American Herbal Pharmacopoeia®
and Therapeutic Compendium

Reishi Mushroom
Ganoderma lucidum

Standards of Analysis, Quality Control, and Therapeutics

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Reporting on the use of proprietary products reflects studies conducted with these and is not meant to be a product endorsement.

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Cover Photograph
Reishi mushroom *Ganoderma lucidum* fruiting body (cultivated)

Photograph courtesy of North American Reishi, Gibons, British Columbia, Canada

NOMENCLATURE

Ganoderma lucidum (Curtis: Fr.) P. Karst.;
Ganoderma japonicum (Fr.) Lloyd syn. *G. sinense* Zhao, Xu et Zhang.

Family

Ganodermataceae

Definition

Reishi mushroom consists of the dried fruiting bodies of *Ganoderma lucidum* (Curtis: Fr.) P. Karst. or *Ganoderma japonicum* syn. *G. sinense* Zhao, Xu et Zhang conforming to the methods of identification and standards provided.

Common Names

United States:	Reishi mushroom (*Herbs of Commerce*), ganoderma.
China:	Ling zhi, ling zhi cao, ling chih, hong ling zhi, chi zhi (*Ganoderma lucidum*); he ling zhi, zi zhi (*Ganoderma japonicum*) (Mandarin).
Japan:	Reishi, mannentake; rokkaku reishi (antler form).
Korea:	Young ji.
Vietnam:	Ling chi.

HISTORY

Numerous legends surrounding reishi mushroom provide an historical record which spans 2000 years. Traditionally, it was used in China by Taoist monks to promote a centered calmness, improve meditative practices, and attain a long and healthy life. Chinese royalty, seeking longevity, held reishi mushroom in high esteem. It became immortalized throughout Chinese culture in paintings, statues, silk tapestries, and on the robes of emperors. Reishi mushroom has also been revered in Japanese culture where it is considered to be the most important of all the Japanese medicinal polypores [sarunokoshikake] (Matsumoto 1979). Traditionally, Chinese and Japanese herbalists referred to six different colors of reishi mushroom: green, black, white, red, yellow, and purple (Hirotani and Furuya 1990; Hsu and others 1986). The characters making up the Chinese name for reishi mushroom [ling zhi] originally depicted a "shaman crying for rain", representing the magical or divine properties which were associated with ling zhi. Reishi mushroom has also been commonly referred to as the "mushroom of immortality", "ten-thousand-year mushroom", "mushroom of spiritual potency", and "spirit plant" (Huang 1993; Liu and Bau 1994).

Reishi mushroom was listed among the superior tonics [shang pin] in the most famous of all Chinese materia medicas, the *Shen Nung Ben Cao Jing* (206 BC-AD 8) (Matsumoto 1979; Unschuld 1986). Superior herbs were among the most highly regarded of all medicines since they were considered to prolong life, prevent aging, boost qi, make the body light and limber, and corresponded to heaven. Reishi mushroom was listed as the most respected out of the 120 superior tonics cited. Specifically, in this text, red reishi was reported to treat binding in the chest, tonify the heart, nourish the center, sharpen the wit, and improve memory. In addition to its physical properties, reishi was said to "cultivate virtue" (Yang 1997).

The cultivation of as many as 38 different types of reishi mushroom was recorded on a stone tablet from the year 1124; this was found at the side of the Seven Buddhas Pavillion in the Mountain of Maiji in the southernmost part of Gansu province (Lin 1994). Interestingly, reishi mushroom was often not included in many of the common materia medicas throughout Chinese history, possibly due to its relative rarity or perhaps due to it being reserved only for use by royalty. It is similarly not included in many of the standard English-language Chinese materia medicas of today.

Because of its widespread use as a tonifier, modern Chinese physicians readily employ reishi mushroom to support immune resistance in patients undergoing conventional chemotherapy and/or radiation treatment for various forms of cancer. Additionally, it is used as an antihepatotoxin, cholesterol-lowering, and hypoglycemic agent and is considered to have marked positive effects on sleep and mental well-being. Though it is popular among consumers in Japan and is widely used by Asian physicians and herbalists, reishi mushroom was only recently included in the *Pharmacopoeia of the People's Republic of China* (2000) and is absent from the *Japanese Pharmacopoeia*.

Figure 1 Reishi mushroom *Ganoderma lucidum*
Source: *Icons of Medicinal Fungi*, Science Press, Beijing, China

IDENTIFICATION

Macroscopic Identification

Both *G. lucidum* and *G. japonicum* are officially accepted in the Chinese pharmacopoeia as reishi, the former producing red reishi [hong ling zhi] and the latter black reishi [he ling zhi]. Both forms are generally sold dried and whole. Following are macroscopic descriptions of both species.

Ganoderma lucidum (Curtis: Fr.) P. Karst. **Fruiting Body:** Annual, persisting many months, growth form highly variable, specimens from North America typically large and shelf-like while those from the tropics and Old World are usually smaller with cap and stalk; intermediate forms exist, including a rare antlered form. **Cap:** Circular to semicircular, fan- or kidney-shaped, 2-20 (35) cm broad, 4-8 cm thick; upper surface smooth or with concentric ripples, corky, tough, with or without varnished appearance; dark red to reddish-brown or reddish-black in center, ochre or yellowish toward the margin, edge itself white when actively growing, flesh yellowish-brown to dark brown. The cap of fresh reishi is soft, cool, moist, and somewhat leathery unless it is old, when it becomes corky and tough. When dry, the cap becomes woody. **Pores:** 1(2) layer(s) of spore-producing tubes, each tube 2-20 mm long; pores minute, dense (4-7 per μm), whitish when fresh, aging or bruising brown. **Stalk:** When present, 3-14 cm long, 0.5-4 cm thick, often twisted, may be enlarged at base, same color and appearance as cap surface.

Antler form: In China and Japan, the rare antlered form of *G. lucidum* is highly prized medicinally. This form develops naturally or is cultivated in environments with little light and high levels of carbon dioxide. The shapes are extremely varied, predominantly being differentiated by their lack of a well-formed cap and their mostly branched and gnarled appearance.

Aroma: Musty, fungus-like. **Taste:** Dependent upon strain. Strains high in triterpenes are characteristically intensely bitter (Kubota and others 1982; Nishitoba and others 1989). Those high in polysaccharides and low in triterpenes are bland or woody. **Fracture:** Tough, fibrous, and tenacious, breaking into strips revealing the different layers of the fruiting body.

Powder: Light to dark brown; soft, spongy, and fibrous.

Distribution: Primarily saprophytic, but may be parasitic. Found primarily on the base, roots, or stumps of hardwoods (especially maples [*Acer* spp.] in North America), rarely on conifers. Cosmopolitan in distribution.

Ganoderma japonicum (Fr.) Lloyd syn. *G. sinense* Zhao, Xu et Zhang. **Fruiting Body:** Annual, persisting many months; stipitate. **Cap:** Circular to semicircular, fan- or kidney-shaped, 2.5-9.5 cm broad, 0.4-1.2 cm thick; upper surface smooth or with concentric ripples, corky, tough, with or without varnished appearance; purplish-black to black, margin narrow, the same color as cap, edge pale brown when actively growing, flesh yellowish-brown to dark brown. The cap of fresh reishi is soft, cool, moist, and somewhat leathery unless it is old, when it becomes corky and tough. When dry, the cap becomes woody. **Pores:** 1(2) layer(s) of spore-producing tubes, each tube 0.3-1 cm long, pores 5-6 per mm, off-white or light to dark brown. **Stalk:** When present, dorsally or laterally attached, 7-19 cm long, 0.5-1 cm thick, often twisted, may be enlarged at base, same color and appearance as cap surface.

Aroma: Smoky or musty. **Taste:** Mildly bitter. **Fracture:** Tough, fibrous, and tenacious, breaking into strips revealing the different layers of the fruiting body.

Powder: Dark brown; soft, spongy, and fibrous.

Distribution: Primarily saprophytic, but may be parasitic. Found primarily on rotten logs or stumps, occasionally on dead bamboo. China and Taiwan.

Other species: *Ganoderma tsugae* Murrill and *Ganoderma applanatum* (Pers.) Pat. can sometimes be traded in the United States as reishi. The cap surface of *G. tsugae* is quite similar to that of *G. lucidum*; however, its flesh is white, it usually has a stalk, and it is confined to conifers (especially hemlocks [*Tsuga* spp.] in North America) (Arora 1986; Lincoff 1984; Ying and others 1987). *G. applanatum* (artist's conk) is easily distinguished from *G. lucidum*. The fruiting body is shelflike, usually lacking a stalk, and is fan-shaped or semicircular in outline. The cap is 5-75 cm broad and 2-20 cm thick, with a hard woody surface that is gray to brown and is not varnished. It is furrowed or ridged and becomes knobby with age. When fresh, the flesh is bright yellow-brown to rusty-brown, brown, or dark brown. The pore surface is white when fresh, turning brown when scratched or old. This species is found on both hardwoods and conifers. While traded domestically, it is not commonly used interchangeably with *G. lucidum* though some harvesters refer to this as reishi.

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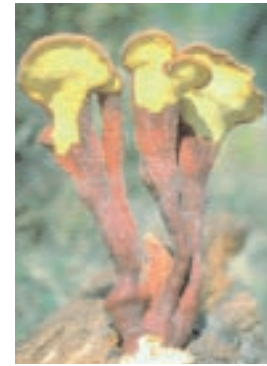2f.

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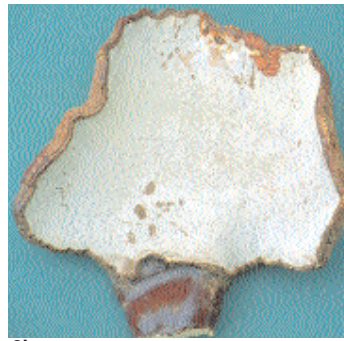**Figures 2a-w** **Various forms of *Ganoderma lucidum* available in commerce**

a. Wild Chinese reishi mushroom. Photograph © 2000 Roy Upton, Soquel, CA.
b. Wild domestic reishi mushroom.
c. Wild domestic reishi mushroom. Photographs © 2000 Roy Upton, Soquel, CA.
d. Wild Chinese reishi mushroom.
e. Cultivated Chinese reishi mushroom. Photograph courtesy of North American Reishi, Gibons, British Columbia, Canada.
f. Cultivated Chinese duanwood reishi mushroom.
g. Cultivated Chinese duanwood reishi mushroom.
h. Cultivated Chinese duanwood reishi mushroom.
i. Cultivated Chinese duanwood reishi mushroom. Photographs Joanne Thompson, Santa Cruz, CA © 2000 American Herbal Pharmacopoeia™.
j. Cultivated Chinese reishi mushroom.
k. Cultivated Chinese reishi mushroom.
l. Cultivated Chinese reishi mushroom.
m. Cultivated reishi mushroom (Texas). Photograph © 2000 Roy Upton, Soquel, CA.
n. Cultivated Chinese reishi mushroom.
o. Wild reishi mushroom. Photograph © 2000 Roy Upton, Soquel, CA.
p. Cultivated Chinese reishi mushroom.

q. Cultivated domestic reishi mushroom.
r. Cultivated domestic reishi mushroom. Photograph © 2000 Roy Upton, Soquel, CA.
s. Cultivated Chinese reishi mushroom antler form. Photograph © 2000 Roy Upton, Soquel, CA.
t. Cultivated Chinese reishi mushroom antler form. Photograph © 2000 Roy Upton, Soquel, CA.
u. Cultivated Chinese reishi mushroom antler form. Photograph © 2000 Roy Upton, Soquel, CA.
v. Cultivated Chinese reishi (poor quality eaten by insects). Photograph © 2000 Roy Upton, Soquel, CA.
w. Cultivated reishi mycelium culture. Photograph courtesy of North American Reishi, Gibons, British Columbia, Canada.

Samples courtesy of Asia Naturals, San Francisco, CA; Gourmet Mushrooms, Sebastopol, CA; Christopher Hobbs, Williams, OR; Mayway Trading, San Francisco, CA; Organotech™, San Antonio, TX; Tai Sang Trading, San Francisco, CA; Teeguarden Herbs, Santa Monica, CA.

3a.

