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Cordyceps, Unlocking nature's benefits for health and wellness

Anuhansi Tanya Pelawatta[1], Pinnaduwage Neelamanie Yapa[1*]

[1]Rajarata Universityof Sri Lanka, Faculty of Applied Sciences, Department of Biological Sciences, 50300, Mihintale, Sri Lanka.
**Corresponding Author: Pinnaduwage Neelamanie Yapa, Rajarata University of Sri Lanka,*

Abstract

Cordyceps spp. are a group of entomoparasitic fungi belonging to the phylum Ascomycota. There are more than thousand species of "Cordyceps" have been identified under four genera, namely, *Cordyceps*, *Ophiocordyceps*, *Elaphocordyceps* and *Metacordyceps*. Those are describing a specific type of entomoparasitic fungi on insect orders including Lepidoptera, Hymenoptera & Hemiptera. As obligate parasites, *Cordyceps* use a mechanism that hijacks of the host nervous system. After infection, the fungi produce secondary metabolites that alter the circadian and diurnal rhythms of the host, leading it to locations with optimal environmental conditions for fungal reproduction. Over the time, the fungus has infected the body of the host and once the suitable environmental condition reached the host dies. By absorbing the nutrients of the carcass, the fungus grows continuously and produce reproductive structures. Cordyceps are usually rich form numerous secondary metabolic components including cordycepin, pentostatin, peroxides, organic acids, oosporeins and polysaccharides. Many of these components are carrying medicinal properties which is important for human health and well-being. In Traditional Chinese Medicine (TCM) a certain species of cordyceps including *Ophiocordyceps sinensis* and *Cordyceps militaris* has been used as medicines for cough, renal disfunction and failures, immunity, anti-inflammatory, antioxidant, and blood sugar regulation. Some properties of *Cordyceps* spp. have been discovered from recent researches in pharmaceuticals. Immunomodulation is one of the recently discovered property from *O. sinensis.* It can enhance the effectiveness of an anti- tuberculosis drug names PA-824. The combination has better effectiveness than the using the drug along against *Mycobacterium tuberculosis*. Apart from headed properties, many *Cordyceps* species are containing compounds which can be using in treatments of various cancer types, to maintaining the gut, liver and renal health and antioxidant compounds. Hence, further studies regarding *Cordyceps* can open a new view on the production of antibiotics and pharmaceuticals which enhance the well-being of human life.

Keywords: *Antibiotics, Entomoparasites, metabolites, Fungi, Secondary*

Introduction

Cordyceps are known as a genus of entomoparasitic fungi in phylum Ascomycetes which almost entirely parasitize on wide ranges of arthropods including order Coleoptera, Hemiptera, Hymenoptera, Diptera and Lepidoptera (Chen et al., 2024). It is one of the largest and most diverse genera in family Claviciputaceae which belonging to the phylum Ascomycota. Majority of these fungal species are distributed among tropical and temperature regions of the world including Europe, North America, Southeast, Eastern and Asian regions (Krishna et al., 2024). All *Cordyceps* spp. are share a common mechanism of their life cycle invading, hijacking and growing on their selected host's body tissues, in order to ensure the growth and the continuation of the generation. Vast majority of them are showing the host specificity, while several species has the ability of growing on considerably broader range of host species. Fewer cordyceps species are selecting a narrow range of fungal species (Hart's truffels) as their hosts. During the parasitic process, *Cordyceps* are maintaining a complex mechanism to facilitate its attachment to the host's body and avoiding the destruction from it's immune system. Through this entire procedure, *Cordyceps* are producing several unique secondary metabolic components which is important in the several stages of its life cycle (Chen et al., 2024; Chou et al., 2024). As secondary components, *Cordyceps* spp. are secreting nucleotides, polysaccharides, steroids, terpenes, proteins derivatives, sugar alcohols, organic acids, and fatty acid derivatives (Chen et al., 2024). Naturally, most of these complex organic metabolic components are responsible with the physiological and structural functions, nutrient requirements, and active metabolic pathways (Chan et al., 2015). Existence of these metabolic components ensure the parasitic life cycle of the fungus while existing as a rich source of organic components, which widely using for studies to discover new drugs with immunomodulatory, antitumor, and hypoglycemic functions (Xiao and Zhong, 2007).

