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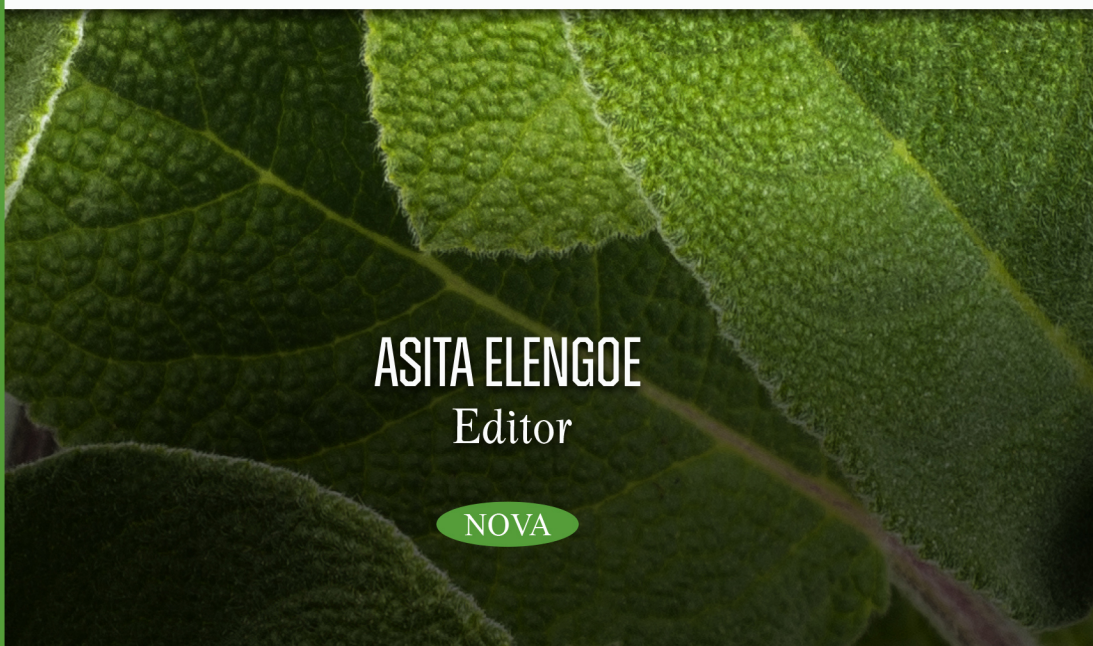

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Specially for my beloved mother, Thavamani
My lovely sisters, Suguna and Vaani
and
My wonderful brother, Tevanraj

Contents

Preface

In December 2019, a novel coronavirus was discovered in Wuhan city, China. People had symptoms of "pneumonia of undetermined cause," which resembled severe acute respiratory syndrome coronavirus (SARS) in 2003. This viral infection was connected to the Huanan seafood market in Southern China. Scientists took sample from patients' lower respiratory tract and sequenced its genome. They found that the virus had 70% homology with the SARS-CoV and 96.3% genetic similarity with the Yunnan bat coronavirus RaTG13. The World Health Organization (WHO) declared that a novel coronavirus found in 2019 (2019- nCoV) or SARS-CoV-2 was the source of this epidemic outbreak on January 12, 2020. The name of the disease is coronavirus disease 2019 (COVID-19). SARS-CoV-2 belongs to beta coronavirus family. It is single-stranded, positive and spherical RNA. It consists of four structural components such as spike (S), envelope (E), membrane (M) and nucleocapsid (N). It is a deadly virus. It is highly transmitted from human to human. Furthermore, there are different types of variants such as variant being monitored (VBM), variant of interest (VOI), variant of concern (VOC) and variant of high consequence (VOHC). Currently, Omicron is considered as VOC because of the reduction in vaccine effectiveness, a disproportionately high number of infections in vaccinated persons, very low vaccine-induced protection against severe disease, reduction of susceptibility to approved therapeutics, failure of diagnostic tests, the severity of the disease, a high number of hospitalization cases, etc.