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Figures 3a-k **Various forms of *Ganoderma japonicum, Ganoderma tsugae,* and *Ganoderma applanatum* in commerce**

a. Wild domestic *Ganoderma tsugae*. Photograph © 2000 Roy Upton, Soquel, CA.
b. Wild domestic *Ganoderma tsugae*. Photograph © 2000 Roy Upton, Soquel, CA.
c. Wild domestic *Ganoderma tsugae*. Photograph © 2000 Roy Upton, Soquel, CA.
d. Cultivated Chinese *Ganoderma tsugae.* Photograph courtesy of Professor Zhi-Bin Lin, Beijing Medical University, Beijing, China.
e. Cultivated Chinese *Ganoderma japonicum.* Photograph courtesy of Greg Geilman.
f. Cultivated Chinese *Ganoderma japonicum.* Photograph © 2000 Roy Upton, Soquel, CA.

g. Cultivated Chinese *Ganoderma japonicum.* Photograph © 2000 Roy Upton, Soquel, CA.
h. Cultivated Chinese *Ganoderma japonicum.* Photograph courtesy of Professor Zhi-Bin Lin, Beijing Medical University, Beijing, China.
i. Unknown species of cultivated reishi. Photograph © 2000 Roy Upton, Soquel, CA.
j. Unknown species of wild domestic reishi growing on hardwood. Washington, DC. Photograph © 2000 Roy Upton, Soquel, CA.
k. *Ganoderma applanatum.* Photograph courtesy of Professor Zhi-Bin Lin, Beijing Medical University, Beijing, China.

Microscopic Identification

Ganoderma lucidum: The mushroom characteristically fractures into tiny strips rather than forming a typical powder. The powder is composed primarily of hyphae of three types: generative, binding, and skeletal with infrequent basidia and basidiospores (spores). Generative hyphae are thin-walled, colorless, and possess clamps which are short appendages branching off. Binding hyphae are also colorless, but with thicker walls, and are highly branched with slender tapering ends. Skeletal or structural hyphae in the primary fruiting body are thick-walled, yellowish-brown, and only slightly branched; skeletal and structural hyphae at the crust of the pileus (cap) are darker in color and show a palisade appearance and rounded ends.

In cross section, the outer part of the cap is coriaceous with enlarged yellow-colored hyphae. The underlying plectenchyma consists of very thin and densely packed hyphae. The inner part of the cap shows a network of gray-colored hyphae approximately 2-7 μm in diameter. While most hyphae run horizontally, a smaller amount run vertically. The vertical tubes at the lower side of the cap are dark brown in color, approximately 200 μm in diameter. Their inner surface is covered with the light hymenial line, forming dark brown basidiospores. The basidia are ellipsoidal or spathulate, infrequent, thin-walled, and numerous. The spores are ovoid or elliptical with a dotted surface and up to 8 μm in length. The spore walls are doubled with the darker inner layer occasionally protruding through the outer hyaline layer, giving a shiny appearance. Starch and calcium oxalate are absent.

Powder: Light brown, fragments of the plectenchyma of the cap, dark brown fragments of the tubes; basidiospores.

Note: It is difficult to differentiate between species of reishi microscopically. All are characterized by the presence of a network of hyphae. It is relatively easy to differentiate between fruiting body and mycelium biomass preparations. The network of hyphae of the fruiting body is well developed while that of the mycelium biomass is sporadic or lacking.

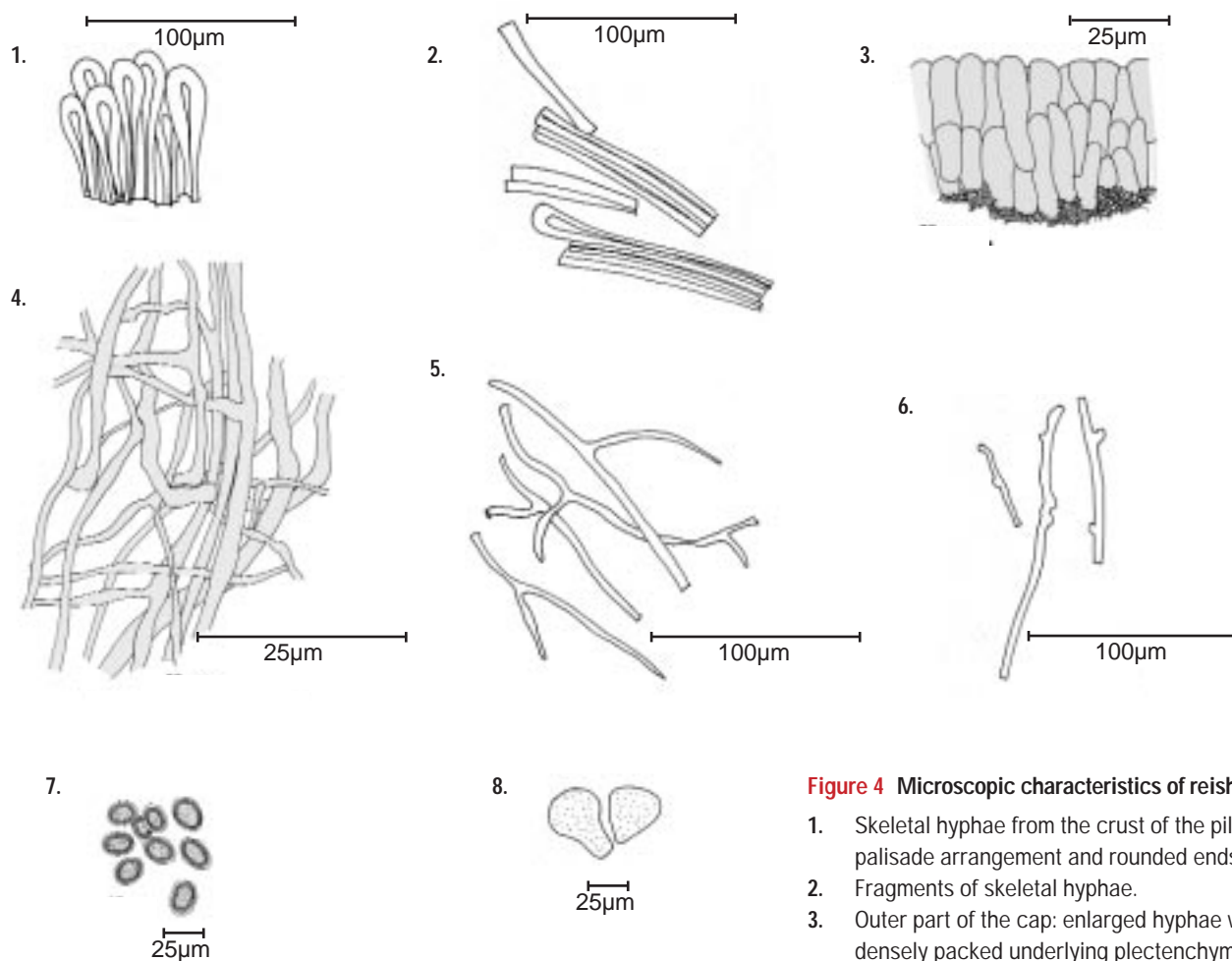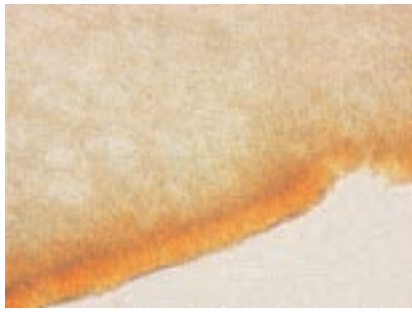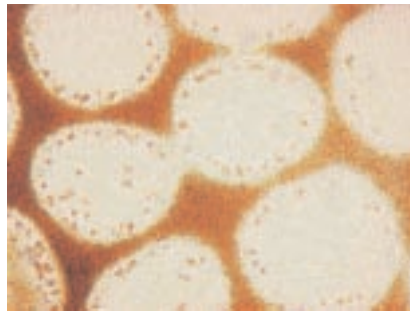**Figure 4** **Microscopic characteristics of reishi mushroom**

1. Skeletal hyphae from the crust of the pileus showing palisade arrangement and rounded ends.
2. Fragments of skeletal hyphae.
3. Outer part of the cap: enlarged hyphae with the densely packed underlying plectenchyma.
4. Inner part of the cap.
5. Binding hyphae.
6. Generative hyphae with clamps.
7. Basidiospores.
8. Basidia.

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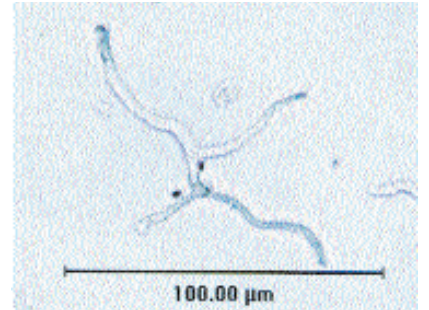
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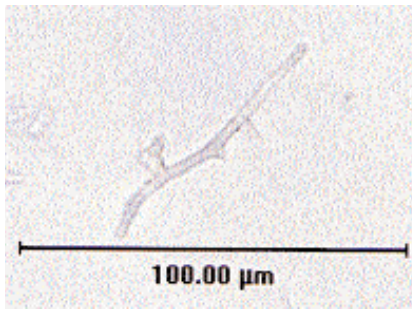
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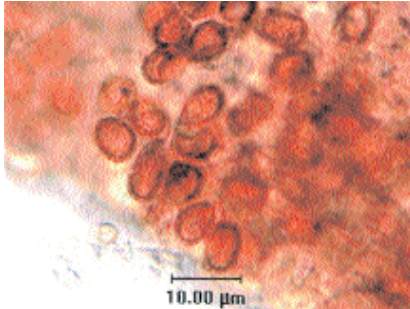
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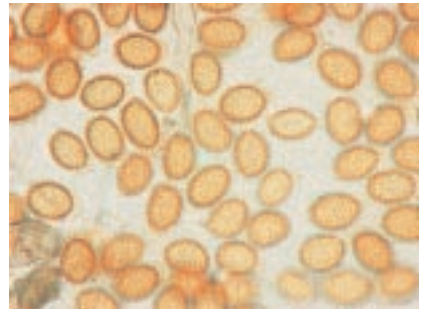
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Figure 5 **Microscopic images of reishi mushroom**
1. Outer part of the cap in cross section.
2. Tubes in cross section.
3. Vertical tubes in longitudinal view.
4. Mycelium of the cap.
5. Skeletal hyphae from the crust of the pileus showing palisade arrangement and rounded ends (400X).
6. Binding hyphae (400X).
7. Generative hyphae with clamps (400X).
8. Basidiospores (1000X).
9. Spores (oil immersion).

COMMERCIAL SOURCES AND HANDLING

Collection

Reishi mushroom is collected after the fruiting body has fully matured. After collecting, dirt and extraneous matter are removed and the fruiting body is dried. Most of the reishi mushroom occurring in trade is cultivated and is characterized by mushroom caps of relatively uniform shape within cultivated lots; sizes may vary. Wild reishi may also be found, the caps of which will be of varying shapes, sizes, and forms. In China, wild reishi mushroom grows predominantly on the roots and stumps of dead oaks and other hardwood trees (Cheung and Li 1986; Ying and others 1987). In Japan, wild reishi mushroom is reported to grow exclusively on old plum trees and is known as Kobai reishi mushroom. It is extremely rare (Matsumoto 1979). In North America, reishi mushroom frequently grows on hardwoods, but it can also be found on conifers (Arora 1986). Currently, the majority of reishi mushrooms in American commerce are imported from Chinese sources. Reishi is under cultivation domestically but supplies of fruiting body are limited. It can be cultivated on wood logs which are often encased with soil and sawdust.

There are numerous strains of reishi which vary widely in size, shape, and color. The average size of reishi mushroom found in San Francisco (Chinatown) ranged from 7.5-12.5 cm for red *G. lucidum* [hong ling zhi/chi zhi] and *G. tsugae* [Songshan ling zhi] and from 10-20 cm for black *G. japonicum* [he ling zhi/zi zhi].

In China, a particular type of reishi, duanwood reishi, is cultivated on linden trees. In Japan, an antler form of reishi is sometimes cultivated and is differentiated by its branched appearance in contrast to the fully developed rounded cap.

Qualitative Differentiation

In traditional Chinese medicine (TCM), the quality of reishi mushroom is predominantly determined by color, shape, and size. Reishi mushroom that is large, deep red, and has a swirled ram's horn pattern is generally considered to be the highest quality. When cultivated, reishi mushrooms are relatively consistent in size, color, and shape. Some buyers prefer the rarer wild fruiting body or cultivated antler form. These will be inconsistent in size, color, and shape and will often have a very gnarled appearance. No correlative pharmacologic information regarding these different types was available.

