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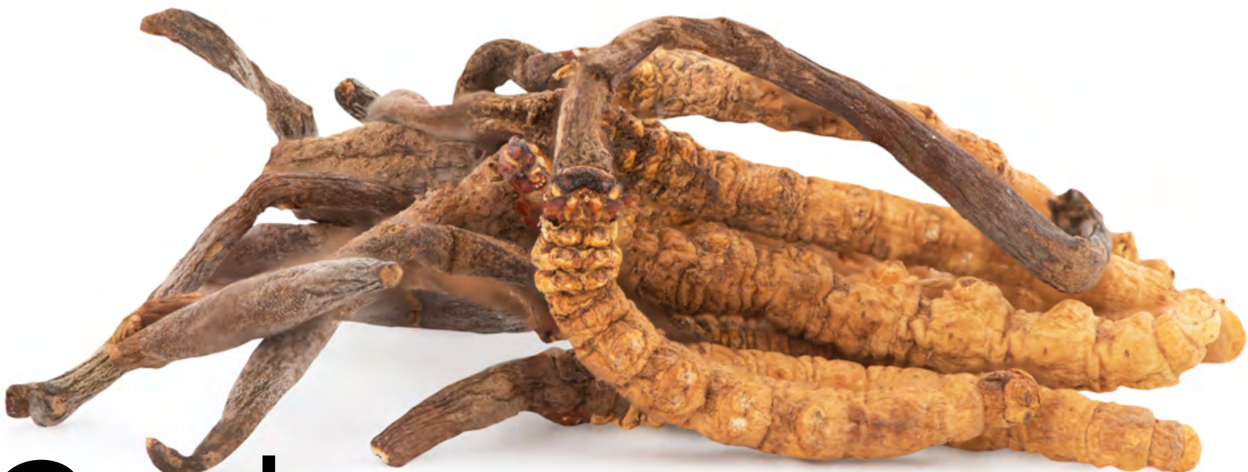
Botanical Adulterants Prevention Program
BOTANICAL ADULTERANTS PREVENTION BULLETIN



Cordyceps *Ophiocordyceps sinensis*. Photo ©2024 wasanajai

Cordyceps

Botanical Adulterants Prevention Bulletin

By Christopher Hobbs, PhD,[a] Roy Upton, RH (AHG),[b] and Stefan Gafner, PhD[c]

[a]University of Massachusetts, 5689 Gold Hill Road, Placerville, CA 95667

[b]American Herbal Pharmacopoeia, PO Box 66809, Scotts Valley, CA 95067

[c]American Botanical Council, 6200 Manor Road, Austin, TX 78723

Correspondence: email

Goal: Because of the great value of cordyceps (*Ophiocordyceps sinensis*, syn. *Cordyceps sinensis*),* its rarity in the wild, and the difficulty of cultivating it, adulteration and substitution frequently occurs. The authenticity of any cordyceps raw material or finished product to be used in dietary or food supplements, or in products falling into another regulatory category,† should be determined, if appropriate, by both DNA and chemical analysis. This is the case even when the mycelium is grown on nutritive substrates such as brown rice (*Oryza sativa*, Poaceae) and the species and strain of the fungal culture used as inoculum is confirmed, because other contaminating fungal species have been observed growing out preferentially over the intended species. Traditional Chinese medical practitioners and consumers familiar with the material known by the Chinese *dong chong xiao cao* (冬虫夏草) may continue to judge identity and quality morphologically but with the understanding that due to its expense, it is a highly adulterated material. This bulletin provides a summary on issues regarding the adulteration of products labeled to contain cordyceps for the herbal products industry, and those with interest in the quality of cordyceps in general. In addition to data on adulteration, the bulletin contains information about the taxonomy, importance in the market, analytical methods to detect adulteration, and consequences for the consumer and the industry.

* In the United States, the American Herbal Products Association (AHPA) has determined that there are three species in commerce that can be labeled as cordyceps: *Ophiocordyceps sinensis*, *Cordyceps militaris*, and *Paecilomyces hepiali*. However, the proposed labeling for the latter two species includes their scientific names added in brackets, i.e., cordyceps (*Cordyceps militaris*) and cordyceps (*Paecilomyces hepiali*).[1]

† Depending on the region, regulations stipulate that cordyceps is sold as a complementary medicine (Australia), dietary supplement (United States), food supplement (Europe), or natural health product (Canada).

Scope: The scope of this bulletin focuses on products sold worldwide under the common name "cordyceps" or "*Cordyceps sinensis*." The third edition of *Herbs of Commerce*[1] allows three species of fungi to be sold under the common name "cordyceps." These include *Ophiocordyceps sinensis*, *Cordyceps militaris* (Cordycipitaceae), and *Paecilomyces hepiali* (reclassified as *Samsoniella hepiali* [Cordycipitaceae] in 2020).[2] *Cordyceps hawkesii*,[‡] which was assigned the common name cordyceps in the second edition of *Herbs of Commerce*,[3] is now recommended to be indicated on dietary supplement labels with its scientific name *Cordyceps hawkesii.*[1] In the United States, for any species used, the fungal part (or form) from which the ingredient is derived must be accurately stated per Compliance Policy Guide 585.525 (e.g., fruiting body, mycelium).[6]

1. General Information

1.1 Common name: cordyceps

1.2 Other common names:

English: caterpillar fungus

Chinese: dong chong xia cao (冬蟲夏草, or 冬虫夏草, meaning "winter worm, summer grass")

French: cordyceps, champignon chenille

German: Cordyceps, Chinesischer Raupenpilz, Tibetischer Raupenpilz, Tibetischer Raupenkeulenpilz

Italian: cordyceps, fungo del bruco

Spanish: cordyceps

Tibetan: yartsa gunbu

1.3 Latin binomial: *Ophiocordyceps sinensis* (Berk.) G.H. Sung, J.M. Sung, Hywel-Jones & Spatafora

1.4 Synonyms: *Cordyceps sinensis* (Berk.) Sacc.,[1] *Sphaeria sinensis* Berk.

1.5 Botanical family: Ophiocordycipitaceae

1.6 Definitions: For the sake of clarity, we will use the following terminology throughout this document.

Wild cordyceps: This is the historical product valued in traditional Chinese medicine (TCM), emerging from the ground and harvested from the wild. Wild cordyceps is comprised of complex of associated species, the primary species of which is now known as *Ophiocordyceps sinensis*. It consists of a club-shaped spore-releasing fruiting body and moth larva produced by fungal parasitism of the ghost moth larva. A more detailed description of this fungi-larva symbiosis is given below (section 1.7).

Cultivated cordyceps fruiting body: This is the fruiting body of accepted cordyceps species and is grown on a nutritive substrate. *Cordyceps militaris* fruiting body is the primary cordyceps fruiting body that has been successfully cultivated on a commercial scale.

Cordyceps: The term cordyceps is used to describe the commercial material in trade. For better clarity, the ingredients in commerce (e.g., *O. sinensis*, *C. militaris*, *S. hepiali*) should be referred to by their scientific names in addition to the common name cordyceps.