Recently, medicinal plants and their phytochemicals become one of the main focuses of interest to hunt for effective, safe to humans and affordable drugs to cope with the current necessities. Indigenous traditional herbal therapy has a long history of treating a wide range of chronic and infectious diseases such as hypertension, diabetes mellitus, obesity, lung, heart and kidney-related diseases, etc. Researchers have demonstrated that medicinal plants that possess anti-viral properties such as *Andrographis paniculata*, *Lindera chunii*, *Dioscorea bulbifera*, *Wistaria floribunda*, *Xanthoceras*

sorbifoli and *Aegle marmelos* showed significant results for anti-HIV activity. A variety of bioactive compounds can inhibit viral entry, viral attachment to the host receptor, viral replication, viral transcription, viral translation, etc.

This book presents 17 chapters. Most of the contributors wrote on plant-derived anti-SARS-CoV-2 viral compounds; metabolomics study of phytochemicals and their therapeutic prospects in SARS-CoV-2 and the role of bioinformatics in the development of sensitive, specific and cost-effective antiviral agents from medicinal plants. These novel approaches can be a feasible strategy that can combat COVID-19 and prevent its comorbidities. Mechanisms of the phytochemicals against SARS-CoV-2 are explained through a variety of new pathways. It is vital to design a plant-based drug for COVID-19 patients. To date, there is no specific treatment for COVID-19. We have also attempted to revisit the pathogenesis of coronavirus through the host, clinical features and diagnostic approach on COVID-19, counteracting SARS-CoV-2 and managing COVID-19 impacts using natural products and medicinal plants and traditional plant-based therapies for SARS-CoV-2 infection.

Acknowledgments

Foremost, I would like to express my sincere gratitude to GOD for His blessings because I could not finish my book on time without Him.

This book acknowledges wholeheartedly and gratefully all my colleagues for their valuable contributions. I cannot resist my temptation to applaud the enthusiasm of these experts which catalyzes my academic passion and catapults me beyond my limitations.

I highly appreciate our contributors for accepting my invitation and sharing their knowledge and research. I produced an excellent quality book with a good teamwork effort. I would like to thank Nova Science Publishers for their kind co-operation at every stage of the book production.

My sincere gratitude also goes to my dear friends who supported me during the completion of this book. Last but not the least, I would like to thank my mother, Thavamani who supported me spiritually throughout my life.

Chapter 1

Introduction: Medicinal Plants and COVID-19

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Abstract

Early in 2020, a serious health problem emerged. An outbreak of the novel SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) epidemic took place in Wuhan, China, in December 2019. It quickly spread around the world. On February 11th, 2020, the World Health Organization (WHO) designated the disease as coronavirus disease (COVID-19). There are four classes of SARS-CoV-2 variants such as variant being monitored (VBM), variant of interest (VOI), variant of concern (VOC) and variant of high consequence (VOHC). However, the Omicron variant is a variant of concern at present because it can develop a more severe disease; reduce the neutralization of antibodies; reduce the effectiveness of treatments or vaccines, etc. Thus, scientists are required to find a new or modified vaccine or treatment for the novel variants of SARS-CoV-2. Phytoconstituents from medicinal plants have been proven to treat a variety of viral infections by inhibiting the pathogenesis of the virus (e.g., viral entry, attachment, replication, etc.). In this chapter, we will discuss the timeline of the COVID-19 pandemic development, SARS-CoV-2 and its variants, and medicinal plants and their biological activities.

Keywords: COVID-19, medicinal plants, SARS-CoV-2, variants

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Introduction

Coronaviruses are a vast family of zoonotic viruses that cause a wide range of illnesses, from severe respiratory infections to the common cold. They can be spread from animals to humans (Elengoe and Selvam, 2022; Elengoe et al., 2022). Certain coronaviruses are found in a population of animals. However, they are not harmful to humans because they are non-infectious diseases. SARS-CoV-2 is the most recent virus that infects humans. It is highly pathogenic to humans. SARS-CoV-2 infection is spread from person to person through droplets developed by infected people's respiratory systems, most commonly while coughing or sneezing. It takes between 2 to 14 days for exposure to onset of symptoms, according to current reports, with a five-day average. Two other recent outbreaks of coronavirus were reported. Middle East Respiratory Syndrome (MERS-CoV) was found to be transmitted to humans from dromedary camels in 2012 (Shereen et al., 2019). The transmission from civet cats to humans was found to be severe acute respiratory syndrome (SARS-CoV) in 2002 (Liu et al., 2020).

