CHAPTER 3 MEDICINALLY IMPORTANT MUSHROOMS

Synopsis

Many edible and non-edible mushrooms have long been used worldwide, especially in the Orient, for medicinal purposes. This Chapter gives a brief summary of the most important and widely used species. In each case their historical and current traditional use is considered together, where appropriate, with their commercial and modern medical applications. Important pharmaceutical products with proven medical applications have been derived from *Ganoderma* spp., *Lentinus edodes, Schizophyllum commune, Tremella fusiformis, Trametes versicolor*, and *Grifola frondosa,* and more recently *Phellinus* and *Hericium erinaceus*.

In addition to their nutritional value, many edible large mushrooms have long been used in the Orient for medicinal purposes. Many non-edible species have also gained important medicinal usage. An old Chinese proverb states that “medicine and food have a common origin”. At present there are at least 270 species of mushroom that are known to have various therapeutic properties (Ying *et al*., 1987). The practice of using fungi, especially mushrooms, in Chinese herbal medicines has been recorded in early records of the “Materia Medica”. The earliest book on medicinal materials in China, the “Shen Noug’s Herbel” (Shen Noug Pen Ts’ao Jing) (100-200AD), recorded the medicinal effects of several mushrooms including *Ganoderma lucidum, Poria cocos, Tremella fuciformis* and others. The most outstanding work on traditional Chinese medicines “Pen Ts’ao Kang Mu” (Compendium of Materia Medica) compiled by Li Shi-Zhen of the Ming Dynasty and published in 1575 documented more than 20 mushroom species, together with a non-mushroom insect-infesting fungus *Cordyceps senensis* which continues to be a major Chinese medicinal fungus (Bensky and Gamble, 1993).

Medicinal mushrooms have become even more widely used as traditional medicinal ingredients for the treatment of various diseases and related health problems largely due to the increased ability to produce the mushrooms by artificial methods. As a result of large numbers of scientific studies on medicinal mushrooms especially in Japan, China and Korea, over the past three decades, many of the traditional uses have been confirmed and new applications developed (Table 1, Wasser and Weis, 1999a). While much attention has been drawn to various immunological and anti-cancer properties of these mushrooms they also offer other potentially important therapeutic properties including antioxidants, anti-hypertensive, cholesterol-lowering, liver protection, anti-fibrotic, anti-inflammatory, anti-diabetic, anti-viral and anti-microbial. These properties will be examined in a later chapter. Clearly, many pharmaceutical companies in the Far East are viewing the medicinal mushrooms as a rich source of innovative biomedical molecules. Many polysaccharide-bound proteins produced by Basidiomycete fungi have been classified as anti-tumour chemicals by the US National Cancer Institute (Jong and Donovick, 1989). Some of the more important and leading medicinal fungi used in the Far East will be briefly summarised. For fuller details of each medicinal mushroom reference should be made to Hobbs (1995), Stamets (1993, 2001) and Mizuno (1995). A recent general paper by Wasser and Weis (1999b) gives detailed general mycological information on several of the most important medicinally valuable Basidiomycetes mushrooms, including biological and ethnomycological properties, taxonomy, morphology, anatomy, description, cultural characteristics, and distributions.

TABLE 1 Cross index of medically active higher Basidiomycetes mushrooms and their medicinal properties (Wasser and Weis, 1999a)

