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### Medicinal mushrooms

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G.M. HALPERN

# Medicinal mushrooms

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**TITOLO**  
Funghi medicinali

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**PAROLE CHIAVE**

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**Summary**

Mushrooms have been used as medicines by humans for 5,000 years or more. This article deals with five healing mushrooms: maitake, reishi/lingzhi, shiitake, *Cordyceps sinensis*, and *Trametes versicolor* [yunzhi]. Many claims are made for medicinal mushrooms. Out of sheer enthusiasm and/or for commercial motives, authors make exaggerated claims. No medicinal mushroom is a cure-all and no mushroom can make the body unassailable to disease. What mushrooms can do is stimulate the immune response, and/or the functions of the body that are already in place for preventing and fighting disease. Maitake is a culinary mushroom that lowers cholesterol, normalizes blood pressure, curbs appetite and helps against diabetes; shiitake, a delicious culinary mushroom, may help prevent AIDS; reishi/lingzhi, the “mushroom of immortality”, has antitumor and antioxidant effects. *Cordyceps sinensis* is anti-aging and stamina-building, as well as anti-diabetic, and lowers cholesterol. *Trametes versicolor*, from which Krestin and PSP, anticancer drugs, are derived is being used clinically. These are fascinating providers of health benefits for patients with chronic conditions, and should help a growing aging population without side-effects or obscene pricing.

**Riassunto**

I funghi sono stati utilizzati in medicina dagli esseri umani per 5.000 anni o più. Questo articolo si occupa di cinque funghi medicinali: maitake, reishi/lingzhi, shiitake, *Cordyceps sinensis* e *Trametes versicolor* [yunzhi]. Sull'onda del puro entusiasmo e/o per motivi commerciali, si è scritto molto sull'argomento. I funghi medicinali non sono la panacea per tutti i mali e nessun fungo può rendere il corpo inattaccabile alle malattie. Quello che i funghi possono fare è stimolare la risposta immunitaria, e/o le funzioni del corpo che sono già in atto per prevenire e combattere la malattia. Maitake è un fungo utilizzato in cucina che abbassa il colesterolo, normalizza la pressione sanguigna, frena l'appetito ed è di aiuto nel controllo del diabete; shiitake, ancora un fungo delizioso utilizzato in gastronomia, può aiutare a prevenire l'AIDS; reishi/lingzhi, il “fungo dell'immortalità”, ha effetti antiossidanti e antitumorali. *Cordyceps sinensis* ha proprietà anti-invecchiamento e di “costruzione”, così come proprietà

anti-diabetiche e di abbassamento del colesterolo. *Trametes versicolor*, da cui sono derivati Krestin e PSP, farmaci antitumorali, è molto utilizzato a livello clinico. Questi elementi sono gli affascinanti fornitori di benefits sanitari a pazienti con patologie croniche, e dovrebbero aiutare la popolazione nell'invecchiamento senza effetti collaterali o prezzi scandalosi.

## Introduction

My father was a mycologist by necessity: he had to find food when he was close to starvation in Eastern Galicia during his childhood, and in Siberia during the family exile of 1916. He taught me about the *cèpes*, chanterelles, and *trompettes-de-la-mort* when we were hiding from the French police and the Gestapo in the Ardèche in 1941, and around Aiguebelette, Savoie, in 1942. It was then I discovered the shapes, the colors, the taste, and the magic of marvelous and accessible foods. During the short breaks outside the refugee camps in Switzerland (1943–1944), I found myself hoping for rain during the late summer or early fall, and would crawl back to the hidden, secret circles where these delicious mushrooms would sprout, sending their odoriferous messages to be captured only by the initiated.

Mushrooms have been used as medicines by humans for 5,000 years or more. Many mushrooms have properties that can improve

health and well-being. But many claims are made for medicinal mushrooms. A few of these claims border on the outlandish. For example, the label on a medicinal mushroom product from China claims the following: “Effective on cancer, AIDS, hepatitis, headaches, colds, and impotence.” Claims like these raise false hopes. Worse, they cause people to be cynical about medicinal mushrooms and herbal remedies in general.

