Outbreak of Coronavirus (SARS-CoV-2) Delta variant (B.1.617.2) and Delta Plus (AY. 1) with fungal infections, Mucormycosis: Herbal medicine treatment

Ravindra B. Malabadi[*1], Kiran P. Kolkar[2], Neelambika T. Meti[3], Raju K. Chalannavar[1]

[1] Department of Applied Botany, Mangalore University, Mangalagangotri-574199, Mangalore, Karnataka State, India*
*[*1]Miller Blvd, NW, Edmonton, Alberta, Canada*
[2]Department of Botany, Karnatak Science College, Dharwad, Karnataka state, India
[3]Plant Biotechnology Laboratory, Rajiv Gandhi Institute of IT and Biotechnology, Bharati Vidyapeeth University, Pune-Satara Road, Katraj, Pune - 411046, Maharashtra State, India
**Corresponding author*

***Abstract*: This review of literature updates the current outbreak of second wave of coronavirus-2 (SARS-CoV-2) mutant Delta variant (B. 1. 617.2) strain and Delta Plus (AY.1) in India followed by the severe black fungus infections, mucormycosis. The mucormycosis, the black fungus infections have been emerged as an additional threat among those recovering from the viral disease, covid-19. Both coronavirus-2 (SARS-CoV-2) mutant strain, B.1.617.2 (Delta variant) and Delta Plus (AY.1) with black fungus has increased covid-19 hospitalizations and killing people in India. The widely accepted treatment of choice for mucormycosis is Amphotericin B. However, these medicines are already exhausted due to the shortage of supply, found very expensive, and fungal strains are resistant during covid-19 outbreak in India. Therefore, traditional herbal medicines with antifungal properties were used as per *Auyverdic* guidelines as an alternative therapy for controlling this deadly black fungus, mucormycosis during the outbreak of covid-19. Herbal medicines with antifungal activities are easily available in rural areas, less expensive, and traditional healers are practicing herbal therapy as an age old practice for controlling mucormycosis. Herbal formulations are very common household remedies in the rural parts of India.**

***Key words:* Black fungus, covid-19, Delta variant, fungal infections, herbal therapy, India, mucormycosis**

I. INTRODUCTION

The outbreak of pneumonia associated novel coronavirus (SARS-CoV-2) disease (Covid-19) has spread quickly throughout the world (Shereen et al., 2020; Malabadi et al., 2021a). As the COVID-19 pandemic enters its second year, new fast-spreading mutant variants, B. 1. 617.2 (Delta strain) and Delta Plus (AY. 1) have caused a surge in infections in many countries, and renewed lockdowns. Many people are of the opinion that Covid-19 is not going to go back to baseline anytime soon and fear is that the deterioration in mental health could linger long after the pandemic has subsided (Fancourt et al., 2021; Pierce et al., 2020). WHO has declared Covid-19 as pandemic which is a major threat to human health (Wu et al., 2020a, 2020b; Shi et al., 2020; V'kovski et al., 2020; Hoffmann et al., 2020; Lima et al., 2020; Yang, 2021; Shin et al., 2020). The Delta variant of coronavirus (SARS-CoV-2) is becoming the globally dominant version of the disease. Similar pandemics have occurred around the globe in recent past. The precautions to contain Covid-19 infection remain in place, and even so, the number of cases and deaths increased every day in India. Therefore, the Covid-19 pandemic poses challenges to healthcare teams around the world.

The outbreak of second wave of coronavirus-2 (SARS-CoV-2) with mutant Delta variant (B.1.617.2) and Delta Plus (AY. 1) in India has been sweeping across the globe (O'Dowd, 2021; Sheikh et al., 2021; Public Health England, 2021). The mutant Delta variant (B.1.617.2) was first detected in India in late 2020, where it is thought to have contributed to the extremely high number of cases during the country's second wave of COVID-19. As of 24 June 2021, mutant Delta variant (B.1.617.2) had spread to 74 countries worldwide, according to the World Health Organization (WHO). The mutant Delta variant (B.1.617.2) currently accounts for more than 91% of UK COVID-19 cases, and is around 40% more transmissible than the Alpha variant (Sheikh et al., 2021; Public Health England, 2021). The so-called Alpha variant (B.1.1.7) was also detected in UK. The small changes in the variants' spike protein may enhance its ability to bind to the ACE2 receptor that it uses to gain entry to human cells (O'Dowd, 2021; Sheikh et al., 2021; Public Health England, 2021). Therefore, separate mutation in the Delta variant (B.1.617.2) may enhance its ability to fuse with human cells once it latches on. If the virus can latch on and fuse more easily, it may be able to infect more of human cells, which may make it easier to overwhelm human immune defences (O'Dowd, 2021; Sheikh et al., 2021; Public Health England, 2021).

The mutant Delta variant (B.1.617.2) is also rapidly spreading in Southeast China and patients are becoming sicker and their conditions deteriorating more quickly than the patients they treated at the start of the pandemic in China.

The 'delta plus' variant is a mutated version of the more aggressive B.1.617.2, or 'delta', strain that drove the second wave of infections in India and has already been listed as a 'variant of concern'. This has been identified as B.1.617.2.1, or AY.1/2, and it is characterised by the K417N mutation in the spike protein of the SARS-CoV2 virus that causes the COVID-19 disease. As of now among the samples sequenced (45,000+) in India, Delta plus variant -- AY.1 --has been observed sporadically in Maharashtra, Kerala and Madhya Pradesh states, India with around 40 cases identified so far and no significant increase in prevalence (www.ndtv.com, 24th June 2021) (www.ndtv.com).

This new Delta plus variant (AY.1) replicated due to the mutation of the existing Delta strain (B.1.617.2) variant first detected in India and this new mutant fuelling an upsurge in infections. This mutated Delta Plus variant (AY.1) infection cases in India are slowly increasing in numbers, are emerging as large parts of India are ending severe lockdowns and restrictions with Covid-19 cases on the decline after a fierce second wave ambushed the nation's health infrastructure in April-May 2021. According to INSACOG (Indian SARS-CoV-2 Genomic Consortia), National Institute of Virology (NIV), Pune, Maharashtra state, India and Institute of Genomics and Integrative Biology (IGIB), a consortium of 28 labs tasked with genome sequencing of the virus causing Covid-19, confirmed that properties of the Delta Plus variant (AY.1) are still being investigated. It is characterized by a mutation in the spike protein, which helps the virus gain entry into human cells. Very little is known about this strain, and Delta Plus (AY.1) which is now in nine countries - US, UK, Portugal, Switzerland, Japan, Poland, Russia and China besides India. "After the report of Delta plus (AY.1) by the Public Health England (PHE), UK on June 11, 2021, retrospective analysis of samples revealed the first occurrence of this lineage from a sample collected from Maharashtra. As of June 18, 2021, 205 sequences of Delta Plus (AY.1) lineage was detected worldwide, with the US and the UK having over half of the known cases. The Delta Plus (AY.1) much like the Delta strain that has spread to 80 countries, is highly infectious and fast-spreading. According to INSACOG, the Delta Plus strain (AY.1) showed "increased transmissibility, stronger binding to receptors of lung cells and potentially reduced monoclonal antibody response.

