

Review:

The endless nutritional and pharmaceutical benefits of the Himalayan gold, *Cordyceps*; Current knowledge and prospective potentials

W.A. ELKHATEEB*, G.M. DABA

Pharmaceutical Industries Division, Department of Chemistry of Natural and Microbial Products, National Research Centre, Tahrir Street, 12311, Dokki, Giza, Egypt. *Email: waillahmed@yahoo.com.

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Abstract. Elkhateeb WA, Daba GM. 2020. Review: The endless nutritional and pharmaceutical benefits of the Himalayan gold, *Cordyceps*; Current knowledge and prospective potentials. *Biofarmasi J Nat Prod Biochem* 18: 74-81. As a traditional medicine, *Cordyceps* has long been used in Asian nations for maintaining vivacity and boosting immunity. Numerous publications on various bioactivities of *Cordyceps* have been investigated in both in-vitro as well as in vivo studies. Nevertheless, the role of *Cordyceps* is still arguable whether it acts as a food supplement for health benefits or a real healing drug that can be prescribed in medicine. The *Cordyceps* industry has developed greatly and offers thousands of products commonly available in a global marketplace. This review will focus on introducing the ecology of *Cordyceps* and their classification. Moreover, elucidation of the richness of extracts originating from this mushroom in nutritional components was presented, with a description of the chemical compounds of *Cordyceps* and its well-known compounds such as cordycepin and cordycepic acid. Furthermore, highlights on natural growth and artificial cultivation of famous *Cordyceps* species were presented. The health benefits and reported bioactivities of *Cordyceps* species as promising antimicrobial, anticancer, hypocholesterolemic, antioxidant, antiviral, anti-inflammatory, organ protective agent, and enhancer for organ function were presented.

Keywords: *Cordyceps*; cultivation; secondary metabolites; traditional medicine

INTRODUCTION

Commonly seen nowadays on shelves of pharmacies and drug stores and recommended for many benefits such as boosting immunity, the genus *Cordyceps* is an ascomycetous traditional medicinal mushroom that is famous for having numerous bioactive compounds. *Cordyceps* have different common names: insect mushroom, caterpillar fungus, Himalayan gold, etc. Still, the name *Cordyceps* originates from the Latin words (cord), which means 'club,' and (ceps), referring to 'head.' The fruiting bodies of these fungi appear from the head of different life stages of various orders of insect species (Zhou et al. 2009; Smiderle et al. 2014; Chen et al. 2000; Peterson 2008; Wang and Yao 2011; Dworecka-Kaszak 2014). The genus *Cordyceps* is classified under the order Hypocreales, family Ophiocordycipitaceae, and phylum Ascomycota. Some genera belong to families Cordycipitaceae and partial Clavicipitaceae, as shown in Table 1 (Pu and Li 1996; Buenz et al. 2005; Sung et al. 2007; Kepler et al. 2012).

Species belonging to the genus *Cordyceps* have a golden history due to their safe use in traditional oriental medicines (Paterson 2008). Also, they were utilized 2000 years ago in China for curing different infectious diseases (Singh et al. 2008; Zhou et al. 2009). Although *Cordyceps* has a wide-reaching distribution, most species have been described from Asia (Boesi Alessandro and Francesca Cardi 2009).

The most famous and widely used species of *Cordyceps* is *C. sinensis* (Berk.) Sacc (syn. *Ophiocordyceps sinensis* (Berk.) G.H. Sung, J.M. Sung, Hywel-Jones & Spatafora). Currently, the preferred scientific name is *Cordyceps sinensis* (Berk.) Sacc. (Devkota et al. 2006). This species has a wide host range, including different species of Lepidopteran larvae (Wang and Yao 2011), numerous Thitarodes caterpillars, and its most common host, the Himalayan bat moth *Hepialus armoricanus* (Chen et al. 2000). *Cordyceps militaris* (also known as orange caterpillar mushroom) is rich in bioactive compounds and hence has medical-biological activities in a similar way to *Cordyceps sinensis* (Shrestha and Sung 2005; Gong et al. 2006; Ma et al. 2007; Huang et al. 2009; Das et al. 2010; Dong et al. 2012). This review discussed ecology, classification, nutritional components, chemical composition, natural growth and artificial cultivation, health benefits, and reported bioactivities of famous *Cordyceps* species.

