book on Small Pox and Measles)' in which he has described the differential diagnosis between smallpox and measles.[12] Based on above-mentioned facts, evidence, it is evident that the Unani system of medicine has discussed epidemics in detail about their causes, pathology, clinical manifestations, prevention, management etc.[13-15] In this review, the possible approach particularly prophylaxis and treatment of epidemic diseases including COVID-19 have been explored which may be useful to combat the pandemic situation of coronavirus disease in the present scenario.

METHODOLOGY

The classical Unani literature mainly Urdu translations, from the period of 9th–20thcentury CE viz. *Firdaus al-Hikmah* (Paradise of Wisdom) of Abu al-Hasan Ali ibn Sahl Rabban al-Tabri (838–870CE), *Kitab al-Mansuri* (*Liber ad Almansorem*), *Kitab al-Hawi* (*Liber Continens*) and *Kitab al-Murshid* of Abu Bakar Muhammad ibn Zakaria Razi (865–925CE), *Kamil al-Sanā* (The Complete Book of the Medical Art) of 'Ali Ibn al-'Abbas al-Majusi (Haly Abbas) (10th Century CE), *Al-Qanūnfi 'l Tib* (The Canon of Medicine) of Ibn Sina(Avicenna) (980–1037CE), *Zakhīrā Khawārizam Shahi* of Ismail ibn Husayn Gorgani (1040–1136CE), *Kitab al-Mukhtarātfi 'l Tib*of Ibn Hubal Baghdadi (1121–1213 CE), *Kitab al-Kuliyāt* of Ibn Rushd (Averroes) (1126-1198 AD), *Kitab al-Ta'seer* of Ibn Zohar (Averroes) (1126-1198 CE), *Kitab al-Fatahfi 'lTadawi Man Jamee Sunuf al-Amrazva al-Shakawi* of Abu Saeed ibn Ibrahim al-Maghrabbi, *'Ilāj al-Amraz* of Hakim Muhammad Shareef Khan (1722–1807CE), *Qarabadeen Azam va Akmal* of Hakim Muhammad Azam Khan (1815–1902CE), *Qarabadeen Najmul Ghani* of Najmul Ghani (b. 1859 CE), *Al-Qarabadeen* and *Makhzan al-Mufredat* of Muhammad Kabeeruddin (1889–1976 CE) were reviewed pertaining to definition, causes, prophylaxis and treatment of epidemic diseases. Other published research papers during the period of 2005 to 2020 CE about antiviral, antipyretic, antitussive, immunomodulatory activities of Unani drugs; SARS CoV-2, COVID-19 etc were also reviewed through search engines like PubMed, Science Direct, Elsevier, Google Scholar, Research Gate etc. The keywords employed for review of this article are Unani medicine, *wabā'-i-amrād* (epidemic diseases), *hummā-i-wabā'i,* (epidemic fever), *tabī'at* (mediatrix naturae), *ajsāmkhabītha* (pathogenic organisms), *hifzmā taqaddam* (prevention), *'ilāj* (treatment), antiviral and immunomodulator Unani drugs, COVID-19, SARS CoV- 2 etc. A total of 130 kinds of literature were reviewed, of them, 89 were selected for the compilation of this manuscript.

RESULTS

Coronavirus Disease-19

Presently, the WHO has registered its grave concern over the alarming situation arising out of novel severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) infections in many countries.[16] This virus is usually transmitted through sneezing or coughing of infected persons.[17] The SARS CoV-2 is an enveloped single-stranded RNA beta coronavirus which genome sequence shared 79.5% sequence identity with severe acute respiratory syndrome-related coronaviruses.[18] It has been observed that the transmission and infectivity of SARS CoV-2 are very high but the mortality is low compare to other coronaviruses such as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle-East respiratory syndrome coronavirus (MERS-CoV)[19] Based on previous studies on SARS-CoV and MERS-CoV, it is supposed that the incubation period of COVID-19 is 2–14 days. Although,

