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MINI-REVIEW

Medicinal properties of *Hericium erinaceus* and its potential to formulate novel mushroom-based pharmaceuticals

Shengjuan Jiang · Songhua Wang · Yujun Sun · Qiang Zhang

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Abstract *Hericium erinaceus* is an important mushroom with edible values and medicinal properties. Both the mycelium and the fruiting bodies contain many bioactive compounds with drug efficacy. Recent evidence demonstrates that it is helpful to various diseases, such as Alzheimer's disease, immunoregulatory, and many types of cancer. Furthermore, emerging pieces of evidence have shown that different active molecules in *H. erinaceus* have different functions on different organs in different diseases via the different mechanisms. Drawing on current research results, this review mainly focuses on the therapeutic effects of *H. erinaceus* on various diseases of multiple physiological systems, including the nervous system, digestive system, circulatory system, and immune system. This paper also discusses systematically the efficient protection of *H. erinaceus* against the diseases from the intricate experimental proofs by using the systematic viewpoints, which provides a framework for future research directions.

Keywords Cytokines · *Hericium erinaceus* · Immunoregulatory · Inflammation · Physiological system

Introduction

Many nutritional foods have been considered as medicine in order to prevent numerous illnesses during the millennial human practice (Francesca and Francesca 2007). The mushrooms, with good tastes and diversity of active biomolecules, are widely used in the diet and clinical therapy (Abdullah et al. 2012; Sun et al. 2008). The interest in edible mushrooms has been increasing in developed countries due to their potential health benefits. *Hericium erinaceus* (HE) is an important wild edible delicacy and is one of the famous four dishes in China. As a kind of edible and pharmaceutical product, it has attracted considerable attention in the past few years. It contains proteins, unsaturated fatty acids, carbohydrates, and a variety of trace elements (Ulziijargal and Mau 2011). The nutraceuticals in HE can be helpful to various diseases of multiple physiological systems, including the nervous system, digestive system, circulatory system, and immune system. Many pieces of research have found that different active molecules in HE have different functions on different organs in different diseases. Furthermore, the mechanisms are different and complicated. So, the daily diet containing HE is beneficial to human health, especially to the patient population. But, the conditions of the environment and the culture medium can greatly influence the contents of HE bioactive compounds in the cultivation course. Thus, in this review, we primarily focus on the characteristics of growth, cultivation, and the nutraceuticals of HE. Furthermore, the highlight of this review is that the medicinal effects of HE and its probable molecular mechanisms are sorted and presented according to the physiological systems. This review is unique in that the possible layered protection reasons of HE against diseases are teased out from the intricate experimental proofs in the available literature by using the systematic viewpoints.

Characteristics and cultivation

H. erinaceus is also called Lion's Mane mushroom or monkey head and is widely found in Asia, Europe, and generally the North temperate latitudes. It is a wood-rotting fungus belonging to the family of the Hericiaceae in the order Russulales within the phylum Basidiomycota. The mature fruiting body is fleshy semi-spherical (Fig. 1a). The soft spines hang from a

S. Jiang (✉) · S. Wang · Y. Sun · Q. Zhang
College of Life Science, Anhui Science and Technology University, Fengyang 233100, Anhui, China
e-mail: jiangsjahstu@126.com

tough, hidden unbranched clump which is attached to the tree. The flesh is white when it is young (Fig. 1c). HE becomes yellowish and brownish when it gets old gradually. Once the browning occurs, the quality of the mature mushroom decreases (Weijn et al. 2013).

HE grows slowly and inhabits high on living beech or oak trunks in pairs in the wild forests. Its growth is greatly influenced by the environmental conditions, such as air circulation, light, temperature, humidity, and pH. As the aerobic fungi, HE is very sensitive to the CO_2 concentration of the environment (Rowan 2002). When the concentration of CO_2 in the growth environment exceeds 0.1 %, the fruiting body will develop into a coral-like deformity mushroom (Fig. 1b, d), which badly affects the flavor and appearance quality of HE.

The artificial cultivation of HE is firstly reported in China in 1988, and it is cultivated by artificial log using bottles and polypropylene bags (Suzuki and Mizuno 1997). In the vegetative and reproductive growth stages, mycelia and fruiting body can be cultivated with many agricultural by-products (Table 1). When HE is cultivated with *Artemisia capillaris* (Choi et al. 2013b) or *Artemisia* (Choi et al. 2012), the ethanolic extracts from HE have stronger activities to lower the cholesterol levels than that from the normal cultivation. It can be concluded that medium can influence the contents of bioactive compounds. The mushrooms can collect minerals from the medium. Many hazardous heavy metals which exist in the culture medium, including Cd (Wang et al. 2007, 2008) and radionuclides, can also be accumulated in the fruiting bodies (Falandysz and Borovicka 2013). For example, cadmium and lead in some edible mushroom (including HE) are found to be higher than legal limits (Zhu et al. 2011). Selenium-fortified food is vital to human health (Falandysz 2008). And cultivation of mushroom on selenium-rich substrates is an effective means to produce the nutritive food. But, the addition of inorganic selenium induces degradative changes in cell organelles (Bhatia et al. 2013). However, organic selenitetriglycerides help the cells to cope with the toxic activity of inorganic selenium ions (Slusarczyk et al. 2013). The results imply that agricultural by-products not only are the good source of energy and nutrition for HE growth and development but also are the sources of the harmful heavy metals. So the safe cultivation influences the nutrition value of HE.

Flavor substance and nutraceuticals

The taste of HE is often described as “seafood like” and is best typified by the taste of shrimp or lobster. Every 100 g of dried HE contains approximately 22.3g crude protein, 3.5g crude fat, 64.8g carbohydrate, and 4.3g moisture by chemical analysis (Mau et al. 2001). The contained soluble sugars include arabitol, glucose, mannitol, myo-inositol, and trehalose. The amount of arabitol is abundant (127.2 mg/g dry weight). It also has 16 kinds of amino acids including seven kinds of essential amino acids. The flavor and the specific odor experienced from eating HE come from a combination of chemical aromatic constituents. The various components in HE yield the specific tastes, such as flavor 5′-nucleotides (Mau et al. 2001) and volatile oil (hexadecanoic acid, linoleic acid, and phenylacetaldehyde). 2-Methyl-3-furanthiol, 2-ethylpyrazine, and 2,6-diethylpyrazine are considered to be principal contributors of the odor (Miyazawa et al. 2008). HE offers a unique variety of phytonutrients, encompassing amylase (Du et al. 2013), herinase (Choi et al. 2013a), laccase (Zou et al. 2012), hericerin (Kobayashi et al. 2012), isohericenone (Kim et al. 2012a), ferulic acid (Xie et al. 2010), geranylated aromatic compound (Yaoita et al. 2012), beta-D-glucan (Dong et al. 2006), trypsin-like proteinases (Gzogian et al. 2005), lectins (Li et al. 2010), polysaccharides (Han et al. 2013), etc. It thus provides a rich source of complete proteins, minerals, and vitamins. So it is the ideal food for patients and those vegan individuals who need alternate sources of the essential nutrients.

