ANNALS OF MULTIDISCIPLINARY RESEARCH, INNOVATION AND TECHNOLOGY (AMRIT)

(A peer-reviewed open access multidisciplinary journal)

www.adtu.in/amrit

REVIEW ARTICLE

PHARMACEUTICAL SCIENCE

A Pragmatic Plan for a COVID-19 Combat-ready Improvised Facemask with an Anti-viral filter: Utilizing North-East Indian Medicinal Plants

Manash Pratim Pathak[1*], Pompy Patowary[2], Aparoop Das[2], Saikat Sen[1],Biplab Kumar Dey[1], Pronobesh Chattopadhyay[3], Satyendra Deka[4]

[1]Faculty of Pharmaceutical Science, Assam down town University, Panikhaiti, Guwahati, Assam-781026, India
[2]Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh-786 004, Assam, India
[3]Division of Pharmaceutical Technology, Defence Research Laboratory, Tezpur-784 001, Assam, India
[4]Pratiksha Institute of Pharmaceutical Sciences, Guwahati-781026, Assam, India
[*]Corresponding author: Manash Pratim Pathak, *Email: manashpharma@rediffmail.com*

Article Chronicle: Received: 12/01/2023 Accepted: 25/05/2023 Published: 26/06/2023

Abstract

To date, no effective anti-viral, immunomodulatory therapies for COVID-19 has been reported, making symptom directed supportive measures as the conventional practice for treatment and defining Personal Protective Equipment (PPE) as preventive devices to control transmission. With the upsurge of positive cases and looking at the severity of the infection, it is the need of the hour to improvise the available PPEs. A holistic approach for a biological protective face mask impregnated with an anti-viral extract may prove to be a novel idea against the epidemic spread of COVID-19. Based on a thorough review of published literatures, we have reported a few of the potent anti-viral ethnomedicines of North East India based on their mechanism of action. The facemask may further be reinforced with 'water repellent' technology. Therefore, the paper aims to apprise the readers of the concept of utilizing herbal resources against COVID-19 pandemic.

Keywords: *Personal Protective Equipment, Facemask, Anti-viral, Water-repellent, North East India, Oxyphenbutazone, Topical Delivery, Transdermal Patches*

1 Introduction

1.1 Clinical Manifestations and General Management of COVID-19

In the past two decades, two highly pathogenic coronavirus viz., the coronavirus accountable for severe acute respiratory syndrome (SARS-Cov) and Middle East respiratory syndrome (MERS-Cov) have been reported(1). In December 2019, the Chinese Center for Disease Control and Prevention, China, isolated a new strain of coronavirus, SARS-Cov-2 which was connected with the pneumonia like outbreak in Wuhan(2). SARS-Cov-2 was officially named coronavirus Disease (COVID-19) on the 11th of February 2020(3) Symptoms in patients infected with COVID-19 include fever, chills, cough, dyspnea and fatigue(4). COVID-19 positive patients suffers from acute respiratory distress syndrome (ARDS) characterized by formation of hyaline membrane and desquamation of pneumocytes as evident from histological examination of the lungs(4). ARDS is followed by a 'cytokine storm' which involves rampage of a considerable amount of proinflammatory cytokines including interleukins (IL)-6, tumour necrosis factor (TNF)-, and IL-12 through bloodstream to the target organs(5). Precisely, till date, no anti-viral, immunomodulatory therapies for COVID-19 has been reported to be effective, making symptom directed supportive measures as the conventional practice for treatment by physicians which includes conventional antiviral or anti-neoplastics like interferon alfa-2b, corticosteroids like methylprednisolone and broad-spectrum antibiotics like meropenem and anti-human IL-6 receptor monoclonal antibody, tocilizumab(4). Lately, hydroxychloroquine as well as remdesivir(6) has reported to been administered as prophylactic as well as therapeutic strategy against COVID-19 cases; however, the results ob-

tained were of mixed nature(7). In an another attempt to counter the growing COVID-19 cases, most recently, convalescent plasma collected from recovered COVID-19 patients was administered to infected patients and the outcome was reported to be satisfactory, however, this treatment needs to undergo various assessment and screening before coming to a final conclusion(8). A number of COVID-19 vaccines namely SII/Covishield, AstraZeneca/AZD1222, Janssen/Ad26.COV 2.S, Sinopharm, Moderna, Sinovac-CoronaVac, Covaxin have now been approved or licensed for human usage and has been administered in humans in different regimen across the world(9) (Kumar et al., 2023). Mass vaccination is being initiated worldwide and India has launched its world's largest vaccination program on full volume across all states, and as of 15th May 2023, 2,206,693,803 vaccine doses has been administered across India(10). All these treatment options are being tried in a trial and error basis and it may take several months or even years to discover a proper therapy to treat COVID-19 patients. So, at this critical juncture, it is the need of the hour to propagate an alternative action plan to limit the ever growing transmission. So, world body such as WHO as well as national body like Indian Council for Medical Research (ICMR), India, has suggested various non-medical preventive and mitigation measures such as social distancing, hand hygiene, coughing/sneezing etiquette, proper use of face mask/cover for general public and devised certain 'Personal Protection Equipment' (PPE) like medical grade facemask, face-shield, protective clothing, goggles, gloves, gown as well as for specific procedures, respirators (i.e., N95 or FFP2 standard or equivalent) and aprons for healthcare personnel to counter the transmission. Controlling the growing transmission should be the main concern and for this, development of a quick solution using locally available resources is the need of the hour.