The constituent concentration varies significantly between the different portions of the fruiting body (Hirotani and Furuya 1990). Quantitatively, the cap yields the richest source of triterpenes, followed by the stem, and then the spores. The underside of the outer layer of the cap yields a higher concentration of triterpenes than the other sections of the cap. Otherwise, the constituent pattern of the various layers of the cap is similar (Miyahara and others 1987). Samples grown on cherry wood reportedly yield higher amounts of triterpenes but grow more slowly and produce less mass than samples grown on oak. When various forms were analyzed during the initial fruiting stage of an antlered form [Saegusa], ganoderic acids and lucidenic acids were reported to be absent. However, these compounds began to develop within 1 week of fruiting, subsequently becoming major constituents (Kohda and others 1985).

At least two particular characteristic constituent patterns have been identified in reishi mushroom cultivars. These are designated as C_{27}, strains rich in lucidenic acid, and C_{30}, strains rich in ganoderic acid. The fruiting body has also been classified as being rich in ganoderic acid A while the mycelium has been most noted for its concentration of ganoderic acid T (Hirotani and Furuya 1990). Comparative constituent analysis was conducted on three strains of Japanese reishi mushroom: red [sekishi], purple [shishi], and black [kokushi]. The red and purple strains analyzed had similar triterpenoid patterns; the black reishi mushroom analyzed contained little acid material (Hirotani and others 1993)

In an effort to yield germanium-rich reishi mushroom, some producers enrich the growing substrate with germanium. Wild reishi mushroom has been reported to yield 1.3-17.8 ppm of germanium. In one cultivation study, enriching the growing medium with germanium dioxide at 1.5 ppm, 5 ppm, and 10 ppm resulted in germanium concentrations of 5.1 ppm, 15.3 ppm, and 24.6 ppm, respectively (Chiang and Chen 1991). Whether this has any pharmacologic effect has not been determined.

Drying

The mushrooms are generally dried in the sun (Liu and Bau 1994) with a sufficient amount of air flow to prevent molding.

Handling

Reishi mushroom should be cleaned of dirt and other foreign matter. Since reishi mushrooms are woody and very hard, they require no other special handling.

Storage

Reishi mushroom should be stored in a cool, dry, dark area protected from insect infestation and moisture. Because of its woody nonvolatile nature, the constituents of reishi mushroom remain stable in normal temperatures and average levels of humidity.

Contamination

Reishi mushroom is prone to both insect infestation and contamination from surface molds on the pore layer, especially if the mushroom is exposed to dampness or is not properly dried.

Preparations

The triterpenes are rather insoluble in cold water but are extractable in ethanol and hot water. These compounds are primarily responsible for the bitter taste associated with reishi. In addition to its high concentration of large molecular weight water-soluble polysaccharides, reishi mushroom

consists of a matrix of the polysaccharide chitin. Chitin is largely indigestible by the human body and is partly responsible for the physical hardness of reishi. Therefore, reishi mushroom must be decocted when making water preparations. For powdered or tableted products, the mushroom must be ground into a very fine powder or made into an extract powder to assure bioavailability. Traditionally, reishi mushroom was slowly simmered for approximately 20-60 minutes prior to adding other herbal ingredients to a decoction.

Decoction:

Boil 2-15 g of chopped or powdered reishi mushroom in approximately 2 L of water. Decoct slowly until 2/3 of the water is reduced.

Alcohol Extract (traditional):

Macerate 90 g of chopped or powdered reishi mushroom in 500 mL of rice wine for at least 10 days (Liu and Bau 1994).

CONSTITUENTS

Triterpenes

More than 100 different highly oxygenated lanostanoid triterpenes have been identified in reishi mushroom. These include multiple pairs of C-3 stereoisomers and C-3/C-15 positional isomers (Shiao and others 1994). The predominant triterpenes are ganoderic acids A-Z. Other triterpenes include ganoderal A and B (Morigiwa and others 1986; Nishitoba and others 1988b), ganoderol A and B (Morigiwa and others 1986), epoxyganoderiol A-C (Nishitoba and others 1988b), ganoderenic acid A-D (Komoda and others 1985), ganodermic acids (Shiao and others 1988), ganoderiol A-I (Nishitoba and others 1988a; Sato and others 1986), ganodermanontriol, ganodermatriol (Sato and others 1986), ganolucidic acids A-E, lucidone A-C, lucidenic acids A-M (Nishitoba and others 1985a, 1985b, 1985c, 1986), lucidadiol, and lucidal (González and others 1999).

Polysaccharides

Numerous bioactive polyglycans (polysaccharides) are contained in all parts of the fruiting body. Among those present in reishi mushroom are neutral polysaccharides (β-1-3, β-1-6 homo D-glucan), acidic glucan and polyglycan, protein-bound heteroglucan, arabinoxyoglucan (a highly branched heteroglucan), a heteroglycan with a β-1-4 core, and peptidoglycans (ganoderan A, B, and C) (Chen and Miles 1996). The basic structure of the major glucans β-1-3 and β-1-6 homo D-glucan is β-1-3 D-glucopyronan with 1-15 units of β-1-6 monogluosyl side chains (Chen and Miles 1996).

Amino Acids (mol %)

Serine (15.2), alanine (14.8), glycine (12.7), threonine (12.4), aspartic acid (9.9), glutamic acid (8.1), proline (6.9), valine (5.3), and other minor amino acids (Hikino and others 1985).

Other Constituents

Steryl esters (ergosterol), adenosine (5'deoxy-5'-methylsulphinyladenosine) (Shiao and others 1994), fungal lysozyme, fatty acids, and a protease (Jong and Birmingham 1992; Miyahara and others 1987; Ying and others 1987).
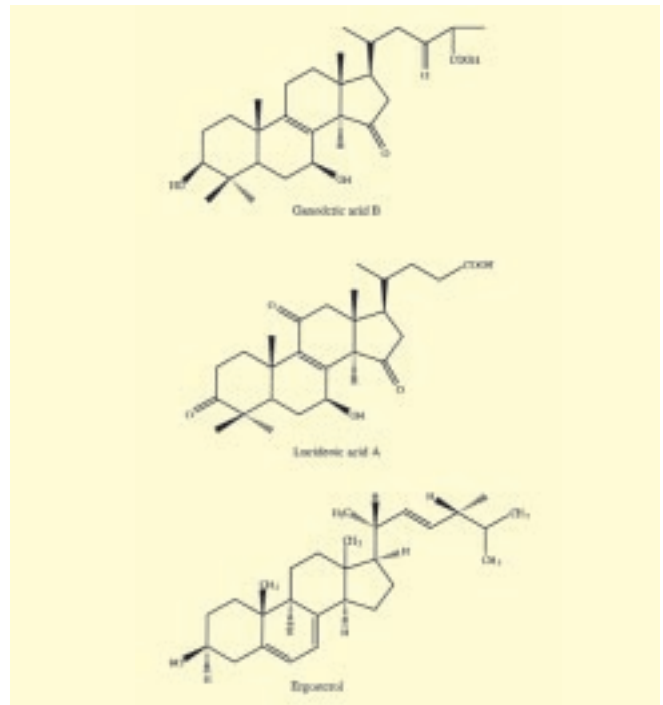

Figure 6 Primary constituents of *Ganoderma lucidum*

ANALYTICAL

Analysis of reishi mushroom can be very complicated due to the large number of triterpenes it contains and because of the significant variation in strains of reishi mushroom that exists. Comprehensive data regarding correlative pharmacological activity of the different strains are lacking.

Spot Test

The following spot test can be helpful for identifying species of reishi mushroom from other botanical substances and is largely specific to *G. lucidum* and *G. japonicum* fruiting bodies.

To 1 g of powder add 15 mL ethanol, shake occasionally, allow to stand overnight, filter, and evaporate 7 mL of the filtrate to dryness. To the residue, sequentially add 3 drops of acetic acid, 1-2 drops of acetic anhydride, and 1 drop of sulfuric acid. After the addition of acetic acid, a subtle brownish to yellow color is produced. With the addition of acetic anhydride, a very faint red color is quickly formed. With the addition of sulfuric acid, a green to pale green color is formed, gradually fading after standing for an extended period.

Note: With this spot test, a particular strain of mycelium biomass and *G. applanatum* produced the same brownish-yellow color in response to acetic acid as that of the fruiting body of *G. lucidum*. However, no other color reaction was observed in response to anhydride and sulfuric acid with these samples.

Thin Layer Chromatography (TLC/HPTLC)

The following thin layer chromatography (TLC) method can be used to help discern characteristic fingerprints of various varieties of reishi mushroom. Because of the wide range of triterpenes contained in reishi, it is difficult to choose one that is most appropriate as a marker compound. Therefore, TLC fingerprinting is considered to be secondary to macroscopic identification.

Sample Preparation
In a 100 mL Erlenmeyer flask, 250 mg of powdered drug are sonicated for 3 minutes with 5 mL methanol. The mixture is filtered. The filtrate is evaporated to dryness and reconstituted with 3 mL methanol. This is the test solution.

Standard Preparation
No standards were available.

Reagent Preparation
Sulfuric acid reagent: While cooling with ice, carefully add 10 mL of sulfuric acid to 90 mL of cold methanol.

Chromatographic Conditions
Stationary Phase:

   HPTLC plates 10 x 10 cm or 20 x 10 cm silica gel 60 with fluorescence indicator (EM Science; Whatman, Macherey & Nagel; or equivalent).

Mobile Phase:

   Dichloromethane:methanol (9:1).

Sample Application:

   5 µL volumes of test solution are applied each as 6 mm bands. Application position should be 8 mm from lower edge of plate.

Development:

   10 x 10 cm or 20 x 10 cm Twin Trough Chamber, saturated for 10 minutes, 5 (10) mL developing solvent per trough (or enough solvent to have a level of 5 mm in chamber), developing distance 70 mm from lower edge of plate. Dry plate with cold air for 5 minutes.
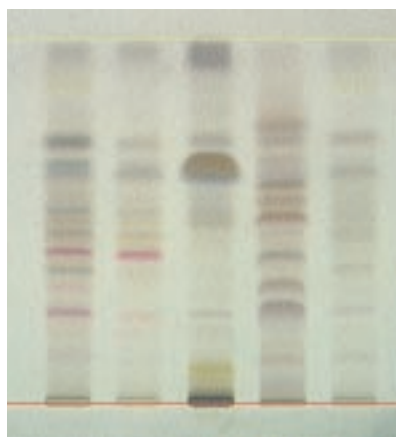
Detection:

   a) UV 254 nm.
   b) Sulfuric acid reagent: Immerse plate in reagent for 1 second, dry in stream of cold air, heat to 110 ˚C for 2 minutes. Examine plate in visible light.
   c) Examine the derivatized plate under UV 366 nm.
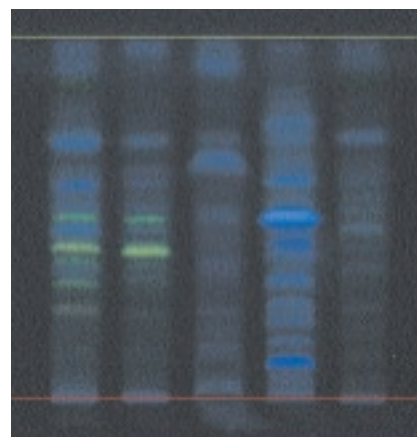
R_f Values:

   Compare to the chromatograms provided.
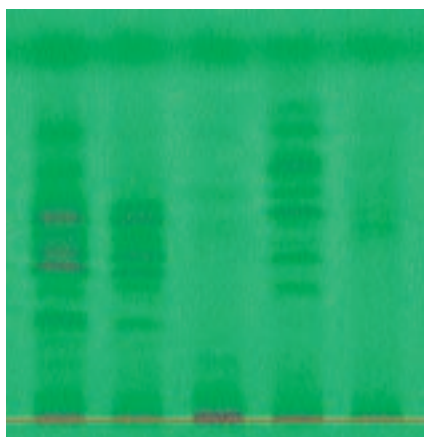
7a.

7b.

7c.

Figures 7a-c HPTLC chromatograms of *Ganoderma lucidum* and *Ganoderma applanatum* fruiting bodies and *Ganoderma lucidum* mycelium

Lane 1: *G. lucidum* fruiting body (duanwood).
Lane 2: *G. lucidum* fruiting body (duanwood).
Lane 3: *G. lucidum* mycelium biomass.
Lane 4: *G. applanatum* fruiting body.
Lane 5: *G. lucidum* fruiting body.

