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Review article

Rationalistic approach in COVID-19 prevention through intervention of Unani medicine prevalent in epidemic – A review

Fatima Khan^{*}, Abdul Nasir Ansari, Mohd Nayab

Department of Ilaj Bit Tadbeer, National Institute of Unani Medicine, Bangalore, India



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ABSTRACT

Introduction: A novel coronavirus virus (2019-nCoV) emerged in China in December 2019 and achieved a high-risk category by the World Health Organization (WHO). The initial symptoms included fever, cough, dyspnea, and sore throat. The present review aims to evaluate the available evidence for the safety and efficacy of *Unani* herbal drugs and formulations in the prevention of *Wabai Amraz* (epidemic diseases) having resemblance to SARS-CoV-2.

Methods: Sources of data for this paper are classical *Unani* textbooks, *Unani* pharmacopeia of India, *Indian Medicinal Plants-An Illustrated Dictionary*, and published articles in various reputed peer-reviewed journals. Collected information was then critically analyzed.

Results: Despite great efforts, no specific treatment has been discovered for coronavirus yet. The best choices, therefore, are prevention and management. The *Unani* system of medicine offers health protection during epidemics. Three important interventions practised during an outbreak are (i) purification of the environment by using certain herbal drugs as fumigants which include vinegar (acetic acid) alone or combined with *Ferula foetida* Regel; (ii) promotion of health and immune modulation by using the pharmacopoeial preparations *Khamira-e-Khashkhash* and *Khamira-e-Marwareed*.

Conclusion: Several single drugs, as well as compound formulations, have been recommended in *Unani* medicine for the prevention and treatment of infectious diseases. The pharmacopoeial preparation *Tiryay-e-Nazla* has been used for respiratory catarrhal inflammations and influenza by *Hakims* of the medieval period. Scientific research on these drugs reveals the presence of many pharmacologically active substances possessing significant antiviral, antipyretic, anti-tussive, and immune-modulatory properties, which can give new insight into infection and epidemic management.

1. Introduction

The recent onset of severe acute respiratory coronavirus syndrome (SARS-CoV) highlights the continuing threat to human health posed by emerging viruses (Holmes and Rambaut, 2004). Coronavirus disease (COVID-19), caused by the SARS-CoV-2 novel coronavirus, is an easily transmitted disease identified in December 2019 and declared a pandemic by WHO on 11 March 2020 while thousands of infections and deaths were reported daily (Galanakis, 2020). On 30th January 2020, the World Health Organization (WHO) officially declared the COVID-19 epidemic as a public health emergency of international concern (Del Rio and Malani, 2020). This virus is a new human-infecting Beta coronavirus, named 2019-nCoV by the WHO and SARS-CoV-2 by the International Committee on Taxonomy of Viruses, based on its genetic

proximity to 2 bat-derived SARS-like coronaviruses, likely originated in chrysanthemum bats (Del Rio and Malani, 2020). The virus spread internationally within one month of the first identification and can be transmitted via close human-to-human contact (Peeri et al., 2020).

The appearance of SARS-CoV-2 marked the third introduction, in the 21st century, of a highly pathogenic and large-scale coronavirus infection into the human population (Guo et al., 2020). Emerging viruses reveal some important general patterns. Firstly, almost all emerging viruses have RNA rather than DNA genomes. Second, almost all emerging viruses have an animal reservoir (Holmes and Rambaut, 2004). Two scenarios were proposed that plausibly explained the origin of SARS-CoV-2: Since SARS-CoV-2 is similar to SARS-CoV-like coronaviruses, bats are likely to act as reservoir hosts for its progenitor. A SARS-CoV-2 progenitor likely spread into humans, acquiring the

^{*} Corresponding author at: Department of Ilaj Bit Tadbeer, National Institute of Unani Medicine, Bangalore, 560091, India.
E-mail address: drfatimakhan021@gmail.com (F. Khan).

genomic features described above through adaptation during undetected human-to-human transmission (Andersen et al., 2020). Six species of coronavirus are known to cause illness in humans. Four viruses-229E, OC43, NL63, and HKU1-are prevalent in immune-competent individuals and generally cause common cold symptoms. The other two strains-severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are zoonotic and have often been related to fatal disease (Zhu et al., 2020). Zoonotic viruses were not known to be highly pathogenic to humans until the outbreak in Guangdong Province, China, of the severe acute respiratory syndrome (SARS-CoV) in 2002 and 2003, and another highly pathogenic coronavirus, Middle East respiratory syndrome coronavirus (MERS-CoV), emerged in Middle Eastern countries. Wild animals, such as bats, have been implicated as the natural host of these viruses in both cases, which have also spilled over to humans, and use civets, and camels as main intermediate hosts (Rodriguez-Morales et al., 2020a). Genomic studies could delineate host factors that predispose individuals to infection acquisition and disease progression (Fauci et al., 2020).

As of 1st September 2021, there have been 216,867,420 confirmed cases and 4,507,837 deaths worldwide and 32,768,880 confirmed cases, and 438,560 deaths in India due to Covid-19, as reported by the WHO (WHO, 2021a). The first case of Covid-19 in India was a student who returned from Wuhan, China on 30th January 2020 (Nikhat and Fazil, 2020).

