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A Review of the Therapeutic Potential of Fungi: Activities Against Severe Diseases and Recent Advances in Fungal Research

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Abstract: Some of the most significant medications ever found are derived from fungi, and they have shown to be essential in the treatment of chronic illnesses. Not only have they prevented millions of deaths, but in certain instances, they have altered about the limits of medical advancement. With new businesses entering the market and hoping so use cutting-edge genomic technologies to speed up the discovery process, this might be about to change. This review looks at the path of discovery for both authorized fungal-derived medications and those undergoing clinical trials for long-term illnesses. We address the potential ecological roles of essential chemicals in nature and with how this connects to these application in human medicine. We demonstrate that how compounds meant to prohibit rival fungi, frequently interact with human receptors drug, sometimes with unanticipated benefits, due to conservation of drug receptors between fungi and people. In addition, we map the locations of medications, antimicrobial substances, and hallucinogenic mushrooms like fungal tree and focus on their distribution with that of all fungal metabolites. Lastly, we look at the self-resistance phenomena with fungi and how to predict the mechanism of metabolites and facilitate the drug discovery and lead optimization process.

Keywords: *Secondary Metabolites Production, Fungal Metabolites Biosynthesis, Application of Fungi in Pharmaceuticals*.

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I. INTRODUCTION

Some but not least significant medications ever found, including both contemporary blockbusters and drugs with historical significance, come from fungi. These substances have become vital in the treatment of long-term illnesses, mainly for immunosuppressants for autoimmune diseases, statins for hypercholesterolemia, and antibiotics and antifungal medications for chronic infections (Abad *et al*, 2018) Fungal-derived metabolites have lately been tested in clinical studies for the treatment of long-term conditions like drug-resistant depression and cancer. There is an enormous abundance microbes, animals, and plants due to world's biomes diversity, including both higher and lower fungi (such as mushrooms) and yeasts and molds. Eukaryotic heterotrophic organisms, fungi are found almost everywhere on Earth. In terms of temperature, pH, organic/inorganic compounds, oxygen, metal, water, salinity, and wastewater, majority of fungal species are able to adapt to harsh conditions. They get their nutrition and carbon from other living things, such as animals (Bahagobati *et al*, 2012) Certain types of fungi are known as biotrophs, meaning they obtain their nourishment from living things like plants and animals. Some species are necrotrophs, meaning they feed on dead or decaying creatures, while others are saprotrophs, meaning they obtain their nourishment from the destruction of host cells. In the past, they were categorized under the kingdom of plants. Due to their unique morphological and structural traits, lack of chlorophyll, a pigment involved in photosynthetic processes, and fungal mode of nutrition acquisition, they were classified as an separate kingdom similar to that of plants and animals (Chadha *et al*, 2014). Many fungal species with diverse morphological traits and a wealth of bioactive components make some of them our friends and some of them our enemies. The majority of these beneficial ingredients developed into mycotoxins, which have negative effects. Food grains and cooked food items are harmed by fungus, which are primarily recognized as food spoilers. Since they causes serious plant diseases, such as rice blast and late potatoes blight, Phytophthora infestans, and Magnaportheoryzae, they are also referred to as plant pathogens. However, fungi are important to humanity because they produce antibiotics like cyclosporine, cephalosporin, and penicillin as well as alkaloids specially ergot alkaloids, enzymes like lipase, food coloring, and fragrance. The fact that mushrooms have a wide range of bioactive compounds, including ergothioneines, glutathiones, lectins, sacharides, phenolics with indole compounds, which

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have a range of biological properties like antimicrobial, antioxidative, and anti-inflammatory, has been supported by the fact that mushrooms have medicinal value. They support the biological control of nematodes. In addition, they serve as a source of proteins, vit D, K^+, Se, riboflavin and niacin, among many other health benefits (Hameed *et al*, 2015). Additionally, they were extremely important in the cure and treatment, even disease prevention of stroke, cancer, Parkinson's, and hypertension. Due to the large number of metabolites that fungi contain, both their positive and negative effects are known. Fungi and their different products are intended to forthcoming microbial cell manufacturing, given the medications manufacturing, enzymes, and food pigments; in reality, most companies currently are based on them (Kim *et al*,. 2005).

