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Lamiaceae in the treatment of cardiovascular diseases

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1. ABSTRACT

Lamiaceae (Labiatae) are an important group of medicinal plants, which have been used for treating heart disease in traditional medicine for centuries. These mainly aromatic plants are used as essential oils, extracts or isolated components (polyphenols, phenolic compounds, terpenes, iridoids *etc.*). Some Labiatae species (more than 30, such as cornmint, lavender, patchouli, rosemary *etc.*) are famous for their use in essential oil production worldwide. In this review, cardioprotective effects of Lamiaceae and their active secondary metabolites, as well as mechanism of action against cardiovascular diseases (hypertension, angina pectoris, hyperlipidemia, thromboembolism, coronary heart disease, heart failure, venous insufficiency, arrhythmia) will be discussed. Use of Labiatae as food or food additives (such as spices) may prevent risk of cardiovascular diseases, diabetes and cancer. This approach is also described as a part of the article. Studies on developing new, effective and safe natural products from Lamiaceae (rich source of flavonoids and other active compounds) are promising and may offer prevention and treatment for patients with coronary disease and other related diseases.

2. INTRODUCTION

Cardiovascular diseases (CVDs) are disorders of the heart and blood vessels and include conditions such as hypertension, hyperlipidemia, thromboembolism, coronary heart disease, and heart failure. Among these conditions, hypertension is the most common, and plays a major role in the development of CVDs (1). According to World Health Organization (WHO), over 17 million people die per year (31% of all global deaths) from CVDs. With the increasing number of diagnoses of CVD, it is projected that mortality will reach 23.3 million before 2030 (2).

Herbs and herbal products have been used for the treatment of several ailments for centuries. More than 2000 plants are known in ethnomedicine, and some of them are traditionally used to prevent or treat people suffering from CVDs and related complications. It is estimated that around 25% of currently commercialized medicines are derived from herbal plants used in traditional medicine. Herbal products are effective against CVD alone or in combination with other drugs, as Mahady *et al.*, (3) noted that hundreds of plant-based products are traditionally used to treat diseases. However, some of the herbs show side effects that sometimes exceed their benefits. Therefore, impact of herbs on biological mechanisms needs to be investigated.

A large number of traditional herbs have been reported, which have efficacy against CVD. Some of the suggested and scientifically proven herbs are *Cynara scolymus (*artichoke), *Allium sativus*-(garlic), *Ginkgo biloba*, *Commiphora mukul*, *Crataegus* species, *Vitis vinifera* (grape), *Crocus sativa (*saffron), and *Camellia sinensis* (tea) (3). These herbs exhibit potent antioxidant and anti-inflammatory activities, which makes them effective against CVD and associated complications. Chemical analysis of these plant extracts revealed that they contain large number of bioactive phytochemicals, which provides unlimited opportunities for the development of new drugs against several diseases, including CVD (4).

Numerous studies reported that species from the Lamiaceae family have potent cardioprotective effects among various medicinal and aromatic herbs (5-8). These plants can be used as crude extracts, essential oils (EOs), or active compounds against CVD (Table 1.) (7; 9; 10). It is important to note that the Lamiaceae family of plants contains various classes of bioactive compounds including flavonoids, terpenoids, and alkaloids. This plant family and their active compounds have shown promising cardioprotective activity *in vitro* and *in vivo* (Table 1, Figure 1, Figure 2). One of the most investigated Lamiaceae species belongs to the *Salvia* genera, known to act as strong cardioprotective agents, which can notably improve myocardial ischemia in patients with CVDs (11). *Salvia*, in combination with other herbs, has a more potent effect. For example, *Salvia* and *Astragalus* show a positive synergistic effect and reduce symptoms of hemorrheology in patients with heart failure (11). However, some studies reported that combination of conventional and alternative medicine may cause herb-drug interactions and result in side effects (2). This review compiles the list of Lamiaceae species with cardioprotective effects, potential mechanisms of their active components, consumption to decrease risks or avoid CVDs, as well as a number of case reports.

3. HERBAL PRODUCTS FOR TREATMENT OF CARDIOVASCULAR DISEASES

Natural plant products are widely used to treat various diseases, including CVD. Based on structures, a wide range of bioactive compounds from plants are used for synthesis of some commercial pharmaceutical drugs. For example, ephedrine isolated from *Ephedra sinica*, (2) semi-synthetic aspirin derived from salicin (isolated from Salix alba), artemisinin isolated from Artemisia annua, alkaloid morphine found in Papaver somniferum, and capsaicin from Capsicum annuum (12). Besides these, several medicinal plants worldwide are used in traditional medicine in the treatment of cardiovascular disorders. For example, *Alium sativum* (garlic) is well known for its hypotensive and hypocholesteremic effects (13), while *Camellia sinensis* (tea) possess cardioprotective effects, which consists of number of flavonoids: catechin (the major), (–)- epicatechin, (–)-epicatechin-3-gallate, (–)- epigallocatechin, and (–)-epigallocatechin-3-gallate, (–)-epigallocatechin-3-gallate *etc.* (13). *Crataegus* spp. is famous for its antihypertensive activity probably due to the large flavonoid content (hyperoside, quercetin, rutin, and vitexin). *Nigella sativa* (black cumin), a well-known spice, contains thymoquinone as the major bioactive constituent with cardiovascular healing effects (13). *Coriandrum sativum* is known as a natural antioxidant and has been shown to increases levels of antioxidants in food.

Table 1. Lamiaceae species with cardioprotective effects *in vitro* and *in vivo*

Scientific name	**Active ingredients**	**Cardioprotective effects and traditional use**	**Reference(s)**
1 .*Ajuga iva* (L.) Schreber	Aqueous extract	• NO-mediated and NO-independent vasorelaxing properties *in vitro* while only the endothelium-independent effect was observed *ex vivo*	(39)
2. *Cedronella canariensis* (L.) Webb. & Berth		• Leaves possess cardiovascular activity	(153)
3. *Clinopodium umbrosum* (M.Bieb.) Kuntze		• Heart tonic	(154)
4. *Dracocephalum moldavica* L.	Flavonoids	• cardioprotective effects against acute ischemia	(155)
5. *Lavandula anguistifolia* Mill.	Essential oils	• **Protects myocardium against isoproterenol induced myocardial infarction that it could be related to its antioxidant properties**	(9)
6. *Leonotis leonurus* (L.) R.Br	Diterpenoid Marrubiin	• Anticoagulant, antiplatelet, and anti-inflammatory effects	(33)
7. *Leonurus cardiaca* L.	Phenolic compounds	• Strengthening cardiac muscle • The healing of heart diseases, Analgesic effect	(41) (156) (157)
8. *Marrubium vulgare* L.		• Protective effect against cardiac complications	(44)
9. *Mentha arvensis* L.		• Beneficial effects of *M. arvensis* in patients with ischemic heart disease	(8)
10. *Mentha* x *piperita* L.	Aqueous extract	• Decreases levels of glucose, cholesterol and triglycerides and increase the high-density lipoprotein cholesterol and HDL-ratio without affecting serum insulin levels in fructose-fed rats	(158)
11. *Mentha pulegium* L.	Polyphenolic compounds (Salvianolic acid B; Salvianolic acid E; Isosalvianolic acid B; Salvialonolic acid I; Salvianolic acid H; Lithospermic acid, luteolin-6,8-C-dihexose; Syringetin; Quercetin)	• Cardioprotective effect	(158)

contd...

Table 1. Contd...

Scientific name	Active ingredients	Cardioprotective effects and traditional use	Reference(s)
12. *Melissa officinalis* L.	Phenolic compounds	• Cardioprotective effect	(159)
13. *Ocimum basilicum*	Rosmarinic acid	• Strongly protect the myocardium against isoproterenol induced infarction • Anticoagulant effect • Cardioprotective effect of rosmarinic acid	(53) (160) (31)
14. *Ocimum gratissimum* L.	Cardioprotectin	• Cardioprotective effect	(161)
15. *Ocimum sanctum* L.		• Hypotensive, cardiac depressant activity	(162)
16. *Origanum vulgare* L.		• Contain cardioprotective flavonoids	(27)
17. *Origanum majorana* L.	Flavonoids (Kaempferol-O-glucuronide; Sakuranetin; Salvialonolic acid; Luteolin-6,8-C-dihexose; Taxifolin; dihydrokaempferide; Luteolin-O-glycoside; Kaempferol-O-sambubioside; Luteolin glucoside; Syringetin; Quercetin)	• Cardioprotective effect	(158)
18. *Orthosiphon thymiflorus* Benth.		• Anti-inflammatory and hypertensive	(36)
19. *Plectranthus barbatus* Andrews	Forskolin (labdane diterpene)	• Cardioprotective activity	(7)
20. Pogostemon cablin (Blanco) Benth.	(*α*-bulnesene) sesquiterpene present in EO	• Anti-PAF (Platelet-Activating Factor)	(163)
21. *Rosmarinus officinalis* L.	Polyphenols and Flavonoids	• Antineoplastic effects	(164) (165) (166)
22. *Salvia hispanica* L.	Seeds α-Linolenic acid	• Prevent cardiovascular diseases, inflammatory and nervous system disorders, and diabetes • precursor of eicosapentaenoic acid and docosahexaenoic acid connected to the antiatherogenic and cardioprotective effects	(167) (168)
23. *Salvia miltiorrhiza* Bunge	Extract Lipophilic tanshinones Salvianolic Acid B	• Antianginal, Hypertension • prevention of LDL-C oxidation • cardiovascular effect	(169) (170) (10) (171)

contd...

Table 1. Contd...

Scientific name	Active ingredients	Cardioprotective effects and traditional use	Reference(s)
34. *Teucrium polium* L.	aqueous-ethanol extract	• Positive effect blood pressure, heart rate and intraventricular pressure	(180) (34)
35. *Teucrium cartaginenses* L.	Methanol extract	• Reduces mean arterial blood pressure	(181)
36. *Stachys inflata* Benth.		• Hydroalcoholic extract attenuates the infarct size following ischaemia	(78)
37. *Scutellaria baicalensis* Georgi.		• Inhibits thrombin-induced production of plasminogen activator inhibitor-1 and interleukin-1ß- and tumor necrosis factor-α-induced adhesion molecule expression in cultured human umbilical vein endothelial cells, anti-thrombotic, anti-proliferative and anti-mitogenic effects of the roots	(182)

Kousar *et al.*, (14) demonstrated that the leaves of *Coriandrum sativum* show significant cardioprotective ability by increasing levels of superoxide dismutase and decreasing levels of serum marker enzymes and peroxidase. Extracts (ethanol and aqueous) of *Curcuma longa* show cardioprotective effects against doxorubicin (DOX) induced cardiotoxicity in rats. Turmeric is rich source of curcuminoids, terpinolone, *p*-cymene, undecanole, 1,8-cineole, *α*-turmerone, and other active secondary metabolites related to its cardioprotective activity (15). Anthocyanins, glucosinolates, isothiocyanates, and phenolic compounds are responsible for the cardioprotective effects of *Raphanus sativus* against myocardial injury induced by isoproterenol (16) in rats.

3.1. Lamiaceae family

The Lamiaceae (Labiatae) family contains medicinal and aromatic plants with around 7,200 species distributed in 240 genera. Current literature data suggests Lamiaceae can act as an antioxidant, antimicrobial and anti-inflammatory agent, while several studies recommend some Lamiaceae species as functional foods (17).

Lamiaceae plants, indigenous to Mediterranean regions and traditionally employed as culinary herbs, also have a long traditional history of use for several medicinal purposes (5, 18, 20). This economically important plant family consists of cultivated and ornamental garden plants (*Salvia splendens*, *Lavandula*, *Teucrium*, *Phlomis*…). Plants of this family are widely used as culinary herbs and spices such as sage (*Salvia*), thyme (*Thymus*), mint (*Mentha*), oregano, and marjoram (*Origanum*), rosemary (*Rosmarinus*), lavender (*Lavandula*), and basil (*Ocimum*). These are also important perfumery ingredients (mint and lavender), flavor additives used in food industries (*Rosmarinus officinalis*, *Ocimum basilicum*, *Origanum majorana*), and as beverages and teas (*Satureja montana*, *Mentha* x *piperita*, *Salvia officinalis*, *Sideritis scardica etc.*). The medicinal properties of the Lamiaceae species are attributed to their high content of volatile (5) and flavonoid compounds. To date, a number of secondary metabolites from the Lamiaceae family of

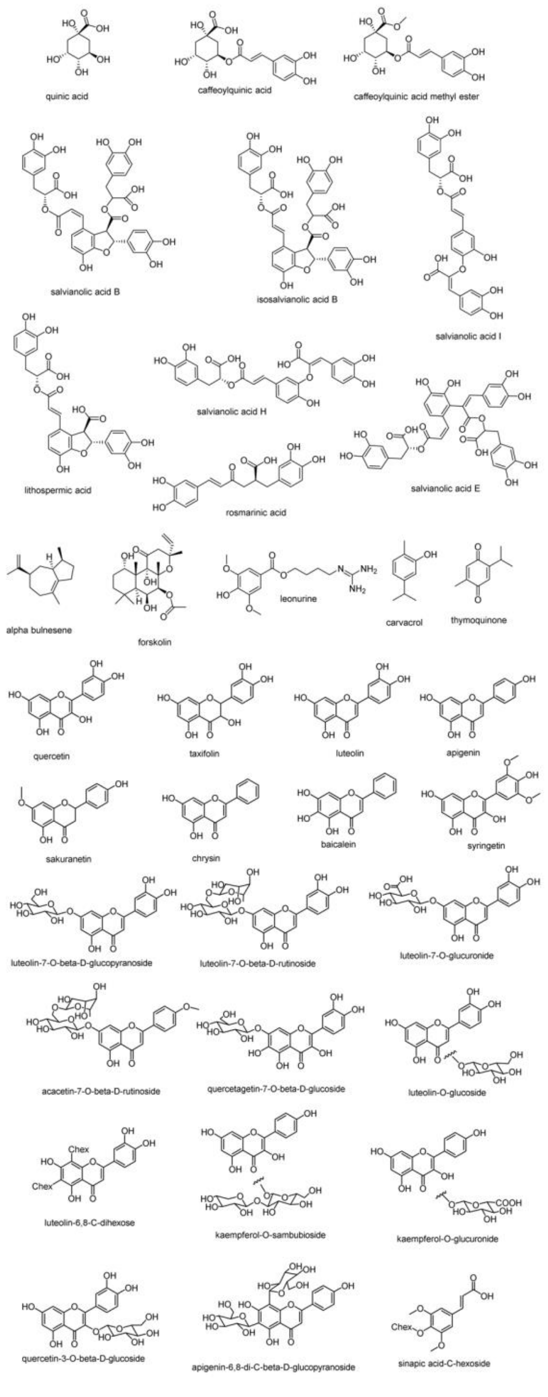

Figure 1. Chemical structures of bioactive Lamiaceae secondary metabolites.

plants are isolated (flavonoids, iridoids, terpenoids *etc.*) and their different biological activities are confirmed (21; 26).

