Cardiovascular effects of the edible immune enhancing products

Shi-Min Yuan

Department of Cardiothoracic Surgery, The First Hospital of Putian, Teaching Hospital, Fujian Medical University, Putian 351100, Fujian Province, People’s Republic of China - E-mail: shiminyuan@126.com

Summary. Objectives: The nutrients, active ingredients and pharmacological effects of the immune enhancing herbs have drawn attention. The pertinent aspects of the edible immune enhancing products are a topic of interest, and their cardiovascular effects warrant deeper understanding. Methods: The data sources of this study are based on retrieval of the literature of edible immune enhancing products from the MEDLINE and China Biology Medicine Disc (CBMdisc) databases between 1990 and 2016. Results: Immune enhancing herbs work by nourishing white blood cells, protecting against toxins, and influencing the innate immune system through alkaloids, flavonoids, saponins and polysaccharides, etc. The cardiovascular effects of the immune enhancing products are closely related to the active ingredients that they contain. They have a common anti-oxidant effect against myocardial ischemia. The anti-angiotensin converting enzyme, calcium antagonistic, acetylcholine-like and non quinidine-like, cellular contractility-strengthening and platelet aggregation inhibiting properties endow them with anti-hypertensive, myocardial protective, anti-arrhythmic, inotropic and lipid-lowering effects. Conclusions: Researches on the active ingredients and cardiovascular effects of the edible immune enhancing products extend their pharmacological application spectrum to heart disorders. The pharmacological effects are closely related to the active ingredients that they contain. Further research on the active ingredients of the products would facilitate the mechanistic study and subsequent drug discovery.

Key words: antioxidants, cardiotonic agents, immunoenhancing factor

Introduction

Chinese medicinal research works have revealed that some medicinal herbs can be of immune modulating effects, either immune enhancing or immune inhibiting. Of the immune enhancing herbs, the majority of them belong to the tonic Chinese medicine, which are further divided into qi-invigorating (such as, Panax Ginseng, Codonopsis pilosula and Radix Astragali, etc.), blood-replenishing (such as, Radix angelicae sinensis, Polygonum multiflorum and Radix paeoniae alba, etc.), yin-nourishing (such as, Radix rehmanniae, Radix ophiopogonis and Asparagus cochinchinensis) and yang-warming herbs (such as, Cornu Corvi nippon parvum, Cistanche desertica and Epimedium brevicornum) (1). Even in Western countries, Echinacea, Astragalus, Panax Ginseng, garlic, ginger, cat’s claw, Origanum vulgare, turmeric, bell pepper, and cloves are commonly recognized as excellent immune boosting herbs, for their specific anti-inflammatory and anti-cancer characteristics by aiding glucose metabolism and moderating the immune response (2). Their immune enhancing effects are largely related to the polysaccharide ingredients, for example, Astragalus polysaccharide and Lycium barbarum polysaccharide. The polysaccharides approach to positive regulation of immune function by stimulating the secretion or proliferation of macrophages, T and B lymphocytes and natural killer cells, modulating the
release of cytokines, promoting the production of antibodies and activating the complement system, etc. (3). Recently, study on immune mechanisms of Achyranthes bidentata polysaccharides revealed that the polysaccharides play an important role in promoting the immune function by impacting on in vivo nerve, endocrine and immune network (4). Some of the edible immune enhancing products, like Ganoderma Lucidum, royal jelly (RJ), Panax Ginseng, lily, mushrooms (Russula, Lion’s Mane Mushroom, straw mushroom and Shiitake mushroom, etc.) and fungus (black and white), that we take in everyday life for immunomodulatory purposes, carry promising anti-cancer and immunomodulatory effects by way of nourishing leukocytes, protecting against toxins and influencing the innate immune system through flavonoids and saponins in addition to polysaccharides, by the example of Ganoderma Lucidum (5). Meanwhile, these products also show cardiovascular effects in lowering blood pressure and treating a heart attack. However, the cardiovascular aspects of the immune enhancing products have not been fully elucidated. This study is designed to evaluate the cardiovascular efficacy of these immune enhancing products.

