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Review

Pharmacological and economical aspects of important species of *Cordyceps sensu lato*: A review

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Abstract

Cordyceps is a well-known endo-parasitic fungus commonly used in traditional Chinese medicine for a long time. The demand for *Cordyceps* is increasing daily because it is commonly used as a nutritional food, medicine, and supplement owing to its natural source. It is very attractive in almost all countries with no side effects. Most *Cordyceps* species have been studied in China, Bhutan, India, Japan, South Korea, and Nepal. We have discussed the important contents of *Cordyceps*, dietary source and nutritional value of Cordyceps, multiple pharmacological properties of four important *Cordyceps* species, *Ophiocordyceps sinensis, Cordyceps militaris, Cordyceps cicadae,* and *Cordyceps tenuipes*, along with the economic status of Cordyceps and its benefits in terms of medicine, supplements, and the cosmetics industry. Owing to the high demand and several benefits of *Cordyceps*, it offers mysterious economic improvements in developed and underdeveloped countries. Therefore, more attention is required to save the endangered species of *Cordyceps* to fulfil the medicinal and nutritional demands worldwide.

Keywords: *Cordyceps,* Pharmacological, *Ophiocordyceps sinensis, Cordyceps militaris*, *Cordyceps cicadae, Cordyceps tenuipes*.

1. Introduction

The *Cordyceps* genus (endoparasites) belongs to the kingdom of fungi and comprises approximately 400 species [1]. It belongs to phylum Ascomycota and is known as "sac fungi" [2]. Its hosts are arthropods, insects in larval form, spiders, mites, and several other fungi. Microscopic sexual structures developed from non-motile spores. Cordyceps manipulate host machinery for survival and reproductive process, *Cordyceps* manipulate their host machinery [3]. It is widely distributed throughout the world, but excessively found in Bhutan, China, India, Japan, Korea, Nepal, and Thailand, due to a favorable humid and warm climate [4], and is mainly distributed in alpine ecosystems in the Tibetan mountains and Himalayas; in China, most *Cordyceps* species are collected from the Tibetan ranges, Gansu, Sichuan, Qinghai, and Yunnan provinces [5]. Since 2000 BC, the genus Cordyceps has been known as a medicinal mushroom with different biological activities [7]. *Cordyceps* extracts have been used as ingredients in Traditional Chinese Medicine (TCM) and have attracted the attention of the pharmaceutical industry for the formulation of pharmaceutical products, supplements, and dietary food products [6]. *Cordyceps militaris*, an important TCM belonging to the Ascomycetes class, has been widely used in East Asia as a traditional crude extract for various disorders. It contains several beneficial active ingredients such as vitamins, functional proteins, polysaccharides, nucleotides, nucleosides, various oils, and sterols, which are utilized for multiple medicinal purposes [8]. More than 350 forms have been discovered in the broad insinuations of insect fungal parasites. Extensive research is being conducted on this species, which has greatly enhanced its medicinal importance. More than 2500 varieties of mushrooms are grown worldwide, and approximately 10 million tons of edible and medicinal mushrooms are distributed worldwide [9]. Like other medicinal herbs, *Cordyceps* is considered an important medicinal herb for the treatment of different disorders [11].

2. Contents of *Cordyceps*

Cordyceps is known for its effectiveness in the treatment of disorders related to the central nervous system, and as a sedative and anticonvulsant agent. They are also effective against respiratory diseases. *Cordyceps* can enhance

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the release of adrenaline from the adrenal glands, play an important role in the contraction of the trachea caused by histamine, and prevent endocrine pulmonary-emphysema (lung disease). *Cordycep*-based traditional medicine can increase plasma corticosterone levels and protect against renal, hypersexual, and hyperlipoedema conditions. Furthermore, it has been used against several types of cancer and helps manage homeostatic conditions. *Cordyceps*-derived polysaccharides have been widely accepted as immunomodulatory, cytotoxic, antitumor, antioxidant, and antibiotic agents [12].

