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Research Article

Review on Yarsagumba (*Cordyceps sinensis*) - An Exotic Medicinal Mushroom

*Sudipta Chakraborty, Sailee Chowdhury, Gouranga Nandi

BCDA College of Pharmacy and Technology 78, Jessore Road (S), Hridaypur, Barasat, Kolkata-127, West Bengal, India

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ABSTRACT

Cordyceps sinensis, popularly known as *Yarsagumba*, is a rare age old mushroom that has been valued extensively in traditional Chinese medicine. People of China and Tibet have been using this for various medicinal purposes since emperors' age. Its unique life cycle and diverse medicinal uses compelled science to show interest during last three decades. The present study reviews about its basic knowledge, claimed uses, their scientific backgrounds and its impact on socio-economic status. Much research work has been carried out leading to isolation of bioactive compounds and many of them undergoing clinical trials too. On the other hand it shows immense effects on the lifestyle and economic status of inhabitants of those high altitude villages where it is found naturally. Despite of its scientific progress, further development is required particularly in formulation of dosage forms and analysis leading to the best utilization of this most costly medicinal mushroom.

Keywords: *Cordyceps sinensis*, medicinal mushroom, yarsagumba

INTRODUCTION

Nature always stands as a golden mark to exemplify the outstanding phenomenon of symbiosis and beside the three important necessities of life – food, clothing and shelter; nature has provided a complete store house of remedies to cure all ailments of mankind. [1]

Today with the advancement in science and technology, remarkable progress has been made in the field of medicine. But despite these developments, of the known 30,000 human diseases or disorders, only one-third can somehow be treated symptomatically with available drugs and that too at a great economic and social cost. [2]

Nature is the only economic source of a number of well established and important drugs. Indian materia medica includes many drugs of natural origin which are derived from different traditional systems and folklore practices. Medicinal plants play a major role and constitute the backbone of Traditional System of medicine [3]. In the recent days, most of the prevailing diseases and some nutritional disorders are treated with natural medicines.[4]

But human interests are not confined only in plants or herbs when medicinal importance is concerned. Beside plants, various traditional system of medicines have indicated different other sources for the treatment of human ailments. Fungus is one such example which, in many cases, shows medicinal uses and has potential of producing novel compounds of medicinal importance. Many of research works have conducted on fungus to utilize it as medicine. [5-7]

One such fungus is *Cordyceps sinensis*, a therapeutic biofactory, is a combination of fungus and dead insect and has been used as a Traditional Chinese medicine (TCM) for centuries. Its effectiveness has been attributed to the Chinese philosophical concept of Yin and Yang and a vast literature exists on this. *Cordyceps* is fascinating *per se*, especially because of its lifestyle on Lepidopteron insects. "Yarsagumba", as it is known in Tibetan and Nepalese language, with both the caterpillar and fungal part in an intact single piece is an item of commerce in many countries as well. [8]

Name and General Description: *Cordyceps sinensis* (Berk.)Sacc., commonly known as cordyceps mushroom and caterpillar fungus, is an ascomycetes fungus and belongs to the family clavicipitaceae. The name *Cordyceps* comes from the Latin words 'cord' and 'ceps' meaning, 'club' and 'head', respectively. These words describe only about the appearance of the fungus. [9]

In Chinese it is called as '*Hia tsao tong tchong*' and '*dong chong xia cao*'. In Tibetan language it is known as '*Yartshagumba' or 'Yarsagumba' or 'Yartsa gunbu'* meaning 'winter-worm summer-grass'! A worm in winter transforms into a kind of 'grass' in the summer. In Himalayan region of India and Nepal, it is called as *Keera ghaas* (insect herb) [9-11]. *Cordyceps* is also known as the Chinese caterpillar fungus because it is a parasitic organism that grows on a rare caterpillar (*Hepialis armoricanus*) until the caterpillar dies and the mushroom sprouts from the caterpillar's head. The term 'Cordyceps' normally refers specifically to the species *C. sinensis*, although there are many species in the genus *Cordyceps* have been reported throughout the world. [9, 12-13]

