

Olive Leaf and Cordyceps

Robert Pastore, Ph.D.

The Bible refers to the olive tree as the “tree of life”. Olives, the ripe fruit of the tree, yield healthy monounsaturated fats and phytochemicals that act as potent antioxidants. Research on the benefits of olive oil abounds in scientific literature. Yet, people are still not aware of the amazing healing powers of another component of the olive tree, the leaves.

The olive tree, botanically designated as *Olea europea*, brings to us a promising herbal product known as olive leaf extract. The ancient Egyptians regarded olive leaf as a symbol of heavenly power, and in keeping with that belief, they extracted its oil and used it to mummify their kings. The healing powers of olive leaf were realized as early as the 1880s when it was utilized to counteract malaria. According to the 1854 *Pharmaceutical Journal of Provincial Transactions* (pp. 363-354), Hanbury stated that a “decoction of the leaves” of the olive tree had been found to be extremely effective in reducing fevers due to a severe, and otherwise often-fatal disease that swept the island of Mytelene in 1843. The olive leaf extract was reported subsequently to be more effective in its fever-lowering properties than quinine. Hanbury recalled that similar observations had been made in France and Spain between 1811 and 1828. It appears that in the early 19th century, Spanish physicians sometimes prescribed olive leaves as a “febrifuge”, and often used them to treat cases of intermittent fever (2). Hanbury concluded that the properties of the tree *Olea europea* deserved more extensive investigation.

In the early 1900s scientists isolated a bitter compound called oleuropein from olive leaf that was thought to give the olive tree its disease resistance. In 1962 an Italian researcher recorded that Oleuropein had the ability to lower blood pressure in animals. Other European researchers validated that claim and also found it to increase blood flow in the coronary arteries, relieve arrhythmia and prevent intestinal muscle spasms. In the years to come, a Dutch researcher identified that a primary ingredient in oleuropein inhibited the growth of viruses, bacteria, fungi and parasites. This chemical was elenolic acid. Further European research determined this compound to have strong bactericidal, antiviral and antifungal capabilities. A safety study on calcium elenolate was tested with laboratory animals and published by the Upjohn pharmaceutical company in 1970. The study concluded that even in doses several hundred times higher than recommended; no toxic or other adverse side effects were discovered.

Health professionals first started using Olive Leaf extract in 1995 when it first became available. Although we do not have a long-term perspective as yet, initial results are very positive. We see a very promising and unique herb with multiple applications. It shows considerable therapeutic action against many

common conditions. In short, it appears to be living up to its unique background and expectations.

Antibacterial, Antiviral, Antifungal

From research and clinical experience to date, many medical doctors use olive leaf as adjuvant care for conditions caused by, or associated with, a virus, retrovirus, bacterium or protozoan, including influenza, the common cold, candida infections, meningitis, Epstein-Barr virus (EBV), encephalitis, herpes I and II, human herpes virus 6 and 7, shingles (Herpes zoster), HIV/ARC/AIDS, chronic fatigue, hepatitis B, pneumonia, tuberculosis, gonorrhea, malaria, dengue, severe diarrhea, and dental, ear, urinary tract and surgical infections. Of course, its application is used under the supervision of a medical professional. No one should attempt to treat themselves.

In the Journal of Pharmacy and Pharmacology, Volume 51, Number 8, 1 August 1999, researchers concluded that standardized olive leaf extract can be considered a potential source of promising antimicrobial agents for treatment of intestinal or respiratory tract infections in man.

According to a study published in Antiviral Res. 2005 Jun;66(2-3):129-36, oleuropein inhibited the in vitro infectivity of the viral hemorrhagic septicemia virus (VHSV), a salmonid rhabdovirus. Furthermore, olive tree leaf extract drastically decreased VHSV titers and viral protein accumulation (virucidal effect) in a dose dependent manner when added to cell monolayers 36 h post-infection. On the other hand, both the olive tree leaf extract and oleuropein were able to inhibit cell-to-cell membrane fusion induced by VHSV in uninfected cells, suggesting interactions with viral envelope. Therefore, we propose that olive tree leaf extract could be used as a potential source of promising natural antivirals, which have demonstrated to lack impact on health and environment. In addition, oleuropein could be used to design other related antiviral agents.

