Medicinal mushrooms as a new source of natural therapeutic bioactive compounds

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Received 19 March 2019
Accepted 17 April 2019

Egyptian Pharmaceutical Journal 2019, 18:88–101

In the ancient books of traditional medicines, medicinal mushrooms were occupying the headlines, and the main topics were confirming to their miraculous therapeutic powers. The presence of various phenolic compounds, polysaccharides, and terpenoids and other compounds, is the reason for their potent biological activities as anticancer, antioxidant, antimicrobial, antiaging, hepatic protective, hypoglycemic, hypocholesterolemic, and much more biological activities are discovered every day. Many mushroom genera are famous for their promising therapeutic capabilities. One of the mushrooms genera attracting attention is *Cordyceps* which has long been used in Asian countries for maintaining long and healthy life. Numerous studies on different metabolic activities of *Cordyceps* have been performed both *in vitro* and *in vivo*. This review describes the importance of medicinal mushrooms with focus on *Cordyceps* as an example of globally commercialized mushrooms.

Keywords:
bioactive, medicinal mushrooms, natural product

Egypt Pharmaceut J 18:88–101

1687-4315

Introduction

Mushrooms are known from centuries to be used as food and medicine. They are a group of macrofungi belonging to ascomycetes and basidiomycetes, and they obtain their nutrition through being saprotrophs, parasites, or symbiotic as mycorrhiza [1]. Mushrooms have a reproductive phase (fruiting bodies) and a vegetative phase (mycelia) [1]. Mushrooms have a high nutritional value due to their contents of proteins, fats, volatile oils, carotenoids, phenolic compounds, flavonoids, and vitamins such as vitamins B1, B2, B3, C, and ergosterol that can be easily converted into vitamin D2 [1–3]. Nowadays, medicinal mushrooms are regarded as functional foods, and exist as over-the-counter health supplements used in complementary and alternative medicines [4]. The diversity of compounds extracted from mushrooms has attracted attention as a mine for novel compounds with new action mechanisms or potential activities against current life-threatening diseases [3]. Generally, biologically active compounds exist as components of their cell wall (polysaccharides such as β-glucans), proteins, or as organic secondary metabolites (steroids, terpenes, phenolic compounds, among others). The activity of these compounds depends strongly on many factors such as the type of mushroom, its development stage, and its growing conditions [5]. Various biological activities have been reported for extracts and/or compounds extracted from mushrooms such as anticancer, anti-inflammatory, hypoglycemic, antimicrobial, antioxidant, immunomodulatory, antiviral, hepatoprotective, anti-neurodegenerative, antiangiogenic, and hypocholesterolemic activities [6–8].

Bioactive compounds in medicinal mushrooms

Various compounds are responsible for the therapeutic activities of many mushrooms genera. The main group of compounds will be highlighted as follows.

Polysaccharides represent the major compounds existing in medicinal mushrooms, and they exhibit antioxidant, anticancer, antidiabetic, anti-inflammatory, antimicrobial, and immunomodulatory activities [9–11]. Glucan polysaccharides especially β-glucans have been reported to exhibit antimicrobial activity, hypoglycemic, and enhance immunity through the activating macrophages [12–14]. Biologically active glucans were extracted previously from mushroom mycelia and fruiting bodies of many mushrooms such as *Pholiota nameko* [15], *Caripia montagnei* [16], *Agaricus blazei* [17], and *Lactarius rufus* [18]. Other glucans with biological activities were isolated from different mushrooms such as lentinan from *Lentinula edodes* [19], pleuran

from *Pleurotus ostreatus* [20], maitake D-fraction isolated from *Grifola frondosa* [21], Schizophyllan from *Schizophyllum commune* [22], and ganoderan A and B, from *Ganoderma lucidum* [3].