Discussion of Chromatograms

7a) UV 254 nm: The chromatograms of reishi mushroom differ among the various samples. The samples on Lanes 1 and 2 are relatively consistent and represent samples cultivated on duanwood in China. In the fruiting body samples on Lanes 4 and 5, prominent bands are seen at R_f = 0.23, 0.36, 0.40, and 0.47. Two additional bands (not prominent on plates shown) appear in the upper R_f region at 0.58 and 0.68. Another is seen in the upper R_f region at approximately R_f = 0.9. The chromatogram of the mycelium (Lane 3) shows no prominent bands under these viewing conditions. The chromatogram of *G. applanatum* (Lane 4) shows a similar pattern as that seen for *G. lucidum*; however, the band at R_f = 0.23 is missing and there is an additional band at R_f = 0.76. Only a few faint bands are observed in the last reishi mushroom sample showing considerable difference of constituent concentration in various samples of *G. lucidum*.

7b) Sulfuric acid reagent, visible light: The differences in the various samples are best observed under these conditions. The chromatogram of the fruiting body samples shows two prominent dark pink bands at R_f = 0.23 and 0.40, a weak pink band at R_f = 0.32, and a gray band at R_f = 0.36. Additional gray bands are seen at R_f = 0.52 and 0.65. Two dark broad zones are seen at R_f = 0.61 and 0.71. The chromatogram of *G. applanatum* has three dark bands at R_f = 0.23, 0.32, and 0.39, but no pink bands. There is also

a sequence of six bands between R_f = 0.48 and 0.75. The chromatogram of the mycelium shows a dominant strong band at R_f = 0.62 and a weaker band directly above. Another weak band is also seen at R_f = 0.23.

7c) UV 366 nm: The chromatogram of the reishi fruiting body sample on Lane 1 shows five yellow or yellow-green bands of varying intensity between R_f = 0.23 and 0.5. Two to three additional faint blue bands and a faint yellow band are seen above these. The two lower bands in the fruiting body sample on Lane 2 are much fainter than in the sample on Lane 1. The chromatogram of the mycelium only shows a few faint blue bands. The chromatogram of *G. applanatum* shows a dominant blue band at R_f = 0.5 and several other faint and darker blue bands above and below this.

8a.

8b.

8c.

Figures 8a-c HPTLC chromatograms of various samples of reishi mushroom

Lane 1: *G. lucidum* antler form.
Lane 2: *G. lucidum* antler form.
Lane 3: *G. lucidum* fruiting body (wild).
Lane 4: *G. lucidum* fruiting body (cultivated).
Lane 5: *G. lucidum* fruiting body (cultivated).
Lane 6: *G. lucidum* fruiting body (domestically cultivated).
Lane 7: *G. lucidum* fruiting body (commercial sample, Chinatown San Francisco).
Lane 8: *G. lucidum* fruiting body (commercial sample reddish-black, Chinatown San Francisco).
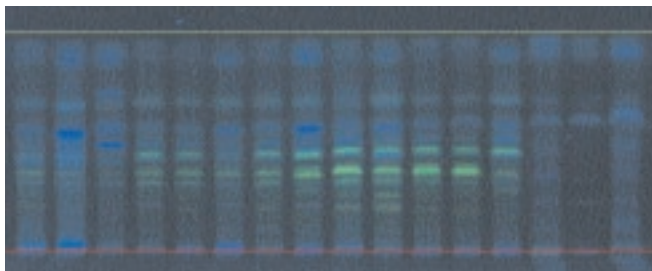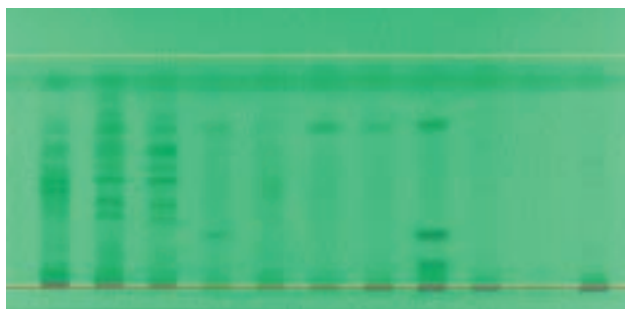**Lane 9:** *G. lucidum* fruiting body (domestically cultivated).
Lane 10: *G. lucidum* fruiting body.
Lane 11: *G. lucidum* fruiting body (duanwood).
Lane 12: *G. lucidum* fruiting body (duanwood).
Lane 13: *G. japonicum* fruiting body (black, Chinatown San Francisco).
Lane 14: *G. lucidum* mycelium biomass.
Lane 15: *G. lucidum* mycelium biomass.
Lane 16: *G. lucidum* mycelium biomass.

Discussion of Chromatograms
8a & c) UV 254 & UV 366 nm: The chromatograms of all the cultivated fruiting body samples (Lanes 4-13) are relatively consistent, showing the same bands as previously described under the same conditions, irrespective of variety and location of cultivation. The antler forms represented in Lanes 1 and 2 show similar bands in the lower and middle R_f region, but they are of significantly less intensity than those of the full fruiting body samples. The bands observed in the wild-harvested North American reishi (Lane 3) are similarly very faint. Few bands are seen in the mycelium samples (Lanes 14-16) at UV 254, and few faint blue bands are observed at UV 366.

8b) Sulfuric acid reagent, visible light: A relatively consistent pattern of bands is seen in all fruiting body samples including the antler form and wild-harvested domestic samples, though subtle differences in these patterns are observed. Each of these samples are showing approximately 8-10 prominent bands at almost identical R_f values. A characteristic pattern is seen in the two samples of reishi cultivated on duanwood (Lanes 11 and 12). A clear pattern is established for the mycelium samples (Lanes 14-16). These are characterized by the prominent band at R_f = 0.62 and additional faint bands above and below. The slight differences between these samples may be due to the different substrates on which the mycelium was cultivated (brown rice and soy).

9a.

9b.
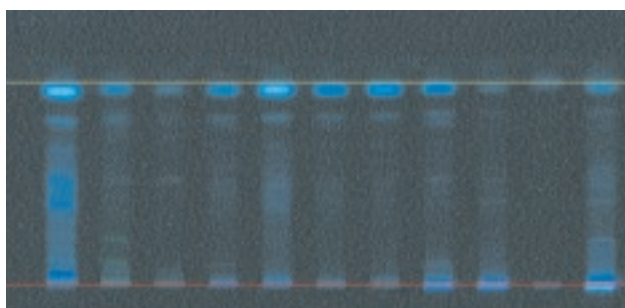
9c.

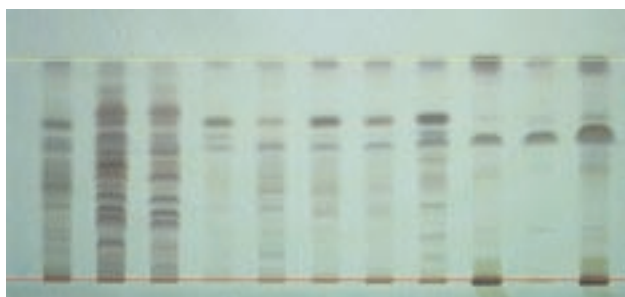**Figures 9a-c** HPTLC chromatograms of various samples of reishi mushroom

Lane 1: *G. lucidum* antler form.
Lane 2: *G. applanatum* fruiting body (wildcrafted, Alaska).
Lane 3: *G. applanatum* fruiting body.
Lane 4: *G. lucidum* fruiting body (wild).
Lane 5: *G. lucidum* fruiting body.
Lane 6: *G. japonicum* fruiting body.
Lane 7: *G. lucidum* fruiting body.
Lane 8: *G. japonicum* fruiting body.
Lane 9: *G. lucidum* mycelium biomass.
Lane 10: *G. lucidum* mycelium biomass.
Lane 11: *G. lucidum* mycelium biomass.

**Discussion of Chromatograms**
9a) UV 254 nm: All bands are too faint for proper characterization.

9b) Sulfuric acid reagent, visible light: The chromatographic pattern of the particular antler form shown here (Lane 1) differs slightly from those previously seen. The pattern of bands shown in these two samples of *G. applanatum* (Lanes 2 and 3) are similar to each other with both showing considerably more prominent and characteristic reddish-brown bands than are observed in *G. lucidum*. The bands for fruiting bodies of the reishi mushroom (Lanes 4-8) are similar to those already described, including those of *G. japonicum* (Lanes 6 and 8), with the bands of one sample of *G. japonicum* (Lane 8) much more prominent than the others. The patterns of the mycelium samples (Lanes 9-11) are characteristically similar to those already described.

9c) UV 366 nm: These conditions are not optimal for observing characteristic patterns of reishi mushroom or mycelium. However, the antler form (Lane 1) shows several faint blue bands, including one that is prominent near the solvent front. The two *G. applanatum* samples (Lanes 2 and 3) show prominent blue bands in the lower middle R_f region with a faint blue band in the lower R_f region and a few other faint bands in the upper R_f region. The bands observed in the other reishi mushroom and mycelium samples are very faint. *G. japonicum* (Lane 8) also shows a prominent blue band near the middle R_f region. Most of the *G. lucidum* samples show a faint yellowish band in the upper R_f region.
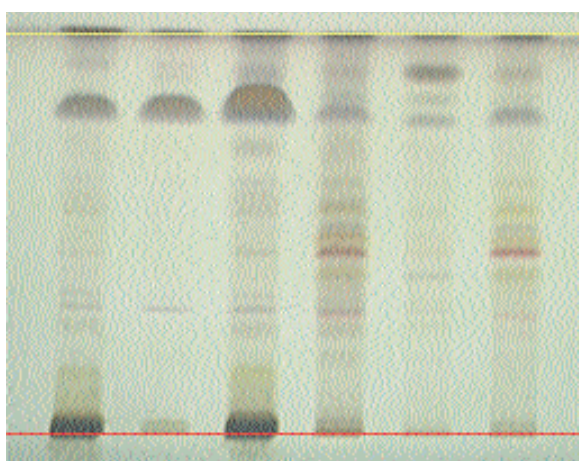
10.

Figure 10 HPTLC chromatogram of reishi mycelium biomass (sulfuric acid reagent, visible light)

Lane 1: *G. lucidum* mycelium.
Lane 2: *G. lucidum* mycelium.
Lane 3: *G. lucidum* mycelium.
Lane 4: *G. lucidum* fruiting body (domestically cultivated).
Lane 5: *G. lucidum* fruiting body (wild).
Lane 6: *G. lucidum* fruiting body (duanwood).

Discussion of Chromatogram
The chromatogram of the mycelium shows a dominant strong band at $R_f = 0.8$ and a weaker band directly above. There is a weak band at $R_f = 0.3$. The chromatogram of the fruiting bodies shows two prominent dark pink bands at $R_f = 0.3$ and 0.44, a gray band at $R_f = 0.8$, and several additional bands throughout.

Qualitative Standards

Foreign Matter:	Not more than 2%.
Ash:	Not more than 3.2% (Pharmacopoeia of the People's Republic of China 2000).
Acid Insoluble Ash:	Not more than 0.5% (Pharmacopoeia of the People's Republic of China 2000).

THERAPEUTICS

Pharmacokinetics

While it has been reported that pharmacokinetic data of reishi and reishi constituents are available in the Chinese literature, these data were not obtainable for review.

Pharmacodynamics

Reishi mushroom is one of the most widely researched botanicals in Asia. Numerous pharmacological studies have been conducted, most of them in China and Japan, primarily evaluating the polysaccharide and triterpene fractions. Several scientific congresses have focused on the chemistry and medical applications of reishi, and several research organizations are dedicated to this subject.

Most of the reported activity of reishi mushroom has been centered around four therapeutic actions: immune-enhancing, cardiovascular-regulating, hypoglycemic, and hepatoprotectant. Since the majority of research has been reported in Asian-language journals, it has been difficult for non-native Asian researchers to assess the quality of study design and to interpret the conclusions. Most of the English-language reports are in abstract form or presentation summaries. Such reports are not subject to peer review, as occurs in formal journal submissions. The preparations of reishi used in these studies are poorly defined. Therefore, in the absence of more extensive translation, non-Asian reviewers are unable to make full use of the extensive data that are available. The review provided here is based on the information in the available English-language studies and English-language reports from Asian studies.