1.2 Recent Update on COVID-19

On 31^{st} December 2019, the WHO Country office in China received the first report of an outbreak of pneumonia like unknown cause and on 5^{th} January 2020, it issued its first guidance on the novel coronavirus. Within a few weeks, the virus rapidly spread from its origin in Wuhan City of Hubei Province of China to the rest of the world spreading its routes to India as well. On 11^{th} March 2020, WHO designated "coronavirus disease 2019" (Covid-19) a global pandemic. As of May 31^{st}, 2023 in 231 countries, about 689,549,946 cases have been confirmed, 661,991,715 cases recovered with over 6,884,636 total deaths reported. In India, on May 31^{st},, 2023, about 44,990,588 cases have been confirmed with 44,454,496 cases recovered and over 531,870 total deaths reported(11). The May 3^{rd}, wave which started in late 2021 presented a devastating effect in India where confirmed cases and casualties surpassed the May 1^{st}, and May 2^{nd}, waves of COVID-19. The first two years of the COVID-19 pandemic were characterized primarily by recurrent mutations in the SARS-CoV-2 Spike protein to a number of residues, including K417, L452, E484, N501, and P681, that expressed in several variants such as Alpha, Beta, Gamma, and Delta. However, in the third year of the pandemic comprising the spring of 2022, there was the appearance of Omicron and its sublineages, which resulted in mutations at various amino acid residues that appeared to be prominent during the summer and autumn of 2022(12). On May 4^{th}, May 2023, the WHO Director-General declared that COVID-19 to be no longer a public health emergency of international concern (PHEIC)(13).

2 Ethnomedicinal Plants with Antiviral Efficacy

Several effective herbal therapies are under evaluation in clinical trials for viral diseases to prove their effectiveness and safety. 'The Times of India' also stated that there is a strong need to bring traditional medicine into the mainstream for the fight against COVID-19. Assam and northeast India (NEI) as a whole is a treasure trove of medicinal plants and herbs and is renowned for its rich fauna. This region is important for conservation of biodiversity because of its high species diversity and high level of endemism. The Institute of Bioresources and Sustainable Development (IBSD), Manipur, India, in collaboration with Botanical Survey of India (BSI), Kolkata, India has recently released a 'Compendium of Antiviral Medicinal Plants of North East India' having information on around seventy medicinal plants having documented anti-viral activities(14). Numerous studies reported the existence as well as efficacy of antiviral plants and herbs in this region (Table 1). Tulsi plant (*Ocimum sanctum, OS*), clove (*Syzygium aromaticum*, SZ) and ginger (*Zingiber officinale*, ZO) are some of the plants that are abundantly available locally and are reported to having potent anti-viral efficacy. Hot aqueous extract of OS was found to be effective against Newcastle disease virus (NDV) and Infectious bursal disease virus (IBDV) in chicken embryo fibroblast (CEF) (in vitro) cell culture as well as in chickens (in vivo)(15). Moreover, crude extract of OS has also shown potent anti-viral activity against endemic avian influenza H9N2 virus(16). Apigenin, found in OS extract, was found to be having improved binding properties in H1N1 influenza virus proteins neuraminidase and hemagglutinin when screened with molecular docking. Aqueous extracts of SZ and ZO was found to be very effective against Feline calicivirus, a surrogate for human norovirus(17) as well as essential oil of SZ was found to be effective against H1N1 virus strains18.

In vitro study of another species of Ocimum, Ocimum gratissimum, commonly called as Ram Tulsi, has shown to exhibit potent inhibition of HIV-1 and HIV-2 and expresses cytotoxicity by the inhibition of reverse transcriptase and pro-viral DNA replication of HIV-1, mitigating the antiviral potential of the plant(28). The extracts of some common potent medicinal plants abundantly found in Northeast India viz. *Dillenia indica* (Vernacular name: Outenga), *Odina wodier* (Vernacular name: Jia) , *Moringa oleifera* (Vernacular name: Sajana) exhibited significant antiviral activity against herpes simplex virus type I (HSV-1) at non-toxic concentrations(29). Again, the same study reported *Morus alba* (Vernacular name: Nuni) and *Butea monosperma* (Vernacular name: Polash) to have antiviral efficacy at higher concentration tested in African green monkey kidney cells (Vero cells). Pteridophytes are known to be the primitive vascular plant groups. An article assessed and outlined 4 such pteridophytes, of Arunachal Pradesh of NEI with ethno medicinal value as an antiviral. It

