



## **CORDYCEPS, AN ENDANGERED MEDICINAL PLANT : A SHORT REVIEW**

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*Cordyceps* is a genus of A fungi (sac fungi) that includes about 400 species. All *Cordyceps* species are endoparasitoids, parasitic mainly on insects and other arthropods (they are thus entomopathogenic fungi); a few are parasitic on other fungi. Until recently, the best known species of the genus was *Cordyceps sinensis* (John and Matt, 2008) first recorded as *yartsagunbu* in Nyamnyi Dorje's 15th century Tibetan text *An ocean of Aphrodisiacal Qualities* (Winkler, 2008a). In 2007, nuclear DNA sampling revealed this species to be unrelated to most of the rest of the members of the genus; as a result, it was renamed *Ophiocordycepssinensis* and placed in a new family, the Ophiocordycipitaceae.

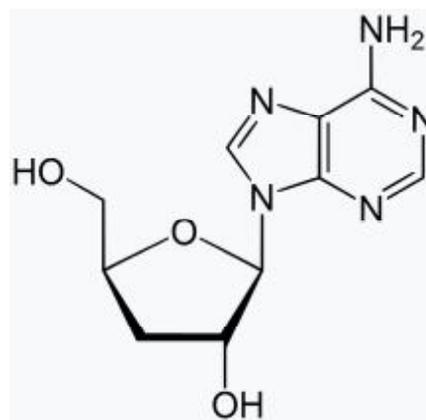
The generic name *Cordyceps* is derived from the Greek word *kordyle*, meaning “club” and the Latin stem *-ceps*, meaning “head”. Several species of *Cordyceps* are considered to be medicinal mushrooms in classical Asian pharmacologies, such as that of traditional Chinese (Halpern, 2007; Zhu *et al.*, 1998) and Tibetan medicines.

When a *Cordyceps* fungus attacks a host, the mycelium invades and eventually replaces the host tissue, while the elongated fruit body (ascocarp) may be cylindrical, branched, or of complex shape. The ascocarp bears many small, flask-shaped perithecia containing asci. These, in turn, contain thread-like ascospores, which usually break into fragments and are presumably infective. Some current and former *Cordyceps* species are able to affect the behavior of their insect host: *Ophiocordyceps unilateralis* (formerly *Cordyceps unilateralis*) causes ants to climb a plant and attach there before they die. This ensures the parasite's environment is at an optimal temperature and humidity, and that

maximal distribution of the spores from the fruit body that sprouts out of the dead insect is achieved (Hughes *et al.*, 2010). Marks have been found on fossilised leaves that suggest this ability to modify the host's behavior evolved more than 48 million years ago (Sung *et al.*, 2007).

The genus has a worldwide distribution and most of the approximately 400 species (Holiday *et al.*, 2004) have been described from Asia (notably Nepal, China, Japan, Bhutan, Korea, Vietnam) species are particularly abundant and diverse in humid temperate and tropical forests.

Some *Cordyceps* species are sources of biochemicals with interesting biological and pharmacological properties (Holiday, 2005), like cordycepin; the anamorph of *C. subsessilis* (*Tolypocladium inflatum*) was the source of ciclosporin—an immunosuppressive drug helpful in human organ transplants, as it inhibits rejection (Chun *et al.*, 2011). Fingolimod, a sphingolipid used to treat Multiple Sclerosis, is modified myriocin which was isolated from *Isariasinclairii*, the anamorph stage of *Cordyceps sinclairii* (web ref).



Cordycepin, a compound isolated from the caterpillar fungus

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*Cordyceps* have a long history of use in traditional medicine. One of the earliest clear records is a Tibetan medical text authored by ZurkharNyamnyiDorje in the 15th century outlining the tonic propensities of Yartsaganbu (*Cordyceps sinensis* renamed now to *Ophiocordyceps sinensis*), especially as an aphrodisiac. Although, there are often-repeated claims of thousands of years of use in traditional Chinese medicine, so far no clear textual source has surfaced.

