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Chinese medicinal fungus *ophiocordyceps sinensis*: a review

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Abstract

Cordyceps species, such as *C. sinensis, C. militaris, C. pruinosa, and C. ophioglossoides* are highly valued in traditional medicine. The entomopathogenic fungus Ophiocordyceps sinensis, previously known as Cordyceps sinensis, has been used for centuries in traditional Chinese medicine to treat various ailments. Recently, its use has surged due to rising living standards and increased focus on health. This growing demand has led to excessive wild harvesting. Fortunately, research has shown that artificially cultivated and fermented mycelial products of *O. sinensis* exhibit similar pharmacological effects as their wild counterparts. The development of laboratory cultures is expected to enhance its application in treating various conditions. This review provides an overview of the *cordyceps* interaction with the host, bioactive compounds, traditional uses and pharmacological properties of *O. sinensis* components.

Key words: cordyceps sinensis, superoxide dismutase, reactive oxygen species, pharmacological properties.

Introduction

Mushrooms, which were previously known for their food and nutritional benefits, are currently gaining popularity for their significant therapeutic potential. In spite of being used in functional foods, they are also included in nutraceuticals, mycotherapy products and dietary supplements. [1,2] . A variety of pharmacological effects are shown by medicinal mushrooms including anti-microbial ,antidiabetic, cytotoxic, antioxidant, hepatoprotective, antiallergic, anticancer, immunomodulatory , prebiotic properties, antihyperlipidemic, and anti-inflammatory among others[2,3,4,5].

One such mushroom is the *Ophiocordyceps sinensis* belongs to Ascomycetes. It is a parasite mainly on insects and other Orthropods. Cordycepin and Cordycepic acid are the main components of the *O. sinensis*. Nucelosides, polysaccharides, sterols and number of bioactive substances found in O. sinensis have been used to treat kidney disease, fatigue, hyperlipidemia, infertility, renal failure, arrhythmias, and a number of cardiac conditions[6].

***Cordyceps* interaction with the Host:** The fungus *Ophiocordyceps sinensis* is also referred to as the Chinese Caterpillar Fungus, "Hia Tsao Tong Tchong" and "Hea Tsaon Tsong Chung" in earliest translations of English, or "Dong Chong Xia Cao" (summertime grass or winter worm) in Chinese.[7].

Cordyceps typically infects insects at various developmental stages, from larvae to adults. The spread of fungal conidia on the insect's surface initiates the infection. After the settlement of conidia on the surface it will germinate within few hours under favourable conditions. Under unfavorable circumstances, conidia can secrete enzymes such as peroxidases and Cu-Zn superoxide dismutase (SOD).

By producing reactive oxygen species (ROS) in response to heat and UV light, these enzymes helps in protecting conidia from harmful substances. Additionally, Conidia also release certain hydrolytic enzymes, like lipases, chitinases, and proteases, which breakdown the insect integument and are essential for infecting the host. These enzymes create a pathway for conidia penetration and supply nutrition to the germinating conidia.

An appressorium is a tiny germ tube that arises from the conidia as the infection increases and gets started to thicken at its distal end.It has been observed that appressorium is known to exert mechanical pressure on the Cordyceps. The plate-like structure known as the penetration plate is formed by the germ tube once it has entered the insect's integument.

The penetration plate develops secondary hyphae that penetrate the epidermal layer and extend into the insect's hemocoel. Protoplast bodies arise from these hyphae and move throughout the insect's hemocoel. The fungus will continue to spread throughout the host's tissues and organs. During its growth, the filamentous fungus may release multiple harmful secondary metabolites into the body of its host. At the end of the fungal life cycle, these metabolites kill the host, which is an insect. They have a strong insecticidal effect. (Fig no.1) Eventually, under favourable circumstances, fruiting body production will take place[8].

