CORDYCEPS

Cordyceps militaris (L.) Fr.

Family

Cordycipitaceae, a family of parasitic fungi.[1]

Parts Used

Fruiting body (stroma).

Description

Cordyceps is a genus of parasitic fungi that grows on the larvae of insects. When these fungi attack their host, they replace its tissue and sprout long, slender stems that grow outside the host's body. They eventually kill the host which then mummifies. The remains of the insect and the fungi have been hand-collected, dried and used as a combination in traditional Chinese medicine (TCM) for centuries to treat fatigue, sickness, kidney disease and low libido. However, the natural fungus has been harvested to the extent that it is an endangered species. Of the more than 400 species of Cordyceps discovered, two have become the focus of health research: *Ophiocordyceps sinensis* (formerly referred to by its synonym *Cordyceps sinensis*) and *Cordyceps militaris*. Most scientific research has been conducted on *O. sinensis*, which is the only one included in the Chinese Pharmacopoeia (2015). Considering several complications regarding *O. sinensis* (see below), the species *C. militaris* has attracted more attention from scientists and the industry over recent years.[2]

O. sinensis is native to the Tibetan Plateau. *C. militaris* is native to Asia, North America and Europe. The long-term process of symbiosis between the *O. sinensis* fungus and the larvae of the ghost moth (Lepidoptera: Hepialidae) (from autumn

to spring) is time-consuming, and the harvesting process of *O. sinensis* from its natural site makes it expensive. The growing demand for this species, and its high prices due to limited natural resources, have led to the search for alternative sources. The solution to this issue is a related species, namely *C. militaris*. A survey conducted during 2007 showed that the yield of natural *O. sinensis* had decreased by more than 90% in the previous 25 years. Since 1999, *O. sinensis* has been listed as an endangered species under the second class of state protection in China. Various actions have been taken to protect this species. *C. militaris* does not present the same sustainability issues. This fungus is also cultivated on a large scale and presents a more sustainable option than *O. sinensis*.[3,4,5]

C. militaris naturally has slow growth in butterfly and moth larvae and is difficult to find in the wild due to its rarity. Thus, many investigators have been focusing on the artificial cultivation of *C. militaris* using cutting-edge technology. Hence, artificial cultures have become a more favourable solution for the biotechnological production of *C. militaris*. This species was found to have a similar composition to *O. sinensis* and subsequent studies have demonstrated that *C. militaris* has higher bioactivity in comparison with *O. sinensis*. *C. militaris* is easier to culture and mass produce than *O. sinensis* so has become a good alternative in terms of being time and cost effective.[6]

Traditional and Empirical Use

Cordyceps is known as a functional mushroom for energy and endurance. These fungi have a long tradition of use in Asian herbal medicine because of their adaptogenic and tonic effects and their ability to reduce fatigue and stimulate the immune system in humans. Cordyceps is derived from two Latin words *cord* and *ceps* representing 'club' and 'head' respectively, describing its appearance as club fungi. The species name *militaris* means "upright, resembling part of a uniform". A vast amount of literature exists about cordyceps mushrooms, some of which is scientific, and some popular myth and even hype. Also known as caterpillar fungus, the fact that cordyceps grown in the wild consumes insects' bodies from the inside out inspired the hit HBO series "The Last of Us", and the video game from which it is adapted, in which a zombie apocalypse is caused by a fungus pandemic. However, humans are not the natural host for cordyceps. Therefore, it is not well adapted to infect or colonise human hosts.[7,8]

Used in TCM for thousands of years, cordyceps has always been expensive and was such a sought-after and valued commodity that it was strictly reserved for use by the emperor and his family. The inhabitants of China, Tibet, Nepal and India have consumed Cordyceps spp. for centuries in order to adapt their bodies to difficult high mountain conditions such as low ambient temperature, high atmospheric pressure and reduced oxygen content in the environment. In TCM, cordyceps is understood to tonify both yin and yang. Due to this balance it can be taken safely over long periods and is commonly used as a tonic herb. In the energetic understating of TCM the action is related to the kidney and lung channels. The kidneys being the organ that manages elimination and blood quality, cordyceps has been prescribed in TCM to counteract various types of anaemia, also increasing blood production and quality. TCM recommends the use of Cordyceps spp. for treating several human disorders such as cardiovascular and respiratory diseases, disorders of the liver and kidney, cancers, diabetes, infectious and parasitic diseases and sexual dysfunctions.[9,10,11]

