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REVIEW ARTICLE

Indian Medicinal Herbs' Pharmacological Interventions in the Management of COVID-19

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-nCoV2) has spread rapidly day-by-day worldwide. Unfortunately, no medicine is available to treat human coronavirus infection. Vaccines, interferon treatments, and small-molecule medicines are potential possibilities for controlling or preventing developing 2019-nCoV infections. On the other hand, new intervention shares are likely to take months to years to emerge. Furthermore, the majority of currently available antiviral medications frequently result in the development of viral resistance, as well as adverse effects, viral re-emergence, and viral dormancy. The pharmaceutical industry is increasingly relying on phytochemical extracts, medicinal plants, and aromatic herbs to develop lead molecules, focusing on alternative antiviral medications. The discovery of these natural compounds' antiviral actions has revealed how they disrupt the viral life cycle, including during viral entry, replication, assembly, and discharge, as well as virus-specific host targets. There are currently no effective or licensed medications to combat SARS-CoVs. However, numerous alternative treatments and cures have been offered. Given the SARS-CoV outbreak's persistence, this review study will highlight many antiviral chemical elements isolated from medicinal and aromatic plants, natural goods, and herbal medications. This review demonstrates that numerous potentially beneficial aromatic herbs and phytochemicals, including coronaviruses, are awaiting assessment and exploitation for therapeutic use against genetically and functionally diverse viral families.

Keywords: Antiviral activity, Coronavirus, COVID-19, Herbal medicine, Medicinal plants, Phytochemicals, SARS-CoV, Severe acute respiratory syndrome

INTRODUCTION

The therapeutic action of medicinal plants has been known in this burgeoning field of biotechnology for decades. Plant research has sparked a surge of interest around the worldwide in recent years, due to its potential for use in traditional medical systems to cure a wide range of disorders. Several medicinal plants have been identified, and current scientific methods have been employed to investigate their validity, safety, and efficacy in therapeutic applications. Antiviral activity has been reported in various medicinal plants against certain extremely pathogenic microbe strains. Many pharmacological qualities are vital in discovering novel bioactive or phytochemical substances that can be used to target or treat human ailments like the COVID-19 pandemic. Many scientists and researchers currently screen and identify natural compounds from medicinal plants that can treat coronavirus illnesses, which is significant for drug development.

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The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, formerly known as 2019-nCoV) has spread quickly throughout China and the rest of the world [Figure 1]. Our study focuses on utilizing medicinal plants as herbal components in pharmaceutical formulations. A potentially lethal coronavirus (SARS-coV-2) has triggered a pandemic (COVID-19) that is extremely dangerous and has prompted governments worldwide to declare an emergency. COVID-19 researchers are being employed to create effective testing assays to detect carriers, treatments to lower the severity of infection more quickly, and vaccines to protect individuals from controlling and averting this pandemic.[1]

Many researchers are working on the use of medicinal plants that play a key role in this critical moment. Indeed, medicinal plants may play an important role in diagnosing infected and recovered individuals, developing vaccines to prevent infection, and treating symptoms with antivirals. COVID-19 (New Coronavirus) is a previously unknown coronavirus strain that first appeared in the Chinese city of Wuhan in December 2019. The virus is related to the ones that cause SARS and middle-east respiratory syndrome (MERS) and the MERS. The World Health Organization (WHO) designated the coronavirus epidemic a worldwide health emergency on January 30, 2020.

According to the WHO, COVID-19 is the official term for infection caused by this unique corona virus. The name was derived from the letters "co" for corona, "vi" for the virus, and "d" for disease, as well as the fact that the outbreak initially occurred in China in November of 2019. More than 35 pharmaceutical and biotechnology companies, government agencies, and research institutes have revealed research activities to develop COVID-19 vaccines and drugs. The Bill and Melinda Gates Foundation has pledged $100 million, while the UK government has set up a USD 26 million vaccine development fund.

