PLANT-BASED DIETARY ITEMS WITH PROPHYLACTIC AND THERAPEUTIC ACTION AGAINST NOVEL CORONAVIRUS

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The ever-flourishing human survival and dominance during the current Anthropocene era in the earth's history has seemingly been punctuated by the deaths of millions of human beings on account of the COVID-19 calamity. Within a year of the onset of the pandemic, humanity has proved its biotechnological might of the twenty-first century through developing many safe and efficacious vaccines by exemplary global co-ordination and ethical collaboration. We now aptly learned how a minuscule virus SARS-CoV-2 quite insidiously reached every nook and corner of the globe and resulted in an unprecedented loss and devastation of global economic activities. Curiously, the COVID-19 pandemic has raised several puzzling questions of life science. Among others, the most crucial question that intrigued scientists, why did a new strain of Coronavirus emerge with ten times greater infectivity than its predecessors? The enigmatic intra-molecular maneuvers in virus structure further ensured the evolution of many more variants with much greater infectivity. Despite the availability of efficacious vaccines, the absence of potent curative medicines and the evolution of escape mutations are the most important reasons for the future possibility of recurrence of the virus. So, predictive pandemic monitoring preparedness must be in place to contain epidemics or pandemics through herbal immune boosters, non-pharmaceutical measures and conservation of biodiversity as per the concept of planetary health. Alleviation of disease symptoms through dietary modification and supplementation has been an age-old practice. To date, many bioactive compounds of plant origin with immense prophylactic and therapeutic potential have been selected as biomedicines. The present article reviews the possibility of some food and drink items whose bioactive molecules could serve as physiological masks against novel Coronavirus and variants. Sprouts of peanuts, soybean, grapes, licorice, turmeric, black cumin, black pepper, snake gourd, cloves, cinnamon, citrus fruits, tea, neem, *shatavari,* and *ashwagandha* have been selected as anti-SARS-CoV-2 food and beverage items based on preclinical pharmacological screening studies. Since food items described above have been traditionally used, there is no doubt of their adverse side effects or toxicity.

Keywords: SARS-CoV-2, pandemic, infectious disease, COVID-19, evolution, planetary health, biodiversity, healthcare, medicine, ecology.

Introduction

The COVID-19 pandemic is an ecological consequence of biodiversity loss on account of endangerment and extinction of species. In nature's law, such stressors often serve as an essential prerequisite for the evolution of new infectious agents with life-threatening capabilities through mutations and re-combinations. The world recently eye-witnessed an unprecedented loss and devastation of the global economy and human life on account of COVID-19, unparalleled in human history. Owing to scientific advancements in aviation technologies, information communication technology, roads and waterways transportation technologies, the world has now shrunk into a global village. The global human population can travel to their planetary destinations at much ease and comfort, searching for livelihood. However, the menace of the spread of infectious diseases is also growing at a similar pace.

We aptly learned how a minuscule virus, SARS-CoV-2 originated at Wuhan city of China, spread to every nook and corner of the world within a short time like a forest fire! According to some scientific estimates, globally more than 300 infectious diseases have emerged among humans during 1940 and 2004 and concomitantly infectious diseases also appeared in wildlife, domesticated animals, wild plants and crop species (Jones et al., 2008). It is estimated that about 60-80 per cent of humans' infectious diseases are of zoonotic origin, i.e., infectious agents transferred from animals to humans. The underlying causes of such emergence are believed to be based on changes in land use, agricultural or other food production practices, or wildlife hunting, increasing rates of contact or encounters between humans and animals. The Nipah virus, SARS-CoV, MERS CoV, and current SARS-CoV-2 are prominent examples of zoonotic virus originated through spillover from wild bats. It is believed that half of the zoonotic diseases that have emerged in humans since 1940 are on account of human activities, while about 20 per cent are through the evolution of drug resistance (Keesing et al., 2010). The world's ecologists and medical scientists have reached a consensus that human activities increasingly play active roles in the emergence of deadly infectious diseases. Therefore, all the consequences like lockdown, the shutdown of the global economy, unprecedented human sufferings and death toll on account of the COVID-19 pandemic have been brought about by human beings themselves, unfortunately, being oblivious to the harsh realities of nature and its philosophy. It reminds us of the famous quote by a French writer, Jean Bruller, "All of humanity's troubles are because we do not know what we are and cannot agree on what to become."