1.1. Coronavirus disease 2019

1.1.1. Causative agent

Coronaviruses belong to the subfamily *Coronavirinae* in the family of *Coronaviridae* of the order *Nido virales*, and this subfamily includes four genera: *Alpha coronavirus*, *Beta coronavirus*, *Gamma coronavirus*, and *Delta coronavirus*. The genome of CoVs is a single-stranded positive-sense RNA (Chen et al., 2020b). They were termed coronaviruses (Latin: corona = crown) based on their morphology as spherical virions with a core-shell and surface projections resembling a solar corona. Alpha- and beta-coronaviruses come from bats while gamma- and delta-viruses come from pigs and birds. Beta-coronaviruses can cause severe effects among the seven subtypes of coronaviruses that can infect humans (Velavan and Meyer, 2020). A densely glycosylated spike (S) protein is used by the virus to penetrate host cells which binds to the angiotensin-converting enzyme 2 (ACE2) receptor with a high affinity (Del Rio and Malani, 2020). It was found that the SARS-CoV-2 genome sequence is 96.2% identical to a bat CoV RaTG13, while it shares 79.5% of SARS-CoV's identity. Based on the results and evolutionary analysis of the virus genome sequencing, the bat was suspected to be a natural host of virus' origin, and SARS CoV- 2 might be transmitted from bats via unknown intermediate hosts to infect humans (Guo et al., 2020). Genomic studies showed that only five nucleotides differed between SARS coronavirus and SARS-CoV-2 and stressed that 2019-nCoV emerged from SARS CoV (Rodriguez-Morales et al., 2020b).

1.1.2. Intermediate host

The new COVID-19 originates from the SARS-CoV-2 virus. The most likely natural reservoirs for SARS-CoV-2 are bats, but it is suspected that the virus crossed the species barrier to humans via another intermediate animal host. This intermediate host may have been a domestic food animal, a wild animal, or a domesticated wild animal that has not yet been identified (WHO, 2020a). It is believed that pangolins could be the intermediate host for SARS-CoV-2 (Kakodkar et al., 2020).

1.1.3. Transmission

The three main transmission routes for COVID-19 are 1) droplet transmission, 2) contact transmission, and 3) aerosol transmission (Adhikari et al., 2020). COVID-19 is transmitted primarily from symptomatic people to others who are in close contact through respiratory droplets, through direct contact with infected people, or contact with

contaminated objects and surfaces. Transmission from a pre-symptomatic case can also occur before symptom onset (WHO, 2020b). Viral RNAs may be found in nasal discharge, sputum, and occasionally in blood or feces (Wu et al., 2020). Transmission via contact with droplets from human respiratory activities such as talking, coughing, sneezing, and aerosols generated during clinical procedures is expected. The origin of droplets can be nasopharyngeal or oropharyngeal and these are normally associated with saliva (Sabino-Silva et al., 2020).

1.2. Disease spectrum

1.2.1. Incubation period

The incubation period for COVID-19, which is the time between virus exposure (being infected) and the onset of the symptoms, is on average is 5–6 days but may take up to 14 days (WHO, 2020b). For the COVID-19 virus, the reproductive number – the number of secondary infections generated by one infected person – is known to be between 2 and 2.5, higher than for influenza. Mortality for COVID-19 is between 3% and 4% higher than for influenza (WHO, 2020c). The virus spreads faster than its two predecessors but has less fatality (Singhal, 2020). Currently designated variants of concern by WHO are Alpha B.1.1.7, Beta B.1.351, Gamma P.1, and Delta B.1.617.2 (WHO, 2021b). COVID-19 efficiently replicates in the upper respiratory tract and appears to cause a less abrupt symptom onset (Heymann and Shindo, 2020).

1.2.2. Symptoms and signs

The clinical course of infection tends to have three main patterns: a mild disease with symptoms of the upper respiratory tract, non-life-threatening pneumonia, and extreme pneumonia with acute respiratory distress syndrome (ARDS) (Heymann and Shindo, 2020). Symptoms typically start with non-specific syndromes which include fever, dry cough, and tiredness. Multiple systems may be involved such as respiratory (coughing, shortness of breath, sore throat, rhinorrhea, hemoptysis, and chest pain), gastrointestinal (diarrhea, nausea, and vomiting), musculoskeletal (muscle ache), and neurological (headache or confusion) (Wu et al., 2020). The elderly and people with underlying medical problems are more likely to develop serious illnesses such as chronic bronchitis, emphysema, heart disease, or diabetes (Filatov et al., 2020). The postulated mechanism for organ damage is the "cytokine storm" or "cytokine cascade". COVID-19 infection is accompanied by an aggressive inflammatory response with the release of a large amount of pro-inflammatory cytokines in an event known as "cytokine storm". The host immune response to the SARS-CoV-2 is hyperactive resulting in an excessive inflammatory reaction leading to organ damage (Jiang et al., 2020).

1.2.3. Diagnosis

COVID-19's golden clinical diagnostic method is the detection of nucleic acid in a sampling of mucosal secretions obtained via a nasal or throat swab. Respiratory tract samples are tested by real-time PCR (Polymerase Chain Reaction) and further confirmed by next-generation sequencing (Guo et al., 2020). X-rays of the chest and other imaging methods may reveal ground glass irregularities, patchy consolidation, alveolar exudations, and interlobular involvement. Lymphopenia appears to be common, with elevated inflammatory markers such as C-reactive proteins and proinflammatory cytokines (Velavan and Meyer, 2020).

1.2.4. Complications

Acute respiratory distress syndrome (ARDS), arrhythmia, shock, acute kidney injury, acute heart injury, liver disease, and secondary infection were among the complications. The poor clinical result was attributed to the seriousness of the disease (Guo et al., 2020).

1.3. Management

Treatment is symptomatic. Ensuring proper isolation is the first step for patients and healthcare workers to avoid transmission to other contacts (Singhal, 2020). To date, no specific treatment for the SARS-CoV-2 infection is 100% effective. Symptomatic and supportive care is the principal strategy. Anti-HIV drugs like Remdesivir, antiviral drugs like lopinavir/ ritonavir, and ribavirin had been tried to treat the SARS disease with apparently favorable clinical response (Wu et al., 2020). According to World Health Organization (WHO), the initial clinical trial results from the United Kingdom (UK) showed that dexamethasone, a corticosteroid, can be lifesaving for patients who are critically ill with COVID-19 (WHO, 2020b). Convalescent plasma or immunoglobulins were used as a final resort to improve the rate of survival. In 2014, the WHO advocated the use of convalescent plasma obtained from Ebola virus disease patients as an empirical therapy during outbreaks. One potential reason for the effectiveness of convalescent plasma therapy is that viremia can be suppressed by convalescent plasma antibodies (L. Chen et al., 2020a). For hypoxic patients, it is suggested that oxygen is given by nasal prongs, a face mask, a high-flow nasal cannula (HFNC), or non-invasive ventilation. Mechanical ventilation may also be necessary. In certain cases, renal replacement therapy may be required (Singhal, 2020).

