ISSN 0974-3618 (Print)
0974-360X (Online)

www.rjptonline.org

REVIEW ARTICLE

Therapeutic Herbal Plants: A Review of Selected Animal Models for Coronary Heart Disease

R. Dhevi[1]*, K. Gayathri[2]
[1]Department of Siddha Medicine, Tamil University, Thanjavur, TamilNadu.
[2]Assistant Professor, Department of Biochemistry, Vels University, Chennai, Tamil Nadu.
*Corresponding Author E-mail: **rdhevi23@gmail.com**

ABSTRACT:
Dietary factors play a key role in the development of various human diseases, including cardiovascular diseases. Epidemiological studies have shown that diets rich in fruits, herbs and spices are associated with a low risk of cardiovascular disease. Herbal treatment has attracted particular attention of modern medicine because of its widespread health use around the world, and the cherished belief that it helps in maintaining good health warding off illnesses and providing more vigor. To date, many favorable experimental effects of herbal preparations have been reported. If folk wisdom is not ignored, it may teach us valuable lessons. It is a great challenge for scientists all over the world to make a proper use of herbal plants and enjoy its maximum beneficial effect to prevent cardiovascular disease. This review has been made indicating an overall view of the efficacy of herbal treatment in cardiovascular diseases.

KEYWORDS: Cardiovascular diseases, herbal treatment, folk medicine, Dietary factors.

INTRODUCTION:
Coronary artery disease (CAD) starts with the formation of atherosclerotic plaques in the coronary arteries. The arteries harden and narrow due to buildup of a material called plaque on their inner walls. The buildup of plaque is known as atherosclerosis. As the plaque increases in size, the insides of the coronary arteries get narrower and less blood can flow through them. Eventually, blood flow to the heart muscle is reduced, and, because blood carries much-needed oxygen, the heart muscle is not able to receive the amount of oxygen it needs. Reduced or cutoff blood flow and oxygen supply to the heart muscle can result in: unstable angina, acute myocardial infarction and sudden death. [1]

World Health Organization (WHO) recognized the ten leading killer disease worldwide. Coronary heart disease was one among them.

Received on 21.02.2018 Modified on 10.04.2018
Accepted on 08.06.2018
Research J. Pharm. and Tech 2018; 11(11): 5197-5204.
DOI: 10.5958/0974-360X.2018.00949.6

It makes up 15.9% of all deaths making it the most common and are the number one cause of death globally: more people die annually from CADs than from any other cause. In the year 2015 CAD affected 110 million people and resulted in 8.9 million deaths. Rates are higher among men than women. People with cardiovascular disease or who are at high cardiovascular risk need early detection and management using counseling and medicines. [2]

Framingham Heart Study in USA played vital role in defining the risk factors for CAD incidence in general population. Major risk factors of CAD are sedentary lifestyle, cigarette smoking, hypertension, high LDL cholesterol, low HDL cholesterol and diabetes mellitus. [3] Other factors that influence CAD risk are obesity, family history of premature CAD, excessive alcohol, depression, hyper-triglyceridaemia, insulin resistance small dense LDL particles, lipoprotein A, serum homocysteine and abnormalities in several coagulation factors. Psychosocial and socioeconomic factors are also important. Multiple studies have revealed that CHD is a significant problem in India, mainly hypercholesterolaemia and hypertriglyceridaemia are widespread. [4]

Epidemiological transition, with increasing life expectancy and demographic shifts in population age-profile, combined with lifestyle related increases in the levels of cardiovascular risk factors is accelerating CHD epidemic in India. CHD prevalence in urban populations increased from 3.5% in 1960s to 9.5% in 1990s. In rural areas it increased from 2% in 1970s to 4% in 1990s. The role of lifestyle modification in the prevention and treatment of CAD in Indians has been reviewed recently. [4,5] To achieve the goal of preventing cardiovascular diseases it is important to avoid the occurrence of the major risk factors themselves.

Herbal medicine is the root of various traditional medicine systems around the world. Botanicals are a chemical source that directly provides approximately 25% of currently used crude drugs, with another 25% derived from chemically altered natural products. [6] Various traditional medicine systems around the world, including ancient Chinese medicinal system, Indian medicinal system (composed of two major branches—Unani and Ayurveda) and Amazonian ethnomedicine, rely heavily on herbs for health preservation and healing. Herbal medicines have been described in traditional texts and used as antimicrobial, anti-inflammatory and antiviral medicine for the cure of allergies, infections, wound healing and fever.[7]

It is no surprise, then, that the use of alternative medicine, such as botanicals and nutritional supplements, has become popular with arthritis patients and is on the rise. An increasing number of people in the United States, as many as 42% use complementary or alternative medicine approaches to help meet their personal health problems.[8,9] Keeping this in view now a day researchers are much interested in the evaluation of herbal medicines in coronary heart diseases. This review describes the currently available herbal plants with scientific evidences that are challenging to cardiovascular disorders.