In 1965, the history of human coronaviruses started when Tyrrell and Bynoel discovered that a virus known as B814 can pass through them (Kahn and McIntosh, 2005). In human embryonic tracheal organ cultures collected from the respiratory system, it was discovered. The virus developed a common cold symptom. Later that decade, researchers discovered a collection of related human and animal viruses. They named them based on their crown-like appearance. They found that 7 different types of coronaviruses can infect humans. SARS was first discovered in 2002 in southern China. It rapidly spread to 28 other countries. More than 8,000 persons have been infected by July 2003, with 774 of them died. In 2004, there were just four more occurrences in a brief outbreak. The coronavirus causes fever, headache, as well as respiratory problems including cough and breathing shortness. MERS began in 2012 in Saudi Arabia (Rossi et al., 2020). Approximately all of the nearly 2,500 cases had resulted in individuals living in or traveling to the Middle East. This coronavirus is less infectious, but more lethal than its SARS-CoV because it caused the death of 858 individuals. It has the same respiratory symptoms as the flu, but it can also lead to kidney failure (Rossi et al., 2020).

SARS-CoV-2 infection, which would be the fifth pandemic after the 1918 influenza epidemic, has currently infected people all across the world. For the time being, we can follow the first warning and subsequent breakout of a cluster of unique instances of human pneumonia in Wuhan, China, which

began in late December 2019 (Elengoe, 2020). 1st December 2019 was the earliest date of symptom initiation. The patients had symptoms such as fever, malaise, dry cough, and dyspnea. These symptoms were identified as viral pneumonia. Initially, due to the area and pneumonia symptoms, the disease was called Wuhan pneumonia by the press. Results of whole-genome sequencing indicated that a novel coronavirus is a causal factor (Singhal, 2020). As a result, this virus is the 7th member of the coronavirus family to infect humans (Kumar et al., 2020). The virus can cause pneumonia, respiratory failure, respiratory difficulties, liver problems, septic shock, and death (Kumar et al., 2020).

The World Health Organization (WHO) temporarily termed the new 2019 coronavirus virus novel (2019-nCoV) on 12th January 2020, then on 12th February 2020, it was formally named coronavirus disease 2019 (COVID-19) (Guo et al., 2020; Elengoe, 2020). Since COVID-19 first appeared in China three years ago, it has grown and expanded rapidly to other countries around the world, posing a global threat. Following the 1918 Spanish flu (H1N1), 1957 Asian flu (H2N2), 1968 Hong Kong flu (H3N2), and 2009 Pandemic flu (H1N1), which killed an estimated 50 million, 1.5 million, 1 million, and 300,000 people, the WHO eventually determined that COVID-19 was a pandemic (Liu et al., 2020). COVID-19 killed 6,730,560 million people (Worldometer, 2022).

Timeline of COVID-19 Pandemic Development

On 31 December 2019, Wuhan Municipal Health Commission notified the World Health Organization about the pneumonia cases in Wuhan City, Hubei Province, China, with an unidentified cause. A novel coronavirus was then eventually discovered. The unknown illness was initially termed as 2019-nCoV and then was referred to as COVID-19. On 1st January 2020, the WHO set up an IMST (Incident Management Support Team) across the three levels of the organization: headquarters, regional headquarters and country level, placing the organization on the immediate ground to deal with the outbreaks. Authorities shut down the Huanan seafood market, which was speculated to be the origin of the mysterious illness. This is because from the first 27 recorded patients, most cases were epidemiologically related to the Huanan Seafood Wholesale Market, a wet market located in the city of Wuhan, which sells not only seafood and live animals, including poultry and wildlife, where some of the patients infected with the pneumonia-like disease were the market

dealers and vendors. According to a retrospective report, the first reported case dates back to 8th December 2019 (Jenny and Sara, 2020; World Health Organization (WHO), 2020).

