Chapter

Therapeutic Properties and Anti-Lipidemic Activity of *Cordyceps sinensis*

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Abstract

Cordyceps sinensis is an entomophagous medicinal mushroom, which is mainly endemic to the Tibetan Plateau including the adjoining high altitude areas. The fungus attacks many lepidopteran larvae caterpillars and mummifies it. The larvae along with the mummified insect are highly valued for their medicinal property. *Cordyceps sinensis* is one of the most efficient and expensive medicinal mushrooms in traditional medicinal systems such as those in China and Tibet, having multiple medicinal and pharmacological properties. It has been used to treat respiratory and immune disorders; pulmonary diseases; renal, liver, and cardiovascular diseases; hyposexuality; and hyperlipidemia. The extract of this mushroom and its bioactive compounds are noteworthy for their ability to regulate lipid metabolism and thereby exhibit anti-lipidemic activity. Cordycepin in particular, which is a bioactive compound existing in *Cordyceps sinensis*, has been identified as one of the primary compounds of interest in this aspect. Despite the global and scientific interest exerted toward *Cordyceps sinensis*, it appears to be of utmost importance that the price and other market factors owing to the rarity of this herb are managed through artificial means of synthesis.

Keywords: caterpillar, cholesterol, *Cordyceps sinensis*, ethnopharmacology, triglycerides

1. Introduction

Edible mushrooms have been widely used around the world for their high nutritional and therapeutic value as well as in the form of a functional food. Additionally, they have been highly appreciated for their medicinal and therapeutic applications from a traditional perspective as well. This is owing to the availability of a vast variety of bioactive compounds such as polysaccharides, proteoglycans, terpenoids, phenolic compounds, steroids, and lectins, which are available in copious amounts in all its components [1]. *Cordyceps sinensis* is a highly valued fungus in this aspect which thrives at very high altitudes, especially in meadows on the Himalayan Plateau [2]. As a medicinal fungus of a long and illustrious history, *Cordyceps sinensis* is an ascomycetes fungus [3]. An image of this fungus is shown in **Figure 1**. Although it is not actually a mushroom in the taxonomic sense, it has been regarded as a medicinal mushroom throughout history. The name *Cordyceps* comes from the Latin words "cord" and "ceps," meaning "club" and "head," respectively [3]. The term "*Cordyceps*"

Figure 1.
Cordyceps sinensis *growing on a caterpillar.*

usually refer to the specific species *Cordyceps sinensis*, but there are also many other species that come under the genus *Cordyceps*.

The medicinal value of this fungus was first recognized more than 2000 years ago in China and the recognition passed onto the rest of Asia [3]. Early records of *Cordyceps sinensis* as a medicine is as old as the Qing Dynasty in China and this information has been mentioned in *Ben Cao Cong Xin* (New Compilation of Materia Medica) written by Wu Yiluo in around 1757 [4]. However, knowledge of this fungus reached Western scientific audiences only in 1726, when it was introduced at a scientific meeting in Paris. The first specimens were carried back to France by a Jesuit priest, who chronicled his experiences with *Cordyceps sinensis* during his stay at the Chinese Emperor's court [4].

Various names have been used to identify *Cordyceps sinensis* in various languages and cultures, where the most common forms of reference are shown in **Table 1**. In historical and general usage, the term "*Cordyceps*" refers specifically to the species *Cordyceps sinensis* (Berk.) Sacc (syn *Ophiocordyceps sinensis* (Berk.) G.H. Sung, J.M. Sung, Hywel-Jones & Spatafora.), which is the most widely used *Cordyceps* species. Berkeley, the British mycologist, first described this fungus in 1843 as *Sphaeria sinensis* Berk., while later on in 1878, Saccardo renamed it as *Cordyceps sinensis* [5]. The currently accepted scientific name is *Cordyceps sinensis* (Berk.) Sacc.

The taxonomic classification of *Cordyceps sinensis* is shown in **Table 2**.