Allium sativum:

Garlic has been widely recognized as agent for prevention and treatment of cardiovascular and other metabolic diseases, atherosclerosis, hyperlipidemia, thrombosis, hypertension and diabetes. Effectiveness of garlic in cardiovascular diseases was more encouraging in experimental studies, which prompted several clinical trials. Many clinical trials showed a positive effect of garlic on almost all cardiovascular conditions. [10] These biological responses have been largely attributed to,

i) Reduction of risk factors for cardiovascular diseases and cancer,
ii) Stimulation of immune function,
iii) Enhanced detoxification of foreign compound,
iv) Hepatoprotection and antimicrobial effect
v) Antioxidant effect.

The Protective effect of garlic on atherosclerosis can be determined by the following study.

Several groups of investigators studied the effects of long term (2-9 months) feeding of garlic and garlic preparations (2% garlic powder in diet) on experimental atherosclerosis induced by a high-cholesterol diet in rabbits. [11, 12, 13, 14, 15, 16 & 17] Most of these studies reported a statistically significant reduction in atheromatous lesions, particularly in the aorta, that averaged about 50%.

The chronic effects of garlic on lipid metabolism in rats were also encouraging. The duration of these studies was at least 4 weeks. Garlic and garlic protein administration in hypercholesterolemic rats induced by a high-cholesterol diet, significantly reduced serum cholesterol, triglyceride and LDL cholesterol, but there was no effect on serum HDL. [18, 19, 20, 21 & 22] Total lipid content and cholesterol levels in liver were also decreased in rat after chronic garlic consumption. Abramoviz *et al*. (1999) investigated the effect of allicin as an active component of garlic on the formation of fatty streaks in aorta and lipid profile in mice. [23] While no significant differences were observed between blood lipid profiles, the microscopic evaluation of formation of fatty streaks in the aortic sinus showed that values for mice in the allicin treated groups were significantly lower by nearly 50%.

Epidemiological study shows an inverse correlation between garlic consumption and reduced risk of cardiovascular disease progression. [24, 25] The wealth of scientific literature supports the proposal that garlic consumption have significant cardioprotective effect, which includes both animal and human studies.

***Hibiscus rosa sinensis*:**

The flowers of *Hibiscus rosa sinensis (Fam: Malvaceae)* [HRS], has been reported in the ancient Indian medicinal literature with beneficial effects in heart diseases. [26] In recent times, both experimental and clinical studies have shown that the dried flower powder of HRS has significant protective effects in ischemic heart disease [IHD]. [27, 28]

In a study Cardioprotective effect of the *Hibiscus rosa sinensis* flowers in an oxidative stress model of myocardial ischemic reperfusion injury in rat was investigated. Dried pulverized flower of *Hibiscus rosa sinensis* was administered orally to Wistar albino rats (150–200 gms) in three different doses [125, 250 and 500 mg/kg in 2% carboxy methyl cellulose (CMC)], 6 days per week for 4 weeks. Thereafter, rats were sacrificed and the baseline changes in cardiac endogenous antioxidants such as superoxide dismutase,

reduced glutathione and catalase were determined and the hearts were subjected to isoproterenol induced myocardial necrosis.

There was significant increase in the baseline contents of thiobarbituric acid reactive substances (TBARS) [a measure of lipid per oxidation] with both doses of *Hibiscus Rosa sinensis*. In the 250 mg/kg treated group, there was significant increase in superoxide dismutase, reduced glutathione, and catalase levels but not in the 125 and 500 mg/kg treated groups. Significant rise in myocardial thiobarbituric acid reactive substances and loss of superoxide dismutase, catalase and reduced glutathione (suggestive of increased oxidative stress) occurred in the vehicle treated hearts subjected to in vivo myocardial ischemic reperfusion injury. It may be concluded that flower of *Hibiscus rosa sinensis* (250 mg/kg) augments endogenous antioxidant compounds of rat heart and also prevents the myocardium from isoproterenol induced myocardial injury. [29]

***Ocimum sanctum*:**

The Tulsi plant or Holy Basil is an important symbol in many Hindu religious traditions. Tulsi's extracts are used in ayurvedic remedies for common colds, headaches, stomach disorders, inflammation, heart disease, various forms of poisoning, and malaria. Traditionally, the herb is taken in many forms: as an herbal tea, dried powder, fresh leaf, or mixed with ghee. Essential oil extracted from Karpoora Tulsi is mostly used for medicinal purposes and in herbal toiletry. For centuries, the dried leaves of Tulsi have been mixed with stored grains to repel insects.

Ocimum sanctum, in India is a local herb containing potent antioxidants flavanoids (orientin, vicenin) and phenolic compounds (eugenol, cirsilineol, apigenin). [11] The ancient systems of medicine including Ayurveda, Greek, Roman, Siddha and Unani, have mentioned its therapeutic applications in cardiovascular disorders, diabetes and asthma. [12, 13] However, only few studies are presently available that documents its cardioprotective potential.

