CHEMISTRY OF CORDYCEPS SINENSIS: A WONDER DRUG FOR ACCLIMATIZATION PURPOSE IN UNREACHED HIGH ALTITUDE AREAS OF HIMALAYAN HILLS

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ABSTRACT - High altitude area of Himalayan hills along Indo-Tibetan border especially 11000-14000 ft above Mean Sea Level is considered to be unreached and unexplored due to adverse climatic conditions. Cordyceps sinensis (Berk.) Sacc. is much valued traditional medicine of this area because of its prominent nutraceutical and medicinal properties. Cordycepin (up to 120 ppm) is the bioactive component of this mushroom. Its utilization for performance enhancement and human acclimatization in the high altitude by curing hypoxia conditions is well established. Hence, nutritional supplements containing C. sinensis may be beneficial for local inhabitants and our Armed Forces deployed in unreached high altitude regions.

KEY WORDS: Cordyceps sinensis, acclimatization, cordycepin, Performance enhancement, unreached locations.

I. INTRODUCTION

Cordyceps sinensis (Berk.) Sacc. (Ascomycetes) is a high value medicinal mushroom of western Himalayan region. It grows in the unreached high altitude areas along Indo-Tibetan border. It is known as “Dong Chong Xia Cao” in the local regions, which means it is worn in winter season and grass in summer season. It is an entomogenous fungus that parasitizes the larvae of Lepidopterean moth Hepialus armoricanus and hence it is also known as caterpillar mushroom. Cordyceps has fungal stroma and larval sclerotium as body parts and it is used as such in different nutraceutical and pharmaceutical preparations. Both the body parts have been found to contain similar biochemical constituents.

C. sinensis is considered as a wonder drug in Traditional Chinese Medicines (TCM), and the ancient medicinal practitioners of China termed it as “Panacea of all ills” due to its benefits in high altitude regions. C. sinensis is reputed in the literature for replenishing the kidney and smoothing the lungs, and it is also prescribed for immuno-modulation, treatment of respiratory, liver, muscle, cardiovascular diseases, hyposexuality and hyperlipidemia. It acts as performance enhancer and its importance came into the notice to world when a group of nine Chinese women athletes, who were fed up by hyperlipidemia, shattered nine world records in world outdoor track field championships in Germany in 1993.

C. sinensis is endemic to alpine habitats on the Tibetan plateau, and it is having cramped geographical distribution. The collection of C. sinensis from natural habitat is a very tough task and it is very rarely available in the far reaches of high cold and arid hills at an altitude between 11,000 ft to 14,000 ft (msl). In India, Munisyari and Dharchula region of Uttarakhand has been identified as a place of occurrence of C. sinensis. Presently, many more places along the Indo-Tibet and Indo-Nepal boarder particularly Milam, Laspa, Darti and Johar valley have also been identified as hot-spots for its natural occurrence. C. sinensis is highly demanded in the international market and it fetches the price of INR 10 - 15 Lakh/kg. C. sinensis has been overexploited in the last three decades, and is bearing the ecological pressure of extinction from ecosystem, which is a very dangerous alarming situation for this species.

Worldwide the efforts of in vitro laboratory culture of this fungus have been undergone to cater the needs of human consumption, and for survival of this species under its natural habitat. Owing to high potency of performance enhancing activity of C. sinensis, Defence Institute of Bio-Energy research (DIBER) has already developed the protocol for in-vitro mycelium culture of this mushroom, and this technology has been transferred to the industries for human welfare. Based on morphology, genetics and biochemical assessment, this in vitro cultured mycelium has been reported very similar to natural samples of C. sinensis.

Cordyceps has been assessed for its chemical composition and bioactive ingredients. Cordycepin (3′-deoxyadenosine), adenosine and N-6-(2-hydroxyethyl) adenosine have been identified as quality indexing ingredients of Cordyceps. Cordycepin is a principal bioactive compound of C. sinensis; it is an important nucleoside analog and secondary metabolite of extra-cellular origin. The observation reveals that a little variation in the nutritional components is observed in different wild samples of Cordyceps, but there is a distinct variation in the secondary metabolites in natural samples as well as in cultivated samples. A considerable difference in the concentration of Cordycepin and other bioactive molecules was observed in different culture methodologies, which are having modifications in culture parameters such as light, temperature, Oxygen concentration and substrate used.

II. BIOCHEMICAL COMPOSITION

C. sinensis samples differ significantly in chemical composition because of their different geographical origins and culture conditions. In various cases, analytical methods are major reasons for the considerable differences in the biochemical compositions. C. sinensis samples have been studied for their nutraceutical and bioactive constituents.
2.1. Nutritional constituents:

2.1.1. Carbohydrates

Carbohydrates are the macromolecules having formula C\(_n\)(H\(_2\)O)\(_m\), where \( y \leq n \). Carbohydrates are primarily the energy providing bio-molecules required for our daily energy need. *Cordyceps sinensis* is a rich source of carbohydrates and is composed of monosaccharides, disaccharides, oligosaccharides including cyclofurans, beta-glucans; beta-mannans,; and complex polysaccharides. It contains 43-48% total carbohydrates out of which only 25 -30% have been assessed by anthrone method. Chemically, it contains 40.5% glucose, 35.4% mannose and 14% galactose units. It contains 26 – 29% of polysaccharides. In the fungal kingdom, and particularly in *Cordyceps* spp., polysaccharides are the best known and understood medicinally active compounds.\(^7\) Polysaccharides effectively regulate blood sugar and facilitate anti-metastatic and anti-tumor effects.\(^8\)

2.1.2. Proteins

Proteins are the second next abundant bio-molecule after carbohydrates which are required for body building and body maintenance. *C. sinensis* contains 22 -28% crude proteins. It is having almost 12 amino acids including 8 essential amino acids, which are necessary for human body. Essential amino acids cannot be synthesized by the body but are necessary for good health. Amino acids are essential for developing the muscles, tendons, organs, glands, nails and hair. Growth, repair and maintenance of all cells are dependent upon amino acids.\(^9\)

2.1.3. Fat and lipid

*C. sinensis* is having 4.8-6.5% fat content consisting of twenty-eight saturated and unsaturated fatty acids and their derivatives. There are two major classes of unsaturated fatty acids - Omega-6 & Omega-3 class and Omega-9 class. Fatty acids regulate blood pressure, cholesterol and triglyceride levels, and are having a positive impact on cardiovascular system.\(^10\)

2.1.4. Crude fibers

*C. sinensis* being as a mushroom contains 6.8-10.5% crude fabric. Fibres are very important for digestive tract as they increase the surface area of food and make the digestion process easier.\(^11\)

2.1.5. Vitamins

*C. sinensis* contains vitamin B-1, B-2, B-12, and E. Vitamin B-1 is essential for proper functioning of central and peripheral nervous system. Vitamin B-2 is essential for energy metabolism, cell formation and growth. Vitamin B-12 is essential for carbohydrates, proteins and fats metabolism pathways and it improves the function of nervous system. Vitamin E is essential in keeping the cells of muscle, heart, testes, liver and nerves alive and functioning.

2.1.6. Minerals\(^12\)

Various macro and micronutrients are present in *C. sinensis* which are adding the value to its nutritional benefits. Mineral contents of *C. sinensis* are discussed below.

- **Potassium**
  
  Potassium is important in maintaining fluid and electrolyte balance in the body. Potassium regulates heart condition and supports osmotic pressure. *C. sinensis* contains 4.75 - 6.30 mg/g of potassium contents.

- **Sodium**
  
  Sodium is an important element for mineral metabolism. Sodium maintains electric potential in tissues. It is essential for osmotic pressure regulation and proper nerve functioning. *C. sinensis* contains 2.15 - 3.20 mg/g of sodium contents.

- **Calcium**
  
  Calcium is a fundamental material used in mineralization of bones, and its presence is essential for proper functioning of muscles and nerves. *C. sinensis* contains 360-520 ppm of calcium contents.

- **Magnesium**
  
  Magnesium is an essential nutritional component for a healthy diet. *C. sinensis* contains 210-240 ppm of magnesium contents. Over 300 biochemical reactions in the body are regularized by magnesium. Magnesium maintains regular heart rhythm, supports a healthy immune system and keeps bones strong.

- **Iron**
  
  Iron is involved in oxygen transport and regulation of cell growth and differentiation. *C. sinensis* contains 14.6 – 16.2 ppm of iron contents. A deficiency in iron limits oxygen delivery to cells, resulting in fatigue and poor work performance.

- **Copper**
  
  Copper is an essential microelement for the health of all living organisms. *C. sinensis* contains 3.0-4.0 ppm of copper contents. Copper plays an important role in facilitating iron uptake in human body.

- **Manganese**
  
  Manganese acts as a co-enzyme to assist metabolic progression in the human body. *C. sinensis* contains 2.0 - 3.0 ppm of manganese contents Manganese helps to maintain healthy bone structure and is involved in building essential enzymes for developing bones. Manganese is also actively involved in forming connective tissues, absorption of calcium, proper functioning of the thyroid and regulation of blood sugar levels.

- **Zinc**
Zinc is an essential trace element for cell growth and division and to strengthen immune system. Zinc accelerates the renewal of the skin cells and is essential for maintaining healthy vision. $C. \text{sinesis}$ contains 11.6 – 18.4 ppm of zinc contents.

2.2. Bioactive ingredients

2.2.1. Nucleosides

$C. \text{sinesis}$ contains various types of nucleosides including adenosine, 2-deoxyadenosine, 3-deoxyadenosine (cordycepin), guanosine and N-6-(2-hydroxyethyl) adenosine. These nucleosides are very beneficial and play important role in the regulation of various physiological processes in the central nervous system, if consumed as nutraceuticals. They have great participation in DNA and RNA synthesis. The energy regulation of human body is dependent on phosphorylation process of these nucleosides. Cordycepin and adenosine has been identified as major bioactive components of $Cordyceps$ spp.

