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Therapeutic Properties of *Pleurotus* species (Oyster mushrooms) for Atherosclerosis: A Review

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Abstract

Atherosclerosis is an impairment of artery walls made up of two membrane layers, intima and media. Oxidative stress, hypertension, and hypercholesterolemia are the three main factors causing atherosclerosis. These conditions are frequently found together and may cause atherogenesis to rapidly occur. The edible genus *Pleurotus* is commonly known as Oyster mushrooms. *Pleurotus* spp. has been proven to have valuable medicinal attributes. Hence, they have been listed among “mushroom nutriceuticals” and categorized as both functional foods and medicinal mushrooms. In this review, we report the benefits of *Pleurotus* spp. for the prevention and treatment of atherosclerosis via reduction of oxidative stress, hypertension, and hypercholesterolemia in terms of the therapeutic compounds responsible. This review revealed that at least ten different types of *Pleurotus* spp. have been reported to have anti-atherogenic capabilities, with six of them possessing high levels of anti-atherogenic compounds such as ACE inhibitor peptide, ergothioneine, chrysin, and lovastatin. Hence, it has been demonstrated that *Pleurotus* spp. has great potential for use as food or extracts from fruiting bodies or mycelium in an alternative therapy for atherosclerosis, through prevention and treatment of oxidative stress, hypertension, and hypercholesterolemia.
Keywords


Atherosclerosis

Atherosclerosis is the most prevalent life-threatening disease in modern society. Atherosclerosis is an impairment of the artery walls, which are made up of two membrane layers, intima and media [3]. It is the underlying cause for most cases of cardiovascular disease (CVD) such as coronary heart disease and stroke [2]. Oxidative stress, hypertension, and hypercholesterolemia are the main risk factors for CVD [2,3]. They are linked together by many ways to cause atherosclerosis. Thus, compounds able to reduce these factors may prevent and/or treat atherosclerosis [3,4,5]. Oxidative stress and hypertension could initiate the atherogenesis by causing endothelial cell damage [4,5]. This may cause the membrane to become permeable to low-density lipoprotein (LDL) leakages, leading to the formation of atherosclerotic plaque [4,3,5]. High levels of cholesterol (hypercholesterolemia) lead to high level of LDL and increase the risk of LDL leakages. Hypercholesterolemia also induces the expression of low-density lipoprotein receptor (LDL-R) gene in macrophage cells, eventually triggering the formation of macrophages-LDL or macrophages-cholesterol accumulation [6].
Oxidative stress in atherogenesis

Cardiovascular disease risk factors, such as hypercholesterolemia, hypertension, diabetes, excessive alcohol use and smoking lead to the increase of reactive oxidative species (ROS) which eventually lead to oxidative stress [2,3]. The reactions involved are catalyzed by oxidant enzymes such as NADPH oxidase, xanthine oxidase, and cyclooxygenase [2,3]. The formation of superoxide may contribute to the reduction of nitric oxide (NO-) bioactivity and an increase in peroxynitrite (ONOO-) formation. Nitrite oxide (NO-) is known to have anti-atherogenic properties by causing vasodilation and offering protection to vascular membrane [2,3]. The formation of peroxynitrite (ONOO-), on the other hand, will cause the lipid oxidation process to occur. Enzymes like lipoxygenase (LO) and myeloperoxidase (MPO) are oxidant enzymes that may be involved in lipid oxidation, either via ONOO- or hydrogen peroxide (H$_2$O$_2$), as a tool of oxidant [5]. The link between the ROS and enzyme (oxidant and antioxidant) systems in the production and detoxification of ROS is summarized in Figure 1. This oxidative stress mechanism eventually activates the inflammation signal. Oxidation may then trigger the expression of pro-inflammatory signals, which then induce the expression of adhesion molecule such as vascular cell adhesion molecule (VCAM-1), intracellular adhesion molecule (ICAM-1), and endothelial-leukocyte adhesion molecule-1 (E-selectin) [3]. The expression attracts more monocytes to differentiate into macrophages and adhere to the site of an injured endothelial membrane [7]. It is known that oxidized LDL (ox-LDL) is an important initiator for many atherosclerotic pathways [8]. The fusion of many macrophages and ox-LDL will cause the
formation of foam cells [9]. This progresses to a fatty streak and aortic lesions, which in turn may lead to severe endothelial injury and development of fibrous plaque [10].