Mycelium: The generative vegetative portion of fungal growth consisting of a mass of hyphae that itself does not include the reproductive body of the organism. Fungal mycelium is sometimes propagated through cell culture in fermentation tanks.

Mycelium biomass: This is prepared from a nutritive substrate inoculated with spores of a target fungi (e.g., *Cordyceps militaris*) and allowed to grow until saturated with primordia but not allowed to emerge fully into fruiting bodies. The entire mass is then ground and sold as a dietary supplement ingredient. Mycelium biomass products contain varying amounts of mycelium to biomass substrate. For labeling purposes, this should be declared as mycelium biomass to differentiate it from pure mycelium and fruiting body products. The biggest impact on the chemical composition of mycelium-based ingredients is genetics (variation between strains in a breeding program). Differences in the metabolome can also be due to processing (drying method, drying temperature, and type of extraction if an extraction occurred) (J. Daoust [M2 Ingredients] email to S. Gafner, April 1, 2024).

1.7 Taxonomic considerations: The hosts in the parasitism of wild cordyceps consist of a number of species of larvae of the ghost moth from the genus *Thitarodes* (Hepialidae) on which the ascomycete fungus *Ophiocordyceps sinensis* can grow. The host caterpillar becomes infected by resident fungi in the soil and eventually is digested and filled with mycelium, subsequently forming a stroma/sporocarp (fruiting body) which projects from the top of the head of the parasitized caterpillar body (also known as the sclerotium). The occurrence of wild cordyceps is most notably in the Tibetan plateau, which is also known as Qinghai-Tibet Plateau.[7,8] The fungal species *O. sinensis* is most widely associated with wild cordyceps in this region, but other species of fungi (and bacteria) living in the soil around the microbial ecosystem of the caterpillar in the time it is developing underground are also present. Many of these will be present on and inside the sclerotium of the caterpillar and the fruiting body of *O. sinensis* when the caterpillar fungus is taken out of the soil. These additional soil fungi may consist of more than 100 different fungal species from 13 different genera nearly all on the outside of the sclerotia, with a minimal presence inside the caterpillar. The exact identity of these fungi is determined by the environment in the soil and associated plants and microorganisms where it grows.[9,10] Based on the comparative phylogenetic work of Sung,[11] the relationship between the fungi and moth is extremely ancient (ca. 122 million years), and the proposed ancestor of *O. sinensis* was shown to be intimately associated with animal parasitism through evolutionary history and until present time. The occurrence in separate and relatively isolated regions and the variety of host species are thought to be among the reasons why the fungus described as *O. sinensis* exhibits a substantial intraspecific genetic diversity.[8]

The complex of fungi, but principally *O. sinensis*,[9,12] sometimes digests the entire caterpillar and produces a club-shaped fruiting body, the combination of which becomes "wild cordyceps"; sometimes the caterpillar continues to pupate and produce an adult moth. In the natural system, this relationship responds to environmental conditions and finds a balance between the benefits of the fungi and the moth.

As is often the case, early classification of the large group of ascomycetous fungi (fungi that produce spores in sacs), which include the families of Clavicipitaceae (to which *O. sinensis* was formerly placed) and Ophiocordycipitaceae, (to which *O. sinensis* was recently placed),[8] was based mainly on morphology and specifics of the life cycles of the organisms. These methods, while helpful, can be misleading since two very genetically divergent organisms (classified using DNA sequences and placed in different species or even genera) can look very similar and have similar chemical profiles based on the identical or similar environmental conditions in which they evolved. Genetically different organisms evolving in the same or similar environments over millions of years can lead to observable and measurable similarities that would potentially cause harvesters to gather them without distinction.

Confusion regarding the application of the correct Latin name or binomial for cordyceps partly arises because fungi have two distinct reproductive stages in their life cycle: the teleomorph (sexual) phase and anamorph (asexual, i.e., mycelium that does not produce a fruiting body) phase. The entire fungus comprising the sexual and asexual phases is known as the holomorph. In the past, the asexual and sexual phase of cordyceps could be placed in different genera, resulting in two distinct binomials for one organism. For wild cordyceps, the accepted Latin name for the fungus mainly responsible for producing the fruiting body from the head of the caterpillar is now *Ophiocordyceps sinensis*, while the asexual phase was known as *Hirsutella sinensis.*[13] However, since the latest International Code of Botanical Nomenclature (ICBN, which includes review and revision of nomenclature for taxa in the Kingdom Fungi),[14] a declaration of "one fungus, one name" is now part of taxonomic rules. Thus, *H. sinensis* is no longer officially recognized as a valid name.

As many as 92–118 additional species of fungi have

Cordyceps *Ophiocordyceps sinensis.* Photo ©2024 Steven Foster been isolated from wild cordyceps,[9] and of those, about 10 are commercially produced and sold in the marketplace. These fungal species are often easier to cultivate than *O. sinensis*, which requires special growth conditions such as cooler temperatures. It has been reported that the anamorph of *O. sinensis* (formerly *Hirsutella sinensis*, see 1.6) grows slowly even at its optimum growth temperature (15–20°C).[13] Growth is inhibited when the temperature exceeds 25°C. However, *Samsoniella hepiali* (previously known as *Paecilomyces hepiali*, sold as Cs-4 or CBG-CS2 and often labeled as "cordyceps"), as well as other species isolated from wild cordyceps, grow quickly and are suitable for large-scale production, and today, are one of the primary sources of "cordyceps" included in dietary supplement products.[15] Most, if not all, of these occur on the outside tough layers of the sclerotium (cortex) on the stroma of the fruiting body and the outside of the club-shaped fruiting body. These additional fungal species may provide a similar chemical profile and have similar biological effects as wild cordyceps, but they do not have the long history of use and cultural reverence that has made wild cordyceps an important medicinal ingredient throughout Asia.

1.8 Nomenclature: Many cordyceps dietary supplements sold in the United States and much of the scientific literature internationally lists the scientific name as *Cordyceps sinensis*. While this is the former scientific name for one of the fungal species that can be sold as cordyceps listed in the *American Herbal Products Association's Herbs of Commerce*, 3rd edition,[1] the fungus has been re-classified as *Ophiocordyceps sinensis* (see section 1.3). United States dietary supplement law requires that the Standardized Common Name as established by *Herbs of Commerce* be listed in product labeling and requires accurate declaration of the plant part (in this case, fungal part); therefore, dietary supplements must indicate if the ingredient is made from a particular species that correlates with a Standardized Common Name (SCN) or Other Common Name (OCN) as established by *Herbs of Commerce* and differentiate whether the ingredient is derived from a mycelium product or from the fruiting body. In Canada[16] and the United States,[1] the name "cordyceps" can be used for both the stroma of *O. sinensis* and the cultured mycelia of *S. hepiali*. While cordyceps is also sold in the European Union as a food supplement, no regulation regarding the composition of "*Cordyceps sinensis*" could be retrieved by the authors. There are also no formal rules regarding the proper labeling of mycelium biomass products with the exception that the part of the plant from which an ingredient is derived must be disclosed (i.e., labeled as "mycelium biomass").

