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Phytochemicals: Novel Antiviral Therapeutic Approach for Prevention of Lung Injury and Respiratory Infection during COVID 19

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Abstract

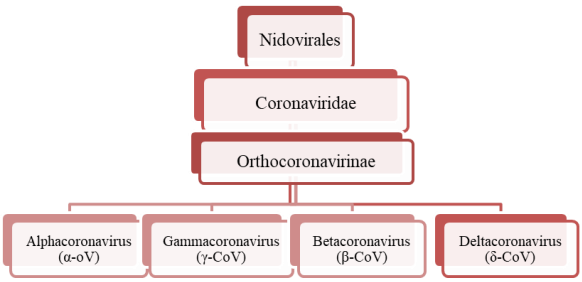
Corona virus spreads from human to human or human to animal via airborne droplets. Corona virus penetrates human cells via the membrane ACE-2 exopeptidase receptor. There are no specific anti-virus medications or vaccinations available to treat this sudden and fatal sickness during COVID-19 except vaccination. Still, it will take months, if not years, to create these antiviral drug therapies to combat against this pandemic. Phytochemicals have a huge significant anti-inflammatory activity, which can reduce the lung injury like major inflammation occurring in the lungs of a covid19 patient. Early studies have indicated that, polyphenol compounds, such as quercetin, curcumin, reservatol etc inhibit the synthesis of different enzymes which helps in SARS CoV2 propagation. To improve the symptoms of COVID-19 infected patients, supportive care and non-specific treatment are now required. As an alternate measure, fast application of herbal medicine or phytochemicals can help with this specific indication. Phytochemicals are a potent class of compounds generated from plants that have less adverse effects due to the lack of additives, preservatives, and excipients. The new COVID19 variants are much dangerous than the early ones which is a major drawback for the early developed vaccines. As a result, the focus of this review will be on certain phytochemicals and their mechanism of action that may be used to manage and prevent SARS-CoV-2 and its major variants emerging now-a-days.

Keywords: SARS-CoV-2; Phytochemicals; Herbal medicine; COVID-19

Introduction

"Phytochemicals isolated from different medicinal plants can address multiple therapeutic targets simultaneously with very less toxic effect on the human body, as evidenced by their widespread use in the treatment of various infectious diseases, including viral infections and their complications. Because infection with any of the Coronaviridae family viruses, including SARS-CoV-2, can cause severe pulmonary damage and respiratory infections, hence plant-derived secondary metabolites like phytochemicals may be useful in reducing these pulmonary complications leading to subsequent reduction of severe respiratory symptoms" [1]. "Phytochemicals those acts upon the respiratory as well as lung injury diseases include proinflammatory and oxidant mediators like TNF alpha, IL-1, IL-6, IL-8, IL-1, NF-B, MMPs, iNOS, MAPK, COX-2, and Reactive Oxygen Species" [2-4]. "Most of those studies are in vitro and in vivo screening of phytochemicals against coronaviruses, computer docking models studies on predicting the antiviral effects of these compounds against the coronavirus family members such as SARS-CoV, MERS-CoV, and SARS-CoV-2" [5,6]. "Natural polyphenol compounds like quercetin, kaempferol, myricetin, apigenin, and resveratrol have been shown significant anti-coronavirus activity in those studies [7-10]. Cho and colleagues discovered that geranylated flavonoids (tomentin A-E) isolated from Paulownia tomentosa (Thunb.) Steud. (Paulowniaceae) inhibited the papain-like protease, which is required for SARS-CoV propagation". SARS-CoV-2 is a key source of calamity in the twenty-first century. On 30 January 2020, the World Health Organization (WHO) designated COVID-19 a "public-health emergency of international significance"

during the second meeting of the Emergency Committee. Covids (CoVs) are individuals from the Order Nidovirales and Orthocoronavirinae subfamily of the Coronaviridae family. The four genera that make up this subfamily are as follows:



The α-and β – CoV genera have been found to contaminate warm blooded animals, though the δ-and γ – CoVs have been displayed to generally infect birds. While the 2019-nCoV disease isn't the principal extreme respiratory contamination flare-up brought about by Coronaviruses, these viruses have recently caused SARS and MERS in the Middle East region [1,2]. This outline will give you an elevated perspective of novel phytochemical drugs that can be effective against COVID-19 treatment.