The COVID-19 pandemic provides a once-in-a-lifetime opportunity for biotechnologists all over the world to confront this problem head-on. The world is now looking to the biotech sector to discover solutions that will help humans battle and overcome the current crisis while deepening our understanding of viral infections and preparing us for possible future outbreaks. The government, research organizations, biotech firms, and pharmaceutical companies have teamed

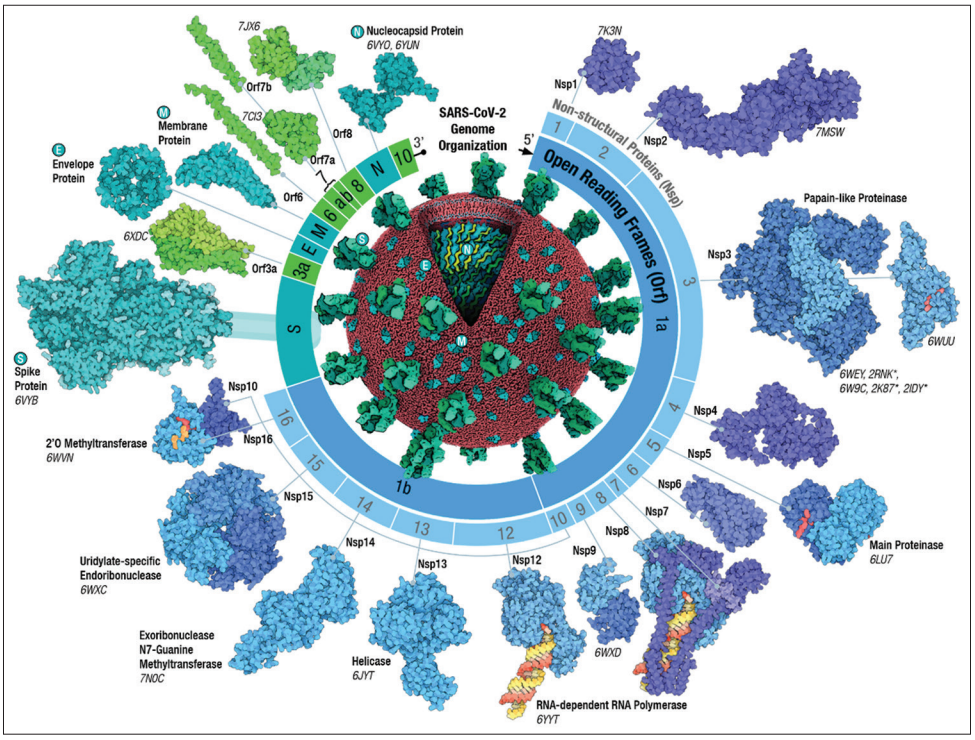

Figure 1: Severe acute respiratory syndrome coronavirus 2 adopted Yadav *et al*. (2021) role of structural and non-structural proteins and therapeutic targets of SARS-CoV-2 for COVID-19. Cells 10: 821. doi.org/10.3390/cells10040821)

up to produce diagnostic tools, medications, and vaccinations to fight this conflict. As a result, biotechnology has emerged as a frontrunner in the fight against COVID-19. Medicinal plants are valuable sources of ingredients that can be used to develop pharmacopoeia, non-pharmacopoeia, and synthetic drugs. Apart from that, these plants have played an important role in the evolution of human cultures worldwide. Herbal medicine has numerous advantages, including easier access than prescription medications, stabilizing hormones and metabolism, natural healing, immune system strength, and less adverse effects. Given the necessity of immunity-boosting measures during the COVID-19, it is critical to take supplements containing resistant components such as vitamin A, C, E, D, B-complex, zinc, and copper, which will help your body fight viruses. Modern technologies and approaches are being used in herbal medicine research and development. The application of modern technologies and procedures can substantially impact the scientific validity, quality improvement, and standardization of herbal medicines when used in conjunction with accepted Western scientific and ethical standards in herbal medicine research and development.

