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Ophiocordyceps sinensis: An entomopathogenic Medicinal fungus of the Himalayas

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A B S T R A C T

Ophiocordyceps sinensis (Berk.) (Genus: *Ophiocordyceps*, Family: Ophiocordycipitaceae), commonly known as the Chinese caterpillar fungus, is a high-altitude, entomopathogenic fungus with significant medicinal and economic properties across the Himalayan and Tibetan Plateau regions. This fungus parasitizes larvae of ghost moths (*Thitarodes* spp.) and is used in traditional Asian medicine for over three centuries. Known for its wide pharmacological effects, ranging from anti-inflammatory and immunomodulatory to anti-cancer and aphrodisiac properties, *O. sinensis* remains integral to both traditional remedies and modern pharmacology. The fungus is ecologically constrained to alpine regions (3,000–5,000 m) and its collection has become a vital income source in parts of China, Nepal, Bhutan and India. However, increasing demand, overharvesting, and habitat degradation have led to its endangered status. Despite decades of research, artificial cultivation of the fungus remains difficult, making large-scale production challenging. Efforts are ongoing to develop sustainable cultivation and harvesting methods. To ensure its sustainability, conservation measures such as regulated harvesting, habitat restoration, community-based management and further scientific research are urgently required.

Introduction

Ophiocordyceps sinensis (Berk.), the Chinese Caterpillar Fungus is a parasitic fungus belongs to the genus *Ophiocordyceps* and Ophiocordycipitaceae family based on a molecular phylogenetic study. Earlier it was classified under the genus Cordyceps in the Clavicipitaceae family (Sung *et al.,* 2007; Dan *et al.,* 2021). It is found in Bhutan, southwestern China (Gansu, Qinghai, Sichuan, Tibet, Yunnan), northern India (mostly Himachal Pradesh, Sikkim and Uttarakhand) and Nepal, thriving at elevations of 3,000–5,000 meters (Li *et al.,* 2011). The common name of species varies from place to place. It is popularly known as the Chinese caterpillar fungus in English, YartsaGunbu in Tibet, Dong Chong Xia Cao in China, Tockukaso in Japan, Yarsagumba in Nepal and Keerajadi in India (Belwal *et al.,* 2019). The fungus parasitizes soil borne larvae of *Hepialus*/*Thitarodes*, belonging to the order *Lepidoptera* (Pegler *et al.,* 1994) and is widely used in the treatment of inflammation, cancer, chronic kidney disease, weakness after sickness, sexual dysfunction, tuberculosis, coughing, anaemia, and back and knee pains etc (Xu *et al.,* 2016; Pegler *et al.,* 1994) and has been used as a medication in China for over 300 years (Wang, 1694).*O. sinensis* has been officially classified as an endangered species in 2012 by the Convention on International Trade in Endangered Species (CITES) Management Authority of China because of limited wild population and over-harvesting (CITES Management Authority of China, 2012).

Since 1964, *C. sinensis* has been listed as a drug in the official Chinese Pharmacopoeia (Lin and Li, 2011). Both the dead larva and fruiting body have been valued as traditional medicine and health food in China for centuries. In traditional Chinese medicine, the caterpillar fungus is primarily used as a tonic to enhance the immune system. Modern pharmacological research has revealed its therapeutic benefits for a variety of conditions, including respiratory, renal, liver, nervous system and cardiovascular diseases (Wei *et al.,* 2021). Due to its extremely high price, ranging from USD $20,000 to $40,000 per kg, it is often referred to as “soft gold” in China.

Despite its widespread value, efforts to develop efficient methods for the commercial cultivation of fruiting bodies have not yet succeeded. *O. sinensis* has both a sexual stage (teleomorphic) and an asexual stage (anamorphic). Due to overharvesting and limited yield, the market price of natural *O. sinensis* (teleomorphic) remains exceptionally high (Li *et al.,* 2019). Harvesting caterpillar fungus has become an essential livelihood for mountain communities in Nepal, contributing 21.1% of total household income and 53.3% of cash income, making it the second largest income source after farming. Similarly, in Tibet, the collection of caterpillar fungus accounts for on average 40% of rural cash income (Shrestha and Bawa, 2014a; Winkler, 2008 and Winkler, 2010). This review paper provides a comprehensive summary of the taxonomy, morphology, lifecycle, host associations, pharmacological applications and socio-economic importance of *O. sinensis*, while highlighting the urgent need for conservation strategies.

