

## Some Antiviral Mushrooms of Nepal

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### Abstract

The present paper is a review based on published papers to highlight about some potential antiviral mushrooms, which are also found in Nepal. Nepalese mushrooms have not been yet analyzed and investigated so far for their antiviral properties except antioxidant and ACE-Inhibition sources on 62 Nepalese mushrooms as evidence-based complementary and alternative medicine.

The published paper from abroad includes the species like: *Calvatia gigantea*, *Cordyceps militaris*, *Cortinarius caperatus*, *Fomes fomentarius*, *Ganoderma lucidum*, *Grifola frondosa*, *Hericium erinaceus*, *Inonotus hispidus*, *Inonotus obliquus*, *Lentinula edodes*, *Omphalotus illudens*, *Ophiocordyceps sinensis*, *Phellinus ignarius*, *Pleurotus citrinopileatus*, *Pleurotus eryngii*, *Pleurotus ostreatus*, *Polyporus umbellatus*, *Russula delica*, *Schizophyllum commune*, *Scleroderma citrinum*, *Tremella sp.* and *Trametes versicolor*, which are also found in the natural temperate (*Schima – Castanopsis - Rhododendron – Quercus*) forests of Kathmandu valley. This paper may provide the researchers a glimpse to the aspects of experiment and lead to investigate on medicinal, antiviral and antibacterial properties of mushrooms found in Nepal. Gautam & Adhikari (2007) have screened *Ophiocordyceps sinensis* for its chemical compound.

### Keywords

Antiviral compounds, mushrooms, alternative medicine, antibacterial properties,

### Introduction

Nepal, lying in the central Himalayan belt, is considered as the center for immense myco-diversity (Adhikari 2000, 2009, 2012, 2014). Till now, about 1300 species of mushrooms are recorded. The list, taxonomic status, habit and habitat, records of reporters, and distribution details can be seen in "Mushrooms of Nepal" (Adhikari 2000, 2014). Hence the details of availability for each mushroom are not given here. Many Nepalese wild and exotic edible mushrooms have been screened for their nutraceutical values (Adhikari, 2000; Adhikari *et al.*, 2018; Bhattarai *et al.*, 2018; Adhikari *et al.*, 2019). Several mushrooms have been analyzed and reported for their antiviral compounds from abroad. In Nepal, about 75 species are known to have medicinal properties (Adhikari, 2008c; Bang *et al.*, 2014), have reported antioxidant and ACE-Inhibition sources of 62 Nepalese wild mushroom species.

Mushrooms have many bioactive compounds

that possess anti-cancer, antibacterial, antifungal, antiviral, antioxidant, and anti-inflammatory activities. The limitation of natural antiviral compounds in the market and the viruses becoming more resistant to currently available medicines warranted the need for the new antiviral prescriptions without side effects. Antiviral compounds isolated from the mushrooms have shown potent activity against human diseases such as immuno deficiency virus, influenza, herpes simplex virus, hepatitis B and C viruses, etc. Enzymatic and non-enzymatic antioxidant compounds such as superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, glutathione S-transferase, ascorbate peroxidase, vitamin C, vitamin E, and glutathione play vital roles in neutralizing oxygen and thereby protecting cells from damage.

### Review and Discussion

The following mushrooms have been reported to yield antiviral compounds, which are naturally

available in the nearby Kathmandu valley forests. This report may provoke the researchers to investigate the hidden new compounds in Nepalese mushrooms.

Piraino & Brandt (1999) isolated an antiviral compound (RC-183 exhibiting HSV-1 and HSV-2) from *Cortinarius caperatus* (Pers.) Fr. [= *Rozites caperata* (Pers.) Karst. (gypsy mushroom)], which is the edible mushroom.

