Unani perspective on COVID-19 and the possible role of Tiryaq Wabai in its management: A Review

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Abstract

Science has uncovered much about SARS-CoV-2 and made extraordinary and unprecedented progress on the development of COVID-19 vaccines, but there is still great uncertainty as the pandemic continues to evolve. We are simply moving to a new phase of the pandemic. Tiryaq Wabai, is on the polyherbal medicine used for centuries by Unani doctors as preventative medicine in epidemics. It consists of three ingredients: Sibr (Aloe barbadensis), Zafraan (Crocos sativus), and Mur-Makki (Commiphora myrrha). All the three ingredients of Tiryaq Wabai have various pharmacological activities like immunomodulatory, antitussive, expectorant, and antiviral activity which provide a strong basis for its prophylactic use for covid-19 infection. Further, research on this important prophylactic Unani formulation Tiryaq Wabai in Covid-19 is the need of the hour.

Keywords: Tiryaq; Epidemic; Covid-19; Unani medicine

Introduction

Traditional medicine is being used widely and rapidly in developing as well as developed countries. Up to 65% of India’s population and 80% in Africa depend on traditional medicine to help meet their health needs. The Unani Medicine, also referred to as Greco-Arabic medicine, Arabic medicine or Unani Tibb, is based on Hippocratic four-humour theory; Dam (blood), Balgham (phlegm), Safra (yellow bile), and Sauda (black bile) 1,2, and the four qualities of living human body states such as hararat (hot), barudat (cold), ratubat (moist) and yabusat (dry).1 Unani medicine uses medicinal products of plant, mineral, and animal origin but mostly plant origin drugs are used for therapeutic and preventive measures.1 In many Arab and Eastern Asian countries, Unani is still prevalent. However, in many countries where conventional medicine is readily available, Unani medicine and herbal products are increasingly being used. India has acknowledged and granted its official status as an alternative healthcare system 1.

In Unani medicine, the disease state is caused by the instability of Mizaj (temperament) or Akhlat (humour), and health maintenance is carried out by applying the various steps to align six critical health fundamentals in the polar dimensions. i.e. Ashab-Sitta-Zarooria: 1. Hawa-e-Muheet (Air), 2. Makool wa Mashrubat (food and drinks), 3. Harkat wa Sukon-e-Badani (Rest and physical activity), 4. Harkat wa Sukun-e-Nafsani (psychological activity and repose), 5. Nuam wa yaqza (Sleep and wakefulness), 6. Ishifrah and Ihtabas (Elimination and retention). The applied aspect of Unani medicine deals with various measures to maintain or restore health 1,5,6.

‘Magneus Felsoof’ introduced Tiryaq (Theriac) as a semisolid dosage form. Indrumakhas I (Andromachus I) has improved Tiryaq by adding flesh of snakes in it 7. The term Theriac refers to medicinal substances initially used by the Greeks from the 1st to the 19th century A.D. The name theriac originated from the old Greek word thēr, “wild animal.” 8,9 By the 8th century, Islamic medicine prescribed Tiryaq for treating complicated diseases which resisted simple drug treatment. Caliphs and Princes requested the manufacture of Tiryaq mixtures which were thought to have wondrous curative and anti-toxic properties, and whose ingredients may well reach into the hundreds. Ibn Sina (Avicenna) explained how Tiryaq was prepared and utilized in the Canon of Medicine. The Al-Biruni pharmacopoeia (973-1048) contained a variety of drugs known as tiryaq 10. The Theriac’s prominent role was to neutralize the effects of...
2. Background and Current Scenario of Epidemics of Acute Respiratory Viral Infections

One of the earliest winter outbreak reports of respiratory infectious disease can be found in the "Book of Epidemics," an ancient Greek text was written about 400 BC by Hippocrates. Many respiratory viruses have since been established as these epidemics' etiologic agents. Until the 16th century, all sorts of epidemics were typically reported by laypeople without scientific knowledge and without an understanding of aetiology, pathogenesis, natural history, characteristic pathognomonic signs, or any of the modern ways we now diagnose, recognize, and classify different diseases. Even various conditions, such as measles and smallpox, have long been confused. A massive outbreak of influenza-like disease followed Carolus's (Charlemagne's) army through Europe in 876–877, having first arrived in Italy to spread northward, a geographic trend frequently recorded for other influenza pandemics occurring between 1510 and 1761 and even killing dogs and birds. Another epidemic, "cough that spread like the plague" in 927 AD, again first reached Italy and spread northward to affect the entire European continent and caused sickness and death in humans, dogs, and birds. Researchers have hypothesized that this was the first known pandemic of influenza, a possibility consistent with its arrival in southern Europe and its rapid spread northward.

Acute respiratory tract infections of viral origin contributed to a severe burden on health care services and society. Respiratory tract infections pose a critical health problem, as they are a leading cause of mortality in children globally, especially in developing countries, causing approximately 19% of all deaths among children under five years and 8.2% of all disability and premature mortality. New respiratory infections have become increasingly significant in modern infectious diseases, since the acute severe respiratory syndrome outbreak in 2003, the influenza A (H1N1) pandemic in 2009, and the influenza A (H7N9) pandemic in 2013. Acute respiratory viral infections usually start in the upper respiratory tract as the port of entry is the nose, mouth, or eyes, and spread to the lower parts of the airways occurs within two to four days. The most common infections in the upper tract include rhinitis, laryngotraheobronchitis, sinusitis, pharyngitis, episcleritis, and laryngitis. Lower-tract conditions are more severe, including tuberculosis, bronchitis, bronchiolitis, and influenza.