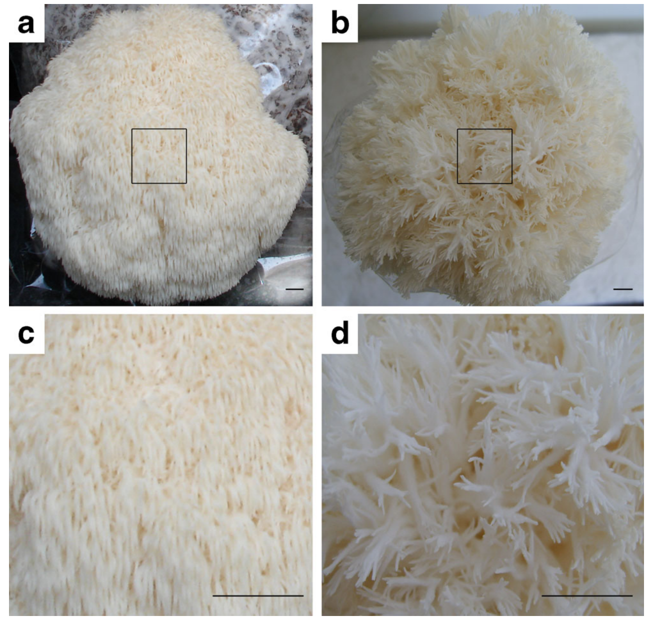

Fig. 1 Images of HE. **a** is the mature normal HE. **b** is the mature coral-like deformity HE. **c** is the part magnifications of **a. d** is the part magnifications of **b**. The *scale bar* is 5 mm

Medicinal effects on physiological systems

A variety of constituents from HE are known to have health-promoting activities and therapeutic potential, including anti-tumor, cytotoxicity, hemagglutination, immunomodulatory activities, etc. Different bioactive molecules have diverse

Table 1 Agricultural by-products used to cultivate the mycelia and fruiting body of HE at different developmental stages

Developmental stages	Organ	Medium	References
Vegetative growth	Mycelia	PDA medium, yeast malt medium, oak sawdust medium	Imtiaj et al. 2008
		Rice bran, wheat bran, barley bran, soybean powder, Chinese cabbage, egg shell	Ko et al. 2005
		Tofu whey	Zhang et al. 2012
Reproductive growth	Fruiting body	Textile industry wastes (alder sawdust, rye straw, hemp, flax shive)	Siwulski et al. 2010
		Sunflower seed hulls	Figlas et al. 2007
		Agro wastes (rice straw, sugarcane bagasse, soybean dregs)	Hu et al. 2008
		Artemisia capillaris	Choi et al. 2013b
		Artemisia	Choi et al. 2012

functions. All things considered, the biological activities of HE are involved in four main physiological systems (Fig. 2a).

Effects on the nervous system

The nervous system plays the leading role in the organism. The basic structure and functional unit of the nervous system are nerve cells, which are a kind of highly specialized cell. The functions of HE on the nervous system are divided into two types.

In the first type, HE can regulate the growth and development of the neurons and accessory structures. For example, the exo-biopolymer purified from the liquid culture broth of HE mycelium enhances the growth of rat adrenal nerve cells and the extension of the neurites of a PC12 cell (Park et al. 2002). The extracts from mycelia and dried fruit body stimulate neurite outgrowth of the cultured neural hybrid clone NG108-15 cells (Wong et al. 2007). Ethanol extracts of HE enhance the neurite outgrowth of PC12 cells (Mori et al. 2008). The extracts of HE can promote normal development of cultivated cerebellar cells and regulate the process of myelin genesis process in vitro (Kolotushkina et al. 2003). The extracts from HE exert neurotropic action and improve the myelination process in the mature myelinating fibers (Moldavan et al. 2007). Aqueous extract of HE fresh fruit bodies can promote functional recovery following crush injury to the peroneal nerve in adult female Sprague-Dawley rats (Wong et al. 2009a, 2011). Dilinoleoyl-phosphatidylethanolamine and 3-hydroxyhericenone F from HE have the protective activity against endoplasmic reticulum stress-dependent Neuro2a cell death (Ueda et al. 2008; Nagai et al. 2006). All the process are involved in the axonal protein synthesis and the expressions of *c-Jun*, *c-Fos*, and genes in the protein kinase B (Akt) and mitogen-activated protein kinase (MAPK)-signaling pathways, which are related with the cell survival and neurite outgrowth. The expressions of the genes and proteins can promote the regeneration of axons and reinnervation of motor end plates and neuromuscular junction (Wong et al. 2012).

In the second type, HE can coordinate the functions of neurons which are associated with the complex neurodegeneration diseases. Alzheimer's disease (AD), depression disorder, anxiety, and cognitive impairment are related with the

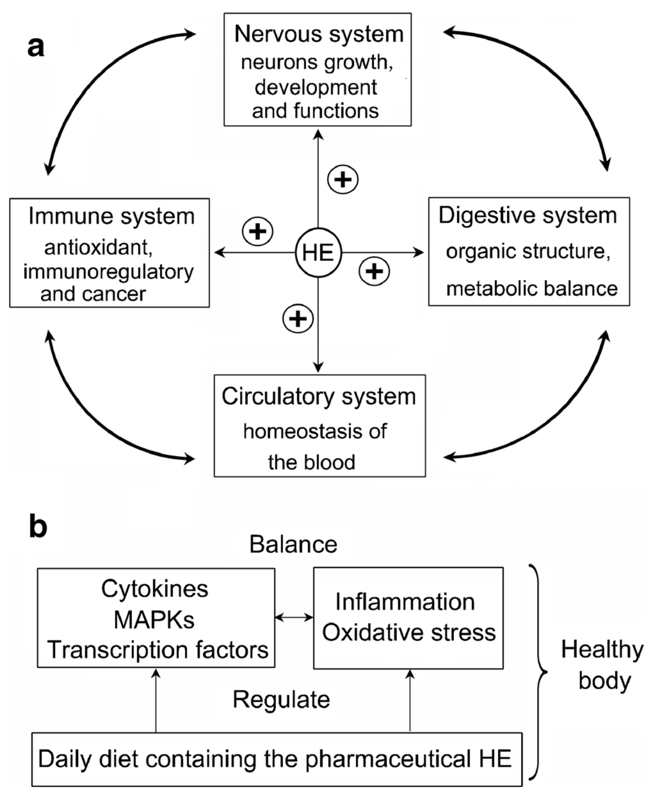

Fig. 2 Possible protections of HE on the organism. **a** Physiological systems influence each other and closely cooperate with each other (indicated by *left right arrow*). HE could regulate the physiological functions (mainly including the nervous system, digestive system, circulatory system, and immune system) of the organisms (indicated by *circled plus*). **b** The factors (cytokines, MAPKs, and transcription factors) are related with the inflammation and oxidative stress in the human body (indicated by *left right arrow*). HE could regulate the balance among them. So, the daily diet containing the pharmaceutical HE could help humans to keep a healthy body

pathological changes and progressive function loss of the neurons. The pathophysiology of these diseases is multifactorial and complex (Anand et al. 2014). The disease courses are the combined actions of complex disease gene regulatory networks (Goodall et al. 2013). As a medicinal mushroom, HE can prevent impairments of spatial short-term and visual recognition memory induced by amyloid β peptide in AD (Mori et al. 2011). HE can improve sleep quality, ameliorate depression and indefinite complaints, relieve menopausal syndromes (Nagano et al. 2010), and alleviate the mild cognitive impairment (Mori et al. 2009).

