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Entomopathic Mushroom: Cordyceps sinensis

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Entomopathic fungi usually attach to the external body surface of insects in the form of microscopic spores. The most common and important entomopathic fungus is Cordyceps. C. sinensis has long been used in folk medicine and is known to have remarkable medicinal properties. It has been determined that there is perhaps a greater biodiversity of compounds within different strains of this single species. Due to the great difference in the concentration of native compounds, a wide range of quality is found in Cordyceps cultivated from different strains and utilizing different culture methodology. Due to its peculiar characteristics, habitat, morphology and being a store house of medicinal properties, it is a highly prized mushroom.

The world of mushrooms has always been fascinating and mystic to man owing to their sudden appearance in numbers, groups, rings, bunches and also in isolation as a single attractive and imposing structure. Man has been fascinated with this biological entity since time immemorial and references about the mushrooms are available in most ancient literatures like Vedas and Bible. Mushrooms have always been a source of good health and have been used since time immemorial as medicines. Their medicinal significance has been widely appreciated all throughout the world and are thus extensively been used in the form of nutriceuticals, nutraceuticals and pharmaceuticals. The studies suggest that mushrooms are pro-biotic i.e. they help our body strengthen itself and fight off illness by maintaining physiological homeostasis by restoring the balance of the body. The compounds present in mushrooms are regarded as Host Defense Potentiators (HDPs) which have immune system enhancement properties and are currently extensively used for treatment of cancers and other malignancies and to increase general body health.

Entomopathic fungi usually attach to the external body surface of insects in the form of microscopic spores (usually asexual). Under the right conditions of temperature and humidity, these spores germinate, grow as hyphae and colonize the insect's cuticle; eventually they bore through it and reach the insects' body cavity (hemocoel). Then, the fungal cells proliferate in the host body cavity, usually as walled hyphae or in the form of wall-less protoplasts (depending on the fungus involved). After some time the insect is usually killed and new propagules are formed in or on the insect if environmental conditions are again right. The entomopathic fungi include taxa from several of the main fungal groups and do not form a monophyletic group. Many common and important entomopathic fungi are in the order Hypocreales of the Ascomycota: the asexual (anamorph) phases Beauveria, Metarhizium, *Nomuraea*, *Paecilomyces=Isaria*, *Hirsutella* and the sexual (Teleomorph state Cordyceps *(Ophiocordyceps)*.

Cordyceps is a fungus of subphylum Ascomycotina, class Pyrenomycetes, order Clavicipitales and family Clavicipitaceae and includes more than 300 species found worldwide. A new classification of *Cordyceps* species has been suggested on the basis of chemo-taxonomy of partial nucleotide sequence of 18S rDNA obtained from four different species. *Cordyceps* species are parasitic, mainly on insects and other arthropods. Some of these are also parasitic on other fungi like the subterranean, truffle-like *Elaphomyces* and also on spiders. The mycelium invades and eventually replaces the host tissue, while the elongated fruiting body (stroma) may be cylindrical, branched, or of complex shape. The genus has a worldwide distribution and most species have been described from Asia (notably China, Japan, Korea and Thailand). *Cordyceps* species are particularly abundant and diverse in humid temperate and tropical forests. Some *Cordyceps* species are sources of important biochemical substances like cordycepin which has very high medicinal properties. The species that parasitizes the vegetable caterpillar, *Cordyceps sinensis*, is the most famous amongst all

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the species of *Cordyceps* and has been considered a precious ingredient of high medicinal importance.

Ethno-mycological and traditional uses

C. sinensis, a parasitic fungus in the alpine regions has been highly valued in Traditional Medicinal System of China, Nepal, Tibet and India. In interior mountain areas, it is also locally known as 'Yarsha Gamboo', Keera ghas' and 'Keera jhar'. The Tibetan name 'Yarsha Gamboo' means 'summer-grass winter-worm'. Tibetans believe that during winter time it lives as a 'worm' and later, as metamorphosis occurs at the start of the spring season, this worm transforms into a kind of 'grass'. Two distinct phases have been recognized during the entire transformation process. Firstly, the 'grass' starts growing form the head of the larvae. The worm at this particular stage, appears to be white, is alive and can be seen moving over the ground. The blade-like part can be seen protruding out from the head of the insect like a tiny horn. This horn like structure continues to grow further. Ultimately, the worm or the insect dies and transforms into a brownish-yellow coloured 'root' like structure of the grass.

