The unholy consortium between Sars cov-2 and Mucormycosis and identification of some potential antifungal herbs: A review

Abstract:

Background:

There has been a rise alarming in the number of mucormycosis post covid-19 infection. The enigmatic relationship of Sars COV-2 and Mucormycosis yet remains to be fully understood. So far as the treatment is concerned, mankind is yet to discover a potent therapeutic drug that could effectively be used to treat this deadly fungal infection. Since ages, mankind has always looked towards nature and perhaps herbals are the best options to go to, in our quest for searching effective antifungal drugs against the ruthless and invasive Mucorales.

Methods:

A comprehensive literature search was conducted across PubMed database, LILACS, the Cochrane Register of Controlled Trials, Google Scholar and others using key words Covid-19, Sars Cov-2, Mucormycosis, Rhizopus, vaccine, steroids, antifungal drugs and herbals. Full texts of the retrieved articles published in English were accessed.

RESULTS:

A handful of medicinal plants such as *Satureja khuzestanica Jamzad*, *Thymus danensis* and *Thymus carmanicus*, *Thymus vulgaris L*, *Lavandula angustifolia*, *Mentha piperita* and some species of pepper such as *Piper sp*., *Piper tuberculatum* and *P. hispid um* have all shown to have a promising anti-fungal effect on Mucorales fungus.

CONCLUSIONS:

Limited knowledge and resources on antifungal (anti-Mucorales) due to lack of adequate research and clinical studies limits our search for identification of potent antifungal herbs. An intensified research and evaluation for antifungal herbs can boost the identification, design and development of newer drugs with lesser adverse drug reactions and better mortality rate.

Keywords: Covid-19, Sars Cov-2, Mucormycosis, Rhizopus, vaccine, steroids, antifungal drugs, herbals.

Introduction:

Mucormycosis is an Angio invasive disease caused by saprophytic fungi that is characterised by extensive angioinvasion that results in vessel thrombosis, subsequent tissue infraction and necrosis. It is caused by fungi of the Mucorales order of the class of Zygomycetes(1)**.**

The disease was first described by Furbinger in Germany in 1876 (2). Mucorales fungi are the next commonest pathogen, after the genus aspergillus sp [I believe that in this line it would be clearer as I wrote in blue. In addition scientific names are written in capital letters and italics] in patients with haematological malignancy, solid organ transplantation and haematopoietic stem cell transplantation(3). The major route of transmission occurs through inhalation of sporangiospores, although other routes such as direct Implantation into injured skin, ingestion of spores, contact from contaminated soil and intravenous transmissions in drug users are some other

known routes. Usually, nasal inoculation is followed by rapid progression, extending to neighbouring tissues, including the orbit, and sometimes to the brain(4). [Check spaces in text] On the basis of clinical presentations, mucormycosis are classified accordingly such as rhinocerebral, cutaneous, pulmonary, renal, gastrointestinal and disseminated and other uncommon rare forms, such as peritonitis, renal, endocarditis, osteomyelitis etc.(2) Various studies have demonstrated that patients with diabetes mellitus, haematological malignancy and chemotherapy, solid-organ transplant recipients on Immunosuppressive therapy, iron overload, chronic kidney failures, extensive skin injury, human immunodeficiency syndrome and prolonged neutropenia are at increased risk of acquiring mucormycosis (1–4).
There has been an alarming rise and considerable amount of mucormycosis infection post covid-19 treatment, reported across various parts of the world. However, the exact cause and mechanism of the association between the two diseases largely remains idiopathic. The study aims to understand the co-relation between the existence of these two diseases. It is also understood that most of the drugs used as antifungal treatments have various drawbacks in terms of toxicity, efficacy as well as cost and their frequent use has also led to the development of resistant strains. Medicinal plants are considered a rich source of antimicrobial agents and can be used as antimicrobial remedies. Although there has been extensive research done on medicinal plants and their antifungal properties against many fungal species, studies on antifungal properties of medicinal plants for Mucorales remains scarce or limited to date. The study aims to identify some potential herbals with anti-Mucorales (antifungal) properties.

Methods:
A comprehensive literature search was conducted across PubMed database, LILACS, the Cochrane Register of Controlled Trials, Google Scholar and others using key words Covid-19, Sars Cov-2, Mucormycosis, Rhizopus, vaccine, steroids, antifungal drugs and herbals. Full texts of the retrieved articles published in English were accessed.

