COSTLIEST FUNGUS OF THE WORLD – ITS BIOLOGY, HARVEST AND TRADE

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The costliest fungus, Ophiocordyceps sinensis or commonly known as Caterpillar fungus, is widely distributed in upper hilly regions of the Himalaya in China, Tibet, Nepal, Sikkim, Bhutan and India. It is a peculiar insect pathogenic fungus with a larva of moths at the base and the fruiting body of fungus at the top. The life cycle of this fungus is also very interesting. The wide use of this fungus in the Traditional Chinese Medicine of China has made the fungus as costliest of the world. The characteristics and medicinal importance of the fungus in general has been discussed before going to the study of caterpillar fungus. The morphology, life cycle, harvesting, medicinal importance, and trade of Caterpillar Fungus have been elaborated. The overharvesting of this Caterpillar fungus by collectors is affecting the ecosystem of the alpine regions of Himalaya leading to the threat of many endangered plant and animal species of that area. All these aspects have been discussed.

The Himalayan regions of India are the important repository of plant biodiversity due to altitudinal gradients from temperate to alpine regions with temperature and climatic variations. Thus these regions with varied landscape features are the natural reservoir of many important and rare medicinal plants of the world including some rare lichens and fungi having varied types of habitats. So plant materials of Himalaya are the main source of many highly valued drugs in modern medicine causing a great global demand for pharmaceutical industry. Raw materials are used for the synthesis of many drugs after separation, purification and characterization of active principles from the crude extract. Plants are used as Traditional medicines in our neighbouring countries China as well as in our country in Ayurveda, Siddha, Unani and Folk medicines in tribal areas.

Recent reports of overharvesting “Himalayan Viagra” in The Times of India¹ on July 11, 2020 and its recent inclusion in the Red List of Threatened Species of International Union for Conservation of Nature (IUCN) has attracted great attention on this fungus to the scientists and the common people. Again this fungus, known for aphrodisiac and rejuvenation properties, has been categorised as ‘Vulnerable’ in the red List of IUCN¹. This is one of the costliest fungus of the world whose market price in the International markets founds to be Rupees 20 lakh per kg¹. The overharvesting of this fungus for its high price has made its scarcity in the natural habitat of Himalayas. According to the opinion of Vivek Saxena, the Indian representative of IUCN, “the purpose of putting the fungus in the Red List under the vulnerable category is to ensure that proper Government policies are implemented in order to conserve it so that it remains in the wild”¹. Himalayan Viagra is also widely known as Caterpillar Fungus, The scientific name of this fungus is Ophiocordyceps sinensis (Berk) Sacc.

IUCN is the International Union for Conservation of Nature and was established in 1964 to include the threatened species of the world in a book called Red Book. The aim of the organisation is to produce the world’s most comprehensive information on the global conservation status of animal, fungi and plant species. The IUCN Red

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list in the Red Book is the indicator of the health of the biodiversity of the world. Its headquarters are in Gland, Switzerland. The Red list of the Red Data Book contains only the list of the endangered species into nine categories on the basis of the risk of global extinction.

These nine categories are i) Not Evaluated ii) Data Deficient iii) Least Concern iv) Near Threatened v) Vulnerable vi) Endangered vii) Critically Endangered viii) Extinct in the wild ix) Totally Extinct (Fig.1).

The Red List of Animals in India as per IUCN has been maintained by the ENVIS Centre (Environmental Information System) on Faunal Diversity by Zoological Survey of India under the Ministry of Environment, Forestry and Climate Change, Government of India. Similarly the Red list of Plants and Fungi in India has been done by the ENVIS Centre on Floral Diversity by the Botanical Survey of India under the same ministry of the Government of India.

As Fungi are growing in varied habitats with extreme temperature and climate variations it was thought that this plants are not impervious or vulnerable to environmental change. But the IUCN has evaluated the conservation status of 280 species of fungus till December 2019. Recently the Red List of Fungi of IUCN has noted five fungal species as vulnerable to critically endangered. In comparison with the nearly 1.5 million to 5 million fungal species throughout the world, very low number of endangered species have been recorded in fungi due to some difficulties in monitoring the fungal population. There are other reasons also as most fungi are not visible in the naked eye before forming their fruit bodies and secondly they may not occur in the same place every year. Thus it is very difficult to track fungi in the normal habitat.