*Lentinula edodes* (Berk.) Singer (shiitake, mrigre chyau) has lentinan and KS-2, as antiviral compounds. It grows on dead woods of *Quercus* and *Castanopsis* trunk and branches. Nowadays, it is cultivated in Nepal as edible ones. *Lentinula edodes*, the tasty culinary staple ingredient, has antiviral activities (anti-HVC) against the hepatitis C virus, herpes simplex virus, and human immunodeficiency virus as influenza. The best way to get the benefits of shiitake is to eat them. They can also be found as medicinal mushroom blends, in tinctures and dried products (Suzuki *et al.*, 1989; Matsuhisa *et al.*, 2015). In 1980, Tochikura, Nakashima and Yamamoto found that lentinan sulfate (extract of shiitake mycelium) blocks HIV cell to cell infection at 85.9% – 96.9% rates, and so does PSK extracted from the medicinal mushroom *Trametes versicolor* (L) Lloyd [= *Coriolus versicolor* (L.) Quel, (turkey tail)]. *T. versicolor* has been analyzed and found to have PSP and PSK. It is a common species, which grows on dead woods of different species.

Recently, Brandt & Piraino (1999) identified a new class of antiviral compounds from mushrooms. *Fomes fomentarius* (L.) Fr. (hoof fungus, iceman or tinder fungus, Ghoda tap chyau), showed its activity in hot water extracts. It grows on living and dead tree trunks of various woods. *Inonotus obliquus* (Ach. ex Pers.) Pilat (Chaga or cinder conk) is said to have anti-cancer and antiviral properties. It grows on living and dead tree trunks *Quercus* and *Castanopsis* species,

The screening of mycochemicals from the basidiocarp of *Ganoderma lucidum* (Curtis.) Karst. (reishi, Dadhu chyau) is found to possess ganaderiol-F, ganoderic acid- $\beta$ , lucidumol. It is a widespread common species from tropical to the temperate region and grows on the rhizosphere region of different trees, causing die-back

diseases of economic plants (Adhikari 2006ab; Adhikari *et al.* 2006; Parajuli *et al.*, 1999ab). It is cultivated in Nepal. *Ganoderma lucidum* is an antiviral powerhouse fungus, which is woody, and therefore not edible. It has been recognized as a medicinal mushroom for thousands of years. The genomic sequencing showed that it could combat many viruses, such as influenza, herpes, Epstein-Barr, and hepatitis, including the very virulent and dangerous H1N1 strain of flu. The substances called triterpenes are one of the main beneficial compounds in reishi alongside the beta-glucans. Triterpenes are very bitter-tasting, making reishi rather inedible. It can be found in chips, capsule powder, and tincture form (Chen *et al.*, 2012; El-Mekkawy *et al.*, 1998)).

The fruit body of *Grifola frondosa* (Dicks.) Gray (maitaki, hen of woods, Marmo shrymo) possesses 1-6 glucans. It grows on *Quercus* tree trunk in temperate regions and is a delicious species. Nepalese are fond of eating this species. It has a broad range of medicinal properties. In a Japanese study, this mushroom extract was found to be active against influenza, which stimulated the production of antiviral cytokines such as TNF-alpha. It was found more powerful when combined with shiitake mushroom extract (Gu *et al.*, 2007).

*Hericium erinaceus*, *Schizophyllum commune*, and *Ganoderma lucidum* were selected for evaluation of their in-vitro anti-dengue virus serotype 2 (DENV-2) activities, which were found to be more productive. Hot aqueous extracts (HAEs), ethanol extracts (EEs), hexane soluble extracts (HSEs), ethyl acetate soluble extracts (ESEs), and aqueous soluble extracts (ASEs) were prepared from the selected mushrooms to calculate the effectiveness (Ellan. *et al.*, 2019). The mushrooms showing vigorous antiviral activities are polypores, so-called woody conks, are now believed (through ongoing DNA research), to be the ancestors of most antibacterial and antiviral compounds. *Calvatia gigantia* (Batsch) Lloyd and *Polyporus umbellatus* Fries also show substantial antiviral activities (Ellan *et al.*, 2019).

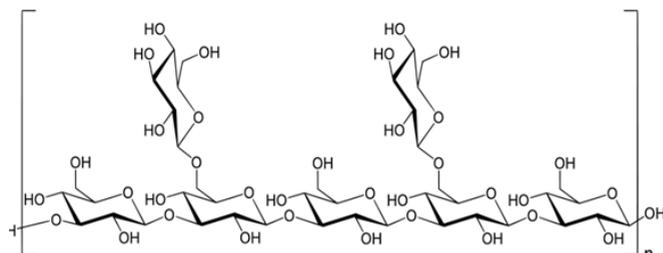
*Pleurotus ostreatus* (Jaqu.) Kumm, (oyster mushroom, Kanya chyau, Marmo shyamo) produces a ubiquitin-like protein with anti-HIV activity. It also grows on *Quercus* and *Castanopsis*

tree trunks. It is also a delicious species and cultivated in Nepal. Most of the antiviral compounds from mushrooms are water-soluble and relatively heat-stable.