Fascinating research at York University School of Medicine, New York, published in Biochem Biophys Res Commun. 2003 Aug 8;307(4):1029-37, found that olive leaf extract inhibited HIV-1, and was not cytotoxic to healthy cells. The following summarizes the study in technical detail. Olive leaf extract inhibits acute infection and cell-to-cell transmission of HIV-1. Olive leaf extract also inhibits HIV-1 replication. No cytotoxicity on uninfected target cells was detected.

To identify viral and host targets for olive leaf extract, researchers characterized gene expression profiles associated with HIV-1 infection and olive leaf extract treatment using cDNA microarrays. HIV-1 infection modulates the expression patterns of cellular genes involved in apoptosis, stress, cytokine, protein kinase C, and hedgehog signaling. HIV-1 infection up-regulates the

expression of the heat-shock proteins hsp27 and hsp90, the DNA damage inducible transcript 1 gadd45, the p53-binding protein mdm2, and the hedgehog signal protein patched 1, while it down-regulates the expression of the anti-apoptotic BCL2-associated X protein Bax. Treatment with olive leaf extract reverses many of these HIV-1 infection-associated changes. Treatment of HIV-1-infected cells with olive leaf extract also up-regulates the expression of the apoptosis inhibitor proteins IAP1 and 2, as well as the calcium and protein kinase C pathway signaling molecules IL-2, IL-2Ralpha, and ornithine decarboxylase ODC1.

In the journal *Mycoses* Volume 46 Page 132 - March 2003 Volume 46 Issue 3-4, researchers investigated the antimicrobial effect of olive leaf extract against bacteria and fungi. The microorganisms tested were inoculated in various concentrations of olive leaf water extract. Olive leaf extract killed almost all bacteria tested, within three hours. Dermatophytes, *Candida albicans* and *Escherichia coli* were killed following three to 24 hour incubation in the presence of 15% (w/v) plant extract. These findings suggest an antimicrobial potential for olive leaf extract. It seems that olive leaf extract might be a great adjuvant protocol for *Candida albicans* yeast vaginitis

Many people who live stressful lives or who may be particularly susceptible to colds and viruses may benefit from long-term use of olive leaf as a preventative agent. Medical doctors have reported unexpected benefits of olive leaf, including improved psoriasis, normalization of heart beat irregularities, diminished cravings, less pain from hemorrhoids, toothaches and chronically achy joints.

Heart disease

The Mediterranean diet, rich in fruit, vegetables, and olive oil is correlated with a lower incidence of coronary heart disease (CHD). Natural antioxidants contained in the Mediterranean diet might also play a role in the prevention of cardiovascular diseases, through inhibition of LDL oxidation. Researchers tested this hypothesis "in vitro" by inducing LDL oxidation with copper sulphate and preincubating the samples with oleuropein.

Oleuropein effectively inhibited copper sulfate induced LDL oxidation, as assessed by various parameters. We demonstrate in this investigation that polyphenolic components of the Mediterranean diet interfere with biochemical events that are implicated in atherogenetic disease, thus proposing a new link between the Mediterranean diet and prevention of CHD (*Life Science*. 1994;55(24):1965-71).

Research suggests that olive leaf may be a true anti-viral compound because it appears to selectively block an entire virus specific system in the infected host. It then appears to offer healing effects not addressed by pharmaceutical antibiotics. Olive leaf's broad killing power includes an ability to interfere with critical amino acid production for viruses; an ability to contain viral infection and/or spread by inactivating viruses by preventing virus shredding, budding or assembly at the cell membrane; the ability to directly penetrate infected cells and stop viral replication.

What makes this product so unique is the fact that it is standardized to contain a minimum of 20% oleuropein per capsule. The actual content can be as high as 23%. Remember, oleuropein is the active antibacterial, antiviral, antifungal and antiparasitic component of olive leaf. Inferior products abound, partially due to confusion. For example, Pastore Formulations Olive Leaf contains 500 mg of olive leaf extract, standardized to 20% oleuropein per capsule and many people only focus on the "500 mg". Sure, I have found 500 mg capsules of olive leaf in health food stores, but the usual amount of oleuropein (the active component) is only 6%. The highest percent of oleuropein I have ever found in a bottle of olive leaf is 12%, and that cost \$40.00 per bottle for 60 capsules. Additionally, many olive leaf extract supplements do not contain the listed amount of oleuropein. Many medical doctors employ olive leaf extract for most bacterial, viral, parasitic, and fungal conditions. There are many unique uses for this medicinal herb.

