Indian Medicinal Plants and Formulations and Their Potential Against COVID-19–Preclinical and Clinical Research

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The cases of COVID-19 are still increasing day-by-day worldwide, even after a year of its first occurrence in Wuhan city of China. The spreading of SARS-CoV-2 infection is very fast and different from other SARS-CoV infections possibly due to structural differences in S proteins. The patients with severe diseases may die due to acute respiratory distress syndrome (ARDS) caused by systemic inflammatory reactions due to the excessive release of pro-inflammatory cytokines and chemokines by the immune effector cells. In India too, it is spreading very rapidly, although the case fatality rate is below 1.50% (https://www.statista.com), which is markedly less than in other countries, despite the dense population and minimal health infrastructure in rural areas. This may be due to the routine use of many immunomodulator medicinal plants and traditional AYUSH formulations by the Indian people. This communication reviews the AYUSH recommended formulations and their ingredients, routinely used medicinal plants and formulations by Indian population as well as other promising Indian medicinal plants, which can be tested against COVID-19. Special emphasis is placed on Indian medicinal plants reported for antiviral, immunomodulatory and anti-allergic/anti-inflammatory activities and they are categorized for prioritization in research on the basis of earlier reports. The traditional AYUSH medicines currently under clinical trials against COVID-19 are also discussed as well as furtherance of pre-clinical and clinical testing of the potential traditional medicines against COVID-19 and SARS-CoV-2. The results of the clinical studies on AYUSH drugs will guide the policymakers from the AYUSH systems of medicines to maneuver their policies for public health, provide information to the global scientific community and could form a platform for collaborative studies at national and global levels. It is thereby suggested that promising AYUSH formulations and Indian medicinal plants must be investigated on a priority basis to solve the current crisis.

Keywords: COVID-19, AYUSH medicine, Indian medicinal plants, Indian traditional medicine, immunomodulators, antiviral agents
1 INTRODUCTION

A novel coronavirus-induced pneumonia, which was later called coronavirus disease 2019 (COVID-19), has rapidly increased to an epidemic scale and affected whole human population globally (WHO, 2020a). In India, the first case of COVID-19 was an imported case from Wuhan, China on January 30, 2020 traced in Kerala (Sahasranaman and Kumar, 2020) and the death rate of COVID-19 in India is 1.45%, as of 12th December, 2020 (Worldometers, 2020). Severe acute respiratory syndrome-related coronavirus (SARS-CoV-2) has become a pandemic hazard to global public health worldwide.

Coronaviruses (CoVs) are large viruses comprising of four genera, namely alpha, beta, gamma, and delta. The beta-coronavirus class includes severe acute respiratory syndrome (SARS) virus (SARS-CoV), Middle East respiratory syndrome (MERS) virus (MERS-CoV), and the COVID-19 causative agent SARS-CoV-2. (Li G. et al., 2020). The novel SARS-CoV-2 is a beta CoV that shows 88% similarity to two bat-derived SARS-like CoVs (bat-SL-CoVZC45 and bat-SL-CoVZXC21), about 50% identical to the sequence of MERS-CoV, and 70% similarity in genetic sequence to SARS-CoV (Cheng and Shan, 2020). Although there is an extremely high resemblance between SARS-CoV and the novel SARS-CoV-2, the SARS-CoV-2 is spreading rapidly as compared to the SARS-CoV, which may be explained by structural differences in the S proteins (Rabaan et al., 2020).

The SARS-CoV-2 S protein has been found as a significant determinant of virus entry into host cells using angiotensin converting enzyme 2 (ACE2) receptor similar to SARS-CoV. Whereas the binding affinity of virion S glycoprotein and ACE2 is reported to be 10–20 folds higher in SARS-CoV-2 as compared to that of SARS-CoV (Song et al., 2018).

Severe cases of COVID-19 are reported to have increased plasma concentrations of pro-inflammatory cytokines, including interleukins (IL-6 and IL-10), tumor necrosis factor (TNF)-α, granulocyte-colony stimulating factor (G-CSF), monocyte chemoattractant protein 1 (MCP1), and macrophage inflammatory protein (MIP)1α (Yuki et al., 2020). Akin to the common viral infections, the antibody profile against the SARS-CoV virus manifests a typical pattern of IgM and IgG antibody production. The IgG antibody is believed to play a protective role, as the SARS-specific IgG antibodies last for a longer time while IgM antibodies disappear at the end of 12 weeks. The latest reports show a significant reduction in the number of CD4+ and CD8+ T cells in the peripheral blood of SARS-CoV-2-infected patients, besides activation of other pro-inflammatory cytokines such as nuclear factor-κB (NF-κB), interferon regulatory factor 3 (IRF3) and type I Interferons (IFN-α/β) (Li G. et al., 2020). A recent report shows that many patients died from acute respiratory distress syndrome (ARDS) caused by the cytokine storm, which is a deadly uncontrolled systemic inflammatory response resulting from the release of large amounts of pro-inflammatory cytokines and chemokines by immune effector cells in SARS-CoV infection (Guo et al., 2020).

Although the pathogenesis of COVID-19 is still not clear, patients with COVID-19 show non-specific symptoms ranging from no symptoms (asymptomatic) to severe pneumonia and death. However, the most common symptoms include fever, non-productive cough, dyspnea, myalgia, fatigue, diarrhea, lung damage, normal or decreased leukocyte counts, and radiographic evidence of pneumonia, which are similar to the symptoms of SARS-CoV and MERS-CoV infections (WHO, 2020b; Rothan and Byrareddy, 2020). Complications include ARDS, acute heart injury, and secondary infections (Guo et al., 2020).

The present conventional strategy of the disease control includes isolation of cases and tracing their contacts, providing optimal care to these infected cases, reducing chances of secondary infections by early diagnosis, and rapid development of effective diagnostic, preventive and therapeutic strategies, including vaccines (WHO, 2020b). The treatment approach for COVID-19 is supportive care, which is supplemented by the combination of broad-spectrum antibiotics, antivirals, corticosteroids and convalescent plasma (Yang et al., 2020).

Scientists are working hard to develop effective treatments. As of October 18, 2020, more than 3611 clinical trials (with more than 100 complementary medicines) on COVID-19 are either ongoing or enrolling patients, and new ones are being added every day, as the case count rockets globally. The drugs being tested range from repurposed flu treatments to failed ebola drugs, to malaria treatments that were first developed decades ago (Lythgoe and Middleton, 2020). There is scale-up development of vaccines across the world by many pharmaceutical companies as well as research organizations. These treatments undergoing trials may require months or years to develop and hit the market, meaning that an immediate treatment or control mechanism should be found, if possible (Table 1).

Considering the current situation, various treatment modalities have been well-thought-out, including traditional medicine, which has been widely used during the past epidemic outbreaks, including SARS and H1N1 influenza (Luo et al., 2020). Until now three countries including India, China, and South Korea, have issued guidelines on traditional regimes for the prevention and management of COVID-19 (Ang et al., 2020).

The Indian Traditional System of Medicine is one of the oldest systems of medical practice in the world and has played an essential role in providing health care service to human civilization, right from its inception. India has the exclusive distinction of its own recognized traditional medicine; Ayurveda, Yoga, Unani, Siddha, and Homoeopathy (AYUSH) (Adhikari and Paul, 2018). These systems are based on definite medical philosophies and represent a way of achieving a healthy lifestyle with conventional and established ideas on the prevention of diseases and the promotion of health. The basic treatment approach of all these systems is holistic and the pharmacological modalities are based on natural products of plants, animals, or mineral origin. Given this, there is a resurgence of interest in AYUSH systems, which have helped the nation in the pandemic crisis due to plague, cholera, Spanish flu, etc. in the past. Hence, by repurposing the traditional uses of Indian medicinal plants and formulations, new treatment options
### TABLE 1 | Details of clinical trials completed on AYUSH drugs for COVID-19 (Source: www.ctri.nic.in).

| Ctri No./Treatment details | Study title | Type of trial (design of study) | Recruitment status | Remarks |
|----------------------------|-------------|---------------------------------|-------------------|---------|
| CTRI/2020/04/024883 ZINGIMR-H | Clinical research on safety and efficacy of ZingiVir-H as an add on therapy in COVID-19 patients | Interventional (Other) | Completed | Zingivir H consumption with standard of care in COVID 19 confirmed patients showed a remarkable recovery compared to that of placebo |
| CTRI/2020/05/025161/Herbal formulation-aayudh advance | To study the effectiveness of herbal formulation - aayudh advance as a supplementary treatment for the corona virus 2019 (COVID-19) infected patients | Interventional (randomized, parallel group, active controlled Trial) | Completed | “Aayudh advance”, when given concomitantly with standard of care, was found to be 100% safe, devoid of any drug-drug interaction, effective as virucidal to reduce viral load, and increased the recovery rate when compared to standard of care alone when tested in mild symptomatic COVID-19 patients |
| CTRI/2020/05/025215/Kabasura kudineer | Effectiveness of Siddha medicine, kabasura kudineer and vitamin C-zinc supplementation in the management of mild COVID-19 patients | Interventional (randomized, parallel group Trial) | Completed | The role of vitamin C with zinc supplementation in the management of COVID 19 is still not clear. Therefore, study will compare the effect of kabasura kudineer and vitamin C with zinc supplementation in terms of negative conversion of SARS CoV-2 infection |
| CTRI/2020/05/025275/Ayurveda rasayana along with conventional guidelines for health care workers | Role of chyawanprash in the prevention of COVID-19 in health care workers | Interventional (randomized, parallel group Trial) | Completed | No adverse effect was found in the study |
| CTRI/2020/05/025276/Ayurveda protocol | Effect of ayurvedic intervention in COVID-19 positive cases | Interventional (single arm Trial) | Completed | Ayurveda treatment protocol includes sanshamani, nagaradi kwath, amalaki churna and golden milk improved the strength of the patient |
| CTRI/2020/05/025397/Purified aqueous extract of cocculus hirsutus (ACCH) | A study to evaluate the effect and safety of a phytopharmaceutical drug in treatment of coronavirus infection | Interventional (randomized, parallel group Trial) | Completed | Clinical improvement was observed in covid patients in terms of disease severity |
| CTRI/2020/05/025425/Chyawanprash (an ayurvedic herbal preparation) | Ayurvedic intervention (chyawanprash) in the prevention of COVID-19 pandemic among health care personnel | Interventional (single arm Trial) | Completed | This remedy was found to be a possible safe prophylactic remedy for COVID-19 |
| CTRI/2020/06/025527/Amrta karuna syrup | Clinical trial on immunity and antiviral for quarantine patients of COVID-19 | Interventional (randomized, parallel group, active controlled Trial) | Completed | The formulation was found to be immunomodulatory |
| CTRI/2020/06/025556/Virulina® along with standard treatment protocol | A clinical trial to know the effect of Virulina® along with standard treatment in COVID-19 positive patients | Interventional (randomized, parallel group, placebo controlled Trial) | Completed | The formulation was found to boost the immunity of the patients and help ease the symptoms |
| CTRI/2020/06/025590/Astha 15 capsule | A clinical trial to evaluate safety and efficacy of polyherbal capsule Astha-15 used as an add on therapy with standard care of therapy as an immunity booster in the suspected and COVID-19 diagnosed patients | Interventional (randomized, parallel group, placebo controlled Trial) | Completed | A better recovery rate was observed |
| CTRI/2020/06/025592/Immunity kit | Use of herbal medicine like tulsi, amruth (giloy), turmeric, ashwagandha as add on treatment in COVID-19 patients | Interventional (single arm Trial) | Completed | Upon using the ayurvedic formulation as add on treatment, the recovery was better in terms of signs and symptoms of COVID-19 patients |
| CTRI/2020/06/026221/Arogya Kashayam-20 | Intervention of ayurvedic medicine (arogyakashyam) in COVID-19 positive cases (asymptomatic and mild symptomatic) | Interventional (randomized, parallel group, active controlled Trial) | Completed | The unani regimen was found to be effective against the mild symptoms of covid 19 |
| CTRI/2020/06/026227/Khamara marwared Triyaq-e-Arba Unani joshanda/ decoction behidana (Cordia oblonga) 3 gm, unnaB (Zephyrus jugulue) 5 in number, sapistan (Cordia myxa) 9 in numbers | A study on unani regimen for prevention of high/moderate risk population of COVID-19 | Interventional (non-randomized, multiple arm Trial) | Completed | Improvement was found in immune status of covid patients |
| CTRI/2020/06/025801/Tablet. Bresol and tab. Septilin | Role of herbal immunomodulators in mild COVID-19 confirmed cases | Interventional (randomized, parallel group, active controlled Trial) | Completed | Use of herbal immunomodulators as add on treatment, improved the recovery rate of COVID-19 patients |
| CTRI/2020/07/026337/Add-on personalized ayurveda intervention to ICMR guideline on Covid-19 | The COVID-19 study with ayurveda add-on to ICMR guideline | Interventional (randomized, parallel group trial) | Completed | Efficacy of treatment was measured in terms of average stay of patients in the hospital to become covid negative |

(Continued on following page)
There are plenty of data supporting the effectiveness of herbs in treating the viral infection. For instance, in controlling the contagious disease spread in the Guangdong Province of China during the 2003 SARS outbreak (Zhang et al., 2020). There are convincing pieces of evidence to establish that traditional Chinese medicine (TCM) has favorable effect in the treatment or prevention of SARS (Yang et al., 2020). A combination of modern and traditional therapy might reduce the severity of the disease, intensity of symptoms, death rate, and side effects. Similar are the observations for Shuanghuanglian (A Chinese medicine) a liquid composed of a blend of honeysuckle, Chinese skullcap, and forsythia, which is claimed to have antiviral, antibacterial, and immunomodulatory effects (https://www.bioworld.com/). Since AYUSH encompasses five different systems of medicine, rich in a variety of traditional formulations, it is likely to have a better chance than other systems to come up with a satisfactory solution to the COVID-19 crisis. Ayurveda means ‘Science of life’. It provides a complete system to have a long and healthy life. It is derived from the concepts of “Dinacharya” - daily regimes and “Ritucharya” - seasonal regimes to maintain a healthy life. Uplifting and maintaining the immunity is duly emphasized across the Ayurveda’s classical scriptures.

The Unani system of medicine, known as Greco-Arab Medicine, is built on the four conditions of living (hot, sodden, frosty, and dry) and four humors of Hippocratic hypothesis namely, blood, yellow bile, dark bile, and mucus. Epidemics, referred to as waba in the Unani system of medicine, are thought to occur if any contagion or ajsam-i-khabitha, finds a place in air and water. Furthering the view, Ibn-e-Sina (980–1035 CE) stated that epidemics spread from one person to another, and one city to another ‘like a message’ (Sina, 1878).

AYUSH systems of medicine propagate general preventive measures aimed at preventing the spread of infection such as social distancing, hygiene and anti-septic measures (sanitization of surroundings), improvement of immunity, and promotion of general health (dietary modifications and herbal drugs). The present article elucidates some traditional Indian AYUSH formulations with proven antiviral, anti-asthmatic, and immunomodulatory activities, however their role in combating COVID-19 needs to be established. Clinical trials of AYUSH medicines like Ashwagandha, Yashhtimadhu, Guduchi, Pippali, and AYUSH-64 on patients, health workers, and those working in high-risk areas have been initiated in India by the Ministry of AYUSH, Ministry of Health and Family Welfares, and the Council of Scientific and Industrial Research (CSIR) with the technical support of Indian Council of Medical Research (ICMR) (Table 1).

**2 POTENTIAL TRADITIONAL INDIAN/ AYUSH FORMULATIONS FOR THE MANAGEMENT OF COVID-19**

**TABLE 1** (Continued) Details of clinical trials completed on AYUSH drugs for COVID-19 (Source: www.ctri.nic.in).

| CTR No./Treatment details | Study title | Type of trial (design of study) | Recruitment status | Remarks |
|---------------------------|-------------|---------------------------------|--------------------|---------|
| CTR/2020/07/026371/1. Kabasura kudineer 2. Shakti drops 3. Turmeric plus tablets | Kabasura kudineer, shakti drops and turmeric plus in the management of COVID-19 | Interventional (Others) | Completed | Better recovery rate was observed in terms of signs and symptoms of stage 1 and 2 of COVID-19 cases on addition of ayurvedic medicines, thereby improving the quality life of stage 1 and 2 of COVID-19 patients |
| CTR/2020/07/026433/1. Dashamulla kwatha and pathyadi kwatha with trikatu churna 2. Sansamani vati 3. AYUSH 64 4. Yastimadhu Ghanaavati | Effect of ayurveda medicine in COVID-19 mild symptoms | Interventional (randomized, parallel group, active controlled Trial) | Completed | No adverse reaction was observed and improvement in signs and symptoms |
| CTR/2020/07/026570/Cap. IP | Safety and efficacy of ayurvedic capsule in mild to moderate COVID-19 infection | Interventional (randomized, parallel group Trial) | Completed | Improvement was observed in respiratory symptoms of covid patients |
3 AYUSH RECOMMENDATIONS FOR MANAGEMENT OF COVID-19

Based on the different systems of Indian Medicine, separate recommendations have been issued from time to time from the Ministry of AYUSH (Government of India) for the management of COVID-19. These different approaches are being followed by the Hospitals as per their specialization, mainly as adjuvants to modern medicine, which could be potentially relevant for COVID 19 treatment. Details of recommended formulations are described below and depicted in Table 2 (Ayurveda), Table 3 (Unani) and Table 4 (Siddha).
TABLE 3 | AYUSH recommended prophylactic approach through Unani formulation. Ref: AYUSH Ministry of Health Corona Advisory–D.O. No. S. 16030/18/2019- NAM; dated: 06th March, 2020.

| Name of the formulation | Composition | Proof of activity related to COVID-19 | References |
|-------------------------|-------------|------------------------------------|------------|
| Arq-e-Ajeeb             | Camphor     | B,C                                | Chen et al. (2013), Ziment and Tashkin (2000) |
|                         | Menthol     | B,C                                | Taylor et al. (2020), Ziment and Tashkin (2000) |
|                         | Thymol      | C                                  | Al-Khalaf (2013) |
| Asghand safoof          | Withania somnifera (L.) Dunal (root) | A,B,C                             | Rasool and Varalakshmi (2006), Pant et al. (2012), Sahni and Srivastava (1993) |
| Habb-e-Bukhar           | Cinchona officinalis L. (bark) | B                                  | Devaux et al. (2020) |
|                         | Tinospora cordifolia (Willd.) Miers (stem) | A,B,C                             | Alsuhaibani and Khan (2017), Pruthvish and Gopinatha (2018), Tiwari et al. (2014) |
|                         | Bambusa bambos (L.) Voss (stem) | A                                  | Sriraman et al. (2015) |
|                         | Acacia arabica (Lam.) Willd. (gum) | C                                  | Rijal and Karmakar (2015) |
|                         | Zingiber officinalis (rhizome) | C                                  | Alamgeer et al. (2018) |
| Habb-e-Hindi zeeqi      | Aconitum chasmanthum Stapf ex Holmes (root) | C                                  | Bagheerwal (2011), Arya and Kumar (2005) |
|                         | Calotropis procera (Alton) W.T. Alton (root) | A,C                               | Zhou et al. (2006), Chang et al. (2013), Khan et al. (2015) |
|                         | Withania somnifera | A,C                               | Kabra et al. (2019) |
| Habb-e-Mubarak          | Myrica esculenta | A                                  | Shukla et al. (2010), Arunadevi et al. (2015) |
|                         | Zingiber officinalis | A                                  | Gerlach et al. (2019), Koochek et al. (2003) |
|                         | Myrtus communis (pearl) | A                                  | Khan et al. (2009), Beaulieu et al. (2013) |
| Khamira-e-Banafsia      | Viola odorata L. (flower) | B,C                                | Jin et al. (2019), Koochek et al. (2003) |
| Khamereea               | Myrtus communis (pearl) | A                                  | Khan et al. (2019), Beaulieu et al. (2013) |
| marwareed               | Bambusa bambos (L.) Voss (stem) | C                                  | Muniappan and Sundararaj (2003) |
|                         | Vataire indica L. (gum) | B,C                                | Meena and Ramaswamy (2019) |
|                         | Sunita album L. (stem) | B,C                                | Paulipandi et al. (2012), Gupta and Chahal (2016) |
|                         | Linum usitatissimum L. (seed) | B,C                               | Mahmood et al. (1996), Boskabady et al. (2011) |
| Lacoq-e-Katan           | Cordia myxa L. (fruit) | A,B,C                              | Liang et al. (2019), Rafieian-kopaei et al. (2017) |
|                         | Ziziphus jujuba Mill. (fruit) | A,B,C                             | Ali et al. (2015), Rashid (2014), Ranjabar et al. (2013) |
|                         | Viola odorata L. (flower) | B,C                                | Yu et al. (2016), Hong et al. (2015), Masaik et al. (2018) |
|                         | Atthea officinalis L. (seed) | C                                  | Gerlach et al. (2019), Koochek et al. (2003) |
|                         | Cassia fistula L. (seed) | A,B,C                              | Bonaterra et al. (2020) |
|                         | Cassia angustifolia M. Vahl (leaves) | A                                  | Laxmi (2015), Indrasetiawan et al. (2019), Antonismy et al. (2019) |
|                         | Ficus carica L. (fruit) | C                                  | Jassim and Naj (2003) |
|                         | Cordia myxa L. (fruit) | C                                  | Al-Snafi (2013) |
|                         | Prunus amygdalas Batsch (seed oil) | B,C                               | Musarra-Pizzo et al. (2019), Musikanthi et al. (2019) |
| Roghan-e-Baboonia        | Matricaria chamomilla L. (flower) | A,C                               | Amirghofran et al. (2000), Singh O. et al. (2011) |
| Sarbat-e-sadr           | Bornyho mori (coconos) | A                                  | Soumya et al. (2019) |
|                         | Ziziphus jujuba Mill. (fruit) | A,B,C                             | Yu et al. (2016), Hong et al. (2015), Masaik et al. (2018) |
|                         | Tachyspermum ammi (L.) Sprague (seed) | A,B                              | Shruhi et al. (2017), Roy et al. (2015) |
|                         | Glycyrrhiza glabra L. (root) | A,B,C                              | Mitra Mazumder et al. (2012), Ashraf et al. (2017), Patel et al. (2009) |
|                         | Foeniculum vulgare Mill. (fruit) | C                                  | Rather et al. (2016) |
|                         | Achochoda vasica Nees (leaves) | A,B,C                              | Vnothapoophan and Sundar (2011), Singh et al. (2010), Gibbs (2009) |
|                         | Onosma bracteatum Wall. (leaves) | C                                  | Patel et al. (2011) |
|                         | Malva sylvestris L. (seed) | C                                  | Martins et al. (2017) |
|                         | Hysoopos officinalis L. (whole plant) | B                                  | Behbahi et al. (2009) |
|                         | Ficus carica L. (fruit) | A,B,C                              | Patil et al. (2013), Camero et al. (2014), Abe (2020) |
|                         | Cordia myxa L. (fruit) | C                                  | Oza and Kulkami (2017) |
|                         | Papaver somniferum L. (flower) | B,C                                | Chattopadhyay and Nal (2007) |
|                         | Onosma bracteatum Wall. (flower) | C                                  | Patel et al. (2011) |
| Sharbat-e-Toot siyah     | Morus nigra L. (fruit) | A,C                                | Lim and Choi (2019) |
| Triyaq-e-Arabia          | Laurus nobilis L. (berries) | A                                  | Auri et al. (2016) |
|                         | Bergenia ciliata (haw.) Sternb. (stem) | A                                  | Rajbandari et al. (2013) |
|                         | Aristocchias indica L. (root) | C                                  | Mathew et al. (2011) |
|                         | Commiphora myrrha (Nees) Engl. (gum) | C                                  | Su et al. (2015) |

Note: A = Provide the references Mallik and nayak (2014), Sengottuvelu et al. (2012), and Welli et al. (2011)!- Immunomodulators; B = Antiviral; C = Anti-allergic/Antiasthmatic/Anti-inflammatory/Respiratory disorders.