Mycological Data [9,12]

Kingdom:	Fungi
Phylum:	Ascomycota

*Author for Correspondence: E-mail: sudislg3@gmail.com

Fig. 1: A mature Cordyceps sinensis in its natural habitat [14]

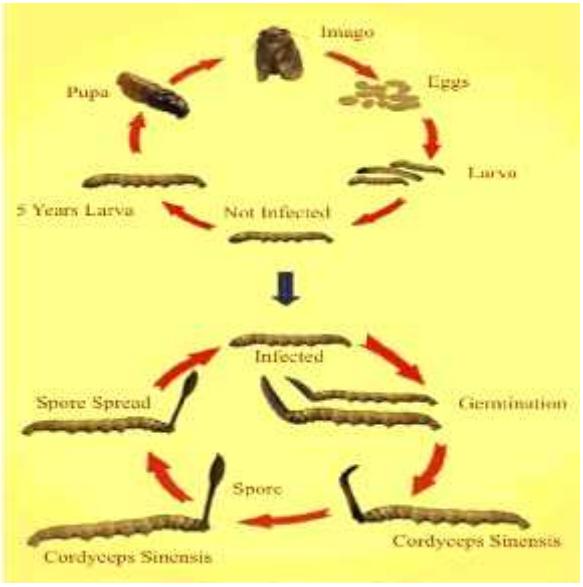


Fig. 2: Life cycle of Cordyceps sinensis [17]

Fig. 3: Dried Cordyceps sinensis ready for market

Fig. 4: Distribution area of cordyceps sinensis [15]

Class: Ascomycetes
Order: Hypocreales
Family: Clavicipataceae
Genus: Cordyceps
Species: C. sinensis (Berk.) Sacc.

Lifecycle: It is a mushroom which grows on a larva of ghost moth. During the summer and early autumn, mature fruiting bodies of *Yarsagumba* release millions of ascospores in the air which infect the larva and germinate inside its body. The fungal cells spread throughout the body through the circulatory system. As the larva is subterranean in habit, it continues digging the soil and enters inside from its rear part in a vertical position. During the winter season, the fungal cells rapidly proliferate inside the larva body and consume all the internal organs of the larva except its exoskeleton. Then the fungal cells convert into the compact white mass inside the body of larva, which is called endosclerotium. It is a dormant stage in the life cycle which can resist unfavorable environmental snow cold condition. When outer temperature slowly rises up at the beginning of the spring, the endosclerotium starts germinating and extrudes through the head part of the larva and ultimately protrudes through the soil.

This part called stroma gets fully mature in the summer (fruiting bodies) and again produces ascospores, which infect the larvae in that region. At this season the collectors start collecting this fungus.

The life cycle needs one year to complete. In spring and summer it grows out of the host larva and forms a mushroom fruiting body above the ground, but grows inside the host larva during
autumn and winter. [15-16]

Morphology: The fruit body is dark brown to black; and the 'root' of the organism, the larval body pervaded by the mushroom's mycelium appears yellowish to brown in color. It is 5-15 cm long and 0.14 to 0.4 cm thick. There are two types are available in market based on the colour. The whitish yellow is larger and good in quality. The other type is of copper colour and it is smaller as well as qualitatively compromised. [13, 18]

Distribution: It grows in high mountains at an altitude of 3,600 – 4,200 meters above sea level. It is found in Nepal Himalaya, Tibet, Bhutan, Sichun, Qunghai, Xizang and Yunnan provinces of China. In India it is mainly found in higher altitudes of Kumaun Himalaya and Garhwal Himalaya and also in higher altitudes of Arunanchal Pradesh and Sikkim. [10]

History And Traditional Uses: The medicinal value of the *Cordyceps* species has been recognized since ancient times in China and the surrounding Orient. The first written record of the *Cordyceps* species comes from China, in the