In India, COVID-19 patients, especially severely ill or immunocompromised, have a higher probability of suffering from invasive mycoses. India is currently battling the second wave of Covid-19 (the Delta Plus strain, AY.1) with black fungus infections that has pushed up the number of patients requiring hospitalisation (Prakash and Chakrabarti, 2021; Garg et al., 2021). As a result of black fungus infections, vomiting, nausea, gastrointestinal bleeding and abdominal pain symptoms have also been described, but less frequently, and vomiting is most common in the pediatric population and abdominal pain is the most prevalent in critically ill covid-19 patients (Prakash and Chakrabarti, 2021; Garg et al., 2021). The devastation of the pandemic resulted in millions of deaths, economic strife and unprecedented curbs on social interaction has already had a marked effect on the people’s mental health (Fancourt et al., 2021; Pierce et al., 2020; Mahase, 2020; Holmes et al., 2020).

Over the past 30 years, several coronaviruses have crossed the species barrier into humans, causing outbreaks of severe, and often fatal, respiratory illness (Zhou et al., 2020a, 2020b; Malabadi et al., 2021a, 2021b, 2021c, 2021d; Shin et al., 2020; Yang, 2021). Since SARS-CoV was first identified in animal markets, global viromics projects have discovered thousands of coronavirus sequences in diverse animals and geographic regions (Wu et al., 2020a, 2020b; Wang et al., 2020; Shereen et al., 2020; Malabadi et al., 2021a, 2021b). Phylogenetic analysis of the complete viral genome (29,903 nucleotides) revealed that the virus was the most closely related (89.1% nucleotide similarity) to a group of SARS-like coronaviruses (genus Betacoronavirus, subgenus Sarbecovirus) that had previously been found in bats in China (Zhou et al., 2020a, 2020b; Wu et al., 2020a, 2020b; Shi et al., 2020; V’kovski et al., 2020; Hoffmann et al., 2020; Lima et al., 2020; Yang, 2021; Shin et al., 2020). This outbreak highlights the ongoing ability of viral spill-over from animals to cause severe disease in humans. The outbreak of 2019-novel coronavirus disease (COVID-19) that is caused by SARS-CoV-2 has spread rapidly around the globe, and becomes a Public Health Emergency of International Concern (Wu et al., 2020a, 2020b; Shi et al., 2020; V’kovski et al., 2020; Hoffmann et al., 2020; Lima et al., 2020; Yang, 2021; Shin et al., 2020). Severe acute respiratory syndrome coronavirus- 2 (SARS-CoV-2) infects host cells through ACE2 receptors, leading to coronavirus disease (COVID-19)-related pneumonia, while also causing acute myocardial injury and chronic damage to the cardiovascular system (Zhou et al., 2020a, 2020b; Wu et al., 2020a, 2020b; Shin et al., 2020; Yang et al., 2021). Therefore, particular attention should be given to cardiovascular protection during treatment for COVID-19.

The human to human spreading of the coranavirus (SARS-CoV-2) occurs due to the close contact with an infected person, exposed to coughing, sneezing, respiratory droplets or aerosols and fecal to oral transmission. These aerosols can penetrate the human body (lungs) via inhalation through the nose or mouth (Shin et al., 2020; Shereen et al., 2020; Malabadi et al., 2021a). The coronavirus (SARS-CoV-2) designated as COVID-19 prominently affect the respiratory tract (both lower and upper respiratory tract), with the initial symptoms of common cold, fever, dry cough, fatigue, general feeling of being unwell, runny nose, aches and pains, nasal congestion, loss of taste or smell, loss of speech or movement, headache, sore throat, a rash on skin, or discolouration of fingers or toes, conjunctivitis, shortness of breath, chest pain or pressure, and diarrhoea to severe pneumonia, difficulty in breathing and ends with the patient death (Wu et al., 2020a, 2020b; Zhou et al., 2020a, 2020b;Wang *et al*. 2020; Malabadi et al., 2021a). Infection with these highly pathogenic coronaviruses (SARS-CoV-2) could result in the acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) followed by the failure of the lung function and death (Wu et al., 2020a, 2020b). The incubation period of the coronavirus disease is 14 days and the time from onset of symptom to developing pneumonia is 4 days (Wu et al., 2020a, 2020b; Zhou et al., 2020a, 2020b; Malabadi et al., 2021a). Therefore, interaction between virus SARS-CoV-2 and host may be responsible for its unusual high morbidity and mortality (Wu et al., 2020a, 2020b; Zhou et al., 2020a, 2020b).

Coronavirus (SARS-CoV-2) is a respiratory RNA virus and undergoes mutation as a part of evolutionary biology. The outbreak of second wave in India by Severe Acute Respiratory Syndrome-2 (SARS-CoV-2) is a life threatening viral disease (Covid-19). This coronavirus Delta variant (B.1.617.2) fuelling India crisis is the newest 'variant of concern' and is spreading globally. The mutation in the spike protein of coronavirus (SARS-CoV-2) has increased the viral transmission rate and virus is more infectious than before. All the viruses mutate, and SARS-CoV-2 does not mutate particularly quickly compared with other viruses. But having spread explosively, it has had abundant opportunities to shape-shift through random mutation. This has resulted in more hospitalization and death of covid-19 patients in India. Therefore, outbreak of mutant B.1.617. 2 (Delta variant) in India is called as the Silent killer and appears to be highly transmissible. Therefore, WHO has concluded that the coronavirus Delta variant (B.1.617.2) that has spread catastrophically in India has seeded itself in dozens of countries. The spread of coronavirus variants of concern across the planet has raised fears that, the virus will find ways to remain elusive, potentially circumventing vaccines. However, the more the virus infects, replicates, spreads, the more it gives this virus a chance to mutate and continue to evade antibody responses.