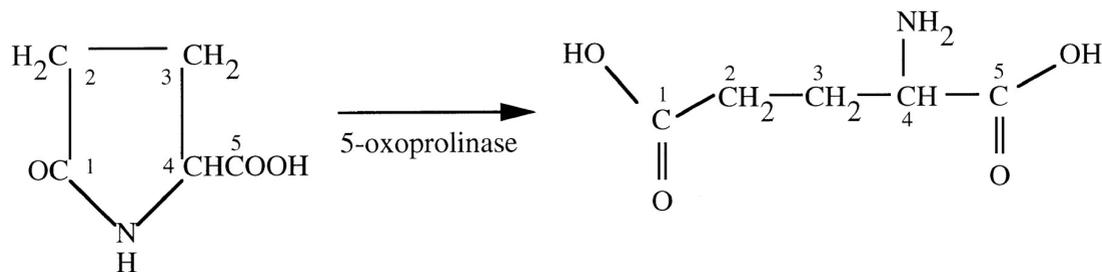
Furthermore, most of the mushrooms mentioned and their mycelia can be cultured commercially to significant levels. The antiviral compounds are found to be present both in the mycelium and in the fruiting bodies. Wang *et al.*, (2000) isolated ubiquitin-like protein from *Pleurotus ostreatus* mushroom for the antiviral, translation-inhibitory, and ribonuclease activities.

Several mushrooms show to be effective against respiratory viruses like the common cold and even the flu virus, which is difficult to prevent and treat due to their ability to mutate quickly. Not all antiviral compounds work in the same manner in all conditions. There is some evidence that mushrooms might be harmful when treating the novel coronavirus. They have potent constituents called beta-D-glucans, beta-glycosides, and other substances that need to be disintegrated before or after entry.

In 1950, Cochran and Lucas found the antiviral effects of *Calvatia gigantea* (giant Lentinan a [beta-glucan](#) isolated from the shiitake mushroom.



Conversion of pyroglutamic acid to glutamate by 5-oxoprolinase



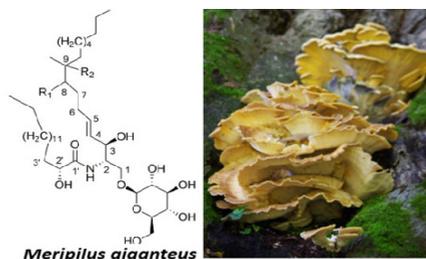
Pyroglutamic acid

Glutamic acid

puffball, football mushroom) and *Agaricus campestris* L. (meadow mushroom) to protect mice from poliomyelitis virus. In 1966, Cochran *et al.* discovered that *Boletus edulis* Bull. (king bolete, porcini), *Calvatia gigantea*, *Suillus luteus* (L.) Roussel, (Slippery Jack), *Lentinus edodes*, and *Piptoporus betulinus* (Bull.) Karst. (birch polypore) were effective against the flu-causing influenza viruses. In 1980, Tochikura, Nakashima, and Yamamoto found that lentinan sulfate (extract of shiitake mycelium (LEM) blocks HIV cell to cell infection 85.9% – 96.9% at similar rates, and so does PSK from the medicinal mushroom *Trametes versicolor*. *Calvatia gigantea* contains calvacine, a compound with potent anti-cancer and antiviral activity (but cannot be used since it causes unacceptable side effects). *Calvatia gigantea* is used in Nepal to treat and heal pack soars (Shrest & Kropp, 2009). It is also used in syphilis and anesthetic conditions.

Cordyceps is an entomopathogenic or entomophilous (parasitic habit on larvae and pupae of insects), pleomorphic fungi distributed worldwide. The nucleosides in *Cordyceps* are in focus nowadays.