	Antifungal	Antiinflammatory	Antitumour	Antiviral (e.g. anti-HIV)	Antibacterial & Antiparasitic	Blood pressure regulation	Cardiovascular disorders	Hypercholesterolemia, hyperlipidemia	Antidiabetic	Immunomodulating	Kidney tonic	Hepatoprotective	Nerve tonic	Sexual potentiator	Chronic bronchitis
1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**
Auriculariales			+			+	X	X							X
Auricularia auricula-judas (Bull.) Wettst.															
Tremellales		+	+					+	+	+		+			X
Tremella fuciformis Berk.						+									+
Tremella mesenterica Rits.:Fr.															
Polyporales															
Schizophyllum commune Fr.:Fr.		X	X		X					X	X	X			
Dendropolyporus umbellatus (Pers.:Fr.)			X							X		X			X
Jül.	+		X	X	X	X			X	X		+			+
Grifola frondosa (Dicks.:Fr.) S.F. Gray															
Fomes formentarius (L.:Fr.) Fr.			+		+										
Fomitopsis pimicola (Schw.:Fr.) P. Karst.		+	+		+							+			
Trametes versicolor (L.:Fr.) Lloyd			X	X	X						X	X			
Piptoporus betulinus (bull.:Fr.) P. Karst.	+		+		+										
Hericium erinaceus (bull.:Fr.) Pers.			+							X			X		X
Inonotus obliquus (Pers.:Fr.) Bond.et Sing.		X	X							X		X			
Lenzites betulina (L.:Fr.) Fr.			+				+								
Laetiporus sulphurous (Bull.:Fr.) Murr.	+		+												
Ganodermatales															
Ganoderma lucidum (Curt.:Fr.) P.Karst		X	X	X	X	X	X			X	X	X	X	X	X
Ganoderma applanatum (Pers.) Pat.			+	+	+					+					
Agaricomycetideae															
Agaricales s.l.															
Pleurotaceae															
Lentinus edodes (Berk.) Sing.		X	X	X	X	X		X	X	X	X	X		X	
Pleurotus ostreatus (Jacq.:Fr.) Kumm.			+	+	+			+					+		
Pleurotus pulmonarius (Fr.:Fr.) Quél	+		+					+							
Tricholomataceae															
Flammulina velutipes (Curt.:Fr.) P.Karst.	+	X	X	+						X					
Oudemansiella mucida (Schrad.:Fr.) v. Höhn.	X														
Armillariella mellea (Vahl.:Fr.) P.Karst.	+					X	X						X		
Hypsizygus marmoreus (Peck) Bigel.			X												
Marasmius androsaceus (L.:Fr.) Fr.		X											X		
Agaricaceae															
Agaricus bla\ei Murr.			X												
Agaricus bisporus (J.Lge) Imbach			+							X	X				
Pluteaceae															
Volvariella volvacea (Bull.:Fr.) Sing.			+	+	+			+							
Bolbitiaceae															
Agrocybe aegerita (Brit.) Sing.	+		+					+					+		

X = commercially developed mushroom product (drug or dietary supplement)

\+ = non commercially developed mushroom product.

Ganoderma lucidum and Ganoderma tsugae:

G. lucidum and related species have the longest historical usage for medicinal purposes, dating back at least four millennia (Zhao and Zeuny, 1994). In Japan it is called *Reishi* or *Mannetake* (10,000 year mushroom) and in China and Korea it is variously called *Ling Chu, Ling Chih* and *Ling Zhi* (Mushroom of Immortality). It is the mushroom most depicted in ancient Japanese, Korean and Chinese Art and has been extensively depicted in Chinese royal tapestries. Reishi is also widely used in the Orient as a talisman to protect a person or home against evil. The fungus grows in many parts of the world and in Japan is to be found mainly on old plum trees. Originally, rare and expensive it can now be artificially cultivated, which makes it more accessible and affordable.

The mushroom and mycelium contain steroids, lactones, alkaloids, polyssacharides and triterpenes. Pharmacologically, a number of the water-soluble polysaccharides have demonstrated antitumour and immunostimulating activities. At least 100 different alcohol-soluble triterpenes have been identified including highly oxidised lanostane-type triterpenoids such as ganoderic, ganoderenic, lucidenic, and ganolucidic acids. These triterpenoids have been shown to possess adaptogenic and antihypertensive as well as anti-allergic properties.