It is my clinical opinion that the key to the benefits of olive leaf extract can be enhanced by mixing the active component with another potent immune supporting compound.

After exhaustive research, I decided to combine olive leaf extract standardized to 20% oleuropein with cordyceps standardized to 7% cordycepic acid, in one 600mg capsule.

Cordyceps

Cordyceps is one of the most rare and treasured herbs, and it has been an important ingredient in Chinese medicine for thousands of years. It can be found on isolated places in southwestern China, especially in the provinces of Tibet, Sichuan, Qinghai, Guise and Yunnan, in locations over 3,500 meters.

Cordyceps could be the next Ginseng due to its reported effects on increasing energy levels, sex drive and athletic performance. You may remember mention of cordyceps in the news It was virtually unknown to the Western part of the world until the Chinese womens track team broke records in 1993 and was found to be part of their dietary supplements.

The pharmacologically active components of cordyceps are cordycepin (deoxyadenosine) and cordycepic acid.

In addition to its immune supporting characteristics, a study presented at the American College of Sports Medicine annual meeting (1999), showed that cordyceps significantly increases maximal oxygen uptake and anaerobic threshold, which may lead to improved exercise capacity and resistance to fatigue.

Exercise Performance

In a review published in The American Journal of Clinical Nutrition 2000 Aug; 72(2 Part 2):624S-636S, selected herbals and their effects on human exercise performance were examined. With regard to cordyceps, controlled studies found improvements in exercise performance when test subjects used a standardized extract.

Hepatitis B

Cordyceps sinensis had been used to treat 25 patients with chronic hepatitis B. The comprehensive index, including T lymphocyte subsets (CD4, CD8), hyaluronic acid(HC) and precollagen type III(PC III), were observed before and after treatment. After 3 months of treatment, CD4 and CD4/CD8 ratio increased significantly ($P < 0.05$), while HA and PC III decreased significantly ($P < 0.05$) compared with the control. The results suggest that the beneficial effects might be obtained by using Cordyceps sinensis to adjust the T lymphocyte subsets level and to treat hepatic fibrosis on patients with chronic hepatitis B.

Cordyceps Sinensis is a plant that has been used in traditional Chinese medicine to restore energy, promote longevity, stimulate the immune system, and to improve quality of life. Ancient records claim that it is beneficial for the heart, circulatory system, liver, kidneys, respiratory system, and sex organs (Gong HY, Wang KQ, Tang SG. Hunan Yi Ke Da Xue Xue Bao 2000;25:248-250.

Hypertension (animal study)

In the journal Life Science 2000 Feb 25; 66(14):1369-76, a protein constituent of cordyceps sinensis was found to have a hypotensive and vasorelaxant effects.

In the study, cordyceps sinensis significantly suppressed the mean arterial pressure (MAP) in a dose-dependent manner and induced the maximal hypotensive response with a 58 ± 4 mm Hg (from 107 ± 6 to 49 ± 3 mm

Hg) change in MAP and a over 45 min action duration. In aortic rings precontracted with phenylephrine treatment with Cordyceps sinensis between 0.5 and 500 microg/ml induced dose dependent relaxation. Maximal vasorelaxant response evoked by 150 microg/ml Cordyceps sinensis was 68.9 +/- 7.3%. Furthermore, Cordyceps sinensis -induced vasorelaxation is mediated by the endothelium possibly by stimulating the release of the nitric oxide and endothelium-derived hyperpolarizing factor.

In conclusion, the present study revealed that presence of a constituent in Cordyceps sinensis which reduces MAP by relaxing the vascular beds directly. However, the effect may be caused by a single active ingredient or by the combined action of many active agents found in the Cordyceps sinensis extract.

Liver metabolism (animal study)

In the British Journal Nutrition 2000 Feb; 83(2):197-204, Cordyceps sinensis stimulated an increase in hepatic energy metabolism and blood flow in dietary hypoferric anemic mice.