In China, "cordyceps" (lower case and not italicized) has been proposed as the term to describe any cordyceps fungus-host complex (i.e., 虫草 in Chinese), while the term "cordyceps fungus" (虫草菌) should be used when referring only to the fungal (fruiting body) part of cordyceps. The common name "Chinese cordyceps" (冬虫夏草 or 中国虫草) specifies the *O. sinensis*-ghost moth caterpillar complex (wild cordyceps) and is the only "*Cordyceps*" species listed in the Chinese pharmacopoeia.[17] Fungi that have been isolated from *O. sinensis*, such as *S. hepiali* or *Clonostachys rosea* (Bionectriaceae, syn. *Gliocladium roseum*, Hypocreaceae) are considered to be Chinese cordyceps-associated fungi as they are only distantly related to *O. sinensis*.[18] There is evidence that fungi related to *O. sinensis* were used traditionally to improve physical stamina and enhance longevity: One example is *O. xuefengensis*, also known as Xuefeng cordyceps, which grows in mountainous regions of Hunan province.[19]

1.9 Plant/fungus part, form, and production method: Traditionally, wild cordyceps (Figure 1) is considered to consist of the fruiting body attached to the head of one of several species of ghost moth caterpillars. During harvest of wild cordyceps, drying and handling, the club-shaped fruiting body can sometimes become separated from the caterpillar, which drastically reduces the economic value of the product. For this reason, collectors and distributors of wild cordyceps might put the two pieces together by gluing or by pushing a stick or wire through the caterpillar and fruiting body, or both. Obtaining *O. sinensis* fruiting body by inoculating larvae of ghost moths is challenging, but apparently has been done successfully, according to Li et al.[20] From 2014 to 2016, over 17 tons of cordyceps from artificial cultivation of *O. sinensis* using the caterpillar *Hepialus xioajinensis* have been obtained.[20] Culturing *O. sinensis* by liquid fermentation, and of *C. militaris* (*bei chong cao* [北虫草] in Chinese, meaning "North cordyceps"),

Figure 1. Wild cordyceps (*Ophiocordyceps sinensis*). Images provided by Eric Brand (Legendary Herbs)

have also been researched widely and implemented in commercial production as alternatives to wild cordyceps. Today, *C. militaris* is the primary species of cultivated cordyceps fruiting body that is in trade.

The common usage of wild cordyceps in China is in tea form or cooked with duck meat or chicken in Chinese cuisine. The pieces of wild cordyceps are often soaked in wine or powdered and mixed with a liquid to drink or a soup. (Yi "Jacky" Chang [Johncan Mushroom] email to S. Gafner, May 9, 2018).

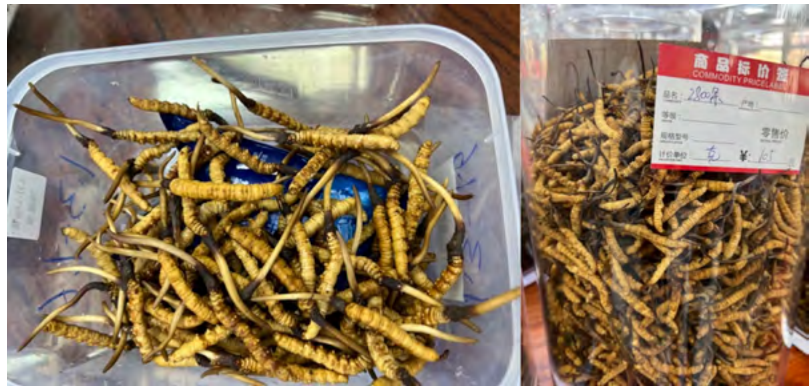


Figure 2. Cultivated cordyceps (*Ophiocordyceps sinensis*), fresh (left), dried and ready for sale (right). Images provided by Eric Brand (Legendary Herbs)

1.10 General use(s): Wild cordyceps is named *yartsa gunbu* in Tibetan. It was first written about by the Tibetan doctor Zurkhar Namnyi Dorje in the 15th century. It also was mentioned as a valuable medicine in many other TCM books.[21,22] According to the *Pharmacopoeia of the People's Republic of China*,[23] cordyceps is "beneficial for lung and kidney, activating blood circulation to dissipate blood stasis and treating virtual cough and haemoptysis," as well as lowering impotence and spermatorrhea, and alleviating pain of the knee and waist. In recent popular advertising, cordyceps promotes sexual potency, energy, and vitality, and has anti-aging benefits. Modern scientific research has produced a number of clinical trials of various quality and four meta-analyses, all involving its beneficial effects on the kidneys with transplant patients and treating chronic and diabetic-related kidney disease.[24-29] These clinical trials demonstrate some effectiveness of cordyceps for drug-induced nephropathy, though researchers concluded that the clinical trials they reviewed, while generally positive, were underpowered, i.e., carried out with inadequate patient numbers.

2 Market

2.1 Importance in trade: The markets for cordyceps in Asia and in other parts of the world are distinctly different. The main market for wild cordyceps is China, where it is used as traditional medicine but also frequently offered as a luxury gift. Wild cordyceps is also popular in other East Asian countries such as Japan and Korea, where it is mostly used as medicine. Additionally, *O. sinensis* fruiting bodies are widely available throughout Chinatowns in North America. Cunningham and Long[30] reviewed the pricing of wild cordyceps from 2002 to 2017, with average costs per kilogram ranging from 20,000 Chinese Yuan (CNY, ca. $2,400) in 2002 to ca. 175,000 CNY (ca. $27,600) in 2012. Price spikes were due to increased exports and speculations by businessmen of increased future demand at the end of 2007 and a lower harvest due to bad weather and increased capital flow into the market in 2012, which led to a general increase in prices for ingredients used in TCM. Price drops were observed at the end of 2008 due to the price spike in the previous year and changes in monetary policy on the national level, and in mid-2015 as the government implemented a new anticorruption policy. Given that wild cordyceps mushrooms often were used as a luxury gift to government officials, the anticorruption regulations led to a marked decrease in gift-giving and, hence, a drop in demand for cordyceps. On the other hand, it led to the emergence in trade of fresh wild cordyceps shipped by air to wealthy Chinese with claims that the nutritional value of the fresh wild cordyceps was three times as high as for the dried mushroom.[31]

The arrival of cultivated *O. sinensis* grown in conjunction with an insect host (Figure 2) is a major new development at Chinese wholesale markets. After years of research challenges, the techniques necessary to cultivate cordyceps by inoculating an insect host have matured to the point that commercial materials have reached wholesale markets. For example, at the Qingping herbal market in Guangzhou, cultivated cordyceps currently is being sold for approximately half the price of the wild material, which typically costs over $25,000 per kilogram.