In this context, traditional systems of medicine are being explored for providing preventive, supportive, and rehabilitative care to patients. This paper presents an overview of Covid-19, the Unani concept of infectious and epidemic diseases and their preventive measures and a possible approach to the management of Covid-19 with Unani medicine.

1.3.1. Prevention

Standard guidelines for reducing exposure and the transmission of a variety of infections have been established by the WHO. These guidelines include daily hand cleaning; covering the nose and mouth; avoiding close contact with others who are infected; seeking medical attention in the event of fever and cough; avoiding direct unprotected contact with live animals and surfaces; mitigation of the consumption of raw or undercooked animal products and proper handling of raw meat, milk or animal organs to prevent cross-contamination. (Khan et al., 2020).

Non-pharmaceutical public health interventions to control infectious disease outbreaks are isolation, quarantine, community containment by social distancing (Wilder-Smith and Freedman, 2020). Precautions for airborne transmission should be taken during procedures that generate aerosols, such as intubation, suction, and tracheostomy (Singhal, 2020). The safety of individuals and society must also be robust. The World Health Organization (WHO), the Center for Disease Control and Prevention (CDC), and the Food and Agriculture Organization (FAO) provided guidance and containment measures for common citizens, physicians, travelers, and infectious patients to avoid transmission to a healthy population (Rodriguez-Morales et al., 2020b). Promotion of public health initiatives, including hand-washing, respiratory hygiene, and social distancing; readiness of health systems for chronically ill patients requiring isolation, oxygen, and mechanical ventilation; improving the prevention and control of infection in health care facilities, with particular attention to nursing homes; and postponement or cancellation of large-scale public services; (Bedford et al., 2020). The COVID-19 outbreak alerts us that a carefully planned stockpile of PPE and other essentials is key to effective infectious disease preparedness and the optimal function of HCP (Zhang et al., 2020). With the progression of the disease, clinical symptoms become serious and psychological issues in infected patients change; psychological intervention should, therefore, be targeted and adapted as necessary (Duan and Zhu, 2020). Several safe and effective vaccines prevent people from getting seriously ill or dying from COVID-19. This is one part of managing COVID-19, in addition to the main preventive measures. As of 3 June 2021, WHO has evaluated that the following vaccines against COVID-19

have met the necessary criteria for safety and efficacy: AstraZeneca/Oxford vaccine, Johnson and Johnson, Moderna, Pfizer/BionTech, Sinopharm, and Sinovac. Approved COVID-19 vaccines provide a high degree of protection against getting seriously ill and dying from the disease, although no vaccine is 100% protective (WHO, 2021c).

2. Methodology

Unani classical books available in the National Institute of Unani Medicine library were searched for information related to epidemic diseases. Six important textbooks of Unani medicine were reviewed. *Al-Qanoon fil Tib* of Ibn Sina (Avicenna), *Kitab al-Hawi* of Zakariya Razi (Rhazes), *Kitab-al-Kulliyat* by Ibn Rushd (Averroes), *Zakhira Khawarizam Shahi* by Ahmad Hasan Jurjani (Ismail Gorgani), *Kitab al-Mukhtarat fil-Tib* by Ibn Hubal Baghdadi and *Moalejat Sharha Asbab* by Najeebuddin Samarqandi. Other published books and journals were also consulted for further details. For information on SARS-CoV-2 and Covid-19, the major scientific databases, namely PubMed, Science Direct, Springer, Elsevier, and Scopus were searched for the most recent information regarding the pandemic. The search words used were 'SARS-CoV-2', 'Covid-19', 'history', 'prevalence', 'symptoms', and 'transmission'. An Internet search on the same search engines, as well as Google Scholar, was searched for scientific evidence regarding Unani drugs prescribed during epidemics. For this search, the terms used were 'waba', 'influenza', 'epidemic', 'immunomodulatory', and 'bioactive compounds, along with the names of single herbs, like *Commiphora myrrha*, Nees, *Crocus sativus* Linn., and *Aloe barbadensis*, Mill., according to their use. A time restriction was not specified to extract the most useful information, hence, articles published from 1951 to 2021 were included in the final manuscript.

3. Infections and epidemic diseases in Unani medicine

3.1. A brief introduction to the Unani system of medicine

The Unani System of Medicine was pioneered in Greece and developed by Arabs into an elaborate medical science based on the framework of the teachings of *Buqrat* (Hippocrates) and *Jalinoos* (Galen). Unani Medicine has since been known as Greco-Arab Medicine. According to the Hippocratic philosophy, this system is based on four humours: blood, yellow bile, phlegm, and black bile, and the four characteristics of living human body conditions, such as hot, cold, wet, and dry (Ahmad, 1983). The Unani Medicine System (USM), also known as Arab medicine, has been recognized by the World Health Organization (WHO) as an alternative system for meeting the health care needs of the human population. India acknowledged it as one of the alternative health care systems and has given it official status. Up to 80% of the population in Africa and 65% in India depend on traditional medicine to help meet their health care needs (Husain and Sofi, 2010) and these medicines may include the use of herbal medicines, animal components, and minerals.

3.2. Concept of infectious diseases and epidemics in Unani medicine

Across the ancient ages, the history of infectious diseases has been documented. Hippocrates (460–377 B.C.) was possibly the first physician to report the numerous clinical symptoms of many infectious diseases, which are currently referred to as influenza, diphtheria, tuberculosis, mumps, and malaria (Parvez et al., 2016). The infectious and epidemic diseases are caused by the invasion of foreign bodies, which attack the humours. The main things affected by the "*Ladia*" or *adva* (infection) and *Waba* (epidemic) are:

1. The humours
2. The heart and other significant organs such as the stomach and liver.
3. *Hararat-e-Gharizia* or vital heat (Khan, 1981)

The text *Ibne Khatima* refers to the mechanism and immediate causes

Table 1
Single drugs prescribed in Unani medicine for respiratory disease.