This article will review recent findings on five major medicinal mushrooms: Maitake [*Grifola frondosa*], a culinary mushroom that lowers cholesterol and helps against diabetes, among other things; Shiitake [*Lentinula edodes*], the delicious culinary mushroom that some believe can help prevent AIDS; Reishi/Lingzhi [*Ganoderma lucidum*], the “mushroom of immortality” and its antitumor and antioxidant effects; *Cordyceps sinensis*, the anti-aging and stamina-building mushroom that generated so many headlines in 1993 when the coach of the Chinese

women’s track team credited it for helping his runners break three world records in a single week; and Yunzhi [*Trametes versicolor*] the mushroom from which Krestin and PSP, some of the anticancer drugs, are derived.

## *Grifola frondosa*

*Grifola frondosa* is a polypore mushroom that grows in clusters at the base of trees, particularly oaks. The mushroom is commonly known among English speakers as **Hen of the Woods**, **Ram’s Head** and **Sheep’s Head**. In the United States’ supplement market, as well as in Asian grocery stores, the mushroom is known by its Japanese name “Maitake”, which means “dancing mushroom”. The fungus is native to the northeastern part of Japan and North America, and is prized in traditional Chinese and Japanese herbology as a medicinal mushroom, an aid to balance out altered body systems to a normal level. In Japan, the Maitake can grow to more than 50 pounds

(20 kilograms), earning this giant mushroom the title “King of Mushrooms.” Maitake is one of the major culinary mushrooms used in Japan.

The underground tubers from which maitake arises have been used in traditional Chinese and Japanese medicine to enhance the immune system. Researchers have also indicated that whole maitake has the ability to regulate blood pressure, glucose, insulin, and both serum and liver lipids, such as cholesterol, triglycerides, and phospholipids, and may also be useful for weight loss.

This year (2009), a phase I/II human trial, conducted by Memorial Sloan–Kettering Cancer Center, showed that maitake could stimulate the immune system of breast cancer patients. Small experiments with human cancer patients have shown that maitake can stimulate NK cells. An *in vivo* experiment showed that maitake could stimulate both the innate immune system and adaptive immune system.

*In vitro* research has shown that maitake can induce apoptosis in cancer cell lines (human prostatic cancer cells, Hep 3B cells, SGC-7901 cells, murine skin carcinoma cells) as well as inhibit the growth of various types of cancer cells (canine cancer cells, bladder cancer cells). Small studies with human cancer patients, revealed that a

portion of the maitake mushroom, known as the “Maitake D-fraction”, possesses anti-cancer activity. *In vitro* research demonstrated the mushroom has potential anti-metastatic properties. In 1997, the U.S. Food and Drug Administration (FDA) approved an Investigational New Drug Application for a portion of the mushroom. Research has shown that maitake has a hypoglycemic effect, and may be beneficial for the management of diabetes. Maitake lowers blood sugar due to the presence of an alpha glucosidase inhibitor.

#### *Lentinula edodes*

The **Shiitake** (*Lentinula edodes*) is an edible mushroom native to East Asia, which is cultivated and consumed in many Asian countries, as well as being dried and exported to many countries around the world. It is a feature of many Asian cuisines including Chinese, Japanese, Korean and Thai. In the East, the shiitake mushroom has long been considered a delicacy as well as a medicinal mushroom. In Chinese, it is called *xiānggū* (香菇, literally “fragrant mushroom”). Two Chinese variant names for high grades of *shiitake* are *donggo* (Chinese: 冬菇, “winter mushroom”) and *huāgū* (花菇, “flower mushroom”, which has a flower-like cracking pattern on the mushroom’s upper

surface); both are produced at colder temperatures.

Research has demonstrated that the shiitake mushroom: stimulates the immune system; contains a cholesterol lowering compound known as eritadenine; possesses anti-bacterial properties; possesses anti-viral properties (including anti-HIV and anti-HSV-1); contains a proteinase inhibitor; reduces platelet aggregation.

Active Hexose Correlated Compound (AHCC) is an  $\alpha$ -glucan rich compound isolated from shiitake. AHCC is a well tolerated compound that possess antioxidant activity, and is metabolized via the CYP450 2D6 pathway. Research has indicated AHCC possesses the following activity: increasing resistance to pathogens *in vivo* (influenza virus, West Nile encephalitis, bacterial infection; various infectious agents); producing an anti-cancer effect (human hepatocellular carcinoma patients); enhancing immune function (controlled trial)

Lentinan<sup>®</sup>, a compound isolated from shiitake, is used as an intravenous anti-cancer agent; it was developed by the Japanese pharmaceutical company Ajinomoto, and designed to treat cancers of the stomach. Human clinical studies have associated lentinan with a higher survival rate, higher quality of life, and lower re-occurrence of cancer (hepatocellular carci-

noma, gastric cancer, colorectal cancer, pancreatic cancer). The City of Hope National Medical Center is currently conducting clinical trials to determine if a select portion of the shiitake mushroom, which includes lentinan, can inhibit lung cancer.

