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Overview of Covid-19; its prevention and management in the light of Unani medicine

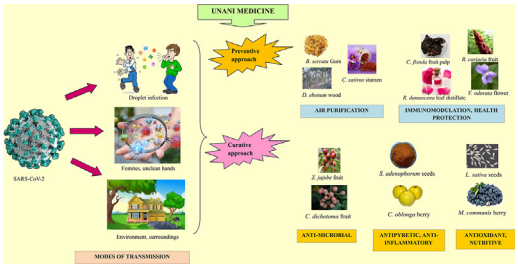
Sadia Nikhat [a,1], Mohammad Fazil [b,*,1]

[a] Dept. of Ilaj bit Tadbeer, School of Unani Medical Education and Research, Jamia Hamdard, New Delhi 110062, India
[b] HAK Institute of Literary and Historical Research in Unani Medicine, CCRUM, Jamia Millia Islamia Campus, New Delhi 110025, India

HIGHLIGHTS

- Covid-19 is an ongoing pandemic caused by a new coronavirus named as SARS-CoV-2.
- SARS-CoV-2 has structural similarity with bat coronavirus and SARS-coronavirus.
- Researches are being done to develop effective vaccines and drugs for the disease.
- Unani medicine has effective preventive measures for epidemic diseases.
- Phytochemicals in herbal drugs can potentially help in reducing the disease burden.

GRAPHICAL ABSTRACT



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ABSTRACT

Since December 2019, a respiratory pandemic named as coronavirus disease 2019 (Covid-19) caused by a new coronavirus named as SARS-CoV-2, has taken the world by storm. The symptoms are fever, malaise, and cough which resolve in a few days in most cases; but may progress to respiratory distress and organ failure. Transmission is through droplet infection or fomites, but other modes such as airborne transmission and oro-fecal transmission are also speculated. Research is underway to develop effective vaccines and medicines for the disease. In such a scenario, we present the measures described in Unani system of medicine for health protection during epidemics. Unani is a traditional system of medicine developed during the middle ages, which employs natural drugs of herbal, animal and mineral origin for treatment. In Unani medicine, during an epidemic, apart from isolation and quarantine, three measures are of utmost importance, (i) purification of surroundings using certain herbal drugs as fumigants or sprays, (ii) health promotion and immune-modulation, and (iii) use of health-protecting drugs and symptom-specific drugs. Drugs such as *loban* (*Styrax benzoides* W. G. Craib), *sandroos* (*Hymenaea verrucosa* Gaertn.) *za'fran* (*Crocus sativus* L.), vinegar etc. are prescribed in various forms. Scientific researches on these drugs reveal the presence of a number of pharmacologically active substances, which may provide a new insight into the management of infections and epidemics.

Abbreviations: SARS-CoV, severe acute respiratory syndrome coronavirus; MERS-CoV, Middle-East respiratory syndrome coronavirus; Covid-19, coronavirus disease 2019; WHO, World Health Organization; SARS-CoV-2, SARS coronavirus-2; NSAIDs, non-steroidal anti-inflammatory drugs; ACE2, angiotensin converting enzyme-2; AYUSH, Ayurveda, Yoga, Unani, Siddha, and Homeopathy; RNA, ribose nucleic acid.

* Corresponding author.
E-mail addresses: sadianikhat@jamiahamdard.ac.in (S. Nikhat), fazilmd00@gmail.com (M. Fazil).

[1] The authors contributed equally to the manuscript at all stages.

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1. Introduction

Since the beginning of the 21st century, three coronaviruses have caused disastrous outbreaks of pneumonia in human beings: Severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002–03 and Middle-East respiratory syndrome coronavirus (MERS-CoV) in 2012 (Čivljak et al., 2020). The ongoing Covid-19 (Coronavirus disease 2019) is the third coronavirus epidemic of zoonotic origin to occur in the present century (Sun et al., 2020), which spread from a single city in China to the entire country within 30 days (Wu and McGoogan, 2020); and spread to nearly 72 countries in less than three months (Chinazzi et al., 2020). In essence, it is known to have affected '*all continents except Antarctica*' (Acharya, 2020). On 12th March 2020, Covid-19 was declared a pandemic by the World Health Organization (WHO) (Gautret et al., 2020). As of 17th April 2020, there have been 2,074,529 confirmed cases and 139,378 deaths worldwide due to Covid-19 as reported by the WHO (WHO, 2020).

In India, the first case of Covid-19 was a student who returned from Wuhan, China on 30th January 2020 (Sahasranaman and Kumar, 2020). By 14th April 2020, there have been a total of 13,387 cases and 437 deaths in the country. Although community transmission is not reported, clusters of cases have been identified (WHO, 2020).

The causative agent of Covid-19 was tentatively named as 2019 n-CoV (2019 novel coronavirus) by WHO on 12th January 2020 (Sun et al., 2020). On 11th February 2020, it was officially named as SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) by the International Committee on Taxonomy of Viruses (Gautret et al., 2020; Rasmussen et al., 2020). It is now understood that SARS-CoV-2 has a 96.2% structural similarity with a bat coronavirus (CoV RaTG13) and 79.5% similarity with SARS-CoV. However, its spike (S) glycoprotein has a 10–20 times higher affinity to human ACE2 receptors as compared to SARS-CoV, leading to more chances of human-to-human transmission; though having a lesser mortality rate (average 3.4%) than that of SARS (9.6%) and MERS (35%) respectively (Guo et al., 2020).

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, and the development of effective diagnostic, preventive and therapeutic strategies, including vaccines (WHO, 2020). In the absence of any proven treatment option, many drugs are under investigation to control this disease with a potentially fatal outcome. Chloroquine is one of the widely used drugs, with in vitro evidence that it reduces viral replication (Deponti et al., 2017). A combination of hydroxychloroquine and azithromycin has also been found to have a significant synergistic effect in reducing viral load and early recovery (Gautret et al., 2020). For severe disease, the use of steroids, passive antibodies, and selective cytokine blockade is suggested (Mehta et al., 2020). The role of NSAIDs and corticosteroids, however, is still controversial and not advisable at present (Russell et al., 2020). Antivirals such as interferon-α, lopinavir/ritonavir, ribavirin, etc. are also being used as a tentative treatment for Covid-19 (Dong et al., 2020). Yet, as of now, there are no specific antiviral drugs or vaccines verified to be effective against SARS-CoV-2, hence the emphasis is being laid on preventive measures and symptomatic treatment (Jean et al., 2020).

In this context, traditional systems of medicine are being explored for providing preventive, supportive and rehabilitative care to patients. Although no direct evidence is available, some uncontrolled studies on traditional medicines suggest that they may have a direct efficacy on the virus. Unani medicine is one of the officially recognized traditional medicine systems of India, which are represented by the acronym AYUSH, i.e. Ayurveda, Yoga, Unani, Siddha and Homeopathy (Weeks, 2020). Unani, also sometimes referred to as the Greco-Arabian system of medicine originated with the teachings of Hippocrates and was improved and systematized by Arabian physicians. It was introduced into India during the 11th–13th century in the Mughal period (Subbarayappa, 2001). Unani system of medicine has a detailed description of drugs that are utilized in many infectious diseases, including respiratory infections (Vohora, 1986). Some of these drugs have been demonstrated to have specific antiviral (Cagno et al., 2015) and immunomodulatory (Nigar and Itrat, 2013) activity in various scientific studies. In this paper, we present an overview of Covid-19 and SARS-CoV-2, Unani concept of infectious and epidemic diseases and their preventive measures, and a possible approach to the management of Covid-19 with Unani medicine.

2. Methodology

The authors searched the Unani medicine books available in Jamia Hamdard library for information related to epidemic diseases. Five important textbooks of Unani medicine were reviewed. *Al-Qanoon fil Tib* (The Law in Medicine) of Ibn Sina (980–1035 CE), *Kitab al-Hawi* (The Comprehensive Book of Medicine) of Zakariya Razi (865–925 CE), *Kitab al-Kulliyat* (The Complete Book on Medicine) by Ibn Rushd (1126–1198 CE), *Kitab al-Mansoori* (Book dedicated to Caliph Mansoor) by *Zakariya Razi* (865–925 CE), and *Kitab al-Mukhtarat fil-Tib* (The Book on Choice of Medicine) by Ibn Hubal Baghdadi (1121–1213 CE). Other published books and journals were also consulted for further details. For information on SARS-CoV-2 and Covid-19, we searched major scientific databases namely Pubmed, Science Direct and Springer for the most recent information regarding the pandemic. The search words used were 'SARS-CoV-2', 'Covid-19', 'history', 'prevalence', 'symptoms', and 'transmission'. Internet search on the same search engines and also Google Scholar was also done to search for scientific evidence regarding Unani drugs prescribed during epidemics. For this search, we used the terms 'air purification', 'influenza', 'epidemic', 'immunomodulatory', and 'bioactive compounds' along with the names of drugs, according to their use. Time restriction was not made to extract the most useful information. The articles published during 2005–2020 were hence included in the final manuscript.