At the beginning of January 2020, China announced a total of 44 alleged mystery disease patients. WHO posted on social media that there was a cluster of cases of pneumonia -with no deaths- in Wuhan, Hubei province on 4th January 2020 (Jenny and Sara, 2020; World Health Organization (WHO), 2020). The isolated virus from bronchoalveolar lavage fluid samples from patients with extreme pneumonia, Chinese researchers have detected beta coronavirus as the pathogenic factor of this new infectious illness. The novel coronavirus is then reported by China as the source of the epidemic. Coronaviruses are a broad group of viruses that can develop different degrees of illness, from mild colds to serious lethal diseases. Typically present in animals, some can infect humans and spread among humans. Both SARS and MERS are attributable to coronavirus (Hu et al., 2020; World Health Organization (WHO), 2020).

China records the first death linked to the new coronavirus on 9th January 2020. A 61-year-old man was admitted to Wuhan hospital with many serious health issues. Other than respiratory failure and extreme pneumonia, the man also had abdominal tumors and chronic liver disease (Jenny and Sara, 2020). The first genetic sequence of the novel coronavirus was released on the virological website on 10th January and on 12th January 2020. China shares the genetic sequence of the novel coronavirus publicly, allowing countries to test and track any potentially infected individuals (Hu et al., 2020).

On 13 January 2020, authorities announced a case of COVID-19 in Thailand, the first case reported outside of China. The patient is a 61-year-old female from Wuhan with no record of visiting the Huanan Seafood Market. On 16th January 2020, Japan announced another imported case of COVID-19. The Chinese national, a male in his 30s, also did not report a connection to the Huanan seafood market. The first case of 2019-nCoV was confirmed by South Korea on 20th January 2020. The patient did not register a visit to the markets in Wuhan (Jenny and Sara, 2020).

Subsequently, many patients with no history of Huanan Seafood Wholesale Market exposure were found. Several familial clusters of infection were reported. Infections also occurred within healthcare facilities. All of these events presented ample proof of human-to-human transmission of the new virus (Hu et al., 2020).

Since this epidemic clashed with the lunar New Year, movement between towns and villages before the festival promoted the spread of viruses in China.

This new coronavirus pneumonia eventually came to other areas in the region of Hubei as well as other parts of China. Within 1 month, the virus had dispersed to all 34 provinces of China. The number of reported cases unexpectedly increased, with thousands of new cases confirmed daily at the end of 15th January 2020 (Hu et al., 2020; World Health Organization (WHO), 2020).

On 25th January 2020, 2019-nCoV entered more nations. Australia announced the first case of 2019-nCoV on the continent, with three more cases identified by health officials later in the day. France reported a new case, the first in Europe. Malaysia also recorded the first four cases, while Canada announced the first case. On 30th January 2020, the WHO announced the outbreak of coronavirus a global health crisis of international concern. On 11th February 2020, the International Committee on Virus Taxonomy called the novel coronavirus as 'SARS-CoV-2' and the WHO named the disease 'COVID-19.' The outbreak of COVID-19 in China peaked in February. According to the National Health Commission of China, the cumulative number of cases kept growing sharply at the beginning of February at an average rate of more than 3,000 newly reported cases each day (Hu et al., 2020; Jenny and Sara, 2020). China has introduced extraordinarily stringent public health initiatives to regulate COVID-19. The city of Wuhan was closed on 23rd January 2020, and all travel and transportation connections to the city were stopped. In the next few weeks, all outdoor events and meetings were prohibited, and public facilities were closed both in most towns and in the countryside. As a result of these steps, the regular number of cases in China has begun to decline gradually. However, amid the gradual decrease in China, the worldwide transmission of COVID-19 has escalated since late February (Hu et al., 2020).

At the beginning of March 2020, the number of COVID-19 cases exceeded 100,000 and more than 100 countries registered COVID-19 cases (Jenny and Sara, 2020). The higher frequency transmission of SARS-CoV-2 and the accessibility of international flights made it possible for COVID-19 to spread rapidly throughout the world. On 11th March 2020, WHO Director-General Tedros Adhanom Ghebreyesus called the worldwide outbreak of COVID-19 a pandemic. Since March, while COVID-19 has been effectively regulated in China, the number of cases in Europe, the USA, India and other regions has jumped dramatically (WHO,2020). As of 16th January 2023, 671,375,204 positive cases; 6,730,560 death cases and 642,681,552 recovered cases have been reported throughout the world (Worldometer, 2022).