Given the difficulties involved in harvesting, *Cordyceps sinensis* has been highly priced. It is basically the costliest fungus or medicinal mushroom throughout the world, hence known as "fungal gold" or "soft gold" [6]. The price of *Cordyceps sinensis* has been shown to grow approximately 20% annually and to date is probably 1000% the price which existed 10 years ago [7]. Pricing is achieved by inspecting the size and firmness of the larval host, which is often tested by squeezing it between two fingers; the stiffer it is, the higher the price [8]. The color is also observed when pricing, where a saturated yellowish-brown color is preferred than the pale ones [9]. Other physical characteristics taken into account when assessing quality are size, weight, smell, taste, and robustness [9]. The texture of good-quality specimens is relatively fleshy while the taste is bitter. Despite its cost and rarity, the unprecedented medicinal applications of *Cordyceps sinensis* have made it a highly valued indispensable component of the traditional Chinese and Tibetan medicine.

DOI: http://dx.doi.org/10.5772/intechopen.92616

Language	Vernacular name
Chinese	Dong chong xia cao
Tibetan	Yartsa gunbu
Hindi	Keeda jadi
Nepali language	Yarcha gumba

Table 1.
Vernacular names used for Cordyceps sinensis.

Classification	Category
Kingdom	Fungi
Division	Ascomycota
Class	Sordariomycetes
Order	Hypocreales
Family	Ophiocordycipitaceae
Genus	*Cordyceps*
Species	*sinensis*

Table 2.
Taxonomic classification of Cordyceps sinensis.

Although *Cordyceps sinensis* has been used for a wide range of medicinal applications, it is only apt that its anti-lipidemic properties are given due attention. For this purpose, it is important that other aspects of this fungus are compiled herein prior to highlighting its effects against lipid-related disorders. Thus, this chapter has been structured in a manner which provides a holistic overview of *Cordyceps sinensis*, where any reader can refer to this write-up and obtain an overall understanding of this medicine prior to delving into its anti-lipidemic effects.

2. The life cycle of *Cordyceps sinensis*

Cordyceps sinensis fungus begins off its wondrous life cycle with the combination of an underground caterpillar (insect)—mostly Lepidoptera larvae, which generally lives about 15 cm underground. One of the special factors, which affect the initial point to begin the life of *Cordyceps sinensis* and which enable its identification from other fungi, is the low temperature that is required for its life cycle. This particular temperature is believed to be below approximately 21°C [6]. The life of the caterpillar fungus which begins under these conditions carries out a slow growing procedure thereafter.

The underground caterpillars which survive by feeding on the underground roots start to shed off their skin in the later part of summer and autumn seasons. Therefore, their skin becomes more vulnerable to fungal spores. Fungal spores, which begin to interact with the chemicals on the skin of these caterpillars, release a fungal mycelium, which then starts infecting the caterpillar to its death. With its death, a formation of a stalk-like structure of the mushroom grows out of the upper part of the head of the dead caterpillar and that particular structure emerges above to the ground surface in the season of spring. The infected larvae after its death become a rigid structure due to the production of the fungal sclerotia, which could pause the germination for a while to produce spores. Right after the end of the winter season, the formation of the mushroom body continues, and along with that, the perithecial stroma grows upward in order to emerge above the ground soil, thereby concluding its life cycle.

3. Ethnopharmacological uses of *Cordyceps sinensis*

Cordyceps sinensis is presently regarded as a highly priced fungus at present due to its precious medicinal value especially in the field of traditional Chinese medicine (TCM). This is primarily for the treatment of kidney disease, fatigue, sexual dysfunctions, diabetes, and cancers, which are highly prevalent nowadays. *Cordyceps sinensis* is also regarded as a Bhutanese indigenous medicine other than TCM [10]. It is said that the *Cordyceps* organism was discovered by yak herders in the Himalayas of ancient Tibet and Nepal who, recognizing the ardent behavior of their animals after grazing on *Cordyceps* at high altitudes in the spring, sought the causal agent for their own usage and medical applications [3]. The capless mushroom was then incorporated into TCM ever since starting with kidney, lung, and heart ailments, male and female sexual dysfunction, fatigue, cancer, hiccups, and serious injury, to relieve pain, and the symptoms of tuberculosis and hemorrhoids, to restore general health and appetite and to promote longevity [3].

A tabulated description of the health benefits of *Cordyceps sinensis* in their traditional applications against disease conditions and scientific studies, which have verified its potency, is listed in **Table 3**.