3.1 Ayurvedic Approaches

3.1.1 AYUSH Kwath

Ministry of AYUSH promotes the use of AYUSH kwath, which is a ready-made formulation for health promotion of the masses. The formulation is made of four herbs Ocimum sanctum L. leaves, Cinnamomum verum J. Presl. stem barks, Zingiber officinalis Rosoce rhizomes and Piper nigrum L. fruits. The formulation is sold in the market with different names like ‘AYUSH Kwath’, ‘AYUSH Kudineer’ or ‘AYUSH Joshanda’. It is available in powder and tablet forms in the market. These herbs are
reported to boost immunity (Carrasco et al., 2009; Niphade et al., 2009; Alsuhaibani and Khan, 2017; Bhalla et al., 2017) and are active remedies to various viral diseases (Mair et al., 2016; Ghoke et al., 2018; Pruthvish and Gopinatha, 2018).

3.1.2 Samshamani Vati

Samshamani vati (Guduchi ghana vati) is an ayurvedic formulation used in all types of fevers. It is also used as an antipyretic and anti-inflammatory remedy (Patgiri et al., 2014). Samshamani vati is made of aqueous extract of *Tinospora cordifolia* (Willd.) Miers (family Menispermaceae), and reported to be an immunomodulator (More and Pai, 2011) due to the synergistic effect of the various compounds present. It is also effective in various viral diseases (Sachan et al., 2019).

3.1.3 AYUSH-64

AYUSH-64 tablet is composed of *Alstonia scholaris* (L.) R. Br. bark, *Picrotoxis kurrooa* Royle ex Benth. rhizomes, *Swertia chirayita* (Roxb.) H. Karst. whole plant, and *Cacalpinia crista* L. seed pulp. Because of its antimalarial activity, AYUSH-64 is considered to be effective among the high-risk coronavirus population. Researchers have reported that each of its constituents is effectively antiviral, anti-asthmatic, and immunoboosting (Sharma et al., 1994; Siddiqui et al., 2012; Sehgal et al., 2013; Panda et al., 2017; Win et al., 2019; Woo et al., 2019).

### 3.1.4 Agasthya Hareetaki

Agastya Haritaki Rasayana is a popular ‘Avaleha kalpana’, used in the management of various respiratory infection and comprises more than 15 herbal ingredients. Most of its ingredients showed antiviral, anti-asthmatic, anti-inflammatory, and immunomodulatory activities (Mouhajir et al., 2001; Tripathi and Upadhyay, 2001; Balasubramanian et al., 2007; Vadnere et al., 2009; Patel and Asdaq, 2010; Pathak et al., 2010; Jain et al., 2011; Kumar et al., 2011; Lampariello et al., 2012; Jiang et al., 2013). The above literature suggests the symptomatic management of COVID-19 by Agastya Haritaki.

### 3.1.5 Anuthaila

Anuthaila consists of about twenty ingredients and out of them *Leptadenia reticulata* (Retz.) Wight and Arn. has been reported in allergic response, treatment of asthma, bronchitis, and throat trouble (Mohanty et al., 2017). Similarly, *Ocimum sanctum* L. is recommended for a wide range of conditions including, cough, asthma, fever, and malaria (Cohen, 2014) and *Sesamum indicum* L. oil for dry cough, asthma, migraine, and

### TABLE 4 | AYUSH recommended prophylactic approach through formulations of Siddha system of medicine. Ref: AYUSH Ministry of Health Corona Advisory—D.O. No. S. 16030/18/2019-NAM; dated: 06th March, 2020.

| Name of the formulation | Composition | Proof of activities related to COVID-19 |
|-------------------------|-------------|----------------------------------------|
| Ahatodai manapagu (siddha) | Adhatoda vasica Nees (leaves) | A,B,C |
| Kabasura kudineer (siddha) | Saccharum officinarum L. | C |
| | Zingiber officinalis Roscoe (rhizome) | A,B,C |
| | Piper longum L. (fruit) | A,B,C |
| | Syzygium aromaticum (L.) Merr. and L.M. Perry (fruit) | A,B,C |
| | Tragia involucrata L. (leaves) | A,B,C |
| | Anacyclus pyrethrum (L.) Lag. (root) | A,B,C |
| | Adhatoda vasica Nees (leaves) | A,B,C |
| | Tinospora cordifolia (Willd.) Miers (stem) | A,B,C |
| | Andrographis paniculata (Burm.f) Nees (whole plant) | A,B,C |
| | Sida acuta Burm.f. (root) | A,B,C |
| | Cyperus rotundus L. (rhizome) | A,B,C |
| | Terminalia chebula Retz. (pulp) | A,B,C |
| | Nilavembu kudineer (siddha) | Andrographis paniculata (Burm.f) Nees (whole plant) | A,B,C |
| | Plectranthus vettiveroides (Jacob) N.P.Singh and B.D.Sharma (root) | A,B,C |
| | Vetiveria zizanoides (L) Nash (root) | A,B,C |
| | Zingiber officinalis Roscoe (rhizome) | A,B,C |
| | Piper Nigrum L. (fruit) | A,B,C |
| | Cyperus rotundus L. (rhizome) | A,B,C |
| | Santalum album L. (stem) | A,B,C |
| | Trichosanthes cucumerina L. (whole plant) | A,B,C |
| | Mollugo cerviana (L) Ser. (whole plant) | A,B,C |

Note: A = Immunomodulators; B = Anti-viral; C = Anti-allergic/Antiasthmatic/Anti-inflammatory/Respiratory disorders.
respiratory infections (Nagpurkar and Patil, 2017). There are reports on S. indicum seeds with Tachyspermum ammi (L.) Sprague seeds for dry cough, asthma, lung diseases, and common cold (Patil et al., 2008). On the basis of above literature, Anuthaila justifies its use in corona virus pandemic condition (Table 2).

### 3.2 Unani Approaches

#### 3.2.1 Triyaq-e-Araba

Triyaq-e-Araba is an important Unani formulation used as a detoxifying agent. It contains Laurus nobilis L. berries, Bergenia ciliata (Haw.) Sternb. stem, Aristolochia indica L. roots and Commiphora myrrha (Nees) Engl. It has been reported by several authors as a potent antiviral agent (Aurori et al., 2016), including against SARS-CoV (Loizzo et al., 2008). Further, B. ciliata is found to be effective against the influenza virus-A and herpes simplex virus-1 (HSV-1) (Rajbhandari et al., 2003), whereas its active principal, bergenin, has been found to be effective against hepatitis C virus (HCV) and HIV virus (Ahmad et al., 2018). On the basis of this literature, Triyaq-e-Araba could be one of the effective antiviral medicine and certifies its use against COVID-19.

#### 3.2.2 Roghan-e-Baboona

Roghan-e-Baboona is an Unani remedy utilized as an anti-inflammatory agent (Zaia et al., 2016). The flowers of Matricaria chamomilla L. are the main ingredient of Roghan-e-Baboona. It is composed of the flowers of M. chamomilla, which is found effective for acute viral nasopharyngitis (Srivastava et al., 2010), as well as for sore throat (Kyokong et al., 2002).

#### 3.2.3 Arq-e-Ajeeb

Arq-e-Ajeeb is a liquid preparation that contains thymol, menthol, and camphor. Thymol is a promising candidate for topical application as an antiviral agent for herpetic infections (Lai et al., 2012; Shariri-Rad et al., 2017). Menthol has been reported as an anti-inflammatory agent (Zaia et al., 2016). The Unani physicians have a very successful history of treating Nazla wabi (Swine flu) using Arq -e-Ajeeb. These studies support the use of Arq-e-Ajeeb for COVID-19.

#### 3.2.4 Khamira-e-Banafsha

Khamira-e-Banafsha is a semi-solid Unani formulation prepared by adding decoction of flowers of Viola odorata L. to a base of sugar or sugar with honey and used for cold-cough as expectorant and for the treatment of ailments of respiratory system and chest diseases, bronchitis, whooping cough, fever, expectorant, antipyretic etc. Further, V. odorata has been reported to suppress the viral load and increase antiretroviral drug efficacy (Gerlach et al., 2019), decrease the thickness of the alveolar wall, hemorrhage area, and alter the epithelial lining of bronchiolo of the lungs (Koochek et al., 2003). The above literature supports its use for the management of COVID-19.

#### 3.2.5 Laooq-e-Sapistan

Laooq-e-Sapistan is a semisolid sugar-based polyherbal Unani formulation extensively used by the masses in India for the treatment of cold and cough, whooping cough, and phlegm. It reduces inflammation of the pharynx, tonsils, and irritation or infection. The jelly like sticky mass of ripe fruit of Cordia myxa L. is the main ingredient, which has been reported as antiviral and antitussive (Jamkhande et al., 2013). Another important constituent is Ziziphus fruit, which contains betulinic acid. Literature showed the down-regulation of IFN-y level by betulinic acid in mouse lung, thus enhancing immunity and suggested as potential therapeutic agent for viral infections (Hong et al., 2015). Aqueous extract also reported increasing thymus and spleen indices as well as enhance the T-lymphocyte proliferation, hemolytic activity, and natural killer (NK) cell activity (Yu et al., 2016). Viola odorata L., one of its ingredients, suppresses the viral load (Gerlach et al., 2019). Hence, the literature supports the use of AYUSH formulation Laooq-e-Sapistan in COVID-19.

#### 3.2.6 Sharbat-e-Sadar

Sharbat-e- Sadar is an Unani polyherbal syrup formulation and is widely used for common cold, cough and respiratory diseases. Trachyspermum ammi (L.) Sprague, an important ingredient, reported to neutralize antibodies for Japanese encephalitis virus (Roy et al., 2015), and a glycoprotein was found to proliferate B-cells (Shruthi et al., 2017). Adhatoda vasica Nees inhibits HIV-Protease (Singh et al., 2010), Bombys mori was reported to increase immune responses against viral infection (Li et al., 2018). Other ingredients such as Glycyrrhiza glabra L., Ficus carica L., Onosma bracteatum Wall., and Ziziphus jujuba Mill. also possess the antiviral and immunomodulatory activities, as summarized in Table 5.

#### 3.2.7 Khameera Marwareed

Khameera marwareed is a compound, sugar-based, semisolid Unani formulation used as an immunomodulator. It has been reported to stimulate the immune system through T helper 1 (Th1) type cytokine response and maintains the body in a healthier position to fight against viral infections (Khan et al., 2009). Its ingredients showed powerful antiviral activities by inhibiting replication (Benencia and Courrèges, 1999).

#### 3.2.8 Asgandh Safoof

Asgand (Withania somnifera (L.) Dunal) is a very popular Indian medicinal plant. The root powder is used in the Unani system of medicine as an immunomodulator. It is reported that the root’s extract significantly increases the CD4+ and CD8+ counts (Bani et al., 2006) and blood profile, especially WBC and platelet counts (Agarwal et al., 1999). Aqueous suspension showed potent inhibitory activity toward mitogen-induced proliferative response of T-lymphocytes and prevent SARS-CoV-2 entry by disturbing connections between viral S-protein receptor binding domain and host ACE2 receptor (Balkrishna et al., 2020). The above literature supports the preventive use of Asgandh safoof against COVID-19.

#### 3.2.9 Habb-e-Bukhar

Habb-e-Bukhar is a polyherbal tablet formulation of Unani system of medicine, prescribed in elephantiasis and malarial fever. The main ingredient of Habb-e-Bukhar is cinchona bark. Its active constituent quinine is being used by some
| Category | Botanical name/Common name/Family/Part | Immunomodulatory activity | Anti-viral activity | Anti-allergic/anti-asthmatic/anti-inflammatory/respiratory disorders |
|----------|---------------------------------------|---------------------------|--------------------|---------------------------------------------------------------|
| C1.1     | *Acacia catechu* (L.f.) Wild./Khadira/Fabaceae/Leaves, bark, heartwood | Aqueous and alcoholic extract increased phagocytic response showed by peritoneal macrophages. The extracts inhibited TNF-α and the production of NO, IL-10. Dose: 100 and 200 mg/kg Sunil et al. (2019) | Aqueous, hydroalcoholic and n-butanol extract showed anti HIV-1 activity by inhibiting viral protein and Tat IC_{50}: 1.8 μg/ml Nutan et al. (2013) | Aqueous extract of leaves showed inhibitory effects on histamine synthesis in rat peritoneal as well as mast cells. Dose: 100 mg/kg Prasad et al. (2009), Negi and Dave (2010) |
| C1.2     | *Adhatoda vasica* Nees/Adusa/Acanthaceae/Leaves | Methanolic extract of leaves inhibit DTH reactiveness, increased the percentage neutrophil adhesion, promoting increased phagocytic activity vis-a-vis increased concentration of lytic enzymes for more effective killing. Dose: 400 mg/kg Vinthapaopoo and Sundar (2011) | Ethanolic leaf extract inhibit the activity of HIV-Protease. HIV-protease plays a significant part in the replication cycle. Singh et al. (2010) | Ethanol extract inhibited IC_{50} dependent caspase mediator release. Dose: 20 mg/kg Gibbs (2009), Hossain and Hoq (2016) |
| C1.3     | *Aegle marmelos* (L.) Correa/Bael/Rutaceae/Root, stem bark, fruits | Alcoholic extract stimulates immune system by acting through cellular and humoral immunity. Dose: 100 and 500 mg/kg Patel and Asdaq (2010) | Purified seselin showed inhibitory potential over multiple SARS-COV-2 targets and holds a high potential to work effectively as a novel drug for COVID-19. Nivetha et al. (2020) | Ethanol extract inhibits production of nitric oxide (NO) by rat peritoneal cells, anti-histamine effect, and membrane stabilization activity. Dose: 200 mg/kg Kumari et al. (2014) |
| C1.4     | *Anacyclus pyrethrum* (L.) Lag./Akkal kadha/ Asteraceae/Root | Petroleum ether extract inhibit DTH reactivity, increased the percentage of T and B lymphocytes and also suppresses lymphoproliferation in splenocytes. Dose: 10 μM Parighati et al. (2016) | Methanolic leaf extract showed significant inhibition of DENV infected THP-1 cells. IC_{50}: 100 μg/ml Sharma N. et al. (2019) | Andrographolide attenuate allergic asthma by inhibition of the NF-kappaB signaling pathway. Dose: 0.1, 0.5, and 1 mg/kg Bao et al. (2009) |
| C1.5     | *Andrographis paniculata* (Burm.f.) Nees/ Kalmegh/Acanthaceae/Leaves | Isolated compound of andrographolide modulate immune responses by regulating macrophage phenotypic polarization and MAPK and PI3K signaling pathways regulate macrophage polarization. Dose: 10 μg/ml (In vitro) and 1 mg/kg (In vivo) Wang et al. (2010) | Alcoholic extract inhibit the viral titer in A549 cells transfected with SRV. They showed the activity through p38 MAPK/Nrf2 pathway. Dose: 50 μg/ml Churiyah et al. (2015), Wintachai et al. (2015) | Alcoholic extract of leaves in mouse model of ovalbumin- (OVA) induced allergic asthma significantly increased the expression of the envelope and NS1 proteins in DENV-infected THP-1 cells. IC_{50}: 100 μg/ml Sharma N. et al. (2019) |
| C1.6     | *Carica papaya* L./Papaya/Caricaceae/Leaves, fruits | Alcoholic extract of fruit pulp and seed enhanced phagocytic activity of peritoneal macrophages is correlated with T helper 1 cytokine response. Interferon-gamma increases the phagocytosis process. Dose: 0.11 g/ml extract every day using a gastric cannula Amin et al. (2019) | Aqueous extract of the C. papaya leaves increases the expression of the envelope and NS1 proteins in DENV-infected THP-1 cells. IC_{50}: 100 μg/ml Sharma N. et al. (2019) | Alcohol extract of leaves in mouse model of ovalbumin- (OVA) induced allergic asthma down regulates IL-4, IL-5, eotaxin, TNF-α, NF-κB, and INOS levels thus exhibit anti-inflammatory effect. Dose: 100 mg/kg Inam et al. (2017) |
| C1.7     | *Cassia occidentalis* L./Kasundra/Fabaceae/Aerial part, seeds | Isolated rheum suppresses the functional responses of the T- and B-lymphocytes and also suppresses lymphoproliferation in splenocytes. Dose: 10 μM Panigrahi et al. (2016) | Alcohol extract showed that the plant possessed an anti-HIV property through inhibition of viral reverse transcriptase activity. IC_{50}: >100 mg/ml Estani et al. (2012) | Isolated anthraquinone showed anti-inflammatory potential by decreasing mRNA expression of Th1/Th2 cytokine in lung tissue. Dose: 250, 500 and 2000 mg/kg Xu et al. (2018) |
| C1.8     | *Cocculus hirustus* (L.) Diels/Patalagarudi/ Menispermaceae/Whole plant | Methanolic extract showed significantly enhanced specific and non-specific activity on various immune paradigm in cyclophosphamide induced immunosuppressed animals. Dose: 200 mg/kg Malik and nayak (2014) | Found effective against all strains of dengue virus and SARS CoV 2 in in vitro studies, hence under phase 2 clinical trial as phytopharmaceutical drug against COVID 19 at 12 centers. (https://www.clinicaltrialsarena.com/news/sun-pharma-covid-19-trial/) | The methanolic leaf extract showed significant analgesic activity in mice as well as significant anti-inflammatory activity using in vitro and in vivo rat models. Dose: 100 mg/kg Sengottuvelu et al. (2012) |
| C1.9     | *Cordia myxa* L./Sapistan/Boraginaceae/Fruits | Aqueous extract of C. myxa fruits significantly increased the delayed type hypersensitivity (DTH), mitotic index (MI) of bone marrow and spleen cells Ali et al. (2015) | Dichloromethane, ethyl acetate, and methanol stem extracts showed anti-viral potential against HIV-1 using the syncytia formation assay. IC_{50}: 21.8 μg/ml Rashid et al. (2014) | Dichloromethane extract inhibit the oxidant stress factors that lead to progression of colitis. Dose: 100 mg/kg Ranjhan et al. (2013) |
TABLE 5 | (Continued) List of Indian Medicinal Plants/AYUSH drugs with proven immunomodulatory, antiviral and anti-allergic/anti-inflammatory/anti-asthmatic activity having potential for exploring against COVID 19 categorized for prioritization on the basis of their earlier reports.