**Methods**

Medical literature of the edible immune enhancing products including Ganoderma Lucidum, RJ, Panax Ginseng, lily, mushrooms and fungus is retrieved from the MEDLINE and China Biology Medicine Disc (CBMdisc) databases from 1990 to present. The articles on cardiovascular effects (anti-hypertensive, myocardial protective, anti-arrhythmic, inotropic and lipid-lowering effects) of these products are comprehensively collected and reviewed.

**Results**

**Ganoderma lucidum**

Ganoderma Lucidum, also named Reishi, is one of the noticeable herbs. It is also known as Lingzhi in China, and is regarded as herb of spiritual potency due to the associated longevity, health and spiritual power (6). Ganoderma lucidum has been under in-depth research, showing potent cardiovascular activities in improving myocardial function by protecting against myocardial ischemia and hypoxia, improving oxygen metabolism, hemodynamics and rheology, etc. Furthermore, its important ingredients polysaccharides and Germanium element are found to accelerate metabolism, defer cell senescence and induce the production of interferon.

Ganoderma lucidum tincture showed significant inotropic effects on the isolated toad heart and in vivo rabbit heart, probably by improving cardiac contractility and increasing cardiac output (7).

Clinical observations revealed that all preparations of Ganoderma lucidum had substantial anti-hypertensive effects with a total effective rate of 84.5% in the treatment of hypertension in the elderly patients. Moreover, Ganoderma lucidum can synergistically enhance the pharmacological effects of other anti-hypertensive agents. This anti-hypertensive effect of Ganoderma lucidum was proposed to be attributable to ribosidoadenine and ganoderic acids that it contains and to the reduced production of angiotension (8). Hu and Cai (9) observed that Ganoderma lucidum polysaccharides significantly inhibited nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity in the aorta of deoxycorticosterone acetate (DOCA) salt hypertensive rats. Zhang et al. (10), in their double-blinded placebo-controlled study, found that plasma nitric oxide increased significantly one month after Ganoderma lucidum additive was supplemented. Tran et al. (11) administered auto-digested Reishi extract to spontaneous hypertensive rats and disclosed its higher inhibitory effect against angiotensin converting enzyme (ACE) than that of the hot-water extract (11).

The sporophores, mycelium, fermentation broth and dry powder of Ganoderma lucidum all could enhance the hypoxic endurance of the experimtmental animals. Injection of the total alkaloids of Ganoderma lucidum could increase the canine coronary flow by 62% and decrease coronary resistance. Ganoderma lucidum (菌灵芝) syrup at a dose of 6 mL, twice daily, for 2-6 months for the treatment of coronary artery disease showed a total effective rate of 71.7-89.6% for angina, 69.1-83.3% for electrocardiographic ischemic changes and, 86% for decreasing cholesterol (12).

Research on the herbal preparation of Ganoderma lucidum on experimental thrombosis revealed that it
could significantly reverse the hypercoagulation state reduced by thrombin reduction and remarkably prolong the activated partial thromboplastin time, prothrombin time and thrombin time. The results indicated that *Ganoderma lucidum* might inhibit both internal and external thrombin (13). When *Ganoderma lucidum* extract was given to 33 patients in a dosage of 110 mg, four times daily, orally taken, for 2 weeks, the whole blood viscosity and plasma viscosity were significantly decreased and the blood pressure was reduced simultaneously, however, no changes were found in hematocrit and erythrocyte sedimentation rate after treatment (14). *Ganoderma lucidum* polysaccharide preparation can significantly inhibit thrombus formation, reduce the content of fibrinogen, and obviously prolong the activated partial thromboplastin time in the experimental mice, and the water-soluble parts of *Ganoderma lucidum* have shown anti-aggregant effects, where adenosine, uridine and purine have been identified as the charging ingredients (15). Crude extract of the fruiting bodies of *Ganoderma lucidum* also showed significant anti-aggregant activities, and it was found that lucidenolactone of the extract was a platelet aggregation inhibitor from the chloroform soluble fraction (16).

**Panax Ginseng**

Panax Ginseng (Araliaceae) belongs to Panax Ginseng C.A. Meyer, originated in China and Korea. The active compounds in Panax Ginseng are believed to be ginseng saponin, ginseng essential oils, β-sitosterol and glucostetin, prostisol, daucosterol, choline, ethanolamine, spermine and 16 kinds of amino acids, vitamins, ginseng polypeptide, ginseng polysaccharide, ginseng flavonoid glycosides and pectin, etc., more important active ingredients of which are ginsenoside, ginseng essential oil, ginseng polysaccharide, ginseng polypeptide, prostisol and ginseng flavonoid (17).