Effects on the digestive system

The digestive system contains a series of hollow organs joined in a long, twisting tube from the mouth to the anus. The stomach is a big food storage and mixer. *Helicobacter pylori* is a gram-negative, microaerophilic bacteria found in the stomach. It is the main pathogenic factor of chronic gastritis, peptic ulcers, and even adenocarcinoma of the distal stomach (Blaser 2006). Ethanol extracts and ethyl acetate fractions of HE can inhibit the growth of *H. pylori* in vitro (Shang et al. 2013). In addition, the freeze-dried fruiting bodies of HE can decrease the gastric mucosal damage and edema and provide cytoprotection against ethanol-induced gastric ulcers in rats (Abdulla et al. 2008). Ethanol extract from HE cultivated with *Artemisia* can relieve the gastric mucosal damage induced by ethanol-HCl in rats (Choi et al. 2012). In the digestive system, the liver is a central regulator of glucose homeostasis. The liver also produces bile, the digestive juice to digest fat from the food. Since the liver receives absorbed nutrients, liver function is influenced by the food components (Wiernsperger 2013). The hepatic triacylglycerol levels can be reduced by daily diet containing HE (Hiwatashi et al. 2010). The methanol extract from HE cultivated with *Artemisia* changes the expressions of typical enzymes and the hepatic structure, which implies that the extract has a strong protective effect on CCl_4-induced hepatic damage in rats (Choi et al. 2005). In addition, HE protects against necrosis of the liver administered by intraperitoneal injection (Kim et al. 2012b). To give full play to the HE beneficial effects, its mycelia substitutes 5 % of wheat flour to make bread (Ulziijargal et al. 2013).

Effects on the circulatory system

The circulatory system permits blood and lymph circulation to transport nutrients (such as glucose and triglyceride), oxygen, carbon dioxide, hormones, etc. The essential material in the body can nourish the cells, stabilize temperature and pH, and maintain the homeostasis of the body. The methanol extract from HE cultivated with *Artemisia* has a potent inhibitory effect on the proliferation of vascular smooth muscle cells (Choi et al. 2005). If the concentrations of the nutrients in the blood are disequilibrated, the diseases appear gradually. The exo-polymer produced in submerged mycelial culture of HE can significantly reduce the plasma triglyceride, total cholesterol, low-density lipoprotein cholesterol, phospholipid, and liver total cholesterol level, which imply that it has the hypolipidemic effect in rats by oral administration (Yang et al. 2002, 2003). The HE extracts by organic solvents weaken the polydipsia symptom and lower the blood glucose level of the streptozotocin-induced diabetic rats (Wang et al. 2005). Hericenone b potently inhibits platelet aggregation induced by collagen through blocking the collagen signaling transductions both in human and rabbit platelets (Mori et al. 2010).

Effects on the immune system

The immune system protects an organism against diseases with layered defenses of increasing specificity. The effects of HE on the immune system can be divided into three types.

One involves the antioxidant activities. Oxygen free radicals and lipid peroxides are very damaging compounds. They belong to the oxidative stress which contributes to the tissue and cell injury. An imbalance between reactive oxygen species levels and antioxidant defenses occurs in many different diseases (Alzoghaibi 2013). So, antioxidants have been widely used in dietary supplements and investigated for the prevention of diseases. The ethanol, methanol, and hot water extracts of HE have the free-radical-scavenging activities, including reducing power ability, chelating effects on ferrous ions, DPPH free-radical-scavenging activity, β-carotene bleaching, and inhibition of lipid peroxidation (Fui et al. 2002; Mau et al. 2002; Abdullah et al. 2012; Zhang et al. 2012). And different processing of the fruiting body can affect the antioxidant properties (Wong et al. 2009b). Besides, HE polysaccharides can decrease lipid peroxidation level and increase antioxidant enzyme activities in renal ischemia reperfusion animals in vivo (Han et al. 2013). Polysaccharides from HE significantly enhance skin antioxidant enzyme activities and collagen protein levels in a dose-dependent manner, implying the anti-skin-aging activities (Xu et al. 2010). Therefore, HE is a good source of exogenous antioxidants which might be considered the important remedies to ameliorate pathological alterations in oxidative stress-related disease.

Another one deals with the immunoregulatory. When foreign substances (antigens) invade the body, dendritic cells (DCs) process antigens, present them on the cell surface, and act as messengers between the innate and the adaptive immune responses. The maturation of DCs is an important process in the initiation and regulation of immune responses (Guerder et al. 2013). The water-soluble components from HE enhance the expressions of cluster of differentiation (CD, including CD80, CD83, CD86, and CD205) and major histocompatibility complex (MHC) molecules and induce the maturation of human DCs (Kim et al. 2010). Natural killer (NK) cells destroy compromised host cells, such as tumor cells or virus-infected cells. The water extracts of HE indirectly activate the cytolytic ability of NK cells possibly via the induction of interleukin-12 (IL-12) and interferon-γ (IFN-γ) in splenocytes (Yim et al. 2007). Inflammation, which is one of the first immune responses, is triggered when innate immune cells detect infection or tissue injury. Molecular targets of inflammation include cytokines such as IL and tumor necrosis factor-α (TNF-α), chemokines, cyclooxygenase-2 (COX-2), prostaglandins, inducible nitric oxide synthase (iNOS), nitric oxide (NO), etc (Laveti et al. 2013). Induction of these molecules promotes the recruitment and activation of leukocytes, which are critical for removing foreign particles or host debris (Newton and Dixit 2012). The water extract from HE can induce IL-1β expression in macrophages at a transcriptional level by enhancing the activation of transcription factors, nuclear factor kappaB (NF-κB), NF-IL6, and activator protein 1 (AP-1) in murine macrophage RAW 264.7 cell line (Son et al. 2006b). It induces iNOS gene expression followed by NO production in macrophages via enhancing the activation of NF-κB (Son et al. 2006a). It also up-regulates production of nitric oxide and expression of cytokines (IL-1β, TNF-α, and TNF-β) mediated by activated macrophages (Lee et al. 2009a, b). The water extracts also induce intercellular adhesion molecule-1 (ICAM-1) expression at both protein and mRNA levels in human monocyte cell line. The induction is activated through extracellular signal-regulated kinase (ERK)- and reactive oxygen species (ROS)-dependent signaling pathways which result in the subsequent activations of transcription factors (NF-κB, AP-1, SP-1, and STAT-1) (Kim et al. 2011c). Based on the above effects of HE, extracts significantly enhance the acceleration of wound healing in rats (Abdulla et al. 2011). And, an HE-containing diet enhances the immunity and disease resistance of shrimp against the *Vibrio alginolyticus* (Yeh et al. 2011). Inflammation normally can eliminate the invaders and restore the tissue physiology. However, when inflammation becomes chronic, increasing pieces of evidence show that it can cause several pathology types (Vendramini-Costa and Carvalho 2012). HE can provide a protective effect against LPS-induced inflammation (Jin et al. 2009b) by suppressing the generation of excessive active pro-inflammatory mediators, such as NO, ROS, prostaglandin E2 (Kim et al. 2012c), IL-1β, and TNF-α (Jin et al. 2009a). It could be concluded that HE might regulate the inflammatory process by increasing or decreasing both signals that initiate and maintain inflammation and signals that shut the process down.

