

## Review

# ***Salvia miltiorrhiza*: Chemical and pharmacological review of a medicinal plant**

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***Salvia miltiorrhiza* is a well-known traditional Chinese herb, belongs to the family of Labiatae, is used in many parts of the world to treat various conditions due to their excellent medicinal values. It is rich sources of tanshinone I, tanshinone II, miltirone and salvianolic acid and a wide range of chemical compounds. Extracts of the plant, particularly those from the root, possess useful pharmacological activities. Particular attention has been given to anti-oxidant activity, anti-microbial activity, antivirus activity, anti-cancer, anti-inflammatory, cardiovascular disease and so on. An account of chemical constituents and biological activities is presented and a critical appraisal of the ethnopharmacological issues is included in view of the many recent findings of *S. miltiorrhiza*. The aim of this review is to up-date and to present a comprehensive analysis of traditional uses, pharmacological reports and phyto-constituents isolated from the plant.**

**Key words:** *Salvia miltiorrhiza*, biological activities, medicinal plant.

## INTRODUCTION

*Salvia miltiorrhiza*, named Danshen in Chinese, is a traditional Chinese medicinal herb. It is a perennial flowering plant in the genus *Salvia*, highly valued for its roots in traditional Chinese medicine. Native to China and Japan, it grows between 90-1200 m elevation, preferring grassy places in forests, hillsides, and along stream banks in the west and southwest provinces of China. The plant is a deciduous perennial. It grows to between 30–60 cm high. Leaves are simple or divided, depending on their position on the stem. Flower petals are purple or blue held within a dark purple calyx (Figure 1). The specific epithet *miltiorrhiza* means "red juice extracted from a root" (Clebsch et al., 2003).

Danshen is the dried root of *S. miltiorrhiza* (*Labiatae*) and is one of the most versatile Chinese herbal drugs, sometimes described as Chinese sage or red sage root (Figure 2). Danshen was used infrequently in ancient Chinese's medicine, yet it has become an important herb in modern Chinese clinical practice. It has been used clinically to treat and prevent cardio-vascular disease, hyperlipidemia, and cerebro-vascular disease throughout the world (Cheng et al., 2007). The transformation of Danshen from a rarely used and minor component of formulas to a key herb is a story that sheds light on the evolution of the Chinese medical tradition (Figure 3). Now, *S. miltiorrhiza* is often widely used in combination

with other herbs.

Remedies containing *S. miltiorrhiza* are used to treat a diversity of ailments, particularly cardiac and vascular disorders such as atherosclerosis ("hardening" of the arteries with cholesterol plaques) or blood clotting abnormalities. The ability of *S. miltiorrhiza* to "thin" the blood and reduce blood clotting is well documented, although the herb's purported ability to "invigorate" the blood or improve circulation has not been demonstrated in high-quality human trials. Because *S. miltiorrhiza* can inhibit platelet aggregation and has been reported to potentiate the blood-thinning effects of warfarin, it should be avoided in patients with bleeding disorders, prior to some surgical procedures, or when taking anticoagulant (blood-thinning) drugs, herbs, or supplements.

In modern Chinese clinical treatment, *S. miltiorrhiza* is one of the most commonly used Chinese herbs. It appears in numerous formulations, often as the key ingredient. In addition, *S. miltiorrhiza* is sometimes given as a single herb remedy, and is even prepared in injection form for intravenous administration. The elevation of *S. miltiorrhiza* to an important herb took place in China. Thus the reasonable and systematic use of *S. miltiorrhiza* is the main content of traditional Chinese's medicine modernization. However, there is little information available in literature about a comprehensive analysis of



**Figure 1.** *Salvia miltiorrhiza*, leaves and flowers.



**Figure 2.** *Salvia miltiorrhiza*, red Radix.



**Figure 3.** Danshen is the dried root of *Salvia miltiorrhizae*.

identification of pharmacologically important molecules, and biochemical and pharmacological studies of this useful plant, as well as possible directions for future research.