History

Since from the principal appearance in December 2019, in Wuhan, China, novel Covid encouraged pneumonia, which was named Covid sickness 2019 (COVID-19) by the WHO on February 11, 2020, has quickly sped up in pandemic size. The new Covid was named extreme intense respiratory disorder Covid 2 by the global viral grouping commission around the same time (SARS-CoV-2). Coronavirus cases have been found in various countries all through the world, including the United States, India, Germany, Brazil, and France [3].

Genome Structure

Coronavirus is a pleomorphic or circle formed encased molecule containing single-abandoned (positive-sense) RNA coupled to a nucleo-protein inside a network protein capsid. Club-molded glycoprotein bulges distend from the envelope. A hemagglutinin-esterase protein is likewise found in a couple of Covids (HE). In the genome of a typical CoV, there is something like six ORFs. Aside from Gamma Covid, which encodes nsp1, the foremost ORFs (ORF1a/b) encode sixteen nsps and cover around 66% of the genome length (nsp1-16). ORF1a and ORF1b are connected by an edge shift, bringing about two polypeptides: pp1a and pp1ab. Virally encoded chymotrypsin-like protease (3CLpro) or mainprotease (Mpro) and one or papain-like proteases are utilized to change over these polypeptides into 16nsps CoVsgRNAs are utilized to decipher all underlying and highlight proteins [4]. Four primary underlying proteins contain spike (S), film (M), envelope €, and nucleocapsid (N) proteins are encoded by ORFs on the 33% of the genome close to the 30-end. Distinctive CoVs train explicit underlying and embellishment proteins, for example, 3a/b protein, HE protein, and 4a/b protein, notwithstanding these four essential primary proteins. These notable proteins play various significant parts in genome assurance and infection expansion. The Covid membrane contains three or four viral proteins. The membrane (M) glycoprotein is the most plentiful primary protein; it traverses the layer multiple times, with a little NH2-terminal bit outside the infection and a long COOH end (cytoplasm space) inside the virion. The peplomers are comprised of spike protein (S), which is a sort I film glycoprotein. S protein is, indeed, the significant inducer of killing antibodies. There is an atomic collaboration between the envelope proteins that directs the development and content of the crown viral film. But when S is required, M assumes a vital part in the intracellular creation of viral particles. In the presence of tunicamycin coronavirus produce less spike protein, noninfectious virions that consolidate M yet without S [5].

Symptoms

Coronavirus defilement manifestations and markers show up after a brooding time of generally 5.2 days. From the beginning of COVID-19 manifestations until the finish of the investigation, the time went from 6 to 41 days, with a middle of 14 days. The span of time differs relying upon the patient's age and invulnerable framework condition. It used to be that patients over the age of 70 had a more limited future than those younger than 70. The most well-known signs and indications of COVID-19 disease are fever, hack, and sleepiness, while different side effects incorporate sputum creation, migraine, haemoptysis, the runs, dyspnoea, and lymphopenia. The chest CT examine affirmed pneumonia, yet it additionally uncovered strange abnormalities like RNAaemia, intense respiratory enduring disorder, unexpected heart harm, and the development of stupendous glass opacities, all of which lead to mortality. A few patients had a couple of fringe ground-glass opacities in the subpleural districts of their lungs, which doubtlessly incited a fundamental and limited resistant reaction, bringing about long haul irritation. Shockingly, treatment with interferon inward breath at times had no logical effect and rather seemed to bother the circumstance by causing deteriorating aspiratory opacities [6,7].

Transmission Route

- Inward breath of suspended respiratory emissions, for example, beads delivered when a tainted individual hacks, sniffles, or talks, or direct contact with a contaminated patient are the fundamental courses of infection transmission.