Table 1: Chemical constituents of *Cordyceps sinensis*

Constituents	Compounds
Sterols	Ergosterol, Cerevisterol, α-sitosterol. [24]
	Ergosteryl-3-*O*-α-D-glucopyranoside, Ergosterol peroxide. [25]
	3-*O*-ferulylcycloartenol, Daucosterol , Stigmasterol, Stigmasterol 3-*O*-acetate , Fungisterol. [26]
	Cholesterol, Campesterol, Dihydro brassicasterol. [27]
Nitrogenous compounds	Uracil, Guanosine, Thymidine, Tridine, Dideoxyuridine, Guanine, Inosine. [28-29]
	Adenine, Hypoxanthine, Adenosine, Cordycepin. [29-30]
	Caffeine, Tetracosanamide. [24]
	Cordycedipeptide A. [31]
	Dideoxyadenosine, Inosine, Guanosine, Uridine. [19,29,32]
	Cordyceamides A, Cordyceamides B, Aurantiamide acetate. [33]
	Thymine, Cordysinin A, Cordysinin B, Cordysinin C, Cordysinin D, Cordysinin E. [26]
Polysaccharides	D-glucan, Cordysinocan, Mannoglucan, D-mannitol. [34-36]
Proteins and related compounds	Cadaverine, Spermidine, Spermine, Putrescine. [19]
	Flazin , Perlolyrine. [26]
	Cordymin, L-tryptophan. [37-38]
Fatty acids and other organic acids	Lauric acid, Myristic acid, Penta decanoic acid, Palmitoleic acid, Linoleic acid, Oleic acid, Stearic acid, Docosanoic acid , Lignoceric acid. [39]
	Palmitic acid, Succinic acid. [24,26]
Phenolics and acids	*p*-hydroxybenzoic acid, Vanillic acid, Syringic acid, *p*-methoxybenzoic acid, *p*-hydroxyphenylacetic acid , 3,4-dihydroxyacetophenone, 4 hydroxyacetophenone, protocatechuic acid , acetovanillone, salicylic acid, Furancarboxylic acid. [26]
Isoflavones	Trihydroxyisoflavone, Glycitein, Daidzein, Orobol, Genistein. [26]
Vitamins	B1, B2, B12, E, and K. [28]
Inorganics	K, Na, Ca, Mg, Fe, Cu, Mn, Zn, Pi, Se, Al, Si, Ni, Sr, Ti, Cr, Ga. [28]
Volatile compounds	Aldehydes: Benzaldehyde, Benzene acetaldehyde, Nonanal , Decanal
	Alcohols: Phenylethyl alcohol, 2-(methylthio)-3-pyridinol, 7-octadien-1-ol
	Aromatics: Azulene, 2,6-dimethylnaphthalene, 1,6-dimethyl-naphthalene
	Phenols: 2-methyl-phenol , Butylated hydroxytoluene
	Acids: Phosphonic acid. [40]

year AD 620, at the time of the Tang Dynasty (AD 618–AD 907) which spoke of a creature whose annual existence alluded to a transformation from animal to plant in summer, and then again from plant to animal in winter. [19-21]

Tibetan scholars wrote of the healing animal/plant through the 15th to 18th centuries, but knowledge of this only reached to the Western scientific audiences in 1726 and again in 1757 during the Qing Dynasty when Wu-Yiluo written "New Compilation of Materia Medica" which is scientifically reliable depiction of the *Cordyceps* mushroom. [9,19-20, 22]

Traditionally it has been used as tonic and sexual stimulant for both sexes. For the same reason perhaps it has been named as "Himalayan herbal Viagra". It is used in case of sexual impotency. Other uses are in diarrhea, headache, cough, rheumatism, asthma, allergic rhinitis, irregular menstruation and in liver diseases. People have their own knowledge for the use of this in different diseases. [20, 23]

Chemical Constituents: Journey of *Cordyceps sinensis* has been started as a Traditional Chinese medicine in Tibet and China. With the advancement of time it spread to Nepal and other parts of the world. Science and technology helped it for more rationale use. Much research work is carried out towards isolation of bio active chemical components of *Cordyceps sinensis*. Some of these are summarized in the Table 1.