Mucormycosis post covid-19 treatment: Associated risk factors
The novel coronavirus disease COVID-19 is a highly contagious viral infection first reported in Wuhan, China, which subsequently spread worldwide.(5) Despite many people having recovered from the viral infection, very little is known about possible clinical sequelae that may persist after the viral infection. A study in Italy found that in patients who had recovered from COVID-19, 87.4% reported persistence of at least 1 symptom. At 60-day follow-up, (55%) reported with three or more symptoms, fatigue (53%), dyspnoea (43%), joint pain (27%) and chest pain (22%). It is also noted that COVID-19 was associated with worsened quality of life among 44% of patients.(6) Among many other complications, there is a spurt of mucormycosis in recovered and fresh Covid-19 cases reported around the world. A considerable number of studies on mucormycosis have been published across various journals, unearthing the incidences and various clinical features of mucormycosis among the

post covid-19 recovered population. These studies and case reports suggests that post covid-19 treatment, the fungal infection is largely attributed to the low immunological functions which could be associated with various predisposed factors and underlying causes like age, comorbidities, uncontrolled Diabetes mellitus, post-transplant, malignancy, rampant use of corticosteroids during the covid-19 infection period etc.(7–9)
Some of the underlying causes for the covid-19 associated mucormycosis are enlisted in the table (table 1.1 [Is written with a capital letter])
[Table 1 put the references]

Table 1: Most common cause of COVID-19 associated Mucormycosis (CAMCR)

	Factors/underlying conditions	CAMCR
1	Uncontrolled Diabetes mellitus	diabetogenic state" in SARS CoV-2 infection-SARS CoV-2 induces damage of pancreatic islets, resulting in acute Diabetes and Diabetic ketoacidosis
2	Immunosuppression by steroids	rampant use of corticosteroids/glucocorticoids leading to immunosuppression in patient
3	Prolonged ICU stays	immunocompromised patients with predisposing factors and longer duration of ICU stay.
4	Co-morbidities	Dampening of immune system - Diabetes mellitus, Hypertension, obesity, cardiac disorders, respiratory disorders, renal disorders
5	Malignancies	neutropenia and immunodeficiency associated with chemotherapy and post-transplant steroid treatment- acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML) and chronic myeloid leukaemia (CML), bone marrow transplant (BMT)
6	Post-transplant	nadir of immunosuppression - solid organ transplant recipients e.g., lungs

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Diabetes mellitus and COVID-19 associated Mucormycosis (CAMCR)
While reviewing the published COVID-19-associated mucormycosis (CAMCR) cases (total 41), it was found that, CAMCR was typically seen in 94% of the patients with diabetes mellitus of which 67% were patients with poorly or uncontrolled Diabetes mellitus. Diabetes mellitus, a "classic" risk factor for mucormycosis, is associated with increased morbidity and mortality in COVID-19(10). A multicentred epidemiologic study of COVID-19 disease-associated Mucormycosis (CAM), across India also found that uncontrolled diabetes mellitus was the most common underlying disease among CAM and non-CAM patients (11) The "diabetogenic state" in SARS CoV-2 infection and its severity, could be suggested by the evidence that

SARS CoV-2 induces damage of pancreatic islets, resulting in acute Diabetes and Diabetic ketoacidosis. These could be supported by high expression of angiotensin-converting enzyme 2 (ACE2) receptors in pancreatic islets, along with increased insulin resistance due to cytokine storm(10)(12). Diabetes mellitus is the single most common risk factor being reported as prominent underlying predisposed risk factor for mucormycosis in various studies. Although many other organs and tissues are also affected, studies have shown that the clinical manifestation is mostly attributed to rhino-orbital and rhino-orbital-cerebral presentation in Diabetic patient. There are various studies, reviews and case presentations reported on the linkage of uncontrolled Diabetes with COVID-19- associated mucormycosis across various journals which indicates that Diabetes mellitus is a high-risk factor for the infection of mucormycosis in immunocompromised individuals(6,10)
[Check spaces and punctuation in text]