SARS-CoV-2

The SARS-CoV-2 is a beta coronavirus, which has a genome of roughly 30 kb and is large, spherical, encapsulated, positive-sense, single-stranded RNA (Richman et al., 2016). Spike glycoprotein (S), membrane (M), envelope (E), and nucleocapsid (N) proteins make up its four primary structural components (Fehr and Perlman, 2015). SARS-CoV-2 uses its spike to block the activity of neutralizing antibodies because neutralizing antibodies are playing an important role in blocking viral particles from binding with the host cell for infection to occur. Spike protein contains S1 and S2 domains. The S1 domain interacts with the host cell receptor known as Angiotensin Converting Enzyme 2 (ACE-2) to trigger a conformational shift in the S protein. The virus penetrates the host cell by mediating membrane fusion with the host cell membrane through the S2 domain.

Since the start of the COVID-19 pandemic, genetic lineages of SARS-CoV-2 have been emerging and spreading globally. There are four classes of SARS-CoV-2 variants such as variants being monitored (VBM), variant of interest (VOI), variant of concern (VOC) and variant of high consequence (VOHC). Alpha (B.1.1.7 and Q lineages), Beta (B.1.351 and descendent lineages), Gamma (P.1 and descendent lineages), Delta (B.1.617.2 and AY lineages), Epsilon (B.1.427 and B.1.429), Eta (B.1.525), Iota (B.1.526), Kappa (B.1.617.1), 1.617.3, Mu (B.1.621, B.1.621.1) and Zeta (P.2) are the variants being monitored (Table 1). According to the World Health Organization (WHO) data, there are no variants of interest as of 12th October 2022. However, Omicron (B.1.1.529, BA.1, BA.1.1, BA.2, BA.3, BA.4 and BA.5 lineages) are the variants of concern (Table 2). Currently, there are no variants of high consequence have been identified in the United States of America. Omicron was identified in South Africa. Its first outbreak occurred in November 2021. It has the potential to increase transmissibility; cause more severe disease (e.g., increased hospitalizations, morbidity and mortality rates); reduce neutralization by some emergency use authorization (EUA) monoclonal antibody treatments; and reduction in neutralization by post-vaccination sera. Moreover, it has the potential to reduce the effectiveness of treatments or vaccines, or diagnostic detection failures. Therefore, there is an urgency to develop a new or modified vaccine or effective treatments for new variants of SARS-CoV-2.

Table 1. List of SARS-CoV-2 variants being monitored

WHO label	PANGO lineage	Nextstrain clade	First outbreak	Earliest sample	Designated VOC	Designated VOI	Designated VBM	Current circulation	Mutations
Alpha	B.1.1.7 and Q lineages	20I (V1)	United Kingdom	20th Sept 2020	December 29, 2020	-	September 21, 2021	No	69-70del, N501Y, P681H
Beta	B.1.351 and descendent lineages	20H (V2)	South Africa	May 2020	December 29, 2020	-	September 21, 2021	No	K417N, E484K, N501Y
Gamma	P. 1 and descendent lineages	20J (V3)	Brazil	Nov 2020	December 29, 2020	-	September 21, 2021	No	K417T, E484K, N501Y
Delta	B.1.617.2 and AY lineages	21A	India	Oct 2020	June 15, 2021	-	April 14, 2022	No	L452R, T478K, P681R
Epsilon	B.1.427 B.1.429	21C	United States	July 2020	March 19, 2021	February 26, 2021 June 29, 2021	September 21, 2021	No	I4205V, D1183Y, S13I, W152C, L452R
Eta	B.1.525	21D	United Kingdom	December 2020	-	February 26, 2021	September 21, 2021	No	E484K, ΔH69/ΔV70 deletion, N439K, Y453F
lota	B.1.526	21F	United States	November 2020	-	February 26, 2021	September 21, 2021	No	E484K, S477N, L5F, T95I, D253G, E484K, D614G and A701V

Table 1. (Continued)

