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Entomopathogenic Mushroom (*Cordyceps* sp.) as Immunity Booster

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Abstract

Cordyceps are a dietary therapeutic mushroom that's been used for centuries to improve the immune system and boost energy levels. Cordyceps were first used in the mountains of Tibet thousands of years ago as a remedy for fatigue and recovery from illness. The mushroom grows naturally on a caterpillar at elevations of 12,000 feet above sea level in throughout the world. Many benefits to using its extracts including a reduction of inflammation and oxidative stress, the leading causes of most disease. This makes cordyceps, along with chaga mushrooms, a good anti-aging and recovery supplement. Adenosine levels help increase the body's supply of adenosine triphosphate (ATP) which is a primary source of energy during physical activity and also increase the body's natural production of nitric oxide optimizing oxygen absorption and improving lung and liver function.

Introduction

Mushrooms which are having medicinal properties have been known since thousands of years to produce biometabolites which are used or studied as possible treatment for many diseases. Most of the cancer-related deaths can be prevented or reduced by modifying our diet with mushrooms, because they contain antioxidants. The name Cordyceps has been derived from two Latin words, i.e., cord and ceps meaning club and head, respectively. *Cordyceps militaris* belongs to the phylum Ascomycota classified in the order hypocreales, as spores are produced internally inside a sack, called ascus (Wang *et al.*, 2011). It is an entomopathogenic fungus, which often grows parasitically on lepidopteron larvae and pupae of insects and spiders. It normally inhabits on the surface of insect's pupae in winters and leading to the formation of fruiting body in summers justifying its name as "winter-worm summer-grass". There have been a variety of pharmacologically active compounds reported from *Cordyceps* sp. Among them Cordycepin has received much attention due to its broad-spectrum biological activity and medicinal value.

Pharmaceutical and Therapeutic Ability of *Cordyceps* sp.

Cordyceps species is also known as traditional Chinese medicine (TCM) as it has wide applications in pharmaceutical and health sector (Russell and Paterson 2008). These Therapeutic development and Drug are also used for the treatment of COVID-19. This medicinal mushroom was in the limelight during the Chinese National Games in 1993, when a group of women athletes broke nine world records, committed that they had been taking *Cordyceps* regularly. It has been seen previously reported that *Cordyceps* also

enhances physical stamina making it very useful for the elderly people and athletes.

How Does It Work?

Cordyceps might improve immunity by stimulating cells and specific chemicals in the immune system. It may also have activity against cancer cells and may shrink tumor size, particularly with lung or skin cancers. The structure of Cordycepin is very much similar with cellular nucleoside, adenosine and acts like a nucleoside analogue. Once inside the cell, Cordycepin gets converted into mono-, di- and tri-phosphates that inhibit the activity of enzymes like ribose-phosphate pyrophosphokinase and 5-phosphoribosyl-1-pyrophosphate amidotransferase which are used in de novo biosynthesis of purines.

Recent literature further confirms that *Cordyceps* enhances cellular energy in the form of ATP (adenosine tri-phosphate). Upon hydrolysis of phosphates from ATP, lots of energy is released which is further used by the cell. The studies by many researchers in the past on *Cordyceps* have demonstrated that it has anti-bacterial, anti-fungal, larvicidal, anti-inflammatory, anti-diabetic, antioxidant, anti-tumor, pro-sexual, apoptotic, immunomodulatory, anti-HIV and many more activities. *Cordyceps* has a long history of use as a lung and kidney tonic, and for the treatment of chronic bronchitis, asthma, tuberculosis and other diseases of the respiratory system. The cardiovascular effects of *Cordyceps* are being noticed more frequently by researchers as it works through variety of possible ways either by lowering high blood pressure via direct dilatory effects or mediated through M-cholinergic receptors resulting in improvement in the coronary and cerebral blood circulation. Thus, *Cordyceps* has implications at the therapeutic level as well by rectifying the abnormalities in rhythmic contractions (also known as cardiac arrhythmia). *Cordyceps* extract has also been found as a promising source to increase cardiac output up to 60 % in augmentation with conventional treatment of chronic heart failure. The product from wild type and cultured *Cordyceps* has also been shown to significantly decrease blood viscosity and fibrinogen levels preventing myocardial infarction. Another study showed that the fermentation products of Cs-4 reduce myocardial oxygen consumption in animals under experimental lab conditions revealing dramatic anti-anoxic effects. These studies provide strong evidence that Cs-4 and its fermentative solution prevents platelet aggregation stimulated by collagen or adenosine di-phosphate (ADP).