In the following study male albino wistar rats were orally fed with hydroalcoholic extract of *Ocimum sanctum* (25, 75, 150 mg/kg) once daily for one month and in addition received Isoproterenol (85 mg/kg, sc) on the 29th and 30th day. On the 31st day, 24 hr after second dose ISP administration, animals were sacrificed. Isoproterenol treated animals exhibited significant myocardial cell injury and infiltration of inflammatory cells. Chronic *Ocimum sanctum* 75 and 150 mg/kg treatment significantly restored the activities of antioxidant enzymes CAT, SOD and GSHPx ($P < 0.05$) compared to Isoproterenol control. *Ocimum sanctum* only at 25 mg/kg dose significantly restored GSHPx activity and failed to significantly increase the activities of other antioxidants CAT and SOD as compared to Isoproterenol control.

The extent of necrosis was also evaluated by measuring myocardial CK-MB isoenzyme activity. [30] The observation that Os (75 mg/kg) treatment significantly prevented leakage of CK-MB and thereby preserved the myofibre architecture as compared to ISP control group, demonstrates its cardioprotective effect. Os treatment at 75 mg/kg dose showed significant improvement in the degree of myonecrosis, infiltration of inflammatory cells, vacuolar changes and oedema compared to the ISP-control, elucidating its myocardial salvaging effects. [31]

***Curcuma longa*:**

Turmeric (*Curcuma longa*) is a member of the ginger family, Zingiberaceae. It's also called tumeric or kunyit in some Asian countries. [32] *Curcuma longa*, common Indian dietary pigment and spice has been shown to possess a wide range of therapeutic utilities in the traditional Indian medicine. It's role in wound healing, urinary tract infections, liver ailments are well-documented. [33] The active component of turmeric identified as curcumin exhibits a variety of pharmacological effects including antioxidant, adaptogenic, anti-inflammatory and anti-infectious activities. [34, 35]

In a study adult male Wistar rats, 10 to 12 weeks old, weighing 150 to 200 g were used. *Curcuma longa* at the doses of 25, 50, 100 & 200 mg/kg were screened in the murine model of isoproterenol induced myocardial necrosis and the optimum dose exhibiting maximum cardioprotective effect was evaluated. *Curcuma longa* (100 mg/kg) was found to be the most effective in functional recovery of the heart and favorable restoration of biochemical and histopathological alterations. [29]

***Commiphora mukul*:**

The plant Commiphora mukul grows abundantly in the states of Karnataka, Gujarat and Rajasthan in India. The oleoresin secreted by this plant, known as guggul is one of the most reputed drugs in ayurveda and has been used for treatment of gout, arthritis, rheumatism, obesity and inflamation etc in traditional system of medicine. [26] Pharmacological studies showed that guggulipid lowered blood lipids in patients of obesity, [36] increased the coagulation and prothrombin time in hyperlipemic subjects, [37] increased fibrinolytic activity [38] and decreased the platelet adhesive index, [39] Guggulipid is effective against myocardial infarction [40] and known to cause thyrogenic effect.[41]

The hyperlipemic activity of guggulipid is mainly due to guggulsterone, as the other components appear to exert significant synergistic effects with regard to lipid lowering action. [42, 43] As guggulipid, guggulsterone also inhibit platelets aggregation and provide protection against myocardial ischemia induced by isoproterenol.[44]

Cardio protective and lipid lowering activity of synthetic guggulsterone and its two isomers [E; 4, 17(21) Cis-pregnandiene-3, 16- di – one] and [Z; 4, 17(20) trans-pregnandiene-3, 16- di – one] was determined in isoproterenol induced myocardial ischemia in rats. Ischemia was produced by intraperitonial injections of aqueous solution of dl-isoproterenol hydrochloride (85mg/kg) for five consecutive days. [45] The drug (guggulsterone isomers E or Z or mixture of guggulsterone E+Z (7:3w/w) were macerated with aqueous gum acacia and fed orally at the dose of 50mg/kg once daily for five days. The control animals received same amounts of normal saline and vehicle for five days simultaneously with isoproterenol. At the end of the experiment, blood was withdrawn after four hours of the last drug administration and serum was prepared. Rats were sacrificed. Biochemical Parameters such as CK, SGOT, SGPT, ALP, Ca-ATPase, phospholipase, lipid peroxide, total cholesterol, phospholipids, glycogen and cytosolic xanthine oxidase were analysed. [46, 47, 48] The results demonstrate that Z-isomer of guggulsterone at the same doses exerted more cardioprotective and antioxidant activity than E-isomer. Therefore it is suggested that Z guggulsterone is a suitable and better replacement for the natural drug isolated from C.mukul.

***Zingiber officinale*:**
Ginger has several medicinal properties. These properties come from the properties of zingerone present in the ginger. In India, the roots of ginger have been known for its distinct medical products and therefore as a home remedy. It has been used for cold-induced disease, nausea, asthma, cough, colic, heart palpitation, swellings, dyspepsia, loss of appetite, and rheumatism. Japanese research indicates that ginger has a tonic effect on the heart. It has been found to lower blood pressure by restricting blood flow in peripheral areas of the body. Further studies show that ginger can lower cholesterol levels by reducing cholesterol absorption in the blood and liver.

