

## Antiviral Potential of Mushrooms in the Light of their Biological Active Compounds

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**Abstract:** Life-threatening diseases, especially those caused by viruses, require searching and investigation in order to find potent compounds and drugs. Mushrooms are promising sources of compounds showing bioactive potency whenever tested. This review highlights extracts and compounds originated from mushrooms fruiting bodies and or mycelia. Further studies are encouraged to discover novel potent antiviral compounds/ extracts or evaluate already known compounds extracted from those edible medicinal mushrooms.

**Keywords:** Medicinal Mushrooms, antiviral activities, cordycepin, ganoderic acid

### 1. INTRODUCTION

In contrast to bacterial illness, viral illness cannot be treated or controlled by traditional antibiotics so specific drugs or antiviral agents are urgently needed. Viruses play a major role in serious infections in children and adults and sometimes lead to the need for admission to intensive care units and hospitalization, especially in cases of encephalopathy or severe respiratory distress. Parainfluenza viruses, Influenza, herpes viruses, syncytial respiratory virus, and adenoviruses are the most frequent pathogens of these severe infections [1].

Antiviral properties of mushrooms were evaluated not only for whole extracts but also for some isolated compounds. The fractions and compounds showing antiviral effects were extracted from both fruiting bodies and mycelia. They can inhibit virus replication directly via inhibition of viral enzymes, viral nucleic acids synthesis, or prevention of virus adsorption and uptake into mammalian cells. In addition, they can inhibit virus replication indirectly by stimulation of the immune system by their polysaccharides or other complex molecules [2, 3].

Truffles are typical symbiotic ectomycorrhizal mushrooms and thus must grow in association with host plant. On the other hand, the antimicrobial activities of desert ectomycorrhizal Mushrooms (Truffles) have been investigated decades ago by many researchers who studied extracts of *Terfezia clavervii* which exhibited antiviral activity. [4, 5].

Ectomycorrhizal mushrooms (Truffles) contain a variety of biochemical components, including steroids, pheromones, flavonoids, anthocyanine, carotenoids, oligosaccharide and volatile organic compounds such as dimethyl-sulfide and bisulfide, butanedione, butyrate, hexenone, ethyl-, methyl- and propylphenol and methylthiomethane. Till now, limited studies were conducted on truffles though they represent unexplored sources with potential therapeutic activities due to containing antiviral, antioxidant, antimicrobial, hepatoprotective, immune-modulating, anticarcinogenic, antidepr-

essant and sedative bioactive compounds [6, 7]. Truffle extracts showed Antiviral activity as reported by **Hussan and Al-Ruqaie**, [8].

On the other hand, a study describing the antiviral properties of methanolic extracts and aqueous extracts from other mushroom species such as *Boletus edulis* Bull. (Boletaceae), *Lentinula edodes* (Berk.) Pegler (Omphalotaceae), and *Pleurotus ostreatus* (Jacq.: Fr.) P. Kumm. (Pleurotaceae) against Human herpes virus 1 (HSV-1) showed that the methanolic extracts had lower anti-HSV-1 activity than the aqueous extracts [9]. **Amoros et al.** [10] tested extracts obtained from the basidiocarps of 121 Basidiomycota mushroom species as anti-HSV (types 1 and 2), anti-vesicular stomatitis virus, and anti-poliovirus. The study reported that 11% of these extracts inhibited one or more than one virus, with more active species belonging to the Cortinariaceae and Tricholomataceae families than to the Boletaceae and Russulaceae families. Dichloromethane and Methanol extracts prepared from 57 types of wood-decaying fungi were tested for the ability to inhibit HIV-1 reverse-transcriptase enzyme *in vitro* [11]. The results demonstrated that the methanolic extracts inhibited the reverse transcriptase activity more strongly than the dichloromethane extracts where *Poria monticola* Murrill (Polyporaceae) and *Laetiporus sulphureus* (Bull.) Murrill (Fomitopsidaceae) were the most active species [11]. **Lee et al.**, [12] reported that A hot water extract prepared from *Porodaedalea pini* (synonym: *Phellinus pini*; Hymenochaetaceae) basidiocarps showed strong inhibitory effect against Coxsackievirus B3 (CVB3) through preventing its plaques formation on HeLa cell lines. An aqueous extract obtained from *Phellinus igniarius* was showed also antiviral activities against influenza virus (Types A and B), including H1N1 and human H3N2 [13].

Ganodermediol, applanoxidic acid G triterpenoids, and lucidiol isolated from *Ganoderma pfeifferi* Bres. (Ganodermataceae) and other *Ganoderma* species showed antiviral activities against influenza virus type A *in vitro*, showing half-maximal inhibitory concentrations [IC<sub>50</sub>] of 0.22, 0.19, and 0.22 mmol/L, respectively, in Madin-Darby canine kidney cell lines [14]. Also, ganodermediol showed activities against lip exanthemas and other signs caused by HSV-1, with an IC<sub>50</sub> value equal to 0.068 mmol/L in Vero cell lines [14]. Antiviral effects of aqueous extracts prepared from mycelia of 11 Basidiomycota species were tested against avian influenza and human influenza A viruses. In those studies, the following fungal species were well identified as potential sources of antiviral agents: (Polyporaceae), *Ischnoderma benzoinum* (Wahlenb.) P. Karst., *Fomitopsis officinalis* (Vill.) Bondartsev & Singer (synonym: *Laricifomes officinalis*; *Daedaleopsis confragosa* (Bolton) J. Schröt., *Cerioporus mollis* (Sommerf.) Zmitr. & Kovalenko (synonym: *Datronia mollis*; Fomitopsidaceae) *Lenzites betulina* (L.) Fr., *Trametes gibbosa* (Pers.) Fr., and *T. versicolor* (L.) Lloyd (Polyporaceae) [15, 16].