Taxonomic History of the caterpillar fungus

In 1842, Westwood mistakenly identified *Ophiocordyceps sinensis* as *Clavariaentomorhiza* (Dicks.) Westwood (Westwood, 1842), a species previously described by Dickson as *Sphaeriaentomorhiza* Dicks. in 1785 from England (Dickson, 1785). Westwood's *Clavaria entomorhiza* was later recognized as a new fungal species by Berkeley in 1843, who renamed it *Sphaeria sinensis* Berk. In 1857, Berkeley referred to the species as *Cordyceps sinensis*, while reviewing *Cordyceps* species in the United States, although he did not provide an explanation for this nomenclatural change (Berkeley, 1857). Subsequently, Pier Andrea Saccardo (1878, 1883) reclassified the species under the genus *Cordyceps*, naming it *Cordyceps sinensis* (Berk.) Sacc. Later, Sung *et al.,* (2007) divided the genus *Cordyceps* into four distinct genera including *Cordyceps*, *Ophiocordyceps*, *Metacordyceps* and *Elaphocordyceps* and reclassified *C. sinensis* under *Ophiocordyceps*, renaming it *Ophiocordyceps sinensis*. The term *Ophiocordyceps sinensis* refers to the stroma (fungal part), while the caterpillar belongs to various species of *Thitarodes* (Hepialus) and other related genera within the family Hepialidae, commonly known as ghost moths, bat moths, or swift moths.

Medicinal uses of Ophiocordyceps sinensis

The use of *Caterpillar fungus* (*Ophiocordyceps sinensis*) in traditional medicine can be traced back to Tibet and Nepal. The earliest known reference to its medicinal use dates back to the late 15th century, found in a document written by ZurkharNyamnyiDorje (Wylie:)(a Tibetan doctor), which mentions the fungus's use as an aphrodisiac. Wang Ang in 1694 first mentioned the use of *O. sinensis* in the traditional Chinese Medicine. For over 300 years, *O. sinensis* has been employed in the treatment of a wide range of ailments, including hyposexuality, bronchial asthma, respiratory diseases, malignant tumors, bronchitis, diabetes, renal failure, asthenia, hyperlipidemia, and hyperglycemia (Li *et al.,* 2002, 2015; Chen *et al.,* 2010). Studies also indicate that *Ophiocordyceps sinensis* plays a key role in regulating several physiological systems in the human body such asthe respiratory, cardiovascular, immune, circulatory, hematogenic and glandular systems, particularly under stressful conditions (Dai *et al.,* 2009). Additionally, *O. sinensis* is recognized for its anticancer, hypocholesterolemic, hypotensive, vasorelaxant, anti-fatigue, and antidepressant properties. The fungus contains a variety of active phytochemicals such as organic acids, phenolic acids, amino acids, nitrogenous compounds, nucleosides, nucleotides, fatty acids, sterols, and polysaccharides, each contributing to its diverse pharmacological actions (Sen *et al.,* 2023).

Morphological characteristics of *Ophiocordyceps sinensis*

Ophiocordyceps sinensis consists of two distinct parts: the basal caterpillar, which contains the fungal endosclerotium and the upper stroma. The caterpillar is typically yellowish, measuring 3.5–4 cm in length, while the stroma is dark brown or black, ranging from 4 to 10 cm. Each caterpillar supports a single stroma that grows from its head and exhibits a clavate, sublanceolate or fusiform shape. The caterpillar is solid and intact, with clearly distinguishable body parts, including the head, neck, body segments and legs.

The stroma is further divided into two regions: the basal stem and the upper head. The stem is slender, glabrous, 2.5–8.5 cm long and 2–3 mm wide, characterized by longitudinal furrows or ridges. The head is swollen and fusiform, measuring 1–2.5 cm in length and 3–5 mm in width. This region represents the fertile part of the stroma, with a distinct sterile apex that is laterally compressed and furrowed, measuring 2–4 mm in both length and width. The head's surface appears granular due to the projecting openings or ostioles of the perithecia.