3. Coronavirus disease 2019

3.1. Causative agent

SARS-CoV-2 is a coronavirus belonging to the genus β-coronaviruses, sub-genus botulinum (Sun et al., 2020). It is the seventh in the family of coronaviruses which is known to infect humans (Andersen et al., 2020). Coronaviruses are a group of enveloped viruses with a spherical shape, having a non-segmented, single-stranded RNA genome with club-like projecting spikes on their surface (Phan, 2020a). SARS-CoV-2 was first isolated from bronchoalveolar lavage samples from three patients suffering from pneumonia of unidentified cause (Zhu et al., 2020). Structurally, the genome of SARS-CoV-2 is similar to other β-coronaviruses. It has a long coding strand on which five ORFs are identified: including ORF1ab polyprotein, spike (S) glycoprotein, envelope protein, membrane protein, and nucleocapsid protein (Phan, 2020a). The S glycoprotein is the primary target of antibodies and vaccines as it is surface-exposed (Walls et al., 2020).

Two distinct features have been identified in the genome sequence: (i) Structural and biochemical studies have identified that SARS-CoV-2 receptor-binding domain (RBD) in the spike protein has a high affinity to human or human-like angiotensin converting enzyme-2 (ACE2) receptors; and (ii) a second feature is a polybasic cleavage at the junction of sub-units S1 and S2 of the spike, which may determine the infectivity and host range of the virus (Andersen et al., 2020).

Mutations and deletions have also been identified in the genome sequence of virus samples isolated from patients across countries, which indicate genetic diversity and evolution of the virus (Phan, 2020b). Genetic analysis of 103 genomes has indicated that SARS-CoV-2 has evolved into two major types, designated as S and L. The L-type is more prevalent, found in about 70% of the cases in Wuhan (Tang et al., 2020).

3.2. Modes of transmission

In the earliest stage of the epidemic, as 55% of the patients were related to a seafood and wet animal market, a likely zoonotic origin was suggested (Sun et al., 2020). Researches have indicated that SARS-CoV-2 has close structural resemblance with bat coronaviruses, supporting the theory that SARS-CoV-2 was derived from bats. Snakes have also been suggested as a likely wildlife repository of the virus. However, there was an exponential rise in unrelated cases since late December 2019 (Sun et al., 2020). Since bats are a natural reservoir of various coronaviruses, a zoonotic angle is not entirely ruled out. But statistics reveal that the disease is spreading rapidly by human-to-human transmission (Guo et al., 2020).

SARS-CoV-2 has been detected in broncho-alveolar secretions, sputum, saliva, throat and nasopharyngeal secretions of infected persons (Phan, 2020b). About 50–80% transmission of the virus is from asymptomatic carriers, hence transmission through speech droplets is considered as a significant mode of transmission of the disease. The virus can be transmitted directly through speech droplets, or through fomites (Anfinrud et al., 2020). Based on reports, it is estimated that 44% of the transmission can occur before the onset of symptoms (He et al., 2020). SARS-CoV-2 binds to the ACE2 receptors, which are present in abundance in the lungs and gastrointestinal tract. Viral RNA has also been detected in feces. Hence, an oro-fecal route of transmission is also considered. Air-borne transmission is not completely ruled out (Ling et al., 2020). There is also evidence that the virus can be transmitted through tears and body fluids if they come into contact with the mucosa of eyes, mouth or nose. Depending on the route of entry, the virus binds to ACE2 receptors and infects type-2 pneumocytes, ciliated bronchial epithelium of lungs (Rodriguez-Morales et al., 2020), or enterocytes of the small intestine. The virus has also been isolated in blood, indicting more routes of transmission (Guo et al., 2020).

3.3. Disease spectrum

The incubation period of Covid-19 ranges from 1 to 14 days, averaging 5–6 days in most patients. Though an incubation period of up to 24 days has been reported in some cases (Jean et al., 2020). The disease affects males and females equally, although a slight male predominance has been observed (Guo et al., 2020). The initial symptoms are fever with chills, dry cough, and malaise in 83–98% of cases. Sputum production is seen in about one-third. Other symptoms include shortness of breath, abdominal pain, diarrhea, headache and vomiting in a few cases (del Rio and Malani, 2020). If pulmonary inflammation worsens, hypoxemia occurs which may lead to cardiac arrest. Elderly patients and those with underlying diseases such as chronic obstructive pulmonary disease, cardiovascular disease, hypertension, etc. have a more chance of developing acute respiratory distress syndrome, organ failure or other conditions leading to death (Guo et al., 2020).

Most patients have a good prognosis, with mild flu-like symptoms (del Rio and Malani, 2020). However, a small percentage, particularly the elderly and those with underlying diseases may develop complications such as arrhythmia, shock, acute renal failure, acute cardiac injury, acute respiratory distress syndrome, etc. (Guo et al., 2020). Overall, the case fatality rate is estimated to be 2–3% (Rodriguez-Morales et al., 2020), while it is as high as 8–15% in older adults (del Rio and Malani, 2020).

Laboratory findings include a decreased white cell count in 70% patients, prolonged prothrombin time in 58% patients, and elevated lactate dehydrogenase in about 40% of the patients (del Rio and Malani, 2020). Interleukin-6 (IL-6), Interleukin-10 (IL-10), Tumor necrosis factor-α (TNF-α) are increased. Bilateral patchy infiltrates are seen on chest radiograph and ground-glass opacities are seen on chest CT scan (del Rio and Malani, 2020). Histopathological examination of biopsy tissues has demonstrated the desquamation of pneumocytes, formation of hyaline membrane and bilateral diffuse alveolar damage in lung, liver and cardiac tissue (Rodriguez-Morales et al., 2020).

4. Infectious and epidemic diseases in Unani medicine

4.1. A brief introduction to Unani System of Medicine

Unani system of medicine has its roots in ancient Greece, in the teachings of Hippocrates (460–377 BCE). The name Unani reflects its Hellenistic origin and is derived from the *Yunan*, the ancient name of Greece (Husain et al., 2010). Unani medicine flourished to its zenith during medieval ages (500–1500 CE) in the Muslim world, mostly in the Arabian peninsula, Persia, Egypt, Syria, ancient Mesopotamia, etc. Ergo it is also referred to as Greco-Arabian medicine and Persian medicine in different parts of the world (Islam, 2018). In India, it is integrated into the national healthcare system and officially named as Unani medicine (Subbarayappa, 2001). Unani medicine is based on the Hippocratic concepts of *mizaj* (temperament) and *akhlat* (humors) (Husain et al., 2010). Famous scholars of Unani medicine include Ibn Sina (Latinized as Avicenna, 980–1035 CE), Zakariya Razi (Latinized as Rhazes, 865–925 CE), Ibn Rushd (Latinized as Averroes, 1126–1198 CE), and many more (Islam, 2018).

4.2. Concept of infectious diseases and epidemics in Unani medicine

The 'germ theory of disease' was established as late as 1683 CE with the development of the first microscope (Foster, 1970). For obvious reasons, the concept of microbes as disease-causing agents does not find a direct reference in Unani medicine. However, there is an adequate understanding that certain *ajsam-i-khabitha* (literally translated as 'bad substances') can migrate from the diseased to healthy persons, and may cause diseases (Sina, 1878). This theory of contagion is advocated by a number of Unani scholars. According to Jalinoos (Latinized as Galen, 131–199 CE), '*a physician should always keep an eye on changes of weather and air*' (Qadeer, 2001). A treatise of Zakariya Razi (865–925 CE), *Kitab fi al-jadari wa-al-hasbah* (Book on Smallpox and Measles) describes the modes of spread of the two diseases and their differential diagnosis. In May 1970, it was regarded as "the first scientific treatise on the subject" by WHO (Islam, 2018). According to Ibn Sina (980–1035 CE), 'air and water are contaminated only after admixture of *ajsam-i-khabitha*, which does not happen otherwise'. He further states, 'such contamination can also be brought about if the dead bodies of people dying due to an epidemic are not disposed of properly' (Sina, 1878). Evidently, he had knowledge of microbes being present in the body even after death, which could potentially infect others.