- It's conceivable that viral RNA is conveyed in minute particles of spit, like breathed in air or when talking, however this still can't seem to be shown. The viral burden in salivation tops at the hour of show and stays high for essentially the principal seven day stretch of indicative sickness, before continuously declining yet being discernible for basically an additional 20 days.
- The virus can also be transmitted by fomites. It keeps going as long as 24 hours on cardboard, and as long as 72 hours on plastic and tempered steel. Irresistible beads and body liquids can sully the epithelium of the human conjunctiva, causing visual issues that can advance to respiratory ailment.
- At later stages of infection, virus persistence has been discovered in anal swabs, blood, and serum, implying additional shedding mechanisms and the possibility of transmission via the oral-fecal or body fluid routes [11-17].

Importance of Phytochemicals

Ayurveda, Siddha, and Unani are examples of herbal medicines that are beneficial in treating a variety of ailments. These honed systems date back 5000 years, and they may be seen and documented in ancient writings. Plants produce phytochemicals to protect themselves from environmental threats such as water fluctuations and microbes, as well as to retain their unique colour, aroma, flavour, and texture. Furthermore, new research has shown that they have major effects on human health, despite the fact that they are not considered necessary nutrients. According to research, these phytochemicals have the power to prevent certain substances in food, drink, and the air we breathe from becoming carcinogenic. Furthermore, it will reduce the edoema that promotes cancer growth. Phytochemicals also help to regulate hormones and minimise oxidative damage to cells, which can lead to a range of disorders. According to researchers, over 4,000 phytochemicals have been identified so far, but only a small percentage of them have been thoroughly investigated. These phytochemicals can be found in a wide variety of plants, but they're mostly found in meals like vegetables, fruits, green tea, coffee, cereals, and beans. Because their translational potential is generally undervalued, phytochemicals go overlooked in current therapeutic research and development [18,19]. Despite the fact that these drugs are controversial, there is a long history of their use in non-Western medicine. A single plant may have a variety of phytochemical elements that function alone or in tandem with other substances to produce the desired pharmacological effect. The search for novel antiviral drugs has frequently been unsuccessful due to viral resistance, viral dormancy, and repeated contamination in immune-compromised patients. The majority of antiviral therapy techniques are non-specific for viruses. In medical research, the advancement in developing antiviral drugs is the main focus. Phytochemicals' antiviral effects have been important at various phases of viral development [20]. Phytochemical-derived pharmaceutical formulations have made a significant commitment to viral contamination. Antiviral chemicals have been used for quick screening from plant extracts and fractions due to the availability of reasonable, proficient, and quick bioassay techniques. Phytochemicals deliver basic raw materials for major antiviral medications, rather than manufactured antiviral treatments. In a variety of viral infections, phytochemicals have taken the place of synthetic medications as life-saving drugs. Surprisingly, the use of this medicine has been passed down the generations through word of mouth, with the majority of them becoming lost over time due to a lack of proper documentation. The study of these phytochemicals could help progress their use in clinical settings to prevent or treat a variety of diseases. Many Indian medicinal herbs have anti-inflammatory, antiviral, and antioxidant qualities, thus they may be a good choice for COVID-19 treatment. To logically establish its appropriateness, standard clinical trials should be conducted [21,22].

Roles of Phytochemicals in the Covid-19 Management

Curcumin

According to new molecular docking studies, curcumin has a greater binding capability to receptors, preventing the COVID-19 virus from entering the body. SARS-spike CoV-2's glycoprotein connects to ACE2, allowing membrane fusion and virus infection via endocytosis. According to in silico docking studies, curcumin may constrain ACE2 to inhibit COVID19 transit to the cell, showing that spike glycoprotein could be a possible target for pharmacological virus entry constraint [23] (Figure 1).

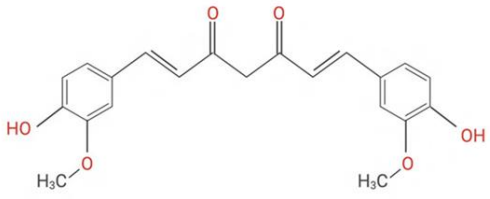


Figure 1: *Molecular Structure of Curcumin.*

The amount of spike proteins in cultures of Vero E6 cells infected with SARS-CoV to examine how curcumin affects viral replication. According to their findings, curcumin suppressed SARS-CoV replication at EC50 values more than 10 M [24]. Employed molecular docking to look into the impact of curcumin and other phytochemicals in regulating COVID-19 illness. Curcumin's binding energies and inhibition constants are generally low. According to the researchers, curcumin has a latent