CORDYCEPS ECOLOGY

Many *Cordyceps* species grow by feeding on insect larvae and sometimes on mature insects. *Cordyceps* grows on insects, crickets, cockroaches, bees, centipedes, black beetles, and ants. From the genus *Cordyceps*, there are several species known to have medical value, only a few are cultivated, and the most common and well-known are

Cordyceps sinensis (Figure 1) and *Cordyceps militaris* (Figure 2) (Halpern Georges 2007). *Cordyceps* may also grow on other arthropods and the fungus *Elaphomyces* Nees.

Table 1. The current classification system of *Cordyceps* (*Cordyceps* sensu lato)

Genus	No. of species
Partial Clavicipitaceae	
<i>Drechmeria</i>	2
<i>Hypocrella</i>	50
<i>Metacordyceps</i>	4
<i>Metarhizium</i>	35
<i>Nomuraea</i>	3
<i>Pochonia</i>	3
<i>Podocrella</i>	4
<i>Regiocrella</i>	2
<i>Sphaerocordyceps</i>	2
<i>Tyrannicordyceps</i>	5
Total: 10	110
Ophiocordycipitaceae	
<i>Blistum</i>	1
<i>Didymobotryopsis</i>	3
<i>Elaphocordyceps</i>	1
<i>Haptocillium</i>	8
<i>Hirsutella</i>	78
<i>Hymenostilbe</i>	22
<i>Ophiocordyceps</i>	155
<i>Paraisaria</i>	2
<i>Perennicordyceps</i>	4
<i>Polycephalomyces</i>	12
<i>Purpureocillium</i>	3
<i>Syngliocladium</i>	5
<i>Synnematium</i>	1
<i>Tolypocladium</i>	39
<i>Trichosterigma</i>	1
Total: 15	335
Cordycipitaceae	
<i>Akanthomyces</i>	13
<i>Ascopolyporus</i>	7
<i>Beauveria</i>	31
<i>Beejasamuha</i>	1
<i>Cordyceps</i>	175
<i>Coremiopsis</i>	2
<i>Engyodontium</i>	5
<i>Gibellula</i>	21
<i>Hyperdermium</i>	2
<i>Insecticola</i>	2
<i>Isaria</i>	83
<i>Lecanicillium</i>	21
<i>Microhilum</i>	1
<i>Phytocordyceps</i>	1
<i>Pseudogibellula</i>	1
<i>Rotiferophthora</i>	27
<i>Simplicillium</i>	8
<i>Torrubiella</i>	66
Total: 18	467
Total: 3 families, 43 genera, and 912 species	

Note: The data is counted from Catalogue of Life: <http://www.catalogueoflife.org/>, accessed in June 2017)



Figure 1. *Cordyceps sinensis* (Collector: Soraj25; Locality: Nepal, Mid-Western, Jumla, Nepal, hosted by <http://mycoportal.org>)



Figure 2. *Cordyceps militaris* (Collector: Marjan Kustera; Locality: Gabrovac, Serbia, hosted by <http://mycoportal.org>)

Classification of the genus *Cordyceps* was previously within the family Clavicipitaceae, order Hypocreales (the old genus *Cordyceps* Fr.). Currently, many genera have segregated from the genus *Cordyceps*, such as *Metacordyceps*, *Tyrannicordyceps* (placed in family Clavicipitaceae); *Elphcordyceps*, *Ophiocordyceps* (in family Ophiocordycipitaceae); *Sphaerocordyceps*, and remaining *Cordyceps* species (placed in *Incertae sedis* within Hypocreales). Due to their special nutritional and healing values, *Cordyceps* is widely spreading in China, with a huge existing domestic market. In the Chinese market, *Cordyceps* is known as ‘Dongchong Xiacao (worm in winter, an herb in summer; *O. sinensis* (Berk.) Sung et al. 2007), which is the most expensive type and only produced from the Tibetan Plateau; other *Cordyceps* species in the markets are termed ‘fake Dongchong Xiacao.’

THE NUTRITIONAL COMPONENTS IN *CORDYCEPS*

Cordyceps is rich in various compounds considered nutritional such as vitamins (K, B1, B2, B12, and E); essential amino acids. Additionally, many mono-, di-, and oligosaccharides and many complex polysaccharides were found in *Cordyceps* besides trace elements (Na, K, Zn, Ca, Mg, Al, Fe, Cr, Cu, Mn, Zr, Pi, Se, Si, Sr, Ti, Ga, V, and Ni), proteins, nucleosides, and sterols. *Cordyceps* contains considerable quantities of polysaccharides, representing 3-8% of the mushroom's total weight, and these polysaccharides usually originate from fruiting bodies. *Cordyceps* polysaccharides are considered the major biologically active compounds besides nucleotides (Zhou et al., 2009; Mishra and Yogesh, 2011; Elkhateeb et al., 2019).