Table 1: Medicinal Plants of Northeast India With Reported Antiviral Activity

Medicinal Plant	**Effective against (Virus)**	**Association with humans/symptoms**	**References**
Ocimum sanctum	Newcastle disease virus	Yes/mild conjunctivitis and influenza-like symptoms, minimally pathogenic in humans	(19)
Ocimum sanctum	H9N2	Yes/flu like illness	(20)
Ocimum sanctum, *Syzygium aromaticum*	H1N1	Yes/febrile respiratory illness, influenza, vomiting, diarrhea	
Syzygium aromaticum, *Zingiber officinale*	Feline calicivirus	Yes/ diarrhea, vomiting, and abdominal cramping	(21)
Ocimum gratissimum	HIV-1 and HIV-2	Yes, acquired immunodeficiency syndrome	(22)
Azardirachta indica,	HSV-1	Yes/ labial herpes, ocular keratitis, genital disease and encephalitis and morbidity in immunocompromised patients	(23)
Dillenia indica, *Odina wodier*, *Moringa oleifera*,	HSV-1		
Solanum torvum	HSV-1		
Aegle marmelos	coxsackieviruses	Yes/ aseptic meningitis, myocarditis, respiratory illness	(24)
Andrographis paniculata	Flavivirus	Yes, dengue fever, dengue hemorrhagic	25
Andrographis paniculata	or dengue virus	fever and/or dengue shock syndrome	25
Acorus calamus L	DENV2 (dengue virus)	Yes, dengue fever	(26)
Curcuma longa	SARS-CoV-2 main proteinase (Mpro)	Yes, Cough, Shortness of breath or, Fatigue, Muscle or body aches, Headache, loss of taste or smell	(27)

includes *Adiantum capillus veneris*, *Equisetum ramosissimum*, *Helminthostachys zeylanica* and *Pteris vitata*(30).A recent systematic report on use of plants by the indigenous tribes from the Chirang Reserve Forest found some indigenous plants including *Aglaia spectabilis*, *Bischofia javanica*, *Digitalis grandiflora*, *Dysoxylum gotadhora* and 11 other plants31 which showed anti-enteroviral activity against type 71, BrCr strain enterovirus, with rupintrivir as a positive control. Meliacine and meliacaprin are peptides isolated from *Melia azedarach*, a deciduous tree native to northeastern India. These peptides were found to exhibit an antiviral activity when examined on Vesicular stomatitis (VSV), polio and HSV viruses in cell cultures in vitro with no cytotoxic effect(32). Aqueous extract of *Azadhiracta indica* (Vernacular name: Neem) bark significantly inhibited HSV-1 entry and viral glycoprotein mediated cell-cell fusion in a cell culture model(23). *Solanum torvum* (Vernacular name: Tita-bhekuri) is a wild edible plant of Northeast India. The extracted glycosides torvanol A and torvoside H from the fruits of *S. torvum* exhibited antiviral potency against HSV-1(33). Furthermore, the in vitro antiviral activity of marmelide extracted from *Aegle marmelos* (Vernacular name; Bael), the holy plant of India, was found to possess potent anti-viral potency against human coxsackieviruses(34). The methanolic extract of *Andrographis paniculata* (Vernacular name: Kalmegh), showed the highest antiviral inhibitory effect on a serotypic Dengue virus (DENV)-1 by antiviral assay based on cytopathic effects(25). A systematic review of plants of the Himalayan countries have been documented which were screened in vitro and in vivo against viral pathogens involved in bronchitis caused by viruses including influenza, rhinoviruses, adenoviruses, coronavirus and respiratory syncytial virus. Out of those, the effective ethnomedicines were mostly documented from India(35). NEI forms an exclusive biogeographic territory encircling some of the major recognized biomes worldwide and is also one of the biodiversity hotspots of the world with about 50% of India's biodiversity(36). It has become imperative to screen the above mentioned plants in detail not only for their in-vitro and in-vivo activity of the extracts but also for their antiviral based mechanism of actions.