Ginsenoside Rb is extracted from the stem leaves and roots of Panax Ginseng, one of the plants of the genus Panax, including Rb1, Rb2 and Rb3. Pharmacological studies showed ginsenoside Rb could significantly enhance hypoxic tolerance of mice, and improve electrocardiographic changes of pituitrin-induced acute myocardial ischemia in rats (18). It was also evidenced in canine acute myocardial infarction model that Ginsenoside Rb could remarkably decrease myocardial infarct size, decrease serum creatine kinase (CK) and lactate dehydrogenase activities, reduce serum free fatty acid and lipid peroxide contents and increase SOD activity (19). In canine acute myocardial infarction model, ginsenoside Rb pretreatment by the duodenal route at doses of 25 and 50 mg/kg, brought about a series of promising hemodynamic improvements, including reduction of heart rate, mean arterial pressure, maximal rising rate of left ventricular pressure (+dp/dt max), left ventricular end diastolic pressure (LVEDP), left ventricular work index and total periphery resistance, along with increase of stroke index, +dp/dt max and coronary blood flow, and decrease of coronary vascular resistance. Meanwhile, cardiac oxygen consumption and myocardial oxygen utilization rate were also decreased (20). In cTnT R141W transgenic mouse model of dilated cardiomyopathy, long-term administration of ginsenoside Rb1 significantly improved cardiac function and reduced mortality by 50%. Histological analysis of the cTnT R141W–heart showed ginsenoside Rb1-attenuated myocardial disarray and decreased interstitial fibrosis, and Western blot analysis indicated that ginsenoside Rb1 treatment significantly downregulated heparin-binding epidermal growth factor-like growth factor (HB-EGF) and pSTAT3 expressions, which, however, overexpressed steadily in the placebo mice (21).

The calcium antagonistic effect of panaxadiol saponins (PDS) has been investigated in the isolated working rabbit hearts with myocardial ischemia and reperfusion injury. PDS of different concentrations 40, 80, 160 and 320 mg/L was perfused into the heart with cardioplegic solutions at 30 min and 60 min after aortic crossclamp, respectively. After reperfusion, the myocardial calcic contents were lower in the PDS 40, 80 and 160 mg/L groups, being lowest in the PDS 160 mg/L group, but no significant difference was noted between the PDS 320 mg/L group and the control group. As a supplement to the cardioplegic solution, PDS of 40-160 mg/L showed calcium antagonistic effect on myocardial ischemia and reperfusion injury in a dose-dependent manner; whereas PDS of 320 mg/L failed to show any calcium antagonistic effect (22). The hemodynamic effects of ginsenosides, panaquolons and eleutherosides were comparatively
evaluated on isolated working rat heart by Cao et al. (23), who found all three ingredients had marked negative inotropic action with reduced arterial blood pressure, left ventricular systolic pressure and ±dp/dt\textsuperscript{max} and rise of LVEDP similar to verapamil. Ginsenosides showed the most powerful effects, followed by panaquolons and eleutherosides.

**RJ**

The composition of RJ is more complex. RJ (dry weight) contains mostly proteins, account for 36-55%, followed by sugar, amino acids, nucleic acids and a variety of fatty acids. It also contains sterols, phospholipids, vitamins, enzymes and inorganic elements. Research shows that RJ has a variety of pharmacological effects, such as anti-hypertensive, anti-fatigue, anti-allergic, anti-bacterial, sex hormone-like effect, anti-oxidant, immune enhancing and myocardial protective effects in experimental diabetic rats and it can also protect against viral myocarditis. It has been found that RJ may lower blood pressure by directly dilate blood vessels (24,25). RJ proteins were found to inhibit renin activity in spontaneously hypertensive rats (26). With RJ preparation injected into the vein of the experimental rabbit, arterial blood pressure, heart rate and left ventricle pressure decreased in a dose-dependent manner (27). It was therefore believed that the pharmacological effect of RJ depended on acetylcholine impacting on the heart and blood vessels (27). With increasing concentrations between 1:1000-1:100, the effect of RJ on myocardial contractility and heart rate of isolated toad heart was gradually suppressed in a close dose dependence, similar to the M-type effects of acetylcholine on the heart, unrelated to β-receptor activation (28). Matsui et al. (29) found active anti-hypertensive components of RJ might be derived from the gastrointestinal enzyme production of bioactive peptides, i.e., the ACE inhibitory peptides isolated from the di- and tri-peptides of RJ hydrolysate. Lu and Lin (32) stated that, although major RJ protein-1 did not show an effect on the activity of ACE, it might inhibit the activity of ACE peptides, thereby decreasing the diastolic blood pressure of the spontaneously hypertensive rats by 22.7 mmHg in average (30).