S. No.	Binomial name and family	Genus	Species	Unani name	Part used	Method of use in Unani medicine	Active ingredients	Mode of action	References
1.	<i>Achyranthes aspera</i> Linn., Amaranthaceae	<i>Achyranthes</i>	<i>A. aspera</i>	chirchita	Root ashes	Oral	Achyranthine, betaine glycosides, saponins	Pectoral, astringent anti-inflammatory	(Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003), (MoHFW, 2007a)
2.	<i>Mentha arvensis</i> Linn. Var., Lamiaceae	<i>Mentha</i>	<i>M. arvensis</i>	nana	Leaves	Oral and local application	Essential oil- menthol, menthyl acetate, L-menthone, limonene	Antibacterial, antifungal antifebrile	(Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003), (MoHFW, 2008)
3.	<i>Valeriana officinalis</i> Linn., Valerianaceae	<i>Valeriana</i>	<i>V. officinalis</i>	sumbul-ut-teeb	Rhizome	Oral	Actinidine, valerene, β -sitosterol, choline, Terpene, valerenic acid	Anti-spasmodic, stimulant	(Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003), (MoHFW, 2007b)
4.	<i>Hyssopus officinalis</i> Linn., Lamiaceae	<i>Hyssopus</i>	<i>H. officinalis</i>	zufa	Leaves	Oral	Marrubiin, ursolic acid, glucoside, essential oil	Expectorant	(Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003), (MoHFW, 2007c)
5.	<i>Ocimum basilicum</i> Linn., Lamiaceae	<i>Ocimum</i>	<i>O. basilicum</i>	faranjmushk	Seeds	Oral	Essential oil, linalool, thymol, flavonoids	Antibacterial, demulcent	(Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003)
6.	<i>Adhatoda vasica</i> Nees., Acanthaceae	<i>Adhatoda</i>	<i>A. vasica</i>	arusa	Dried leaves	Oral	Vasicine, vasicinone, trypsin, β -sitosterol-D-glucoside, Quercetin	Expectorant, Anti-spasmodic, Febrifuge, Depurative	(Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003)
7.	<i>Onosma bracteatum</i> Wall., Boraginaceae	<i>Onosma</i>	<i>O. bracteatum</i>	gaozaban	Dried leaves	Oral	Glycosides, flavonoids, tannin, phenolic compounds	Refrigerant, demulcent, tonic	(Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003), (MoHFW, 2008)
8.	<i>Foeniculum vulgare</i> Mill., Apiaceae	<i>Foeniculum</i>	<i>F. Vulgare</i>	badiyan	Dried ripe fruit	Oral	Essential oil, flavonoids, anethole, limonene, Fixed oil	Anti-bacterial, anti-oxidant, anti-inflammatory	(Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003), (MoHFW, 2007b)
9.	<i>Viola odorata</i> Linn., Violaceae	<i>Viola</i>	<i>V. odorata</i>	banafsha	Flowers and leaves	Oral	Anthocyanin, violin, flavonoids, tocopherol, rutoside, mucilage	Expectorant, anti-inflammatory, antimicrobial, antipyretic	(Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003), (MoHFW, 2007d)

of the plague and other pandemics according to humor theory. The immediate source, he says, is the air alteration that people breathe (Luisa and Arvide, 2018). An eminent Unani physician Galen (129–200 CE) postulated that certain pollutant-related diseases tend to be carried by wind and thus spread more quickly as they enter the human body through the respiratory tract (Spinelli, 2020). Fever during an epidemic arises due to a change in the quality and composition of air (Baghdadi, 2007). According to Rhazes, an epidemic affects those whose bodies are full of morbid humours or the waste products of the body that have not been excreted (Razi, 2008). People with weak immunity or having co-morbid conditions are more susceptible to develop disease easily (Rushd, 1987). Avicenna in his book *Al Qanoon fil Tibb* (Canon of Medicine) mentioned the possible symptoms of epidemics as shortness of breath, dry cough, fever, increased thirst, nausea, loss of appetite, anxiety, depression, sleeplessness, weakness, giddiness, fatigue, increased pulse rate, and diarrhea (Sina, 2010). According to the eminent Unani physician Ibn Hubl Baghdadi, hoarseness of voice, headache, sore throat and expectoration may also be present (Baghdadi, 2004).

The 13th-century Persian scholar *Najeebuddin Samarqandi* mentioned a type of epidemic influenza in his treatise *Al-asbab wal Alamat* (The Book of Causes and Symptoms). In the translated version of the book, published under the name *Moalejat Sharah Asbab*, a disease

called *Nazla-e-Wabaiya* (epidemic influenza) is named in the chapter of *Anaf al-Anza* (Influenza) (Nikhat and Fazil, 2020). *Samarqandi* states that *Nazla-e-Wabaiya* 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 afflicted with *Nazla-e-Wabaiya* may also suffer from cough, diarrhea, and delirium. Pleurisy and pneumonia, if present, worsen the prognosis (Samarqandi, 2009).

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 contemporary knowledge of infection reinforces the fact that Unani medicine can play a significant role in combating current health problems.

3.2.1. General preventive measures during epidemics

In India, the number of COVID-19 cases is increasing day by day. With the epidemic spreading in many nations, segregation, social distancing, routine use of masks, and daily hand washing are general practices used to try to prevent further infections. The future rate of infections depends greatly on how quickly the curve is flattened (Spinelli, 2020).

Unani Medicine has long recognized the influence of surroundings

Table 2
Compound formulas as adjuvant therapy as prescribed in Unani medicine.