Traditional Chinese Medicine (TCM)

Traditional Chinese medicine or TCM is known as a systematic healthcare system which developed from clinical experiences (Matos et al., 2021; Wu et al., 2025). Even though the origin of TCM remains unclear, most of the archeological structures which belonging to the TCM dating back to several millennia (Matos et al., 2021). In the core modalities of TCM, one important part is using the herbal medicines to treat diseases. As the herbal medicines in TCM, plant parts, animal parts, mineral remedies and fungal structures has been used through several thousand years of history. Within the fungal ingredients which commonly using for the TCM, *DongChongXiaCao*

(Winter worm-summer grass) is referring for the famous "Caterpillar fungi" or *Ophiocordyceps sinensis*. It is a rare species of cordyceps family which surviving in high altitudes (3,000-4,000 meters) such as Qinghai and Tibet plateau (Chellapandi and Saranya, 2024). With the gradual growth, the fungi parasitize the larvae of ghost moth species which belonging to the order *Lepidoptera*, under the genus *Thitarodes* (Formerly classified under genus *Hepialus*). After infecting the fungal parasite, the larva is turned into a sclerotium which covered by the intact exoskeleton of the insect to withstand the winter, which is regarded as "winter worm". In the late spring or early of the summer of the next year, a clavate stroma of the fungus grows from the sclerotium and emerged from the ground appearing as a herb, which is regarded as "summer grass" (Wang and Yao , 2011). It was one of the high-demanding medicinal ingredients in TCM, which has been used for treating lung diseases, boost immunity, enhancing vitality and strengthen the immune system (Paterson, 2008; Chellapandi and Saranya, 2024). Instead of *O. sinensis*, *Cordyceps militaris*, *Cordyceps purinosa* and *Cordyceps ophiglossoides* has been used in various aspects in TCM such as a tonic, herbal drink, reduce inflammations and a medicine for blood sugar management (Paterson, 2008).

Modern research outcomes- Immunomodulatory properties of *Cordyceps* spp.

Immune system is one of the most complex systems in a human body which has complicated defense mechanisms against the infective agents. Immunomodulation is a process of modifying immune responses in a positive or negative administration of a drug or certain components (Saroj et al., 2012). In recent years, researches regarding the immunostimulatory and immunomodulatory properties of cordyceps species as well as the secondary metabolite extracts has been significantly increased. From recent researches, mycelial extractions and bioactive compounds of various cordyceps species have been studied with the production of various cytokinin production such as interleukin (IL)-1β, IL-2, IL-6, IL-8, IL-10, IL-12, and tumor necrosis factor (TNF)-α and phagocytosis stimulation of immune cells of the immune system (DAS et al., 2020). Immunomodulation is a broader process rather than immunostimulation, it alters the immune system, whether by turning it up or turning it down. Many cordyceps species extractions including *O. sinensis* has the immunomodulation properties too. The extractions of *O. sinensis* has the potential of splenocyte stimulation and enhanced Th1-type cytokine expression from the splenocytes. Importantly, the same treatment significantly enhanced the natural killer cell activity of the splenocytes and enhance the effectiveness of an anti- tuberculosis drug names PA-824 (Jang et al., 2015). Another widely using cordyceps species for pharmaceutical industry is *Cordyceps militaris*. Mycelial extractions of *C. militaris* has the ability of activation of macrophages and enhancement of phagocytosis. As the bioactive components which responsible for immunomodulation were polysaccharides in *C. militaris*, including a mixture of arabinose, galactose, glucose, mannose, and Xylose (Liu et al., 2024).

Antitumor properties

The amount of people who are suffering from cancers and tumors in the world will continue to grow steadily, according to the latest report about the trend of global cancer released by the World Health Organization (WHO). According to the official reports of WHO, nearly 10 million deaths has been observed from various types of cancers and each year, nearly 400,000 children has been develop various types of cancers (WHO, 2026). Developing drugs against cancers and tumors are incredibly challenging because cancer cells are containing mutants, vary from the structure and the function even inside the same tumor and sharing many similar functions with normal cells in the body. When developing anti cancerous treatments, various *Cordyceps* spp. have been provided promising results. Especially, the component which known as cordycepin has discovered as a successful anti -tumor agent, specially against several cancer types (Jin et al., 2018). Cordycepin has the ability of induce cancer cell apoptosis in caspase-dependent pathways, a primary mechanism of apoptosis, which governing by a family of protease enzymes named caspases. Apoptosis of Human liver cancer (HepG2) cells were induced by the activation of caspase, interaction between Fas and FADD, and modulation of the protein levels of Bid and tBid (Shao et al., 2016). Cordycepin also decreased human bladder carcinoma cells (T24 cells) survival. That was regulating by the activation of A3 adenosine receptor of the cells and the subsequent inactivation of Akt pathways, leading to the increases in cleaved Caspase-3 and apoptosis (Cao et al., 2017). Instead of cordycepin, polysaccharides, Beauvericin, Ergosterol and cordycemaides are also responsible for the activation of tumor suppression pathways. (Xiao and Zhong , 2007).