Polysaccharide fractions, as well as ethanol and aqueous extracts of *Lentinula edodes* (Shiitake) exhibited antiviral activity against bovine herpesvirus 1 and poliovirus 1 and replication, and researchers have documented that extracts activities on both virus strains are found at the time replication begins [17]. *Agrocybe*, which is an individual illudane-illudane bis-sesquiterpene, prepared from *Cyclocybe salicaceicola* Vizzini (synonym: *Agrocybe salicaceicola*; Agaricaceae) showed weak antiviral effects against respiratory syncytial virus, with an IC<sub>50</sub> of 100 µmol/L [18].

Extracts and total polysaccharide fractions prepared from aqueous extracts of mushrooms belonging to the genera *Lentinus*, *Ganoderma*, *Daedaleopsis*, *Pleurotus*, *Trametes*, *Inonotus*, and *Laetiporus* showed fully suppressed infectious activity of West Nile virus. In addition, some fungal compounds can show inhibitory activities on human immunodeficiency virus (HIV). It has been reported that PSP from *Trametes versicolor* and polysaccharides from PSK krestin can inhibit HIV-1 replication *in vitro*. They show immunostimulatory effect, krestin provides support to the killer cells of the immune system, and the polysaccharide-protein complex inhibiting HIV reverse transcriptase activity and the attachment of HIV-1 gp120 to CD4 surface receptor [11, 19, 20, 21]. Furthermore, a sample of melanin (SI = 12.5) obtained from *I. obliquus* exerted activity against vaccinia virus. Also, extracts from larch polypore (SI = 2) and Chaga (SI = 2) possessed certain antiviral potential [16]. Additional studies on chemical metabolites from fungi (*Inonotus obliquus*) that inhibit the replication of VARV can detect compounds/fractions with various mechanisms of action, which is relevant for the therapeutic drug development against smallpox infections. [22].

## 2. EXAMPLES OF SOME COMPOUNDS WITH POTENT ANTIVIRAL ACTIVITIES

### 2.1. Cordycepin and its Analogs

Cordycepin (also named 3'-deoxyadenosine) is a purine nucleoside that differs in structure from adenosine in the absence of oxygen atom in the 3' position of its ribose moiety [23]. Cordycepin was

originally isolated from the medicinal mushroom *Cordyceps militaris* [24], but currently it can be produced synthetically due to its potent biologically active properties such as anticancer, antifungal, inhibition of platelet aggregation, and antiviral activities [25-27]. Generally, the action mechanisms of cordycepin is still under investigation, but some studies have explained those activities in relation to its ability to inhibit several protein kinases [28, 29].

The antiviral activity of cordycepin has been previously reported against many viruses such as inhibiting influenza viral genome replication [30, 31], inhibiting HIV-1 reverse transcriptase [32], murine leukemia virus and Epstein-Barr virus (EBV) [33, 34], inhibiting rota-virus through stimulating the host induced Type I Interferon response in cells [35], in addition to many plant viruses [36].

### 2.2. Ganoderic Acids

Ganoderic acids are the bioactive Triterpenes produced by *Ganoderma* species [37]. Some of the reported Ganodermic acids are A, AM1, B,  $\beta$ , C1, C2,C6, D, Df, DM, E, F, G, H,J,K, Mc, Me, Nf, Mk, N, P, R, S, Sz,T, TR,TQ, X, and Y[37]. Studies on ganoderic acids revealed that they exhibit various biological activities such as anti-thrombosis [38], anti-tumor [39], and neuroprotective activities [40]. Moreover, ganoderic acids can selectively inhibit the activities of eukaryotic DNA polymerase [41]. One of the promising activities exerted by ganoderic acids is their antiviral activities against many viruses such as HIV-1 [42]. Ganoderic acid originated from *Ganoderma lucidum* suppressed hepatitis B virus replication [43].

### 2.3. Future Trends

Mushrooms are functional food and are rich source of assortment of bioactive compounds that offer great therapeutic potential for the prevention and control of several diseases [3, 44]. Hence, isolation and identification of bioactive compounds from mushrooms crude extracts are required in order to specify which compound is responsible of the observed antiviral activity. Optimization of submerged culture conditions for mushrooms mycelial growth as well as strain improvement by genetic manipulation should be applied on large scale in order to overproduce the desired compounds. Further research and clinical trials have to be carried out to validate mushrooms as source of bioactive molecules with potential antiviral application.

## 3. CONCLUSION

In conclusion, Studies from different countries have shown that polysaccharides, as well as other fungal compounds (nucleosides, proteins, terpenoids, glycoproteins, etc.) exert antiviral effect against many viruses pathogenic for humans such as orthopoxviruses, herpes, hepatitis viruses, West Nile, human immunodeficiency, and influenza. Biologically active compounds prepared from the same fungal species can show antiviral activities against different viral pathogens.

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