Terpenes are the compounds responsible for the antioxidant, anticancer, and anti-inflammatory activities among many other biological activities exerted by mushrooms [1,23]. The fruiting bodies and spores of Lingzhi or Reishi mushroom (*G. lucidum*) were previously reported as a source of several triterpenes such as ganoderic acids, lucidenic acids, and lanostane-type triterpenic acids [24–27]. On the other hand, various sterols and triterpenes such as inotodiol, trametenolic acid, ergosterol, and ergosterol peroxide were previously isolated from the chaga mushroom (*Inonotus obliquus*) [6,28,29].

Phenolic compounds are responsible for antioxidant activities in mushroom extracts through acting as decomposers of peroxidase, inactivators of metals, oxygen scavengers, or inhibitors of free radicals [30]. Phenolic compounds include phenolic acids, oxidized polyphenols, hydroxybenzoic acids, flavonoids, tannins, hydroxycinnamic acids, stilbenes, and lignans [31]. A long list of phenolic compounds were isolated from mushrooms. Examples are the polyphenol, myricetin, isolated from *Craterellus cornucopioides* [32], pyrogallol isolated from *Agaricus bisporus* [33], grifolin and grifolin derivatives extracted from *Albatrellus ovinus* [34]; hericenones C, D, E, F, G, H isolated from *Hericium erinaceus* [35].

On the other hand, mushrooms produce many bioactive proteins and peptides, such as lectins, fungal immunomodulatory proteins, ribosome-inactivating proteins, and laccases [1]. The antifungal peptide pleurostrin was from *P. ostreatus* [36]. The antiviral peptide (SU2) was isolated from *Russula paludosa* [37]. The antifungal peptide, agrocybin, was extracted from *Agrocybe cylindracea* [38]. The peptide Cordymin, exhibiting anti-inflammatory activity, was isolated from *Cordyceps sinensis* [39] and from *Cordyceps militaris* [40].

There are many genera of medicinal mushrooms known for their use as a source of therapeutic bioactive compounds such as *Metacordyceps* spp. (Fig. 1), *Ganoderma* spp. (Fig. 2), Jelly Mushroom

Figure 1

Metacordyceps spp.

Figure 2

Ganoderma spp.

Auricularia spp. (Fig. 3), and Truffles Ex. *Termania* (Fig. 4, photographs taken by Waill A. Elkhateeb).

In this review, *Cordyceps* will be discussed in detail as an example of a promising source of therapeutic bioactive compounds.

Cordyceps

The fruiting bodies of *Cordyceps* fungi often erupts from the head of the larva and adult stages of many different species of insects [41]. *Cordyceps* are entomophagous fungi from the phylum Ascomycota, family Ophiocordycipitaceae, order Hypocreales, and they are known to parasitize many orders of insects at different life stages from larva to adult stages [42–45]. Numerous species within the genus have a golden reputation due to their long safe history of use in traditional medicines [42]. They have been used for more than2000 years in China for treating infectious diseases [41,46,47]. The *Cordyceps* genus contains some of the most highly prized and revered of all medicinal fungi. Grasslands, providing habitat for Thitarodes ghost moths and thus for *C. sinensis*, are a particularly important habitat [48].

The most famous and widely used species of *Cordyceps* is *C. sinensis* (Berk.) Sacc. The host range of this species is wide, including different species of Lepidopteran larvae [43,44,49] A similar species, *C. militaris* (L.:Fr.) link or as commonly known, the orange caterpillar fungus [50], has a similar chemical composition and medicinal biological activities as *C. sinensis* [51–53].

Cordyceps in the wild

Generally, *Cordyceps* species feed on insect larvae and sometimes they also parasite on mature insects. *Cordyceps* grow on all groups of insects – crickets, cockroaches, bees, centipedes, black beetles, and ants, to name a few. Although there are several species known to have medical value, only a few are cultivated and the most popular and well known are *C. sinensis* and *C. militaris* [54]. However, *Cordyceps* are not limited to insects and may grow on other arthropods. This group belongs to the order Hypocreales, which includes 912 known species that are assigned to the families Cordycipitaceae and Ophiocordycipitaceae [55–57]. *Cordyceps* only refers to the macrofungi, and these macrofungi were previously placed in the old genus *Cordyceps*

Figure 3

Jelly mushroom *Auricularia* spp.