The researchers from Flinders University and La Trobe University in Australia used high-performance computer modelling of the form of the SARS-CoV-2 virus at the beginning of the pandemic to predict its ability to infect humans and 12 domestic and exotic animals. The results showed that SARS-CoV-2 bound to ACE2 on humans cells more tightly than any of the tested animal species, including bats and pangolins. Humans showed the strongest spike binding consistent with the high susceptibility to the virus, but very surprising if an animal was the initial source of infection in humans. The computer modeling found that the virus ability to bind to bat ACE protein was poor relative to its ability to bind to human cells by the Professor David Winkler, La Trobe University, Australia. The researchers explained that if one of the animals species tested was the origin, it would normally be expected to show the highest binding to the virus.

Mutations in the spike gene can make the virus inherently "better" at infecting people or can help the virus to escape the neutralising antibodies. This means if the virus mutates in the "right way", it can re-infect someone who has already recovered from covid-19. Some mutations weaken the virus while others may make it stronger, enabling it to proliferate faster or cause more infections (Malabadi et al., 2021a, 2021b, 2021c). Therefore, vaccination campaign must be rationalised and implemented with all due speed which will reduce SARS-CoV-2 transmission as much as possible while the vaccine is rolled out (Malabadi et al., 2021d). Therefore, Government of India has implemented new lock down measures to bend the epidemic curve, including the possibility of a state government lockdown (Malabadi et al., 2021d). The Serosurvey by the Indian Council of Medical Research in January 2021 has suggested that only 21% of the Indian population had antibodies against SARS-CoV-2. Hence India is far away from reaching herd immunity.

In another major breakthrough, the anti-COVID therapeutic drug known as 2-DG (2-deoxy-D-glucose) has been developed by the Institute of Nuclear Medicine and Allied Sciences (INMAS), a leading laboratory of the Defence Research and Developmental Organization (DRDO) -CSIR Laboratoris, Government of India, New Delhi, India in collaboration with Dr Reddy’s Laboratories (DRL) in Hyderabad. Telangana, India (**India. com. News Desk, 2021).** The Anti-Covid-Oral-drug is known as 2-DG (2-deoxy-D-glucose) launched for the first time under the Emergency Use for controlling Covid-19 in India. This is a kind of pseudo glucose molecule in the drug which stops virus in its tracks. The 2-DG (2-deoxy-D-glucose) drug comes in powder form in a sachet, which is taken orally by dissolving it in water. It accumulates the virus-infected cells and prevents virus growth by stopping viral synthesis and energy production. Its selective accumulation in virally infected cells makes this drug unique. DRDO, New Delhi, Government of India, New Delhi, India and Dr Reddy’s lab had gone through the complete clinical trials and conducted clinical trials across 30 hospitals and on a large number of patients. In efficacy trends, patients treated with 2-DG (2-deoxy-D-glucose) showed a faster symptomatic cure than the standard of care (SoC) on various endpoints. The Drugs Controller General of India (DGCI) approved the oral drug for emergency use as an adjunct therapy in moderate to severe coronavirus (Covid-19) patients (**India. com. News Desk, 2021).**

Another good news is that indigenously developed covid-19 vaccine **Covaxin** (India's indigenous COVID-19 vaccine by Bharat Biotech, Hyderabad, Telangana, India is developed in collaboration with the Indian Council of Medical Research (ICMR) and National Institute of Virology (NIV), Pune, Maharashtra, India neutralises the mutant (B.1.167. 2 and B.1.168) Delta variants of SARS-CoV-2 and works against new strain. Therefore, Bharath Biotech, Covaxin has now received Emergency USE Authorizations for covid-19 treatment in India. In addition to this, another covid-19 vaccine, Covishild (Serum Institute of India, Pune, Maharashtra, India) also neutralises the mutant (B.1.167 and B.1.168) and B. 1. 617.2 (Delta variant) variants of SARS-CoV-2. This has been tested only in few blood samples of the infected people. Large scale clinical trials are undergoing and results are yet to be confirmed. Furthermore, initial clinical experiments confirmed that Moderna and Pfizer-BioNTech COVID-19 (mRNA Lipid nanoparticle) vaccines (Malabadi et al., 2021d) were also found effective and neutralizes the new variant (B.1.167 and B.1.168) and B. 1. 617.2 (the Delta Variant of Concern) with new mutations in India (www.ndtv.com, 2021). Two weeks after receiving a second dose, the Pfizer-BioNTech vaccine appeared to provide 79% protection against infection with the Delta variant, compared with 92% protection against the Alpha variant.

The study by Oxford University researchers, published in the journal Cell, investigated the ability of antibodies in the blood from people, who were vaccinated with the two-shot regimens, to neutralize the highly contagious Delta and Kappa variants, a statement said. “There is no evidence of widespread escape suggesting that the current generation of vaccines will provide protection against the B.1.617 lineage,” the paper said, referring to the Delta and Kappa variants by a commonly used code. An analysis by the Public Health England (PHE), UK showed that vaccines made by Pfizer Inc and AstraZeneca offer high protection of more than 90 per cent against hospitalization from the Delta variant.

The Oxford University researchers also analysed re-infection patterns in people who had previously had COVID-19. The risk of re-infection with the Delta variant appeared particularly high in individuals previously infected by the Beta and Gamma lineages that emerged in South Africa and Brazil, respectively.

The COVID-19 pandemic and the resulting economic recession have negatively affected many people’s mental health and created new barriers for people already suffering from mental illness (Fancourt et al., 2021; Pierce et al., 2020; Mahase, 2020; Holmes et al., 2020). Therefore, major concern is that the COVID-19 pandemic has had a bad effect on our daily life. People are facing challenges that can be stressful, overwhelming, and cause strong emotions in adults and children (Fancourt et al., 2021). Public health actions, such as social distancing, are necessary to reduce the spread of COVID-19, but they can make people feel isolated and lonely and can increase stress and anxiety (Fancourt et al., 2021; Pierce et al., 2020; Mahase, 2020; Holmes et al., 2020).

Psychological stress can cause many health issues: Feelings of fear, anger, sadness, worry, numbness, or frustration, 2) Changes in appetite, energy, desires, and interests, 3) Difficulty concentrating and making decisions, 4) Difficulty in sleeping or nightmares, 5) Physical reactions, such as headaches, body pains, stomach problems, and skin rashes, 6) Worsening of chronic health problems, 7) Worsening of mental health conditions (Fancourt et al., 2021; Pierce et al., 2020; Mahase, 2020; Holmes et al., 2020).

This comprehensive review updates about outbreak of new coronavirus (SARS-CoV-2) mutant variant of concern, B.1. 617.2 (Delta variant) in India is followed by the severe fungal infections caused my mucormycosis in covid-19 patients. Further, herbal medicine treatment formulations with antifungal activity has been recommended on bases of literature survey for controlling mucormycosis.