During the 14th-century plague pandemic, Spanish scholar Ibn Khatima (1364–1369 CE) mentioned in his treatise *Tahsil garaḍ al-qasid fi-tafsil al-maraḍ al wafid* (succeeding in clarifying pest disease) that 'I have observed that a person who comes in close contact with a patient of plague will start suffering from the same symptoms' (Cambra, 2018; Rehman, 1991), indicating a good understanding of disease transmission.

Epidemics, referred to as *waba* in Unani medicine, are thought to occur if such contagion or *ajsam-i-khabitha*, as they are referred to, find a place in air and water (Sina, 1878). Zakariya Razi (865–925 CE) states in *Kitab al-Mansoori* (Book dedicated to Caliph Mansoor), most epidemics spread in the autumn season, especially if the preceding summer season was humid, and the wind is still (Razi, 1991). In this context, the direction of winds is given utmost significance. As Ibn Hubal Baghdadi (1121–1213 CE) mentioned in his treatise *Kitab al-Mukhtarat fil-Tib* (The Book on Choice of Medicine), if southern winds are replaced by northern winds, then catarrhal illnesses will occur in abundance (Baghdadi, 2004). Because, as stated by Razi in the 15th volume of his treatise *Kitab al-Hawi* (The Comprehensive Book of Medicine), southern winds are warmer while the northern winds are colder, and this change

of temperature makes people more susceptible to respiratory infections (Razi, 2008).

Furthering the view, Ibn Sina (980–1035 CE) stated that epidemics spread from one person to another, and one city to another 'like a message' (Sina, 1878). Zakariya Razi (865–925 CE) stressed this fact and stated that '*there will always be something common in patients of epidemics, whether a place, food, drink or travel history*' (Razi, 2008). During the 14th-century plague pandemic, Arabian scholar Ibn Khatib (1313–1374 CE) stressed that 'most of the people who come in contact with a plague victim will die'. In the same context, he states, 'the disease spreads through clothes, utensils and jewelry' (Ober and Aloush, 1982; Rehman, 1991), thus stressing on transmission through fomites. In the same vein, this statement stresses on social distancing and isolation, two important aspects of prevention in the current pandemic.

The 13th-century Persian scholar Najeebuddin Samarqandi (d. 1222 CE) mentioned about a type of epidemic influenza in his treatise *Al-asbab wa-Alamat* (the book of causes and symptoms). In the translated version of the book, published by the name of *Sharah Asbab*, the disease is mentioned by the name of *Nazla-e-Wabaiya* (epidemic influenza) in the chapter on *Anaf al-Anza* (Influenza). About *Nazla-e-Wabaiya*, Samarqandi states that it is associated with fever, sneezing, sore throat, nasal irritation and malaise. Specifically, weakness sets in early in the disease. He further states that a patient of *nazla-e-wabaiya* may also suffer from cough, diarrhea, and delirium. Pleurisy and pneumonia, if present, worsens the prognosis (Samarqandi, 2010).

It is evident that despite the inability to observe microbes, Unani scholars could envision and comprehend their sources and reservoirs, modes of transmission of infections, and potential causes of infections turning into epidemics. The theories and observations closely resemble the contemporary knowledge of infections, which reinforce the fact that Unani medicine can play a significant role in combating current health problems.

4.3. General preventive measures during epidemics

The preventive measures for epidemic diseases are collectively aimed towards the improvement of immunity, prevention of spread of infection, hygiene and anti-septic measures and promotion of general health. Host defenses are given particular importance (Rushd, 1987). According to Razi (865–925 CE), people who remain physically active and exercise regularly have a lesser susceptibility to epidemic diseases (Razi, 2008). Patients having a weak constitution and those suffering from underlying diseases are said to be more susceptible during epidemics (Sina, 1878).

The basic measure advised is to avoid places where an epidemic is spread. In case it is not avoidable, then a person advised to stay at a well-ventilated place, preferably distant from the ground. When interacting with a patient, care should be taken that the air currents may not be directed from a patient to a healthy person (Razi, 1991). During epidemics, it is also advised to avoid unnecessary physical exertion (Razi, 2008; Sina, 1878) and to stay in properly ventilated places with optimum temperature, neither too hot nor too cold (Rushd, 1987).

4.4. Sanitization of surroundings

Immense stress is placed on purification and sanitization of surroundings during epidemics because it is the primary medium which facilitates the spread of infections. Before the era of chemical-based air purifiers, Unani physicians employed medicinal herbs as decoction or distillate for spray, or as fumigants to keep the air free of contaminants.

Homes should be sprayed with diluted vinegar to keep the air clean. It may be mentioned here that in Unani texts, vinegar implies the one made from sugarcane (*Saccharum officinarum* L., Poaceae) unless specified otherwise. *Arq-e-Gulab* (*Rosa damascena* Herrm.) should be applied on the body and curtains etc. If the air smells foul, then fumigation with *sandal* (*Santalum album* L.) and camphor is also advisable. Fumigation with herbs like *Qust* (*Saussurea costus* (Falc.) Lipsch.), *kundur* (*Boswellia serrata* Roxb. ex Colebr.), *ood* (*Paeonia emodi* Royle.) and *Murr* (*Commiphora myrrha* Nees Engl.) is also advisable (Rushd, 1987). According to Zakariya Razi, some aromatic drugs can destroy infectious agents and should be used as fumigants during epidemics. For instance *amber* (*Liquidambar acalycina* H. T. Chang), *loban* (*Styrax benzoides* W. G. Craib), *sandroos* (*Hymenaea verrucosa* Gaertn.) *za'fran* (*Crocus sativus* L.), *aabnoos* (*Diospyros ebenum* J. Koenig ex Retz.), *mastagi* (*Pistacia lentiscus* L.), *mushk* (*Moschus moschiferus* L.), *izkhar* (*Cymbopogon jwarancusa* (Jones) Schult.), *abhal* (*Juniperus communis* L.), *zanjabeel* (*Zingiber officinale* Roscoe), *sibr* (*Aloe vera* L.), olive gum, etc. (Razi, 2008). *Mushk* however, is now banned for use, as the *Musk* deer is an endangered species in many parts of the world, including India (Bhat, 2016). Information about these drugs is presented in Table 1.

It is pertinent mentioning here that in the contemporary world, herbal fumigants and sprays are rarely used for the purpose specified in traditional medicine. Sporadic researches have been published on the efficacy of herbal drugs as fumigants (Bhatwalkar et al., 2019), but much of the potential is yet to be discovered. Also, we could not find any clinical trials on the health effects of herbal fumigants. Probably, for this reason, the studies, if at all conducted, report the effect of these drugs as insecticidal, acaricidal, etc. For some drugs such as *H. verrucosa*, *O. europaea*, etc., no studies were found where the drugs have been used for fumigation, although many herbal drugs are used as household incense in some countries (Lemenih et al., 2003). Hence, we rely on the information that they contain volatile oils rich in alcohol (J. Kim et al., 2016), terpenoids (Ludwiczuk et al., 2017), etc. which may offer an anti-microbial effect on fumigation. However, the health effects of fumigation, along with quality control of drugs is needed before reaching a conclusion.

4.5. Dietary modifications

During epidemics, it is advised to avoid meat, sweets, and fruits with high water content. If meat has to be taken, then that of birds found on mountains may be preferred over animal meat. Fish should be entirely avoided (Rushd, 1987). These restrictions were placed probably because the zoonotic spread of infections was speculated, and fish and animals living near the ground were more likely to be infected than those living at higher altitudes. It is also advised to consume citrus and sour fruits, especially grapes, apples, lemon, etc. Oxymel prepared with *Arq-e-Gulab* is believed to provide effective protection during epidemics (Razi, 1991; Rushd, 1987). Overeating and under-eating both are considered harmful as they have adverse effects on the bodily constitution. Staying thirsty was also known to be detrimental (Sina, 1878).

4.6. Health protecting drugs

Unani scholars have prescribed certain drugs that may be used as health protecting drugs during epidemics. Both single herbs and compound formulations have been prescribed in this regard. *Imli* (*Tamarindus indica* L.), *revand chini* (*Rheum australe* D. Don), *gul-e-banafsha* (*Viola odorata* L.), *halela* (*Terminalia chebula* Retz.), *amaltas* (*Cassia fistula* L.), *turanjabeen* (*Alhagi pseudalhagi* (M. Bieb.) Desv. ex B. Keller & Shap.), and *aab-e-anar* (*Punica granatum* L.) are said to afford protective effects during epidemics. According to Ibn Rushd, these drugs have a cleansing effect on body humors (Rushd, 1987). Vinegar may also be taken orally, as part of diet or salad, etc. (Razi, 1991). Since the dosage and dosing pattern of these drugs is not specified in classical textbooks of Unani medicine, we suggest that they may be used according to the guidelines of Unani pharmacopeias (Anonymous, 2009).