In consideration of our biosphere's extremely fragile ecological state, the Rockefeller Foundation, in collaboration with Lancet Commission, recently propounded the idea of planetary health in 2015 to highlight increasing threats of deadly infectious diseases for human health and well-being at a global scale (Horton, 2015). This emphatically states planetary health to be the health of human civilization and the state of the natural systems. It depends and calls for international collaborations and concerted exceptional actions for an outright check on jumps or spillover of viruses and other infectious microorganisms at the source itself. Such exceptional actions by protecting global biodiversity and scrupulously addressing climate change issues by human beings would save billions of dollars on frequent vaccine discoveries and production. Above all, great havoc and panic of pandemics would also be curtailed. As per the World Health Organization report, in January 2021, there have been 102 million confirmed cases of COVID-19 and 2.2 million deaths on record. While in India, the infection tally touched 10.7 million with 1.5 lakh deaths even after a complete lockdown of economic activities for about three months and restricted activities. During September 2020, the pandemic situation in India was the worst, with an infection rate as high as 100,000 cases and deaths of more than 1000 per day. As of February 2021, the daily infection and death rate declined to 10000-13000 and 127, respectively. Nevertheless, the world is curiously waiting for some effective targeted medicines yet to be discovered. The global hunt for potent therapeutics, effective

vaccines and vaccine administration against SARS-CoV-2 are the new buzzwords of all government's agenda and daily news and analysis in global media. The Government of India in its union budget for 2021-22 has allocated Rs. 350000 million for vaccination programmes.

Recalling the last ten months of unusual situations has been frightening and terrifying for all of us. Reports on discriminative and partisan behavior on the part of hospital administration, cynicism among medical professionals, particularly during the pandemic, were social stigmas. Therefore, society must value and appreciate healthcare professionals' efforts as Corona warriors and healthcare professionals must also adhere to the bioethics of medical profession (Narayan, 2006). Despite the world's largest vaccination program currently undertaken against COVID-19, lack of specific medicine and fear of immunity evading variants are important reasons for the pandemic's recurrence shortly. Vital know-how and true education on ways and means to provide relief from the anticipated crisis caused by Damocles sword of COVID-19 would be the need of the hour. Consistent with the views described above, the article aims at educating readers on some scientifically and pharmacologically studied anti-SARS-CoV-2 plant-based dietary foodstuff, non-alcoholic beverages and herbs commonly available in our vicinity as functional food medicines. It has two-pronged actions, preventive and curative, in case of infections through a broad range of variants of COVID-19. Introduction of SARS-CoV-2 with the mode of transmission, pathogenesis, mortality and current medicines along with dietary therapy have been briefly presented in subsequent paragraphs of the article. Although modern pharmaceutical technologies have greatly supported the identification and isolation of plant-based bioactive compounds of prophylactic and therapeutic values against viral diseases, their accessibility to common people is highly restricted due to expensive extraction processes from live plants. Routine production of nutraceuticals such as quercetin, resveratrol, flavonoids and alkaloids could be undertaken at an industrial scale through *in vitro* culture technologies (Narayan, 2015; Narayan, 2016).