Figure 4

Truffles Ex. *Tirmania* spp.

Fr. (Clavicipitaceae, Clavicipitales). Owing to their special edible and medicinal values, *Cordyceps* is very popular in China, where a huge domestic market exists [56].

Important components of *Cordyceps*

Cordyceps have a wide range of various compounds, some are characterized as nutritional compounds, since they possess all the important amino acids, vitamins such as K and E, besides the water-soluble B vitamins (B1, B2, and B12). In addition, they contain many sugars, including monosaccharides, disaccharides, and oligosaccharides, and many complex polysaccharides, proteins, sterols, nucleosides, and trace elements (Na, K, Ca, Mg, Al, Fe, Cu, V, Pi, Se, Ni, Sr, Si, Ti, Cr, Ga, Zn, and Zr). *Cordyceps* contains abundance of polysaccharides, which represents in the range of 3–8% of the overall weight, and commonly originated from the fruiting bodies. *Cordyceps* polysaccharide is one of the main bioactive components [41].

Cordyceps sinensis natural products

Ophiocordyceps sinensis (≡*C. sinensis* (Berk.) Sacc.) is the most expensive and the most extensively studied *Cordyceps* species. *C. sinensis* contains crude fats, proteins, fiber, carbohydrate, cordycepin (30-deoxyadenosine), cordycepic acid (D-mannitol), polysaccharide, and a series of vitamins. The therapeutic applications of *Cordyceps* are focusing mostly on the major effects of increasing utilization of oxygen and production of ATP, besides stabilizing sugar metabolism in the blood. Such activities may be attributed to compounds such as cordycepin, cordycepic acid and numerous vitamins, polysaccharides and trace elements. Although all the medically active compounds of *C. sinensis* are still unknown, at least two chemical compounds, cordycepin and cordycepic acid, have been purified and identified as medically important active compounds. It is now believed that cordycepic acid is, in fact, D-mannitol, and that cordycepin is 30-deoxyadenosine, a purine alkaloid [41].

Cordyceps militaris natural products

Of all the *Cordyceps* species, *C. militaris* has been most successfully cultivated and most intensively studied. Most *Cordyceps* products in the marketplace are developed from the fruiting bodies of cultivated *C. militaris*. According to chemical analysis, *C. militaris* contains cordycepin, adenosine, polysaccharide, mannitol, trehalose, polyunsaturated fatty acids, δ-tocopherol, p-hydroxybenzoic acid, and β-(1→3)-D-glucan [42,43,58–61].

Cultivation and growing of *Cordyceps*

The natural fruiting bodies of *Cordyceps* are very rare and are costly to collect. Moreover, natural populations of key *Cordyceps* species are decreasing rapidly due to overcollection [62], presenting the need for increased cultivation of *Cordyceps in vitro* using an artificial medium [63,64]. Examples of some medicinally important *Cordyceps* species such as *C. sinensis*, artificial *O. sinensis*, C. militaris, and artificial C. militaris *are shown in* Fig. 5.

The growth of *C. sinensis* on sabouraud's dextrose with yeast extract broth medium was investigated using different carbon sources, nitrogen sources, and additives (vitamins and minerals) [65,66].

Sucrose was the best carbon source for *C. sinensis* growth, while beef extract and yeast extract were the best nitrogen sources. Moreover, using folic acid significantly increased the yield, and adding calcium chloride and zinc chloride as micronutrients and macronutrients, respectively, increased the total yield significantly [67].

One of the remarkably important artificial techniques for *C. sinensis* culturing was using sterile rice media at 9–13°C for 40–60 days, followed by lowering temperature to 4°C for inducing stroma production [68]. It should be mentioned that the *Cordyceps* mycelium growth depends on different factors such as growth media, temperature, pH, and some environmental factors [69], but after trying different media, potato dextrose agar was proven to be the best medium using a pH range of 8.5–9.5 at 20–25°C [70].

