

Review on: Pharmacological Activity of *Caterpillar fungus* (Keeda Jadi)

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www.jrasb.com || Vol. 2 No. 3 (2023): June Issue

Received: 26-05-2023

Revised: 06-06-2023

Accepted: 16-06-2023

ABSTRACT

In this review we focus about the pharmacology, biological characteristics and therapeutic uses of *Caterpillar fungus* (*Keeda jari*) which is also known as *keeda ghaas*, *Yarsa gamba*. It is found at high Himalayan mountains of India, Nepal and Tibet. It is found between 350 and 5000 meters above sea level. It is an entomo-fungal combination of a larva of small moth, *Hepialus armoricanus* and a parasite fungus *Cordyceps sinensis*. *Cordyceps* is best known medicine for increasing physical stamina and sexual functions. It has been proven to improve liver, kidney, and lung functioning in addition to being routinely used to treat people with heart disease. Numerous investigations have shown that it possesses a wide range of biological functions and pharmacological potential despite not being harvested in a sustainable or deliberate manner.

Keywords- Lecturers' Engagement, PLIS, Ethical Leadership, Public Universities.

I. INTRODUCTION

As a tonic and/or narcotic, Chongcao, also known as the sexual stage of the fungus *Ophiocordyceps sinensis*, has been utilised by humans for a significant amount of time. However, safety concerns were voiced after it was discovered that substantial concentrations of arsenic were present in the soil where wild *Ophiocordyceps sinensis* thrives [1]. This led to the questioning of whether or not it was safe to consume. *Ophiocordyceps sinensis* was shown to have a number of beneficial effects in clinical studies, including the ability to stop bleeding, remove phlegm, and strengthen the kidneys and lungs. In addition to the therapy of non-small cell lung cancer, liver cancer, and breast cancer [2,3], this substance has the potential to be used as an adjuvant in the treatment of 21 additional illnesses. It has

been demonstrated that chongcao can treat a broad variety of illnesses, including cancer, diabetes, hypertension, liver disease, and heart disease [4,5,6,7,8,9]. This is the case despite the fact that chongcao is known to have adverse effects on human health. In recent years, the cost of *O. sinensis* has increased as a result of an increase in demand coupled with a decrease in available supply. In 2016, the China Food and Drug Administration (CFDA) rigorously limited its manufacture and sale due to the presence of arsenic in the natural fruiting bodies. This was done despite the fact that the cost of the product was rising. Arsenic is a pollutant in the environment that has been demonstrated to inhibit the migration of neurons, the maturation of cells, and the proliferation of neural progenitor cells [1,10]. Because of the lack of availability and the safe clinical usage, other

Ophiocordyceps-related fungi and conidial forms of artificially created *O. sinensis* fermentation mycelia have been used as alternatives in Chinese medicine and healthy food [11,12].

Researchers are in agreement that *Hirsutella sinensis* is a unique anamorph of *O. sinensis* [11,15,16,17]. Additionally, they believe that additional species, such as *Paecilomyces hepialid*, *Gliocladium roseum*, and *Tolypocladium sinensis*, represent endoparasitic fungi that are widely found in wild *O. sinensis* [18,19]. *Ophiocordyceps* powder (*Hirsutella sinensis* species), *Ophiocordyceps* powder (*Paecilomyces hepialid* species), *Ophiocordyceps* powder (*Gliocladium roseum* species), and *O. mortierella* mycelium powder (*Tolypocladium sinensis* species) are all examples of the four species isolated from *O. sinensis* that have been successfully cultured. Mycelia from the *Ophiocordyceps* mushroom can be fermented into one of four different standardised products [20,21,22,23,24], all of which find widespread application as components of traditional Chinese medicine [25].