some researchers believe that this period could be 0–24 days in certain cases.[20]The SARS CoV-2 produces pneumonia-like clinical manifestations such as fatigue, fever, dry cough, muscular pain, breathlessness, sore throat, nasal congestion, headache, vomiting, diarrhoea etc particularly in the beginning of the disease, but in severe cases, acute respiratory distress syndrome, hypoxemia, septic shock, metabolic acidosis, coagulation disorders develop rapidly. Certain asymptomatic cases do not have such clinical presentations except mild fatigue and low-grade fever. Such patients are usually carrier of SARS CoV-2 and can transmit the infection to other .[21]Till dates, there is no curative treatment or vaccine has been developed which can combat the COVID-19. Only general preventive measures such as stay away from the exposure, hand washing with soap and water for 20 seconds, use of alcohol-based sanitizer, wearing of surgical /N95/ N99 face masks etc are adopted to prevent the spread of the disease. Based on clinical need, certain supportive management such as rehydration therapy, antipyretic and antitussive drugs, oxygen support etc are given to patients of COVID-19.[22] Certain antimalarial drugs such as chloroquine and hydroxychloroquine have been clinically used in some patients of South Korea and China which exhibited little therapeutic effects. Similarly, azithromycin along with hydroxychloroquine has also been reported to possess an insignificant effect.[23] Clinical trials on sarilumab and Remdesivir against rapidly spreading COVID-19 are being carried out by few reputed biotechnological firms including National Institute of Health of the United States of America.[24]

The lockdown imposed and implemented in many parts of the world to break the cycle of infection, promisingly decreased the growth rate, increased doubling time of COVID-19 cases particularly in India and to ramp up health infrastructure but has led to the migration crisis, several psychiatric conditions such as stress, anxiety, depression, suicides, panic disorders among the people [25] apart from slowing down the global economy.[26]

UNANI SYSTEM OF MEDICINE

Brief introduction

The principle fundamentals of Unani system of medicine are based on the teachings of Greek philosopher and scholar, Hippocrates (460–370BC), whose humoral theory which presupposes the presence of four bodily senses of humour, *dam* (sanguine), *balgham* (phlegm), *safrā* (yellow bile) and *sawdā* (black bile) with their corresponding temperamental qualities of hot-moist, cold-moist, hot-dry and cold-dry respectively[8]. Later, this system has been further developed and codified through systemic experimentations carried out mostly by Arab and Persian physicians and scholars such as Razi (865–925CE), Ibn al-'Abbas al-Majusi (930–994 CE), Ali Ibn Sina (980–1037CE)[27], Abu Sahal Masihi (d. 1010 CE) etc. These scholars had propounded another theory namely *umūre tabī'iyya* (basic physicochemical components of the human body) which is composed of seven components viz. *arkān*(elements), *mizāj*(temperament), *akhlāt*(humour), *a'dā'* (organs), *arwāh*(pneuma), *quwā*(faculties) and *af'āl*(functions)[9]. The survival of the living body is not possible in the absence of any one of these components. Furthermore, any qualitative or quantitative derangement in the constituents of the components as mentioned above may cause disease condition. Thus the main aim of an Unani physician during treatment of diseases is to bring back the homeostasis or equilibrium primarily by aiding bodily faculties' viz. *tabī'at mudabbir-i-badan* (*medicatrix naturae*).[28] This is an inherent power of the body which provides self-preservation or adjustment and restore any disturbance in the constitutional state of an individual[10]. he four principles of treatment adopted in Unani medicine are *Ilāj bi'l-Tadbīr* (regimental therapy), *Ilāj bi'l-Ghizā* (diet therapy), *Ilāj bi'l-Dawā* (pharmacotherapy) and *Ilāj bi'l-Yad* (surgery).[29]

Concept of epidemics in Unani Medicine

In Unani medicine, the *wabā'* is defined as contaminated or putrefied changes in the air.[30] The equivalent term for *wabā'* is epidemic as mentioned in the Standard Unani Medical Terminology book published by the Central Council for Research in Unani Medicine, Ministry of AYUSH, Government of India.[10] Ibn Sina stated that sometimes the *ajsām khabītha* (pathogenic organisms) contaminates the water which may ultimately change the quality of air and causes fever in a large group of the population at a very short period .[31] The historical events testify that many infectious diseases such as meningitis, tuberculosis, leprosy, rabies and smallpox were prevalent in olden days. Hippocrates described the clinical manifestations of many infectious diseases which are presently named as tuberculosis, mumps, influenza, diphtheria, malaria etc. Galen proposed miasma theory of transmission of contagious diseases. According to him, certain infectious diseases viz. cholera, plague, chlamydia etc spreads through a noxious form of bad air which contains harmful vapours or poisonous elements that enters in the human body by inhalation or skin pores. Razi has described the complete picture of smallpox and measles[12] in *Kitab fi al-Jadariva al-Hasbah*(*De Variolis et Morbiliis/* Book on Small Pox and Measles) which has been considered as the first scientific treatise on this subject by the WHO in May 1970 CE.[32] He is regarded as a great epidemiologist who explored many aspects of epidemic diseases. He has advocated in *Kitab al-Hawi* (*Liber Continens*), that "*when zoonotic diseases are epidemic, the human being should avoid being in close contact with animals*'.[34] Likewise, a historian namely Magner LN has quoted that since ancient time, it is observed that an infectious disease is transmitted through wild or domesticated animals directly or via insect vectors.[33] Razi has further stated that the