➢ *Beneficial Effects*

- Antibiotic Products
- Pharmaceutic Products
- Anticancer
- Plant growth regulator
- Colorant producer
- Edible and Nutrients
- Health Benefits
- Cheese Making

➢ *Harmful Effects*

- Plant Diseases
- Mycotoxins
- Food Destroyer

II. SECONDARY METABOLITES PRODUCTION

Most widely used technologies, microbial fermentation is typically tailored in businesses to generate secondary metabolites and are applied in the production of relevant items. This technique is used to grow crops in liquid environments while immersed, and it is a very simple and easy way to increase the production of commodities and affect the control parameters. Solid-state condition fermentation technique is used in microbial culture cultivation for the agro-industrial production of bioactive chemicals. With this type of technology, there is less moisture present in the solid support. Because fungi grow well in low water conditions, this technique works well for them and is also reasonably priced. This process is helpful for producing secondary metabolites in addition to primary metabolites.

➢ *Biosynthesis of Fungal Metabolites*

Mycotoxins to antibiotics are many secondary metabolites generated by fungi, and metabolic routes which lead to the synthesis of these compounds are also very varied. Three common metabolic pathways are involved in their synthesis: Acetate pathway (embrace fatty acids synthesis), polyketides, and other compounds, Shikimic Acid pathway, (embrace aromatic amino acids synthesis), with alkaloids and the mevalonic acid pathway,embrace steroids synthesis, terpenoids, and other compounds. Secondary metabolites are typically categorized using the routes, which are typically described as occurring after the participation of enzymes or their intermediates. Many enzymes which play pivotal role in these pathways are dimethylallyl tryptophan synthetases, polyketide synthases, nonribosomal peptide synthetases, and many more. Many other enzymes used as building blocks to obtain different fungal products are acetyl co-A, and mevalonate. Dimethylallyl diphosphatereal (synthesized by Mevalonic acid binding with three molecules of acetyl co-A) play pivotal role in steroids, terpenes, and gibberellins synthesis. Slight modifications with the help of these enzyme in the biological synthesis pathway produce a extensive secondary metabolites with comprehensive applications in different field of medicine, food, and agriculture. Acetyl-CoA and amino acids are examples of primary metabolite precursors that are necessary for the synthesis of secondary metabolites. According to one research (Richter et al. 2014), beauvericin was produced by modifying the expression system of Aspergillus niger. Another study looks at the biosynthesis of artemisinin using Saccharomyces cerevisiae, Escherichia coli, and Artemisia annua engineering. The results are grouped into two operons, which are subsequently transformed into strain of *E. coli* to achieve efficient compound production.

➢ *Pharmaceuticals Applications of Fungi*

Penicillin, derived from the fungus P. *notatum*, has ushered in new era of therapeutic uses in the realms of pharmaceutical and biotechnology. This discovery has motivated several researchers to discover new antibiotics. Subsequently, most pharmaceutical companies began to screen for microorganisms around the middle of the 1950s (Dreyfuss *et al* 1994). All of the other microorganisms' fungi turned out to be the best producers of useful compounds, and they were also used as a defense against other harmful fungi and bacteria. Fungal secondary metabolites exhibit many advantageous actions, such as antibacterial, and anti-cancer properties. Based on the specific condition it is important to select the appropriate metabolite to be treated. Penicillium, Aspergillus, Chromocleista, and Pestalotiopsis release fungal alkaloids that have antiparasitic, antimicrobial, and anti-HIV characteristics (Ma *et al*. 2016). The physiological spectrum exhibited by phenolics protects against oxidative stress, inflammation, allergies, and other conditions. Antibiotic resistance, which eventually renders traditional therapies useless, is a major concern in pharmaceutical applications. Microorganism-derived chemicals are used to increase the susceptibility of medications to disease-causing mediators. Due to the presence of specialised metabolites, fungi, exhibit a variety of biological activities. For instance, taxol (anticancer), penicillin (antibacterial), lovastatin (hypolipidemic), and caspofungin (antifungal) properties (Macheleidt *et al*. 2016). Griseofulvin, (bioactive molecule) derived from P. *griseofulvum*, is used to treat skin and nails infection. As an effective uncompetitive reversible inosine monophosphate dehydrogenase inhibitor, the rate-limiting enzyme responsible for the *de novo* synthesis of guaosine nucleotides and mycophenolic acid and sometime antibiotics (Clutterbuck *et al*. 1932). The polysaccharide-protein combination found in medicinal mushrooms boosts innate immunity, which has anticancer effects in both people and

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animals (Mohmand *et al*. 2011). Numerous studies carried out globally have confirmed the medicinal mushrooms benefits and bioactive ingredients identification they contain, including proteins, glycoproteins, terpenoids, and polysaccharides.

