**Caterpillar Mushroom *Cordyceps militaris*-Ultimate Traditional food.**

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**Introduction**

Edible mushrooms are extensively utilized due to their considerable nutritional and medicinal benefits as a functional meal. Furthermore, they have garnered significant recognition for their curative and medicinal applications (Chang and Miles, 2004). The bioactive substances found in medicinal mushrooms include a variety of polysaccharides, proteoglucans, terpenoids, phenolic compounds, steroids, and lectins. The chemicals in question exhibit a diverse array of therapeutic activities and possess the ability to function as agents that modulate the immune system, combat cancer, combat viruses, neutralize oxidants, and reduce inflammation. There are at least 12,000 species which can be considered as mushroom with 2000 are edible. About 300 species have been grown experimentally and 60 are cultivated commercially (Badalyan, 2012; Villares *et al.,* 2012).

*Cordyceps* *militaris* commonly known as orange caterpillar, keedha jaddi and Himalayan gold is an ascomycete entomopathogenic fungus comes under class of significant value, is known to flourish at elevations the Himalayan plateau's chilly, green, alpine meadows are located over 3800 meters above mean sea level (MSL) (Alessandro and Francesca, 2009; Sharma *et al*., 2015a, b; 2016). Due to the inherent challenges associated with the harvesting process, the product has been assigned a rather high price point. Despite being expensive and difficult to find, the remarkable therapeutic uses of Cordyceps have established it as a highly esteemed and essential element in traditional Chinese and Tibetan medicine, People living in various countries, including China, Tibet, Nepal, and India, have long included Cordyceps spp. in their diets as a means of helping their bodies adjust to the strenuous environmental conditions present in high-altitude mountainous regions. The aforementioned conditions encompass reduced ambient temperatures, elevated air pressure, and diminished oxygen concentrations in the immediate vicinity. *Cordyceps* spp, is frequently recommended in the context of traditional Chinese medicine as a therapeutic intervention for various human ailments, includes diseases of the heart, lungs, liver, and kidneys, cancer, diabetes, illnesses brought on by viral and parasitic agents, and sexual dysfunction. This chapter provides a comprehensive examination of contemporary advancements in *C. militaris* research, focusing on the assessment of its active chemical constituents, the pharmacological impacts, and the recent developments in product research and development. *C. militaris* is a parasitic fungus that specifically targets Lepidoptera larvae. This particular fungus has a long history of traditional medicinal use in China. The substance known as the widely recognized components of this substance include cordycepin (3'-de-oxyadenosine) and its derivatives, ergosterol, polysaccharides, glycoprotein, and peptides containing -aminoisobutyric acid. The presence of polysaccharides and cordycepin in *C. militaris* contributes to its anti-inflammatory, antioxidant, anti-tumor, anti-metastatic, and immunomodulatory properties (Das *et al.,* 2010). According to Wang *et al*. (2014), the study observed the impacts of hypoglycaemic, steroidogenic, and hypolipidemic activities.

**Geographical source**

The wide variety of species being covered here can be found all over the world, but especially in humid, temperate and tropical habitats in Asia, which includes places like Korea, Japan, Nepal, and China. The presence of multiple species indicates the widespread distribution of organisms throughout a wide range of biological niches on Earth. (Olatunji *et al.,* 2018, Hajek & Leger 1994). Different and coordinated methods allow the Cordyceps species to link up with their related hosts. After avoiding detection by the host's immune system and producing protective secondary metabolites, organisms carry on with their life cycles by modifying their appearance to take advantage of the host for growth and survival. New pharmaceuticals may be found thanks to this phenomenon (Hajek & Leger, 1994). As a result of their potential as a source of natural substances with varied biological functions, the worth of these species has increased significantly. (Olatunji *et al.,* 2018). Due to the high cost of acquiring and processing wild Cordyceps species, laboratory-grown specimens have become more popular in recent years. (Wang *et al.,* 2022).