C. militaris cultivation is much easier than *C. sinensis* in both solid and broth media using numerous carbon and nitrogen sources [71,72]. Farming of *C. militaris* mycelium using artificial media has lately been developed specially for the purpose of Cordycepin production using different methods such as surface culture [73] and submerged culture [74,75]. Cereals such as rice have been commonly used with some organic substrates for commercial production of *C. militaris* stromata [76,77]. Other successful substrates include cottonseed coats, wheat grains, bean powder, corn grain, corn cobs, millet, and sorghum [78–81].

Mycelia production for the purpose of biologically active compounds is also possible and has been conducted in submerged culture [53,81,82]. *C.*

Figure 5

Medicinally important *Cordyceps* species: (a) *Cordyceps sinensis* mature fruiting body in the wild, (b) *C. sinensis* dug out from soil, (c) dryC. *sinensis* product, (d) artificial *Ophiocordyceps sinensis* on living caterpillars, (e) Cordyceps militaris growing in the wild, (f) artificial C. militaris growing on insects, (g) artificial Cordyceps militaris growing on a culture medium (photographs taken by Ting-Chi Wen and Waill A. Elkhateeb).

militaris cultivation has been further advanced, resulting in a high yield of stromata production and high content of Cordycepin [75,83]. *C. militaris* cultivation was also investigated using different media [84–86].

Uses and health benefits of *Cordyceps*

Species of *Cordyceps* are widely researched due to the endless list of medicinal biological activities exerted by their extracted compounds as shown by some examples in Tables 1 and 2, Fig. 6 with various medical and

Table 1 Common therapeutic effects of different *Cordyceps* spp.

Therapeutic effects	*Cordyceps* spp.	Major bioactive compounds	References
Antitumor	*Cordyceps sinensis*	Cordycepin	Yalin *et al.* [99]
		Cordyglucans	Yang *et al.* [100]
		Monosaccharide saponins	Paterson [42]
		EPSF	Zhang *et al.* [101]
	Cordyceps militaris	Cordycepin and mannitol	Liu *et al.* [43]
Antidiabetic effects	*Cordyceps sinensis*	Cordymin	Vestergaard *et al.* [102]
			Qi *et al.* [103]
	Cordyceps militaris	Cordycepin, adenosine	Yun *et al.* [61]
Anti-inflammatory	*Cordyceps sinensis*	Cordycepin	Liu *et al.* [104]
		Adenosine	Fan *et al.* [112]
	Cordyceps militaris	β-(1→3)-D-glucan	Smiderle *et al.* [58]
Antioxidant activity	*Cordyceps sinensis*	Exopolysaccharide fraction, EPSF	Wang *et al.* [113]
		CPS-1	
		CME-1	
	Cordyceps militaris	Polysaccharide (PSC)	Wang *et al.* [114]
Antimicrobial activity	*Cordyceps sinensis*	Cordycepin	Liu *et al.* [104]
		Ergosterol	Seitz [105]
	Cordyceps militaris	Mannitol, trehalose, polyunsaturated fatty acids, δ-tocopherol and p-Hydroxybenzoic acid	Reis *et al.* [59]
Anti-influenza	*Cordyceps* militaris	Polysaccharide (PSC)	Ohta *et al.* [60]
Anticonvulsant activity	*Cordyceps sinensis*	Adenosine	Yang *et al.* [106]

nutritional values. The main uses of *Cordyceps* have been known in oriental old medicine for curing respiratory diseases such as asthma and bronchial cases, as well as for providing body with energy and for boosting sexual power.

Modern research now confirms the efficiency of *Cordyceps* in many other fields. One of the breakthroughs of modern research has been the discovery of cordycepin, which has a strong antimicrobial activity against almost all species of bacteria. *Cordyceps* showed strong activity against tuberculosis and human leukemia, as shown in many clinical trials in Asia and elsewhere [54].