Experimental hypoferric anemia was induced in mice by feeding with an iron-free diet for 6 weeks. They were then given extract from Cordyceps sinensis and were placed on an Fe-containing recovery diet for 4 weeks. During the 4-week Cordyceps sinensis-extract treatment, consistent increases were observed in liver beta-ATP: inorganic phosphate value by liver ³¹P NMR spectroscopy, representing the high energy state, and in blood-flow rate as determined by ²H NMR spectroscopy of deuterated water (D₂O) uptake after intravenous injection of D₂O. The hematological variables (the packed cell volume and the hemoglobin level) and the hepatic intracellular pH, which was determined from the NMR chemical shift difference between the inorganic phosphate peak and the alpha-phosphate peak of ATP, were not significantly different between Cordyceps sinensis-extract-treated and control mice. As blood flow and energy metabolism are thought to be linked, the Cordyceps sinensis-extract-increased hepatic energy metabolism in the dietary hypoferric anaemic mice was concluded to be due to increased hepatic blood flow.

Cancer (animal study)

Researchers at Norman Bethune University of Medical Sciences, Changchun, released animal data on Cordyceps inhibiting the growth of tumors, prolonging the survival period of mice implanted with S180 tumor cells, inhibiting the growth and metastasis of Lewis pneumonic cancer in the implanted mice, increasing the plasma content of cortisol and testosterone in normal rats, and elevating the weight of sexual organs in normal and castrated rats (Chung Kuo Chung Yao Tsa Chih 1997 Feb; 22(2):111-3, Anticarcinogenic effect and hormonal effect of Cordyceps. [Article in Chinese], Liu J, Yang S, Yang X, Chen Z, Li J).

Lupus (animal study)

Animal research indicates that *Cordyceps sinensis* (CS) is effective in improving the survival of lupus mice. In the study *Cordyceps sinensis* treated lupus mice for 8 weeks had a progressive reduction in anti-ds-DNA production (optical density value decreased from 0.172 +/- 0.009 to 0.112 +/- 0.015) when compared with the control group (optical density value increased from 0.141 +/- 0.036 to 0.198 +/- 0.047). In clinical presentation, the treated group had a reduction in lymphadenopathy, a delayed progression of proteinuria, and an improvement in kidney function. Histologic analysis of kidney tissue indicated that H 1-A could inhibit the mesangial proliferation that was evident in lupus nephritis. However, there was no significant change in immune complex deposition. The studies reveal that the *Cordyceps sinensis* may be potentially useful for treating systemic lupus erythematosus in human patients, and they provide some questions for further investigation of the pathogenesis of systemic lupus erythematosus and lupus nephritis (J Lab Clin Med 1999 Nov; 134(5):492-500).

Sugar Control (animal study)

Cordyceps sinensis extract significantly lowered the plasma glucose level in normal, streptozotocin (STZ)-induced diabetic and epinephrine-induced hyperglycemic mice. Administration of *Cordyceps* to STZ-induced diabetic mice significantly increased the activity of hepatic glucokinase. A significant reduction in the hepatic glucose output was observed following the infusion of *Cordyceps* using the perfused rat liver. *Cordyceps* also significantly decreased protein content of facilitative glucose transporter isoform 2 (GLUT2) from rat liver following *Cordyceps* administration. These effects presumably contribute to the hypoglycemic activity (Biol Pharm Bull 1999 Sep; 22(9):966-70).

Antitumor Sterols

Researchers University of British Columbia, Vancouver, Canada, isolated antitumor sterols from the mycelia of *Cordyceps sinensis*. The two antitumor compounds, 5 alpha,8 alpha-epidioxy-24(R)-methylcholesta-6,22-dien-3 beta-D-glucopyranoside and 5,6-epoxy-24(R)-methylcholesta-7,22-dien-3 beta-ol are present in standardized extracts of *Cordyceps sinensis*. Two previously known compounds, ergosteryl-3-O-beta-D-glucopyranoside and 22-dihydroergosteryl-3-O-beta-D-glucopyranoside were also isolated.. The *Cordyceps* sterols were found to be a greater inhibitor to the proliferation of K562, Jurkat, WM-1341, HL-60 and RPMI-8226 tumor cell lines by 10 to 40% at (Phytochemistry 1999 Aug; 51(7):891-8).

Kidney Injury

Cordyceps sinensis has been used as a Chinese medicine for a long time in the treatment of nephritis (any of various acute or chronic inflammations of the kidneys, such as Bright's disease.)

The current hypothesis about the pathogenesis of immunoglobulin A nephropathy (IgAN) is that nephritogenic IgA immune complexes (IgAIC) go to the kidney to stimulate resting mesangial cells to release cytokines and growth factors. These cytokines and growth factors cause mesangial cell proliferation and release chemical mediators that lead to the glomerular injury.