II. COVID-19: BLACK FUNGAL INFECTIONS-MUCORMYCOSIS

The basal fungal lineages have been classified into 4 main groups during the evolution of the fungal lineage, 1) Ascomycota (Sac fungi) and 2) Basidiomycota (Club fungi), 3) Chytridiomycota, and 4) Zygomycota (Saprophytic filamentous fungi) (Hibbett et al., 2007; Petrikkos et al., 2012; Mendoza et al., 2015). Among these 4 groups, only Zygomycotan fungi are known to infect humans. Hence, fungal infections caused by zygomycetes have been called Zygomycosis, and the term “Zygomycosis” is often used as a synonym for “Mucormycosis (Aggarwal et al., 2015; Skiada et al., 2018; Petrikkos et al., 2012; Hibbett et al., 2007; Mendoza et al., 2015). Zygomycota is further classified mainly based on morphology, including the ability to form coenocytic (aseptated) hyphae and zygospores (sexual spores) (Petrikkos et al., 2012; Hibbett et al., 2007; Mendoza et al., 2015). In Zygomycota, there are 10 known orders, two of which, the Mucorales (filamentous fungi) and Entomophthorales, contain species that can infect humans, and the infection has historically been known as mucormycosis (Prakash and Chakrabarti, 2021; Aggarwal et al., 2015; Hibbett et al., 2007; Petrikkos et al., 2012; Mendoza et al., 2015; Skiada et al., 2018). Mucormycetes belong to the order Mucorales, subphylum *Mucoromycotina* (Hibbett et al., 2007). Mucorales represents a heterogeneous group of filamentous fungal saprobionts or facultative parasites, usually found in soil, compost, animal feces, decaying vegetables, agricultural debris, or other organic matter and in association with plants, fungi, animals, and humans as opportunistic pathogens (Prakash and Chakrabarti, 2021; Hassan and Voigt, 2019; Montaño and Voigt, 2020; Chakrabarti and Singh, 2014; Chander et al., 2015). Many are cosmopolitan components of the biosphere, ubiquitously occurring in all the climatic zones of the Earth (Hassan and Voigt, 2019; Montaño and Voigt, 2020). Mucormycosis (previously called Zygomycosis) is a serious but rare emerging fungal infection caused by a group of molds called mucormycetes with high morbidity and mortality (Aggarwal et al., 2015; Hibbett et al., 2007; Mendoza et al., 2015; Petrikkos et al., 2012; Skiada et al., 2018). This life-threatening disease is caused by ubiquitous fungi in the order mucorales, predominantly by *Rhizopus* species including *R. delemar* and *R. oryzae*. Other common causative organisms include species of *Mucor*, *Lichtheimia* (previously *Absidia*), *Apophysomyces*, *Rhizomucor*, and *Cunninghamella* (Baldin and Ibrahim, 2017). The pathogenicity of mucorales (saprophytic filamentous fungi) is largely believed to be due to the endocellular excretions and production of subtilisins, chitinases, proteinases and antioxidant proteins (e.g., superoxide dismutase, catalase and peroxidase (Hameed et al., 2017). The genus Mucor has several species, the more common ones being *Mucor amphibiorum*, *M. circinelloides*, *M. hiemalis*, *M. indicus*, *M. racemosus*, and *M. ramosissimus* (Prakash and Chakrabarti, 2021; Hameed et al., 2017).

Mucor (saprophytic colonizers) and Rhizopus species belongs to mucorales are commercially important species. The genus Rhizopus, specifically, has been majorly exploited to produce lactic acid, fumaric acid, amylases, pectinases, steroids, lipases, ureases, and tannases, whereas genus Mucor is considered a good source for cellulases, phytases, proteases, ethanol, lipids and food colorants (Hameed et al., 2017). The genera of zygomycetes (Mucor and Rhizopus) can be a great source of natural antioxidants and these natural antioxidants can be termed as "microbial antioxidants" because of microbes/fungi being their source of origin (Hameed et al., 2017).

Currently in India, another major health issue is black fungus infections in covid-19 patients admitted in hospitals is known as mucormycosis (Garg et al., 2021; Alekseyev et al., 2021; Mehta and Pandey, 2020; Sarkar et al., 2021; Song et al., 2020). Fungi of the basal lineage order mucorales are able to cause infections in animals and humans (Hassan and Voigt, 2019). COVID-19 patients, especially severely ill or immunocompromised, have a higher probability of suffering from invasive mycoses (Garg et al., 2021; Alekseyev et al., 2021; Mehta and Pandey, 2020; Sarkar et al., 2021; Song et al., 2020). Most of the Covid-19 patients admitted in the hospitals in India are suffering from mucormycosis and ends up with loss of eye vision and death. Mucormycosis is also observed in recovered Covid-19 patients with other health disorders (Prakash and Chakrabarti, 2021). Steroids reduce the inflammation in the lungs for Covid-19 patients. Therefore, steroids will help the human body to stop some of the damage that can happened when the body's immune system goes into overdrive to fight off coronavirus. However, steroids also reduced the immunity and push up blood sugar levels in both diabetics and non-diabetic Covid-19 patients. Mucorales have the great affinity for blood vessels, invade rapidly, and disseminate widely. Furthermore, hemorrhagic necrosis is the hallmark of mucormycotic tissue lesions (Prakash and Chakrabarti, 2021; Chakrabarti and Singh, 2014; Chander et al., 2015; Hassan and Voigt, 2019). The rate of mortality and morbidity caused by mucormycosis, a well-known, life-threatening disease especially in Covid-19 patients with a compromised immune system has increased rapidly during the last decades, especially in developing countries (Chakrabarti and Singh, 2014; Chander et al., 2015; Hassan and Voigt, 2019). The mucoralean fungi are dreaded to cause the fatal disease in a broader range of human and animal hosts compared with other opportunistic fungi (Hassan and Voigt, 2019). The main hallmarks of this infection include the invasion of blood vessels, infarction, thrombosis, and tissue necrosis, which are exhibited at the latest stages of the infection (Hassan and Voigt, 2019; Montaño and Voigt, 2020). Angioinvasion, thrombosis, and tissue necrosis are the most common hallmarks of mucormycosis (Prakash and Chakrabarti, 2021; Montaño and Voigt, 2020).