Because different *Ophiocordyceps* species may have varying effects on a person's health, it is essential that any products claiming to contain *O. sinensis* undergo a rigorous authentication process before being put on the market. In the past, positive identification of *O. sinensis* was accomplished through the use of morphological description, microscopic identification, and chemical composition analysis [23,26,27,28,29]. Due to the absence of objective standards or a particular component index in these processes [30,31,32,33,34], correctly identifying and separating *O. sinensis* from the numerous cultivated *O. mycelia* can be a difficult task. Additionally, while the polymerase chain reaction (PCR) has been effectively used to identify *Ophiocordyceps sinensis* (*O.S.*) fruiting bodies [14,15,35], it is not possible to use PCR to identify cultivated *Ophiocordyceps* mycelia because the drying process affects the integrity of the DNA genome [18,36,37]. Because determining the species of a mushroom is an essential and vital step in maintaining quality control and standardisation of herbal treatments, it is of the utmost importance that methods be developed to authenticate *O. sinensis* as well as the four farmed strains of *O. mycelia* listed above. Finding proteins in the species that are characteristic of fungi could be one method to accomplish this goal. Because the sequence of amino acids in the fungal protein might differ across different types of fungi, it can be utilised as a reliable method for determining the species [38,39]. However, despite the fact that these proteins are thought to be among the *O.S.*'s bioactive components, very little research has been done on them and very few reports have been written on them [40]. As a result of its segmented quadruple mass filter, improved selectivity, and increased ion transmissibility, biological mass

spectrometry [38,39,41,42,43,44,45,46] has developed into a potent instrument for the analysis of proteomes. However, the information that is currently available is insufficient to characterise the protein produced by the fungus at the genus level. An illustration of this would be the flag peptide that was discovered in the digested *O. sinensis*-related products.

Geographical Distribution

The sole locations on Earth where you may find *Ophiocordyceps sinensis* are in Bhutan, southern China, northern India (mainly Himachal Pradesh, Sikkim, and Uttarakhand), and Nepal, at elevations between 3,000 and 5,000 metres. Tibet, Gansu, Qinghai, Sichuan, and Yunnan are the Chinese provinces where you can find it most frequently[48].

Caterpillar fungus Pharmacology Activity

A remarkable nutritional supplement and therapeutic fungus *Cordyceps* species especially *C. sinensis*, is a key source of information for Traditional Chinese Medicine[49]. The discovery of novel antibiotics in this fungus has been one of the high points of contemporary study. One of these, cordycepin, is extremely efficient against a variety of bacteria species that have shown resistant to other, more widely used antibiotics[50]. The herb cordyceps is used to treat asthma, renal, immunological disorders, chronic obstructive pulmonary illnesses, and low blood pressure. It also strengthens the heartbeat. Both men and women use it as an aphrodisiac and as a cure for impotence[51].

Enhances physical stamina

The most well-known medical use of cordyceps is for boosting athletic endurance. Clinical studies have demonstrated that cordyceps boosted cellular ATP10. An increase in cellular ATP increases useable energy and strengthens internal balancing mechanisms, which enhances oxygen utilization[52]. Such effects might be brought on by the presence of adenosine, cordycepin, cordycepin acid, d-mannitol, polysaccharides, vitamins, and trace minerals. When people utilize cordyceps, these characteristics lead to physical improvement, increased endurance, and anti-fatigue[53].

Effects on heart

Patients with heart disease and stroke survivors have historically been treated with *C. sinensis*. The cardiovascular system is impacted by *C. sinensis* in a variety of ways, including decreased myocardial oxygen consumption, improved myocardial ischemia, and anti-platelet aggregation. *C. sinensis* can improve myocardial ischemia by increasing nutritive myocardial blood flow and inhibiting arrhythmia brought on by aconitine, barium chloride, and adrenaline.[54]. Patients with chronic heart failure have reported an improvement in their overall quality of life because to it, and it also treats renal hypertension.

Maintain liver function

It has been demonstrated that *C. sinensis* improves the liver's effectiveness in functioning.