Constituents

Polysaccharides (e.g. beta-glucans), adenosine, cordycepin, cordycepic acid, ergosterol, fatty acids, phenolic compounds

Actions

Immunomodulator, adaptogen, anti-inflammatory, antioxidant, antihyperglycaemic, antitumour, neuroprotective, antiaging, antimicrobial, hypolipidemic, tonic[12,13]

Pharmacological Activity

Much of the research on cordyceps is limited to animal or lab studies, so conclusions about its effects on humans is based on traditional use.[14]

Anti-inflammatory Activity

Research suggests cordyceps decreases inflammatory markers in animals. Taking cordyceps seems to reduce levels of inflammatory factors

such as C-reactive protein and interleukin (IL)-6, IL-18, and tumor necrosis factor-alpha. However, their effects on inflammation in humans remain unknown.[15]

Antitumour Effects

Test-tube and animal studies suggest cordyceps may have the potential to treat cancer, as well as some side effects of cancer treatments. However, these effects have not been shown in humans and more research is needed.[16]

Antiaging Activity

Research in mice suggests cordyceps has antiaging properties. While these findings are promising it is unknown whether they apply to humans. The elderly have traditionally used cordyceps to reduce fatigue and boost strength and libido. Researchers believe their antioxidant content may explain their antiaging potential.[17]

Immunomodulating Activity

Some evidence shows that cordyceps may both strengthen the immune system and suppress it due to its adaptogenic nature, which may prove useful in circumstances such as following an organ transplant or in individuals with autoimmune conditions. However, human studies are limited, and more in-depth research is necessary to substantiate these findings.[18]

A recent review catalogued the immunomodulatory effects of different extracts of cordyceps, namely total extracts, polysaccharides and cordycepin. The researchers found that different cordyceps extracts have different immunomodulatory functions. They said total extracts using water or 50% ethanol and polysaccharides from cordyceps could be used to treat tumours, allergies and viral infections because these ingredients tend to drive the immune response toward type 1 immunity. Total extracts using 70 to 80% ethanol and cordycepin could be used as immunosuppressive agents for delayed-type hypersensitivity and tend to drive the immune response toward type 2 immunity. They said detail mechanisms of total extract by different solution should be further investigated. [19]

An ethanol extract of cordyceps was shown to enhance cell-mediated immunity in healthy Korean men. A total of 1.5g per day was taken orally by 39 healthy volunteers in the experimental group. The researchers found that the interleukin-2 and the interferon-γ were significantly increased after the four weeks treatment compared with the 40 people in the placebo group. In addition, they observed that cordyceps could increase natural killer cell activity and T cell proliferation. They posited that the extract could serve as a safe immunomodulator to increase cell-mediated immunity in healthy male adults. [20]

Antifatigue Activity

The use of cordyceps was relatively unknown in the West until it was credited for the success of female Chinese track and field athletes at the National Games in Beijing in September 1993. Wang Junxia ran 10,000 metres 42 seconds faster than any woman before and also broke the women's world record in the 3,000 metres by two seconds. Her teammate, Qu Yunxia, set a new women's world record in the 1,500 metres. At all three distances, additional Chinese women finished under the previous world records. The incredible rapid ascendency of the Chinese women's track program led to speculation that illicit drug use was responsible for their success, especially after reports that former East German sports scientists were hired to help train Chinese athletes. Their coach attributed the athlete's success to intensive training as well as a stress-relieving tonic prepared from powdered seahorse and *C. sinensis*. Though the performance of these athletes was surrounded with scepticism (and alleged doping which has never been formalised but was written in a letter by the athletes after they retired), interest in the potential ergogenic effects of cordyceps has remained. However, only a few human studies concerning supplementation with a mushroom mixture (containing, among others, *C. militaris*) have shown an improvement in tolerance to high-intensity exercises.[21,22]