The other relates to cancer. Cancer cells possess strong capacities to grow uncontrollably and resist the usual mechanisms of cell death. They invade nearby parts of the body through the lymphatic system or bloodstream (Ramaswami et al. 2013). When the canceration of the normal cells begins, the balance of the complex cellular signal networks is interrupted. The matrix metalloproteinase (MMP) 2 and MMP-9 mediate many of the changes in the microenvironment during tumor progression (Kessenbrock et al. 2010). Daily intraperitoneal injections of HE extractions can reduce the expression of MMP-2 and MMP-9, thereby blocking migration and invasion of cancer cells to the lungs. Furthermore, they down-regulate the phosphorylations of ERK, c-Jun N-terminal kinase (JNK), and MAPK (Kim et al. 2013). Cell apoptosis can prevent the development of cellular cancerization. HE enhances doxorubicin (Dox)-mediated apoptotic signaling by reducing cellular FADD-like interleukin-1-converting enzyme inhibitory protein (c-FLIP) expression via JNK activation (Lee and Hong 2010). The aqueous and ethanolic extracts induce apoptosis of U937 human monocytic leukemia cells by activation of mitochondria-mediated caspase-3 and caspase-9 (Kim et al. 2011a). In addition, the mycelia and culture broth of HE also show chemopreventive effects via induction of nuclear factor E2-related factor-antioxidant response element (Nrf2-ARE) pathway and induce the cellular defense (Jin et al. 2009c). Although the causes of cancers are diverse, complex, and only partially understood, the discovery of the efficient therapies is ongoing. The agglutinin from an HE fruiting body exhibits potent mitogenic activity toward mouse splenocytes. And, it also shows the antiproliferative activity toward hepatoma (HepG2) and breast cancer (MCF7) cells (Li et al. 2010). The water-soluble polysaccharides from HE have significant antiartificial pulmonary metastatic tumor effects in mice by increasing the amounts of CD4 cells and macrophages (Wang et al. 2001). Crude protein extracts of HE show cytotoxicity on human cervical cancer HeLa cells (Lee et al. 2010). Daily intraperitoneal injections of HE extractions significantly reduce tumor weights and inhibit neo-angiogenesis inside the tumors (Kim et al. 2011b). In brief, the anticancer processes mainly involve activation of macrophages, inhibition of angiogenesis, reduction of phosphorylation MAPKs, and induction of cell apoptosis.

In-depth understanding of HE against the diseases

From the above medicinal proofs, we can conclude that the different active molecules in HE have different functions on different organs in different diseases via the different mechanisms. All the functional pieces of evidence seem to be scattered and have no correlation. However, by deep analyses, the understanding of the HE protections on the organism can be summarized in three aspects.

Viewed from a global viewpoint, HE might devote itself to regulate the overall physiological functions of the organisms (Fig. 2a). The structure and function of the human body are extremely complex. In the precise human body, different systems have their own unique functions. The digestive system is responsible for working on the food ingestion, absorption, and transportation of nutrients and eliminating the unwanted food from the body in the form of feces. The circulatory system plays a vital role in homeostasis and the distribution of blood, nutrients, and hormones to the various body organs. The immune system identifies a variety of threats and protects the organism against disease or other potentially damaging foreign bodies. The nervous system, which is one of the most complex systems, controls and regulates the different systems of our body. However, all physiological systems cannot be viewed in isolation because they influence each other and closely cooperate with each other under the direct or indirect regulations of the nervous system. In general, the physiological systems should be evaluated from the whole body. And, the disorder of any system would disturb the balance of the whole-body homeostasis. The complication is that one disease in one system might trigger the pathological changes of other systems. For example, type 2 diabetes is associated with a higher risk of vascular disease, hypoglycemia, and inflammation (Samaras and Sachdev 2012). The amyloid-β peptide (Aβ) can induce oxidative stress (Wang et al. 2013) and inflammation response in the AD (Bungart et al. 2013). However, some pieces of evidence imply that Alzheimer's disease may not originate within the brain (Viscogliosi and Marigliano 2013), and some scientists find that gut bacteria impacts human behavior in the neurodevelopmental disorders (Hsiao et al. 2013). So, it can be concluded that organisms may be studied as a holistic complex system, and the cure of a disease might be started from seeking the real decisive incentives underlying the symptoms of the diseases on the whole. As an edible and medicinal product, HE has been proved to have the medicinal effect on the four main physiological systems, which implies that HE might perform the regulative roles in the body.

Analyzed from the inducements of the diseases, HE can be conducive to reducing or eliminating the risk factors of the diseases which are caused by inflammation and oxidative stress (Fig. 2b). Although the exact pathogenesis of many complicated diseases of humans is unclear, more and more pieces of evidence testify that inflammation and oxidative stress are hallmarks of the majority of diseases (Holmes 2013; Schott and Revesz 2013; Gubandru et al. 2013). Chronic inflammation plays the roles in the tumor onset, growth, and metastatic progression (Woller and Kuhnel 2014). As a major physiological hallmark of malignancy, cancer-related inflammation has an important value in diagnosis, treatment, and prognosis in esophageal cancer (Zhang et al. 2013a). Inflammatory development is correlated with cognitive impairment in AD patients (Shen et al. 2013). AD exhibits extensive oxidative stress which reveals the full spectrum of oxidative damages to neurons (Wang et al. 2013). Oxidative stress accelerates the proliferation of colorectal cancer cells (Kang et al. 2013). The weak expressions of obesity-related pro-inflammatory cytokines can effectively lower the blood glucose level in mice (Zhou et al. 2013). Acute blood glucose fluctuation is associated with enhanced oxidative stress (Zhang et al. 2013b). Costantini et al highlights the effects of natural antioxidants on the prevention and cure of liver cancer (Costantini et al. 2014). Many scientists have noticed the roles of inflammation and oxidative stress in the progression of many diseases. And, they have intended to identify the core cancer genes and pathways for all tumor types at various clinical time points by using the genomic data (Kandoth et al. 2013). But, few, if any, studies have shown how the diseases are triggered (Mishra et al. 2012). Nevertheless, as an edible and pharmaceutical product, HE, which has the exact antioxidant and immunoregulatory activities, could play important roles in the prevention of the diseases.

Viewed from the inside molecular mechanisms, HE can be beneficial to the prevention of the diseases by regulating the expressions of the cytokines, MAPKs, and the transcription factors (Fig. 2b). Through deep analysis, the main effects of the diseases involve the alterations of mitogen-activated protein kinases (including MAPKs, ERK, p38, and JNK), activations of transcription factors, and the inductions of cytokines. Mitogen-activated protein kinase pathways regulate cellular proliferation, differentiation, migration, survival, and apoptosis. Many inherited or acquired human diseases stem from abnormalities in MAPK-signaling pathways and the inflammatory cytokines (Kim and Choi 2010). For example, inflammation and oxidative stress alter the risk of colorectal cancer by interacting with MAPK-signaling genes (Slattery et al. 2013). In gastric and esophageal cancer, the MAPK pathway regulates the expression of human leukocyte antigen-A (HLA-A), the signal of disease progression, and poor prognosis (Mimura et al. 2013). NF-κB regulates the expression of inflammation-associated enzymes and cytokine genes. And it has a cross talk with p38 and reactive oxygen species during inflammation and cancer initiation and progression (Hoesel and Schmid 2013). The cytokine IL-6 is often expressed in the tumor microenvironment of multiple cell types (Zhang et al. 2013c). Although the detailed molecular mechanisms remain obscure, HE, as an edible and medicinal product, can regulate the expressions of related signal molecules. Thus, HE might be considered as a new potential health-enhancing food.