Some important compound formulations are also prescribed during epidemics. Ibn Rushd (1126–1198 CE) has given a description of a medicine, about which he made a curious claim, '*whoever has used this formulation during an epidemic remained protected from it*'. The composition is as follows: *Sibr* (*Aloe vera* L.) and *Murr makki* (*Commiphora*

Table 1
Drugs prescribed for sanitization of environment during epidemics.

S. no.	Botanical name & family	Unani name	Part used	Method of use in Unani medicine	Mode of Action/rationale for use	References
1.	Acetic acid (vinegar)	*Sirka*	Whole	Spray	Antimicrobial	(Ezz Eldin et al., 2019; Razi, 2008)
2.	*Boswellia serrata* Roxb. ex Colebr., Styracaceae	*Kundur*	Oleo-gum resin	Fumigation	Reduction of airborne bacteria	(Bhatwalkar et al., 2019; Rushd, 1987)
3.	*Cinnamomum camphora* (L.) J. Presl., Lauraceae	*Kafoor*	Essential oil	Fumigation	Insecticidal, acaricidal	(Fu et al., 2015; Kim et al., 2007; Sina, 1878)
4.	*Crocus sativus* L., Iridaceae	*Za'fran*	Stamen	Fumigation	Contains volatile oils with anti-microbial activity[a]	(Amini et al., 2017; Rushd, 1987)
5.	*Cymbopogon jwarancusa* (Jones) Schult., Poaceae	*Izkhar*	Root	Fumigation	Insect repellant	(Razi, 2008; Zhang et al., 2011)
6.	*Diospyros ebenum* J. Koenig ex Retz., Ebenaceae	*Aabnoos*	Wood	Fumigation	Contains essential oils[a]	(Maridass et al., 2008; Razi, 2008)
7.	*Hymenaea verrucosa* Gaertn., Leguminosae	*Sandroos*	Resin	Fumigation	Contains diterpenoids[a]	(Baghdadi, 2004; Crowther et al., 2015)
8	*Juniperus communis* L., Cupressaceae	*Abhal*	Berry	Fumigation	Volatile oil contains terpenes[a]	(Orav et al., 2010; Sina, 1878)
9.	*Liquidambar acalycina* H. T. Chang, Altingiaceae	*Amber*	Gum	Fumigation	Contains diterpenoids and triterpenoids[a]	(Crowther et al., 2015; Razi, 2008)
10.	*Olea europaea* L., Oleaceae	*Zaitoon*, Olive	Gummy exudate from tree	Fumigation	Leaves and oil contain triterpenoids[a]	(Ludwiczuk et al., 2017; Razi, 2008)
11.	*Paeonia emodi* Royle., Paeoniaceae	*Ood*	Root	Fumigation	Contains essential oil having salicylaldehyde, *trans*-myrtanol etc.[a]	(Rushd, 1987; Verma et al., 2015)
12.	*Pistacia lentiscus* L., Anacardiaceae	*Mastagi*	Gum-resin	Fumigation	Insecticial	(Bachrouch et al., 2010; Razi, 2008)
13.	*Rosa damascena* Herrm., Rosaceae	*Arq-e-Gulab*	Distillate of petals	Application on curtains etc.	Insecticidal	(J. Kim et al., 2016; Rushd, 1987)
14.	*Santalum album* L., *Santalaceae*	*Sandal safaid*	Heartwood	Fumigation	Insecticidal	(J. Kim et al., 2016; Sina, 1878)
15.	*Saussurea costus* (Falc.) Lipsch., Compositae	*Qust*	Root	Fumigation	Insect repellant and toxic	(Razi, 1991; Sagheer et al., 2013)
16.	*Styrax benzoides* W. G. Craib, Styracaceae	*Loban*	Resin	Fumigation	Reduction of air-borne bacteria	(Bhatwalkar et al., 2019; Sina, 1878)
17.	*Zingiber officinale* Roscoe, Zingiberaceae	*Zanjabeel*	Rhizome	Fumigation	Insecticidal and insect repellant	(Chaubey, 2013; Rushd, 1987)

[a] Studies about these drugs as fumigants were not found on any of the search engines. However, researches have shown that they contain volatile oils with biologically active substances such as alcohols, terpenes, etc. (mentioned in the table) which may provide air-purifying effects on fumigation. Hence, these findings provide a rationale for future research.

Table 2
Drugs prescribed for the protection of health during epidemics.

S. no.	Botanical name & family	Unani name	Part used	Method of use in Unani medicine	Mode of action/rationale for use	References
1.	Acetic acid (vinegar)	*Sirka*	Whole	Spray	Antimicrobial, antioxidant, anti-obesity	(Ho et al., 2017; Razi, 1991)
2.	*Alhagi pseudalhagi* (M. Bieb.) Desv. ex B. Keller & Shap., Leguminosae	*Turanjabeen*	Resinous exudates from fruit and stem	Oral	Anti-microbial, anti-oxidant, hepatoprotective, anti-pyretic	(Imani et al., 2020; Rushd, 1987)
3.	*Cassia fistula* L., Leguminosae	*Amaltas*	Pulp	Oral	Immunomodulatory, antioxidant, hepatoprotective	(Rahmani, 2015; Rushd, 1987)
4.	*Crocus sativus* L., Iridaceae	*Za'fran*	Stamen	Oral	Immunoregulatory, anti-inflammatory	(Rushd, 1987; Zeinali et al., 2019)
5.	*Juglans regia* L., Juglandaceae	*Jauz*	Jam made of fruits	Oral	Neuroprotective, cardioprotective	(Hayes et al., 2016; Razi, 1991)
6.	*Morus nigra* L., Moraceae	*Toot*	Jam made of fruits	Gargle	Anti-inflammatory, antimicrobial	(Lim and Choi, 2019; Razi, 1991)
7.	*Punica granatum* L., Lythraceae	*Anar*	Fruit juice	Oral	Anti-microbial, anti-fungal, anti-viral, antioxidant	(Bassiri-Jahromi, 2018; Rushd, 1987)
8.	*Rheum australe* D. Don, Polygonaceae	*Revand Chini*	Rhizome	Oral	Antimicrobial, antioxidative, anti-inflammatory	(Pandith et al., 2018; Rushd, 1987)
9.	*Rhus coriaria* L., Anacardaceae	*Sumaq*	Fruit	Gargle	Antibacterial against oral bacteria	(Razi, 1991; Vahid-Dastjerdi et al., 2014)
10.	*Rosa damascena* Herrm., Rosaceae	*Arq-e-Gulab*	Distillate of petals	Gargle	Antioxidant; contains alcohols	(Razi, 1991; Sharafati Chaleshtori et al., 2018)
11.	*Tamarindus indica* L., Leguminosae	*Imli*	Pulp	Oral	Analgesic, anti-inflammatory	(Komakech et al., 2019; Rushd, 1987)
12.	*Terminalia chebula* Retz., Combretaceae	*Halela*	Fruit	Oral	Anti-bacterial	(Rushd, 1987; Saxena et al., 2017)
13.	*Viola odorata* L., Violaceae	*Banafsha*	Flowers	Oral	Anti-microbial, anti-fungal	(Parsley et al., 2018; Rushd, 1987)

myrrha Nees Engl.), one part each, *za'fran* (*Crocus sativus* L.), 2 parts. The drugs should be finely powdered and taken in a dose of 2.4 g per day (Rushd, 1987). For epidemics involving respiratory diseases, gargling with a solution of *sumaq* (*Rhus coriaria* L., decoction), *rub-e-toot* (*Morus nigra* L.), *rub-e-jauz* (*Juglans regia* L.) and *arq-e-gulab* (*Rosa damascena* Herrm.) before sleep is advised (Razi, 1991). Information about the use of these drugs is provided in Table 2.

5. Possible approach to prevention and management of Covid-19 in the light of Unani medicine

In light of the above-summarized information, the symptoms of Covid-19 closely resemble those of *nazla-e-wabaiya* described in Unani books. Fever, malaise, cough, etc. are the initial symptoms, which may be associated with diarrhea (del Rio and Malani, 2020). Similar symptoms have been described by Unani scholars regarding *nazla-e-wabaiya* (Samarqandi, 2010). People with an underlying disease or a weak constitution have been described by Ibn Sina (980–1035 CE) as being more susceptible to epidemic diseases and having a poor prognosis (Sina, 1878). Besides, the modes of transmission of infection, importance of quarantine and air purification have also been outlined in sufficient detail (Rushd, 1987).