S. No.	Unani name	Chief ingredient	Ingredients	Action and Uses	Dose	References
1.	Khamira-e-Khashkhash	<i>Papaver somniferum</i> capsule	<i>Papaver somniferum</i> capsule 25 in no., <i>Papaver somniferum</i> seeds ground in water, <i>Cucurbita moschata</i> seeds ground in water, <i>Prunus amygdalus</i> ground in water every 12 ml, white sugar 500 g	Catarrh, coryza, cough	5–10 g	(CCRUM, 1984), (Lateef, 1951)
2.	Khamira-e-Marwareed	<i>Mytilus margaritifera</i> Pearl	<i>Mytilus margaritifera</i> pearl 25 g, <i>Bambusa arundinacea</i> dried exudate 25 g, <i>Santalum album</i> wood 3 g, <i>Ambra grisea</i> 10 g, White sugar 1 ½ kg, <i>Rosa damascena</i> distillate 1 lit., <i>Borago officinalis</i> distillate 1 lit	Heart tonic, Brain tonic, nervine tonic, palpitation	3–5 g	(CCRUM, 1984), (Lateef, 1951)
3.	Laoq-e-Nazli	<i>Papaver somniferum</i> seed	<i>Glycyrrhiza glabra</i> root 20 g, <i>Althea officinalis</i> seed 25 g, <i>Cydonia oblonga</i> seed 25 g, <i>Cydonia oblonga</i> kernel 10 g, <i>Acacia nilotica</i> gum 10 g <i>Cochlospermum religiosum</i> gum 15 g, <i>Papaver somniferum</i> black and white seed each 20 g, White Sugar 500 g	Catarrh, bronchitis, coryza	5–10 g	(Lateef, 1951), (MoHFW, 2009)
4.	Sharbat-e-Banafsha	<i>Viola odorata</i> flowers	<i>Viola odorata</i> flowers 125 g, white sugar 1 kg	Fever, cold, cough	25–50 ml	(CCRUM, 1984), (Lateef, 1951)
5.	Sharbat-e-Toot Siyah	<i>Morus nigra</i> juice	<i>Morus nigra</i> juice 1 liter, white sugar 1.5 kg	Cold, cough, sore throat, tonsillitis, diphtheria	20–40 ml	(CCRUM, 1984), (Lateef, 1951)

and ecological conditions on the state of health of human beings. In addition to treating disease conditions, Unani Medicine puts great emphasis on disease prevention and on promoting existing health through the principles of the six vital factors (*Asbab-e-Sitta Zarooriyah*) of life. It accentuates the importance of maintaining an acceptable environmental balance and keeping air, water, and food free of all potential pollutants and pathogens (MoHFW, 2019). Improving immunity with immune modulators is, according to classic Unani experience, one of the primary strategies used for disease prevention and health maintenance. The treatment and prevention of infectious and epidemic diseases are thus based on the following principles of Unani medicine:

1. Avoid contact with polluted air, water, and food, depollute or cleanse them.
2. Normalize and purify the humours by administering blood purifiers.
3. Administer suitable drugs along with other classical therapies.
4. Use the *Advia Tiryaqia* and *Fad-e-Zaher* (antidotal drugs) for protection from infection and epidemics.
5. Tone up the heart and protect the vital heat from being reduced or otherwise exhausted (Khan, 1981).

3.2.2. Dietary modifications

Consumption of vitamin-rich foods and functional foods can strengthen the immune system which helps the body fight viruses. Ascorbic acid (Vitamin C) plays a protective role, as it promotes immune function and is essential for tissue repair and growth. It also limits the susceptibility of the lower respiratory tract to infection under certain conditions. Vitamin C-rich foods include citrus fruits, kiwi, and broccoli. Certain vegetables, such as carrots, spinach, and sweet potato, are rich in vitamin A, which play an important role in immune function and are believed to minimize infectious susceptibility. Vitamin D and E supplementation can improve resistance to COVID-19. Supporting the immune system is now one of the top well-being priorities of individuals globally (Galanakis, 2020).

3.2.3. Health protecting drugs

About 25,000 plant-based formulations have been used in folk remedies in Indian medicine (Pundarikakshudu and Kanaki, 2019). The use of such medications is considered to enhance host immunity during the occurrence of epidemics and pandemics and they are emphasized by ancient physicians (Jurjani, 2010). Single drugs and compound Unani formulations can be beneficial and used in upper respiratory tract infections for possible immune-boosting / symptomatic relief. Though many medicinal plants have been identified, more research must be carried out to develop remedies specific to SARS-CoV-2. Various Indian medicinal plants that have been widely used for respiratory diseases have been included in Table 1 and compound formulations in Table 2.

3.3. A possible approach to the prevention and management of COVID-19 from the perspective 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 and cough are the initial symptoms, which may be associated with diarrhea. Similar symptoms have been described by Unani scholars regarding *Nazla-e-wabaiya*. With this information, the following preventive measures and management options were suggested to fight epidemics and may be beneficial in the prevention and treatment of COVID-19 as well.

3.3.1. Preventive measures

Foods rich in water content should be avoided, as well as alcohol, excess sleep, and fornication (Razi, 2008). Light, nutritive, and easily digestible food should be given in small quantities at short intervals and meat and fish should also be avoided (Rushd, 1987). Houses should be fumigated with acetic acid (Sirka), *Hing* (*Ferula foetida* Regel.), *Mastagi* (*Pistacia lentiscus* Linn.) (Razi, 2008), and *Sandal safaid* (*Santalum album* Linn.) (Baghdadi, 2007; Sina, 2010). It is recommended that people should stay indoors and traveling should be avoided (Jurjani, 2010). A small quantity of vinegar should be given at certain intervals as it is antimicrobial and lowers body temperature. Citrus or Vitamin C-rich foods like grape juice, lemon juice, and pomegranate juice should be given (Sina, 2010).

Islamic teachings outlining how to protect the public from death during a pandemic and illness date back to the very beginning of Islam. One of the basic elements of Islamic education is the maintenance of good personal and community hygiene. Allah's Messenger-the last Prophet, Prophet Mohammad PBUH (Peace Be Upon Him) advised that those with infectious diseases should not be kept with healthy people. He also said that "If we learn that the plague epidemic has started in a country, we should not go there; if we are in that country, we should not flee from there" which is also based on today's concept of quarantine and social distancing (Jawziyya, 2008; Ashraf et al., 2020).