Cordyceps was shown to be potent in increasing the maximum amount of oxygen and to improve respiratory function [47]. There are a number of components like deoxynucleosides produced by *C. sinensis*, such as the compounds 2′, 3′ deoxyadenosine which is marketed under the trade name 'Didanosine' in the USA as a medication for the treatment of AIDS. Similarly, Quinic acid derived from Cordycepin (3′ deoxyadenosine) present in *Cordyceps* is found to have antiviral and antibacterial properties [87,88]. Numerous studies have verified the benefits of *C. sinensis* in treating disturbances in heart rhythm such as cardiac arrhythmia and chronic heart failure [47].

Antitumor and anticancer activities of Cordyceps

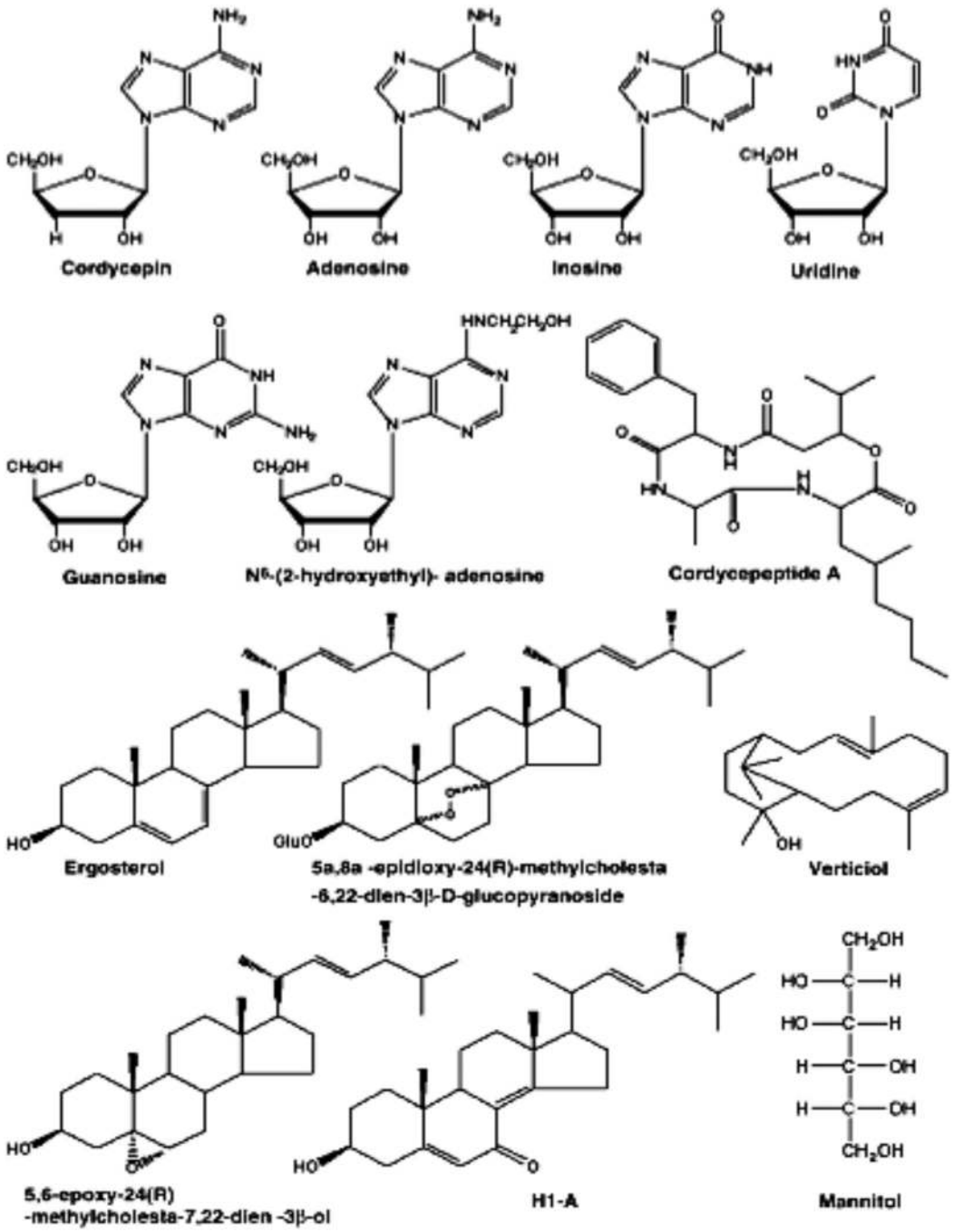
Various biologically active compounds exerting an anticancer activity were extracted from *Cordyceps*.