Although, *in vitro* and animal models provide preliminary support for some of the traditional medicinal uses, there are no clinical studies demonstrating health benefits in humans or for “elderly populations, improved sexual drive and virility” and “improved renal function” (Khan *et al.*, 2012). Some polysaccharide components and cordycepin, which have some anticancer activity in preliminary *in vitro* and animal studies (Khan *et al.*, 2012), have been isolated from *C. militaris*.

*Cordyceps sinensis* on the Tibetan Plateau rose dramatically by 900% between 1998 and 2008, or an annual average of over 20%. However, the value of large-sized caterpillar fungus has increased more dramatically than smaller size *Cordyceps*, regarded as lower quality (Winkler, 2008). In parts of eastern Asia (such as China), the *Cordyceps* fungus are rare and worth high prices.

Year	% Price increase	Price/kg (Yuan)
1980s		1,800
1997	467% (incl. inflation)	8,400
2004	429% (incl. inflation)	36,000
2005		10,00060,000

### Find a vitamin or supplement

#### Cordyceps

#### Other names

Caterpillar Fungus, Caterpillar Mushroom, Cs-4, Champignon Chenille, Chinese Caterpillar Fungus, Cordyceps sinensis, Dong Chong Xia Cao, Dong Chong Zia Cao, Hsia Ts’Ao Tung Ch’Ung, Ophiocordyceps sinensis, Tochukaso, Vegetable Caterpillar.

#### Cordyceps overview information

Cordyceps is a fungus that lives on certain caterpillars in the high mountain regions of China. Supplement makers are able to get enough of the product to sell because cordyceps will reproduce in the laboratory. Cordyceps is used to treat coughs, chronic bronchitis, respiratory disorders, kidney disorders, nighttime urination, male sexual problems, anemia, irregular heartbeat, high cholesterol, liver disorders, dizziness, weakness, ringing in

the ears, unwanted weight loss, and opium addiction. It is also used for strengthening the immune system, improving athletic performance, reducing the effects of aging, promoting longer life, and improving liver function in people with hepatitis B. Some people use cordyceps as a stimulant, a tonic, and an “adaptogen,” which is used to increase energy, enhance stamina, and reduce fatigue.

#### How does it work?

Cordyceps might improve immunity by stimulating cells and specific chemicals in the immune system. It may also have activity against cancer cells and may shrink tumor size, particularly with lung or skin cancers.

Cordyceps are a type of fungus, better known as a species of edible medicinal, nutritionally beneficial mushrooms. While closely related to other mushrooms, cordyceps aren’t technically the same as most mushrooms and instead are classified as a powerful form of *Ascomycetes* fungus. Cordyceps are harvested in high mountain regions of the world, especially parts of the Himalayas in China, and are actually grown on the backs of caterpillars! Considered to be “exotic” healers, cordyceps mushrooms have been mostly rare for much of history (considering they’re only found above altitudes of 3,800 meters above sea level during certain times of the year and in only certain parts of the world where these special caterpillars exist). Yet they have a reputation for being “a precious longevity-promoting herb.”

#### Research and studies on cordyceps

Prized for their natural ability to fight free radicals, infections and inflammation, cordyceps are impressive disease-fighting mushrooms that have been used for centuries to reduce symptoms of respiratory disorders, coughs, colds, liver damage and much more. They’re a true “superfood” in the way that they fight the effects of aging and stress, help keep the body free from disease, and also increase energy levels. Cordyceps fungus is parasitic in nature because it grows on a type of caterpillar and then winds up eating its own host! The base of the mushroom forms from the insect’s larva and is dark brown to black, attaching itself to the organism and growing about six inches long. Once it fully matures, cordyceps actually consume more than 90 percent of the infected insect. They then swell up and enlarge to become about 300–500 milligrams in weight.

The first people to discover cordyceps’ benefits initially observed animals eating the wild fungus and growing strong in the process. Farmers and herders began to use the fungus in powder form and to make tonics and teas. Some of the first uses for these tonics were increasing milk production and improving reproductive capacity of

livestock. Later on, people began drying cordyceps in sunlight to preserve their benefits.

It's believed that the many anti-inflammatory benefits of cordyceps come from their ability to positively affect the immune system, fighting oxidation damage, and stimulating protective cells that keep the body free from mutations (like cancerous cells) and infections. Studies have found that cordyceps can act like natural cancer treatments in some cases, preventing the growth of tumors (especially in the lungs and on the skin).