3.3.2. Suggested management

Nazla-e-wabaiya is managed with anti-inflammatory, immunomodulatory, and antipyretic herbs such as a decoction of *behidana* (*Cydonia oblonga* Mill., Rosaceae) 3 g, *unnab* (*Ziziphus jujuba* Mill., Rhamnaceae) 5 no., *sapistan* (*Cordia dichotoma* Forst.f., Boraginaceae) 9 no., and *khaksi* (*Sisymbrium irio* Linn., Cruciferae) 5 g. In case of associated diarrhea, *habb-ul-aas* (*Myrtus communis* L., Myrtaceae) and *tabasheer* (*Bambusa bambos* (L.) Voss, Gramineae) are also prescribed. If pneumonia or pleurisy occurs, *qairooti aarad-e-karsana* (10 g), *Aloe vera* L. (sap; 1 g), *Crocus sativus* L. (stamen; 1 g) are crushed, mixed, and warmed slightly; then applied to the chest wall and covered with a cotton bandage

Table 3
Ingredients of *tiryqa-e-nazla* (CCRUM, 1984), (Lateef, 1951).

S. No.	Binomial name and family	Genus	Species	Unani name	Part used	Method of use in Unani medicine	Active ingredients	Mode of action	Dose	References
1.	<i>Hyoscyamus niger</i> Linn., (Solanaceae)	<i>Hyoscyamus</i>	<i>H. niger</i>	ajwain khurasani	Seeds	Decoction	Hyoscyamine, hyoscyne	Sedative, narcotic, astringent	300 g	(Khare, 2007), (Nadkarni, 1976), (MoHFW, 2008)
2.	<i>Lavandula steochas</i> Linn., (Papilionaceae)	<i>Lavandula</i>	<i>L. steochas</i>	ustukhuddoos	Flowers	Decoction	Polyphenols, essential Oil, oleanolic acid, Acacetin, luteolin	Antibacterial, antiseptic, anti-spasmodic	50 g	(Khare, 2007), (Nadkarni, 1976), (CCRUM, 1992)
3.	<i>Coriandrum sativum</i> Linn., (Umbelliferae)	<i>Coriandrum</i>	<i>C. sativum</i>	kishneez khushk	Fruit	Decoction	Volatile oil, flavonoid, Coumarins, coriandrins	Stimulant, anti-inflammatory	100 g	(Khare, 2007), (Nadkarni, 1976), (MoHFW, 2007b), (CCRUM, 2011)
4.	<i>Papaver somniferum</i> Linn., (Papaveraceae)	<i>Papaver</i>	<i>P. somniferum</i>	post khashkhash	Capsule	Decoction	Isoquinoline alkaloids, Organic acids	Narcotic, sedative, Analgesic, anti-spasmodic	300 g	(Khare, 2007), (Nadkarni, 1976), (CCRUM, 2011), (Khare, 2007), (Nadkarni, 1976), (MoHFW, 2007c)
5.	<i>Papaver somniferum</i> Linn., (Papaveraceae)	<i>Papaver</i>	<i>P. somniferum</i>	tukhm-e-khashkhash	Seeds	Decoction	Fixed oil, neutral substances, resins	Nutritive, demulcent emollient, spasmolytic	400 g	(CCRUM, 1997), (CCRUM, 2011) (Khare, 2007)
6.	<i>Lactuca sativa</i> Linn., (Compositae)	<i>Lactuca</i>	<i>L. sativa</i>	tukhm-e-kahu	Seeds	Decoction	Lactucarium, lactupicrin, lactucerin	Sedative, expectorant, antiseptic, demulcent	200 g	(CCRUM, 2011) (Khare, 2007)
7.	<i>Althea officinalis</i> Linn., (Malvaceae)	<i>Althea</i>	<i>A. officinalis</i>	gul-e-khatmi	Flower	Decoction	Mucilage, flavonoids, polyphenolic acids	Demulcent, anti-tussive, expectorant	100 g	(CCRUM, 2011), (Nadkarni, 1976), (CCRUM, 1987)
8.	<i>Glycyrrhiza glabra</i> Linn., (Papilionaceae)	<i>Glycyrrhiza</i>	<i>G. glabra</i>	rubb-us-soos	Extract	Powder added after preparing a decoction	Glycyrrhizin, triterpene, saponin, asparagin	Demulcent, antiallergic, expectorant, Anti-inflammatory	100 g	(CCRUM, 2006), (Khare, 2007), (Nadkarni, 1976), (MoHFW, 2007b)
9.	<i>Cochlospermum gossypium</i> , DC (Cochlospermaceae)	<i>Cochlospermum</i>	<i>C. gossypium</i>	kateera	Gum	Powder added after preparing a decoction	Acidic oligosaccharides	Sedative, bechic, Demulcent, astringent	50 g	(CCRUM, 2006), (Khare, 2007), (Nadkarni, 1976)
10.	<i>Rosa damascene</i> Mill., (Rosaceae)	<i>Rosa</i>	<i>R. damascene</i>	gul-e-surkh	Petals	Powder added after preparing a decoction	Essential oil, organic acid, fat, resin	Astringent, expectorant, laxative, cardiac tonic, Anti-oxidant	50 g	(MoHFW, 2007d), (Khare, 2007), (Nadkarni, 1976)
11.	<i>Acacia arabica</i> Willd. Var., (Mimosaceae)	<i>Acacia</i>	<i>A. arabica</i>	gond keekar	Gum	Powder added after preparing a decoction	L-arabinose, aldobiouronic acid, L-rhamnose	Astringent, demulcent, expectorant	50 g	(CCRUM, 2006), (Khare, 2007), (Nadkarni, 1976)
12.	<i>Commiphora myrrha</i> , Nees. (Burseraceae)	<i>Commiphora</i>	<i>C. myrrha</i>	mur-makki	Gum	Powder added after preparing a decoction	Acidic polysaccharides, Volatile oil	Anti-inflammatory, antiseptic, antiviral, Bacteriostatic, expectorant	50 g	(MoHFW, 2007c), (Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003)
13.	<i>Triticum aestivum</i> Linn., (Gramineae)	<i>Triticum</i>	<i>T. aestivum</i>	nishasta-e-gandum	Wheat starch	Powder added after preparing a decoction	Tocopherol, Protein, lipid, lysine, minerals	Antipyretic, demulcent, emollient, tonic	50 g	(CCRUM, 2006), (Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003)
14.	<i>Citrus aurantifolia</i> (Christm) Swingle (Rutaceae)	<i>Citrus</i>	<i>C. aurantifolia</i>	sat-e-leemu	Juice	To be added after preparing a decoction	Vitamins, minerals, alkaline salts, 1,3-Beta-glucan hydrolase	Antiscorbutic, stomachic, refrigerant	3 g	(CCRUM, 2011), (Khare, 2007), (Nadkarni, 1976)