Table 2 List of major *Cordyceps*-based companies

Cordyceps align="12pt 0cm" company align="12pt 0cm"	Country of the origin
Aloha Medicinals	USA *www.alohamedicinals.com align="12pt 0cm"* align="12pt 0cm" align="12pt 0cm"
Doctors Best	USA *www.drbvitamins.com*
Host Defense Mushrooms	USA *https://hostdefense.com*
Perfect supplements	USA *www.perfectsupplements.com*
Paradise	USA *https://paradiseherbs.com*
Solaray	USA *www.naturalhealthyconcepts.com align="12pt 0cm; text-align: left"* align="12pt 0cm; text-align: left" align="12pt 0cm; text-align: left"
Oregon's Wild Harvest	USA *www.oregonswildharvest.com*
Real Herbs	USA *www.irealherbs.com*
Mushroom Science	USA *https://mushroomscience.com*
Herbsense	China *www.herbsens.com*
	Czech *www.terezia.eu*
ZeinPharma	Germany *www.zeinpharma.com*
The Really Healthy	UK */www.healthy.co.uk*

Cordycepin has an antitumor activity in B16 melanoma cells [89,90]. Cordycepin induced apoptosis in Mouse Leydig tumor cell *in vitro* [91]. Also, it inhibits cell proliferation and further apoptosis of human colorectal carcinoma using SW480 and SW620 *in vitro* [92,93]. *C. militaris* was found to inhibit U937 cells grown in a dose-dependent manner and also in the treatment of human leukemia [94].

Figure 6



Typical chemical structures of common compounds found within *Cordyceps* spp. [64].

Cordyceps has shown promising activities in inhibiting the growth of cancer cells [95] and in some cases could reduce tumor size [96,97]. Moreover, some *Cordyceps* species have anti-leukemia activities [92,98].

Hypoglycemic and hypocholesterolemic effects of Cordyceps

Cordyceps are found to regulate and also lower blood sugar levels by improving metabolism of glucose [107]. Furthermore, *Cordyceps* can increase secretion of glucokinase and hexokinase which are glucose-regulating enzymes secreted by the liver [108]. Polysaccharides are the key players in showing the hypoglycemic activity of *Cordyceps*. Hypercholesterolemia is an indicator for high risk of cardiovascular attack. Many studies have reported the role of *C. sinensis* in lowering the total cholesterol level and the level of triglycerides. It also helps in increasing the ratio of the good cholesterol (high-density lipoprotein cholesterol) to bad cholesterol (low-density lipoprotein cholesterol) [109].

Improving kidney functions

The results of some clinical trials have shown that the administration of *C. sinensis* could significantly

improve kidney function and overall immunity of patients suffering from chronic renal failure [110]. The mechanism of kidney-enhancing activity of *Cordyceps* is owing to its capability to elevate 17-ketosteroid and 17-hydroxycorticosteroid levels in the body, protect sodium pump activity of tubular cells, accelerate tubular cells regeneration, and reduce calcium content in certain tissues [110–114].