In diabetic rat model, RJ (400 mg/kg, twice daily) were given for 8 weeks, decreased malondialdehyde (MDA), elevated serum superoxide dismutase (SOD) activity and alleviated myocardium pathologic changes were found in addition to a reduced blood glucose level (31). Xing and Meng (32) treated 27 patients with viral myocarditis with RJ (30 mL, thrice daily) and observed significant improvement of left ventricular function. The myocardial protective effects were considered to be due to taurine-enriched RJ that might improve lipid fluidity of the cellular membrane and alleviate the ultrastructural changes of the myocardium.

**Russula**

The fruit bodies of *Russula* are rich in amino acids, polysaccharides, a variety of essential mineral elements of the human body, fatty acids and cholesterol. *Russula* polysaccharide has excellent functions in lowering blood glucose and lipid levels of mice model with diabetes and hyperlipidemia (33,34). Lou et al. (35) and Zeng et al. (36) observed that *Russula* polysaccharides could significantly increase myocardial contraction of isolated frog heart for one fold and there was a period of premature beat and compensatory interval. The active ingredients of *Russula* fruit bodies, such as amino acid and essential mineral elements, could increase SOD activity of the brain, heart and liver of the experimental mice and increase the glutathione, while reducing the MDA contents.

**Lily**

The Chinese herbal medicine Lily contains some active ingredients, such as alkaloids, saponins, phospholipids and polysaccharides, etc., and nutrients, such as starch, proteins, amino acids, vitamins and microelements. Lily is good at moisturizing the lung and stopping cough, clearing away the heart evil in the pericardium, and calming the nerves and strengthening the immunity (37). *Baihe Nignshe Decoration* (百合宁神汤) is an effective prescription for treating depression. It is composed of lily, fried *Semen Ziziphi Sponosae*, *Albizia julibrissin*, and caulis 30 g each, and *angelica* 10 g, salvia 15 g and licorice 6 g, decorated taken for twice, one dose daily and 10 more doses after complete
resolution of the symptoms. With this decoration, Lü (38) treated “heartache” (with electrocardiographic evidences of coronary insufficiency, conduction block and T wave changes) for 7-60 days. The total effective rate was 90%.

**Tremella**

*Tremella* polysachrides (TP) is the main active ingredient of *Tremella*. It has a variety of pharmacological effects, such as regulation of human immune function, ant-tumor, ant-radiation and anti-aging, etc. TP has the effect of scavenging oxygen free radicals and anti-lipid peroxidation. This result suggested that TP have anti-apoptotic effects to myocardiocytes. In an *in vitro* experiment of cultured separated neonate rat cardiomyocytes and an *in vivo* experiment in mice, in which TP-pretreated groups were peritoneally injected with D-galactose intragastric administration of 100, 200 and 400 mg/kg TP, respectively. Results showed that Na⁺-K⁺-ATPase activities of the cardiomyocytes were normal control group > TP-pretreated group > apoptosis-induced group; apoptotic indices were apoptosis-induced group > TP-treated group > normal control group in *in vitro* study; while the apoptotic indices detected by TUNEL in *in vivo* study were 400 mg/kg TP group < 200 mg/kg TP group < positive control group. Myocardial homogenate MDA and lipofuscin were significantly lower in 200 and 400 mg/kg TP groups than in positive control, and significantly lower in 400 mg/kg TP than in 200 mg/kg TP group; while the activities of glutamione peroxide dismutase and SOD were significantly higher in all three TP groups than in positive control; among which the 400 mg/kg TP group showed the highest activity of glutamione peroxide dismutase (39).