Immunosuppression by steroids

In the backdrop of this COVID-19 expression, various studies have indicated that immunocompromised individuals with prolonged systemic corticosteroid use are more susceptible to mucormycosis. Corticosteroids are commonly used as adjuvant therapy for acute respiratory distress syndrome because of their anti-inflammatory effects. However, it is highly controversial for patients with severe viral pneumonia infections.(13). Over the past 20 years, case reports and various studies have indicated the growing number of mucormycosis following Bone marrow transplants (BMT) and Haematological malignancies (HM) which is due to prolonged treatment of the patients with steroids and immunosuppressive agents (14). In a comparative study of influenza-associated mucormycosis (IAM) versus COVID-19 associated mucormycosis (CAM), patients with CAM and IAM, respectively, received steroids as an adjuvant treatment either for viral pneumonia or underlying medical conditions. The use of steroids was a prominent risk factor for the development of mucormycosis in 66.7% of patients with viral pneumonia(15). The acute increase in mucormycosis could be associated with the immunocompromising effects of corticosteroids along with microangiopathy in Diabetes and possible peripheral microthrombi in COVID-19. This could be further supported by the high incidence of diabetes in our population and widespread use of corticosteroids such as Dexamethasone and methylprednisolone as a part of treatment intervention for COVID-19. Patients become more susceptible to secondary infections, due to the immunosuppressive nature of glucocorticoids.(16)

Prolonged ICU stays:

Mucormycosis are very severe infections that may be acquired in the ICU or when acquired elsewhere, may require critical care. Infections caused by filamentous fungi such as mucormycosis infections represent a major burden in the ICU. Over years a high proportion of cases are diagnosed in the ICU. This could be attributed to the challenges in diagnosis due to the non-specific signs and symptoms of the condition. Some characteristic clinical presentation includes progressing necrotizing lesions in the rhino-sinusal area, skin, lungs and soft tissues of immunocompetent hosts such as patients in the ICU. There is a lack of epidemiological data concerning to ICU stay but gradually mucormycosis is frequently being reported as individual case reports or

as small series in ICUs. Study from one centre found that 37% of mucormycosis cases were diagnosed in patients treated in the ICU.(17). Despite the latest advances in ICU standard of care, the global ICU mortality for mucormycosis remained very high, reaching 71.6%. A French multi-centre cohort indicates that the prognosis of mucormycosis in ICU remained poor, especially in those with haematological malignancies, in older patients, malnutrition and those with accumulate numerous predisposing factors(18). All these studies may suggest that immunocompromised patients with various predisposing factors, healthcare-acquired infections, excessive or prolonged overuse of corticosteroids associated with prolonged ICU stay especially after COVID-19 infections could be a major cause for mucormycosis infections.

Co-morbidities and malignancies:
Prevalence of comorbidities and malignancies among the covid-19 infected population has contributed to severity and high mortality rate. Various studies have revealed that common comorbidities such as Diabetes mellitus, Hypertension, obesity, cardiac disorders, respiratory disorders, renal disorders etc. has been found to dampen the immunological functions, leaving the Covid-19 infected person in more critical condition.(7). A multicentre observational study involving 465 individuals diagnosed with mucormycosis revealed that co-morbid illnesses such as chronic kidney disease 93 (20%), Cardiovascular 67 (14.4%), Pulmonary 30 (6.5%), Liver disease 24 (5.2%), Neurological 18 (3.9%) were prevalent.(19). There is a rise in the reported case of mucormycosis among patients with haematological malignancies (HM) such as acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML) and chronic myeloid leukaemia (CML) and in bone marrow transplant (BMT) recipients over last two decades. These could be due to neutropenia and immunodeficiency associated with chemotherapy and post-transplant steroid treatment leading to diminished or dampened immune functions in an individual. (14) The chances of survival increase in cases with better controlled comorbid conditions. These comorbidities and malignancies greatly affect the outcome of patient's infection and mortality.

Post-transplant
Mucorales are angioinvasive and can infect any organ system however in solid organ transplant recipients, lungs are the predominant site of infection. Post-transplant of any organs, they can virtually affect every organ, such as the skin, gastrointestinal, genitourinary, cardiovascular, musculoskeletal systems as well as infections of surgical wounds.(20). Studies have shown that infection is most commonly acquired during the nadir of immunosuppression between one- and six-months post transplantation. These could be associated with increased immunosuppression for the treatment of rejection or anti-rejection therapy and enhanced incidence of fungal infection.(21). Invasive fungal infections (IFIs) occur in up to almost 20% of recipients of renal transplantation. Among all the Mucorales, Rhizopus species is the most common, accounting for 35%–73% of cases, followed by Mucor (13%–37%) and ~~Mycocladus~~ [It is important to put the current names of the fungi: *Lichtheimia sp* (formerly *Absidia sp, Mycocladus sp*)] (0%–13%).(20). A