In modern times, *Cordyceps sinensis* appears to be actively used by the elderly people and athletes as well to boost their energy [16]. Experiments show that although *Cordyceps sinensis* could be used as an energy booster, only a small portion of extra energy could be achieved due to the increase of cellular adenosine triphosphate (ATP) when it is taken as an herbal supplement. The energy output and its oxygen capacity help with treating cold intolerance and decreasing fatigue. It is also noteworthy that compared with other medicinal herbs, *Cordyceps sinensis* has

Disease	Description and effect	References
Cancer	*Cordyceps sinensis* has been able to demonstrate the inhibition of colorectal cancer cells	[11]
Liver fibrosis	Experiments have shown that ergosterol in cultured mycelium *Cordyceps sinensis* has an anti-inflammatory as well as an antifibrotic effect *Cordyceps sinensis* culture had helped in the inhibition of hepatocytes and hepatic stellate cell activation	[12]
Respiratory	*Cordyceps sinensis* is used to ease various kinds of diseases associated with the lungs and the respiratory system such as phlegm, cough, and various other diseases associated with the bronchial and asthma	[13]
Kidney	Studies showed that consumption of *Cordyceps sinensis* stem helps in increasing 17-ketosteroid and 17-hydroxycorticosteroids levels in the human body resulting in the prevention of kidney disease. In the meantime, the consumption of *Cordyceps sinensis* by patients with renal failure has helped them decrease their blood pressure by 15%	[14]
AIDS/HIV	*Cordyceps sinensis* has been used to treat HIV infections in West Africa	[15]

Table 3.
Disease conditions which have ethnopharmacologically utilized Cordyceps sinensis *and studies elucidating their scientific verifications.*

DOI: http://dx.doi.org/10.5772/intechopen.92616

a very low toxicity and side effects over its benefits. Studies show that health issues like nausea, diarrhea, and diseases such as dry mouth have not been experienced by the patients who have taken *Cordyceps sinensis* [5].

4. Anti-lipidemic effects of *Cordyceps sinensis*

Age-related diseases are rising as a common issue in the present era due to the evolutionary changes that take place in the dietary patterns and lifestyle changes of humans. Studies which are being carried out to mitigate these rising health issues show methodological approaches to prevent and mitigate them by utilizing the medicinal values of traditional medicines across the globe.

Complications related to lipid metabolism have been identified as an age-related disease condition [17]. As a detrimental health effect related to lipid metabolism, the incidence of obesity has also been increasing steadily in the developed and developing countries worldwide. Analysis of the global burden of obesity revealed that there were 396 million adults with obesity in 2005 and that the expected number is projected to be 573 million individuals in 2030, without the application of an adjustment for secular trends [18]. Excessive fat accumulation that increases the risk of adverse health effects is one of the definitions of obesity [19]. It is a condition that is implicated as a risk factor for various diseases such as hypertension, coronary heart disease, and type II diabetes [20].

Hyperlipidemia is another age-related disease condition. This occurs due to the presence of too much low-density lipoprotein (LDL) in the blood, while it threatens the health of the circulatory system, risking the blockage of arteries with the deposition of fats and lipids. In addition, hyperlipidemia acts as the root cause of diabetes and functional depression in organs such as the liver, heart, and kidney [3, 4].

Cordyceps sinensis has been used in modern times for the treatment of lipid-related disorders. A summary of the anti-lipidemic effects of *Cordyceps sinensis* is shown in **Figure 2**. The fruiting body part of *Cordyceps sinensis* contains a composition of nucleosides, exopolysaccharides (EPS), proteins, and sterols. These bioactive components which play a significant role in treating diseases are also