However, nephritogenic IgAIC in humans is still unknown. To solve this problem previously, researchers established an in vitro model that showed that cultured human mesangial cells (HMC) stimulated with interleukin-1 (IL-1) plus IL-6 (proinflammatory chemicals) can cause mesangial cell proliferation, increasing production of chemical mediators and superoxide anion (a powerful free radical that damages tissue).

An in vivo model also proved that this culture medium may lead to renal injury with hematuria (blood in urine) and proteinuria (protein in urine). Therefore, to fractionate the crude components that can be used in the treatment of patients with IgAN, researchers cultured HMC, and then an HMC activating model with HMC incubated with IL-1 and IL-6 was established.

Cordyceps significantly inhibited the HMC activation by IL-1 plus IL-6. The acute toxicity test with male Institute of Cancer Research mice showed no liver toxicity or mutagenicity. Then the researchers established an IgAN animal model with R36A (Pneumococcal C-polysaccharide purified from Streptococcus pneumoniae) as antigen and anti-R36A IgA monoclonal antibody to form nephritogenic IgA-IC, which can induce hematuria and proteinuria in mice with IgA deposition in the mesangial area. The mice in the IgAN model fed Cordyceps extract in diet had significant reduction of hematuria and proteinuria together with histopathologic improvement. These results gave researchers a new regimen for the treatment of patients with IgAN. (J Lab Clin Med 1999 Jan; 133(1):55-63).

Liver Health (animal study)

Researchers from the Faculty of Pharmaceutical Sciences, Mukogawa Women's University, Nishinomiya, Japan, found that Cordyceps sinensis extract stimulated an increase in Kupffer cells in the liver. Kupffer cells are very important cells in the liver that are responsible for phagocytosis (engulfing of pathogens, toxins, etc) - think of "pac man" Jpn J Pharmacol 1999 Apr; 79(4):505-8.

Lung Cancer and Melanoma (animal study)

Researchers investigated the effect of the *Cordyceps sinensis* extract on liver metastasis of Lewis lung carcinoma (LLC) and B16 melanoma (B16) cells in mice. *Cordyceps* extract showed a strong cytotoxicity against LLC and B16 cells, while cordycepin (3'-deoxyadenosine), an active component of *Cordyceps* was not cytotoxic against these cells. These findings suggest that *Cordyceps* has an anti-metastatic activity that is probably due to components other than cordycepin, in my opinion the active component was cordycepic acid (Jpn J Pharmacol 1999 Mar; 79(3):335-41)

A study published in Am J Chin Med 1998; 26(2):159-70, indicated that *Cordyceps sinensis* increases the expression of major histocompatibility complex class II antigens on human hepatoma cell line HA22T/VGH cells. Previous studies suggest that down-regulation of the major histocompatibility complex (MHC) antigens on the cell surface of certain tumors results in an escape of immune surveillance. *Cordyceps sinensis* is well known for its modulatory effect on host immune system.

Liver Cancer (human cell research)

The extract of *Cordyceps sinensis* was found to increase the MHC class II antigen expression on HA22T/VGH cells with the percentage of L243(+) cells 40.2 +/- 2.5 and RMFI 6.6 +/- 0.4; whereas cells without treatment disclosed the percentage of L243(+) cells 17.2 +/- 1.4 and RMFI 5.4 +/- 0.3, respectively ($p < 0.05$). There was a dose-related increase in the degree of fluorescence intensity in terms of RMFI on VGH-CS-ME-82 induced cells. The RMFI in cells treated with IFN-gamma 0, 0.2 and 5 ng/ml were 5.4 +/- 0.3, 8.2 +/- 0.4, and 24.9 +/- 1.5, respectively; whereas the RMFI in cells co-incubated with VGH-CS-ME-82 (40 micrograms/ml) and IFN-gamma 0, 0.2 ng/ml and 5 ng/ml were 6.7 +/- 0.2 ($p < 0.05$), 9.2 +/- 0.9 ($p < 0.1$) and 29.5 +/- 1.2 ($p < 0.005$), respectively. We conclude that VGH-CS-ME-82, either alone or with IFN-gamma induction, increases the MHC class II antigen expression on hepatoma cell line HA22T/VGH, which will shed light into the present immunotherapy, and make the host immune surveillance more effective against tumor cells with down-regulated MHC class II antigen expression.