For thousands of years, the seasonal cycle of respiratory viral diseases has been commonly known as regular epidemics of common cold and influenza disease that strike the human population in temperate regions. Besides, epidemics from viruses such as SARS-CoV and the newly emerging SARS-CoV-2 arise in the winter months. SARS-CoV, Middle East respiratory coronavirus syndrome (MERS-CoV), influenza, adenovirus, human bocavirus, human metapneumovirus, parainfluenza virus, rhinovirus, RSV, and other common respiratory pathogens have been identified as a cause of pneumonia. Additionally, these viruses can cause co-infections in community-acquired bacterial pneumonia.

2.1. Covid-19

A cluster of patients was admitted to hospitals with an initial diagnosis of an uncertain aetiology of pneumonia in late December 2019. These patients were epidemiologically linked to a wholesale market of seafood and wet animals in Wuhan, Hubei Province, China. The pathogen was
confirmed to be a distinct clade from the β-coronaviruses related to the MERS and SARS27,31. On February 11, 2020, the World Health Organization (WHO) declared a new name for the 2019-nCoV epidemic: Coronavirus Disease 2019 (COVID-19). Concerning the virus itself, the International Committee on Virus Taxonomy has designated 2019-nCoV as a SARS-CoV-2.28 The WHO declared the outbreak of SARS-CoV-2 on January 30, 2020, to be a public health emergency of international concern. SARS-CoV-2 has a more robust transmission capacity than the SARS-CoV, which caused a SARS outbreak in 200332. Coronaviruses are enveloped, positive single-stranded, large RNA viruses infecting humans, and a wide variety of animals33. It is pleomorphic or spherical particles, 150 to 160 nm in size, unsegmented, nucleoprotein, capsid, matrix, and S-protein. Essential viral proteins are nucleocapsid protein (N), membrane glycoprotein (M), and spike glycoprotein (S). COVID-19 differs from other coronaviruses by encoding a different glycoprotein having properties of acetyl esterase and hemagglutination (HE)34. In 1966, Tyrrell and Bynoe first identified coronaviruses, which cultivated the viruses in patients with common colds. They were called coronaviruses (Latin: corona → crown), based on their morphology as spherical virions with a central shell and surface projections resembling a solar corona. There are four subfamilies, including alpha-, beta-, gamma- and delta coronaviruses. Although alpha and beta-coronaviruses come from mammals, particularly bats, gamma and delta viruses come from pigs and birds33.

Coronavirus is one of the major pathogens affecting the human respiratory system30. Respiratory droplets mainly transmit SARS-CoV-2 from person to person, customarily released when an infected person coughs or sneezes. Since droplets typically fall within a few meters, the transmission risk will decrease if people stay at least 1 m apart. Transmission is assumed not to occur through the inhalation of aerosols typically, but there are regards that the virus may be aerosolized during certain events or procedures (e.g., singing, intubation, or the use of nebulizers) and that it may persist in aerosols for more than 3 hours35. COVID-19 can also be present in the stool and urine of patients with diarrheal symptoms besides with aerosol and large respiratory droplets36. Transmission may occur from symptomatic or asymptomatic patients, where the rates of secondary infection vary between 0.5% and 5% SARS-CoV-2 has been shown to remain stable in aerosolized form for up to 3 hours, in cardboard for 24 hours, and plastic or stainless steel for three days36.

Following an incubation period of 1 to 12.5 days (average estimates vary from 5 to 6 days), COVID-19 symptoms appear, but they can last for as many as 14 days. The time from the onset of symptoms of COVID-19 to death ranged from 6 to 41 days, with an average of 14 days. This time depends on the patient’s age and immune system status. It was lower in patients > 70 years of age relative to those less than 70 years of age30. Early reports suggest fever (88%) and dry cough (67.7%) are the most common symptoms, which are associated with many other viral syndromes (Figure 1). Noticeably, rhinorrhoea (4.8%) and gastrointestinal symptoms (diarrhoea 4% to 14%, nausea or emesis 5%) appear to be uncommon in COVID-1936.

Infection with SARS-CoV-2 can activate innate and adaptive immune responses. Nevertheless, uncontrolled innate inflammatory responses and impaired adaptive immune responses can damage the tissue, both locally and systemically. Lymphopenia is a typical occurrence in patients with severe COVID-19, with significantly reduced numbers of CD4+ T cells, CD8+ T cells, B cells, natural killer (NK) cells, and a decreased percentage of monocytes, eosinophils, and basophils. The increase in neutrophils’ count and neutrophils’ ratio to lymphocytes typically suggest higher severity of the disease and poor clinical outcome. Additionally, exhaustion markers, such as NKG2A, on cytotoxic lymphocytes, including NK cells and CD8+ T cells, are upregulated in patients with COVID-1937. The identification of SARS-CoV-2-specific IgM and IgG in patients, combined with RT-PCR-based tests, provided the basis for disease diagnosis35,37.

Figure 1: Symptoms of COVID-19

Source: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answer-s-hub/q-a-detail/q-a-coronaviruses#:~:text=symptoms
To date, no anti-viral drugs with specific effects have been identified, and the primary therapeutic strategy focused on symptomatic support. Upon hospitalization, partial patients demonstrated low treatment effectiveness and experienced severe pneumonia, pulmonary oedema, acute respiratory distress syndrome (ARDS), or multiple organ failure. Information about the clinical features of refractory COVID-19 has been scarce.