Host range and habitats

C. sinensis is an entomophagous fungus of the family Clavicipitaceae. It parasitizes a range of grass root boring caterpillars, most commonly the Thitarodes (*Hepialus armoricanus*, family Hepialidae). In all, around 40 species of *Hepialus* moth have been recognized in the Tibetan Plateau region and around 30 of these species can be infected by *C. sinensis*. The mycelium of the fungus grows in soil and colonizes the buried larvae (caterpillar) of this moth. The caterpillar becomes mummified by the growth of the mycelium and hence is given the name, "caterpillar fungus". It has been reported that *C. sinensis* has evolved and developed a special adaptation to improve chances of reproductive success. Reproduction is highly host-specific. Every single spore fragments into around 32 million propagules. These tiny propagules get attached to the larval stage of the insect. The larvae is then forced to move closer to the surface of ground (non-infected larvae will not hibernate close to the ground surface). The mycelium, which is composed of white thread like structures called hyphae, grows inside the body of the insect in the form of a cottony mesh. The hyphae fill the interior of the entire caterpillar and mummify it, leaving behind the larval exoskeleton filled with only the white mycelium of fungus. When alpine grasses start sprouting, a fruiting body develops which, surprisingly, always emerges out from the head of the caterpillar (larvae). This fruiting body is usually 5-10 cm long, brown colored and club-shaped. The propagules present on the fruiting body are dispersed by the wind and can attach to new host insects. The fruiting body resembles grass sprouting but the difference is the colour which is dark blue to black.

Native occurrence of this entomophagus fungus is mostly confined to the high Himalayan Mountains in Tibet, Nepal and India, at an altitude

ranging from 3000 to 5000 m. The most common occurrence of this fungus is between 3500 and 4500 m elevation in cold and arid environment. *C. sinensis* is endemic to the Tibetan Plateau including the adjoining high altitude areas of the Central and Eastern Himalayan range (covering areas of Nepal, Bhutan and Uttarakhand, Sikkim, Himachal Pradesh and Arunachal Pradesh in India). It is found in the high altitudes of Pithoragarh, Uttarakhand and other provinces at locations above 7000 ft. It is also common in the grasslands and shrub lands of the Tibetan Plateau including west Sichuan, North Yunnan and major areas of Qinghai and West Gansu. The distribution of *C. sinensis* is limited to those areas where the average annual precipitation is above the range 350-400mm. This caterpillar fungus thrives very well in sub-alpine and alpine grasslands or meadows and in open dwarf shrub lands. Extensive research has been conducted on the ecology, collection, utilization, trade route, management and significance and species diversity of *C. sinensis* in various parts of India, Tibet, Michigan, Bhutan, China and Korea.

Collection and trade

Years back this fungus was collected and traded from Tibet to China in exchange for tea and other commercial goods like silk, grains, etc. The most appropriate time for harvesting of this fungus starts with the arrival of the spring season, in about starting of May. Local villagers and nomads search for the fungus in the grasslands and shrub lands. But the harvesting is slightly a difficult process as only the stroma or the grass-like part of the fungus is visible over the surface which too is quite short, not longer than 2-5cm and has to be lifted out with the help of a sharp knife. Extreme care has to be taken while pulling out the fungus from the ground surface because if the stroma breaks off from the head of the larvae, it directly affects the commercial value of the mushroom resulting in a decline in its market rate.

During the harvesting season, all other activities come to a standstill as everyone is focused on gathering more and more of the fruiting bodies. This has often led to many blooded wars in these areas. The Ministry of Population and Environment, Govt. of Nepal has banned its collection, trade and transportation. However, in Tibet it is an open trade. In some areas of Tibet, even the schools announce vacations for 15-20 day in late May so that the students can also help in the collection and harvesting of this precious mushroom. The daily collection may vary from 250g to as much as 5kg.