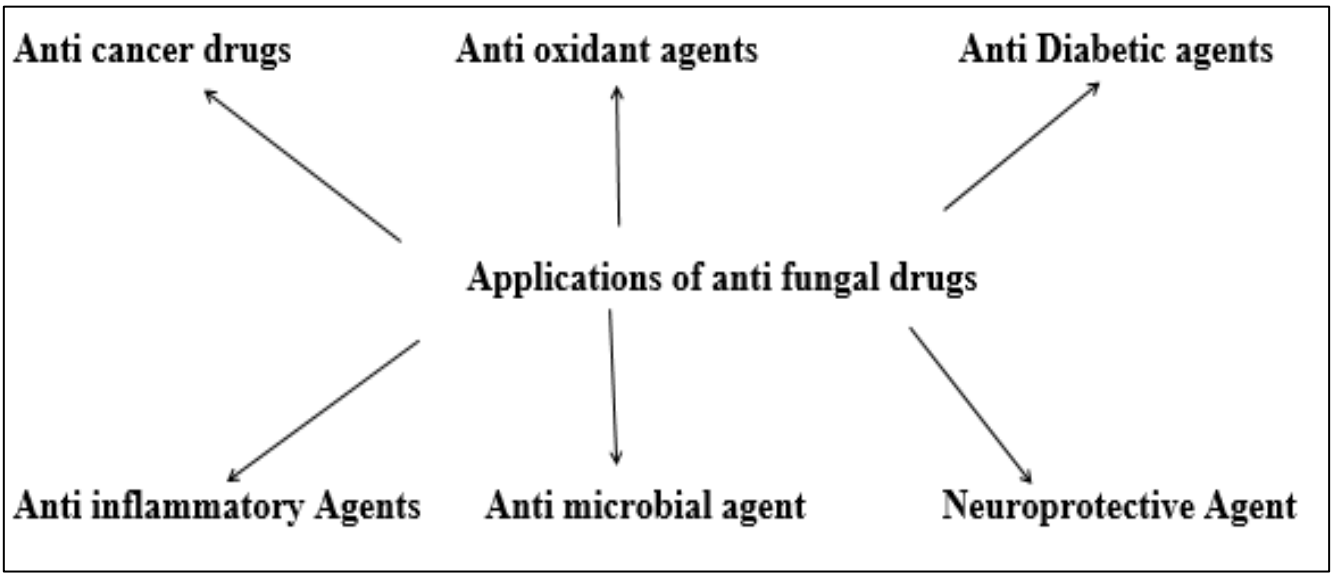

Fig 1 Therapeutic Uses of Fungi

III. FUNGI AS SOURCES OF ANTIBIOTICS PROPERTY

The fermentation process is widely utilized to chemical synthesis, ethanol, enzymes, and antibiotics. Antibiotics are produced using fungi like P. *chrysogenum*, P. *notatum*, and *Cenococcum* sp. (Yadav *et al*. 2019). The "Antibiotic" was first introduced in 1941 by Selman Waksman to describe a microbe's tiny particle that stimulates the growth of other bacteria. On September 3, 1928, when washing the Staphylococcus-loaded plates, Alexander Fleming saw that P. *notatum* (mold) formed clear infection area and create zone of inhibition. He came to the conclusion that the mold contained a chemical that killed germs since it prevented the bacterial growth on the plate. But while working at Oxford University, Ernst Chain and Howard Florey separated that material from the mold after ten years and gave it the name penicillin (Goyal *et al*. 2016). The Alexander Fleming discovered Penicillin function as a catalyst for antibiotic production for chemotherapy, inspiring other researchers to extract new compounds from fungi. Over the following 50 years, a number of antibiotics were discovered; of them, a very less number of chemicals classes were derived from fungi (Karwehl *et al* 2017). Then, pleuromutilin, fusidic acid, and cephalosporins from the same penicillins class — specifically, the beta-glucan antibiotics were added. All-purpose antibiotics called cephalosporins are typically used by individuals who are allergic to penicillin and to treat infections that are resistant to the antibiotic. Compared to penicillins, cephalosporin C is said to have a wider spectrum of antibacterial activity. Godtfredsen *et al*. (1962) isolated fusidic acid, a fusidane-type triterpenoid, by evaluating the antimicrobial potential of a few fungal extracts. According to Beekman and Barrow (2014), the antibiotic screening shown effective action against *Neisseria meningitides*, B *subtilis*, S *pneumoniae*, M *tuberculosi*, Corynebacterium diphtheria, S *aureus*, and *C tetani*. When taken orally as an antibiotic, the identical metabolite that was identified from the fungus Acremonium fusidioides has been effective against some infections of Gram-positive bacteria. The antibiotics discovery and their curative use in the 1950s revolutionized both the treatment and prolongation of life. Antibiotics are useful in treating a variety of physiological conditions, such as reducing cholesterol, as well as