### *Ganoderma lucidum*

**Língzhī** (traditional Chinese: 靈芝 simplified Chinese: 灵芝; Japanese: *reishi*; Korean: *yeongji*, hangul: 영지) is the name for one form of the mushroom *Ganoderma lucidum*, and its close relative *Ganoderma tsugae*. *Ganoderma lucidum* enjoys special veneration in Asia, where it has been used as a medicinal mushroom in traditional Chinese medicine for more than 4,000 years, making it one of the oldest mushrooms known to have been used in medicine. The word *lingzhi*, in Chinese, means “herb of spiritual potency” and has also been described as “mushroom of immortality”. Because of its presumed health benefits and apparent absence of side-effects, it has attained a reputation in the East as the ultimate herbal substance. Lingzhi is listed in the American Herbal Pharmacopoeia and Therapeutic Compendium. *Ganoderma lucidum* produces a group of triterpenes, called ganoderic acids, which have a molecular structure similar to steroid hor-

mones. It also contains other compounds many of which are typically found in fungal materials including polysaccharides such as beta-glucan, coumarin, mannitol, and alkaloids.

Lingzhi may possess anti-tumor, immunomodulatory and immunotherapeutic activities, supported by studies on polysaccharides, terpenes, and other bioactive compounds isolated from fruiting bodies and mycelia of this fungus. It has also been found to inhibit platelet aggregation, and to lower blood pressure (via inhibition of angiotensin-converting enzyme), cholesterol and blood sugar.

Laboratory studies have shown anti-neoplastic effects of fungal extracts or isolated compounds against some types of cancer. In an animal model, *Ganoderma* has been reported to prevent cancer metastasis, with potency comparable to Lentinan from shiitake mushrooms.

The mechanisms by which *G. lucidum* may affect cancer are unknown and they may target different stages of cancer development: inhibition of angiogenesis (formation of new, tumor-induced blood vessels, created to supply nutrients to the tumor), mediated by cytokines, cytotoxicity, inhibiting migration of the cancer cells and metastasis, and inducing and enhancing apoptosis of tumor cells.

Additional studies indicate that ganoderic acid has some protective effects against liver injury by viruses and other toxic agents in mice, suggesting a potential benefit of this compound in the treatment of liver diseases in humans, and *Ganoderma*-produced sterols inhibit lanosterol 14 $\alpha$ -demethylase activity in the biosynthesis of cholesterol. *Ganoderma* compounds inhibit 5-alpha reductase activity in the biosynthesis of dihydrotestosterone. Recently the group of M. Noguchi conducted a double-blind, placebo-controlled randomized and dose-ranging study in 50 men >50y with lower urinary tract symptoms [LUTS]; doses were given qd. The extract of *G. lucidum* was well tolerated and an improvement in International Prostate Symptom Score [IPSS] was observed. The recommended daily dose of *G. lucidum* in men with LUTS is 6 mg.

Besides effects on mammalian physiology, *Ganoderma* is reported to have anti-bacterial and anti-viral activities. *Ganoderma* is reported to exhibit direct anti-viral with the following viruses; HSV-1, HSV-2, influenza virus, vesicular stomatitis. *Ganoderma* mushrooms are reported to exhibit direct antimicrobial properties with the following organisms: *Aspergillus niger*, *Bacillus cereus*, *Candida albicans*, and *Escherichia coli*.

Some oriental preparations containing lingzhi extract are marketed

as a *weight loss aid*. They are advertised as a “slimming formula” in Japanese markets and lingzhi is combined with other herbal extracts. Research is scarce to show the validity of these claims in terms of lingzhi as a weight loss aid.