droplets *inhalation is more contagious and an infected person should avoid visiting the houses of others*'[34] which seeds the idea of quarantine or isolation. At another place, Razi has quoted that '*those people whose waste products are not regularly and properly excreted from the body, they are more prone to acquire infection of epidemic diseases*'.[35] According to him, the epidemic diseases are usually occurring during hot weather especially when raining has started.[13] When the direction of the air is changed from south to north, the prevalence of throat and chest diseases is increased. Smallpox and acute fever are very common during autumn. He has also asserted that the movement of people from non-contaminated to contaminated place causes infections.[35] Another renowned Unani scholar, Ibn Sina has stated that the body secretion is contaminated by foreign bodies before getting an infection.[36] The contamination of the air is caused found when the bodies died during an epidemic are not disposed of properly.[3,31] The air may also get contaminated and putrefied due to rotten fruits, vegetables, accumulated water at one place, dead animals etc. Such contaminated air can produce infection in the human being which manifests as body pain, excessive sweating, halitosis, bilious vomiting and diarrhoea, changes in urine etc. The diseases produce through such type of contamination are called *amrad-i-wafidā* which is the synonym of epidemic disease.[37] Ibn Khatima (1369 CE) stated that the human body is surrounded by minute bodies which when entered in the human body may cause disease.[36] Eventually, the ancient Unani scholars were fully aware of the presence of microbial organisms in the environment. Though the germ theory was completely understood after the invention of the microscope in 1683 CE [3] Another terminology, *humma-i-wabaī* is mentioned in the classical Unani literature which is referred to epidemic fevers caused by putrefied changes in the air.[15,38] Such putrefied air when inhaled produces septicaemia resulting in malicious fever, difficulty in breathing and deaths.[15] Ibn Zohar stated that he observed certain patients who died despite having mild fever and simultaneously some patients recovered completely when their place of stay and use of cold and dry food items was modified. He further asserted that inhalation of contaminated air disrupts the normal functioning of the heart and the patient has died due to heart failure.[38] The severity of the infection during an epidemic is assessed by respiratory distress and foul smell of breath.[35] The Unani physicians have described the detail clinical manifestations of epidemic diseases viz. redness in the eye, hotness in the chest, polyuria, increased viscosity of urine, loss of appetite, ulcers around the mouth etc. It is also noted that some patients do not have a high-grade fever but internally burning sensation and anxiety is felt.[35] *Nazlā-i-Wabaīyā* (epidemic coryza and catarrh) is mentioned in Unani literature which clinical features are sore throat, sneezing, body ache, fever.[88] dry cough, difficulty in breathing, vertigo, diarrhoea, fatigue etc.[89] Theses manifestations are very much similar to COVID-19 like conditions.

Certain diagnostic features for the diagnosis of epidemic diseases have been explained by the Unani scholars such as changes in the contents of stool and colour of saliva.[35] Presently, the real-time fluorescence (RT-PCR) is usually applied as a diagnostic tool to detect the positive nucleic acid of SARS-CoV-2 in the oropharyngeal swab, sputum and secretions of the lower respiratory tract.[39] Based on keen observation and profound intellect, the ancient Unani scholars were fully aware of changes in the respiratory rate, the pattern of breathing, colour of tongue and saliva which were all were used as a diagnostic tool in olden days but nowadays the salivary swab is taken for PCR test as confirmatory one. Apart from the detailed description of epidemic diseases in general, the Unani medicine has also given detail description of certain specific diseases which have been categorized as an epidemic in earlier days such as *hasba* (measles), *judariyya* (smallpox)[13,30,31,37,41] *tā'ūn* (plague).[40] *judhām* (leprosy) etc[31].

Adoption of Preventive measures during epidemics

General measures

In Unani medicine, various general preventive measures are mentioned to prevent epidemic diseases. The purity of atmospheric air is vital for the preservation of health; hence it is advocated by Hippocrates to stay in open, airy, entry of sun rays light, ventilated places to stay healthy. It is stated that the spread of epidemic fever is increased in a crowded place. Thus, people should avoid going and staying in such places. Razi has advised keeping away from the place where plague is endemic or epidemic. He further suggested that in the case of armed forces or guests are to visit such places, they should prefer to stay at high altitude. It is also advised that the contaminated or putrefied air should not be inhaled. The healthy persons should avoid close contact of infected persons. In the case of close contact, the healthy person should sit against the wind. It is recommended that when the heat is felt in the body, they should leave that place and should reside in a cold room whose doors and windows are in the northern direction. This may prevent the contamination of air from certain infections such as measles, smallpox and plague. The children should take more precautions than adults because they are more susceptible to infections during the epidemic. Excessive exertion or strenuous physical work should be avoided to restore bodily faculties,[13] but regular moderate exercise should be performed which will help to excrete waste products from the body since these subjects are not prone to get the infection during the epidemic.[35] The patients of any infection during the endemic or epidemic should be isolated at home which testifies the concept of home quarantine in Unani medicine.[13,30] The cloth screen of the door or window should be placed after dipping in the rose water. The people should be advised to take vinegar along with plain water daily.[13] The dietary habit of healthy people and patients

