

## **Cordyceps sinensis: A review on pharmacology, biological characteristics, and traditional uses**

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### **ABSTRACT**

This review focuses on the pharmacology, biological characteristics, and conventional use of "Keeda jadi," a significant folk remedy. In the wild, it can be found in the high Himalayan ranges in India, Nepal, and Tibet at high altitudes of 350–5000 m. A tiny moth larva, *Hepialus armoricanus*, and the parasitic fungus *Cordyceps sinensis* make up this entomo-fungal hybrid. The most well-known medical use of cordyceps is for enhancing sexual and physical endurance. It has been traditionally used to treat individuals with heart disease and also found to boost liver, kidney and lung functions. Because of its therapeutic qualities, *C. sinensis* is special and valued. Many 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. Hence, scientific knowledge and awareness are essential for the future prospects of cordyceps, including trade, sustainable harvesting, conservation, and production methods.

**Keywords:** Cordyceps sinensis, Pharmacology, Traditional uses, Cordycepin

### **INTRODUCTION**

Due to its rich biodiversity, the Indian Himalaya region is regarded as a true bazaar of herbal treasure. Important medicinal and fragrant plants thrive in this area and have several folkloric uses. A very significant folklore medicine known as Keeda jadi, Keeda ghaas, Yarsa gumba, Yarsa gunbu, etc. is widely found in the alpine parts of the Indian Himalaya, primarily in Arunachal Pradesh and Uttarakhand, generally at the altitudes of 3500-5000 m [1-3]. *Hepialus armoricanus*, a tiny moth larva (Lepidoptera; caterpillar host), and the parasitic fungus *Cordyceps sinensis* make up this entomo-fungal hybrid. The fungus's mycelium colonises the moth larvae that have been buried by growing in the soil. The mycelium's expansion causes the caterpillar to become mummified. The mycelium of the fungus creates a fruiting body that emerges from the head of the larva when alpine grasses begin to sprout in the summer [2].

Unknown Cordyceps (Berk.) Sacc. is a fungus that belongs to the Clavicipitales order, class

Pyrenomycetes, Ascomycotina subphylum, and Clavicipitaceae family. Many studies have been conducted in the past on *Cordyceps sinensis* from the Indian Himalaya on a variety of topics, including their medicinal potential, market worth, commerce, conservation tactics, collection methods, and history [1,2,4-7].

Due to its extraordinary therapeutic characteristics, *cordyceps sinensis* has been utilised as a traditional medicine since ancient times. It is used to treat asthma, renal injuries, bronchitis, cough, resistance of the respiratory tract, blood pressure, weakness, immunity strengthening, lung malfunction, and irregular menstruation, according to research [5,8]. It is also used to prepare formulations that are energising and revitalising.

There are several additional *Cordyceps* species that are present, but historically, the term "Cordyceps" has only ever been used to refer to the species *C. sinensis*, which has long been prized in Traditional Chinese Medicine. Since *Cordyceps* is only naturally found at extremely high altitudes in the Himalaya, it is incredibly challenging to gather. It has long been one of the most expensive medicinal fungus because of these challenges [9].

## PHARMACOLOGY

A remarkable nutritional supplement and therapeutic fungus, *Cordyceps* species, especially *C. sinensis*, is a key source of information for Traditional Chinese Medicine. The discovery of novel antibiotics in this fungus has been one of the high points of contemporary study. One of these, cordycepin, is particularly efficient against a wide range of bacteria, even those that have developed resistance to other widely used antibiotics. The herb *cordyceps* is used to treat asthma, renal, immunological disorders, chronic obstructive pulmonary illnesses, and low blood pressure. It also strengthens the heartbeat. It is used in treatment for impotence, as an aphrodisiac in both men and women. Some additional health benefits of *Cordyceps* are given below:

- **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. The efficiency of oxygen utilisation is improved by a rise in cellular ATP, which also increases the amount of useful energy and enhances the internal balance system. Such effects could be brought on by the presence of adenosine, cordycepin, cordycepin acid, d-mannitol, polysaccharides, vitamins, and trace minerals. When people utilise *cordyceps*, these characteristics lead to physical improvement, increased endurance, and anti-fatigue.

- **Effects on heart**

Patients with heart disease and stroke survivors have long 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 ischaemia by increasing nutritive myocardial blood flow and inhibiting arrhythmias brought on by aconitine, barium chloride, and adrenaline [11]. It has promoted an increase in the overall quality of life in the patients suffering from chronic heart failure and has curative role in renal hypertension [12,13].

- **Maintains 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 inhibits hepatic fibrosis [14]. 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. Polysaccharide of *C. sinensis* action on liver fibrosis and inhibit stellate cell activation and TGF $\beta$  1 expression [15].