Due to its bitter taste, lingzhi is traditionally prepared as a hot water extract. Thinly sliced or pulverized lingzhi (either fresh or dried) is added to a pot of boiling water, the water is then brought to a simmer, and the pot is covered; the lingzhi is then simmered for two hours. The resulting liquid should be fairly bitter in taste, with the more active red lingzhi more bitter than the black. The process may be repeated. Alternatively, it can be used as an ingredient in a formula *decoction* or used to make an extract (in liquid, capsule, or powder form). The more active red forms of lingzhi are far too bitter to be consumed in a soup.

### *Cordyceps sinensis*

There are over 680 documented varieties of *Cordyceps*, and one of the most well known varieties of these is *Cordyceps sinensis*. The Latin etymology describes *cord* as “club”, *ceps* as “head”, and *sinensis* as “from China”. The mushroom is known in Tibetan as *yartsa gunbu* or *yatsa gunbu*.

Caterpillar fungi are the result of a parasitic relationship between the fungus *Cordyceps* and the larva of the ghost moth (*Thitarodes*), several species of which live on the Tibetan Plateau (Tibet, Qinghai, West-Sichuan, SW-Gansu & NW Yunnan, all in China, and the Himalayas India, Nepal, Bhutan). The fungus germinates in living organisms (in some cases the larvae), kills and mummifies the insect, and then the *Cordyceps* grows from the body of the insect. *C. sinensis* is a complex traditional Chinese herb with multiple fungi living in its caterpillar and stroma. Its maturation from early May to late June is associated with dynamic changes in proliferation and predominance of the fungi.

It is known in the West as a medicinal mushroom and its use has a long history in Traditional Chinese medicine as well as Traditional Tibetan medicine.

The “caterpillar” [technically it is a larva, since it is hairless] prone to infection by the fungus lives underground in alpine grass and shrublands on the Tibetan Plateau and the Himalayas at an altitude between 3000 m and 5000 m. Spending up to five years underground before pupating, the caterpillar is attacked while feeding on roots. The fungus invades the body of the *Thitarodes* caterpillars, filling its entire body cavity with mycelium and eventually killing

and mummifying it. The caterpillars die near the tops of their burrows. The dark brown to black fruiting body (or mushroom) emerges from the ground in spring or early summer, always growing out of the forehead of the caterpillar. The long, usually columnar fruiting body reaches 5-15 cm above the surface and releases spores.

The first mention of *Cordyceps sinensis* in traditional Chinese Medicine was in Wang Ang’s 1694 compendium of material medica, *Ben Cao Bei Yao*. In the 18th Century it was listed in Wu Yiluo’s *Ben cao cong xin* (“New compilation of Materia Medica”).

The entire fungus-caterpillar combination is hand-collected for medicinal use.

The fungus is a medicinal mushroom which is highly prized by practitioners of Tibetan medicine, Chinese medicine and traditional herbal Folk medicines, in which it is used as an aphrodisiac and as a treatment for a variety of ailments from fatigue to cancer. It is regarded as having an excellent balance of yin and yang as it is apparently both animal and vegetable (though it is in actuality not vegetable, but fungi). Assays have found that *Cordyceps* species produce many pharmacologically active substances. They are now cultivated on an industrial scale for their medicinal value.

Laboratory-grown *C. sinensis* mycelium has similar clinical efficacy and less associated toxicity. Only one toxicity case of constipation, abdominal distension, and decreased peristalsis, two cases of irregular menstruation, and one case report of amenorrhea following ingestion of tablets or capsules containing *C. sinensis* have been reported. In Chinese medicine *C. sinensis* is considered sweet and warm; it enters the Lung and Kidney channels; the typical dosage is 3-9 grams.

An experiment noted *Cordyceps sinensis* may protect the liver from damage. In 1990, a study was undertaken in which 32 hepatitis B sufferers were given 3,750 mg of *Cordyceps* a day for 30 days. Positive antibodies to the virus changed to negative in 21 patients. In 23 patients, tests showed that liver function had improved.