Considered a type of natural "immuno-potentiating drug," corycep supplements are now used to bring the immune system back to normal following life-threatening infections or illnesses. Cordyceps can help control autoimmune disorders, excessive inflammation and tissue damage while speeding up healing time. Additionally, research shows that cordyceps can act like mild stimulants or "adaptogen herbs," fighting stress or fatigue and naturally increasing energy levels. Some of the most researched benefits of corceypys also include improving athletic performance, increasing immunity against viruses and even promoting longevity.

In addition to fighting cancer, cordyceps are used to help treat:

- respiratory infections like chronic bronchitis
- coughs, colds and the flu
- reproductive problems and sexual dysfunction
- kidney disorders
- bladder infections and urination problems
- asthma
- hepatitis B
- low circulation and irregular heartbeats
- heart disease and high cholesterol
- liver disorders
- muscle weakness
- chronic fatigue syndrome and low energy
- dizziness

## Benefits of Cordyceps

### 1. Increase Immune Function and Have Anti-Aging Effects

Pharmacological and biological studies have found that cordyceps positively impact immune function and benefit the cardiovascular, respiratory, endocrine and reproductive systems. Cordyceps can help fight cancer and immunological disorders because they contain inflammation-lowering polysaccharides, modified

nucleosides and cyclosporines. Animal studies have demonstrated benefits to heal autoimmune diseases like leaky gut syndrome and antitumor activity in various types of cancers when either synthetic or natural and cordycep supplements are administered.

Some evidence shows that taking cordyceps supplements during or following chemotherapy can lower symptoms of the treatment and increase the body's defense mechanisms. There's also evidence that they help restore normal fat mobilization and reduce oxidative damage, which contributes to nearly every chronic disease from heart disease to cognitive decline.

Research done by the School of Pharmaceutical Sciences at Peking University in Beijing found that cordycep extract supplements had anti-aging effects on mice and improved activity of antioxidants, including superoxide dismutase and glutathione peroxidase. Cordyceps also lowered the level of lipid peroxidation and monoamine oxidase activity that contributed to aging in the mice. All results pointed to the fact that cordycep supplementation is effective for improving functioning of the brain, immune system and reproductive/sexual functions.

### 2. Improve Stamina and Athletic Performance

A 2010 study published in the *Journal of Alternative and Complementary Medicine* demonstrated that supplementation with Cs-4 (*Cordyceps sinensis*) improved exercise performance and contributed to overall markers of wellness in older adults. Considered an energizing adaptogen (similar to other superfood herbs like maca or cocoa), cordyceps can help fight fatigue, treat muscle aches and prevent weakness.

Several studies suggest that cordyceps can improve physical abilities, endurance and stamina partially because they boost the body's supply of ATP, one of the primary sources of energy during exercises. Cordyceps contain adenosine, a type of nucleic acid that is a component needed to make ATP. One 2007 study done by The Hong Kong University of Science and Technology found that higher production of ATP helped athletes keep up with intense workouts and extend the length of time they could stay active at a high level.

### 3. Act Like a Natural Aphrodisiac

Traditionally, people of both sexes took tonics made from cordyces to enhance their libidos and reproductive function. It appears that cordycep supplements can help the body utilize oxygen more efficiently and improve blood flow, which is important for physical health and sexual function. Improved endurance, anti-fatigue effects and

lower levels of inflammation at the root of most diseases are several other reasons that cordyceps improve fertility. Thus, cordyceps can be utilized as a natural treatment for infertility and a natural remedy for impotence.

#### 4. Fight Diabetes

Two active constituents in cordyceps, d-mannitol cordycepin and 3'-deoxyadenosine, are partially responsible for various physiological actions that help control insulin and blood sugar levels. In animal studies, cordyceps supplements have helped combat hypoglycemic effects in normal and diabetic mice. This shows cordyceps may be useful to naturally treat diabetes.

#### 5. Improve Liver Function and Detoxification

Cordyceps appear to help improve liver function, especially in people with damaged livers due to disorders like hepatitis B. Because the liver helps remove toxins from the body, enhanced liver function is one way that cordyceps positively impact the immune system.