**Auricularia auricula**

*Auricularia auricula* is a kind of edible and medicinal fungi belonging to Basidiomycetes. The nutrients of black fungus are very rich, rich in sugar and protein, and there are plentiful microelements, such as calcium and iron. *Auricularia auricular* polysaccharide (AAP) is a natural active ingredient in the black fungus. Ye *et al.* (40) fed myocardial infarct rat model with oral AAP at three different does of 50, 100 and 200 mg/kg/day for 20 days. The average myocardial infarct size in the AAP groups was significantly smaller than that in the ischemia group. The level of serum lactate dehydrogenase induced by regional myocardial ischemia was significantly decreased in the AAP group compared to the ischemia group. Thus, AAP may prevent myocardium from ischemic injury as an anti-oxidant agent.

**Discussion**

Wang *et al.* (41) analyzed 189 medicinal herbs enlisted in the textbook *Pharmacology of Chinese Traditional Medicine* and found that 95 (50.3%) herbs have cardiovascular effects. The cardiovascular herbs distribute in blood-activating herbs (100%), liver-calming herbs (87.5%), tonifying herbs (82%), and resuscitation-inducing herbs (80%), etc. The pharmacological effects of the medical herbs have been proved to be closely related to the active ingredients that they contain. Researches of ingredient-effect relations of the common cardiovascular herbs have made better understanding of pharmacological mechanisms, and different herbal ingredients have different pharmacological effects in acting mechanisms and potency of effect (Table 1).

With the development of economy and steady improvement of people’s living standards, the desire for health maintenance is growing rapidly. The edible immune enhancing products, popularly known as health food, are drawn much attention. This has also led to the research and further understanding on the pharmacology and long-term effects of these products. It is firstly recognized their immune enhancing nature, and the intake pathway, absorbility and curative effect are highly valued. Decothing processing as used in the traditional herbal medicine is usually regarded as a favorable way for obtaining as more as possible active ingredients, however, it is not so practical for the herbal health food products, but to take herbal tea is a substitute method of it, instead.

The edible immune enhancing products that are discussed in the present article are heterogeneous in terms of classification of traditional Chinese medicine, pharmacological effects and active ingredients, etc. The ingredients and pharmacological effects of *Ganoderma Lucidum*, *Panax Ginseng* and even RJ have undertaken
<table>
<thead>
<tr>
<th>Herbal ingredients</th>
<th>Anti-hypertension</th>
<th>Lipid-regulation</th>
<th>Anti-thrombosis protection</th>
<th>Anti-arrhythmia</th>
<th>Inotropic activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alkaloids</strong></td>
<td>Direct inhibition of aortic smooth muscle contraction (42); α₁ receptor blockade of vascular smooth muscle (43); Inhibition of acetylcholinesterase activity (43); Calcium antagonist-like effect (43); Inhibition of synthesis &amp; release of endothelin &amp; reduction of plasma renin activity (43); Direct vasodilation (46);</td>
<td>Increase the activity of lecithin-cholesterol acyltransferase; Increase NO level; Decrease CRP content (44)</td>
<td>Inhibit platelet aggregation (42); Increase oxyradical scavenging capacity (42); Anti-lipid peroxidation (42)</td>
<td>Non quinidine-like effect (42,45); Shorten the A-H interval of His bundle electrocardiogram (45)</td>
<td>Directly enhancement of myocardial contractile force (42)</td>
</tr>
<tr>
<td><strong>Saponins</strong></td>
<td>Downregulate nuclear factor κB expression (46); Decrease CRP content, vascular cell adhesion factor-1 &amp; monocyte chemotactic protein-1 (46)</td>
<td>Decrease platelet aggregation &amp; platelet aggregation time (46); Prolong thrombus formation time (46); Improve prostacyclin and NO levels (46); Enhance synthesis &amp; secretion of tissue type plasminogen activator in the vascular endothelial cells (46)</td>
<td>Relieve cell morphology changes &amp; maintain DNA synthesis (46).</td>
<td>Non-quinidine-like effect (46)</td>
<td>Inhibit Na⁺-K⁺-ATPase of myocardium</td>
</tr>
<tr>
<td><strong>Flavonoids</strong></td>
<td>Reduce endothelin (43); Increase NO (43); Improve endothelial function (43); Inhibit ACE activity &amp; synthesis of angiotensin II (43)</td>
<td>Lower plasma cholesterol &amp; triglyceride</td>
<td>Inhibit platelet aggregation &amp; thrombus formation; Decrease blood viscosity</td>
<td>Decrease myocardial oxygen consumption (43); Dilate coronary artery (43); Protect against oxidant free radicals (43)</td>
<td>Non-quinidine-like effect (47)</td>
</tr>
</tbody>
</table>