### PHYTOCHEMICAL CONSTITUENTS ISOLATED FROM *Salvia miltiorrhiza*

Up to today, more than seventy compounds have been isolated and structurally identified from *S. miltiorrhiza* with various concentrations (Yong et al., 2009). The main components of *S. miltiorrhiza* can be divided into two groups (Table 1), hydrophilic compounds such as salvianolic acids, and lipophilic chemicals, including diterpenoid and tanshinones. Most of these compounds are colored, providing the reddish appearance of the roots. The second group of components, labeled tanshinone I, tanshinone II, cryptotanshinone, were first described by researchers in 1968, though investigations had been underway since the pigments were isolated from *S. miltiorrhiza* in 1934. More recently, nearly 40 variants of the basic tanshinone structures have been found in the roots. The tanshinones are unique chemical constituents, and similar compounds are not found in other Chinese herbs. The total tanshinone content of the roots is about 1%, with tanshinone I and II and cryptotanshinone being present in the largest amount. In one recent study, the concentration of *Radix Salvia miltiorrhiza* yielded tanshinone II 0.29%, cryptotanshinone 0.23% and tanshinone I 0.11%.

Among the tanshinones, tanshinone I, tanshinone IIA and cryptotanshinone are the major bioactive constituents and have various kinds of pharmacological effects including antibacterial, antioxidant, antitumor activities, prevention of angina pectoris and myocardial infarction. Despite the pharmacological activities, potential risks regarding combination use of *S. miltiorrhiza*, and drugs have been observed. For example, Clinical reports have suggested the possibility of interactions between warfarin and *S. miltiorrhiza*, which could result in increased anticoagulation (Yu and Chan, 1997; Izzat and Yim, 1998; Chan, 2001). Danshen is listed in the Chinese Pharmacopoeia for the treatment of cardiovascular and cerebrovascular diseases. The major active constituents of Danshen include tanshinones (Lee et al., 1987), which have been reported to have anti-platelet (Chan, 2001; Yu et al., 1997), cardio protective (Au-Yeung et al., 2001; Fu et al., 2007; Wu et al., 1993), anti-inflammatory (Kim et al., 2002), hepato-protective (Lee et al., 2003), vasodilatory effects and diminution of cancer cell proliferation (Lee Chen et al., 2008; Liu et al., 2001) effects in preclinical studies. Its product, Fu fang Dan shen Di wan, extracting curative ingredients, mainly from the plant, is now available in sixteen countries and becomes the first Chinese herbal medicine approved by the Food and Drug Administration for clinical tests in the United States. The water-soluble compounds of *S. miltiorrhiza* are mainly

this plant. This review is intended to provide the currently information on traditional Chinese's medicine knowledge,

**Table 1.** Components isolated from *Salvia miltiorrhiza*

Hydrophilic compounds	Lipophilic chemicals
sal-vianic acid A,B,C	tanshinone I ,IIA,IIB, V ,VI
salvianolic acid A,B,C,D,E,G	cryptotanshinone
rosmarinic acid	isotanshinone I ,II,IIB
methyl rosmarinate	isocryptotanshinone
monomethyl lithospermate	hydroxytanshinone IIA
dimethyl lithospermate	methyl tanshinonate
ethyl lithospermate	dan-shenxinkum A,B,C,D
lithospermic acid B	dihydroisotanshinone I
protocatechualdehyde	neocryptotanshinone
isoferulic acid	deoxyneocryptotanshinone
baicalin	salviol
isoperatorin	nortanshinone
ursolic acid	Tanshindiol A,B,C
$\beta$ -stirosterol	miltirone
daucosterol	1-dehy-dromiltirone
stigmasterol	1-dehydrotanshinone II A
tigo-genin	1-detoisocryptotanshinone
5(3-hydroxypropyl)-7-methoxy-2-(3-methoxy-4-hydroxyphenyl)-3-benzofurancarbaldehyde	3 $\alpha$ -hydroxytanshinone II A
	1,2-dihydrotan-shinqunone
	formyltanshinone
	methylenedihydrotanshinone
	7 $\beta$ -hydroxy-8-13-abietadiene 11, 12-dione
	ferruginol
	4-methylenemiltirone
	tanshinlactone
	dihydrotanshinlactone
	danshen-spiroketallactone
	epidanshenspiroketallactone
	cryptoac-etalide
	miltiodiol
	miltipolone
	nor-salvioxide
	1,2,5,6-tetramethylhydroxytanshinone I
	2-isopropyl-8-methylphenanthrene-3,4-dione

phenolic acid compounds, including single phenolic acids and polyphenolic acids. Single phenolic acids include protocatechuic aldehyde, protocatechuic acid, caffeic acid, and 3,4-dihydroxyphenyl lactic acid, also called danshensu, whereas polyphenolic acids include rosmarinic acid, lithospermic acid, salvianolic acid A, salvianolic acid B, and other salvianolic acids (Jing et al., 2008).