Traditional Chinese Medicine has been used to try to prevent liver illness, and cordyceps is one of the main components of TCM. Patients with liver diseases such as viral hepatitis A, chronic hepatitis B, chronic hepatitis C, hepatitis fibrosis, etc. respond very well to cordyceps. It improves liver function, immunological activity of organic cells, and reduces hepatic fibrosis.[55]. The majority of Cordyceps' bioactive substance for liver protection, which varies depending on the species, are Cordyceps polysaccharides. The liver fibrosis can be significantly reduced by *C. sinensis*, and it can also speed up the breakdown of collagen. The liver fibrosis-inhibiting effects of *C. sinensis* polysaccharide on stellate cell activation[56].

Maintain kidney functions

By raising the blood levels of 17-hydroxycorticosteroids and 17-ketosteroids, *C. sinensis* may improve kidney function. According to studies *C. sinensis* extract is employed as a medicinal medication for treating kidney illnesses such glomerular sclerosis and chronic renal diseases in general. The high toxicity medication cyclosporin, which is used during kidney transplantation, causes substantial renal damage in many patients who take it[56].

According to the study, patients who received *C. sinensis* in addition to cyclosporin had a considerably lower rate of kidney injury than those who just received cyclosporin[57].

Maintain lung's function

The bronchi are significantly relaxed by *C. sinensis*, the adrenal glands produce significantly more adrenaline, and it also affects how histamine causes the trachea to constrict. Additionally, it has expectorant, anti-asthmatic, and anti-tussive properties and prevents pulmonary emphysema.[58]. Numerous studies have demonstrated the effectiveness of *C. sinensis* in treating a variety of respiratory conditions, including as bronchitis, chronic obstructive pulmonary disease, and asthma. It has been demonstrated that *C. sinensis* extract inhibits tracheal contractions, which is crucial for asthma sufferers as it allows for more ventilation to the lungs[59].

Improve sexual function

Traditional Chinese Medicine has long utilized *C. sinensis* to treat both male and female sexual issues, including hypo libido and impotence. It has been demonstrated to enhance sperm count and survival, decrease infertility, and boost libido and quality of life in both men and women. Clinical studies on humans have similarly shown that *C. sinensis* is useful in preventing diminished sex desire and virility. Additionally, *C. sinensis* has similar effects to sex steroids in mice[60].

Antibacterial properties

C. sinensis was capable of killing germs. Gram-positive and Gram-negative bacteria were both suppressed by the antibacterial protein CSAP that was

isolated from *C. sinensis* cultivated mycelia, while fungus and yeast were not significantly inhibited.[61]. *Staphylococcus aureus*, *E. coli*, *Bacillus subtilis*, and *Bacillus thuringiensis* were all susceptible to the antibacterial properties of the fermentation broth of *C. sinensis*[62].

Antioxidant properties

C. sinensis has antioxidant properties. The antioxidant efficacy of water extracts from diverse natural sources of *C. sinensis* and cultivated Cordyceps mycelia was assessed using three distinct test methods: the xanthine oxidase assay, the induction of hemolysis assay, and the lipid peroxidase assay. The findings indicated that Cordyceps had potent anti-oxidant properties in all assays.[63]. Water-soluble polysaccharide CPSI, a galactosaminogalactan containing glucose, mannose, and galactose as its monosaccharides, was isolated from *C. sinensis* and shown antioxidant activity in vitro, including the ability to scavenge hydroxyl radicals, the ability to reduce, and the ability to chelate Fe²⁺.

Antitumor activities

The extract of *C. sinensis* has been acknowledged as a traditional therapy, utilized in Traditional Chinese Medicine for the prevention and treatment of cancer and various other diseases. *C. sinensis* has the capacity to suppress the formation of tumors. The primary bioactive components in cordyceps that have antitumor effect include polysaccharides, sterols, and adenosine[64]. Cordyceps polysaccharides' antitumor activity has been amply shown the effects of cordyceps extract have been examined²⁹, and 28 novel antitumor substances have continuously been identified. The ethyl acetate extract of Cordyceps displayed the most powerful action. Different Cordyceps extracts also shown higher cytotoxicity on the B16 cell line. The extract may include the chemicals ergosterol and adenosine[65].