Treatment of liver disorders

Cordyceps is universally involved as a cotreatment of chronic hepatitis B and C. Extract mixture of *Cordyceps* in combination with other medicinal mushrooms in addition to the antiviral drug, lamivudine, was used for treating hepatitis B [41,115]. On the other hand, daily consumption of *Cordyceps* improved liver functions in patients suffering from posthepatic cirrhosis [41].

Reduction of fatigue

Cordyceps has been used from 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. Nowadays, *Cordyceps* is used by athletes to fight fatigue and weakness and to increase endurance and improve energy levels. Additionally, the results of clinical trials involving elderly patients with chronic fatigue indicated that treatment with *C. sinensis* resulted in improvement of fatigue, increasing cold intolerance [35,93,116].

Cordyceps protect the organs and glands

C. sinensis also has obvious effects on other organ systems [117]. For example, in the central nervous system, *C. sinensis* has cooling, anticonvulsant, and sedative activities. For the respiratory, *C. sinensis* has a strong relaxant activity on the bronchi, considerably, and also plays a key role in the contraction of trachea caused by histamine. It also has an anti-asthmatic effect and prevents pulmonary emphysema. Concerning the endocrine system, *C. sinensis* increases the secretion of adrenaline and has effects as a male hormone. Polysaccharides extracted from *Cordyceps* can increase corticosterone level in the plasma.

Cordyceps is used in traditional medicine for decades to improve fertility in men. A study has proven the positive effect of using *C. militaris* mycelium on sperm motility, morphology, productivity, and enhancement of sexual activity. Moreover, consuming *Cordyceps* resulted in improving liver function tests in patients suffering from posthepatic cirrhosis [118].

Anti-inflammatory activity of Cordyceps

Generally, cordycepin is the metabolite responsible for the anti-inflammatory activity of many *Cordyceps* species [119–121]. Ethanolic extracts of cultured mycelia and fruiting bodies of *C. militaris* exhibited an anti-inflammatory effect [119]. On the other hand, an alkaline extract of *C. militaris* showed a potent *in-vivo* anti-inflammatory effect against nociception and peritonitis in mice [85]. Adenosine is another compound existing in *Cordyceps* species with a wide spectrum of activities related to preventing tissue damage such as anti-inflammatory properties [104,122–124].

The methanolic fraction of *C. militaris* fruiting bodies exerted an anti-inflammatory activity resulting from

Table 3 Cosmetic products containing *Cordyceps sinensis* and *Cordyceps militaris* extracts and their functions

Product name	Function	Company name	Reference
Cordyceps (mushroom extract)	Improved lungs and kidney function	Organika	*https://organika.com*
Cordyceps	Support healthy immune and vascular systems	Moon Juice	*https://moonjuice.com*
Ultra *Cordyceps* plus	Support lung health and liver function	Drbvitamins	*www.drbvitamins.com*
Host Defense *Cordyceps*	Promotes healthy kidney function and augments oxygen uptake	Host defense	*https://hostdefense.com*
Perfect *Cordyceps*	Boost the immune system and improve sexual function	Perfect Supplements	*www.perfect-supplements.com*
Paradise herbs Tibetan *Cordyceps*	Support physical activity, performance, stamina and resistance	Paradise Herbs	*https://paradiseherbs.com*
Solaray *Cordyceps*	Protect against throat infections and promotes healthy cholesterol levels	Naturally Healthy Concepts	*www.naturalhealthyconcepts.com*
Oregon's wild harvest *Cordyceps*	Cardiovascular, respiratory and immune support	Oregon's Wild Harvest	*www.oregonswildharvest.com*
Cordyceps	Boosts energy and immunity and supports cardiovascular health	Ireal herbs	*www.irealherbs.com*
Cordyceps CS–4	Provide the immune health benefits	Mushroom Science	*https://mushroomscience.com*

Figure 7

Cordyceps products made in China: (a) *Cordyceps sinensis* powder capsule (*www.naturessunshine.comwww.naturessunshine.com*), (b) *C. sinensis* powder capsule (*www.alibaba.comwww.alibaba.com*), (c) *C. militaris* soup (*www.aliexpress.comwww.aliexpress.com*), (d) *Cordyceps* mycelia extract powder as food supplements (*www.alibaba.comwww.alibaba.com*), (e) *Cordyceps*-king capsule (www.ecvv.com), (f) *C. sinensis* cream (*www.aliexpress.comwww.aliexpress.com*).

the presence of cordycerebroside A, soyacerebroside I, and glucocerebroside, which prevented the accumulation of the pro-inflammatory iNOS protein [125].