An Entomopathogenic Fungus

It is known as an entomopathogenic fungus because *Cordyceps* usually infects insects at different stages of their development ranging from insect larvae to adult. Insect's epidermis is covered with a thick layer of cuticle (procuticle and epicuticle) which is also known as integument. Insect's

integument comprises chitin, proteins and lipids. Beside this, it also contains variety of enzymes and phenolic compounds. Epidermis is formed by a single layer of epithelial cells followed by a thick layer of procuticle. Procuticle is differentiated into an inner soft part known as an endocuticle while the outer hard part is called exocuticle. Epicuticle and wax are known to constitute the outermost covering of the cuticle. This not only serves as a protective barrier against pathogenic organisms but also prevents water loss and acting as an interface between insect and its environment. Further a short germ tube protruding out of the conidia starts thickening at the distal end which is known as appressorium. This appressorium maintains a kind of mechanical pressure on the germinating germ tube further improving the penetration effect of germ tube so as to reach into the insect's haemolymph. As the germ tube penetrates the epicuticle layer of insect's integument, it starts forming a plate-like structure called penetration plate. The penetration plate further produces secondary hyphae, which cross the epidermal layer and reach into the haemocoel of insect's body. From these hyphae, protoplast bodies bud off and start circulating into the insect's haemocoel. Fungus now starts growing into a filamentous mode invading internal organs and tissues of the host. During growth inside the host, fungus produces various kinds of toxic secondary metabolites, which are insecticidal. These secondary metabolites take the insect to its final life stage and ultimately insect dies out. Fungal mycelium emerges out through the cuticle and lead to the formation of fruiting body under suitable environmental conditions. Finally the insects become sluggish and then die; the mycelium modifies and develops into a sclerotium, which remains covered by the integument of the dead insect.

Metabolites Isolated from *Cordyceps*

Cordyceps, especially its extract has been known to contain many biologically active compounds like Cordycepin, cordycepic acid, adenosine, exopolysaccharides, vitamins, enzymes etc. Out of these, Cordycepin, i.e., 3-O-deoxy adenosine isolated from ascomycetes fungus *C. militaris*, is the main active constituent which is most widely studied for its medicinal value having a broad-spectrum biological activity.

Medicinal Uses of Cordycepins

- Immune system stimulator,
- Respiratory diseases,
- Antitumor properties,
- Sexual potentiator,
- Kidney, liver and heart problems,
- Athletes/ sportsmen stamina,
- Acute and chronic hepatitis cancer.



Figure 1: *Cordyceps militaris* (Artificial and Natural)

Conclusion

Cordyceps being an ancient medicinal mushroom used as a crude drug for the welfare of mankind in old civilization is now a matter of great concern because of its unexplored potentials obtained by various culture techniques and being an excellent source of bioactive metabolites with more than 21 clinically approved benefits on human health including antidiabetic, anti-tumor, anti-oxidative, immunomodulatory, sexual potentiator and anti-

ageing effects (Das *et al.*, 2010). Cordycepin alone has been widely explored for its anti-cancer/ anti-oxidant activities, thus, holding a strong pharmacological and therapeutic potential to cure many dreadful diseases in future. Further investigations need to be focused on to study the mechanistic insight into the mysterious potential of this medicinal mushroom on human health and promoting its cultivation strategies for commercialization and ethno pharmacological use of this wonderful herb against the COVID-19.

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