Perithecia are distributed around the swollen head and vary in shape, being subtruncate or oblate, ovoid, globose or ellipsoid. The asci are cylindrical or slightly tapering at both ends, either straight or curved, with a capitate, hemispheroid apex. Ascospores are hyaline, filiform, multiseptate and slightly tapering at both ends (Shrestha *et al.,* 2010; Sung *et al.,* 2007).

Hosts species of Ophiocordyceps sinensis

The insect host species of *Ophiocordyceps sinensis* mainly belong to the family Hepialidae (Lepidoptera) (Chu *et al.,* 2004). *Thitarodesarmoricanus* Oberthür was the first host species of *O. sinensis* to be reported and biologically characterized in China. Since 1980s numerous efforts have been made to study the insect species associated with *O. sinensis*, revealing a broad host range that includes over 50 species within Hepialidae (Wang and Yao, 2011). The classification of the host larva has evolved over time, with Pereira (1854) initially identifying it as a species of *Agrotis* based on Mr. Doubleday's observation. Gray (1858) later reclassified it as *Gortyna* (Noctuidae), while Soubeiran and Thiersant (1874) and Lohwag (1923) attributed it to *Hepialus* and *Phassus* within Hepialidae. Several *Hepialus* species, including *H. armoricanus*, *H. oblifurcus* and *H. biruensis* have been confirmed as hosts (Chu, 1965; Gao *et al.,* 1992; Chen *et al.,* 2002). Recent studies indicate that 50–70 moth species, predominantly *Thitarodes* (Hepialus) along with a few species of *Hepialiscus*, *Forkalus* and *Bipectilus* serve as hosts of *O. sinensis* (Li and Tsim, 2004; Liu *et al.,* 2005; Cheng *et al.,* 2007). Maczey *et al.,* (2010) identified two new *Thitarodes* (Hepialus) species as hosts from Bhutan.

Life cycle

The life cycle of *O. sinensis* in its insect hosts typically spans 2 to 3 years. The stalked fruiting body known as the perithecial stroma develops from the head of the dead caterpillar and emerges from the soil in alpine meadows of Bhutan, China, India and Nepal by early spring. During late summer, the stroma releases thread-like ascospores from the perithecia. The primary insect hosts, caterpillars from the family *Hepialidae,* inhabit the soil and feed on the roots of plants from over 19 angiosperm families. Multiple *Thitarodes* species are associated with *O. sinensis*, though only a few, such as *T. armoricanus* and *T. jianchuanensis* are well-studied. These caterpillars are most susceptible to fungal infection after molting, particularly during late summer and autumn. The highest rates of infection occur when 4^{th} to 5^{th} instar larvae shed their old cuticles and begin forming new ones (Zhu *et al.,* 2004).

The precise mechanism of fungal entry into the caterpillar remains unclear. Following entry, the fungus proliferates vegetatively within the host, filling its body with thread-like hyphae. The fungus extensively invades the host's tissues, eventually leading to its death. As the fungus produces sclerotia the host caterpillar becomes rigid (Buenz *et al.,* 2005; Stone, 2008; Li *et al.,* 2006; Zhu *et al.,* 1998). The fungus grows from the dead caterpillar's head, forming a small stroma bud before soil freezing in winter. This bud resumes growth in the following spring and early summer, emerging as a mature fruiting body (Pegler *et al.,* 1994).

Economic importance and trade of *Ophiocordyceps sinensis* in the Himalayan Belt

The commercial collection of *O. sinensis* serves as a major source of income for local communities in the Himalayan regions of Southwest China, Tibet, Nepal, Bhutan and India. According to Belwal *et al.,* (2019), global production of the fungus ranges between 84.2 and 182.5 tons per year[1]. The highest yield is reported from the Tibetan Plateau, with an estimated 80 to 175 tons annually, followed by Nepal (1.0–3.2 tons/year), India (1.7–2.8 tons/year) and Bhutan (0.5–1.5 tons/year) (Winkler, 2009). It contributes between 40% and 90% of collector households' cash income in these regions [53](Winkler, 2008). China is the leading global producer, responsible for 95–96% of total output, while Nepal, India, and Bhutan contribute approximately 1.2–1.8%, 1.5–2.0%, and 0.6–0.8%, respectively (Shrestha and Bawa, 2013).