2.1. Nitrogenous compounds

In biological systems, both nitrogenous bases and nucleosides may play major roles [13]. Nitrogenous compounds such as nucleosides, adenosine, cordycepin, guanosine, inosine, thymidine, and uridine have been isolated from *Cordyceps*. Cordycepin is an important compound used in TCM for various diseases. It is a derivative of adenosine isolated from different *Cordyceps* species and is widely used for cancer treatment because of its remarkable anti-angiogenic, anti-metastatic, and anti-proliferative properties with apoptosis induction [14]. Six important nitrogenous compounds extracted from different *Cordyceps* species are shown in Table 1 along with their molecular weights and PubChem CID, which disclose all information about a chemical compound.

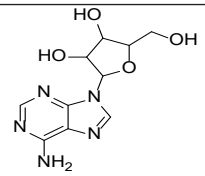
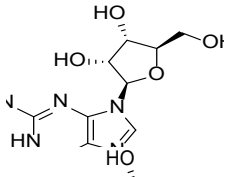
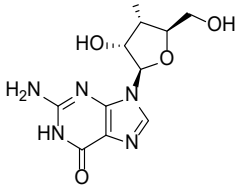
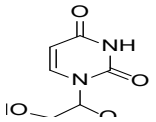
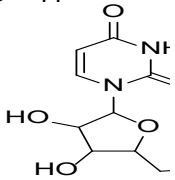
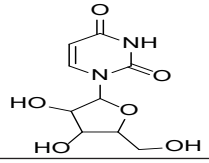
2.2. Polysaccharides

Polysaccharides are important components of *Cordyceps*, with certain pharmacological properties. *Cordyceps* fruiting bodies contain approximately 3-8 percent of polysaccharides in weight [15]. Polysaccharides in the form of extracellular polysaccharides, intracellular polysaccharides, exopolysaccharides, heteropolysaccharides, mannoglucans, and D-glucans are spread in various species of the *Cordyceps* genus and possess several biological activities, such as immunomodulatory, hypolipidemic, hyperglycemic, steroidogenic, anti-cancerous, anti-metastatic, anti-diabetic, anti-inflammatory, and anti-oxidative, to manage fatal diseases [16]. Twenty-one important polysaccharides extracted from the different *Cordyceps* species are shown in Table 2.

2.3. Sterols

Sterols are important functional components of *Cordyceps* and are naturally occurring organic compounds that belong to the lipid classification of biomolecules. *O. sinensis* is an important source of functional sterols with apoptosis-inducing properties. *Cordyceps*-derived sterols

Table 1. Nitrogenous compounds extracted from different *Cordyceps* species.

Chemical Name/ PubChem CID	Molecular Formula	Molecular Weight (g/mol)	Source	Chemical Formula
Adenosine/ 60961	$C_{10}H_{13}N_5O_4$	267.24	*Cordyceps militaris* *Ophiocordyceps sinensis*	
Cordycepin/ 6303	$C_{10}H_{13}N_5O_3$	251.24	*Cordyceps militaris* *Ophiocordyceps sinensis*	
Guanosine/ 135398635	$C_{10}H_{13}N_5O_5$	283.24	*Cordyceps militaris* *Ophiocordyceps sinensis*	
Inosine/ 135398641	$C_{10}H_{12}N_4O_5$	268.23	*Cordyceps militaris,* *Ophiocordyceps sinensis*	
Thymidine/ 5789	$C_{10}H_{14}N_2O_5$	242.23	*Cordyceps militaris* *Ophiocordyceps sinensis*	
Uridine/ 6029	$C_9H_{12}N_2O_6$	244.2	*Cordyceps militaris,* *Ophiocordyceps sinensis*	

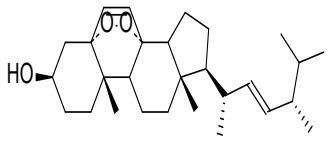
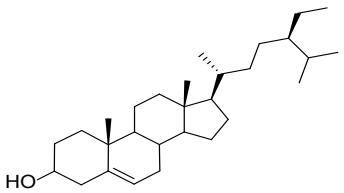
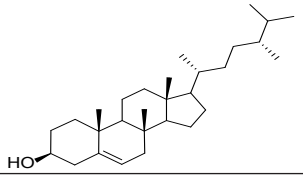
have a range of medicinal properties, including cytotoxicity and antimicrobial activity [17]. Ergosterol peroxide, a derivative of ergosterol found in various species of the genus C*ordyceps*, such as *O. sinensis* and *C. cicade*, has the ability to improve TGF-beta 1 induced stimulation and is beneficial for the prevention of renal fibroblasts [18]. It also inhibits proliferation of cancer cell lines.