(Samarqandi, 2009). The details of these formulations are mentioned in Table 4. *Qairooti* is the name of the ointments specifically prescribed for chest diseases. *Qairooti aarad-e-karsana* is a polyherbal Unani formulation based on the following ingredients: *aarad-e-karsana* (*Pisum sativum* L., Papilionaceae; flour; 150 g), *tukhm-e-hulba* (*Trigonella foenum-graecum*, Fabaceae; flour; 150 g), *kalonji* (*Nigella sativa* L., Ranunculaceae; seeds; 60 g), *asl-us-soos* (*Glycyrrhiza glabra* L., Leguminosae; root; 60 g), *aqar qarha* (*Anacyclus pyrethrum* DC., Compositae; root; 50 g), *roghan-e-gul* (*Rosa damascena*, Rosaceae; oil) and beeswax (100 g) (CCRUM, 1984). In the textbook of *Zakheera Khwarzam Shahi* by Ismail Jurjani, the use of *tiryqs* during epidemics is mentioned as an herb to strengthen the heart and keep the body faculties strong (Jurjani, 2010). *Tiryqa* refers to any substance or drug that neutralizes a poison or counteracts its effects (CCRUM, 2012), and as such, *tiryqa-e-nazla* can be

used. *Tiryqa-e-nazla* is a *la'iq* which is a semisolid preparation used in lungs and pharynx diseases. It is used to prevent colds and coughs. Since most herbal drugs are bitter, sugar is used in the formulation of compound products. The composition of *tiryqa-e-nazla* is given in Table 3.

3.3.2.1. Preparation. The first seven herbs are soaked in 6 liters of water overnight and boiled the next day until the quantity of water is reduced to half. The decoction is then strained and mixed with a base of sugar 3 kg and *sat-e-leemu* (*Citrus aurantifolia*) and triturated until it becomes white. The rest of the herbs are powdered, including *kishneez khushk* (*Coriandrum sativum* Linn.; 50 g), then strained and added to the previously made base.

3.3.2.2. Dose. It is prescribed in a dose of 10 g in the morning or at

Table 4
Herbs prescribed in Unani medicine for *nazla-e-wabaiya* (epidemic influenza) (Samarqandi, 2009).

S. No.	Binomial name and family	Genus	Species	Unani name	Part used	Method of use in Unani medicine	Active ingredients	Mode of action	References
1.	<i>Cydonia oblonga</i> Mill., Rosaceae	<i>Cydonia</i>	<i>C. oblonga</i>	behidana	Berry	Decoction for oral use	Hydroxycinnamic derivatives	Anti-oxidant	(MoHFW, 2007c), (Khare, 2007), (Nadkarni, 1976)
2.	<i>Ziziphus jujube</i> Mill., Rhamnaceae	<i>Ziziphus</i>	<i>Z. jujube</i>	unnab	Fruit	Decoction for oral use	Betulinic acid	Anti-proliferative on some influenza viruses, anti-inflammatory	(CCRUM, 2006), (Khare, 2007), (Nadkarni, 1976)
3.	<i>Cordia dichotoma</i> Forst.f., Boraginaceae	<i>Cordia</i>	<i>C. dichotoma</i>	sapistan	Fruit	Decoction for oral use	Hydroquinones, steroids, flavonoids, terpenoids	Anti-microbial, anti-oxidant, antiulcer on Gastric mucosa	(CCRUM, 1992), (Khare, 2007), (Nadkarni, 1976)
4.	<i>Sisymbrium irio</i> Linn., Cruciferae	<i>Sisymbrium</i>	<i>S. irio</i>	khaksi	Seeds	To be mixed after preparing a decoction	Isorhamnetin, linolenic, oleic, and erucic acid	Anti-bacterial, febrifuge, expectorant	(MoHFW, 2008), (Khare, 2007), (Nadkarni, 1976)
5.	<i>Bambusa bambos</i> (L.)Voss, Gramineae	<i>Bambusa</i>	<i>B. bambos</i>	tabasheer	Manna	Decoction for oral use	Coumaran, adipic acid ester, palmitic acid, α -elemol	Anti-helminthic, anti-inflammatory, Anti-diarrhoeal	(CCRUM, 2011), (Khare, 2007), (Nadkarni, 1976)
6.	<i>Myrtus communis</i> Linn., Myrtaceae	<i>Myrtus</i>	<i>M. communis</i>	habb-ul aas	Berry	Decoction for oral use	Tannins, flavonoids (anthocyanins, quercetin, gallic acid, etc.)	Intestinal motility, anti-oxidant	(Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003)
7.	<i>Aloe barbadensis</i> Mill. Liliaceae	<i>Aloe</i>	<i>A. barbadensis</i>	elwa	Leaf sap	For local application on the chest wall	Anthraquinones, mannans, resin	Anti-inflammatory, antimicrobial	(Khare, 2007), (Nadkarni, 1976), (MoHFW, 2007b)
8.	<i>Crocus sativus</i> Linn., Iridaceae	<i>Crocus</i>	<i>C. sativus</i>	za'fran	Stamen	For local application on the chest wall	Crocetin, crocin	Expectorant, nerve tonic	(Khare, 2007), (Nadkarni, 1976), (Prajapati et al., 2003)
9.	<i>Acacia arabica</i> Willd. Var (Mimosaceae)	<i>Acacia</i>	<i>A. arabica</i>	gond babool	Gum	To be mixed after preparing a decoction	D-arabinose, D-rhamnose, aldobouronic acid	Astringent, demulcent, expectorant	(CCRUM, 2006), (Khare, 2007), (Nadkarni, 1976)
10.	<i>Nerium indicum</i> Mill. (Apocynaceae)	<i>Nerium</i>	<i>N. indicum</i>	kaneer	Root	To be mixed after preparing a decoction	Glucoside, essential oil	Resolvent, attenuant	(MoHFW, 2007b), (Khare, 2007), (Nadkarni, 1976), (CCRUM, 2008)