WHO label	PANGO lineage	Nextstrain clade	First outbreak	Earliest sample	Designated VOC	Designated VOI	Designated VBM	Current circulation	Mutations
Kappa	B.1.617.1	21B	India	December 2020	-	May 7, 2021	September 21, 2021	No	L452R, E484Q, P681R
N/A	B.1.617.3	19B	India	February 2021	-	May 7, 2021	September 21, 2021	No	L452R, E484Q, D614G, P681R
Zeta	P.2	21K	Brazil	January 2021	-	February 26, 2021	September 21, 2021	No	E484K, D614G
Mu	B.1.621 B.1.621.1	21H	Colombia	January 2021	-	-	VBM: September 21, 2021	No	R346K, E484K, N501Y, D614G, P681H

Table 2. List of SARS-CoV-2 variants concern lineages under monitoring (WHO) (as of 13th January 2023)

WHO Label	Pango lineage	Nextstrain clade	First outbreak	Relation to circulating VOCs	Earliest sample	Mutations
Omicron	BA.2.75	22D	India	BA.2 sublineage	31.12.2021	BA.2.75: BA.2 + S:K147E, S:W152R, S:F157L, S:I210V, S:G257S, S:D339H, S:G446S, S:N460K, S:Q493R reversion BA.2.75.2: BA.2.75 + S:R346T, S:F486S, S:D1199N
Omicron	BF.7	22B	China	BA.5 sublineage	24.01.2022	BA.5 + S:R346T
Omicron	BQ.1	22E	United Kingdom	BA.5 sublineage	07.02.2022	BQ.1 and BQ.1.1: BA.5 + S:R346T, S:K444T, S:N460K
Omicron	XBB	22F	United States	Recombinant of BA.2.10.1 and BA.2.75 sublineages, i.e., BJ1 and BM.1.1.1, with a breakpoint in S1	13.08.2022	BA.2+ S:V83A, S:Y144-, S:H146Q, S:Q183E, S:V213E, S:G252V, S:G339H, S:R346T, S:L368I, S:V445P, S:G446S, S:N460K, S:F486S, S:F490S XBB.1.5: XBB + S:F486P

Table 3. List of medicinal plants and their mechanism

No.	Plant species	Bioactive compound	Virus	Mechanism	Reference
1.	*Andrographis paniculata*	Andrographolide	SARS-CoV-2	– Inhibits viral replication	Shi et al., 2020
2.	*Justicia adhatoda* L.	Anisotine	SARS-CoV-2, Human influenza virus	– Blocks RBD of the SARS-CoV-2 spike protein and prevents host attachment through ACE2 receptor	Ghosh et al., 2021
3.	*Allium sativum* L.	Ajoene, allicin, alliin, allyl methyl thiosulfinate, methyl allyl thiosulfinat, allitridin, diallyl sulfide, garlicin,lectin	Human influenza virus, SARS-CoV-2	– Inhibits viral replication	Rouf et al., 2020
4.	*Mangifera indica*	Mangiferin	Human influenza virus	– Inhibits viral adsorption	Al-Rawi et al., 2019
5.	*Aloe vera* (L.) Burm.f.	Feralolide, 9-dihydroxyl-2-O-(z)-cinnamoyl-7-methoxy-aloesin, aloeresin, quercetin, catechin hydrate, and kaempferol	SARS-CoV-2	– Inhibits viral replication	Mpiana et al., 2020
6.	*Bombax ceiba* L.	Kaempferol-3-O-(6″-O-Ep-coumaroyl)-β-D-glucopyranoside	SARS-CoV-2	– Inhibits the ORF 3a protein of SARS-CoV-2	Zhang et al., 2015
7.	*Cyperus rotundus* L.	Humulene epoxide, and caryophyllene oxide	SARS-CoV-2	– Inhibits the activity of spike glycoprotein, papain-like protease (PLpro), 3-chymotrypsin-like protease (3CLpro) and RNA-dependent RNA polymerase (RdRp)	Amparo et al., 2021
8.	*Azadirachta indica* A. Juss.	Gedunin, pongamol, and azadirachtin	SARS-CoV-2	– Inhibits viral replication	Nesari et al., 2021
9.	*Piper nigrum* L.	Guaiol	SARS-CoV-2	– Inhibits viral replication	Pandey et al., 2021