recurrent pulmonary mucormycosis after lobectomy in a non-smoking patient without any known predisposing risk factors has also been reported in a case study(22). Donor-derived fungal infection has also been reported in two patients developed renal mucormycosis following transplantation of kidneys from the same infected donor (23). A person with post-transplant history either with or without a history of mucormycosis infection, when infected with SARS COV-2 is more prone to get fungal infection due to the immunosuppressed conditions. These could be the result of prolonged and excessive of immunosuppressive drugs, steroids, comorbidities, use of immunosuppressive therapies and other underlying risk factors(24).

Treatment/mitigation of mucormycosis:

The therapeutic approach to mucormycosis is multimodal which includes antifungal agents, surgical debridement and correction of the underlying predisposing factor of the disease. The treatment outcome in mucormycosis, thus mostly depends on the influence or correction of underlying metabolic condition and immunosuppressive state such as neutrophil recovery in neutropenic patients, steroid tapering in patients receiving corticosteroids etc.(25). Several other factors such as heterogeneity, pleiotropic clinical presentation, the multitude of the fungal species, factors related to surgery (e.g., timing, radicalness), can all contribute to the outcome of the treatment and management of mucormycosis.(26). Given that cases of mucormycosis infection in post covid-19 patients is mostly due to the predisposed risk factors associated with prolonged use of corticosteroids for acute respiratory distress syndrome, the treatment is critical and challenging.

Primary antifungal therapy for mucormycosis is mostly based on polyene, as Amphotericin B deoxycholate (AmB) remains the only licensed antifungal agent for the treatment of mucormycosis. However, lipid formulations of AmB (LFABs) are significantly less nephrotoxic and can be safely administered at higher doses for a longer period of time as compared to AmB which is recommended against, due to substantial toxicity, but may be the only option in resource limited settings (27,28)he global guidelines for diagnosis and management of mucormycosis recommends the first-line treatment with high-dose liposomal amphotericin B, while intravenous isavuconazole and intravenous or delayed release tablet Posaconazole are also recommended with moderate strength(28). While some class of drugs based on azoles such as fluconazole, itraconazole, isavuconazole and voriconazole have been studied, studies suggest that fluconazole and voriconazole are not active against mucormycosis however itraconazole may yield some activity but may not be superior to posaconazole(25)(27)(29). [Put a parenthesis for the three bibliographies] Various studies have demonstrated that Posaconazole can be used as salvage options for patients with mucormycosis who are intolerant of polyene therapy. It also appears to be safe alternate drug despite dosing for months to years of administration(27). Adjunctive therapy with Isavuconazole and Posaconazole, hyperbaric oxygen, and recombinant cytokines, granulocyte transfusions can be considered for selected patients. Few studies also suggest that hyperbaric oxygen could be used as an adjuvant therapy in treating mucormycosis. This is based on the idea that increased oxygen concentration in tissues may increase neutrophil antifungal activity and the

polyenes induced putative oxidative killing mechanism (30). Usually, hyperbaric oxygen therapy is well tolerated with low risk of adverse events(31)

A prompt initiation of treatment plan with amphotericin B and surgery are critical for successful management of mucormycosis and has been found to improve the mortality rate (29). The surgical intervention is essential due to the angio-invasive nature of the agents of mucormycosis that results in the formation of extensive thrombosis in the blood vessels leading to tissue infarction and necrosis that may impair or hinder the penetration of antifungal agents to the site of infection. Therefore, surgical debridement of necrotic tissues is essential for complete eradication of mucormycosis from the body (27,28,32).

Search Result:
A thorough literature search for antifungal properties against Mucorales was conducted across various data base. However, to date, there are only few works available on antifungals specifically against mucormycosis. A handful of known or identified herbals with specific antifungal properties against mucormycosis are discussed below.