3.2. Cardioprotective effects of Lamiaceae species and their active compounds

The Lamiaceae species, which are a rich source of antioxidants (polyphenolic compounds), possess promising benefits to decrease the risk of CVDs through the suppression of inflammation (27). One of the plants of the Lamiaceae family, Satureja hortensis, is traditionally well known for the treatment of CVDs and associated complications (28). It has been reported that methanol extract of S. hortensis has an inhibitory effect on blood platelet adhesion, aggregation, secretion and also has blood anticoagulant activity (29). Further studies revealed that monoterpenes (such as carvacrol), flavonoids and phenolic acids (like labiatic acid) present in S. hortensis are responsible for its anti-platelet properties. Another plant of this family, *Leonurus turkestanicus,* has been shown to be effective against cardiovascular, stomach, and other related diseases (30). In a study, camphor, limonene, tannins, triterpenoids, coumarins, cineole, and flavonoids, present in *Lavandula aguistifolia,* showed significant antioxidant properties and decreased cardiac tissue damage and strengthened myocardial membrane (31). *Stachys schimperi* possess cardioprotective effects on DOX-induced cardiotoxicity in rats. Isoscutellarein 7-O-β-D-glucopyranoside, found in methanol extract of this species, showed notable free radical scavenging activity, with mild protection against DOX-induced cardiotoxicity as shown by histopathological analysis. *In vivo* experiments in rats with isoproterenol-induced myocardial infarction showed that rosmarinic acid, found in high quantities in the leaves of basil (*Ocimum basilicum*), exhibited cardioprotective effects, which could be related to the antioxidant activities of rosmaniric acid. (31). Another example is *Plectranthus barbatus* (*syn. Coleus forskohlii*), which has been shown to be anti-atherogenic and cardioprotective (32). In that study, rats with myocardial infarction were administered the treatment (obtained from the dry, tuberous roots of the plant) for 20 days-post MI. The authors speculated that forskolin (labdane diterpene), found in the roots, is responsible for these activities (Table 1, Figure 1)

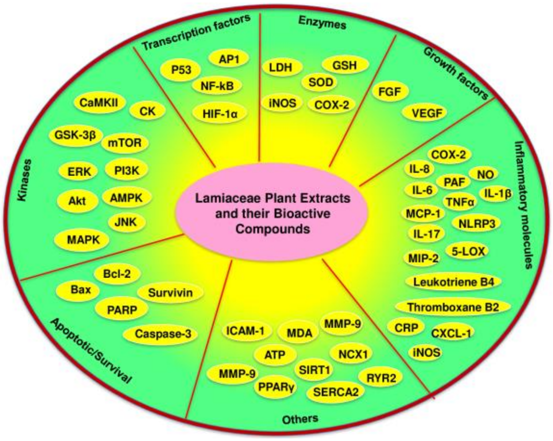

Figure 2. Molecular targets of Lamiaceae plant extracts and their bioactive compounds.

Marrubiin (labdane diterpenoid), a major compound of *Leonotis leonurus* plant extract, has shown anticoagulant, antiplatelet, and anti-inflammatory properties (33). Further, a study *in vivo* showed that the marrubiin in *L. leonurus* plant extract prolonged activated partial thromboplastin time (APTT). In addition, *in vitro* studies further revealed that the extract of *Leonotis leonirus*, as well as marrubiin, inhibit platelet aggregation through the inhibition of the binding of fibrinogen to glycoprotein IIb/IIIa receptor (33). In a study using human umbilical vein endothelial cells HUVECs, ethanol extract of *Teucrium polium* induced anti-angiogenic effects (34). Moreover, a combination of *T. polium* and tranilast (an analog of a tryptophan metabolite) remarkably increased anti-angiogenic properties.

Thymoquinone (2-Isopropyl-5-methylbenzo-1, 4-quinone), which is the major component of some spices belonging to the Lamiaceae family (mainly from *Thymus* genera), showed healing effects against coronary artery diseases, urinary system failures, hypertension, diabetes, apoptosis, inflammation, and oxidative stress. The cardioprotective effect of Thymoquinone is related to its antioxidant and anti-inflammatory activity (35).Comprehensive investigation on antihypertensive activity of leaf extract and compounds isolated from *Orthosiphon* species have also been studied and showed that isolated components (Methylripariochromene A, Orthochromene A, Neoorthosiphol A and B and Tetramethylscutell) decreased systolic blood pressure (36). In a study using rats, EO of *Lavandula angustifolia* has shown to protect isoproterenol-induced myocardial infarction. The authors concluded that *Lavandula* EO decreased cardiac tissue damage and provided strength to the myocardial membrane. This remarkable cardioprotective effect of *L. anguistifolia* EO was found associated with its antioxidant activity (9) (Table 1).

4. CARDIOVASCULAR DISEASES MITIGATED THROUGH ANTI-INFLAMMATORY EFFECT OF HERBS

Inflammation is one of the common causative factors of several diseases, including CVDs. Although it is not clearly proven that inflammation directly contributes to heart disease, CVD patients are reported to have increased level of inflammation. Various epidemiological and clinical studies have shown that increased inflammation has strong relationships with risk of cardiovascular diseases (37). Several inflammatory markers have been detected in CVD patients, but high-sensitivity C-reactive protein (CRP) is noted as the most clinically reliable and accessible inflammatory marker. A number of agents that can reduce inflammation associated CVD have been discovered, including 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, in the form of statins (38). However, it is not well known whether reduction of CRP really lowers cardiovascular risk. Therefore, there is a dire need of agents that can reduce the risk of CVD effectively and safely.

Because of their biologic properties as shown in Figure 2, Lamiaceae can reduce the risk factors of CVD and decrease the incidence of occurrence. Among several herbs, aqueous extract of *Ajuga iva* has shown to possesses vasorelaxing properties *in vitro* (39). Vasorelaxation of *Ajuga iva* extract was found to be influenced by nitric oxide (NO) modulation, as NO regulates the functional activity of inflammatory cell types including macrophages (39). *Lavandula anguistifolia* EOs inhibited platelet-activating factor (PAF), an inflammatory phospholipid mediator. Inhibition of PAF leads to protection of myocardium against isoproterenol-induced myocardium infraction in rats

(9). Ethyl acetate extract of *L. anguistifolia* also inhibits lipopolysaccharide (LPS)-induced inflammation in RAW264.7 macrophages through suppression of iNOS/NO signaling, IL1β, and cyclooxygenase (COX)-2 genes (40). Thus, modulation of inflammation by these plants contributes to reduction of CVD.

Leonurus cardiaca has been studied for its efficacy in strengthening cardiac muscle, which could be the potential factor in reduction of risk of CVD (41). Although the mechanism of strengthening muscle is not known, polyphenol rich extract of this plant is reported to mitigate inflammation by inhibiting the PAF secretion induced by staphylococcal peptidoglycan (42). The methanol extract of *Marrubium vulgare* at doses of 10, 20, and 40 mg/kg has shown to protect isoproterenol-induced acute myocardial infarction (43). Furthermore, 40 µg/mL of *M. vulgare* aqueous fraction has shown to decrease ischaemia-reperfusion (I/R) injury in rats (44). These findings suggest that the *M. vulgare* has cardioprotective properties. Although the mechanism of action for their cardioprotective activities is not clear, it can be speculated that this property is mediated through its anti-inflammatory activity, since it inhibits inflammatory molecule COX-2.

Mentha arvensis, which is used around the world, has shown cardioprotective effects through the inhibition of inflammation. At 100µg/ml, extract of this plant exhibited strong inhibitory activity against IL-8 secretion in AGS cells, which might be associated with CVD (45). Another species of mentha, *M. piperita*, also possess an anti-inflammatory effect against acute and chronic inflammation (46). The anti-inflammatory effect was mediated through suppression of tumor necrosis factor-alpha (TNF-α), vascular endothelial growth factor (VEGF), and fibroblast growth factor-2 (FGF-2) (47). This anti-inflammatory activity of *M. piperita* could be associated with suppression of CVD, since CVD patients have increased inflammation. Moreover, *M. modarresi* exhibits cardioprotective effects (48). *M. pulegium* has also shown anti-inflammatory as it strongly reduces IL-6, MCP-1, and TNF-α secretion in murine RAW 264.7 macrophages (49). These studies affirm the use of Lamiaceae is beneficial as cardioprotective and anti-inflammatory agents.

Melissa officinalis has been used as traditional medicine in several African countries as calming agent, antispasmodic, and cardioprotective agent. The anti-inflammatory activity of EO obtained from this plant's leaves was observed in carrageenan and experimental trauma-induced hind paw edema in rats (50). *M. officinalis* extract has also exhibited protective effects against reperfusion-induced lethal ventricular arrhythmias in rats. Moreover, lyophilized aqueous extract of *M. officinalis* leaves can be used for the treatment of benign palpitations, as heart palpitation is a common complaint that is associated with a marked distress and makes the condition difficult to treat. A study conducted in healthy volunteers treated with 500 mg lyophilized aqueous extract of *M. officinalis* leaves (or placebo) twice a day for 14 days showed reduced frequency of heart palpitation episodes (51). In another randomized, double-blind clinical trial, *M. officinalis* was found to be cardioprotective, as it is effective in improvement of lipid profile, glycemic control, and reduction of inflammation (52). Extracts of *Ocimum* species also play a significant role in cardiac functions. Ethanol extract of aerial parts of *O. basilicum* and *O. sanctum* have shown protective effect on isoproterenol-induced myocardial infarction in rats (53; 54). This cardioprotective effect of *Ocimum* species may be mediated through suppression of inflammation. The anti-inflammatory activity of *O. basilicum* EO was shown against carrageenan and different other mediator-induced paw edema in rats. It inhibited arachidonate metabolism, a mediator of inflammation, in rats (55). Methanol extract of *O. sanctum* leaves was also shown to inhibit inflammation in isoproterenol-induced myocardial infraction in rats. Pre-treatment of this extract inhibited 5-lipoxygenase, COX-2, levels of leukotriene B4 and, thromboxane B2 induced by isoproterenol in rats (56).

Origanum majorana has been used traditionally against various ailments, including cardiac disease. In isoproterenol-induced myocardial infarcted rats, sweet marjoram leaf powder and marjoram leaf aqueous extract increased the relative heart weight, alleviated myocardial oxidative stress, and the leakage of heart enzymes, such as creatine phosphokinase, lactate dehydrogenase and aminotransferase (57). *In vitro* studies revealed that

EO from oregano leaves exerts an anti-inflammatory effect on LPS-treated murine macrophage RAW264.7 cells. This EO also inhibited the expression and secretion of interleukin (IL)-1β, IL-6, and tumor necrosis factor-alpha (TNF-α) in RAW264.7 cells treated with LPS (58). Besides its EO, ethanol oregano (*Origanum vulgare*) extract also suppressed propionibacterium acnes-induced inflammation *in vivo* and *in vitro* (59). Thus, the cardioprotective effect of *Origanum* species could be due, in part, to the, anti-inflammatory properties.

Plectranthus barbatus extract has shown to reduce the production of pro-inflammatory cytokines, indicating its anti-inflammatory potential (60). Other *Plectranthus* species have also been shown to have inflammation reduction properties. In an LPS-induced rat model, *Plectranthus amboinicus* attenuated the increase in the expression of circulating proinflammatory cytokines TNF-α and IL-8 (61). Extracts of *Plectranthus zeylanicus* prepared with n-hexane or dichloromethane potently suppressed 5-lipooxygenase activity in stimulated human neutrophils (62). Although the cardioprotective effects of *Plectranthus* species are scarcely reported, this anti-inflammatory property may be a causative factor in cardioprotection. Rosemary leaves have shown anti-inflammatory effects in experimental models and are also used against various ailments. Dietary supplementation of rosemary in a rat model attenuated cardiac remodeling by improving energy metabolism. It improved diastolic function, and reduced hypertrophy after myocardial infarction (63).