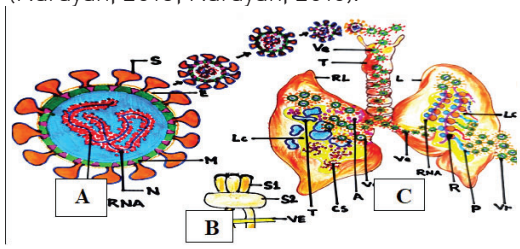

Fig. 1 (A). Diagrammatic representation of SARS-CoV-2 structure and pathogenicity in human lungs; A. Structure of SARS-CoV-2 (S-spike, E-envelope, M-membrane, N-nucleoprotein, RNA) B. Structure of spike (S1 & S2-receptor binding proteins; VE-virus envelope) C. Structure of human lungs, mode of viral invasion, and host-pathogen interaction (Ve- viral invasion, T-trachea, RL-right lung, Lc-lung cell, T-killer T-cells, CS-cytokine storms, A-anti-bodies, L-left lung, RNA, R-ribosomes, P-proteins, Vr-newly formed virus particles

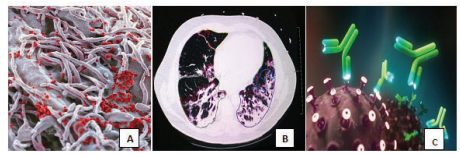

Fig. 1 (B). Infection, pathogenesis and control of COVID-19; A. Human cell studded with SARS-CoV-2 particles red in color (Credit: Dr Katherine Davies, National Infection Service/SPL/nature) B. Scanned image of lung damaged through COVID-19 (Credit: Nathan Laine/ Bloomberg/ Getty/ nature) C. Artist's conceptualization on monoclonal antibodies binding with spikes of coronavirus (Credit: Sci-comm Studio/ Science photo library/ nature)

Morbidities, mortalities, and medical interventions for combating COVID-19

Although there are some rapid test methods to confirm infection through SARS-CoV-2, such as rapid antigen or antibody tests, real-time PCR is the most accurate confirmatory diagnosis method, detecting viral genome in nasal, throat swabs or blood samples. The incubation period of the virus is reported to be between 1 to 14 days; however, much-enhanced infectivity of SARS-CoV-2 compared to SARS-CoV and MERS CoV is attributed to the transmission through asymptomatic as well as pre-symptomatic carriers. This type of transmission within healthy individuals constitutes a large proportion (of about 80) of infected persons. Moreover, SARS-CoV-2 could also be transmitted during the latency period. These are the reasons why COVID-19 is spreading like wildfire. The case fatality rate of COVID-19 worldwide is around 3-5 per cent so far; however, it may go much higher in elderly persons, co-morbidity conditions and among people who are immunosuppressioned reported to be at 14.8 per cent (Taghizadeh-Hesary and Akbari, 2020). Some common symptoms of COVID-19 include a flu-like illness with fever, sore throat, cough, fatigue, dyspnoea. However, in select groups of people, elderly or co-morbid patients, disease progression aggravates as acute respiratory distress syndrome (ARDS), septic shock and multi-organ failure, finally leading to mortality. Currently, symptomatic healthcare facility is being provided to patients since no specific anti-viral medicines are in place. Milder symptoms occur because of the presence of viral antigens in the host and proportionate defensive immune reaction or response by the host; thereby, cellular and humoral or innate immunity produces viral-specific T-cells (CD4+, CD8+) and virus-specific antibodies. Hence, patients with milder symptoms are being treated with those medicines that block viral entry to host cells, also block replication to alleviate symptoms and reduce infectivity. Thereby, the viral transmission is curtailed. Severe cases of COVID-19 are characterised by ARDS responsible for health deterioration and mortality of patients. ARDS is caused by cytokine releasing syndrome, which occurs when the host immune system hyperactively responds to the viral genome inside cells. The hyperactive response involves large-scale production and release of pro-inflammatory cytokines such as IL-6, IL-1, etc., and chemokines and their vigorous circulation in the cytoplasm of cells (Fig. 1 A). Such conditions cause damage to vascular endothelium and parenchyma cells of lung tissues (Fig. 1B). Consequently, patients with damaged swollen lungs often encounter breathing difficulties and urgently require life support intervention through ventilators. If the situation further aggravates, septic shock and multi-organ failure may occur, resulting in patients' deaths. Therefore, severe ARDS cases require prophylactic immune modulation and anti-viral in addition to the life support system. Allopathic drug hydroxychloroquine (HCQ) has been used as prophylaxis and therapeutic against COVID-19 because of its multi-action effects on virus multiplication. Nafamostat and camostat can inhibit viral fusion with host cells; thereby, entry of viruses into host cells could be prevented. Viral protease inhibitors like lopinavir, ritonavir, and nelfinavir, could prevent proteolytic cleavage of viral polyprotein precursors into functional units, thereby multiplication of virus is prevented. Remdesivir and ribavirin can