Medicinal plants with antifungal properties against Mucorales [All scientific names are written in italics]

It is also understood that most of the drugs used for antifungal treatments have various drawbacks in terms of toxicity, efficacy as well as cost and their frequent use has also led to the development of resistant strains (33,34) In our study, we have identified some of plant species with potential antifungal properties especially against Mucorales. Medicinal plants are considered a rich source of antimicrobial agents and can be used as antimicrobial remedies to prevent or treat various fungal infections. A review study on effective medicinal plants on important fungal strain and diseases suggest that certain plants exhibit antifungal activities against specific fungal species. The ethanolic extract of *Satureja khuzestanica Jamzad* leaves exhibited antifungal activity against saprophytic fungi Rhizopus sp. and Mucor sp. with minimal inhibitory concentration (625-5000 microg/ml). A study also found that *Thymus danensis* and *Thymus carmanicus* oils showed inhibitory effect even at low concentration (300µl/L) against Rhizopus stolonifera at 600µl/L. Plate assays of the essential oil of *Lavandula angustifolia* and *Mentha piperita* also showed that the different concentrations of essential oils had antifungal activity against Rhizopus stolonifera.(33). The results of the investigated antifungal activity of the essential oil of *Thymus vulgaris L*. and its constituent thymol and p-cymene against Rhizopus oryzae shows that essential oil and thymol significantly inhibited mycelial development and germination of sporangiospores. Thus**,** relating their interaction with ergosterol, the essential oils of Thymus vulgaris and thymol possess strong antifungal activity which could be used in the treatment of mucormycosis(34). Another study also indicates the promising anti-Rhizopus oryzae activity of *Piper sp*., *Piper tuberculatum* and P*. hispidum* against planktonic cells, biofilm formation, and rhizopuspepsin. These essential oils possess a promising antifungal activity and could be useful in formulating adjuvants to limit the growth of R. oryzae(35).

Evaluating the antifungal potential of essential oil of *Syzygium aromaticum* (L.) against some common fungal pathogens of plants and animals including Mucor sp., and other fungal species, it was found that the fungus species were inhibited by the clove oil when tested through agar well diffusion method. The study concluded with findings that the antifungal action of clove oil is due to its high eugenol content present in *Syzygium aromaticum* (L.)(36). A summary of some medicinal herbs with potential antifungal (anti Mucorales) properties are enlisted in the table. (Table 1.2) [Table 1.2 put the active substance of plants with antifungal properties and the reference]

Plant	**Parts of plant**	**action**	**Mucorales**
Satureja khuzestanica Jamzad	leaves	inhibitory	Rhizopus sp., Mucor sp., [All scientific names are written in italics]
Thymus danensis, Thymus carmanicus	Essential oil	inhibitory	Rhizopus stolonifera
Lavandula angustifolia, Mentha piperita	Essential oil	fungistatic activity	Rhizopus stolonifera
Thymus vulgaris L	Essential oil	inhibit mycelial development and germination of sporangiospores	Rhizopus oryzae
Piper sp., Piper tuberculatum and P. hispidum	Essential oils	Against planktonic cells, biofilm formation, and rhizopuspepsin	Rhizopus oryzae
Syzygium aromaticum (L.)	Essential oil	inhibitory	Mucor sp.,

Table 1.2 Some medicinal herbs with potential antifungal (anti Mucorales) properties

Discussion:

The main purpose of this article is to draw the attention of the medical and pharmaceutical researchers towards herbal medicine. The identification of new medicinal plants with strong antifungal properties against Mucorales fungal species could pave a way for the design and develop newer drugs with more efficacy and fewer side effects against the existing drugs.

The authors aim to understand the enigmatic relationship between covid-19 and mucormycosis. There is an alarming rise in the number of deadly fungal infections such as mucormycosis among the population especially after COVID-19 infection. Post covid-19 treatment, the fungal infection could be largely attributed to the low immunological functions associated with various predisposed factors and underlying

causes such as age, comorbidities, uncontrolled Diabetes mellitus, post-transplant, malignancy, rampant use of corticosteroids during the covid-19 infection period etc. These unusual association between the two diseases could be due to multiple factors however, Diabetes is the single largest known factor for the mucormycosis. Mucormycosis infection is caused by several fungi of the order Mucorales belonging to the class of Zygomycetes. An active ketone reductase system found in the Mucorales species such as Rhizopus enables them to thrive in hyperglycaemic or high glucose and acidotic environment. Studies have also demonstrated that the serum present in healthy individuals could potentially inhibit Rhizopus unlike the serum present in Diabetic ketoacidosis patients which promotes its growth. These could also be associated with an impaired glutathione pathway which leads to decreased phagocytic activity in these patients. (4)

The burden of viral infection and overuse of corticosteroids during infection period could possibly led to dampening of immune system giving an opportunity to opportunistic and invasive fungus such as Mucorales. Age and immune mechanism play a significant role during infection. Various studies have also observed that, patients who survived the infections were mostly younger adults, free from any underlying predispositions such as Diabetes, Cardiovascular disorders, Renal disorders and other immune deficiencies etc.