Cerevisterol is an ergostanoid found in various fungi. Wang et al. explored the importance of the anti-mycobacterial and anti-fungal activities of Cerevisterol in *C. morakotii* BCC 56811. Beta-Sitosterol is a very significant phytosterol found in different plants and fungal species and four very beneficial sterols (beta-sitosterol, campesterol, cholesterol, and ergosterol) were very first time determined by utilizing the experimental techniques (pressurized liquid extraction, trimethylsilyl derivation and GC-MS analysis) by Yang et al., in *Cordyceps species, O. sinensis, C. liangshanensis, C. gunnii,* and *C. militaris* [19]. Table 3 shows some important sterols extracted from different Cordyceps species, along with their molecular weights and PubChem CID, which reveals all information on the respective chemical compounds.

Table 2. Polysaccharides extracted from different *Cordyceps* species.

Chemical Name	Source	Chemical Name	Source
C-3	*Cordyceps cicadae*	CS-F3	*Ophiocordyceps sinensis*
CG-1	*Metacordyceps gunni*	CS-F10	*Ophiocordyceps sinensis*
Ch-1	*Cordyceps hawkesii*	CS-F30	*Ophiocordyceps sinensis*
Ch-2	*Cordyceps hawkesii*	CS-81002	*Ophiocordyceps sinensis*
CI-A	*Cordyceps cicadae*	CSP-1	*Cordyceps militaris*
CI-P	*Cordyceps cicadae*	CSP-2	*Cordyceps militaris*
Ck_1-A	*Cordyceps kyushuensis*	CSP-3	*Cordyceps militaris*
Ck_3-A	*Cordyceps kyushuensis*	CT-4N	*Ophiocordyceps sinensis*
CM-1	*Cordyceps militaris*	CO-1	*Tolypocladium ophioglossoides*
CMB	*Cordyceps militaris*	SCP-1	*Ophiocordyceps sinensis*

Table 3. Sterols extracted from different *Cordyceps* species.

Chemical Name/ PubChem CID	Molecular Formula	Molecular Weight (g/mol)	Source	Chemical Formula
Ergosterol peroxide/ 5351516	$C_{28}H_{44}O_3$	428.6	***Ophiocordyceps sinensis Cordyceps cicade***	
Cerevisterol / 10181133	$C_{28}H_{46}O_3$	430.7	***Cordyceps morakotii***	
Beta-Sitosterol/ 222284	$C_{29}H_{50}O$	**414.7**	*Ophiocordyceps sinensis Cordyceps liangshanensis Metacordyceps gunni Cordyceps militaris*	
Cholesterol/ 5997	$C_{27}H_{46}O$	**386.7**	*Ophiocordyceps sinensis Cordyceps liangshanensis Metacordyceps gunni Cordyceps militaris*	
Campesterol/ 173183	$C_{28}H_{48}O$	**400.7**	*Ophiocordyceps sinensis Cordyceps liangshanensis Metacordyceps gunni Cordyceps militaris*	

2.4. Proteins and amino acids

Proteins comprise 18 amino acids, including aspartic acid, threonine, serine, glutamate, proline, glycine, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, lysine, histidine, cysteine, and tryptophan. After hydrolysis, the amino acid content was generally 20– 25%, the lowest was 5.53%, and the highest was 39.22%. The maximum quality of Glutamate [20].