Cardiovascular Effects

Human Clinical Studies

The ability of reishi mushroom to inhibit platelet aggregation after oral administration, as revealed by human peripheral blood samples, has been reported. This activity has been associated with a water-soluble component from reishi that is a derivative of adenosine (5'deoxy-5'-methylsulphiny-ladenosine) (Kawagishi and others 1993; Tao and Feng 1990). In one clinical trial of 15 healthy volunteers and 33 patients with atherosclerotic disease, statistically significant ($P < 0.01$) inhibition of platelet aggregation was observed following administration of 1 g of reishi mushroom 3 times daily for 2 weeks. After treatment with reishi, the length and width of induced thrombi was reduced by approximately 10% to 15% (Tao and Feng 1990). However, in another

study, inhibition of platelet aggregation was not observed in 5 HIV-positive hemophiliacs given 0.9 g daily of an extract of reishi mushroom standardized to contain 150 mg of adenosine per 100 g of extract (patients consumed the equivalent of 1.35 mg of adenosine daily) (Gau and others 1990).

In a study of hypertensive patients, which included a placebo control group, whole blood viscosity, plasma viscosity, and blood pressure were significantly reduced ($P < 0.01$ compared with pretreatment values) in 33 patients (15 male, 18 female) given oral doses equivalent to 1.3 g reishi (110 mg of dried reishi mushroom extract) each time, 4 times daily for 2 weeks. A reduction in a variety of symptoms including dizziness (58.8%), headache (75.0%), chest tightness (53.8%), and insomnia (64.7%), was also observed in the reishi-treated group while no significant changes were observed in the placebo group (Cheng and others 1993).

In a study of patients with heart disease, a cold water infusion of reishi mushroom (concentration and dosage undefined) was administered to 35 patients. Symptoms (undefined), electrocardiogram (ECG), and primary blood dynamic parameters reportedly improved in 85.7% of patients (Wang and Zheng 1994).

Animal and In Vitro Studies

Administration of the adenosine derivative 5'deoxy-5'-methylsulphinyladenosine from reishi (50 μg/mL) resulted in a 20% to 50% inhibition of platelet aggregation in vitro. The mechanism of action was unclear but was suggested to be due to the activation of platelet phospholipase; inhibition of platelet-activating factor (PAF) was ruled out (Kawagishi and others 1993). Inhibition of thrombus formation and a significant decrease in weight and length of a thrombus was observed in rabbits ($P < 0.01$) (Wen and others 1997).

Spontaneously hypertensive rats were given an undisclosed amount of reishi mushroom powder as part of the diet. After 4 weeks, the systolic blood pressure in treated rats was reported to be significantly lower than that of the controls though no statistical analysis was provided (Jong and Birmingham 1992). Inhibition of angiotensin-converting enzyme (ACE) and subsequent hypotensive activity has been reported in laboratory animals, suggesting one mechanism of action. At least ten lanostane triterpenes (known as ganoderic acids) with mild in vitro ACE-inhibiting effects have been identified in a 70% MeOH extract of reishi. Of these, ganoderic acid F exhibited the highest inhibitory effect ($IC_{50} = 4.7 \times 10^{-6}$ M) while the others were relatively insignificant (10^{-5} M) (Morigiwa and others 1986).

In modern Chinese medicine, reishi mushroom is used as a hypocholesterolemic agent. In an in vivo study where mevinolin was administered as a positive control, several oxygenated triterpenes from reishi were reported to inhibit HMG-CoA reductase, the rate-limiting enzyme in the cholesterol biosynthetic pathway. Using rat liver slices from animals initially fed cholestyramine, the incorporation of (2-3H) acetate and (2-14C) mevalonate into cholesterol was reduced in the presence of the test compounds from reishi. In addition, a few triterpenes containing oxygenated functional groups at C-15 and a hydroxyl group at C-26 of the

triterpene have been demonstrated to inhibit cholesterol biosynthesis (Shiao and others 1994). Several of these compounds have been shown to reduce cholesterol absorption in experimental animals fed a 2% cholesterol diet, presumably by occupying the sterol receptors in the intestinal tract. They were reported to be more potent than β-sitosterol and, like β-sitosterol, are poorly absorbed (Shiao and others 1994). Thus, the reported cholesterol-lowering activity may be due to a combination of inhibiting cholesterol absorption from dietary sources and inhibition of synthesis of endogenous cholesterol.

According to a secondary review, a tincture of reishi mushroom, which contains the triterpene fraction, demonstrated a significant cardiotonic effect on the isolated frog heart, as well as on the pentobarbital sodium-inhibited heart. The effect was also noted in mammals; thus, for example, intraperitoneal (ip) injection of 3 g/kg of a tincture of the fruiting body increased contraction amplitude of the rabbit heart in situ by 41%. In anesthetized cats, low intravenous (iv) infusion of a reishi extract (hot alcohol) caused bradycardia and a cardiotonic effect, while iv injection of an undefined reishi preparation to anesthetized dogs increased coronary blood flow by 44% compared to predrug values (Chang and But 1986).

Immunomodulatory Effects

Human Clinical Studies
In the United States, reishi mushroom is most often recommended for its immune-supporting effects. This is based primarily on animal studies showing a host-mediated attack against implanted tumors and on the use of reishi and other mushroom polysaccharide fractions in supporting immune resistance of patients undergoing conventional chemo- and/or radiation therapy for various forms of cancer. English-language reports of clinical studies are quite limited in this area for reishi mushroom (there is more data for other mushroom polysaccharides, mainly *Polyporus*, *Coriolus*, and *Lentinus*, which are believed to have the same mechanism of action as the reishi polysaccharides). In one placebo-controlled study, it was reported that 3 g of a reishi mushroom extract (10:1 concentration of hot water extract) was administered orally to 48 patients with advanced tumors (breast, renal, gastric) for 30 days. A marked immune-modulating effect with an increase in T lymphocytes including T helpers as well as a decrease in CD8s, was reported in patients whose immunologic parameters were initially compromised. Little effect was seen in patients with normal immune indicies. The extract was also reported to lessen side effects due to chemo- and/or radiation therapy and enhanced postoperation patient recovery as compared to controls (Kupin 1992). No specific values or statistical analysis were provided.

Animal and In Vitro Studies
A number of in vitro immune-modulating activities have been reported for polysaccharides derived from reishi mushroom. In one study, a polysaccharide was reported to enhance concanavalin A-induced murine T cell prolifera-

tion. The polysaccharide, when combined with d-matrine (an alkaloid), decreased interleukin 2 (IL-2) expression and inhibited T cell proliferation (Jong and Birmingham 1992). Reishi mushroom polysaccharides were reported to promote production of IL-2 in a concentration-dependent manner in a mixed lymphocyte culture and additionally enhanced the cytotoxicity of T lymphocytes by 100% at a concentration of 200 μg/mL (Lei and Lin 1992).

Additional studies on cytokine effects by researchers Wang and others (1997) indicated that administration of reishi polysaccharides (100 μg/mL) resulted in 5.1-, 9.8-, and 29-fold increases in interleukin (IL-1β), tumor necrosis factor (TNF-α), and IL-6, respectively, in macrophage cultures as compared to controls. In addition, the release of interferon (IFN-γ) from T lymphocytes was greatly promoted with reishi polysaccharides (25-100 μg/mL). When splenocytes were treated with reishi alone, the increase in cytokine production was nonsignificant, but when pretreated with reishi and hydrocortisone (0.025-1 μg), the increase was significant ($P < 0.01$) (Zhang and others 1993). This effect on cytokines IL-2 and IL-3 was reportedly associated with a potentiation of their mRNA expressions at the transcriptive levels (Qing and others 1998). Intraperitoneal administration of 25 and 50 mg/kg of reishi mushroom polysaccharides in 24-month-old mice once daily for 4 days enhanced the activity of DNA polymerase-α in splenocytes by 44% and 58.8%, respectively. Administration of 50, 100, and 200 μg/mL polysaccharides restored the IL-2 production of splenocytes from aged mice to the levels of that of young mice (Lei and Lin 1993). Other studies support the ability of reishi mushroom polysaccharides to restore the level of IL-2 production that has been inhibited by aging; in at least three studies, this was demonstrated in aged mouse splenocytes (Lei and Lin 1991, 1993; Zhang and others 1993). An additional study in mice showed that reishi mushroom can promote cell proliferation in murine splenocytes (Xiao and others 1994).

Reishi mushroom has also been shown to exhibit a protective effect against immune suppression from exposure to γ-irradiation. Mice exposed to 400 rads γ-irradiation experienced markedly depressed leukocytes; however, both the relative spleen weights and leukocyte counts of mice treated with a reishi mushroom extract (400 mg/kg for 35 days; extract ratio undefined) were significantly ($P < 0.01$) higher than those of the controls. Cellular immunocompetence in γ-ray-treated mice measured by ^{3}[H]-thymidine incorporation with splenic cells stimulated by phytohemagglutinin (PHA), concanavalin A, and endotoxin (LPS) revealed that the blastogenic response of splenocytes to both PHA and ConA were higher in the groups treated with reishi than in the controls. It was suggested the extract assisted in the recovery of cellular immunocompetence in irradiated mice, a finding consistent with modern clinical use of reishi mushroom to protect cancer patients from immunosuppression due to radiation therapy for cancer (Chen and Hau 1995). However, nonsignificant results were reported by another group of researchers who exposed mice to 500 and 650 cGγ-irradiation and measured the 30-day survival and hemor-

rhagic parameters in animals treated with the same reishi preparation (Hsu and others 1990). More recently, another group of researchers reported that a hot water extract of reishi mushroom prevented hydroxyl radical- and UV irradiation-induced DNA damage. A polysaccharide isolated from the same extract was as effective as the total extract demonstrating this to be among the active compounds (Kim and Kim 1999).

Through the use of DNA labeling and gel electrophoresis, it was shown that treatment with reishi polysaccharides markedly induced leukemic-cell apoptosis and, in combination with mononuclear cell-conditioned media, additionally triggered the maturation of 40% to 45% of the undifferentiated cells (Wang and others 1997). This same activity was reported earlier by another group of researchers (Lieu and others 1992). Researchers Wang and others (1997) concluded the antitumor activity of reishi polysaccharides in laboratory animal models was not due to direct tumorocidal activity but rather to an enhancement of host immune responses attacking foreign cells. Another researcher reported direct cytotoxicity of reishi mushroom triterpenes to tumor cells in vitro and in animals. In this study, synthetic analogs of phosphodiesters of reishi oxysterols were administered ip to mice with breast and liver tumors (P815) (dosing regimen not disclosed). The researchers reported an increased lifespan in the mice given the synthetic compounds and also reported the compounds were more selective against tumor cells than normal cells. Specific data on how these conclusions were reached were lacking (Luu 1992).

In summarizing the immune-modulating effects of reishi mushroom polysaccharides, researchers Lin and Lei (1994) state reishi mushroom polysaccharides significantly promote mixed lymphocyte response, antagonize the inhibitory effects of immunosuppressive and antitumor drugs, display a biphasic effect on IL-2 activity, increase both L3T4+ and Lyt 2+ cell subpopulations, enhance cytotoxic activity of T lymphocytes, and promote the secretion of IL-1 in peritoneal exudate cells. Chang (1994a) concluded that the polysaccharide fraction, with β-glucans, has stimulatory effects on the white blood cell lines: leukocytes, monocytes, macrophages, natural killer (NK) cells, lymphokine-activated killer (LAK) cells, tumor-infiltrating lymphocytes (TIL), and other lymphocytes. He considers these actions to be responsible for the antiviral, antitumor, antiinflammatory, granulopoietic, and bactericidal effects that have been reported for reishi mushroom in laboratory animal studies. He further suggests that reishi mushroom's broad immune-supporting activity and low toxicity make it particularly useful for immune support of patients undergoing radiotherapy, chemotherapy, or major surgery (Chang 1994a). These immunological effects are consistent with the modern application of reishi among herbal practitioners. Nevertheless, well-designed clinical trials regarding the immunological effects of well-characterized reishi preparations are needed to determine the clinical efficacy of this herb for human use.

Antitumor Effects

Animal and In Vitro Studies

Numerous studies have reported on the antitumor activity of reishi mushroom in animals (Lee and others 1994; Lieu and others 1992; Lin and Tome 1991; Maruyama and others 1989; Sone and others 1985; Wang and others 1993). This activity is primarily associated with polysaccharides in general and, specifically, polysaccharides with the branched (1–3)-β-D-glucan moiety (Sone and others 1985).

Antitumor activity has also been reported for reishi triterpenes. In one study, polysaccharides from various species of Ganoderma were administered to ICR/S1c mice with implanted Sarcoma 180 tumor cells. Considerable antitumor activity was reported for all species with varying degrees of inhibitory activity elicited by the polysaccharides as shown in Table 1 (Wang and others 1993).