The brain regulates the behavioral and physiological responses to given signals. It also coordinates not only external sensory inputs from the environment but also internal challenges from the body to maintain the physiological homeostasis (McEwen and Gianaros 2011). The comprehensive physiological responses of different systems lead to protection and adaptation of the organism to the stress and adversity-related challenges (McEwen and Gianaros 2010). Although our knowledge of the mechanisms of the body and diseases is still in its infancy, the daily diet containing the edible and medicinal HE (about 50g FW for adult) could help humans to keep a healthy body. It seems clear that diet cures more than doctors. The disease prevention and treatment by the intake of the potential medicinal food could open up a new possible direction of medical research. Unfortunately, the clear mechanisms of the bioactive components found in HE are limited. More large-scale prospective studies are needed to investigate the detailed molecular curative mechanisms of *H. erinaceus* and to develop the effective *H. erinaceus* pharmaceuticals.

Conclusions

As an edible and medicinal product, *H. erinaceus* can regulate the expressions of cytokines, MAPKs, and the transcription factors at the molecular level. And, *H. erinaceus* can also influence the inflammation reactions and oxidative stress of the cells. Based on the combined effects of the molecular and cellular levels, *H. erinaceus* performs the medicinal functions on the tissues, organs, and organisms. So *H. erinaceus* has the potential to formulate novel mushroom-based pharmaceuticals.

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Conflict of interest The authors have no conflict of interest.

References

Abdulla MA, Noor SM, Sabaratnam V, Abdullah N, Wong KH, Ali HM (2008) Effect of culinary-medicinal lion's mane mushroom, *Hericium erinaceus* (Bull.: Fr.) Pers. (*Aphyllophoromycetideae*), on ethanol-induced gastric ulcers in rats. Int J Med Mushrooms 10:325–330

Abdulla MA, Fard AA, Sabaratnam V, Wong KH, Kuppusamy UR, Abdullah N, Ismail S (2011) Potential activity of aqueous extract of culinary-medicinal Lion's Mane mushroom, *Hericium erinaceus* (Bull.: Fr.) Pers. (*Aphyllophoromycetideae*) in accelerating wound healing in rats. Int J Med Mushrooms 13:33–39

Abdullah N, Ismail SM, Aminudin N, Shuib AS, Lau BF (2012) Evaluation of selected culinary-medicinal mushrooms for antioxidant and ACE inhibitory activities. Evid Based Complement Alternat Med 2012:464238

Alzoghaibi MA (2013) Concepts of oxidative stress and antioxidant defense in Crohn's disease. World J Gastroenterol 19:6540–6547

Anand R, Gill KD, Mahdi AA (2014) Therapeutics of Alzheimer's disease: past, present and future. Neuropharmacology 76:27–50

Bhatia P, Aureli F, D'Amato M, Prakash R, Cameotra SS, Nagaraja TP, Cubadda F (2013) Selenium bioaccessibility and speciation in biofortified *Pleurotus* mushrooms grown on selenium-rich agricultural residues. Food Chem 140:225–230

Blaser MJ (2006) Who are we? Indigenous microbes and the ecology of human diseases. EMBO Rep 7:956–960

Bungart BL, Dong L, Sobek D, Sun GY, Yao G, Lee JC (2013) Nanoparticle-emitted light attenuates amyloid-beta-induced superoxide and inflammation in astrocytes. Nanomedicine 10:15–17

Choi WS, Kim CJ, Park BS, Lee SE, Takeoka GR, Kim DG, Lanpiao X, Kim JH (2005) Inhibitory effect on proliferation of vascular smooth muscle cells and protective effect on CCl_4-induced hepatic damage of HEAI extract. J Ethnopharmacol 100:176–179

Choi WS, Jang DY, Nam SW, Park BS, Lee HS, Lee SE (2012) Antiulcerogenic activity of scoparone on HCl/ethanol-induced gastritis in rats. J Korean Soc Appl Biol Chem 55:159–163

Choi BS, Sapkota K, Choi JH, Shin CH, Kim S, Kim SJ (2013a) Herinase: a novel bi-functional fibrinolytic protease from the monkey head mushroom, *Hericium erinaceum*. Appl Biochem Biotechnol 170:609–622

Choi WS, Kim YS, Park BS, Kim JE, Lee SE (2013b) Hypolipidaemic effect of *Hericium erinaceum* grown in *Artemisia capillaris* on obese rats. Mycobiology 41:94–99

Costantini S, Colonna G, Castello G (2014) A holistic approach to study the effects of natural antioxidants on inflammation and liver cancer. Cancer Treat Res 159:311–323

Dong Q, Jia LM, Fang JN (2006) A beta-D-glucan isolated from the fruiting bodies of *Hericium erinaceus* and its aqueous conformation. Carbohydr Res 341:791–795

Du F, Wang HX, Ng TB (2013) An amylase from fresh fruiting bodies of the monkey head mushroom *Hericium erinaceum*. Prikl Biokhim Mikrobiol 49:29–33

Falandysz J (2008) Selenium in edible mushrooms. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev 26:256–299

Falandysz J, Borovicka J (2013) Macro and trace mineral constituents and radionuclides in mushrooms: health benefits and risks. Appl Microbiol Biotechnol 97:477–501

Figlas D, Gonzalez Matute R, Curvetto N (2007) Cultivation of culinary-medicinal lion's mane mushroom *Hericium erinaceus* (Bull.: Fr.) Pers. (*Aphyllophoromycetideae*) on substrate containing sunflower seed hull. Int J Med Mushrooms 9:67–73

Francesca L, Francesca V (2007) Wild food plants of popular use in Sicily. J Ethnobiol Ethnomed 3:15

Fui HY, Shieh DE, Ho CT (2002) Antioxidant and free radical scavenging activities of edible mushrooms. J Food Lipids 9:35–46

Goodall EF, Heath PR, Bandmann O, Kirby J, Shaw PJ (2013) Neuronal dark matter: the emerging role of microRNAs in neurodegeneration. Front Cell Neurosci 7:178

Gubandru M, Margina D, Tsitsimpikou C, Goutzourelas N, Tsarouhas K, Ilie M, Tsatsakis AM, Kouretas D (2013) Alzheimer's disease treated patients showed different patterns for oxidative stress and inflammation markers. Food Chem Toxicol 61:209–214

Guerder S, Joncker N, Mahiddine K, Serre L (2013) Dendritic cells in tolerance and autoimmune diabetes. Curr Opin Immunol 25:670–675

Gzogian LA, Proskuriakov MT, Ievleva EV, Valueva TA (2005) Trypsin-like proteinases and trypsin inhibitors in fruiting bodies of higher fungi. Prikl Biokhim Mikrobiol 41:612–615

Han ZH, Ye JM, Wang GF (2013) Evaluation of in vivo antioxidant activity of *Hericium erinaceus* polysaccharides. Int J Biol Macromol 52:66–71

