Global Journal of Medical research
Volume 12 Issue 4 Version 1.0 May 2012
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN : 0975-5888

The Beneficial Effects of Herbs in Cardiovascular Diseases

By Ipseeta Ray Mohanty , Suresh Kumar Gupta , Nimain Mohanty , Daniel Joseph & Yeshwant Deshmukh
MGM Medical College, Navi Mumbai

*Introduction -*The history of medicine dates back perhaps to the origin of human race and since time immemorial, man has made use of plants for the treatment of disease. Application of various herbal preparations which are highly effective for curing many diseases seem to have been in practice as early as 400 BC. The earliest reference to the use of medicinal herbs as a cure for a disease was found in Ebers Papyrus (2600 BC). In India, references to the curative properties of herbs in Rig Veda (period estimate between 3500-1800 BC) seem to the earliest records of use of plants in medicine. However, these references are very brief. More detailed account is available in the Ayur veda (about 2500 BC), the Indian System of Medicine. After the Vedas, appeared the two most important works on Indian System of Medicine, the Charak-Samhita (1000 BC) and Susruta-Samhita (800 BC). The Unani system of medicine further enriched the Herbal Materia Medica. Sheikh Abu Ali Seena (980-1033 AD), the author of AL QANOON described various plant medicines in his book Adviya Qalbia (Mamtani and Mamtani, 2005).

GJMR-B Classification : NLMC Code: WG 120, QV 770, QV 676

Strictly as per the compliance and regulations of:

The Beneficial Effects of Herbs in Cardiovascular Diseases

Ipseeta Ray Mohanty α , Suresh Kumar Gupta σ , Nimain Mohanty ρ , Daniel Joseph ω & Yeshwant Deshmukh ¥

I. Introduction

The history of medicine dates back perhaps to the origin of human race and since time immemorial, man has made use of plants for the treatment of disease. Application of various herbal preparations which are highly effective for curing many diseases seem to have been in practice as early as 400 BC. The earliest reference to the use of medicinal herbs as a cure for a disease was found in Ebers Papyrus (2600 BC). In India, references to the curative properties of herbs in Rig Veda (period estimate between 3500-1800 BC) seem to the earliest records of use of plants in medicine. However, these references are very brief. More detailed account is available in the Ayur veda (about 2500 BC), the Indian System of Medicine. After the Vedas, appeared the two most important works on Indian System of Medicine, the Charak-Samhita (1000 BC) and Susruta-Samhita (800 BC). The Unani system of medicine further enriched the Herbal Materia Medica. Sheikh Abu Ali Seena (980-1033 AD), the author of AL QANOON described various plant medicines in his book Adviya Qalbia (Mamtani and Mamtani, 2005).

Herbs have been used in medical treatment and some derivates (aspirin, digitalis) have become the mainstay of pharmacology. Medicinal plants have been observed to possess numerous activities with regard to cardiovascular system viz. antiplatelet, hypolipidemic, anti-inflammatory, hypoglycemic and hypotensive actions. For cardiovascular diseases, herbal treatments have been used in patients with congestive heart failure, systolic hypertension, angina pectoris, atherosclerosis, cerebral insufficiency, venous insufficiency, and arrhythmia.

This review compiles herbal medicines that affect the cardiovascular system both in terms of efficacy and safety as gleaned from the scientific literature that is available. The purpose of this review article is to critically evaluate the available evidence for the role of medicinal herbs in prevention and treatment of cardiovascular diseases. In order to simplify, these herbs are categorized under the primary diseases they treat. Nonetheless, most herbal medicines have multiple cardiovascular effects that may frequently overlap.

Author α: Dept of Pharmacology, Dr Ipseeta Ray Mohanty Professor MGM Medical College Kamothe, Navi Mumbai.
E-mail : ipseetamohanty@yahoo.co.in
Author ω ¥ : Dept of Pharmacology.
Author ρ : Dept of Paediatrics, MGM Medical College, Navi Mumbai.
Author σ :Department of Clinical Research and Pharmacology, Delhi Institute of Pharmaceutical Sciences & Research, New Delhi.

