**Catterpillar Mushroom *(Cordyceps militaris)*- An Ultimate Traditional food**

**Irfan Javaid1, Shaheen Kauser Jan1, Ali Anwar1 and Farooq Ahmad Bhat1,**

1Division of Plant Pathology, Faculty of Agriculture, SKUAST-K Wadura, sopore-193201, Jammu and Kashmir, India,

**\*Corresponding author: irfanskuast@gmail.com**

**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 medical and therapeutic uses (Chang and Miles, 2004). Medicinal mushrooms exhibit a wide range of bioactive components, including 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 over 3,800 meters above mean sea level (MSL) among the frigid, grassy, alpine meadows of the Himalayan plateau (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, Throughout several generations, populations residing in various places such as China, Tibet, Nepal, and India have traditionally included *Cordyceps* spp. in their dietary practices as a strategy to adapt their bodies to the demanding environmental conditions prevalent in high-altitude mountainous areas. 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, including cardiovascular and respiratory disorders, liver and kidney impairments, cancers, diabetes, infectious and parasitic diseases, as well as sexual dysfunctions.

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 cordycepin (3'-de-oxyadenosine) and its derivatives, together with ergosterol, polysaccharides, glycoprotein, and peptides containing α-aminoisobutyric acid, are extensively acknowledged constituents of this entity.

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. The present study utilized a new extract derived from fermented mulberry leaves with *C. militaris* to investigate its impact on lipid metabolism. The experimental study involved the administration of an extract to obese C57BL/6 mice that were fed a high-fat diet (HFD) for a duration of 12 weeks. The results of this intervention demonstrated a significant reduction in the levels of triglyceride, glucose, total cholesterol, and low-density lipoprotein. Additionally, an increase in the production of high-density lipoproteins was detected. The quantity of abdominal fat and the dimensions of adipocytes shown a decrease in comparison to the control groups. Additionally, the study observed a decrease in the Fas cell surface death receptor, as well as a suppression of adipocyte protein 2 and peroxisome proliferator-activated receptor-γ mRNA expression (Lee *et al.,* 2019). In recent studies, it was observed that strawberry extracts, when subjected to fermentation *with C. militaris*, exhibited heightened amounts of secondary metabolites. Additionally, these extracts demonstrated varying degrees of suppression of adipogenesis in a 3T3-L1 cell line (Liu *et al.,* 2011, Guo *et al.,* 2020) The provided extract also demonstrated a correlation between dosage and the inhibition of differentiation in 3T3-L1 preadipocytes, resulting in a reduced ability to develop into adipocytes. Furthermore, no detrimental effects on cellular viability were observed. A decrease in lipid accumulation was observed, along with an increase in levels of adipocyte markers such as peroxisome proliferator-activated receptor-γ, adiponectin, and CCAAT/enhancer binding protein-α. Additionally, there was continuous expression of monocyte chemoattractant protein, which is a marker for pre-adipocytes (Shimada *et al.,* 2008)

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 therapeutic management of developing disorders such as cancer, SARS, AIDS, and Swine flu. The viability of human cancer cells, namely 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 strongly inhibited as demonstrated by electrophoresis analysis (SDS PAGE) and gel filtration (Park *et al.,* 2009). In a study conducted by Zhang *et al.,* (2010), it was observed that the MCMP strain, which is a water-soluble polysaccharide derived from mycelium, exhibited anti-tumor effects when incubated for 48 hours against Hep-G2 cells, Hela cells, and mesangial cells. In their study, Wong *et al.,* (2011) conducted 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. According to Wong *et al.,* (2011), there is a higher level of expression of the gene in cancer and inflammatory cells compared to normal cells, where the expression is relatively modest.