3. Pharmacologically and systematically important species of *Cordyceps*

There are more than 400 species of *Cordyceps* found in different countries, and almost all species of *Cordyceps* are medically important because of their active ingredients that are used as functional foods, traditional alternative medicines, crude herbs, supplements, and essential oils. In this review, we have mentioned the importance of these four species in terms of their diversity and economic and medicinal values. Table 4 shows a summary of the systematic positions of the four selected species of *Cordyceps*. Figure 1 presents images of these species in their natural habitat, and Table 5 shows the pharmacological activities of the selected species.

3.1. *Ophyocordyceps sinensis*

Ophyocordyceps sinensis is an important medicinal species worldwide. Figure 1 shows the natural habitat of *O. sinensis*.

3.1.1. Morphological characteristics

Morphologically, *O. sinensis* has peculiar characteristics with bright colored stromata, dark brown to black colored appearance, rarely branched, dusky pigments along with a tough nature to flexible stromata arising from the prothorax of the host with a length of approximately 40-100*2-5 mm, with a sterile tip and continuous head through the stipe, larger than the stipe [21].

3.1.2. Host

The hosts of *O. sinensis* are larvae of *Ahamus, Bipectilus, Forkalus, Thitarodes,* and *Hepialiscus* species that are still embedded vertically in saturated soil [22].

3.1.3. Distribution

Ophiocordyceps sinensis is commonly found in different regions of Tibet, China (Gansu, Sichuan, Qinghai, and Yunnan), Japan, Bhutan, Nepal, and India [23].

3.1.4. Pharmacological properties

Ophiocordyceps sinensis has several bioactive contents such as Cordycepin (3'deoxyadenosine, $C_{10}H_{13}N_5O_3$), adenosine ($C_{10}H_{13}N5O_4$), ergosterol ($C_{28}H_{44}O$) with nucleosides and nucleobases as the major isolated compounds. Adenosine-containing *O. sinensis* extract contributes to the hypotensive and vaso-relaxant functions of the fungus [24]. The simple extract and partly distilled sections were observed for their ability to inhibit superoxide anions and release elastase to explore the chemical components and biofunctions of *O. sinensis* mycelia. In addition, five new compounds, cordy lines A – E, were identified [25].

Sterol derivatives are vital to the *O. sinensis* band. Chromatography using a silica gel column and HPLC was used for the separation and purification of *O. sinensis* H1-A sterols. We were initiated to quash active human mesangial cells (HMC) and relieve the clinical histological improvement of IgAN (Berger's disease). A study found that pure H1-A might be useful for the treatment of systemic lupus erythematosus, and H1-A has been suggested to be active in the signal transaction control of autoimmune disorders, apoptosis, and protein modulation of Bcl-2 and Bcl-XL. *Ophyocordyceps sinensis* contains a large quantity of polysaccharides, which range from 3% to 8% of the total weight and are usually derived from strong fermentation in mycelium and broth fruiting bodies. Polysaccharides demonstrate highly potent antiplatelet activity that could include adenylate cyclase/cyclic AMP activation and subsequent inhibition of intracellular signals such as Akt and MAPK, resulting in the inhibition of platelet activation. Early herbal pharmacopeia reported an improvement in mushroom activity in the protection of lung-neck phlegm resolution, homeostasis, and erectile dysfunction. According to the traditional Chinese medicine theory, the main effect of *O. sinensis* is to enrich the lungs, which involves chronic lower back pain, cold resistance, excessive mucus and tears, chronic cough, and wheezing. *Ophyocordyceps sinensis* also has antibacterial activity, decreases asthma, reduces blood pressure, and increases heartbeat [26].

3.2. *Cordyceps militaris*

Cordyceps militaris has several biological activities and has been used as edible mushroom worldwide, figure 1 shows *C. militaris* in its natural habitat [27].

3.2.1. Morphological characteristics

Morphologically *C. militaris* has a very attractive appearance with independent stromata, yellowish or orange in color, 20-100*1-6mm, head continues with the stipe but is wider, cylindrical or a little spherical in shape [27].

3.2.2. Host

Hosts of *C. militaris* are *Coleopteran, Dipteran, Hymenopter* and *Lepidoteran* species, frequently horizontally buried down in the humid soil [27]**.**

3.2.3. Distribution

Cordyceps militaris is widely distributed worldwide [28].