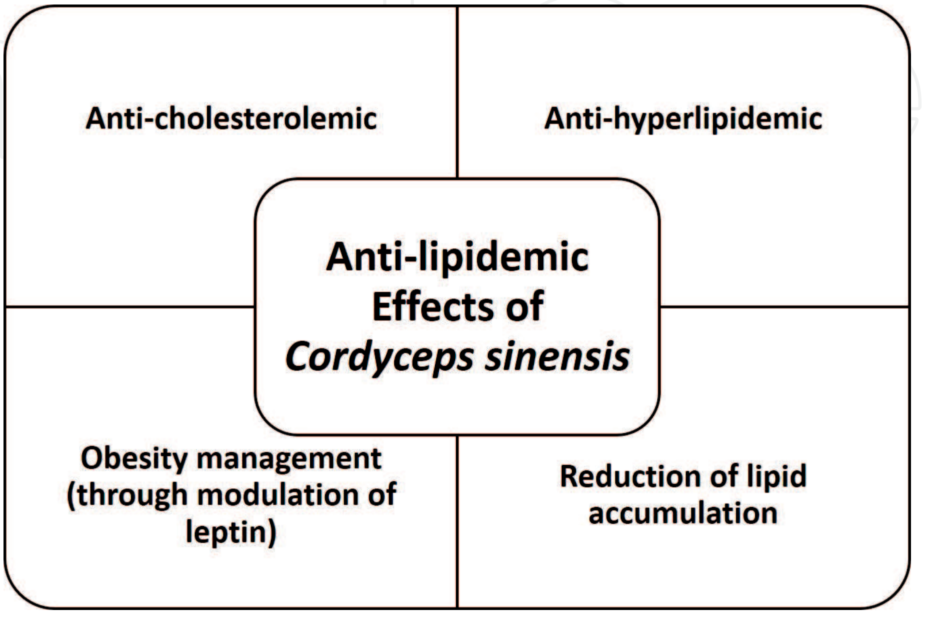

Figure 2.
Schematic depicting the anti-lipidemic effects of Cordyceps sinensis.

used in treating diseases like hyperlipidemia due to their anti-lipidemic and anti-cholesterolemic ability which have demonstrated to lower cholesterol. Treatment of mice with the extract of *Cordyceps sinensis* mycelia has demonstrated to significantly reduce cholesterol and triglyceride concentrations and the synthesis of very-low-density lipoprotein (VLDL, an LDL precursor). Therefore, given these functions, a useful mechanism of action present in *Cordyceps sinensis* for obesity prevention could be considered as the inhibition of preadipocyte differentiation.

In human as well as animal studies, administration of *Cordyceps sinensis* has been associated with a reduction in cholesterol and triglyceride and an increase in the ratio of high-density lipoprotein (HDL) to LDL cholesterol [17]. Whether the causative mechanism for this lipid-balancing effect is through blood sugar stabilization, enhancing liver function, or any other as hitherto unknown cause remains to be seen.

Interestingly, in addition to their mycelium effects obtained from solid-state fermentation, *Cordyceps sinensis* biomass obtained from submerged fermentation has been recognized as an effective agent in lipid metabolism [21]. This hypothesis was supported by some evidence which surfaced about glucan isolated from the *Cordyceps sinensis*. Current interest in the effect of glucans on lipid metabolism mainly is centered on the possibility that the glucans could entrap bile acids in the intestine and thus increase bile acid exclusion in the feces. The results by Freire Dos Santos et al. [22] suggest that *Cordyceps sinensis* biomass supplementation in high-fat diet (HFD)-fed rats for 4 months normalizes the blood lipid and the low testosterone levels induced by HFD. Despite the outcomes of the study, it has to be borne in mind nevertheless that *Cordyceps sinensis* biomass supplementation cannot replace the use of currently available drug regiments for lipid reduction but can easily complement them. It may also enable the use of lower doses of therapeutic drugs, thereby decreasing the risk of dose-related side effects. Furthermore, Freire Dos Santos et al. demonstrated that a long-term intake of HFD caused a significant liver damage which has been reverted by *Cordyceps sinensis* biomass supplementation and, this in turn, normalized decreasing testosterone levels observed in HFD-fed rats.

Leptin, a newly discovered hormonal product of the obesity (ob) gene, is expressed by white adipose tissue. It has been implicated in the regulation of body weight, glucose metabolism, and fertility. Leptin deficiency produces severe obesity, insulin resistance, and impaired glucose tolerance in ob/ob mice, and also, congenital leptin deficiency in humans leads to hyperphagia and marked obesity. Choi suggested that *Cordyceps sinensis* originated EPS are excellent candidates to develop as functional food additives or therapeutic agents for anti-obesity and antidiabetic purposes through improvement in glucose homeostasis and preservation of insulin reserves [23].