Fig. 1a *Ganoderma lucidum* growing naturally on tree stump

Fig. 1b Reishi motif on pavilion door in the Forbidden City, Beijing (Willard 1990**)**

Fig. 1c Contemporary Chinese painting depicting the Phoenix bird holding a Reishi mushroom: both Ancient Chinese symbols of longevity (Willard, 1990)

Fig 1d *G. tsugae*, antler form growing on sterilised sawdust media (Willard, 1990**)**

Fig. 1e *G. lucidum* growing on sterilised sawdust media (Willard, 1990)

This mushroom possesses many different medicinal properties dependent on the stage and environment of its growth (Jong and Birmingham, 1992, Liu, 1999). Traditionally, it has been widely used in the treatment of hepatopathy, chronic hepatitis, nephritis, hypertension, arthritis, neurastheine, insomnia, bronchitis, asthma and gastric ulcers. Scientific studies have confirmed that substances extracted from the mushroom can reduce blood pressure, blood cholesterol and blood sugar levels as well as inhibit platelet aggregations (Table 2). Reishi extracts have been highly effective in alleviating altitude sickness and also in treating myotonia dystrophica. Several major biochemicals such as polysaccharides, proteins and triterpenoids with potent immuno-modulating action have been isolated from *Ganoderma* spp. The major immuno-modulating effects of these active substances include mitogenicity and activation of immune effector cells such as T cells, macrophages and natural killer cells resulting in the production of cytokines, including interleukins, tumour necrosis factor-α and interferons. The therapeutic action of *G. lucidum* as an anti-cancer and anti-inflammatory agent has been associated with its immuno-modulating properties (Wang *et al*., 1977). While the extensive range of traditional medical treatments with this mushroom have not yet been fully substantiated by modern scientific standards they are being extensively scrutinised in the Far East and the USA (Chang, 1995, 1999, Chen and Miles, 1996). In view of its bitter taste and indigestible structure (often similar to varnished wood in appearance) this is not an edible mushroom but, in hot water extracted form, it is available worldwide in tablet and liquid products (Stamets, 1999).

Table 2 Pharmacological effects of whole Reishi extracts *in vivo* and *in vitro* (for references see Hobbs, 1995)

- Analgesic
- Anti-allergic activity
- Bronchitis-preventative effect, inducing regeneration of bronchial epithelium
- Anti-inflammatory
- Antibacterial, against *Staphylococci, Streptococci,* and *Bacillus pneumoniae* (perhaps due to increased immune system activity)
- Antioxidant, by eliminating hydroxyl free radicals
- Antitumor activity
- Antiviral effect, by inducing interferon production
- Lowers blood pressure
- Enhances bone marrow nucleated cell proliferation
- Cardiotonic action, lowering serum cholesterol levels with no effect on triglycerides, enhancing myocardial metabolism of hypoxic animals, and improving coronary artery hemodynamics
- Central depressant and peripheral anticholinergic actions on the autonomic nervous sytem reduce the effects of caffeine and relax muscles
- Enhanced natural killer cell (NK) activity *in vitro* in mice
- Expectorant and antitussive properties demonstrated in mice studies
- General immunopotentiation
- Anti-HIV activity *in vitro* and *in vivo*
- Improved adrenocortical function
- Increased production of Interleukin-1 by murine peritoneal macrophages *in vitro*
- Increased production of Interleukin-2 by murine splenocytes *in vitro*

Key active constituents:
Beta and hetero-Beta-glucans (antitumour, immunostimulating)
Ling Zhi-8 protein (anti-allergenic, immuno-modulating)
Ganodermic acids – triterpenes (anti-allergenic agents, cholesterol and blood pressure reducing)

Estimates place the annual value of *G. lucidum* products worldwide at more than US $ 1.6 billion (Chang and Buswell, 1999).