night for cold, cough, coryza, and catarrh. It is not recommended for those diagnosed with type I and type II diabetes mellitus.

4. Discussion

In India, cases are likely to continue. This increase in infection is mainly due to the ability of the virus to recombine, mutate, block the immune system of the host cells, and infect multiple species as well as cell types. Moreover, discovering the gene pool of SARS-CoV-2 may help accelerate the production of drugs and vaccines (Vellingiri et al., 2020). Modern drugs used in SARS-Cov-2 are not satisfactory in their various clinical outcome measures as they are associated with adverse side effects. The maintenance of anti-oxidant and immune fitness is a rational approach to preventive health care. Studies conducted in the Unani system of medicine have shown that herbal drugs have the potential to reduce the burden of epidemics and improve the quality of life without significant side effects. Having wider safety margins and time-tested efficacy against cold, cough, coryza, and catarrh, the pharmacopoeial preparation *tiryaq-e-Nazla* shows potential as an herbal remedy assessed in future clinical trials for SARS-Cov-2. *Tiryaq* was used by Buqrat (Hippocrates), Ibn Sina (Avicenna), Jalinoos (Galen), Ibn Rushd (Averroes), and Ismail Jurjani (Ismail Gorgani) with patients during past epidemics (Sina, 2010; Jurjani, 2010; Rushd, 1987; Razi, 2008; Khan, 1981). *Tiryaq-e-nazla* may be used for two reasons. First, Unani descriptions correlated with immune-stimulating activity. The second basis for its selection was related to scientific reports regarding its immune-modulating and anti-oxidant activity or related pharmacological actions and therapeutic effects of the individual herbs found in this formulation. *Glycyrrhiza glabra* is known to target the viral replication of SARS-CoV, therefore, it is a promising agent against SARS-CoV-2. A study shows that *Hyoscyamus niger* reduced infections caused by

influenza viruses when screened for antiviral plant properties against bronchitis. *Hyoscyamus niger* was found to be a bronchodilator and had inhibitory effects on the Ca^{2+} channel. This could be used to target the $orf3a$ Ca^{2+} channels that trigger various downstream pathways upon viral infection. Most importantly, various medicinal plants have shown inhibitory effects against ACE (Angiotensin-Converting Enzyme), and these include *Coriandrum sativum* (Vellingiri et al., 2020). A single herb may contain many phytochemical constituents that function alone or in combination with other compounds to produce the desired pharmacological effect (Parasuraman et al., 2014). The antiviral effects of medicinal plants have played a tremendous role at different stages of viral growth (Akram et al., 2018). Plant-derived pharmacological formulations marked a major contribution to the management of viral infections (Newman et al., 2003).

Furthermore, continued research on these herbs and medicinal plants is necessary to promote their usage in clinical practice for the prevention or treatment of various illnesses. Since many Indian medicinal plants exhibit antiviral, anti-inflammatory, anti-oxidant, and immune-modulatory actions, it may be advisable to consider them for the treatment of COVID-19. However, it is essential to carry out standard clinical trials to scientifically prove their efficacy (Vellingiri et al., 2020).

5. Conclusion

Since ancient times, Indian herbs have been used as a treatment and preventive strategy for several diseases, including respiratory viral infections. The benefit of using these herbs in viral respiratory infections is to build immune-stimulating and inflammation-modulating effects which strengthens the immune system (Vellingiri et al., 2020). Almost all the prophylactic and therapeutic measures adopted since two and

half millennia by the Unani physicians are still prevalent, and these have been scrutinized in the light of various scientific studies. Unani medical thought is based on supporting the body so it is protected from diseases in general and infections in particular. The use of *tiryaaqat* (antidotes) may prove useful. Some scientific studies have confirmed that the pharmacopeial preparation *tiryaaq-e-nazla* has major antiviral effects due to several of its ingredients and that the whole preparation has an immunomodulatory impact. As the medicines are graded on the degree of their activity in the Unani System of Medicine, the phytopharmaceuticals used in the treatment of infectious and epidemic diseases, medications of the third and fourth degree as per their temperament and activity, and poisons reported in the literature in use for a long may be studied for further details. This may protect the human being from the hazards and toxic side effects of antibiotics. In this way, a new approach to dealing with infectious, contagious, and epidemic diseases can be developed with more effective potency and fewer hazards. This will certainly be more readily acceptable to the Indian people and to others who accept this system of treatment (Khan, 1981). This review suggests the importance of a few Indian medicinal plants that have been used for several decades in the treatment of various respiratory conditions. The pathways of the plant-based medicines may be used to target to reduce the disease burden. Thus, proactive investments in research on vaccines based on the mechanism of action of certain Indian medicinal plants or phytopharmaceuticals to treat COVID-19 would emerge as a beacon of hope to overcome this fatal infection (Vellingiri et al., 2020).

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Declaration of Competing Interest

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