3.2.4. Pharmacological properties

There have been many attempts to derive beneficial materials from sunken mycelial crops for integration into pharmaceuticals and functional foods. Cultivating this fungus to be used as a medication in large and adequate amounts in technical studies is of vital importance. Various investigators have adjusted the conditions for cultivating fungi, for example, biological components of cultivation, illumination, gene expression, and conditions of traditional culture. Using capillary electrophoresis (CE) and HPLC [23], a simple and rapid method can be used to monitor batch-to-batch dissimilarities in plant yields obtained under optimized conditions. Deep ocean water was used to raise *C. militaris* in a sunken solid environment. Fermentation products are currently being tested for *C. militaris*. The results showed that cordycepin production could be substantially increased [29]. In addition, a solid leftover medium of *C. militaris* was used to prepare highly efficient cordycepin with minimal solvent use [24]. Technologies applied to *C. militaris* cultivation have

Table 4. Systematic position of four species of *Cordyceps sensu* lato.

Kingdom	**Fungi**	**Fungi**	**Fungi**	**Fungi**
Phylum	Ascomycoa	Ascomycoa	Ascomycota	Ascomycota
Sub-phylum	Pezizomycotina	Pezizomycotina	Pezizomycotina	Pezizomycotina
Class	Sordariomycetes	Sordariomycetes	Sordariomycetes	Sordariomycetes
Subclass	Hypocreomycetidae	Hypocreomycetidae	Hypocreomycetidae	Hypocreomycetidae
Order	Hypocreales	Hypocreales	Hypocreales	Hypocreales
Family	Ophiocordycipitaceae	Cordicipitaceae	Cordicipitaceae	Cordicipitaceae
Genus	*Ophiocordyceps*	*Cordyceps*	*Cordyceps*	*Cordyceps*
Species	***Ophiocordyceps sinensis***	***Cordyceps militaris***	***Cordyceps cicadae***	***Cordyceps tenuipes***

Table 5. Pharmacological activities of selected four species of *Cordyceps sensu* lato.

Ophiocordyceps sinensis	***Cordyceps militaris***	***Isaria cicadae***	***Cordyceps tenuipes***
Anti-aging and sexual activities	Anti-malarial agent	Improve lipid profile (decease blood cholesterol and triglycerides)	Anti-cancerous agent
Boost up ATP energy in body	Anti-fatigue agent	Anti-cardiovascular agent	Lower blood sugar level
Prevention of memory loss and Alzheimer's disorders	Prevent sutoimmune disorders	Leukocytes improvement and elevation of spleen index	Neurotrophic factor biosynthesis in the glial cell lines
Anti-leukemia agent	Neuroprotective agent	Anti-immunomodulatory agent	Anti-malarial agent
Anti-viral agent	Anti-microbial agent	Protection of liver, kidney, spleen and thymus	Anti-pathogenic effects
Prevent autoimmune disorders	Anti-bacterial agent	Inhibit the lipid peroxidation of cell membranes	Anti-oxidant agent
Improve lipid profile and cholesterol in body.	Protection of liver disorders.	Elevates the number of peripheral white blood cells.	Anti-hyperglycemic agent.
Anti-oxidant agent	Anti-viral agent	Anti-diabetic agents	Anti-bacterial agent
Anti-fibrotic agent	Prevent chromic kidney disorders	Anti-cancerous agents	
Improve blood circulation and blood sugar metabolism	Anti-fungal agents	Improve eye vision and conditions of chronic eye disease	
Anti-inflammatory agent	Prevent chromic lungs disorders	Treatment of pneumonia	
Prevent chromic kidney disorders	Anti-HIV agent	. Anti-aging agent	
Prevent chromic lungs disorders	Anti-cancer agent	Anti-fatigue agent	
Anti-cancer agent.			
Breast cancer, pre-myelocytic cancer, hepatocellular cancer and liver cancers	Improve sexual disturbance	Anti-bacterial agent	
Protect brain infarctions	Anti-insectidal properties		
Improve stamina	Anti-inflammatory effects		
Improve anemia and sweats at night	Anti-fibrotic effects		
Prevent cardiac arrhythmia.	Anti-oxidant agent		
Improve pain in bones diffractions of knee and lumbar puncture	Anti-aging effects.		
Anti-diabetic agent	Anti-hypoglycemic improvement		
Adjunct therapy in cancer chemotherapeutic treatments	Anti-angiogenic effects		
Anti-leprosy and tuberculosis effects	Anti-diabetic agent		
Hypotensive and vaso-relaxant	Anti-proliferative effects		
Enhance protection against cerebral ischemia	Improve hypolipidemia		
Anti-neoplastic agent	Steroidogenic effects		