**Oxidation of Low-density lipoprotein (LDL) in atherogenesis**

Low-density lipoprotein (LDL) is thought to be pro-atherogenic once structurally modified by oxidation, enzymatic modification, aggregation, or other mechanisms which can convert the LDL to a form identifiable by macrophages scavenger receptors as a foreign substance [3]. The modified LDL would induce the formation of foam cell and then progresses to the development of fibrous plaque or atherosclerotic plaque [3]. The contribution of modified LDL to the formation of foam cell and development of atherosclerotic plaque was initially demonstrated by Goldstein and colleagues in 1979. They found that there was no cholesterol aggregation during incubation of monocytes with high doses of native LDL as opposed to the incubation of monocytes with modified LDL, through which high cholesterol aggregation was observed [11]. Modified LDL, especially oxidized LDL (Ox-LDL), or the LDL modified by oxidation, may damage the endothelial membrane for example by weakening endothelial nitrite oxide (NO⁻) bioavailability and its vascular-protective function. ROS like peroxynitrite (ONOO⁻) and hydrogen peroxide (H₂O₂) trigger the LDL to oxidize. These reactions may be mediated by oxidant enzymes such as lipoxygenase (LO) and myeloperoxidase (MPO). Napoli et al. [12,13] identified the presence of Ox-LDL in the fatty streaks of hypercholesterolemic-human fetal aortas. There are lots of evidences regarding the role of LO and MPO enzymes in the LDL oxidation. For example, Cyrus et al. [14] noted decreasing lipid peroxidation and the occurrence of murine atherogenesis by the absence of LO gene expression. Besides that, Bocan et al. [15]
successfully attenuated the development of atherosclerosis in hypercholesterolemic rabbits by treating them with the known inhibitors of LO. The expression of MPO in human atherosclerotic lesions was identified by Daugherty and colleagues in 1994. MPO is an enzyme generated by neutrophils and monocytes that secrete hypochlorous acid (HOCl) [11], and also nitrating oxidants which cause oxidation and as well as inflammation [4].

**Hypertension and atherosclerosis**

The renin-angiotensin and renin-aldosterone systems are linked together in the regulation of cardiovascular system via monitoring sodium balance, extracellular fluid volume, and structural and functional cardiac and vascular effects. The combination of these two systems is known as the renin-angiotensin-aldosteron system (RAAS). Over-activity of RAAS is associated with the progression of hypertension, stroke, atherosclerosis and other cardiovascular diseases. The most important effector in RAAS, Angiotensin II, not only causes contraction of blood vessels but through its binding to AT$_1$ receptor in the vascular system, may activate several pathways that initiate atherogenesis via inflammation, LDL oxidation and endothelial damage [16]. The activation of AT$_1$ initially triggers NADPH oxidase (NOX) to generate reactive oxygen species (ROS). This causes activation of inflammatory signals, diminishes nitric oxide (NO$^-\$) bioavailability, and finally endothelial dysfunction, as described in the Figure 2 [17,16]. Endothelial dysfunction causes low-density lipoprotein (LDL) leakages and eventually leads to the formation of foam cells [18]. The accumulation of foam cell in the blood vessels initiates the development of atherosclerotic plaque [18].
Regarding the role of angiotensin converting enzyme (ACE) in blood pressure homeostasis, it is an enzyme involved with blood pressure homeostasis. ACE is a dipeptidyl carboxypeptidase in the renin-angiotensin system (RAS) of mammals. ACE is widely distributed in human body such as in kidneys, gastrointestinal tract, lung, liver, brain, testis, ovary and prostate [19,20]. It is called ACE because of its involvement in the conversion of angiotensin I to angiotensin II by breaking the C-terminal dipeptide His9-Leu10 from angiotensin I [21]. Over expression of angiotensin II causes rapid constriction of blood vessels resulting in hypertension. Other than causing constriction by stimulating the formation of angiotensin II, ACE also has the ability to deteriorate bradykinin (potent vasodilator) and other vasoactive peptides. ACE acts by cleaving the active bradykinin into inactive bradykinin\(_{1-7}\) and bradykinin\(_{1-5}\) in kallikrein-kini cascade system [22]. Bradykinin is a potent vasodilator that dilates the arteries, resulting in a drop in blood pressure. It also reduces the blood pressure by inducing other vasodilators such as nitric oxide, prostacyclin, and endothelium-derived hyperpolarizing factor [19].