Tiamyom et al. [17] investigated the effects of *Cordyceps sinensis* extract and *Gymnema inodorum* extract, used alone and combined, on antiadipogenesis in 3T3-L1 cells. Results from this study indicated that both herbs and their combination had inhibitory effects on lipid accumulation in the adipocytes. The pancreatic lipase assay results indicated that *Cordyceps sinensis* extract inhibited the pancreatic lipase activity in a dose-dependent manner. These results suggested that the use of *Cordyceps sinensis* extract alone and in combination with *Gymnema inodorum* extract may be efficacious as a complementary therapy for hyperlipidemia and obesity management.

5. Bioactive compounds of interest

Cordyceps sinensis appears to contain all of the essential amino acids, vitamins E and K, as well as the water-soluble vitamins B1, B2, and B12. In addition, it contains many sugars, including mono-, di-, and oligosaccharides, and many complex polysaccharides, proteins, sterols, nucleosides, and trace elements. Characterization of cordycepin (**Figure 2**) and 2′-deoxyadenosine was reported by nuclear magnetic resonance (NMR) and infrared (IR) spectroscopy in an extract of *Cordyceps sinensis* [24, 25]. Cordycepin has been identified as one of the compounds involved in the anti-lipidemic effects of *Cordyceps sinensis*, and thus, within the context of this chapter needs to be highlighted as the primary bioactive compound involved in lipid metabolism and regulation. Cordycepin inhibits adipocyte differentiation and accumulation of lipid in mature adipocytes [26]. As cordycepin blocks both adipocyte differentiation and lipid accumulation, it has the potential to be an effective therapeutic agent for obesity and obesity-related disorders [26].

Nucleosides have been found in all species of *Cordyceps*, including uridine. A number of polysaccharides and other sugar derivatives, such as cordycepic acid (D-mannitol), have been also identified in *Cordyceps sinensis* [17].

In recent years, much interest has been focused on EPS produced by *Cordyceps sinensis* and its other varieties due to their various biological and pharmacological

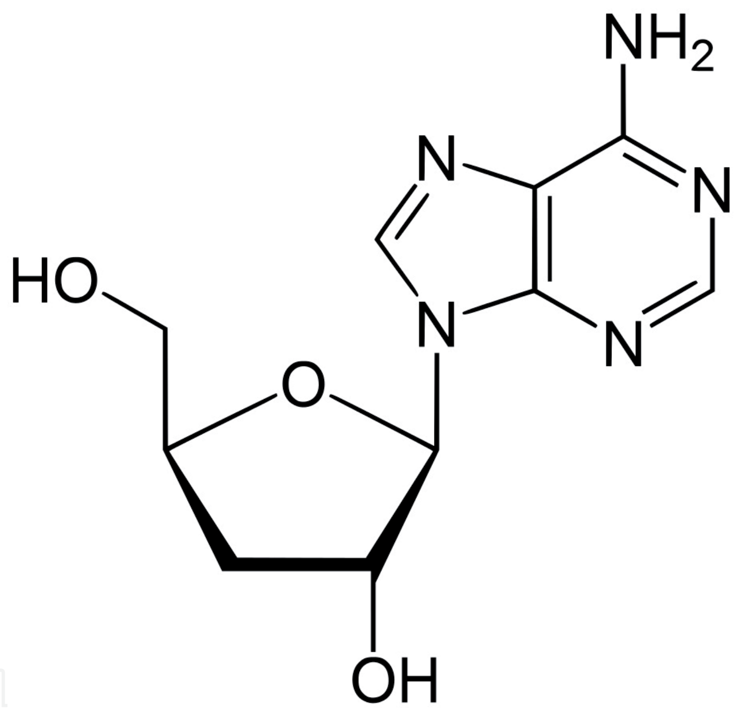

Figure 3.
Chemical structure of cordycepin, which has been isolated from Cordyceps sinensis*.*