According to one report, a glucan derived from a hot water extract of the fruiting body exhibited a relatively high inhibitory activity against the growth of Sarcoma 180 solid tumors in mice treated with successive ip injections of the glucans (Sone and others 1985) (Table 2). Similar findings were reported using reishi mushroom extracts in ICR mice (Lee others 1994; Ohno and others 1998; Yadomae and others 1998). In the studies of Ohno and others (1998) and Yadomae and others (1998), the immune-modulating activity of a hot water and ethanol extract were investigated in murine macrophage cultures. Both extracts enhanced in vitro production of IL-6 and nitric oxide (NO) synthesis dose dependently. Intraperitoneal administration of both extracts protected ICR mice from lethal ip infection of *Escherichia coliform* and displayed significant antitumor activity against a solid form of Sarcoma 180 in the mice (74% inhibition of average tumor growth with 3 out of 10 of the mice showing complete regression). Oral administration of both extracts (2 mg/mouse daily) were also effective against the same tumor model (45% and 63% inhibition, respectively) (Yadomae and others 1998). The β-glucan fraction, ganoderan, similarly enhanced NO production 4-fold and TNF-α production 19-fold as compared to controls in rats (Han and others 1999). The antler form of reishi was reported to yield higher concentrations of β-D-glucans than the normal fruiting body, though specific comparative concentrations were not provided in the report; a water extract (1000 μg/mL) of this antler material (prepared from 10 g/200 mL) was shown to be effective against L929 tumor cell lines. These researchers suggested the antitumor activity was associated with an increase in macrophage activity and a subsequent increase in TNF (Miura and others forthcoming). According to a review of Shiao and others (1994), some of the polysaccharides derived from reishi fruiting body can be described as serving as biological response modifiers in host defense mechanisms against cancer (Shiao and others 1994).

Direct tumorocidal action (as opposed to immunological antitumor activity) was found with two steroidal compounds (ganoderic aldehyde A and ergosta-7,22-diene-2β,3α,9α-triol) isolated from reishi fruiting bodies. These compounds were shown to have significant inhibitory action against human hepatoma PLC/PRF/5 (ED_{50} 2.54 and 1.17

Table 1 Comparison of antitumor† activity of polysaccharide fractions of three species of reishi

Species	Dose (mg/kg ip)	% Inhibition	Complete regression (day 45)	ID_{50} (mg/kg)
G. applanatum (fruiting body)*	3 x 1	62	3/5	1.90
G. applanatum (fruiting body)*	1 x 1	100	5/5	0.15
G. applanatum (mycelium)*	10 x 1	100	5/5	0.74
G. applanatum (mycelium)	3 x 1	76	3/5	2.10
G. lucidum (fruiting body)*	50 x 1	100	5/5	3.21
G. lucidum (fruiting body)*	40 x 1	100	5/5	22.20
G. lucidum (fruiting body)*	100 x 1	100	5/5	8.30
G. lucidum (fruiting body)*	100 x 1	100	5/5	6.30
G. lucidum (fruiting body)*	100 x 1	100	5/5	12.80
G. lucidum (fruiting body)*	100 x 1	95	5/5	34.10

† Represents a host versus tumor-implant response
* Experiments were conducted with primary polysaccharides derived from *Ganoderma* spp., not from crude reishi preparations
Test model: ICR/S1c mice with implanted Sarcoma 180 tumor cells (6 x 10⁶) and an equal number of controls
Source: Wang and others 1993.

Table 2 Comparison of antitumor activities of branched (1-3)-β-D-glucans of reishi mushroom against Sarcoma 180 (solid tumor)

Polysaccharide	db	Dose (mg/kg days)	Avg tumor wt (g) (treated/control)	Growth inhibition	Complete regression
Hot water-II	1/3.1	10 x 10	0.2/9.4	97.9	4/5
Hot water-II polyol		5 x 10	0.8/9.4	91.4	5/6
Cold alkali-II	1/16.8	10 x 10	3.8/9.4	59.6	2/6
Cold alkali-II polyol		5 x 10	2.5/8.3	70.0	2/7
Hot alkali-II	1/23.0	10 x 10	7.4/8.3	10.9	0/7
Alkali residue		5 x 5	9.7/8.3	-17.9	0/7
Extracellular glucan	1/2.7	10 x 10	0.8/9.4	91.6	4/6
Polyol		5 x 10	0.3/9.4	96.8	5/7

db = expressed as the ratio of branched (1-3)-linked D-glucosyl residues to all the (1-3)-linked D-glucosyl residues
Source: Modified from Sone and others (1985).

µg/mL, respectively) and KB cells (ED_{50} 1.25 and 0.89 µg/mL, respectively) in vitro (Lin and Tome 1991). Most recently, ganoderic acids A (IC_{50} 100 µM) and C were shown to inhibit farnesyl protein transferase (FPT) in vitro. Inhibitors of FTP have been shown to inhibit reticular-activating system (RAS)-dependent cell transformation and may represent a potential therapeutic strategy for cancer (Lee and others 1998). In another study, an ergosterol peroxide (EPO) derived from reishi was shown to potentiate the DNA-polymerase-β-inhibitory activity of linoleic acid (LA) in vitro. Administration of LA alone at a concentration of 80 µM resulted in complete inhibition while administration of EPO alone was largely ineffective. However, the combination of 0.25 mM of EPO and a lower dose of LA (just 10 µM) resulted in an almost complete inhibition (Mizushina and others 1998).

In addition to the reported immune-modulating and antitumor effects, oral administration of reishi has also been shown to protect against various degrees of adriamycin-induced (3 mg/kg ip) cellular toxicity in rats. At doses of 3 mg/kg ip, adriamycin resulted in significant decreases in leukocytes and platelets and also resulted in cloudy swelling and vacuolar degeneration in heart, liver, and kidney cells. Cellular toxicity was reportedly significantly reduced in rats pretreated with 500 mg/kg of reishi mushroom for 14 days and then administered every other day (for 4 times) after administration of adriamycin (Hongwei and others 1997). No statistical analysis or values were available.

At this time, there is no evidence that reishi inhibits cancer in humans. Direct tumorocidal action has only been demonstrated in vitro, and the immunological mechanism of antitumor action, attributed to the polysaccharide fraction, has been demonstrated only for implanted tumors, to which the host reacts.

Hypoglycemic Effects
Animal and In Vitro Studies
The two glycans ganoderans A and B were shown to possess strong hypoglycemic actions in normal and alloxan-induced hyperglycemic mice. In one study, both glycans reduced blood glucose levels in alloxan-induced hyperglycemic mice in a dose-dependent (10, 30, and 100 mg/kg ip) fash-

ion with a significant reduction reached in 7 hours at all doses for ganoderan A ($P < 0.01$) and at the two higher doses for ganoderan B ($P < 0.01$). Ganoderan A possessed stronger hypoglycemic activity than ganoderan B (Hikino and others 1985). In another study, ganoderan B and ganoderan C (10, 30, 100 mg/kg ip) similarly reduced blood glucose concentrations in a dose-dependent fashion. After 7 hours of administration of ganoderan B, blood glucose was reduced to 83, 63, and 59% of the control, respectively. After 24 hours, blood glucose was reduced to 90, 86, and 70% of the control at the same dosages. After 7 hours of administration of ganoderan C, blood glucose was reduced to 86, 76, and 59%. After 24 hours of administration of ganoderan C, blood glucose was reduced to 105, 87, and 82% of the control, respectively (Tomoda and others 1986).

In follow-up studies by Hikino and others (1989), three primary mechanisms associated with reishi's hypoglycemic activity were reported: its ability to elevate plasma insulin levels, its ability to enhance glucose utilization in peripheral tissues, and its ability to enhance the metabolism of glucose in the liver (Hikino and others 1989). Using both normal and glucose-loaded mice, blood glucose levels decreased significantly ($P < 0.01$ and $P < 0.05$) in both groups after administration of ganoderan B (30 mg/kg ip). At doses of 100 mg/kg ip, plasma insulin levels similarly increased in both groups but was not statistically significant. These effects were correlated with significant increases in the activity of liver enzymes primarily responsible for glucose metabolism in the liver, specifically glucokinase, phosphofructokinase, and glucose-6-phosphate dehydrogenase, while decreasing glucose-6-phosphatase. It also decreased glycogen synthetase activity in the liver, resulting in a reduction of liver glycogen. It elicited no effect on the binding of insulin on adipocyte receptors or on hexokinase and glycogen phosphorylase. Hepatic cholesterol and triglyceride levels remained unchanged. Hypoglycemic activity was most pronounced 3-7 hours after administration of a water extract of reishi mushroom containing ganoderan B (Hikino and others 1989). In an additional study by the same primary researcher, heteroglycans were found to have relatively weak hypoglycemic activity when compared to the activity of the primary ganoderans (Hikino and Mizuno 1989).

Anti-inflammatory Effects

Animal and In Vitro Studies
Water extracts of reishi mushroom were found to possess significant activity against carrageenin-induced paw edema when administered subcutaneously (sc) to rats. In one controlled study, groups of animals received either saline as a placebo control, indomethacin as a positive control (10 mg/kg sc), or a test article, one of which was a reishi mushroom water extract (2 g/kg). Both indomethacin and reishi mushroom showed significant anti-inflammatory effect ($P < 0.01$) against carrageenin-induced edema at all time intervals from 1-6 hours (Lin and others 1993). Stavinoha and others (1990) investigated the topical anti-inflammatory activity of a water extract and an ether extract of the whole mushroom. Oral administration of 380 mg/kg and 1780 mg/kg of the preparation reduced carrageenin edema in mice by 25% and 47%, respectively. In comparison, hydrocortisone (18 mg/kg) and phenylbutazone (90 mg/kg) reduced swelling by 55% and 37%, respectively. When administered topically, the water extract was reportedly inactive, whereas 50 mg of reishi powder and 220 mg of the ether extract were reported to be comparable to 5 mg of hydrocortisone (Stavinoha and others 1990).

Hepatoprotective Effects

Human Clinical Studies
Clinical information about the hepatoprotective action of reishi was reported in one small uncontrolled trial. Four patients with hepatitis B and elevated bilirubin and SGPT/SGOT levels were given 6 g of a reishi extract (concentration undefined) for 3 months. After 1 month, bilirubin, SGPT, and SGOT levels were significantly reduced ($P < 0.01$); after 90 days all values returned to within normal ranges (Soo 1994).

Animal and In Vitro Studies
A number of studies have focused on the ability of reishi to protect the liver from chemical damage and enhance its detoxifying activity (Jong and Birmingham 1992; Lin and others 1993, 1995; Liu and others 1979a, 1979b). In the studies of Liu and others, treatment with reishi protected against CCl_4-induced hepatic damage and indomethacin-

Table 3 The hepatoprotective effects of reishi mushroom on CCl_4-induced GOT and GPT level increase in rat liver

Group	Dose (mg/kg)	GOT	GPT	% Protection
Normal	—	120.83 ± 4.02	44.18 ± 2.45	—
CCl_4	—	263.58 ± 8.11[*]	84.93 ± 2.29[*]	—
Reishi mushroom	10	253.05 ± 16.26	77.07 ± 8.47	7.38
	30	198.13 ± 19.32[a]	64.37 ± 5.32	45.85
	100	169.52 ± 14.82[a]	52.68 ± 6.20[b]	65.89

Significantly different from normal; [*]$P < 0.001$, Student's t-test

Significantly different from CCl_4 control group; [a]$P < 0.01$, [b] $P < 0.05$, Dunnett's t-test

Source: Lin and others 1995.

induced mouse deaths. Hepatocyte regeneration under the influence of reishi was also noted. However, in the studies of Lin and others, contrary findings regarding the ability of reishi to inhibit CCl_4-induced hepatic damage were reported. In the earlier study, a water extract of reishi (1 g/kg ip) was shown to be ineffective at preventing hepatic damage when given concomitantly with CCl_4 (Lin and others 1993). In the latter study (1995), a significant ($P < 0.01$) reduction in CCl_4-induced hepatic damage, as determined by reductions in SGOT and lactic dehydrogenase (LDH) levels 24 and 48 hours after treatment with a crude reishi extract (30 and 100 mg/kg ip), was observed. The greatest effect was observed at the 100 mg/kg dose.