Aspergillus, *Cryptococus* and *Candida* infections in COVID-19 patients will require early detection by a comprehensive diagnostic intervention (histopathology, direct microscopic examination, culture, (1, 3)-b- D-glucan, galactomannan, and PCR-based assays) to ensure effective treatments (Song et al., 2020; Prakash and Chakrabarti, 2021). The main fungal pathogens for fungal coinfections in severe COVID-19 patients are *Aspergillus*, Candida and pathogenic fungus caused the lung infections are *Mucor* and *Cryptococcus* (Song et al., 2020; 1994; Malabadi and Raghavendra, 1994, 1995, 1998). Mucormycosis is an uncommon but serious rare infection that complicates the course of severe COVID-19 (Chakrabarti and Singh, 2014; Chander et al., 2015; Hassan and Voigt, 2019; Montaño and Voigt, 2020). Covid-19 patients who have been hospitalised particularly those who required oxygen therapy during Covid-19 illness are at a much higher risk of mucormycosis (Garg et al., 2021; Alekseyev et al., 2021; Karimi-Galougahi et al., 2021).

Some cases of mucormycosis in patients with an asymptomatic Covid-19 infection who were not even aware of their diagnosis has been reported. Mucormycosis is a fungal infection that has a high mortality rate of 50 per cent and an increasing number of Covid-19 patients have been developing this infection while still at the hospital or after discharge (Prakash and Chakrabarti, 2021; Garg et al., 2021; Brunet and Rammaert, 2020; Alekseyev et al., 2021; Mehta and Pandey, 2020; Sarkar et al., 2021; Song et al., 2020; Karimi-Galougahi et al., 2021). Covid-19 patients suffering from the black fungal infection (Mucormycosis) typically have symptoms of stuffy and bleeding nose; swelling of and pain in the eye; drooping of eyelids; and blurred and finally, loss of vision (Karimi-Galougahi et al., 2021; Mehta and Pandey, 2020; Sarkar et al., 2021; Chakrabarti and Singh, 2014; Chander et al., 2015). There could be black batches of skin around the nose (Prakash and Chakrabarti, 2021; Alekseyev et al., 2021; Mehta and Pandey, 2020; Sarkar et al., 2021; Brunet and Rammaert, 2020).

Covid-19 patients with diabetes mellitus may be at a higher risk for developing mucormycosis (Garg et al., 2021). Concurrent glucocorticoid therapy probably heightens the risk of mucormycosis (Garg et al., 2021; Prakash and Chakrabarti, 2021). A high index of suspicion and aggressive management is required to improve outcomes (Garg et al., 2021; Song et al., 2020). Physicians caring for critically ill COVID-19 patients must be aware of serious infections that can complicate the course of COVID-19 (Garg et al., 2021; Prakash and Chakrabarti, 2021). A high degree of clinical suspicion is required to diagnose pulmonary mucormycosis (Prakash and Chakrabarti, 2021; Garg et al., 2021). Early diagnosis and timely management are necessary to improve the outcomes in pulmonary mucormycosis (Prakash and Chakrabarti, 2021; Garg et al., 2021). Extensive use of steroids/monoclonal antibodies/broad-spectrum antibiotics may lead to the development/exacerbation of a preexisting fungal disease (Song et al., 2020; Garg et al., 2021; Mehta and Pandey, 2020). Physicians should be aware of the possibility of secondary invasive fungal infections in patients with COVID-19 infection (Song et al., 2020; Garg et al., 2021; Mehta and Pandey, 2020; Aggarwal et al., 2015).

In India, although *Rhizopus* species are the most common cause of the disease, *Apophysomyces elegans*, *A. variabilis* and *Rhizopus homothallicus* are emerging species and uncommon agents such as *Mucor irregularis* and *Thamnostylum lucknowense* are also being reported (Prakash and Chakrabarti, 2021; Chakrabarti and Singh, 2014; Chander et al., 2015). Most cases of mucormycosis resulted from the inhalation of fungal sporangiospores that have been released in the air or from direct inoculation of organisms into disrupted skin or gastrointestinal tract mucosa, ingestion of contaminated food (Prakash and Chakrabarti, 2021; Baldin and Ibrahim, 2017; Skiada et al., 2018). These routes resulted in the rhinoorbital/cerebral, pulmonary, gastrointestinal, or cutaneous infections (Baldin and Ibrahim, 2017). The hallmark of mucormycosis is the ability of the causative organism to aggressively and rapidly invade blood vessels, which resulted in hematogenous dissemination, vessel thrombosis, and subsequent tissue necrosis (Prakash and Chakrabarti, 2021; Baldin and Ibrahim, 2017). Therefore, interactions between invading fungi and endothelial cells lining blood vessels represented a major step in the pathogenesis of mucormycosis (Baldin and Ibrahim, 2017).

Mucormycosis mainly affects people who have health problems or take medicines that lower the body's ability to fight germs and sickness (Prakash and Chakrabarti, 2021; Chakrabarti and Singh, 2014; Chander et al., 2015). Mucormycosis is also called as either a respiratory or a skin infection. Signs of a related sinus or respiratory infection may include: cough, fever, headache, nasal congestion, sinus pain (Prakash and Chakrabarti, 2021; Chakrabarti and Singh, 2014; Chander et al., 2015; Baldin and Ibrahim, 2017). With a skin infection, mucormycosis can develop within any part of body. It may initially occur at the site of skin trauma, but it can quickly spread to another area (Chakrabarti and Singh, 2014; Chander et al., 2015). The symptoms of mucormycosis such as: blackened skin tissue, blisters, fever, redness, swelling, tenderness, and ulcers (Prakash and Chakrabarti, 2021; Chakrabarti and Singh, 2014; Chander et al., 2015; Baldin and Ibrahim, 2017).

Mucorales are ubiquitous and found in soil and air and even in the nose and mucus of healthy people (Prakash and Chakrabarti, 2021; Chakrabarti and Singh, 2014; Chander et al., 2015; Skiada et al., 2018). The most common clinical presentations of mucormycosis are rhino-orbito-cerebral, pulmonary, cutaneous, and disseminated (Chakrabarti and Singh, 2014; Chander et al., 2015; Skiada et al., 2018). The main risk factors for developing mucormycosis are neutropenia due to cancer treatment, hematopoietic and solid organ transplantation, diabetes mellitus, in particular when presenting with ketoacidosis (DKA), and other forms of acidosis (Prakash and Chakrabarti, 2021; Baldin and Ibrahim, 2017). In India, rhino- orbito- cerebral presentation associated with uncontrolled diabetes mellitus (DM) was the predominant characteristic, and isolated renal mucormycosis has emerged as a new clinical entity (Prakash and Chakrabarti, 2021; Chakrabarti and Singh, 2014; Chander et al., 2015).