Salvia hispanica, commonly known as salba, was found to reduce postprandial glycemia in healthy subjects. In an acute, randomized, double-blind, controlled study in 11 healthy individuals, bread baked with salba decreased the postprandial glycemia as well as improved blood pressure, coagulation, and decreased markers of inflammation (64). These effects of salba possibly explain its cardioprotective effects. In a rat model, dietary *S. hispanica* seeds normalized blood pressure, improved heart lipotoxicity, and glucose oxidation induced by a sucrose-rich diet (65). This cardioprotective effect of *S. hispanica* may be mediated through suppression of inflammation, since it decreased levels of inflammatory markers such as IL-6 and TNF-α, as well as xanthine oxidase activity and reactive oxygen species (ROS) contents in rats fed a sucrose-rich diet (66). *S. miltiorrhiza*, another species, also has cardioprotective efficacy. *Salvia miltiorrhiza*, in combination with other extract, attenuated myocardial ischemia/reperfusion (I/R) injury via suppression of NLRP3 inflammasome activation in C57BL6 mice. Moreover, it suppressed serum levels of IL-1β, an indicator of NLRP3 inflammasome activation after I/R injury (67). Thus, it exerts its cardioprotective effects by suppression of NLRP3 inflammasome activation in this I/R injury model.

Plant oils, including thyme, have been shown to mediate anti-inflammatory effects. It has been demonstrated that this oil provides cardioprotective benefits because of the presence of its bioactive components (68). The aqueous methanol extract of aerial parts of *Thymus linearis* benth has shown to decrease heart rate of both normotensive and hypertensive rats (69), thus indicating potential antihypertensive activity t. As *Thymus* extract suppresses inflammatory (TNF-α, IL-1β, IL-6) cytokines (70), it can be concluded that cardioprotective activity of this plant extract might be mediated through its anti-inflammatory activities. *Thymus* extract also showed significant anti-inflammatory properties by reducing nuclear factor (NF)-κB transcription factor protein levels, as well as cytokines such as IL-1β, IL-8, and Muc5ac secretion in cell culture model (71). Moreover, in an animal model, *Thymus* extracts produced 34% inhibition against carrageenan and 22% inhibition against egg albumin-induced paw edema (69). Based on these findings, it is concluded that *Thymus* extract could contribute to reduction of inflammatory responses and exhibit cardioprotective effects.

As I/R injury facilitates and accelerates apoptosis in the myocardium, its suppression by safe, natural compounds can prevent incidence of CVD. Hydro-alcoholic extract of *Teucrium polium* has shown to prevent I/R-induced apoptosis in the isolated rat heart (72). This cardioprotective effect of *T. polium* may be mediated through multiple factors including its anti-inflammatory properties. In a study, *T. polium* extract prevented inflammation induced by carrageenan (73) and LPS-induced colon inflammation (74). It also inhibited inflammatory markers TNF-α and IL-1β in colon tissue of rats (75). Ethyl acetate extract of another species of *Teucrium* has also shown to exhibit an anti-inflammatory effect by blocking both pathways of Arachidonic acid metabolites (COX-2 and lipoxygenase) (76). Extracts obtained from aerial parts of *Stachys inflata* have been used in Iranian folk medicine against rheumatic and other inflammatory disorders. Furthermore, methanol extract of *Stachys inflata* (50-200 mg/kg) inhibited carrageenan-induced paw edema and formalin-induced paw licking in an inflammatory rat model. The hydroalcoholic extract (200 mg/kg) also reduced myeloperoxidase activity, indicating its inflammatory activity (77), and such activity attenuated the infarct size following myocardial I/R (78).

Scutellaria baicalensis is a Chinese herb that has been shown to have cardioprotective effects in experimental animal models. In a study, pretreatment with *S. baicalensis* extract (30 mg/kg) for five days showed significant reduction in myocardial infarct size and a marked increase in the activity of catalase in the liver. This cardioprotective effect of *S. baicalensis* is linked to the suppression of CRP. In a study with 79 men and women diagnosed with moderate osteoarthritis, supplementation of *S. baicalensis* blend suppressed CRP along with other inflammatory markers IL-1β and –IL-6, TNF-α, and hyaluronic acid (79). In mice, it also suppressed cigarette smoke extract and LPS-induced production of TNF-α, IL-17A, macrophage inflammatory protein 2 (MIP2), and chemokine (C-X-C motif) ligand 1 (CXCL-1) in lung tissue. These studies indicate that *S. baicalensis* has inflammatory properties that facilitate its cardioprotective activities.

5. POTENTIAL MECHANISMS OF ACTIVE COMPONENTS WITH CARDIOVASCULAR EFFECT

The extracts of different parts of this Lamiaceae plant family contain varieties of bioactive compounds with cardioprotective and therapeutic properties. Some of these include Leonurine, Rosmarinic acid, Quercetin, Apigenin, Carvacrol, Thymoquinone, Baicalein, and many others (Table 1, Figure 1). These compounds exhibit cardioprotective effects through regulation of multiple molecules including transcription factors, growth factors, inflammatory molecules, enzymes, kinases, apoptotic, survival, and other molecules (Figure 2). How bioactive phytochemicals exert cardioprotection by regulating these molecules will be discussed.

Leonurine, a natural active compound of *Leonurus cardiaca*, has been shown to possess various biological activities, including against CVDs. Leonurine has shown to attenuate myocardium injury through its antioxidative and anti-apoptotic properties and acts as an adjuvant cardioprotective agent. This compound also suppresses apoptotic protein Bax and increases anti-apoptotic gene Bcl-2 to prevent acute myocardial ischemia (80; 81). Apigenin (found in *Apium graveolens* and *L. cardiaca*) has shown similar mechanisms in cardioprotection. It reduces apoptosis of cardiomyocytes by reducing caspase-3 activity, Bax protein expression, and increasing Bcl-2 protein expression. Apigenin also inhibits the phosphorylation of p38 MAPKS during myocardial I/R (82; 83). In H9c2 cardiac myocytes, leonurine increases Akt phosphorylation, expression of hypoxia inducible factor-1α (HIF-1α), survivin, and VEGF (80), which leads to suppression of cardiac cell death. It has been also reported that leonurine also alleviates collagen deposition and myocardial infarction size, inhibits cell apoptosis, and improves myocardial function. These effects of Leonurine were shown to be mediated by increased levels of phosphorylated (p)-PI3K, p-AKT, p-GSK3β and Bcl-2, as well as, decreased levels of caspase3, cleaved-caspase3 and Bax. Thus, Leonurine exerts potent cardioprotective effects by inducing anti-apoptotic effects by activating the PI3K/AKT/GSK3β signaling pathway (84).

Rosmarinic acid displays potent cardioprotective effects due to its ability to increase antioxidant enzymes and gene expression of sarcoplasmic reticulum Ca^{2+} ATPase 2 ($SERCA_2$) and ryandodine receptor-2 (RyR_2), which are involved in Ca^{2+} homeostasis (85). A recent study showed that Rosmarinic acid protects against cardiac fibrosis by activation of AMPKα, inhibition of phosphorylation, and nuclear translocation of Smad3. This compound also induces peroxisome proliferator-activated receptors (PPAR-γ) to attenuate cardiac fibrosis (86). Cardioprotection by Apigenin is also mediated by induction of PPAR-γ as its antagonist reversed the myocardial protection conferred by Apigenin (87). Further study showed that apigenin promoted PI3K/Akt/mTOR pathway and prevented adriamycin-induced cardiotoxicity in the mice (88). Quercetin, which is the component of several plants of *Lamiaceae* family, has potent cardioprotective efficacy *in vitro* and *in vivo*. It downregulates inflammatory molecules NF-κB, AP-1, and MMP-9 (89). Quercetin also inhibits MAPK, JNK, and focal adhesion kinase activities induced by thrombin in endothelial cells, and thus exhibits cardioprotective effects (90). It has also shown to act as cardioprotective agent by inducing antioxidant enzymes GSH, improving ATP, as well as reducing the elevated plasma creatine kinase, cardiac TBARS, and NO(x) contents (91 - 92).

Carvacrol, a natural bioactive compound, possess cardioprotective activities through multiple mechanisms. It has been shown to suppress myocardial ischemic damage in a rat model of acute myocardial infarction by diminishing the infarct size and myocardial enzymes including creatine kinase, lactate dehydrogenase, and cardiac troponin T. Carvacrol also reduced malondialdehyde and elevated activities of the antioxidant enzymes superoxide dismutase, glutathione, and glutathione peroxidase. Besides these, carvacrol was also shown to inhibit caspase-3 activation and Bax expression but upregulated Bcl-2 protein expression (93). Another study showed that Carvacrol upregulated phosphorylated ERK and exhibied anti-apoptotic mechanisms against myocardial I/R injury in rats. Carvacrol also increased the activation of Akt/eNOS pathway in cardiomyocytes leading to cardioprotection (82). Thus, the cardioprotective effects of carvacrol, linked to its antioxidant and antiapoptotic activities, is mediated through MAPK/ERK and Akt/eNOS signaling pathways.

Thymoquinone, the active constituent of *Thymus* species of plants, has been reported to have potential protective effects on the cardiovascular system. In a recent experiment, Thymoquinone has shown to improve cardiac function and reduce infarct size. The mechanism of the cardioprotective effect of Thymoquinone was mediated by a decrease in cardiac lactate dehydrogenase and creatine kinase levels, as well as suppression of apoptosis in myocardial I/R injury in rats (94). It has also been shown that it elevates superoxide dismutase activity and reduces production of hydrogen peroxide and malonaldehyde, thus exhibiting an antioxidative effect. In addition, Thymoquinone up-regulated expression of SIRT1 and inhibited p53 acetylation to protect from cardiac injury (86). Baicalein, an active component from *Scutellaria baicalensis* and *S. lateriflora* plants as well as other Lamiaceae family plants, exhibits cardioprotective effects via multiple molecular mechanisms. Besides its anti-inflammatory effect, it also acts as an antioxidant. It was shown to decrease MDA level and increase SOD and GSH-Px activity, as well as inhibit activation of the MAPK and NF-κB pathways in rats (95 - 96). This compound also exhibited the ability to protect cardiomyocytes against oxidative stress-induced cell injury through the Nrf2/Keap1 pathway (97). Besides these, baicalein downregulates phosphorylation of Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) and expression of Na^{+}/Ca^{2+}-exchangers (NCX1) and upregulates SERCA2 and RYR2 (98). There are several other bioactive compounds from the Lamiaceae family of plants that have cardioprotective activities. We attempted to summarize all of the cardioprotective activities of the bioactive compounds from the Lamiaceae family of plants with their mechanisms; however there are still several other components that are not covered that have similar cardioprotective properties.

6. CARDIOPROTECTIVE PROPERTIES OF LAMIACEAE FAMILY AND FOOD

Aromatic plants appear “fashionable,” since their use is able to positively affect health by reducing the amount of salt in the diet, or by presenting benefits related with their antioxidant properties (99). In fact, in addition to being recognized as a source of proteins, fibers, vitamins, and minerals, they can be considered suppliers of phytochemicals, which take action as antioxidants, antimicrobials, and/or antivirals, for example (100). Generally, the phytochemical function in the plants is to satisfy several biological activities such as seed dispersal and pollination, to serve a structural role, and act in the defense strategies of plant stress conditions such as wounding, infection, and so on (101). Some authors have also underlined their role as phytoalexins or antifeedants (102). Epidemiological studies have demonstrated that among phytochemicals, natural phenolic antioxidants such as antimicrobial, antiviral, antioxidant, anticancer, anti-inflammatory, and antiulcer factors act in preventing cardiovascular diseases. They further demonstrated that their regular intake is associated with a reduced incidence of coronary heart disease (103). It is well established that oxidative stress influences the pathogenesis of heart diseases, such as hypertension, atrial fibrillation, and atherosclerosis (104). In this perspective, phenolic action is related to reactive oxygen species by acting as reducing agents, hydrogen donors, and singlet oxygen quenchers (105).

Due to the importance of phenolic compounds in disease prevention, they were a topic of several reviews (102, 106-111). Plant phenolics include phenolics acids, flavonoids, tannins, and the less common stilbenes and lignans. Flavonoids are the most abundant polyphenols in our diets (106). Phenolics have been considered powerful antioxidants *in vitro* and proved to be more potent than Vitamin C, Vitamin E, and carotenoids. The inverse relationship between fruit and vegetable intake and the risk of oxidative stress associated diseases such as CVDs, cancer, and osteoporosis has been partially ascribed to phenolics. Polyphenols display antioxidant effects (112 - 113), as well as immunomodulatory and vasodilatory properties that may account for their effects on cardiovascular risk reduction. Indeed, dietary intakes of flavanones, anthocyanidins, and other foods rich in flavonoids were associated with reduced risk of death due to coronary heart disease and cardiovascular disease (113).