II. Angina Pectoris

a) *Carthamus tinctorius extract*

Carthamus tinctorius L. (safflower), a Chinese herbal medicine is widely used to prevent and treat cardiac disease in clinical practice. The anti-ischemic effects of a purified extract of C. tinctorius (ECT) both in vivo and in vitro was investigated. For in-vivo studies, an animal model of myocardial ischemic injury induced by left anterior descending coronary artery occlusion was studied. Pretreatment with ECT (100, 200, 400, 600 mg/kg body wt.) protected the myocardium from ischemia injury by limiting infarct size and improving cardiac function. For the in vitro experiment, neonatal rat ventricular myocytes were incubated in H2O2 and the direct cytoprotective effect of ECT against H2O2 exposure was studied. Pretreatment with 100-400 microg/ml ECT prior to H_2O_2 exposure significantly increased cell viability as revealed by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. ECT significantly reduced H2O2 induced cardiomyocyte apoptosis, as detected by Annexin V and flow cytometry. Phosphatidylinositol 3 kinase (PI3K) play a role in the signaling cascade involved in ECT mediated anti-apoptotic effects as the P13K inhibitor (LY294002) blocked the cytoprotective effect conferred by ECT. It was also observed that the rise in the intracellular level of reactive oxygen species (ROS) as assessed by 2',7'-dichlorofluorescin diacetate (DCFH-DA), was significantly inhibited by ECT treatment. The study provides evidence that the cardioprotective effect of ECT in myocardial ischemia is mediated via reducing oxidative stress induced damage and apoptosis (Han et al., 2009).

b) *Sini Decoction*

The cardioprotective activity and mechanism of Sini Decoction (SND) against anti-mitochondrial oxidation injury caused by myocardial ischemia and reperfusion (I/R) was investigated. Kun ming mice were randomly allocated to three groups: Control group, I/R

group and SND-treated group. At the end of experiment, hearts of mice were taken out for estimation of myocardial and mitochondria superoxide dismutase (SOD) activity, myocardium and mitochondrial malondialdehyde (MDA) content, mitochondrial swelling, lactic acid content of myocardium and Mn SOD mRNA expression. SND treatment increased the activity of myocardium and mitochondrial SOD ($P<0.01$), decreased the content of myocardium and mitochondrial MDA ($P<0.01$), decreased the lactic Acid content of myocardium, lighted the swelling of mitochondria ($P<0.01$) and altered the expression of Mn SOD mRNA ($P<0.01$). Sini decoction treatment prevented the mitochondrial oxidation injury caused by myocardial I/R. Cardioprotective effects may be attributed to increase in the expression of MnSODmRNA (Zhao et al., 2008).

c) Sanwei Tanxiang

The effect of Sanwei Tanxiang powder on myocardial pathologic change, myocardium lipid peroxidation and oxidative stress in an anesthetized rat model of I/R was studied. A rat model of regional myocardial I/R was established by 30 min occlusion of the left anterior descending coronary artery followed by 40 min reperfusion. The experimental animals were randomly divided into the sham operation, IR control group, positive control group and Sanwei Tanxiang treatment groups. The changes in myocardial creatine phosphokinase (CK), antioxidant enzymes and lipid peroxidation along with the ultrastructural changes were studied. In Sanwei Tanxiang group's significant myocardial protection, reduction in oxidative stress and improvement in ultrastructral pathological changes was observed as compared with the I/R model group. The authors conclude that the protective effects of Sanwei Tanxiang powder on anesthetized rat's hearts against myocardial I/R injury may be related to the antioxidant activity of Sanwei Tanxiang powder (Kou et al., 2008).