| Category | Botanical name/Common name/Family/Part | Immunomodulatory activity | Anti-viral activity | Anti-allergic/anti asthmatic/anti-inflammatory/respiratory disorders |
|----------|----------------------------------------|---------------------------|-------------------|---------------------------------------------------------------|
| C1.10    | *Curcuma longa* L./Haldi/Zingiberaceae/Rhizome | Lyophilized turmeric was found to decrease spleen weight, decrease the proportion of CD4⁺, CD8⁺ T cells, and decrease phagocytic activity. **Dose:** 1 and 2% (w/w) Kim et al. (2014). Poly saccharide fraction of aqueous extract of C. longa inhibiting the secretion of IL-12 and PGE₂. **Dose:** 0.8–500 μg/ml Chandrasekaran et al. (2013) | Aqueous extract of C. longa suppressed the HBV replication and the transcription of HBV genes in HepG2 cells which produce HBV particles. **Dose:** 200 mg/L and 500 mg/L Kim et al. (2005). Isolated curcuminoids from aqueous extract of curcuma longa exhibited significant inhibitory activity against the neuraminidases from novel influenza H1N1 (WT) and oseltamivir-resistant novel H1N1 (H274Y mutant) expressed in 293 T cells. **IC₅₀:** 6.18 ± 0.64 to 40.17 ± 0.79 μg/ml Dao et al. (2012). Virtual screening of curcumin and its analogue found its activity SARS CoV 2 surface proteins and is under clinical trial. (https://chemrxiv.org/articles/Identification-of-compounds-from-nigella-sativa-as-new-potential-inhibitors-of-2019-novel-coronavirus-COVID-19-molecular-docking-study/12055716/) | Alcoholic extract of C. longa ameliorates food allergy by maintaining Th1/Th2 immune balance in ovalbumin challenged mice. **Dose:** 100 mg/kg Shin et al. (2015) |
| C1.11    | *Cynodon dactylon* (L.) Pers./Doorna/Poaceae/Whole plants | Fresh juice of the grass increased humoral antibody response upon antigen challenge, significant increase in antibody titer in the haemagglutination antibody assay and plaque forming cell assay. **Dose:** 250 and 500 mg/kg Mangathayaru et al. (2009) | Alcoholic dried extract showed virustatic and virucidal activity against porcine reproductive and respiratory syndrome virus (PRRSV) and also significantly inhibits replication of PRRSV. **Dose:** 0.78 mg/ml Pringproa et al. (2014) | Chloroform extract of whole plant produces a bronchodilation via antimuscarinic calcium channel blocking activators and phosphodiesterase inhibition activity. **Dose:** 5, 10, 50 and 100 mg/kg Patel et al. (2013) |
| C1.12    | *Jatropha curcas* L./Euphorbiaceae/Leaves, roots | Phytoconstituents of hydroalcoholic extract ameliorated both cellular and humoral antibody response. **Dose:** 0.25, 0.5, 1 mg/kg Abd-Ala et al. (2009) | Successive extract of J. curcas was evaluated by inhibition of HIV replication as determined by HIV p24 antigen ELISA showed 100% inhibition by methanolic and 97.19% inhibition by aqueous extract. **IC₅₀:** 0.0255–0.4137 mg/ml (aqueous) and 0.00073–0.1278 mg/ml (Methanolic) Dahake et al. (2013) | Isolated jatrophacine showed anti-inflammatory potential to act as COVID-19 treatment in docking studies. (https://chemrxiv.org/articles/Identification-of-compounds-from-nigella-sativa-as-new-potential-inhibitors-of-2019-novel-coronavirus-COVID-19-molecular-docking-study/12055716/) |
| C1.13    | *Mollugo cerviana* (L.) Ser./Grishmasundara/Moluginaceae/Whole plant | Alcoholic extracts increase NO release by peritoneal cells. **Dose:** 25 μg/ml Ferreira et al. (2003) | Alcoholic extract exhibits antiviral properties for both chikungunya virus and dengue virus. **Dose:** 1.8 mg/ml Jain et al. (2019) | Hydroalcoholic extract inhibit the levels of lipid peroxides, acid phosphatase, and gamma-glutamyl transpeptidase activity. **Dose:** 1 mg/g Sadique et al. (1987) |
| C1.14    | *Nigella sativa* L./Kalonji/Ranunculaceae/Seeds | Aqueous extract of N. sativa enhance the proliferative capacity of splenocytes and T lymphocytes, suppression of IFNγ secretion from splenocytes. **Dose:** 10, 50, and 100 g/ml Majdalaweih et al. (2010) | Nigellidine and α- hederin found to have the best potential to act as COVID-19 treatment in docking studies. (https://chemrxiv.org/articles/Identification-of-compounds-from-nigella-sativa-as-new-potential-inhibitors-of-2019-novel-coronavirus-COVID-19-molecular-docking-study/12055716/) N. sativa seeds oil possesses a striking antiviral effect against MCMV infection. **Dose:** 100 mg/100 ml/mouse Umar et al. (2016) | Aqueous extract of seed showed sensory receptors mediating reflex bronchoconstriction and tachykinin receptor antagonists. **Dose:** 3.3% w/w extract Boskabady et al. (2003) |

(Continued on following page)
### TABLE 5 (Continued) List of Indian Medicinal Plants/AYUSH drugs with proven immunomodulatory, antiviral and anti-allergic/anti-inflammatory/anti-asthmatic activity having potential for exploring against COVID 19 categorized for prioritization on the basis of their earlier reports.

| Category | Botanical name/Common name/Family/Part | Immunomodulatory activity | Anti-viral activity | Anti-allergic/anti asthma/anti-inflammatory/respiratory disorders |
|----------|----------------------------------------|---------------------------|---------------------|---------------------------------------------------------------|
| C1.15    | Ocimum sanctum L./Tulsi/Lamiaceae/Leaves | Aqueous extract of leaves showed regulation of IL-2 production and exhibited leukocytosis and augmentation of T & B cells. Dose: 250 mg/kg Goel et al. (2010) | Hydroalcoholic extract showed promising antiviral properties against H1N2 virus by inhibition of a stage in viral intracellular multiplication and non-specific interference with virus-cell interactions. Dose: 135, 67, 33 mg/0.1 ml Ghokhe et al. (2016)Tulsiol and dihydroeugenol have been found effective against SARS CoV 2 in molecular docking studies. (https://papers.ssrn.com/sol3/papers.cfm abstract id = 3554371) | Alcoholic extracts showed anti-asthmatic potential through inflammatory mechanism by inhibiting LTC4, LTA4 and COX-2 in HL-60 cell lines and reduction in inflammation in asthma mice model. IC₅₀: 1–10 μg/mlDose: 100 mg/kg Soni et al. (2019) |
| C1.16    | Phyllanthus emblica L./Amla/Phyllanthaceae/ Fruits | Alcoholic extract of fruits stimulate B and T lymphocyte and restored the interleukin production considerably. Dose: 10 mg to 1 mg/ml Sai Ram et al. (2002) | Chloroform extract decreased the expression or function of HCV NS5B protease in a dose dependent manner and GAPDH remained constant. Dose: 100 μg/ml Javed et al. (2011) | Alcohol extract exhibits anti-inflammatory and anti-oxidant activity by protecting RAW264.7 cells from oxidative damage by increasing glutathione content and total superoxide dismutase activity, suppressing MDA content and decreasing release of pro-inflammatory mediators. IC₅₀: 0.677 ± 0.029 mg/ml Li W. et al. (2020) |
| C1.17    | Solanum nigrum L./Makoi/Solanaceae/Seeds, barriers | Isolated polysaccharides of significant increment in the percentage of CD4⁺ T lymphocyte and a decrease in the percentage of CD8⁺ T lymphocyte of tumor-bearing mice peripheral blood. Dose: 90, 180, 360 mg/kg Li et al. (2009) | Alcohol extract and its fraction inhibit HCV by binding with HCV NS5B protein. Dose: 200 μg/ml Ganta et al. (2017) | Petroleum ether extract of berries inhibits asthma by inhibiting increase in leukocyte and eosinophil count, protection against mast cell degranulation and resisting contraction due to presence of β-sitosterol. Dose: 50, 100 and 200 mg/kg Nirmal et al. (2012) |
| C1.18    | Valeriana wallichii DC./Valerianaceae/Roots | Alcoholic root extract inhibited HCV by binding with HCV NS5B protein.Dose: 250 μg/ml Ganta et al. (2017) | Alcohol extract and its fraction inhibit HCV by binding with HCV NS5B protein. Dose: 200 μg/ml Ganta et al. (2017) | Crude extract showed protection against airway disorders through relax ion of the low K⁺ (25 mM)-induced contractions with a mild effect on the contractions induced by high K⁺ (80 mM). Dose: 0.03–3.0 mg/ml Khan and Gilani (2012) V. negundo leaf oil inhibit COX-2 without much interfering COX-1 pathways. Dose: 500 μL/kg Chattopadhyay et al. (2012) |
| C1.19    | Vitex negundo L./Renuka/Verbanaceae/Leaves | Hydroalcoholic extract of leaves of V. negundo activate the phagocytes cells such as macrophages and neutrophils. Dose: 200 mg/kg Ladi et al. (2016) | Alcohol extract of leaves inhibits HIV-1 reverse transcriptase activity in vitro assay thus exhibits anti-HIV activity. Dose: 200 μg/ml Kannan et al. (2012) | Hydro-alcoholic root extract of W. somnifera showed antiviral properties against IBD virus by cytopathic effect reduction assay. Dose: 25 μg/ml Pant et al. (2012). Withanolone and withaferin a have been found effective against SARS CoV 2 in bioinformatics studies and asgandh extract is under clinical trial. (https://www.researchsquare.com/article/rs-17806/v1), (http://www. bioinformation.net/016/97320630016411.pdf) |
| C1.20    | Withania somnifera (L.) Dunal/Asgand/ Solanaceae/Roots | Aqueous suspension of root showed potent inhibitory activity toward mitogen induced proliferative response of T-lymphocyte and delayed-type hypersensitivity reaction. Dose: 1000 mg/kg Rasool and Varalakshmi (2008) | Hydro-alcoholic root extract of W. somnifera showed antiviral properties against IBD virus by cytopathic effect reduction assay. Dose: 25 μg/ml Pant et al. (2012). Withanone and withaferin a have been found effective against SARS CoV 2 in bioinformatics studies and asgandh extract is under clinical trial. (https://www.researchsquare.com/article/rs-17806/v1), (http://www. bioinformation.net/016/97320630016411.pdf) | Aqueous extract of withania root inhibit histamine and 5-HT in early phase and prostaglandins in delayed phase of inflammatory reaction. Dose: 1000 mg/kg Sahni and Srivastava (1993) |

(Continued on following page)
| Category. Sl no | Botanical name/Common name/Family/Part | Immunomodulatory activity | Anti-viral activity | Anti-allergic/anti-inflammatory/respiratory disorders |
|----------------|----------------------------------------|---------------------------|-------------------|-----------------------------------------------------|
| C1.21 | Zingiber officinale Rosc/Sunthi/Zingiberaceae/ Rhizome | Volatile oil of ginger influences both cell-mediated immune response and nonspecific proliferation of T lymphocyte. \( \text{Dose: 0.125, 0.25, and 0.5 g/kg} \) Zhou et al. (2006) | Aqueous extract effective against HRSV-induced plaque formation on airway epithelium by blocking viral attachment and internalization. \( \text{IC}_{50} > 150 \mu g/ml \) Chang et al. (2013) | Aqueous and alcoholic extract showed anti-inflammatory activity by reducing inflammation through suppression of Th2-mediated immune response. \( \text{Dose: 500 mg/kg (alcoholic extract)/720 mg/kg (aqueous extract)} \) Khan et al. (2015) |
| C2.1 | Abutilon indicum (L.) Sweet/Tuthi/Malvaceae/ Aerial parts | Alcoholic extract showed stimulatory effect on T lymphocytes. Increasing doses of showed higher HA titer value, restoration of WBC count. It also increased lymphocyte and E-rosette formation. \( \text{Dose: 200 and 400 mg/kg Gaikwad and Krishna Mohan (2012)} \) | Alcoholic extract of leaves showed anti-MCV and anti-HSV activities. \( \text{Dose: 0.4 µg/ml Vimalanathan et al. (2009)} \) | Methanolic extract of aerial part showed mast cell stabilizing and anti-inflammatory activity. \( \text{Dose: 250 and 500 mg/kg Mehta and Paranjape (2008)} \) |
| C2.2 | Achyranthes aspera L./Apamarga/Amaranthaceae/Root | Polyphenolic compounds of hydroalcoholic extract showed cytokine based immunomodulatory role. \( \text{Dose: 100 mg/kg Narayan and Kumar (2014)} \) | Alcohol extract showed potential activity against herpes simplex virus type-1 and type-2 by inhibiting the early stage of multiplication in vero cells. \( \text{Mukherjee et al. (2013)} \) | Ethyl acetate fraction from methanolic extract showed in vitro anti-inflammatory activity. \( \text{IC}_{50}: 50 = 76 ± 0.14 \) Khuda et al. (2013) |
| C2.3 | Aloe vera (L.) Burm.f/Ghrit kumari/ Asphodelaceae/Roots, leaves | Aloe vera gel administration did not increase ovalbumin (OVA)-specific cytotoxic T lymphocyte (CTL) generation in normal mice. \( \text{Dose: 100 mg/kg Im et al. (2010)} \) | Isolated anthraquinone showed anti-viral activity by inhibiting virus replication. \( \text{IC}_{50}: 13.70 ± 3.80 \) to 62.31 ± 3.05 Borges-Araglez et al. (2019) | Polysaccharide isolated from gel showed anti-allergy potential by inhibition of type 2 helper T cell (Th2) immune response, increase in IL-10 production and stimulating type 1 regulatory T (Tr1) cells activation. \( \text{Dose: 50 and 100 mg/kg Lee D. et al. (2018)} \) |
| C2.4 | Alistonia scholaris (L.) R.Br./Saptaparni/ Apocynaceae/Bark | Aqueous extract enhanced phagocytic activity. \( \text{Dose: 50 mg/kg Ivo et al. (2003)} \) | Aqueous and alcoholic plant extract showed anti-viral potential against coxsackie B5, polio virus and herpes simplex virus. \( \text{Dose: 2.8 mg/kg Antony et al. (2014)} \) | Aqueous extract showed anti-inflammatory and analgesic activity by in chemical and thermal induced pain models in albino rats. \( \text{Dose: 50, 25, and 50 mg/kg Zhao et al. (2017)} \) |
| C2.5 | Azadirachta indica A.Juss./Neem/Meliaceae/ Leaves | Dried powdered leaves significantly enhanced the antibody titers against new castle disease virus (NCDV) antigen. \( \text{Dose: 2 g/kg Saclekar et al. (1998)} \) | Isolated polysaccharides from aqueous extract of the leaf virucidal against Poliovirus-1 (inhibiting initial stage of viral replication). \( \text{IC}_{50}: 80 \mu g/ml and 77.5 \mu g/ml Faccon-Gahardi et al. (2012)} \) | Isolated leaves extract showed anti-inflammatory potential, which may be attributed to its inhibitory activity on macrophage-derived cytokine and mediators. \( \text{Dose: 50, 100, and 200 mg/kg Kumar et al. (2016)} \) |
| C2.6 | Berberis aristata DC./Daruharidra/ Berberidaceae/Bark | Isolated berberine inhibited the suppressed viral infection-induced up-regulation of TLR7 signaling pathway. \( \text{Dose: 20 mg/kg Yan et al. (2018)} \) | Alcoholic extract showed potent anti-viral activity against both influenza virus a and HSV-1. \( \text{IC}_{50}> 6.25 \mu g/ml \) Rajbhanderi et al. (2009) | Alcohol extract exhibited significant anti-inflammatory activity in carrageenan-induced rat paw edema manner. \( \text{Dose: 300 mg/kg Sinha et al. (2001)} \) |
| C2.7 | Berberis ciliata (Haw.) Sternb./Pashanbhed/ Saxifragaceae/Stem | Alcoholic extract stimulated the expression of CD69 on lymphocytes. \( \text{Dose: 3.13 and 6.25 mg/ml Turnova et al. (2018)} \) | Hydroalcoholic extract of C. sinensis inhibited ADV replication in post-adsorption stage. \( \text{IC}_{50}: 6.62 \mu g/ml Karimi et al. (2016)} \) | Aqueous extract showed anti-inflammatory potential by increasing expression of Th1 cell-specific anti-asthmatic biomarkers (tumor necrosis factor-\( \alpha \) and interferon-\( \gamma \)) and decreasing the expression of anti-asthmatic cytokines in the lungs. \( \text{Dose: 25 µg/ml Heo et al. (2008)} \) |
| C2.8 | Camellia sinensis (L.) Kuntze/Chary/Theaceae/ Leaves | Aqueous extract of C. sinensis changes hematological profile, immuno potentiating cells, cellular response in splenectomised mice. \( \text{Dose: 250 and 500 mg/kg Gomes et al. (2014)} \) | \( \text{Continued on following page} \) | \( \text{Continued on following page} \) |
| Category. Sl no | Botanical name/Common name/Family/Part | Immunomodulatory activity | Anti-viral activity | Anti-allergic/anti-asthmatic/anti-COPD through affecting the expression of specific airway epithelial cell genes that modulate Th1 processes using in vitro assay. Dose: 2,4, 1.2, and 0.6 μg/ml Mambreri et al. (2020) |
|----------------|----------------------------------------|--------------------------|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| C2.9 Cannabis sativa L./Ajaya/Cannabaceae/Leaves | Cannabinoids indicating mainly immunosuppressive effects on macrophages, NK cells, T lymphocytes and their ability to produce cytokines. Dose: 5 mg/day Killestein et al. (2000) | C. sativa inhibited viral DNA synthesis. It inhibit the replication cycle of various types of DNA or RNA viruses Jasim and Naji (2003) Hot water extract C. sativa reduced the plaque forming ability. Dose: 300-500 μg/ml Kurokawa et al. (1993) Hydroalcoholic extract of C. sativa suppressed extracellular HBV DNA production. Dose: 100 μg/ml Indrasetiawan et al. (2019) | Oil extract of C. sativa protective effect against COPD through affecting the expression of specific airway epithelial cell genes that modulate Th1 processes using in vitro assay. Dose: 2,4, 1.2, and 0.6 μg/ml Mambreri et al. (2020) |
| C2.10 Cassia fistula L./Amlatas/Fabaceae/Bark | Hydro alcoholic extract of C. fistula increased antibody titer against salmonella typhimurium ‘O’ antigen and significant enhancement in skin thickness in DNCB sensitized albino rats. Dose: 125 mg/kg, 250 mg/kg and 500 mg/kg (Laxmi 2015) | Hydroalcoholic extract of C. fistula suppressed extracellular HBV DNA production. Dose: 100 μg/ml Indrasetiawan et al. (2019) | Isolated rhein showed anti-inflammatory activity by modulating levels carrageenan-induced hind paw edema, croton oil-induced ear oedema, cotton pellet-induced granuloma and acetic acid-induced vascular permeability models. Dose: 10 mg/kg Antonisamy et al. (2019) |
| C2.11 Cinnamomum verum J.Presl./Daarchini/Lauracea/Stem, bark | Bark suspension increased the phagocytic index in carbon clearance test, neutrophil adhesion and serum immunoglobulin levels and antibody titer values. Dose: 10 and 100 mg/kg Naphade et al. (2009) | Aqueous extract provide treatment against influenza virus infections in vero cells transfected with H7N9 influenza. Brochet et al. (2017) | Isolated procyanidine showed reduction in the filtration in inflammation. Dose: 125 μg/ml 50:1 Sood et al. (2020) |
| C2.12 Cissampelos pareira L./Akamai/Menispermacaeae/Aerial parts, roots | Isolated alkaloid fraction of alcoholic extract modulate both T and B cell mediated immune response. Dose: 100 mg/kg Bafna and Mishra (2010) | Alcoholic extract of aerial part of C. pareira inhibit the viral replication and ability to down-regulate the production of TNF-α, a cytokine implicated in severe dengue disease. IC50 ≥ 125 μg/ml Sood et al. (2015) | Isolated sesquiterpenes from alcoholic extract showed anti-allergic potential against immediate-type as well as delayed-type hypersensitivity. Dose: 100 mg/kg Bafna and Mishra (2010) |
| C2.13 Cypereus rotundus L./Musta/Oypereaceae/ Rhizome | Aqueous, alcoholic, ethyl acetate and total oligomer flavonoids (TOF) extracts of C. rotundus influence humoral-mediated immunity by stimulating B and T cell proliferation. Dose: 1–1000 μg/ml Soumaya et al. (2013) | Aqueous, alcoholic and ethyl acetate extract of C. rotundus inhibited the HBV DNA replication in HepG2.2.15 cell line. IC50 29.0, 21.5, 263.4 μg/l Xu et al. (2015) | Ethyl acetate extract showed anti-inflammatory effects by inhibiting macrophage proinflammatory function by reducing LPS-induced production of IL-1β, TNF-α, COX-2-derived PGE2 and iNOS-ill-synthesized NO. Dose: 1–100 μg/ml Harzi et al. (2011) |
| C2.14 Daphne gnidium L./Lota/Thymelaeaceae/Aerial part | Dichloromethane extract of the aerial exhibited strong antiretroviral activity by interference with HIV co-receptors, CCR5 and CXCR4, Vidal et al. (2012) | Dichloromethane extract of the aerial parts exhibited strong antiretroviral activity and absence of cytotoxicity and pure compounds were active against multidrug-resistant viruses irrespective of their cellular tropism. Dose: 10 μg/ml Vidal et al. (2012) | Ethyl acetate extract showed anti-inflammatory effects by inhibiting macrophage proinflammatory function by reducing LPS-induced production of IL-1β, TNF-α, COX-2-derived PGE2 and iNOS-ill-synthesized NO. Dose: 1–100 μg/ml Harzi et al. (2011) |
| C2.15 Ficus carica L./Anjeer/Moraceae/Leaves, latex | Administration of extract ameliorated both cellular and humoral antibody response Patil et al. (2010) | Resuspension of latex in DMEM containing 1% ethanol able to interfere with the replication of CphV-1. IC50 100 μg/ml Camero et al. (2014) | Tea infusion of leaves showed anti-allergy potential through promotion of dissociation of IgE from FcεRI receptors. Dose: 10 ml/kg Abe (2020) |
| C2.16 Glycyrrhiza glabra L./Mulethi/Fabaceae/Roots, rhizome and leaves | Aqueous root extract showed leukocyte count and phagocytic index increased as well as cellular immune response study, an enhancement in foot pad thickness was observed. Dose: 1.5 g/kg Mitra Mazumder et al. (2012) | Aqueous and alcoholic extracts of G. glabra verified hemagglutination (HA) test data through which amount of virus is quantified from the allantonic fluid of chicken embryos. Dose: 300 μg/ml Arshaf et al. (2017) | Saponin fraction showed anti-asthmatic potential in triple antigen sensitized rats by inhibition of mast cell degranulation. Dose: 100 mg/kg Patel et al. (2009) |
| C2.17 Ilicium verum Hook.f./Takicka/Magnoliaceae/ Fruit | Isolated lectins from I. verum showed immunomodulatory action by stimulating phagocytic function. Dose: 30 and 50 mg/kg Bouadi et al. (2015) | Aqueous, alcoholic and hydroalcoholic extracts exhibited inhibitory effects against NDV and avian reovirus. Dose: 0.24–3.9 mg/ml Ahaj et al. (2020) | 70% alcoholic extract exert antiasthmatic effects through upregulation of Foxp3 regulatory T cells and inhibition of Th2 cytokines. Dose: 50, 100, and 200 mg/kg Sung et al. (2017) |
TABLE 5 | (Continued) List of Indian Medicinal Plants/AYUSH drugs with proven immunomodulatory, antiviral and anti-allergic/anti-inflammatory/anti-asthmatic activity having potential for exploring against COVID 19 categorized for prioritization on the basis of their earlier reports.