**Macroscopic characters**

The stroma has a club- or clavate-shaped morphology, characterized by distinct divisions into fertile and sterile segments. The fertile part, which has dimensions of 10-30 × 5-12 mm, exhibits a coloration ranging from red to darker orange. This region is marked by the presence of ostioles originating from the orange perithecia, resulting in abrasions. The coloration of the specimen ranges from yellow, mild, to crimson orange, with occasional mottling of orange. The sterile region of the specimen measures approximately 30-4 × 5-10 mm in size. The dimensions of the semi-submerged, ovoid perithecia range from 550 to 700 × 250 to 400 micrometres in size. The dimensions of the object are around 350-400 × 3-4 μm. It has a nearly cylindrical shape and consists of eight spores, which eventually separate into several individual spores (Akata, *et al.,* 2016)

***Cordyceps militaris's* Health benefits**

Since ancient times (3000 years), the medicinal mushroom *C. militaris* has been used extensively in China for therapeutic purposes. It is used therapeutically to treat conditions like hyperglycemia, hyperlipidaemia, lung and renal dysfunction, exhaustion, night sweats, infertility problems, cardiac arrhythmias, and other heart ailments. A wide range of pharmacological qualities, such as those that reduce inflammation, function as antioxidants, have anticancer, antimetastatic, immunomodulatory, hypoglycaemic, and steroidogenic actions are all present in *C. militaris* (Das *et al.,* 2010).

1. **Immune Boosting Activity**

Multiple investigations have shown that extracts from this medicinal fungus modulate the immune system. Oral injection of *C. militaris* fruiting body aqueous extracts at 20 mg/kg stimulated macrophage IFN production via IL-18 (Kim *et al.,* 2008). Fresh and dried *C. militaris* extracts exhibit similar immunomodulatory effects in immunosuppressed rats treated with clophosphamide. The quantitative examination of phytochemical components showed that fresh and dried *C. militaris* had similar cordycepin and adenosine concentrations. Fresh extracts had more polysaccharides, total polyphenols, and total flavonoids than dried ones. In a mouse model of sickness, both extracts dose-dependently reversed thymus and spleen suppression. The treatment of these extracts significantly increased IL-2 and IFN-γ production in animal subjects. (Zhu *et al.,* 2013). In another study Kunming mice in good health showed immunological modulation and antioxidant action from *C. militaris* fruiting body extracts. Oral extract dosages of 50, 100, or 200 mg/kg increased thymic and splenic indices. The neutrophil count decreased while the leukocyte count, monocytes, and lymphocytes increased. Eosinophil and basophil numbers were constant. Elevated IL and TNF-α levels were observed in the spleen, while increased antioxidant capacity, glutathione peroxidase, and SOD were found in various organs, including the heart, kidney, and liver. This study found an immune-enhancing effect in healthy people. (Liu *et al.,* 2013).

1. **Anti-obesity activity**

The extracts derived from *C. militaris* have properties that are effective in reducing fat levels. In order to examine its effects on lipid metabolism, the current study used a novel extract made from fermented mulberry leaves with *C. militaris*. In the experimental trial, obese C57BL/6 mice were fed a high-fat diet (HFD) for a period of 12 weeks before receiving an extract. Triglycerides, glucose, total cholesterol, and low-density lipoprotein levels all significantly decreased as a result of this intervention, according to the study's findings. High-density lipoprotein production also appeared to be increasing. In contrast to the control groups, there was a reduction in the amount of abdominal fat and the size of adipocytes. Adipocyte protein 2 and peroxisome proliferator-activated receptor mRNA expression were also suppressed, and the study also noticed a drop in the Fas cell surface death receptor (Lee *et al*., 2019). The production of secondary metabolites increased when strawberry extracts were fermented with *C. militaris*, according to recent investigations. Adipogenesis was also suppressed to varied degrees by these extracts in a 3T3-L1 cell line (Liu *et al*., 2011, Guo *et al*., 2020).

1. **The suppression of cellular proliferation**

Cancer is a prominent contributor to mortality, necessitating the development of an efficacious pharmaceutical intervention. Cordycepin derived from *Cordyceps militaris* has undergone evolutionary changes in the field of pharmacognosy, positioning it as a promising foundation for the Cancer, SARS, AIDS, and the swine flu are examples of emerging diseases that require therapeutic care. As shown by electrophoresis analysis (SDS PAGE) and gel filtration, the viability of human cancer cells, specifically MCF-7 cells with an IC50 of 15.0 uM, 5637 cells with an IC50 of 9.30 uM, and A-549 cells with an IC50 of 8.10 uM, was severely decreased (Park *et al*., 2009). When cultured for 48 hours with Hep-G2 cells, Hela cells, and mesangial cells, the water-soluble polysaccharide known as the MCMP strain—which is generated from mycelium—was found to have anti-tumor properties in a study by Zhang *et al*. (2010). Wong and colleagues (2011) conducted a study, the purification of a protease called Cordymin from the species *Cordyceps militaris*. The researchers observed that this protease had anti-proliferative effects specifically targeting breast cancer cells known as MCF-7. It is of utmost significance to comprehend that *C. militaris* possesses the capability to impede the growth of tumor cells, so rendering it a potential candidate for the advancement of novel therapeutic agents aimed at cancer prevention and treatment. The A3 adenosine receptor (A3 AR) belongs to the family of adenosine receptors and has been found to have potential use in cancer therapy.