The new cultivated cordyceps seen in Chinese markets has a very similar appearance to the natural wild product, as it features the corpse of the host caterpillar with a fungal stroma projecting from its head. The successful cultivation of natural cordyceps on an insect host potentially provides an ecological and affordable alternative to wild-crafted material; however, it also poses risks of marketplace confusion and commercial misrepresentation if cultivated cordyceps is presented

Table 1: Sales Data for Dietary Supplements Labeled to Contain Cordyceps in the United States Natural Channel from 2013–2022[35-38]

Year	Sales [USD$][a]	Sales Rank
2013	1,170,633	67
2014	1,178,792	65
2015	1,435,362	51
2016	1,625,559	57
2017	1,933,032	53
2018	2,532,396	n/a
2019	2,740,052	40
2020	3,482,578	28
2021	3,980,576	28
2022	4,256,857	28

[a]SPINS does not track Whole Foods Market sales, which is a major natural products retailer in the United States, as well as products sold through health professionals or certain special retail markets (e.g., Chinatowns)

n/a: not available

Sources: Smith et al.[35-38] T. Smith (American Botanical Council) e-mail communications, September 2, 2015, September 3, 2015, and June 19, 2018; K. Kawa (SPINS) e-mail communication, July 11, 2016

as wild-harvested cordyceps. In their whole form, wild cordyceps may be distinguished from cultivated material based on organoleptic evaluation, primarily of the annular striations and aroma (E. Brand email to S. Gafner, September 25, 2023). However, these differences are very subtle and likely would not be discerned in mixed batches. Research shows that the chemical profiles between cultivated and wild productions can vary greatly.[32-34] Whether this results in any difference in clinical relevance or benefit is not known.

While rarely seen in TCM wholesale markets, several additional cordyceps products are used as health supplements in China. These products are based on fungal species isolated from wild cordyceps that are cultivated and made into powdered extracts. Prominent products in this category include *H. sinensis* and *S. hepiali* (Cs-4), where their mycelium is produced by fermentation at a commercial scale without the production of a fruiting body.[18] According to Liang and Münster,[31] cordyceps made by fermentation or grown on starch media is of lesser importance in the Chinese trade as Chinese customers generally prefer wild medicines and distrust the fermented or starch-grown products.

The cordyceps dietary supplement markets in Europe and North America are dominated by lower-cost products that are made using cultivated *C. militaris* fruiting body or mycelium biomass products grown on starch-based media or produced in fermentation tanks. Many of the fermentation products are not actual *O. sinensis* mycelium, but ingredients derived from cordyceps associated fungi (section 3). Based on available sales data (excluding online sales, which are not generally available), cordyceps dietary supplements are predominately sold retail in the Natural Channel, with sales in the Mainstream Multi-outlet Channel (also known as Mass Market Channel) accounting for less than 5% of dollar sales compared to the Natural Channel in the years between 2014–2017. The retail sales data (Table 1) show a steady increase in consumer interest in cordyceps dietary supplements over the past decade and particularly over the past five years, in line with a general increase in interest in medicinal mushroom dietary supplements in the United States.

2.2 Supply sources: The fruiting body of wild cordyceps (Figure 1) that includes the caterpillar body is collected from the wild in the Tibetan plateau and surrounding Himalayan mountains and in high-altitude regions of the Chinese provinces Gansu, Qinghai, Sichuan, and Yunnan,[29] where it is an important product for the local economy. Collectors are mostly local people (although the harvest also attracts migrants into the growing areas) who deliver their collected products to brokers (often inhabitants of the village or nearby villages). The material moves through the value chain to contractors, national brokers (mostly Tibetan), and finally to international brokers, who supply cordyceps to the world market.[29] The price of the fruiting body depends on the color, firmness, size of the larva, and the ratio of the fungal fruiting body size to the size of the larva. Since the stroma is easily separated from the sclerotium after drying, the intactness of the wild cordyceps is also a major criterium for its value. Reliable data on annual production are lacking, but an estimate from 2009 suggests the yearly cordyceps production in China is between 80–175 metric tons. Production in other countries such as India, Nepal, and Bhutan was estimated at 3,200–7,500 kilograms.[22] The annual harvest is subject to substantial fluctuations, mostly based on climatic conditions (e.g., drought) that affect the availability of the fungus. Costs for authentic wild cordyceps fruiting body in 2015 and 2016 were estimated to be between $20,000–35,000/kg,[39-41] while wholesale prices in 2018 for Cs-4 made from mycelium were between $8–10/kg (J. Chang [Johncan Mushroom] email to S. Gafner, May 9, 2018).

Since the wild harvest of cordyceps is extremely labor intensive, the supply limited, and the fungus expensive and overharvested in some areas,[31,42] successful

Table 2. Major Chinese Products Based on Cordyceps Isolates (modified from Zhang et al)[48]

Fungus	Product	Notes
Hirsutella sinensis (accepted name *Ophiocordyceps sinensis*), Ophiocordycipitaceae	Bailing capsule	Fermentation product made from the mycelium of *Hirsutella sinensis*, the accepted anamorph of *O. sinensis*. Described in the Chinese Pharmacopeia (CP) starting in 2005. *Hirsutella sinensis* is no longer valid because of the "one organism, one species" taxonomic rule. The ingredient in Bailing capsule is therefore *O. sinensis.*
Samsoniella hepiali (syn. *Paecilomyces hepiali*), Cordycipitaceae	Jinshuibao capsule (Cs-4)	Described in the Chinese Pharmacopoeia since 2000.[49] Although *S. hepiali* is sold in the United States. as a "strain of *C. sinensis*," the two species are only distantly related genetically (see section 3.1.1. for more details) but are accepted by the common name "cordyceps" in Canada and the United States.
Mortierella hepiali, Mortierellaceae	Zhiling capsule	In the CP since 2010; approved for production in China in 1985.
Cephalosporium sinensis (considered a synonym of *O. sinensis*)	Ningxinbao capsule	Approved for production in 1987.
Clonostachys rosea, Bionectriaceae, syn. *Gliocladium roseum*, Hypocreaceae	Xinganbao capsule	Approved for production in 1987.
Pleurocordyceps sinensis, syn. *Paecilomyces sinensis*, Ophiocordycipitaceae	Chongcaojun capsule or Chongcao capsule	Production prohibited since 2001. (*S. hepiali* is official).
Scydalium sp. (a species of unknown taxonomy)	Chongcao capsule	
Tolypocladium sinense, Ophiocordycipitaceae	Bo'ao chongcao oral liquid	Formerly considered an anamorph of *O. sinensis*.

cultivation would lessen the impact on native populations. As such, the availability of cultivated *O. sinensis* or *C. militaris* may alleviate some of the pressure on wild populations. Since the ghost moth can be cultivated,[43] it has been suggested that these larvae be introduced to the Tibetan grasslands to increase the possibility of cordyceps production where it naturally occurs. Inoculation with cultivated *O. sinensis* as well as planting additional native plants for the caterpillar to feed upon is also recommended.[44] So far, these methods have been considered too cost prohibitive for commercial production. However, Li et al[45] reported in 2018 on the successful cultivation of *O. sinensis* on the insect host in an artificial environment on a large scale. As stated in section 2.1, cultivated *O. sinensis* has entered the Chinese wholesale market over the past few years.