should be improved; they should take balanced diet regularly during the epidemic. The rooms where patients are staying should have proper ventilation because an accumulated air at one place may cause more contamination. The physicians may perform counselling of patients suffering from epidemic diseases to boost their morale and psychological power.[35] The patients may be advised to take gargle with decoction which contains *Rhus coraria* Linn., extracts of *Morus nigra* Linn. and *Myristica fragrans* Houtt and rose water daily during the epidemic to keep the infection at bay.[13,15] Prepare liniment with *Myrtus communis*, camphor and sandalwood for application over the chest.[41]

Spraying of Unani drug sanitizers

In Unani medicine, various drugs and preparations are recommended for spraying in the environment as sanitizers. Spray with vinegar (acetic acid) alone[41,42] or along with *Ferula foetida* Regel is useful[30,35] for sanitization of houses, doors, roads and other things. Other formulas for a spray with Unani drugs containing sandalwood, camphor and aqua rose in combination, and spray with rose and vinegar are also advised.[30] Ibn Hubal Baghdadi has recommended another recipe which contains aqua rose, sandalwood, camphor and vinegar as a spray.[15] An eminent Indian Unani physician, Hakim Muhammad Azam Khan has suggested that use of spray with mint water to destroy microorganisms.[41] It is also advised that spray with plain water along with vinegar may be done daily during epidemics.[13] A simple spread of leaves of *Salix caprea* and *Rosa damascena* on the floor is also recommended for sanitization purpose.[15]

Fumigation treatment of the environment with Unani drugs

The classical Unani texts have discussed fumigation with the combustion of drugs during epidemics which have antiseptic, disinfectant, antimicrobial and aromatic properties. Fumigation with *Styrax benzoin* Dry and *Cyperus rotundus* Linn. is advised by Razi.[42] He has recommended another recipe for fumigation which contains Agarwood, Ambargris, sandalwood, *Saussurea lappa* (Decne.) Sch.-Bip., and *Boswellia serrata* Roxb.[30,35] Fumigation may also be done with *Ferulaassa foetida* Regel., *Crocus sativus* Linn., *Cyperus rotundus* Linn., *Acorus calamus* Linn., bitter Almond, *Cymbopogon jwarancusa* (Jones) Schult., *Parmeliaperlata* (Huds.) Ach., and *Tamarix articulata* vahl. in combination. Another formula for fumigation containing peel of pomegranate, sandalwood, camphor, *Salix alba* Linn., applewood, and wood of quince tree is also recommended.[30] It is also advised that fumigation with *Hymenaea verrucosa* Gaertn., *Pistacia lentiscus* Linn., camphor, *Crocus sativus* Linn., *Diospyros ebenum* J Koenig ex Retz., borax, *Laurus noblis* Linn., *Cymbopogon jwarancusa* (Jones) Schult., *Parmelia perlata* (Huds.) Ach., *Juniperus communis* Linn., *Zingiber officinale* Rosc., *Acorus calamus* Linn., *Inulara cemosa* Hook. F., *Coriandrum sativum* Linn., and *Commiphora myrrha* may also be used. Razi has also mentioned that a mixture of camphor, *Acacia Arabica* Wild. var. Indica Benth., *Nigella sativa* Linn., *Asareum europaeum* Linn., *Styrax benzoin* Dry., Agarwood and *Crocus sativus* Linn., be grounded together and make pills which can be used as fumigation after burning them during the epidemic.[35] Another formulation for fumigation which contains *Saussurea lappa* (Decne.) Sch.-Bip., *Boswellia serrata* Roxb., *Commiphora myrrha,* Ambargris, clove, *Acorus calamus* Linn., *Pistacia lentiscus* Linn., musk, camphor, sandalwood and Agarwood is also recommended.[15] Fumigation with just Ambargris[41] and sandalwood along with camphor may also desensitize the environment from pathogenic organisms.[13]