**Hypercholesteremia**

Hypercholesteremia is a condition in which levels of cholesterol in the blood are elevated [23]. High levels of cholesterol leads to the high level of LDL, and hence increases the risk of atherosclerotic plaque formation. Cholesterol homeostasis may be interfered with by a high intake of exogenous cholesterol. It induces disturbances of several regulation pathways such as the cholesterol biosynthetic pathway and expression of LDL-R (low density lipoproteins-receptor) gene in macrophage cells. The expression of LDL-R gene in macrophage is one of the main keys leading to the formation of macrophage-LDL/macrophage-oxLDL or macrophage-
cholesterol accumulation [6]. Besides that, the elevation in the level of cholesterol induces the formation of angiotensin II that up-regulate the expression of AT$_1$ receptors. The activation of AT$_1$ receptor and formation of angiotensin II would then lead to inflammation, vasoconstriction, endothelial dysfunction, and eventually atherosclerosis (Figure 2) [16,17].

However, it must be noted that improvement of the serum HDL is essential in ameliorating atherogenesis, and has been a new target for atherosclerosis therapies [24-26]. HDL is also known as “reverse cholesterol transport” due to its involvement in shipping surplus stored cholesterol to the liver for metabolism and modification [24]. On top of that, HDL has other anti-atherogenic properties such as anti-inflammation, antioxidant, endothelial fixation and anti-thrombosis [24,27-30]. It is believed that the quality of HDL is more important for prevention and treatment of atherosclerosis than quantity [25].

**Role of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase in cholesterol metabolism**

HMG-CoA reductase belongs to a class of proteins located in the endoplasmic reticulum [31]. It has eight transmembrane domains with the active site along the carboxyl terminal in the cytosol [32]. HMG-CoA reductase is a rate-limiting enzyme in the endogenous cholesterol metabolism. It is responsible for catalyzing the conversion of HMG-CoA to mevalonic acid in the mevalonate pathway [33], as shown in the Figure 3. The mevalonate pathway consists of 28 steps. The interference of statin occurs in the second step of the pathway. Statin works by retarding the activity of HMG-CoA reductase from converting the 3-hydroxy-3-methylglutaryl coenzyme A
(HMG-CoA) into L-mevalonate. In some cases, statin has been criticized as having myopathy side effects [34] hence leading to an increase in demands for natural product alternative therapy.

**Edible -mushrooms**

The first reliable evidence of mushrooms being consumed as food was recorded to several hundred years BC in China. The Chinese have used mushrooms in their traditional medicine [35]. Currently, people consume mushrooms for texture, taste and also for their nutritional and medicinal properties. Mushrooms are considered valuable resources in food production as well as a source of lead compounds in the production of drugs [36]. Mushrooms are categorized as a healthy food because they are low in calories and fat, but rich in proteins and minerals [37]. Their benefits to health include immunomodulatory, hypocholesterolemic effects, and anti-tumor effects [38]. Mushrooms are currently considered a natural source in prevention and treatment of cardiovascular disease via various mechanisms like anti-hypertension, cholesterol lowering, and anti-atherosclerotic. Lau et al. [39] reported that protein fraction of fruiting bodies from various types of mushrooms like *Agaricus bisporus* (button mushroom), *Flammulina velutipes* (golden needle), *Lentinula edodes* (shiitake), *Hericium erinaceus* (monkey’s head mushroom), *Pleurotus citrinopileatus* (yellow oyster mushroom), *P. cystidiosus* (abalone mushroom), *P. flabellatus* (pink oyster mushroom), *P. florida* (white oyster mushroom), and *P. pulmonarius* (grey oyster mushroom) possess anti-hypertensive properties through inhibition of ACE. Gil-Ramirez et al. [40] has proven that edible-medicinal mushrooms like *Cantharellus cibarius, Agaricus bisporus, Pleurotus ostreatus, Lentinula edodes, Boletus edulis, Amanita caesarea, Lactarius deliciosus, Lyophyllum shimeji, Agrocybe aegerita, Craterellus cornucopioides, Marasmius oreades*,
Pleurotus eryngii, Lepiota procera, Agaricus blazei, Grifola frondosa and Flammulina velutipes are good alternative sources for hypocholesterolemic activity through the ability to retard the activity of HMG-CoA reductase enzyme. Abdullah et al. [41] reported that 14 species of culinary-medicinal mushrooms (Agrocybe sp., Auricularia auricular-judae, Flammulina velutipes, Ganoderma lucidum, Hericium erinaceus, Lentinula edodes, Pleurotus cystidiosus, P. eryngii, P. flabellatus, P. florida, P. sajor-caju, Schizophyllum commune, Termitomyces heimii, Volvariella volvacea) have anti-oxidant and anti-hypertensive properties. In other work, Pleurotus eryngii, Grifola frondosa (Maitake), and Hypsizygus marmoreus (Bunashimeji), are three species of edible mushrooms that have displayed anti-atherosclerotic effects in apolipoprotein E–deficient mice by lowering of serum total cholesterol concentrations [42].