- **Maintains kidney function**

By raising the blood levels of 17-hydroxy-corticosteroids and 17-ketosteroids, *C. sinensis* may improve kidney function [3]. According to studies, *C. sinensis* extract is utilised as a medicinal medication for treating kidney illnesses such glomerular sclerosis and chronic renal diseases in general [16]. The high toxicity medication cyclosporin, which is used during kidney transplantation, causes substantial renal damage in many patients who take it. Study revealed that patient receiving *C. sinensis* in addition with cyclosporin showed much lower incidence of kidney damage than group receiving only cyclosporine [17].

- **Maintains lung 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. Moreover, it has expectorant, anti-asthmatic, and anti-tussive properties and prevents pulmonary emphysema [18]. According to numerous research, *C. sinensis* is effective in treating a variety of respiratory conditions, such as bronchitis, chronic obstructive pulmonary disease, and asthma [19–21]. It has been demonstrated that *C. sinensis* extract inhibits tracheal contractions, which is crucial for asthma patients since it allows for greater ventilation to the lungs.

## IMPROVES SEXUAL FUNCTION

Traditional Chinese Medicine has long used *C. sinensis* to treat both male and female sexual issues, including hypolibido and impotence. It has been demonstrated to increase 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 drive and virility [22]. In mice, *C. sinensis* also produced effects akin to those of sex steroids [23].

- **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 extracted from cultivated *C. sinensis* mycelia, while fungus and yeast were not significantly inhibited [24]. *Bacillus subtilis*, *Bacillus thuringiensis*, and *Staphylococcus aureus* all exhibited antibacterial action in *C. sinensis* fermentation broth, but *Staphylococcus aureus* and *E. coli* were particularly sensitive [25].

- **Antioxidant properties**

*C. sinensis* possesses anti-oxidant properties. The xanthine oxidase assay, the induction of hemolysis assay, and the lipid peroxidase assay were used to assess the anti-oxidant activity of

water extracts from diverse natural sources of *C. sinensis* and cultured *Cordyceps* mycelia. The findings indicated that *Cordyceps* has potent anti-oxidant properties in all assays [26]. Water soluble polysaccharide CPSI, a glucomannogalactan with the monosaccharide composition of glucose, mannose and galactose, isolated from *C. sinensis* has shown antioxidant activity in vitro, including scavenging effect of the hydroxyl radicals, the reducing power and  $\text{Fe}^{2+}$  chelating activity [26].

- **Antitumor activities**

As a traditional medication used in Traditional Chinese Medicine for the prevention and treatment of cancer and a number of other diseases, *C. sinensis* has the capacity to limit the growth of tumours [27]. The primary bioactive components in cordyceps that have antitumor effect include polysaccharides, sterols, and adenosine. Many studies have been conducted to support the antitumor activity of cordyceps polysaccharides [28], and the effects of cordyceps extract have also been examined [29]. The ethyl acetate extract of *Cordyceps* displayed the most potent action. Various *Cordyceps* extracts also shown higher cytotoxicity on the B16 cell line. Potential chemicals identified from the extract included ergosterol and adenosine [30].

- **Immuno modulating effects**

Both individual components and *C. sinensis* extracts exhibit immune-stimulating and immune-suppressive properties. Immunomodulators have shown promise in the treatment and prevention of conditions and illnesses brought on by certain immunological deficits [31]. Major immunomodulating properties of the active ingredient extracted from cordyceps include lymphoproliferative response, natural killer cell activity, and phytohaemagglutinin-stimulated interleukin-2 and tumour necrosis factor- $\alpha$  production on human mononuclear cells [32]. The immunomodulating properties of mushrooms are linked to their therapeutic effects, which include the suppression of immunological disorders and allergies [33–34]. A study showed that different components of *Cordyceps* polysaccharides enhanced the immune response, spleen index, thymus index, phagocytic function of monocyte-macrophage [35], cellular immune function in chronic renal failure and also improved renal functions [36].

- **Side effects of *C. sinensis***

Although nausea, diarrhoea, and dry mouth<sup>3</sup> illnesses have been noted in a small number of patients, no deaths or significant injuries have been associated with the ingestion of *C. sinensis*. According to one investigation, a patient experienced a systemic allergic reaction after consuming the *Cordyceps* strain Cs-4 [37]. Lead poisoning is one of the most serious adverse effects of cordyceps. Lead is added by the harvesters to make the weight heavier; this is readily visible in the mass of the little, elongated *Cordyceps* and caterpillars. Kidney disease, elevated blood pressure, and decreased fertility in both men and women are all effects of lead poisoning. Women who have been exposed to lead poisoning have also experienced miscarriages and early births. Serious joint pain and motor nerve damage are also consequences. Although cordyceps enhances cardiovascular, renal, and other bodily functions, its lead pollution has detrimental consequences on the patient's health. Since cordyceps are created by parasitizing insects, if the insects had a disease, it might have spread to the cordyceps, making it polluted and dangerous.