In addition, various essential oils, rich in carvacrol and a monoterpenic phenol isomeric with thymol, are recognized to be active against CVDs (114). Since these are the most representative part of EOs deriving from medical and aromatic plants, several pharmacological studies have focused on efforts to investigate the effects of this group of substances on the cardiovascular system (115). Several studies have demonstrated effects on rats. For example, in Carvacrol, approximately 65% of its composition is made up of a phenolic monoterpene cyclic isomer of the monoterpene (present in the EO of oregano), which has been reported to reduce blood pressure and heart rate, inhibit hypertension induced by L-NAME, and induce vasorelaxation (116-117). Citronellol, a monoterpene found in some plants, is used in combination with antihypertensive agents, and was found to produce hypotension and was shown to act as a vasorelaxant molecule. Limonene, one of the most common terpenes in nature and a major constituent of several citrus oils (orange, lemon, mandarin, lime, and grapefruit), is reported to contribute to the reduction and prevention of cardiovascular injuries caused by pulmonary hypertension. Furthermore, (+)-linalool and (-)-linalool can act as both a cardiovascular system stimulant and depressant (118-119). Also, thymol is reported to have a vasorelaxation effect (114).

Most of the aromatic plants belonging to the Lamiaceae family have different biological activities, which are mainly related to both the phenolic and the volatile constituents (121-123). For example, the activity of rosemary is largely due to Carnosol, Carnosic acid, and Rosmarinic acid present in the extract of rosemary; however, α Pinene, (-)-Bornyl acetate, Camphor, and Eucalyptol present in the EO of this plant also contribute to its activity (120-122). Also, minor components can have a potential influence on the biological activity due to the possibility of synergistic effect among their components (123). This aromatic plant can be added directly to the food or incorporated into the food packaging, performing as antimicrobial and antioxidant agent. In addition, rosemary EO and extract has been classified as generally recognized as safe for their intended use, within the meaning of section 409 of the Act Food and Drugs Administration (125-126) and according to the Commission Directive 2010/67/EU and Commission Directive 2010/69/EU, respectively. According to the folk medicine, the uses of rosemary have been described in two monographs, one for rosemary leaf (Rosmarini folium) and other for rosemary oil (Rosmarini aetheroleum) (126, 99). Since aromatic plants, their extracts, and their EOs are gifted of such health promoting features, their 'wise' use in food formulation could be considered as dietary strategies for disease prevention, with a particular focus on cardiovascular diseases. In fact, "nutritional therapy", using functional foods and nutraceuticals as therapeutics, is based on the assumption that food is not only a source of nutrients and energy, but can also provide health benefits. In this view, plant-based food and beverages, consumed as part of a normal diet, can offer additional health benefits beyond basic nutritional functions (127). In general, the exploitation of phenolics or EOs extracted from aromatic plants is important in food against product oxidation, color and odor stabilization, and astringency. Also, EFSA (European Food Safety Agency) has recognized most of them for use as food additives, such as flavorings or antioxidants, but claims regarding health-promoting effects for cardiovascular disease are recognized (100). On the other hand, awareness about the health benefits of nutraceuticals and plant-derived bioactive molecules for reducing the risk and incidence of CVDs is increasing among men and women. Consequently, the demand of herbal preparations rich in antioxidants and anti-inflammatory products is trending (128). Moreover, the demand for medicinal herbal products, nutraceuticals, functional foods, probiotics, and alternative therapies have increased during the past few decades (129) for the replacement of synthetic medicines for treating hypertension, hypercholesterolemia, CVD). However, Hippocrates himself, regarded as the father of medicine (ca.460-370 B.C.), advocated the healing effects of foods. He said: "Leave your drugs in the chemist's pot if you can heal the patient with food". On the other hand, Labiatae are included in the Mediterranean diet recognized in the prevention of cardiovascular diseases, including reduced mortality rate and lower weight gain (130). Thus, a holistic approach is needed for the prevention of CVDs, diabetes, and cancer. Furthermore, re-thinking food formulation (131) and food processes, and the ability to preserve the biological functions of raw ingredients, is necessary. Recently, some researchers have pointed out the necessity towards biomimetics defined as "science which takes inspirations from nature to solve problems". In this contest, biomimetic plant foods (BPFs) can offer solutions for the future with the design of nature-inspired food structures for improved health and well-being (132). In the case of tailor-made foods, designed for preventing CVDs, is very important that the bioactive compounds remain stable during product processing and shelf-life. For this, in the last decade, the use of new, emerging technologies such as high-pressure homogenization, pulsed electric fields, gas-plasma, and other non-thermal technologies were proposed to overcome the nutritional content loss due to the use of severe thermal treatments (132-134).

7. POTENTIAL USE OF LAMIACEAE PRODUCT IN THERAPY

The World Health Organization (WHO) suggests that plants belonging to *Lamiaceae* family, (134) characterized by a long history of use and having therapeutic effects, should also be evaluated for new activities and properties that could be useful in treatment and prevention of different diseases (134). Plants from this family are well known for their antibacterial, antifungal, antioxidant, anticancer (135), and antiviral properties (134). Their exploitation in therapy may be due to the presence of a wide range of bioactive compounds, such as antioxidants and especially, polyphenols (27). According to Bekut *et al.*, (134), the antiviral effects of *Lamiaceae* plants have mainly been shown *in vitro*; however, some effects also have been observed in some trials in healthy volunteers, or inpatients. The EOs, extracts, or other parts of *Lamiaceae* plants have been tested also against CVDs such as hypertension, which is one of the major health concerns in various parts of the world. Arterial hypertension is a chronic medical condition in which the pressure in the arteries exceeds 140/90 mmHg. The incidences of uncontrolled hypertension occur mainly among individuals above 50 years of age (136). High blood pressure can also be affected indirectly by other conditions such as insulin resistance, obesity, kidney failure, nervous system, concomitance, and atherosclerosis (138; 139). Hypertension is estimated to cause 4.5% of the disease burden globally (140 - 141). Generally, biofeedback, relaxation, weight reduction, exercise, drug treatment, smoking cessation, and dietary modifications, (e.g., reduced salt intake and avoidance of excessive alcohol use) are the non-pharmacological methods used, for mid-hypertension (141 - 142). However, alternative herbal medicines are often preferred over modern medicines. A study showed that 25% of modern drugs and 75% of new medicines against virulent diseases are obtained from natural plant resources (143). According to the WHO, about 80% of people rely on traditional medicines (144). A recent study performed by Yang *et al.*, (145) investigated the therapeutic efficacy of *Salvia przewalskii* total phenolic acid extract (SPE) on immune complex glomerulonephritis (ICG) in rats, concluding that SPE could reduce whole blood viscosity and increase the urine excretion of water. Moreover, they demonstrated that SPE could reduce proteinuria, regulate protein and lipid metabolisms, attenuate renal inflammatory cell infiltration, and delay the progression of glomerular lesions in a rat ICG model, providing evidence that SPE has the potential to become a therapeutic drug for glomerulonephritis.

Also, *Rosmarinus officinalis*, a rich source of phenolic phytochemicals exhibiting significant antioxidant, anti-inflammatory, hypoglycemic, hypolipidemic, hypotensive, anti-atherosclerotic, anti-thrombotic, hepatoprotective, and hypocholesterolemic effects, was proposed, due to the interesting pharmacological effects, in the management of metabolic syndrome, defined by a constellation of complex coexisting cardiometabolic risk factors (146).

A study performed by Mihailovic-Stanojevic *et al.* (147) evaluated total phenol and flavonoid contents, antioxidant capacity, free radical scavenging activity, and potential antihypertensive effects of aqueous extract obtained from *Thymus serpyllum* (wild thyme, TE, highly present in Mediterranean diet), in spontaneously hypertensive rats (SHR) and in normotensive Wistar rats. The TE extract, having total phenol content of 2008.33 ± 10.6 mg/L GAE, rosmarinic, and caffeic acids as predominant phenolic compounds, was able to protect against hypertension in experimental model.

A recent study gave an overview about traditional medicinal knowledge of plants as antihypertensive drugs (148). One hundred nighty-two medicinal plant species, belonging to 77 families, were reported to treat hypertension. It was first attempted to document ethno-botanical information using quantitative approaches on hypertension in the study area. The leaves were reported to be the most used plant part (55.1%) while herbs were the most used form (54%). Decoction was reported to be the most common mode of administration (72 reports). The quantitative approaches, such as Family Importance Value (FIV), Relative Frequency of Citation (RFC), and Disease Consensus index (DCI) were used to assess the importance of traditional knowledge obtained in the study. Highest DCI and FIV values were reported for Rutaceae and Lamiaceae. Meanwhile, there are so many of these naturally occurring plant substances covering a wide range that offer a good opportunity of delivering useful medicinal complexes for the management of hypertension. According to this study, *Ficus palmata*, *Senna tora*, *Teucrium polium*, *Valeriana officinalis*, and *Ziziphus mauritiana* were recorded for the first time as anti-hypertensive medicinal drugs. The study performed by Malik *et al.*, (148), provides basic leads for future pharmacological and phytochemical investigation to explore the potential of such plants in herbal drug discovery. Of course, it is thus recommended that strategies for cultivation and conservation of important species be designed. However, some researchers have pointed out the need to build a database platform to discuss the risks and benefits of herbal medicine use with the aim of enhancing their patients' health outcome (149). In fact, according to a study performed in Sierra Leone by James *et al.*, (149), garlic and lemon grass are the most common herbal medicines used among users against hypertension and cardiovascular disease. However, their use, not dependent to the patient's socio-demographic and health factors, is still related to popular traditions. In this perspective, a recent study tried to predict several plant utilities for cardiovascular disease relating the plant phylogeny and its potential as sources of new cardiovascular drugs. In particular, analyzing 139 plant species in 71 plant families, they found 7 plant families (Apiaceae, Brassicaceae, Fabaceae, Lamiaceae, Malvaceae, Rosaceae, and Zingiberaceae) with 45 species which emerged as phylogenetically important exhibiting common cardiovascular mechanisms of action within the family. Particularly, Lamiaceae (*Lavandula stoechas*, *Mentha suaveolens*, *Rosmarinus officinalis*, *Scutellaria baicalensis*, *Salvia miltiorrhiza*) had anticoagulant/thrombolytic effects and they were found to possess anti-atherosclerotic properties.

In other studies, Ferreira *et al.* (151), reported cases on *Salvia hispanica*, commonly known as Chia and belonging to the Lamiaceae family, outlined the need for randomized, double-blind, placebo-controlled clinical trials in order to obtain reliable results to compare with traditional medicine.

According to the recent literature, complementary medicine is higher in women than in men (152). Although a majority of herbal medicines have been traditionally considered beneficial, their use deserves more attention, not only for the increasing trend of their use and the imposed expense on patients, but also for their potential harmful and unknown effects. Some risks, such as herbal medicines interference with other drugs and their incongruity with physiologic status, require physicians to ask their patients about consuming these products, and they should also increase their knowledge of herbal medicines. So, the literature reports emphasize on the necessity of implementing effective training programs to improve knowledge of health providers regarding the consumption, adverse effects, and drug interferences of common herbal medicines and also consider the history of taking herbal medicines at the time of patient visits. In fact, although the plants generally have many potential beneficial effects, they also have potential to cause interactions with antiretroviral and other drugs, resulting in a drastic increase or decrease of drug concentrations.

8. CONCLUSION

Therapeutic effects of Lamiaceae on prevention and regulation of blood pressure and heart failure through antioxidant, anti-inflammatory, hypotensive, anti-atherosclerosis, heart rate-regulating, and vasodilating properties are known in ethnomedicine and nowadays in conventional medicine as well. With increasing interest in herbs as anti-inflammatory agents in the management of chronic inflammation connected to CVDs, research is emerging on the use herbs in foods. Therefore, the use of Lamiaceae as modulators of physiological responses and biological pathways should be extensively studied both *in vitro* studies and in animal trials. Moreover, additional studies regarding the improvement of the delivery of proven active compounds need to be performed. The study of Lamiaceae natural compounds can be a source of inspiration for developing novel or enhanced molecules acting against CVDs. Wide compound diversity present in Lamiaceae species are precious natural resources for inexpensive and safe approaches for cardioprotection. However, synergistic effects of herbs and interaction with commercial drugs need to be thoroughly investigated for future pharmaceutical development of herbal drugs. In addition, it is important to highlight that legal surveillance of herbal-drug interactions should be instituted at a global level.