Biotechnical production of mycelium from cordyceps and cordyceps-associated fungi in fermentation tanks and on starch medium mostly is done in China. *Cordyceps militaris* is another important ingredient produced in China and is the primary source of cultivated cordyceps fruiting body in international trade. Unlike wild cordyceps, fruiting bodies of *C. militaris* have been successfully cultivated on a large scale and are available as dietary supplements in the United States and Europe.[18] A paper published in 2020 estimated Chinese *C. militaris* fruiting body production at 10,100 metric tons/year. Other *C. militaris*-producing countries include Japan, South Korea, and Vietnam.[46] Small-scale production also has been reported from the United States.

3 Adulteration

In international markets, adulteration of cordyceps is one of the major problems in the trade of *O. sinensis*.[47] Labelling products with "*Cordyceps sinensis*" when the actual organism in the product is a different species than *O. sinensis*, and often from a different genus, results in a misbranded product and does not accurately convey to consumers what species they are getting.[15]

As stated in section 2.1, most "cordyceps" dietary supplement products sold on the markets in Europe and North America are made from *C. militaris* or from mycelium obtained via biotechnological methods. Table 2 summarizes the major cordyceps isolates sold widely in China, and since China is a major, perhaps *the* major, supplier of cordyceps raw materials, these species could be used in products sold in the United States.

When consumer products such as capsules and tablets contain authenticated wild-occurring *O. sinensis*, it is difficult to determine whether both the fruiting body and caterpillar were used in their manufacture. Liu et al showed that the contents of adenosine, guanosine, uridine, other nucleosides and polysaccharides, and antioxidant potency are nearly identical in the caterpillar and the fruiting body when the two are analyzed separately from cordyceps.[50] This suggests that the caterpillar is thoroughly digested by the time the fruiting body is formed.

3.1 Known adulterants: Adulteration of *O. sinensis* can be separated into groups: (a) another mushroom or non-mushroom species is sold labeled as *O. sinensis*; (b) *O. sinensis* mycelium or mycelium biomass is labeled as fruiting body; (c) parts of the caterpillar-fungus complex are glued together, or held together by sticks or wires to give the impression of a high-quality material; (d) a considerable amount of substrate is in the finished product, such as brown rice, consequently leaving much less room for fungal biomass; (e) substantial quantities of undeclared excipients or fillers are added; and (f) fake wild cordyceps models made from flour and various pigments have been reported to occur. For the Western markets, the adulteration issues (a), (b), (d), and (e) are the most relevant.

3.1.1 Adulteration with other fungal species*: Ophiocordyceps sinensis* is widely accepted as the correct species for cordyceps, based on extensive research on the chemistry and phylogenetic analysis of the product in the wild and in cultivation. *Cordyceps militaris*, which is being widely used as a substitute for *O. sinensis* in products in the United States, can also be legally sold as cordyceps, and some dietary supplements, but not all, are labeled correctly as *C. militaris*. Based on existing studies on chemistry and pharmacology showing a similarity between both species, *C. militaris* may be the most appropriate species to substitute for *O. sinensis*[51,52] if correctly labeled. Before labeling products as *C. sinensis* or *O. sinensis* (which is the correct binomial), the ingredients should be authenticated by appropriate testing methods, even materials obtained from reputable suppliers. Sometimes, the supplier may not know the identity of each batch of cordyceps raw material.

When considering wild-harvested samples of cordyceps originating from the Tibetan plateau and the surrounding areas and then sold from China and other countries, a number of morphologically-similar species may inadvertently be admixed with *O. sinensis* during harvest. Other potential adulterants of *O. sinensis* from Chinese material added later include *Isaria cicadae* (Cordycipitaceae), *Keithomyces neogunnii* (syn. *Metacordyceps neogunnii*, Clavicipitaceae), *Ophiocordyceps liangshanensis* (syn. *C. liangshanensis*), *O. nutans* (syn. *C. nutans*), and *Tolypocladium guangdongense* (syn. *C. guangdongensis*, Ophiocordycipitaceae).[53]

Because of its rarity, difficulty in insuring the proper species identification, and high price, manufacturers in China and other countries have isolated other species from wild cordyceps and cultured them, producing branded products.[54] A particular case is the fungal ingredient Cs-4, which was originally believed to be a strain of *Cordyceps sinensis* (*O. sinensis*) and is still labeled as such. Subsequently, it was found to be made from a strain of *S. hepiali,*[55,56] a fungus related to *O. sinensis*.[57] Animal (in vivo) and cellular (in vitro) studies performed on *S. hepiali* have demonstrated a variety of biological effects, including anti-inflammatory, anti-stress, antidiabetic, and immunomodulatory benefits that are consistent with TCM uses of cordyceps.[55,58-63] In addition, a number of human clinical trials using Jinshuibao capsules or other products containing *S. hepiali* have been conducted and report improved exercise performance and immunomodulatory effects.[64-69] As previously noted, in Canada and the United States, "cordyceps" is a legally accepted name for *S. hepiali* for Natural Health Product and dietary supplement labeling, respectively. However, there would be greater transparency in specifications and labeling if it were accurately labeled as *S. hepiali*.

Wen et al performed a multi-gene phylogenetic analysis of specimens obtained from herb markets in China and Tibet that included ITS, nrSSU (18S rRNA), *EF-1*α, and RPB1 gene regions.[70] The researchers obtained sequence data from 36 species, among them common adulterants of *O. sinensis*. Samples from China were most closely related to *Metarhizium guizhouense* (syn. *Metarhizium taii*, *Metacordyceps taii*, Clavicipitaceae) a species collected for medicinal purposes in southwestern provinces of China,[19] and those from the Tibetan market were most closely related to *O. sinensis*. Zhang and Wei found that ITS had enough interspecific variation to be useful as a barcode for separating *O. sinensis* from common adulterants.[71]

Luo et al found that *K. neogunnii* and *C. hawkesii* have very similar appearance to each other and to *O. sinensis*.[72] They also determined through the use of ITS sequence data that the two species were very closely related, making separation with this marker difficult.