The mortality of mucormycosis remains high. Treatment includes antifungal agents in combination with surgical intervention (Prakash and Chakrabarti, 2021; Skiada et al., 2018). Antiviral agents with activity against mucorales is isavuconazole (given through an IV or orally), amphotericin B (given through an IV) -based drugs or posaconazole (given through an IV or orally) (Skiada et al., 2018). These 2 systemic anti-fungals are currently available with good mucorales activity- amphotericin B (including the lipid formulations) and the triazole posaconazole (Kontoyiannis and Lewis, 2011). It is important to start one of these classes of antifungal agents as soon as possible, as treatment delays are associated with increased mortality (Kontoyiannis and Lewis, 2011).

The clinical signs and symptoms of mucormycosis are nonspecific and there are no biomarkers to indentify this disease (Kontoyiannis and Lewis, 2011). Mucorales have a strong tropism for invasion of blood vessels, resulting in tissue infarction and necrosis, the pathologic hallmark of mucormycosis (Kontoyiannis and Lewis, 2011). Early recognition and treatment of the infection are critical improving patient survival before invasion, and necrosis become too extensive and the infection disseminates to other organs (Kontoyiannis and Lewis, 2011). Therefore, the management of mucormycosis in hematology patients is very important and key strategies: (1) rapid initiation of effective antifungal therapy and concomitant aggressive attempts for diagnosis, (2) extensive “early” surgical debridement of necrotic lesions, and (3) rapid control of underlying medical condition, when feasible (Prakash and Chakrabarti, 2021; Kontoyiannis and Lewis, 2011). Hyperbaric oxygen therapy is a beneficial adjunct therapy for mucormycosis, particularly diabetic patients with rhinocerebral or extensive cutaneous disease (Kontoyiannis and Lewis, 2011). In addition, high concentrations of oxygen can inhibit the growth of mucorales in vitro and improve the rate of wound healing by increasing the release of tissue growth factors (Kontoyiannis and Lewis, 2011). In general, antifungal therapy of mucormycosis should be highly individualized and continued until there is clinical resolution of signs and symptoms of infection (Kontoyiannis and Lewis, 2011). Many challenges must be overcome to improve the overall outcomes associated with the invasive mucormycosis (Kontoyiannis and Lewis, 2011). The advancement of fungal diagnostics with the implementation of novel fungal biomarkers is a formidable frontier in mucormycosis (Kontoyiannis and Lewis, 2011).

III. COVID-19-MUCORMYCOSIS: HERBAL MEDICINE TREATMENT

Fungi that belong to mucorales cause infections in human is known as mucormycosis (Prakash and Chakrabarti, 2021; Priya et al., 2020; Alekseyev et al., 2021). This is a very serious heath issue and resulted in the large number of Covid-19 hospitalizations and deaths in India. Covid-19 is an infectious disease characterized by inflammatory syndrome, and pneumonia itself leading to the reduced food intake and increased muscle catabolism (Prakash and Chakrabarti, 2021; Priya et al., 2020; Alekseyev et al., 2021). Therefore Covid-19 patients are at high risk of being malnourished, making the prevention of malnutrition and the nutritional management key aspects of care (Fernández-Quintela et al., 2020; Thibault et al., 2021; de Morais, 2021; Laviano et al., 2020; Calder et al., 2020). Among the mucorales, *Rhizopus oryzae* is the most common fungus isolated from clinical specimens of Indian Covid-19 patients with mucormycosis followed by *Lichtheimia corymbifera*, *Mucor racemosus* and *Apophysomyces variabilis* (Priya et al., 2020; Garg et al., 2021). Mucormycosis (Zygomycosis) has emerged as a formidable infection in an increasing population of covid-19 patients with various forms of chronic and/or severe immunosuppression (Garg et al., 2021;Aggarwal et al., 2015;Chakrabarti and Singh, 2014; Chander et al., 2015). In the last 10 years, number of fungal infections have increased at alarming rate particularly during the recent outbreak of coronavirus (SARS-CoV-2) (Prakash and Chakrabarti, 2021; Priya et al., 2020; Garg et al., 2021). In India, considerable numbers of diabetics remain undiagnosed before presentation of mucormycosis, and acted as diabetes-defining illness. (Garg et al., 2021; Alekseyev et al., 2021; Mehta and Pandey, 2020; Sarkar et al., 2021; Song et al., 2020). However, even in timely diagnosis, the window of opportunity is much shorter as fungal infections grow very rapidly *in vivo* (Priya et al., 2020; Garg et al., 2021). Hence fungal infections leading to the cause of mortality and morbidity in immunocompromised individuals.

Another factor is severity of mucormycosis infection is due to its rapid disease progression and angioinvasive character (Prakash and Chakrabarti, 2021; Priya et al., 2020; Alekseyev et al., 2021; Malabadi and Raghavendra, 1994, 1995, 1998). So effective treatment should be initiated before extensive angioinvasion occurs (Priya et al., 2020; Garg et al., 2021). Adding to the plight situation, they are resistant to many antifungals, including flucytosine, ketoconazole, fluconazole, voriconazole, and echinocandins with variable susceptibility to itraconazole (Priya et al., 2020; Garg et al., 2021). Furthermore, Amphotericin B, posaconazole, and ravuconazole are the only promising drugs (Priya et al., 2020). The widely accepted treatment of choice for mucormycosis is Amphotericin B (Priya et al., 2020; Alekseyev et al., 2021). These medicines are very expensive, and poor people can not afford to purchase at their urgent needs. When administering Amphotericin B, it is essential to monitor kidney function due to its high nephrotoxicity incidence (Priya et al., 2020; Alekseyev et al., 2021). Some of the other second-line accepted antifungals include the triazoles, posaconazole and isavuconazole (Priya et al., 2020; Alekseyev et al., 2021). Triazoles inhibit the 14-α-demethylation, which leads to an increase in toxic 14-α-methylsterols that alters the fungal membrane's permeability (Priya et al., 2020; Alekseyev et al., 2021). Covid-19 Patients that are intolerant to Amphotericin B are given posaconazoles. Isavuconazole has an extended spectrum. Because of this, it is the only antifungal used in the treatment of invasive mucormycosis (Priya et al., 2020; Alekseyev et al., 2021). The infection site will determine the clinical presentation. This can manifest as cutaneous, pulmonary, sinusitis, gastrointestinal, or even dissemination (Priya et al., 2020; Alekseyev et al., 2021).