**Pleurotus spp. as a functional food**

Pleurotus is a genus of edible-mushroom commonly known as Oyster mushrooms. This species is widely cultivated especially due to its flavor and texture [43]. They are a good source of protein and carbohydrates. They are rich in minerals, low in fat, and have a short life cycle [44,45]. Mushrooms cultivation of the genus Pleurotus is widely carried out in several countries because of their high adaptability and health benefits. There are many different species in the genus Pleurotus with pharmacological properties, such as P. florida, P. tuber-regium, P. eryngii, P. ostreatus and P. pulmonarius [46].

Pleurotus spp. has been demonstrated in many studies to have valuable medicinal attributes such as immunomodulatory, anti-oxidant, anti-inflammatory, hypocholesterolemic, anti-genotoxic, anti-hyperglycaemic, anti-viral, anti-tumour, anti-Human Immunodeficiency Virus (HIV), anti-
mutagenic, hepatoprotective, anti-ageing and anti-allergic effects, from a diverse sort of extracted compounds [47,48]. They also have been listed among “mushroom nutriceuticals” and hence following categorized as functional foods and medicinal mushrooms [49,48]. In this review, we will present evidence to support the utilization of oyster mushrooms (Pleurotus spp.) for the prevention and treatment of atherosclerosis via oxidative stress, hypertension, and hypercholesterolemia (Table 1).

**Anti-atherogenic Properties of Pleurotus spp**

**Alternative therapy for oxidative stress**

Previous studies have shown that methanol extracts of *P. pulmonarius* are effective in scavenging hydroxyl peroxide (OH⁻) and inhibiting lipid peroxidation with half maximal inhibitory concentration (IC₅₀) 0.48 mg/ml and 0.96 mg/ml, respectively [50]. Water and alkali-extracted polysaccharide of *P. tuber-regium* have been shown to possess strong antioxidant capabilities in scavenging superoxide radical (O₂⁻) and hydroxyl radical (OH⁻). Water-extracted polysaccharide was better than alkali-extracted polysaccharide in scavenging O₂⁻, while alkali-extracted polysaccharide was better than water-extracted polysaccharide in scavenging OH⁻ [51]. Adebayo et al., [52] showed that the polysaccharide produced from the mycelium of *P. pulmonarius* exhibited good antioxidant activity by acting as hydrogen donor. Ergothioneine was proven to be able to be absorbed into endothelial cells membrane via organic cation transporter (OCTN) and hence protect the cells from oxidative stress [53,54]. In addition to that, a review by Paul and Snyder emphasized that a lack of ergothioneine in cells may lead to DNA damage and
protein and lipid oxidation induced by oxidative stress [55]. Ergothioneine was identified in large amount in *Pleurotus* spp. like *P. ostreatus* with 118.91 mg/kg wet weight and 97.35/123.42 mg/l which was higher than portabella mushroom (*Agaricus bisporus*, brown strain), button mushroom (*Agaricus bisporus*, white strain), chanterelle (*Cantharellus cibarius*), black turtle bean, red kidney bean, garlic, broccoli, onion, and spinach [56,54]. However, *in vivo* and clinical studies on the effect of ergothioneine on oxidative stress remain limited [57-60]. Thus, future work can be performed for the validation *in vivo* and clinical studies by investigating the effect of ergothioneine isolated or extracted from *Pleurotus* spp. for anti-atherogenic activities, especially in terms of the protective effect against oxidative damage.