Table 3. (Continued)

No.	Plant species	Bioactive compound	Virus	Mechanism	Reference
10.	*Aegle marmelos* (L.)	Seselin	SARS-CoV-2	– Blocks the activity of main protease (Mpro)	Nivetha et al., 2021
11.	*Citrus sinensis* (L.)	Hesperidin, luteolin, and vitamin C	SARS-CoV-2	– Inhibits spike protein and Mpro activity	Bellavite and Donzelli, 2020
12.	*Zingiber officinale*	6-gingerol, and gingeronone A	SARS-CoV-2	– Inhibits SARS CoV-2 by interacting viral proteases, RNA binding protein, and spike protein – Inhibits main protease and ORF8 of the SARS-CoV-2	Pandey et al., 2021
13.	*Curcuma longa* L.	Curcumin	SARS-CoV-2	– Interacts directly with viral membrane proteins, disrupts viral envelope, inhibits viral protease and induces host antiviral response by boosting immunity	Thimmulappa et al., 2021
14.	*Salvia rosmarinus*	Carnosic acid, carnosol or rosmanol, genkwanin, cirsimaritin or homoplantaginin, ursolic acid	SARS-CoV-2	– Blocks SARS-CoV-2 infection and reduce inflammation	Satoh et al., 2020
15.	*Ocimum tenuiflorum*	Eugenol	SARS-CoV-2	– Inhibits the interaction between spike S1 and ACE2 – Reduces SARS-CoV-2 spike S1-induced activation of NF-κB and the expression of IL-6, IL-1β and TNFα	Paidi et al., 2021

Medicinal Plants

Since ancient times, people use traditional herbs to treat or cure a variety of chronic diseases such as hypertension, diabetes mellitus, lung, kidney and heart-related diseases, etc. Indians use turmeric in their cooking as a spice. They also use neem leaves for chickenpox treatment. Phytoconstituents are a class of promising antiviral agents. They have been intensively to treat different types of viruses such as influenza virus, chicken pox virus, hepatitis B virus, human papillomavirus, rhinovirus, dengue virus type-2, herpes simplex virus-1, poliovirus, adenovirus, Epstein-Barr virus, respiratory syncytial virus, hepatitis C virus, human immunodeficiency virus (HIV), etc. Furthermore, many research studies have been demonstrated that traditional medicine gives better and more effective results than commercial drugs for viral infection. It is cost-effective, has low or no side effects and has a productive therapeutic effect. Ethanopharmacology helps to find novel biologically active compounds from plant sources. Bioactive compounds from medicinal plants have been proven to be effective against viral infections by inhibiting various steps in the pathogenesis of the virus such as viral entry, viral attachment to the host receptor, viral replication, endocytosis, transcription of the viral genome, protein translation, cleavage of the polypeptide, protein synthesis, etc. The uses of medicinal plants in viral infection were collected from the previous research findings (Table 3).

Conclusion

SARS-CoV-2 is a highly pathogenic virus. It can spread rapidly from one person to another person. There are different types of variants. Currently, World Health Organization (WHO) declared Omicron variants as a variant of concern (VOC). In conclusion, natural compounds from medicinal plants may be used as potential drugs for COVID-19 treatment. They can increase the effectiveness of the treatment against Omicron variants. The discovery of novel bioactive substances aids in developing new, safe and effective drugs.

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Chapter 2

The Pathogenesis of Coronavirus through the Host

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Abstract

The presence of the COVID-19 pandemic had brought a major impact on the healthcare and socioeconomic sectors. The emergence of SARS-CoV-2 had caused a high mortality rate across the globe. The virus was first identified in China in the year 2020 and further spread from the country across the world. Human-to-human transmission via respiratory droplets was reported as the major route of transmission. Transmission via fomite and airborne transmission in closed and poorly ventilated settings was also confirmed. Bats were identified as the reservoir for SARS-CoV-2 as bats host many viruses without presenting the clinical symptoms thus SARS-CoV-2 has been indicated as a zoonotic origin. The clinical spectrum of the disease varies from mild, moderate to severe. There are a few steps that involve the entry of SARS-CoV-2 into the human host: attachment, penetration, biosynthesis, maturation and release. Most asymptomatic patients (people without symptoms) can transmit the infection to people who are in close contact or proximity. Some patients have a mild influenza-like illness that cannot be

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differentiated from a simple upper respiratory tract infection. Hospitalization is required for moderate and severe cases. Studies have shown that mainly elderly and immunocompromised patients are the individuals who progress to the severe stages of the disease. Lessons from the understanding of the nature of the virus and its pathogenesis would help in new approaches and improving human health.