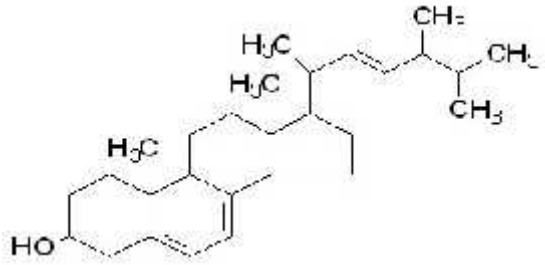
Pharmacological Reports / Bioactivities

Anti-tumor and anticancer activities: Majority of currently used anticancer agents are derived in one way or another from natural sources. Nature have been prime source of highly effective conventional drugs for the treatment of many forms of cancer, and while the actual compounds isolated frequently may not serve as the drugs, they provides lead for the development of potential novel agents. [41]

Investigations have proved that *Cordyceps sinensis* shows anti tumor, free radical scavenging and anticancer effects. It has been suggested that polysaccharides of *Cordyceps sinensis* are may be responsible for these activity. [42-43] The role of polysaccharides in antitumor

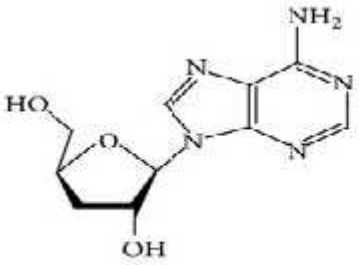
effect is argued in some cases where it is suggested that the effects are may be due to sterols**.** [44-48]

Mechanisms of inhibition of the growth of various cancer cells have also been proposed. It is suggested that cell growth may get arrested for different reasons such as enhancement of immunological function and non-specific immunity, selective inhibition of RNA synthesis, thereby affecting the protein synthesis, restricting the sprouting of blood vessels inducing tumour cell apoptosis, regulation of

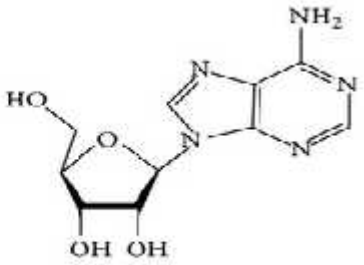


Ergosterol

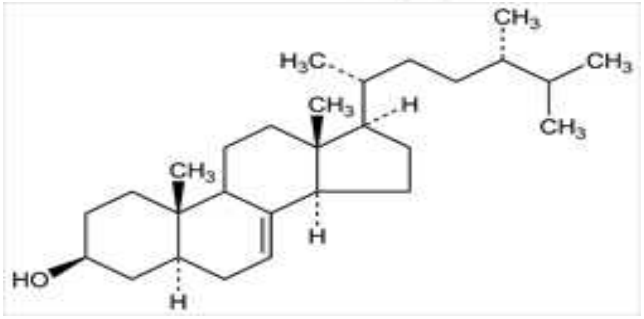
Cadaverine



Cordycepin



Adenosine



Fungisterol

Caffeine

Fig. 5: Some chemical structures

signal pathways, antioxidation and anti-free radical activity, anti-mutation effect, interfering with the replication of tumor-inducing viruses and nucleic acid methylation. [49]

Immunomodulator activities: *Cordyceps sinensis* shows both immunosuppressive and immuno-stimulating functions. Effects of various *codyceps* extracts/fractions have been studied on lymphoproliferative response, natural killer (NK) cell activity, interleukin-2 (IL-2) , tumor necrosis factor (TNF-α) and also on allograft models. It is observed that low-molecular weight part of extracts/fractions mainly shows such kind of effects.[50-53]

Antidiabetic activities: Researchers have demonstrated the hypoglycemic effect on normal and alloxan-diabetic mice and streptozotocin (STZ)-diabetic rats. It is proposed that polysaccharides of *Cordyceps sinensis* are responsible for the said activity. [32, 44]