inhibitory effect on COVID-19 Mpro and could be used as a medicinal drug. Curcumin's anti-inflammatory cytokine properties are becoming more well-known. Curcumin stymies the nuclear factor-B and MAPK pathways, as well as the critical signals that control the production of various pro-inflammatory cytokines. Curcumin suppresses the expression of anti-inflammatory and anti-fibrotic chemokines and cytokines implicated in lung infection, such as IFN, MCP-1, IL-6, and IL-10. Curcumin inhibits RSV replication, TNF-alpha production, and phospho-NF-B down regulation, all of which diminish RSV infection [25,26].

Resveratrol

Resveratrol has been shown to promote ERK1/2 signalling, support cell proliferation, and improve SIR1 signalling, all of which are linked to cellular survival and DNA repair in response to DNA damage. Resveratrol, on the other hand, may prevent MERS-CoV-induced apoptosis by decreasing FGF-2 signalling. In addition, MERS-CoV infection may result in the production of inflammatory cytokines, whereas resveratrol inhibits the NF-B pathway, potentially reducing inflammation. Following MERS-CoV infection, resveratrol reduced the levels of cleaved caspase 3. These changes could be caused by resveratrol's direct inhibition of caspase 3 cleavages, a decrease in virus-induced apoptosis, or a restriction of an upstream process required for caspase 3 cleavages [27] (Figure 2).

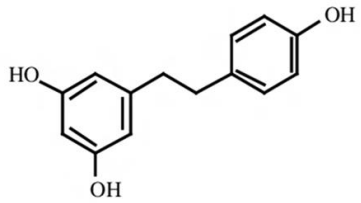


Figure 2: *Molecular structure of Resveratrol.*

TNF production was lowered following resveratrol treatment, showing that the anti-RV effect of resveratrol is achieved via reducing the inflammatory response. Both the 10mg/kg/d and 30mg/kg/d resveratrol-treated groups had significant IFN- levels after RV infection. The proportion of CD4+/CD8+ in resveratrol-treated sets was similar to that in mock-infected clusters, suggesting that resveratrol may aid Rotavirus-infected piglets in maintaining immune function. Rotavirus infection causes diarrhoea, which can be reduced by resveratrol [28]. The mechanism of resveratrol's antiviral action on the Pseudorabies virus. According to the findings, resveratrol inhibited PRV replication in a dose-dependent manner. The inhibition of virus reproduction in the presence of resveratrol was linked to viral reproduction inhibition in host cells, rather than only direct inactivation or inhibition of viral entry into host cells. Due to its capacity to restrict IB kinase activity, which is the key controller in NF-B actuation, resveratrol has been demonstrated to be a powerful inhibitor of both NF-B activation and NF-B-dependent gene expression in other investigations. As a result, resveratrol's ability to inhibit IB kinase breakdown could explain its inhibition of PRV-induced cell passage and gene expression [29]. Despite the absence of evidence for employing resveratrol in persons infected with SARS-CoV-2, the foregoing data imply that it may be worth exploring as an adjuvant antiviral drug, especially in light of the information provided, who exhibited MERS-CoV activity in vitro.

Gallic acid

Gallic Acid disrupted several intra-cellular inflammatory pathways that trigger ulcerative colitis. Nuclear transcription variables, like nuclear factor (NF)-κB and signal transducer and activator of transcription 3 (STAT3), as well as their inflammatory downstream substrates, are suppressed by the Gallic acid. It too decreases the expression and/or action of pro-inflammatory cytokines and inflammatory proteins, including interferon-γ, TNF-α (INF-γ), interleukin (IL)-1β, IL-17, IL-6, IL-23, IL-21, i-NOS, and cyclooxygenase (COX)-2, and diminishes the expression and invasion of neutrophils and CD68+ macrophages into the colon [30,31]. Gallic acid has a unique mechanism for extinguishing the flames of inflammation. It also reduces the production and expression of pro-inflammatory and inflammatory mediators including substance P, bradykinin, COX-2, NF-κB, IL-4, IL-2, IL-5, TNF-α, and IFN-γ. Furthermore, the substance represses the phagocyte or polymorph nuclear (PMN) mediated inflammatory reactions by scavenging ROS and diminishing the myelo peroxidase (MPO) activity [32]. Gallic acid has the ability to restrain HIV-1 integrase, HIV-1 protease dimerization, HIV-1 transcriptase, HCV replication, attachment and penetration of HCV, the herpes simplex virus (HSV)-1, HCV serine protease and attachment and diffusion of HSV-2. In Haemophilus influenza A and B particles are also affected [32,33]. Phenolic compounds function as antiviral agents against a variety of viruses, including HCV and HIV, by interacting with viral proteins and/or RNA via their phenol rings, or by altering MAP kinase signalling in host cell defence. Gallic acid polyphenols executed hydrogen bonds with 1 or 2 of the nucleotide triphosphate entry channels (NTP) amino acids in COVID-19 polymerase (Figure 3).