CHEMICAL COMPOSITION OF THE MOST COMMON *CORDYCEPS* SPECIES

Cordyceps sinensis (Berk.) Sacc.) is considered the most expensive and well-studied *Cordyceps* species. According to different chemical analyses, *C. sinensis* contains proteins, polysaccharides, fats, fiber, and carbohydrates, the famous bioactive compounds cordycepin (30-deoxyadenosine) and cordycepic acid (D-mannitol), and different vitamins (Ohta et al. 2007; Zhou et al. 2009).

The therapeutic potentials of *Cordyceps* depend mainly on the key actions of increased oxygen utilization, ATP production, and sugar metabolism stabilization. Many bioactive compounds originating from *Cordyceps* are responsible for those effects, such as cordycepin, cordycepic acid, polysaccharides, vitamins, and trace elements. The full bioactive compounds existing in *C. sinensis* are not yet identified. However, at least two compounds, cordycepic acid and cordycepin, have been identified and recommended as important bioactive compounds. Of all *Cordyceps* species, *C. militaris* is the only species that has been successfully cultivated and most intensively studied. The majority of *Cordyceps* products available in the markets are developed from the fruiting bodies of cultivated *C. militaris*. According to reported chemical investigations, *C. militaris* contains cordycepin, adenosine, polysaccharide, mannitol, trehalose, polyunsaturated fatty acids, δ -tocopherol, p-Hydroxybenzoic acid, and β -(1 \rightarrow 3)-D-glucan (Reis et al. 2013; Liu et al. 2014; Smiderle et al. 2014; Wen et al. 2017; Elkhateeb et al. 2019).

CORDYCEPS NATURAL GROWTH AND ARTIFICIAL CULTIVATION

The natural growing fruiting bodies of *Cordyceps* are rare, and their collection is an expensive process. Moreover, natural populations of key *Cordyceps* species are decreasing rapidly due to over-collection (Stone 2008;

Zhang et al. 2012), presenting the need for increased *in-vitro* cultivation using the artificial medium. While over 400 species under the genus *Cordyceps* have been identified, only 36 species have been successfully cultivated in artificial media (Sung et al. 1999; Yin and Qin 2009). The first large scale fruiting techniques used for growing *Cordyceps* reduced the natural growing cycle from 5 to 2 years; this technique included breeding the host larvae, *Thitarodes* (*Hepialus*), then placing about 100 larvae into shoe carton sized plastic containers covered with lids, which are filled with grassland soil containing roots and tubers of their natural foods collected from the wild, besides other roots from cultivation. Spores of *C. sinensis* were inoculated after two years, and about 10% of the larvae were actually taken over by *Cordyceps* and grew stromata (Yue et al., 2013). On the other hand, Arora et al. (2013) succeeded in using submerged conditions for culturing *Cordyceps sinensis* at pH 6 and a temperature of 15°C.

In previous studies, the medium used for the growth of *C. sinensis* was Sabouraud's dextrose supplemented with yeast extract broth medium, and different additives, carbon, and nitrogen sources were also investigated (Arora et al. 2009). The highest number of conidia was obtained under the physical stress of freeze-shock (Ren and Yao 2013). Sucrose has been reported as the best-tested carbon source for the growth of *C. Sinensis*. Similarly, beef extract and yeast extract were the best nitrogen sources (Seema et al., 2012). Furthermore, using folic acid meaningfully increased the yield, and adding calcium chloride and zinc chloride as micro and macronutrient increased the yield significantly. One of the optimum artificial techniques for culturing *C. sinensis* was utilizing sterile rice media at 9-13°C for 40-60 days. Then to induce stroma production, the temperature was lowered to 4°C and 13°C for 40 days to develop fruiting bodies (Cao et al. 2015). It should be highlighted that the growth of *Cordyceps* mycelium is mainly affected by some environmental factors and many factors such as temperature, growth media, and pH (Calam 1971). Still, after testing various media, potato dextrose agar was confirmed to be the optimum medium at pH ranging between 8.5-9.5 at 20- 25°C (Ruhul et al. 2008).