prevent viral replication and multiplication by inhibiting viral enzyme RNA-dependent-RNA-polymerase (McKee et al., 2020). Whereas, Sofosbuvir, zanamivir, and oseltamivir could also inhibit viral replication, viral shedding and infectivity. Emodin as a potent inhibitor of the ACE2-S-protein complex for preventing viral entry into host cells is investigated. Azithromycin, Interferon-alpha, Interferon Beta, and convalescent plasma have also been used to assess their efficacy as anti-viral and prophylaxis. Under severe conditions or ARDS, corticosteroids, tocilizumab, anakinra, IVIg, ruxolitinib, upadacitinib, and baricitinib have been assessed as inhibitors or neutralizing agents against interleukins arising as a result of cytokine storms to manage the severity of COVID-19 (Shetty et al., 2020).

Although a plethora of medicines, as mentioned, have been used to combat COVID-19, no specific, effective, and targeted medicine has been recommended so far. There are currently more than 50 vaccine candidates under clinical trials; many of them have reached an advanced assessment stage. Pfizer/ BioNTech, Gamaleya, Moderna RNA-1273, Oxford's adenovirus vectored vaccine (Ch Ad ox1 nCoV-19), Sinopharm, and Covaxin have been assessed for desired efficacy and approved for emergency use (Folegatti et al., 2020; Kim et al., 2021). Some oral and nasopharyngeal vaccines are also being evaluated, and will hopefully be made available by June and July 2021. Though the world's most extensive covid vaccination program has been started in December 2020 and January 2021, its actual impact would be seen in the coming days.

Need and relevance of plant based molecular defense against COVID-19

The evolution of novel viruses capable of causing human diseases is a natural phenomenon that might go on unceasingly unless we change our lifestyle as per the aims and aspirations of the planetary health concept. Although vaccines are the most potent arsenals against infectious diseases, we cannot afford to invest huge money in the R&D of vaccines. We all know that Hydroxychloroquine, a structural analog of quinine extracted from the bark of Cinchona trees for hundreds of years, formed an early line of defense against COVID-19 (Editorial, Nature Plants, 2020). As SARS-CoV-2 spread fast, we increasingly realised the needs and relevance of plant-based medicines and decoctions as prophylaxis and therapeutics because they are easily accessible, inexpensive and effective against COVID-19. Governments of India and China officially approved the integration of Ayurveda and traditional Chinese medicines, respectively, with allopathic prescriptions and efficacious results were also seen in improving symptoms and curing the disease (Vellingiri et al., 2020; Ren et al., 2020). Drug designing and development often involve intense, rigorous, very expensive and highly time-consuming activities. Therefore, consistent innovative efforts are required to develop anti-viral bio-active molecules from plants since they have always served as natural sources of lead molecules as progenitors of many potent drugs currently being utilised against infectious diseases. Above all, many phytochemicals are believed to be of great potential in possessing synergistic potentials/

actions in combination with allopathic medicines, thereby alleviating the latter's harmful side effects (Narayan, 2019).