d) Curcumin

The protective effect of curcumin against myocardial injury was studied. A rat model of myocardial I/R injury was established by occluding the left anterior descending branch of coronary artery for 60 min and subsequently reperfusing for 60 min. Different dose of curcumin (20, 40 mg/kg) were administered by intravenous injection 5 min before the onset of ischemia. The changes in myocardial infarct sizes, the serum CK and lactate dehydrogenase (LDH), the myocardial lipid peroxidation and free fatty acid (FFA) content, the myocardial SOD and glutathione peroxidation (GSHPx) activity were estimated. Curcumin (20, 40 mg/kg) reduced the myocardial infarct sizes, the serum CK and LDH activity. The myocardial lipid peroxidation and FFA content declined significantly. Upregulation in antioxidant enzyme activity was observed. Curcumin exerted protective effects on myocardial I/R injury, which may be attributed to inhibition of lipid peroxidation, augmentation of endogenous antioxidants and improving myocardial metabolism (Cheng et al., 2005).

e) Chuanxiong-phthalide

The cardioprotective effect of Chuanxiong-pathalide A on endothelial cell injury induced by I/R was studied. Myocardial injury was induced of a 30-min normothermic global ischemia followed by 60 min reperfusion. The isolated rat hearts were perfused under constant pressure with Chuanxiong-pathalide A at the concentrations of 0.012 5 mg/ mL, 0.025 mg/mL and 0.05 mg/mL within 10 min followed by a 10-min washout period before the induction of I/R. Pretreatment with Chuanxiong-pathalide A produced a reduction in the incidence of reperfusion-induced ventricular fibrillation (VF) and ventricular tachycardia (VT). Pretreatment of the hearts with high dose of Chuanxiong-pathalide A (0.05 mg/mL) prior to the I/R, reduced the incidence of reperfusion-induced ventricular fibrillation (VF) and ventricular tachycardia (VT) to 37.5% as compared with non-pretreated control group ($P < 0.05$). The duration of occurrence of VF and VT in the group pretreated with Chuanxiong-pathalide A at dosages was significantly shorter than the non-pretreated control group. In the Chuanxiong-pathalide A treated group increase in coronary flow and significant reduction in the oxidative stress in the group pretreated with Chuanxiong-pathalide A as compared to control group was observed. In addition, enzyme immunoassays showed decrease in IL-1beta and TXB2/6-Keto-PGF1alpha ratio. Results demonstrated that chuanxiong-pathalide A pretreatment protected the endothelial function from the injury caused by I/R (Gao et al., 2005).

f) Acanthopanax senticosus saponins

The protective effect of Acanthopanax senticosus saponins (ASS) on myocardial I/R injury was investigated. The myocardial ischemia-reperfusion model was induced by ligating the left anterior descending coronary for 30 min and thereafter reperfusing for 120 min. The changes in myocardial infarct size, the serum CK and lactate LDH activity, serum lipid peroxidation content, SOD and GSH-Px activity and plasma endothelin (ET), angiotensin II (Ang II), prostacycline (PGI2) and thromboxane A2 (TXA2) levels and myocardial FFA content of infarct and non-infarct area were determined. In rats treated by ASS (in a dosage of 25, 50 and 100 mg/kg i.v. at 30 min after coronary occlusion), the myocardial infarct size was significantly reduced, the serum CK and LDH activity, the plasma ET, Ang II and TXA2 level and myocardial FFA content declined, while plasma PGI2 level and PGI2/TXA2 was significantly increased. In addition, serum MDA content declined SOD and GSH-Px activity increased markedly. ASS has protective effect on myocardial I/R injury, which may be due to its function of improving free radicals and myocardial metabolism,

decreasing plasma ET, Ang II and TXA2 levels and increasing plasma PGI2 level and PGI2/TXA2 ratio (Sui et al., 2004).

g) Shuangshen tongguan

The study was conducted to observe the effects of Shuangshen tongguan (SSTG) on infarction size and tumor necrosis factor-alpha (TNF-alpha), intercellular adhesion molecular-1 (ICAM-1) levels in serum during reperfusion injury of acute myocardial ischemia. To induce myocardial I/R injury, anterior descending branch of coronary artery was ligated and released. The size and weight of infarction area and the contents of TNF-alpha, ICAM-1 in serum were assayed by Nitroblue tetrazolium (N-BT) staining and ELISA respectively. The size and weight of infarct area and the contents of TNF-alpha, ICAM-1 in serum were significantly increased in the control group compared with the normal group. However, following treated with SSIG a decrease in TNF-alpha and ICAM-1 was observed. I/R injury resulted in release of TNF-alpha, ICAM-1. SSTG protected myocardium from I/R injury by suppressing over-secretion of TNF-alpha and ICAM-1 and reduced the size and weight of infarct area (Han et al., 2004).