3. Background of Epidemics in Unani Medicine

The epidemic of infectious diseases has been recognized throughout history. Classical literature in ancient Greece and Egypt mentions epidemics that occur between the 17th and the late 19th century A.D. The germ hypothesis was formulated in the middle of the 16th century A.D. It gained much popularity based on the component changes as well as the late 19th century A.D. The germ hypothesis also complemented the ancient explanation of infectious diseases such as Galen’s miasma theory. There is no explicit reference in Unani medicine to the definition of microbes as disease-causing agents. Nevertheless, it is well known that certain ajsam-i-khabita (harmful substances) can move from the diseased to healthy people and cause disease. Epidemics, referred to as waba in Unani medicine, are thought to occur if ajsam-i-khabita is healthy in the air and water. Unani scholars suggest that the spread of epidemics take place through infected air, water, and soil. The air may be impaired due to trouble in the natural equilibrium of the earth or could be due to global warming. Unani scholars proclaimed that certain parts of the earth have changes in intensity/wavelength of rays, which have a harmful effect on that area’s air. The old air near the soil normally gets purified with healthy rays turn out to be infected due to bad changes in the rays. These contaminated vapours can trigger the growth and mutation of the infectious agent. Unani scholars have reported that inadequate management of waste, water collection, and poor community hygiene encourages the production and spread of epidemics. It may be a possible explanation for the rise of epidemics/pandemics in this period. Ibn Sina and Zakariya Razi (865–925 CE) state in Al-qanoon (Canon of Medicine), Kitab al-Mansoor (Caliph Mansoor Book), respectively, the majority of epidemics spread during the autumn season, mainly if the previous summer season was humid and the weather is still windy.

According to Ibn Abbas Majusi (d. 994 A.D.), “Whenever imbalance occurs in the material of the air and decomposition are produced in together the material (Maddah) and quality, producing plenty of bad symptoms (a’rad-rdiyah) and diseases in human beings.” At another place, he says: “Epidemic (Waba) only spreads where the natural air quality changes.” Such variations in the air are either in composition or characteristics. The change in composition occurs when one of its components is unusual or uncommon and this causes epidemics due to the air putrefaction similar to that which occurs in a pond or stagnant water. Every single component of the air does not rot but varies in quality; it may transform into another component as water becomes vapour. The high moisture environment is conducive to epidemics and putrefaction. For fact, stagnant waters are also becoming mudy. This alteration causes hot and harmful fevers (hummiyat-harrah raddiyah), plagues, and other diseases in humans, as well as severe and dangerous animal diseases. Ibn Sina (980–1035 CE) said that epidemics spread from one person to another, and from one city to another ‘like a message’. Zakariya Razi (865–925 CE) emphasized this fact and said that ‘there will always be something common in epidemics patients, whether a place, food, drink or travel history’.

Arab scholar Ibn Khatib (1313–1374 CE) pointed out during the plague pandemic in the 14th century that ‘any people who come into touch with a victim of the plague will die.’ In the same way, the disease is transmitted via clothing, utensils and jewellery, thus stressing transmission through fomites.

The basics of the Unani System of Medicine (USM) being humoral physiology, the temperament of human beings as a whole, individual variations or factors, diseases, foods, drinks, seasons, etc. form the qualitative aspect of this system. Any disruption in the equilibrium of humours causes disease. According to the doctrine of Unani Medicine, there are three causes; bodily predisposition, environmental factors, and a mediating cause. The environmental causes are one of the most typical causes of an epidemic or pandemic.

Rabbab Tabri said that people with excess waste in their bodies are usually affected by the epidemic fever Humma wabaiya/nazle-e-wabaiya. According to Avicenna (980–1037 AD), Humma-e-Wabai is a severe fatal fever caused by contaminated air, spreading rapidly between larger populations. Humma-e-Wabaiya is the form of catastrophic fever triggered by unavoidable changes in climate (qualitatively or quantitatively). As a consequence, Air is impure and eventually induces an irregular Rooh temperature, which results in morbidity and death. As fresh and pure air is essential for health, any contamination in the air may disturb the person’s health, and it depends on the intensity of contamination. Those people are mainly susceptible to a weak immune system, i.e., older and children. Renowned Unani Scholars like Hippocrates (370–460 BC), Galen (130–200 AD), Rhazes (865–925 AD), Avicenna (980–1037 AD) described that there are four etiological factors responsible for Amraz-e-Wabai (epidemic disease), i.e., change in the quality of air, water, earth and celestial bodies.

The following are the two fundamental theories of USM related to the causation of diseases, depending on the mode of origin.

1. Diseases are caused by the imbalance of the humour born inside the body.
2. Diseases are caused by the invasion of foreign bodies, which attack the humour. For instance, a vital organ like the heart may be invaded, affecting its normal functions and stimulating activities, which, as a result, may be disturbed.

The infectious and epidemic diseases belong to the second category. The main things affected by the "Tadia" or adva (infection) and Waba (epidemic) are:

1. The humour
2. The heart and other vital organs like the stomach, liver, etc.
3. Hararat-e-Gharizia or Vital heat

The clinical manifestation of "nazle-e-wabaiya" in the Unani literature simulates clinical presentation of ARIs that propagate in epidemic form as an influenza virus, RSV, type 1, and 2 parainfluenzal, MERS CoV, SARS CoV, SARS-CoV, etc. Unani scholars could not detect and discern these infectious agents because of unadvanced diagnostic methods in the ancient period, but had been aware of their existence and...
named ‘wabai bukharat’ 4. The Persian scholar Najeebuddin Samarqandi (d. 1222 CE) states about Nazla-e-Wabaiya that it is associated with fever, sneezing, sore throat, nasal inflammation, and malaise. Weakness, in particular, develops at an early stage of the disease. He also says that a nazla-e-wabaiyu patient may also have cough, diarrhoea, and delirium 43. The Unani scholars also stated that the infection could complicate and progress to pneumonia (za’tul riya) and pleurisy (za’tul janab) in the elderly, infants, and low immune patients. Some literary findings suggest that Unani scholar was well aware of the ARI epidemic. Hence, their clinical indices and management recommendations may be used as a method for addressing increasingly growing current-era respiratory epidemics 4.