During recent years, caterpillar mushroom has emerged out be an important cash crop traded on a large scale and a new source of income in the rural areas in the higher altitude regions usually above 3000-5000 m. In the river valley of Gori Ganga alone, the number of fungus gatherers at alpine habitats has increased about four-fold since the year 2000. During 2002, nearly 900 persons went to seven different alpine habitats in search of the fungus (average 128 persons per habitat) and collected about 200 g of the fungus worth Rs. 8600, according to the purchase price in the year 2002. This was the price if the material was sold immediately in the alpine habitats. Carrying the collected fungus material a few kilometers down to the local market, the selling price increases to about Rs. 7000 per kg. Since the year 2000, purchase price at the field site and in the local market has increased tremendously and so also the income of a gatherer. Between the year 2000 and 2002, the income of a wild material gatherer had increased by 3.7 times and above four-fold if the material was sold at the field or to the agents in the local market respectively. Factors such as high price of the fungus, very often make the transaction secretive in the local market while due to cross-boundary trade between two countries, the rest of the trade is under the surface. Cost of one kg of the fungus at the final destination (brokers in national and international markets) was much higher than the price paid to the field gatherers in the year 2002 and ranged between Rs. 68,000 and 80,000 in Tibet, while in Nepal a slight increase was noted (Rs. 80,000-90,000). However in the Indian market, the material was sold at the rate of Rs. 1,25,000 to 1,30,000 per kg. Fresh fungus is sold for 9,000-15,000 RMB/Jin (1 Jin=1 metric pound=500g) in Lithang. It is believed that in the International market the fungus may fetch a price between one and two million Rupees per kg (US$ 20,000-40,000). The amount paid varies among the trade channels which start from the wild material gatherers in the field,

then to the brokers and agents who collect the dried material from the various locations and sell it at a higher price. However, rapid and immediate marketing of this fungus is not required as the fungus is usually sold and consumed in a dried form. Its small size and easy storage conditions make the transportation much easier.

Composition of *C. sinensis*

The pharmacological and medicinal significance of *C. sinensis* is mainly due to its bioactive ingredients. The composition properties and structure-activity relationship of these components have been under extensive scrutiny by many researchers and have eventually been rediscovered and modified with respect to the present scenario of disease and abnormalities. It contains a wide variety of potentially important constituents, including polysaccharides, ophiocordin (an antibiotic compound), cordycepin, cordypyridones, nucleosides, bioxanthracenes, sterols, alkenoic acids and exopolymers etc. The constituents of *C. sinensis* were thoroughly studied and a crystalline substance Cordycepic acid was isolated and identified, which was later identified as d- mannitol. Cordycepin and cordycepic acid are regarded as the most important constituents of this fungus and owe high medicinal significance.

Medicinal uses of *C. sinensis*

In the recent past, a variety of medicinal preparations in the form of tablets, capsules and extracts from mushrooms for the treatment of various kinds of ailments, diseases and disorders have been produced and marketed. In 1991, the value of world mushroom crop was estimated to be around 8.5 billion dollars and in the same year 1.2 billion dollars were estimated to have been generated from medicinal products from various medicinal mushrooms. Herbal medicinal preparations from different mushrooms have become a growing business in various parts of the world as for instance, Bhutan is an emerging market for *Cordyceps* and its usage has shown a tremendous increase since last few years. There are data of clinical trials that support the efficacy of *C. sinensis* as a medicinal herb, especially for disorders related to the liver, kidney and immune system. A number of studies indicate that *C. sinensis* (and also its mycelial extract) possess certain anti-cancer, anti-metastatic and immuno-stimulating properties. It is also reported to have anti-oxidant activity.

Since ages, *C. sinensis* has been regarded as panacea of life, imparting youth, vigor and longevity. Other important functions include activation of the immune responses, controlling the blood sugar levels, treatment of Hepatitis B, improvement of the respiratory functions, improvement in the functioning of the heart, maintaining the levels of cholesterol, reduction of the tumor size in cancer patients, protection against free radical damage, reduction of fatigue, combats sexual dysfunction, helping in organ transplantation, improvement in the functioning of kidney and adrenal gland etc.

Nature is the source of all the raw materials that we need. About 2–3 decades ago, most of the drugs were of herbal origin. A variety of reasons under pin why people like to use natural medicines as it is evident that patients are getting even more distressed after using chemically synthesized drugs, rather than natural means like medicinal mushrooms that can conquer life claiming diseases, leaving no side effects on human health. To maintain proper growth, the pharmaceutical industries need innovation and access to high output rate on low-cost materials with reasonable safety. The combination of modern chemistry with bio-based starting materials, like, bio-metabolites, offers the scope for revolutionizing mushroom based pharmaceutical industries. In the near future, bio-metabolites (cordycepin, polysaccharides, etc.) extracted from medicinal mushroom like *Cordyceps* will have a role that compares with that of oil and gas crackers today. It is mentionable that the highest cordycepin production was recently obtained in surface liquid culture using *C. militaris* mutant. Therefore, bio-metabolites, such as cordycepin, polysaccharides and alike materials of *Cordyceps* will be the key future driving force in the realm of green pharmacology and pharmacognosy.

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