Hiwatashi K, Kosaka Y, Suzuki N, Hata K, Mukaiyama T, Sakamoto K, Shirakawa H, Komai M (2010) Yamabushitake mushroom (*Hericium erinaceus*) improved lipid metabolism in mice fed a high-fat diet. Biosci Biotechnol Biochem 74:1447–1451

Hoesel B, Schmid JA (2013) The complexity of NF-kappaB signaling in inflammation and cancer. Mol Cancer 12:86

Holmes C (2013) Review: systemic inflammation and Alzheimer's disease. Neuropathol Appl Neurobiol 39:51–68

Hsiao EY, McBride SW, Hsien S, Sharon G, Hyde ER, McCue T, Codelli JA, Chow J, Reisman SE, Petrosino JF, Patterson PH, Mazmanian SK (2013) Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. Cell 155: 1451–1463

Hu SH, Wang JC, Wu CY, Hsieh SL, Chen KS, Chang SJ, Liang ZC (2008) Bioconversion of agro wastes for the cultivation of the culinary-medicinal lion's mane mushrooms *Hericium erinaceus* (Bull.: Fr.) Pers. and *H. laciniatum* (leers) banker (*Aphyllophoromycetideae*) in taiwan. Int J Med Mushrooms 10: 385–398

Imtiaj A, Jayasinghe C, Lee GW, Shim MJ, Rho HS, Lee HS, Hur H, Lee MW, Lee UY, Lee TS (2008) Vegetative growth of four strains of *Hericium erinaceus* collected from different habitats. Mycobiology 36:88–92

Jin KS, Park JY, Cho MK, Jang JH, Jeong JH, Ok S, Bak MJ, Song YS, Kim MJ, Cho CW, Jeong WS (2009a) Modulation of Nrf2/ARE and inflammatory signaling pathways by *Hericium erinaceus* mycelia extract. Food Sci Biotechnol 18:1204–1211

Jin KS, Park JY, Cho MK, Jang JH, Ok S, Jeong JH, Kim MJ, Song YS, Jeong WS (2009b) Anti-inflammatory effects of *Hericium erinaceus* mycelia hot water extract in murine macrophage Raw 264.7 cells. Ann Nutr Metab 55:334

Jin KS, Park JY, Cho MK, Jang JH, Ok S, Jeong JH, Kim MJ, Song YS, Jeong WS (2009c) Chemopreventive effects of *Hericium erinaceus* mycelia hot water extract in Hepg2 human hepatocarcinoma cells. Ann Nutr Metab 55:334

Kandoth C, McLellan MD, Vandin F, Ye K, Niu B, Lu C, Xie M, Zhang Q, McMichael JF, Wyczalkowski MA, Leiserson MD, Miller CA, Welch JS, Walter MJ, Wendl MC, Ley TJ, Wilson RK, Raphael BJ, Ding L (2013) Mutational landscape and significance across 12 major cancer types. Nature 502:333–339

Kang KA, Kim KC, Bae SC, Hyun JW (2013) Oxidative stress induces proliferation of colorectal cancer cells by inhibiting RUNX3 and activating the Akt signaling pathway. Int J Oncol 43:1511–1516

Kessenbrock K, Plaks V, Werb Z (2010) Matrix metalloproteinases: regulators of the tumor microenvironment. Cell 141:52–67

Kim EK, Choi EJ (2010) Pathological roles of MAPK signaling pathways in human diseases. Biochim Biophys Acta 1802:396–405

Kim SK, Son CG, Yun CH, Han SH (2010) *Hericium erinaceum* induces maturation of dendritic cells derived from human peripheral blood monocytes. Phytother Res 24:14–19

Kim SP, Kang MY, Choi YH, Kim JH, Nam SH, Friedman M (2011a) Mechanism of *Hericium erinaceus* (Yamabushitake) mushroom-induced apoptosis of U937 human monocytic leukemia cells. Food Funct 2:348–356

Kim SP, Kang MY, Kim JH, Nam SH, Friedman M (2011b) Composition and mechanism of antitumor effects of *Hericium erinaceus* mushroom extracts in tumor-bearing mice. J Agric Food Chem 59:9861–9869

Kim YS, Jeon JH, Im J, Kang SS, Choi JN, Ju HR, Yun CH, Son CG, Lee CH, Han SH (2011c) Induction of intercellular adhesion molecule-1 by water-soluble components of *Hericium erinaceum* in human monocytes. J Ethnopharmacol 133:874–880

Kim KH, Noh HJ, Choi SU, Lee KR (2012a) Isohericenone, a new cytotoxic isoindolinone alkaloid from *Hericium erinaceum*. J Antibiot (Tokyo) 65:575–577

Kim SP, Moon E, Nam SH, Friedman M (2012b) *Hericium erinaceus* mushroom extracts protect infected mice against *Salmonella Typhimurium*-induced liver damage and mortality by stimulation of innate immune cells. J Agric Food Chem 60:5590–5596

Kim YO, Lee SW, Oh CH, Rhee YH (2012c) *Hericium erinaceus* suppresses LPS-induced pro-inflammation gene activation in RAW264.7 macrophages. Immunopharmacol Immunotoxicol 34: 504–512

Kim SP, Nam SH, Friedman M (2013) *Hericium erinaceus* (Lion's Mane) mushroom extracts inhibit metastasis of cancer cells to the lung in CT-26 colon cancer-tansplanted mice. J Agric Food Chem 61:4898–4904

Ko HG, Park HG, Park SH, Choi CW, Kim SH, Park WM (2005) Comparative study of mycelial growth and basidiomata formation in seven different species of the edible mushroom genus *Hericium*. Bioresour Technol 96:1439–1444

Kobayashi S, Inoue T, Ando A, Tamanoi H, Ryu I, Masuyama A (2012) Total synthesis and structural revision of hericerin. J Org Chem 77: 5819–5822

Kolotushkina EV, Moldavan MG, Voronin KY, Skibo GG (2003) The influence of *Hericium erinaceus* extract on myelination process in vitro. Fiziol Zh 49:38–45

Laveti D, Kumar M, Hemalatha R, Sistla R, Naidu VG, Talla V, Verma V, Kaur N, Nagpal R (2013) Anti-inflammatory treatments for chronic diseases: a review. Inflamm Allergy Drug Targets 12:349–361

Lee JS, Hong EK (2010) *Hericium erinaceus* enhances doxorubicin-induced apoptosis in human hepatocellular carcinoma cells. Cancer Lett 297:144–154

Lee JS, Cho JY, Hong EK (2009a) Study on macrophage activation and structural characteristics of purified polysaccharides from the liquid culture broth of *Hericium erinaceus*. Carbohydr Polym 78:162–168

Lee JS, Min KM, Cho JY, Hong EK (2009b) Study of macrophage activation and structural characteristics of purified polysaccharides from the fruiting body of *Hericium erinaceus*. J Microbiol Biotechnol 19:951–959

Lee SL, Leong JY, Lim RLH (2010) Comparative cytotoxicity and hemagglutination activities of crude protein extracts from culinary-medicinal mushrooms. Int J Med Mushrooms 12:213–222

Li Y, Zhang G, Ng TB, Wang H (2010) A novel lectin with antiproliferative and HIV-1 reverse transcriptase inhibitory activities from dried fruiting bodies of the monkey head mushroom *Hericium erinaceum*. J Biomed Biotechnol 2010:716515