Effects on immune system

C. sinensis extracts exhibit immune-stimulating and immune-suppressive properties. Immunomodulators can be efficient treatments and preventative measures for conditions brought on by certain immune deficits. Major immunomodulating effects of the active ingredient isolated from cordyceps include lymphoproliferative response, natural killer cell activity, and phytohemagglutinin-stimulated interleukin and tumor necrosis factor- α production on human mononuclear cells. The immunomodulating properties of mushrooms are linked to their therapeutic benefits, which include the reduction of immunological disorders and allergies. A research revealed that several Cordyceps polysaccharide components improved renal functions as well as the immunological response, spleen index, thymus index, monocyte-macrophage phagocytic function, and cellular immune function in chronic renal failure[66]

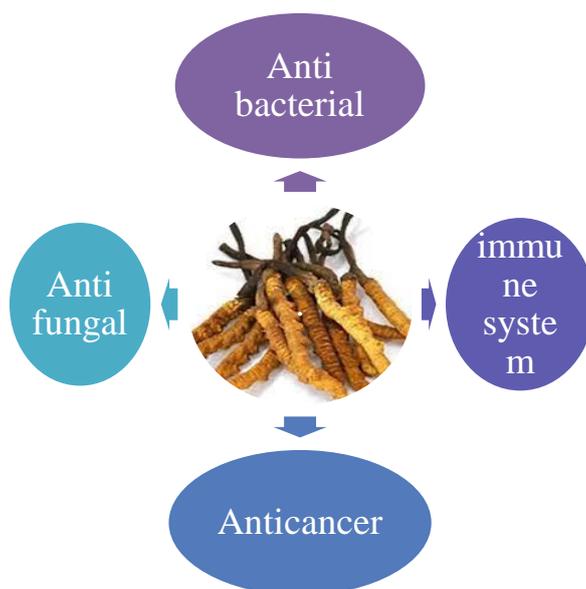


Figure 1: Pharmacological Activity of *C. sinensis*

Phytochemical constituents

Numerous nutritious substances can be found in cordyceps. It includes unprocessed lipids, proteins, fibers, carbs, polysaccharides, cordycepin, cordycepin acid, and vitamins, among other things[67]. It also has sterols, nucleosides, macro- and microelements, as well as mono, di, and oligosaccharides of sugar[68].

Cordycepin and cordycepin acid

It has been suggested that cordycepin and cordycepin acid are significant components of *C. sinensis*. The structural formula of cordycepin, which was initially isolated from *C. militaris*, was determined to be 3'-deoxyadenosine. One of the key therapeutic ingredients is cordycepin acid, an isomer of quinic acid whose structure has been determined to be 1,3,4-trihydroxycyclohexane[69].

The amount of cordycepin acid in *C. sinensis* varies according to the body's stage of growth and ranges from 7 to 29%. It is a complement to other medications and is used for injection.

Polysaccharides

The medicinally useful ingredient, polysaccharides, was abundant and made up 3–8% of the total weight of cordyceps. These have positive effects on blood sugar regulation as well as antimetastatic, antitumor, and immunomodulating properties[70].

An atomic force microscope (AFM) was used to examine the topography of the Cordyceps polysaccharides, which revealed that they had a multi-branched galactomannan structure. Galactomannan was extracted from the water-soluble protein-containing sodium carbonate extract of Cordyceps, and its molecular weight was determined by gel filtration to be separated substance has a 3:5 molar ratio of D-mannose and D-galactose as well as a trace amount of protein.

The molecular weight of polysaccharides is related to their pharmacological action. Polyglucans with

a higher molecular weight often have greater water solubility and more potent anti-tumor action.

Nucleotides

Adenosine, uridine, and guanosine are useful nucleotide components found in cordyceps. Guanosine is the nucleotide found in maximum concentration in both natural and artificial Cordyceps, and artificial Cordyceps also contain more nucleotides than natural Cordyceps[71].