Keywords: pathogenesis, reservoir, SARS-CoV-2, transmission

Introduction

In December 2020, SARS-CoV-2 emerged when a worker from the market which sells live animals and exotic animals in the Hubei province of China presented with fever, dizziness, and cough. After approximately 4 weeks, there were nearly 10000 cases reported across countries and within a short period, the infection had succumbed across the globe (Yuki et al., 2020). Globally, the pandemic has claimed the lives of more than 6.8 million, according to John Hopkins University. It caused substantial morbidity among patients who survived their illnesses. Researchers worked substantially and identified the causative agent of coronavirus disease-2019 (COVID-19) to be severe acute respiratory syndrome-associated coronavirus-2 (SARS-CoV-2) (Li et al., 2020). The virus is primarily transmitted between people through respiratory droplets and contact routes. The disease continues to spread at an alarming rate worldwide. It was declared as a pandemic by the World Health Organization (WHO) (Zheng et al., 2020).

SARS-CoV-2 has been reported to be more infectious compared to SARS-CoV as the reproductive number is higher and this facilitates the rapid spread (Table 1). SARS-CoV-2 has several features which make it more infectious. SARS-CoV-2 binds strongly to the ACE2 receptors due to its differences in the surface protein and this facilitates greater efficiency in the host cell invasion (Wrapp et al., 2020). In addition to that, SARS-CoV-2 also has a greater affinity for the mucosa of the conjunctiva and upper respiratory tract thus leads to a higher infectious rate of SARS-CoV-2 (Wolfel et al., 2020; Hui et al., 2020).

Table 1. The recent outbreak of respiratory viruses and their severity

Types of viruses	Severity of disease caused by the virus	References
SARS-CoV-2	Highly contagious with severe respiratory signs	Meyerowitz et al., 2021 CDC, 2020
MERS	Severe respiratory signs, High mortality rate	Yang et., 2015 Aly et al., 2017
SARS	Contagious and severe respiratory signs	Woodhead et al., 2003

Primary Reservoir and Host of Coronavirus

The origination and transmission of the coronavirus (SARS-CoV-2) are essential to be determined as a preventive strategy to contain the virus. Since the emergence of SARS-CoV-2, potential animal species have been thoroughly studied to identify the possible reservoirs, genomic evolution of the virus and the intermediate hosts (Ji et al., 2020) (Bassetti et al., 2020). Bats are known to harbor a large diversity of coronavirus as there is the presence of anti-SARS-CoV-2 antibodies found in the samples isolated from the *Rhinolopus* sp. which further confirms the viral replication and as a primary reservoir. In the current scenario, researchers have been focusing on raccoon dogs and palm civets (Xiao et al., 2008) as the major reservoir of the infection; however, only the sample obtained from China food market showed positive for coronavirus and this suggests that the palm civet as the secondary host. Snakes were also suggested as a possible host however after genomic similarity findings of a novel coronavirus, bat coronavirus demonstrated approximately 88% similarities, this supports that bats could be the key reservoir of coronavirus (Markotter et al., 2020). Several genomes with sequences similarities have been reported between bat's coronavirus and SARS-CoV and this shows a high genetic similarity between both viruses (Hu et al., 2017).

Researchers suggest that in between the bats and humans, there is an intermediate host which contributes to the role of production of recombinant viruses. They have been extensively studying samples from bats and have concluded that bats can be a potential source of zoonotic diseases due to their ability to harbor many viruses without presenting any clinical symptoms for several months (Misra, 2020). Samples obtained from bats that are infected with CoV can propagate the virus without immunological interference compared to other infected mammals and this makes them an ideal reservoir for viruses (Zhou et al., 2020). Viral outbreaks from several spillovers from