Cordyceps gunnii is said to be a common adulterant of *O. sinensis*.[73] Osathanunkul et al[74] were able to quickly identify and differentiate *O. sinensis* and *C. militaris* with the use of Bar-HRM (high resolution melting), which involves multiplex amplification of the ITS nuclear DNA region coupled with HRM analysis and did not require obtaining sequence data. They were able to confirm the adulteration of a high-priced *O. sinensis* product with *C. militaris*. A 2020 investigation assessed the authenticity of 16 commercial samples labeled as "Chinese cordyceps" or "*dong chong xia cao*" by duplex PCR using the ITS region for fungal species distinction and the COI region to determine the presence of caterpillar DNA. Samples consisted of dried mushroom (n = 11) or finished healthcare products (n = 5) and were purchased online or from a local TCM market in Chengdu, China. Cordyceps and caterpillar DNA were detected in nine dried mushroom samples. The other two dried mushroom samples and two finished products had only cordyceps DNA. No DNA was found in the remaining three products, suggesting that these were made using a different fungus or that the DNA was degraded and could not be amplified.[75]

Based on a variety of scientific research, and for economic reasons, many commercial products that are advertised as "wild cordyceps" or even "*Cordyceps sinensis*" in capsule and tablet form should be viewed as suspect. Raja et al found *Tolypocladium inflatum* (Ophiocordycipitaceae) in two and *Sanghuangporus sanghuang* (syn. *Inonotus sanghuang*, Hymenochaetaceae) in one out of six commercial products labeled to contain *C. sinensis*.[76]

Hobbs also investigated seven products from China and India, five products of unknown origin advertised and available on eBay or Amazon, and seven from domestic sources labeled as "*Cordyceps sinensis*" (n

Cordyceps *Ophiocordyceps sinensis*. Photo ©2024 Steven Foster

= 17) or "*Cordyceps militaris*" (n = 2). While all products labelled and sold as *C. militaris* were authentic, none of the other samples labelled as *C. sinensis* (*O. sinensis*) could be confirmed as authentic based on sequences obtained from two independent labs using ITS 1 and ITS 2 as barcodes, Sanger's method of sequencing, and standard phylogenetic methods (C. Hobbs, unpublished results). With respect to the Chinese products, including cultivated pure mycelium powders, cultures on agar were either contaminated with *Aspergillus* (Aspergillaceae), where sequences could be recovered for two species; two appeared to contain an earthstar *Geastrum* (Geastraceae) species; and sequences could not be obtained from two of the top-selling products, even using short internal primers designed to detect *O. sinensis* SCAR markers based on ITS.[77] Thus, *O. sinensis* ITS sequences could not be obtained from any of these products labeled as containing "cordyceps".

3.1.2 The sale of mycelium-derived materials as cordyceps fruiting body: As with the labeling of the plant part in herbal ingredients, the fungal part is an important and necessary descriptor to characterize a fungal material and needs to be indicated on the product label. Due to much lower costs and the ease of production, *O. sinensis* mycelium preparations are sometimes represented as an economical alternative to the *O. sinensis* fruiting body obtained from the wild.[78] Unfortunately, ingredients derived from mycelium (e.g., mycelium biomass products) have been shown to sometimes be composed mainly of starch and/or maltodextrin (see section 3.1.4).[79] Finally, products made from mycelium that claim to contain the fruiting body are obviously adulterated.[80] Analytical methods to differentiate mycelium from fruiting body have been published by several authors.[33,81-84]

3.1.3 Adulteration by adding pieces of stick or wire, or soaking in concentrated mineral solutions: Besides intentional and unintentional substitution and adulteration with species other than *O. sinensis*, the practice of adding sticks or pieces of wire into cordyceps caterpillar and fruiting bodies has been reported.[85] However, this report could not be confirmed from any other independent published papers and the alleged practice is obscure even in the Chinese literature. If this method of adulteration is suspected, i.e., a given lot weighs significantly more than it should, based on unadulterated lots of the same size, closer scrutiny of the cordyceps batch is warranted. For small amounts, individual samples can be checked with gloved hands, and a handheld magnifier, for odd weights of individuals. Suspected lots can be checked by snapping (breaking) individual caterpillar and fruiting body units to check for wires, etc. For larger lots, x-ray screening can be used. Wu et al reported two case histories of consumers of cordyceps products exhibiting severe signs of lead poisoning.[86] Subsequent testing found abnormally high levels of lead in the cordyceps samples they were taking as well as high lead blood serum levels in the patients. The authors state that "lead bars" have been observed to have been inserted into cordyceps to increase weight. Adulteration of this sort with a toxic heavy metal, besides being fraudulent, is also potentially dangerous, especially when cordyceps products are taken for an extended time. There are also reports that cordyceps fruiting body is sometimes soaked in mineral solutions, such as concentrated lead or aluminum sulfate, to increase weight.[87,88]

3.1.4 Adulteration with plant species glued to caterpillars or molded objects: Adulteration using plant materials, e.g., pieces of *Stachys* (Lamiaceae) or *Hemerocallis* (Asphodelaceae) species, have been reported by multiple authors.[78,89] In these cases, the plant materials are added to or glued to a caterpillar or to a caterpillar-like object modeled using flour and yellow/orange dyes. In the cordyceps market of Hong Kong, this is reported as the most common form of adulteration.[90]

3.1.5 Adulteration with excessive undigested or partially digested substrate: Some studies have analyzed β-glucans and starch/glycogen in commercial cordyceps products containing fungal extracts promoted for their health benefits. Holliday et al[91] published a table comparing the percentage of residual material using various substrates to grow cordyceps mycelium. The percentage of residual grain was 15% for millet, 20-30% for oats, 50-80% for wheat, and 60-80% for brown rice. The lowest yield (1-10%) of cordyceps was found using soybeans as substrate. This is similar to data published by Au et al.,[78] who reported that many of the commercial samples analyzed contained more than 80% soybean. Another study[79] investigating the glucan contents of 19 fruiting bodies from various fungal species as well as 12 commercial fungal supplements purchased online showed that some of the products contained up to 83% α-glucans, the majority of which is likely to be either starch or glycogen. Of the four cordyceps products that were tested during the study, capsules labeled to contain cordyceps mycelium had 13.9 g and 65.5 g/100 g total glucans. The content of α-glucans (relative to the total glucan content) in three of the four products labeled to contain cordyceps mycelium was over 82%, while it was 21.6% in the fourth. Except for three *Agaricus* (Agaricaceae) samples, the relative content of α-glucans was below 10% in the fruiting bodies. One sample with pure mycelium (grown by deep-layer method) had only 3% α-glucans, showing that mycelium (without substrate in the sample) has very little starch or glycogen. However, no formal determinations have been made as to what ratio of mycelium to substrate represents an appropriate quality product. According to Julie Daoust (email to S. Gafner, April 4, 2024), substrate to mycelium ratio is not something that is typically declared since it is hard to measure. The amount of undigested substrate impacts efficacy and dosing. Undigested substrate dilutes the effect of the fungal product, but exactly by how much depends on the product. A suitable approach would be if mycelium producers could create a consensus standard of optimal mycelium yields based on best production practices. No such consensus yet exists.