Effect on Hepatic cells: Effects of *Cordyceps sinensis* on various abnormal hepatic conditions have been demonstrated using different models. It also modulates the cellular immune function and increases the serum complement level in the patients with post-hepatitic cirrhosis. It also shows short-term curative effect in chronic hepatitis B (HBV). [54-57]

Bioactive components of *cordyceps* for liver protection are mostly cordyceps polysaccharides (CPs). The CPs can improve the immunological functions of organic cells, removing harmful components and thus reducing the injury to liver cells. The effects of CPs in protecting the liver were presented as follows: protective effect on immune liver injury, effect on patients with chronic hepatitis B, effect on patients with hepato cirrhosis after hepatitis, protective effect on liver fibrosis. [49]

Effect on Cardiovascular system: *Cordyceps sinensis* shows prominent effects different conditions of cardiovascular system. Mycelia and fruiting bodies of *Cordyceps sinensis* are rich in adenosine and therefore mild hypotensive effect and platelet aggregation inhibition are observed. It shows anti arrhythmic, vasodilating effect, negative inotropic effect and also inhibits thrombus formation. It also found to stimulate erythropoiesis in mouse bone marrow. [22, 58-62]

Effect on kidney: Research works have demonstrated that *Cordyceps sinensis* shows protective effects on different nephrotoxicity. It also found to reduce acute renal failure (ARF) and Chronic renal failure (CRF) in rats. [63-66]

Aphrodisiac and sexual stimulant: *Cordyceps* species and, especially, *C. sinensis* have been appreciated for many centuries in Traditional Chinese Medicine (TCM) for its use as sexual stimulant and health promotion [19].This libido-promoting activity has also been suspected and *Cordyceps* containing products have been consumed for the same purpose for years. But surprisingly there are only few direct evidences in the scientific literature which are

Fig. 6: Steel wires & twigs inserted in Cordyceps sinensis

strong enough to link the known metabolites to the function. It has been showed that *C. sinensis* stimulates corticosteroid production and steroidogenesis in animal models. [22, 44, 67]

Clinical trials of *Cordyceps sinensis* related to above mentioned ailments have been conducted in China and some other parts of the world which are being helpful to calculate doses and to formulate in appropriate dosage form. [22, 44]

Enhancement of physical stamina**:** The best-known medicinal action of *Cordyceps* is in the increase of physical stamina. In 1993, the Chinese National Games brought this mushroom to the attention of the world's sporting authorities. A group of nine women athletes who had been taking *Cordyceps* shattered nine world records. There have been many reports of amazing improvements in performance in various sports due to the intake of *Cordyceps*. [68]

Clinical research has shown that *Cordyceps* increased cellular bio-energy—ATP (adenosine triphosphate) by as much as 55 per cent. Increased synthesis of ATP and faster energy recovery has also been reported. It would seem that *Cordyceps* improves the internal balance mechanism, thus making the utilization of oxygen more efficient. These properties may account for the overall physical enhancement, the extra endurance and the anti-fatigue effects that are seen in humans using *Cordyceps*. [69]

Adulteration: The great demand worldwide and the huge cost of the wild collected variety have led *Yarsagumba* trade far from the ethics. To balance the demand, supply is increased and this has given rise to variations in purity and quality, creating a situation in which there are a large number of counterfeit and adulterated products are being sold. [70]

Cordyceps is found in its natural state as attached to the mummified body of the caterpillar from which it arises. It is harvested as such, dried, and supplied into the market. As it is sold by weight, commonly it has been observed that better quality *Cordyceps* traditionally had fewer inserted sticks or twigs to gain more weight. This practice has been so widespread that it is virtually impossible to find wild collected *Cordyceps* without these fillers inserted. (Fig 6. shows such example)In modern practice metallic wires are inserted into the caterpillar rather than the traditional twig to gain more weight. [9,71-72]

Analytical Approaches and Standardization: The methods for analyzing *Cordyceps* quality have not yet been standardized throughout the world. Different analytical methods and standards are practiced in various places. Almost all of the samples of wild *Cordyceps* have been shown to be very similar in chemical composition, but there is variation in the secondary metabolite compounds present in cultivated *Cordyceps sinensis* and other *Cordyceps* species. The nucleosides, and specifically the deoxy-nucleosides (e.g., Cordycepin), have been determined to be the most reliable indicator of potency. Beside this, some polysaccharides, ergosterol, mannitol, peptides, cordycepic acid are also proposed as markers for quality control.