In Nepal, revenue from the caterpillar fungus represents the second largest income source for collector households, contributing more than >65% of the total household cash income (Shrestha *et al.,* 2014b). In rural and semi-urban areas of Tibet, the fungus accounts for approximately 50% to 80% of per capita rural income (Winkler, 2009). In Bhutan, individual harvesters can earn over USD 2,500 annually from collection activities (Cannon *et al.,* 2009). In India, the fungus plays a significant economic role in states such as Uttarakhand, Sikkim, and Arunachal Pradesh (Negi *et al.,* 2014).

Threat and challenges for *O. sinensis*

Ophiocordyceps sinensis is increasingly threatened by overharvesting, habitat degradation and the impacts of climate change. Studies have suggested that collection of the fungus has contributed to habitat degradation by overexploitation of vegetation essential for the survival of the host larvae, trampling from collectors and livestock and prolonged human activity in collection zones (Shrestha *et al.,* 2014a; Negi *et al.,* 2015; Negi *et al.,* 2020).

The accumulation of non-biodegradable waste and open defecation further threaten environmental health. Despite these challenges, there are currently no proper management practices in place to reduce the ecological footprint of harvesting activities. A sharp decline has been observed in Tibet, where yields dropped from an estimated 100 tons in the 1950s to just 5–10 tons by the 1990s (Hu *et al.,* 2005). Additionally, intensified harvesting has resulted in a 21–46% reduction in aboveground biomass and an 11–19% decrease in overall collection areas (Xu *et al.,* 2015). Local harvester accounts from Nepal further reflect a significant decline in *O. sinensis* availability, underscoring growing concerns over its long-term viability and sustainable use (Shrestha and Bawa, 2013; Yeh and Lama, 2013).

Research on artificial cultivation of *O. sinensis*

The global demand for wild *Ophiocordyceps sinensis* has significantly increased due to its declining production from overexploitation and limited commercial trade. In response, artificial cultivation techniques have been developed to meet market needs, but challenges remain in enhancing cultivation. Researchers have turned to fungi associated with *O. sinensis* as potential substitutes, as their chemical profiles closely resemble those of wild *O. sinensis*. These fungi can also be manipulated to enhance the production of bioactive metabolites. Despite the challenges, advancements in both in vitro (solid and submerged cultures) and in vivo cultivation methods have shown promise in producing bioactive compounds like cordycepin, with some studies even exploring agro-industrial waste as a cost-effective substrate. However, large-scale in vivo production remains limited due to the complex life cycle of the host larvae, which makes it difficult to meet the growing demand (Sharma *et al.,* 2024).

In recent decades, caterpillar fungus, *Ophiocordyceps sinensis* has become a critical source of livelihood for various communities of Himalayan and Tibetan Plateau regions. However, its increasing economic value has led to unsustainable harvesting practices, including overharvesting and the collection of immature specimens. These pressures, coupled with ecological factors such as the decline in moth and larval populations due to the degradation of host plant resources, alterations to soil microhabitats, intensified grazing and the impacts of climate change, have collectively contributed to the reduction in the species' availability. Given the ecological sensitivity of alpine habitats and the socio-economic dependence on this resource, there is an urgent need for the implementation of conservation and sustainable management strategies across its distribution range. Measures such as promoting sustainable harvesting techniques, regulating the number of harvesters per household, limiting the duration of harvesting seasons, managing waste in alpine zones and minimizing habitat degradation, particularly from fuelwood collection are essential. Further research is also necessary to optimize in vivo cultivation methods, conservation policies, and innovations in biotechnology to meet increasing global demand while minimizing environmental impact. Furthermore, national and international collaboration through conservation forums can play a pivotal role in formulating a unified and holistic policy that balances ecological sustainability with community livelihoods.

Author Contributions

Asma Begum: Investigation, formal analysis, writing—original draft. Rajib Kumar Borah: Validation, methodology, writing—reviewing.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

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