*Cordyceps militaris* (L.) Link, *Ophiocordyceps*



*sinensis* (Berk.) Sung, Sung, Hywel-Jones & Spatafora, (= *Cordyceps sinensis* – Yarsagumbu: Yarsa = insect, gumbo = plant – Cordicepine), show vigorous antiviral activities. The fruit bodies of *C. militaris* grow on Lepidoptera pupa and larva in clusters, while the fruit body *O. sinensis* grows singly from the head of caterpillar (*Thitarodes* = *Hepialus*, moths). *O. sinensis* is collected from the alpine zone of Nepal (Darchula, Bajhang, Bajura, Doti, Jumla, Mugu, Humla, Dolpa, Kalikot Manang, Mustang, Jajarkot, Magdi, Gorkha, Rasuwa, Rukkum, Sindhupalchowk, Solukhumbu, and Taplejung districts lying between 3500 and 5000m). It is endemic to the Tibetan Plateau (Adhikari 2008abc) Gautam & Adhikari (2007) have screened the chemicals of *O. sinensis*.

*Cordyceps militaris* has more than ten nucleotides and their related compounds, including adenine, adenosine, inosine, cytidine, cytosine, guanine, uridine, thymidine, uracil, hypoxanthine, and guanosine. *Cordyceps* are known for being antifungal and antibacterial, anti-inflammatory, antioxidant, antitumor, antiapoptosis, and immunomodulatory action, as well as improving fatigue and libido. Therefore, *O. sinensis*' chemical constituents and pharmacological effects (Yarsagumbu) against different diseases provide a reference for the study in the future (Liu *et al.*, 2015). Almost all of the nucleotides and nucleosides in *O. sinensis* can be transformed reciprocally. Early in 1950, cordycepin was first isolated from *C. militaris*, and its structural formula was confirmed as 3'-deoxyadenosine, but it is only found in natural *O. sinensis* with shallow content and cannot be detected in the cultured ones. Cordycepin was separated with a mixture of acetonitrile and water (5:95, v/v) at a flow rate of 1.0 ml/min, which is the commonly used method to extract the composition. Many bioactive components of *O. sinensis* have been obtained, including nucleoside, polysaccharide, sterol, protein, amino acid, and polypeptide. Besides, these constituents' corresponding pharmacological actions were also shown in the study, such as anti-inflammatory, antioxidant, antitumor, antiapoptosis, and immuno modulatory actions. Therefore, *O. sinensis* can use different effects against different diseases and provide a

reference for the study of *O. Sinensis* in the future (Liu *et al.*, 2015). The content of adenosine is much higher in cultured *O. sinensis* than in the natural one. Among them, cultured *O. sinensis* has many adenosines, which are much higher than those in cultured *C. militaris*. Nucleotide named AMP can be degraded to adenosine. The source of inosine in natural *O. sinensis* may be the oxidative adenosine. Many other adenosine analogs such as 2'-deoxyadenosine, 2'3'-dideoxyadenosine, cordycepin triphosphate, and 3'-amino-3'-deoxyadenosine have also been found in *O. sinensis*. Yang and Li introduced three methods to extract adenosine: organic solvent pressurized liquid extraction, boiling water extraction, and ambient temperature water extraction.

## Conclusion

Due to the changing climatic conditions day-by-day, various pathogenic elements are appearing that causes diseases. Scientists are investigating the exact remedy material to keep human beings safe and sound. However, emerging diseases have created havoc. Fungi and mushrooms can be a source of ingredient to treat or eradicate the prevailing disaster, which needs investigation and study, The family Polyporaceae, as a vibrant frontier of new medicines, plays an essential role in nutrient recycling by decomposing aged trees. In a time when new antiviral medication is critically needed, mushrooms are an untapped resource and deserve intensive studies. The most potent effects of medicinal mushrooms are their strong antiviral and immune-enhancing properties. Interestingly, polypores are not known to be poisonous, whereas there are more than 100 species of poisonous gilled mushrooms (Adhikari 2018).

Nepal, with its immense natural biological diversity since time immemorial, is a treasure house for finding out the substance and ingredient of eradicating and preventing the natural calamities. It needs regular investigation, trail, and patience.

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