TRENDS AND GOALS IN BIOTECHNOLOGY OF MEDICINAL PLANTS IN COVID-19

The corona virus-caused COVID-19 pandemic (SARS-coV-2) significantly influences human lifestyle. COVID-19 has a higher death rate of 3% and is more transmissible worldwide due to the progressive increase in cases. This condition necessitates the development of novel vaccines, antibodies, and medicines. The candidate vaccine against the virus (SARS-coV-2) has received special attention, highlighting the need for a rational vaccine design that avoids antigenic determinants that trigger immune responses.[2] Following the establishment of a process for the production of plant-based vaccines, therapeutic enzymes, and antibodies, a rapid method for the generation of candidate vaccines is expected, with the pre-existing anti-(SARS-coV-2) virus antibody that could cross-react with (SARS-coV-2) virus and vaccine based on VLPs assembled with S protein being the primary candidates target for virus neutralization.

Recently, it was discovered to be a powerful inhibitor of SARS-major CoV-2's protease, 3C-like protease, which might suppress SARS-CoV-2 replication in Vero cells.[3] Triterpenes are abundant in licorice, Wolfipori extensa, and polyporus umbellate, many of which have antiviral properties or function as steroidal hormone mimics to influence the immune system of mammals.[4] COVID-19 is likely to be thwarted by the combination of these activities, which impede viral propagation while also relieving pneumonia symptoms and decreasing the viral infection-induced cytokine storm.

Herbal therapies, with their mostly unknown chemical makeup and mechanism of action, do not meet the stringent standards demanded by modern pharmaceuticals. Although the safety and effectiveness of a specific herbal cure could be demonstrated clinically, this results in low patient and physician acceptance. Compared to traditional herbal therapies, future generations of TCM-inspired contemporary medicines should comprise single or mixed bioactive plant natural components with recognized composition and action mechanisms and exhibit similar or greater safety and performance. Furthermore, organizations such as the WHO might play a role in helping to build a framework under which all regions of the world could get access to financing and expertise to study their medicinal plants and exchange their knowledge with the rest of the world medicinal plant biodiversity.

POTENTIALS OF MEDICINAL PLANTS AGAINST HUMAN CORONAVIRUSES

Herbal treatments using medicinal plants are very common in rural and tribal areas. Mainly because they have a great degree of scalability, which makes them more affordable and available than modern medicine. The antiviral potential of medicinal plants against the coronavirus SARS-CoV-2 virus is the topic of this investigation. COVID-19 virus pandemic has become a deadly disease in the

21st century, and no specific medication has been discovered to treat patients infected by this virus. As a result, various important phytochemical groups and their potentials are exhibiting human coronavirus, such as alkaloids, terpenoids, flavonoids, phenolic acid, tannin, and lignins, among others, which have been reported to show their potential against infectious diseases caused by pathogenic microorganismsas shown in Table 1.[5-7]

PLANT BIOTECHNOLOGY SERVICES MARKET 2020 SIZE, THE IMPACT OF COVID-19

The Plant Biotechnology Services Market 2020 Global Industry Research study examines the market's size, growth, share, segments, manufacturers, technologies, major trends, market drivers, challenges, standardization, deployment methods, opportunities, and future road map 2026 projection.

The global "Plant Biotechnology Services Market" (2020–2026) status and position of manufacturers, regions, product types, and end industries, with perspectives of manufacturers, regions, and product types; this report analyses the top companies in the global and main regions, and splits the Plant Biotechnology Services market by product type and applications/end industries. The market trend research method for Plant Biotechnology Services comprises an examination of several aspects affecting the industry, such as government policy, competitive landscape, historical data, market environment, current market trends, future technologies, and technological innovation. The government policy, competitive geography, historical data, market environment, present trends in the market, upcoming technologies, technological innovation, and the technical progress in related industries, as well as market risks, market barriers, opportunities, and challenges, are all part of the Plant Biotechnology Services market trend research process. Between 2020 and 2026, the worldwide Plant Biotechnology Services market is expected to grow significantly during the forecast period. The market was developing steadily in 2020, and with key players adopting more tactics, the market is predicted to rise over the forecasted horizon.