1. **THROMBOLYTIC ACTIVITY**

*C. militaris*, a fungus, has been used in Chinese and Tibetan medicine for its many benefits. It 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**

Mushrooms have the capacity to accumulate a diverse array of secondary metabolites, encompassing phenolic chemicals, polyketides, terpenes, and steroids. Polyphenols have become significant in the field of antioxidants due to their diverse range of biological effects, which encompass activities such as scavenging free radicals, chelating metals, modulating enzymes, and inhibiting LDL oxidation, among other acts (Rodrigo and Bosco, 2006). Li and Xu (1997) provided an explanation for the antioxidant characteristics exhibited by the fruiting bodies of artificially developed *C. militaris*, which were grown under optimal conditions. This study examines the impact of *C. militaris* on the enzymatic activities of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and the inhibition of hydroxyl radicals when assessed in vivo. Previous studies have shown evidence that *C. militaris* has the ability to suppress mitochondrial damage and swelling caused by Fe (+)-L-Cysteine in a concentration-dependent manner. Additionally, it has been observed that C. militaris exhibits a notable effect in scavenging superoxide anions. Furthermore, the impact of C. militaris on the enzymatic activities of CAT, SOD, GPx, and anti-hydroxyl radicals in the liver of mice has been well-documented, revealing a considerable increase. The findings of this study suggest that *C. militaris*demonstrated a protective effect on mitochondria through its ability to scavenge reactive oxygen species, reduce mitochondrial swelling, and enhance the activity of ant oxidases. *C. militaris*has been documented to possess pharmacological properties that contribute to mitochondrial preservation and anti-aging effects. 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 are intricate processes involving the interplay of various soluble substances and cells, which can occur in any tissue as a result of trauma, infections, or injuries caused by post ischemic, toxic, or autoimmune causes (Nathan, 2002). Typically, the human body's response to inflammation is known to be self-limiting. This is achieved through the downregulation of proinflammatory protein expression, the upregulation of anti-inflammatory proteins, and the reversal of vascular changes that initially facilitated the recruitment of immune cells (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. They investigated the extract's impact on the production of various inflammatory markers, including nitric oxide (NO), interleukin-6 (IL-6), tumor necrosis factor (TNF), and lipopolysaccharide (LPS)-stimulated RAW 264.7 cells. The researchers concluded that the hot extract of C. militaris effectively suppressed the production of inflammatory mediators derived from macrophages, and this inhibition was observed to be dependent on the dosage administered. In their study, Fung and Ko (2012) determined that the extract of C. militaris, specifically the polysaccharide component, as well as cordycepin, demonstrated anti-inflammatory properties in both in-vitro and in-vivo models of inflammation using mice. These effects were likely achieved through the reduction of humoral immunity. Furthermore, there have been reports indicating that the reduction of pro-inflammatory cytokine mediator (TNF-alpha) levels by the use of C. militaris extract leads to the inhibition of intestinal inflammation in a mouse model of acute colitis. The study conducted by Patel and Ingalhalli (2013) observed a decrease in the production of inflammatory mediators, including TNF-alpha, NO, and IL-6 secretion, when different concentrations of hot C. militaris were analyzed. This finding suggests a potential inhibitory influence on the production of these mediators. Furthermore, mushrooms have been found to contain anti-inflammatory peptides with varying molecular weights, in addition to their bioactive components. In a study conducted by Wong *et al.,* (2011), Cordymin, a peptide with a low molecular weight of 10,906 Da, was isolated and purified from the species Cordyceps militaris. The efficacy of this peptide has been assessed in its ability to effectively suppress the infiltration of polymorphonuclear cells and the upregulation of C3 protein induced by IR in the brain. Additionally, it has been observed to inhibit the production of interleukin-1β and tumor necrosis factor-α, thereby exerting a neuroprotective effect on the ischemic brain through the suppression of inflammation.