Fig. 1. Pharmacological important species of *Cordyceps sensu* lato.

been thoroughly investigated to produce fruiting bodies that have been cultivated and amplified. Various chemical components of *C. militaris*, such as polysaccharides, carbohydrates, and derivatives of cerebrosides, sterols, nucleotides, nucleosides, proteins (cyclic dipeptides and amino acids), and essential oils, have been isolated. In one study, by determining their effect on free radical NO and cytokines (TNF-α and IL-12), the researchers verified the isolation of ten pure *C. militaris* compounds together with the evaluation of their biological activity [30]. The most active isolated compounds were cordycepin, ergosterol, 3, 4-O-isopropylidene-D-mannitol, D-mannitol and ergosterol peroxide, which inhibited the production of inflammatory mediators and proliferation of human cancer cells. A previous study described the decontamination of the cerebroside, nucleotides, and sterols of *C. militaris* fruiting bodies. The anti-inflammatory activity of the isolated compounds was demonstrated in LPS-stimulated RAW 264.7, by their inhibitory effect on the aggregation of pro-inflammatory iNOS protein and decreased expression of COX-2 proteins. This is the first study to report the cerebroside anti-inflammatory activity of this TCM. Another study discovered non-volatile components of *C. militaris* mycelia [31].

3.3. *Cordyceps cicadae*

Cordyceps cicadae is one of the most important species in terms of medicine worldwide, but very little information is available on this species, and more research is required to explore the properties of *C. cicadae*. Figure 1 shows the natural habitat of *C. cicadae* [32].

3.3.1. Morphological characteristics

Morphologically *C. cicadae* appears as horn-like protuberances on Cicada's mountain heads [32].

3.3.2. Host

Cordyceps cicadae can parasitize multiple hosts [32].

3.3.3. Distribution

Cordycep cicadae, also known as Isaria cicadae Shing is normally distributed in tropical and sub-tropical regions with a temperature of 18-24 ° C and relative humidity of more than 80%. *Cordycep cicadae* generally grow vertically at an altitude of 700-950 m on sunny slopes. *Cordycep cicadae* is most commonly seen in the provinces of Fujian, Zhejiang, Sichuan, Jiangsu in Yunnan and Tibet plateau in China [33]. *Cordyceps cicadae* is distributed mostly in low-altitude mountains and forest regions, in Japan, south of Fukushima, Jeju Island in South Korea, Taiwan's northern mountains and bamboo forests, and in Ruisui, Guangfu and Yuli Townships in Hualien County and also in Thailand's Southeast Asia, North America, and Europe [34].

3.3.4. Pharmacological properties

The metabolic components of *Cordyceps cicadae* include several bioactive medicinal compounds such as adenosine, ergosterol, cordycepin, cordycepic acids, polysaccharides, macrolides, and other metabolites. Recent studies have shown that *C. cicadae* plays a significant role in improving immune regulation and renal function and has anti-diabetic, antioxidant, antibacterial, and antitumorigenic properties. *Cordyceps* cicadae is one of the most popular traditional Chinese medicinal products and has been used in China for approximately 1,600 years, 800 years longer than that of *Ophiocordyceps sinensis. Cordyceps cicadae* show wind and heat dissipation operations, relieves hallucinations, enhances eyesight, prevents eye cloudiness, and promotes explosions. Shi-Zhen Li also reported, *C. cicadae* with the same efficacy as *Periostracum cicada*, was used mostly in the action of childhood seizures and morose nightly weeping of children, shiver and malaria [35].