3 Significance of PPE

Having been through the 2019-2020 experience with COVID-19, the medical committees are well aware of the ongoing challenges and controversies surrounding PPE for healthcare personnel. PPE is used to minimize potential exposure to infective agents and materials thereby providing protection to both healthcare workers and patients. After SARS and MERS pandemic, the importance of PPE was underscored in the recent outbreak of COVID-19. PPE is the only effectual measure within a package that comprises administrative, environmental as well as engineering controls (Infection prevention, 2014). However, the lack of adequate PPE for frontline healthcare workers has grown due to constant up-surging rates of COVID-19 related infection and death. Moreover, before this pandemic, China produced about half the world's face masks(37). Currently, as the infection spread across China, their exports have gradually minimized. Moreover, the uprising in global demand, caused by not only by the number of COVID-19 cases but also by panic buying and stockpiling, misinformation, and irrational use will lead to further scarcity of PPE globally. Though PPE is an important component of standard precautions, inappropriate use of PPE can actually increase infection hazards(38). Therefore, appropriate strategies can be employed to improve compliance with PPE. It has been reported that during the SARS outbreak, healthcare workers accounted for almost 20% of the total cases because of

failure to properly use PPE. Although PPE is usually worn only for short periods, coronavirus can survive for hours on surfaces and viral infection can be spread by surface-to-hand and hand-to-hand contact(39). Some authors have also concluded that coronaviruses survived on hospital PPE longer than the contact duration with an infected patient(40). The key components of PPE are gloves, gowns, aprons, masks, goggles, visors, caps, and theatre footwear.

3.1 The Need for an Effective Face Mask

Inputs from current information suggest that there are mainly two routes of transmission of the COVID-19 virus, which are, respiratory droplets and contact with a contaminated surface. Coughs and sneezes of an infected person generate respiratory droplets and a person in close proximity (within 1m) of the infected person has a very high risk of getting exposed to the generated infective respiratory droplets. Moreover, infective respiratory droplets may also perch on any surface where the virus may remain viable for a considerable time thereby making the environment occupied by an infected person a likely source of transmission. And a non-infected person may become vulnerable to the virus when he/she comes in contact with such an infected person or the surroundings occupied by an infected person. So, it is of utmost important for an infected person as well as health workers that come in contact with the infected person to wear a medical grade face mask. Moreover, a used and discarded facemask may become a vector for that disease as they tend to multiply in its fiber. That is why; a washable, reusable facemask with an anti-viral filter may counter the transmission of SARS-Cov-2 and other deadly viruses. At this critical juncture, development of a reusable antiviral-water-resistant facemask is deemed to be a suitable solution. Using locally available resources and employing simple technology which is cost effective, a state-of-the art facemask may be developed. Medical masks, defined as surgical procedure masks that are flat, pleated or cup shaped, are affixed to the head with straps(3). Studies involving influenza, influenza-like illness, and human coronaviruses suggests that proper use of medical masks may prevent the spread of infectious respiratory droplets from an infected to a non-infected person a well as may prevent potential contamination of the surfaces by these respiratory infectious droplets(3). Growing incident of COVID-19 positives cases worldwide made many countries to implement the use of non-medical home-made masks among general public and vulnerable healthy persons. Many studies strongly suggested universal public masking in the United States (US) both for indoor and public spaces, including public gatherings, markets and also in closed workplaces with the hope of slowing down the transmission(41). Finally, on 3^{rd} April 2020, countries that claimed benefits of home-made face cover were cited by the Ministry of Health and Family Welfare, Government of India and recommended the use of home-made reusable mask for general public and also for people who are not suffering from any medical conditions or having breathing difficulties. On 26th April 2020, WHO advised the decision makers of countries that are currently considering the use of masks, to follow a risk-based approach before allowing use of non-medical masks in the society (q-a-on-COVID-19-and-masks, (WHO, 26th April 2020). Studies reported that medical or surgical mask is 3 fold effective in blocking microorganism transmission expelled by volunteers than the home-made mask(42). However, in another recent study it was reported that neither surgical mask nor cotton mask was effectively able to filter SARS-CoV-2 from cough by infected patients. The study concluded that these masks were unable to filter SARS-CoV-2 due to its microscopic size that ranges between 0.08 to 0.14 m(43). It was also reported that high filter efficiency mask may not solely uplift the global burden of COVID-19 infection(44).

3.2 Improvising Facemasks With the Help of Natural Resources

Overviewing the current status, an antiviral mask may be an effective approach to constrict the spreadability of COVID-19. A number of patents has been filed or subsequently granted on various anti-viral medical devices including facemask. A United States (US) patent, polyphenol tea extract impregnated in a nonwoven fabric was used as filter for design of an anti-viral face mask. This polyphenol tea extract impregnated face mask, capable of maintaining a high virus trapping performance, inactivated the trapped viruses and prevented them from rescattering(45). In another US patent, an anti-viral glove was developed by coating the inner layer with an anti-infective agent consisting of chlorhexidine and pharmaceutically acceptable salts of chlorhexidine with a non-adsorbant lubricating agent, the anti-infective agent was found to be effective within 10 minutes of exposure to a liquid(46). (6) developed a novel type of mask with an antibacterial function using extractant of the Chinese herb Scutellaria baicalensis(47). In another study, an all-natural compound of green tea extract QR-435-impregnated masks was tested in vitro against H3N2 in Madin-Darby canine kidney (MDCK) cells and was found effective in preventing passage of the H3N2 virus(48). Most recently, an invention has been patented relating to antiseptic compositions, particularly, to a nasal antiseptic barrier composition and having antimicrobial, antiviral, and antifungal properties, with ethyl alcohol as the active ingredient(49). Screening the aforementioned traditional north East Indian plants, having a long history of antiviral potency, may provide a herbal extract having potent antiviral activity thereby serving for an established segment of the public health system. A biological protective face mask with an antiviral function may prove to be a novel idea to prevent the epidemic spread of COVID-19 and protect infected person as well as the people involved in healthcare sector. Moreover, even after discarding the proposed facemask, the anti-viral filter will continuously inhibit the virus from multiplication.