protozoal, bacterial, and fungal infections (Berdy 2012). Their resistance began to spread as a result of the increasing usage of antibiotics, which prompted researchers to look for new antibiotics. Antibiotic production, primarily of their analogs, increased exponentially. Antibiotics that benefit human health and alleviate pain are mostly derived from fungi, with Streptomyces being the primary producer of secondary metabolites and antibiotics (about 80% of all known antibiotics). Apart from antibiotics, essential medicinal products derived from fungal sources include lipase, ergot alkaloids, and statin reduce cholesterol synthesis. Determining the amount of secondary metabolites generated from fungi is a complex task. The majority of fungal products have the potential to be used as medications and as future treatments. Polyketide monocerin a functionalised compound, was derived from endophytic fungus called *Exserohilum rostratum* is an example of bioactive substance with antibiotics properties obtained from the plant species Bauhinia guianensis. It has antibacterial properties toward certain bacterial species, including S. *typhimurium* and S. aureus. Conversely, viruses continue to be a major source of catastrophic epidemics of debilitating illnesses and mortality worldwide, especially in regions where antiviral chemotherapy and vaccinations are either unavailable or not readily available in sufficient quantities. Additionally, the current status of viral illnesses is severely restricting the efficacy of medications due to the advent of drug-resistant strains. Consequently, there is an urgent need to identify and develop medications derived from natural sources that can help manage viral infections. After a surplus of highly potent

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and active compounds from fungal sources were isolated and tested for antiviral activity, none of them were able to reach the level of the market. This entry highlights the powerful effects of natural compounds on a number of human pathogenic viruses, including the influenza virus, herpes virus, enterovirus-71, hepatitis virus, respiratory syncytial virus, and human immuno-deficiency virus (Hyde *et al*. 2019). Due to its immune-stimulating activity, Pleurotus mushrooms also demonstrated direct or indirect antiviral effects. Ubiquitin is an antiviral substance that is extracted from the oyster mushroom's fruiting body. Pleurotus tuberregium $-glucans and their derivatives were potent anti-type-1 and type-2 simplex viruses.