Artificial cultivation is achieved by inoculating reared larvae with cultured strains, and the infected larvae are monitored and fed indoors for one or two years. After that, *C. sinensis* could be collected. (Lo et al. 2013). *C. militaris* cultivation is much easier than *C. sinensis* in both solid and liquid media using different carbon and nitrogen sources since *C. militaris* can complete its life cycle when cultured *in-vitro* (Shrestha et al. 2004, Xiong et al. 2010). The artificial cultivation of *C. militaris* mycelium on synthetic media has recently been advanced, especially for cordycepin production, using different methods such as surface culture (Masuda et al. 2007) and submerged culture (Mao et al. 2005). Usually, *C. militaris* stromata production requires 35-70 days (Zhang and Liu 1997; Du et al. 2010). Culture duration depends on many conditions, such as the amount of medium, shape, and volume of the culture container. The development of *C. militaris* stroma cultivation *in-vitro* started with using insects to grow

stromata by Leatherdale (1970), followed by laboratory trials using various organic substrates by Yue et al. (1982). For commercial production of *C. militaris* stromata, cereals, including rice, have been widely used (Wen et al., 2008; Chen et al., 2011). Also, using substrates such as wheat grains, cottonseed coats, corn cobs, corn grain, bean powder, millet, and sorghum has shown promising results (Chen and Wu 1990; Zhang and Liu 1997; Gao and Wang 2008, Wei and Huang 2009). The optimum organic substrate currently used is a mixture of rice and silkworm pupae (Shrestha et al. 2005, Sung et al. 2006; Jin et al. 2009). Furthermore, brown rice, malt, and soybean were important sources of nutrition for *C. militaris* compared to chemical media (Xie et al. 2009). *C. militaris* cultivation needs a relatively low level of nitrogen (Gao et al. 2000) which may explain lower yields when using insects compared to higher yields reached when cereals were used in the culture. Plant hormones such as colchicines, 2, 4-D, and citric acid triamine can promote *C. militaris* stroma production. Also, potassium, calcium, and magnesium salts can increase the yield of fruiting bodies (Xiao et al., 2010).

Mycelia production for the large-scale production of bioactive compounds is also achievable and has been performed in submerged culture (Huang et al., 2006; Xie et al., 2009; Das et al., 2010). *C. militaris* cultivation has been improved, successfully producing a high yield of stromata and elevated cordycepin content (Sun et al., 2009; Du et al., 2010). The production of fruiting bodies has been studied for three successive generations (Hong et al. 2010; Xiao et al. 2010; Shrestha et al. 2012; Xiaoli et al. 2014).

CORDYCEPS AND HEALTH BENEFITS

The genus *Cordyceps* species are extensively studied due to the uncountable number of medical-biological activities used by their extracted compounds, with various medical and nutritional values. In traditional Chinese medicine, the main use of *Cordyceps* has been to treat asthma and other bronchial conditions and give energy and sexual power. Recent research now confirms the competence of *Cordyceps* in many other fields. One of the advances of modern research has been the discovery of cordycepin, which has a potent antibacterial action against the majority of bacterial species that have currently developed resistance to other commonly used antibiotics. *Cordyceps* showed remarkable activity during treating tuberculosis and human leukemia, as shown in many clinical trials in Asia and elsewhere (Halpern Georges 2007). *Cordyceps* was shown to improve the maximum amount of oxygen and improve respiratory function. Other components produced by *Cordyceps sinensis* include the deoxynucleoside 2', 3' deoxyadenosine. Also, Quinic acid derived from cordycepin obtained from *Cordyceps* exerts antimicrobial and antiviral activities. Many studies have reported the potency of *Cordyceps sinensis* in healing heart rhythm disturbances such as chronic heart failure and cardiac arrhythmia (Mishra and Yogesh, 2011; Wang et al., 2012).