A recent double-blind, placebo-controlled study conducted with sedentary adults revealed that those receiving cordyceps supplements for 21 days experienced faster heart rate recovery and were less fatigued than the placebo group. Thirty healthy middle aged sedentary people were instructed to consume two sachets of either cordyceps (1.1g per day) or placebo powder mixed with 250mL of lukewarm water every day for three weeks. The researchers concluded that the ingestion of

cordyceps significantly improved the health-related components in middle-aged sedentary individuals.[23]

Antidiabetic Activity

Research in animals suggests cordyceps may have potential as a diabetes treatment. Some evidence suggests that cordyceps may also protect against kidney disease, a common complication of diabetes. In a review of 22 studies including 1,746 people with chronic kidney disease, those who took cordyceps (more than one species was included) experienced improved kidney function. However, the results were not conclusive and the authors of the review stated that many of the studies were low quality. Therefore, no conclusions could be made about the effects of cordyceps on kidney function in humans with chronic kidney disease.[24]

Lung Activity

While further studies are needed, cordyceps appears to be a safe immunological adjuvant for the treatment of patients with mild-to-moderate COVID-19 according to an August 2023 randomised, double-blind, placebo-controlled study. Sixty-five patients were recruited for the study, with 33 in the cordyceps group and 32 in the placebo group. Cordyceps capsules, administered at a dose of 500mg three times a day along with supportive treatment, showed effectiveness in patients with mild to moderate COVID-19 infection, as evidenced by the proportionately higher number of recoveries on day 5, the relatively shorter time for improvement of clinical symptoms, and the proportionately higher number of patients showing negative RT-PCR tests on day 10.[25]

Miscellaneous Activity

In a 2022 non-randomised controlled pilot trial, consumption of cordyceps (two capsules, twice daily, after meals for 90 days) by patients with benign prostatic hyperplasia contributed to improving the urinary flow, decreasing the size of the prostatic gland and alleviating micturition symptoms as well as having positive effect on

sexual functions.[26]

Indications

- Fatigue, support energy levels, convalescence after infection or illness, stress, improved vitality, general daily health prophylaxis regime, including healthy aging
- Lung support, asthma, upper respiratory infections, coughs
- Kidney support, diabetes
- Cardiovascular health, high blood pressure, hyperlipidaemia
- Inflammation, arthritis

Energetics

Sweet, warm

Use in Pregnancy

There is insufficient reliable information available on the use of the hydroethanolic extract of cordyceps in pregnancy. Avoid using.[27]

Contraindications and Cautions

Theoretically cordyceps might alter the management of autoimmune diseases by either stimulating or suppressing immune function. Advise patients with autoimmune diseases such as multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis or others to avoid or use cordyceps with caution. Theoretically, cordyceps might increase the risk of bleeding if used perioperatively. Advise patients to discontinue cordyceps at least two weeks before elective surgical procedure.[28]

Drug Interactions

These interactions come with the caveat that some of these warnings are based on research using *O. sinensis*.

Avoid combining with cyclosporin (an immunosuppressant medication) unless under strict medical supervision as there are theoretical decreased drug effects. This is because a small clinical study reported that cordyceps reduced the immunosuppressive effects of cyclosporin in patients who had undergone renal transplantation.

Other studies have reported that cordyceps may help improve cyclosporin induced nephrotoxicity.

Concomitant use with other immunosuppressant drugs may potentially be beneficial under strict medical supervision. There are theoretical decreased drug effects due to cordyceps stimulating the immune system however there are possible improved outcomes. This is based on preliminary evidence that suggests in renal transplant patients adjunctive use of cordyceps with immunosuppressive therapy may result in reduced hepatotoxicity and nephrotoxicity, reduced number of infections and reduced drug requirements.

Caution with combining cordyceps and anticoagulant/antiplatelet drugs due to a theoretical increased risk of bleeding. Animal research suggests cordyceps may have antiplatelet effects but this has not been reported in humans.

Monitor with testosterone as there are theoretical additive effects, although the clinical significance is unclear.

Concomitant use with chemotherapy may be beneficial. There are theoretical improved outcomes with chemotherapy however caution is advised with the use of this combination until more data is available. Preliminary evidence suggests cordyceps may improve quality of life and cellular immunity in patients undergoing cancer chemotherapy. [29]

Administration and Dosage

Liquid Extract:	1:5
Alcohol:	30%
Weekly Dosage:	20 to 100mL[30]

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