Lentinus edodes

This fungus is indigenous to Japan, China and other Asian countries with temperate climates. It is to be found in the wild on fallen deciduous trees especially

Fig. 2a *Lentinus edodes* growing naturally on fallen timber

Fig. 2b *L. edodes* fruiting on an oak log (Stametes 1993)

Fig. 2c *L. edodes* growing on sawdust logs

chestnut, beech, oak, shia, alder etc. However, it has been grown artificially for centuries on cut logs which can support seasonal fruiting. In more recent times, mass cultivation has predominantly been achieved by the sawdust culture technology. In China it is known as *Xiang gu* (fragrant mushroom) and as *Shiitake* in Japan because of its historical association with the shia tree. This mushroom has been renowned in Japan and China for thousands of years both as a food and as a medicine. It has a most exotic and delicious taste and is a central part of many Oriental dishes and is increasingly being adopted in the West. There is little difference in flavour or mouth feel between mushrooms cultured on logs and those found in the wild on tree stumps or dead trees. However, sawdust cultured mushrooms now being marketed worldwide are considered to be soft in texture and

less flavoursome. It is undoubtedly the leading mushroom worldwide that can be used both as a nutritious and tasty food and a highly effective medicine.

In Oriental medicine it has been used for a wide range of health problems and its curative properties are well attested to in folk medicine (Hobbs, 1995). It has been particularly valuable in treating high blood pressure and lowering blood cholesterol. The fungus is the source of two well-studied polysaccharide preparations, viz. Lentinan – a cell wall polysaccharide extractable from both the fruit-body and mycelium, and LEM – a protein-bound polysaccharide derived only from the mycelium (Chihara, 1992). Both compounds have demonstrated anti-cancer activity. It is believed that such compounds function by enhancing the immune system rather than attacking the cancer cells directly. Such compounds are increasingly used in Japan as adjuvants to help support immune function in cancer patients during radio- and chemotherapy and can prolong survival times in some types of cancer (Mizuno, 1995).

An immense literature has been, and continues to be, accumulated on these compounds mostly in the Orient but increasingly so in Western scientific and medical journals. Areas of study that will be expanded on in later Chapters will include anti-cancer effects, immune regulatory effects, antiviral effects, bacterial and parasitic infections, hepatoprotective and cardiovascular effects.

Commercial preparations are available as tablets, capsules, or elixirs, and are extensively on sale in most Oriental countries, and increasingly in the USA and Europe, in natural food/medicine markets. Shiitake extracts more often appear in mixtures blended with Reishi, Maitake and others.

Key active constituents

Beta-D-glucan (Lentinan) and heteroglucan-protein (LEM) (anti-tumour, immunostimulating)

Eritadenine (cholesterol-reducing)
Ergosterol (provitamin D-2)
RNA fractions (antiviral nucleic acids)

Phellinus linteus

Fig. 3 *Phellinus* sp. growing naturally on deciduous tree

The fruiting-bodies of this fungus are called ‘song gen’ in Chinese medicine and ‘meshimakobu’ in Japanese. The fungus grows as a parasite mostly on living deciduous trees (but occasionally on *Pinus* spp.) in Japan and Korea but also in

other parts of the world (Teng, 1996). The fungus can now be cultured by log and sawdust technology. However, extensive studies are underway for mycelium culture in fermentors.

In traditional Chinese medicine hot water extracts of the inedible fruit-bodies have been used for an extensive range of ailments and it is believed to work as a 'miracle medicine' refreshing the human body and prolonging longevity (Ying *et al*., 1987). Recent studies have compared hot water extracts of *Phellinus* with the other main anticancer medicinal mushrooms when tested against xenographs. The *Phellinus* extract showed the strongest evidence of tumour proliferation suppression (Mizuno, 2000). It has been extensively studied for effects on digestive system cancers, e.g. gastric, duodenal, colon and rectal and also liver cancer. Special attention has been given to the beneficial effects of such extracts before and after cancer operations or in the adjuvant setting (Aziawa, 1998; Mizuno, 2000).

In recent years, using cultured mycelium of selected strains of *Phellinus,* compounds have been extracted and used in Korea as medicinals – especially for cancer treatment. This resulted from a national project between laboratories in the National Universities and several Pharmaceutical Companies, and the medicinal products now being manufactured by Korean New Pharmaceutical Co. There are a large number of Korean patents on the manufacture of such medicinal products (see Mizuno, 2000). Products as dietary supplements are expected shortly to enter the Japanese health food market.

The medicinal attributes of this fungus will merit close attention in the future (Mizuno, 2000).