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10. REFERENCES

1. B Baharvand-Ahmadi; M Bahmani; A Zargaran. A brief report of Rhazes manuscripts in the field of cardiology and cardiovascular diseases. Int J Cardiol, 207, 190-191 (2016)
DOI: 10.1016/j.ijcard.2016.01.021

2. S Suroowan; F Mahomoodally. Common phyto-remedies used against cardio-vascular diseases and their potential to induce adverse events in cardiovascular patients. Clin Phytoscience 1, 1 (2015)

DOI: 10.1186/s40816-015-0002-3

3. GB Mahady. Medicinal plants for the prevention and treatment of coronary heart disease

4. P Cos; AJ Vlietinck; D Vanden Berghe; L Maes. Anti-infective potential of natural products: How to develop a stronger *in vitro* "proof-of-concept." J Ethno-pharmacol, 106, 290-302 (2006)
DOI: 10.1016/j.jep.2006.04.003

5. M Khoury; D Stien; V Eparvier; N Ouaini; M El Beyrouthy. Report on the medicinal use of eleven Lamiaceae species in Lebanon and rationalization of their antimicrobial potential by examination of the chemical composition and antimicrobial activity of their essential oils. Evidence-based Complement Altern Med, (2016)
DOI: 10.1155/2016/2547169

6. JD Adams; M Wall; C Garcia. Salvia columbariae contains tanshinones. Evidence-based Complement Altern Med, 2, 107-110 (2005)
DOI: 10.1093/ecam/neh067

7. RH Alasbahi; MF Melzig. Plectranthus barbatus: A review of phytochemistry, ethnobotanical uses and pharmacology part 1. Planta Med, 76, 653-661 (2010)
DOI: 10.1055/s-0029-1240898

8. S Gul; H Gul; R Nawaz. Possible Mechanism of Action of Mentha arvensis in. 2, 5-10 (2014)

9. M Ziaee; A Khorrami; M Ebrahimi; H Nourafcan; M Amiraslanzadeh; M Rameshrad; M Garjani; A Garjani. Cardioprotective effects of essential oil of Lavandula angustifolia on isoproterenol-induced acute myocardial infarction in rat. Iran J Pharm Res, 14, 279-289 (2015)
DOI: 10.1109/AINA.2013.98

10. F Chen; L Li; DD Tian. Salvia miltiorrhiza roots against cardiovascular disease: Consideration of herb-drug interactions. Biomed Res Int, (2017)
DOI: 10.1155/2017/9868694

11. JD Adams; R Wang; J Yang; EJ Lien. Preclinical and clinical examinations of Salvia miltiorrhiza and its tanshinones in ischemic conditions. Chin Med, 1, 1-15 (2006)
DOI: 10.1186/1749-8546-1-3

12. C Veeresham. Natural products derived from plants as a source of drugs. J Adv Pharm Technol Res, 3, 200 (2012)
DOI: 10.4103/2231-4040.104709

13. C Liu; Y Huang. Chinese Herbal Medicine on Cardiovascular Diseases and the Mechanisms of Action. Front Pharmacol, 7 (2016)
DOI: 10.3389/fphar.2016.00469

14. F Kousar; N Jahan; S Nosheen. Cardioprotective Potential of Coriandrum sativum. Plant Sci J, 1, 1-6, (2012)

15. EM El-sayed; ASA El-azeem; AA Afify; MH Shabana; HH Ahmed. Cardio-protective effects of Curcuma longa L . extracts against doxorubicin-induced cardiotoxicity in rats. J Med Plants Res, Vol. 5(17), 5, 4049-4058 (2011)

16. I Factor; M Shah; G Shahu; AK Tamrakar; S Malshetthy; S Janadri. Cardiotoxic Activity of Leaves Extract of Raphanus sativus Linn . in Adult Male Albino Rats. Int J Pharm Phytopharmacol Res, (eIJPPR) (2014)

17. K Carovic-Stanko; M Petek; M Grdiša; J

Pintar; D Bedekovic; M Herak Custic; Z Satovic. Medicinal plants of the family Lamiaceae as functional foods - a review. Czech J Food Sci 34, 377-390 (2016)
DOI: 10.17221/504/2015-CJFS

18. S Saljoughian; S Roohinejad; AEDA Bekhit; R Greiner; A Omidizadeh; N Nikmaram; A Mousavi Khaneghah. The effects of food essential oils on cardiovascular diseases: A review. Crit Rev Food Sci Nutr, 58, 1688-1705 (2018)
DOI: 10.1080/10408398.2017.1279121

19. OC Aworh. From lesser-known to super vegetables: the growing profile of African traditional leafy vegetables in promoting food security and wellness, J Sci Food Agricul, (2018)
DOI: 10.1002/jsfa.8902

20. MHH Roby; MA Sarhan; KAH Selim; KI Khalel. Evaluation of antioxidant activity, total phenols and phenolic compounds in thyme (Thymus vulgaris L.), sage (Salvia officinalis L.), and marjoram (Origanum majorana L.) extracts. Ind Crops Prod, (2013)
DOI: 10.1016/j.indcrop.2012.08.029

21. N Mimica-Dukic; B Bozin; M Sokovic; N Simin. Antimicrobial and Antioxidant Activities of Melissa officinalis L. (Lamiaceae) Essential Oil. J Agric Food Chem, (2004)
DOI: 10.1021/jf030698a

22. ŠS Herodež; M Hadolin; M Škerget; Ž Knez. Solvent extraction study of antioxidants from Balm (Melissa officinalis L.) leaves. Food Chem, (2003)
DOI: 10.1016/S0308-8146(02)00382-5

23. H Sadraei; A Ghannadi; K Malekshahi. Relaxant effect of essential oil of Melissa officinalis and citral on rat ileum contractions. Fitoterapia (2003)
DOI: 10.1016/S0367-326X(03)00109-6

24. R Singh; MAM Shushni; A Belkheir. Antibacterial and antioxidant activities of Mentha piperita L. Arab J Chem, (2015)
DOI: 10.1016/j.arabjc.2011.01.019

25. YC Chung; FC Hsieh; YJ Lin; TY Wu; CW Lin; CT Lin; NY Tang; TR Jinn. Magnesium lithospermate B and rosmarinic acid, two compounds present in Salvia miltiorrhiza, have potent antiviral activity against enterovirus 71 infections. Eur J Pharmacol, (2015)
DOI: 10.1016/j.ejphar.2015.02.046

26. C Queffélec; F Bailly; G Mbemba; JF Mouscadet; S Hayes; Z Debyser; M Witvrouw; P Cotelle. Synthesis and antiviral properties of some polyphenols related to Salvia genus. Bioorganic Med Chem Lett, (2008)
DOI: 10.1016/j.bmcl.2008.06.063

27. K Tzima; N Brunton; D Rai. Qualitative and Quantitative Analysis of Polyphenols in Lamiaceae Plants-A Review. Plants 7, 25 (2018)
DOI: 10.1016/0002-9610(47)90150-5

28. R Hamidpour; S Hamidpour; M Hamidpour; M Shahlari; M Sohraby. Summer Savory: From the Selection of Traditional Applications to the Novel Effect in Relief, Prevention, and Treatment of a Number of Serious Illnesses such as Diabetes, Cardiovascular Disease, Alzheimer's Disease, and Cancer. J Tradit Complement Med, 4, 140-144 (2014)
DOI: 10.4103/2225-4110.136540

29. R Yazdanparast; L Shahriyary. Comparative effects of Artemisia dracunculus, Satureja hortensis and

Origanum majorana on inhibition of blood platelet adhesion, aggregation and secretion. Vascul Pharmacol, 48, 32-37 (2008)
DOI: 10.1016/j.vph.2007.11.003

30. N Mamadalieva; D Akramov; E Ovidi; A Tiezzi; L Nahar; S Azimova; S Sarker. Aromatic Medicinal Plants of the Lamiaceae Family from Uzbekistan: Ethnopharmacology, Essential Oils Composition, and Biological Activities. Medicines 4, 8 (2017)
DOI: 10.3390/medicines4010008

31. M Koshma; VJS Reddy; TN Aditya; S Jilani; YS Rani; P Swaroopa; KP College; C Nagar. Review Article. Int Res J Pharm, 4-11 (2017)
DOI: 10.7897/2230-8407.0812244

32. M Jagtap; BK Ashok; SS Chavan; HM Chandola; B Ravishankar. A comparative evaluation of cardioprotective activity of two Makandi (Coleus forskohlii Willd.) formulations against isoproterenol induced myocardial infarction in hyperlipidaemic rats. Indian J Nat Prod Resour, 2, 335-344 (2011)

33. N Mnonopi; RA Levendal; MT Davies-Coleman; CL Frost. The cardioprotective effects of marrubiin, a diterpenoid found in Leonotis leonurus extracts. J Ethnopharmacol, 138, 67-75 (2011)
DOI: 10.1016/j.jep.2011.08.041

34. F Sheikhbahaei; M Khazaei; SN Nematollahi-Mahani. Teucrium polium extract enhances the anti-angiogenesis effect of tranilast on human umbilical vein endothelial cells. Adv Pharm Bull, 8, 131-139 (2018)
DOI: 10.15171/apb.2018.016

35. T Farkhondeh; S Samarghandian; A Borji. An overview on cardioprotective and anti-diabetic effects of thymoquinone. Asian Pac J Trop Med, 10, 849-854 (2017)
DOI: 10.1016/j.apjtm.2017.08.020

36. MK Singh; B Gidwani; A Gupta; H Dhongade; CD Kaur; PP Kashyap; DK Tripathi. A review of the medicinal plants of genus Orthosiphon (Lamiaceae). Int J Biol Chem, 9, 318-331 (2015)
DOI: 10.3923/ijbc.2015.318.331

37. JT Willerson. Inflammation as a Cardiovascular Risk Factor. Circulation 109, II-2-II-10 (2004)
DOI: 10.1161/01.CIR.0000129-535.04194.38

38. ETH Yeh; JT Willerson. Coming of age of C-reactive protein: Using inflammation markers in cardiology. Circulation 107, 370-372 (2003)
DOI: 10.1161/01.CIR.0000053-731.05365.5A

39. J El-Hilaly; B Lyoussi; M Wibo; N Morel. Vasorelaxant effect of the aqueous extract of Ajuga iva in rat aorta. J Ethnopharmacol, 93, 69-74 (2004)
DOI: 10.1016/j.jep.2004.03.020

40. SS Kulabas; H Ipek; AR Tufekci; S Arslan; I Demirtas; R Ekren; U Sezerman; TB Tumer. Ameliorative potential of Lavandula stoechas in metabolic syndrome via multitarget interactions. J Ethnopharmacol, 223, 88-98 (2018)
DOI: 10.1016/j.jep.2018.04.043

41. W K.; S M.; M I. Leonurus cardiaca L. (Motherwort): A review of its phytochemistry and pharmacology. Phytother Res, 27, 1115-1120 (2013)

42. B Sadowska; B Micota; M Rozalski; M

Redzynia; M Rozalski. The immunomodulatory potential of Leonurus cardiaca extract in relation to endothelial cells and platelets. Innate Immun, 23, 285-295 (2017)
DOI: 10.1177/1753425917691116

43. K Yousefi; H Soraya; F Fathiazad; A Khorrami; S Hamedeyazdan; N Maleki-Dizaji; A Garjani. Cardioprotective effect of methanolic extract of Marrubium vulgare L. on isoproterenol-induced acute myocardial infarction in rats. Indian J Exp Biol, 51, 653-660 (2013)

44. A Garjani; D Tila; S Hamedeyazdan; H Vaez; M Rameshrad; M Pashaii; F Fathiazad. An investigation on cardioprotective potential of Marrubium vulgare aqueous fraction against ischaemia-reperfusion injury in isolated rat heart. Folia Morphol, (Poland) 76, 361-371 (2017)
DOI: 10.5603/FM.a2017.0011

45. SF Zaidi; JS Muhammad; S Shahryar; K Usmanghani; AH Gilani; W Jafri; T Sugiyama. Anti-inflammatory and cytoprotective effects of selected Pakistani medicinal plants in Helicobacter pylori-infected gastric epithelial cells. J Ethnopharmacol, 141, 403-410 (2012)
DOI: 10.1016/j.jep.2012.03.001

46. AH Atta; A Alkofahi. Anti-nociceptive and anti-inflammatory effects of some Jordanian medicinal plant extracts. J Ethnopharmacol, 60, 117-124 (1998)
DOI: 10.1016/S0378-8741(97)00137-2

47. M Modarresi; MR Farahpour; B Baradaran. Topical application of Mentha piperita essential oil accelerates wound healing in infected mice model. Inflammopharmacology 2, 1-7 (2018)
DOI: 10.1007/s10787-018-0510-0

48. B R.M.; B D.; B P.; K A.; S J.; K V. Pharmacological action of Mentha piperita on lipid profile in fructose-fed rats. Iran J Pharm Res, 10, 843-848 (2011)

49. F Brahmi; T Nury; M Debbabi; S Hadj-Ahmed; A Zarrouk; M Prost; K Madani; L Boulekbache-Makhlouf; G Lizard. Evaluation of Antioxidant, Anti-Inflammatory and Cytoprotective Properties of Ethanolic Mint Extracts from Algeria on 7-Ketocholesterol-Treated Murine RAW 264.7 Macrophages. Antioxidants 7, 184 (2018)
DOI: 10.3390/antiox7120184

50. A Bounihi; G Hajjaj; R Alnamer; Y Cherrah; A Zellou. *In vivo* potential anti-Inflammatory activity of Melissa officinalis L . essential oil. Adv Pharmacol Sci, (2013)
DOI: 10.1155/2013/101759

51. F Alijaniha; M Naseri; S Afsharypuor; F Fallahi; A Noorbala; M Mosaddegh; S Faghihzadeh; S Sadrai. Heart palpitation relief with Melissa officinalis leaf extract: Double blind, randomized, placebo controlled trial of efficacy and safety. J Ethnopharmacol, 164, 378-384 (2015)
DOI: 10.1016/j.jep.2015.02.007