Polyphenols are phenolic compounds that found in plants, binds with NTP of COVID-19 polymerase, preventing substrate and divalent cations from entering the central active site cavity and supressing the activity of enzyme. Gallic acid binds to COVID-19 polymerase with higher affinity than ribavirin and show good drug resemblance and pharmacokinetic features. Thus, Gallic acid

could be considered as a possible COVID-19 therapeutic option [34].

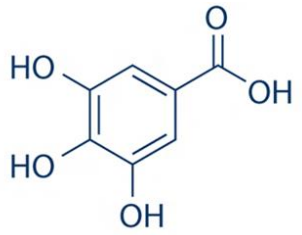


Figure 3: *Molecular Structure of Gallic acid.*

Glycyrrhizin

"Due to the importance of the host cell receptor for virus access, focusing on ACE2 could be a viable prospect for avoiding SARS-CoV-2 integration and, more importantly, preventing the virus from spreading out of the infected cell. Glycyrrhizin has recently been discovered to have the ability to bind with ACE2. Despite the fact that this study was conducted in silico by means of molecular docking, and the in vitro exhibition of an interaction remains to be validated, due to its antiviral effect on SARS-CoV, glycyrrhizin may still be regarded as a latent treatment for COVID-19". Endogenous interferon is produced by glycyrrhizin. Because of current clinical practise on COVID-19 and earlier settlement in management of severe Middle East respiratory syndrome (MERS)-CoV infection, interferon is suggested in all 7 descriptions of the diagnosis and treatment of Pneumonia contaminated by Novel Corona virus issued by the National Health Commission of China.

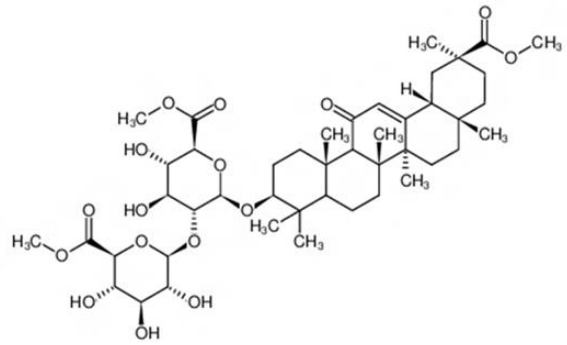


Figure 4: *Molecular structure of Glycyrrhizin.*

While interferon is a broad-spectrum antiviral, it works by blocking DNA and RNA infection replication at various stages of their replication cycles, as well as stimulating immune cell populations to clear virus infections. As a result, glycyrrhizin may be used to treat COVID-19 in an indirect manner. In the absence of a pathogen-specific antiviral or a targeted vaccine, a variety of antiviral medicine has recently been explored for the treatment of COVID-19. Injuring to the liver caused by drugs has become a serious health issue. Glycyrrhizin, which has been shown to protect the liver, could help with COVID-19 treatment [35,36] (Figure 4).