Key active constituents

Beta-glucans (anti-tumour and immunostimulating)
Marketed as Meshima capsules

Poria cocos

Fig. 4 *Poria cocos* sclerotium at base of tree

This fungus, sometimes referred to as *Wolfiporia cocos*, is the most commonly used of all Chinese medicinal fungi. It is called *Hoeleu* or *Fu Ling* in Chinese which refers to the hard *sclerotium* of the fungus. This is a *mycorrhizal* fungus growing in association with the roots of various conifers, especially Chinese red pine. Large tuberculiform structures – the sclerotia – are formed underground and can be collected all year round but especially early autumn (Liu and Bau, 1980). Apart from the medicinal uses, the large sclerotial structures have been used as food in Nigeria and in parts of Eastern and Southern US – “Indian bread”.

Pharmacologically, the polysaccharides – spachyman and pachymaran exhibit strong anti-cancer and immunomodulatory activities. Low-molecular weight tetracyclic triterpenes have considerable immunostimulating and antiviral activities (Hobbs, 1995). The extensive range of traditional medicinal uses are documented in

Hobbs (1995) and Ying *et al*. (1987). The main clinical trials have been concerned with the treatment of viral hepatitis in which *Poria* was one of several herbal ingredients. *Hoeleu* is widely available in Chinese herbal shops in bulk, and is also included in many commercial preparations.

Key active constituents

Polysaccharides – spachyman and packymaran (anti-tumour and immunomodulating)
Tetracyclic triterpenes (immunomodulation and antiviral)

Auricularia auricula

Fig. 5 *Auricularia auricula* growing on fallen timber

This fungus is widely known as Jew's ear (a contraction of Judas' ear), wooden ear, or tree ear and in Japan, *Kikurage*. They are *facultative parasites* growing on trunks of many broadleaf trees or on dead wood (Hobbs, 1995). The fruiting body is gelatinous, elastic, rubber in texture and widely used in Chinese cuisine. However, it is an acquired taste! It is widespread in United States, Europe

and Asia. Historically, it has been used in China both as a food and medicine. It is particularly useful for stopping pain and bleeding, and is regularly prescribed in traditional Chinese medicine to treat haemorrhoids and excessive uterine bleeding (Ying *et al*., 1987). *Kikurage* has a high content of undigestible polysaccharides or dietary fiber.

Pharmacologically, the polysaccharides have been used as immune toxins, anticoagulants and to lower cholesterol. Extracts of *Auricularia* prevent egg implantation in animals terminating early and mid-pregnancy (He and Chen, 1991). Owing to this possible teratogenicity, it is recommended that *Auricularia* extracts should not be taken by pregnant or lactating women and those planning to conceive.

This is believed to be one of the first mushrooms to be artificially cultivated in China. Now extensively cultivated in Asia for culinary and medicinal purposes. As yet there is no cultivation practice on the West.

Key active constituents

Polysaccharides (immune stimulation, anticoagulant, lowering cholesterol).

Hericium erinaceus

Fig. 6 *Hericium erinaceus* growing on fallen log

This is an edible mushroom occurring widely in Japan and China, growing on standing and decayed broadleaf trees such as oak, walnut and beech. It can also cause heart rot in standing trees. Originally collected from the wild, it is now extensively grown artificially on logs and sawdust mixtures making this mushroom available all the year round. It is known in the West as the hedgehog or monkey head fungus and in China as *Shishigashida* because the fruiting body looks like the head of a lion. When air dried and extracted with hot water it is used extensively in traditional Chinese medicine (Houtou), to promote digestion and general vigour, strength and general nutrition. The polysaccharide from this mushroom have cyto-static effects on gastric, oesophageal, hepatic and skin cancers (Mizuno, 1999;

Mizuno *et al*., 1992). Mycelium produced from several *Hericium* spp. and then extracted with hot water formed the basis of a sports drink named Houtou that was used in the 11th Asia Sports Festival (1990) and is believed to have contributed to the remarkable activities of Chinese players!!

It is anticipated that this mushroom will become an important component in future health foods.