With this information, we suggest the following preventive measures and management options in the light of Unani medicine:

5.1. Preventive measures

General measures of isolation, quarantine, and distancing must be followed. Transmission through fomites is highly likely, so care should be taken in handling and disposing of the same. Health care workers, family members and caretakers of the patients should take due precautions. Stay in well-ventilated places reduces the chances of contracting the infection. Razi's advice of avoiding airflow from the patient to a healthy person is remarkable. For this purpose, the patient should face away from healthy people while coughing, sneezing or talking, as the virus may also be excreted through saliva (Razi, 1991).

Sanitization of the environment should always be given special importance as it serves as the medium for lodging and dissemination of the virus. Several drugs (Table 1) have been prescribed for spray, for application on curtains, as sanitizers on the body, and for fumigation. These drugs are mostly aromatic, for instance *loban* (*Styrax benzoides* W. G. Craib), *sandroos* (*Hymenaea verrucosa* Gaertn.) *za'fran* (*Crocus sativus* L.), Rose water, vinegar, etc. which provide a relaxing aroma and are also said to have a clearing effect on microbes (Razi, 1991). Although the clinical effects of most drugs are not published as yet, but as they have a long history of cultural use, their importance cannot be denied abruptly. In the future, herbal drugs may potentially provide a cost-effective and safer alternative to chemical disinfectants (Bhatwalkar et al., 2019).

Health protective measures need a special mention. Unani physicians were aware of the immunomodulatory effects of citrus fruits. Besides, other measures of health promotion during epidemics include having a wholesome diet, avoiding starvation, avoiding meat and fish, and staying hydrated (Razi, 2008; Sina, 1878). Certain drugs have also been prescribed as for the purpose of health promotion (summarized in Table 2), such as *revand chini* (*Rheum australe* D. Don), *gul-e-banafsha* (*Viola odorata* L.), and *halela* (*Terminalia chebula* Retz.) (Rushd, 1987). Prophylactic gargling with a solution of *sumaq* (*Rhus coriaria* L., decoction), *rub-e-toot* (*Morus nigra* L.), *rub-e-jauz* (*Juglans regia* L.) and *arq-e-gulab* (*Rosa damascena* Herrm.) before sleep may be advised (Razi, 1991)

5.2. Suggested management

In *Al Asbab wa-Alamat*, the management of *nazla-e-wabaiya* is done with anti-inflammatory, immunomodulatory and antipyretic drugs such as decoction of *behidana* (*Cydonia oblonga* Mill., Rosaceae) 3 g, *unnab* (*Ziziphus jujube* Mill., Rhamnaceae) 5 no., *sapistan* (*Cordia dichotoma* G. Forst., Boraginaceae) 9 no., and *khaksi* (*Sisymbrium adenophorum* (Wooton & Standl.) Tidestr., Brassicaceae) 5 g. In case of associated diarrhea, *habb-ul aas* (*Myrtus communis* L., Myrtaceae) and *tabasheer* (*Bambusa bambos* (L.) Voss, Poaceae) are also prescribed. *Sheera tukhm e kahu* (*Lactuca sativa* L., Compositae, seed paste) may be given to relieve thirst. If pneumonia or pleurisy occurs, *qairooti aarad karsana* (10 g), *Aloe vera* L. sap (1 g), *C. sativus* L. stamen (1 g) are crushed, mixed and warmed slightly, then they are applied on the chest wall and covered with a cotton bandage (Baghdadi, 2004; Samarqandi, 2010).

The details of these drugs are mentioned in Table 3.

Qairooti is the name of ointments specifically prescribed for chest diseases. *Qairooti aarad karsana* is a polyherbal Unani formulation based on the following ingredients: *Aarad e Karsana* (*Pisum sativum* L., Leguminosae, flour), *Aarad e Hulba* (*Trigonella adscendens* (Nevski) Afan. & Gontsch., Leguminosae, flour) - 60 g each, *Kalonji* (*Nigella sativa* L., Ranunculaceae, seeds), *Asl-us-Soos* (*Glycyrrhiza glabra* L., Leguminosae, root) - 24 g each, *Aqarqarha* (*Anacyclus pyrethrum* (L.) Lag., Compositae, root) - 18 g, *Roghan-e-Sosan* (*Iris ensata* Tunb., Iridaceae, oil) and Bees Wax- both in equal amount, *quantum satis*, to make a paste (Anonymous, 2006).

6. Conclusion

Human civilization has been marred with the occurrence of epidemics, often threatening to have disastrous effects on humankind. Just when we thought we had conquered microbes (Adedeji, 2016; Mohr, 2016), three viruses, belonging to a family hitherto considered less virulent, took the 21st century by storm (Čivljak et al., 2020). The newest of them, SARS-CoV-2, is, fortunately, lesser on virulence than its two recent predecessors, namely SARS-CoV and MERS, but higher in infectivity (Vellingiri et al., 2020). This simply implies that it has more chances of reaching the susceptible population and causing higher mortality. There is also speculation that close to two-thirds of Covid-19 cases from China may have gone undetected (Menkir et al., 2020). Going by the present trends, the cases are likely to increase in the near future (Vellingiri et al., 2020). This is going to place a huge economic burden, especially on developing and under-developed countries (McKibbin and Fernando, 2020).

An important aim of this paper was to apprise the readers about the concept of epidemic diseases in Unani medicine, and also how the theories built largely on observation and clinical experiences aptly provide a comprehensive description of preventive and protective measures for infectious and epidemic diseases. Concepts of sanitation, isolation, air purification and immune-modulation described in Unani medicine remain the basic tenets of infection containment in the contemporary preventive medicine (Chinazzi et al., 2020). This necessitates a keen observation to uncover more treasure of knowledge from this ancient medicine system. Presently, in the absence of any decisive treatment available for Covid-19, stress is being laid on traditional medicine systems for providing the necessary protection (Vellingiri et al., 2020). Herbal medicines have several bioactive compounds such as phenols, vitamins, several antioxidants, etc. with important pharmacological activity. Hence they can play a significant role in reducing the disease burden in the contemporary world (J. Kim et al., 2016; Zeinali et al., 2019).

Intriguingly, it was noticed that among all epidemics, the textbooks of Unani medicine primarily focused on air-borne respiratory infections. Although at some places epidemics involving food and water-borne diseases, and plague, etc. have also been discussed (Razi, 2008; Sina, 1878), but most of the literature is dedicated to air-borne diseases which affect the respiratory system. It is possible because the most prevalent epidemics in the Muslim world during the medieval ages were plague, smallpox, chickenpox, etc. which are transmitted through fomites or respiratory route (Islam, 2018). The methods of air purification, and the

Table 3
Drugs prescribed in Unani medicine for *nazla-e-wabaiya* (epidemic influenza).

S. no.	Botanical name & family	Unani name	Part used	Method of use in Unani medicine	Active ingredients	Mode of action	References
1.	*Cydonia oblonga* Mill., Rosaceae	*Behidana*	Berry	Decoction for oral use	Hydroxycinnamic derivatives	Anti-oxidant	(Baghdadi, 2004; Hamauzu et al., 2005)
2.	*Ziziphus jujube* Mill., Rhamnaceae	*Unnab*	Fruit	Decoction for oral use	Betulinic acid	Anti-proliferative on some influenza viruses, anti-inflammatory	(Hong et al., 2015; Samarqandi, 2010)
3.	*Cordia dichotoma* G. Forst., Boraginaceae	*Sapistan*	Fruit	Decoction for oral use	Hydroquinones, terpenoids, steroids, flavonoids	Anti-microbial, antioxidant, antiulcer on gastric mucosa	(Oza and Kulkarni, 2017; Sina, 1878)
4.	*Sisymbrium adenophorum* (Wooton & Standl.) Tidestr., Brassicaceae	*Khaksi*	Seeds	To be mixed after preparing decoction	β-Sitosterol, stigmasterol, β-sitosterol-β-d-glucoside	Anti-bacterial	(Al-Massarani et al., 2017; Sina, 1878)
5.	*Myrtus communis* L., Myrtaceae	*Habb-ul aas*	Berry	Decoction for oral use	Tannins, flavonoids (anthocyanins, gallic acid, quercetin, etc.)	↓Intestinal motility, anti-oxidant	(Jabri et al., 2016; Sina, 1878)
6.	*Bambusa bambos* (L.) Voss, Poaceae	*Tabasheer*	Manna	Decoction for oral use	Coumaran, palmitic acid, adipic acid ester, α-elemol	Anti-helminthic, anti-inflammatory, anti-diarrhoeal	(Samarqandi, 2010; Vairappan et al., 2015)
7.	*Lactuca sativa* L., Compositae	*Tukhm-e-Kahu*	Seeds paste	For oral use	Folate, β-carotene, lutein, phenolics, vitamins, iron	Anti-inflammatory, anti-diabetic, nutritive	(M. J. Kim et al., 2016; Sina, 1878)
8.	*Aloe vera* (L.) Burm.f., Xanthorrhoeaceae	*Elwa*	Leaf sap	For local application on chest wall	Anthrones, anthraquinones, mannans	Anti-inflammatory	(Arain et al., 2016; Sina, 1878)
9.	*Crocus sativus* L., Iridaceae	*Za'fran*	Stamen	For local application on chest wall	Safranal, crocin	Antioxidant	(Bukhari et al., 2018; Samarqandi, 2010)

drugs prescribed for the same (Table 1) e.g. Vinegar, Rosewater, fumigation with various resins such as *loban*, etc. are extremely noteworthy (Razi, 1991). Convincing scientific evidence is present which advocates the air-purifying activity of most of these drugs (J. Kim et al., 2016).