Inhalation

It is advised that rose petals dipped in vinegar, and sandalwood along with camphor and vinegar may be inhaled regularly by healthy people as a preventive measure during epidemics.[30]

Lifestyle modifications

The consumption of intoxicants,[30,35] excessive sexual intercourse and sleep should be avoided during epidemics. The people are advised to keep away from a crowded place; take *hammām juloosi* (sitz bath), fresh and hot food, plenty of water; and avoid much physical exertion. It is also advised that easily digestible food items should always be consumed periodically during epidemics.[35]

Dietotherapy

During epidemics, meat, sweet edibles should not be consumed. In case of extreme desire, only meat of birds or young goat shall be taken with a mixture of vinegar or grapes juice. Vinegar;[13,42] fruits like grapes, pomegranate, apple, lemon etc should be taken frequently. Cucumber, snake cucumber, pumpkin should be taken routinely. The Unani physicians have recommended that barley water[13] which is prepared with one part of barley and 10/ 14/ 20 parts of plain water[43,44] should be taken daily during epidemics to boost the immune system of the body.[13] The barley water with sugar added is also beneficial.[15,41] Hippocrates has described 10 various benefits of barley water and is considered as diet-cum-drug which is highly recommended in case of fever, acute infections, tuberculosis, diabetes mellitus and other debilitating diseases.[29] The barley contains both soluble and insoluble fibre, protein, vitamins B and E, minerals, selenium, iron, magnesium, flavonoids, anthocyanins etc. The antioxidant property of barley is due to the presence of selenium and vitamin E.[47] Gile Armani (Armenian bole) along with vinegar and plain water is also useful during epidemics.[13] The infusion of *Prunus domestica* Linn., *Tamarindus indica* Linn.,

and mucilage of *Plantago ovate* Forsk., with an admixture of aqua roses and pomegranate juice is also advised.[13] *Prunus domestica* Linn. and pomegranate may also be consumed regularly eaten separately. Vinegar, plain water, Armenian bole, rose water along with *sikanjabeen* (a combination of vinegar and honey) is also recommended regularly during the epidemic. Intake of lentil legume, *Vigna mungo* pulse and pumpkin, butter along with vinegar and asafoetida[35], grapes juice, vinegar, lemon juice, infusion of sumac, unripe grapes, apple, quince, *Citrus medica* Linn. and lemon juices are also beneficial.[30] Camphor water, pomegranate juice, vinegar along with Armenian bole also provides strength to the body during epidemics.[15]In case of cough, sneezing and fever; spinach, *Chenopodium album* Linn., fresh or dry coriander,[45] apple juice,[41] almond oil etc shall be preferred.[45] *Murabba-i-Turanj*, a specific dietetic prepared with *Citrus medica* Linn. and sugar is useful in case of throat and chest diseases during the epidemic.[46]

Pharmacotherapeutics of epidemic diseases

The classical texts of Unani medicine deal with several Unani drugs which have been effectively used by ancient Unani physicians for the treatment of infectious diseases during epidemics.

Specific compound drugs used for the management of epidemic diseases

The following polyherbal pharmaceutical preparations have been recommended for the prevention and treatment of epidemic diseases. (Table 1)

Table 1: Specific compound drugs used for the management of epidemic diseases

Pharmacopoeial preparations	Ingredients and their ratio	Dosage form	Dose/ Method of use	Indications	References
Tiryaq-i-Afayee	*Aloe vera 10 g, Balsamodendron myrrha 5 g, Crocus sativus* 5 g	Powder/ Pills	1-2 g with plain water/ infusion of *Ocimumbasilicum*	Epidemic diseases including fever	13,15,35,41,43,44,48, 49
Qurs-i-Kafoor	*Rosa damascena* 35 g, *Cucumis melo* 52.5 g, *Vitiveria zizanioides* 24.5 g, *Lactuca sativa* seeds 21.5 g, *Cichorium intybus* seeds 7 g, *Lagenaria siceraria* seeds 14 g, Extract of *Iris versicolor* 10.5 g, *Fraxinus ornus* 35 g, *Cinnamomum camphora* 1.75 g	Tablet	One tablet daily	Refrigerant for heart and liver, antipyretic	13,30
Formulation	*Rosa damascena* 10 .5 g, *Gulqand* (a combination of rose petals and sugar) 70 g boil together into the water	Fresh preparation of decoction	Take with an admixture of Rose oil 35 ml or *Khameera-Banafsha* (compound drug)	Epidemic fever	41
Formulation	*Cydonia oblonga* 3 g, *Ziziphus jujuba* 5 No., *Cordia myxa* 9 No.	Fresh preparation of decoction	Take with *Sharbat-i-Banafsha* 25 ml	Coryza and catarrh during an epidemic	88,89