➢ *As Anticancer Agents*

The most common cause of mortality and morbidity worldwide is multi-factorial disorders like cancer, which are predicted to have claimed 9.6 million lives in 2018. It is thought to have something to do with controlling both cell division and proliferation when growth factors are lost (GBD 2015). There are several cancer treatments available, and they are given based on how the disease is progressing. Radiation therapy and chemotherapy are two of the many treatments that have become standard for the cancer treatment. Chemotherapeutic medications are known to have with drawbacks, such as a high rate of side effects, a high failure rate, and a low effectiveness (Hyde *et al*. 2019). Natural products shown extend range of qualities against cancer via promoting apoptotic, antiproliferative, and non-migratory actions via different routes, thereby assisting in the search for an appropriate treatment (Evidente *et al*. 2014). Specialised metabolites are primarily found in fungi; however, bacteria and plants are the primary producers of anticancer medicinal agents. The cytoskyrins identified from C *lunata* indole alkaloids from P *aurantiogriseum*, are examples of specialised metabolites of obtained from fungal have not yet been practicised as cancer-fighting drug. Exhibit demonstrated anticancer properties (Chadha *et al.,* 2014). A specialised metabolite of the leptosin family and a potent anticancer drug, the dimeric di, keto-piperazines were identified from Leptosphaeria sp., which was collected from the marine alga Sargassum tortile (Bugni and Ireland 2004). Fusarium sp.-isolated gallic acid shows as an anticancer agent (Pan *et al*, 2017). It has also been claimed that chaetocochin A–C, which has been used to treat cancer, is produced by the fungus Chaetomium, which is derived from the leaves of the plant species Sapium ellipticum. Additionally, it has been demonstrated in a different study that the deoxypodophyllotoxin that was isolated from Aspergillus *fumigates* has a high anticancer potential (Khaled *et al*. 2013). Another anti-cancer bioactive substance, (+)-epiepoxydon, was identified from Apiospora *montagnei* extracts derived from Polysiphonia violacea, a red alga, and tested against human cancer cell lines (Klemke *et al*. 2004). It was discovered that a tetrapeptide from the green alga Codium *fragiles Fusarium* sp. had antitumor action (Raghukumar 2008). From the two strains of Hypocrea sp., three beneficial substances, cis-9-Octadecenoic acid, Heptadecanoic acid, and 16methyl-methyl ester were identified. Docking scores were used to assess the impact of these compounds on the cancer of skin protein 4,5-Diarylisoxazole Hsp 90 Chaperone. Out of all the compounds, Heptadecanoic acid, 16 methyl, and methyl ester exhibited greater reduction of a protein associated with cancer of skin, with a docking score of −11.4582 Kcal/moL, than Dyclonine, which is a recognized inhibitor of the same protein with a score of −10.058 Kcal/moL (Kandasamy *et al*. 2012). Moreover, a number of mushrooms shows anticancer activity. The polysaccharides of medicinal mushrooms as anti-cancer include lectins, terpenoids, dietary fibers, and hetero beta-glucans and associated protein complexes. The majority of anticancer compounds were extracted from the fruiting bodies, mycelia, and mushroom culture medium of medicinal, including, Flammulina velutipes, Schizophyllum scommune, Lentinus edodes, Trametes versicolor, and Ganoderma lucidum (Wasser and Weis 1999). According to reports, Pleurotus ferulae fruiting body ethanol extract showed significant anticancer effect against lung carcinoma (Choi *et al*., 2004). Higher conc of flavonoids were found in Pleurotus ostreatus specially in fruiting bodies, which is what gives this mushroom its cytotoxic effect against human leukemia (HL-60) cell line *in vitro*. In C57BL/6 mice, beta-glucan derived from Ganoderma lucidium exhibited *in vivo* anticancer action, resulting in prevention of primary lung cancer metastasis. Hericium erinaceus, the therapeutic benefit of mushrooms, has been thoroughly studied *in vivo* in animal models (Li *et al.,* 2014). It was observed that in a mouse model of xenograft tumors, the ethanol extract of this species inhibits the growth of gastric, liver, and colon cancers. According to a report, a single band protein HEP3 as an immunomodulator extracted and shown the ability to inhibit the growth of colon cancer cells in mouse xenograft tumors (Diling *et al*., 2017). Promising compounds derived from fungi in both preclinical and clinical developmental stages include Irofulven, illudin S derived from Omphalotus illudens, which interferes with DNA replication complexes during DNA formation as well as cell division. According to Devi *et al*., 2020 and Topka *et al.,* 2018, the bioactive chemical has demonstrated encouraging results in clinical studies both phase I and phase II against several cancer types, including those of the lungs, pancreatic, breast, blood, CNS many more. Illudin conjugate has higher activity *in vitro* than irufulven and is currently undergoing pre-clinical development. Leptosins F and C, two more powerful anticancer chemicals obtained from Leptoshaeria sp., demonstrated anticancer potential when tested in mice embryos (Sandargo *et al*., 2019).

➢ *As Antioxidant Agent*

Often referred to as inhibitor of oxidation, antioxidants are highly effective against reactive oxygen species (ROS). Finding potent antioxidants that can prevent or treat any disease naturally is a constant endeavor. A prospective source of antioxidants was thought to be fungal species with their secondary metabolites from natural sources, are innovative works for novel and safe antioxidants. Some specialised metabolites that have been outlying from fungi are coumarin an endophytic fungi, isopestacin from Pestalotiopsis microspora, borneol not direct source from fungi, salidarroside, corynesidones B and A, p-tyrosol, 2,14-dihydroxy-7-drimen-12,11-olide, lapachol, 2,3,6,8-tetrahydroxy-1- methylxanthone, rutin, phloroglucinol, 5-

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(hydroxymethyl)-2-furanocarboxylic acid, many more may be the source of novel natural antioxidants with a variation in biological activities, including anticancer properties.

The most well-known chemotherapeutic drugs against a range of cancers are considered to be antioxidants, and fungal metabolites work as antioxidants play key role in reducing the risks of oxidative stress-related diseases (Gupta *et al*., 2020). The fact that potent substances are highly effective against ROS damage with antioxidant activity and other free radicals formed from oxygen, which are involved in assorted diseases, underscores their significance (Bhagobaty and Joshi 2012).