| Category | Botanical name/Common name/Family/Part | Immunomodulatory activity | Anti-viral activity | Anti-allergic/anti-asthmatic/anti-inflammatory/respiratory disorders |
|----------|-----------------------------------------|---------------------------|---------------------|---------------------------------------------------------------|
| C2.18    | Mentha × piperita L./Peppermint/Lamiaceae/Leaves | Hydrodistillate fractions of M. piperita affect the functional responses of human PMNs and PBMCs. **Dose:** 2 mM and 12 µL Cosentino et al. (2009) | Alcoholic extract showed antiviral activity against RSV with a high selectivity index, and significantly decreased the production of NO, TNF-α, IL-6, and PGE2 in lipopolysaccharide-stimulated RAW 264.7 cells. **IC<sub>50</sub>:** 10.41 µg/ml Li et al. (2017) | Essential oil showed antispasmodic activity by regulating prostaglandins and nitric oxide synthase on rat trachea. **Dose:** 1–300 µg/ml de Sousa et al. (2010) |
| C2.19    | Mentha spicata L./Spearmint/Lamiaceae/Leaves | Essential oil showed antispasmodic activity by regulating prostaglandins and nitric oxide synthase on rat trachea. **Dose:** 2 mM and 12 µL Lii et al. (2009) | Aqueous extract exhibits antiviral potential against porcine parvovirus (PPV) in vitro by efficiently killing them and control their multiplication in cells. **IC<sub>50</sub>:** 0.0340 mg/ml Welli et al. (2011) | Ethyl acetate soluble fraction of leaves by inhibit antigen stimulated rat basophile. Prasad et al. (2009) |
| C2.20    | Momordica charantia L./Bitter guard/ Cucurbitaceae/Leaves, fruits and seed | Alcohol and diethyl ether extract has been found that the exposure of neutrophils and macrophages stimulates both their capacity to ingest foreign particles and their intracellular killing activities. **Dose:** 250, 500, 1000 mg/kg Mahamat et al. (2020) | Crude protein fraction of M. charantia strongly inhibited H1N1, H3N2 and H5N1 subtypes. **IC<sub>50</sub>:** 40–200 µg/ml Pongthanapisith et al. (2013) | Alcohol extract showed the highest reduction of LPS-induced NO, iNOS and prostaglandin E2 production and down regulates pro-interleukin-1β and NF-κB activation expression in RAW 264.7 macrophages Li et al. (2009) |
| C2.21    | Morus alba L./Sahatoot/Moraceae/Leaves, fruits | Isolated water soluble polysaccharides stimulates murine RAW264.7 macrophage cells to release chemokines and proinflammatory cytokines. Lee et al. (2013). Alcohol extract of leaves significant increase in the phagocytic index and adhesion of neutrophils. **Dose:** 100 mg/kg and 1 g/kg Bharani et al. (2010) | M. alba fruits juice and its fractions inhibit internalization and replication of MNV-1, whereas it may influence adherence or internalization of FCV-F9 virions. **EC<sub>50</sub>:** 0.005 (MNV-1) and 0.25–0.30 (FCV-F9) Lee et al. (2014) | Juice of M. alba fruits inhibit production of NO and proinflammatory cytokines (TNF-α, IL-6), as well as the expression of NOS2 and PTGS2 in LPS-stimulated RAW264.7 macrophages. **Dose:** 0.1, 0.5, and 1 µg/ml Jung et al. (2019) |
| C2.22    | Nyctanthes arbor-tristis L./Parijata/Oleaceae/Leaves, flowers and seeds | Immunostimulant activity of NAFE seems to be mediated through splenocytes proliferation and increased production of cytokines, especially IL-2 and IL-6 of aqueous extract of Nyctanthes arbor-tristis. **Dose:** 400 and 800 mg/kg Bharshiv et al. (2016) | n-Butanol fraction of alcoholic extract of protected encephalomyocarditis virus (EMCV) infected mice against semliki forest virus (SFV). **Dose:** 125 mg/kg Gupta et al. (2005) | Alcoholic extract showed anti-asthmatic and anti-tussive activity against histamine and acetylicholine cocktail induced asthma and citric acid induce cough in Guinea pig. **Dose:** 100, 200, and 300 mg/kg Mathur et al. (2018). Extracted polysaccharide from leaves aqueous extract reduce the number of cough efforts without influencing the specific airway resistance, it triggers cough reflex provocation. **Dose:** 25 and 50 mg/kg Ghosh et al. (2015) |
| C2.23    | Ocimum basilicum L./Basil/Lamiaceae/Leaves | Hydroalcoholic extract of leaves increased the IFN-γ/IL-4 ratio and decreasing BALF levels of IgE, PLA<sub>2</sub> and TP. **Dose:** 50,300, 600 mg/kg Eftekhar et al. (2019b) | Alcoholic extract inhibit ZIKV replication in vero E6 cells. The extract seems to inhibit the virus at the step of attachment and entry into the host cell. **IC<sub>50</sub>:** 1:134 Singh et al. (2019) | Hydroalcoholic extract showed therapeutic effect on asthma by reducing eosinophil’s, monocytes, neutrophils percentage and increase in percentage of lymphocytes and antioxidant biomarkers levels. **Dose:** 0.75, 1.50, and 3.00 mg/ml Eftekhar et al. (2019a) |
| C2.24    | Oleo europea L./Zaitoon/Oleaceae/Leaves | Isolated oleuropein from hydroalcoholic extract showed lymphocyte activation and proliferation properties. Oleuropein exhibited a high degree of lymphocyte aggregation. **Dose:** 540 µg/ml Randon and Attard (2007) | Aqueous leaves extract showed anti-viral potential against Newcastle disease virus by restricting replication. **Concentration:** 1000 µg/ml Saith et al. (2017) | Essential oil from leaves inhibit NFB activation in monocytes and monocyte derived macrophages. Lucas et al. (2011) |

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TABLE 5 | (Continued) List of Indian Medicinal Plants/Ayush drugs with proven immunomodulatory, antiviral and anti-allergic/anti-inflammatory/anti-asthmatic activity having potential for exploring against COVID 19 categorized for prioritization on the basis of their earlier reports.

| Category | Botanical name/Common name/Family/Part | Immunomodulatory activity | Anti-viral activity | Anti-allergic/anti-inflammatory/respiratory disorders |
|----------|---------------------------------------|---------------------------|---------------------|-----------------------------------------------|
| C2.25    | Panax ginseng C.A.Mey./Ginseng/Araliaceae/Roots | Ginsenosides increased the number of spleen plaque-forming cells, the titer of sera hemagglutinins as well as the number of antigen-reactive T-cells and splenocyte natural killer activity. **Dose:** 10 mg/kg [Buniana et al. (1990)] | Fermented extract improved the survival of human lung epithelial cells, inhibits RSV replication, suppressed the expression of RSV-induced inflammatory cytokine genes and the formation of ROS in epithelial cell cultures. **Dose:** 25 mg/kg [Wang et al. (2012)] | P. ginseng extract showed anti-asthmatic activity by restoring EMBP(eosinophil major basic protein), Muc5ac, CD40, and CD40L expression and mRNA and protein levels of IL-1, IL-4, IL-5, and TNF-α. **Dose:** 20 mg/kg [Kim and Yang (2011)] |
| C2.26    | Peganum harmala L./Harmal/Nitrariaceae/Aerial parts and seeds | Alcoholic extract (80%) of seed showed effects on zymosan-A activated neutrophils (PMNs). **Dose:** 25, 50, and 100 μg/ml [Kim and Yang (2011)] | Alcoholic extract inhibits viral RNA replication and viral polymerase activity. **IC50:** 9.87 μg/ml [Moradi et al. (2017)] | Alkaid fraction of alcoholic extract showed potent antitussive, expectorant and bronchodilating activities in cough models of mice and Guinea pigs. **Dose:** Total extract (1650 mg/kg) and alkaloid fraction (90 mg/kg) [Liu et al. (2015)] |
| C2.27    | Phyllanthus amarus Schumach. and Thonn./Bhui amta/Phyllanthaceae/Whole plant | Alcoholic extract of aerial parts exhibited potent inhibitory action on both phagocytic and CD18 expression of phagocytes. **Dose:** 6.25–100 μg/ml [Jantan et al. (2014)] | Aqueous extract inhibited cellular proliferation and suppressed HBsAg production in human hepatoma cells. **Dose:** 1 mg/ml [Yeh et al. (1993)] | Alcoholic extract attenuates asthma by exhibiting relaxation effect against histamine and acetylcholine induced contraction model in Guinea pigs. **Dose:** 25 mg/kg (in vivo), 10 and 100 mg/ml (in vitro) [Singal et al. (2013)] |
| C2.28    | Picrorhiza kurroa royle ex Benth./Kutki/Plantaginaceae/Rhizome, leaves | Hydroalcoholic extract stimulate cell-mediated and humoral immunities, along with complement activity and phagocytic function. **Dose:** 25, 50, 100 mg/kg [Sharma et al. (1994)] | Isolated iridoids from chloroform fractionated alcoholic extract of inhibit expression of vpr in TREx-HeLa-vpr cells and these iridoid are naturally occurring vpr inhibitors. **IC50:** 0.15 mM for HBsAg and 0.14 mM for HBeAg [Jiang et al. (2013)] | Alcoholic extract attenuates asthma by exhibiting relaxation effect against histamine and acetylcholine induced contraction model in Guinea pigs. **Dose:** 25 mg/kg (in vivo), 10 and 100 mg/ml (in vitro) [Singal et al. (2013)] |
| C2.29    | Piper longum L./Pipli/Piperaceae/Fruits | Aqueous extract possessed a demonstrable immunostimulatory activity, both specific and nonspecific, as evident from the standard test parameters such as haemagglutination titer, macrophage migration index and phagocytic index. **Dose:** 225 mg/kg [Tripathi et al. (1999)] | Butanolic fraction of alcoholic extract possesses remarkable inhibitory HBV activity, against the secretion of hepatitis B virus surface antigen (HBsAg) and hepatitis B virus e antigen (HBeAg). **IC50:** 0.15 mM for HBsAg and 0.14 mM for HBeAg [Jiang et al. (2013)] | Alcoholic extract showed anti-asthmatic potential by exhibiting relaxation effect against histamine and acetylcholine induced contraction model in Guinea pigs. **Dose:** 25 mg/kg (in vivo), 10 and 100 mg/ml (in vitro) [Singal et al. (2013)] |
| C2.30    | Piper nigrum L./Marica/Piperaceae/Fruits | Aqueous extract of P. nigrum capable of promoting the proliferative signaling pathways in splenocytes and enhance murine splenocyte proliferation. **Dose:** 50 and 100 μg/ml [Majdalawieh and Carr (2010)] | Isolated piperamides from P. nigrum inhibit coxsackie virus type B3 (CVB3). It inhibit the proliferation of VSMCs. **IC50:** 21.6 μM to 10.6 μM [Mair et al. (2016)] | Isolated piperamides from P. nigrum inhibit coxsackie virus type B3 (CVB3). It inhibit the proliferation of VSMCs. **IC50:** 21.6 μM to 10.6 μM [Mair et al. (2016)] |
| C2.31    | Pongamia pinnata (L.) Pierre/Karanj/Fabaceae/Seeds | Isolated oil impact on immune cell signaling events needed for continued recruitment of neutrophils/other cells. **Dose:** 0.3 or 0.5 g/kg [Muniandy et al. (2018)] | Aqueous extract interfered with HBsAg and thus probably may prevent HBV entry. **Dose:** 5 mg for 0.18 μg/ml concentrations of the virus [Mathayana et al. (2018)] | Isolated isoflavone and showed inhibitory effects against NO production in LPS-stimulated BV-2 microglial cells thus anti-inflammatory effects. **IC50:** 9.0 μM [Wen et al. (2018)] |
| C2.32    | Punica granatum L./Anar/Punicaceae/Fruit, peel | Aqueous extract showed a significant decrease in nitric oxide levels and TNF-α levels. A significant diminution of INOS, TNF-α and NF-κB expression was also observed. **Dose:** 0.65 g/kg [Labasi et al. (2016)] | Alcoholic extract inhibited influenza a PR8 virus replication in the MDCK cell line, it could suppress the amplification of the infectious influenza viruses. **IC50:** 6.45 μg/ml [Moradi et al. (2019)] | Isolated gallotyl-hexahydroxycphenyl-glucose showed protective effect against acute lung injury and anti-inflammatory activity by inhibiting LPS-induced JNK and NF-κB activation and reduction in expression of the TNF-α, IL-6, and IL-1β genes in lungs. **Dose:** 5, 50, and 100 mg/kg [Pinheiro et al. (2019)] |

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TABLE 5 | (Continued) List of Indian Medicinal Plants/AYUSH drugs with proven immunomodulatory, antiviral and anti-allergic/anti-inflammatory/anti-asthmatic activity having potential for exploring against COVID 19 categorized for prioritization on the basis of their earlier reports.

| Category. Sl no | Botanical name/Common name/Family/Part | Immunomodulatory activity | Anti-viral activity | Anti-allergic/anti asthmatic/anti-inflammatory/respiratory disorders |
|----------------|----------------------------------------|---------------------------|-------------------|-------------------------------------------------|
| C2.33 | Plantago major L./Lahuriya/Plantaginaceae/Whole plants, seeds | Aqueous extract increased lymphocyte proliferation and secretion of interferon-γ at low concentrations (<50 μg/ml), but at high concentrations, it can inhibit this property (<50 μg/ml). **Dose**: 50 μg/ml | Isolated compound of caffeic acid from aqueous extract possesses interesting anti-HSV-1, anti-HSV-2 and anti-ADV-3 activities. Caffeic acid was found to inhibit HSV-1 replication. **EC50**: 15.3 μg/ml | Hydroalcoholic extract showed amelioration of asthma by increasing mean mast cells, alveolar epithelium thickness and glycophosphatidic accumulation. **Dose**: 100 mg/kg |
| C2.34 | Psoralea corylifolia L./Babchi/Fabaceae/Seeds | Hydroalcoholic extract stimulate natural killer cell activity. A positive response was also observed in the ADCC activity of spleen cells. **Dose**: 100 and 200 mg/kg Latha et al. (2000) | Aqueous extract found more effective in suppressing the virosis and reduced the mortality against virosis cellular and biochemical changes. **Kiran Kumar** et al. (2012) | Extract showed novel agent for asthma by inhibiting eosinophils accumulation into airways and modulating Th1/Th2 cytokine balance. **Dose**: 200 and 400 mg/kg Lee and Kim (2008), Wen et al. (2018) |
| C2.35 | Rhodiola rosea L./Rhodora/Crassulaceae/Whole plant | Isolated compound of could promote the activation of T lymphocytes, differentiate them into CD4+ or CD8+ cell, and implement their functions. **Dose**: 12.5, 25, 50 μg | Alcoholic extract inhibit the entry and infection of ebola and marburg viruses. **IC50**: 0.25 μg/ml (ebola virus)4.0 μg/ml (marburg virus) **Cui et al.** (2010) | Isolated salidroside showed protective effect in acute lung injury by decrease in the W/D ratio, myeloperoxidase activity of lung, reducing protein concentration, macrophages in the bronchoalveolar lavage fluid and regulating inflammatory cytokines and NF-κB. **Dose**: 120 mg/kg **Dose**: 500 mg/kg Saneja et al. (2009) |
| C2.36 | Santalum album L./Sandalwood/Santalaceae/Stem | Aqueous extract inhibited cell proliferation, nitric oxide production and CD14 monocyte. **Dose**: 30 mg/ml Gupta and Chaphalkar (2016) | β-Santalol from hexane extract exhibits anti-influenza A/HK (H3N2) virus by inhibition of viral mRNA synthesis. **Dose**: 100 μg/ml Paul pandi et al. (2012) | Alcoholic extract showed in vitro anti-inflammatory activity as compared to Diclofenac. **Dose**: 500 mg/ml Saneja et al. (2009) |
| C2.37 | Saussurea lappa (Decne.) C.B.Clarke/Kutha/Compositae/Roots | Isolated compound of costunolide and dehydrocostus lactone showed suppressive effect on the expression of the hepatitis B surface antigen (HBsAg) in Hep3B cells. **IC50**: 1.0–2.0 μM **Chen et al.** (1995) | Hexane fraction of alcoholic extract suppress the HBoAg production by Hep3B cells. **IC50**: 1.0–2.0 μM **Chen et al.** (1995) | SML0417, epipligulyl oxide and elecampane camphor isolated from roots ameliorates allergic asthma in murine model by inhibiting antigen-induced degranulation, reduction in inflammatory signs and mucin production and expression and secretion of Th2 cytokines. **Lee B. K.** et al. (2018) |
| C2.38 | Sphaeranthus indicus L./Mundi/Asteriaceae/Leaves, flowers | Petroleum ether extract from the flower heads of S. indicus increasing phagocytic activity, hemagglutination antibody titer and delayed type hypersensitivity. **Dose**: 200 mg/kg Balia and Mishra (2007) | Alcohol extract exhibits anti-virus potential against herpes simplex virus (HSV) and mouse corona. **Dose**: 0.4 μg/ml Vimalanathan et al. (2009) | Alcoholic leaves extract inhibit prostanoid synthesis. **Dose**: 100,200, and 400 mg/kg Meher et al. (2011) |
| C2.39 | Syzygium aromaticum (L.) Merr. and L.M. Perry/Leavang/Myrtaceae/FRuits | Aqueous and alcoholic suppressive effects on mouse macrophages and inhibit IL-1β, IL-6, and IL-10. **Dose**: 1000 μg/ml Dibazar et al. (2015). Essential oil increased the WBC count and enhanced DTH response in mice. **Carrasco et al.** (2009) | Hydroalcoholic extract exhibits anti-viral activity against herpes simplex virus-1 evaluated on vero cell line using MTT assay. **IC50**: 8.4 μg/ml Moradi et al. (2018) | Aqueous extract decreases neutrophil count and proteins leakage into bronchoalveolar lavage fluid. **Dose**: 200 mg/kg Chiriguir et al. (2019) |
| C2.40 | Terminalia chebula Retz./Hulāla/Combretaceae/FRuits | Aqueous extract increase in humoral antibody titer and delayed-type hypersensitivity in mice. **Dose**: 100–500 mg/kg Shivaprasad et al. (2006) | Hydroalcoholic extract of prevents the attachment as well as penetration of the HSV-2 to vero cells and efficacy to inhibit virus attachment and penetration to the host cells. **IC50**: 0.01 ± 0.0002 μg/ml Kesarwani et al. (2017) | Carbohydrate polymer from aqueous extract of dried ripe fruit showed antitussive efficacy in citric acid-induced cough efforts. **Dose**: 50 mg/kg **Nosikova et al.** (2013). Ethyl acetate fraction showed antitussive efficacy on sulfur dioxide gas induced cough partially through modulation of opioid receptors. **Dose**: 500 mg/kg Haq et al. (2013) |

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### TABLE 5  (Continued) List of Indian Medicinal Plants/AYUSH drugs with proven immunomodulatory, antiviral and anti-allergic/anti-inflammatory/anti-asthmatic activity having potential for exploring against COVID 19 categorized for prioritization on the basis of their earlier reports.

| Category, SI no | Botanical name/Common name/Family/Part | Immunomodulatory activity | Anti-viral activity | Anti-allergic/anti-inflammatory/anti-asthmatic activity |
|-----------------|----------------------------------------|---------------------------|---------------------|--------------------------------------------------------|
| C2.41           | *Tinospora cordifolia* (Wild.) Miens/Giloe/ Menispermaceae/Stem | Aqueous and alcoholic extract reduced bacterial load as compared to untreated macrophages. *Dose: 100, 200, and 500 μg/ml* Alsuhaibani and Khan (2017) | Methanol and ethyl acetate mixture extract inhibits the growth of HSV. *Dose: 50–100 μg/ml* Pruthvish and Gopinatha (2018) | Hydroalcoholic extract ameliorates asthma through decreasing oxidative stress and inflammation through modulating glutathione homeostasis and regulation of NF-κB and pro-inflammatory genes. *Dose: 100 mg/kg* Tiwari et al. (2014) |
| C2.42           | *Tribulus terrestris* L./Gokhru/Zygophyllaceae/ Whole plant | Saponin fraction increased phagocytic activity in dose dependent manner. *Dose: 50, 100, 200 μg/ml* Tiwari et al. (2011) | Alcohol extract showed antiviral potential against newcastle disease virus evaluated by titering in vivo vero cell line culture. *Dose: 80 μg/ml* Malik et al. (2018) | Hydroalcoholic fruit extract activate mast cell. *EC50: 1% extract with 0.1% HC* Kang et al. (2017) |
| C2.43           | *Ziziphus jujuba* Mill./Unnab/Rhamnaceae/Fruits | Aqueous extract increase thymus and spleen indices as well as enhance the T-lymphocyte proliferation, hemolytic activity and NK cell activity. *Dose: 1.3, 2.6, and 5.2 g/kg* Yu et al. (2016) | Isolated betulinic acid showed antiviral activity on influenza virus by attenuating pulmonary pathology and down-regulation of IFN-γ level. *Concentration: 50 μM* Hong et al. (2015) | Alcoholic extract showed inhibition of expression and activity of COX-2. *Dose: 200, 400, and 600 mg/kg* Mesiak et al. (2018) |
| C2.44           | *Zataria multiflora* Boiss./Satar/Lamiaceae/Whole plant, leaves | Obtained essential oils from hydrodistillation increase in the secretion of TNF-α, IFN-γ, IL-2 and decrease in IL-4. *Dose: 10 μg/one BALB/c and 7 μg/one C57BL/6* Jamali et al. (2020) | Z. multiflora destruction of virus infectivity or inhibition of early phases of viral proliferation cycle. Arabzadeh et al. (2013) | Hydro-alcoholic extract ameliorates allergic asthma by decreasing pro-inflammatory cytokines, increasing expression of anti-inflammatory cytokines gene and number of treg (FOXP3) in splenocytes. *Dose: 200, 400, and 800 μg/ml* Kianmane et al. (2017) |
| C3.1            | *Artemisia absinthium* L./Vilayati afsantin/ Asteraceae/Roots | Alcoholic extract modulates the percentage expression and fluorescent intensity of CD66, CD40 and MHC II molecules on DCs. *Dose: 100 μg/ml* Azeguli et al. (2018) | Decoction effectively suppressed HBV DNA, HBeAg, and HBsAg. *Dose: 15 ml (containing 1 g of dried extract)* Ansari et al. (2018) | Aqueous extract in ovalbumin challenged mice amelorates asthma through promotion of naïve T cell development and reducing activated T cells. *Dose: 0.56 mg/kg* Rifa‘i et al. (2014) |
| C3.2            | *Datura metel* L./Safed dhatura/Solanaceae/ Leaves, fruits and seeds | - | Aqueous and alcoholic extract performed in vero cell line using MTT assay showed good antiviral activity. *IC50: 2.5 mg/ml* Roy et al. (2016) | Decoction effectively suppressed HBV DNA, HBeAg, and HBsAg. *Dose: 15 ml (containing 1 g of dried extract)* Ansari et al. (2018) |
| C3.3            | *Elettaria cardamomum* (L.) Maton/Choteliaichi/ Zingiberaceae/Fruits | Essential oil overlapped with that of various canonical signaling pathways which support its immunomodulator activity. Han and Parker (2017) | Ethyl acetate extract exhibits antiviral activity MDCK cells infected with influenza virus A/Puerto rico/8/34 (H1N1). *IC50: 0.2 μg/ml* Hossain et al. (2018) | The extract obtained from supercritical fluid extraction with carbon dioxide inhibit NF-kappa signaling pathway. *Dose: 0.033%* Souissi et al. (2022) |
| C3.4            | *Emblica ribes* Burm.f./Baberang/Myrsinaceae/ Fruits | - | Ethyl acetate extract increases phagocytosis, WBC and neutrophils count. *Dose: 200–500 mg/kg* Uttara and Mishra (2009) | Isolated embelin attenuates anti-inflammatory activity against carrageenan induced paw edema in rats. *Dose: 20 mg/kg* Mahendran et al. (2011) |
| C3.5            | *Hedychium spicatum* Sm./Kapurkachi/ Zingiberaceae/Rhizome | Alcoholic extract increased phagocytosis, WBC and neutrophils count. *Dose: 200–500 mg/kg* Uttara and Mishra (2009) | Aqueous extract of leaves inhibits plaque formation of both of the two strains of HSV-1 in vero E6 cells. *Dose: 125 mg/kg* Bebahani (2009) | Aqueous extract attenuates anti-histaminic action against histamine-induced bronchospasms in Guinea pig. *Dose: 200 mg/kg* Ghidlyal et al. (2012) |
| C3.6            | *Hyosopus officinalis* L./Zoofa/Lamiaceae/ Flowers, leaves | Aqueous extract of leaves affects the levels of some cytokines (such as IL-4, IL-6, IL-17, and IFN-γ) in asthmatic mice. By detection of the expressions of MMP-9 and TIMP-1 and the morphological changes. *Dose: 0.04 g/10 g* Ma et al. (2014) | Aqueous extract of leaves affects the levels of some cytokines (such as IL-4, IL-6, IL-17, and IFN-γ) in asthmatic mice. By detection of the expressions of MMP-9 and TIMP-1 and the morphological changes. *Dose: 0.04 g/10 g* Ma et al. (2014) | (Continued on following page)
### TABLE 5 (Continued)