3.1.6 Adulteration with binders, fillers, and carriers used for cultivation of the mycelium: Au et al investigated fruiting bodies of *O. sinensis* (n = 19), *C. hawkesii* (n = 11), *O. liangshanensis* (n = 1), and *C. militaris* (n = 2), obtained from local markets in China, along with five samples claiming to be wild cordyceps using macroscopic criteria and polarized light microscopy.[78] Some adulterants may clearly be differentiated macroscopically; however, based on the data presented by these researchers, the differentiation between *Ophiocordyceps* and *Cordyceps* may not be achieved with a high level of confidence. Additionally, eight bulk samples labeled as fermented cordyceps mycelium and seven samples of cordyceps dietary supplements in capsule form were analyzed. Among the five samples of wild cordyceps from local markets was a product made using a caterpillar and a *Hemerocallis* species, another from *Cordyceps* species and an unidentified plant, and two made with flour pressed into the form of a caterpillar and a *Hemerocallis* species. The authors were able to identify soy powder in nine of the 15 bulk and capsule products. The researchers emphasize that only a small amount of material is necessary for microscopic evaluations, and that microscopy is a useful method for differentiation of fruiting bodies of *Cordyceps* and *Ophiocordyceps* species in whole or powdered form. Cordyceps mycelium obtained by fermentation was characterized by translucent or transparent clumps or granules. Mycelium grown on a grain medium was identified by the presence of starch granules or features characteristic of plants such as trichomes, palisade cells, calcium oxalate prisms, or fragments of the seed coat (testa).

3.2 Sources of information confirming adulteration: Numerous articles focus on authenticating cordyceps, and either documented or likely adulterants can be found in the extensive published literature.[74-76,78,86,91-95] A majority of the reported data is from ingredients sourced in Asia, including samples from China,[75,78,86,92,93] Hong Kong,[78] Taiwan,[95] Thailand,[74] and Vietnam.[94] Two papers provide some insight into the quality of cordyceps supplements in the United States.[76,91] In 2004, Holliday et al[91] proposed a quality index for cordyceps based on the sum of N6-(2-hydroxyethyl)adenosine, adenosine, and cordycepin, a nucleoside analogue, though cordycepin is often not present in *O. sinensis* or only occurs in trace amounts. The sum of these three constituents was between 0–0.071% in mycelium-based products compared 0.071–0.100% in wild cordyceps. The authors reported that nearly all products sold on the American market "contained no detectable amount of cordyceps", but that some of these were composed entirely of rice flour or powdered nutmeg (*Myristica fragrans*, Myristicaceae).[91] A 2017 paper analyzed six commercial products labeled to contain "Cordyceps sinensis". Two of these were made from *T. inflatum*, one from *Sanghuangporus sanghuang*, and the remaining three samples were devoid of DNA of sufficient quality to allow identification.[76] *Tolypocladium inflatum* has also been identified using DNA analysis (Sanger sequencing, using the Internal Transcribed Spacer [ITS] 1 and ITS 2 gene regions as barcodes) by one of the authors from commercially available raw materials in the United States, labeled and sold as *C. sinensis* (C. Hobbs, unpublished results).

3.3 Accidental or intentional adulteration: Accidental or intentional adulteration can result from the collection of cordyceps in the wild. Of the many species that grow throughout the Tibetan highlands on *Hepialus armoricanus* or other species of *Hepialus* caterpillars, several look very similar to *O. sinensis*.[96] Wang and Yao described 32 species of *Cordyceps* growing in alpine areas in China and nearby nations.[97] The same authors also found 57 species of other insects, including moths, that are actual or potential hosts for *O. sinensis*.[97] This indicates potential inadvertent collection of other species of infected caterpillars, in both the host and parasite.

Because of its rarity and high value, wild cordyceps is likely to be intentionally adulterated with other species as well as fillers like flours, starches, and maltodextrin. Unintentional adulteration of finished products occurs because manufacturers may accept the certificate of analysis (CoA) from suppliers without appropriate verification.

3.4 Frequency of occurrence: For cordyceps products in powder, liquids, capsules, or tablets, the expectation is that adulteration is common and widespread, for reasons detailed above. An outlier to the publicly available data is an investigation of 100 commercial samples of wild cordyceps obtained from markets in Hong Kong. All of these samples had the genetic marker for *O. sinensis*.[98]

3.5 Possible safety/therapeutic issues: Safety is not an issue in the commercial market where substitution of species associated or isolated from wild cordyceps is concerned, although not all *Ophiocordyceps* species are safe to eat, as evidenced by a series of case reports documenting poisoning in 60 Vietnamese patients due to ingestion of *Paraisaria heteropoda* (syn. *Ophiocordyceps heteropoda,* Ophiocordycipitaceae).[99] Fortunately, the most common forms of cordyceps traded other than *O. sinensis* (e.g., *C. militaris,* and others), share similar safety, chemical, and pharmacological profiles.

In cases of cordyceps, the most important consequence of substitution is the economic loss for the buyer. Authentic wild *O. sinensis* commands a very high price.

A primary safety risk is due to adulteration with wires, lead bars, or mineral salts to increase weight (section 3.1.3). The two case reports of poisoning in humans due to lead-contaminated cordyceps do not reveal if the elevated lead content is due to environmental contamination or adulteration. However, the high lead content (20 mg/g) determined in a sample of cordyceps powder used by one of the patients may point to an intentionally adulterated product.

4. Analytical Methods to Detect Adulteration

Several analytical methods have been proposed to authenticate *O. sinensis* fruiting body and mycelium, including macroscopic, microscopic, genetic, and marker constituent-based approaches.

4.1 Macroscopic and microscopic analysis: Morphological analysis is an appropriate low-cost testing method when the morphologically characteristic parts of the fruiting body are present but has the disadvantage that the closely related species listed above can be difficult to differentiate visually. Macroscopic and microscopic characteristics of *C. hawkesii*, *C. militaris*, *O. liangshanensis*, and *O. sinensis* have been reported by Au et al[78] and Liu et al,[87] while Kang et al[100] provide features of caterpillars infected by *C. gunnii*, *O. liangshanensis*, *O. sinensis*, and *Paraisaria gracilis* (syn. *C. gracilis*, Ophiocordycipitaceae). Microscopic differentiation of closely related species is nevertheless challenging, limiting this as a definitive identification tool. The investigation of Liu et al[87] reported that the primary morphological and microscopic features of the six species (*C. gunnii*, *C. militaris*, *O. barnesii*, *O. liangshanensis*, *O. sinensis,* and *P. gracilis*) examined were similar but that differentiating diagnostic differences exist, allowing distinction among the species. However, information about the number of specimens upon which these determinations were based and whether they fully encompassed the spectrum of variable characteristics inherent in each species was not provided in the paper. Au et al[78] collected 38 *O. sinensis* samples along with suspected adulterating species from mainland China and Hong Kong markets in the form of crude material, capsules, and fermented products. The gross exterior features of each sample were examined and described organoleptically (observation, measurement, touching, smelling, and tasting) and included multiple *Cordyceps* species as well as *Hemerocallis* species. The investigators provide detailed descriptive and illustrative descriptions outlining their findings that can help in the proper identification of select materials used as cordyceps.

Macroscopic and microscopic assessment is especially useful to detect undeclared starch or fragments from grains used to produce cordyceps mycelium biomass as well as other plant species and adulterating or contaminating substances such as lead or maltodextrin. Macroscopic and microscopic analyses can both be used to readily differentiate between fruiting body and mycelium biomass ingredients before and, in the case of microscopy, after comminution.