Most of the potent activities in presence of anti-oxidants work as potetial therapies that cure and avoid different disorders associated with reactive oxygen species (ROS). Some examples of biological activities with potential therapies are anti-artherosclerotic, anti-inflammatory, anti-viral, and anti-mutagenic (Pimentel *et al.*, 2011). A *candidus*, P *roquefortii*, E *falconensis*, and *Mortierella* sp. are among the fungal species that are known to produce potent compounds having antioxidant properties. Two new compounds of Acremonium sp. were reported to demonstrate highly potent to reduce ROS. Through the bioreformation of four oxidative products 1, 2, 3, and 4-tetrahydronaphthalene, a novel component isolated from the marine Halorosellinia oceanica type of endophytic fungus was sesquiterpenoid—presented a unique method of biological oxidation devoid of interrupting the stimulating alicyclic structure (Pan *et al*. 2008).

In another investigation more than eleven different types of mushrooms were examined with their antioxidant properties. Every Scleroderma leaf exhibits efficacious activity with an IC50 value of < 20 µg/mL. Certain species, including Leucogaster rubescens, Geopora clausa, R. pedicellus, and Rhizopogon couchii, showed moderate activity and values of IC50 in between 20 and 40 µg/mL. Some species exhibited mild antioxidant activity with IC50 values > 50 µg/mL, including M *tuberiformis*, G *monticola*, E *muricatus*, R *subaustralis*, and R. *nigrescens* (Stanikunaite *et al*. 2007). It has been demonstrated that parasitenone, a bioactive substance extracted from the marine fungus Aspergillus *parasiticus*, which was itself derived from red alga, specifically Carpopeltis cornea, has the ability to scavenge free radicals (Abdel-Lateff 2004). The ROS reducing properties as antioxidant, mushrooms have also drawn attention from researchers. According to a study, Elaphomyces granulates fruiting body's ethanolic extract and syringic acid shown strong ROS reducing activity against myelomonocytic HL-60 cells, with IC50 values of extract 41µg/mL and syringic acid 0.7 µg/mL, Syringic acid had a strong antioxidant effect that was almost as strong as that of vitamin C with IC50 value of 0.5 µg/mL, a well-known ROS reducing property (Stanikunaite *et al*. 2009).

- *As Antidiabetic Agents*

Diabetes, is a condition characterized by up regulation of blood glucose levels due to contrast insulin production cause the inability of people with diabetes to effectively utilize insulin in their bodies. Type-1 diabetes, an insulin-dependent diabetes, is characterized by an inability of the pancreas to make insulin due to impairment in the function of the β cells that secrete insulin (Meier *et al*., 2005). according to a report, all over the world, there are 5–10% known instances of type-1, primarily affecting children and teenagers.

Patients with type-2 diabetes also called insulin non dependent diabetes are treated with hypoglycemic agents are due to enabling to metabolize insulin or create enough of it. Type-2 diabetes disease accounts 90–92% and is mostly affected age more than 50 people (Hameed *et al*., 2015). approximately 7-9% of World's population is affected by type-2 condition. In a review of 2017 report, in India about 73 million cases, 114 million in China and 30 million in the USA were recorded.

If this condition is not treated in timely manner, kidney failure, cardiovascular problems, and even death may occur (Huang *et al*., 2018). The fungal species, including Agaricus bisporus, Tremella fuciformis, C. aegerita, and Cyclocybe cylindracea, belong to the Basidiomycota and are used to treat type-2 diabetes because their diets contain fewer digestible carbohydrates, which helps patients avoid having higher blood glucose levels (Poucheret *et al*. 2006).

In the treatment of diabetes, a variety of bioactive metabolites that are extracted from both therapeutically lower and higher fungi have antihyperglycemic action, either as isolated compounds or as extracts. According to Bugni Ireland (2004), the endophytic fungus Cosmospora sp. produced the bioactive metabolite Aquastatin-A, which has antidiabetic properties against type-2 diabetes. Tyrosine phosphatases are proteins that modulate cellular processes that rely on tyrosine phosphorylation. This chemical inhibits these enzymes. Another endophytic fungus called Pseudomassaria sp. includes insulin mimic, which can lower blood glucose levels and be a novel treatment for diabetes (Strobel and Daisy 2003). It was claimed that β-glucan, which was extracted from the dried fruiting bodies of Agaricus subrufescens, had antidiabetic properties.