Healthy lifestyles necessarily encompass healthy diets and regular exercise to maintain an optimum cellular currency of energy and ATP molecules required for our body to sustain all routine activities cyclically. Fresh food items involving whole food grains, pulses, oils, vegetables, fruits, milk and yogurt constitute a healthy diet that provide all necessary nutrients to our body. Optimum availability of cellular ATP molecules and dietary nutrients is an essential prerequisite for a healthy and resilient immune system to fight off invading viruses and microorganisms naturally. However, such nutritional foodstuffs are not available to all because of socioeconomic disparities. Nonetheless, processed and preserved food habits are also growing parallel to meet the needs of taste-based culture and quick fix lifestyles in urban settlements to buy more time for greater ease, comfort, and enjoyment. Such lifestyles have resulted in the greater vulnerability of all age groups of people to communicable and non-communicable diseases. Hence, there is a growing need to educate people on functional foods and drinks as dietary medicines to save themselves from pain and agonies of respiratory viral diseases, including COVID-19.

Functional food items against SARS-CoV-2

Sprouted peanuts (*Arachis hypogaea*) and grape (*Vitis vinifera*) skins contain a high resveratrol concentration, a stilbenoid and natural polyphenol, which has been demonstrated *in vitro* to inhibit the expression of nucleocapsid protein of MERS-CoV. It also inhibits virus-induced cell apoptosis, hence suggested to be effective for inhibition of multiplication of SARS-CoV-2 as well as virus-mediated apoptosis of host cells (McKee et al., 2020). Therefore, sprouted peanuts may serve as a curative diet as a medicine against COVID-19. Takahashi et al., 2015 have demonstrated through *in vitro* assays that soybean (*Glycine max*) contains ACE2 inhibiting substance, which was identified as nicotianamine (ACE2iSB). Since the ACE2 enzyme serves as receptor for viral spike proteins, nicotianamine could inhibit SARS-CoV-2 to find entry into host cells.

Fig. 2. (A) Dried chopped roots of licorice and food preparation with root extract, candies and confectionaries (B) Sprouts of soyabean

Therefore, sprouted soybean as foodstuff may also be used to block entry of SARS-CoV-2 into host cells, thereby preventing COVID-19 infections (Fig. 2 (B)). Licorice (*Glycyrrhiza glabra*) or *mulethi* is dried roots, conventionally used to chew for clearing sore throat. The root extract is used to prepare candies and confectionery items which can benefit COVID-19 patients upon consumption as a therapeutic diet. Pharmacologically, licorice extract contains glycyrrhizin which has been demonstrated through *in vitro* assays as a potent inhibitor of SARS-CoV-2 entry into host cells and also the multiplication of viruses more effectively than standard anti-viral Rivabirin (Cinatl et al., 2003). Further, Bailly et al. (2020) reported that glycyrrhizin blocks enzyme ACE2 and SARS-CoV-2 attachments based on molecular docking studies, thereby viral entry into host cells would be prevented.