Understandably, Unani medicine does not mention epidemics and pandemics as separate entities, and a common term '*waba*' is used for those diseases which affect a large geographical area. This is probably for two reasons, first and foremost, global communication was not possible in medieval ages like today; and second, travel over very long distances would have rarely occurred, hence the occurrence of a pandemic would have been a remote possibility, practically unlikely.

It is a likely possibility that epidemics will continue to occur, and with the emergence of new organisms, may be more aggressive than ever (Jones, 2020). Hence, the need arises to develop new effective methods of infection control that are accessible to the maximum population. Most of the Unani herbal drugs described in this manuscript are cheap, easy to administer and available in most parts of the world. Our review suggests that proactive researches on Unani medicines can generate credible evidence regarding their role in health promotion and disease prevention.

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References

Acharya, K.P., 2020. Resource poor countries ought to focus on early detection and containment of novel corona virus at the point of entry. Clin. Epidemiol. Glob. Heal. https://doi.org/10.1016/j.cegh.2020.03.001.

Adedeji, W.A., 2016. The treasure called antibiotics. Ann. Ibadan Postgrad. Med. 14, 56–57.

Al-Massarani, S.M., El Gamal, A.A., Alam, P., Al-Sheddi, E.S., Al-Oqail, M.M., Farshori, N.N., 2017. Isolation, biological evaluation and validated HPTLC-quantification of the marker constituent of the edible Saudi plant Sisymbrium irio L. Saudi Pharm. J. SPJ Off. Publ. Saudi Pharm. Soc. 25, 750–759. https://doi.org/10.1016/j.jsps.2016.10.012.

Amini, M., Ghoranneviss, M., Abdijadid, S., 2017. Effect of cold plasma on crocin esters and volatile compounds of saffron. Food Chem. 235, 290–293. https://doi.org/10.1016/j.foodchem.2017.05.067.

Andersen, K.G., Rambaut, A., Lipkin, W.I., Holmes, E.C., Garry, R.F., 2020. The proximal origin of SARS-CoV-2. Nat. Med. https://doi.org/10.1038/s41591-020-0820-9.

Anfinrud, P., Bax, C.E., Stadnytskyi, V., Bax, A., 2020. Could SARS-CoV-2 be transmitted via speech droplets? medRxiv https://doi.org/10.1101/2020.04.02.20051177 2020.04.02.20051177.

Anonymous, 2006. National Formulary of Unani Medicine. 1st ed. Ministry of Health and Family Welfare, Govt. of India, New Delhi.

Anonymous, 2009. The Unani Pharmacopoeia of India. Part-1st. VI. Ministry of Health and Family Welfare Department of Ayush. Ministry of Health and Family Welfare, Govt. of India, New Delhi.

Arain, I.U., Husnain, A., Talat, A., 2016. Effects of aloe vera in local massage oils in alternative medicine for the treatment of joint pains: a double blind study. Ann. King Edward Med. Univ. 22, 8. https://doi.org/10.21649/akemu.v22i1.789.

Bachrouch, O., Jemâa, J.M. Ben, Talou, T., Marzouk, B., Abderraba, M., 2010. Fumigant toxicity of Pistacia lentiscus essential oil against Tribolium castaneum and Lasioderma serricorne. Bull. Insectology 63, 129–135.

Baghdadi, I.H., 2004. Kitab al-Mukhtarat fil-Tib. Central Council for Research in Unani Medicine, New Delhi.

Bassiri-Jahromi, S., 2018. Punica granaturn (pomegranate) activity in health promotion and cancer prevention. Oncol. Rev. 12, 1–7. https://doi.org/10.4081/oncol.2018.345.

Bhat, G.A., 2016. Musk deer trade and worldwide depletion. Environ. Policy Law 46, 137–148.

Bhatwalkar, S.B., Shukla, P., Srivastava, R.K., Mondal, R., Anupam, R., 2019. Validation of environmental disinfection efficiency of traditional Ayurvedic fumigation practices. J. Ayurveda Integr. Med. 10, 203–206. https://doi.org/10.1016/j.jaim.2019.05.002.

Bukhari, S.I., Manzoor, M., Dhar, M.K., 2018. A comprehensive review of the pharmacological potential of Crocus sativus and its bioactive apocarotenoids. Biomed. Pharmacother. https://doi.org/10.1016/j.biopha.2017.12.090.

Cagno, V., Civra, A., Kumar, R., Pradhan, S., Donalisio, M., Sinha, B.N., Ghosh, M., Lembo, D., 2015. Ficus religiosa L. bark extracts inhibit human rhinovirus and respiratory syncytial virus infection in vitro. J. Ethnopharmacol. 176, 252–257. https://doi.org/10.1016/j.jep.2015.10.042.

Cambra, L.M.A., 2018. The causes of the black death described by Ibn Khatima in his work Tahsil Al-Garad. Am. Res. J. English Lit. 4. https://doi.org/10.21694/2378-9026.18015.

Chaubey, M.K., 2013. Biological activities of Zingiber officinale (Zingiberaceae) and Piper cubeba (Piperaceae) essential oils against pulse beetle, Callosobruchus chinensis (Coleoptera: Bruchidae). Pakistan J. Biol. Sci. 16, 517–523. https://doi.org/10.3923/pjbs.2013.517.523.

Chinazzi, M., Davis, J.T., Ajelli, M., Gioannini, C., Litvinova, M., Merler, S., Pastore y Piontti, A., Mu, K., Rossi, L., Sun, K., Viboud, C., Xiong, X., Yu, H., Halloran, M.E., Longini, I.M., Vespignani, A., 2020. The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. Science (80-.), eaba9757 https://doi.org/10.1126/science.aba9757.

Čivljak, R., Markotić, A., Kuzman, I., 2020. The third coronavirus epidemic in the third millennium: what's next? Croat. Med. J. 61, 1–4. https://doi.org/10.3325/cmj.2020.61.1.

Crowther, A., Veall, M.A., Boivin, N., Horton, M., Kotarba-Morley, A., Fuller, D.Q., Fenn, T., Haji, O., Matheson, C.D., 2015. Use of Zanzibar copal (Hymenaea verrucosa Gaertn.) as incense at Unguja Ukuu, Tanzania in the 7-8th century CE: chemical insights into trade and Indian Ocean interactions. J. Archaeol. Sci. 53, 374–390. https://doi.org/10.1016/j.jas.2014.10.008.

Deponti, G.N., da Silva Naue, W., Hervé, B.B., Piekala, D.M., Glaeser, S.S., de Fraga Gomes Martins, L., Dias, A.S., 2017. Perme Intensive Care Unit Mobility Score: analysis of mobility improvement in critical care patients admitted to a university hospital in Brazil. J. Crit. Care 42, 399. https://doi.org/10.1016/j.jcrc.2017.09.091.

Dong, L., Hu, S., Gao, J., 2020. Discovering drugs to treat coronavirus disease 2019 (COVID-19). Drug Discov. Ther. 14, 58–60. https://doi.org/10.5582/ddt.2020.01012.

Ezz Eldin, H.M., Sarhan, R.M., Khayyal, A.E., 2019. The impact of vinegar on pathogenic Acanthamoeba astronyxis isolate. J. Parasit. Dis. 43, 351–359. https://doi.org/10.1007/s12639-019-01098-3.

Foster, W.D., 1970. A History of Medical Bacteriology and Immunology, a History of Medical Bacteriology and Immunology. Cox & WaymanLtd, Great Britain https://doi.org/10.1016/c2013-0-04334-4.

Fu, J.T., Tang, L., Li, W.S., Wang, K., Cheng, D.M., Zhang, Z.X., 2015. Fumigant toxicity and repellence activity of camphor essential oil from Cinnamonum camphora Siebold against Solenopsis invicta workers (Hymenoptera:Formicidae). J. Insect Sci. 15, 129. https://doi.org/10.1093/jisesa/iev112.