| Category | Botanical name/Common name/Family/Part | Immunomodulatory activity | Anti-viral activity | Anti-allergic/anti-asthmatic/anti-inflammatory/respiratory disorders |
|----------|----------------------------------------|---------------------------|--------------------|--------------------------------------------------|
| C3.7     | Inula racemosa Hook./Puskara/Asteraceae/ Root | Polysaccharide fraction of water extract showed immunomodulatory action by stimulating phagocytic function. **Dose:** 100–200 mg/kg | - | Pet. Ether extract shows anti-asthmatic potential by mast cell degranulation. **Dose:** 50 and 100 mg/kg Vadnere et al. (2009) |
| C3.8     | Lepidium sativum L./Chansur/Cruciferae/Whole plants | Protein extract of lepidium sativum alter the proliferation induced by Con-A. **Dose:** 100 mg/kg | - | Isolated fractions from ethanol extract of whole plant inhibit bronchospasm induced by histamine and acetylcholine. Rehman et al. (2012), Prasad et al. (2009) |
| C3.9     | Leptadenia reticulata (Retz.) Wight and Am./Meethi dodli/Apocynaceae/Root, stem bark | Alcoholic extract increased haematological profile, GSH, SOD, CAT activity and decreased LPO levels in cyclophosphamide-induced rats. **Dose:** 100–200 mg/kg | - | Ethyl acetate fraction inhibit pro-inflammatory cytokines (IL-2, IL-6, TNF-α) and release of prostaglandin to prevent inflammation. **Dose:** 600 mg/kg Mohanty et al. (2015) |
| C3.10    | Magnolia officinalis var. officinalis/Himchampa/ Magnoliaceae/Bark | Isolated compound magnolol and honokiol from petroleum ether extract of bark provoked IFN7 transcripts (magnolol) and reinforcing the host antiviral response via NF-κB pathways (Honokiol). **Dose:** 35 mg/L | - | Aqueous extract exhibits anti-allergic actions through inhibition of local immunoglobulin E, histamine release and TNF-α production in 48/80 induced systemic anaphylaxis in rats. **Dose:** 0.001–1 g/kg Shin et al. (2001). Polyphenolic rich extract of Magnolia officinalis suppressed the production of inflammatory mediators, NO, pro-inflammatory cytokines, TNF-α and IL-6, and inhibition of TLR3 and NF-κB activation. **Dose:** 10 and 200 mg/kg Fang et al. (2015) |
| C3.11    | Mucuna pruriens (L.) DC./Kaunchbeej/Fabaceae/ Seeds | M. pruriens modulate the immune components like TNF-α, IL-6, IFN-I, IL-1b, iNOS and IL-2. **Dose:** 100, 200 and 400 mg/kg | - | Alcoholic extract of seeds of M. pruriens act on opioid receptor that located on airway passage and produce inhibitory effect. **Dose:** 500 mg/kg Nuzhat et al. (2013) |
| C3.12    | Piper betle L./Paan/Piperaceae/Leaves | Alcoholic extract of P. betle leaves showed lymphocyte proliferation, interferon-γ receptors and the production of nitric oxide. It suppressed phytohaemagglutinin stimulated peripheral blood lymphocyte proliferation. **Dose:** 500 mg/kg | - | Alcoholic extract of leaves decreased histamine and GM-CSF produced by an IgE-mediated hypersensitive reaction, and inhibited eotaxin and IL-8 secretion in a TNF-α and IL-4-induced allergic reaction. **Dose:** 10 mg/ml Wirotesangthong et al. (2008) |
| C3.13    | Sesamum indicum L./Tila/Pedaliaceae/Seed | Essential oil suppress cellular immunity with the domination of Th2 responses and also modulate macrophages, dendritic cells proinflammatory functions. **Dose:** 100 µg/ml Khorrani et al. (2018) | - | Aqueous extract reduce LPS induced inflammatory gene expression. **EC50:** 100 ng/ml Deme et al. (2018) |
| C3.14    | Sida cordifolia L./Beejband/Malvaceae/Seeds | S. cordifolia increased production of T-cell precursor and passive influences on the production of cytokines. **Dose:** 2 gm/kg | - | Alcoholic extract of seed inhibit paw edema and granuloma formation. **Dose:** 200 and 400 mg/kg Singh S. et al. (2011) |
| C3.15    | Swertia chirayata (Roxb.) H.Karst./Chirayata/ Gentianaceae/Whole plant | Chloroform extract inhibit expression of viral protein R in heLa cells harboring the TREX plasmid encoding full-length vpr (TREX-HeLa-vpr cells. **Dose:** 10 µM Woo et al. (2019) | - | Chloroform fraction exhibits bronchodilator effect by Ca2+ channel blockade. **Dose:** 0.1–3.0 mg/ml Khan et al. (2012) |

(Continued on following page)
| Botanical name/Common name/Family/Part | Immunomodulatory activity | Anti-viral activity | Anti-allergic/anti-inflammatory/anti-asthmatic activity |
|--------------------------------------|---------------------------|-------------------|-------------------------------------------------------|
| Tychosporum ammi (L.) sprague/Ajwain/| Aqueous seed extract: Aqueous extract effectively reduced the hemorrhage area, alveolar wall thickness and septum rupture, and alteration of the epithelial lining of bronchioles of lungs. | Seed oil: Neutralize antibody for Japanese encephalitis virus. Dose: 0.5 mg/ml | Alcoholic extract of aerial part showed anti-inflammatory effect against carrageenan induced granuloma. |  |
| Tylophora indica (Willd.) Miers | | | Alkaloidal fraction inhibit proliferation of B-cell enriched murine splenocytes and activated macrophages in releasing NO and promoted phagocytosis. |  |
| V. odorata/L./Banafsha/Violaceae/Flowers - | | | Isolated glycoprotein from aqueous extract of seed proliferate B-cell enriched murine splenocytes and activated macrophages in releasing NO and promoted phagocytosis. |  |
| Ahatodai Manapagu | | | Alcoholic extract of aerial part showed anti-inflammatory activity (Rastogi et al., 2020) |  |
| Nilavembu Kudineer | | | Ahatodai Manapagu is composed of Adathoda vasica Nees leaves, which contains alkaloids like vasicine, the active ingredient in various cough syrups. A. vasica has been used in the Indian medicinal system for thousands of years, to treat various types of respiratory disorders (Sampath Kumar et al., 2010). Vinothapooshan et al. suggested that its extract positively modulates the immunity of the host (Vinothapooshan and Sundar, 2011). |  |
| Kabasura Kudineer | | | Kabasura Kudineer is a traditional formulation used in the Siddha system of medicine for managing common respiratory complaints such as flu and cold. Siddha practitioners also recommended this formulation for severe phlegm, dry cough, and fever. It is made up of more than ten herbal ingredients, and each ingredient has a unique pharmacological activity in respiratory disorders. Hence, the ministry of AYUSH recommends its use for symptomatic management in COVID-19. |  |

3.2.10 Sharbat-e-Toot Siyah
Sharbat-e-Toot Siyah is composed of the juice of Morus nigra L. in a sugar base and is used to treat tonsillitis and sore throat. It has been reported as anti-inflammatory and analgesic and inhibits the pro-inflammatory cytokines (Chen et al., 2016). Very recently, it has been reported to enhance immunomodulatory activity (Lim and Choi, 2019).

3.2.11 Laook-e-Katan
Laook-e-Katan is a sugar-based semisolid Unani formulation composed of Linum usitatissimum L. seed, which contains alpha linolenic acid and has been reported to have antiviral, anti-inflammatory, and immunomodulatory activities (Lee et al., 2004; Erdinest et al., 2012; Miccadei et al., 2016). In Unani, it is recommended for respiratory disorders (Table 3).

3.3 Siddha Approaches

3.3.1 Nilavembu Kudineer
Nilavembu Kudineer is a polyherbal Siddha formulation prescribed for the prevention and management of viral infections and fevers. It acts as an immunomodulator and plays a defending role against dengue fever and chikungunya. Recent studies showed that formulation has antiviral and antimicrobial actions, which makes it suitable for viral fevers, malaria, and typhoid fever (Mahadevan and Palraj, 2016). Previously, studies proved that most of its constituents are effective as antiviral, anti-asthmatic, and immunobooster agents (Carrasco et al., 2009; Wang et al., 2010; Jin et al., 2011; Chang et al., 2013; Wintachai et al., 2015; Mair et al., 2016).

3.3.2 Ahatodai Manapagu
Ahatodai Manapagu is composed of Adathoda vasica Nees leaves, which contains alkaloids like vasicine, the active ingredient in various cough syrups. A. vasica has been used in the Indian medicinal system for thousands of years, to treat various types of respiratory disorders (Sampath Kumar et al., 2010). Vinothapooshan et al. suggested that its extract positively modulates the immunity of the host (Vinothapooshan and Sundar, 2011).

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Kabasura Kudineer is a traditional formulation used in the Siddha system of medicine for managing common respiratory complaints such as flu and cold. Siddha practitioners also recommended this formulation for severe phlegm, dry cough, and fever. It is made up of more than ten herbal ingredients, and each ingredient has a unique pharmacological activity in respiratory disorders. Hence, the ministry of AYUSH recommends its use for symptomatic management in COVID-19.
In addition to Ayurvedic, Unani, and Siddha formulations recommended by AYUSH there are some homeopathic formulations such as Arsenicum album, Brayonia alba, and Rhus toxicodendrum have been recommended which have not been included due to controversies over the use of homeopathic medicines. These formulations are prepared by dilutions in such a way so that no single detectable molecule is present in the final formulation, which results in controversy (Ernst, 2010). The criticism is due to non-evidential rationale to determine the biological effects of solutions containing unmeasurable starting material (Kaur, 2013).

Further, advancements in pathogenesis and understanding of diseases provide a wider platform to report the pharmacological limitations and opportunities of these highly diluted homeopathic medicines. Day by day, it is becoming more challenging for a pharmacologist to validate the therapeutic claims of homeopathic medicines through experiments. Low acceptance of homeopathic formulations is due to the absence of standardized protocols to justify their pharmacological potential. A major concern is to develop evidence-based validated methods and advancements in the homeopathic system to justify its measurable dilutions, which will help in understanding the mechanism of action and acceptability of homeopathic medicine (Table 4).

### 3.4 Routinely Used Common Indian Medicinal Plants for Exploring Against COVID-19

Ashwagandha, giloe, ginger, cinnamon, tulsi, black pepper, black cumin, amla, turmeric, garlic, and flax seeds have been traditionally used as herbal remedies for multiple diseases since ancient times. These herbs have been utilized in food preparations and traditional medicines in several countries. However, in India, their culinary use is very common and they are a part of kitchen in every house. Similarly, there are some traditional Indian formulations such as Chyawanprash, Triphala, and Rooh Afza etc. that are very commonly used in Indian territory as a part of daily used nutritional supplements. These plants and formulations are very common and at least one of them is being used daily by every Indian, irrespective of religion/community/financial status. The above-mentioned herbs and formulations have been proved potent scientifically for their immunomodulatory, antioxidant, and anti-infective properties, which might be one of the reasons behind the lower death rate of Indians per million of population due to COVID-19 even with minimum health infrastructure.

#### 3.4.1 Allium sativum L. (Garlic)

Various research has been conducted in vivo to highlight the effect of *A. sativum* in immunomodulation using garlic oil extract. The results showed reduction in serum TNF-α, ICAM-1 and immunoglobulin (G and M) levels confirming the enhancement in immune system activity (Kamel and El-Shinnawy, 2015). Pre-treatment with aqueous garlic extract showed notable antiviral effects mainly by reduction in infectivity and titer of virus against the velogenic strain of Newcastle disease virus in embryonated chicken eggs (Arify et al., 2018). *A. sativum* also showed antiviral effect against avian influenza virus H5N2 on Vero cells (Rasool et al., 2017). Its defensive effect on allergen-induced airway inflammation in rodent model showed significant reduction in inflammatory cell count, eosinophil infiltration and serum IgE modulation of Th1, Th2, and Th3 cytokines, upregulation of Th-1, Th-3 and simultaneous down-regulation of Th-2 expression. (Hsieh et al., 2019). Old extract of *A. sativum* showed modulation of airway inflammation established in BALB/c mice by reduction in percentage of eosinophil, lavage and serum IgG1 levels, and perivascular inflammation. The study suggested the attenuation of allergic airway inflammation by aged garlic extract (Zare et al., 2008). It has been found that fresh raw garlic extract showed anti-inflammatory effects by decreasing production of prostaglandin E2 (PGE2), IL-6, IL-1β, nitric oxide (NO), and leukotrienes (LT D4 and E4) in lipopolysaccharide activated RAW264.7 cells (Jeong et al., 2016).

#### 3.4.2 Cinnamomum verum J.Presl. (Cinnamon) or Cinnamomum zeylanicum Blume

*C. verum* essential oil and powder exhibited anti-oxidant, immunomodulator, and antiviral activity in Newcastle disease virus in chickens mainly by modulating total protein, globulin, total antioxidant capacity, and lysozyme activity, and significantly increased phagocytic activity (Islam et al., 2017). Another study reported that *C. zeylanicum* essential oil when blended with other essential oils showed effective antiviral potential against H1N1 and HSV1 viruses. Reduction in virus infectivity has been observed with 99% at 60-min contact time and more than 99.99% after 60 min for both H1N1 and HSV1 viruses (Brochet et al., 2017). Its bark extract exhibited immunomodulatory activity and significantly increased serum immunoglobulins, phagocytic index, neutrophil adhesion, and antibody titer (Niphade et al., 2009). Procyanidine polyphenols (Type A) extracted from *C. zeylanicum* bark showed anti-inflammatory potential in edema induced by carrageenan (Vetal et al., 2013). Alcoholic extract of bark suppressed intracellular release of TNF-α (murine neutrophils) and leukocytes (pleural fluid) as well as inhibition of TNF-α gene expression in lipopolysaccharide-stimulated human peripheral blood mononuclear cells (Joshi et al., 2010).

#### 3.4.3 Curcuma longa L. (Turmeric)

Aqueous extract of *C. longa* decreased relative spleen weight and modulation in hemato logical changes indicating the potential of *C. longa* as an immunomodulator in cyclophosphamide-immunosuppressed *in vivo* model. The study observed promising effects of turmeric as an immunomodulator by representing spleen cells in younger mice (Mustafa and Blumenthal, 2017). *C. longa* extract also showed antiviral potential against dengue virus in *in vitro* and *in vivo* studies on Huh7-tit-1 cells and a remarkable reduction in viral load has been observed by in *in vivo* model (Ichsyani et al., 2017). Water and ethanolic crude extracts have been found to be antiviral in...
H5N1 also showed upregulated TNF-α as well as IFN-β mRNA expression, highlighting its promising role in the inhibition of the replication of viruses (Sornpet et al., 2017). Turmeric extract has been found to be anti-allergic in mice immunized with ovalbumin and alum. Attenuation of food allergy by maintaining balance of Th1/Th2 has been reported. Extract has been found to cause reduction in Th2 and increase in Th1 cell-related cytokines. Further, increased levels of IgE, IgG1 and mMCP-1 levels were also decreased proving effects of turmeric in allergic disorders mainly, asthma and food allergies (Shin et al., 2015). Various other studies also reported anti-inflammatory effects of C. longa either alone or in combination (Lee et al., 2020).

3.4.4 Linum usitatissimum L. (Flax Seed)
Heteropolysaccharide, extracted from flax seed hull possessed immunomodulatory activity and anti-hepatitis B virus potential. It significantly stimulated mRNA expression of TNF-α, NO and IL exhibiting immune responses in murine macrophages. Antiviral activity has been reported through inhibition of expression of surface antigen as well as envelop antigen and also interfered with DNA replication. The study suggested its promising potential as an immunostimulant and vaccine adjuvant (Liang et al., 2019). The study suggested its promising potential as an immunostimulant and vaccine adjuvant (Liang et al., 2019). It showed anti-inflammatory and immunomodulatory potential in obesity-associated insulin resistance. Its oil in co-culture with 3T3-L1 adipocytes-RAW 264.7 macrophages of C57BL/6 mice reported shifting the cytokines toward anti-inflammatory with a decrement in TNF-α. Immunomodulation has been observed through an increase in levels of Th2-related cytokine (IL-4), serum anti-ova IgG1, and IgE, and a decrease in Th-1 related cytokines (TNF-α and IFN-γ) and anti-ova IgG levels (Palla et al., 2015). Another study reported the immunomodulatory activity of phenolic components of flax seed mainly through reduction in cell-mediated immune responses (Kasote et al., 2012). Immunomodulation has been observed through an increase in levels of Th2-related cytokine (IL-4), serum anti-ova IgG1, and IgE, and a decrease in Th-1 related cytokines (TNF-α and IFN-γ) and anti-ova IgG levels (Palla et al., 2015). Another study reported the immunomodulatory activity of phenolic components of flax seed mainly through reduction in cell-mediated immune responses (Kasote et al., 2012).

3.4.5 Nigella sativa L. (Black Cumin)
Nigella sativa L’s bioactive compounds have been observed as potential inhibitors of COVID-19 in molecular docking studies. Nigellidine gave energy complex at active site (6LU7) with energy scores closest to chloroquine and better than hydroxychloroquine and favipiravir whereas α-hederin gave energy complex at the active site (2GTB) with energy scores better than chloroquine, hydroxychloroquine, and favipiravir (Salim and Noureddine, 2020). The alcoholic seed extract has shown immunosuppressive activity on a phytohemagglutinin and immunostimulating effect on non-phytohemagglutinin (PHA) stimulated proliferation (Alshatwi, 2014). The thymoquinone-rich oil showed suppression of cytokine signaling molecules, and PGE2 in T-lymphocytes as well as enhanced PGE2 release in adrenocarcinomic human alveolar basal epithelial A549 cells (Koshak et al., 2018).

3.4.6 Ocimum sanctum L. (Tulsi)
Hydro-alcoholic extract of Ocimum sanctum inhibited intracellular multiplication of virus. It also inhibits non-specific interference with virus-cell interactions in H9N2 viruses. (Ghoke et al., 2018). The immunomodulatory potential of alcoholic leaves extracts at IC50 value of 73.3 μg/ml showed reduction in hepatic parasite and, skewing of the humoral response toward Th1 type (Bhalla et al., 2017). O. sanctum inhibits leukotiene-C4-synthase, leukotiene-A4-hydrolase and cyclooxygenase-2 activities in cultured HL-60 cells and causes a significant reduction in OVA-induced lung inflammation (Soni et al., 2015).

3.4.7 Phyllanthus emblica L. (Amla)
Amla has been reported to significantly relieve chromium-induced immunosuppressive effect on lymphocyte proliferation and led to restoration in production of IL-2 and INFγ (Sai Ram et al., 2002). Phenolics from emblica has been found to increase splenocytes proliferation. Geraniin and isocorilagin showed significant immunostimulatory effects (Liu et al., 2012). Ethanolic extract of amla strongly reduced levels of pro-inflammatory cytokines and increased levels of anti-inflammatory cytokine (Bandyopadhyay et al., 2011). An isolated compound (1, 2, 4, 6-tetra-O-galloyl-β-d-glucose) of P. emblica showed antiviral potential against HSV by HSV-1 inactivation, which leads to inhibition of early infection indulging attachment and penetration of virus, suppression of intracellular growth and inhibited gene expression of HSV-1 E and L along with DNA replication (Xiang et al., 2011).

3.4.8 Piper nigrum L. (Black Pepper)
Piperamides isolated from P. nigrum fruits showed significant inhibition of coxsackie virus type B3 in a cytopathic effect inhibition assay (Mair et al., 2016). Aqueous extract of P. nigrum acted as a potent modulator of the macrophages and significantly enhanced splenocyte proliferation in a dose-dependent manner (Majdalawieh and Carr, 2010). The isolated alkaloid from P. nigrum exhibited anti-inflammatory effect in RAW 264.7 cells stimulated by LPS and significant inhibition in iNOS-mediated NO and IL-1β, IL-6, and TNF-α. It also demonstrated anti-inflammatory activity in edema induced by carrageenan (Pei et al., 2020). Reports have confirmed the improvement of ovalbumin-induced nasal epithelial barrier dysfunction in allergic rhinitis mouse model. Further, protection of epithelium integrity, enhancement in E-cadherin tight junction protein as well as inhibition of the degraded levels of zonula occludens-1 and occluding in the nasal passage have been reported. Additionally, enhancing the activation of Nrf2/HO-1 signaling showed anti-allergic and anti-asthma activities (Bui et al., 2020).