4.2 Genetic testing: For identification of fungal species, the preferred method is often aligning and comparing DNA sequences from the organism under tests with known sequences where the species identification has been confirmed by independent laboratories using DNA barcoding, preferably coupled with phylogenetic analysis.[76] Since several fungal species may be present on the surface of a fruiting body, care has to be taken to use a representative sample or to use DNA metabarcoding assays that can detect multiple fungi and determine the relative contents of the species. One disadvantage is that DNA analysis cannot determine whether fruiting body or mycelium is in the sample, thus requiring coupling with morphology, microscopy, or chemical analyses. Additionally, mycelium biomass-based ingredients may predominantly consist of grain used to grow the mycelium and, hence, the grain DNA may be preferentially amplified depending on the primers used. Finally, there are some known challenges when extracts from fruiting bodies or mycelium are used, particularly the lack of DNA of sufficient quality to enable amplification and sequencing.[101]

DNA barcoding using the ITS region is used most often, and the ITS region is widely accepted as the standard barcode for *Ophiocordyceps, Cordyceps*, and fungi as a group.[76,102-108] Over 1000 accessions of *O. sinensis* are available on GenBank, along with a number of other closely related species. Separation is reliable between *C. militaris* and *O. sinensis* since these have sufficient genetic distance. Other species more closely related to *O. sinensis* can be separated with high probability of identity as long as at least several ITS sequences for each of the possible other species are available on GenBank, preferably from different labs for independence of the data. Checking several sequences from GenBank for the same species and marker, then looking for variation, is crucial for proper specificity. However, ITS does not work in all groups of fungi, and ITS data have been criticized because of intraspecific variability, lack of consistency for different ITS molecules in the same sample, lack of coverage (certain DNA regions are not available for some taxa of interest), and because the quality of sequence data available on GenBank is inadequate in some cases. Since the ITS region may not work in every case, other barcode regions have been proposed, such as protein-coding DNA markers like TEF1α, a region that will act as a universal barcode.[108-110]

4.3 Identification based on chemical marker compounds or chemical fingerprints: In addition to DNA analysis, chemical testing is essential for determining the relative quality of any cordyceps sample. Studies have shown that nucleosides, notably adenosine and related derivatives, are important bioactive constituents in cordyceps, as typified by cordycepin,[111-114] and these are the most widely used chemical markers for identification. However, *O. sinensis* has been shown in some studies to be devoid of cordycepin,[115,116] but it is found in abundance in *C. militaris*[117,118] and even *T. inflatum*.[119] High-performance liquid chromatography (HPLC) or high-performance thin-layer chromatography (HPTLC),[120-123] nuclear magnetic resonance (NMR),[124] and capillary electrophoresis[125-127] methodologies can show quantitatively or semi-quantitatively the level of cordycepin and other marker compounds for standardization.[113,128] Adenosine is widely used in China as a quality marker, and quantification methods are available in the Chinese Pharmacopoeia.[49] The amino acid ornithine may be a suitable marker to distinguish

Cordyceps *Ophiocordyceps sinensis.* Photo ©2024 Steven Foster between wild cordyceps and products made from cordyceps mycelium based on two metabolomic studies.[83,84] D-Mannitol (cordycepic acid) is often cited as a specific marker for cordyceps identification, but D-mannitol is not a specific marker for *O. sinensis* as it is a common fungal constituent found in species of *Agaricus*, for instance.[129,130] Complex polysaccharides specific to the genus *Cordyceps* have been mentioned as important active compounds, but they are difficult to characterize and quantify.[131] Several publications have used metabolomic approaches to distinguish wild cordyceps from mycelium-based ingredients and *C. militaris*.[33,81-84] In summary, the nucleoside content and pattern in commercial samples appears to be relevant for quality confirmation of important active compounds as well as species identification, although with caution,[123] but measurements of single marker constituents are not sufficient to unequivocally identify *O. sinensis* or other commercially available cordyceps species. Metabolomic approaches likely represent the most robust approach to distinguish among *O. sinensis* and cordyceps-associated products using fungal metabolites. A combination of analytical methods including physical, chemical, and genetic likely will produce the best results.

5. Conclusions

Cordyceps is a cultural treasure from the mountain regions in Bhutan, India, Nepal, and the Tibetan Autonomous Region, as well as other regions of China. It is more valuable by weight than gold because of its rarity and dwindling supplies in the wild. The species most responsible for historically important cordyceps from the Himalayan region is *O. sinensis*. However, other closely related species were also used in traditional medicine in China and surrounding countries.

Approximately 10 fungal species have been cultured from wild cordyceps. Many of them are offered in commercial products throughout Asia, and some are also in products sold in the United States and other countries. While some of these ingredients (e.g., Cs-4 derived from *S. hepiali*, *H. sinensis*, or *C. militaris* fruiting body) have been studied in several clinical trials, the value to health of some of the other marketed products is less certain.

Some of these other species have been subjects of published studies that include careful identification by physical, chemical, and DNA analysis, and evidence of their pharmacological activity in support of their health benefits exists. Proper identification of raw materials is essential since adulteration is common due to the high cost of cordyceps. Chemical assays using cordycepin, adenosine and other nucleosides, and polysaccharides, or genetic testing (utilizing primarily the ITS) are the most widely used methods for identification and quality determination, though cordycepin is often lacking in *O. sinensis* and occurs in higher concentrations in species such as *C. militaris*. Therefore, methods based on marker constituent analysis are less than definitive due to the variability in their presence and concentrations in *O. sinensis* and some of the species permitted for interchangeable use.

In addition to adulteration with unacceptable species, the intentional adulteration of cordyceps fruiting body formed from flour, sometimes with intact caterpillar fruiting body attached, is quite common in Hong Kong.

The most relevant quality labeling issue in United States and international markets is the distinction between fruiting body and mycelium biomass products. Determination of the fungal part (fruiting body versus mycelium) can be achieved through morphological, chemical, and genetic testing when material is in its crude form in which appropriate morphological identification characteristics and intact and/or DNA is present. When cordyceps is traded in its whole form, the undeclared addition of metals or twigs or the substitution with other fungi can be easily detected. For powdered cordyceps, diluents like starch or maltodextrin can be observed under the microscope. However, once extracted, standard physical, chemical, and genetic texts may not detect these impurities. For extracts, chemical testing can differentiate between fruiting body and mycelium preparations and give an indication of relative quality, though identification to species may not be accomplished as various fungal species contain the same marker constituents. Additionally, the composition of marker constituents in cultivated cordyceps is impacted by genetics (variation between strains in a breeding program). Morphological and genetic methods are not fit for purpose without intact morphological features or intact DNA, respectively. Further, genetic testing alone does not provide an indication of quality. Thus, the combination of various testing methodologies provides the highest assurance of species identification, purity, and quality.

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Revision summary

Version # , Author,	Date Revised	Section Revised	List of Changes
Version 1, C. Hobbs, R. Upton, S. Gafner	N/A	N/A	None