Impressed with glycyrrhizin's medicinal efficacy, Prof. Hong Ding of Wuhan University proposed that diammonium glycyrrhizinate in combination with Vitamin C might exhibit synergistic action in blocking SARS-CoV-2 multiplication in COVID-19 patients as a very effective drug and approved its clinical trials (Editorial Nature, 2020). Recently, Sinha et al. (2020) has reported another bioactive compound, glycerin A, in addition to glycyrrhizic acid from licorice extract (Fig. 2 (A)), which binds with viral Nsp-15 endoribonuclease and blocks replication of the virus inside host cells based on molecular docking studies. Red raspberry, grapes, broccoli, red onion, black tea and leafy vegetables contain quercetin, a natural flavonoid that has been demonstrated to possess a broad range of anti-viral properties. Quercetin displays multi-target action on virus activities, viral entry, viral replication and virus particle assembly. These therapeutic actions of quercetin are further augmented by the co-administration of Vitamin C, which exerts immune-modulatory activity and can also recycle oxidized quercetin. Therefore, co-administration of Vitamin C and quercetin is a safe, effective and inexpensive anti-viral and immune modulation approach for both prophylaxes of high-risk populations and treatment of both mild and severe cases (Biancatelli et al., 2020). Curcumin is a natural polyphenolic compound extracted from turmeric (*Curcuma longa*), a trendy coloring and flavoring food item. It has been successfully used as a bioactive phytochemical with high curative potential for many diseases; therefore, medicinal efficacy of curcumin is approved by the US food and drug administration (FDA). Several studies on anti-viral activities have pointed out the multi-mechanistic roles of curcumin in inhibition of viral entry, replication of the viral genome, and viral multiplication. Curcumin molecules have been demonstrated through molecular docking techniques to interfere with SARS-CoV-2 protease and spike glycoprotein binding with target receptors; thereby, viral entry to cells and replicating the viral genome is inhibited (Utomo et al., 2020). It has also been demonstrated to possess anti-inflammatory and antifibrotic effects by reducing the expression of chemokines and cytokines in human lung infection; thereby, acute respiratory distress syndrome (ARDS) caused by them would be improved. ARDS is the main cause of deaths of COVID-19 patients the world over, requiring a mechanical supply of oxygen to patients through ventilators. Rahman (2020) reported an interesting finding of *Nigella sativa* or black cumin or *kalonji*, which in combination with zinc might be very effective in curing COVID-19 patients. *N. sativa* seeds contain unsaturated fatty acid, proteins, alkaloids, saponins, and essential oil. Thymoquinone and nigellimine are believed to be bioactive components of seeds that can act against SARS-CoV-2 since nigellimine share structural similarities with chloroquine and hydroxychloroquine, so it is expected to perform analogous functions of HCQ. Whereas thymoquinone can inhibit the entry of SARS-CoV-2 into cells, nigellimine can enhance Zn's uptake by host cells similarly, as demonstrated for HCQ. It is known that Zn inhibits proteolytic processing of viral polyprotein precursor; thereby, viral replication is inhibited. Oleoylethanolamide (OEA) is derived from omega-9-monounsaturated fatty acid, oleic acid, which is abundantly present in sunflower oil, olive oil, canola oil, avocado fruits and cheese. OEA has been experimentally demonstrated in clinical trials to decrease angiotensin

receptors' affinity to SARS viruses, thereby prohibiting viral entry into host cells. OEA can also decrease the production of pro-inflammatory cytokines in obese patients; therefore, OEA may serve as potential ARDS symptoms alleviating molecules for COVID-19 patients. Lakshmi et al. (2020) have provided evidence through molecular docking studies for anti-SARS-CoV-2 activities of some Indian ethnomedicinal plants, *Trichosanthes cucumerina* (Snake gourd) and *Piper nigrum* (Black pepper), which are also traditionally used as vegetable and spice, respectively. Cucurbitacin E, cucurbitacin-B, isocucurbitacin-B and bryonolic acid *T. cucurmerina* can inhibit SARS-CoV-2. Main protease 3CLpro, is used to process polyprotein precursor, thereby inhibiting the multiplication of the virus. Whereas piperine of *Piper nigrum* is also an inhibitor of 3CLpro, they together can also serve as immune modulators without adverse side effects. *Cinnamomum verun* (cinnamon) and *Syzygium aromaticum* (cloves) herbal extracts have been used to test their efficacy against SARS-CoV *in vitro* assay and observed to be inhibitory of viral entry into host cells, thereby preventing disease development (Zhuang et al., 2009). Given the structural homology between SARS-CoV and SARS-CoV-2, cinnamon and clove are also expected to inhibit SARS-CoV-2.

Functional drinks and kitchen garden herbs against SARS-CoV-2

Citrus fruits such as oranges and lemons are used in the preparation of refreshing drinks; if the powdered peel is also mixed with a drink, it provides neutraceuticals such as hesperidin, naringin, and Vitamin C, which have been pharmacologically demonstrated to be highly medicinal against COVID-19 based on molecular docking (Fig. 3 (A)). Hesperidin is most abundantly present in peels of citrus fruits. Hesperidin and naringin are bioactive