3.4.9 Tinospora cordifolia (Willd.) Miers (Giloe)
In vitro screening of T. cordifolia silver nanoparticles against chikungunya virus cell showed significant antiviral potential (Sharma V. et al., 2019). Alcoholic leaves extract of T. cordifolia significantly decreases intracellular reactive oxygen species (ROS) in chikungunya patients with high levels of intracellular ROS in persisting polyarthralgia by ex vivo treatment (Banerjee et al., 2018). An in vitro study revealed the antiviral potential of crude stem extract of T. cordifolia against HSV in Vero cell lines by inhibiting the growth of
Aqueous extract of T. cordifolia stem significantly increase INFγ and IL levels (IL-1, IL-2, IL-4) in isolated chicken peripheral blood mononuclear cells (PBMCs) against infectious bursal disease virus. Further, immunomodulatory potential via the toll like receptor (TLR)-mediated pathway was also concluded (Sachan et al., 2019). The hydro-alcoholic extract of T. cordifolia stem in drinking water caused enhancement of cellular immunity as well as humoral immunity in broiler chicks (Nety et al., 2017). Chloroform extract significantly prevented pro-inflammatory biomarkers (IL-6, IL-1β and PGE2) and decreased paw edema (p ≤ 0.05) with no toxicity reported when conducted in RAW264.7 macrophages (Philip et al., 2018).

3.4.10 Withania somnifera (L.) Dunal (Ashwagandha)

Multiple studies have proved that Ashwagandha has antiviral and immunomodulatory potential. Very recently, an in silico study concluded that Withaferin-A exhibits antiviral potential against SARS-CoV-2 through inhibiting RNA polymerase with higher binding energy than hydroxychloroquine and other drugs used against SARS-CoV-2. Another study on withanone showed blockage of SARS-CoV–2 entry and also its subsequent infection by interrupting electrostatic interactions between the RBD and ACE2 (Balkrisna et al., 2020). Grover and colleagues through molecular docking reported the potential of withaferin A against HSV through inhibition of DNA polymerase enzyme (Grover et al., 2011). W. somnifera molecular mechanism has been elucidated by using network ethnopharmacological technique and reported that withanolide-phystosterol combination is a good immunomodulator (Chandran and Patwardhan, 2017). W. somnifera formulation (supplemented with minerals) has been reported to improve both cellular and humoral immunity as well as hematological profile in addition to the significant inhibition in mouse splenocytes (Trivedi et al., 2017). Aqueous root extract of W. somnifera attenuates production of pro-inflammatory cytokines and transcription factor in collagen-induced arthritis (Khan et al., 2018). A study in 2018 showed that W. somnifera significantly inhibited mRNA expression of inflammatory cytokines and promotes the mRNA expression of the anti-inflammatory cytokine in HaCaT cells (Sikandan et al., 2018).

3.4.11 Zingiber officinale Roscoe (Ginger)

Fresh ginger aqueous extract showed antiviral activity against human respiratory syncytial virus in human respiratory tract cell lines (HEp-2 and A549) and decreased the plaque counts in a dose-dependent manner. It also stimulated the secretion of IFN-β that contributes to counteracting against viral infection (Chang et al., 2013). It also showed antiviral potential against avian influenza virus H9N2 on Vero cells in a dose-dependent manner (Rasool et al., 2017). Oral administration of Soft gel capsules containing a Z. officinale in combination showed immunomodulatory and anti-inflammatory properties parallel to those exerted by positive control, and gene expression data highlighted overall same transcriptional remodeling (Dall’Acqua et al., 2019). A study on essential oil of ginger reported immunomodulatory effects by improving the humoral immunity in cyclophosphamide-immunosuppressed mice in a dose-dependent manner (Carrasco et al., 2009). Oral administration of alcoholic ginger extract to allergic rhinitis patients showed significant reduction in total nasal symptom scores (TNSS), with overall improvement in rhino conjunctivitis quality of life questionnaire (Yamprasert et al., 2020). The aqueous and alcoholic extracts of rhizome decreased goblet cell hyperplasia, infiltration of inflammatory cells in airways with reduced total and differential counts of eosinophils and neutrophils in mouse model (Khan et al., 2015) (Table 5).

3.5 Routinely Used Indian Natural Health Supplements to Explore for Use Against COVID 19

3.5.1 Chyawanprash

Chyawanprash is an Ayurvedic polyherbal health supplement, which is made up of concentrated extracts of nutrient-rich herbs and minerals. Chyawanprash comes under Awaleha (electuaries/ herbal jams) due to its consistency, and composed of Amla fruit as a base, which is considered as the most active Rasayana to improve strength, stamina, and vitality.

Although several types of research have been published on Chyawanprash to report its health benefits against various ailments, the study reports antioxidant (Anil and Suresh, 2011) free radical scavenging (Bhattacharya et al., 2002) antibacterial, antiviral, anti-inflammatory, antiallergic, and antitrombotic effects (Gupta et al., 2017). In a randomized controlled trial, it was found effective for pulmonary tuberculosis as an adjunct to antitubercular drugs. (Debnath et al., 2012; Sharma R. et al., 2019). An experimental study showed that Chyawanprash pre-treatment reduced plasma histamine levels and IgE release when rats and mice were challenged with allergen- and ovalbumin-induced allergy, suggesting its anti-allergic potential. NK cell activity was significantly increased by Chyawanprash treatment. On treating dendritic cells with Chyawanprash, there was a significant increase in immunity marker levels as well as phagocytic activity that proves its immunomodulatory activity (Sastry et al., 2011).

3.5.2 Triphala

Triphala is a well-known polyherbal Ayurvedic medicine consisting of equal proportions of fruits of Phyllanthus emblica L., Terminalia bellerica (Gaertn.) Roxb. and Terminalia chebula Retz. in the form of powder for digestive and refreshing action. Triphala is associated with many of the therapeutic potentials such as antioxidants, antiinflammatory, antineoplastic, antimicrobial, antiabetic, etc. (Peterson et al., 2017). Alcoholic extract of Triphala showed specific antimicrobial activity (Tambekar and Dahikar, 2011), broad-spectrum antimicrobial activity against antibiotic-resistant bacteria isolated from humans (Peterson et al., 2017).

Triphala extract was found more active than the NSAID drug, indomethacin, in improving arthritic and inflammatory effects and reduced expression of inflammatory mediators.
through inhibition of NF-κB activation (Kalaiselvan and Rasool, 2015). In LPS-stimulated macrophages, Triphala inhibited the production of inflammatory mediators, intracellular free radicals, and inflammatory enzymes (Reddy et al., 2009; Kalaiselvan and Rasool, 2016). It has been shown to reduce multiple cell signaling pathways of inflammation and oxidative stress and prevented the noise-stress induced changes in rats thereby strengthening the cell-mediated immune response (Prasad and Srivastava, 2020). A clinical study of Triphala showed immunostimulatory properties on T cells and NK cells, however did not change the cytokine levels in healthy volunteers (Phetkate et al., 2012). The individual constituents of Triphala have also showed immunomodulatory activity (Aher and Wahi, 2011). The stated data on Triphala reveals that it is a powerful polyherbal formulation with countless therapeutic uses for maintaining homeostasis as well as the cure and management of various disease.

3.5.3 Sharbat Rooh Afza

Rooh Afza is a well-known refreshing formulation with global acceptance. It is a concentrated squash prepared as sugar syrup with distillates of numerous medicinal plants including seeds of khurfa (Portulaca oleracea L.), kasni (Cichorium intybus L.), angoor (Vitis vinifera L.), nilofar (Nymphaea alba L.), Neel Kamal (Nymphaea nouchali Burm. f.), kamal (Nelumbo nucifera Gaertn.), gazoaban (Borago officinalis L.), badiyan (Coriandrum sativum L.), fruits/juices of santara (Citrus × sinensis (L.) Osbeck), ananas (Ananas comosus (L.) Merr.), seb (Malus domestica (Suckow) Borkh.), berries (Rubus fruticosus L.), vegetables like palak (Spinacia oleracea L.), gazar (Cichorium endivia L.), kasni (Cynara cardunculus L.), and pudina (Mentha arvensis L.). Rooh Afza boosts the energy system of the body by naturally refreshing. Although there is no evidence on Rooh Afza revealing its therapeutic value, its constituents have been reported as potently antiviral, immunomodulatory, and antiallergic against respiratory disorders.

The flower extract of P. oleracea possessed significant antioxidant and protective effects against DNA damage induced by necrotic effects (Dogan and Anuk, 2019). V. vinifera fruits exhibit anti-asthmatic activity by inhibiting cellular response and subsequent production of inflammatory cytokines (Arora et al., 2016). A study on N. alba flower has been reported against inflammatory activity in Swiss Albino mice using acute inflammatory models in a dose-dependent manners (RS et al., 2013). The immunoregulatory and anti-HIV-1 enzyme activities of N. nucifera suggest that it could be potentially important against virus development (Jiang et al., 2011).

Thus, it can be perceived that Rooh Afza not only provides natural refreshness to the body but also has antioxidant, immunomodulatory, and anti-inflammatory/antiviral activities. However, to validate the scientific data on the therapeutic value of Rooh Afza, experimental research should be undertaken to prove its role in health benefits therapeutically.

The above studies encourage further investigations of traditional medicinal plants for their preventive use against coronavirus infection. The herbs could be taken individually or synergistically at appropriate concentrations as candidates for developing potential therapeutic tools against COVID-19.

3.6 Potential Indian Medicinal Plants for Exploring Against COVID-19

There are many other Indian medicinal plants, which are either part of AYUSH recommendations as such or as ingredients of formulations or are known for improving immunity with antiviral and anti-allergic/anti-inflammatory potential and can offer potential leads against COVID-19. Table 5 provides a list of 83 medicinal plants categorized on a priority basis as per their reported properties. Category 1 (C1) includes 21 “Most promising drugs” which have already shown activity against Coronaviruses/HIV/Dengue viruses with their immunomodulatory and anti-allergic/anti-inflammatory properties. Category 2 (C2) is composed of 44 “Equally promising drugs” which reportedly have shown anti-viral, immunomodulatory, and anti-allergic/anti-inflammatory activities. Category 3 (C3) represents 18 “Possibly promising drugs” which have been reported to show anti-viral/immunomodulatory and/or anti-allergic/anti-inflammatory activities.

Listed medicinal plants and AYUSH recommended formulations could help as the potential alternate therapeutics for management and cure of COVID-19. However, this needs scientific explorations and validation of their preclinical and clinical studies. Since there is such a rich diversity, many other medicinal plants and their bioactive fractions need the attention of the scientific community to be explored against COVID-19.

4 CONCLUSION

The SARS-CoV-2 has become a threat to human population due to non-availability of approved vaccines or drugs for its treatment. Many herbs that have been reported to work as an immunity booster against other viral infections, and to possess anti-allergic/anti-inflammatory activities, need to be tested against COVID-19. Indian Traditional Medicines have a wide potential for being used in these tough times either for prophylaxis or as adjuvant, owing to their longstanding use in community, ancient references and scientific evidence about their safety and clinical efficacy. The AYUSH ministry, Govt of India has issued several advisories from time to time, considering the strength and evidence of these systems of medicines and making considerable efforts to encourage researchers to explore herbal products for COVID-19. Interventions and herbal formulations from different AYUSH systems have the support of evidence for their immunity-enhancing, anti-inflammatory and antiviral effects. These herbal remedies may, therefore, provide some respite until the availability of trial-tested drug or vaccine to combat the COVID-19 menace. Further, it was noted that a major portion of public and private funding were dedicated to AYUSH trials. More than 50% of these trials were sponsored by the government and various stakeholders associated with the Ministry of AYUSH. It is expected that the results of these clinical studies will be disseminated soon at the public platform so that the policymakers from the AYUSH systems
of medicines may reframe their policies for public health and provide information to the global scientific community, which could form a platform for collaborative studies at the national and global levels. The medicinal plant species discussed in this review and categorized for their preclinical and clinical investigation may be taken up by research organizations on priority basis, as this may result in the development of lead molecule against SARS-CoV-2 and COVID-19. Keeping in view the potential of AYUSH medicines and medicinal plants of India, the herbal drug, manufacturers, and the national and global research organizations should develop necessary strategies for furtherance of preclinical and clinical research on these promising therapeutic leads.

REFERENCES

Abd-Alla, H. L., Moharram, F. A., Gaara, A. H., and El-Safty, M. M. (2009). Phytoconstituents of Jatropha curcas L. Leaves and their immunomodulatory activity on humoral and cell-mediated immune response in chicks. Zeitschrift fur Naturforsch C. 64 (7-8), 495–501. doi:10.1515/znc-2009-7-805

Abe, T. (2020). Fig (Ficus carica L.) leaf tea suppresses allergy by acceleration of IgE-receptor complexes. Biosci. Biotechnol. Biochem. 84 (5), 1013–1022. doi:10.1080/09168451.2020.1722608

Adhikari, P. P., and Paul, S. B. (2018). History of Indian traditional medicine: a medical inheritance. Asian J. Pharm. Clin. Res. 11 (1), 421. doi:10.22159/ajpcr.2018.v11i1.21893

Agarwal, R., Diwanay, S., Patki, P., and Patwardhan, B. (1999). Studies on medicines and medicinal plants of India, the herbal drug, COVID-19. Keeping in view the potential of AYUSH development of lead molecule against SARS-CoV-2 and clinical investigation may be taken up by research manufacturers, and the national and global research organizations should develop necessary strategies for furtherance of preclinical and clinical research on these promising therapeutic leads.

AUTHOR CONTRIBUTIONS

SA: conceptualization, methodology, writing - reviewing and editing; SZ and BP: data curation, writing - original draft preparation; PB, GG, and AP: visualization, investigation; RP and MA: software, validation.

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Bhargavi, S. E. R., Asad, M., Dhamangi, S. S., and Chandrakala, G. K. (2010). Immunomodulatory activity of methanolic extract of Morus alba Linn. (mulberry) leaves. Pak. J. Pharm. Sci. 23 (1), 63–68.

Bharjorie, C. K., Garg, S. K., and Bhatia, A. K. (2016). Immunomodulatory activity of aqueous extract of Nycanthes arbor-tristis flowers with particular reference to splenocytes proliferation and cytokines induction. Indian J. Pharmacol. 48 (4), 412–417. doi:10.4103/0253-7613.166210

Bhattacharya, S. K., Bhattacharya, D., Sairam, K., and Ghosal, S. (2002). Effect of bioactive tannoid compounds of Emblica officinalis on ischemia-reperfusion-induced oxidative stress in rat heart. Phytotherapy 9 (2), 171–174. doi:10.1078/0944-7163-00990

Bonaterra, G., Bronischewski, K., Hunold, P., Schwarzbach, H., Heinrich, E. U., Fink, C., et al. (2020). Anti-inflammatory and anti-oxidative effects of Phytohusil® and root extract of althaera officinalis L. On macrophages in vitro. Front. Pharmacol. 11, 290. doi:10.3389/fphar.2020.00290

Borges-Argáez, R., Chan-Balan, R., Cetina-Montejo, L., Ayora-Talavera, G., Saños-Perez, P., Gómez-Carballo, J., et al. (2019). In vitro evaluation of anthraquinones from Aloe vera (Aloe barbadensis Miller) roots and several derivatives against strains of influenza virus. Ind. Crop. Prod. 132, 468–475. doi:10.1016/j.indcrop.2019.02.056

Boskabady, M. H., Kiani, S., Jandaghi, P., Zarei, T., and Zarei, A. (2003). Comparison of antitussive effect of Nigella sativa with codeine in guinea pig. Iran. J. Med. Sci. 28 (1), 111–115.

Boskabady, M. H., Shafei, M. N., Saberi, Z., and Amini, S. (2011). Pharmacological effects of Rosa damascena. Iran. J. Basic Med. Sci. 14 (4), 295–307. doi:10.22038/ijbms.2011.5018

Boudai, H., Necib, Y., and Bahi, A. (2015). Immunomodulatory activity of lectins extracted from illicium Verum. Int. J. Pharm. Sci. Res. 31 (1), 129–131.

Brochet, A., Guiblot, A., Haddioui, L., and Roques, C. (2017). Antibacterial, antifungal, and antiviral effects of three essential oil blends. Microbiologyn 6 (4), e00459. doi:10.1002/mib.459

Buchinemi, M., Rajesh Kumar, M., Kodagi, B. I., Pathapati, R. M., SalmakamHarita, M., et al. (2014). Evaluation of anti-inflammatory and analgesic activity of azadirachta indica (leaf) extract in chemical and thermal induced pain models in rats. Int. J. Toxicol. Pharmacol. Res. 4 (6), 144–147.

Bui, T. T., Fan, Y., Piao, C. H., Nguyen, T. Y., Shin, D. U., Jung, S. Y., et al. (2020). Piper Nigrum extract improves OVA-induced nasal epithelial barrier dysfunction via activating Nrfl2/HO-1 signaling. Cell. Immunol. 351, 104035. doi:10.1016/j.cellimm.2019.104035

Buriana, K., Hristo, N., Christina, H., and Petkov, V. D. (1990). Immunomodulatory activity of ginsenoside Rg1 from panax ginseng. Jpn. J. Pharmacol. 54 (4), 447–454. doi:10.1254/jjp.54.447

Camero, M., Mariano, M., Lovo, A., Elia, G., Leão, M., Buonavoglia, C., et al. (2014). In vitro antiviral activity of Ficus carica latex against caprine herpesvirus-1. Nat. Prod. Res. 28 (22), 2031–2035. doi:10.1080/14786419.2014.918120

Carrasco, F. R., Schmidt, G., Romero, A. L., Sartoretto, J. L., Caparroz-Asses, S. M., Bersani-Amado, C. A., et al. (2009). Immunomodulatory activity of zingerib officinale Roscoe, salvia officinalis L. And syzygium aromaticum L. Essential oils: evidence for humoral- and cell-mediated responses. J. Pharm. Pharmacol. 61 (7), 961–967. doi:10.1211/jpp.61.07.0017

Chandran, U., and Patwardhan, B. (2017). Network ethnopharmacological evaluation of the immunomodulatory activity of Withania somnifera. J. Ethnopharmacol. 197, 250–256. doi:10.1016/j.jep.2016.07.080

Chandrasekaran, C., Sundarajan, K., Edwin, J., Gururajag, R., Mundkinajeddu, D., and Agarwal, A. (2013). Immune-stimulatory and anti-inflammatory activities of Curcuma longa extract and its polysaccharide fraction. Pharmacogn. Res. 5 (2), 71–79. doi:10.4103/0974-8490.110527

Chang, J. S., Wang, K. C., Yeh, C. F., Shieh, D. E., and Chiang, L. C. (2013). Fresh ginger (Zingiber officinale) has anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines. J. Ethnopharmacol. 145 (1), 1–14. doi:10.1016/j.jep.2012.10.043

Chattopadhyay, D., and Naik, T. (2007). Antivirals of ethnomedicinal origin: structure-activity relationship and scope. Mini Rev. Med. Chem. 7 (3), 275–301. doi:10.2174/138955707780059844

Chattopadhyay, P., Hazarika, S., Dhiman, S., Upadhyay, A., Pandey, A., Karmakar, S., et al. (2012). Vitex negundo inhibits cyclooxygenase-2 immunomodulatory cytokerin-mediated inflammation on carragenan-induced rat hind paw edema. Pharmacogn. Res. 4 (3), 134–137. doi:10.4103/0974-8490.99072
targets HIV-1-infected cells and infectious viral particles to potentiate the efficacy of antiretroviral drugs. *Medicines* 6 (1), 33. doi:10.3390/ medicines6010033

Ghildiyal, S., Gautam, M. K., Joshi, V. K., and Goel, R. K. (2012). Pharmacological evaluation of extracts of Hedychium spicatum (Ham-ex-Smith) rhizome. *Ancient Sci. Life* 31 (3), 117–122. doi:10.4103/0257-7941.103189

Ghoke, S. S., Sood, R., Kumar, N., Pateriya, A. K., Bhatia, S., Mishra, A., et al. (2018). Evaluation of antiviral activity of Ocimum sanctum and Acacia arabica leaves extracts against H9N2 virus using embryonated chicken egg model. *BMC Complement. Altern. Med.* 18 (1), 174. doi:10.1186/s12906-018-2238-9

Ghosh, K., Nosalova, G., Ray, A., Sivova, V., Nosal, S., and Ray, B. (2015). Extracted polysaccharide from Nyctanthes arbor-tristis leaves: chemical and antitussive properties. *Int. J. Biol. Macromol.* 75, 128–132. doi:10.1016/j.ijbiomac.2015.01.021

Gibbs, B. F. (2009). Differential modulation of IgE-dependent activation of human basophils by amboxrol and related secretory anlogues. *Int. J. Immunopathol. Pharmacol.* 22 (4), 919–927. doi:10.1177/0394633X0900200407

Goel, A., Singh, D. K., Kumar, S., and Bhatia, A. K. (2010). Immunomodulating property of Ocimum sanctum by regulating the IL-2 production and its mRNA expression using rat’s splenocytes. *Asian Pac. J. Trop. Med.* 3 (1), 8–10. doi:10.1016/S1995-7845(10)60021-1

Gomes, A., Datta, P., Sarkar, A., Dasgupta, S. C., and Gomes, A. (2014). Black tea (Camellia sinensis) extract as an immunomodulator against immunocompetent and immunodeficient experimental rodents. *Orient. Pharm. Exp. Med.* 14 (1), 37–45. doi:10.4103/1530-034X.130342

Grover, A., Agrawal, V., Sandilya, A., Bisaria, V. S., and Sundar, D. (2011). Non-nucleoside inhibition of Herpes simplex virus DNA polymerase: mechanistic insights into the anti-herpetic mode of action of herbal drug withaferin A. *BMC Bioinf.* 12 (Suppl 13), S22. doi:10.1186/1471-2105-12-S13-S22

Guán, S., He, J., Guo, W., Wei, J., Lu, J., and Deng, X. (2017). Adjuvant effects of salidroside from *Rhodiola rosea* L. on the immune responses to ovalbumin in mice. *Immunopharmacol. Immunotoxicol.* 39 (3), 738–745. doi:10.3109/08923973.2011.567988

Guán, S., Xiong, Y., Song, B., Song, Y., Wang, D., Chu, X., et al. (2012). Protective effects of salidroside from Rhodiola rosea on LPS-induced acute lung injury in mice. *Immunopharmacol. Immunotoxicol.* 34 (4), 667–672. doi:10.3109/08923973.2011.605175

Gul, S., Ahmed, S., Kifli, N., Uddin, Q. T., Tahir, N. B., Hussain, A., et al. (2014). Multiple pathways are responsible for Anti-inflammatory and Cardiovascular activities of Hordeum vulgare L. *J. Transl. Med.* 12 (1), 316. doi:10.1186/s12967-014-0316-9

Gulati, K., Ray, A., Debnath, P. K., and Bhattacharya, S. K. (2002). Pharmacological evaluation of *Carica papaya* ameliorates allergic asthma via down regulation of IL-4, IL-5, eotaxin, TNF-α, NF-κB, and iNOS levels. *Phytomed.* 32, 1–7. doi:10.1016/j.phymed.2017.04.009

Indrastasriawan, P., Aoki-Utsubo, C., Hanafi, M., Hartati, S. R. I., Wahyuni, T. S., Kameoka, M., et al. (2019). Antiviral activity of cananga odorata against hepatitis B virus. *Kobe J. Med. Sci. 65* (2), E71–E79.