Fig 1. Nine groups in IUCN Red List

Before discussing the details of the caterpillar fungus (**Ophiocordyceps sinensis**), it will be wise to give a general idea of the fungus in brief.

**General Idea Of The Fungus**

In addition to higher plants, FUNGI (sing. Fungus) are among the most widely distributed organisms on the planet and are of great economical and medicinal importance. Fungi are basically plants without any chlorophyll but now they are placed in a separate kingdom like plants and animals. The discipline dealing with fungi is called Mycology. The word Fungus comes from the Latin word meaning mushrooms which are a reproductive structure of some fungi. The common people have an idea that the fungus means mushroom. But most of fungi do not produce mushroom like structure. The Fungi containing different varieties of living organisms come under the group Eumycota. Few fungi are unicellular as for example Yeast having individual oval or cylindrical cells. But most of the fungi are multicellular having a thread like structure called Hyphae (sing. Hypha) forming a network of filaments which cannot be seen in the naked eye. But the mass of hyphae called mycelium can be seen in the naked eye. It can grow on a surface of the soil or on decaying materials or in a liquid and even on living tissue². They are ubiquitous in terrestrial habits. They are also associated with plants, animals and sometimes in saprophytic, mutualistic or mycorrhizal and parasitic forms. Reproduction may be asexual, sexual orparasexual but most of them produce large number of haploid spores which can undergo mitotic division to produce multicellular haploid individuals. Reproductive structures are varied and of short duration. About 14,400 species are recorded from India approximately under 45 classes, 120 orders, 345 families and 2660 genera.

The giant Honey Mushroom (**Armillaria solidipes**) is the largest organism on earth spreading across more than 2400 acres of underground soil in eastern Oregon which is at least 2400 years old². Some most economically important species of fungi are edible Mushrooms, Penicillin producing fungus **Penicillium notatum**, unicellular Yeast which is used in Bakery and Brewing industry and many others. There are some fungi which have symbiotic
association with plants or animals giving benefit to both species. Many trees form symbiotic relationship with fungi by connecting the roots of plants with the underground parts of fungus. This relationship is called Mycorrhizae. Through this mycorrhizal process, the hyphae of the fungus absorbs minerals from the soil and transfer them to roots of trees and thus helping trees to take more nutrients as well as to maintain air and water flow in the soil around the roots. In this relationship the fungus is also getting benefit by taking organic nutrients like sugars and amino acid from plants.

Fungi are eukaryotic organisms as their cells have clearly defined nuclei with all organelles like mitochondria, endoplasmic reticulum, Golgi apparatus, vacuoles, various types of vesicles and Peroxisomes like that of higher plant and animal cells. Some fungal cells also contain another organelles called Woronin body or organelle complex at the tip of the hyphae called Spitzenkörper. This organelle is called the “Vesicle supply centre” which regulates the initiation, maintenance and direction of hyphal growth (Fig.2).

Fig.2. Multinucleate hyphae of Neurospora crassa. Nuclei showing green and Schizenkörper (arrows) at the tips of the growing Hyphae. (Taken From Reference 3).

**Ophiocordyceps Sinensis**

*Ophiocordyceps* is a genus of Fungi under the family Ophiocordycipitaceae under the Division Ascomycetes or Ascomycota in the order Hypocreales. It is an insect-pathogenic fungus discovered by the British Naturalist Alfred Russel Wallace in 1859. Some fungi have an intimate relationship with many insects and some arthropod species like spiders, mites and ticks to form symbiosis, mutualism and parasitism.

The genus *Ophiocordyceps* was first scientifically described by a British mycologist Tom Petch in 1931 with about 140 species that grow on insectu. Petch identified four species of *Ophiocordyceps* such as *O.blattae* growing on Cockroach, *O.unilateralis* on ants, *O. peltata* and *O. rhizoideaon* Coleoptera larva, A few species of Ophiocordyceps was reported that is growing on Termites. Berkley first identified caterpillar fungus as *Sphaeria sinensis* in 1843 and later Saccardo named it as Cordyceps sinensis and afterwards Sung and others gave a name to this fungus as *Ophiocordyceps sinensis* in 2007.