(continued)
Table 1 (continued). Cardiovascular effects of herbal ingredients

<table>
<thead>
<tr>
<th>Herbal ingredients</th>
<th>Anti-hypertension</th>
<th>Lipid-regulation</th>
<th>Anti-thrombosis protection</th>
<th>Myocardial protective</th>
<th>Anti-arrhythmia</th>
<th>Inotropic activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polysaccharides</td>
<td>Reduce lipid peroxidation (43); Regulate the release of vasoactive factors (43); Protect endothelial cell function (43)</td>
<td>Enhance phagocytic capacity of low density lipoprotein of macrophages (49); Induce macrophages to produce NO &amp; α-TNF (49).</td>
<td>Induce change of configuration &amp; activate antithrombin (50); Activate serum protease inhibitor (50)</td>
<td>Protect against oxidant free radicals &amp; against myocardial remodeling (49)</td>
<td>Antagonize chloroform-induced ventricular arrhythmias in mice (49)</td>
<td>Increase cardiac output; Dilate coronary artery (49)</td>
</tr>
</tbody>
</table>

ACE: angiotensin converting enzyme; ATP: adenosine triphosphate; cAMP: cyclic adenosine monophosphate; CRP: C-reactive protein; DNA: deoxyribonucleic acid; TNF: tumor necrosis factor; NO: nitric oxide.

Table 2. Cardiovascular effects of the edible immune enhancing products

<table>
<thead>
<tr>
<th>Edible products</th>
<th>Dosage form /active ingredient</th>
<th>Cardiovascular effects</th>
<th>Subjects</th>
<th>Mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Ganoderma lucidum</em></td>
<td>Tincture</td>
<td>Inotropic</td>
<td>Isolated toad heart</td>
<td>Improve cardiac contractility</td>
</tr>
<tr>
<td></td>
<td>All preparations/ribosidoadenine and ganoderic acids</td>
<td>Anti-hypertensive</td>
<td>Elderly patients</td>
<td>Decrease the production of angiotension</td>
</tr>
<tr>
<td></td>
<td>Polysaccharide</td>
<td>Anti-hypertensive</td>
<td>Hypertensive rats</td>
<td>Inhibit NADPH oxidase activity</td>
</tr>
<tr>
<td></td>
<td>Additive</td>
<td>Anti-hypertensive</td>
<td>Hypertensive patients</td>
<td>Increase nitric oxide level</td>
</tr>
<tr>
<td></td>
<td>Auto-digested Reishi extract</td>
<td>Anti-hypertensive</td>
<td>Spontaneous hypertensive rats</td>
<td>Inhibit ACE activity</td>
</tr>
<tr>
<td></td>
<td>Sporophores, mycelium, fermentation broth and dry powder</td>
<td>Myocardial protective</td>
<td>Experimental animals</td>
<td>Enhance the hypoxic endurance</td>
</tr>
<tr>
<td></td>
<td>Total alkaloids</td>
<td>Myocardial protective</td>
<td>Canine</td>
<td>Increase the coronary flow &amp; decrease coronary resistance</td>
</tr>
<tr>
<td></td>
<td>Syrup (6 mL, twice daily, for 2-6 months)</td>
<td>Myocardial protective</td>
<td>Patients with coronary artery disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extract</td>
<td>Anti-aggregant</td>
<td>Patients</td>
<td>Decrease blood and plasma viscosity</td>
</tr>
<tr>
<td></td>
<td>Polysaccharide</td>
<td>Anti-aggregant</td>
<td>Mice</td>
<td>Prolong the activated partial thromboplastin time</td>
</tr>
</tbody>
</table>

(continued)
thorough investigations; while those of the reminders, including lily, *Russula* and fungus have not. From the view of ingredient-effect relations, the immune enhancing and cardiovascular effects of these edible products are attributable more to the polysaccharides. In another word, the polysaccharides play a major role in the multiple target effects of the cardiovascular pharmacology of these products, probably leading to a somewhat weaker action than the conventional cardiovascular herbs. Moreover, there has not been enough research on lily and *Russula* (Table 2).