Islam, M. R., Oomah, D. B., and Djuara, M. S. (2017). Potential immunomodulatory effects of non-dialyzable materials of cranberry extract in poultry production. *Poultry Sci.* 96 (2), 341–350. doi:10.3388/pwsp302

Iwo, M. I., Soemardjji, A. A., Retnoingrum, D. S., Sukrasnoand, U. A., M. (2000). Immunostimulating effect of *Pulea* (Alstonia scholaris L. B.R., Apocynaceae) bark extracts. *Clin. Hemorheol. Microcirc.* 22 (6), 177–183.

Jain, A., Choubey, S., Singour, P. K., Rajak, H., and Pawar, R. S. (2011). Sida cordifolia (Linn) - an overview. *J. Ayurveda Integr. Med.* 2 (2), 131–131. doi:10.1234/jaim.v2i2.29005

Jiang, Y., Tzi Bun, N. G., Zhaokun, L. I. U., Wang, C., Ning, L. I., and Qiao, W., et al. (2011). Protective effects of *Nyctanthes arbor-tristis* against dengue and chikungunya virus through in-vitro evaluation. *J. Ayurveda Integr. Med.* 11 (3), 329–335. doi:10.3329/ajmbr.v11i3.16302

Jamali, T., Kovovsi, G., and Ardestani, S. K. (2020). *In-vitro and in-vivo anti-breast cancer activity of OEO* (Oliveria decumbens vent essential oil) through promoting the apoptosis and immunomodulatory effects. *J. Ethnopharmacol.* 248, 112313. doi:10.1016/j.jep.2019.112313

Jamkhande, P. G., Barde, S. R., Patwekar, S. L., and Tidke, P. S. (2013). Plant profile, phytochemistry and pharmacology of Cordia dichotoma (Indian cherry): a review. *Asian Pac. J. Trop. Biomed.* 3 (12), 1009–1012. doi:10.1016/S2221-1691(13)60194-X

Jantun, I., Ilangkovan, M., Yuandianai Mohamad, H. F. (2014). Correlation between the major components of *Phyllanthus amarus* and *Phyllanthus urinaria* and their inhibitory effects on phagocytic activity of human neutrophils. *BMC Complement. Altern. Med.* 14 (1), 429. doi:10.1186/1472-6882-14-429

Jassim, S. A. A., and Naji, M. A. (2003). Novel antiviral agents: a medicinal plant perspective. *J. Appl. Microbiol.* 95 (3), 412–427. doi:10.1046/j.1365-2672.2003.02026.x

Javed, T., Ashfaq, U. A., Riaz, S., Rehman, S., and Riazuddin, S. (2011). *In-vitro antiviral activity of Solanum nigrum against Hepatitis C Virus*. *Viril. J.* 8 (1), 26. doi:10.1164/j.viril.2010.05.096

Jeong, Y. Y., Ryu, J. H., Shin, J. H., Kang, M. J., Kang, J. R., Han, J., et al. (2016). Comparison of anti-oxidant and anti-inflammatory effects between fresh and aged black garlic extracts. *Molecules* 21 (4), 430. doi:10.3390/ molecules21040430

Jiang, Y., Tzi Bun, N. G., Zhao kun, L. I. U., Wang, C., Ning, L. I., Qiao, W., et al. (2011). Immunoregulatory and anti-HIV-1 enzyme activities of antioxidant...
Kumar, S., Kamboj, J., Suman, and Sharma, S. (2011). Overview for various aspects of the health benefits of piper longum Linn. Fruit. J. Acupunct. Meridian Stud. 4 (2), 134–140. doi:10.1007/s12590-011-0020-4

Kumar, S., and Pandey, A. K. (2014). Medicinal attributes of Solanum xanthocarpum fruit consumed by several tribal communities as food: an in vitro antioxidant, anticancer and anti HIV perspective. BMC Complementary Altern. Med. 14 (1), 112. doi:10.1186/1472-6882-14-112

Kumari, K. D. K. P., Weerakoon, T. C. S., Handunnetti, S. M., Samarasinghe, K., and Suresh, T. S. (2014). Anti-inflammatory activity of dried flower extracts of Aegle marmelos in Wistar rats. J. Ethnopharmacol. 151 (3), 1202–1208. doi:10.1016/j.jep.2013.12.043

Kurokawa, M., Ochiai, H., Nagasaki, K., Meki, M., Xu, H., Kadota, S., et al. (1993). Antiviral traditional medicines against herpes simplex virus (HSV-1), poliovirus, and measles virus in vitro and their therapeutic efficacies for HSV-1 infection in mice. Antiviral Res. 22 (2-3), 175–188. doi:10.1016/0166-3542(93)90094-Y

Kyokong, O., Charuluxananan, S., Muangmingsuk, V., Rodanant, O., Subornsug, C., and Suresh, T. S. (2014). Anti-infective activity of Punica granatum peel biomass. J. Ethnopharmacol. 153 (1), 318–329. doi:10.1016/j.jep.2013.11.028

Lee, J. S., Synytsya, A., Kim, H. B., Choi, D. J., Lee, S., Lee, J., et al. (2013). Antiviral traditional medicines against herpes simplex virus (HSV-1), poliovirus, and measles virus in vitro and their therapeutic efficacies for HSV-1 infection in mice. Antiviral Res. 22 (2-3), 175–188. doi:10.1016/0166-3542(93)90094-Y

Lee, D., Kim, H. S., Wei, C. L., Lin, C. F., and Tsai, Y. C. (2012). Inhibition of herpes simplex virus type 1 by thymol-related monoterpenoids. Antiviral Res. 98 (3), 318–321. doi:10.1016/j.antiviral.2011.12.002

Lee, Y. C., and Kim, S. H. (2008). Immunomodulatory effect of Juglans sinensis, a medicinal nut. Foodborne Pathog. Dis. 5 (3), 210. doi:10.1089/fpd.2008.0057

Lee, S. Y., Cho, S. S., Li, Y. C., Bae, C. S., Park, K. M., and Park, D. H. (2020). Antinflammatory activity of momordica charantia L. (Cucurbitaceae) leaf diethyl ether and methanol extracts on Salmonella typhi -infected mice and LPS-induced phagocytic activities of macrophages and neutrophils. Evidence based complementary Altern. Med. 2020, 1–11. doi:10.1155/2020/5248346

Lee, Y. C., and Kim, S. H. (2008). Immunomodulatory effect of Juglans sinensis, a medicinal nut. Foodborne Pathog. Dis. 5 (3), 210. doi:10.1089/fpd.2008.0057

Lee, D., Kim, H. S., Wei, C. L., Lin, C. F., and Tsai, Y. C. (2012). Inhibition of herpes simplex virus type 1 by thymol-related monoterpenoids. Antiviral Res. 98 (3), 318–321. doi:10.1016/j.antiviral.2011.12.002

Lee, J. S., Synytsya, A., Kim, H. B., Choi, D. J., Lee, S., Lee, J., et al. (2013). Antiviral traditional medicines against herpes simplex virus (HSV-1), poliovirus, and measles virus in vitro and their therapeutic efficacies for HSV-1 infection in mice. Antiviral Res. 22 (2-3), 175–188. doi:10.1016/0166-3542(93)90094-Y

Lee, Y. C., and Kim, S. H. (2008). Immunomodulatory effect of Juglans sinensis, a medicinal nut. Foodborne Pathog. Dis. 5 (3), 210. doi:10.1089/fpd.2008.0057

Lee, D., Kim, H. S., Wei, C. L., Lin, C. F., and Tsai, Y. C. (2012). Inhibition of herpes simplex virus type 1 by thymol-related monoterpenoids. Antiviral Res. 98 (3), 318–321. doi:10.1016/j.antiviral.2011.12.002

Lee, J. S., Synytsya, A., Kim, H. B., Choi, D. J., Lee, S., Lee, J., et al. (2013). Purification, characterization and immunomodulatory activity of a pectic polysaccharide isolated from Korean mulberry fruit Oddi (Morus alba L.). Int. Immunopharmacol. 17 (3), 858–866. doi:10.1016/j.intimp.2013.09.019

Lee, S. Y., Cho, S. S., Li, Y. C., Bae, C. S., Park, K. M., and Park, D. H. (2020). Antinflammatory activity of momordica charantia L. (Cucurbitaceae) leaf diethyl ether and methanol extracts on Salmonella typhi -infected mice and LPS-induced phagocytic activities of macrophages and neutrophils. Evidence based complementary Altern. Med. 2020, 1–11. doi:10.1155/2020/5248346

Lee, Y. C., and Kim, S. H. (2008). Immunomodulatory effect of Juglans sinensis, a medicinal nut. Foodborne Pathog. Dis. 5 (3), 210. doi:10.1089/fpd.2008.0057

Lee, D., Kim, H. S., Wei, C. L., Lin, C. F., and Tsai, Y. C. (2012). Inhibition of herpes simplex virus type 1 by thymol-related monoterpenoids. Antiviral Res. 98 (3), 318–321. doi:10.1016/j.antiviral.2011.12.002

Lee, J. S., Synytsya, A., Kim, H. B., Choi, D. J., Lee, S., Lee, J., et al. (2013). Purification, characterization and immunomodulatory activity of a pectic polysaccharide isolated from Korean mulberry fruit Oddi (Morus alba L.). Int. Immunopharmacol. 17 (3), 858–866. doi:10.1016/j.intimp.2013.09.019

Lee, S. Y., Cho, S. S., Li, Y. C., Bae, C. S., Park, K. M., and Park, D. H. (2020). Antinflammatory activity of momordica charantia L. (Cucurbitaceae) leaf diethyl ether and methanol extracts on Salmonella typhi -infected mice and LPS-induced phagocytic activities of macrophages and neutrophils. Evidence based complementary Altern. Med. 2020, 1–11. doi:10.1155/2020/5248346

Lee, Y. C., and Kim, S. H. (2008). Immunomodulatory effect of Juglans sinensis, a medicinal nut. Foodborne Pathog. Dis. 5 (3), 210. doi:10.1089/fpd.2008.0057

Lee, D., Kim, H. S., Wei, C. L., Lin, C. F., and Tsai, Y. C. (2012). Inhibition of herpes simplex virus type 1 by thymol-related monoterpenoids. Antiviral Res. 98 (3), 318–321. doi:10.1016/j.antiviral.2011.12.002

Lee, J. S., Synytsya, A., Kim, H. B., Choi, D. J., Lee, S., Lee, J., et al. (2013). Purification, characterization and immunomodulatory activity of a pectic polysaccharide isolated from Korean mulberry fruit Oddi (Morus alba L.). Int. Immunopharmacol. 17 (3), 858–866. doi:10.1016/j.intimp.2013.09.019

Lee, S. Y., Cho, S. S., Li, Y. C., Bae, C. S., Park, K. M., and Park, D. H. (2020). Antinflammatory activity of momordica charantia L. (Cucurbitaceae) leaf diethyl ether and methanol extracts on Salmonella typhi -infected mice and LPS-induced phagocytic activities of macrophages and neutrophils. Evidence based complementary Altern. Med. 2020, 1–11. doi:10.1155/2020/5248346

Lee, Y. C., and Kim, S. H. (2008). Immunomodulatory effect of Juglans sinensis, a medicinal nut. Foodborne Pathog. Dis. 5 (3), 210. doi:10.1089/fpd.2008.0057
of most active free radical scavenging derivatives of embelin - a Structure-activity relationship. Chem. Pharm. Bull. 59 (8), 913–919. doi:10.1248/cpb.59.913

Mahmood, N., Piacente, S., Piazza, C., Burke, A., Khan, A. I., and Hayt, A. J. (1996). The anti-HIV activity and mechanisms of action of pure compounds isolated from Rosa damascena. Biochem. Biophys. Res. Commun. 229 (1), 73–79. doi:10.1006/bbrc.1996.1759

Mair, C., Liu, R., Atanason, A., Schmidtke, M., Dirsch, V., and Rollinger, J. (2016). Antiviral and anti-proliferative in vitro activities of pipermides from black pepper. Planta Med. 81 (S 01), S1–S381. doi:10.1055/s-0036-1596830

Majdalawieh, A. F., Hmaidan, R., and Carr, R. I. (2010). Nigella sativa modulates inflammatory, anti-bacterial and anti-diarrhoeal activity of Ziziphus jujuba. Microb. Pathog. 50 (6), 427–432. doi:10.1016/j.micpath.2011.03.018

Mathur, K., Mathur, A. K., Issrani, R., Ambani, S. R., and Goyal, M. (2016). Anti-inflammatory, antipruritic and mast cell stabilizing activity of Aristolochia indica. J. Basic Med. Sci. 15 (4), 422–427. doi:10.20388/jbms.2015.1307

Mathew, J. E., Kaitheri, S. K., Dinakaranvachala, S., and Jose, M. (2011). Anti-inflammatory, antipruritic and mast cell stabilizing activity of Aristolochia indica. Indian J. Basic Med. Sci. 14 (5), 422–427. doi:10.20388/ijbms.2011.5077

Mathur, K., Mathur, A. K., Issrani, R., Ambani, S. R., and Goyal, M. (2016). Anti-inflammatory, antipruritic and mast cell stabilizing activity of Aristolochia indica. J. Basic Med. Sci. 14 (5), 422–427. doi:10.20388/ijbms.2011.5077

Mehta, A. A., and Panarjape, A. N. (2008). Investigation into the mechanism of action of abutilon indicum in the treatment of bronchial asthma. Global J. Pharmacol. 2 (2), 23–30.

Messa, A. M., Poh, H. W., Bin, O. Y., Elsadaw, L., and Alsayed, B. (2018). In vivo anti-inflammatory, anti-bacterial and anti-diarrheal activity of Ziziphus jujuba fruit extract. Open Access Maced. J. Med. Sci. 6 (5), 757–766. doi:10.3889/oamjms.2018.168

Miccaeli, S., Masella, R., Mileo, A. M., and Gessani, S. (2016). ω3 polyunsaturated fatty acids as immunomodulators in colorectal cancer: new potential role in adjuvant therapies. Front. Immunol. 7, 486. doi:10.3389/fimmu.2016.00486

Mishra, A., Thakur, M., and Alok, S. (2016). Evaluation of immunomodulatory activity of polysaccharide fraction of Inula racemosa, Bombax ceiba and Allium sativum. Int. J. Pharm. Sci. Res. 7 (9), 3749–3755. doi:10.13040/IJPSR.0975-8232

Mitra Mazumder, P., Pattanayak, S., Parvani, H., Sasmal, D., and Rathinavelusamy, P. (2012). Evaluation of immunomodulatory activity of Glycyrrhiza glabra L. roots in combination with zing. Asian Pac. J. Trop. Biomed. 2 (1), S15–S20. doi:10.1016/S2221-1691(12)60122-1

Mohnaty, S. K., Swamy, M. K., Siddha, S. K., Prakash, L., Subbanarashib, A., and Maniyam, A. (2015). Analgesic, anti-inflammatory, anti-lipooxygenase activity and characterization of three bioactive compounds in the most active fraction of Leptadenia reticulata (Retz.)wight & -ravala medicinal plant. Iran. J. Pharm. Res. 14 (3), 933–942. doi:10.22037/ijpr.2015.7101

Mohnaty, S. K., Swamy, M. K., Sinniah, U. R., and Anuradha, M. (2017). Leptadenia reticulata (Retz.) Wight & Arn. (jivanti): botanical, agronomical, phytochemical, pharmacological, and biotechnological aspects. Molecules 22 (6), 1019. doi:10.3390/molecules22061019

Moradi, M. T., Karimi, A., Alidadi, S., and Hashemi, L. (2018). In vitro anti-herpes simplex virus virus, antioxidant potential and total phenolic compounds of selected iranian medicinal plant extracts. Iranian J. Tradit. Knowl. 17 (2), 255–262.

Moradi, M. T., Karimi, A., Rafieian-Kopaei, M., and Fotouhi, F. (2017). In vitro antiviral effects of Peganum harmala seed extract and its total alkaloids against Influenza virus. Microb. Pathog. 110, 42–49. doi:10.1016/j.micpath.2016.07.014

Moradi, M. T., Karimi, A., Shahrami, M., Hashemi, L., and Ghaffari-Goocheh, M. S. (2019). Anti-influenza virus activity and phenolic content of pomegranate (punica granatum L.) peel extract and fractions. Avicenna J. Med. Biotechnol. 11 (4), 285–291.

More, P., and Pai, K. (2011). Immunomodulatory effects of Tinospora cordifolia (Guduchi) on macrophage activation. Biol. Med. 3 (2), 134–140.

Mouhair, F., Hudson, J. B., Rejdali, M., and Towers, G. H. N. (2001). Multiple antiviral activities of endemic medicinal plants used by Berber peoples of Morocco. Pharm. Biol. 39 (5), 364–374. doi:10.1076/phbi.39.5.364.5892

Mukherjee, H., Ojha, D., Bag, P., Chandel, H. S., Bhattacharyya, S., Chattjee, T. K., et al. (2013). Anti-herpes virus activities of Achyranthes aspera: an Indian ethnomedicine, and its triterpene acid. Microbiol. Res. 168 (4), 238–244. doi:10.1016/j.micres.2012.11.002

Muniandy, K., Gothai, S., Badran, K. M. H., Kumar, S. S., Esa, N. M., and Arulselvan, P. (2018). Suppression of proinflammatory cytokines and mediators in LPS-Induced RAW 264.7 macrophages by stem extract of alternanthera sessilis via the inhibition of the NF-κB pathway. J. Immunol. Res. 2018, 1–12. doi:10.1155/2018/8430684

Muniappa, M., and Sundararaj, T. (2003). Antiinflammatory and antitussive activity of ambusa arundinacea. J. Ethnopharmacol. 88 (2-3), 161–167. doi:10.1016/S0378-7417(03)00183-1

Murthy, K., and Mishra, S. H. (2016). Velvet bean roots stimulates humoral and cellular mediated immunity and offers protection against cyclophosphamide induced myelosuppression. Int. J. Phytomed. 8 (1), 69–79.

Musarap-Pizzo, M., Ginetra, G., Smeriglio, A., Pennisi, R., Sciortino, M. T., and Mandalari, G. (2019). The antimicrobial and antiviral activity of polyphenols from almond (prunus dulcis L.) skin. Nutrients 11 (10), 2535. doi:10.3390/nu11102355

Mustafa, R., and Blumenthal, E. (2017). Immunomodulatory effects of turmeric: proliferation of spleen cells in mice. J. Immunoassay Immunoc. 38 (2), 140–146. doi:10.1080/15321819.2016.1227835

Nagarkar, B., Nirmal, P., Narkhe, A., Kulkarni, O., Harsulkar, A., and Patil, N. M. (2017). A review on sesame oil crop. J. Agric. Food Sci. 2 (1), S15–S20. doi:10.7897/2277-4343.06114

Nagray, C., and Kumar, A. (2014). Antineoplastic and immunomodulatory effect of polyphenolic components of Achyranthes aspera (PCA) extract on urethane induced lung cancer in vivo. Mol. Biol. Rep. 41 (1), 179–191. doi:10.1007/s11033-013-2850-6

Negi, B. S., and Dave, B. P. (2010). In vitro antiviral properties of Ascaris acuta and its phytochemical analysis. Indian J. Microbiol. 50 (4), 369–374. doi:10.1016/j.ijmp.2010.09.001

Nety, S., Koley, K. M., Choudhary, M., Chourasia, D., and Kumar, V. (2017). Comparative study of immunomodulatory effect of tinospora cordifolia stem and azadirachta indica extract in broiler chicks. Vet. Pract. 18 (2), 286–288.
Niphade, S. R., Asad, M., Chandrakala, G. K., Toppo, E., and Deshmukh, P. (2009). Immunomodulatory activity of Cinnamomum zeylanicum bark. Pharm. Biol. 47 (12), 1168–1173. doi:10.1186/2045-7020-30-19234

Nirmal, S. A., Patel, A. P., Bhawar, S. B., and Pattan, S. R. (2012). Antihistaminic and antiallergic actions of Solanum nigrum berries: possible role in the treatment of asthma. J. Ethnopharmacol. 142 (1), 91–97. doi:10.1016/j.eph.2012.04.019

Nivetha, R., Bhuvaraganav, S., and Janarthanan, S. (2020). Inhibition of multiple SARS-CoV-2 proteins by an antiviral biomolecule, seselin from Aegle marmelos deciphered using molecular docking analysis. Res. Square [Epub ahead of print]. doi:10.21203/rs.3.rs.31134/v1

Nosalova, G., Jurecek, L., Chatterjee, U. R., Majee, S. K., Nosal, S., and Ray, B. (2013). Antinutritive activity of the water-extracted carbohydrate polymer from terminalia chebula on citric acid-induced cough. Evidence Based Complementary Altern. Med. 2013, 1–7. doi:10.1155/2013/650134

Nutan, S. K., Modi, M., Dezzutti, C. S., Kulshreshtha, S., Rawat, A. K. S., Srivastava, S. K., et al. (2013). Extracts from Acacia catechu suppress HIV-1 replication by inhibiting the activities of the viral protease and Tat. Vet. J. 10 (1), 309. doi:10.1186/1743-422X-10-309

Nuzhat, S., Khan, R. A., and IQbal, A. (2013). Anti-tussive effect and gross toxicities of methanol extract of mucuna pruriens (L.) DC. in comparison of codeine phosphate. Int. J. Pharmac. 4 (6), 62–65. doi:10.7897/2230-8407.04514

Orhan, I. E., Mesiak, M. A., Jabeen, A., and Kan, Y. (2016). Immunomodulatory properties of various natural compounds and essential oils through modulation of human cellular immune response. Ind. Crop. Prod. 8 (1), 117–122. doi:10.1016/j.indcrop.2015.11.088

Oza, M. J., and Kulkarni, Y. A. (2017). Traditional uses, phytochemistry and pharmacology of the medicinal species of the genus Cordia (Boraginaceae). J. Pharm. Pharmacol. 69 (7), 755–789. doi:10.1111/jpp.12715

Palla, A. H., Khan, N. A., Bashir, S., Ur-Rehman, N., Iqbal, J., and Gilani, A. H. (2015). Pharmacological basis for the medicinal use of Linum usitatissimum (Flaxseed) in infectious and non-infectious diarrhea. Indian J. Pharmacol. 47 (6), 789–796. doi:10.4103/0974-8520.141958

Patil, V. V., Bhangale, S. C., and Patil, V. R. (2010). Studies on immunomodulatory activity of icus carica. Int. J. Pharm. Sci. Res. 2 (4), 97–99.