**Alternative therapy for hypertension**

Lau *et al.* [39] discovered several types of protein fractions from nine different types of mushrooms, including *Pleurotus* spp., with high inhibitory activity towards ACE. They then suggested that active proteins from mushrooms for the anti-hypertensive properties are those proteins with 3 to 10 kDa molecular masses. Abdullah *et al.*, [41] investigated ACE activity from hot water extract of selected medicinal mushrooms and demonstrated that *Pleurotus* spp. possessed the best ACE inhibitory activity with low IC$_{50}$ values (*P. cystidiosus*, 0.054 mg/mL; *P. eryngii*, 0.067 mg/mL; *P. flabellatus*, 0.058 mg/mL; *P. florida*, 0.050 mg/mL; *P. pulmonarius*, 0.056 mg/mL) compared to other mushroom species. Jang *et al.* [61] previously characterized a new ACE inhibitory peptide from the fruiting bodies of *P. cornucopiae*. Besides that, D-mannitol (sugar alcohol) extracted via hot water extraction of *P. cornucopiae* showed anti-hypertensive effect by inhibiting ACE activity and reducing the blood pressure of hypertensive
D-mannitol has been reported to be able to protect heart and myocardial from damage by previous works on *Cordyceps sinensis* [63,64]. A hot water extract, protein fraction, polysaccharide fraction and 6% dry powder of *Pleurotus nebrodensis* were shown to prevent and also ameliorate hypertension on hypertensive rats [65]. A preparation of ethyl acetate fraction from *Pleurotus eryngii* done by Wang et al. [66] has been patented for the prevention and treatment of hypertension in animal model. The fraction is believed to contained antihypertensive agents, however the identified compounds were not revealed in that publication.

**Alternative therapy for hypercholesterolemia**

Lovastatin is a natural statin first discovered in the fermentation broth of *Aspergillus terreus* in 1978 by Albert and colleagues with name mevinolin. Later it was officially recognized as lovastatin [67,68]. Lovastatin has been clinically accepted as a great compound to reduce LDL cholesterol via inhibiting the activity of HMG-CoA reductase [68]. *Pleurotus* spp. has earlier been reported to produce large amount of lovastatin/ mevinolin in the fruiting bodies ranged from 50-5991 µg/g dry weight [69,70]. Mevinolin produced from *Pleurotus* spp. such as *P. sapidus*, *P. saca* and *P. ostreatus* have displayed good inhibitory of HMG-CoA reductase activity [70]. The extraction of lovastatin from *Pleurotus* spp. done by Gunde-Cimerman and his co-workers were via 12 hours’ incubation of the fruiting bodies with water: methanol [1:1] at 30 °C [70,40]. Alarcon et al. [71] successfully identified the presence of lovastatin ranged from 5 to 70 mg/l in mycelium liquid culture from 4 different strains of *P. ostreatus* and in the fruiting bodies was ranged from 0.40 to 2.07% [71].
Recent studies have shown that *Pleurotus ostreatus* exhibited a very convincing ability to improve the lipid profile of high-fat diet fed on par to simvastatin (synthetic hypolipidemic) at 10% (w/w) biomass dosage, by reducing the amount of triglyceride and LDL, the bad cholesterol, but elevating the level of HDL, the good cholesterol [72]. *Pleurotus ostreatus* also showed a significant reduction in plasma $\beta$-lipoprotein (lipoprotein for LDL) and pre-$\beta$-lipoprotein (lipoprotein for VLDL) and increment in $\alpha$-lipoprotein (lipoprotein for HDL) in hypercholesterolemic rat supplemented with 5% (w/w) dry powder of *P. ostreatus* fruiting bodies [73,74]. Anandhi *et al.* [75], suggested that chrysin (5,7-dihydroxyflavone) is the compound responsible for hypocholesterolemic activities from *Pleurotus ostreatus*. Chrysin was identified as a major component in ethanolic extract of *Pleurotus ostreatus* [76]. Therefore, further study is required to validate the effect of chrysin in lowering cholesterol level and hence to be a new therapeutic compound for hypercholesterolemia besides lovastatin.

In other research on *Pleurotus eryngii*, the excreted polysaccharides from submersion culture of *P. eryngii* displayed inhibition of macrophage and ox-LDL (foam cells) accumulation via down regulation of the ox-LDL scavenger receptor on macrophage CD36 [77]. In hypercholesterolemic rats with diets supplemented with 5% (w/w) dry powder of *Pleurotus eryngii* fruiting bodies showed improvement in the atherogenic lipid profile due to lowered plasma $\beta$ and pre-$\beta$-lipoprotein, while increasing $\alpha$-lipoprotein and also reduced the level of low-density lipoprotein (LDL), triglyceride, plasma total cholesterol, phospholipid, total lipid and LDL/ HDL (High-density lipoprotein) ratio [78]. Fruiting bodies of *P. florida* have been reported to have hypocholesterolemic capability in elevating HDL/ LDL ratio and decreasing total cholesterol, lipid and glyceride levels of liver and plasma [79]. Diets supplemented with ethyl
acetate and methanol extract of *P. citrinopileatus* (0.5 g/ kg body weight daily) showed reduction in total cholesterol and triglycerides levels, and increments of HDL levels in hyperlipidemic hamsters [80].