Razi has highlighted the therapeutic value of *Tiryaq-i-Afayee* during epidemics. He said that '*in my knowledge, those who took this drug during the epidemic did not suffer from the epidemic diseases*'[35]. Many renowned Unani physicians and scholars quoted in their classical texts that Galen had used *Tiryaq-i-Afayee* frequently during the epidemic.[15,41,43,44,49]

Supportive compound drugs used for the management of epidemic diseases

The following pharmacopoeial preparations have been recommended for the treatment of fever, common cold, cough, general debility and other complains of infectious diseases. (Table 2)

Table 2: Supportive compound drugs used for the management of epidemic diseases

Pharmacopoeial preparations	Ingredients and their ratio	Dosage form	Dose/ Method of use	Indications	References
Sharbat-i-Khaksi	*Foeniculum vulgare 100 g, Borago officinalis* leaves 60 g, *Sisymbrium irio 100 g, Ziziphus jujuba 100 g, sugar 1.5 kg,* Glycerine 400 g, Citric acid 4 g, Sodium benzoate 2 g	Syrup	25 ml	fever	50,51

Table 2: *(Continued)*

Pharmacopoeial preparations	Ingredients and their ratio	Dosage form	Dose/ Method of use	Indications	References
Sharbat-i-Banafsha	*Viola odorata* flowers 125 g, sugar 1.5 kg	Syrup	25-50 ml	fever, cough, common cold, pneumonia, pleurisy	43,48,52
Sharbat-i-Neelofar	*Nympha alba* flowers 30 g, sugar 900 g	Syrup	25-50 ml	Pneumonia, pleurisy, fever, headache	43
Khameera Marwareed	Pearl 25 g, *Bambusa arundinacea* 25 g, *Santalum album* 25 g, Ambergris 10 g, sugar1.5 kg, aqua *Rosa damscena* 1 lit, aqua *Borago officinalis* 1 lit	Semisolid	3-5 g	General tonic, immunomodulator, cardiac and brain tonic	53,54,55

Specific and supportive single drugs used for the management of epidemic diseases

In Unani medicine, the following specific and supportive single drugs are used for the treatment of various clinical features of epidemic diseases. Certain scientific studies have has proved n that these drugs possess antiviral, antioxidant, antitussive, expectorant, immunomodulator, antipyretic activities etc. (Table 3)

Table 3: Specific and Supportive single drugs used for the management of epidemic diseases

Single drugs	Dose	Indications	References
Behi dana (*Cydonia oblonga)*	3-5 g	Antioxidant, immunomodulator, antiallergic, anti-influenza, antipyretic, antitussive	53,56,57
Unnab (*Ziziphus jujuba*)	5-7 pieces	Antiinfluenza, immunomodulator and antioxidant, expectorant, antitussive, antipyretic	53,57-59
Sapistan (*Cordia myxa*)	9-15 pieces	Immunomodulator, antioxidant, antitussive, expectorant, antipyretic	53,57,60,61
Karanjwa (*Caesalpiniabonducella*)	3-5 g	Antipyretic, antimicrobial, anti-inflammatory, immunomodulator	53,57,63

DISCUSSION

The aforementioned survey has elucidated the detail description of epidemic diseases about their prevention and management. In Unani medicine, the epidemic is referred as *wabā'*[10] which defined as changes in the air due to contamination[30] by *ajsām khabītha* (pathogenic organisms) and produces fever and other clinical manifestations in a large group of the population at a time.[31] The causes, pathology, clinical features and management of certain epidemic diseases viz. smallpox, measles,[37,40] plague,[40] leprosy[31] etc are mentioned in classical Unani literature in detail. The ancient Unani physicians have described various general measures for prevention of epidemic diseases such as isolation at home; avoid visiting in a crowded place and close contact with infected persons[13], use gargle containing Unani drugs etc[13,15]. They have mentioned that certain Unani drugs are used as a spray for sanitization of the environment. The spray with vinegar[41,42], sandalwood, camphor, aqua rose,[30] mint water[41] etc are very much useful and still in vogue. Since a long time, vinegar is known to have disinfectant, antimicrobial[63,64] and antioxidant properties. These effects are due to the presence of polyphenols, micronutrients and other bioactive constituents in the vinegar. [64] EzzEldin et al., 2019 has reported that vinegar possesses significant antiparasitic effect against *Acanthamoeba astronyxis* isolate. [63] Misra et al., 2012 has revealed the antibacterial effect of dichloromethane and methanol extracts of callus, somatic embryo and seedlings of *Santalum album* Linn. and sandalwood oil against nine Gram-negative and Gram-positive bacteria. They also found that the somatic embryo extract possesses significant antibacterial effect compared to that of sandalwood oil and matured tree leaves. This activity is due to the presence of terpenoids, saponin, phenolics and tannins constituents.[65] Sokolova et al., 2017 has reported the antiviral activity of aliphatic and alicyclic camphor imines against influenza virus (H_1N_1).[66] The aqueous and methanol extracts of rose petals exhibited antiviral effect against Human Immunodeficiency Viruses (HIV). Citronellol and geraniol isolated from the rose essential oil showed antiviral activity against Herpes Simplex Virus-1 and Haemophilus parainfluenza type-3. The antibacterial activity of rose water has been reported against various bacteria such as *E. coli*, *P. aeruginosa*, *B. subtilis*, *S. Aureus*, *Chromobacterium violaceum*, *Erwinia carotovora* etc.[68] Vetas D et al., 2017 has reported the significant antibacterial activity of sage and spearmint essential oils against Planktonic