4. “Tiryaq Wabai” as Prophylactic in Unani Medicine Against Epidemics

The name of the polyherbal wording justifies its effect, e.g., ‘Tiryaq’ refers to ‘antidote’ and ‘Waba’ to ‘epidemic.’ The medicine was used as a prophylactic antidote against epidemics and as an antidote to poisoning. Unani supports disease prevention by prescription of certain medicines and regimes to improve immunity and overall body health. An epidemic history has taught ancient Unani practitioners to encourage preventive measures during epidemics, such as cleanliness and hygiene, the isolation of sick patients, care of patients with infectious material, and usage of prophylactic medicine, and general tonics before and during infective seasons. Tiryaq was explicitly planned to accomplish similar goals by Unani scholars 4.

Prevention of wabai amraz with Tiryaq Advia is recommended in the Unani system of medicine since ancient times. As a prophylactic drug, Tiryaq is generally recommended for toxicity prevention (sepsis). Tiryaqiyyat is the formulation that reinforces the rooh so that Rooh can neutralize the body’s toxicity. Tiryaqiyyat enhances the rooh, activates hararte-harariza, and allows Tabiyat to avoid morbid substances 17. Avicenna mentioned that those who use Tiryaq in good health would not be affected by infection because it helps reinforce the rooh and maintain health 39. Ismail Jurjani states that Tiryaq is used to protect the heart during epidemics, maintain the faculties, and avoid sepsis. Jalinoo said that people who used Tiryaq Wabai as prophylaxis had not been affected by infectious diseases 16.

Tiryaq is characterized in various diseases by a prophylactic function and effectiveness. Some important Tiryaq is mentioned in Table 1. Tiryaq Wabai identified as Muhaﬁze fasade akhlat (preventing hormonal disorders) and Muhaﬁze ufoonat (preventing infection) and therapeutically Tiryaq Wabai are indicated for the prevention of wabai amraz (epidemic disorders) during waba (epidemic). Tiryaq Wabai is based on three ingredients (Table 2), namely Sibr (Aloe barbadensis), Zafran (Crocus sativus), and Mur-Makki (Commiphora myrrha). Sibr is described to be Muhaﬁze fasade akhlat (preventing hormonal disorders), Daf-e-Ufoonat (antiseptic), Muharrick-e-Kabid (a liver stimulant). Zafran is defined to be Muharriki-e-Hurarat Ghereezia (stimulate innate immunity), muhaﬁze fasade akhlat (preventing hormonal disorders), daf-e-Ufoonat (antiseptic), muhaﬁze tabiyat (immunomodulator), muqawwiwe jigar (liver tonic), mufarrah qawa (exhilarant). Mur-Makki is described to be moharrik (a stimulant) and daf-e-taffun (antiseptic) 13-15,17-19,46.

Table 1: Some important Tiryaq mentioned in different Qarabaadeen (Unani Pharmacopoeia)