Hepatoprotective actions of reishi have been attributed to both the triterpenes and the polysaccharides. Part of the hepatoprotective activity attributed to reishi was suggested to be due to a superoxide and hydroxyl radical scavenger-like action (IC_{50} of reishi water extract 12.66 mg/mL) with antioxidant activity reportedly equivalent to 0.54 mM ascorbic acid (Lin and others 1995) (Table 3). Antioxidant activity was observed with polysaccharide and triterpene fractions of reishi which were active over a range of 40-400 μg/mL (ED_{50} 180 and 200 μg/mL, respectively; $P < 0.01$). The terpenes were most active (ED_{50} 40 μg/mL) (Zhu and others 1999). In a review article, it was reported that a reishi mushroom extract administered concurrently with glutathione was more effective than either alone in limiting CCl_4-induced liver damage in rats. Blood transaminase levels, lipid peroxidation values, and histological findings were monitored. The effect was reported to be particularly notable in protecting against liver necrosis and hepatitis (Jong and Birmingham 1992).

Hepatoprotective activity was reported to be correlated with an inhibition of β-glucuronidase, a correlative marker of hepatic injury, by ganoderenic acid A (Kim and others 1999a). Ganoderic acid C, derived from *G. tsugae,* was also shown to elicit a significant hepatoprotective effect against CCl_4-induced hepatotoxicity in mice to a degree that was reportedly greater than the noted hepatoprotectant milk thistle (*Silybum marianum*). SGPT and SGOT levels in the controls were approximately 6500 and 2700 dL, respectively. After oral administration of ganoderic acid (0.2 mg/kg), SGPT and SGOT levels were approximately 2000 and 800 units/dL, respectively, after 24 hours. In comparison to controls (6500 units/dL), before and after SGPT and SGOT levels for milk thistle (concentration undefined) were approximately 4300 and 1500 units/dL, respectively. Another study found that ganoderic acid A exhibited potent antihepatotoxic activity against CCl_4-induced liver damage in mice and suggested this activity to be due to inhibition of β-glucuronidase (Kim and others 1999a). Other triterpenes of reishi caused a slight but nonsignificant reduction in liver enzymes (Su and others 1993).

A study compared the hepatoprotective effects of polysaccharides isolated from various plants, including *Aloe barbadensis, Lentinus edodes, G. lucidum,* and *Coriolus versicolor.* The polysaccharide isolated from reishi was shown to be the most effective of those studied for increasing the activity of glutathione *S-*transferase in mouse hepatocytes (Kim and others 1999b).

Other Effects

Reishi mushroom has a long history of use in TCM for treatment of chronic bronchitis (Tasaka and others 1988). In one small uncontrolled study of 20 patients with chronic bronchitis, reishi mushroom was administered for 4 months. According to the review, in all but 2 patients there was a significant decline in blood cholinesterase activity, suggesting a reduction in the excitability of the parasympathetic nerves (Chang and But 1986).

The use of reishi to decrease herpes zoster pain and lesions was reported in 4 individuals. Four patients (mean age of 65) with herpes zoster were treated solely with an aqueous extract of reishi (17 g dry reishi yielded 1 g powdered extract). The extract was administered orally in daily doses of 6.4 and 12.8 g (equivalent to 36 and 72 g dry reishi, respectively, in 3 divided doses). In 1 patient, postherpetic neuralgia dramatically decreased on two different occasions, one after 4 days of treatment with reishi and the other after 10 days of treatment. In both instances treatment was continued for approximately 45 days then discontinued, and the pain remained absent for at least several months. In another patient with severe herpes zoster requiring hospitalization, the 36 g equivalent dose failed to provide relief. After 20 days, the dose was doubled. Pain diminished over a 10-day period and subsequently diminished further over a 45-day treatment period. The patient reported being pain free after 7 months of taking reishi. Reishi was discontinued and the patient remained symptom free for at least 11 months. In the third patient, severe pain and lesions resolved over a period of 7 days of treatment with reishi (equivalent to 36 g daily). Discontinuation of reishi resulted in a return of the pain with subsequent resolution when reishi was readministered. Treatment was continued for another 7 days. The patient remained free of herpetic pain and lesions for at least 14 years. The last patient presented with neuralgia and itching which further developed into lesions and edematous erythema. After 3 days of treatment with reishi (equivalent to 36 g daily), progression ceased, lesions began to crust, and pain decreased. Skin lesions had almost completely resolved after 3 weeks (Hijikata and Yamada 1998).

Specific antiviral activities have been reported for a variety of reishi constituents. Significant in vitro cytopathic inhibitory activity against herpes simplex virus (HSV-1 and 2) and vesicular stomatitis virus (VSV) has been observed. An acidic protein-bound polysaccharide exhibited the most potent antiherpetic activity (EC_{50} 300-520 μg/mL) (Eo and others 1999a, 1999b). Antiviral activity of reishi against human immunodeficiency virus (HIV) has also been reported in vitro. In at least two studies, low molecular weight fractions of an aqueous extract and a total ethanolic extract of reishi mushroom were shown to strongly inhibit HIV-1 in the in vitro XTT antiviral assay (Kim and others 1994, 1996); in the latter study, low molecular weight fractions of an aqueous extract strongly inhibited viral replication. In another study, triterpenes isolated from a methanolic extract

of reishi (ganoderiol F and ganodermanontriol) were also shown to exhibit anti-HIV-1 activity (IC values of 7.8 μg/mL^{-1}). This study showed that a number of lanostadiene-type triterpenes had relatively strong anti-HIV-1 activity while the lanostene triterpenes and ergostane compounds had no activity (El-Mekkawy and others 1998). No details regarding this study were available. In another study, polysaccharides derived from reishi were reported to have antifibrotic activity as determined by reduction of collagen in the liver. Reductions in serum aspartate transaminase, alanine transaminase, alkaline phosphatase, and total bilirubin were also observed (Park and others 1997).

Bioassay-guided fractionation studies were undertaken to investigate the analgesic activities of reishi (Koyama and others 1993). In a dose-dependent manner, ganoderic acids A, B, G, and H (3-5 mg/kg sc) significantly reduced acetic acid-induced pain in mice ($P < 0.05$ - $P < 0.001$). In some cases, the effect observed was equal to, or greater than, 30-100 mg of aspirin.

Reishi has also been reported to be effective in treating a wide variety of other conditions, including migraines, lupus, hepatitis, dengue fever, asthma, arthritis, skin allergies, insomnia, gastric ulcer, and epilepsy. These assertions were reportedly based on clinical observation over a period of 6 years with 474 patients (Soo 1996). No substantiating data regarding these effects were available. A methanolic extract of the antler form of reishi has been reported to inhibit melanin synthesis in melanoma (Miura and others forthcoming).

Mycelium Research

Numerous compounds with biological activity have been isolated from reishi mushroom mycelium preparations, and a significant amount of data regarding mycelium exists. Some of the constituents contained in the mycelium are the same as those contained in the fruiting body while others are unique to the mycelium. Like the fruiting body, the primary constituents of pharmacologic interest include sterols, lactones, alkaloids, polysaccharides (most specifically β-glucan), and various lanostane oxygenated triterpenes. Similarly, identical pharmacological effects of the mycelium have been reported for the central nervous, cardiovascular, immune, and respiratory systems and for its ability to inhibit biosynthesis and absorption of cholesterol. It has been reported to have both immunostimulant and immunosuppressive activity and antiallergic, antitumor, and liverprotective effects. While all attempts to gather the available primary literature have been made, no primary human clinical data were retrieved.

It is very difficult to evaluate the data regarding various reishi mushroom mycelium preparations and to determine their clinical effectiveness. Most of the data do not clearly delineate the type of preparation used in the studies. Various terminology is used, including mycelia, mycelium, mycelia extract, cultured medium, and mycelia fermentation product. Some of the preparations are characterized on undisclosed amounts of specific constituents, and the designs of the study are often unclear. More importantly, an extrapola-

tion of the findings of the available studies and the use of commercial mycelium biomass products as are available in the United States cannot be made definitively. Mycelium products in the United States are mycelium biomass preparations in which mycelium is cultivated on a grain medium. The constituent profile of mycelium biomass products is significantly different than the fruiting body and also varies greatly between mycelium preparations. Similarly, findings of studies utilizing specific polysaccharide or protein fractions cannot be used to substantiate the effectiveness of orally administered commercial reishi mushroom mycelium biomass products because of a potential lack of bioavailability. Lastly, most of the studies reviewed used concentrations of isolated constituents that are magnitudes higher than what is available in crude mycelium biomass preparations. Therefore, a review of these data did not appear to be relevant to the use of mycelium products in the United States.

Additional studies have been conducted regarding compounds derived from the spores. Spore preparations are generally not available and the data are similarly limited.

Conclusion

There is a tremendous amount of data on the chemistry and pharmacology of reishi mushroom, but relatively little information on its clinical applications. Much of the research has focused on the ability of the reishi polysaccharides to enhance specific and nonspecific immune responses; as a result, a wide array of medical indications associated with immune functions have been claimed but remain to be substantiated. In some cases, the data are readily subject to misinterpretation. For example, animal models showing antitumor activity actually reveal a host-defense type mechanism that is unlikely to apply to human cancers. In addition, while the immunological activity is associated with reishi extracts, the materials used in the studies are primarily water soluble polysaccharide fractions. These may or may not be present in high enough concentrations in commercial preparations to be effective or they may be biologically unavailable.

Unfortunately, the majority of data available on reishi is in Asian-language journals that are not easily accessed by English-speaking reviewers. The majority of data that are available in English occur in abstract form or secondary brief summaries with limited details and lack critical review. In most cases, there are no details of the test substance, preparation methods, dosages used, and study designs. In general, clinical and laboratory animal studies did not include placebo controls or did not include comparative statistical analysis. This makes a critical review of the available data very difficult and limits our full knowledge of the level of efficacy of reishi. There are a number of English-language studies that are well designed that support many of the uses outlined in these review articles. However, most of these data have been ascertained from in vitro or animal studies, similarly limiting our understanding of reishi in humans. Based on the available literature, it is clear that reishi has great potential as a therapeutic agent and warrants further clinical investigation in humans.

According to the pharmacology reports, the cardiovascular effects (lower cholesterol, lower blood pressure, reduced blood glucose, reduced platelet aggregation) and some of the liver-protective actions of reishi can be primarily attributed to the triterpenes (these are soluble in alcohol or alcohol-water mixtures) while the immunological, anti-inflammatory, and some of the liver-protective effects can be primarily attributed to the polysaccharides (which are soluble in water preparations).

Actions Supported by Modern Pharmacology

Clinical: Inhibits platelet aggregation (Cheng and others 1993; Tao and Feng 1990); in immunologically compromised subjects, increases T lymphocyte and T helper cells and decreases T suppressor cells; improves immunocompetancy after chemo- and/or radiation therapies (Kupin 1992).

Animal and In Vitro: Analgesic (Koyama and others 1993); anti-inflammatory (Lin and others 1993; Stavinoha and others 1990); antitumor (Lee others 1994; Lieu others 1992; Lin and Tome 1991; Maruyama and others 1989; Sone and others 1985; Wang and others 1993; Yadomae and others 1998); antiviral (Eo and others 1999a, 1999b; Kim and others 1994, 1996); hepatoprotective (El-Mekkawy and others 1998; Kim and others 1999a; Lin and others 1993, 1995; Liu and others 1979a, 1979b); hypoglycemic (Hikino and others 1985; Tomoda and others 1986); hypocholesterolemic (Shiao and others 1994); hypotensive (ACE inhibitor) (Morigiwa and others 1986); immune-modulating: increases IL-1-β, IL-2, and IL-6 (Lei and Lin 1992; Wang and others 1997; Zhang and others 1993), increases cytotoxicity of T lymphocytes (Lei and Lin 1992), increases TNF-α in macrophage cultures (Wang and others 1997); inhibits platelet aggregation (Kawagishi and others 1993).

Actions Supported by Traditional or Modern Experience or Authoritative Data

Immunomodulator, tonic, sedative, antidepressive.

Medical Indications Supported by Clinical Trials

From the available studies, it appears that reishi can be used to inhibit platelet aggregation (Cheng and others 1993; Tao and Feng 1990). This action, which is attributed to the triterpenes, is consistent with the Chinese use of reishi alcohol extracts for the treatment of cardiovascular diseases. For these uses, reishi is given alone, or in combination with other botanicals, on a regular basis. However, to our knowledge, reishi preparations have not been compared to known antiplatelet agents. The limited clinical data (Kupin 1992) also supports the use of reishi in improving immunological parameters in patients undergoing conventional chemo- and/or radiation therapies for the treatment of cancer and in speeding restoration of immunocompetency after conventional cancer therapies have been concluded. For these purposes, the powder, hot water extract, powdered extracts, or polysaccharide fractions are utilized.