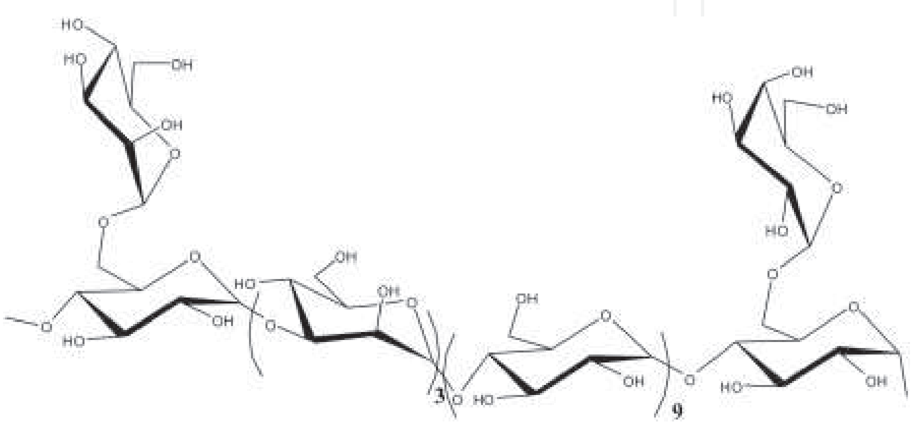

Figure 4.
Chemical structure of CPS-2, which was isolated by Wang et al. [27]. The structure was found to be mostly of α-(1 → 4)-d-glucose and α-(1 → 3)-D-mannose, branched with α-(1 → 4,6)-d-glucose every 12 residues on average.

activities. These polysaccharides are effective in regulating blood sugar and appear to have antimetastatic and antitumor effects [27]. *Cordyceps sinensis* contains proteins, peptides, polyamines, and all essential amino acids as well [28]. Sterol-type compounds have also been found in *Cordyceps sinensis*, including ergosterol, delta-3 ergosterol, ergosterol peroxide, 3-sitosterol, daucosterol, and campesterol [27, 28]. Twenty-eight saturated and unsaturated fatty acids and their derivatives have been isolated from *Cordyceps sinensis* [14]. Polar compounds of *Cordyceps sinensis* extracts include many compounds of alcohols and aldehydes; polycyclic aromatic hydrocarbons produced by *Cordyceps sinensis* as secondary metabolites were also reported. A water-soluble polysaccharide (CPS-2), isolated from the cultured *Cordyceps sinensis*, was obtained by hot water extraction, anion exchange, and gel permeation chromatography by Wang et al. [14]. The changes in blood urea nitrogen and serum creatinine in this particular study revealed that CPS-2 could significantly relieve renal failure caused by fulgerizing kidney. An image of this polysaccharide is shown in **Figure 3**. It is believed that there are several other polysaccharides as such with therapeutic potential in terms of lipid regulation in *Cordyceps sinensis* (**Figure 4**).

6. Other health benefits of *Cordyceps sinensis*

Cordyceps sinensis appear to have a variety of other health benefits which do not necessarily stem from its traditional medicinal applications. Some of them are shown in **Table 4**.

Disease condition	Part of fungus being used	Effect	References
Diabetes	Fruiting body and mycelia	Antiproliferative activity toward breast cancer cells (MCF-7)	[29]
Oxidative damage	Fruiting bodies	Antioxidant	[30]
Immune injury	Fruiting bodies and mycelia	Immune modulating	[31]
Melanogenesis	Mycelia	Anti-tyrosinase activity	[32]

Table 4.
Scientifically verified beneficial properties of Cordyceps sinensis, *which are not part of its ethnopharmacological uses.*

7. Conclusions

Although there is a higher and more favorable medicinal value in traditional medicines such as *Cordyceps sinensis*, the limitations should be considered as well in order to reveal its undiscovered potential of treating lipid-related diseases. However, as the availability of *Cordyceps sinensis* is gradually being decreased in the West, care should be taken when meeting the consumer demands, especially when it comes to the cultivation and growth of the herb. Moreover, as the natural *Cordyceps sinensis* is becoming rare, methods are in the process of being developed for the artificial production of this fungus with the same chemical constituents or even better. The world is now awakening to the importance of this fungus, and the price factor appears to play an important role in the marketplace. A lot of research is still pending on this fungus especially from the medical side. With the present research nevertheless, it is noteworthy that *Cordyceps sinensis* has been identified