3.3 Salient Features of an Antiviral Extract-impregnated Face Mask

While designing a face mask the following points may be considered:

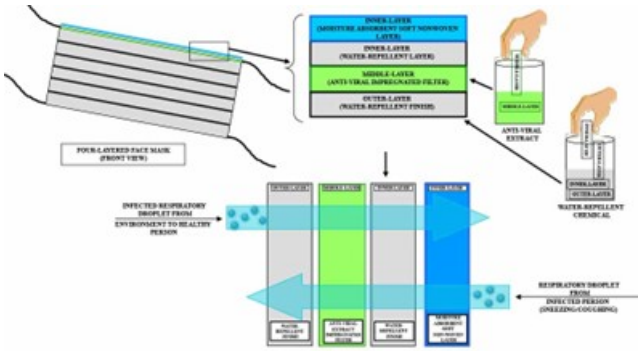

Figure 1: A basic design for an antiviral extract-impregnated face mask

• It should bridge the gap between unapproved disposable masks and expensive, approved replaceable cartridge respirators.
•An effective face mask may be prepared comprising of two to four layers of polypropylene based nonwoven fabric or 100% cotton woven fabric.
•A filtration medium comprising a nonwoven fabric formed of continuous thermoplastic filaments that restrict the penetration of macromolecules size >0.5 micron.
•The outer most layer that contacts the face may be of a material that permits more comfortable wearing of the mask.
•The middle layer may be made of nonwoven polypropylene-based fabric fabricated to an anti-viral herbal extract filter.
•The fabric should be lightweight and somewhat porous with heat/moisture exchanging properties
•The biological agent forming part of porous segment of the mask should extend across the nasal and mouth portions of the face of a wearer. A basic design for an antiviral extract-impregnated face mask has been depicted in (Figure 1).

3.4 Reinforcing the Anti-viral Impregnated Facemasks With Water-repellent Technology

Although there are reports and findings of anti-viral medicinal plant or their essential oils, water-repellant face mask or anti-viral face mask are available, however, no literature was found where the combination of both the anti-viral coating or impregnation and water-repellent finish was demonstrated in any type of facemask. Incorporation of 'water-repellent' or 'hydrophobic' technology in fabric is an old technique dated back to 1920(50). Since then, this technology has been rigorously utilized in various sector including health and medical field. This technology protects the health workers from exposure to body fluids accidentally from an infected patient. Numerous studies have been carried out to improvise medical masks using this technology. Shen and his team developed a water-repellant surgical mask where effects of repellent finish and layering order on the fluid resistance, filtration ability and differential pressure of surgical face masks were studied and found that the repellent finish decreased the filtration ability of the cover layer, without affecting the filtration ability of the filtration layer(51).The FDA has listed 5 major tests to determine the barrier performance and safe use of face mask including, fluid resistance, filtration efficiency, air exchange, flammability and biocompatibility. Among these, filtration efficiency is the most widely accepted one(52). Also, three-dimensional (3D) printing has been used to prepare drug-containing nose masks specifically tailored to the patient. (53), designed a 3D-printed anatomically customized wound dressings using silver, zinc and copper as the anti-microbial agents in the shape of a nose and ear(53). Moreover, an improved face mask can also be designed containing the anti-viral agent encapsulated within micro miniature cells of the mask in which, such capsules may be ruptured to allow their contents be released to the cells of the mask effecting the destruction of viruses passing through the mask when the wearer breathe(54).

4 Conclusion

The main aim of this paper was to apprise the readers about the concept of utilizing herbal resources against COVID-19. Nosocomial transmission of COVID-19 associated severe ARDS to patients and healthcare workers has been a notorious characteristic of this disease. Moreover, it is a likely possibility that epidemics will continue to occur, and with emerging new organisms, may be more violent than ever, as the virus mutates. Therefore, the need arises to develop novel effective methods of infection control that are both cost-effective and accessible to the maximum population. Hence, a holistic approach of integrating and introducing a specific herbal extract-impregnated face mask can be turned into practice by taking the aforementioned approaches and processed for further preclinical and clinical trials. India is the country where the world's oldest living healthcare system originated and therefore it's time to combat the crisis using its traditional healthcare might.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgments

The authors are grateful to the Faculty of Pharmaceutical Science, Assam Down Town University, Panikhaiti, Guwahati, Assam, 781026, India, for their necessary support.