Some analytical methods have been designed for standardization purpose. Gas chromatography with mass spectroscopic detection (GC/MS) method can be used for quantification of the target compounds in *cordyceps*. Better reliability has been observed in HPLC-Mass spectroscopic detection method. [22,72-73]

1) High performance liquid chromatography (HPLC)

HPLC is a conventional method for analysis of non-volatile compounds. For most cases, HPLC with UV–vis detection is the prevailing technique, which has been widely used for determination of components in Chinese medicine. Using HPLC coupled with UV detector, ergosterol, adenosine, cordycepin, and other nucleosides, Polysaccharides, Amino acids in *Cordyceps* were determined. [72-73]

2) Gas chromatography (GC): GC–MS have been employed for analysis of the essential oil of *C. sinensis* and many compounds are identified. Verticiol, a compound resembling with verticine, has been found in *C.* sinensis which indicates anti-tussive and expectorant effects of *C. sinensis.* [72-73]

3) Capillary electrophoresis (CE): High performance capillary electrophoresis (HPCE), a powerful tool in natural product analysis, has been applied for the analysis of compounds found in *Cordyceps.* With the help of this technique mainly nucleosides such as cordycepin, adenosine, guanosine, hypoxanthine, uracil, etc have been analyzed. [73]

Socio-Economic Impact: In nature *C. sinensis* is found only at high altitudes on the Himalayan plateau and therefore difficult to harvest. Because of such difficulties, *Cordyceps* has always been one of the most expensive medicinal fungi known. Its high price had relegated it exclusively to members of the Emperor's court. It has been beyond the reach of the average people. Despite its cost and rarity, the unparalleled medicinal possibilities for *Cordyceps* spp. have made it a highly valued staple of traditional Chinese medicine.[19]

Market survey and the trend in the trade indicate that the price of *Yarshagumba* varies largely due to the quality and

the place too. Estimates show that the price may go up to $ 9000 to $10000 per kg for average quality and for good quality products it may rise to $ 500000 per kg.[15]

This stream of cash income to rural communities from collection and trade of *Yarshagumba* has caused a far-reaching transformation of social and economic conditions in the last two decades. The income derived through the collection and trade of this precious myco-medicinal herb has led to an empowerment of marginal communities living in extremely remote locations who used to secure their survival only through rustic and agricultural activities.

But where money is involved challenges are bound to come and so in this case too. It has been reported that during April to July (collection season of the fungus) schools are declared closed in some area of Nepal and Tibet for collection of fungus! Unfair trade like work/rice/milk etc against fungus has also been heard. The local communities fought over access to caterpillar fungus resources, and some of these turn violent resulting in a few deaths each year too.[15,74]

CONCLUSION

Cordyceps sinensis, a traditional Chinese medicine, has always been prerogative to the richer section of the society. But as the time has progressed researchers shown interest to know the scientific base of the traditional uses. Today many of the claimed uses have got its scientific reason. Clinical trials are going on for some isolated compounds too. But the research work, vast knowledge and uses are limited to the countries where it is found mostly. Therefore study leading to its propagation by tissue culture and its chemical contents should be emphasized. All the possible measures need to be taken to make it available in global medicinal arena as this myco-medicinal herb has got so many benefits to offer us. Modern medicinal science should not forget its diversity of pharmacological effects which have the ability to make someone strong as an elephant, fast as a horse and beautiful as a peacock!

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