Gautret, P., Lagier, J.-C., Parola, P., Hoang, V.T., Meddeb, L., Mailhe, M., Doudier, B., Courjon, J., Giordanengo, V., Vieira, V.E., Dupont, H.T., Honoré, S., Colson, P., Chabrière, E., La Scola, B., Rolain, J.-M., Brouqui, P., Raoult, D., 2020. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int. J. Antimicrob. Agents 105949. https://doi.org/10.1016/j.ijantimicag.2020.105949.

Guo, Y.R., Cao, Q.D., Hong, Z.S., Tan, Y.Y., Chen, S.D., Jin, H.J., Tan, K. Sen, Wang, D.Y., Yan, Y., 2020. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status. Mil. Med. Res. 7, 11. https://doi.org/10.1186/s40779-020-00240-0.

Hamauzu, Y., Yasui, H., Inno, T., Kume, C., Omanyuda, M., 2005. Phenolic profile, antioxidant property, and anti-influenza viral activity of Chinese quince (Pseudocydonia sinensis Schneid.), quince (Cydonia oblonga Mill.), and apple (Malus domestica Mill.) fruits. J. Agric. Food Chem. 53, 928–934. https://doi.org/10.1021/jf0494635.

Hayes, D., Angove, M.J., Tucci, J., Dennis, C., 2016. Walnuts (Juglans regia) chemical composition and research in human health. Crit. Rev. Food Sci. Nutr. 56, 1231–1241. https://doi.org/10.1080/10408398.2012.760516.

He, X., Lau, E.H., Wu, P., Deng, X., Wang, J., Hao, X., Lau, Y.C., Wong, J.Y., Guan, Y., Tan, X., Mo, X., Chen, Y., Liao, B., Chen, W., Hu, F., Zhang, Q., Zhong, M., Wu, Y., Zhao, L., Zhang, F., Cowling, B.J., Li, F., Leung, G.M., 2020. Temporal dynamics in viral shedding and transmissibility of COVID-19. medRxiv https://doi.org/10.1101/2020.03.15.20036707 (2020.03.15.20036707).

Ho, C.W., Lazim, A.M., Fazry, S., Zaki, U.K.H.H., Lim, S.J., 2017. Varieties, production, composition and health benefits of vinegars: a review. Food Chem. https://doi.org/10.1016/j.foodchem.2016.10.128.

Hong, E.-H., Song, J.H., Kang, K. Bin, Sung, S.H., Ko, H.-J., Yang, H., 2015. Anti-influenza activity of betulinic acid from Zizyphus jujuba on influenza A/PR/8 virus. Biomol. Ther. (Seoul). 23, 345–349. https://doi.org/10.4062/biomolther.2015.019.

Husain, A., Sofi, G., Dang, R., Kumar, N., 2010. Unani system of medicine - introduction and challenges. Med. J. Islam. World Acad. Sci. 18 (1), 27–30.

Imani, G., Mehrpoya, M., Khalilian, A., Dastan, D., Imani, B., 2020. Effects of cinnamon extract on complications of treatment and eradication of Helycobacter pylori in infected people implication for health policy/practice/research/medical education. J. Herbmed Pharmacol. J Herbmed Pharmacol 9. https://doi.org/10.15171/jhp.2020.xx.

Islam, A., 2018. Origin and development of unani medicine: an analytical study. Intellect. Discourse 26, 23–49.

Jabri, M.A., Rtibi, K., Sakly, M., Marzouki, L., Sebai, H., 2016. Role of gastrointestinal motility inhibition and antioxidant properties of myrtle berries (Myrtus communis L.) juice in diarrhea treatment. Biomed. Pharmacother. 84, 1937–1944. https://doi.org/10.1016/j.biopha.2016.11.008.

Jean, S.-S., Lee, P.-I., Hsueh, P.-R., 2020. Treatment options for COVID-19: the reality and challenges. J. Microbiol. Immunol. Infect. https://doi.org/10.1016/j.jmii.2020.03.034.

Jones, D.S., 2020. History in a crisis-lessons for Covid-19. N. Engl. J. Med. 1–3.

Kim, S. Il, Na, Y.E., Yi, J.H., Kim, B.S., Ahn, Y.J., 2007. Contact and fumigant toxicity of oriental medicinal plant extracts against Dermanyssus gallinae (Acari: Dermanyssidae). Vet. Parasitol. 145, 377–382. https://doi.org/10.1016/j.vetpar.2006.12.021.

Kim, J., Jang, M., Shin, E., Kim, Jeongmin, Lee, S.H., Park, C.G., 2016a. Fumigant and contact toxicity of 22 wooden essential oils and their major components against Drosophila suzukii (Diptera: Drosophilidae). Pestic. Biochem. Physiol. 133, 35–43. https://doi.org/10.1016/j.pestbp.2016.03.007.

Kim, M.J., Moon, Y., Tou, J.C., Mou, B., Waterland, N.L., 2016b. Nutritional value, bioactive compounds and health benefits of lettuce (Lactuca sativa L.). J. Food Compos. Anal. https://doi.org/10.1016/j.jfca.2016.03.004.

Komakech, R., Kim, Y.-G., Matsabisa, G.M., Kang, Y., 2019. Anti-inflammatory and analgesic potential of Tamarindus indica Linn. (Fabaceae): a narrative review. Integr. Med. Res. 8, 181–186. https://doi.org/10.1016/j.imr.2019.07.002.

Lemenih, M., Abebe, T., Olsson, M., 2003. Gum and resin resources from some Acacia, Boswellia and Commiphora species and their economic contributions in Liban, south-east Ethiopia. J. Arid Environ. 55, 465–482. https://doi.org/10.1016/S0140-1963(03)00053-3.

Lim, S.H., Choi, C.I., 2019. Pharmacological properties of morus nigra L. (Black Mulberry) as a promising nutraceutical resource. Nutrients 11. https://doi.org/10.3390/nu11020437.

Ling, L., Joynt, G.M., Lipman, J., Constantin, J.M., Joannes-Boyau, O., 2020. COVID-19: a critical care perspective informed by lessons learnt from other viral epidemics. Anaesth. Crit. Care Pain Med. S2352-5568 (20), 30029–30031. https://doi.org/10.1016/j.accpm.2020.02.002.

Ludwiczuk, A., Skalicka-Woźniak, K., Georgiev, M.I., 2017. Terpenoids. In: Badal, S., Delgoda, R. (Eds.), Pharmacognosy: Fundamentals, Applications and Strategy. Academic Press, Jamaica, pp. 233–266. https://doi.org/10.1016/B978-0-12-802104-0.00011-1.

Maridass, M., Ghanthikumar, S., Raju, G., 2008. Preliminary phytochemical analysis of diospyros species. Ethanobotanical Leafl 12, 868–872.

McKibbin, W.J., Fernando, R., 2020. The global macroeconomic impacts of COVID-19: seven scenarios. SSRN Electron. J. https://doi.org/10.2139/ssrn.3547729.

Mehta, P., McAuley, D.F., Brown, M., Sanchez, E., Tattersall, R.S., Manson, J.J., 2020. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 395, 1033–1034. https://doi.org/10.1016/S0140-6736(20)30628-0.

Menkir, T.F., Chin, T., Hay, J.A., Surface, E., Martinez de Salazar, P., Buckee, C., Mina, M.J., Khan, K., Watts, A., Lipsitch, M., Niehus, R., 2020. Estimating the number of undetected COVID-19 cases exported internationally from all of China. medRxiv https://doi.org/10.1101/2020.03.23.20038331 (2020.03.23.20038331).

Mohr, K.I., 2016. History of antibiotics research. In: Stadler, M., Dersch, P. (Eds.), Current Topics in Microbiology and Immunology. Springer, Cham, pp. 237–272. https://doi.org/10.1007/82_2016_499.

Nigar, Z., Itrat, M., 2013. Evaluation of a Unani polyherbal formulation (Tiryaqe wabai) as an immunostimulator in elderly persons. Anc. Sci. Life 33, 117. https://doi.org/10.4103/0257-7941.139054.

Ober, W.B., Aloush, N., 1982. The plague at Granada, 1348-1349: Ibn Al-Khatib and ideas of contagion. Bull. N. Y. Acad. Med. 58, 418–424.

Orav, A., Koel, M., Kailas, T., Müürisepp, M., 2010. Comparative analysis of the composition of essential oils and supercritical carbon dioxide extracts from the berries and needles of Estonian juniper (Juniperus communis L.). Procedia Chemistry, 161–167 https://doi.org/10.1016/j.proche.2009.12.023.