Liver Protection (animal study)

In order to evaluate the effect of *Cordyceps sinensis* on aminoglycoside (AG) induced nephrotoxicity, Gentamycin was imposed on the young and old rats with *Cordyceps* administration. Aminoglycosides are any of a group of broad-spectrum antibiotics, such as streptomycin and gentamycin used to treat

infections caused by gram-negative bacteria. The renal tubular injury was ameliorated as evidenced by less prominent increment of BUN, SCr, sodium excretion, urinary NAGase and less severity of histopathological changes as compared with control. In addition, the use of Cordyceps could promote an earlier recovery of renal oxygen consumption, insulin clearance, and sodium absorption in isolated perfused kidney from Cordyceps treated rat than that from control. Possible mechanisms of Cordyceps on drug-induced nephrotoxicity include: (1) Accelerating the regeneration of tubular cells; (2) Protecting the sodium pump activity of tubular cells; (3) Attenuating the tubular cell lysosome hyperfunction stimulated by phagocytosis of AG as well as decreasing the tubular cell lipoperoxidation in response to toxic injury; (4) Reducing the tissue calcium content (Chung Kuo Chung Hsi I Chieh Ho Tsa Chih 1996 Dec; 16(12):733-7. Experimental study on effect of Cordyceps sinensis in ameliorating aminoglycoside induced nephrotoxicity).

Human Leukemic U937 Cells.

Researchers at the Department of Medical Research, Veterans General Hospital-Taipei, Taiwan, Republic of China, investigated the effect of Cordyceps sinensis on the proliferation and differentiation of human leukemic U937 cells using an in vitro culture system. The results showed that Cordyceps extract had an activity that could significantly inhibit the proliferation of U937 cells resulting in a growth inhibition rate of 78-83%.

Furthermore, antibody neutralization studies further revealed that the tumoricidal and differentiating effects of Cordyceps extract were mainly derived from the elevated cytokines, especially IFN-gamma and TNF-alpha. These two cytokines acted synergistically on inhibiting cell growth and inducing differentiation of the target U937 cells (Life Sci. 1997;60(25):2349-59).

References

Lu, Mary, Effect of Cordyceps sinensis and artemisinin in preventing recurrence of lupus nephritis. *Alternative Medicine Review*, May, 2003.

HY Gong, KQ Wang, SG Tang, Effects of Cordyceps sinensis on T lymphocyte subsets and hepatofibrosis in patients with chronic hepatitis B. *Alternative Medicine Review*, Dec, 2002.

Hanbury D. On the febrifuge properties of the olive (*Olea europea*, L.), *Pharmaceutical Journal of Provincial Transactions*, pp. 353-354, 1854.

Cruess WV, and Alsberg CL, The bitter glucoside of the olive. *J Amer. Chem. Soc.* 1934; 56:2115-7.

Veer WLC et al. A Compound isolated from *Olea europea*. *Recueil*, 1957; 76:839-40.

Panizzi L et al. The constitution of oleuropein, a bitter glucoside of the olive with hypotensive action. *Gazz. Chim. Ital*; 1960; 90:1449-85.

Renis HE, In vitro antiviral activity of calcium elenolate, an antiviral agent. *Antimicrob. Agents Chemother.*, 1970; 167-72.

Petkov V and Manolov P, Pharmacological analysis of the iridoid oleuropein. *Drug Res.*, 1972; 22(9); 1476-86.

Zarzuelo A et al, Vasodilator effect of olive leaf, *Planta Med.*, 1991; 57(5):417-9.

The evaluation of long-term effects of cinnamon bark and olive leaf on toxicity induced by streptozotocin administration to rats. *J Pharm Pharmacol* 1999 Nov;51(11):1305-12.

Bao TT, Wang GF, Yang JL. Pharmacological actions of *Cordyceps sinensis*. *Chung Hsi I Chieh Ho Tsa Chih*. 1988 Jun;8(6):352-4, 325-6.

Bok JW, Lermer L, Chilton J, Klingeman HG, Towers GH. Antitumor sterols from the mycelia of *Cordyceps sinensis*. *Phytochemistry*. 1999 Aug;51(7):891-8.

Bucci LR. Selected herbals and human exercise performance. *Am J Clin Nutr*. 2000 Aug;72(2 Suppl):624S-36S.

Chiou WF, Chang PC, Chou CJ, Chen CF. Protein constituent contributes to the hypotensive and vasorelaxant activities of *Cordyceps sinensis*. *Life Sci*. 2000 Feb 25;66(14):1369-76.