**THROMBOLYTIC ACTIVITY**

*C. militaris* may boost immune function, vigor, and overall health. However, the effects of this event on thrombolysis—the enzymatic breakdown of blood clots—are poorly explored. Drugs that dissolve blood clots are often associated with thrombolytic action. This field of study is crucial to cardiovascular health, including stroke and heart attack. If Cordyceps militaris possesses thrombolytic activity, it could help treat certain illnesses. Further detailed research is needed to demonstrate this intervention's efficacy and safety for these goals. If this subject has improved or been studied after my last update, I would not know about it. To get the most accurate and up-to-date information on Cordyceps militaris' thrombolytic action, consult scholarly literature, medical databases, or healthcare professionals who are aware of recent advances. Patel and Ingalhalli (2013) observed the presence of fibrin binding activity in the fibrinolytic enzyme derived from *C. militaris*. This activity enables the destruction of fibrin, suggesting its potential application in thrombolytic therapy. This particular characteristic offers a viable substitute for the expensive fibrinolytic enzymes commonly employed in the treatment of cardiovascular conditions associated with aging in humans.

1. **ANTI-OXIDATIVE PROPERTY**

A wide variety of secondary metabolites, including phenolic compounds, polyketides, terpenes, and steroids, can accumulate in mushrooms. Due to their wide spectrum of biological effects, which include functions like scavenging free radicals, chelating metals, regulating enzymes, and blocking LDL oxidation, among others, polyphenols have grown in importance in the field of antioxidants (Rodrigo and Bosco, 2006). The antioxidant properties displayed by the fruiting bodies of artificially generated *C. militaris* that were grown under ideal conditions were explained by Li and Xu (1997). In this study, we investigate the effects of *C. militaris* on the in vivo catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and hydroxyl radical inhibition enzymatic activities. Previous research has demonstrated that *C. militaris* has the capacity to inhibit Fe (+)-L-Cysteine-induced mitochondrial swelling and damage in a concentration-dependent manner. A considerable effect in scavenging superoxide anions has also been noted for *C. militaris*. Additionally, it has been extensively studied how *C. militaris* affects the enzymatic activities of CAT, SOD, GPx, and anti-hydroxyl radicals in the liver of mice. In a study conducted by Dong *et al*. (2014), it was demonstrated that the extract derived from *C. militaris* had anti-oxidative properties, namely by effectively regulating the levels of superoxide dismutase and glutathione peroxide.

1. **ANTI-INFLAMMATORYPROPERTY**

Inflammations, which can develop in any tissue as a result of trauma, infections, or damage brought on by post-ischemic, toxic, or autoimmune causes, are complex processes involving the interaction of several soluble chemicals and cells (Nathan, 2002). The body's reaction to inflammation is often known to be self-limiting. This is accomplished by reversing vascular modifications that initially made it easier for immune cells to recruit, upregulating anti-inflammatory protein expression, and downregulating proinflammatory protein expression (Cook *et al*., 2005). The advantageous immune response to external stimuli or damage to bodily tissues has been documented to lead to the reinstatement of the original structure and functionality of the tissue. In their study, Jo *et al.,* (2010) demonstrated the anti-inflammatory properties of a hot water extract derived from *Cordyceps militaris*, a traditional herbal remedy. Fung and Ko (2012) found that the extract of *C. militaris*, specifically the polysaccharide component, as well as cordycepin, displayed anti-inflammatory activities in both in-vitro and in-vivo types of inflammation using mice. Additionally, there have been findings showing that using a *C. militaris* extract to lower levels of the pro-inflammatory cytokine mediator (TNF-alpha) inhibits intestinal inflammation in a mouse model of acute colitis. When varied concentrations of heated *C. militaris* were tested, Patel and Ingalhalli's (2013) study found a decrease in the production of inflammatory mediators, including TNF-alpha, NO, and IL-6 secretion. This result raises the possibility of an inhibitory effect on the synthesis of these mediators. In addition to their bioactive components, mushrooms have been revealed to possess anti-inflammatory peptides with a range of molecular weights.