*Cordyceps* can relieve acute kidney failure brought on by an adverse toxic reaction to aminoglycoside antibiotics. Studies have shown that *Cordyceps* has significant kidney-protective effects against gentamycin and kanamycin. In a controlled study of patients who had developed a condition called 'gentamycin kidney toxicity', half the patients were given an extract of the cultured mycelium of *Cordyceps* while still taking gentamycin. The control group continued to receive the gentamycin and addi-

tional drugs to neutralize its toxicity. By the sixth day, 89% of the *Cordyceps* group had made a complete clinical recovery from the toxicity of gentamycin; in comparison, only 45% of the control group recovered. A large, placebo-controlled clinical study of *Cordyceps* in kidney-transplant patients was conducted at Nanfang Hospital and Taizhou Medical School, in China, to test its ability to protect the kidneys from cyclosporine toxicity. Sixty-nine stable kidney-transplant patients were randomly assigned to two groups: one group of 39 patients received a placebo, while the other 30 patients received *Cordyceps*. All the patients received cyclosporine, and throughout the 15-day trial, they were monitored for signs of kidney toxicity. Researchers found less kidney toxicity in the *Cordyceps* group, and the longer patients took the mushroom powder, the less toxicity there was. Based on their findings, the doctors who conducted the trial now recommend *Cordyceps* for kidney-transplant patients on cyclosporine. It is interesting to note, that cyclosporine is produced by another species of *Cordyceps*, *C. subsessilis*, or at least its anamorphs.

Researchers have noted that the Caterpillar fungus has a hypoglycemic effect; *Cordyceps* is effective in lowering both blood glucose and plasma insulin, improving

glucose metabolism by enhancing insulin sensitivity, and improving oral glucose tolerance. It appears to lower blood sugar levels through specific polysaccharides (CS-F10 and CS-F30). Studies have conclusively demonstrated higher tolerance to cold (66 elderly subjects), improvement in fatigued patients (117 subjects), increased SOD levels (37 subjects). It is also possibly the most active natural medicine vs. arrhythmias (>75% improved).

A classical major indication is chronic respiratory disease (COPD, chronic bronchitis, chronic asthma) where the rate of success averages 90% when compared to placebo ( $p < 0.01$ ); treatment was 4 weeks in 200 patients, with a daily average dose of 3-4.5 g. Another classical indication is erectile dysfunction; in 2 studies vs. placebo, improvement was >65%.

Bioxanthracenes from *Cordyceps pseudomilitaris* BCC 1620 demonstrated anti-malarial activity. *Cordyceps sinensis* supplement enhances recovery from taxol-induced leucopenia.

The group of J.S. Zhu has reported at the Symposium on the effects of CordyMax™ on lipids in patients with moderate hyperlipidemia; the study lasted 8 weeks and was placebo-controlled. LDL levels were reduced by 5.4% ( $p = 0.002$ ), oxLDL by 22.9% ( $p = 0.001$ ); HDL in females in-

creased by 31.1% ( $p < 0.001$ ), and in all subjects the atherosclerotic index was reduced by 29% ( $p < 0.001$ ).

The same group examined the anti-fatigue and endurance enhancement properties of CordyMax® with use of sports physiology methods. In double-blind clinical trials with use of an incremental work rate protocol on a cycle ergometer and/or treadmill, they found that CordyMax increased VO<sub>2</sub>max by 7.0%, anaerobic threshold by 12.6%, maximal ventilation by 10.4% and maximal work rate by 5.9%, indicating improvement of aerobic exercise capacity in healthy sedentary adults of advanced age. In healthy young athletes and by use of a constant work rate protocol, CordyMax therapy increased O<sub>2</sub> pulse by 7.6% and reduced heart rate (HR) by 2.2%, RER by 2.5%, and lactic acid by 10.5% during endurance exercise, indicating improvement of cardiovascular and metabolism functions during endurance exercise. CordyMax also accelerated HR recovery 3 min post maximal exercise by 6.3%. In summary, CordyMax supplementation influences favorably aerobic capacity and cardiovascular, pulmonary, and metabolic functions during maximal and endurance exercise, improves fatigue and endurance performance, and facilitates recovery from exercise.