Water-soluble salvianolic acid A and salvianolic acid B were successfully isolated and purified from *S. miltiorrhiza* by high speed counter current chromatography and ultrasound assisted extraction (Yin et al., 2009; Juane et al., 2010). The isolated salvianolic acid A exhibited considerable higher antioxidant capacity than

salvianolic acid B. *S. miltiorrhiza*, exhibits a much stronger activity in free radical scavenging and antioxidance than those of vitamin E. Thus, salvianolic acid A and salvianolic acid B are the major antioxidant components in *S. miltiorrhiza*, also many other good benefits (Table 1).

#### **TOXICITY OF *Salvia miltiorrhiza***

At the higher dosage levels, *S. miltiorrhiza* may on rare occasions cause dry mouth, dizziness, lassitude,

numbness, shortness of breath, and other symptoms that will usually disappear spontaneously without interrupting the treatment. Rare Chinese Materia Medica notes that *S. miltiorrhiza* is not suitable for patients who have deficiency but not stasis, or deficiency accompanied by cold, or with tendency to bleed. *S. miltiorrhiza* has very low acute toxicity, with an LD50 by injection of 40-80 g/kg. The Pharmacopoeia of the People's Republic of China indicates a recommended dosage of 9-15 g per daily dose in decoction form. In a few instances, higher doses are administered, up to 20 g per day, in the treatment of inflammatory diseases, including viral hepatitis. According to English-Chinese Rare Chinese Materia Medica, up to 30-60 g can be used in cases of angina and heat-type arthritis. The relatively high dosage of *S. miltiorrhiza*, compared to most other Chinese herbs may be attributed to the relatively low level of active constituents and their poor solubility in water.

It is recommended that *S. miltiorrhiza*, or its preparations used for treatment of poor blood circulation, not be combined with coumadin (Warfarin), as there is a possibility of increasing the anticoagulant effects. Such effects may be rare and are likely to be dose dependent, as the mechanism appears to be a simple additive effect of anticoagulant activity of *salvia* along with that produced by Warfarin. Therefore, persons using coumadin should either avoid using *S. miltiorrhiza*, or use it in relatively low dosage while paying attention to blood coagulation tests that are routinely performed for persons taking the drug. The doses are based on scientific research, publications or traditional use. Because most herbs and supplements have not been thoroughly studied or monitored, safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients even within the same brand. Combination products often contain small amounts of each ingredient and may not be effective. The dosing for unproven uses should be approached cautiously, because scientific information is limited in these areas. There are no standard or well-studied doses of *S. miltiorrhiza*, and many different doses are used traditionally. Further studies through long-term bioassays are required to determine the chronic toxicity of the plant on the body.

## PHARMACOLOGICAL ACTIVITIES OF *Salvia miltiorrhiza*

### Anticancer activity

Cancer is one of the leading causes of death, and the main bioactive chemicals from *S. miltiorrhiza* play an important role in the prevention in several cancer cells. Several observations made in the past are suggestive of anti-cancer effect of the plant and its constituents.

Recently, a high throughput screening of 76 medical plants identified tanshinone IIA as one of the promising

cytotoxic compounds in human leukemia cells (Efferth et al., 2008). Tanshinone IIA, extracted from the dried root of *S. miltiorrhiza*, is one of the potential anticancer components, despite its traditional application was in the treatment of cardiovascular diseases in China (Zhou et al., 2005). Experiments have shown that tanshinone IIA exerted cytotoxic effect on a number of human tumor cell lines (Wu et al., 1991; Ryu et al., 1997). Studies revealed that induction of apoptosis was the key factor in contributing to the cytotoxic property of tanshinone IIA (Yuan et al., 1998; Sung et al., 1999; Yuan et al., 2004; Sung et al., 2005; Liu et al., 2006; Wang et al., 2007). Triggering of the apoptotic pathway has been considered as one of the more promising strategies for anticancer therapy (WHu and Kavanagh, 2003). Therefore, the anti-cancer potential of tanshinone IIA has been explored.