Oza, M.J., Kulkarni, Y.A., 2017. Traditional uses, phytochemistry and pharmacology of the medicinal species of the genus Cordia (Boraginaceae). J. Pharm. Pharmacol. https://doi.org/10.1111/jphp.12715.

Pandith, S.A., Dar, R.A., Lattoo, S.K., Shah, M.A., Reshi, Z.A., 2018. Rheum australe, an endangered high-value medicinal herb of North Western Himalayas: a review of its botany, ethnomedical uses, phytochemistry and pharmacology. Phytochem. Rev. 17, 573–609. https://doi.org/10.1007/s11101-018-9551-7.

Parsley, N.C., Kirkpatrick, C.L., Crittenden, C.M., Rad, J.G., Hoskin, D.W., Brodbelt, J.S., Hicks, L.M., 2018. PepSAVI-MS reveals anticancer and antifungal cyclovioIacins in Viola odorata. Phytochemistry 152, 61–70. https://doi.org/10.1016/j.phytochem.2018.04.014.

Phan, T., 2020a. Novel coronavirus: from discovery to clinical diagnostics. Infect. Genet. Evol. https://doi.org/10.1016/j.meegid.2020.104211.

Phan, T., 2020b. Genetic diversity and evolution of SARS-CoV-2. Infect. Genet. Evol. 81. https://doi.org/10.1016/j.meegid.2020.104260.

Qadeer, A., 2001. Tareekh-e-Tib wa Akhlaqiyat. 1st ed. (New Delhi).

Rahmani, A.H., 2015. Cassia fistula Linn: potential candidate in the health management. Pharm. Res. 7, 217–224. https://doi.org/10.4103/0974-8490.157956.

Rasmussen, S.A., Smulian, J.C., Lednicky, J.A., Wen, T.S., Jamieson, D.J., 2020. Coronavirus disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. Am. J. Obstet. Gynecol. https://doi.org/10.1016/j.ajog.2020.02.017.

Razi, Z., 1991. Kitab al-Mansoori. Central Council for Research in Unani Medicine, New Delhi.

Razi, Z., 2008. Kitab al-Hawi. Central Council for Research in Unani Medicine, New Delhi.

Rehman, S.Z., 1991. Daur-e-Jadeed Aur Tib. Tibbi Academy, Bhopal.

del Rio, C., Malani, P.N., 2020. COVID-19—new insights on a rapidly changing epidemic. Jama https://doi.org/10.1001/jama.2020.3072.

Rodriguez-Morales, A.J., Bonilla-Aldana, D.K., Sah, R., 2020. COVID-19, an emerging coronavirus infection: current scenario and recent developments – an overview. J. Pure Appl. Microbiol. 14 (1), 1–9 6150 14.

Rushd, I., 1987. Kitab al-Kulliyat. 2nd ed. Central Council for Research in Unani Medicine, New Delhi.

Russell, B., Moss, C., Rigg, A., Hemelrijck, M. Van, 2020. COVID-19 and treatment with NSAIDs and corticosteroids: should we be limiting their use in the clinical setting ? Ecancer 14, 1–3. https://doi.org/10.3332/ecancer.2020.1023.

Sagheer, M., Ali, K., Hasan, M.U., Rashid, A., Sagheer, U., Alvi, A., 2013. Repellent and toxicological impact of acetone extracts of nicotiana tabacum, pegnum hermala, saussurea costus and salsola baryosma against red flour beetle, tribolium castaneum (herbst). Pak. J. Zool. 45, 1735–1739.

Sahasranaman, A., Kumar, N., 2020. Network structure of COVID-19 spread and the lacuna in India's testing strategy. SSRN Electron. J. https://doi.org/10.2139/ssrn.3558548.

Samarqandi, N., 2010. Sharah Asbab. Aijaz Publishing House, New Delhi.

Saxena, S., Lakshminarayan, N., Gudli, S., Kumar, M., 2017. Anti bacterial efficacy of Terminalia chebula, Terminalia bellirica, Embilica officinalis and Triphala on salivary Streptococcus mutans count - a linear randomized cross over trial. J. Clin. Diagn. Res. 11, ZC47–ZC51. https://doi.org/10.7860/JCDR/2017/23558.9355.

Sharafati Chaleshtori, F., Saholi, M., Sharafati Chaleshtori, R., 2018. Chemical composition, antioxidant and antibacterial activity of Bunium persicum, Eucalyptus globulus, and rose water on multidrug-resistant listeria species. J. Evidence-Based Integr. Med. 23. https://doi.org/10.1177/2515690X17751314.

Sina, I., 1878. Al Qanoon Fil Tibb. Munshi Nawal Kishore, Lucknow.

Subbarayappa, B.V., 2001. The roots of ancient medicine: an historical outline. J. Biosci. https://doi.org/10.1007/BF02703637.

Sun, P., Lu, X., Xu, C., Sun, W., Pan, B., 2020. Understanding of COVID-19 based on current evidence. J. Med. Virol. https://doi.org/10.1002/jmv.25722.

Tang, X., Wu, C., Li, X., Song, Y., Yao, X., Wu, X., Duan, Y., Zhang, H., Wang, Y., Qian, Z., Cui, J., Lu, J., 2020. On the origin and continuing evolution of SARS-CoV-2. Natl. Sci. Rev. https://doi.org/10.1093/nsr/nwaa036.

Vahid-Dastjerdi, E., Sarmast, Z., Abdolazimi, Z., Mahboubi, A., Amdjadi, P., Kamalinejad, M., 2014. Effect of Rhus coriaria L. water extract on five common oral bacteria and bacterial biofilm formation on orthodontic wire. Iran. J. Microbiol. 6, 269–275.

Vairappan, C.S., Nagappan, T., Hui, L.T., 2015. Chemical constituents and biological activities of essential oils from four species of bamboo genus Schizostachyum. J. Trop. Biol. Conserv. 12, 127–136.

Vellingiri, B., Jayaramayya, K., Iyer, M., Narayanasamy, A., Govindasamy, V., Giridharan, B., Ganesan, S., Venugopal, A., Venkatesan, D., Ganesan, H., Rajagopalan, K., Rahman, P.K.S.M., Cho, S.G., Kumar, N.S., Subramaniam, M.D., 2020. COVID-19: a promising cure for the global panic. Sci. Total Environ. 725, 138277. https://doi.org/10.1016/j.scitotenv.2020.138277.

Verma, R.S., Padalia, R.C., Chauhan, A., Yadav, A., Chanotiya, C.S., 2015. Essential oil composition of Himalayan Peony (Paeonia emodi Royle). J. Essent. Oil Res. 27, 477–480. https://doi.org/10.1080/10412905.2015.1039664.

Vohora, S.B., 1986. Unani Joshandah drugs for common cold, catarrh, cough and associated fevers. J. Ethnopharmacol. 16, 201–211. https://doi.org/10.1016/0378-8741(86)90090-5.

Walls, A.C., Park, Y.J., Tortorici, M.A., Wall, A., McGuire, A.T., Veesler, D., 2020. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. Cell https://doi.org/10.1016/j.cell.2020.02.058.

Weeks, J., 2020. Call to action: announcing the traditional, complementary and integrative health and medicine COVID-19 support registry. 26, 1–3. https://doi.org/10.1089/acm.2020.29083.jjw.

World Health Organization (WHO), 2020. Coronavirus Disease 2019 (COVID-19) Situation Report-88. World Health Organization.

Wu, Z., McGoogan, J.M., 2020. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA - J. Am. Med. Assoc. 323, 1239–1242. https://doi.org/10.1001/jama.2020.2648.

Zeinali, M., Zirak, M.R., Rezaee, S.A., Karimi, G., Hosseinzadeh, H., 2019. Immunoregulatory and anti-inflammatory properties of Crocus sativus (Saffron) and its main active constituents: a review. Iran. J. Basic Med. Sci. 22, 334–344. https://doi.org/10.22038/ijbms.2019.34365.8158.

Zhang, J.S., Zhao, N.N., Liu, Q.Z., Liu, Z.L., Du, S.S., Zhou, L., Deng, Z.W., 2011. Repellent constituents of essential oil of Cymbopogon distans aerial parts against two stored-product insects. J. Agric. Food Chem. 59, 9910–9915. https://doi.org/10.1021/jf202266n.

Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., Zhao, X., Huang, B., Shi, W., Lu, R., Niu, P., Zhan, F., Ma, X., Wang, D., Xu, W., Wu, G., Gao, G.F., Tan, W., 2020. A novel coronavirus from patients with pneumonia in China, 2019. N. Engl. J. Med. 382, 727–733. https://doi.org/10.1056/NEJMoa2001017.