Lipid oxidation and its prevention by antioxidants is a subject of concern to diverse fields of research. Their benefits have been demonstrated in many clinical investigations. Zingerone is an example of a β-adrenoceptor blocker. These β-adrenoceptor blockers have been found to inhibit lipid oxidation in canine and swine models and it has been suggested that the inhibition of lipid oxidation may provide additional cardioprotective effects for β-adrenoceptor blockers. The use of β-adrenoceptor blockers (an example of which is zingerone) is well established in the treatment of various cardiovascular disorders. [49]

In a study, ethanolic Z. officinale (ZO) extract (200 mg/kg) pretreatment for 20 days in isoproterenol (ISO)-treated rats significantly increased the levels of endogenous myocardial antioxidants (catalase, superoxide dismutase and tissue glutathione), decreased the levels of serum marker enzymes (lactate dehydrogenase, creatine kinase, aspartate transaminase and alanine transaminase) and increased myocardial lipid peroxides. Histological examination of rat's heart section confirmed myocardial injury with ISO administration and near normal pattern with ethanolic *Zingiber officinale* extract pretreatment. The results of the present study, for the first time, provide clear evidence that the ethanolic *Zingiber officinale* extract pretreatment enhances the antioxidant defense against ISO-induced oxidative myocardial injury in rats and exhibit cardioprotective property. [50]

***Emblica officinalis*:**
Emblica officinalis or Amla is one of the richest natural sources of vitamin C, containing up to 720 mg/100g of fresh pulp and 921 mg/100cc of pressed juice. This is approximately 20 times the vitamin C content of an orange. Amalaki fruit has, in fact, has been used sucessfully to treat human scurvy. It is also effective in the treatment of amlapitta (peptic ulcer), as well as in non-ulcer dyspepsia. [51, 52]

The alcoholic extract of *Emblica officinalis* (1gm/kg) given to isoprotenol-pretreated rats resulted in an increase in cardiac glycogen and a decrease in serum LDH, suggesting a cardioprotective action. It also demonstrated a statistically significant reduction in serum cholesterol levels and an antiatherogenic effect in rabbits. [53, 52]

The effects of amla on low-density lipoprotein (LDL) oxidation and cholesterol levels were investigated in vitro and in vivo using Cu (2+)-induced LDL oxidation and cholesterol-fed rats. SunAmla and ethyl acetate (EtOAc) extract of amla significantly inhibited thiobarbituric acid (TBA)-reactive substance level in the Cu $(2+)$-induced LDL oxidation and the effects were stronger than those of probucol. In addition, the administration of Sun Amla (at a dose of 20 or 40 mg/kg body weight/day) or EtOAc extract of amla (at a dose of 10 or 20 mg/kg body weight/day) for 20 days to rats fed 1% cholesterol diet significantly reduced total, free and LDL-cholesterol levels in a dose-dependent manner, and

EtOAc extract of amla exhibited more potent serum cholesterol-lowering effect than SunAmla in the same amount. Furthermore, the oxidized LDL level in serum was markedly elevated in cholesterol-fed control rats as compared with normal rats, while it was significantly decreased by the administration of SunAmla or EtOAc extract of amla. Moreover, the serum TBA-reactive substance level was also significantly decreased after oral administration of SunAmla or EtOAc extract of amla. These results suggest that amla may be effective for hypercholesterolemia and prevention of atherosclerosis. [54]

***Terminalia Chebula*:**

The dried ripe fruit of *Terminalia chebula* (Combretaceae), is used extensively in Ayurveda and is widely distributed throughout India, Burma and Sri Lanka. It is commonly known as black myroblans in English and has traditionally been used in the treatment of asthma, sore throat, vomiting, hiccough, diarrhoea, bleeding piles, gout and heart and bladder diseases. [55] An herbal formulation containing *T. chebula* under the name 'TRIPHALA' is a very popular traditional medicine for the treatment of chronic disorders including diabetes. It is reported to have antioxidant and free radical scavenging activities. [56] It has shown effectiveness against cancer cells [57] and helicobacter pyloris. [58]

Cardioprotective effect of ethanolic extract of *Terminaliachebula* fruits (500 mg/kg body wt) was examined in isoproterenol (200 mg/kgbody wt) induced myocardial damage in rats. In isoproterenol administeredrats, the level of lipid peroxides increased significantly in the serum and heart. A significant decrease was observed in the activity of the myocardial marker enzymes with a concomitant increase in their activity in serum. Histopathological examination was carried out to confirm the myocardial necrosis. *T. chebula* extract pretreatment was found to ameliorate the effect of isoproterenol on lipid peroxide formation and retained the activities of the diagnostic marker enzymes. [59] This study confirms the cardioprotective activity of *Terminaliachebula.*

***Terminalia arjuna*:**

Terminalia arjuna is a medicinal plant of the genus *Terminalia*, widely praised & used by Ayurvedic physicians for its curative properties in organic/functional heart problems like angina, hypertension, deposits in arteries etc. Research suggests that Terminalia is useful in alleviating the pain of angina pectoris, and in treating heart failure and coronary artery disease. Terminalia may also be useful in treating hypercholesterolemia. [60] The cardioprotective effects of terminalia are thought to be caused by the antioxidant nature of several of the constituent flavonoids and oligomeric proanthocyanidins, while positive inotropic effects may be caused by the saponin glycosides.