Anticancer activities of *Cordyceps*

Various *Cordyceps-originated* bioactive compounds have a promising anticancer activity that was previously reported (El-Hagrassi et al., 2020). For example, cordycepin showed antitumor activity against B16 melanoma cells (Yoshikawa 2004 and 2007). In addition, cordycepin inhibited the mammalian target of rapamycin complex 1 in gallbladder cancer cells in-vitro, resulting in loss of cancer cell viability and apoptosis (Wong et al. 2010; Ferreira et al. 2010; Wu et al. 2014). *C. militaris* was found to inhibit U937 cell growth in a dose-dependent manner and limit human leukemia (Park 2005). *Cordyceps* has shown promising results in slowing and inhibiting the growth of cancer cells (Santhosh Kumar et al. 2014) and, in some cases, could reduce tumor size (Nakamura et al. 2003). Clinical trials on cancer patients have been conducted in many Asian countries, showing talented results in reducing tumor size (Wang et al. 2001), improving tolerance for chemotherapy and/or radiation (Zhou et al. 1998), and stimulating the immune system which, hence, enhances the efficiency of chemotherapy (Shin et al. 2003). Crude extract of *C. militaris* showed potent anticancer activity in a xenograft mouse model with RMA cell-derived tumors (Park et al., 2017). Additionally, some *Cordyceps* species have anti-leukemia activities and better suppressive effects of chemotherapy on bone marrow function as a model for cancer treatment (Liu et al. 2008; Wong et al. 2010; Ferreira et al. 2010).

Hypoglycemic and hypocholesterolemic effects

Cordyceps are found to regulate and lower blood sugar levels by improving glucose metabolism and conserving hepatic glycogen (Zhao et al., 2002; El-Hagrassi et al., 2020). *Cordyceps* can increase the secretion of glucokinase and hexokinase, which are glucose-regulating enzymes secreted by the liver (Kim et al., 2017). Polysaccharides are the key player in showing the hypoglycaemic activity of *Cordyceps*. For example, CS-F30, a polysaccharide extracted from *C. sinensis* culture mycelium, has been reported for its promising hypoglycaemic effect (Kiho 1996). Additionally, the plasma glucose level was reduced quickly after intravenous administration of CS-F30 in normal and streptozocin-induced diabetic mice (Kiho 1996). Another polysaccharide (CS-F10) was purified from a hot-water extract of *C. sinensis* cultured mycelia and consists of galactose, glucose, and mannose in a molar ratio of 43:33:24. CS-F10 lowers the plasma glucose level in normal, adrenaline-induced hyperglycaemic, and diabetic mice. Hypercholesterolemia is an indicator of a high risk of cardiovascular attack. El-Hagrassi et al. (2020) reported the role of *C. militaris* in lowering the total cholesterol level and the level of triglycerides. A hot-water extract of *C. sinensis* mycelia has been found to reduce total cholesterol concentration in the serum of mice by reducing LDL (low-density lipoprotein) hypocholesterolemic activities (El-Hagrassi et al., 2020). A hot-water extract of *C. sinensis* mycelia has been found to reduce total cholesterol concentration in the serum of mice by reducing LDL and very-low-density lipoprotein and increasing good cholesterol concentration (HDL cholesterol) (Koh 2003).

Improving kidney functions and liver disorders

Some clinical trials revealed that the administration of *C. sinensis* could significantly improve kidney function and boost the overall immunity of patients diagnosed with chronic renal failure (Guan et al. 1992). Additionally, treating patients with gentamicin-induced kidney damage helped recover 89% of normal kidney function in a relatively short time (Zhou et al. 1990). The mode of kidney enhancing the action of *Cordyceps* is explained by its ability to protect sodium pump activity of tubular cells, increase 17-ketosteroid and 17-hydroxycorticosteroid levels in the human body, reduce the content of calcium in certain tissues, and accelerate the regeneration of tubular cells (Zhou et al. 1990; Xu et al. 1995; Wang et al. 1998). *Cordyceps* is commonly used for the treatment of chronic hepatitis B and C. Using the antiviral drug, lamivudine, plus mixed extracts of *Cordyceps* with other medicinal mushrooms showed promising results for treating hepatitis B (Wang and Shiao 2000; Ng and Wang, 2005; Zhou et al. 2009). On the other hand, daily consumption of *Cordyceps* improved liver functions in patients who have post-hepatic cirrhosis (Zhu and Liu 1992; Zhou et al. 2009). *Cordyceps* extracts are used to help in the healing of both chronic hepatitis B and C (Wang and Shiao 2000).