Paulpandian, M., Kannan, S., Thangam, R., Kaveri, K., Gunasekaran, P., and Rejeeth, C. (2012). In vitro anti-viral effect of β-santalol against influenza virus replication. Phytomed. 19 (3–4), 231–235. doi:10.1016/j.phymed.2011.11.006

Pei, H., Xue, L., Tang, M., Tang, H., Kuang, S., Wang, L., et al. (2020). Alkaloids from black pepper (piper nigrum L.) exhibit anti-inflammatory activity in murine macrophages by inhibiting activation of NF-κB pathway. J. Agric. Food Chem. 68 (7), 2406–2417. doi:10.1021/acs.jafc.9b07754

Peterson, C. T., Denniston, K., and Chopra, D. (2017). Therapeutic uses of triphala in ayurvedic medicine. J. Altern. Complementary Med. 23 (8), 607–614. doi:10.1089/acm.2017.0083

Phetkate, P., Kummalue, T., U-Prayta, Y., and Kietnun, S. (2012). Significant increase in cytotoxic T lymphocytes and natural killer cells by triphala: a clinical phase I study. Evidence Based Complementary Altern. Med. 2012, 1–6. doi:10.1155/2012/239856

Philip, S., Tom, G., and Vasumathi, A. V. (2018). Evaluation of the anti-inflammatory activity of Tinospora cordifolia (Willd.) Miers chlorof orm extract – a preclinical study. J. Pharm. Pharmacol. 70 (8), 1113–1125. doi:10.1111/jphp.12932

Pinheiro, A., Mendes, A., Neves, M., Prado, C. M., Bittencourt-Mernak, M. L., Santana, F., et al. (2019). Galloyl-hexahydroxydiphenoyl (HHDPP)-Glucose isolated from punica granatum L. Leaves protects against lipopolysaccharide (LPS)-Induced acute lung injury in BALB/c mice. Front. Immunol. 10, 1978. doi:10.3389/fimmu.2019.019728

Pongthanasipit, V., Ikuta, K., Puthavathana, P., and Leelamanit, W. (2013). Antiviral protein of Momordica charantia L. inhibits different subtypes of influenza A. Evidence Based Complementary Altern. Med. 2013, 729081. doi:10.1155/2013/729081

Prasad, R., Lavania, R. D., Manviand Gupta, R. (2009). Role of herbs in the management of asthma. Pharm. Rev. 3 (6), 247–258.

Prasad, S., and Srivastava, S. K. (2020). Oxidative stress and cancer: chemopreventive and therapeutic role of triphala. Antioxidants 9 (1), 72. doi:10.3390/antiox9010072

Pravansa, S., Thippeswamy, B. S., and Veerapur, V. P. (2012). Immunomodulatory and antioxidant effect of Leptadenia reticulata leaf extract in rodents: possible modulation of cell and humoral immune response. Immunopharmacol. Immunotoxicol. 34 (6), 1010–1019. doi:10.3109/08923973.2012.689767

Pringproa, K., Khonghiran, O., Kunanoppadol, S., Potha, T., and Chuammitri, P. (2014). In vitro virucidal and virustatic properties of the crude extract of cynodon dactylon against porcine reproductive and respiratory syndrome virus. Vet. Med. Int. 2014, 1–5. doi:10.1155/2014/947589

Pruthvish, B., and Gopinath, S. M. (2018). Antiviral prospective of Tinospora cordifolia on HSV-1. Int. J. Curr. Microbiol. Appl. Sci. 7 (1), 3617–3624. doi:10.20546/ijcmas.2018.701.425

Rabaan, A. A., Al-Ahmed, S. H., Haque, S., Sabi, R., Tiwari, R., Malik, Y. S., et al. (2020). SARS-CoV-2, SARS-CoV-1, and MERS-CoV: a comparative overview. Le Inf. Med. 28 (2), 174–184.

Rafiean-kopaei, M., Shakiba, A., Sedighi, M., and Bahmani, M. (2017). The analogic and anti-inflammatory activity of Linum usitatissimum in babI/c mice. J. Evidence Based Complementary Altern. Med. 22 (4), 892–896. doi:10.1177/2156587217714741

Raghavendhara, S., Tripathi, P. K., Ray, P., and Patel, A. K. (2019). Evaluation of medicinal herbs for Anti-CHIKV activity. Virology 533, 45–49. doi:10.1016/j.viro.2019.04.007

Rahman, M. M., Alam, M. N., Ulla, A., Sumi, F. A., Subhan, N., Khan, T., et al. (2017). Cardamom powder supplementation prevents obesity, improves glucose intolerance, inflammation and oxidative stress in liver of high carbohydrate high fat diet induced obese rats. Lipids Health Dis. 16 (1). 151. doi:10.1186/s12944-017-0539-x

Rai, S. N., Birla, H., Zaheer, W., Singh, S. S., and Singh, S. P. (2017). Immunomodulation of Parkinson’s disease using Muscuna pruriens (Mp.). J. Chem. Neuroanat. 85, 27–35. doi:10.1016/j.chemneu.2017.06.005

Raj, C. D., Shabi, M. M., Brahateeswaran, D., and Mahesh, N. (2006). Anti-inflammatory activity of Tylophora indica in albino rats. J. Pharmacol. Toxicol. 1 (5), 490–492. doi:10.3923/jpt.2006.490.492

Rajbhandari, M., Mentel, R., Jha, P. K., Chaudhary, R. P., Bhattarai, S., Gwali, M. B., et al. (2009). Antiviral activity of some plants used in Nepalese traditional...
medicine. Evidence Based complementary Altern. Med. 6 (4), 517–522. doi:10.1093/ecam/nem156
Rajbhandari, M., Wegner, U., Schöpke, T., Lindequist, U., and Mentel, R. (2003). Inhibitory effect of Bergenia ligulata on influenza virus A. Pharmazie 58 (4), 268–271.
Ramesh, B. N., Girish, T. K., Raghavendra, R. H., Naidu, K. A., Prasada Rao, U. J., S., and Rao, K. S. (2014). Comparative study on anti-inflammatory and anti-inflammatory activities of Caesalpinia crista and Centella asiatica leaf extracts. J. Pharm. BioAllied Sci. 6 (2), 86–91. doi:10.4103/0975-7406.129172
Randon, A. M., and Attard, E. (2007). The in vitro immunomodulatory activity of oleuropein, a secoiridoid glycoside from olea europaea L. Pharmacogn. Res. 7 (3), 263–267. doi:10.4103/0974-8490.157977
Roy, S., Mukherjee, S., Pawar, S., and Chowdhary, A. (2016). Evaluation of in vitro anti-viral activity of Datura metel Linn. against rabies virus. Pharmacogn. Res. 8 (4), 265–269. doi:10.4103/0974-8490.188874
RS. J. J., Jagadesh, S., Ganesan, S., K. V. R., and Eerike, M. (2013). Anti inflammatory activity of ethanolic extract of Nymphaea Alba flower in Swiss albino mice. Int. J. Med. Res. Health Sci. 2 (3), 474–478. doi:10.5958/j.
2319-8862.2.3.082
Sachan, S., Dhamma, K., Latheef, S. K., Samad, H. A., Mariappan, A. K., Munuswamy, P., et al. (2019). Immunomodulatory potential of tinospora cordifolia and CpG ODN (TLR21 agonist) against the very virulent, infectious bursal disease virus in SPF chickens. Vaccines 7 (3), 106. doi:10.3390/vaccines7030106
Sadekar, R. D., Kolte, A. Y., Barmase, B. S., and Desai, V. F. (1998). Immunopotentiating effects of Azadirachta indica (Neem) dry leaves powder in broilers, naturally infected with IBD virus. Indian J. Exp. Biol. 36 (11), 1151–1153.
Sadique, J., Chandra, T., Thennmozhi, V., and Elango, V. (1987). The anti-inflammatory activity of Eucosmienta littorale and Mollugo cerviana. Biochem. Med. Metab. Biol. 37 (2), 167–176. doi:10.1016/0885-4505(87)90023-5
Saharanaman, A., and Kumar, N. (2020). Network structure of COVID-19 spread and the lacuna in India’s testing strategy. arXiv:10.2139/sern.3558548.
Sahni, Y. P., and Srivastava, D. N. (1993). Anti-inflammatory activity of Withania somnifera: possible mode of action. J. Appl. Anim. Res. 3 (2), 129–136. doi:10.1080/09712119.1993.9705964
Sai Ram, M., Neetu, D., Yogesh, B., Anju, B., Dipti, P., Pauline, T., et al. (2002). Cyto-protective and immunomodulating properties of Amla (Emblica officinalis) on lymphocytes: an in vitro study. J. Ethnopharmacol. 81 (1), 5–10. doi:10.1016/S0378-7741(01)00942-4
Salhi, R. H., Odisho, S. M., Al-Shammari, A. M., and Ibrahim, O. M. S. (2017). Antiviral effects of Olea europaea leaves extract and interferon-beta on gene expression of newcastle disease virus. Adv. Anim. Vet. Sci. 5 (11), 436–445. doi:10.17582/journal/aavs/2017/5.11.436.445
Salim, B., and Noureddine, M. (2020). Identification of compounds from nigella sativa as new potential inhibitors of 2019 novel coronavirus (Covid-19): molecular docking study. chemRxiv:10.26434/chemxrxiv.20205716.v1.
Sampath Kumar, K. P., Bhownik, D., Tiwari, P., and Kharel, R. (2010). Indian traditional herbs Adhatoda vasa and its Medicinal application. J. Chem. Pharm. Res. 2 (1), 240–245.
Sanjai, A., Kasli, K., Kaushik, D., Kumar, S., and Kumar, D. (2009). Antioxidant, analgesic and anti-inflammatory activities of santalum album linn. Planta Med. 75 (04), 102. doi:10.1055/s-2009-1216540
Sasai, T. M., Dr., N., Dr., et al. (2011). Quantification of immunity status of dabur Chayaowanprash - a review part-2 (clinical studies). Indian J. Appl. Res. 4 (3), 205–211. doi:10.15373/2249555a/mar2014/61
Seddik, R., Chauhan, A., Gilhotra, U. K., and Gilhotra, A. (2013). In vitro and in vivo evaluation of antithromstatic activity of picrorhiza kurroa plant. Int. J. Pharm. Sci. Res. 4 (9), 3440–3443. doi:10.13040/IJPSR.0975-8232
Sengottuvelu, S., Rajesh, K., Sherief, S. H., Duraisami, R., Vasudevan, M., and Nandhakumar, J., et al. (2012). Evaluation of analgesic and anti-inflammatory activity of methanolic extract of Cocculus hirsutus leaves. J. Res. Educ. Indian Med. 18, 175–182.
Sharifi-Rad, J., Salehi, B., Schnitzler, P., Ayatollahi, S. A., Kobarfard, F., Fathi, M., et al. (2017). Susceptibility of herpes simplex virus type 1 to monoterpenes thymol, carvacrol, p-cymene and essential oils of Sinapis arvensis L., Lallemanita royleana Benth. and Pulicaria vulgaris Gaertn. Cell. Mol. Biol. 63 (8), 42–47. doi:10.14715/cmb/2017.63.8.10
Sharma, M. L., Rao, C. S., and Duda, P. L. (1994). Immunostimulatory activity of Picrorhiza kurroa leaf extract. J. Ethnopharmacol. 41 (3), 185–192. doi:10.1016/0378-7671(94)90031-0
Sharma, N. N., Mishra, K. P., Chanda, S., Bhardwaj, V., Tanwar, H., Ganju, L., et al. (2019). Evaluation of anti-dengue activity of Carica papaya aqueous leaf extract and its role in platelet augmentation. Arch. Virol. 164 (4), 1095–1110. doi:10.1007/s00705-019-01479-2
Sharma, R., Martins, N., Kuca, K., Chaudhary, A., Kabra, A., Rao, M. M., et al. (2019). Chayaowanprash: a traditional indian bioactive health supplement. Biomolecules 9 (5), 161. doi:10.3390/biom9050161
Sharma, V., Kaushik, S., Pandit, P., Dhill, D., Yadav, J. P., and Kaushik, S. (2019). Green synthesis of silver nanoparticles from medicinal plants and evaluation of their antiviral potential against chikungunya virus. Appl. Microbiol. Biotechnol. 103 (2), 881–891. doi:10.1007/s00253-018-9488-1
Sharma, V., Thakur, M., Chauhan, N. S., and Dixit, V. K. (2010). Immunomodulatory activity of petroleum ether extract of Anacyclus pyrethrum. Pharmac. Biol. 48 (11), 1247–1254. doi:10.3109/18881766.2010.5730602
Shin, H. S., Seo, H. J., Jung, S. Y., Choi, D. W., Kwon, D. A., Bae, M. J., et al. (2015). Turmeric (Curcuma longa) attenuates food allergy symptoms by regulating type 1/type 2 helper T cells (Th1/Th2) balance in a mouse model of food allergy. J. Ethnopharmacol. 175, 21–29. doi:10.1016/j.ethph.2015.08.038
Shin, T. Y., Kim, D. K., Chae, B. S., and Lee, E. J. (2001). Antiinflammatory action of magnolia officinalis on immediate hyperresponsivity reaction. Arch. Pharmac. Res. 24 (3), 249–255. doi:10.1007/BF02978266
Shivaprasad, H. N., Kharya, M. D., Rana, A. C., and Mohan, S. (2006). Preliminary immunomodulatory activities of the aqueous extract of Terminalia chebula. Pharm. Biol. 44 (1), 32–34. doi:10.1080/02698830600535042
Weili, H., Baoan, C., HongYing, Z., XueBing, W., DuanHong, X., and RuiLiang, C. (2011). Antiviral activity of fermented ginseng extracts against a broad range of influenza viruses. *Viruses* 10 (9), 471. doi:10.3390/10090471

Welli, H., Baocan, C., HongYing, Z., XueBing, W., DuanHong, X., and RuiLiang, C. (2011). Antiviral activity of Mentha spicata Linn. extracts against porcine parvovirus in vitro. *Jiangou J. Agric. Sci.* 27 (3), 556–560.

Wen, R., Lv, H., Jiang, Y., and Tu, P. (2018). Anti-inflamatory isoflavones and isoflavanones from the roots of Pongamia pinnata (L.) Pierre. *Biorg. Med. Chem. Lett.* 28 (6), 1050–1055. doi:10.1016/j.bmcl.2018.02.026

WHO (2020a). Coronavirus disease (COVID-19) outbreak. Emergencies Dis.

WHO (2020b). Rolling updates on coronavirus disease (COVID-19). Events as they happen. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019 (Accessed December 19, 2020).

Win, N. N., Kodama, T., Lae, K. Z. W., Win, Y. Y., Ngwe, H., Abe, I., et al. (2019). Bis-iridoid and iridoid glycosides: viral protein R inhibitors from Picrorhiza kurroa and Chinese jujube extracts in mice. *J. Ethnopharmacol.* 205, 105021. doi:10.1016/j.jep.2020.105021

Win, N. N., Kodama, T., Lae, K. Z. W., Win, Y. Y., Ngwe, H., Abe, I., et al. (2019). Bis-iridoid and iridoid glycosides: viral protein R inhibitors from Picrorhiza kurroa collected in Myanmar. *Fitoterapia* 134, 101–107. doi:10.1016/j.fitote.2019.02.016

Wintachai, P., Kaur, P., Lee, R. C. H., Ramphan, S., Kuadkritkan, A., Wikan, N., et al. (2013). Activity of andrographolide against chikungunya virus infection. *Sci. Rep.* 3 (1), 14179. doi:10.1038/srep14179

Wirotesangthong, M., Inagaki, N., Tanaka, H., Thanakijcharoenpath, W., and Yagi, K. (2015). Activity of andrographolide against chikungunya virus infection. *Front. Pharmacol.* 6, 170. doi:10.3389/fphar.2016.00170

Wu, W., Li, Y., Jiao, Z., Zhang, L., Wang, X., and Qin, R. (2019). Phyllanthin and hypophyllanthin from Phyllanthus amarus ameliorates immune-inflammatory response in ovalbumin-induced asthma: role of IgE, Nrf2, iNOS, TNF-α, and IL-4. *S. Immunopharmacol. Immunotoxicol.* 41 (1), 55–67. doi:10.1080/08923973.2018.1545788

Xiang, Y., Pei, Y., Qu, C., Dai, Z., Ren, Z., Yang, K., et al. (2011). In vitro anti-herpes simplex virus activity of I2,6-A6-tetra-O-galloyl-β-D-glucose from Phyllanthus emblica L. (Euphorbiaceae). *Phytother. Res.* 25 (7), 975–982. doi:10.1002/ptr.3368

Xu, H. B., Ma, Y. B., Huang, X. Y., Geng, C. A., Wang, H., Zhao, Y., et al. (2015). Bioactivity-guided isolation of anti-hepatitis B virus active sesquiterpenoids from Cassia occidentalis L. on ovalbumin-induced allergies in a mouse model of allergic asthma. *J. Ethnopharmacol.* 171, 131–140. doi:10.1016/j.jep.2015.05.040

Xu, W., Hu, M., Zhang, Q., Yu, J., and Su, W. (2018). Effects of anthraquinones from Cassia occidentalis L. on ovalbumin-induced allergies in a mouse model of allergic asthma. *J. Ethnopharmacol.* 221, 1–9. doi:10.1016/j.jep.2018.04.012

Yang, H., Huang, Z., Aiping, Y., Qi, L., Ning, D., Tu-Lin, L., et al. (2019). Jatrophacine, a 4,5-seco-rhamnoflaned diterpenoid with potent anti-inflammatory activity from Jatropha curcas. *Nat. Prod. Res.* 1–5. doi:10.1080/14786419.2019.1660656

Yang, Y., Islam, M. S., Wang, J., Li, Y., and Chen, X. (2020). Traditional Chinese medicine in the treatment of patients infected with 2019-new coronavirus (SARS-CoV-2): a review and perspective. *Int. J. Biol. Sci.* 16 (10), 1708–1717. doi:10.7150/ijbs.45538

Ye, H. F., Hong, C. Y., Huang, Y. L., Liu, T. Y., Choo, K. B., and Chou, C. K. (1993). Effect of an extract from Phyllanthus amarus on hepatitis B surface antigen gene expression in human hepatoma cells. *Antiviral Res.* 20 (3), 185–192. doi:10.1016/0166-3542(93)90019-F

Yu, Z. p., Xu, D. D., Lu, L. F., Zheng, X. D., and Chen, W. (2016). Immunomodulatory effect of a formula developed from American ginseng and Chinese jujube extracts in mice. *J. Zhejiang Univ. Sci. B.* 17 (2), 147–157. doi:10.1631/jzus.B1500170

Yuki, K., Fujigoi, M., and Koutsogiannaki, S. (2020). COVID-19 pathophysiology: a review. *Clin. Immunol.* 215, 108427. doi:10.1016/j.clim.2020.108427

Zaia, M. G., Cagnazzo, M., di, O., Feita, K. A., Soares, E. G., Faccioli, L. H., et al. (2016). Anti-inflammatory properties of menthol and menthone in Schistosoma mansoni infection. *Front. Pharmacol.* 7, 170. doi:10.3389/fphar.2016.00170

Zare, A., Farzaneh, P., Pourpak, Z., Zahedi, F., Moin, M., Shahabi, S., et al. (2008). Purified aged garlic extract modulates allergic airway inflammation in Balb/c mice. *Iran. J. Allergy Asthma Immunol.* 7 (3), 133–141.

Zaveri, M., Khandhar, A., and Jain, S. (2008). Quantiﬁcation of baicalein, chrysin, biochanin-A and ellagic acid in root bark of Oroxylum indicum by RP-HPLC with UV detection. *Eurasion J. Anal.Chem.*

Zhang, T., Wu, Q., and Zhang, Z. (2020). Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. *Curr. Biol.* 30 (7), 1346–1351.e2. doi:10.1016/j.cub.2020.03.022

Zhang, T., Wu, Q., and Zhang, Z. (2020). Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. *Curr. Biol.* 30 (7), 1346–1351.e2. doi:10.1016/j.cub.2020.03.022

Zhou, H., Deng, Y. M., and Xie, Q. M. (2006). The modulatory effects of the essential oil of ginger on the cellular immune response in vitro and in vivo in mice. *J. Ethnopharmacol.* 105 (1–2), 301–305. doi:10.1016/j.jep.2005.10.022

Ziment, I., and Tashkin, D. P. (2000). Alternative medicine for allergy and asthma. *J. Allergy Clin. Immunol.* 106 (4), 603–614. doi:10.1067/mia.2000.109432