Polysaccharide derived from the Ophiocordyceps sinensis mycelia was shown to have antidiabetic effect in diabetic mice produced with streptozotocin and alloxan, where blood levels of insulin rose and glucose fell (Li *et al*, 2006). Drugs with hypogycemic qualities can be made from the fruiting bodies of Antrodia cinnamomea (Huang *et al*, 2018). Because they improve insulin sensitivity and resistance as well as glucose absorption, the Inocutis levis extracts offer therapeutic potential against diabetes and help control blood glucose levels.

According to a report, bisporus extract has antidiabetic properties since it reduces glucose levels in diabetic rats with streptozotocin (Jeong *et al*, 2010). Certain pharmacological glucose lowering mushroom products, including Tremella, Ophiocordyceps sinensis, and Reishi-Max capsules are marketed as anti-diabetic with the claim that they lower type-

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2 diabetes patients specially fasting glucose levels (De Silva *et al.*, 2012).

SX-Fraction, a different mushroom product, is thought to be the best alternative for increasing sensitivity of insulin (Preuss *et al*., 2007) and also combining medicinal mushroom products with other medications.

➢ *As Anti-Inflammatory Agents*

Living things experience inflammation naturally. When this process gets out of control then cause illnesses, including psoriasis, arthritis, cancer, heart, and Alzheimer's also. Antihistamines and steroidal and nonsteroidal anti-inflammatory medications are among the treatment options available to treat disorders associated to inflammation. Even with a few notable successes, treating inflammatory illnesses still need a lot more work. Our ability to treat inflammatory illnesses with modern medicine depends on the cyclooxygenase enzyme, which changes arachidonic acid toward the reason for prostaglandins synthesis.

Despite the amazing advancements in non-synthetic drugs and our reliance on them, more than 80-85% of the world's population still uses traditional medicine because they cannot afford western medications. Important sources of naturally occurring compounds with anti-inflammatory properties are fungi and their metabolites (Deshmukh et al. 2012). Bioactive substances include penidepsidone A, penisclerotiorin A, diaporthein B, diaporthein C, 3-methylorsellinic acid, and aculeatusquinone the fungus P *sclerotiorum* yielded, aculeatusquinone C, 3-methylorsellinic acid, and examined these structures using X-ray diffraction, spectroscopic techniques, and also with quantum chemical calculations. These substances were examined on generation of the nitric oxide in lipo-polysaccharide induced microgial cells for examined anti-inflammatory properties. Acleatusquinone C, A, and 3-methylorsellinic acid, out of all the extracted chemicals, demonstrated more anti-inflammatory action than indomethacin, a recognized anti-inflammatory medication (affirmative control) (Zhao *et al.*, 2020). Few new bioavailable components from a fungus Penicillium sp. TJ403-2 that was isolated originating from sea sand have been reported by another recently conducted study.

13β and 12βHydroxy Conidiogenone C, and 12β-Hydroxy Conidiogenone D were the chemicals in question. X-ray crystallography experiments, HRESIMS, and one- and two-dimensional NMR investigations all helped to clarify their structures. The anti-inflammatory properties of each substance were investigated in relation to LPS-induced NO generation.

The compounds NF-κB-activated pathway was demonstrated by immuno-fluorescence and western blot tests, underscoring its potential as a beginning for the creation of new non rebellious agents (Li *et al.*, 2020). Some Anti-inflammatory compounds can be found in mushrooms. Ergosterol, a vitamin D precursor, is available in notable amounts in edible mushrooms, such as Agaricus bisporus fruiting bodies, and has been shown to have non rebellious properties. According to Muszynska (2018), pleuran, a specialised metabolite extracted from the fruiting bodies of oyster mushrooms, exhibited non rebellious properties.

In Raw 254.7 cells, the ethanolic extract of Elaphomyces granulatus, two minor compounds such as syringic acid and syringaldehyde, shows antiinflammatory properties as COX-II inhibitors, an enzyme that is responsible for inflammation. More COX-II inhibitors were produced by syringic acid and syringaldehyde, whose IC50 values were 0.3 and 3.4 µg/mL, respectively. The IC50 value of NS-397, a positive control that is known as COX-II inhibitor and was found to be 0.21 µg/mL. At 50 µg/mL, its ethanolic extract shows 67% inhibition of COX-II (Stanikunaite *et al*., 2009).