The group of Prof. J.Y Wu, at the Hong Kong Polytechnic University has engineered a mycelial strain of *Cordyceps sinensis* named Cs-HK-1. Both the ethanol- and water-extract have demonstrated powerful anti-tumor effects in animal (human transgenic) tumors. Kunming mice, each carrying a weight of 6% body-weight on the tail in a 40cm-deep water pool at 25°C could swim twice as long after being fed Cs-HK-1, when compared to ClNa controls. Outside of the East, the world was largely unaware of *Cordyceps*. This changed, when the fungus caught the world's attention due to three female Chinese athletes, Wang Junxia, Qu Yunxia, and Zhang Linli. These athletes broke 5 world records for 1,500, 3,000 and 10,000 meters in 1993 at the National Games in Beijing, China. The amount of new world records being set at a single track event caused much attention and suspicion. Following the races, the women were expected by some to fail drug tests for anabolic steroids. However, the athletes' tests revealed no illegal substances, and coach Ma Junren told reporters that the runners were taking *Cordyceps sinensis* and turtle blood at his request. However for the Sydney Olympics, Ma Junren withdrew some of his athletes at the last minute. It was speculated that a new doping test would have revealed

illegal doping, thus half a dozen Chinese field and track athletes were left home.

### *Trametes versicolor*

*Trametes versicolor* - formerly known as *Coriolus versicolor* and *Polyporus versicolor* - is an extremely common polypore mushroom which can be found throughout the world. *Versicolor* means 'of several colours' and it is true that this mushroom is found in a wide variety of different colours. *T. versicolor* is commonly called Turkey Tail in the United States because of its resemblance to the tail of the wild turkey. *T. versicolor* is recognized as a medicinal mushroom in Chinese medicine under the name *yun zhi* (simplified Chinese: 云芝, traditional Chinese: 雲芝). In China and Japan *T. versicolor* is used as in immunoadjuvant therapy for cancer. *Polysaccharide-K* (*Krestin*, *PSK*), is a protein-bound polysaccharide isolated from *Trametes versicolor*, which is used as an immune system boosting agent in the treatment of cancer in some European countries as well as China and Japan. *PSK* is extracted from the mycelial strain CM-101 and is approximately 62% polysaccharide and 38% protein. The glucan portion of *PSK* consists of a beta 1-4 main chain and beta 1-3 side chain, with beta 1-6 side chains.



The polypeptide portion is rich in aspartic, glutamic, and other amino acids and is orally bioavailable. In Japan, PSK is approved as an adjuvant for cancer therapy and is covered by government health insurance.

The success of Krestin inspired Chinese researchers to develop a *Trametes versicolor* extract of their own called PSP (*Polysaccharide-Peptide*). PSP was first isolated from cultured deep-layer mycelium of the COV-1 strain of *Trametes versicolor* in 1983. PSP may contain at least four discrete molecules, all of which are true proteoglycans. PSP differs from PSK in its saccharide makeup, lacking fucose and containing arabinose and rhamnose. The polysaccharide chains are true beta-glucans, mainly 1-4, 1-2 and 1-3 glucose linkages with small amounts of galactose, mannose, and arabinose linkages. PSP can be easily delivered by oral route.

PSK has documented anticancer activity *in vitro*, *in vivo* and in human clinical trials. Research has also demonstrated that PSK can reduce mutagen-induced, radiation-induced, and spontaneously-induced cancer development. PSK has shown to be beneficial as an adjuvant in the treatment of gastric, esophageal, colorectal, breast and lung cancers. Human clinical

trials suggest PSK can reduce cancer recurrence when used as an adjuvant and research has demonstrated that the mushroom can inhibit certain human cancer cell lines *in vitro*.

In a double-blind, placebo-controlled randomized study, physicians at the Queen Mary Hospital of the University of Hong Kong evaluated the effects of a 28-day administration of PSP on patients who had completed conventional treatment for advanced non-small cell lung cancer (NSCLC), a very aggressive form of lung cancer. Thirty-four patients, with no significant difference in their baseline demographic, clinical, or tumor characteristics, or previous treatment regimens, were enrolled into each of the PSP and placebo groups. After 28 days of treatment, there was a significant improvement in the number of white blood cells, and percent of body fat among the PSP-treated patients, but not the placebo-treated patients; this difference was statistically very significant. Although the evaluable PSP patients did not improve in NSCLC-related symptoms, there were significantly less PSP patients withdrawn due to disease progression than their control counterparts: 5.9% and 23.5%, respectively. There was no reported adverse reaction attribu-

table to PSP. Researchers concluded that PSP treatment appeared to be associated with slower deterioration in patients with advanced non-small cell lung cancer.

The United State's top ranked cancer hospital, the MD Anderson has reported that it is a "promising candidate for chemoprevention due to the multiple effects on the malignant process, limited side effects and safety of daily oral doses for extended periods of time."

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