Key active constituents

Beta-D-glucans (antitumour)
Ergosterol (provitamin D)
Cyathane derivatives (nerve growth stimulators)

Grifola frondosa

This fungus forms large fan-shaped mushroom heads that often fuse together in masses at the base or on the roots of broadleaf trees. It can invade the core of the tree as a *parasite* causing extensive decay. It is often called 'Hen of the Woods' or 'Sheep's Head' while it is more often called in Japan, Maitake, which mean '*dancing nymph'*. In the early stages it is sought after for its delicious taste and excellent aroma. Previously, it was only collected from the wild and, consequently, was highly prized and priced. Since the late 1970s, it can be artificially cultivated on logs or sawdust mixtures and now many thousands of tons are being grown in Asia and more recently USA (Chen, 1999). In traditional Chinese medicine it has been used for improving spleen and stomach ailments, calming nerves and treating haemorrhoids (Hobbs, 1995). Maitake is a component of a wide range of Chinese medicines.

Fig. 7a *Grifola frondosa* growing naturally at base of tree.

Fig. 7b *G. frondosa* growing on sawdust mixture

Recent studies have shown that polysaccharides and polysaccharide-protein complexes from this mushroom have significant anti-cancer activity (Hishida *et al*., 1988, Kurashige *et al*., 1997). A limited number of clinical studies in Japan and the USA have shown that a purified fraction of polysaccharide is highly effective against cancers of the breast, lung, liver, prostate and brain. Details of clinical trials will be discussed later. Other fractions from *G. frondosa* exhibit immunological enhancement together with properties of anti-HIV, antihypertension, antidiabetic, and antiobesity (Zhuang and Mizuno, 1999). It is interesting to note that the β-glucan fractions from this mushroom are now being used by over 3,000 health professionals in the US for the prevention and treatment of :

Flu and common infection (bacteria and viruses)

AIDS (HIV)

Diabetes mellitus

Hypertension

Hypercholesterolemia

Urinary tract infections (particularly for women) (Professor Konno – personal communication).

Capsules with dried Maitake form widely accepted dietary supplements and apart from the Far East are now being extensively marketed in US and in Europe. Other examples are Maitake tea, whole Maitake powder and a Maitake drink.

Key active constituents:

1,3 and 1,6 Beta glucans (antitumour and immunomodulating)
Commercial product “Grifolan”

Flammulina velutipes

This is one of the most popular edible mushrooms in China and Japan where it is known as *Enokitake*. In nature it grows on stumps or decayed wood of hardwood trees as a typical mushroom. It is now mostly produced by artificial cutivation from jars of sawdust mix. After growth through the sawdust medium and as the primordia form on the surface, a plastic collar is placed around the neck of the jar and with special environmental conditions, results in the formation of elongated stipes and tiny mushroom heads. While they may be cooked in various ways they can also be used directly in salads. This is a major edible mushroom. It can be slightly salty and bitter in taste and is used in traditional Chinese medicine to treat liver diseases and gastric ulcers. Polysaccharides from this mushroom have been shown to inhibit the growth of cancers in a number of xenograph models. Flammulin, a basic simple protein from *F. velutipes* is able to markedly inhibit tumour cells (Komatsu *et al*., 1963). Flammulin has been purified to a crystalline state and clinical trials are now in progress (Zhang *et al*., 1999). The first scientific paper stating that edible mushrooms were effective against a solid tumour was with *Flammulina*.

A new antitumour glycoprotein has been isolated from cultured mycelium of this fungus - Proflamin. It is useful in combination therapy with other chemotherapy agents (Ikekawa, 1995).

Furthermore, an epidemiological study in Nagano Prefecture, Japan showed that the cancer death rate among farmers producing *F. velutipes* was remarkably lower than that of other people in the Prefecture and in Japan overall (Ikekawa, 2001).