3.4. *Cordyceps tenuipes*

Cordyceps tenuipes is a newly discovered species with very little information available; therefore, more research is required to explore the importance of *C. tenuipes* in different regions of the world. Figure 1 shows the natural habitat of *C. tenuipes* [36].

3.4.1 Morphological characteristics

Morphologically, *Cordyceps tenuipes* have a golden silky yellow color, and Eolrukmal and Hukpyobeom appear in the larval stage with unusual markings[36].

3.4.2. Host

Cordyceps tenuipes are usually parasitic with sexual and asexual morphs on lepidopteran pupae [37].

3.4.3. Distribution

Cordyceps tenuipes are broadly found worldwide, especially in Europe, South Asia, North America, Oceania, and Africa [37].

3.4.4. Pharmacological properties

Studies have shown that *C. tenuipes* and its effective principles have a wide range of pharmacological activities, including immune suppression, anticancer, insect resistance, antibacterial, antiviral, anti-depression, anti-aging, antioxidant, blood sugar control, blood lipid control, and liver resistance [37]. Therefore, this mushroom is widely used in East Asian nations as a tonic and medicine. *Paecilomyces tenuipes*, a famous Chinese entomopathogenic medicinal fungus, from many years, has been used in medicine in China, Japan, Korea, and other countries. *Paecilomyces tenuipes* has gradually become notable for its antidepressant, antitumor, and immunomodulatory effects

because it includes polysaccharides, adenosine, cordycepin, sterols, and cyclopeptides. *Paecilomyces tenuipes* possesses anticancer activity in vivo and exhibits significant cytotoxicity against cancer cell lines [38].

5. Economic values of *Cordyceps*

The broad spectrum of *Cordyceps* values the international market in terms of food, medicine, and supplements. Raw crude *Cordyceps* or its powdered extracts play an important role in improving the economy of various countries, such as Bhutan, China, India, Japan, Korea, and Nepal. Consequently, because of its several health benefits, *O. sinensis* is one of the most expensive and highly used fungi in the Himalayan region. The requirement for *O. sinensis* is around twenty-five hundred individuals per kilogram. Figure 2 represents the average price scale of *O. sinensis* in the drug market and non-market transactions, and a graphical representation shows the fluctuation of the market price every year from June 2013 to June 2019. In 2014 and 2016, the price was higher than that in other years (190000 Yuan per kg). The demand for *O. sinensis* in the Chinese market is very high, reaching approximately 70-100 tons annually [39].

6. Dietary source and nutritional value of *Cordyceps*

There are several edible mushrooms in the world, among which *Cordyceps* mushrooms contain a wide range of nutritionally important components, including various types of essential amino acids; vitamins such as B1, B2, B12, and K; different types of carbohydrates such as monosaccharides, oligosaccharides, and several medicinally important polysaccharides, proteins, sterols, nucleosides, and other suggested elements. *Cordyceps* contains monosaccharides, disaccharides, oligosaccharides, multiple compound polysaccharides, proteins, sterols, nucleosides, and trace elements. *Cordyceps* contains an excess of polysaccharides, which account for 3–8% of the entire weight and are generally extracted from the fruiting bodies as the most bioactive component [40].