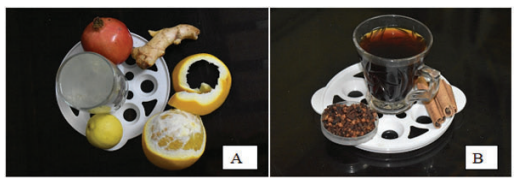

Fig. 3. (A) Juice of orange and lemon mixed with powdered rind of citrus fruits (B) Tea prepared with cinnamon and cloves

flavonoids shown as inhibitors of viral ACE2 and 3CLpro enzymes, which are crucial for viral entry into host cells and multiplication. In contrast, Vitamin C, hesperidin, and naringin can counteract cytokine storms in severe patients, thereby improving ARDS symptoms of COVID-19 patients (Meneguzzo et al., 2020). Bhardwaj et al. (2020) and Ghosh et al. (2020) have reported their findings on tea leaves' bioactive molecules as therapeutics against COVID-19. Tea leaves are a popular non-alcoholic drink in India and many parts of the world. Botanically, tea is *Camellia sinensis* leaves used to manufacture various tea types such as green tea, black tea and oolong tea through different processing methods (Fig. 3 (B)). In molecular docking and molecular dynamics studies, it has been found that oolonghomobisflavan-A, the most abundant polyphenol molecules of tea leaves, was the most potent inhibitor of the main protease (Mpro) of SARS-CoV-2, which can block viral multiplication. When Mopar inhibitory activities of tea leaf constituents were compared with repurposed synthetic allopathic drugs, atazanavir, darunavir, and lopinavir, tea leaf constituents such as olonghomobisflavan-A, theasinensin-D, and theaflavin-3-O-gallate showed superiority

over allopathic drugs. While in green tea, out of 8 polyphenols studied, all exhibited good inhibitory activity against Mopar. However, three polyphenols, epigallocatechin gallate, epicatechingallate and gallocatechin-3 gallate, were the best performers. *Azadirachta indica* or neem is considered one of the most popular medicinal plants, is the source of nimbolin-A, Minocin and cycloartanols which inhibit E and M proteins of SARS-CoV-2; when consumed by COVID-19 patients, these bioactive molecules can interrupt the synthesis of virus particles consequently viral load is considerably reduced. Nimbin-A was the most potent in binding affinity, as demonstrated in molecular docking (Borkotoky et al., 2020).

Fig. 4. (A) *Asparagus racemosus* plant (B) *Withania somnifera* flowering twig

Asparagus racemosus or *shatavari* (Fig. 4 (A)) is a well-known traditionally used Indian herb to enhance immunity, longevity and mental functions. *In silico* study was conducted to identify and evaluate phytoconstituents of the root extract against SARS-CoV-2. Steroidal saponins such as Asparoside-D and Asparoside-C were observed to inhibit spike receptor-binding domains of SARS-CoV-2 by forming stable bonds between them. Whereas Asparoside-D and Asparoside-F were able to form stable bonds with viral NSP15 endoribonuclease, viral entry into host cells and multiplication is inhibited. Quite interestingly, the above binding affinity between phytoconstituents of *A. racemosus* and SARS-CoV-2 proteins was greater than the currently prescribed drug Remdesivir against COVID-19 (Chikhale et al., 2020). *Withania somnifera* is a well-known Ayurvedic herb used as an immunomodulator, anti-inflammatory, anti-viral and anti-oxidant (Fig. 4 B). In the wake of COVID-19, this medicinal herb's phytoconstituents were screened using computational methodologies such as molecular docking and dynamics studies. Withanoside X was found to be a potent inhibitor of SARS-CoV-2 vital proteins, receptor binding domains of spike proteins, and NSP-15 endoribonuclease (Chikhale et al., 2020). Subsequently, Kumar et al. (2020) demonstrated that withanone (active withanolides) could inhibit SARS-CoV-2 main protease (Mopar) and check virus multiplication. Further, Kumar et al. (2020) reported that withanone and withaferin-A stably interact with catalytic sites of TMPRSS2 enzyme of the host that cleaves virus-bound ACE2 receptor and facilitate subsequent membrane fusion of virus and host cells, thereby preventing viral entry into host cells. Straughn et al. (2020), while searching for an alternative natural product to alleviate ARDS symptoms, found that withaferin-A, a steroidal lactone of ashwagandha, could reduce cytokine storms, hence, improves ARDS conditions in severe COVID-19 patients. It also checks the viral entry into host cells by interfering with receptor binding domains of viral S-proteins. Chewing fresh raw leaves of *W. somnifera* empty stomach for a fortnight improves symptoms of allergic rhinitis reactions comparable to anti-histamine, cetirizine. As withaferin-A was observed to be a potent prophylactic and therapeutic against SARS-CoV-2 on account of its multiple actions against the virus consumption of fresh leaves could effectively reduce susceptibilities of allergic rhinitis prone people to respiratory