Kaczka EA, Trenner NR, Arison B, Walker RW, Folkers K. Identification of cordycepin, a metabolite of *Cordyceps militaris*, as 3'-deoxyadenosine. *Biochem Biophys Res Commun*. 1964;14:456-7.

Kuo YC, Tsai WJ, Shiao MS, Chen CF, Lin CY. *Cordyceps sinensis* as an immunomodulatory agent. *Am J Chin Med*. 1996;24(2):111-25.

Manabe N, Azuma Y, Sugimoto M, Uchio K, Miyamoto M, Taketomo N, Tsuchita H, Miyamoto H. Effects of the mycelial extract of cultured *Cordyceps sinensis* on in vivo hepatic energy metabolism and blood flow in dietary hypoferric anaemic mice. *Br J Nutr*. 2000 Feb;83(2):197-204.

Manabe N, Sugimoto M, Azuma Y, Taketomo N, Yamashita A, Tsuboi H, Tsunoo A, Kinjo N, Nian-Lai H, Miyamoto H. Effects of the mycelial extract of cultured *Cordyceps sinensis* on in vivo hepatic energy metabolism in the mouse. *Jpn J Pharmacol*. 1996 Jan;70(1):85-8.

Wang SM, Lee LJ, Lin WW, Chang CM. Effects of a water-soluble extract of *Cordyceps sinensis* on steroidogenesis and capsular morphology of lipid droplets in cultured rat adrenocortical cells. *J Cell Biochem.* 1998 Jun 15;69(4):483-9.

Xu WH. Water-soluble constituents of *Cordyceps sinensis* (Berk.) Sacc.--the nucleosides. *Chung Yao Tung Pao.* 1988 Apr;13(4):34-6, 63.

Zhang SS, Zhang DS, Zhu TJ, Chen XY. A pharmacological analysis of the amino acid components of *Cordyceps sinensis* Sacc. *Yao Hsueh Hsueh Pao.* 1991;26(5):326-30.

Zhao-Long W, Xiao-Xia W, Wei-Ying C. Inhibitory effect of *Cordyceps sinensis* and *Cordyceps militaris* on human glomerular mesangial cell proliferation induced by native LDL. *Cell Biochem Funct.* 2000 Jun;18(2):93-7.

Zhu JS, Halpern GM, Jones K. The scientific rediscovery of a precious ancient Chinese herbal regimen: *Cordyceps sinensis*: part II. *J Altern Complement Med.* 1998 Winter;4(4):429-57.

Zhu JS, Halpern GM, Jones K. The scientific rediscovery of an ancient Chinese herbal medicine: *Cordyceps sinensis*: part I. *J Altern Complement Med.* 1998 Fall;4(3):289-303.

Bok JW, Lermer L, Chilton J, Klingeman H, Towers GN (1999) Antitumour sterols from the mycelia of *Cordyceps sinensis*. *Phytochemistry* 51:891-898.

Chen DG (1995) Effects of JinShuiBao capsule on the quality of life of patients with chronic heart failure. *Journal of administration of traditional Chinese medicine* 5 (suppl):40-45.

Chen GZ, Chen GL, Tang QM, Sun T, Shai J, Henshall J, Ngu M (1987) Effects of alcoholic extract *Cordyceps sinensis* on T-lymphocyte subsets. *Bulletin of Hunan medical college* 12:4:311-314.

Guo QC, Zhang C (1995) Clinical observation of adjunctive treatment of 20 diabetic patients with JinShuiBao capsule. *Journal of administration of traditional Chinese medicine* 5 (suppl):22.

Huang Y, Lu J, Zhu B, Wen Q, Jia F, Zeng S, Chen T, Li Y, Cheng G, Yi Z (1987) Toxicity study of fermentation *Cordyceps mycelia* B414. *Zhongchengyao Yanjiu* 10:24-25.

Khio T, Tabata H, Ukai S, Hara C (1986) A minor protein-containing galactomannan from a sodium carbonate extract of *Cordyceps sinensis*. *Carbohydrate research* 156:189-197.

Kiho T, Hui J, Yamane A, Ukai S (1993) Polysaccharides in Fungi XXXII. Hypoglycaemic activity and chemical properties of a polysaccharide from the cultured mycelium of *Cordyceps sinensis*. *Biological and pharmaceutical bulletin* 16:12:1291-1293.