In addition, the mechanism of *S. miltiorrhiza*-induced apoptosis in human hepatoma HepG2 cells indicated that *S. miltiorrhiza* deplete intracellular thiols, which, in turn, causes MPT (mitochondria permeability transition) and subsequent increase in ROS (Reactive oxygen species) generation, and eventually apoptotic cell death (Liu et al., 2001). Neo-tanshinolactone isolated from *S. miltiorrhiza* have property to *in vitro* against several human cancer cell lines, significant inhibition against two human breast cancer cell lines 10-fold more potent than tamoxifen citrate, it also potently inhibited an estrogen receptor over-expressing breast cancer cell, it can be a candidate as an anti-breast cancer medicine (Wang et al., 2004). Furthermore, some related study in Colo 205 human colon cancer cells investigated the effect of tanshinone I on human colon cancer cells, a result proposed tanshinone I induce apoptosis in Colo 205 cells through both mitochondrial-mediated intrinsic cell-death pathways and p21-mediated G0/G1 cell cycle arrest (Su et al., 2008). Besides the above-mentioned cancer cells, the anticancer effects of tanshinones on the highly invasive human lung adenocarcinoma cell line, CL1-5 is studied by many scientists. Tanshinone I significantly inhibited migration, invasion, and gelatinase activity in macrophage-conditioned medium-stimulated CL1-5 cells *in vitro* and also reduced the tumorigenesis and metastasis in CL1-5-bearing severe combined immunodeficient mice. These effects are mediated at least partly through the interleukin-8, Ras-mitogen-activated protein kinase, and Rac1 signaling pathways (Lee et al., 2008).

### Anti-inflammatory activity

Inflammation is involved in the pathological process of many diseases, which are associated with the production of inflammatory cytokines, such as Interleukins, and tumor necrosis factor alpha (Straub, 2007). The elevated cytokine level likely contributes to the increased incidence of inflammatory diseases, neurodegenerative diseases, menopause and cardiovascular diseases (Vural et al.,

2006). Tanshinone has strongest inhibition on prostaglandin D2 production, tanshinone IIA exerts anti-inflammatory effects via inhibition iNOS gene expression and NO production, inhibition of inflammatory cytokine.

Experimental studies have shown that tanshinone can inhibit leukocyte chemotaxis and therefore, may have therapeutic effect on acute and subacute inflammation (Kang et al., 2000; Yagi and Takeo, 2003). *In vitro* and *in vivo* studies have shown that the anti-inflammatory mechanism of tanshinone may be related to inhibition of inflammatory cell cytokine production and arachidonic acid metabolism (Kim et al., 2002).

Tanshinone IIA isolated from *S. miltiorrhiza* has also been shown to possess anti-inflammatory activity. The present studies confirmed that tanshinone IIA serves as a phytoestrogen and exerts anti-inflammatory effects by inhibiting NO, IL-1 beta, IL-6, TNF-alpha and iNOS production and mRNA expression. The effects are apparently mediated via an ER-dependent (estrogen receptor) pathway in LPS (Lipopolysaccharide) activated RAW 264.7 cells since it could be blocked by ICI. The inhibition of cytokine production by tanshinone IIA may account for the antagonism of cell infiltration, suggesting that tanshinone IIA may be used as an anti-inflammatory drug against inflammatory disorders during menopause by limiting the early phases of macrophage infiltration. These results may explain the effectiveness of the traditional use of *S. miltiorrhiza* as an anti-inflammatory herbal medicine.

### Antimicrobial activity

Micro-organisms are involved in the pathogenesis of many diseases and cause deterioration of a variety of products. Despite the progress in understanding the life cycle and control of many pathogens, nearly all the diseases affecting millions of people in developing countries are still caused by micro-organisms. Scientific findings concluded *S. miltiorrhiza* fraction, and its components (Cryptotanshinone and dihydrotanshinone I) show antibacterial activity against broad range of bacteria, including the broad range of gram positive bacteria, and gram-negative bacteria, and superoxide radicals are considered important in the antibacterial actions of the agents (Lee et al., 1999). Clinical application of *S. miltiorrhiza* can be effective in prevention of inflammatory diseases induced by gram-negative bacteria, Lipopolysaccharide (LPS) has been implicated as one of the major causes of gram-negative bacteria-induced sepsis that are life-threatening syndromes occurring in intensive care unit patients. This related study showed *S. miltiorrhiza* is able to block the lethal toxicity of LPS in mice via suppression of TNF-alpha release and protection on liver injury (Wan et al., 2006).