Antioxidants can help regulate a cytokine storm triggered by infection since reactive oxygen species (ROS) play an essential role in inflammatory response. Glycyrrhizin appears to be able to prevent virus-induced intracellular ROS generation. By reducing the activation of c-Jun N-terminal kinase (JNK), nuclear factor kappa beta (NFkB), p38, and redox-sensitive signalling pathways that are known to be appropriate for virus reproduction, Glycyrrhizin can restrict virus reproduction. SARS-COV-2 can generate a persistent inflammatory or cytokine strom reaction, which can trigger coagulation and complete cascades, resulting in multiple organ failures. According to the records, Glycyrrhizin appeared to be a specific inhibitor of thrombin. Records appeared that glycyrrhizin could be a specific inhibitor of thrombin. These finding suggest that glycyrrhizin can help COVID-19 multisite mechanism patients [37,38].

Withanone

Kumar et.al investigated the ability of Withanone (active withanolides extracted from Ashwagandha) to bind a extremely conserved protein, Mpro of SARS-CoV-2. They discovered that withnone binds to the substrate-binding pocket of SARS-CoV-2 Mpro with sufficient adequacy and binding energies that match those of a N3 protease inhibitor previously claimed. Comparative to N3 inhibitor, withanone were binds with the highly preserved residues of corona virus protease. Molecular dynamics replication was used to assess the interaction stability of these compounds. For N3 inhibitor the interaction free energies deliberated via MM/GBSA (Figure 5).

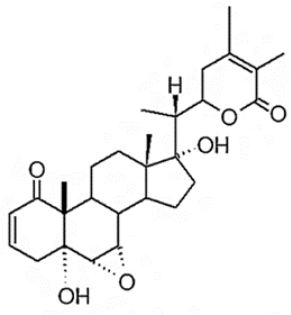


Figure 5: *Molecular Structure of Withanone.*

According to the information available at the time predicted that these natural compounds may have the potential to hinder the efficient activity of SARS-CoV-2 protease (a crucial protein for virus endurance), and therefore (i) may save time and cost required for designing/development, and early screening of anti-COVID drugs, (ii) could have limited therapeutic value for the management of original deadly corona virus disease, (iii) warrants prioritized advance approval within the research facility and clinical trials [39]. According to, Withanone docked exceptionally

well in the binding border of AEC2-RBD complex, and that stimulations revealed that shifted somewhat towards the interface centre. The electrostatic component of interaction free energies of ACE2-RBD complex was significantly reduced by Withanone. Two salt bridges were also discovered at the contact; withanone destabilised these salt bridges, decreasing their occupancies. They hypothesize; such an entrance of electrostatic interactions between the RBD and ACE2 would impede or damage COVID-19 access and contamination [40].

Colchicine

When colchine binds with unpolymerized tubulin heterodimers, it forms a stable compound that successfully restrains microtubule dynamics. Colchine may also be a non-selective NLRP3 inflammasome inhibitor. Initially thought to be solely a microtubule polymerization and leucocyte invasion inhibitor, it is presently assumed that a substantial portion of colchicine is responsible for NLRP3 inflammasome inhibition. Colchicine supress's pyrin-like domains interaction through inhibiting the activation of P2X7 receptor and polymerization of ASC [41]. Furthermore, colchicine inhibits mitochondrial transport and as a result, ASC approximation to NLRP3, indicating that microtubules facilitated mitochondrial transfer to generate the optimum locations for NLRP3 inflammasome activation. Colchicine appears to limit IL-1b production in dose-dependent manner as a response to several NLRP3 inflammasome inducers. For instance, Colchine was beneficial in silencing interleukin IL-1b, IL-6 and IL-18 in the case of acute coronary syndrome, which was attributed to inflammasome suppression [42,43] (Figure 6).

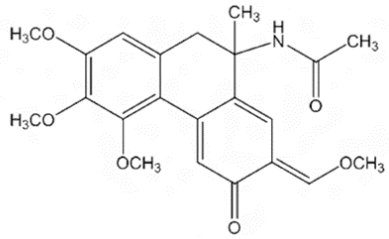


Figure 7: *Molecular structure of Colchicine.*

GRECCO-19 will be a planned, open-labeled, randomized, controlled trial to assess the effectiveness of colchicine in the prevention of COVID-19 problems. Patients with SARS-CoV-2 infection confirmed by a research lab (beneath RT PCR) and a clinical picture that includes temperature of more than 37.50C and at least 2 out of the following symptoms will be included: i. persistent throat pain, ii. Persistent coughing pain, iii. Fatigue/ tiredness, IV. Anosmia and/or ageusia, v. PaO2<95 mmHg. Patients will be randomly assigned to either a colchicine or control group (1:1) [44].

