Commonly called Cordyceps, *Ophiocordyceps sinensis* (formerly Cordyceps sinensis) is a parasitic fungus that colonizes the internal organs of Lepidoptera larvae, especially the moths *Hepialus armoricanus* and *Thitarodes* spp. The invading fungus consumes the moth larva (i.e., caterpillar) and eventually forms a protective sclerotium from which the fungal fruiting body emerges. In the Tibetan language the fungus is called Yartsa gunbu, which means “summer grass–winter worm” and describes well this strange life form. Early in the summer, a structure that appears to be a blade of grass extends out of the head of what was a caterpillar in the previous winter. However, the “grass” is actually the fruiting body of *O. sinensis* that is ready to release its spores. This unusual fungus occurs naturally at 3000 m and above throughout Tibet, Nepal, and China. Although *O. sinensis* may be the most well-known species, there are many other species with similar life histories in the closely related genus Cordyceps. There are more than 680 described species of Cordyceps distributed among six continents within which the fungal taxa occupy a range of climatic zones, habitats, and host species. Those presently cultivated for medicinal purposes and used as a health supplement include *O. sinensis*, *O. militaris*, *O. sobolifera*, *O. subsessilus*, *O. ophioglossoides*, and others. It is well established that *O. sinensis* has been used for hundreds of years in Traditional Chinese Medicine (TCM) for its power to strengthen the body, boost the immune system, and increase virility. Treatment with *O. sinensis* may also be prescribed for various ailments of the kidney and heart. It is also used for treatment of hepatitis B and is reported to have antioxidant properties. This brief scientific summary of *O. sinensis* takes a look at recent scientific study of this intriguing fungus.
ACTIVE SUBSTANCES
Some of the most important substances found in *O. sinensis* with potential medicinal use include polysaccharides, a nucleoside called cordycepin and a sterol known as ergosterol. In particular, the fruiting body (i.e., mushroom) is said to improve sexual performance and fertility, possess antioxidant properties, control diabetes, and provide relief from fatigue and ailments of the liver. Each of these unique features will be discussed in turn.

TESTOSTERONE PRODUCTION
*Ophiocordyceps sinensis* is said to improve sexual performance and fertility. One of the most essential controlling factors of male reproductive function and sexual activity is testosterone. Hsu et al. (5) tested the components in *O. sinensis* with in vivo and in vitro stimulatory effects on mouse Leydig cells, the producer of testosterone. Purified mouse Leydig cells were treated with one of three extracted fractions of *O. sinensis*: F1 (water soluble polysaccharide), F2 (water soluble protein) and F3 (poorly water soluble polysaccharide and protein). Fractions were then tested in vitro for effects on steroidogenesis, i.e., the biological process that generates and transforms steroids. More importantly, the fractions of *O. sinensis* with positive effects were then fed to mice to determine their in vivo effect on levels of testosterone in plasma. Figure 1 shows the effects of *O. sinensis* fractions at each of two doses on testosterone production in purified normal mouse Leydig cells.

It can be clearly observed in figure 1 that fraction 1 (water soluble polysaccharide) does not have a statistically significant effect on testosterone production. In contrast, *O. sinensis* fractions F2 and F3 stimulated in vivo and in vitro testosterone secretion in mice. Further

![Figure 1.](image)

The effects of *Ophiocordyceps sinensis* fractions on testosterone production in purified normal mouse Leydig cells. The cells were incubated for 3 h in *O. sinensis* fractions of 3 or 10 mg/ml (5).
studies showed that F2 induced testosterone production in a dose- and time-dependent manner, with a maximal response at 3 mg/ml (5). Testosterone production in response to fraction F3 was also dose- and time-dependent, but as the concentration of F3 increased to 6 and 10 mg/ml, testosterone returned to basal level. It is possible that *O. sinensis* fraction F3 contains stimulatory as well as inhibitory substances and at high concentrations these effects may cancel each other, whereas F2 lacks such inhibitory components.

**ANTIOXIDANT EFFECT**

*Ophiocordyceps sinensis* has been reported to have antioxidant properties. However, it is not clear which substances are responsible for these effects. Melanins, which are dark-brown to black pigment macromolecules, may have strong antioxidant activity. Dong et al. (6) isolated and identified melanin from *O. sinensis* and then tested the antioxidant activity of each pigment. The study suggested that extracted melanin has strong antioxidant activities. There is almost no melanin formation in natural fruiting bodies or in submerged culture of mycelium. Thus, *O. sinensis* melanin is probably exogenous in origin and may be formed by secretion of phenol oxidases into the growth medium which in turn oxidize phenolic compounds of various origins. Alternatively, phenols may be secreted into the medium where they are autoxidized or are oxidized by enzymes released from the fungus. Dong and colleagues further studied the antioxidant scavenging activity of *O. sinensis* melanin on DPPH•, a stable free radical that has important pharmacological consequences. The activity reached more than 80% at concentrations over 40 µg/ml, which was slightly higher than that of two comparison antioxidants, BHT and α-tocopherol.

Dong et al. (6) also evaluated the effectiveness of melanin from water extract of *O. sinensis* at scavenging free radicals. They surmised that no other known compounds, including polysaccharides, mannitol, and cordycepin, can explain the antioxidant activity of *O. sinensis*. Thus, it was concluded that melanin may be the primary scavenger of free radicals.