DOI: http://dx.doi.org/10.5772/intechopen.92616

as a traditional medicine which is able to regulate lipid levels and demonstrated anti-lipidemic activity. Cordycepin appears to be an important bioactive compound in this aspect, and it is without a doubt that further research will be able to elucidate more bioactive compounds existing in *Cordyceps sinensis* which are able to collectively involve in lipid metabolism and regulation. The potency of *Cordyceps sinensis* would highly depend on its chemical constituents, viz., the cordycepin and polysaccharides that make up the fruiting body, mycelium, or spores. However, further experimental, epidemiological, and clinical studies are needed to identify other molecular targets, resolve the relationships between *Cordyceps sinensis* intake and anti-lipidemic activity, and explore the optimum dosing, efficacy, and safety alone and in combination with existing anti-cholesterolemic and anti-triglyceridemic pharmaceutical therapies.

Acknowledgements

The authors wish to thank the Australian College of Business & Technology, Kandy Campus, for the facilities provided to put this write-up together.

Conflict of interest

The authors declare no conflicts of interest, financial, or otherwise.

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References

[1] Mehra A, Zaidi KU, Mani A, Thawani V. The health benefits of *Cordyceps militaris*—A review. KAVAKA. 2017;**48**(1):27-32

[2] Chang ST, Miles PG. Mushrooms: Cultivation, Nutritional Value, Medicinal Effect and Environmental Impact. 1st ed. Boca Raton, FL, USA: CRC Press; 2004

[3] Joshi RK. Phytochemical and medicinal aspect of *Cordyceps sinensis* (Berk.): A review. Journal of Medicinal Plants Studies. 2016;**4**(1):65-67

[4] Hobbs CH. Medicinal Mushrooms: An Exploration of Tradition, Healing, and Culture. Vol. 251. Santa Cruz, CA: Botanica Press; 1995

[5] Devkota S. Yarsagumba [*Cordyceps sinensis* (Berk.) Sacc.]: Traditional utilization in Dolpa District, Western Nepal. Our Nature. 2006;**4**:48-52

[6] Panicker S. *Cordyceps* the fungal gold—A review. Advances in Research. 2017;**11**(3):1-16

[7] Zhou XW, Li LJ, Tian EW. Advances in research of the artificial cultivation of *Ophiocordyceps sinensis* in China. Critical Reviews in Biotechnology. 2014;**34**:233-243

[8] Jordan JL, Sullivan AM, Lee TDG. Immune activation by a sterile aqueous extract of *Cordyceps sinensis* mechanism of action. Immunopharmacology and Immunotoxicology. 2008;**30**:53-70

[9] Singh RP, Pachauri V, Verma RC, Mishra KK. Caterpillar fungus (*Cordyceps sinensis*)—A review. Journal of Eco-friendly Agriculture. 2008;**3**:1-15

[10] Panda AK, Swain KC. Traditional uses and medicinal potential of *Cordyceps sinensis* of Sikkim. Journal of Ayurveda and Integrative Medicine. 2011. DOI: 10.4103/0975-9476.78183

[11] Rao YK, Fang SH, Tzeng YM. Evaluation of the anti-inflammatory and anti-proliferation tumoral cells activities of *Antrodia camphorata*, *Cordyceps Sinensis*, and *Cinnamomum osmophloeum* bark extracts. Journal of Ethnopharmacology. 2007;**114**(1):78-85

[12] Yamaguchi Y, Kagota S, Nakamura K, Shinozuka K, Kunitomo M. Antioxidant activity of the extracts from fruiting bodies of cultured *Cordyceps sinensis*. Phytotherapy Research. 2000;**14**(8):647-649

[13] Wang N, Li J, Huang X, Chen W, Chen Y. Herbal medicine *Cordyceps sinensis* improves health-related quality of life in moderate-to-severe asthma. Evidence-Based Complementary and Alternative Medicine. 2016. DOI: 10.1155/2016/6134593

[14] Wang Y, Yin H, Lv X, Wang Y, Gao H, Wang M. Protection of chronic renal failure by a polysaccharide from *Cordyceps sinensis*. Fitoterapia. 2010;**81**(5):397-402

[15] Adotey G, Quarcoo A, Holiday J, Saaka B. Effect of Immunomodulating and antiviral agent of medicinal mushrooms (immune assist 24/7TM) on CD4+ T-lymphocyte counts of HIV-infected patients. International Journal of Medicinal Mushrooms. 2011;**13**(2):109-113