Sterols

Ergosterol, -3-ergosterol, ergosterol peroxide, 3-sitosterol, deco sterol, and campestral are among the sterol-type substances found in cordyceps.

Ergosterol is an essential precursor of vitamin D2 and has significant therapeutic benefit. Free ergosterol levels in natural Cordyceps vary considerably, although they are definitely greater in the mycelia of the plant.

Protein and amino acids

The range of 29–33% for the crude protein content of cordyceps. The protein is made up of 18 amino acids, and it is typically stated that 20 to 25 percent of those amino acids remain after hydrolysis[72]. The main pharmacological constituents are arginine, glutamate, tryptophan, and tyrosine; among these, glutamate, arginine, and aspartic acid have the largest content. The commercial preparation of Cordyceps has a greater amino acid content than the mycelia of *C. sinensis*, which is comparable to the level in the fruiting body of *C. sinensis*.

Fatty acids and metals

Both saturated and unsaturated fatty acids are present in cordyceps. The amount of unsaturated fatty acids is 57.84%. With 38.44%, linoleic acid has the largest amount, followed by 17.9% for oleic acid[73]. Content of saturated fatty acids is 42.16%. The two acids with the greatest concentrations—palmitic acid (21.86%)

and octadecanoic acid (15.78%)—are present. Unsaturated fatty acids perform the unusual task of lowering blood lipid levels and preventing cardiovascular illnesses.

The number of metals in *Cordyceps* varies depending on the species and metal elements it contains high levels of zinc, magnesium, and manganese are crucial for warming the kidney and promoting renal healing[74].

II. MARKET POTENTIAL

Wild-harvested and naturally occurring plants are valued more highly in traditional medical practices because they are thought to have more therapeutic effects; as a result, their costs are higher. Since ancient times, *cordyceps* has been regarded for its therapeutic benefits, and this practice is still prevalent today. The fungus is traditionally exchanged for its weight in silver or gold in China[75]. In Chinese marketplaces, *cordyceps* is still quite valuable; one kilogram of the fungus was sold for Rs. 1,00,0007. In Nepal, the cost of a kilogram of available fungus can range between NR (Nepali Rupees) 30,000 and 60,000, whereas Uttarakhand in India produces the most *cordyceps*, with unofficial average prices of Rs. 2,50000 to 3,00000 per kilogram[76].

The majority of the peasants in the districts of Chamoli and Pithoragarh are responsible for collecting *cordyceps*. As a result, the harvesting of *Cordyceps* has caused significant changes in the economics and way of life of the villages. The Government of Uttarakhand has created regulations and procedures for the sustainable gathering of *cordyceps* and has delegated responsibility to "Van Panchayats[77].

III. TRADITIONAL SIGNIFICANCE OF STUDY

Due to its distinctiveness and value as a medicinal plant, *C. sinensis*[78]. Due to its abundance, locals in many areas of the Himalayan region gather it to improve their standard of living, but they are not well-versed in collecting methods or conservation practices[79]. It is frequently believed that *C. sinensis* collecting poses a harm to the Himalayan ecosystem where it flourishes. Given the significance of *cordyceps*, it is necessary to educate the locals and communities about science and to provide them with training in sustainable harvesting and conservation salvaging[80].

IV. CONCLUSION

Numerous investigations have shown that it possesses a wide range of biological functions and pharmacological potential despite not being harvested in a sustainable or deliberate manner. To resolve the

numerous claims and controversies in the present period scientifically is one of our difficulties. Due of the material's high price and rarity, *Cordyceps* has faced more difficulties than most other plants. Mycelium cultivation in the lab, standardization, the creation of suitable dosage forms, and carrying out rapid stability tests of the same are the only areas that require attention. Therefore, scientific knowledge and awareness are essential for the future prospects of *cordyceps*, including commerce, sustainable harvesting, conservation, and production methods.

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