The research on the Global Plant Biotechnology Services Market 2020 provides a general review of the industry, including definitions, classifications, applications, and the industrial chain structure. The Global Plant Biotechnology Services Market Share research includes growth trends, competitive landscape analysis, and major regions development status for international markets. Manufacturing processes and cost structures are examined, and development policies and plans are developed. Import/export consumption, supply and demand figures, cost, price, income, and gross margins are all included in this report. This study examines each manufacturer's manufacturing sites, capacity, production, ex-factory price, revenue, and market share in the global market for Plant Biotechnology Services.

CHALLENGES AND OPPORTUNITIES DURING COVID-19 PANDEMIC

Pharmaceutical and biotechnology businesses worldwide are stepping up to meet the COVID-19 pandemic's difficulties. The COVID-19 pandemic reveals several flaws in human nature. Plant science is ideally positioned to contribute significantly to these concerns. The COVID-19 pandemic has been a serious obstacle for researchers, but it has also provided several chances for new scientific endeavors, particularly in plant biotechnology. Biotechnology research is critical for developing major pandemic interventions such as vaccine development and medication discoveries.

FUTURE PERSPECTIVES

Prospects for the future continue to develop efficient antiviral chemotherapeutics that are cost-effective and have few side effects and those that may be used in combination with other medications to improve the treatment of corona virus-infected patients. Because there are no preventive vaccines or active antiviral medications available to treat numerous viruses, eradicating these illnesses appear challenging. On the other hand, natural products provide a rich source of biodiversity for developing

Table 1: A partial list of antiviral plants inhibiting coronaviruses (CoV)

Medical plants	Antiviral compound (s)	Virus	Antiviral effects	References
Capsicum annuum (Peppper) *Curcuma longa* (turmeric) *Mentha longifolia* L.,(Mint)	Glucoside, curcumin, oleuropein, luteolin- 7, epicatechingallate, catechin, demethoxycurcumin, glucoside, and apigenin-7	Coronavirus (CoV)	COVID-19 Mpro All these antiviral compounds inhibited protein. However, further investigations are required to confirm their future applications	[8]
Tylophora indica (antamool)	Tylophorine	Corona viruses	Tylophorine-based biomolecules exhibit broad spectrum potential for inhabiting coronaviruses	[9]
Lycoris radiata (red spider lily)	Lycorine	Severe acute respiratory syndrome (SARS)-CoV	Lycorine could be a potential reagent for antiviral drug development	[10]
Psoralea corylifolia (babchi)	Bavachinin, psoralidincorylifol	SARS-CoV	The ethanol extract of these secondary metabolites demonstrated their high activity against SARS-CoVPLpro	[11]
Withania somnifera (L.) duna (asvagandha)	withanolide WS-1, withanolide A to Y, somnirol, withasomniferin A	SARS-CoV	enzyme function thereby block spike proteins ability (SARSCOV-2) to fuse with host cell receptor-ACE-2	[12]
Tinospora cordifolia (guduci)	Tinosporin, Tinosporide, Cordifolide, Phenyl prophyl glycoside	Corona viruses	Hot in potency relieves fever, Rejuvenative	[13]
Andrographis paniculata (kalamegha)	andrographolide, neoandrographolide, deoxy andrographolide others 14 – deoxy andrographolide	Corona viruses	Antiviral, antipyretic, antiperiodic, immune enhancement, hepatoprotective, vermicidal, Hypoglycemic, thrombolytic	[14]
Ocimum tenuiflorum (tulsi)	Bornylacetate, cadinene, eugenol, eugenol methyl ether, methyl chavicol, limonene	Corona viruses	Antiviral, Antifungal, antibacterial, adaptogenic (anti-stress), hypoglycaemic, antispasmodic	[13]
Ocimum basilicum (Vana tulsi)	Quercetin, luteolin apigenin, kaempferol, flavanoids, isoeugenol, Vitamin A, C, Calcium, phosphorous, Beta – carotene	Corona viruses	Inhibitory activity in HIV – 1, fungistatic, anti-allergenic, Cytotoxic, Antispasmodic	[15]
Zingiber officinale roscoe (ardraka)	Alpha curcumene, citral, citronellol, gingerol, zingiberenes, zingiberol, zingerone, gingerols, gingerenone A	Corona viruses	Antihistaminic, antioxidant, anti-inflammatory, hypoglycaemic, bioavailability enhancer, hypolipidemic	[16]
Curcuma longa L. (haridra)	Curcumene, curcumenone, curcone, cineole, curzerenone, eugenol, procurcumenol	Corona viruses	Antioxidant, anti-inflammatory, antihistamine, antiseptic, hypocholesterolenic	[17]