Key active ingredients:

Beta-glucan-protein (antitumour and immunomodulating)
Beta-glycoprotein-Proflamin (antitumour)

Fig. 8a *F. velutipes* growing naturally on tree stump

Fig. 8b *F. velutipes* growing artificially on sawdust mix

Pleurotus ostreatus

The fruit-body of this mushroom is oyster-shaped and hence the common name Oyster Mushroom. It grows in layered clusters on deciduous trees in many parts of the world. It is one of the easiest to grow, most often on straw or sawdust

Fig. 9a *P. ostreatus* growing on decayed timber

logs, and has become one of the most popular edible mushrooms with a pleasant odour and taste. In the Sung dynasty (A.D. 420-479) it was referred to as “the mushroom of flower heaven” (Stamets, 1993, Hobbs, 1995).

Fig. 9b *P. ostreatus* growing on sawdust mixture

The medicinally beneficial effects of *Pleurotus* spp. were discovered independently on different continents. The awareness of their medicinal properties comes not only from Asia but from the folklore of central Europe, South America and African (Gunde-Cimerman, 1999). While first artificially cultivated in USA, production is now worldwide. There have been a number of studies suggesting a

role in numerous diseases with its anti-cancer activity, immunomodulating effects, and antiviral, antibiotic and anti-inflammatory activities. The major cause of death in the Western hemisphere is coronary artery disease with hypercholesterolemia as a primary risk factor. Drug therapy for lowering cholesterol has made considerable use of the pharmacologic agent lovastatin (mevinolin) and its analogues. Species of the genus *Pleurotus* are excellent producers of lovastatin and as such, *Pleurotus* could be considered as a functional food with natural cholesterol-lowering ability (Gunde-Cimerman, 1999). However, large scale production of lovastatin from fruit-bodies is not deemed commercially viable because of variability in fruit-body composition. Lovastatin is normally found only in the lamella and basidiospores and not in the stipe and cap. Mycelial cultivation could be the way ahead.

Key active constituents:

Beta-glucans (antitumour, immunomodulation)
Lovastatin (cholesterol-lowering)

Trametes (Coriolus) versicolor

This is a fungus with many synonyms but *Trametes* is now the accepted genus name. The multicoloured cap resembles a 'turkey tail' and occurs as overlapping clusters on dead logs in most parts of the world. This is not an edible fungus but hot water extracts have been used in traditional Chinese medicine from historical times for a wide range of ailments (Ying *et al*., 1987). Modern studies have produced two extremely important compounds, PSK or "Krestin", a water-soluble protein-bound polysaccharide and PSP, a polysaccharide-peptide both derived from mycelial cultures of the fungus. PSK has been shown to act directly on tumour cells (cytostatic and cytotoxic) as well as indirectly in the host to boost cellular

Fig. 10 *Trametes versicolor* growing naturally on fallen timber

immunity (Tsukagoshi, 1984). PSK also shows antiviral activity through stimulation of interferon production. PSP is a powerful immunostimulant and anti-cancer agent (Yang, 1993, Ng,1998). There have been a wide range of clinical trials for a range of human cancers. In most cases when taken with traditional chemotherapy or radiotherapy there have been significant increases in patient longevity. In 1987 “Krestin” accounted for 25% of the total expenditure of anti-cancer agents in Japan (Fukushima, 1989). A polysaccharopeptide isolated from this mushroom has been shown to inhibit the HIV-1 (Collins and Ng, 1997) while a polysaccharide showed chemopreventitive activity in an *in vitro* model (Kun *et al*., 1999). PSP and PSK are

just beginning to be available in the US and Europe. These compounds will be extensively discussed in later Chapters.

Key active constituents:

Beta-glucan-proteins (antitumour, antiviral, immunomodulating)
Ergopsterol (provitamin D2)

Tremella mesenterica and T. fuciformis

This fungus is commonly known as the “white auricularia” or “white jelly fungus”, and in Japan, *Shirokikurage*, with a jelly-like, translucent fruiting-body which usually grows on deciduous trees in warm climates worldwide. It can now be grown artificially and is being increasingly consumed in Asia.