**DIABETES TREATMENT**

Oxidative stress may play an important causal role in the onset and development of diabetes. To evaluate the potential role of *O. sinensis* in mitigating diabetes progression, El Ashry et al. (3) tested the combined effects of *O. sinensis* and taurine, an amino acid widely distributed in animal tissues, against glibenclamide, a standard synthetic oral hypoglycemic drug. They evaluated the effects of these natural products both in vivo and in vitro on rats that had diabetes induced by exposure to streptozotocin (STZ). Diabetic rats were orally administered glibenclamide, *O. sinensis*, or taurine, or a combination of *O. sinensis* and taurine, for a period of 21 d.

The results clearly showed that glibenclamide, *O. sinensis*, taurine and *O. sinensis*/taurine combination induced a significant reduction in serum glucose level. El Ashry et al also demonstrated an elevation in insulin level and an increase in percent β cell function when used in STZ diabetic rats. Although glibenclamide was most effective at controlling hyperglycemia,
increasing insulin level, and improving β cell function and islet destruction, the natural products were relatively better at enhancing insulin resistance and antioxidant function. There was no significant difference between O. sinensis and glibenclamide in the reduction of fructosamine levels. Finally, El Ashry and colleagues surmised that the anti-diabetic effects of O. sinensis and taurine may be due to pancreatic or extra-pancreatic action.

**FATIGUE REDUCTION**

Koh et al. (7) studied the fatigue reduction effects of hot water fraction of O. sinensis by testing the swimming endurance capacity of fraction-fed mice in an adjustable-current swimming pool. The mice administered the O. sinensis fraction received either 150 or 300 mg/kg/d while the control group received 0.9% NaCl by weight. Time to fatigue at a flow rate of 8 l/min was then estimated for each mouse. After 7 d of treatment, swimming time of mice that received O. sinensis fractions increased significantly compared to controls. Koh and coworkers suggest that the effect of the hot water fraction on recovery from exhaustion might be explained by improved resistance to stress-induced exercise and enhanced immune system function. These results suggest that the hot water fraction of O. sinensis reduces fatigue and also prolongs the swimming time of mice. These effects may be related to the enhancement of immunity.

Kumar et al. (8) supplemented exercising rats with O. sinensis mycelia powder and observed over 15 d a 2.9-fold and 1.32-fold increase in swimming-time-to-fatigue over the placebo
and non-supplemented exercise groups, respectively, without observing increases in body or muscle mass. To understand the molecular basis of endurance enhancement, Kumar et al. evaluated the expression of skeletal muscle metabolic regulators AMPK-1α, PPAR-δ, and PGC-1α. Increased expression of these genes induces marked changes in the metabolism of skeletal muscle, including increases in glycogen breakdown, glycolysis, glucose uptake, and fatty acid oxidation, together with many changes in gene expression that promote endurance. Supplementing *O. sinensis* to exercising rats significantly activated AMPK-1α, PGC-1α, and PPAR-δ in the red gastrocnemius muscle. It is important to note that in comparison to control rats, *O. sinensis* supplementation without exercise significantly activated all three metabolic regulators. Thus, *O. sinensis* supplementation with or without exercise improves exercise endurance capacity by activating skeletal muscle metabolic regulators. Moreover, Koh et al. (7) showed that the hot water fraction of *O. sinensis* has stress-reducing effects.

**LIVER EFFECT**

An earlier study of 33 sufferers of chronic hepatitis B treated with cultured *O. sinensis* mycelia showed that the fungus (a) improves liver function; (b) promotes negative transfer HbsAg, i.e., the surface antigen of the hepatitis B virus; (c) markedly raises plasma albumin; (d) helps patients resist high gamma globulin; and (e) enhances immunocompetence. It is suggested that the fungus may be a treatment for chronic hepatitis B patients that adjusts protein metabolism and corrects inversion of albumin and globulin. Since inflammation has been reported to be associated with chronic diseases, inhibitory dietary factors of the fungus may be beneficial in such cases.

*Ophiocordyceps sinensis* also reduced the hepatic content of malondialdehyde and the serum concentrations of transaminases and alkaline phosphatase in rats with hepatic fibrosis. An anti-fibrotic action was indicted by these results. (1)
Conclusions

*Ophiocordyceps sinensis* is a fungus that parasitizes moth larvae. The fungus has been used medicinally for hundreds of years because of its unique biological activities. In this summary, some of these activities have been discussed. The most important substances for medicinal potential in *O. sinensis* are polysaccharides, cordycepins and sterols. One particular study showed that *O. sinensis* may influence reproductive function by stimulating testosterone secretion. Results also suggest that a weakly water-soluble polysaccharide and protein fraction from the fungus stimulate testosterone secretion at intermediate doses, but may be inhibitory at high concentrations.

It has been demonstrated that the fungus has antioxidant activity; however, the biochemical causes are unknown for this effect. More recently, melanin has been implicated as the component responsible for scavenging free radicals. Earlier studies showed that *O. sinensis* induces a significant reduction in serum glucose level and increases insulin resistance and percent β cell function when used in STZ diabetic rats.

The fungus has anti-fatigue and stress-reducing effects. These effects were demonstrated in mice that prolonged their swimming time with less fatigue after being administered fractions of the fungus. Even treatment against hepatitis B is possible, since *O. sinensis*

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has been shown to improve liver function.