Both experimental and clinical studies have also reported beneficial effects of the dried bark powder of TA in ischemic heart disease (IHD). [61,62,63] In a recent study, chronic oral administration of crude bark of *Terminalia arjuna* augmented endogenous antioxidants of rat heart and prevented oxidative stress associated with *invitro* IR injury of the heart. Reinforcement of endogenous defense, through enhancement of antioxidants and induction of HSP has been identified as a promising strategy of myocardial protection. [65,66]

In another study oral administration of TA for 12 weeks in rabbits caused augmentation of myocardial antioxidants; superoxide dismutase (SOD), catalase (CAT) and glutathione (GSH) along with induction of heat shock protein72 (HSP72). In vivo ischemic-reperfusion injury induced oxidative stress, tissue injury of heart and haemodynamic effects were prevented in the TA treated rabbit hearts. The study provides scientific basis for the putative therapeutic effect of TA in ischemic heart disease. [67]

***Withania somnifera*:**

Withania somnifera is classified in Ayurveda as a rasayana, a group of plant-derived drugs that promote physical and mental health, augment resistance against disease and diverse adverse environmental factors, and revitalize the body in debilitated conditions and increase longevity. Studies indicate that Withania somnifera possesses anti-inflammatory, antistress, antioxidative and rejuvenating properties. It also appears to exert a positive influence on the endocrine, cardiopulmonary, and central nervous systems. Study results show that it helps in the maintenance of myocardial antioxidant status and contributes to the significant restoration of most of the altered haemodynamic parameters in heart disease. [68]

A study was designed to evaluate the cardioprotective potential of hydro-alcoholic extract of *Withania somnifera* on the basis of haemodynamic, histopathological and biochemical parameters in the isoprenaline-(isoproterenol) induced myocardial necrosis in rats and to compare with Vitamin E, a known cardioprotective antioxidant.

Wistar albino male rats (150–200 g) were divided into six main groups: sham, isoprenaline control, *Withania somnifera*/Vitamin E control and *Withania somnifera*/Vitamin E treatment groups. *Withania somnifera* was administered at doses 25, 50 and 100

mg/kg and Vitamin E at a dose of 100 mg/kg, orally for 4 weeks. On days 29 and 30, the rats in the isoprenaline control and *Withania somnifera*/Vitamin E treatment groups were given isoprenaline (85 mg/kg), subcutaneously at an interval of 24 hr. On day 31, haemodynamic parameters were recorded and the hearts were subsequently removed and processed for histopathological and biochemical studies. A significant decrease in glutathione (P<0.05), activities of superoxide dismutase, catalase, creatinine phosphokinase and lactate dehydrogenase (P<0.01) as well as increase in lipid peroxidation marker malonyldialdehyde level (P<0.01) was observed in the hearts of isoproterenol control group rats as compared to sham control.

On histopathological examination, myocardial damage was further confirmed. The result show that *Withania somnifera* (25, 50 and 100 mg/kg) exerts a strong cardioprotective effect in the experimental model of isoprenaline-induced myonecrosis in rats. Among the different doses studied, *Withania somnifera* at 50 mg/kg dose produced maximum cardioprotective effect.Augmentation of endogenous antioxidants, maintenance of the myocardial antioxidant status and significant restoration of most of the altered haemodynamic parameters may contribute to its cardioprotective effect (Mohanty Ipseeta *et al*., 2004). [69]

Grape seed:

Increasing evidence shows that red wine consumption has cardioprotective effects. These effects have been attributed to the polyphenolic compounds in grapes. Following study reveals the effects of red grape seed proanthocyanidins on the recovery of postischemic function in isolated rat hearts.

Two groups of rats were fed 50 and 100 mg doses of proanthocyanidin- rich extract for 3 weeks and another group was untreated and served as controls. The animals were then anesthetized and the hearts were isolated and subjected to 30 min of ischemia followed by 2 h of reperfusion. Coronary effluents were collected during the third minute of reperfusion for measurement of oxygen free radicals by using electron spin resonance spectroscopy.

In rats treated with 50 and 100 mg grape seed proanthocyanidins/kg, the incidence of reperfusion-induced ventricular fibrillation was reduced from its control value of 92% to 42% and 25%, respectively ($P < 0.05$ for both). The incidence of ventricular tachycardia showed the same pattern. In rats treated with 100 mg proanthocyanidins/kg, the recovery of coronary flow, aortic flow, and developed pressure after 60 min of reperfusion was improved by 32%, 8%, 98% 8%, and 37%,3%, respectively ($P < 0.05$ for all) compared with untreated control rats. Electron spin resonance studies indicated that proanthocyanidins significantly inhibited the formation of oxygen free radicals. In rats treated with 100 mg roanthocyanidins/kg, free radical intensity was reduced by 75%,7% ($P < 0.05$) compared with the control rats. Flavonoids, which increase the antioxidant capacity of cells and tissues, are probably responsible for the antioxidant property of red wine. [70, 71]

Epidemiologic evidence indicates that consumption of red wine is beneficial in the prevention of coronary artery disease, [72] and this beneficial effect could be attributed to antioxidants present in the polyphenol fraction of red wine. [73] Grape seed proanthocyanidins have cardioprotective effects against reperfusion-induced injury via their ability to reduce or remove, directly or indirectly, free radicals in myocardium that is reperfused after ischemia. [74]

CONCLUSIONS:

Herbal medicines have been used for centuries and their potential benefits have been corroborated by high prevalence of their use worldwide. For cardiovascular disorders, many herbal treatments are available with limited scientific assessment. Some herbal medicines (crude extracts and pure compounds) that have been studied extensively for their cardioprotective effects such as trilinolein, garlic and other herbal products may be beneficial as effective pharmacological. Further basic and clinical studies are needed to elucidate the pharmacological effects of these herbal products and their potential impact on the prevention and treatment of coronary heart disease.