| S.N. | Tiryaq name | Dose | Action/Uses | Ref. |
|------|-------------|------|-------------|-----|
| 1.   | Tiryaq wabai/ Tiryaq a’f/yi’i | 2 gm with Arq badyaan | Beneficial in Haija (cholera), Chechok (smallpox), and Taoon (Plague) and Removes animal poison. According to Jalinoo, if any person takes it in an epidemic of Taoon, then he is not suffering from this disease. | 13-15,17,19,46 |
| 2.   | Tiryaq nazla | 14 g | Relieves in colds, prevent cough, beneficial in eye pain and Atishk (syphilis) | 13-15,17-19,47,48 |
| 3.   | Tiryaq al-asnaan | 1 or 2 drops | To prevent toothache due to cold | 14,15,17-19,46,47,49 |
| 4.   | Tiryaq al-dharab/zarab | 3-5 gm | Beneficial in Zarab (dysentery), Zo’f-i-mi’da (weakness of stomach), Zo’f-i-am’a (weakness of intestine), Qabz (constipation) Dard-i-shikam (stomach pain), to strengthen the Aza-e-rueso (vital organs), Mujarrab (tested in Ishual-i-mida (stomach purgation) | 15-17,19,47 |
| 5.   | Tiryaq Faroq | 4 g in snake bite, 2 g in scorpion bite | Mufattitay Sadde Kabid (Lion devourer), anti-inflammatory, Beneficial in Istisqa’ (Ascites), Varqaan-i-suddi (Obstructive Jaundice, Dard-i-gurd (pain in the kidney), and Qoolinj (Colic). To prevent Haja (cholera) and the antidote for the snake, scorpion, and other poisonous animal bites. | 13,15,39,47,48,50 |
| 6.   | Tiryaq arba | 4.5 g with Luke warm water | The antidote for the scorpion and other poisonous animal bites. Beneficial in Qoolinj (Colic), liver, and spleen diseases. | 13-15,17-19,39,46,47,49-52 |
| 7.   | Tiryaq Kabir | 4.5 g | Use as an antidote for all kinds of poisonous animal bites. | 15,47 |
| 8.   | Tiryaq tyn mahhtoom | 3.5g | Antidote for poison | 15,47 |
| 9.   | Tiryaq al-tyn | 3.5g before or after a meal | Antidote for poison | 19,50 |
| No. | Drug Name | Dosage | Uses |
|-----|-----------|--------|------|
| 10. | Tiryaq tyn-Romi | 3.5g | The antidote for all kinds of poisons and any poisonous animal bites |
| 11. | Tiryaq thamania/samania | 3.5g with Luke warm water | The antidote for the scorpion and other poisonous animal bites. Beneficial in liver and spleen diseases. |
| 12. | Tiryaq baligun nafa | 14g | The antidote for the snake bite |
| 13. | Tiryaq ashkari | 7g | The antidote for the scorpion bite, instant relief in wound pain |
| 14. | Tiryaq sartan | 4.5g | The antidote for the mad dog bite |
| 15. | Tiryaq al-dhahab/zahab | 3.5g | Beneficial in Melancholia, epilepsy, juzam (leprosy), Istsqa' (Ascites), yarqaan (Jaundice), bawasir (Hemorrhoids). Protect from epidemic diseases when used with Roghan banafsha |
| 16. | Tiryaq habbe utraj | Local application | Use as an antidote for all kinds of poisonous animal bites. |
| 17. | Tiryaq afyoon | 9g | The antidotes for opium (Afyoon) cannabis (Bhang) and belladonna (Yabroojus sanam) poisoning |
| 18. | Tiryaq sagheer | 4.5g | The antidote for all kinds of poisonous animal bites. According to Sheikh al-raees, in animal bites, it is more beneficial than Tiryaq arba. |
| 19. | Tiryaq aqrab | 7g with Luke warm water | The antidote for the scorpion bite, beneficial in Qoolinj and intestinal pain |
| 20. | Tiryaq rateela | 3.5g | The antidote for all kinds of poisonous animal bites. |
| 21. | Tiryaq habbe utraj | 7g | The antidote for the scorpion bite |
| 22. | Tiryaq Muhammad zakarya | 7g | The antidote for all kinds of poisons and any poisonous animal bites |
| 23. | Tiryaq yohina saryaani | 4.5g | The antidote for the scorpion bite |
| 24. | Tiryaq musannif kunnash buqrati | 3.5 to 4.5g | The antidote for all kinds of poisons and any poisonous animal bites |
| 25. | Tiryaq shekh bu ali sina | 4.5g | The antidote for all kinds of poisons, Muqawwi-i-qalb (heart tonic), Muqawwi-i-bah |
| 26. | Tiryaq mathana | 5 gm | Beneficial in diseases of kidney, bladder and uterus |
| 27. | Tiryaq 'adhra/azra | 4.5g | Beneficial in sar’a (epilepsy), Khatqaan (Palpitation) and diseases of liver and spleen |
| 28. | Tiryaq al-rahah | 2g with majoon supari pak | beneficial in leucorrhoea (Sailanur reham) |
| 29. | Tiryaq al-markah | 6g with Luke warm water | The antidote for the scorpion bite, beneficial in quling, intestinal and visceral pain |
| 30. | Tiryaq akbar | 3 gm | Beneficial in epidemic diseases, vertigo, epilepsy, hematemesis, stomach pain, liver pain, jaundice, urinary inconsistency, arthritis, amenorrhoea, palsy. The antidote for any poisonous animal bites and also the antidote for all kinds of poisons |
| 31. | Tiryaq athanasiya | 1g with Luke warm water | Beneficial in cough, hematemesis, the pain of liver, stomach, spleen. |
| 32. | Tiryaq dara’il suhtah | ½ to 4½ g | The antidote for all kinds of poisons and any poisonous animal bites |
| 33. | Tiryaq al-tihal | 1g | Beneficial in diseases of the spleen |
| 34. | Tiryaq ‘aam al-nafa’a | 1g | The antidote for all kinds of poisons and any poisonous animal bites |
| 35. | Tiryaq didan | 1gm | Used to get rid of roundworms in humans |
| 36. | Tiryaq al-kabid | 1gm | Beneficial in diseases of the liver |
4.1. Method of preparation of Tiryaqat wabai

Take all the ingredients of pharmacopeial quality. Clean the drugs Zafran, Sibr and Mur-Makki, by removing foreign matter. Dry the drugs in the shade, powder the drugs Sibr and Mur-Makki separately in a pulveriser and pass through a sieve of mesh number 80. Zafran, are ground in a dry mortar (Kharal), with Arg Ghulab (Rosewater) 10 tola (120 ml). Mix the powder of Sibr Zard and Mur-Makki to the Zafran paste and make the pill manually to get the tablets of 500 mg. Then tablets are wrapped with Warq-e-Nuqra (silver foils) 14,15,17,46.

4.2. Dose: 1-2 tablets of 500 mg thrice weekly Orally 14,46.

4.3. Actions: Muhaqize fasade akhlat (preventing humoral disorders) and Muhaqize ufoonat (preventing infection). Antidote, Chemoprophylactic during the epidemic 14,46.

4.4. Therapeutic uses: Infectious disease, plague, chickenpox, cholera, any epidemic outbreak 14,46.

Table 2: Component of “Tiryaq Wabai.”

| Constituent (Unani Name)/ Botanical Name | Part Used | Temperament | Actions | Ratio of drug | Ref. |
|-----------------------------------------|-----------|-------------|---------|---------------|------|
| Sibr (Aloe barbadensis) | Fresh and dried juice of leaves pulp | Hot and dry 2° | Tiryaq, Mushil, Mudir haiz, Mohallil-e-waram, muharrik kabid | 2 | 14,18,46, 53 |
| Mur-Makki (Commiphora myrrha) | resin | Hot 3° and dry 2° | Tiryaq, Muharrik, Dafe taffun, Munaffis Balgham, Mudir haiz | 1 | 14,18,46, 53 |
| Zafran (Crocus sativus) | Dried stigma and styles | Hot 2° and dry 1° | Tiryaq, Mudir bowl, Muqawwi jigar, Muqawwi asab, Mudir haiz, Muqawwi bah | 1 | 14,18,46, 53 |

5. Scientific studies

The use of immunomodulators has the potential to stimulate innate and acquired defence processes such as cytokines, which enables the body to aid itself. Many disorders such as viral infections, different cancers and autoimmune diseases can be managed with immunostimulant drugs. A study evaluated the immunostimulant effect of Tiryaq Wabai in immunocompromised elderly patients to validate the Unani claims. The test group was treated with Tiryaq Wabai 500mg thrice a week in capsule form, while the control group was given roasted wheat flour, a placebo in the dose of 500mg thrice a week for 45 days. Significant improvement was observed in TLC, ALC, Lymphocyte % and CD4 count and CD8 counts in the test group in comparison to the control group. An increase in CD4 and CD8 counts indicate a significant positive effect on the proliferation and differentiation of lymphocytes. The result suggests the immunostimulant activity of test drug Tiryaq Wabai and recommends its use in conditions where immunostimulant is required 16.