Mau JL, Lin HC, Ma JT, Song SF (2001) Non-volatile taste components of several speciality mushrooms. Food Chem 73:461–466

Mau JL, Lin HC, Song SF (2002) Antioxidant properties of several specialty mushrooms. Food Res Int 35:519–526

McEwen BS, Gianaros PJ (2010) Central role of the brain in stress and adaptation: links to socioeconomic status, health, and disease. Ann N Y Acad Sci 1186:190–222

McEwen BS, Gianaros PJ (2011) Stress- and allostasis-induced brain plasticity. Annu Rev Med 62:431–445

Mimura K, Shiraishi K, Mueller A, Izawa S, Kua LF, So J, Yong WP, Fujii H, Seliger B, Kiessling R, Kono K (2013) The MAPK pathway is a predominant regulator of HLA-A expression in esophageal and gastric cancer. J Immunol 191:6261–6272

Mishra A, Liu S, Sams GH, Curphey DP, Santhanam R, Rush LJ, Schaefer D, Falkenberg LG, Sullivan L, Jaroncyk L, Yang X, Fisk H, Wu LC, Hickey C, Chandler JC, Wu YZ, Heerema NA, Chan KK, Perrotti D, Zhang J, Porcu P, Racke FK, Garzon R, Lee RJ, Marcucci G, Caligiuri MA (2012) Aberrant overexpression of IL-15 initiates large granular lymphocyte leukemia through chromosomal instability and DNA hypermethylation. Cancer Cell 22:645–655

Miyazawa M, Matsuda N, Tamura N, Ishikawa R (2008) Characteristic flavor of volatile oil from dried fruiting bodies of *Hericium erinaceus* (Bull.: Fr.) Pers. J Essent Oil Res 20:420–423

Moldavan MG, Gryganski AP, Kolotushkina OV, Kirchhoff B, Skibo GG, Pedarzani P (2007) Neurotropic and trophic action of lion's mane mushroom *Hericium erinaceus* (Bull.: Fr.) Pers. (*Aphyllophoromycetideae*) extracts on nerve cells in vitro. Int J Med Mushrooms 9:15–28

Mori K, Obara Y, Hirota M, Azumi Y, Kinugasa S, Inatomi S, Nakahata N (2008) Nerve growth factor-inducing activity of *Hericium erinaceus* in 1321N1 human astrocytoma cells. Biol Pharm Bull 31:1727–1732

Mori K, Inatomi S, Ouchi K, Azumi Y, Tuchida T (2009) Improving effects of the mushroom Yamabushitake (*Hericium erinaceus*) on mild cognitive impairment: a double-blind placebo-controlled clinical trial. Phytother Res 23:367–372

Mori K, Kikuchi H, Obara Y, Iwashita M, Azumi Y, Kinugasa S, Inatomi S, Oshima Y, Nakahata N (2010) Inhibitory effect of hericenone B from *Hericium erinaceus* on collagen-induced platelet aggregation. Phytomedicine 17:1082–1085

Mori K, Obara Y, Moriya T, Inatomi S, Nakahata N (2011) Effects of *Hericium erinaceus* on amyloid beta (25-35) peptide-induced learning and memory deficits in mice. Biomed Res 32:67–72

Nagai K, Chiba A, Nishino T, Kubota T, Kawagishi H (2006) Dilinoleoyl-phosphatidylethanolamine from *Hericium erinaceum* protects against ER stress-dependent Neuro2a cell death via protein kinase C pathway. J Nutr Biochem 17:525–530

Nagano M, Shimizu K, Kondo R, Hayashi C, Sato D, Kitagawa K, Ohnuki K (2010) Reduction of depression and anxiety by 4 weeks *Hericium erinaceus* intake. Biomed Res 31:231–237

Newton K, Dixit VM (2012) Signaling in innate immunity and inflammation. Cold Spring Harb Perspect Biol 4:a006049

Park YS, Lee HS, Won MH, Lee JH, Lee SY, Lee HY (2002) Effect of an exo-polysaccharide from the culture broth of *Hericium erinaceus* on enhancement of growth and differentiation of rat adrenal nerve cells. Cytotechnology 39:155–162

Ramaswami R, Harding V, Newsom-Davis T (2013) Novel cancer therapies: treatments driven by tumour biology. Postgrad Med J 89:652–658

Rowan FS (2002) How terrestrial organisms sense, signal, and respond to carbon dioxide. Integr Comp Biol 42:469–480

Samaras K, Sachdev PS (2012) Diabetes and the elderly brain: sweet memories? Ther Adv Endocrinol Metab 3:189–196

Schott JM, Revesz T (2013) Inflammation in Alzheimer's disease: insights from immunotherapy. Brain 136:2654–2656

Shang X, Tan Q, Liu R, Yu K, Li P, Zhao GP (2013) *In vitro* anti-*Helicobacter pylori* effects of medicinal mushroom extracts, with special emphasis on the Lion's Mane mushroom, *Hericium erinaceus* (higher *Basidiomycetes*). Int J Med Mushrooms 15:165–174

Shen Y, Yang L, Li R (2013) What does complement do in Alzheimer's disease? Old molecules with new insights. Transl Neurodegener 2:21

Siwulski M, Sobieralski K, Mankowski J (2010) Comparison of mycelium growth of selected species of cultivated mushrooms on textile industry wastes. Acta Sci Pol 9:37–43

Slattery ML, Lundgreen A, Wolff RK (2013) Dietary influence on MAPK-signaling pathways and risk of colon and rectal cancer. Nutr Cancer 65:729–738

Slusarczyk J, Malinowska E, Krzyczkowski W, Kuras M (2013) Influence of inorganic and organic selenium on number of living mycelial cells and their ultrastructure in culture of *Hericium erinaceum* (Bull.: Fr. Pers.). Acta Biol Hung 64:96–105

Son CG, Shin JW, Cho JH, Cho CK, Yun CH, Chung W, Han SH (2006a) Macrophage activation and nitric oxide production by water soluble components of *Hericium erinaceum*. Int Immunopharmacol 6:1363–1369

Son CG, Shin JW, Cho JH, Cho CK, Yun CH, Han SH (2006b) Induction of murine interleukin-1 beta expression by water-soluble components from *Hericium erinaceum*. Acta Pharmacol Sin 27:1058–1064

Sun YJ, Zhou ZY, Chen Y, Zhou LW (2008) Influence of intracellular polysaccharide from *Morchella esculenta* on acute liver injury caused by carbon tetrachloride in mice. Edible Fungi China 27:41–42, 45

Suzuki C, Mizuno TX (1997) Cultivation of Yamabushitake (*Hericium erinaceum*). Food Rev Int 13:419–421

Ueda K, Tsujimori M, Kodani S, Chiba A, Kubo M, Masuno K, Sekiya A, Nagai K, Kawagishi H (2008) An endoplasmic reticulum (ER) stress-suppressive compound and its analogues from the mushroom *Hericium erinaceum*. Bioorg Med Chem 16:9467–9470

Ulziijargal E, Mau JL (2011) Nutrient compositions of culinary-medicinal mushroom fruiting bodies and mycelia. Int J Med Mushrooms 13:343–349

Ulziijargal E, Yang JH, Lin LY, Chen CP, Mau JL (2013) Quality of bread supplemented with mushroom mycelia. Food Chem 138:70–76