Clear protocols for how to employ these therapies are lacking. Some practitioners report positive effects when reishi is used in conjunction with conventional therapies, beginning the reishi as early as possible prior to, and throughout, chemo- and/or radiation therapies. Follow-up therapy can continue for several days (or until leukocyte counts return to normal) and up to several months. In China, concomitant use of reishi and other botanicals with conventional cancer therapies is commonly used. Other practitioners believe reishi should be given prior to, discontinued during, and readministered after, conventional therapies are completed.

Medical Indications Supported by Traditional or Modern Experience or Authoritative Data

In modern herbal therapies, reishi is applied in two primary ways: according to traditional principles of Chinese herbalism and incorporated into western herbal therapies based on its pharmacological activities, irrespective of traditional Chinese diagnostic and therapeutic indications. For information regarding its use in traditional chinese medicine (TCM), see Traditional Chinese Medicine Supplement.

In western herbal therapies, reishi is primarily used for its tonic properties, especially its use as an immunomodulator. For this purpose, it is often used in conjunction with chemo- and/or radiation therapies in the treatment of cancer as a means to help in the prevention of opportunistic infections and to counter side effects associated with conventional therapies. Reishi is also integrated into many treatment protocols for those infected with HIV with the primary goal being to enhance immune resistance and prevent opportunistic infections. For both of these purposes, reishi is most often combined with other similarly acting immune-modulating botanicals, such as astragalus (*Astragalus membranaceus*), ligustrum (*Ligustrum lucidum*), schisandra (*Schisandra chinensis*), and other mushrooms and polypores, including grifola (*Grifola umbellata*) and poria cocos (*Wolfiporia cocos*).

Reishi is additionally used as a general tonic for deficiency syndromes associated with tiredness and fatigue and, contrastly, as a calmative for insomnia due to restlessness and an overactive mind. Occasionally, reishi is used as a mild analgesic when pain is associated with stress and tension.

Substantiated Structure and Function Claims

Based on a review of the available literature, reishi supports a number of biological processes. It primarily supports general and specific immune resistance (Chang 1994a; Lin and Lei 1994). Specifically, in in vitro and animal studies, reishi has been shown to increase IL-1-β, IL-2, and IL-6 production or release (Lei and Lin 1992; Wang and others 1997; Zhang and others 1993), increase cytotoxicity of T lymphocytes (Lei and Lin 1992), and increase TNF-α in macrophage cultures (Wang and others 1997). Reishi also affects various mechanisms associated with regulation of blood sugar levels. Specifically, in animal studies, reishi and

its constituents have been shown to elevate plasma insulin levels, enhance glucose utilization in peripheral tissues, and enhance the metabolism of glucose in the liver (Hikino and others 1989). Animal and in vitro studies have also shown reishi to inhibit cholesterol biosynthesis, cholesterol absorption (Shiao and others 1994), and platelet aggregation (Tao and Feng 1990).

Dosages

Although widely used by consumers and health professionals, the effective dosage for humans has not been well established. According to a review by Chang (1994b), the *Ben Cao Gang Mu of Li Shi-Zhen* included reishi mushroom in a formula at approximately 22-108 mg daily of crude herb. In studies using the β-glucan receptor on human white blood cells, it was determined that doses of 0.05 mg/kg of β-glucan could elicit white blood cell microbial killing activity in vivo. Based on β-glucan concentration of reishi mushroom (minimum of 0.19% of a water soluble β-1,3-glucan fraction), this translates into a relative effective dose of approximately 300 mg. Additionally, dose-dependent biological activity of β-glucan on β-glucan receptors is reportedly observed over a 100-fold range. This further suggests the maximal effective dose of crude reishi mushroom, based on this assay, to be approximately 35 g daily (a recommendation consistent with the empirical use of reishi mushroom) (Chang 1994b). However, bioavailability and absorption studies are necessary before attempting to use the β-glucan-receptor model to establish an accurate dose for reishi mushroom. Researchers Liu and Bau (1994) recommend a dosage range of 3-15 g. The *Pharmacopoeia of the People's Republic of China* has recently included a monograph for reishi citing a dosage of 6-12 g daily which has been adopted here.

Powder:
>   6-12 g daily (Pharmacopoeia of the People's Republic of China 2000).

Decoction:
>   Approximately 375 mL twice daily.

Tincture (1:5):
>   10 mL 3 times daily (Huang 1993).

Rice Wine Extract:
>   30 mL twice daily (Liu and Bau 1994).

S AFETY P ROFILE

Classification of the American Herbal Products Association

Class 1: Herbs that can be safely consumed when used appropriately (McGuffin and others 1997).

Side Effects

No side effects were reported in the available clinical literature. Clinicians have reported occasional mild digestive upset and skin rashes in sensitive individuals. These side effects are usually of short duration. Because reishi mushroom inhibits the rate-limiting enzyme HMG-CoA reduc-

tase in the cholesterol biosynthesis pathway, it may also interfere with coenzyme Q10 synthesis. Coenzyme Q10 deficiency has been reported to be a risk factor for cardiovascular disease (Folkers and others 1990).

Contraindications

There are no reported contraindications cited in the literature. However, immune-modulating substances such as reishi mushroom should be used with extreme care or avoided completely in organ transplant patients utilizing immunosuppressive agents or in patients with autoimmune diseases.

Interactions

Reishi mushroom has been shown to potentiate the sedative action of reserpine and chlorpromazine and to antagonize the central stimulant activity of amphetamines (Chang and But 1986). It has also been reported to increase barbital- and pentobarbital-induced sleeping times in human clinical studies (Chen and Miles 1996). Due to its reported platelet aggregation-inhibitory activity, patients using anticoagulants should seek the advice of their primary health care provider before using reishi mushroom. Because of its inhibitory action on HMG-CoA reductase, reishi mushroom may potentiate the effects of lovastatin and other similarly acting cholesterol-lowering medications. Reishi mushroom has been reported to potentiate the antioxidant effects of glutathione (Song and Burmingham 1992). Because of its reported immune-enhancing activity, use of reishi mushroom may be contraindicated in conjunction with post organ transplant immunosuppressive agents. Reishi mushroom polysaccharides have been shown to antagonize the immunosuppressive effects of morphine in vitro and in vivo (Lu and Lin 1994a, 1994b).

Pregnancy, Mutagenicity, and Reproductive Toxicity

No data available.

Lactation

No data available.

Carcinogenicity

No data available.

Influence on Driving

Based on a review of the available literature and modern use, no negative effects are to be expected.

Precautions

Reishi mushroom extracts have been shown to contain a complex mixture of allergens (Horner and others 1993). In one experiment, 16% of 115 patients with asthma reacted positively when skin prick tested for potential allergenicity to reishi mushroom spores (Cutten and others 1988). Those with sensitivities to fungi and mushrooms should proceed carefully when using reishi mushroom products. It has been suggested that use of reishi mushroom should be discontin-

ued prior to surgery due to a reported vasodilatory action (Chen and Miles 1996) and its platelet inhibitory activity. Due to its reported hypoglycemic activity, those using hypoglycemic medications should consult with their health professional before using reishi preparations.

Overdose

No data available.

Treatment of Overdose

No data available.

Toxicology

A variety of fruiting body preparations have been reported to possess very low toxicity. Toxicology studies of reishi mushroom at Hunan Medical College, Hunan, China reported that intragastric administration of an alcohol extract at 1.2 and 12 g/kg daily for 30 days had no effect on the growth and development of animals; nor were any abnormalities in liver function, ECG, or major organs observed. Similarly, there were no toxic reactions observed in dogs administered 12 g/kg daily of a cold alcohol extract for 15 days and a hot alcohol extract at 24 g/kg daily for 13 days (the extracts were of undefined strength). According to a review by Soo (1994), 5000 mg/kg of a hot water extract administered orally to mice for 30 days failed to induce any changes in body weight, hematological parameters, or organ weight. The LD_{50} of an ip injection of an undefined reishi preparation in mice was reported to be 38.3 ± 1.048 g/kg (Chang and But 1986). Another source gave an LD_{50} for a reishi mushroom syrup (undefined potency) as 69.6 mL/kg in mice (route of administration not noted) and 4 mL/kg intragastric in rabbits (Huang 1993).

INTERNATIONAL STATUS

United States
> Regulated as a dietary supplement.

China
> Included in the *Pharmacopoeia of the People's Republic of China* (2000). Approved for the treatment of dizziness, insomnia, palpitations, shortness of breath, and cough and asthma due to consumption.

Japan
> Not included in the Japanese pharmacopoeia. Not used in Kampo medicines.

Reishi Mushroom
Ling Zhi   靈芝

THERAPEUTICS

Taste and properties:
Bland, sweet, or bitter depending on cultivar. Neutral to warming.

Channels of entry:
Heart, liver, lung, spleen, kidney.

Functions:
Nourishes and calms shen, relieves cough, tonifies qi and blood, supplements the kidneys, and stabilizes the will.

Nourishes the Heart and Calms the Spirit (Shen)

Ling zhi nourishes the heart and strengthens qi and blood. It is used to treat symptoms of heart and spleen deficiency manifesting as symptoms of insomnia, forgetfulness, fatigue, listlessness, and poor appetite. For insomnia: use in combination with dang gui (*Angelica sinensis*), bai shao (*Paeonia albiflora*), suan zao ren (*Ziziphus spinosa*), and long yan rou (*Arillus longan*), or with long yan rou and sang shen (*Morus alba*).

Relieves Coughs and Arrests Wheezing

Ling zhi dispels phlegm, relieves cough, and arrests wheezing. It is used to treat cough due to cold, cough with profuse sputum, accelerated respiration, chronic asthma, and inability to sleep due to dyspnea. For asthma and coughing: use with dang shen (*Codonopsis pilosula*), wu wei zi (*Schisandra chinensis*), gan jiang (*Zingiber officinale*), and ban xia (*Pinellia ternata*).

Tonifies Qi and Nourishes Blood

Ling zhi has traditionally been used to strengthen the body and tonify qi. It is used alone to treat qi and blood deficiency with weak digestion, poor appetite, listlessness, loose stool, and fatigue. Other symptoms may include dizziness and soreness of the lower back associated with liver imbalance and kidney deficiency.

Other Effects

In modern Chinese medicine, reishi has been used to treat angina pectoris, high cholesterol, hypertension, hepatitis, and leukopenia.

Actions

Nourishes the heart and calms shen, relieves coughing and arrests wheezing, tonifies qi, and nourishes blood.

Indications

According to the *Shen Nung Ben Cao Jing* (206 BC-AD 8) ling zhi was described as a superior medicinal agent [shang pin]. The superior herbs were among the most highly regarded of all medicines as they were considered to prolong life, prevent aging, boost qi, make the body light and limber, and corresponded to heaven. Specifically, red reishi was reported to treat binding in the chest, tonify the heart, nourish the center, sharpen the wit, and improve memory. In

Figure 11 Reishi mushroom *Ganoderma lucidum*
Photograph courtesy of North American Reishi, Gibons, British Columbia, Canada

addition to its physical properties, reishi was said to "cultivate virtue" (Yang 1997).

Additionally, reishi can be used for disturbed and restless shen, deficient blood and qi, insomnia due to disturbed shen, coughing and wheezing, and chronic asthma. According to the *Pharmacopoeia of the People's Republic of China* (2000), reishi is also used for dizziness, insomnia, palpitations, shortness of breath, and cough and asthma due to consumption.

In a unique study, the effects of reishi (250 mg of powdered extract; concentration undefined) on the pulse was investigated in healthy human subjects (12 males and 2 females). Subjects were not allowed to consume alcohol, caffeine, or have any medication and were required to rest for 30 minutes prior to recording pulses. The largest amplitude of pulse pressure was recorded with a pressure inducer affixed to the skin. Administration of reishi reportedly increased pulse amplitude extensively, though statistical analysis was not given and no control was included. The effects reached maximum amplitude at 30 minutes and was maintained for 90 minutes (Wang and others 1994).

Standard Formulas

Information regarding use in classic formulas is lacking.

SAFETY PROFILE

Side Effects

None cited in the literature. According to classic texts, the superior herbs [shang pin], among which reishi is classified, are said to be nontoxic and to cause no harm even when taken in large amounts for long periods of time (Yang 1997). Clinicians have reported occasional mild digestive upset and skin rashes in sensitive individuals.

Contraindications

None cited in the literature.

Interactions

None cited in literature.

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TABLE OF CONTENTS

9 781929 425105