References

[1] T. Chen, D. Wu, H. Chen, W. Yan, D. Yang, G. Chen, K. Ma, D. Xu, H. Yu, H. Wang *et al.*, "Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study," *bmj*, vol. 368, 2020.

[2] N. Zhu, D. Zhang, W. Wang, X. Li, B. Yang, J. Song, X. Zhao, B. Huang, W. Shi, R. Lu *et al.*, "A novel coronavirus from patients with pneumonia in china, 2019," *New England journal of medicine*, 2020.

[3] "Rolling updates on coronavirus disease (COVID-19)," 2020. [Online]. Available: https://www.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen

[4] Z. Xu, L. Shi, Y. Wang, J. Zhang, L. Huang, C. Zhang, S. Liu, P. Zhao, H. Liu, L. Zhu *et al.*, "Pathological findings of covid-

19 associated with acute respiratory distress syndrome," *The Lancet respiratory medicine*, vol. 8, no. 4, pp. 420–422, 2020.

[5] Y. Li, M. Chen, H. Cao, Y. Zhu, J. Zheng, and H. Zhou, "Extraordinary gu-rich single-strand rna identified from sars coronavirus contributes an excessive innate immune response," *Microbes and infection*, vol. 15, no. 2, pp. 88–95, 2013.

[6] M. Wang, R. Cao, L. Zhang, X. Yang, J. Liu, M. Xu, Z. Shi, Z. Hu, W. Zhong, and G. Xiao, "Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-ncov) in vitro," *Cell research*, vol. 30, no. 3, pp. 269–271, 2020.

[7] S. Rathi, P. Ish, A. Kalantri, and S. Kalantri, "Hydroxychloroquine prophylaxis for covid-19 contacts in india," *The lancet infectious diseases*, vol. 20, no. 10, pp. 1118–1119, 2020.

[8] C. Shen, Z. Wang, F. Zhao, Y. Yang, J. Li, J. Yuan, F. Wang, D. Li, M. Yang, L. Xing *et al.*, "Treatment of 5 critically ill patients with covid-19 with convalescent plasma," *Jama*, vol. 323, no. 16, pp. 1582–1589, 2020.

[9] K. Rakesh, S. Gupta, and A. Gupta, "Current status and future challenges with coronavirus (covid-19): an update on vaccines," *Life Research*, vol. 6, p. 1–6, 2023. [Online]. Available: https://www.tmrjournals.com/article.html?J_num=14&a_id=2476

[10] WHO, "WHO COVID19(Homepage)," 2023. [Online]. Available: https://covid19.who.int/region/searo/country/in

[11] "Reported cases and deaths by country or territory," 2023. [Online]. Available: https://www.worldometers.info/coronavirus/#countries

[12] D. Focosi, R. Quiroga, S. McConnell, M. C. Johnson, and A. Casadevall, "Convergent evolution in sars-cov-2 spike creates a variant soup from which new covid-19 waves emerge," *International journal of molecular sciences*, vol. 24, no. 3, p. 2264, 2023.

[13] WHO, "Statement on the fifteenth meeting of the IHR (2005) Emergency Committee on the COVID-19 pandemic," 2023. [Online]. Available: https://covid19.who.int/region/searo/country/in

[14] P. Mukherjee and A. Mao, "Compendium of the anti-viral medicinal plants of northeast india," *Institute of Bioresources and Sustainable Development, Imphal and Botanical Survey of India, Kolkata*, pp. 5–10, 2021.

[15] P. Varshney, S. Dash, A. Bhatia *et al.*, "In vitro and in vivo antiviral potential of hot aqueous extract of ocimum sanctum and argemone mexicana leaves," *Medicinal Plant Research*, vol. 3, 2013.

[16] S. Ghoke, R. Sood, N. Kumar, A. Pateriya, S. Bhatia, A. Mishra, R. Dixit, V. Singh, D. Desai, D. Kulkarni *et al.*, "Evaluation of antiviral activity of ocimum sanctum and acacia arabica leaves extracts against h9n2 virus using embryonated chicken egg model," *BMC complementary and alternative medicine*, vol. 18, no. 1, pp. 1–10, 2018.

[17] H. A. Aboubakr, A. Nauertz, N. T. Luong, S. Agrawal, S. A. El-Sohaimy, M. M. Youssef, and S. M. Goyal, "In vitro antiviral activity of clove and ginger aqueous extracts against feline calicivirus, a surrogate for human norovirus," *Journal of food protection*, vol. 79, no. 6, pp. 1001–1012, 2016.

[18] A. Brochot, A. Guilbot, L. Haddioui, and C. Roques, "Antibacterial, antifungal, and antiviral effects of three essential oil blends," *Microbiologyopen*, vol. 6, no. 4, Aug. 2017.