Research done by the Department of Analytical Chemistry at the Academy of Chinese Sciences found that cordyceps have positive influence on oxidative stress; energy metabolism; and amino acid, protein and choline metabolism thanks to their role in helping with digestive organ function. Over a period of eight weeks, metabolic disorders, signs of liver disease and heart damage in mice were significantly improved with daily oral administration of cordyceps.

One reason that positive effects of both the liver and heart were observed together is that a healthier liver also allows for better digestion and utilization of fatty acids, so therefore cordyceps are known to help improve triglyceride levels and benefit heart health.

#### 6. Fight Respiratory Infections

Research has demonstrated that cordyceps help alleviate symptoms of several respiratory illnesses, including working as a natural remedy for chronic bronchitis, coughs and asthma. Supplementation can help improve detoxification and circulation so the amount of oxygen reaching the lungs improves. In animal studies, cordyceps have also shown the ability to increase the number of T-helper cells that fight infections while not increasing the the number of T-suppressor cells. This makes them beneficial for speeding up the time it takes to fight off illness once an infection or virus sets in.

#### History of *Cordyceps* and Interesting Facts

Cordyceps (species name *Cordyceps sinensis*) are considered a time-honored superfood that first originated

in Traditional Chinese Medicine at least 5,000 years ago. Their medicinal uses were described in old Chinese medical books, and traditional holistic healers have been using them to cure dozens of diseases without the use of chemical medications for generations. Local folk healers were said to use *Cordyceps* either alone or in combination with other TCM herbal treatments to fight more than 20 different ailments, such as bronchitis and heart disease. Cordyceps and other medicinal plants have long been used in Chinese, Christian and Hindu religious ceremonies and are believed to be linked to longevity and immortality. In Ayurvedic medicine, for example, mushrooms are said to be beneficial for enhancing “vigor and vitality.” According to the *Journal of Ayurveda Integrative Medicine*, traditional healers in Sikkim recommended the fungus/mushrooms, including coryceps, “for all illnesses as a tonic, because they claimed that it improved energy, appetite, stamina, libido, endurance, and sleeping patterns.”

#### How to use *Cordyceps* Plus Potential Side Effects

For many decades, cordyceps were difficult to obtain, expensive and not widely used. Today, wild cordyceps are still not easy to come by, but luckily scientists have figured out how to reproduce cordyceps synthetically in laboratory settings, making them much more widely available to the public. Supplements are now available in most health food stores at much more affordable prices and appear to offer the same benefits as the wild varieties. Another advantage of growing controlled species of cordyceps is being able to control contamination, such as harmful bacteria and heavy metals.

#### *Cordyceps* Dosage

It's now possible to purchase cordyceps tablets, powders and capsules from most health food stores and over the Internet. Many people take them by mouth, but some even like to open the capsules and use the powder in teas, soups and stews (how they were traditionally taken in China for hundreds of years). Dosage depends on the reason they are being used, but usually the recommended amount is to take about five to 10 grams of cordyceps once or twice per day. Follow the dosage advice on the product label, or speak with an herbalist about treating a specific condition. You don't necessarily need to take them every day if you're only trying to prevent future illnesses and boost your immune system. In that case, once or twice a week with a lower dose works well.

#### Side Effects and Interactions

*Cordyceps* are considered safe for most people, but there are some potential side effects to be aware of, especially for pregnant women and people with a history

of autoimmune diseases. If you're pregnant or breast-feeding, you likely want to steer clear of taking cordyceps since their safety hasn't been well-researched or confirmed in this population.

For anyone with a known autoimmune disease (for example, lupus, rheumatoid arthritis, multiple sclerosis), some doctors warn that *Cordyceps* might worsen the problem. Because they stimulate the immune system, it's possible that *Cordyceps* can interfere with medications for these diseases or overactivate certain immune cells. The same warning goes for anyone with a known bleeding or blood clot disorder, since medical mushrooms can sometimes interfere with proper blood clotting.