52. A Asadi; F shidfar; M Safari; M Malek; AF Hosseini; S Rezazadeh; A Rajab; S Shidfar; S Hosseini. Safety and efficacy of Melissa officinalis (lemon balm) on ApoA-I, Apo B, lipid ratio and ICAM-1 in type 2 diabetes patients: A randomized, double-blinded clinical trial. Complement Ther Med, 40, 83-88 (2018)
DOI: 10.1016/j.ctim.2018.07.015

53. F Fathiazad; A Matlobi; A Khorrami; S

Hamedeyazdan; H Soraya; M Hammami; N Maleki-Dizaji; A Garjani. Phyto-chemical screening and evaluation of cardioprotective activity of ethanolic extract of Ocimum basilicum L. (basil) against isoproterenol induced myocardial infarction in rats. DARU, J Pharm Sci, 20, 1 (2012)
DOI: 10.1186/2008-2231-20-87

54. M Sharma; SK Gupta; K Kishore; DS Arya. Cardioprotective potential of Withania sominifera in isoproterenol induced myocardial infaction in rats. J Mol Cell Cardiol, 33, A110 (2001)
DOI: 10.1152/ajprenal.00141.2013

55. S Singh. Mechanism of action of antiinflammatory effect of fixed oil of Ocimum basilicum Linn. Indian J Exp Biol, 37, 248-252 (1999)

56. S Kavitha; F John; M Indira. Amelioration of inflammation by phenolic rich methanolic extract of Ocimum sanctum Linn. leaves in isoproterenol induced myocardial infarction. Indian J Exp Biol, 53, 632-40 (2015)

57. G Ramadan; NM El-Beih; NMS Arafa; MM Zahra. Preventive effects of egyptian sweet marjoram (Origanum majorana L.) leaves on haematological changes and cardiotoxicity in isoproterenol-treated albino rats. Cardiovasc Toxicol, 13, 100-109 (2013)
DOI: 10.1007/s12012-012-9189-4

58. C Cheng; Y Zou; J Peng. Oregano essential oil attenuates raw264.7 cells from lipopolysaccharide-induced inflammatory response through regulating nadph oxidase activation-driven oxidative stress. Molecules 23, 1-12 (2018)
DOI: 10.3390/molecules23081857

59. L Te Chuang; TH Tsai; TJ Lien; WC Huang; JJ Liu; H Chang; ML Chang; PJ Tsai. Ethanolic extract of origanum vulgare suppresses propionibacterium acnes-induced inflammatory responses in human monocyte and mouse ear edema models. Molecules 23, 1-11 (2018)
DOI: 10.3390/molecules23081987

60. P Kapewangolo; AA Hussein; D Meyer. Inhibition of HIV-1 enzymes, antioxidant and anti-inflammatory activities of Plectranthus barbatus. J Ethno-pharmacol, 149, 184-190 (2013)
DOI: 10.1016/j.jep.2013.06.019

61. DB Akinbo; AA Onyeaghala; JO Emomidue; SO Ogbhemhe; HC Okpoli. Phytochemical and anti-inflammatory activities of aqueous leaf extract of Indian borage (oregano) on rats induced with inflammation. Cancer Biomarkers, 22, 257-265 (2018)
DOI: 10.3233/CBM-170893

62. M Napagoda; J Gerstmeier; S Wesely; S Popella; S Lorenz; K Scheubert; A Svatoš; O Werz. Inhibition of 5-lipoxygenase as anti-inflammatory mode of action of Plectranthus zeylanicus Benth and chemical characterization of ingredients by a mass spectrometric approach. J Ethnopharmacol, 151, 800-809 (2014)
DOI: 10.1016/j.jep.2013.11.004

63. BP Murino Rafacho; PP Dos Santos; ADF Gonçalves; AAH Fernandes; K Okoshi; F Chiuso-Minicucci; PS Azevedo; LAM Zornoff; MF Minicucci; XD Wang; SA Rupp De Paiva. Rosemary supplementation (Rosmarinus oficinallis L.) attenuates cardiac remodeling after myocardial infarction in rats. PLoS ONE

12, 1-17 (2017)
DOI: 10.1371/journal.pone.0177521

64. V Vuksan; AL Jenkins; AG Dias; AS Lee; E Jovanovski; AL Rogovik; A Hanna. Reduction in postprandial glucose excursion and prolongation of satiety: Possible explanation of the long-term effects of whole grain Salba (Salvia hispanica L.). Eur J Clin Nutr, 64, 436-438 (2010)
DOI: 10.1038/ejcn.2009.159

65. A Creus; M Ferreira; M Oliva; Y Lombardo. Mechanisms Involved in the Improvement of Lipotoxicity and Impaired Lipid Metabolism by Dietary a-Linolenic Acid Rich Salvia hispanica L (Salba) Seed in the Heart of Dyslipemic Insulin-Resistant Rats. J Clin Med, 5, 18 (2016)
DOI: 10.3390/jcm5020018

66. MR Ferreira; SM Alvarez; P Illesca; MS Giménez; YB Lombardo. Dietary Salba (Salvia hispanica L.) ameliorates the adipose tissue dysfunction of dyslipemic insulin-resistant rats through mechanisms involving oxidative stress, inflammatory cytokines and peroxisome proliferator-activated receptor ?. Eur J Nutr, 57, 83-94 (2018)
DOI: 10.1007/s00394-016-1299-5

67. Y Wang; X Yan; S Mi; Z Li; Y Wang; H Zhu; X Sun; B Zhao; C Zhao; Y Zou; K Hu; X Ding; A Sun; J Ge. Naoxintong attenuates Ischaemia/reperfusion Injury through inhibiting NLRP3 inflammasome activation. J Cell Mol Med, 21, 4-12 (2017)
DOI: 10.1111/jcmm.12915

68. CE Smith. Plant Oils and Cardiometabolic Risk Factors: The Role of Genetics. Curr Nutr Rep, 1, 161-168 (2012)
DOI: 10.1007/s13668-012-0018-y

69. Alamgeer; MS Akhtar; Q Jabeen; HU Khan; S Maheen; Haroon-Ur-Rashid; K Sabeha; S Rasool; MNH Malik; K Khan; MN Mushtaq; F Latif; N Tabassum; AQ Khan; H Ahsan; W Khan. Pharmacological evaluation of antihypertensive effect of aerial parts of Thymus linearis Benth. Acta Pol Pharm - Drug Res, 71, 677-682 (2014)

70. ME Cam; AN Hazar-Yavuz; S Yildiz; B Ertas; B Ayaz Adakul; T Taskin; S Alan; L Kabasakal. The methanolic extract of Thymus praecox subsp. skorpilii var. skorpilii restores glucose homeostasis, ameliorates insulin resistance and improves pancreatic ß-cell function on streptozotocin/nicotinamide-induced type 2 diabetic rats. J Ethnopharmacol, 231, 29-38 (2019)
DOI: 10.1016/j.jep.2018.10.028

71. M Oliviero; I Romilde; MM Beatrice; V Matteo; N Giovanna; A Consuelo; C Claudio; S Giorgio; F Maggi; N Massimo. Evaluations of thyme extract effects in human normal bronchial and tracheal epithelial cell lines and in human lung cancer cell line. Chem Biol Interact, 256, 125-133 (2016)
DOI: 10.1016/j.cbi.2016.06.024

72. M Mahmoudabady; FS Talebian; NA Zabihi; A Rezaee; S Niazmand. Teucrium polium L . Improved Heart Function and Inhibited Myocardial Apoptosis in Isolated Rat Heart Following Ischemia-Reperfusion Injury. 159-167 (2018)

73. F Rahmouni; L Hamdaoui; T Rebai. *In vivo* anti-inflammatory activity of aqueous extract of Teucrium polium against

carrageenan-induced inflammation in experimental models. Arch Physiol Biochem, 123, 313-321 (2017)
DOI: 10.1080/13813455.2017.1333517

74. G F.; T A.K.; P S.; L A. Terpenes from essential oils and hydrolate of Teucrium alopecurus triggered apoptotic events dependent on caspases activation and PARP cleavage in human colon cancer cells through decreased protein expressions. Oncotarget 9, 32305-32320 (2018)
DOI: 10.18632/oncotarget.25955

75. AH Abdolghaffari; A Baghaei; F Moayer; H Esmaily; M Baeeri; HR Monsef-Esfahani; R Hajiaghaee; M Abdollahi. On the benefit of Teucrium in murine colitis through improvement of toxic inflammatory mediators. Hum Exp Toxicol, 29, 287-295 (2010)
DOI: 10.1177/0960327110361754

76. SM Mukarram Shah. A possible anti-inflammatory mechanism of ethyl acetate extracts of Teucrium stocksianum Bioss. BMC Complementary and Alternative Medicine 15, 1-6 (2015)
DOI: 10.1186/s12906-015-0834-x

77. N Maleki; A Garjani; H Nazemiyeh; N Nilfouroushan; AT Eftekhar Sadat; Z Allameh; N Hasannia. Potent anti-inflammatory activities of hydroalcoholic extract from aerial parts of Stachys inflata on rats. J Ethnopharmacol, 75, 213-218 (2001)
DOI: 10.1016/S0378-8741(01)00194-5

78. A Garjani; N Maleki; H Nazemiyeh. Effects of hydroalcoholic extract from aerial parts of the sterile stems of Stachys inflata on myocardial infarct size in rats. 165-170 (2004)

79. BH Arjmandi; LT Ormsbee; ML Elam; SC Campbell; N Rahnama; ME Payton; K Brummel-Smith; BP Daggy. A Combination of Scutellaria Baicalensis and Acacia Catechu Extracts for Short-Term Symptomatic Relief of Joint Discomfort Associated with Osteoarthritis of the Knee. J Med Food, 17, 707-713 (2014)
DOI: 10.1089/jmf.2013.0010

80. X Liu; L Pan; Q Gong; Y Zhu. Leonurine (SCM-198) improves cardiac recovery in rat during chronic infarction. Eur J Pharmacol, 649, 236-241 (2010)
DOI: 10.1016/j.ejphar.2010.08.056

81. XH Liu; PF Chen; LL Pan; R De Silva; YZ Zhu. 4-Guanidino-n-butyl syringate (Leonurine, SCM 198) protects H9c2 rat ventricular cells from hypoxia-induced apoptosis. J Cardiovasc Pharmacol, 54, 437-444 (2009)
DOI: 10.1097/FJC.0b013e3181bae160

82. Y Chen; L Ba; W Huang; Y Liu; H Pan; E Mingyao; P Shi; Y Wang; S Li; H Qi; H Sun; Y Cao. Role of carvacrol in cardioprotection against myocardial ischemia/reperfusion injury in rats through activation of MAPK/ERK and Akt/eNOS signaling pathways. Eur J Pharmacol, 796, 90-100 (2017)
DOI: 10.1016/j.ejphar.2016.11.053

83. J Hu; Z Li; L ting Xu; A jun Sun; X yan Fu; L Zhang; L lin Jing; A dong Lu; Y fei Dong; Z ping Jia. Protective effect of Apigenin on ischemia/reperfusion injury of the isolated rat heart. Cardiovasc Toxicol, 15, 241-249 (2015)
DOI: 10.1007/s12012-014-9290-y

84. L Xu; X Jiang; F Wei; H Zhu. Leonurine protects cardiac function following acute myocardial infarction through anti-

apoptosis by the PI3K/AKT/GSK3ß signaling pathway. Mol Med Rep, 18, 1582-1590 (2018)
DOI: 10.3892/mmr.2018.9084

85. S Javidanpour; M Dianat; M Badavi; SA Mard. The cardioprotective effect of rosmarinic acid on acute myocardial infarction and genes involved in Ca2+homeostasis. Free Radic Res, (2017)
DOI: 10.1080/10715762.2017.1390227

86. Y Lu; Y Feng; D Liu; Z Zhang; K Gao; W Zhang; H Tang. Thymoquinone attenuates myocardial ischemia/re-perfusion injury through activation of SIRT1 signaling. Cell Physiol Biochem, 47, 1193-1206 (2018)
DOI: 10.1159/000490216

87. UB Mahajan; G Chandrayan; CR Patil; DS Arya; K Suchal; YO Agrawal; S Ojha; SN Goyal. The protective effect of apigenin on myocardial injury in diabetic rats mediating activation of the PPAR-? pathway. Int J Mol Sci, 18 (2017)
DOI: 10.3390/ijms18040756

88. W Yu; H Sun; W Zha; W Cui; L Xu; Q Min; J Wu. Apigenin Attenuates Adriamycin-Induced Cardiomyocyte Apoptosis via the PI3K / AKT / mTOR Pathway. 2017 (2017)

89. SK Moon; GO Cho; SY Jung; SW Gal; TK Kwon; YC Lee; NR Madamanchi; CH Kim. Quercetin exerts multiple inhibitory effects on vascular smooth muscle cells: Role of ERK1/2, cell-cycle regulation, and matrix metalloproteinase-9. Biochem Biophys Res Commun, 301, 1069-1078 (2003)
DOI: 10.1016/S0006-291X(03)00091-3

90. NC Kaneider; B Mosheimer; N Reinisch; JR Patsch; CJ Wiedermann. Inhibition of thrombin-induced signaling by resveratrol and quercetin: Effects on adenosine nucleotide metabolism in endothelial cells and platelet-neutrophil interactions. Thromb Res, 114, 185-194 (2004)
DOI: 10.1016/j.thromres.2004.06.020