Table 3: Scientific studies and chemical constituents of different Components of “Tiryaq Wabai.”

| Drugs | Chemical constituents | Activities |
|-------|-----------------------|------------|
| Sibr (Aloe barbadensis) | Acemannan, Alanine, arginine, aspartic acid, cysteine, glutamic acid, glycine, histidine, hydroxyproline, isoleucine, leucine, lysine, methionine, phenylalanine, proline, threonine, serine, tyrosine, valine, Aloe-emodin, aloetic acid, anthranol, aloin A & B, anthrace, anthranol, barbaloin, chrysophanic acid, emodin, ethereal oil, ester of cinnemonic acid, isobarbaloin, resi-stannol, Auxins, gibberellins, Arachidonic acid, γ-linolenic acid, triglycerides, triterpenoid, potassium sorbate, salicylic acid, uric acid, Acetic acid, citric acid, formic acid, fumaric acid, lactic acid, malic acid, pyruvate, succinic acid and tartaric acid, Minerals such as calcium, chlorine, chromium, copper, iron, magnesium, manganese, phosphorous, potassium, sodium and zinc 54–58. | Anti-viral, Immunomodulatory, Anticancer activity, Antioxidant effects, Antidiabetic effects, Anti-inflammatory, Wound healing, Anti-ulcer effects, Antihyperlipidemic activity 59–67. |
| Mur-Makki (Commiphora myrrha) | alpha-elemene, cuminic aldehyde, eugenol, metacresol, pinene, limonene, diterpenes, and sesquiterpenes, delta elemene, beta-bourbonene, beta-elecone, beta-caryophyllene, gama-elecone, alpha-humulene, dehydroaromandendrene, 9-epi-caryophyllene, gama-muurolene, allo aromadendrene, curzerene, gama-cadinene, delta-cadinene, beta-sesquiphellandrene, selina-3,7(11)-diene, elemol, caryophyllene alcohol, caryophyllene oxide, cis-beta-elecone Katayoun, furanogermacra-1E,10(15)-diene-6-one, 2-methoxyfuranogermacra-1(10),4-diene, T-cadinol, 3a-hydroxy-T-cadinol, epicurzerenone 68–70. | Anti-viral, Immunomodulatory, Analgesic, Anticancerous, Antioxidant activity, Anti-microbial activity, Anti-fungal activity, Anti-inflammatory, Antihyperlipidemic, Hepatoprotective effect 70–79. |
| Zafran (Crocus sativus) | Crocin, picrocrocin, safranal, carotenoids including zeaxanthin, lycopen, and various α- and β-carotenes, carotenes, crocetin, picrocrocin, zeaxanthin 80–83. | Anti-viral, Immunomodulatory, Antinociceptive, anti hypertensive, Anticonvulsant, Antilissive, Antigenototoxic, cytotoxic, Axioytic, anti-inflammatory, Anti-Alzheimer effect 84–93. |
5.1. Anti-viral activities and their Mechanism of different Components of “Tiryaq Wabai.”

5.1.1. Sibr (Aloe barbadensis)

The research examines Aloe Vera’s anti-viral activity and conducts molecular docking with COVID-19 main protease (3CLpro/Mpro) to classify possible COVID-19 protein inhibitors as well as the ADME analysis. The binding affinity of ligands indicates that the most potent ligands to be used as potential COVID-19 Mpro inhibitors are three ligands (6, 1 and 8) obtained from the range of 10 Aloe Vera compounds. In conclusion, Lipinski’s rule of five based on ADME analysis approves ligand 6 to be the best drug candidate 94. In another study, two anthraquinones, aloesaparinin-1 (1) and aloesaparinin-ll (2) were isolated from A vera roots, and seven derivatives were obtained from these isolated compounds. These compounds were tested by the cytopathic effect reduction assay (CPE) against two strains of influenza virus AH1N1. The anti-viral activity was determined by the ability of compounds to prevent virus replication on Madin Darby Canine Kidney cells (MDCK). Results showed both compounds were most effective if applied at concentrations of 50 μM and 100 μM 6. In another study, the ability of compounds to prevent virus replication on Madin Darby Canine Kidney cells (MDCK) was significantly reduced. Bioaron C aqueous extract) against representatives of picornaviridae families and non-enveloped RNA viruses 95. Other studies have shown an unusual viral function of saffron extract and its main ingredients. The result suggested that aqueous saffron extract was not active in some doses (i.e. a mild activity) against HIV-1 and HSV-1 virions, but that crocin and picrocrocin suggested important anti-HSV-1 and anti-HIV-1 activities.

5.1.2. Zafran (Crocus sativus)

Soleymani et al96 explore the anti-viral function of saffron extract and its main ingredients. The result suggested that aqueous saffron extract was not active in some doses (i.e. a mild activity) against HIV-1 and HSV-1 virions, but that crocin and picrocrocin suggested important anti-HSV-1 and anti-HIV-1 activities.

Mechanism: Crocin prevented the HSV replication of virions in Vero cells before and after entry. Crocin carotenoid inhibited the penetration of HSV in the target cells as well as disrupted virus replication after cell entry. Picrocrocin also prevents the entry and replication of viruses.