and Biofilm *Staphylococcus aureus* cells in comparison to the sodium hypochlorite[69]. Li et al., 2017 has revealed the promising *in vitro* antiviral, anti-inflammatory and antioxidant activities of ethanol extract of *Mentha piperita* leave. The antiviral activity of the test drug against the respiratory syncytial virus (RSV) was reported due to the presence of phenolic acid and flavonoid bioactive compounds.[70]

The review also discussed fumigation treatment to sanitize the environment for which many drugs are listed in the classical texts. For instance, fumigation with *Styrax benzoin,*[42] sandalwoods*, Boswellia serrata,*[30,35] camphor,[30] *Zingiber officinale*, *Acorus calamus* etc has been recommended. Many scientific studies have also proved their insecticidal, disinfectant and antimicrobial properties when they are used in the form of fumigation. Bhatwalkar et al., 2019 has carried out a study on validation of environmental disinfection efficacy of traditional Ayurvedic fumigation practices in which it has been reported that the fumigation with garlic peel (*Allium sativum*), turmeric (*Curcuma longa*), carom seeds (*Trachyspermum ammi*) and loban powder (*Styrax benzoin*) separately decreased the average airborne bacterial colony forming units (cfu)/m3 compare with non-fumigated control.[71] Upadhyaya I et al., 2015 has reported that the two plants derived antimicrobial agents such as trans-cinnamaldehyde and eugenol[72] which are commonly found in *Cinnamomum zeylanicum* and *Syzygium aromaticum* (Linn.) Merr and Perry., respectively[73] showed potential effects when applied as fumigation treatment against *Salmonella enteritidis* on embryonated eggshell.[72] The classical text reveals that camphor was used as fumigant when the Black Death was prevalent in ancient time. Camphor is reported to have many activities like insecticidal, antiviral, antimicrobial, analgesic, antitussive etc.[67] Fu et al., 2015 has reported the potential insecticidal activity of camphor essential oil against the red imported fire ant (RIFA)[74] Kim J et al., 2016 has reported the significant insecticidal activity of *Santalum album* and *Rosa damascena* in contact toxicity tests against male and female spotted wing drosophila (SWD) with LD50 values of 3.40 ug/ fly and 2.18 ug/ fly against male SWD and of 8.91 ug / fly and 5.61 ug/ fly against female SWD, respectively.[75] Chaubey, 2013 investigated the repellent, insecticidal and antiovipositional activities of *Zingiber officinale* and *Piper cubeba* essential oils against pulse beetle and *Callosobruchus Chinensis* (Coleoptera: Bruchidae), in which both essential oils produced promising fumigant and contact toxicity, especially against C. Chinensis adults.[76] Liu et al., 2013 has revealed the potent insecticidal activity of the essential oil obtained from rhizomes of *Acorus calamus* against the booklouse (Liposcelisbostrychophila).[77]

It is advised to take various modified diets such as vinegar,[13,42] barley water,[15,41] *murabba-i-turanj*[46] etc, and fruits like grapes, pomegranate, apple, lemon,*Prunus domestica*, *Tamarindusindica* etc[13] during the epidemic. The two important flavonoids such as hesperidin and hesperetin are usually found in citrus fruits which possess antioxidant and anti-inflammatory activities.[78] A study has reported that an ethanol extract of fresh *Prunus domestica* Linn. exhibited significant free radical scavenging capacity and antioxidant activity.[79] Barathikannan et al., 2016 has reported the significant α-Glucosidase inhibition, antimicrobial and antioxidant activity of *Punica granatum* fruit peel extract[80]. The ethanol extract of the seed coat of *Tamarindus indica* Linn. exhibited antioxidant activity. Similarlytamarindienal, an active constituent isolated from the fruit pulp showed fungicidal and antibacterial activities[73].