Cordyceps antioxidant and antiaging activities

Protecting against damage of cells by free radicals is one of the biological activities exerted by *Cordyceps* species extracts. This activity corresponds to polysaccharide fraction [64,114,126,127]. *C. sinensis* has potent antioxidant and antiaging properties.

Cordyceps side effects

Cordyceps is generally safe in recommended dosages and no major side effects were reported. [53].

Figure 8

Cordyceps products made in the USA: (a) *Cordyceps sinensis* powder capsules (*hostdefense.comhostdefense.com*), (b) fruiting body extract of *C. sinensis* (*www.nusapure.comwww.nusapure.com*), (c) *C. sinensis* powder sachets with coffee (*www.iherb.comwww.iherb.com*), (d) *C. sinensis* antistress capsules (*https://organika.comhttps://organika.com*), (e) *Cordyceps* powder capsules (www.paradiseherbs.com), (f) *C. sinensis* powder capsules (*https://usahealthyinc.comhttps://usahealthyinc.com*), (g) *Cordyceps* powder capsules (*www.drbvitamins.comwww.drbvitamins.com*).

Global market of *Cordyceps*

The *Cordyceps* industry is strong and growing. Various products were commercialized for compounds originated from *Cordyceps* species. Some major *Cordyceps*-based companies are listed in Table 2, and examples for some cosmetics-containing *C. sinensis and C. militaris* extracts and their beneficial functions are declared in Table 3. Global production of just *O. sinensis* is estimated to be in the region of 85–185 tons [128] with further tonnage provided by other *Cordyceps* species. The harvesting and sale of noncultivated *Cordyceps* can have a significant impact on household incomes in the regions in which it is collected [64,129–131]. The intense global interest and value assigned to *Cordyceps* has led to a large range of commercial products

Figure 9

Cordyceps products made in different Asian and European countries: (a) *Cordyceps sinensis* supplement capsules made in Japan (*https://cordyceps.tokyohttps://cordyceps.tokyo*), (b) *C. sinensis* supplement capsules made in Thai (*www.amazon.comwww.amazon.com*), (c) *Cordyceps* tea sachets made in South Korea (*www.alibaba.comwww.alibaba.com*), (d) *Cordyceps* powder capsules made in Czech (*www.terezia.euwww.terezia.eu*), (e) *C. sinensis* capsules made in Germany (*www.zeinpharma.comwww.zeinpharma.com*), (f) *C. sinensis* capsules made in the UK (*www.healthy.co.ukwww.healthy.co.uk*).

derived from these fungi all over the world as shown in Figs 7–9.

Medicinal mushrooms keep surprising us by their promising biological activities [3,7,54,132,133] in a way that encourage studying their effects *in vitro* and *in vivo* in order to discover their potent compounds to win the war with the currently spreading life-threatening diseases.

Future trends

Being functional foods, mushrooms represent a prolific source of bioactive compounds with countless therapeutic capabilities working toward preventing

and controlling many diseases. A large number of mushrooms originated from biologically active compounds have been isolated and have been reported previously. Several studies explored promising activities of mushrooms, and those studies were conducted using crude extracts of mushrooms. Further researches are required in order to isolate and identify bioactive compounds responsible for such biological activities. Moreover, clinical trials and more in-vivo experiments have to be carried out to confirm mushrooms' capabilities as sources of compounds having medical applications.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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