Of the different species of the genus *Ophiocordyceps*, the most costliest Fungus of the world is *O. Sinensis* (Berk) Sacc w. This species is commonly known as CATERPILLAR FUNGUS which is terrestrial and growing by parasitizing larvae of moths and produces fruiting bodies used in Traditional Chinese Medicine. This ascomycete entomaphagus parasitic fungus *O. Sinensis* is commonly known as the Chinese Caterpillar Fungus or Dong Chong Xia Cao (winter worm, summer grass) or “Hia Tsao Tong Tchong” and “Hea Tsaon Tsong Chung”. In the interior mountain areas of Tibet, it is locally known as “Yarsha Gamboo”, “Keera Ghas” and “Keerajhar”. In India it is known by the name of “Ghas Ki kira” or Kira Jhar or Ghas Ki jhar or keerajari or Yartsa Gunba in the local alpine zones of Himalayas and Gadavira or Yarsagumba in Nepal.

In India it is widespread in the upper hilly regions of district Pithoragarh of Uttarakhand in the snow meadows at the altitude of 3200m and also in some areas of Kumaon hills and also in Nepal and Bhutan. In Hindi this fungus is called *Keera jari*, keera meaning “insect” and “jari” meaning root. *O.sinensis* is also found along the border lines with Nepal and China. In China this is endemic in the Tibetan plateau and in high mountain areas (3000- 5000 m) in Sichuan, Quinghai, Yunnan around Himalaya. The global distribution of fungus is shown in Fig.3. This fungus is widely collected from seven districts of Nepal particularly in the Dolpa district which is the major warehouse for the supply from Nepaly. The First Chinese Emperor used this herbal medicine as a tonic for longer life, The legendary Chinese beauty Yang KueFei (719 – 756 AD) is the regular user of this medicine as her fountain of youth. The Chinese athletes took this fungus regularly and held many world records.
Morphology of Ophiocordyceps Sinensis

The parasitic fungus O. sinensis is a combination of fungi and larva of host insect. It consists mainly of two parts (i) the caterpillar of insect at the base containing fungal Endosclerotium within the caterpillar (Basal Part) formed after infection through mycelium and (ii) the upper part called Stroma. The caterpillar is usually yellowish on the soil and the stroma at the top is dark brown or black (Fig. 4). The body of the uninfected caterpillar (normal) is like the larva of silkworm with 3-5 cm in length and 3-8 mm in diameter. The body parts of the caterpillar after mummification due to infections are clearly visible as head, neck, body segments and sometimes legs. The stroma is clear with slender basal stem of 2.5 – 8.5 cm long and 2 – 3 mm wide while upper head is 1 – 2.5 cm. long and 3 – 5 mm wide. The head is the fertile region of the fungus called stroma. This morphological structure is peculiar in having the upper part as stroma of the fungus O. sinensis and the basal part belongs to the larva (caterpillar) of the insect which is pervaded by the mycelium of the fungus (Fig. 3). Thus this fungus invades the caterpillars, eats the soft tissue and mummifies the larva and to complete the life cycle at the cost of insect.

Life Cycle of Fungus Using Larva

The larva of the insect Hepialus armaricanus remains for long time in soil then changes into caterpillar via pupal stage. During summer, the larva are very active and crawl on the soil for taking food by eating grass roots or often crawl on the trees to eat food and then come back to soil to spend the winter in the underground. When the larva are active on the soil, the fungus also becomes active at the same time. The spores, called ascospores, of the fungus (Ophiocordyceps) spreads in air and then fall into the soil by rain or dews and attached on the body of the larva. At winter the infected larva crawled deep into the soil for passing the hibernating stage. But the fungal spore inside the larva starts to germinate taking nutrients from the internal organs of the larva through mycelium which ultimately captures the whole body of the larva leading to the death of larva or caterpillar. At this stage the dead caterpillar is called “winter worm”. In the coming summer, the mycelia grow out of the head of dead larva or caterpillar as stroma to form fruit body above the ground whose base is attached with the dead
caterpillar. This upper part of the fungus in the figure 3 is its fruiting body which will produce ascospores (sexual stage). As the protruding fruiting body of the fungus resembles a grass sprout in the forest it is called YARSA GAMBA meaning ‘winter insectsummer grass’. The ascospores will infect fresh larva after coming out of the fruiting body. Thus growth and reproduction of O. Sinensis requires a host insect and there are some micro organisms (Biotic Factor) that also help during infection of larva under the ground. Although the function of these micro organisms are not confirmed. The infection and sporulation of the fungus depends on the temperature, humidity and intensity of light of that area. The loose soil in that area facilitates the movement of spores into the soil to increase the infection of the larva. The low temperature in the winter and difference in the day and night temperatures help in the vertical movement of larva leading to the increase in probability of infection. The growth and reproduction of this Caterpillar fungus has host specificity on a particular larva of Hepialus. This parasitic complex with infected (mummified ) caterpillar and fungus has a good demand in China as these are used in (mummified) caterpillar and fungus has a good demand in China as these are used in a very popular and most valued Traditional Chinese Medicine that can treat many diseases like cancer, hyperglycaemia, hypertension, and others and China is exporting medicine produced from this fungus to other countries and thus making it costliest of the world.