Antifungal drugs used as medication has many side effects and covid-19 patients have failed to develop the resistance due to many health disorders such as diabetes, cancer, organ transplant, and high blood pressure. Some of the covid-19 patients were already on the long term medications such as corticosteroids, blood pressure medications, cancer treatment have failed to develop the resistance against mucormycosis (Garg et al., 2021; Priya et al., 2020). This is the bottom line and has promoted the fungal infections in the covid-19 patients. These fungi rarely affect the immunocompetent, but rather immunocompromised patients (Alekseyev et al., 2021). This mainly occurs in those that are on hemodialysis, high-dose glucocorticoids, have trauma like extensive burns and with uncontrolled diabetes mellitus (Alekseyev et al., 2021). To diagnose suspected mucormycosis, an extensive history, physical exam and imaging is crucially important (Alekseyev et al., 2021).

Covid-19 patients should be considered at high risk of malnutrition (Thibault et al., 2021). Acute malnutrition induced by Covid-19 infection would therefore, be associated with increased loss in muscle mass and weakening of immune defences prompted in the severity of the Covid-19 (Thibault et al., 2021; de Morais, 2021; Fernández-Quintela et al., 2020; Laviano et al., 2020; Calder et al., 2020). People infected with Covid-19 requiring an intensive care unit admission often requires nutrition therapy as part of supportive care. Chronic diseases, malnutrition, or COVID-19 itself can compromise meeting nutritional needs. Obesity and excessive adiposity, but especially low muscle mass are risk factors for COVID-19 patients (Thibault et al., 2021; de Morais, 2021; Fernández-Quintela et al., 2020; Laviano et al., 2020; Calder et al., 2020). There is a direct correlation among nutrition, immune system, and coronavirus disease (SARS-CoV-2). The nutrients and bioactive molecules such as melatonin, vitamins, proteins, carbohydrates in the diet (foodstuffs) influences the immunity and the nutritional status of the covid-19 patient (Malabadi et al., 2021c; Thibault et al., 2021; de Morais, 2021; Fernández-Quintela et al., 2020; Laviano et al., 2020; Calder et al., 2020). The covid-19 patients were also addressed with the deficient nutritional status probably due to anorexia, nausea, vomiting, diarrhea, hypoalbuminemia, hypermetabolism, and excessive nitrogen loss (Thibault et al., 2021; de Morais, 2021; Fernández-Quintela et al., 2020; Laviano et al., 2020; Calder et al., 2020). Therefore, nutritional therapy appears as the first-line treatment and should be implemented into standard practice. Optimal intake of all nutrients, mainly those playing crucial roles in immune system, should be the top priority of the well-balanced diet system (de Morais, 2021; Fernández-Quintela et al., 2020; Thibault et al., 2021; Laviano et al., 2020; Calder et al., 2020).

Several plant natural bioactive compounds interact with the angiotensin-converting enzyme 2 (ACE2) receptor, the gateway for severe acute respiratory syndrome (SARS) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Thibault et al., 2021; de Morais, 2021; Fernández-Quintela et al., 2020; Laviano et al., 2020; Calder et al., 2020; Malabadi et al., 2021a). Natural plant bioactive compounds can also reduce the inflammatory response induced by SARS-CoV-2. These plant active compounds are the most potential beneficial tools in the nutritional management of COVID-19 patients (de Morais, 2021; Thibault et al., 2021; Fernández-Quintela et al., 2020; Laviano et al., 2020; Calder et al., 2020). High biological value proteins, fatty acids (omega 3), vitamins A and C, dietary fibre, selenium and copper present anti-inflammatory effects; polar lipids have an anti-thrombotic effect; vitamins A, C and D protect against respiratory infections; vitamin E, iron, and zinc improve the immune function; and vitamins C, A and E, and omega 3 fatty acids present antioxidant effects (Thibault et al., 2021; de Morais, 2021; Fernández-Quintela et al., 2020; Laviano et al., 2020; Calder et al., 2020). Consumption of carbohydrates with a higher glycaemic index should be avoided since this contributes to inflammation (de Morais, 2021). Natural bioactive compounds found in plants and sea food, namely revesterol, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), capsaicin, and curcumin, among others, have been associated with anti-inflammatory effects (Laviano et al., 2020; Calder et al., 2020; Thibault et al., 2021; de Morais, 2021; Fernández-Quintela et al., 2020). There is also important connection between gut microbiota and immunity, probiotics and prebiotics revealed a protective effect and are promising compounds for a dietary therapy of COVID-19 patients. Nutritional therapy is an essential component for the successful treatment and recovery of COVID-19 patients (Fernández-Quintela et al., 2020; Thibault et al., 2021; de Morais, 2021; Laviano et al., 2020; Calder et al., 2020). These medicinal plants are also important source of other type of beneficial compounds including the ingredients for functional foods. These functional foods promoted the better health to prevent chronic illness (Vaidya and Devasagayam, 2007; Malabadi et al., 2021a, 2021c, 2021d, 2021e, 2021f).

Therefore, plants have been considered as traditional source of antifungal medicines for the past many years (Malabadi et al., 2021a; Malabadi et al., 2005; Malabadi, 2005, 2008; Malabadi and Vijayakumar, 2005, 2007, 2008; Malabadi et al., 2007; Malabadi et al., 2010a; Malabadi et al., 2012a, 2012b, 2012c, 2012d; Chalannavar et al., 2012; 2013a, 2013b, 2015; Sasi et al., 2021; Aqil and Ahmad, 2003; Suresh et al., 2010; Mehmood et al., 1999). A broad spectrum of medicinal plants was used as traditional remedies for various infectious diseases. Indian traditional herbal medicine is very famous since India is leading in the medicinal systems of Ayurveda and Siddha (Malabadi and Nataraja, 2002a, 2002b ; Malabadi et al., 2021a, 2021e, 2021f; Kulkarni et al., 2020; Swamy et al., 2016; Malabadi, 2008; Malabadi and Vijayakumar, 2005, 2007 2008; Malabadi et al., 2009, 2010a, 2010b, 2011a, 2011b; Malabadi et al., 2012a, 2012b, 2012c, 2012d; Malabadi et al., 2016a, 2016c, 2016d; Malabadi et al., 2017a, 2017b; Malabadi et al.. 2018). *Ayurveda* system of healthcare takes holistic approach towards disease management and preservation of health in which salutogenesis (maintaining optimum health and immune status) is a major aspect.