**ANTI- MICROBIAL AGENT**

The advancement of antibiotics stands as a significant scientific accomplishment during the past seven decades. According to Fuchs (2004), these chemicals are purported to exhibit various modes of action, such as disrupting metabolic processes or affecting organismal structures. The study conducted by Park *et al*. (2009) shown that the protease extract derived from *C. militaris* had inhibitory effects on the growth of *Fusarium oxysporum* in a concentration-dependent manner. According to the findings of Patel and Ingalhalli (2013), it was proposed that the utilization of a particular acidic polysaccharide derived from *C. militaris*, when cultivated on germinated soybeans, exhibited therapeutic properties in combating influenza virus infection. According to the findings of Wong *et al*. (2011), it was observed that Cordymin, a protease derived from *C. militaris*, has inhibitory effects on HIV-1 reverse transcriptase.

1. **FERTILITY ENHANCER**

The majority of those affected by infertility are currently seeking medical treatment, making it a widespread problem that affects a large number of people (Glazener *et al*., 1987). Due to a change in emphasis from synthetic medications to natural herbal therapies, there has been an increase in the use of herbal extracts as agents for improving animal fertility (Dada and Ajilore, 2009). Chang *et al*. (2008) explained the effects of cordycepin produced from *C. militaris* on the improvement of both sperm quality and quantity in their investigation. This rise in cordycepin has been found to have a positive effect on testosterone and estradiol-17 levels, leading to an augmentation in the proportion of sperm cells exhibiting motility. According to Patel and Ingalhalli (2013), it has been proposed that cordycepin could potentially contribute to the augmentation of semen output and enhancement of sperm quality in boars. The study conducted by Hong *et al*. (2011) provided evidence of the enhancing impact of *Cordyceps militaris* on the synthesis of testosterone in male murine rodents.

**ANTI CHOLESTEROL AGENT**

Hypercholesterolemia poses a significant socioeconomic challenge for both the general population and healthcare practitioners, primarily because of the robust association between lipid abnormalities and cardiovascular disorders (Morsy and Fouad, 2008). The accumulation of LDL cholesterol is highly atherogenic and exerts a toxic effect on vascular cells. Consequently, the development of atherosclerosis, hypertension, obesity, diabetes, and impaired organ function, such as in the liver, heart, and kidneys, can occur (Jain *et al.,* 2010).

The specific mechanism responsible for the lipid balancing impact of this phenomenon, whether it involves stabilizing blood sugar levels, improving liver function, or another yet undiscovered cause, has yet to be determined (Patel & Ingalhalli, 2013). There has been a growing scientific interest in the assessment of traditional remedies and alternative medicines as viable treatments for reducing cholesterol levels.

**ANTI DIABETIC PROPERTY**

Type 1 or type 2 diabetes mellitus (DM) is a long-term metabolic disorder of the endocrine system caused by deficits in insulin secretion, increased cellular resistance to insulin, or a combination of these factors. Outcome of this phenomenon is distinguished by an excessively elevated concentration of glucose in the bloodstream, commonly referred to as hyperglycemia, which results in significant harm to the organs of the body (Wong *et al.,* 2011). At now, there are a variety of therapeutic medications for diabetes mellitus (DM) that are commercially available. Despite the wide array of pharmaceutical options, a significant proportion of these medications exhibit high toxicity levels and exorbitant costs, hence exacerbating adverse consequences for the patient. Consequently, their attempts to modify the progression of diabetic problems become unsuccessful. Certain medications have the potential to elevate the occurrence of renal tumors, hepatic damage, and acute hepatitis. Singh *et al* 2008 studied the predominant focus of antidiabetic research lies in the advancement of antihyperglycemic medicines that possess a high degree of safety and are devoid of undesirable side effects, including but not limited to nausea, diarrhea, hepatic complications, and weight gain Malviya *et al*. (2010). Zhang *et al*. (2006) and Dong *et al*. (2010) in their investigation, gave diabetic Sprague-Dawley rats either a water extract or an alcohol extract of Cordyceps militaris. The study team discovered that through improving glucose metabolism, this extract significantly reduced blood glucose levels.

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