7. Supplements of *Cordyceps*

Regular use of dietary supplements is best known to reduce the risk of infection, maintain good nutrition, and optimize homeostasis. Therefore, research into complete package energy foods is in high demand, which can have active, non-toxic, antioxidant, and energetic properties. Figure 3-6 demonstrates the detailed information of important extracts of *C. militaris* and *O. sinensis* used in terms of medicine/supplements, mostly used to boost energy levels, improve the immune system, and treat several other diseases worldwide. A sportsman looks for a large amount of physical and psychological energy during the training. During this time, athletes consume a large amount of energy and other substances to retain their physical energy and strength [29]. Thus, individuals looking for a complete package of energy, and we know that it is therefore not possible to give them a complete package of energy and substances through food and nutritional specialists who are facing many problems in this regard [24]. One of the energy sources is Cordyceps, which is gaining a great deal of attention as a food supplement or full energy kit for athletes' health. The modern use of *Cordyceps* in Sikkim, India, has been found among most local folk healers/modern healers who take advantage of Cordyceps to treat 21 ailments. One research group from China claimed that *Cordyceps* helps in the removal of lactate, enhances the metabolism of lactate energy in mice cells, and allows athletes to perform more anaerobically [30]. There are a few other studies on the curative impact of *Cordyceps* involving different research models and clinical trials in voluntary athletes [26]. Clinical research has shown that *Cordyceps* increases cellular bio-energy ATP concentration [15] by increasing useful energy and improving internal mechanisms, resulting in increasingly efficient oxygen use.

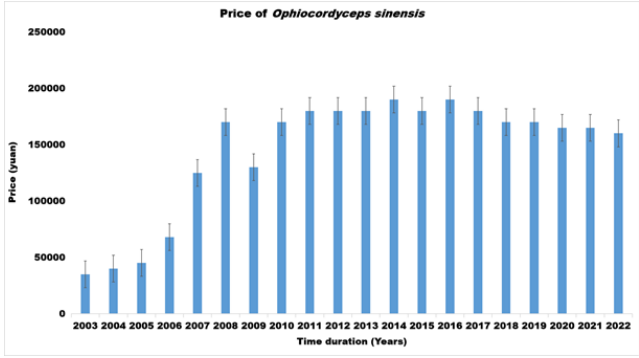


Fig. 2. Trends in the price of *Ophiocordyceps sinensis* from 2003 to 2022.

8. Benef ts of *Cordyceps* in cosmetics industry

Cordyceps is very beneficial for various skin disorders and has received more attention in the pharmaceutical and cosmetic industries because various products of *Cordyceps* species have potential for skin care and delay the aging process. The high concentration of free radicals due to metabolic reactions in the human body contributes to several metabolic disorders during aging. Currently, numerous compounds are synthesized as antioxidant ingredients in cosmetics, which have certain toxic contents and worse effects; consequently, there is a need for more research on the use of natural antioxidants that could be harmonious with the body. *Ophiocordyceps sinensis* extracts are useful as anti-tyrosinase and anti-elastase agents, and provide protection from the harsh effects of sunlight along with anti-collagenase activity. A very important chemical compound of *Cordyceps*, "Cordycepin" possesses various medicinal activities and is an active ingredient for skin care, anti-photo aging and anti-pigmentation processes, therefore utilized in various cosmetics products. Ultraviolet radiation is the main cause of DNA damage and results in photoaging and skin carcinoma, whereas *Cordyceps* extracts have the potential to become photoprotective agents and decrease the risk of skin cell carcinoma [41].

9. Conclusions and future directions

Several aspects of *Cordyceps* have been discussed in this review, indicating that *Cordyceps* is one of the best sources of natural food and novel treatments for fatal health issues, and most importantly, improves the economy of different countries. Several species of *Cordyceps* are the most important herbs and medicinal mushrooms, with several bioactivities against heart-related disorders, respiratory problems, and cardiovascular complications, and can lower serum triglycerides and maintain the lipid profile. *Cordyceps* mushroom-based diet could also improve the nutritional requirements of the body, boost energy le-

vels, and improve blood supply. This diet enhances blood circulation in the heart and brain, releases stress, and improves blood pressure. *Cordyceps* extracts contain antioxidants that can restrict cellular destruction and have been presented as anti-inflammatory agents. *Cordyceps* has no prominent side effects and possesses several health benefits; therefore, pharmaceutical companies should pay more attention to FDA-approved medication based on *Cordyceps* because our society relies more on herbal treatments and medicines from plant sources, and it is their general thinking that plant-based or natural medicines are harmonious for mankind. Although several plant-based medicines have severe side effects, pharmaceutical companies are required to overcome these side effects and produce novel medicines from *Cordyceps* to treat fatal diseases.

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