Andrographolide

Andrographolide inhibited the production of IFN, IL-2, and IL-6 in T cells, lowering the cellular and humoral adaptive immune response. Andrographolide inhibited dendritic cells' ability to transmit antigen to T lymphocytes. In an ovalbumin-induced asthma rat model, andrographolide therapy reduced serum immunoglobulin, IL-4, IL-13, IL-5, and Th2 cytokine levels. Andrographolide prevents angiogenesis by reducing migration, invasion, the adhesion molecule ICAM-1, and endothelial cell proliferation [45]. The andrographolide prevented NF-βfrom binding with DNA, lowering the production of pro-inflammatory proteins such iNOS and COX-2. A research to see how andrographolide affects the production of insulinomatumours. A research to see how andrographolide affects the production of insulinomatumours. Andrographolide inhibits insulinoma tumour growth by concentrating the TLR4/NF-βsignalling pathway [46,47] (Figure 7).

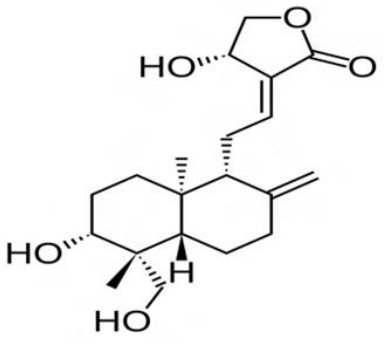


Figure 7: *Molecular structure of Andrographolide.*

Andrographolide inhibited the production of free radicals in neutrophils. Andrographolide was responsible for the production of IFN-γ, NK cells, IL-2, and TNF-γ. The andrographolide increased the cytotoxic capability of lymphocytes by raising the expression of CD markers and TNF-gamma production [48]. Using in silico methods such as target analysis, molecular docking, ADME prediction, and toxicity prediction, evaluated andrographolide as a potential inhibitor of SARS-main COV-2's protease (Mpro). Andrographolide was successfully coupled to the SARS-CoV-2 Mpro binding site. This molecule also adheres to Lipinski's rule, making it a viable candidate for testing in biochemical and cell-based assays to see if it may be utilised to combat COVID-19 [49].

Astaxanthin

In humans, astaxanthin essentially constricts histopathological increase in provocative cell signalling nf kappa-B (NFkB) processes, and diminishes TNF- in humans, many pro-inflammatory cytokine levels are also declining, which may have implications for keeping the lungs healthy and reducing the effects of SARS-CoV-2 infection Other major inflammatory mediators, such as IL-1b, IL-6, CRP, COX-2, iNOS, PGE-2, and

nitric oxide (NO), were also reported to be lowered by astaxanthin [50]. In vitro, found that astaxanthin administration causes nuclear factor B/p65 to localise and the levels of inflammatory cytokines (TNF-, IL6) to drop, as well as a significant increase in cell proliferation. Apoptosis in alveolar epithelial cells has also been found to be inhibited by astaxanthin. In addition to limiting NF-kB pathway activation, a decrease in the M1/M2 macrophage phenotypic proportion is linked to lower levels of inflammatory cytokines [51]. In primary cultured cells, this molecule also facilitates the release of T helper 1 cytokines like IFN- and IL-2 without producing significant cytotoxicity. Astaxanthin affects the immune system and improves the immunological response by boosting the creation and development of natural killer cells, granulocytes, T and B lymphocytes, and monocytes [52] (Figure 8).