[16] Zhu JS, Rippe J. CordyMax enhances aerobic capability, endurance performance, and exercise metabolism in healthy, mid-age to elderly sedentary humans. In: Proceedings of the American Physiological Society's (APS) Annual Scientific Conference, Experimental Biology. Washington, DC: Convention Center; 2004. pp. 28-31

[17] Tiamyom K, Sirichaiwetchakoon K, Hengpratom T, Kupittayanant S, Srisawat R, Thaeomor A, et al. The effects of *Cordyceps sinensis* (Berk.) Sacc. and *Gymnema inodorum* (Lour.) Decne. Extracts on adipogenesis and lipase activity *in vitro*. Evidence-based Complementary and Alternative Medicine. 2019. DOI: 10.1155/2019/5370473

[18] Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. International Journal of Obesity. 2008;**32**:1431-1437

[19] Kahn SE, Hull RE, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006;**444**(7121):840-846

[20] Guilherme A, Virbasius JV, Puri V, Czech MP. Adipocyte dysfunctions linking obesity to insulin resistance and type 2 diabetes. Nature Reviews. Molecular Cell Biology. 2008;**9**(5):367-377

[21] Chimilovski JS, Habu S, Bosqui Teixeira RF, Thomaz-Soccol V, Noseda MD, Pedroni Medeiros AB, et al. Antitumour activity of *Grifola frondosa* exopolysaccharides produced by submerged fermentation using sugar cane and soy molasses as carbon sources. Food Technology and Biotechnology. 2011;**49**:359-363

[22] Freire Dos Santos L, Rubel R, Bonatto SJ, et al. *Cordyceps sinensis* biomass produced by submerged fermentation in high-fat diet feed rats normalizes the blood lipid and the low testosterone induced by diet. EXCLI Journal. 2012;**11**:767-775

[23] Choi JW. Anti-diabetic effect of the exopolysaccharides (EPS) produced from *Cordyceps sinensis* on *ob/ob* mice. Korean Society for Biotechnology and Bioengineering Journal. 2011;**26**:33-40

[24] Chen SZ, Chu JZ. NMR and IR studies on the characterization of cordycepin and 2′-deoxyadenosine. Zhongguo Kangshengsu Zazhi. 1996;**21**:9-12

[25] Segelken R. Cyclosporin mold's sexual state found in New York Forest Cornell Students' discovery could target additional sources of nature-based pharmaceuticals. Cornell University Science News. 2002

[26] Takahashi S, Tamai M, Nakajima S, et al. Blockade of adipocyte differentiation by cordycepin. British Journal of Pharmacology. 2012;**167**(3):561-575

[27] Wu JW, Chen X, Siu KC. Isolation and structure characterization of an antioxidative glycopeptide from mycelial culture broth of a medicinal fungus. International Journal of Molecular Sciences. 2014;**15**:17318-17332

[28] Vasiljevic JD, Zivkovic LP, Cabarkapa AM, Bajic VP, Djelic NJ, Potparevic BM. *Cordyceps sinensis*: Genotoxic potential in human peripheral blood cells and antigenotoxic properties against hydrogen peroxide by comet assay. Alternative Therapies. 2016;**22**:S213-S221

[29] Ma L, Zhang S, Du M. Cordycepin from *Cordyceps militaris* prevents hyperglycemia in alloxan-induced diabetic mice. Nutrition Research. 2015;**35**(5):431-439

[30] Zhang G, Huang Y, Bian Y, Wong JH, Ng TB, Wang H. Hypoglycemic activity of the fungi *Cordyceps militaris*, *Cordyceps sinensis*, *Tricholoma mongolicum* and *Omphalia lapidescens* in streptozotocin-induced diabetic rats. Applied Microbiology and Biotechnology. 2006;**72**:11521-11526

[31] Nathan C. Points of control in inflammation. Nature. 2002;**420**(6917):846-852

[32] Aramwit P, Bang N, Ratanavaraporn J, Nakp T, Srichana T. An anti-cancer cordycepin produced by *Cordyceps militaris* growing on the dead larva of *Bombyx moris* silkworm. Journal of Agricultural Science. 2014;**4**(4):42-53