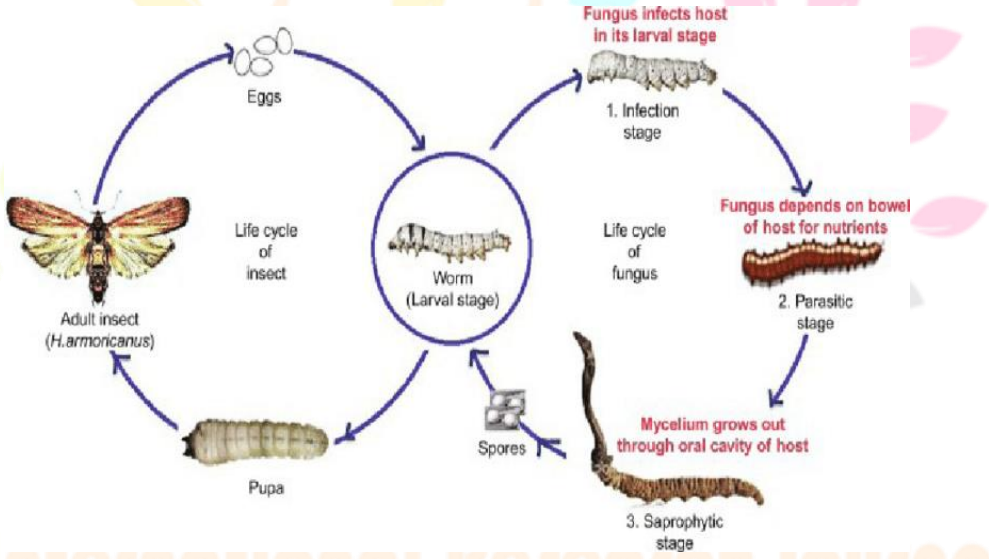

Fig no 1: Cordyceps sinensis developmental phases in the host caterpillar Hepialus armoricanus [8].

Bioactive compounds of *o. sinensis*: Many bioactive substances, like polysaccharides, ergosterol, nucleosides, cordycepin, and cordycepic acid, have been isolated and purified from *O. sinensis* by scientists. Numerous investigations have revealed that these substances, whether under single or combination circumstances, it clearly exhibits various pharmacological properties[9]. Artificially farmed O. sinensis produced higher levels of polysaccharides, adenine, and adenosine than naturally occurring specimens, according to a recent study by Wang et al. (2015a). Additionally, their research indicated that water extracts from the cultured samples exhibited enhanced antioxidant capability[10].

Cordycepic acid and cordycepin: Cordycepin, chemically known as 3′-deoxyadenosine, was initially isolated from Cordyceps militaris in 1951 and later from *O. sinensis* in 1996[11]. The biological activities of cordycepin have been widely documented, and it has been used to treat a variety of ailments including its anti-inflammatory properties[12], cell proliferation[13], and platelet activation[14]. According to Wong et al. (2010), cordycepin's effects on AMP-activated kinase (AMPK) signalling and mTOR are likely the cause of many of the biological effects that have been described[15].

The isomer of cordycepic acid is quinic acid, which was initially identified from c.sinensis in 1957[16] and later it was identified as d-mannitol[17]. One of the main byproduct of plants is mannitol, which is found in carrots, lichens, and edible fungi. O. sinensis has a 7–29% cordycepic acid concentration, which varies with growth [18].

Polysaccharides: A class of structurally varied macromolecules known as polysaccharides and it has been shown to have immunological, anti-tumour, and antioxidative effects. Complex galactomannans with several branches and a variety of connections between neighbouring monosaccharaides that create helical and tiny ring structures are known as polysaccharides.[9]. Most polysaccharides are colorless, odorless, and have high stability and solubility in water. Miyazaki et al. (1977) carried out the first study on the polysaccharide structures from naturally occurring *O. sinensis*. Since then, a substantial amount of scientific study has been carried out in China and Japan to find potentially beneficial polysaccharides.[19].

Usually, fruiting bodies, fermented mycelia, fermentation cultures, and broth include polysaccharides, which range from 3 to 8% in concentration in O. sinensis[20]. Several investigations have demonstrated that O. sinensis polysaccharides exhibit a variety of biological effects, including antioxidant, immunomodulatory, apoptosis, anticancer, and cardiovascular protection[9]. Therefore, more studies concentrating on polysaccharide separation, purification, functional processes, and mechanisms will lead to novel findings and increased uses of O. sinensis.

Additional bioactive substances: In addition to the previously noted key bioactive compounds, *O. sinensis* yields numerous other bioactive components such as ergsterol, crude proteins, nucleotides, amino acids, metal elements and fatty acids which exhibit various pharmacological functions[9]. **Nucleotides** such as adenosine, uridine, and guanosine are potent bioactive constituents found in *O. sinensis*[21].

Ergosterol is a sterol which is particularly present in fungi that serves as a precursor to vitamin D2, which has significant health benefits and medicinal applications. Ergosterol mainly exists in two forms like free ergosterol and esterified ergosterol, each having distinct physiological functions[22].

Fatty acids can be categorized into two types: saturated and unsaturated. Unsaturated fatty acids are physiologically active substances that have the special ability to lower blood lipid levels and preventing the development of cardiovascular disease[9].