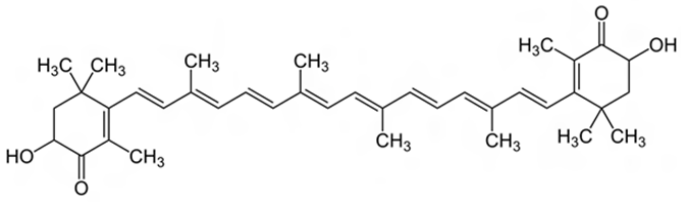


Figure 8: *Molecular structure of Astaxanthin.*

Immunomodulation by natural bioactive compounds, in combination with COVID-19, may be able to provide further therapeutic assistance in several diseases, particularly through discriminating immunosuppression is necessary for autoimmune disorders. In a human model, dietary astaxanthin regulates immunological response while also protecting against oxidative damage and inflammation. Overall, cell-mediated and humoral immune responses were improved by astaxanthin. Immune markers such as mitogen-induced lymphocyte proliferation in B and T cells, LFA-1 expression, and IFN- and IL-6 production all rose significantly [53]. When respiratory epithelial cells are infected with the virus, dendritic cells phagocytose it and transmit antigens to T lymphocytes. Effector T cells kill infected epithelial cells, whereas cytotoxic CD8+ T cells produce and release pro-inflammatory cytokines that cause cell death. The infection and cell death both trigger and amplify the host's innate immune response. COVID-19 has characteristics that indicate a lower amount of lymphocytes and neutrophils, as well as CD8+T and CD4+ T cells in the peripheral blood specify disease severity [50].

Emodin

Emodin's antiviral activity is proved by its capacity to block casein kinase 2 that is employed by various viruses to phosphoryate proteins required for their survival [54]. Emodin damaged the lipid bilayer in a similar way, resulting in the inactivation of the enclosed virus [55]. Emodin can disrupt the SARS-CoV S protein and ACE2 interaction. SARS-CoV and Vero E6 cell interaction was also blocked by preincubating S protein or S protein-pseudo typed retrovirus with emodin. These findings suggested that emodin could prevent SARS-CoV infection by blocking the S protein-ACE2 interaction site, in addition to disrupting the viral envelope [56] (Figure 9).

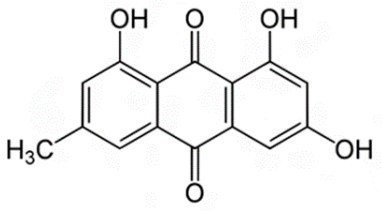


Figure 9: *Molecular Structure of Emodin.*

Promazine is a three-ringed phenolic compound that has been found to have anti-sars-cov action. Emodin and promazine inhibited the s protein and ace2 in a dose-dependent manner. These findings suggest that side chains other than the anthraquinone structure play a role in s protein and ace2 binding. Promazine possesses anti-SARS characteristics via blocking viral entry and protein processing, according to these results [56,57]. With a K1/2 value of roughly 20 M, emodin can inhibit the 3a ion channel of coronaviruses SARS-CoV and HCoV-OC43, as well as virus discharge from HCoV-OC43. Viral ion channels, they say, could be a suitable target for antiviral drug development [58]. According to, emodin can inhibit the 3a ion channel of coronaviruses SARS-CoV and HCoV-OC43, as well as virus discharge from HCoV-OC43, with a K1/2 value of around 20 M. They claim that viral ion channels could be a promising target for antiviral medication development [59-65].

Conclusion

The World Health Organization has declared the new corona virus (COVID-19) a Public Health Emergency of International Concern because it is causing an increasing number of episodes of pneumonia. According to the WHO, public health specialists around the world are concerned about the virus, and numerous governments have taken precautionary measures to tackle it. Government authorities in all countries are working hard to decrease person-to-person interaction by permitting area-wide public place closures, as well as a number of other public safety measures such as social surveillance. Thousands of years of expertise in pandemic and endemic disease therapy have been gathered. Herbal Medicines has accumulated thousands of years of experience in the treatment of pandemic and endemic diseases. Complementary and alternative treatments for patients with SARS-CoV-2 infection are still needed urgently, and herbal medicine experiences are certainly worth examining. Fighting an existing pandemic also provides an opportunity to see how

effective phytomedicine is at treating infectious diseases that are still developing. Numerous phytochemicals have been found to exhibit inhibitory and immunomodulatory effect against HIV proteases, suggesting that they could be promising COVID-19 medicines [66-72]. COVID-19 symptoms may be alleviated with the usage of these phytochemicals. Despite the finding of numerous phytochemicals, much more study is needed before a SARS-CoV-2 specific treatment can be developed. As a result, it's critical to look into the effects of these prescription phytochemicals on SARS-CoV-2.

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