**Economic and Medicinal Importance of Fungi in General**

Fungi have many economic and medicinal importance to man. Our daily lives are closely connected with fungi and also in combination with some bacteria it can help in recycling by transforming dead materials to some essential components of the soil. Fungi are also important for increasing growth of many trees including some crop plants through mycorrhizal associations.

Edible mushrooms are taken by human beings for their nutritional values. Yeasts like Saccharomyces cerevisiae are used for bread making and S. ellipsoideus are used in the production of alcohol. Fungi also have played an important role in producing many antibiotics. The first antibiotic Penicillin produced from the fungus Penicillium notatum was discovered accidentally by Alexander Fleming in 1928 in his laboratory at St. Mary’s Hospital in London. There are number of different stories about the discovery of Penicillin but the usual story is that the culture of Staphylococcus aureus remained in his laboratory during his holiday time for few days. After returning from his leave, he found that his culture was contaminated with fungal colony and growth of the bacterium Staphylococcus was inhibited in a zone by the fungus. Fleming identified the fungus as Penicillium and was given the name of this inhibitory substance as Penicillin. He could not purify it but predicted that Penicillin has a great potential value for clinical purposes if we can produce it in a large scale. Penicillin was purified in 1940 by Howard Florey, Ernst Chain, Norman Heatley and others in Oxford University which has been used for the first time as a trial in Radcliffe Infirmary in Oxford. Then American Scientists and Industrial experts started production of Penicillin in mass scale to distribute the wonder drug during World War II by reducing the death of soldiers from infected wounds. The recovery rate was from 94% to 100%. Britain also became self sufficient in Penicillin production by 1947. Other medicines are also isolated from fungi like Vitamin A, Vitamin B 12, some steroids, alkaloids and some enzymes like Amylase, Cellulase, Zymase etc.

**Medicinal Importance of O.Sinensis**

The caterpillar fungus Ophiocordyceps sinensis is known in Tibet as Yartsagunbu, in Hindi as Keera jari in different areas of Himalayas. The dried club shaped fruiting body with the larva has a great medicinal value. This is used traditionally as a medicinal herb to strengthen lungs and kidneys, increase energy and vitality, stop haemorrhage, decrease phlegm and treat fatigue and more recently as aphrodisiacs and tonic known as Himalayan Viagra. It is one of the costliest medicinal herbs in the world with a market value of US Dollar 128,000 in China. The use of this herb as a traditional medicine has a long history in Tibet and China. The collection and use of this herb was known in Tibet as early as at least 1000 years ago but the reference of its use was found in the text of Tibetan Medicine from 1439 to 1475 in a book on “An Ocean of Aphrodisiacal Qualities — A Special Work on Yartsa Gunbu” by Zurkhar Nyamnyi Dorji. In Traditional Chinese Medicine (TCM), it was mentioned by Wang Ang in 1694 in a book on “The Complete Essentials of Materia Medica”. The first Western report was found in 1736 by the Jesuit priest Du Halde who was treated by the Emperor’s physician at the Imperial Court with Cordyceps (older name of Ophiocordyceps)18-19. It has been used as Folk Medicine in rural areas (Ethnobotanical use) to treat about 21 ailments including erectile dysfunction, female aphrodisiacs, malignant tumours, bronchial asthma, bronchitis, cough and cold, jaundice, alcoholic hepatitis.
and others. In the mountainous Northern Yunnan province the Tibetan people used this herb for improving eyesight in the treatment of Calcium deficiency in children, diabetes associated nephropathy and to strengthen immune system. In India villagers of Uttarakhand and Garhwal Himalayas used this fungus for medicinal purposes as in Tibet, Nepal and Bhutan. It is now used as an important raw material in the Oriental medicine around the world due to its many medicinal properties. In village areas it is taken by cooking with duck meat or with hen’s meat to treat patients suffering from cancer and asthenia or abnormal loss of strength with duck meat. It is used with hen’s meat to treat hyposexuality and male impotence. In some areas of Nepal the caterpillar fungus is powdered and combined with the rhizome of plant *Dactylorhiza hatagirea* for consumption or mix with honey and cow’s milk for tonic and aphrodisiac. It is also used as a powerful tonic in the name of Himalayan Viagra. Western Medical Research on *O. Sinensis* suggests anti-tumour, anti-viral and anti-cancer activities, immune-modulating effects, antioxidant, reduction of cholesterol and increase of stamina and libido. Several research papers on this myco-medicine are being published specially in East Asia. This medicine is also popular in Japan and Korea. It is not so popular in Western market as such but the bio-active compounds isolated from this complex fungus are used for medicinal purposes. Pharmaceuticals derived from *O. Sinensis* and related species are used widely in Western medicine. The most important of them is Cyclosporin which is used to prevent rejection after transplant surgery and to treat auto immune disorder and Ergotamine which can be used to treat migraine and for induction of child birth.