viruses, including SARS-CoV-2. Given *ashwagandha's* immense utilities in the management of COVID-19, Tillu et al. (2020) also opined that it might be a better and safer substitute for containment of COVID-19 as compared to Hydroxychloroquine.

Conclusion

A pandemic of the magnitude of COVID-19 is a once-in-a-century event. Although the devastating impact of COVID-19 has been enormous on the global economy and human life so far, the present generation of humanity must view it as an opportunity to be an eye-opener for learning valuable environmental lessons. CORONA, an acronym could mean: Compensation or Reversal of Nature's Agony. It reminds us, why did Coronavirus emerge? Because human beings never compensated for the exploitations they caused of nature and natural resources. A minuscule virus, SARS-CoV-2, emerged as an arsenal of Mother Nature to take revenge of ruthless human behavior towards wildlife and threatened species of the planet earth. Investigations for ascertaining the biodiversity source of SARS-CoV-2 are underway at Wuhan. We never got better insights into ecological theory: biodiversity loss is slow poisoning. COVID-19 is an eye-opener for the present generation. Ecologically, biodiversity loss and climate change have been serving as predisposing factors for the emergence of novel Coronavirus, SARS-CoV-2. We do perceive the adverse effects of climate change in our daily life observations. However, unlike climate change, the harmful impacts of biodiversity loss as a silent killer cannot be realised while damage is being inflicted; when catastrophic consequences become apparent, it would be too late to contain it. What exactly happened through COVID-19? Human beings never anticipated the harmful effects of trade and trafficking in wildlife. However, the sudden emergence of SARS-CoV-2 made everybody panic as an international health emergency was declared which abruptly brought about lockdown of all human activities. The global death toll on account of COVID-19 is approaching the 2.3 million mark as of now, and infection and death rates are gradually declining in India and many parts of the world. However, some vaccines have been approved and administered — a matter of great hope and expectations for normalcy. Since pandemics often show a long scaring tail, herbal prophylactics and immunity boosters would stand the test of time. Scientifically, our everyday dietary needs hold great promise. Growing needs of potent preventive nutraceuticals against COVID-19 necessitated pharmacological researches to identify and isolate bioactive compounds from botanical sources that serve our dietary needs. Research and innovations for COVID-19 combat continued with the hunt for potent inhibitors of SARS-CoV-2 proteins and enzymes such as S-proteins, M-proteins, 3CLprotease, Papain-like protease, RdRP, NSP-15 endoribonuclease, ACE2 of host for blocking viral replication in host cells, thereby containment of the disease COVID-19. To date, many compatible bioactive compounds of dietary plant foodstuff origin have been identified that block viral and host enzymes instrumental for viral multiplication in host cells and disease development. Dietary foodstuffs with prophylactic and therapeutic action against COVID-19 virus have been selected — soybean, peanuts, licorice, grapes, avocado, citrus fruits, turmeric, black cumin, black pepper, sunflower seeds, snake gourd, cinnamon, cloves, black and green tea, neem,

shatavari and *ashwagandha* which could be conveniently used as functional foods and drinks against a broad spectrum Covid-variants. Nevertheless, current discoveries of potent prophylaxis, targeted medicines, and vaccines are just emergency measures to tide over the crisis; the ultimate solution to pandemics lies in follow-up and scrupulous adherence to the planetary health concept.

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