CONFLICT OF INTEREST:

There is no conflict of interest in this review paper.

REFERENCES:

1. Ross, R. The pathogenesis of atherosclerosis: a perspective for the 1990s. Nature. 1993; 362: 801-809.
2. GBD 2015 Mortality and Causes of Death, Collaborators. "Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015". *Lancet*. 2016; 388 (10053): 1459–1544.
3. Grundy SM *et al*., Primary prevention of coronary heart disease: guidelines from Framingham. Circulation 1998; 97: 1876-1887.
4. Reddy KS and Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. Circulation 1998; 97: 596-601.
5. Enas EA, Yusuf S, Sharma S. Coronary artery disease in South Asians. Indian Heart J. 1998; 50: 105-113.
6. Huxtable RJ. The pharmacology of extinction. J Ethnopharmacol. 1992; 37: 1-11.
7. Borchers AT *et al*., Inflammation and native American medicine: the role of botanicals. Am J Clin Nutr 2000; 72: 339-347.
8. Soeken KL, Miller SA, Ernst E. Herbal medicines for the treatment of rheumatoid arthritis: a systematic review. Rheumatology 2003; 42: 652-9.

9. Kessler RC *et al*., Long-term trends in the use of complementary and alternative medical therapies in the United States. Ann Intern Med. 2001; 135: 262–268.
10. Sanjay Banerjee K, Subir Maulik K. Effect of garlic on cardiovascular disorders: a review. Nutrition Journal. 2002; 1: 1-14.
11. Jain RC. Onion and garlic an experimental cholesterol atherosclerosis in rabbits. Artery. 1975; 1**:** 115-125.
12. Jain RC. Effect of garlic on serum lipids, coagulability and fibrinolytic activity of blood. Am J Clin Nutr. 1977; 30**:**1380-1381.
13. Bordia A, Verma SK, Vyas AK, Khabya BL, Rathore AS, Bhu N, Bedi HK. Effect of essential oil of onion and garlic on experimental atherosclerosis in rabbits. Atherosclerosis. 1977; 26: 379-386.
14. Chang MLW and Johnson MA. Effect of garlic on carbohydrate metabolism and lipid synthesis in rats. J Nutr. 1980; 110: 931-936.
15. Kamanna VS and Chandrasekhara N. Effect of garlic on serum lipoproteins cholesterol levels in albino rats rendered hypercholesteremic by feeding cholesterol. Lipids. 1982; 17: 483-488.
16. Mand JK *et al*., Effect of garlic on experimental atherosclerosis in rabbits. Ind Heart J. 1985; 37: 183-188.
17. Betz E and Weidler R. Die Wirkung von Knoblauchextrakt auf die atheerogenese bei kaninchen. *In:* Betz, E. (Ed.), Die anwendung aktueller methoden in der arteriosklerose. Forschung. 1989; 304-311.
18. Rajasree CR, Rajmohan T, Agusti KT. Biochemical effects of garlic on lipid metabolism in alcohol fed rats. Ind J Exp Biol. 1999; 37**:** 243-247.
19. Mathew BC, Daniel RS. Hypolipidemic effect of garlic protein substituted for caseinin diet of rats compared to those of garlic oil. Ind J Exp Biol. 1996; 34**:** 337-340.
20. Qureshi AA, Din ZZ, Abuirameileh N, Burger WC, Ahmed Y, Elson CE. Suppression of avian hepatic lipid metabolism by solvent extracts of garlic: impact on serum lipids. J Nutr. 1983; 113: 1746-1755.
21. Kamanna VS and Chandrasekhara N. Hypocholesteromic activity of different fractions of garlic. Ind J Medical Res. 1984; 79: 580-583.
22. Chi MS. Effect of garlic products on lipid metabolism in cholesterol-fed rats. Proc Soc Exp Biol Med. 1982; 171: 174-178.
23. Abramovitz D *et al*., Allicin-induced decrease in formation of fatty streaks (atherosclerosis) in mice fed a cholesterol-rich diet. Coron Artery Dis. 1999; 10: 515-519.
24. Kendler BS. Garlic (*Allium sativum*) and onion (*Allium cepa*): a review of their relationship to cardiovascular disease. *Prev Med*. 1987; 16(5): 670-685.
25. Keys A. Wine, garlic and CHD in seven countries. Lancet. 1980; 1(8160): 145-146.
26. Nadkarni AK, Nadkarni KM. India Materia Medica with Ayruvedic, Unani-Tibbi, Siddha, Allopathic, Homeopathic, Naturopathic & Home Remedies 1954; Volume 1, 3rd edition. Bombay (India): Popular Book Depot.
27. Jonadet M *et al*., In vitro enzyme inhibitory and in vivo cardioprotective activities of hibiscus (Hibiscus sabdariffa L). J Pharm Belg. 1990; 45: 120-124.
28. Yamasaki H, Uefuji H, Sakihama Y. Stress proteins and myocardial protection. Arch Biochem Biophys. 1996; 332: 183-186.