### Botany

The wild form of *C. sinensis* is rare and expensive consequently, a strain isolated from the wildform (Cs-4, or *Paecilomyces hepialid* (Chen) is cultivated industrially and more commonly used. Issues of substitution with other species and contamination have been described (Sung *et al.*, 2007; Zhu *et al.*, 1998; Li *et al.*, 2006 and Holiday *et al.*, 2008).

### History

*Cordyceps* is valued for its activity in restoring energy promoting longevity and improving of life of human beings (Zhu *et al.*, 1998).

### Chemistry

Other classes of constituents found in wild *C. sinensis* include the following proteins peptides, all essential amino acids and polyamines, saccharides and sugar derivatives, sterols fatty acids and other organic acid, vitamins (including B<sub>1</sub>, B<sub>12</sub>, E and K) and inorganic elements (Zhu *et al.*, 1998; Holiday *et al.*, 2008; Li *et al.*, 2006). Cordycepin and other unique compounds have been identified using thin layer and gas Chromatography, high performance liquid chromatography and capillary electrophoresis. Water, ethanol, methanol and ethyl acetate extracts have been described for the whole fungus and mycelium as well as for other parts of the fungus (Li *et al.*, 2006; Paterson, 2008; Ng, 2005).

### Pharmacology

*In vitro* evaluation and animal studies of *Cordyceps* and its chemical constituents suggest potential therapeutic application however despite a significant number of clinical studies, the overwhelming majority had poor methodologies. Very few large randomized, controlled clinical trials have been conducted (several of which evaluated *Cordyceps* in combination with other agents), making definite statements about the efficacy of *Cordyceps* premature (Holiday *et al.*, 2008; Paterson,

2008; Wojcikowski *et al.*, 2004).

### Ageing

Traditionally, *Cordyceps* has been used in the elderly population to improve weakness, importance and fatigue associated with ageing (Holiday *et al.*, 2008; Ji *et al.*, 2009). However, the methodology of such studies is often poorly documented improvements in self-reported symptoms have been described as malondialdehyde levels (Zhu *et al.*, 1998 Ng and Wang, 2005). Other anti oxidant effect, hydroxyl radical scavenging activity and decreases in lipid peroxidation are thought to be responsible for the anti ageing effects (Ng, and Wang, 2005; Wang *et al.*, 2009 and Won *et al.*, 2009) as well as effects on the adrenergic and dopamine system (Nishizawa *et al.*, 2007). Increases in learning and memory have been shown in experiments in aged mice (Ji *et al.*, 2009).

### Cancer

Numerous *in vitro* and animal experiments have been conducted on aqueous and ethanol extracts of *Cordyceps* as well as with cordycepin and oxypiperazines extracted from the mycelium. The extracts enhanced cytokinin activity and induced cell cycle arrest and apoptosis, thereby reducing tumour cell proliferation and enhancing survival time (Holiday *et al.*, 2008; Rao *et al.*, 2007; Zhang *et al.*, 2008; Chen *et al.*, 2009; Wu *et al.*, 2007; Lee *et al.*, 2009; Zhang *et al.*, 2006; Matsuda *et al.*, 2009). An experiment with animal suggests a protective role for *Cordyceps* in radiation and chemotherapy induced injury, with increased survival times demonstrated in mice (Liu *et al.*, 2008; Liu *et al.*, 2006).

### Cardiovascular effect

*Cordyceps* has a long history of traditional medicinal use in heart disease (4). Reduced heart rate and restoration from arrhythmias have also been shown in animals (Zhu *et al.*, 1998; Ng and Wang, 2005). Long term open label clinical studies in cardiac failure have described *Cordyceps* effect in improving cardiac function arrhythmias and overall quality of life, but, are yet to be substantiated by large high quality clinical trials (Zhu *et al.*, 1998; Chiou *et al.*, 2000;).

Fibrinolytic action of a *Cordyceps* extract has been shown *in-vitro* on bovine and human serum (Li *et al.*, 2007). Platelet aggregation has been inhibited in rabbits and in human platelets *in-vitro* (Ng and Wang, 2005; Cho *et al.*, 2007; Koh *et al.*, 2003).