1. **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 method of action mostly involves disruptions in cell wall production, alterations in plasma membrane permeability, interference with chromosomal replication, or inhibition of protein synthesis (Tenover, 2006). 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. The research conducted by Wong et al. (2011) has revealed the potent antifungal properties of the pure cytotoxic antifungal protease derived from the fruiting bodies of C. militaris. This protease has been found to have significant antifungal activity against many fungal species, including *Fusarium oxysporum, Bipolaris maydis, Mycosphaerella arachidicola, Rhizoctonia solani,* and *Candida albicans*. 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**

Infertility is a prevalent issue that impacts a significant number of individuals, with a majority of affected individuals currently seeking medical intervention (Glazener *et al.,* 1987). There has been an increasing trend in the utilization of herbal extracts as agents for enhancing fertility in animals, which can be attributed to a shift in focus from synthetic pharmaceuticals to natural herbal remedies (Dada and Ajilore, 2009). In their study, Chang et al. (2008) provided an explanation on the impact of cordycepin derived from *C. militaris* on the enhancement of both sperm quality and quantity. Previous studies have indicated that the addition of *C. militaris* has been associated with elevated levels of cordycepin in the bloodstream. 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. The findings of this study indicate that there were no detected alterations in the body weight, food consumption, and water intake of the rats. However, it was noticed that the concentration of testosterone in the serum of the rats was dramatically elevated by the administration of *C. militaris*. Hence, the utilization of *C. militaris* fruiting bodies cultivated on the drone bee medium presents a potential avenue for the application of integrative medicine in addressing reproductive disorders arising from inadequate testosterone levels in males.

1. **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). Hypercholesterolemia is characterized by the accumulation of elevated levels of low-density lipoprotein (LDL) cholesterol in the extracellular subendothelial space of arteries. This 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).

In both human and animal trials, the administration of Cordyceps has been linked to a decrease in cholesterol and triglyceride levels, as well as an increase in the ratio of high-density lipoprotein to low density lipoprotein cholesterol. 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, with a particular focus on their efficacy and minimal or nonexistent side effects.

1. **ANTI DIABETIC PROPERTY**

Diabetes mellitus (DM) is a chronic metabolic condition within the endocrine system that arises from deficiencies in insulin secretion (type 1), heightened cellular resistance to insulin (type 2), or a combination of these factors. The 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. This encompasses a range of oral antidiabetic medicines, including sulfonylureas, biguanides, glinides, tolbutamide, phenformin, rosiglitazone, and repaglinide. 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. According to the study conducted by Singh et al. in 2008, it was found that... Presently, 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. According to the study conducted by Malviya et al. (2010), In a study conducted by Zhang et al. (2006), the researchers examined the anti-diabetic properties of a crude extract derived from the fruiting bodies and mycelia of various medicinal fungus, such as *C. militaris, C. sinensis, Omphalia lapidescens,* and *Tricholoma mongolicum*. In their study, Dong et al. (2010) administered either a water extract or alcohol extract of *Cordyceps militaris* to diabetic Sprague-Dawley rats. The researchers found that this extract led to a noteworthy decrease in blood glucose levels by enhancing glucose metabolism. Additionally, the extract exhibited a potent inhibitory effect on the concentration of total cholesterol and triglycerides.

In a study conducted by De Silva *et al.,* (2012), the authors demonstrated the potential anti-diabetic properties of different fractions of C. militaris in mice with streptozotocin-induced diabetes. The experimental group revealed a significant decrease in blood glucose levels. The researchers reached the conclusion that the aqueous extract of *C. militaris* included a molecule that exhibited properties of an insulin sensitizer. This compound was found to enhance insulin production and alleviate insulin resistance in rats with type II diabetes. According to Patel and Ingalhalli (2013), the authors proposed that the utilization of cordycepin derived from *C. militaris* resulted in the inhibition of diabetes regulating genes via deactivating NF-Kb-dependent inflammatory responses. Diabetes mellitus is commonly observed to be accompanied by hormonal and neurochemical alterations that have been linked to the presence of anxiety and depression. There exists a hypothesis suggesting that the vanadium complex of vanadium-enriched *C. militaris* (VECM) may have potential benefits in the prevention of depression in individuals with diabetes. Additionally, it is believed that VECM may have an impact on insulin action and perhaps have favorable effects on treatment satisfaction and mood. *Cordyceps militaris* has been documented to exhibit an activity similar to that of antidepressants, which mitigates the induction of diabetes.

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