5.1.3. Mur-Makki (Comniphora myrrha)

Alamri et al71 examined the effect of Myrrh extract on Vero cells infected with Herpes Virus Type-1. The findings showed that Vero cells were toxic to high concentrations (10% and 5%) while lower concentrations (2%,1%, 0,5%) protected Vero cells against the cytopathic effect of HSV-1.

Mechanism: Treated Vero cells will result in a decrease in IL-1B levels, which in turn will reduce cytokine production due to HSV-1, including IL6 and IL8.

Table 4: Immunomodulatory activities and their Mechanism of different Components of “Tiryaq Wabai.”

| Drug | Immunomodulatory activity | Mechanism | Ref. |
|------|---------------------------|-----------|-----|
| Sibr (Aloe barbadensis) | Ahluwalia et al100 research indicate that AVH200® (A. barbadensis Mill. dried frozen inner leaf gel extract) has an in vitro suppressive effect on human blood T cells. | Reduced expression of CD25 among CD3+ T cells and suppression of T cell proliferation, and also reduced the expression of CD28 on CD3+ T cells; ↓ secretion of IL-2, IFN-γ and IL-17A in PBMC cultures | 100 |
| | Dziewulska et al research assess the effect of herbal extracts on selected mechanisms of immunity in clinically stable pigeons and pigeons inoculated with type 1 pigeon paramyxovirus (PPMV-1). The test indicates that aloe vera extract has immunomodulatory properties and can be used effectively for viral disease prevention, immune enhancement and as an alternative treatment for viral diseases. | Aloe vera activated both cell and humoral immunity, as shown by the higher expression of genes encoding CD4 and CD8 surface receptors | 101 |
| | One research found that dietary supplementation with Aloe vera prevented immunosuppression caused by transportation stress, injection and bacterial infection; treatment also increased Serum lysozyme concentrations (SLC) tested in pacu (Piaractus mesopotamicus) after heat-killed infection with Aeromonas hydrophila. | Prohibited falls of both respiratory leukocyte burst and haemolytic activity of complement system caused by transport. | 102 |
| | Madan et al found Aloe Vera extract (300 | It stimulates the proliferation of stem cells → ↑ to | 103 |
| Study                                                                 | Action/Effect                                                                                                                                                                                                 | Reference |
|----------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| Aleem et al.                                                         | mg/kg, i.p) have immunostimulatory action total white blood cells. It also ↑ plaque-forming cells in the spleen and circulating antibody titre → ↑ humoral immune response                                                | 104       |
|                                                                     | On mice confronted with S. typhimurium DT104, an in vivo anti-microbial activity and immunomodulation effects of aloe peel extracts were tested. The faecal shedding of S. typhimurium DT104 ↓ significantly and the intestinal Salmonella specific IgA and IgG titers ↑ significantly in mice fed with aloe peel extracts | 105       |
| Mesbah et al.                                                       | Aloe Vera treatment significantly ↓ the clinical signs of experimental autoimmune encephalomyelitis (an animal model of multiple sclerosis) and delayed onset of disease                                  | 106       |
|                                                                     | The immunomodulatory activity of PAG in immunosuppressed and Candida albicans infected mice has been investigated. The findings show clearly that Aloe Vera gel has immunomodulatory activity.                  | 107       |
|                                                                     | Another study showed that aloe vera improved the capacity of broiler chickens with humorus responses to viral infection.                                                                                | 108       |
|                                                                     | Another study found that rainbow trout (Oncorhynchus mykiss) fortified with aloe vera powder had improved immunity parameters, leading to significantly lower mortalities in the challenge with S. parasitica compared to the control.  | 109       |
| Farahnejad et al.                                                   | Acemannan (major polysaccharide) → activates macrophages → enhanced phagocytic and candidacidal activities                                                                                           | 110       |
|                                                                     | Zafran (Crocus sativus)                                                                                     | 111       |
| Khajuria et al.                                                     | Cellular immunity: 1. ↑ in adhesion of neutrophils, 2. attenuation of cyclophosphamide-induced neutropenia, 3. ↑ in the phagocytic index in carbon clearance assay | 111       |
|                                                                     | Humoral immunity: 1. ↑ in serum immunoglobulin levels 2. ↑ thymus gland weight and hemagglutination titre value                                                                                         | 111       |
| Kadri et al.                                                        | ↑ Arthus reaction and Delayed-type hypersensitivity reactions. Both reactions are important in evaluating humoral and cellular immune responses, respectively. A.R. is a hypersensitivity type III reaction, which depends on the production of specific antibodies against an | 112       |
significantly (P ≤ 0.05) ↓ in mice treated with cyclosporine as compared with mice treated with the extracts of C. sativus. These findings suggest that C. sativus extract exerted some positive effects on the metaphase index of bone marrow or spleen cells, and accordingly an enhancement of immune functions.

Another research found that myrrh suspension facilitated the healing and reconstruction of damaged tissue when used for a relatively short period (less than 2 weeks) and when suspended in low concentration.

Another research showed that Commiphora has a strong antioxidant and can defend against lead-induced hepatic oxidative damage and immunotoxicity by reducing lipid peroxidation and enhancing the mechanisms of antioxidant and immune defence.

Abdel-Aziz et al study indicate that myrrh can improve the cellular immunity of schistosomiasis infected mice. This study showed that serum anti-schistosomal antibodies of mice infected with Schistosoma mansoni were ↓ significantly (p<0.0001) after three weeks of the treatment with myrrh compared with the infected non-treated group.