### Diabetes

Animal studies suggest *Cordyceps* particularly the extract of polysaccharide decreases blood glucose levels by improving glucose metabolism and enhancing insulin



*Cordyceps* beginning its growth from a wasp



*Cordyceps militaris*



*Cordyceps militaris*



Chinese soup of silkie, seahorse and cordyceps



*Cordyceps ophioglossoides*



*Cordyceps militaris*



*Cordyceps fungus*



*Cordyceps sinensis*

sensitivity (Li *et al.*, 2006; Ng and Wang, 2005; Lo *et al.*, 2006; Lo *et al.*, 2004; Zhang *et al.*, 2006; Zhao *et al.*, 2002; Balon *et al.*, 2002; Hockaday *et al.*, 2002).

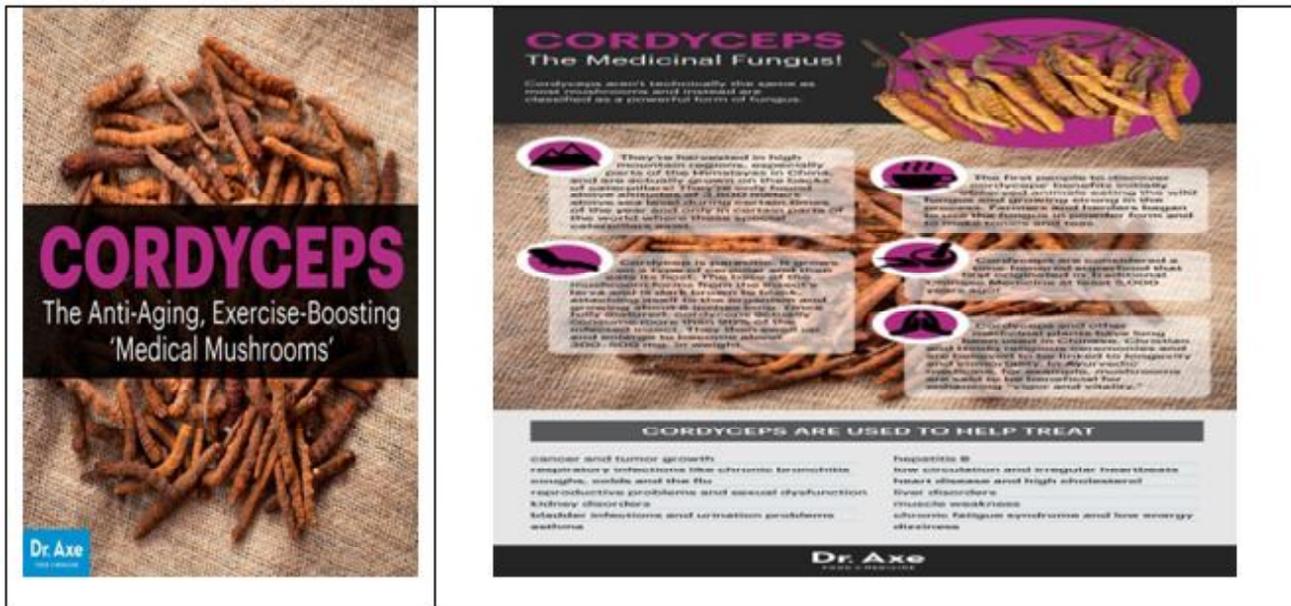
### Hepatic function

Hepatoprotective effects of *Cordyceps* extracts have

been demonstrated in animal model (Ng and Wang, 2005; Ko *et al.*, 2010). Open label clinical studies conducted in patients with active hepatitis and posthepatic cirrhosis reported improvements in liver function tests (Holiday *et al.*, 2008; Zhu *et al.*, 1998; Ng and Wang, 2005).