Many bio-active compounds have been isolated from this fungus such as Cordycepin, Cordycepic Acid, Adenosine, Exo-polysaccharides, Vitamins, Enzymes etc. Of these CORDYCEPIN is an antibiotic having anti-tumour effect, insecticidal effect and antibacterial effect. This antibiotic is already available in the market through Tokyo Chemical Industry Ltd. but it is still now for Laboratory use and Research purposes only. Bioactive compounds isolated from this fungus and their properties of pharmacological actions are discussed later.

Global trade of caterpillar fungus is widely circulated after creating many world records by Chinese athletes in 1993 in World Athletic Championships in Stuttgart. Other countries came to know that Chinese athletes are getting so much energy by taking dietary supplements of *O. sinensis* as a tonic to build up strength and energy.

### Harvesting and Trade

The harvesting of the fungus generally starts from the month of May to June or July depending on the climate and condition of the snow of that area. Sometimes it is very difficult for harvesters as they have to recline on the slope of the mountain to search and collect the fungus which is protruding very little above the ground such as 1-2 cm. It is then dried in the shade and then stored in air tight containers to avoid moisture. Qinghai province and Tibet Autonomous Regions of China are the major collection centres of Yarsagumba. In 2017 the total collection of this fungus in that area was about 10 tons meeting the 10% of the total national production. This brought per capita income of local population as 20,000 Yuan (= US Dollar 3120).

In India some collections have been done in remote areas of Nanda Devi Biosphere Reserve which is located in Garhwal and Kumaon regions of Uttarakhand in the Western Himalaya. This landscape falls under Chamoli, Bageshwar and Pithorgarh district of Uttarakhand. The annual harvest varied from 300 to 1150 of caterpillar fungus per household. But the number of harvest is gradually decreased due to the greater collection and high demand. Again the overharvesting is also done by the villagers as this is the only earning source of many rural people. They
do not think about its future conservation. In comparison to India more and more collections of this fungus are done in Nepal, Bhutan and Sikkim. The top three fungus producing districts of Nepal is Jumla, Dolpa and Darchula. The average annual production in Jumla is about 201 kg. After collection of the caterpillar fungus, it is cleaned thoroughly to remove soil and dirt generally through toothbrush. It is then dried in the shade and then stored in airtight container to avoid moisture and is ready for market (Fig.5).

The commercial demand of fungus depends on the ratio of the length of the larva and stroma or quantitatively as the amount of fungus present in one pound (about 500 gms). In each pound the number of fungus present varies from 800 to 1500 specimens. The medicinal potency of Yartsa Gunbu is maximum if the stroma is slightly shorter than the larva or at least not much longer which depends on the time of harvesting (Figure 6)²⁹-³⁰. The main objective is to collect the caterpillar fungus early in the season so that the fruit body is not much developed and thus collectors try to collect the fungus at early stage. If the fruit body is mature and starts to disperse asci or spores, the larva of the fungus begins deterioration and the market value and demand will be less³¹.