Cordyceps as antioxidant and antiaging activities

One of the most potent bioactivities reported for *Cordyceps* extracts is their ability to protect cells from being damaged by free radicals. This activity corresponds to polysaccharide fraction (Yu et al. 2007; Wang et al. 2012). *Cordyceps sinensis* has potent antioxidant and anti-aging properties (Yamaguchi et al., 2000; Ji et al., 2009). Also, many studies elucidated the antioxidant effect of extracts obtained from *C. militaris* (El-Hagrassi et al., 2020). The fruiting bodies extract of *C. militaris* showed strong DPPH radical scavenging activity, which indicated high antioxidant activity. In contrast, the fermented mycelia extract had stronger total antioxidant activity and reduced capability (Dong et al. 2014). *Cordyceps* has been used for centuries as a remedy for weakness and fatigue by residents living in the high mountains of Tibet to give them energy which is achieved by increasing cellular ATP (Holliday et al. 2008). Nowadays, athletes utilize *Cordyceps* to overcome weakness and fatigue, increase endurance and boost energy levels (Liu et al. 1997). Moreover, clinical trials connecting chronic fatigue with aging patients revealed that treatment with *C. sinensis* improved fatigue and dizziness, increasing cold intolerance and amnesia (Mizuno et al. 1999; Chen et al. 2013; Wu et al. 2014).

Cordyceps for organs and glands protection

Cordyceps sinensis also has clear effects on other organ systems (Chen 1995; Zhang and Yuan 1997; Guo and Guo 2000; Xu 2006). For example, *C. sinensis* has sedative, anticonvulsant, and cooling effects on the central nervous system. In the respiratory system, *C. sinensis* has a potent relaxant action on bronchi, noticeably increases secretion of adrenaline from the adrenal glands, and participates in tracheal contraction caused by histamine; it also has an

expectorant antitussive and anti-asthmatic effects, and it also inhibits pulmonary emphysema. In the endocrine system, *C. sinensis* has effects as a male hormone. Polysaccharides extracted from *Cordyceps* can increase corticosterone levels in plasma. *Cordyceps* has been used in traditional medicine for decades to improve men's fertility. A study has proven the positive effect of using *C. militaris* mycelium on sperm motility, morphology, productivity, and enhancement of sexual activity (Lin et al. 2007). *Cordyceps* extracts contain adenosine, deoxyadenosine, corresponding adenosine type nucleotides, and nucleosides, which help stabilize heartbeat and correct heart arrhythmias (Pelleg and Porter 1990).

Cordyceps as anti-inflammatory

Commonly, the famous cordycepin is the compound causing the anti-inflammatory activity of numerous *Cordyceps* species (Won and Park 2005; Kim et al. 2006; Yang et al. 2011). *C. militaris* ethanolic extracts of cultured fruiting bodies and mycelia exerted an anti-inflammatory activity on the chick embryo chorioallantoic membrane angiogenesis and the croton oil-induced ear edema in mice (Won and Park 2005). On the other hand, an alkaline extract of *C. militaris* showed a strong anti-inflammatory effect against formalin-induced nociception and LPS-induced peritonitis in mice due to containing a potent anti-inflammatory compound (linear β - (1R3)-D-glucan) (Smiderle et al. 2014; Park et al. 2015). Adenosine is also extracted from *Cordyceps* species with numerous activities related to avoiding tissue damage as anti-inflammatory properties (Nakav et al. 2008; Tsai et al. 2010; Liu et al. 2015).

Cordyceps as antiviral agents

Many studies reported that cordycepin extracted from *C. militaris* could inhibit infection with the human immunodeficiency virus (Mueller et al. 1991). Cordycepin has shown antiviral activities against different viruses such as plant viruses and human viruses (influenza virus, Epstein-Barr virus, murine leukemia virus) (Ryu et al. 2014). The mode of killing or inhibiting actions of cordycepin is not fully understood, but several studies have elucidated the ability of cordycepin to inhibit numerous protein kinases (Glazer and Kuo 1977; Jin et al. 2011; Elkhateeb et al. 2019). On the other hand, crude extract of fruiting bodies of *C. militaris* showed promising in-vitro antirotavirus SA-11 agent activities (El-Hagrassi et al., 2020).

Cordyceps side effects and safety

Cordyceps is generally safe in the recommended dosage, and no major side effects were reported. (Das et al. 2010).

CONCLUDING REMARK

Cordyceps and its bioactive components and metabolites are golden mines with therapeutic potential against various fatal diseases. Developing new techniques

capable of cultivating species other than *Cordyceps militaris* can contribute to producing enough quantities of bioactive compounds such as cordycepin and cordycepic acid, which also may lower the cost of this expensive medicinal mushroom. On the other hand, further *in vivo* studies should be conducted in order to evaluate the clinical activities of *Cordyceps* metabolites which can be a step toward certifying its use as a medical drug.

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