Currently, the options available for the treatment of mucormycosis is very limited against the rapidly growing numbers of the infection. Several studies have also indicated that most of the available antifungal drugs have various drawbacks in terms of toxicity, efficacy and cost. Various predisposing risk factors associated with low immune functions, as well as increase in resistance to the currently used antifungal drugs is intensifying the need for conducting pharmacological investigations to develop new antifungal drugs that could selectively act on new targets with least side effects.

The use of medicinal plants for the treatment of various diseases including infectious diseases such as mucormycosis is not new to mankind. Significant number of drugs has been developed through plants and their derivatives. Although there has been extensive research done on medicinal plants and their antifungal properties against many fungal species, studies on antifungal properties of medicinal plants for Mucorales remains scarce or limited to date. The phytocompounds derived from various parts of the plants are of great importance in the production of antifungal drugs. Medicinal plants such as *Satureja khuzestanica Jamzad*, *Thymus danensis* and *Thymus carmanicus*, *Thymus vulgaris L*, *Lavandula angustifolia* and *Mentha piperita* have been shown to exhibit interesting antifungal effect against the Mucorales. Studies have demonstrated that these medicinal herbs can inhibit the fungal activity of Mucorales such as Rhizopus sp., Mucor sp., Rhizopus stolonifera and Rhizopus oryzae etc. [All scientific names are written in italics] Some herbals such as *Lavandula angustifolia* and *Mentha piperita* inhibits the fungal growth through fungistatic activity.

Medicinal herbs like *Thymus vulgaris L* could potentially inhibit the mycelial development and germination of sporangiospores, whereas the essential oil extracts of Piper sp., Piper tuberculatum and P. hispidum acts against planktonic cells, biofilm formation, and rhizopuspepsin. Essential oil extracts of *Syzygium aromaticum (L.) is*

also known to produce inhibitory effect on the [in this line delete cusiva style] *mucor sp.,* [Scientific names begin with capital letter]

All these medicinal herbs have shown a promising anti-fungal effect on Mucorales fungus. Medicinal plants and their derivatives are the potential source that can lift the lid on the burden of mucormycosis infections. To this day, hundreds of thousands of plant species have been studied for their medicinal properties such as antimicrobial, antifungal, antiparasitic etc. However, many more plants yet remain to be studied and explored. The limited numbers of resource available on antifungal properties of plants against mucormycosis greatly limits our study and therefore understanding the exact mechanism of these herbal and fungal interaction is beyond the scope of our present work. More evidences on identified plants could perhaps allow us to understand their interaction with these powerful angioinvasive fungus.

Future Directions

Anti-fungal and anti-Mucorales drugs are still limited in the arsenal of modern healthcare system. This has resulted in the higher mortality rate in the affected population especially after covid-19 pandemic. Several studies have demonstrated that plants or herbal medicine can be of great influence and potential in the discovery of newer drugs. However, there has been very few researches or study conducted on the anti-Mucorales herbs. Government agencies like Ministry of AYUSH, various national and international healthcare institutions, pharmaceutical industries and FDA etc. could play more crucial role by funding various studies across the world. Identification of more herbs or plants with potential anti-fungal properties through high-quality research can accelerate the process of newer drugs discovery. Adequate number of studies with high methodological qualities, using advanced and sophisticated techniques in pharmacognosy along with standard RCTs can boost the pursuit of newer and effective drugs against mucormycosis.

Conclusions:

There are multiple factors responsible for the dampening of immune system which provides an opportunity to invasive Mucorales to attack the patients after covid-19 infection. Some herbals could be a potential asset in the discovery and development of newer antifungal drugs. However, extensive and intensified research should be carried out to further identify, design and develop new and safer antifungal drugs that can be powerful to treat mucormycosis.

Abbreviations:

AYUSH- Ayurveda Yoga & Naturopathy Unani, Siddha and Homeopathy
ICU- Intensive Care Unit
FDA- Food and Drug Administration

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