## PHYTOCHEMICAL CONSTITUENTS

Many different nutritional substances can be found in cordyceps. It includes unprocessed lipids, proteins, fibres, carbs, polysaccharides, cordycepin, cordycepin acid, and vitamins, among other things. It also has sterols, nucleosides, macro- and microelements, as well as mono, di, and oligosaccharides of sugar.

- **Cordycepin and Cordycepin acid**

It has been suggested that cordycepin and cordycepin acid are significant components of *C. sinensis* [3]. The structural formula of cordycepin, which was initially isolated from *C. militaris*, was determined to be 3'-deoxyadenosine [38]. One of the key therapeutic ingredients is cordycepic acid, an isomer of quinic acid whose structure has been determined to be 1,3,4-trihydroxycyclohexane [39]. Depending on the body's stage of growth, Cordycepin acid content in *C. sinensis* ranges from 7 to 29% [40]. It is utilised as a supplement in various medications as well as for injection [41].

- **Polysaccharides**

The medicinally useful ingredient, polysaccharides, is abundant in cordyceps, making up 3–8% of its total weight [25,42]. They have antimetastatic, antitumor, and immunomodulating properties in addition to being excellent blood sugar regulators [28–29,32,43–44]. An atomic force microscope (AFM) was used to examine the topography of the Cordyceps polysaccharides, which revealed that they have 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 23 kDa. The compound isolated is composed of D-mannose and D-galactose in a molar ratio of 3:5 and small portion of protein [46]. Pharmacological activity of polysaccharides is correlated with the molecular weight. Higher molecular weight of polygucans tends to have greater water solubility and have more effective anti-tumour activity.

- **Nucleotides**

Adenosine, uridine, and guanosine are useful nucleotide components found in cordyceps. Guanosine is the nucleotide with the highest content in both natural and artificial Cordyceps, and artificial Cordyceps also have higher nucleotide content than natural Cordyceps [47].

- **Sterols**

Cordyceps contain number of sterol-type compounds ergosterol,  $\delta$ -3-ergosterol, ergosterol peroxide, 3-sitosterol, daucosterol and campeasterol. Ergosterol has important medicinal value and is an important precursor to Vitamin D<sub>2</sub>. The content of free ergosterol varies significantly in natural Cordyceps but evidently found higher in the mycelia of Cordyceps.

- **Protein and amino acids**

Around 29–33% of crude protein can be found in cordyceps [48]. 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. The four main pharmacological ingredients are arginine, glutamate, tryptophan, and tyrosine; of these, glutamate, arginine, and aspartic acid have the largest quantity [49]. The commercial preparation of Cordyceps has a higher amino acid content than the mycelia of *C. sinensis*, which is comparable to the content 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 content, followed by 17.9% for oleic acid. Content of saturated fatty acids is 42.16%. The two acids with the highest

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 amount of metals in Cordyceps varies depending on the species and metal elements [25]. High levels of Zn, Mg, and Mn are crucial for warming the kidney and promoting renal healing [50].

## MARKET POTENTIAL

Wild-harvested and naturally occurring plants are valued more highly in traditional medical practises because they are thought to offer more therapeutic effects; as a result, their costs are higher. From ancient times, cordyceps has been cherished for its therapeutic benefits, and this practise is still prevalent today. The fungus is traditionally exchanged for its weight in silver or gold in China. In Chinese marketplaces, cordyceps is still very valuable; one kilogramme of the fungus was sold for Rs. 1,00,0007. While Uttarakhand is India's top producer of cordyceps, with unofficial average prices of Rs. 2,50000 to 3,00000 for a kilogramme, the price may vary between NR (Nepali Rupees) 30,000 and 60,000 for a kilogramme in local areas of fungus availability [5,7]. 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 economy and way of life of the villages. The Government of Uttarakhand has created regulations and procedures and delegated responsibility to "Van Panchayats" for the sustainable collecting of Cordyceps [7].

## TRADITIONAL SIGNIFICANCE OF THE STUDY

*C. sinensis* is unique and valuable for its various medicinal properties. Locals in many parts of the Himalayan region collect it due to its availability in order to improve their standard of living, but they are not well-versed in collection methods or conservation practises. The Himalayan ecosystem where *C. sinensis* flourishes is sometimes thought to be in danger due to the collecting. Given the significance of cordyceps, it is necessary to educate the villagers and locals about science and to provide them with training in sustainable harvesting and conservation salvage.

## CONCLUSION

Many 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 challenges. Due to the material's high price and rarity, Cordyceps has faced more difficulties than most other herbs. Mycelium culture in the lab, standardisation, the creation of suitable dosage forms, and carrying out rapid stability studies of the same are the only areas that require attention. Hence, scientific knowledge and awareness are essential for the future prospects of cordyceps, including trade, sustainable harvesting, conservation, and production methods.

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