2.2.1.1. Cordycepin

Cordycepin or 3'-deoxyadenosine is a major bioactive component of $C. \text{sinesis}$. It is produced by this mushroom in hypoxia conditions. Cordycepin is the extracellular secondary metabolite of $C. \text{sinesis}$, which is produced under stressed environmental conditions in high altitude regions. Initially, this molecule was isolated from $C. \text{militaris}$. Characterization of this molecule was carried out by Chen and Chu using nuclear magnetic resonance (NMR) and infrared spectroscopy (IR) in an extract of $C. \text{sinesis}$.

The structure of cordycepin is as under. (Fig. 1)

![Fig.1 Molecular structure of Cordycepin or 3'-deoxyadenosine](image)

There is a lack of oxygen on C-3 in ribose sugar and hence it is an excellent terminator of transcription process. When Cordycepin is introduced to bacterial cell undergoing DNA replication, it produces a defective DNA that triggers bacteria cell to undergo apoptosis (programmed cell death). It also inhibits the m-RNA formation in some bacteria. Cordycepin is very effective against all sorts of bacteria that have developed resistance to the other antibiotics. It also shows anti-viral properties due to 3-deoxy positions. The best known medicinal action of $Cordyceps$ is to increase of physical stamina and to cure hypoxia conditions at high altitude regions. $Cordyceps$ improves the internal balance mechanism, thus making the utilization of oxygen more efficient. By curing the hypoxia conditions it helps in acclimatization of humans in unreached high altitude regions. The concentration of cordycepin in different $Cordyceps$ strains differ significantly, even in some cases it is not detectable. In natural samples cordycepin contents may vary from negligible to 120 ppm.

2.2.1.2. Adenosine

Adenosine is composed of adenine and ribose sugar, and it is a very essential nucleoside for living organisms. It gives energetic nucleotides viz. adenosine monophosphate (AMP), adenosine diphosphate (ADP) and adenosine triphosphate (ATP) on phosphorylation. All these nucleotides are intensively involved in metabolism, and regulate the energy requirement of various human physiological processes. Further; it is well known that these nucleotides are essential for DNA repair process and m-RNA synthesis. Different strains of $C. \text{sinesis}$ show variability in adenosine contents, RP-HPLC chromatogram shows 30-250 ppm adenosine content in different samples. The molecular structure of adenosine is given below (Fig. 2)

![Fig.2 Molecular structure of Adenosine](image)

2.2.2. Polyphenols

Phenolic compounds have been proven a major class of phytochemicals, which are accountable for inhibiting the oxidative damage caused by free radicals. $C. \text{sinesis}$ contains a variety of polyphenolic compounds including flavonoids, flavonols and proanthocyanidins. Polyphenolics were extracted with the help of water and alcohol. The concentration of phenolic compounds was higher in the alcoholic extracts, when compared with the water extracts. The polyphenol content in $C. \text{sinesis}$ is given below. [Fig 3]

![Fig. 3 Relative Polyphenol contents in $C. \text{sinesis}$.](image)
2.2.3. Sterols

Various sterols are reported in *Cordyceps* spp. including Delta-3 ergosterol, ergosterol, ergosterol peroxide, 3-sitosterol and campesterol. Sterols such as campesterol can prevent ‘bad’ cholesterol from being absorbed into the bloodstream. Instead of clogging up arteries and impairing artery function, the cholesterol is eliminated as waste with the help of these sterols. In this manner, sterols in the *C. sinensis* may reduce the risk of coronary heart disease.

2.2.4. Cordycepic acid

Cordycepic acid or D-mannitol is well known polyhydroxy alcohol present in *C. sinensis*. It is an active component of *C. sinensis*. *C. sinensis* has 6-8% of cordycepic acid content besides the nucleoside analogues. It has diuretic action and is used as a prophylaxis against post-operative acute renal failure. The molecular structure of cordycepic acid or D-mannitol is given below.

![Molecular structure of cordycepic acid](image)

III. CONCLUSION

*C. sinensis* grows in high altitude regions especially 11000-14000 ft above mean sea level of western Himalayan region. It is very well known for its beneficial effects in the high altitude regions especially performance enhancing capabilities and curing hypoxia conditions. Local inhabitants and our soldiers deployed in high altitude regions are much desirous to get support for their acclimatization under this challenging situation. The chemical study of *C. sinensis* is definitely a great effort to support nutraceutical industries in developing pharmaceuticals and nutraceuticals for our local inhabitants and soldiers. This will be the way, by which they will be able to face adverse climatic conditions in efficient manner in unreached Himalayan locations. From this study, it is evident that *C. sinensis* has good nutritional value and it contains variety of chemical constituents like cordycepic acid, polyphenols, polysaccharides, sterols and free amino acids. Nucleosides like cordycepin and adenosine are the potent bioactive molecules in *C. sinensis*. Besides the performance enhancing capabilities and curing hypoxia conditions cordycepin has been proven to be effective against a variety of bacterial and viral infections. Thus, in future more R&D efforts are required for developing nutraceuticals and pharmaceuticals from *C. sinensis* to support local inhabitants and our Armed Forces deployed in far reaches of high altitude regions to protect our international boundaries along Indo-Nepal and Indo-Tibatan borders.

REFERENCES