This article points out primarily the ingredient-effect relation of the traditional Chinese medicine, and extends it into the edible immune enhancing products. However, lack of prospective randomized control studies, heterogeneous research works to each product, and lack of special criteria for curative effect judgment constitute the main drawbacks of this study. It is very important to take dosage form, extraction methods and use of effective components and drug delivery into consideration. Mechanisms of these edible immune enhancing products need to be further elucidated in the future.

**Conclusions**

The cardiovascular effects of the herbs are closely related to the active ingredients that they contain. According to the ingredient-effect relations, immune enhancing products play cardiovascular effects dominantly with polysaccharides. They have so much in common that their antioxidant effects play an important role in the protection against myocardial ischemia. The anti-ACE (of *Ganoderma lucidum* and of RJ), calcium antagonistic (of *Panax Ginseng*) acetylcholine-like (of RJ) and anti-platelet aggregation properties (at least of *Ganoderma lucidum* and *Panax Ginseng*) endow these products with anti-hypertensive, myocardial protective, anti-arrhythmic, inotropic and lipid-lowering effects. This article primarily offers information for extending the pharmacological application spectrum of edible im-

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**Table 2 (continued). Cardiovascular effects of the edible immune enhancing products**

<table>
<thead>
<tr>
<th>Edible products</th>
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<th>Cardiovascular effects</th>
<th>Subjects</th>
<th>Mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Panax Ginseng</em></td>
<td>Ginsenoside</td>
<td>Myocardial protective</td>
<td>AMI rat model</td>
<td>Anti-oxidant capacity</td>
</tr>
<tr>
<td></td>
<td>Ginsenoside</td>
<td>Myocardial protective</td>
<td>AMI canine model</td>
<td>Hemodynamic improvement</td>
</tr>
<tr>
<td></td>
<td>Ginsenoside</td>
<td>Myocardial protective</td>
<td>Isolated working rabbit heart</td>
<td>Calcium antagonistic effect</td>
</tr>
<tr>
<td>Royal jelly</td>
<td>Royal jelly protein</td>
<td>Anti-hypertensive</td>
<td>Spontaneous hypertensive rats</td>
<td>Inhibit RAA system</td>
</tr>
<tr>
<td></td>
<td>Royal jelly</td>
<td>Myocardial protective</td>
<td>Diabetic rat model</td>
<td>Anti-oxidant capacity</td>
</tr>
<tr>
<td><em>Russula</em></td>
<td>Polysaccharide</td>
<td>Lipid-lowering</td>
<td>Mice</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Polysaccharide</td>
<td>Myocardial protective</td>
<td>Isolated frog heart</td>
<td>Anti-oxidant capacity</td>
</tr>
<tr>
<td><em>Lily</em></td>
<td>Decoration</td>
<td>Myocardial protective</td>
<td>Patients with coronary artery disease</td>
<td>Improve myocardial ischemia</td>
</tr>
<tr>
<td><em>Tremella</em></td>
<td>Polysaccharide</td>
<td>Myocardial protective</td>
<td>Cultured rat myocardiocytes</td>
<td>Anti-oxidant capacity</td>
</tr>
<tr>
<td><em>Auricularia auricula</em></td>
<td>Polysaccharide</td>
<td>Myocardial protective</td>
<td>AMI rat model</td>
<td>Anti-oxidant capacity</td>
</tr>
</tbody>
</table>

CE: angiotensin-converting-enzyme inhibitor; AMI: acute myocardial infarction; NADPH: nicotinamide adenine dinucleotide phosphate.
mune enhancing products to heart disorders. Investigations on cell membrane ion channel and endothelial function have provided new ideas for the cardiovascular pharmacology of the products. Further research on active ingredients of the herbs would facilitate the mechanistic study and subsequent research of drug discovery.

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29. Matsui T, Yukiyoshi A, Doi S, Sugimoto H, Yamada H,

Correspondence:
Prof. Shi-Min Yuan
The First Hospital of Putian, Teaching Hospital, Fujian Medical University, 389 Longdejing Street, Chengxiang District, Putian 351100, Fujian Province, People’s Republic of China
Tel: 86 594 6923117
E-mail: shiminyuan@126.com