The first ever research on the benefit of oyster mushroom (*P. ostreatus*) diet in humans was conducted by Schneider *et al.* [81]. Based on that study, a daily intake of oyster mushroom soup (30 g dried oyster mushroom per soup) by 20 subjects (9 male, 11 female; age 20–34 years) led to a significant reduction in triacylglycerol concentration, oxidized-LDL rates, and total cholesterol levels with -0.44mmol/l, -7.2U/ml, and -0.47mmol/l, respectively. However, the presence of mevinolin compound was not detected in this study [81].

**Conclusion**

Based on the review, *Pleurotus* spp. has great potential as part of an alternative therapy for atherosclerosis through the prevention and treatment of oxidative stress, hypertension, and hypercholesterolemia, either directly as food or extracts from fruiting bodies or mycelium. However, a comparison study about how *Pleurotus* spp. may be best used is needed for further investigation. Among the *Pleurotus* species, *P. ostreatus* exhibited the best candidate for prevention and treatment of atherosclerosis due to the fact that it has been proven to contain a large amount of anti-atherosclerotic agents such as ergothioneine, lovastatin, and chrysin. Further investigations are also essential to elucidate its mechanisms and determine the compounds responsible for the anti-atherogenic properties. Further evaluation and clinical trials are also
needed to validate the effectiveness of anti-atherogenic agent from *Pleurotus* spp. in human metabolism conditions.

**AcknowledgementS**

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**References**


Oxidation Precede Monocyte Recruitment into Early Atherosclerotic Lesions. Journal of Clinical Investigation 100 (11):2680


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Table 1: *Pleurotus* spp. with reported anti-atherogenic properties and compounds.

<table>
<thead>
<tr>
<th><em>Pleurotus</em> spp.</th>
<th>Anti-atherogenic properties</th>
<th>Compound</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. citrinopileatus</em></td>
<td>Antioxidant, Hypocholesterolemia</td>
<td></td>
<td>[82,80]</td>
</tr>
<tr>
<td><em>P. cornucopiae</em></td>
<td>Anti-hypertensive</td>
<td>ACE inhibitor peptide</td>
<td>[61,62]</td>
</tr>
<tr>
<td><em>P. eryngii</em></td>
<td>Antioxidant, Anti-hypertensive, Hypocholesterolemia</td>
<td>Ergothioneine</td>
<td>[77,66,41,56,54]</td>
</tr>
<tr>
<td><em>P. florida</em></td>
<td>Antioxidant, Hypocholesterolemia</td>
<td></td>
<td>[41,79]</td>
</tr>
<tr>
<td><em>P. nebrodensis</em></td>
<td>Anti-hypertensive</td>
<td></td>
<td>[65]</td>
</tr>
<tr>
<td><em>P. ostreatus</em></td>
<td>Hypocholesterolemia</td>
<td>Chrysin,</td>
<td>[69-</td>
</tr>
<tr>
<td>Species</td>
<td>Effect</td>
<td>Compound</td>
<td>Reference</td>
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<tr>
<td><em>P. pulmonarius</em></td>
<td>Antioxidant, Anti-hypertensive</td>
<td>Ergothioneine,Lovastatin</td>
<td>71,73,72,76,75,56,54[1]</td>
</tr>
<tr>
<td><em>P. saca</em></td>
<td>Hypocholesterolemia</td>
<td>Lovastatin</td>
<td>69,70[1]</td>
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<td><em>P. sapidus</em></td>
<td>Hypocholesterolemia</td>
<td>Lovastatin</td>
<td>69,70[1]</td>
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<tr>
<td><em>P. tuber-regium</em></td>
<td>Antioxidant</td>
<td></td>
<td>51[1]</td>
</tr>
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</table>
Figure 1: Reactive oxygen species (ROS) systems in the activation of inflammation and lipid oxidation
Figure 2: The relationship between hypercholesterolemia, hypertension and endothelial dysfunction
Figure 3: Mevalonate pathway