Ex-Ginseng Vitamin C. [Today on Medicine]



Performance of Anti-Aging & Exercise

**Immune system and anti-inflammatory effects**

Aside from limited data from clinical studies conducted in renal transplant recipients and chronic hepatitis patients (Zhu *et al.*, 1998; Ng and Wang, 2005; Li *et al.*, 2009; Liu *et al.*, 2003). Different fractions of *Cordyceps* extract (either aqueous or ethanol based) appear to have different effects and therefore an immunomodulator function for *Cordyceps* has been proposed (Kuo *et al.*, 2007; Yoon *et al.*, 2008; Zhou *et al.*, 2008; Jordan *et al.*, 2008; Cheung *et al.*, 2009; Jordan *et al.*, 2008; Kuo *et al.*, 2007; Kuo *et al.*, 2001). But, potential anti-inflammatory action has not been studied (Zhu *et al.*, 1998; Ng and Wang, 2005; Kim *et al.*, 2006). In mice, enhanced splenocyte proliferation increased plasma corticosterone decreased production of immunoglobulin E and modulation of cytokine and CD4+ and CD8+ cell production were reported (Jordan *et al.*, 2008;

Cheung *et al.*, 2009; Jordan *et al.*, 2008; Kuo *et al.*, 2001; kuo 2007; Kuo *et al.*, 2007). An infection and attenuated disease severity in lupus-prone autoimmune mice were also described (Kuo *et al.*, 2005; Chen *et al.*, 2009; Ka *et al.*, 2006).

**Physical performance**

Tests in animals such as the mouse swim test generally showed increased time to exhaustion. Unpublished data on studies in elderly volunteers revealed increased energy levels and oxygen-carrying capacity following six weeks of *Cordyceps* treatment over placebo (Zhu *et al.*, 1998; Holiday *et al.*, 2008). In three clinical trials *Cordyceps* was found (Herda *et al.*, 2008; Earnest *et al.*, 2004; Colson *et al.*, 2005). In another clinical trial *Cordyceps* 3.15g (as Cs-4) taken daily for 5 weeks had no effect compared with placebo (Parcell *et al.*, 2004).

### Renal function

Almost all the clinical studies evaluating the effect of *Cordyceps* renal function are poor methodology which are used *Cordyceps* in combination with other mixed preparation (Wijikowski *et al.*, 2004). Improved renal function as demonstrated by increases creatine clearance and decreases in blood urea nitrogen and serum creatine (Holiday *et al.*, 2008; Zhu *et al.*, 1998; Wijikowski *et al.*, 2004). These findings are supported by histological studies in animals (Zhu *et al.*, 1998; Ng and Wang, 2005; Wijikowski *et al.*, 2004; Shahed *et al.*, 2001).

### Respiratory effects

*In-vitro* studies suggest aqueous extract of *Cordyceps sinensis* have a stimulatory effect on ion transport in human airway epithelial cells, possibly because of Cordycepin and adenosine (Yue *et al.*, 2008).

### Sexual dysfunction

Experiment in castrated rats showed a mild effect on sexual function. Decreased in erection and mount latency were demonstrated but no effect on ejaculation latency was found (Ji *et al.*, 2009). However, action on steroidogenesis and testosterone have been shown (Huang *et al.*, 2004; Wong *et al.*, 2007; Hsu *et al.*, 2003).

### Other effects

Inhibition of osteoclast differentiation in mice has been described (Mizuha *et al.*, 2007). Stimulation of erythropoiesis has been reported as well as well as antibacterial, anti-fungal and anti-microbial activity (Ng and Wang, 2005).

### Dosage

Dosing supported by product quality data is unavailable and many herbal supplements contain varying undefined levels of this product *Cordyceps* 3 to 6 g/day has been used in patients with long-term renal failure for periods ranging from days to years (Holiday *et al.*, 2005; Zhu *et al.*, 1998; Wijikowski *et al.*, 2004).

### Lactation and Pregnancy

Information regarding safety and efficacy in pregnancy and lactation is lacking. Experiments were conducted on mice which suggest *Cordyceps* has an effect on plasma testosterone levels (Huang *et al.*, 2004; Wong *et al.*, 2007; Hsu *et al.*, 2003; Mizuha *et al.*, 2009).

### Interaction

The American College of Cardiology Writing Committee on Complementary and Integrative Medicine suggests that a risk of potentiation of anticoagulants and monoamine oxidase inhibitors exists (Vogel *et al.*, 2005;).

### Adverse Reaction

In the study conducted in children with asthma a combination preparation containing *Cordyceps* did not affect blood cell counts or renal or liver function tests (Won *et al.*, 2009).

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