Fungal infectious diseases have a significant impact on public health. Fungi cause more prevalent infections in immunocompromised individuals mainly in covid-19 patients undergoing transplantation related therapies, and malignant cancer treatments. Plant active compounds with antifungal activity can be considered as an option of new and improved alternative formulations in the antifungal therapy (Malabadi et al., 2012a, 2012b, 2012c, 2012d). Hence there is an urgent need for the efficient treatment of fungal infections using herbal medicine approach which will protect covid-19 patients for the speedy recovery with a better quality life. Therefore, the combination of herbal and dietary therapy would be an added advantage for controlling the black fungus infections during covid-19 hospitalization. The medicinal plants with antifungal activities have been listed in the following Table-1.

Table-1: Medicinal plants with antifungal activities

Number	Family	Botanical & common name
1	*Myrtaceae*	(Guava) *Psidium guajava*
2	*Meliaceae*	(Neem) *Azidarachta indica*
3	*Zingiberaceae*	(Ginger) (*Zingiber officinale*)
4	*Fabaceae*	Mulethi or Liquorice (*Glycyrrhiza glabra*)
5	*Zingiberaceae*	**Turmeric** (*Curcuma longa* L.)
6	*Myrtaceae*	(Cherry) *Eugenia uniflora*
7	*Mimosaceae*	*Mimosa tenuiflora*
8	*Solanaceae*	(Brinjal) *Solanum melongena*
9	*Euphorbiaceae*	(Indian Copperleaf) *Acalypha indica*
10	*Menispermaceae*	Guduchi (Amruthballi) *Tinospora cordifolia*
11	*Apiaceae*	Indian pennywort (Gotukola) *Centella asiatica*
12	*Amaranthaceae*	Mountain Knot Grass (Gorakhbuti or Chhaya) *Aerva lanata*
13	*Verbenaceae*	(Indian privet or Wild. Jasmine) *Clerodendrum inerme*

14	*Apocynaceae*	(Trellis-vine) *Pergularia daemia*
15	*Plumbaginaceae*	(Wild white leadwort) *Plumbago zeylanica*
16	*Amaryllidaceae*	(Garlic) *Allium sativum*
17	*Lythreaceae*	(Henna tree) *Lawsonia inermis*

18) *Citrus limon*, 19) *Bryophyllum pinnatum* (leaves), 20) *Caesalpinia bonducella* (seeds), 21) *Delonix regia* (flower), 22) *Hedychium spicatum* (fruits), 23) *Mangifera indica* (leaves), 24) *Murraya coenigii* (leaves), 25) *Syzgium cumini* (seeds). 26) *Cichorium intybus* (roots), 27) *Ficus religiosa* (leaves), 28) *Trigonella foenum-graecum* (leaves), 29) *Pistacia integerrima* (stems), 30) *Rheum emodi* (roots), 31) *Clitoria ternatea* (Whole plant), 32) *Costus speciosus* (rhizome), 33) Catharanthus roseus (Whole plant), 34) Tulsi (Ocimum sanctum) (Whole plant), 35) Kutki (*Picrorhiza kurroa*), 36) *Terminalia chebula*, 37) *Terminalia bellerica* (Combretaceae), 38) *Emblica officinalis* (Family Euphorbiaceae), 39) Amla (*Phyllanthus emblica*), 40) Aloe vera (*Aloe barbadensis*), 41) Lavang (*Syzygium aromaticum*), 42) Dalchini (*Cinnamomum verum*), 43) *Glycyrrhiza glabra*, 44) *Hibiscus sabdariffa*, 45) *Cichorium intybus*, 46) *Chrysanthemum coronarium*, 47) *Nigella sativa*, 48) *Anastatica hierochuntica*, 49) *Epilobium hirsutum*, 50) *Polygonum cuspidatum*, 51) *Vaccinium macrocarpo*, 52) *Withania somnifera*, 53) *Alpinia officinarum*, 54) *Astragalus membranaceus*, 55) *Cassia alata*, 56) *Ecklonia cava*, 57) *Glycyrrhizae uralensis*, 58) *Houttuynia cordata*, 59) *Lindera aggregata*, 60) *Lycoris radiata*, *Mollugo cerviana*, 61) *Polygonum multiflorum*, 62) *Pyrrosia lingua*, 63) *Saposhnikoviae divaricate*, 64) *Moringa oleifera* (Drumstick; Nuggekai in Kannada), 65) *Cissampelos pariera* Linn (Kannada name-Padavali), 66) *Momordica charantia* (Kannada- Hagalkai): Bitter melon, 67) *Acacia caesia* (Family-Mimosaceae) (Kaadu siege in Kannada). **68**) *Achyranthes bidentata* (Family-Amaranthaceae) (Aane hatti in Kannada), **69**) *Argmone mexicana* (Family-Papaveraceae) (Aarishina datura in Kannada), **70**) *Cassia hirsuta* (Family-Caesalpiniaceae). **71**) *Chenopodium ambrosioides* (Family-Chenopodiaceae). **72**) *Commelina benghalensis* (Family-Commelinaceae). **73**) East Indian lemon grass or Malabar or Cochin grass is native to India (*Cymbopogon flexuosus*) (Family-Poaceae). **74)** *Ecballium laterium*, 75) *Piptadenia colubrina* (Mimosaceae), 76) *Schinus terebinthifolius* (*Anacardiaceae*), 77) *Parapiptadenia rigida* (*Fabaceae*), and 78) *Ajania fruticulosa* (*Asteraceae*).

IV. CONCLUSION

The outbreak of coronavirus (SARS-CoV-2) Delta variant (B.1.617. 2) and Delta plus (AY.1) in India has created havoc resulted in the more hospitalization and killing more people. In addition, currently in India, Covid-19 patients admitted in the hospitals are suffering from black fungus infections known as mucormycosis is an additional headache and burden. Mucormycosis has emerged as an important opportunistic infection, especially in severely immunosuppressed hosts. The uncontrolled diabetes mellitus remained the most important risk factor for most of the Covid-19 cases. The antifungal drugs are out of stock due to shortage in supply and found more expensive during this critical period of Covid-19 outbreak. Most of the fungi are resistant to the available antifungal drugs. Therefore, herbal and nutritional therapy is an essential component for the successful treatment and recovery of COVID-19 patients. There are many medicinal plants with antifungal activities have been reported and tested during this coronavirus outbreak and found successful. The clinical trials are yet to be confirmed. Therefore, there is a ray of hope for the controlling fungal infections during this coronavirus (SARS-CoV-2) outbreak. The bioactive molecules of medicinal plants were also directly interact with fungus and inhibit the fungal growth. This has been reported by many research groups around the world. Herbal extract formulations are useful as per the local traditional healers recommendation which is one of the common traditional practice in the rural part of India. Further phytochemical research is important to provide the relevant information for the development of potential bioactive compounds that benefit the development of new therapeutic needs for fungal infections.

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