Boskabady et al investigated the Crocus sativus extract on human lymphocytes’ cytokines and T helper 2/T helper one balance. Various concentrations of the extract substantially inhibited lymphocyte cell viability in peripheral blood mononuclear cells stimulated with phytohemagglutinin. They were even inhibiting IFN-γ secretion in stimulated cells and IL-10 secretion both in stimulated and non-stimulated cells at high concentrations of extract (500 μg / ml). The findings indicate that saffron could have therapeutic effects on inflammatory conditions linked to increased development of Th2 cytokines such as asthma.

A study investigates the effects of myrrh supplementation on WBC numbers in the blood before and during an injury. The result showed treatment with myrrh induced an initial ↑ in WBC levels that persisted through the post-injury healing period.

Another research indicated that C. sativus hydroethanolic extract reduced histamine level in asthmatic guinea-pigs prevent ↑ serum histamine level, ↓ eosinophil counts in lung lavage

Mur-Makki (Commiphora myrrh) A study investigates the effects of myrrh supplementation on WBC numbers in the blood before and during an injury. The result showed treatment with myrrh induced an initial ↑ in WBC levels that persisted through the post-injury healing period.

Another research found that myrrh suspension facilitates the healing and reconstruction of damaged tissue when used for a relatively short period (less than 2 weeks) and when suspended in low concentration.

Another research showed that Commiphora has a strong antioxidant and can defend against lead-induced hepatic oxidative damage and immunotoxicity by reducing lipid peroxidation and enhancing the mechanisms of antioxidant and immune defence.

Abdel-Aziz et al study indicate that myrrh can improve the cellular immunity of schistosomiasis infected mice. This study showed that serum anti-schistosomal antibodies of mice infected with Schistosoma mansoni were ↓ significantly (p<0.0001) after three weeks of the treatment with myrrh compared with the infected non-treated group.

Significantly ↓ mean serum level of IL-2, non significantly ↓ level of gamma interferon (IFN-γ)

Significant macrophage activation observed with the release of nitric oxide was encouraged by non-cytotoxic defence from a saffron corm. After proteoglycan therapy, fast activation of protein kinase C and NF-kappa B was achieved, which may clarify nitric oxide synthase induction. The rapid apoptosis of macrophages was promoted in proteoglycan concentrations ranges from 10 to 1,000 ng/ml, possibly due to their activation. This molecule did not prevent in vitro migration or invasion of human tumour cells. The results supported a plausible immune-modulating activity for Crocus proteoglycan.

Specific stimulation of PKC activity, probably triggered by the ↑ calcium levels caused by treatment with this glycoconjugate.

The compound alters plasma membrane permeability on HeLa cells, causing calcium influx → ↑ intracellular calcium levels and activation of PKC induce NF-kB DNA-binding (a process necessary to activate iNOS transcription and NO production in macrophages)

↑ the ratio of IFN-c to IL-4, which indicates a ↑ Th1/Th2 balance

Another study indicated that C. sativus hydroethanolic extract reduced histamine level in asthmatic guinea-pigs

prevent ↑ serum histamine level, ↓ eosinophil counts in lung lavage
Table 5: Classification and structure of critical chemical constituents of the component of *Tiryaq Wabai*

| Drug name                  | Classification | Chemicals      | Structures | PubChem CID |
|----------------------------|----------------|----------------|------------|-------------|
| *Sibr* (*Aloe barbadensis*)| polysaccharide | Acemannan       |            | 72041       |
| anthraquinone glycoside    | Aloin          |                |            | 14989       |
| anthraquinone glycosides   | Aloe-emodin    |                |            | 10207       |
| omega-6 fatty acid         | γ-linolenic acid |               |            | 5280933     |
| *Mur-Makki* (*Commiphora myrrha*) | sesquiterpenoids | alpha-elemene |            | 80048       |
| natural organic compound   | Cuminic aldehyde |             |            | 326         |
| phenylpropanoids           | eugenol        |                |            | 3314        |
| Category                              | Compound                          | Chemical Formula | Molecular Weight |
|---------------------------------------|-----------------------------------|------------------|------------------|
| organic compound                     | metacresol                        | ![metacresol](image) | 342              |
| aromatic monoterpenoids               | curzerene                         | ![curzerene](image) | 572766           |
| Zafran (*Crocus sativus*)             | diterpenoids                      | ![Crocin](image)  | 5281233          |
|                                       | monoterpenic glycoside             | ![picrocrocin](image) | 130796           |
| organic compound                     | safranal                          | ![safranal](image) | 61041            |
| carotenoid alcohols                  | zeaxanthin                        | ![zeaxanthin](image) | 5280899          |
| acyclic carotene                     | lycopene                          | ![lycopene](image) | 446925           |
| carotenoids                          | crocetin                          | ![crocetin](image) | 5281232          |
6. Conclusion and discussion

It is a likely possibility that epidemics will continue to occur, and with the emergence of new organisms may be more aggressive than ever. Hence, the need arises to develop new effective methods of infection control that are accessible to the maximum population. Prevention of *wabai amraz* with *Tiryaq* Advia is recommended in the Unani system of medicine since ancient times. As a prophylactic drug, *Tiryaq* is generally recommended for toxicity prevention (sepsis). *Tiryaqiyat* is the formulation that reinforces the *Rooh* so that *Rooh* can neutralize the body’s toxicity. *Tiryaqiyat* enhances the *rooh*, activates *hararte-gharizia*, and allows Tabiyat to avoid morbidity substances. All the three ingredients of *Tiryaq Wabai* have various pharmacological activities like an immunomodulatory, antitussive, expectorant, antiviral activity which provide a strong basis for its prophylactic use for covid-19 infection. Further, research on this important prophylactic Unani formulation *tiryaq* e *wabai* in Covid-19 is the need of the hour. Greater impetus on research in the Unani system of medicine will not only boost trade and practice of herbal products but will also help in spreading the traditional Indian knowledge to other parts of the world.

Conflicts of Interest: None

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