29. Ipseeta Mohanty, Dharamvir Singh Arya and Suresh Kumar Gupta Effect of *Curcuma longa* and *Ocimum sanctum* on myocardial apoptosis in experimentally induced myocardial ischemic-reperfusion injury. BMC Complementary and Alternative Medicine. 2006; 6:3.
30. Rona G *et al*., Pathogenesis of isoproterenol-induced myocardial alterations: functional and morphological correlates. Recent Adv Stud Card Struct Metab. 1973; 3: 507-525.
31. Arya1 DS *et al*., Myocardial salvaging effects of *Ocimum sanctum* in experimental model of myocardial necrosis: a haemodynamic, biochemical and histoarchitectural assessment. Current science. 2006; 91: 667-672.
32. Egan S. Curcumin, a Major Constituent of Turmeric, Corrects Cystic Fibrosis Defects. Science. 2004; 23: 600-602.
33. Ammon HPT *et al*., Curcumin: a potent inhibitor of Leukotriene B4 formation in rat peritoneal polymorphonuclear neutrophils (PMNL). Planta Med. 1992; 58**:** 26-31.
34. Nirmala C and Puvanakrishnan R. Protective role of curcumin against isoproterenol induced myocardial infarction in rats. Mol Cell Biochem. 1996; 159(2): 85-93.
35. Srinivas L, Shalini VK, Shylaja M: Turmerin: A water soluble antioxidant peptide from turmeric (*Curcuma longa*). *Arch-Biochem Biophys.* 1992; 292(2):617-623.
36. Kuppuranjan K *et al*., Effect of guggulu (Commiphora mukul Engl) on serum lipids in obese, hypercholesterolemic and hyperlipidemic cases. J. Assoc. Physicians India. 1978; 26: 367-374.
37. Tripathi SN, Shastri VVS, Satyavati GV. Experimental and clinical studies on the effect of guggulu (Commiphora mukul) in hyperlipemia and thrombosis. Ind J Med Res. 1968; 90: 62-68.
38. Baldav VS *et al*., Effect of commiphora mukul (guggul) on fibrinolytic activity and platelet aggregationin coronary artery disease. Rajasthan Med J. 1980; 19: 84-90.
39. Bordia A and Chuttani SK. Effect of gum guggulu on fibrinolysis and platelet adhesiveness in coronary heart disease. Ind J Med Res. 1979; 70: 992-1001.
40. Satyavati GV, Dwarkanath C, Tripathi SN. Experimental studies on the hypocholesterrolemic effect of Commiphora mukul Engl (Guggul). Ind J Med *Res.* 1969; *57*: 1950-1957.
41. Singh AK, Prasad GC, Tripathi SN. *In vitro* studies on thyrogenic effect of commiphora mukul (guggulu) Ancient Sci. Life 1982; 2: 23-29.
42. Satyavati GV. Guggulipid:A promisinghypolipidemic agent from gum guggul (Commiphora wightii). In economic and medicinal plant reseach. Plants and Traditional Medicine 1991; Academic Press, New York. 5: 47-82.
43. Chander R, Khanna A K, Kapoor NK. Lipid lowering activity of guggulsterone from *Commiphora mukul* in hyperlipemic rat. Phytotherapy Res. 1996; 10: 508-511.
44. Mester M, Mester L, Nityanand S. Inhibition of platelet aggregation by 'Guggulu' steroids. Planta Medica. 1979; 37: 367-369.
45. Kaul S and Kapoor NK. Cardiac sarcolemma enzymes and liver microsomal cytochrome P450 in isoproterenol treated rats. Ind. J. Med. Res. 1989; 90: 62-68.
46. Kaul S, Singh V, Kapoor NK. Protective effect of Colcenol on biochemical changes produced in coronary ligation induced ischemia. Ind. J. Exp. Biol. 1990; 28: 981-984.
47. Kaul S and Kapoor NK. Sracolemma membrane enzyme changes in myocardial necrosis induced by isoproterenol and salvage by drugs. Biomembrane in health and disease. A.M. Kidwai, R.K Uprett and P.K.Roy.(Ed). 1991; Today & Tomorrow Printer. New Delhi, India. 439.
48. Bessy OA, Lowry OH, Brock MJ. A method for the rapid determination of Alkaline Phosphatase with five cubic mililitres of serum. J Biol Chem. 1946; 164: 321-338.
49. Yeun- Chih Huang *et al*. A new aspect of view in synthesizing new type β-adrenoceptor blockers with ancillary antioxidant activites. Bioorganic and Medicinal Chemistry. 2001; 9: 1739-1746.
50. Ansari MN, Bhandari U, Pillai KK. Ethanolic Zingiber officinale R. extract pretreatment alleviates isoproterenol-induced oxidative myocardial necrosis in rats. Indian J Exp Biol. 2006; 44: 892-897.
51. Singh BN and Sharma PV. Effect of amalaki on amlapitta. J Res Ind Med. 1971; 5: 223-230.
52. Thakar CP and Mandal K. Effect of Emblica officinalis in cholesterol-induced atherosclerosis in rabbits. Ind J Med Res. 1984; 79: 142-146.
53. Chawla YK, Dubey P, singh R. Treatment of dyspepsia with amalaki (Emblika officianilis), an ayurvedic drug. Vagbhata.