Eighteen amino acids were found in **crude protein**, including aspartic acid, glycine, valine, methionine, isoleucine, glutamate, threonine, serine, proline, tryptophan, phenylalanine, histidine, tyrosine, lysine and cysteine with a crude protein concentration between 29.1 and 33%[23]. Amino acids are usually expressed as 20–25% after hydrolysis; The minimum is 5.53% and the greatest is 39.22%. Aspartic acid, glutamate, and arginine have the largest quantities, whereas tyrosine, glutamate, arginine, and tryptophan are the main pharmacological components.[24].

Zinc, magnesium, and manganese are examples of **metal elements** that are important for the growth and maintenance of gonad function[25].

Traditional uses of *o. sinensis*:

The fungus, mushroom, or herb is known as gumba by the inhabitants of North Sikkim; "winter (yarsa) and summer (gumba)" is how its Tibetan name is interpreted. In literary works, "gunba" or "Gonba" have also been used in instead of "gumba." The local Nepalese refer to it as Keera Jhar, or insect herb. It is also called as Himalayan Viagra.

When yaks, goats, lambs, and other animals grazed in the forest and consumed C. Sinensis, the local herders noticed that the animals were strong and robust. Its therapeutic qualities were found as a result of this finding. Locals and herders then used the powdered fungus combined with jaggery to increase milk yield and improve the health and vitality of their cattle. Later, its advantageous medical qualities

were studied, with an emphasis on harvesting only the above-ground portion (fruiting body/stroma), which was first processed by sun-drying. After consuming it for themselves, they were convinced of its therapeutic benefits in boosting vigor and energy. Eventually, they noticed that it had aphrodisiac properties, and they frequently gave it as gifts to friends and family from Gangtok and the neighborhood.

At present, the product is used by regional traditional healers to treat a variety of illnesses, either by itself or in combination with other medicinal herbs. They apply an empirical trial-and-error technique to treat various illnesses, determining dosage based on their experience. To increase libido and desire, men and women alike usually take one piece of C. sinensis with a cup of milk. The Bhutia community rises one piece of C. Sinensis in a cup of locally manufactured alcohol (chang) for an hour, and then drinks it as a tonic in the morning and evening.

When preparing and drinking C. sinensis, some people choose to use hot water rather than alcohol. C. sinensis is used as therapeutic agent for wasting disorders and diabetes by certain traditional healers.By mixing it with a decoction of ginseng root and texus leaf; it is used in cancer treatment. Nepalese reports also mention similar procedures[26,27,28].

Long-term and consistent use of C. Sinensis for 21 different conditions has been noted by local traditional healers or folk healers. These conditions include cancer, erectile dysfunction, benign prostatic hyperplasia (BHP), jaundice, alcoholic hepatitis, diabetes, bronchial asthma, bronchitis, TB, and others.[29]. It's used by many traditional healers and senior citizens to treat erectile dysfunction and lengthen life expectancy[30].

Reported pharmacological activities:

Pharmacology: Cordyceps species, particularly *C. sinensis,* is highly valued as both a nutritional supplement and medicinal mushroom, serving as a crucial material source in Traditional Chinese Medicine. The identification of novel antibiotics within this mushroom represents a major breakthrough in contemporary research. One such substance is cordycepin, which has shown to be quite successful against a variety of bacteria that show resistance to other widely used antibiotics. Asthma, immunological disorders, renal problems, and chronic obstructive lung illnesses are among the conditions for which cordyceps is utilized. It also strengthens heartbeats and controls low blood pressure. Both men and women can benefit from its aphrodisiac properties and use it to cure impotence. The following are some more health advantages of cordyceps:

- **Increases physical stamina**
- **Effects on heart**
- **Maintains liver, kidney, lungs function**
- **Improves sexual function**
- **Anti-bacterial and anti-oxidant properties**
- **Immunomodulating properties**
- **Anti-tumour effects [31].**

Conclusion

Ultimately, Ophiocordyceps sinensis, which is also referred to as Cordyceps sinensis or Yarsagumba, is a highly prized medicinal fungus that possesses a multitude of potential health advantages. Its traditional and modern uses include boosting the immune system, enhancing athletic performance, improving respiratory and cardiovascular health, managing blood sugar levels, and promoting overall vitality. The bioactive compounds in Ophiocordyceps sinensis, such as polysaccharides and beta-glucans, contribute to its therapeutic effects, making it a popular supplement for promoting health and longevity.

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