In addition, ethanol extracts of *S. miltiorrhiza* had antimicrobial activities on *Porphyromonas gingivalis*, *A. actinomycete mcomitans*, *Streptococcus mutans*,

*Lactobacillus*, and the minimum inhibitory concentrations were 15.62, 15.62, 62.50 and 15.62 mg/ml. The pH of the solution was influential to its antimicrobial activity. According to above, ethanol extracts of *S. miltiorrhiza* have an antimicrobial activity on oral pathogenic microbes (Deng et al., 2006). The hexane and chloroform fractions of *S. miltiorrhiza* evidenced profound antimicrobial activity, and inhibited resistant gene expression against *Staphylococcus aureus* and MRSA (methicillin-resistant *Staphylococcus aureus*) (Ji won et al., 2007). Thus, *S. miltiorrhiza* is expected to be recognized as natural sources for the development of new functional drugs.

### Antivirus activity

Water soluble extracts of the herbal plant, *S. miltiorrhiza* exhibited the potent effect against HIV-1 integrase activity *in vitro* and viral replication *in vivo*. The isolated components from *S. miltiorrhiza* are potent anti-HIV inhibitors. IC50 for inhibition of processing by HIV-1 integrase was found to be 0.83 microM for lithospermic acid and 0.48 microM for lithospermic acid B, both inhibitors strongly suppressed the acute HIV-1 infection of H9 cells with IC50 values of 2 and 6.9 microM for lithospermic acid and lithospermic acid B, respectively, suggested and indicated that these two selective integrase inhibitors hold promise as a novel class of therapeutic drugs for AIDS based on their high potencies and absence of cytotoxicity (Abd-Elazem et al., 2002).

The enteroviruses are a genus of ssRNA viruses associated with several human and mammalian diseases. Historically, the most significant has been the Poliovirus. Other types are coxsackievirus and echovirus. Enterovirus are the most common cause of aseptic meningitis and can cause serious disease, especially in infants and the immuno-compromised human enteroviruses (family Picornaviridae) infect millions of people worldwide each year, resulting in a wide range of clinical outcomes ranging from unapparent infection to mild respiratory illness (common cold), hand, foot and mouth disease, acute hemorrhagic conjunctivitis, aseptic meningitis, myocarditis, severe neonatal sepsis-like disease, and acute flaccid paralysis. *S. miltiorrhiza* extracts (ethyl acetate extract and water extract) possess antiviral activity and have potential for the development as an anti-enterovirus 71 agent (Wu et al., 2007).

### Antioxidant activity

Today, new developments in bio-medical science emphase the involvement of free radicals in many diseases. There is increasing evidence to suggest that many degenerative diseases such as brain dysfunction, cancer, heart disease and immune system decline could

be the result of cellular damage caused by free radicals and that anti-oxidants may play an important role in disease prevention (Aruoma et al., 1998). Studies have also shown that phenolic compounds are potent scavengers of free radicals and as such, are potentially useful in the prevention of a number of diseases (Zainol et al., 2003). Up to date, more than twenty phenolic acids isolated from *S. miltiorrhiza* have been well studied (Li et al., 2009). The commonly used anti-oxidants, butylated hydroxyanisole and butylated hydroxytoluene are synthetic chemicals and the possible toxicity of these anti-oxidants has resulted in their reduced usage (Ito et al., 1985). Due to health concerns, natural anti-oxidants have been extensively employed in recent years (Yen et al., 2003). Water-soluble salvianolic acid A and salvianolic acid B were isolated and purified from the crude extract of *S. miltiorrhiza*. The related results showed that salvianolic acid A and salvianolic acid B exhibited high total antioxidant activities. Their EC50 values were  $1.35 \pm 0.00$  and  $1.43 \pm 0.01$  g/ml, respectively.