91. I Chis; D Baltaru; A Dumitrovici; A Coseriu; B Radu; R Moldovan; A Muresan. Protective effects of quercetin from oxidative/nitrosative stress under intermittent hypobaric hypoxia exposure in the rat's heart. Physiol Int, 105, 233-246 (2018)
DOI: 10.1556/2060.105.2018.3.2.3

92. LA Ahmed; HA Salem; AS Attia; ME El-Sayed. Enhancement of amlodipine cardioprotection by quercetin in ischaemia/reperfusion injury in rats. J Pharm Pharmacol, 61, 1233-1241 (2009)
DOI: 10.1211/jpp/61.09.0014

93. W Yu; Q Liu; S Zhu. Carvacrol protects against acute myocardial infarction of rats via anti-oxidative and anti-apoptotic Pathways. Biol Pharm Bull, 36, 579-584 (2013)
DOI: 10.1248/bpb.b12-00948

94. J Xiao; ZP Ke; Y Shi; Q Zeng; Z Cao. The cardioprotective effect of thymoquinone on ischemia-reperfusion injury in isolated rat heart via regulation of apoptosis and autophagy. J Cell Biochem, 119, 7212-7217 (2018)
DOI: 10.1002/jcb.26878

95. R Shi; Z Wei; D Zhu; N Fu; C Wang; S Yin; Y Liang; J Xing; X Wang; Y Wang. Baicalein attenuates monocrotaline-induced pulmonary arterial hypertension by inhibiting vascular remodeling in rats. Pulm Pharmacol Ther, 48, 124-135 (2018)

DOI: 10.1016/j.pupt.2017.11.003

96. M Kumar; ER Kasala; LN Bodduluru; V Dahiya; M Lahkar. Baicalein protects isoproterenol induced myocardial ischemic injury in male Wistar rats by mitigating oxidative stress and inflammation. Inflamm Res, 65, 613-622 (2016)
DOI: 10.1007/s00011-016-0944-z

97. G Cui; S Chui Wah Luk; RA Li; KKK Chan; SW Lei; L Wang; H Shen; GPH Leung; SMY Lee. Cytoprotection of baicalein against oxidative stress-induced cardiomyocytes injury through the Nrf2/Keap1 pathway. J Cardiovasc Pharmacol, 65, 39-46 (2015)
DOI: 10.1097/FJC.0000000000000161

98. F Zhao; L Fu; W Yang; Y Dong; J Yang; S Sun; Y Hou. Cardioprotective effects of baicalein on heart failure via modulation of Ca2 + handling proteins *in vivo* and *in vitro*. Life Sci, 145, 213-223 (2016)
DOI: 10.1016/j.lfs.2015.12.036

99. R Ribeiro-Santos; D Carvalho-Costa; C Cavaleiro; HS Costa; TG Albuquerque; MC Castilho; F Ramos; NR Melo; A Sanches-Silva. A novel insight on an ancient aromatic plant: The rosemary (Rosmarinus officinalis L.). Trends Food Sci Technol, 45, 355-368 (2015)
DOI: 10.1016/j.tifs.2015.07.015

100. M Carocho; MF Barreiro; P Morales; ICFR Ferreira. Adding molecules to food, pros and cons: A review on synthetic and natural food additives. Compr Rev Food Sci Food Saf, 13, 377-399 (2014)
DOI: 10.1111/1541-4337.12065

101. M Muchuweti; E Kativu; CH Mupure; C Chidewe; AR Ndhlala; MAN Benhura. Phenolic composition and antioxidant properties of some spices. Am J Food Technol, 2, 414-420 (2007)
DOI: 10.3923/ajft.2007.414.420

102. M Naczk; F Shahidi. Extraction and analysis of phenolics in food. J Chromatogr A, 1054, 95-111 (2004)
DOI: 10.1016/j.chroma.2004.08.059

103. ML McCullough; JJ Peterson; R Patel; PF Jacques; R Shah; JT Dwyer. Flavonoid intake and cardiovascular disease mortality in a prospective cohort of US adults. Am J Clin Nutr, 95, 454-464 (2012)
DOI: 10.3945/ajcn.111.016634

104. TU De Andrade; GA Brasil; DC Endringer; FR Da Nóbrega; DP De Sousa. Cardiovascular activity of the chemical constituents of essential oils. Molecules 22 (2017)
DOI: 10.3390/molecules22091539

105. C Proestos; IS Boziaris; GJE Nychas; M Komaitis. Analysis of flavonoids and phenolic acids in Greek aromatic plants: Investigation of their antioxidant capacity and antimicrobial activity. Food Chem, 95, 664-671 (2006)
DOI: 10.1016/j.foodchem.2005.01.049

106. J Dai; RJ Mumper. Plant phenolics: Extraction, analysis and their antioxidant and anticancer properties, Molecules, (2010)
DOI: 10.3390/molecules15107313

107. S Umar Lule; W Xia. Food Phenolics, Pros and Cons: A Review. Food Rev Int, 21, 367-388 (2005)
DOI: 10.1080/87559120500222862

108. I Molnár-Perl; Z Füzfai. Chromatographic, capillary electrophoretic and

capillary electrochromatographic techniques in the analysis of flavonoids. J Chromatogr A, 1073, 201-227 (2005)
DOI: 10.1016/j.chroma.2004.10.068

109. JK Prasain; CC Wang; S Barnes. Mass spectrometric methods for the determination of flavonoids in biological samples. Free Radic Biol Med, 37, 1324-1350 (2004)
DOI: 10.1016/j.freeradbiomed.-2004.07.026

110. E de Rijke; P Out; WMA Niessen; F Ariese; C Gooijer; UAT Brinkman. Analytical separation and detection methods for flavonoids. J Chromatogr A, 1112, 31-63 (2006)
DOI: 10.1016/j.chroma.2006.01.019

111. PCH Hollman; A Cassidy; B Comte; M Heinonen; M Ric. The Biological Relevance of Direct Antioxidant Effects of Polyphenols for Cardiovascular health in humans is not established. J Nutr, 989-1009 (2011)
DOI: 10.3945/jn.110.131490.989S

112. TL Zern; ML Fernandez. Recent Advances in Nutritional Sciences Cardioprotective Effects of Dietary. The Journal of Nutrition 2291-2294 (2005)

113. P Portincasa; G Calamita. Phytocompounds modulating Aquaporins: Clinical benefits are anticipated. Food Chem, 274, 642-650 (2019)
DOI: 10.1093/jn/135.10.2291

114. D Peixoto-Neves; KS Silva-Alves; MDM Gomes; FC Lima; S Lahlou; PJC Magalhães; VM Ceccatto; AN Coelho-De-Souza; JH Leal-Cardoso. Vasorelaxant effects of the monoterpenic phenol isomers, carvacrol and thymol, on rat isolated aorta. Fundam Clin Pharmacol, 24, 341-350 (2010)
DOI: 10.1111/j.1472-8206.2009.00768.x

115. MRV Santos; F V. Moreira; BP Fraga; DP de Sousa; LR Bonjardim; LJ Quintans. Cardiovascular effects of monoterpenes: A review. Brazilian J Pharmacogn, 21, 764-771 (2011)
DOI: 10.1590/S0102-695X2011005000119

116. Y Aydin; Ö??? Kutlay; S Ari; S Duman; K Uzuner; S Aydin. Hypotensive effects of carvacrol on the blood pressure of normotensive rats. Planta Med, 73, 1365-1371 (2007)
DOI: 10.1055/s-2007-990236

117. J Magyar; N Szentandrássy; T Bányász; L Fülöp; A Varró; PP Nánási. Effects of terpenoid phenol derivatives on calcium current in canine and human ventricular cardiomyocytes. Eur J Pharmacol, 487, 29-36 (2004)
DOI: 10.1016/j.ejphar.2004.01.011

118. JFA Bastos; ÍJA Moreira; TP Ribeiro; IA Medeiros; AR Antoniolli; DP De Sousa; MR V Santos. Hypotensive and vasorelaxant effects of citronellol, a monoterpene alcohol, in rats. Basic Clin Pharmacol Toxicol, 106, 331-337 (2010)
DOI: 10.1111/j.1742-7843.2009.00492.x

119. M Höferl; S Krist; G Buchbauer. Chirality influences the effects of linalool on physiological parameters of stress. Planta Med, 72, 1188-1192 (2006)
DOI: 10.1055/s-2006-947202

120. E Arranz; J Mes; HJ Wichers; L Jaime; JA Mendiola; G Reglero; S Santoyo; M Villalva; L Jaime; E Aguado; JA Nieto; G Reglero; S Santoyo. Anti-Inflammatory and Antioxidant Activities from the Basolateral Fraction of Caco-2 Cells

Exposed to a Rosmarinic Acid Enriched Extract. J Agric Food Chem, 13, 384-390 (2018)
DOI: 10.1021/acs.jafc.7b06008

121. N Babovic; S Djilas; M Jadranin; V Vajs; J Ivanovic; S Petrovic; I Zizovic. Supercritical carbon dioxide extraction of antioxidant fractions from selected Lamiaceae herbs and their antioxidant capacity. Innov Food Sci Emerg Technol, 11, 98-107 (2010)
DOI: 10.1016/j.ifset.2009.08.013

122. B Teixeira; A Marques; C Ramos; NR Neng; JMF Nogueira; JA Saraiva; ML Nunes. Chemical composition and antibacterial and antioxidant properties of commercial essential oils. Ind Crops Prod, 43, 587-595 (2013)
DOI: 10.1016/j.indcrop.2012.07.069.

123. AI Hussain; F Anwar; SAS Chatha; A Jabbar; S Mahboob; PS Nigam. Rosmarinus officinalis essential oil: Antiproliferative, antioxidant and antibacterial activities. Brazilian J Microbiol, 41, 1070-1078 (2010)
DOI: 10.1590/S1517-83822010000400027

124. FDA. Food and drug administration (FDA). Code of federal regulations (CFR).Title 21: Food and drugs. Chapter I e Food and drug administration, department of health and human services (Continued), subchapter B e Food for human consumption, Part 18. (2014).

125. FDA. Food and drug administration (FDA). Code of federal regulations (CFR). Title 21: Food and drugs. Chapter I e Food and drug administration, department of health and human services (Continued), Subchapter B e Food for human consumption, Part 1. (2014).

126. European Pharmacopoeia. European directorate for the quality of medicines (EDQM) (5th ed., pp. 2377e2379). Strasbourg: Council of Europe (2005)

127. M Iriti; S Vitalini; G Fico; F Faoro. Neuroprotective herbs and foods from different traditional medicines and diets. Molecules, 15, 3517-3555 (2010)
DOI: 10.3390/molecules15053517

128. M Pandey; RK Verma; SA Saraf. Nutraceuticals: New era of medicine and health. Asian J Pharm Clin Res, 3, 11-15 (2010)

129. A Rahal; A Kumar. Cardiovascular Diseases: Can Herb-Based Antioxidant and Anti-Inflammatory Functional Products Be a Solution? React Oxyg Species, (2016)
DOI: 10.20455/ros.2016.877

130. I Garcia-Mantrana; M Selma-Royo; C Alcantara; MC Collado. Shifts on gut microbiota associated to mediterranean diet adherence and specific dietary intakes on general adult population. Front Microbiol, 9, 1-11 (2018)
DOI: 10.3389/fmicb.2018.00890

131. A Zamora; B Guamis. Opportunities for Ultra-High-Pressure Homogenisation (UHPH) for the Food Industry, Food Engineering Rev, (2015)
DOI: 10.1007/s12393-014-9097-4

132. DT Do; J Singh; I Oey; H Singh. Biomimetic plant foods: Structural design and functionality. Trends Food Sci Technol, 82, 46-59 (2018)
DOI: 10.1016/j.tifs.2018.09.010

133. F.Patrignani, C. Mannozzi, S. Tappi, U. Tylewicz, F. Pasini, V. Castellone, Y. Riciputi, P. Rocculi, S. Romani, M. F.