The Unani literature also contains certain evidence-based specific pharmacopoeial preparations for the prevention and management of epidemic diseases. *Tiryaq-i-Afayee* which contains *Aloe vera, Balsamodendron myrrha, Crocus sativus*, is considered as the drug of choice in this regard.[15,41,43,44,49] Scientific studies have reported that the ingredients of *Tiryaq Afayee* possess significant antiviral activity. For instance, Choi et al., 2019 have reported that *Aloe vera* ethanol extract (AVE) significantly decreases the viral replication of green fluorescent protein labelled influenza A virus in Madin-Darby Canine Kidney (MDCK) cells. The study also demonstrated that the antiviral activity of AVE is due to the presence of quercetin, catechin hydrate and kaempferol in the extract[81]. Li et al., 2014 has reported that aloe-emodin, an important anthraquinone glycoside present in *Aloe vera* possesses significant antiviral activity against influenza A virus in MDCK cells via up-regulating galectin-3 and thioredoxin as well as down-regulating nucleoside diphosphate kinase A[82]. Soleymani et al., 2018 has reported that crocin and picrocrocin isolated from Iranian saffron extract exhibited potent antiviral effect against HSV-1 and HIV-1.[83] A study has reported that *Tiryaq-i-Wabai*, a pharmacopoeial formulation which contains same ingredients as *Tiryaq-i-Afayee*, possesses significant immune-stimulating activity in a small group of immuno-compromised subject. This study has revealed that the total leucocyte count (TLC), lymphocyte percentage, absolute lymphocyte count (ALC) and CD_4 count were significantly increased in comparison to the control group.[8]

Apart from specific drugs, certain other formulations such as *Sharbat-i-Khaksi, Sharbat-i-Banafsha, Sharbat-i-Neelofar* and *Khameera Marwareed* are also recommended based on clinical manifestations of infectious diseases. A study has reported that an aqueous extract of *Sisymbriumirio*, chief ingredient of *Sharbat-i-Khaksi*[50] possesses promising antipyretic activity against yeast-induced pyrexia in rats.[85] Another study has reported the potential antibacterial activity of silver nanoparticles (Ag NPs) synthesized by using an aqueous extract of *Sisymbrium irio* against multi-drug resistant bacterial strains like *Pseudomonas aeruginsa* and *Acenetobacter baumanii* which produces ventilator-associated

pneumonia.[86] *Viola odorata* Linn. is the main ingredient of *Sharbat-i-Banafsha*. Tafazoli et al., 2019 has reported that the *Viola odorata* Linn. oil possesses significant effect to control fever in febrile neutropenic children.[87] Khan et al., 2009 has reported that *Khamira Marwareed* showed promising immunopotentiating effect in mice in terms of increasing haemoglobin, RBCs, WBCs, IgG, IgG2a and IgG2b levels[54].

Certain single Unani drugs such as *Cydonia oblonga*, *Ziziphus jujuba*, *Cordia myxa* and *Caesalpinia bonducella* are studied for different activities which may be effective in COVID like conditions.[53] Hamauzu et al., 2005 has revealed that the phenolic extract of *Cydonia oblonga* exhibits significant antioxidant activity against linoleic acid peroxidation system and DPPH radical scavenging system, and antiviral activity against influenza virus.[56] A study has revealed the significant antioxidant and immunological activities of purified polysaccharides of *Ziziphus jujuba* Cv. Muzao.[58] Ali et al., 2015 has revealed that an aqueous extract of the fruit of *Cordia myxa* Linn. exhibited an immunomodulatory effect in terms of increasing cell-mediated immunity in immunized mice with hydatid cyst fluid.[60] Archana et al., 2005 have reported the significant antipyretic and analgesic properties of the extract of *Caesalpinia bonducella* seed Kernel in animal models.[63]

CONCLUSION

The Unani classical and contemporary material surveyed has yielded substantial key information and practical solutions in the prevention and control of epidemic diseases and COVID like conditions. Almost all the prophylactic and therapeutic measures adopted since two and half millennium by the Unani physicians are still in vogue and these have been scrutinized in the light of various scientific studies cited in the manuscript. Hence, it is reasonable to conclude that the observation and experimentation carried out by Unani scholars with the then-available knowledge and resources in managing various epidemic diseases has led the foundation to further strengthen and develop the current understanding of epidemiology. More ever the analytical review carried out amply proves that Unani system of Medicine has all the potential in preventing and managing epidemic diseases including COVID like conditions.

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