➢ *Fungi As Antimicrobial Property*

Numerous of mushrooms produce antimicrobial properties to cover them from pathogenic microbes, insects and protozoa also. Some of the fungal components demontrated as antibacterial against both gram positive and negative bacteria and antimicrobial in contrast to yeast, mycelial fungi like dermatophytes and food grown pathogenic Distillation of these naturtally derived compounds have great medicinal value in pharmaceuticals. According to the average geometric mean of the MIC of the various drugs were as follows: amphotericin B (AMB), 0.56 µg/ml; liposomal amphotericin B membrane inhibitor; 0.36 µg/ml; itraconazole, 0.57 µg/ml; voriconazole, 0.46 µg/ml; posaconazole (POS), 0.45 µg/ml sequelene synthesis inhibitor; and caspofungin cell wall synthesis inhibitor, 0.46 µg/ml (Lass *et al*., 2008). These drugs are demonstraed as traditional and antifungal drugs. The production of antimicrobial properties of compounds by variety of fungal species has been suspected and for centuries utilised by humankind.The antimicrobial agent pramanicin (R.C. Crouch *et al*.,1991) and their related fatty acid (Schwartz *et al.*,1992)

➢ *Fungi As Neuroprotection*

Many compounds from various fungal species demonstrated as strong neuroprotective properties. There are neuroactive compounds in medicinal mushrooms that enhance nerve function. Numerous therapeutic mushrooms, such as Pleurotus giganteus, Hericum erinacus, Ganoderma sp., Lignosus rhinocerotis, and Antrodia camphorata, are beneficial for enhancing the nervous system especially peripheral. Erinacines and hericenones, areterpenoid class produced by the mycelia and maturing body of Hericium erinaceus. Through the MAPK/ERK pathway, that can trigger the production of neurotropic growing factor *(Thongbai et al., 2015*). A neuroprotective compound found in Malaysian medicinal mushroom an sclerotium extract Lignosus rhinocerotis promotes neuronal development (Eik *et al., 2012).* (Neuronal outgrowth is stimulated by G. neo-japonicum (Seow *et al.*, 2013). According to Phan and Sabaratnam (2012), P. giganteus contains a significant quantity of uridine, which exhibits neuronal development trigger development activity. The Hericicaceae family's Laxitextum incrustatum and Dentipellis fragilis contain erinacine-type molecules, which are cyanide diterpenoids that promote nerve development factors (Gong *et al*., 2020). The insect-linked ascomycetes create the fungimod chemical. In addition to being utilized as a novel treatment for multiple

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sclerosis, Isaria sinclairii is an effective immunomodulator that supress immunity was approved by the US FDA in 2010. It is also used to treat apoptosis and grafting *(Hyde et al., 2019).*

IV. PRESENT AND FUTURE SCOPE OF THE STUDY

Since ancient times, excellent model organisms of fungi in biological and natural study, and more recently, they have also been crucial to the creation of natural medicines. Fungal-derived specialised metabolites are the main source of assist molecules in the contemporary pharmaceutical business. Numerous new chemical and pharmaceutical industries are emerging in both industrialized and developing nations as a result of the need for natural therapies. Numerous government initiatives should be taken to study and creation of fungal based medicines-based metabolites have received approval from various nations inside their borders. In India as well, a number of programs in the research sectors for the therapies development from fungal are ratified by the DBT, DST, CSIR, ICMR, and ICAR governments. These days, one of the most popular subjects in scientific research is the growing of mushrooms and the separation of the chemical compounds found within. Even in many Indian cities' more rural regions, mushroom farming is becoming more and more popular. More recent business people are working in the sector of mushroom production and marketing them for human use in both fresh and dry forms.

V. CONCLUSION

"A Review of the Therapeutic Potential of Fungi" clearly states that the review and focuses on therapeutic aspects. In this we mainly focus on the Activities Against various severe diseases scope of fungi in research. Recent Advances in Fungal Research signals currency and relevance to ongoing scientific investigation. Fungi represent a largely untapped resource in the search for novel therapeutic agents. Their ability to produce a wide array of bioactive compounds has demonstrated significant potential in combating severe diseases such as cancer, neurodegenerative disorders, and various infectious conditions. Traditional medicinal fungi, along with newly discovered species, have shown promising pharmacological effects through antimicrobial, anticancer, antioxidant, and immunomodulatory activities. Advances in molecular biology, fungal genomics, and biotechnological techniques have further accelerated the discovery and development of fungal metabolites with clinical relevance. Despite the progress made, more comprehensive studies, including clinical trials and safety evaluations, are needed to translate these natural products into effective therapeutic agents. Continued interdisciplinary research and investment in fungal biotechnology could lead to innovative treatments and broaden the scope of fungi in modern medicine.

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