Besides, *S. miltiorrhiza* aqueous fraction which contains salvianolic acid B and rosmarinic acid displays strong anti-lipoperoxidant activity via scavenging superoxide anion radical; *S. miltiorrhiza* component, Danshensu(3-(3,4-dihydroxyphenyl) lactic acid) and tanshinone scavenge superoxide anion free radicals or lipid free radicals;

Danshen, processed from the roots of *S. miltiorrhiza*, is ranked as one of the most important commercial herbs in China. Its annual output is around 5000–7000 tons. As we know, the leaf biomass of *S. miltiorrhiza* constitutes a considerable proportion of the whole plant. However, large amounts of leaves are discarded as waste during root harvest time. Compared with the corresponding root extracts, leaf extracts of *S. miltiorrhiza* possess considerable amounts of total phenolics, similar phenolic composition and significant antioxidant activities. HPLC and correlation analysis show that salvianolic acid B and rosmarinic acid constitute the most abundant phenolic compounds. They are the major contributors to antioxidant activities. In light of these valuable bioactivities, leaves of *S. miltiorrhiza* considered as waste materials have a good commercial potential to be utilized as promising natural antioxidants in the food, pharmaceutical or cosmetic industries, not only for the low cost but also for the large amounts available (Li and Wang, 2009; Matkowski et al., 2008).

### Cardiovascular pharmacology

For several decades, *S. miltiorrhiza* extract has been widely used in clinics in China, Korea, Japan and other Asian countries for the treatment of various-microcirculatory disturbance-related diseases, such as cardiovascular disease, cerebrovascular disease, and a number of studies have been carried out in attempts to identify the biological actions and the mechanism

underlying such actions (Feldman et al., 2000). A lot of reports also demonstrated that *S. miltiorrhiza* is able to relax coronary arteries, elicit an antioxidant salvage effect upon the myocardium, reduce intimal thickness in air-injured carotid arteries, inhibit platelet aggregation, and prevent low-density lipoprotein (LDL) oxidation (Chen et al., 2001).

*S. miltiorrhiza* had demonstrated its effectiveness in reduction of infarct size and mortality rate in rats with acute myocardial infarction. The antioxidant effect and possible feature of angiogenesis of *S. miltiorrhiza* had been suggested as the main factor in protecting ischemic myocardium. Salvianolic acids, as the main active components of aqueous extract of *S. miltiorrhiza*, exhibit potential effects to prevent myocardial injury induced by infarction in clinical and animal experiments. Subsequently, with the development of the molecule biology of the new technology, the functional proteomics reveals the effect of *S. miltiorrhiza* aqueous extract against vascular atherosclerotic lesions (Yu-Chiang et al., 2010).

In a word, *S. miltiorrhiza* has a key role which cannot be substituted in the prevention and treatment of cardiovascular related disease. Such as myocardial protection, myocardial infarction and acute myocardial infarction, coronary heart disease, congenital heart disease treatment, ischemic heart disease prevention and anti-anginal, cardiac disease with contractile failure prevention, anti-atherosclerosis, arterial restenosis prevention, arterial intima prevention, chronic cor pulmonale treatment, ventricular fibrillation prevention and treatment, portal hypertension effect, hypolipidemic activity and so on (Ji W et al., 2008).

### Conclusion

Overall, *S. miltiorrhiza* is a well-known medicinal plant that is frequently prescribed in various indigenous systems of medicines, especially those of China and Korea. Its most widespread traditional uses have been for the treatment of cardiovascular disease, microcirculation disorders, liver fibrosis, cancer, insomnia, poor memory and mental agitation. The Fufang Danshen Diwan medicine extracting curative ingredients, mainly from *S. miltiorrhiza* is now undergoing clinical tests in the US and European Union, which are going well. Although a small step forward, the clinical tests's success has cast light on the development and globalization of traditional Chinese's medicine.

Now, some bio-active compounds have been isolated, and various ketones have been identified in *S. miltiorrhiza* including tanshinoneI, tanshinoneII, miltirone and salvianolic acid. *S. miltiorrhiza* was particularly rich in salvianolic acid and may, therefore be considered as a natural source of these commercially important antioxidants. The collective results obtained for the in vitro pharmacology activity of *S. miltiorrhiza* provide scientific support for the use of these plants in traditional medicine.

The worldwide consumption of *S. miltiorrhiza* and its extracts is on the rise due to the increase in popularity of alternative medicine in the prevention and treatment of cardio-vascular diseases. However, extensive pharmacological mechanisms of *S. miltiorrhiza* are deficient. The idea of some research has continued to narrow. Therefore, It is important to note that most of the research done on *S. miltiorrhiza* employs in vitro-based studies and in vivo tests should be encouraged.

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