1987; 5: 24-26.
54. Kim HJ *et al*. Influence of amla (Emblica officinalis Gaertn.) on hypercholesterolemia and lipid peroxidation in cholesterol-fed rats. J Nutr Sci Vitaminol (Tokyo). 2005; 51: 413-418.
55. Kirtikar KR and Basu BD. *Terminalia chebula*. In Indian Medicinal Plants Volume 1. 2nd edition. Kirtikar, K.R. and Basu, B.D (Ed.), Allahabad: Lalit Mohan Basu Publications. P 1935; 1020-1023.
56. Cheng HY *et al*. Antioxidant and free radical scavenging activities of *Terminalia chebula*. Biol Pharm Bull. 2003; 26: 1331-1335.
57. Saleem A et al. Inhbition of cancer cell growth by crude extract and the phenolics of *Terminalia chebula* Retz. fruit. J Ethnopharmacol. 2002; 81: 327-336.
58. Malekzadeh F et al. Antibacterial activity of black myroblan (*Terminalia chebula* Retz.) against *Helicobacter pylori*. Int J Antimicrob Agents. 2001; 18: 85-88.
59. Suchalatha S and Shyamala Devi CS. Protective effect of *Terminalia chebula* against experimental myocardial injury induced by isoproterenol. Indian Journal of Experimental Biology. 2004; 42: 174-178.
60. Miller AL. "Botanical influences on cardiovascular disease". Altern Med Rev. 1998; 3: 422-431.
61. Dwivedi S. Antianginal and cardioprotective effects of *Terminalia arjuna*, an indigenous drug, in coronary heart disease. Journal Association Physician India. 1994; 42: 287–289.
62. Bharani A, Ganguli A, Mathur LK, Jamra Y Raman PG. Efficacy of *Terminalia arjuna* in chronic stable angina: a doubleblind, placebo-controlled, crossover study comparing *Terminalia arjuna* with isosorbide mononitrate. Indian Heart Journal. 2002; 54: 170–175.
63. Sumitra M et al. Experimental myocardial necrosis in rats: role of arjunolic acid on platelet aggregation, coagulation and antioxidant status. Molecular and Cellular Biochemistry. 2001; 224: 135-142.
64. Gauthaman K et al. Effect of chronic treatment with bark of *Terminalia arjuna*: a study on the isolated ischemic reperfused rat heart. Journal of Ethnopharmacology 2001; 75: 197-201.
65. Caroline CG, Mohamed A, Magdi HY. Heat stress proteins and myocardial protection: experimental model or potential clinical tool? The International Journal of Biochemistry and Cell Biology. 1999; 31: 559–573.
66. Suzuki K et al. Heat shock protein 72 enhances manganese superoxide dismutase activity during myocardial ischemia-reperfusion injury, associated with mitochondrial protection and apoptosis reduction. Circulation. 2002; 106: I270-I276.
67. Gauthamana SK et al. *Terminalia arjuna* (Roxb.) protects rabbit heart against ischemic-reperfusion injury: role of antioxidant enzymes and heat shock protein. Journal of Ethnopharmacology. 2005; 96: 403-409.
68. Mohanty I et al. Mechanisms of cardioprotective effect of Withania somnifera in experimentally induced myocardial infarction. Basic Clin Pharmacol Toxicol. 2004; 94: 184-90.
69. Mohanty Ipseeta et al. Mechanisms of Cardioprotective Effect of *Withania somnifera* in Experimentally Induced Myocardial Infarction. Basic & Clinical Pharmacology and Toxicology. 2004; 94: 184-190.
70. Bagchi D, Bagchi M, Stohs SJ. Free radicals and grape seed proanthocyanidin extract: importance in human health and disease prevention. Toxicology. 2000; 148: 187-197.
71. Hollman PC, Hertog MG, Katan MB. Role of dietary flavonoids in protection against malignancy and coronary heart disease. Biochem Soc Trans. 1996; 24: 785–789.
72. Rimm EB, Giovannucci EL, Willett WC. Prospective study of alcohol consumption and risk of coronary disease in men. Lancet. 1991; 338: 464-486.
73. Hertog MGL, Feskens EJM, Kromhout D. Antioxidant flavonols and coronary heart disease risk. Lancet 1997; 16: 349-699.
74. Tunde Pataki et al. Grape seed proanthocyanidins improved cardiac recovery during reperfusion after ischemia in isolated rat hearts. Am J Clin Nutr. 2002; 75: 894- 9.