[19] L. K. Csatary, R. W. Moss, J. Beuth, B. Torocsik, J. Szeberényi, and T. Bakács, "Beneficial treatment of patients with advanced cancer using a newcastle disease virus vaccine (mth-68/h)," *Anticancer research*, vol. 19, no. 1, pp. 635–638, 1999.

[20] Y. Lin, M. Shaw, V. Gregory, K. Cameron, W. Lim, A. Klimov, K. Subbarao, Y. Guan, S. Krauss, K. Shortridge *et al.*, "Avian-to-human transmission of h9n2 subtype influenza a viruses: relationship between h9n2 and h5n1 human isolates," *Proceedings of the National Academy of Sciences*, vol. 97, no. 17, pp. 9654–9658, 2000.

[21] M. H. Lee, B.-H. Lee, J.-Y. Jung, D.-S. Cheon, K.-T. Kim, and C. Choi, "Antiviral effect of korean red ginseng extract and ginsenosides on murine norovirus and feline calicivirus as surrogates for human norovirus," *Journal of ginseng research*, vol. 35, no. 4, p. 429, 2011.

[22] J. B. Jackson, S. Y. Kwok, J. J. Sninsky, J. S. Hopsicker, K. J. Sannerud, F. S. Rhame, K. Henry, M. Simpson, and H. H. Balfour, Jr, "Human immunodeficiency virus type 1 detected in all seropositive symptomatic and asymptomatic individuals," *J. Clin. Microbiol.*, vol. 28, no. 1, pp. 16–19, Jan. 1990.

[23] V. Tiwari, N. A. Darmani, B. Y. J. T. Yue, and D. Shukla, "In vitro antiviral activity of neem (azardirachta indica l.) bark extract against herpes simplex virus type-1 infection," *Phytother. Res.*, vol. 24, no. 8, pp. 1132–1140, Aug. 2010.

[24] K. Mena, C. Gerba, C. Haas, and J. Rose, "Risk assessment of waterborne coxsackievirus," *Journal of the American Water Works Association*, vol. 95, no. 7, pp. 122–131+12, Jul. 2003.

[25] S. L. Abd Kadir, H. Yaakob, and R. Mohamed Zulkifli, "Potential anti-dengue medicinal plants: a review," *J. Nat. Med.*, vol. 67, no. 4, pp. 677–689, Oct. 2013.

[26] X. Yao, Y. Ling, S. Guo, W. Wu, S. He, Q. Zhang, M. Zou, K. S. Nandakumar, X. Chen, and S. Liu, "Tatanan a from the acorus calamus l. root inhibited dengue virus proliferation and infections," *Phytomedicine*, vol. 42, pp. 258–267, 2018.

[27] V. D. Kharisma, A. Agatha, A. N. M. Ansori, M. H. Widyananda, W. C. Rizky, T. G. A. Dings, M. Derkho, I. Lykasova, Y. Antonius, I. Rosadi *et al.*, "Herbal combination from moringa oleifera lam. and curcuma longa l. as sars-cov-2 antiviral via dual inhibitor pathway: A viroinformatics approach," *Journal of Pharmacy & Pharmacognosy Research*, vol. 10, no. 1, pp. 138–146, 2021.

[28] S. Pandey, S. Singh, N. Kumar, and R. Botany, "Antiviral, antiprotozoal, antimalarial and insecticidal activities of ocimum gratissimum l," *Asian Journal of Pharmaceutical Research and Development*, vol. 5, pp. 1–9, 12 2017.

[29] D. Goswami, P. K. Mukherjee, A. Kar, D. Ojha, S. Roy, and D. Chattopadhyay, "Screening of ethnomedicinal plants of diverse culture for antiviral potentials," 2016.

[30] A. Benniamin, "Medicinal ferns of north eastern india with special reference to arunachal pradesh," 2011.

[31] S. K. Panda, R. Das, P. Leyssen, J. Neyts, and W. Luyten, "Assessing medicinal plants traditionally used in the chirang reserve forest, northeast india for antimicrobial activity," *J. Ethnopharmacol.*, vol. 225, pp. 220–233, Oct. 2018.

[32] A. Y. Al-Rubae, "The potential uses of melia azedarach l. as pesticidal and medicinal plant, review," *American-Eurasian Journal of Sustainable Agriculture*, vol. 3, no. 2, pp. 185–194, 2009.

[33] D. Arthan, J. Svasti, P. Kittakoop, D. Pittayakhachonwut, M. Tanticharoen, and Y. Thebtaranonth, "Antiviral isoflavonoid sulfate and steroidal glycosides from the fruits of solanum torvum," *Phytochemistry*, vol. 59, no. 4, pp. 459–463, Feb. 2002.