Kiho T, Yamane A, Hui J, Usui S, Ukai S (1996) Polysaccharides in fungi XXXVI. Hypoglycaemic activity of a polysaccharide (CS-F30) from the cultured mycelium of *Cordyceps sinensis* and its effect on glucose metabolism in mouse liver. *Biological and pharmaceutical bulletin* 19:2:294-296.

Kiho T, Ookubo K, Usui S, Ukai S, Hirano K (1999) Structural features and hypoglycaemic activity of a polysaccharide (CS-F10) from the cultured mycelium of *Cordyceps sinensis*. *Biological and pharmaceutical bulletin* 22:9:966-970.
Li L, Bao TT, Song ZY (1992) A preliminary study on the mechanisms of lowering cholesterol by *Cordyceps sinensis* Cs-4. *Pharmacology clinics Traditional Chinese medicine*. 8:2:6-9.

Liang YL, Liu, Y, Yang JW, Liu C (1997) Studies on pharmacological activities of cultivated *Cordyceps sinensis*. *Phytotherapy research* 11:3:237-239.

Lin CY, Ku FM, Kuo YC, Chen CF, Chen WP, Chen A, Shio MS (1999) Inhibition of activated human mesangial cell proliferation by the natural product of *Cordyceps sinensis* (H1-A): An implication for treatment of IgA mesangial nephropathy. *Journal of laboratory and clinical medicine* 133:1:55-63.

Manabe N, Azuma Y, Sugimoto M, Uchio K, Miyamoto M, Taketomo N, Tsuchita H, Miyamoto H (2000) Effects of the mycelial extract of cultured *Cordyceps sinensis* on in vivo hepatic energy metabolism and blood flow in dietary hypoferric anaemic mice. *British journal of nutrition* 83:197-204.

Pegler DN, Yao YJ, Li Y (1994) The chinese 'caterpillar fungus'. *The mycologist* 8:1:3-5.

Quio YL, Ma XC (1993) Treatment of 32 tussive patients with JinShuiBao. *Chinese journal of integrated traditional and Western medicine* 13:11:660.

Shao G, You ZH, Cu, XC, Wang XT, Zhu DC, Wang SY, Liao SZ, Shi XZ, Huang JR (1990) Treatment of hyperlipidaemia

with *Cordyceps sinensis*: A double blind placebo control trial. International journal of oriental medicine 15:2:77-80.

Wang Q, Zhao Y (1987) Comparison of some pharmacological effects between *Cordyceps sinensis* (Berk.) Sacc. and *Cephalosporium sinensis* Chen sp. Nov [English abstract 704]. Bulletin Chinese material medica 12:11:682-684.

Xiao Y, Huang XZ, Chen G, Wang MB, Zhu JS, Cooper CB (1999) Increased aerobic capacity in healthy elderly humans given a fermentation product of *cordyceps* CS-4. Medicine and science in sports and exercise 31:5 (suppl):S174.

Xu F (1992) Pharmaceutical studies of submerged culture of *cordyceps* mycelia in China. Chinese pharmaceutical journal 27:4:195-197.

Zhu JS, Halpern GM, Jones K (1998a) The scientific rediscovery of an ancient Chinese herbal medicine: *Cordyceps sinensis* Part 1. The journal of alternative and complementary medicine 14:3:289-303.

Zhu JS, Halpern GM, Jones K (1998b) The scientific rediscovery of a precious ancient Chinese herbal regimen: *Cordyceps sinensis* Part 2. The journal of alternative and complementary medicine 4:4:429-457.

Selected abstracts

[Inhibits Liver Fibrosis](#) - Hepatobiliary Pancreat Dis Int. 2004

[Fertility](#) - Biol Reprod. 2004

[Antioxidant and Memory Enhancing](#) - Arch Pharm Res. 2003

[Hematogenic Lung Metastasis](#) - Receptors Channels. 2003

[T Lymphocytes](#) - Br J Pharmacol. 2003

[Anti-tumour and immuno-stimulating activities](#) - Phytother Res. 2003

[Testosterone Production](#) - Life Sci. 2003

[Inflammatory Mediators](#) - Toxicol Appl Pharmacol. 2003

[Asthma](#) - Zhongguo Zhong Yao Za Zhi. 2001

[Antifatigue and Antistress](#) - Biol Pharm Bull. 2003

[Hypocholesterolemic Effect](#) - Biol Pharm Bull. 2003