Health benefits and human well being

Rather than using for pharmaceutical extractions and production of new medicines, *Cordyceps* are much popular among people as a nutrient rich source from minerals, proteins, amino acid derivatives and phenolic components (Liu et al., 2019; Ashraf et al., 2020). Abundant number of bioactive components and secondary metabolites are present in *Cordyceps* such as proteins derivatives, carbohydrates such as arabinose, fatty acids, volatile compounds, carotenoids, phenolic compounds, flavonoids, minerals (Fe, Ca, Mg, Ni, Sr, Na, Ti, Pi, Se, Mn, Zn, Al, Si, K, Cr, Ga, V and Zr) and vitamins (B1, B2, B12, E and K) (Hur, 2008; Elkhateeb et al., 2019; Ashraf et al., 2020). Because of that, *Cordyceps* spp. are now using as a dietary supplement as well as a herbal medicine by various states including United States and Eastern Asian countries such as China (Das et al., 2010).

Cultivation of *Cordyceps*

In natural environments, *Cordyceps* spp. are growing on specific host species. But, when comes to mass production, cereal-based substrates such as rice, wheat, oats, and barley, which provide essential nutrients for mycelial colonization and metabolite biosynthesis for cordyceps cultvation. Supplementation with suitable nitrogen sources and trace elements further enhances growth, fruiting body formation, and cordycepin accumulation (Sharma *et al.*, 2024; Shrikhandia *et al.*, 2026). In contrast, submerged liquid fermentation is primarily used for rapid mycelial biomass production under controlled environmental conditions, including optimized pH, temperature, aeration, agitation, and nutrient availability. It offers advantages such as shorter cultivation periods, reduced contamination risks, easier process control, and scalability for industrial production, although fruiting body development is generally absent under submerged conditions (Paterson, 2008; Shrikhandia *et al.*, 2026). The selection of cultivation substrates, carbon and nitrogen sources, light exposure, temperature, and oxygen availability significantly influences fungal growth and the synthesis of secondary metabolites. Recent advances have focused on optimizing cultivation media using agro-industrial residues, mixed grain substrates, and insect-derived materials to improve productivity while reducing production costs. Furthermore, the integration of bioprocess engineering, controlled fermentation systems, and strain improvement has enhanced biomass yield and metabolite production, supporting the commercial development of *Cordyceps*-derived nutraceuticals and pharmaceuticals. Nevertheless, the establishment of standardized cultivation protocols and efficient large-scale production systems remains a major research priority to ensure consistent product quality and maximize the accumulation of valuable bioactive compounds (Sharma *et al.*, 2024; Shrikhandia *et al.*, 2026).

Conclusion

Cordyceps is a group of entomoparasitic fungal species which belonging in to the phylum Ascomycota. As an obligate parasite, *Cordyceps* are using various types of metabolic compounds for ensure their life cycle. They are usually rich form numerous secondary metabolic components including cordycepin, Pentostatin, peroxides, organic acids, polysaccharides, volatile components, and mineral nutrients. In Traditional Chinese Medicine (TCM) a certain species of cordyceps and their extractions including *O. sinensis*, *C. militars* and *C. purinosa* has been used as medicines for cough, renal disfunction and failures, immunity, anti-inflammatory, antioxidant, and blood sugar regulation. Some properties of *Cordyceps* spp. have been discovered from recent researches in pharmaceuticals. Immunomodulatory is one of the recently discovered property from *O. sinensis.* It can enhance the effectiveness of an anti -tuberculosis drug names PA-824. The combination has better effectiveness than the using the drug along against *Mycobacterium tuberculosis*. Apart from that, many *Cordyceps* spp. are containing compounds which can be used in treatments of various cancers including several types of hepatic cancers. Because of being a high profitable industry, selected *Cordyceps* spp. are now cultivated in media, including cereal based and liquid fermentation methods. Further researches and studies regarding the bioactive compounds, metabolite extraction methods and cultivation optimization techniques can enhance the *Cordyceps* biotechnological applications.

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