**Trade of Caterpillar Fungus**

The only important source of income of the villagers of Alpine Himalayan areas of China, Tibet, Bhutan, Nepal and India is through collection of this fungus and selling these to the brokers who are coming directly to the site for their business leading to about 70- 90% cash income to villagers. Some households have 26,600 Dollar per season so most of them are leaving their usual business on Yak and sheep herds as it requires more annual labour than collecting and selling fungus. A similar process occurs in Bhutan, Nepal and India. Thus people in these areas have realized profits more in collecting fungus than farming and herding of animals. The annual household cash income from the collection of caterpillar fungus is about 64.5% and 53.3% in Jumla and Dolpa district of Nepal respectively and 80-100% in Bhutan. In Uttarakhand of India this income is found to be 98% in Nandakini valley, 60 – 78% in Gori valley and 74% in Nandadevi Biosphere Reserve.²⁹-³⁰ As the brokers are collecting raw materials directly from the villagers, so they do not follow any rules or in other words they follow informal trade channel for sending them to China through Indo –Nepal border. The Government of India, Nepal and Bhutan are now taking steps to control illegal trade and over-exploitation of this fungus by the villagers.

In Bhutan steps are taken to restrict the collection of fungus through permit system with a nominal fee. The collectors have to collect 2 out of 5 specimens from the ground and only three members from each household will be able to join the team. Authorised persons will collect these specimens from the collector after payment in cash which will then go to the International market through auction by Government to avoid illegal trade.

In China the policy made by the Chinese Government is very strict. Collectors have to apply for the permit to the local Government and no collection activities are allowed in the core zone of nature reserves where habitat destructions are strictly forbidden to conserve these important fungi. The violation of rules by anybody can result in heavy penalties and confiscation of permits.

In Nepal the caterpillar fungus is protected under Forest Act of Nepal 1993 and Forest regulations Act 1995. The Government gives permission to the collector after receiving royalty from collectors and traders without any other restrictions.

Fig. 6. Trade flow for Caterpillar Fungus (Taken from Reference 28)
In India the collection and sale of fungus are not regulated by law but the State Government has made some guidelines to stop illegal smuggling. State Government of Uttarakhand has protected the fungus under the Indian Forest Act 1927 and has made some guidelines. The permission for the collection and trade is to be taken from the village level Forest Council (Van Panchayat) while collection and trade is completely prohibited from the Reserve Forest. Collectors may sell the raw materials to Village Council and then they sell to the buyers authorised by the Forest Department at a fixed price. But the traders and local villagers of India are still doing illegal trade due to huge differences in price margin from legal and illegal trade. These fungi are going illegally to various towns and cities of Nepal. Then it flows mainly to China and other countries at a high price. Thus smuggling of the species is going on across borders for higher profits\(^28,31\) (Fig. 6).

**Ecological Pressure and Threats**

During the collection time of the Caterpillar fungus, villagers are going in great numbers in the alpine regions of the Himalayas with their tents, fuel, food other consumables as well as their domestic animals for longer period of time leading to overgrazing by domestic animals, chopping of woods for firewood by the collectors. Overcrowding of villagers in the alpine zone for longer period during harvesting are affecting the ecosystem and also affect many threatened animal species of the area. Again these anthropogenic pressures are also affecting the river systems of the Himalayas through pollution and habitat destruction. All these uncontrolled harvestings for longer periods in same area may lead to decline in the sustainability of this fungus in near future. Again the deposit of huge non-degradable garbage near the camp of the harvester have a deleterious effect on caterpillar fungus, surrounding environment and the population of birds, rare and threatened animals and plants of that localities. So the control of hazardous harvesting and implementation of sustainable scientific harvesting must be done for the survival of the species and the environment of alpine landscape. The team members from Nanda Devi Biosphere Reserve have already started environmental and conservation awareness programme to people associated with harvesting and trade of caterpillar fungus in the Himalayas. They also have taken an objective to target young people and students to discuss the medicinal importance of the fungus, anthropogenic pressure on their only important earning species and the environment, market and trade issues. This will help to get their cooperation in the management of conservation and sustainable of the valuable species. Villagers agreed to the minimum use of plastic and clean the meadows from non-degradable wastes while returning home after harvesting is over. The policy should be made by the Government of India to search alternative areas for production of more caterpillar fungus so that rotational harvesting can be done to save land and species. The Project leader is also planning to arrange for alternative source of income instead of depending solely on caterpillar fungus which will help to save the rare and costly fungus as well as the environment. The parallel venture has also been taken to build factory for producing medicine from the fungus in addition to the selling of raw materials to the International market.