novel antivirals, new structure-activity connections, and effective medical and therapeutic approaches to viral diseases. The ability of a virus to rapidly evolve during replication, as seen in HIV and HSV, is a major issue with antiviral medications that target specific viral proteins or genes. Influenza viruses that are resistant to oseltamivir, acyclovir, and other nucleoside and nucleotide analogue anti-herpes medications. These substances prevent the virus from replicating and spreading to new neighbouring cells by selectively inhibiting thymidine kinase (TK), an enzyme that the virus possesses but that human cells lack. This prevents the virus from being able to synthesise its own DNA.[20]

When evaluating the antiviral activity of medicinal herb preparations, numerous factors should be considered, including the extraction procedures utilized, since acetone extracts or methanol fractions have the highest antiviral activity.[21] It is, therefore, necessary to determine the precise methodology for extract preparation, the portions of the plants to be utilized, the appropriate season(s) for material collection, and the details of the application modality from the commencement of a

prospective study on aromatic herbal medicines[22] [Hudson, 1990]. Although most studies in this area are still in the early stages, more research on the identification of active substances, the description of underlying mechanisms an analysis of efficacy, and potential *in vivo* applications is recommended to aid in the discovery of effective antiviral chemotherapeutics. Additional research should look into the possibilities of combining the treatments with other natural substances or regular medicines, as a multi-target solution could help reduce the ability of drug-resistant virus strains to infect people. We believe that natural therapies, including aromatic herbs, essential oils generated from medicinal plants, and pure oil compounds, will continue to play an important role in creating and advancing anti-corona virus medications.

CONCLUSION

Medicinal plants and natural products are still seen as viable options for preventing and treating various ailments. Since the COVID-19 pandemic broke out in December 2019, different traditional herbal medications have been used with excellent results among COVID-19 patients, primarily in China. This review discussed the potential uses of medicinal plants and/or natural products to prevent or even treat COVID-19. Although studies evaluating the anti-SARS-CoV-2 effects of medicinal plants are still insufficient and immature, some natural products with IC50 values <10 μM could be considered promising anti-SARS-CoV-2 agents because they could block SARS-CoV-2 life-cycle related proteins such as the cellular receptor ACE2, papain-like, or chymotrypsin-like proteinases. However, several limitations have been identified in terms of the specificity of the action exerted by such products, sustainable sourcing of the species, dose ranges used, and appropriate controls. While there are several indications that these plant-derived products may aid in the fight against COVID-19 infection, more research is needed to determine the clinical usefulness of such products against COVID-19 disease.

Furthermore, aside from the necessity for clinical validation of their effectiveness and safety, the bioavailability of natural compounds with potential anti-SARS-CoV-2 properties, such as tannins, should be studied. Prospective and interventional studies are needed to investigate herbal mixes, medicinal plants, or natural items with anti-SARS-CoV-2 properties. A combination of natural goods or herbal combinations with anti-COVID-19 medicines that have been validated could be a viable preventive and therapeutic option to investigate.

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