[34] L. Badam, S. S. Bedekar, K. B. Sonawane, and S. P. Joshi, "vitro antiviral activity of bael (aegle marmelos corr) upon human coxsackieviruses B1-B6. the journal of communicable diseases," vol. 34, pp. 88–99, 2002.

[35] R. Amber, M. Adnan, A. Tariq, and S. Mussarat, "A review on antiviral activity of the himalayan medicinal plants traditionally used to treat bronchitis and related symptoms," *J. Pharm. Pharmacol.*, vol. 69, no. 2, pp. 109–122, Jan. 2017.

[36] A. Mao, T. Hynniewta, and M. Sanjappa, "Plant wealth of northeast india with reference to ethnobotany," 2009.

[37] K. Bradsher and L. Alderman, "The world needs masks. china makes them, but has been hoarding them," *New York Times*, vol. 13, 2020.

[38] J. Hinkin, J. Gammon, and J. Cutter, "Review of personal protection equipment used in practice," *British journal of community nursing*, vol. 13, no. 1, pp. 14–19, 2008.

[39] J. M. Gwaltney Jr and J. O. Hendley, "Transmission of experimental rhinovirus infection by contaminated surfaces," *American journal of epidemiology*, vol. 116, no. 5, pp. 828–833, 1982.

[40] L. Casanova, W. A. Rutala, D. J. Weber, and M. D. Sobsey, "Coronavirus survival on healthcare personal protective equipment," *Infection Control & Hospital Epidemiology*, vol. 31, no. 5, pp. 560–561, 2010.

[41] M. Gandhi and D. Havlir, "The time for universal masking of the public for coronavirus disease 2019 is now," in *Open forum infectious diseases*, vol. 7, no. 4. Oxford University Press US, 2020, p. ofaa131.

[42] A. Davies, K.-A. Thompson, K. Giri, G. Kafatos, J. Walker, and A. Bennett, "Testing the efficacy of homemade masks: would they protect in an influenza pandemic?" *Disaster Med. Public Health Prep.*, vol. 7, no. 4, pp. 413–418, Aug. 2013.

[43] S. Bae, M.-C. Kim, J. Y. Kim, H.-H. Cha, J. S. Lim, J. Jung, M.-J. Kim, D. K. Oh, M.-K. Lee, S.-H. Choi *et al.*, "Effectiveness of surgical and cotton masks in blocking sars–cov-2: a controlled comparison in 4 patients," *Annals of internal medicine*, vol. 173, no. 1, pp. W22–W23, 2020.

[44] D. Pradhan, P. Biswasroy, P. K. Naik, G. Ghosh, and G. Rath, "A review of current interventions for covid-19 prevention," *Archives of medical research*, vol. 51, no. 5, pp. 363–374, 2020.

[45] K. Nashimoto and Y. Tashiro, "Gargling cup, antiviral mask, antiviral filter, antifungal, antibacterial, and antiviral filter air cleaner and air-cleaner humidifier," 1999, uS Patent 5,888,527.

[46] S. Modak and Sampath, "Antiviral glove," USA Patent 5 133 090, 1992.

[47] Y.-F. Wang, F. Kang, S.-J. You, C.-H. Tsai, and G.-L. Lin, "Preparation and characteristic of antibacterial facemasks with chinese herbal microcapsules," *Aerosol and Air Quality Research*, vol. 17, no. 8, pp. 2119–2128, 2017. [Online]. Available: https://doi.org/10.4209%2Faaqr.2017.06.0208

[48] J. S. Oxford, R. Lambkin, M. Guralnik, R. A. Rosenbloom, M. P. Petteruti, K. DiGian, and C. LeFante, "Preclinical in vitro activity of qr-435 against influenza a virus as a virucide and in paper masks for prevention of viral transmission," *American journal of therapeutics*, vol. 14, no. 5, pp. 455–461, 2007.

[49] J. Willimann and Sampath, "Antimicrobial and Antiviral Composition," USA Patent 10 307 452, 2019.

[50] J. T. Williams, *Waterproof and water repellent textiles and clothing*. Woodhead Publishing, 2017.

[51] H. Shen and K. K. Leonas, "Study of repellent finish of filtration ability of surgical face masks," *International Nonwovens Journal*, no. 4, pp. 1 558 925 005os–1 400 403, 2005.

[52] K. K. Leonas, C. R. Jones, and D. Hall, "The relationship of fabric properties and bacterial filtration efficiency for selected surgical face masks," *JTATM*, vol. 3, pp. 1–8, 2003.

[53] Z. Muwaffak, A. Goyanes, V. Clark, A. W. Basit, S. T. Hilton, and S. Gaisford, "Patient-specific 3d scanned and 3d printed antimicrobial polycaprolactone wound dressings," *International journal of pharmaceutics*, vol. 527, no. 1-2, pp. 161–170, 2017.

[54] J. Lemelson, "Face Mask and Method," USA Patent 4 856 509, 1989.