**Bioactive Constituents and Their Pharmacological Properties**

Besides Cordycepin there are other bioactive compounds isolated from *O. sinensis (=Cordyceps sinensis)* such as Adenosine, Polysaccharides, Ergosterol, Serine Protease (CSP), Cordymin, Cordycemissides A and B, Cordycepic acid and others\(^32\). Many of these compounds isolated from this fungus both in vivo and in vitro activate immune systems of the body. Of these components Cordycepin is found to be the most vital due to its various nutraceutical and therapeutic potential with innumerable health benefits. Bioactive compounds present in caterpillar fungus are proteins, fats, essential amino acids, volatile oils, carotenoids, flavonoids, phenolic compounds, minerals (Fe, Ca, Mg, Sr, Na, Ti, Se, Mn, Zn, Al, K, Cr, V, Zr) and Vitamins (B1, B2, B12, E and K) as well as various types of Carbohydrates like monosaccharides, oligosaccharides, polysaccharides, sterols, nucleosides etc\(^33\).

Cordycepin, nucleoside analogue, is first isolated from the fermented broth of *Cordyceps militaris*. The chemical structure of Cordycepin has two heterocyclic rings of which one is Imidazole.Cordycepin is a derivative of the nucleoside Adenosine differing from the latter by the absence of Oxygen in the 3’ position of its ribose entity (Fig. 7). The pharmacological activities of Cordycepin are found as anti microbial, antitumour, anti-mutagenic, anti-metastatic, anti-diabetic, anti-inflammatory, immune-modulatory, anti diabetes, anti-hypertension, anti-arthritis, hepato protective, anti-ageing etc. This fungus is also known as Traditional Chinese Medicine (TCM) as it was used long back in China in the pharmaceutical and health sector as nutraceuticals (26). The term Neutraceutical in the diet was first introduced by Dr Felice by joining the two words “Nutrition” and “Pharmaceutical” and define it
as food which imparts good health as well as prevent various diseases. Several pharmaceutical and nutraceutical preparations are made from the dry powder of *Ophiocordyceps* or *Cordyceps*.

In traditional procedures Cordycepin and other bioactive compounds are extracted from the fungus grown in natural conditions. Owing to over exploitation of the specimen from the Himalayas, it cannot meet the demand of the market.

Thus Scientists are trying to cultivate this fungus both *in vivo* and *in vitro* in the field and laboratory respectively as well as in the synthesis of Cordycepin from the cultivated specimens. There are two methods for the synthesis of Cordycepin like Microbial Fermentation and *in vitro* process. Recently Genetic Engineering techniques are used following Gene over expression, Gene knock out and Gene editing methods.

From the survey conducted by the Grand View Research Team, it has been found that the Global nutraceutical market size could reach US Dollar 722.49 billion by 2027 and the major key companies like Abbott, Amway, Danone SA, Nestle SA, Pepsi Co. and others are doing research and development in nutraceutical production. It has been estimated that Global Cordycepin market will be US Dollar 1 billion by 2026 where China will be the main supplier followed by India, Nepal and Bhutan. Some work has already been done on the mechanism of action of Cordycepin showing effect on i) the inhibition of Purine biosynthetic pathway; ii) the RNA chain termination and iii) interference of m TOR signal transduction.

However, further research work is needed to know the exact mechanism of the action of Cordycepin and other biomolecules on human body having high potential of pharmacological, therapeutic and nutraceutical value. As this wonderful fungus is edible so it will be a good preventive medicine for various ailments in future.

Fig. 7. Chemical structures of some known and potent bioactive compounds in *Cordyceps*. (A) Cordycepin (B) Adenosine (C) Cordycepic acid (D) Ergosterol (E) Structure of (a) and (b). (a) Cordyceamides A (b) Cordyceamides B. (F) Linoleic acid (G) Oleic acid (H) Palmitic acid. (Taken from Reference 33).

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