It has a long historical use in traditional Chinese medicine as an immune tonic and for treating debility and exhaustion together with many other ailments including skin-care. It contains acidic polysaccharides especially glucuronoxylomannan, readily extracted with hot water giving a smooth and stable solution used in Oriental cuisine. The polysaccharides of this fungus show anti-cancer activity and can enhance immune functions (Hobbs, 1995). Clinical trials have shown it to be effective in treating radio- and chemo-therapy-induced leukopenia, boosting immunological functions and stimulating leukocyte activity (Hu and But, 1987). Med Myco Ltd. (Israel) have developed a submerged fermentation method to produce Tremellastin from *T. mesenterica* mycelium which contains 50% glucuronoxylomannan, together with proteins rich in amino acids, dietary fibre and vitamins of the B group. Dietary supplements from *Tremella* are only now beginning to expand into the Asian market, and they will certainly be of special significance in the cosmetic industry.

Fig. 11a *T. mesenterica* growing naturally on deciduous tree

Fig. 11b *T. fuciformis* growing naturally on deciduous tree

Key active constituents:

Acidic polysaccharides (glucuronoxylomannan) (antitumour, immunostimulatory, antidiabetic, skin enhancing)

Cordyceps sinensis and C. sobolifera

The fungi grow as *parasites* in larvae of Lepidoptera, gradually taking over the entire larval body. The diseased larvae bury themselves in the soil and die. Later the fungal mass or *stroma* grows out of the pupa and can be identified and collected.

The caterpillar fungus or *Tochukaso* has been highly regarded in Chinese medicine for many centuries. It is not a mushroom type fungus and the fruiting structure cannot be cultivated or cultured. The complete structure can be used in many forms, whole, powdered or extracted and has many applications in Chinese medicine (Hobbs, 1995; Halpern, 1999). Anti-cancerr polysaccharides have been isolated from several species of C*ordyceps* and some have been shown to have hypoglycaemic activity as well (Jones, 1997; Itami and Yahagi, 1990; Kun 1998). A major concern with herbal medicine using *Cordyceps* collected from nature is quality and safety.

However, the pure mycelium of these parasitic fungi can now be easily cultivated in fermentors and is attracting considerable interest as an agent to treat fatigue and improve motor function (Mizuno, 1999). The major chemical, pharmacological and toxicological studies on *Cordyceps sinensis* have been reviewed for English and Chinese literature by Zhu *et al*. (1988a,b). These studies show that the main activities of the fungus are in oxygen-free-radical scavenging.

Fig. 12 *Cordyceps* spp. stroma growing out of colonised insects

With this particular fungus it is clear that there will be increased usage of fermenter-produced mycelium. Such methods use selected media under aseptic conditions, providing better quality and homogeneity through process control.

Key active constituents:

Galactomannans (antitumour, immunostimulating)
Cordycepin
Sterols

Schizophyllum commune

This is a small, whitish fungus with no stalk which grows on dead trees throughout the year. It is a very common fungus and has worldwide distribution (Hobbs, 1995). Pharmacologically it is extremely important because it produces the polysaccharide Schizophyllan which shows considerable anti-cancer activity in xenograph and clinical practice. There have been numerous clinical trials with Schizophyllan which will be discussed later (Ooi and Liu, 2000).

Key active constituents:

Beta-glucans (antitumour and immunomodulation).

Fig. 13a *S. commune* growing naturally on dead deciduous tree

Fig. 13b *S. commune* view of underside of fruitbody

Agaricus blazei

This mushroom was first discovered in the USA in the 1940s but its main commercial cultivation now occurs in Japan and Brazil. In Japan it is called *Himematsutake* and is one of the most expensive medicinal mushrooms. A novel polysaccharide-protein complex has been shown to be highly active against a variety of xenographs (Ito *et al*., 1997).

Key active constituents:

Beta (1,3)-D-glucan, Beta (1-4)-D-glucan, Beta (1-6)-D-glucan (antitumour and immune enhancing)
Proteoglucans (antitumour).

Fig. 14 *Agaricus blazei*, Himematsutake or the Almond Portobella, grown in cased leachate cow manure (Stamets, 2000)

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