Vendramini-Costa DB, Carvalho JE (2012) Molecular link mechanisms between inflammation and cancer. Curr Pharm Des 18:3831–3852

Viscogliosi G, Marigliano V (2013) Alzheimer's disease: how far have we progressed? Lessons learned from diabetes mellitus, metabolic syndrome, and inflammation. J Am Geriatr Soc 61:845–846

Wang JC, Hu SH, Su CH, Lee TM (2001) Antitumor and immunoenhancing activities of polysaccharide from culture broth of *Hericium spp*. Kaohsiung J Med Sci 17:461–467

Wang JCY, Hu SH, Wang JT, Chen KS, Chia YC (2005) Hypoglycemic effect of extract of *Hericium erinaceus*. J Sci Food Agric 85:641–646

Wang SH, Zhang H, Fu MQ, Chen QY, Zhou ZY, Lu XM (2007) Anti-oxidative responses of *Agrocybe aegerita* mycelia to cadmium stress. Chin J Appl Ecol 18:1813–1818

Wang SH, Zhang H, Cui YR, He QY, Zhang Q (2008) Effects of cadmium stress on the antioxidative system in *Ganoderma lucidum* mycelia. Chin J Appl Ecol 19:1355–1361

Wang X, Wang W, Li L, Perry G, Lee HG, Zhu X (2013) Oxidative stress and mitochondrial dysfunction in Alzheimer's disease. Biochim Biophys Acta. doi:10.1016/j.bbadis.2013.1010.1015

Weijn A, van den Berg-Somhorst DB, Slootweg JC, Vincken JP, Gruppen H, Wichers HJ, Mes JJ (2013) Main phenolic compounds of the melanin biosynthesis pathway in bruising-tolerant and bruising-sensitive button mushroom (*Agaricus bisporus*) strains. J Agric Food Chem 61:8224–8231

Wiernsperger N (2013) Hepatic function and the cardiometabolic syndrome. Diabetes Metab Syndr Obes 6:379–388

Woller N, Kuhnel F (2014) Virus infection, inflammation and prevention of cancer. Recent Results Cancer Res 193:33–58

Wong KH, Sabaratnam V, Abdullah N, Naidu M, Keynes R (2007) Activity of aqueous extracts of lion's mane mushroom *Hericium erinaceus* (Bull.: Fr.) Pers. (*Aphyllophoromycetideae*) on the neural cell line NG108-15. Int J Med Mushrooms 9:57–65

Wong KH, Naidu M, David RP, Abdulla MA, Abdullah N, Kuppusamy UR, Sabaratnam V (2009a) Functional recovery enhancement following injury to rodent peroneal nerve by lion's mane mushroom, *Hericium erinaceus* (Bull.: Fr.) Pers. (*Aphyllophoromycetideae*). Int J Med Mushrooms 11:225–236

Wong KH, Vikineswary S, Noorlidah A, Rani KU, Murali N (2009b) Effects of cultivation techniques and processing on antimicrobial and antioxidant activities of *Hericium erinaceus* (Bull.: Fr.) Pers. extracts. Food Technol Biotechnol 47:47–55

Wong KH, Naidu M, David P, Abdulla MA, Abdullah N, Kuppusamy UR, Sabaratnam V (2011) Peripheral nerve regeneration following crush injury to rat peroneal nerve by aqueous extract of medicinal mushroom *Hericium erinaceus* (Bull.: Fr) Pers. (*Aphyllophoromycetideae*). Evid Based Complement Alternat Med 2011:580752

Wong KH, Naidu M, David RP, Bakar R, Sabaratnam V (2012) Neuroregenerative potential of lion's mane mushroom, *Hericium erinaceus* (Bull.: Fr.) Pers. (higher *Basidiomycetes*), in the treatment of peripheral nerve injury (review). Int J Med Mushrooms 14:427–446

Xie CY, Gu ZX, You XJ, Liu GX, Tan YX, Zhang H (2010) Screening of edible mushrooms for release of ferulic acid from wheat bran by fermentation. Enzyme Microb Technol 46:125–128

Xu H, Wu PR, Shen ZY, Chen XD (2010) Chemical analysis of *Hericium erinaceum* polysaccharides and effect of the polysaccharides on derma antioxidant enzymes, MMP-1 and TIMP-1 activities. Int J Biol Macromol 47:33–36

Yang BK, Park JB, Song CH (2002) Hypolipidemic effect of exo-polymer produced in submerged mycelial culture of five different mushrooms. J Microbiol Biotechnol 12:957–961

Yang BK, Park JB, Song CH (2003) Hypolipidemic effect of an exo-biopolymer produced from a submerged mycelial culture of *Hericium erinaceus*. Biosci Biotechnol Biochem 67:1292–1298

Yaoita Y, Yonezawa S, Kikuchi M, Machida K (2012) A new geranylated aromatic compound from the mushroom *Hericium erinaceum*. Nat Prod Commun 7:527–528

Yeh SP, Hsia LF, Chiu CS, Chiu ST, Liu CH (2011) A smaller particle size improved the oral bioavailability of monkey head mushroom, *Hericium erinaceum*, powder resulting in enhancement of the immune response and disease resistance of white shrimp, *Litopenaeus vannamei*. Fish Shellfish Immunol 30:1323–1330

Yim MH, Shin JW, Son JY, Oh SM, Han SH, Cho JH, Cho CK, Yoo HS, Lee YW, Son CG (2007) Soluble components of *Hericium erinaceum* induce NK cell activation via production of interleukin-12 in mice splenocytes. Acta Pharmacol Sin 28:901–907

Zhang ZF, Lv GY, Pan HJ, Pandey A, He WQ, Fan LF (2012) Antioxidant and hepatoprotective potential of endo-polysaccharides from *Hericium erinaceus* grown on tofu whey. Int J Biol Macromol 51:1140–1146

Zhang M, Zhou S, Zhang L, Ye W, Wen Q, Wang J (2013a) Role of cancer-related inflammation in esophageal cancer. Crit Rev Eukaryot Gene Expr 23:27–35

Zhang W, Zhao S, Li Y, Peng G, Han P (2013b) Acute blood glucose fluctuation induces myocardial apoptosis through oxidative stress and nuclear factor-κB activation. Cardiology 124:11–17

Zhang Y, Yan W, Collins MA, Bednar F, Rakshit S, Zetter BR, Stanger BZ, Chung I, Rhim AD, di Magliano MP (2013c) Interleukin-6 is required for pancreatic cancer progression by promoting MAPK signaling activation and oxidative stress resistance. Cancer Res 73:6359–6374

Zhou R, Lin ZH, Jiang CS, Gong JX, Chen LL, Guo YW, Shen X (2013) Marine natural product des-O-methyllasiodiplodin effectively lowers the blood glucose level in db/db mice via ameliorating inflammation. Acta Pharmacol Sin 34:1325–1336

Zhu F, Qu L, Fan W, Qiao M, Hao H, Wang X (2011) Assessment of heavy metals in some wild edible mushrooms collected from Yunnan Province, China. Environ Monit Assess 179:191–199

Zou YJ, Wang HX, Ng TB, Huang CY, Zhang JX (2012) Purification and characterization of a novel laccase from the edible mushroom *Hericium coralloides*. J Microbiol 50:72–78