Caboni, F. Gardini, R. Lanciotti, M. Dalla Rosa, F. Patr. Effect of high pressure homogenization on the shelf-life and functionality of organic kiwifruit juice, Frontiers Microbiol, 10 (2019)
DOI: 10.3389/fmicb.2019.00246

134. M Bekut; S Brkic; N Kladar; G Dragovic; N Gavaric; B Božin. Potential of selected Lamiaceae plants in anti(retro)viral therapy, Pharmacological Res, (2018)
DOI: 10.1016/j.phrs.2017.12.016

135. MS Dilip Kumar Chanchal , Shashi Alok, Surabhi Rashi, Rohit Kumar Bijauliya, Rahul Deo Yadav and. Various medicinal plants used in the treatment of anticancer activity. Int. J. Pharm. Sci. Res. 9(4):1424-1429
DOI: 10.13040/IJPSR.0975-8232.9(4).1424-29

136. ZFT and ARK Syer Ree Tee, Xin Yun Teoh, Wan Abdul Rahman Wan Mohd Aiman, Ahmad Aiful, Calvin Siu Yee Har. The Prevalence Of Hypertension And Its Associated Risk Factors In Two Rural Communities In Penang, Malaysia. IeJSME 2, 27-40 (2010)

137. J.R.; Ghosh, A. R. Bandyopadhyay, Comparative evaluation of obesity measures?: relationship with blood pressures and hypertension. Singapore Med J, 48, 1-4 (2007)

138. J Heisler; PM Glibert; JM Burkholder; DM Anderson; W Cochlan; WC Dennison; Q Dortch; CJ Gobler; CA Heil; E Humphries; A Lewitus; R Magnien; HG Marshall; K Sellner; DA Stockwell; DK Stoecker; M Suddleson. Eutrophication and harmful algal blooms: A scientific consensus. Harmful Algae 8, 3-13 (2008)
DOI: 10.1016/j.hal.2008.08.006

139. World Health Organization WHO Monographs on selected medicinal plants. Geneva:World Health Organization (2002)

140. CRL Cardoso; GF Salles. Prognostic Importance of Ambulatory Blood Pressure Monitoring in Resistant Hypertension: Is It All that Matters?, Current Hypertension Reports, (2016)
DOI: 10.1007/s11906-016-0693-y

141. NJ Farpour-Lambert; Y Aggoun; LM Marchand; XE Martin; FR Herrmann; M Beghetti. Physical Activity Reduces Systemic Blood Pressure and Improves Early Markers of Atherosclerosis in Pre-Pubertal Obese Children. J. Am. Coll. Cardiol, (2009)
DOI: 10.1016/j.jacc.2009.08.030

142. IB Puddey; LJ Beilin. Alcohol is bad for blood pressure. In: Clinical and Experimental Pharmacology and Physiology (2006)
DOI: 0.1111/j.1440-1681.2006.04452.x

143. L Bedoya; P Bermejo; M Abad. Anti-Infectious Activity in the Cistaceae Family in the Iberian Peninsula. Mini-Reviews Med Chem, (2009)
DOI: 10.2174/138955709788167600

144. JB Calixto. Twenty-five years of research on medicinal plants in Latin America: A personal view, J Ethnopharmacol, (2005)
DOI: 10.1016/j.jep.2005.06.004

145. Y Yang; ZP Wang; SH Gao; HQ Ren; RQ Zhong; WS Chen. The effects of salvia przewalskii total phenolic acid extract on immune complex glomerulonephritis. Pharm Biol, (2017)
DOI: 10.1080/13880209.2017.1383486

146. FV Hassani; K Shirani; H Hosseinzadeh. Rosemary (Rosmarinus officinalis) as a potential therapeutic plant in metabolic syndrome: A review: Naunyn-Schmiedeberg's Archives of Pharmacology. (2016)
DOI: 10.1007/s00210-016-1256-0

147. N Mihailovic-Stanojevic; A Belšcak-Cvitanovic; J Grujic-Milanovic; M Ivanov; D Jovovic; D Bugarski; Z Miloradovic. Antioxidant and Antihypertensive Activity of Extract from Thymus serpyllum L. in Experimental Hypertension. Plant Foods Hum Nutr, (2013)
DOI: 10.1007/s11130-013-0368-7

148. K Malik; M Ahmad; RW Bussmann; A Tariq; R Ullah; AS Alqahtani; AA Shahat; N Rashid; M Zafar; S Sultana; SN Shah. Ethnobotany of anti-hypertensive plants used in Northern Pakistan. Front. Pharmacol, 9 (2018)
DOI: 10.3389/fphar.2018.00789

149. PB James; H Kamara; AJ Bah; A Steel; J Wardle. Herbal medicine use among hypertensive patients attending public and private health facilities in Freetown Sierra Leone. Complement Ther Clin Pract, 31, 7-15 (2018)
DOI: 10.1016/j.ctcp.2018.01.001

150. E Guzman; J Molina. The predictive utility of the plant phylogeny in identifying sources of cardiovascular drugs. Pharm. Biol, 56, 154-164 (2018)
DOI: 10.1080/13880209.2018.1444642

151. C de Souza Ferreira; L de F de Sousa Fomes; GES da Silva; G Rosa. Effect of chia seed (Salvia hispanica L.) consumption on cardiovascular risk factors in humans: A systematic review. Nutr. Hosp, 32, 1909-1918 (2015)
DOI: 10.3305/nh.2015.32.5.9.394

152. H Tajadini; K Divsalar; M Mehrabani; AA Haghdoost; Z Esmaili; M Shadkam; M Moradi. The Frequency of Using Herbal Medicines Among Patients With Hypertension in Kerman, Iran, 2012-2013. J Evidence-Based Complement Altern Med, 20, 199-202 (2015)
DOI: 10.1177/2156587215573141

153. RE López-García; D Martín-Herrera; V Darias; RM Rabanal. Study of the Hypoglycaemic, Diuretic and Cardiovascular Activity of Cedronella canariensis var.canariensis (L.) W. & B. Phytotherapy Research 10, 541-543 (1996)

154. Rana M S; Samant Ss. Diversity, indigenous uses and conservation status of medicinal plants in Manali wildlife sanctuary, North western Himalaya. Indian J Tradit Knowl 10, 439-459 (2011)

155. J Jiang; X Yuan; T Wang; H Chen; H Zhao; X Yan; Z Wang; X Sun; Q Zheng. Antioxidative and cardioprotective effects of total flavonoids extracted from Dracocephalum moldavica L. against acute ischemia/reperfusion-induced myocardial injury in isolated rat heart. Cardiovasc Toxicol, 14, 74-82 (2014)
DOI: 10.1007/s12012-013-9221-3

156. A Shekari; MH Mahdipour; V Nazeri; M Shokrpour. The reproductive biology of motherwort (Leonurus cardiaca L.). 12, 109-116 (2018)

157. M Rezaee-Asl; M Sabour; V Nikoui; S Ostadhadi; A Bakhtiarian. The Study of Analgesic Effects of Leonurus cardiaca L. in Mice by Formalin, Tail Flick and Hot Plate Tests. Int Sch Res Not, 2014, 1-5

(2014)
DOI: 10.1155/2014/687697

158. A Taamalli; D Arráez-Román; L Abaza; I Iswaldi; A Fernández-Gutiérrez; M Zarrouk; A Segura-Carretero. LC-MS-based metabolite profiling of methanolic extracts from the medicinal and aromatic species Mentha pulegium and Origanum majorana. Phytochem Anal, 26, 320-330 (2015)
DOI: 10.1002/pca.2566

159. A Skendi; M Irakli; P Chatzopoulou. Analysis of phenolic compounds in Greek plants of Lamiaceae family by HPLC. J Appl Res Med Aromat Plants, 6, 62-69 (2017)
DOI: 10.1016/j.jarmap.2017.02.001

160. M Aalikhani Pour; S Sardari; A Eslamifar; M Rezvani; A Azhar; M Nazari. Evaluating the anticoagulant effect of medicinal plants *in vitro* by cheminformatics methods. J Herb Med, 6, 128-136 (2016)
DOI: 10.1016/j.hermed.2016.05.002

161. KS Prabhu; R Lobo; AA Shirwaikar; A Shirwaikar. Ocimum gratissimum: A Review of its Chemical, Pharmacological and Ethnomedicinal Properties. Open Complement Med J, 1, 1-15 (2009)
DOI: 10.2174/1876391X00901010001

162. S Singh; HMS Rehan; DK Majumdar. Effect of Ocimum sanctum fixed oil on blood pressure, blood clotting time and pentobarbitone-induced sleeping time. J Ethnopharmacol, 78, 139-143 (2001)
DOI: 10.1016/S0378-8741(01)00336-1

163. YC Tsai; HC Hsu; WC Yang; WJ Tsai; CC Chen; T Watanabe. a-Bulnesene, a PAF inhibitor isolated from the essential oil of Pogostemon cablin. Fitoterapia 78, 7-11 (2007)
DOI: 10.1016/j.fitote.2006.09.016

164. EA Offord; K Macé; C Ruffieux; A Malnoë; AMA Pfeifer. Rosemary components inhibit benzo(a)pyrene-induced genotoxicity in human bronchial cells. Carcinogenesis 16, 2057-2062 (1995)
DOI: 10.1093/carcin/16.9.2.057

165. H Haraguchi; T Saito; N Okamura; A Yagi. Inhibition of lipid peroxidation and superoxide generation by diterpenoids from Rosmarinus officinalis. Planta Med, (1995)
DOI: 10.1055/s-2006-958094

166. P Mena; M Cirlini; M Tassotti; KA Herrlinger; C Dall'Asta; D Del Rio. Phytochemical profiling of flavonoids, phenolic acids, terpenoids, and volatile fraction of a rosemary (Rosmarinus officinalis L.) extract. Molecules 21, 1-15 (2016)
DOI: 10.3390/molecules21111576

167. LA Muñoz; A Cobos; O Diaz; JM Aguilera. Chia Seed (Salvia hispanica): An Ancient Grain and a New Functional Food. Food Reviews Internat, 29, 394-408 (2013)

168. J Karbowska; Z Kochan. Salvia hispanica (chia) as a promising source of n-3 polyunsaturated fatty acids with antiatherogenic and cardioprotective properties. Postepy Higieny i Medycyny Doswiadczalnej 72, 307-317 (2018)

169. X-L Lei; GCY Chiou. Studies on cardiovascular actions of Salvia miltiorrhiza. Am J Chin Med, 14, 26-32 (1986)
DOI: 10.1142/S0192415X86000053

170. G Chen; RX Liu; WG Zhang; B Wang; J Fu; YG Feng; XB Zhang; F Wu; X Ma. Effect of Salvia miltiorrhiza Bunge injection on anticardiolipin antibody production induced by beta2 glycoprotein. Acta Pharmacol Sin (2001)

171. J Wang; X Xiong; B Feng. Cardiovascular effects of salvianolic acid B. Evidence-based Complement Altern Med, (2013)
DOI: 10.1155/2013/247948

172. CM Sá; AA Ramos; MF Azevedo; CF Lima; M Fernandes-Ferreira; C Pereira-Wilson. Sage tea drinking improves lipid profile and antioxidant defences in humans. Int J Mol Sci, 10, 3937-3950 (2009)
DOI: 10.3390/ijms10093937

173. WS Itani; SH El-Banna; SB Hassan; RL Larsson; A Bazarbachi; HU Gali-Muhtasib. Anti colon cancer components from lebanese sage (Salvia libanotica) essential oil: Mechanistic basis. Cancer Biol Ther, 7, 1765-1773 (2008)
DOI: 10.4161/cbt.7.11.6740

174. J Damašius; PR Venskutonis; V Kaškoniene; A Maruška. Fast screening of the main phenolic acids with antioxidant properties in common spices using on-line HPLC/UV/DPPH radical scavenging assay. Analytical Methods 6, 2774-2779 (2014)

175. A López-Cobo; AM Gómez-Caravaca; J Švarc-Gajic; A Segura-Carretero; A Fernández-Gutiérrez. Determination of phenolic compounds and antioxidant activity of a Mediterranean plant: The case of Satureja montana subsp. kitaibelii. J Funct Foods, 18, 1167-1178 (2015)
DOI: 10.1016/j.jff.2014.10.023

176. C-Z Wang; SR Mehendale; T Calway; C-S Yuan. Botanical Flavonoids on Coronary Heart Disease. Am J Chin Med, (2011)
DOI: 10.1142/S0192415X1100910X

177. T Khouya; M Ramchoun; A Hmidani; S Amrani; H Harnafi; M Benlyas; YF Zegzouti; C Alem. Anti-inflammatory, anticoagulant and antioxidant effects of aqueous extracts from Moroccan thyme varieties. Asian Pac J Trop Biomed, 5, 636-644 (2015)
DOI: 10.1016/j.apjtb.2015.05.011

178. A Marculesku; L Vlase; D Hanganu; C Dragulescu; I Antonie; O Neli-Kinga. Polyphenols Analyses From Thymus Species. Proc Rom Acad, Series B 3, 117-121 (2007)

179. A Vallverdú-Queralt; J Regueiro; M Martínez-Huélamo; JF Rinaldi Alvarenga; LN Leal; RM Lamuela-Raventos. A comprehensive study on the phenolic profile of widely used culinary herbs and spices: Rosemary, thyme, oregano, cinnamon, cumin and bay. Food Chem, 154, 299-307 (2014)
DOI: 10.1016/j.foodchem.2013.12.106

180. S Niazmandu; T Hassannia; M Esparham; M Derakhshan. Cardiovascular effects of Teucrium polium L. extract in rabbit. Pharmacognosy Magazine (2011)
DOI: 10.4103/0973-1296.84244

181. S Catalayud; R Bello; B Beltrán; E Primo-Yufera; J Esplugues. Cardiovascular effects of the methanol and dichloro-methanol extracts from Teucrium cartag-inenses L. Phyther Res, 12, 44-45 (1998)
DOI: 10.1002/(SICI)10991573(19980-201)12:1%3C68::AIDPTR188%3E3.0.CO;2-B

182. Y Huang; S-Y Tsang; X Yao; Z-Y Chen. Biological properties of Baicalein in cardiovascular system. Curr Drug Target -Cardiovascular Hematol Disord, (2005) DOI: 10.2174/1568006043586206

Abbreviations: CVDs-Cardiovascular diseases; EOs-essential oils; DOX -doxorubicin; CRP-C-reactive protein; PAF-platelet-activating factor; TNF-α-tumor necrosis factor-alpha; ROS - reactive oxygen species; MIP2 -macrophage inflammatory protein 2; ICG-complex glomerul-onephritis; DCI-Disease Consensus index

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