h) Sasanquasaponin

The effects of sasanquasaponin (SQS), a traditional Chinese herb's in ameliorating I/R injury was assessed. Further, the possible role of intracellular Cl- homeostasis on SQS's protective effects during I/R was also elucidated. An in vivo experimental ischemia model was induced in mice (weight 27-45 g) using ligation of left anterior descending coronary artery. In vitro model of isolated perfused heart and isolated cultured ventricular myocytes were used. The in vivo results showed that SQS inhibited cardiac arrhythmias during I/R. Incidence of arrhythmias during I/R, including ventricular premature beats and ventricular fibrillation, was significantly decreased in the SQS-pretreated group ($P<0.05$). Results in perfused hearts showed that SQS suppressed the arrhythmias, prevented I/R induced decrease in contract force and promoted the force recovery from reperfusion. Furthermore, in-vitro intracellular Cl- concentrations ([Cl-]i) were measured using a fluorescence method in isolated ventricular myocytes. SQS slightly decreased [Cl-]i in non-hypoxic myocytes and delayed the hypoxia/reoxygenation-induced increase in [Cl-]i during ischemia and reperfusion ($P<0.05$). Our results showed that SQS protected mice against I/R-induced cardiac injury. Modulation of intracellular Cl- homeostasis by SQS plays a role in its anti-arrhythmia effects during I/R (Lai et al., 2004).

i) Psidium guajava L, Limonium wrightii and Okinawan medicinal plants

Effects of the aqueous extracts of Psidium guajava L. and Limonium wrightii, (medicinal herbs growing in Okinawa) at concentrations known to possess antioxidant activity were evaluated in an in vivo model of global I/R. Results were further compared with those of quercetin and gallic acid, major antioxidative components of P. guajava L. and L. wrightii, respectively. Both extracts significantly attenuated ischemic contracture during ischemia and improved myocardial dysfunction after reperfusion. Both plant extracts restored high-energy phosphates and reduced lipid peroxidation in the reperfused hearts. Quercetin and gallic acid also exerted similar beneficial effects. These results indicate that P. guajava L. and L. wrightii both have cardioprotective effects against myocardial I/R injury in isolated rat hearts, primarily through their antioxidant actions (Sakanashi, 2003).

j) Astragalus membranaceus

The effect of components isolated from Astragalus membranaceus on myocardial I/R injury was investigated. Myocardial I/R injury was induced by ligating the left anterior descending coronary artery. The effect of total saponins, total flavonids and astragaloside i.v. isolated from A. membranaceus on hemodynamics during acute myocardial ischemia, Na(+)-K(+)-ATPase activity, cAMP and MDA contents in the ischemic myocardium were assessed. The total saponins, total flavonids and astragaloside i.v. prevented the decline in cardiac function in rat heart injured by I/R in vivo, and decreased Na(+)-K(+)-ATPase activity in the ischemic myocardium. Results demonstrate that the total saponins increased the cAMP content and the total flavonids decreased the level of MDA production in the ischemic myocardium. The cardioprotective effects of different components isolated from A. membranaceus on the cardiac function in the process of I/R may be attributed to improving energy metabolism and antioxidant activity in the ischemic myocardium (Zhou et al., 2000).

k) Ginkgo biloba extract

Ginkgo biloba leaf extract (GBLE) contains many different flavone glycosides and terpenoides. GBLE showed significant antioxidant activity, exerted an anti-inflammatory effect on inflammatory cells (by suppressing the production of active oxygen and nitrogen species), a relaxing effect on vascular walls, an antagonistic action on platelet-activating factor, an improving effect on blood flow or microcirculation, and a stimulating effect on neurotransmitters. GBLE inhibited the oxidative decomposition of low-density lipoprotein (LDL), reduced the cell death in various types of neuropathy, and prevented the oxidative damage to mitochondria. The study using a model of I-R injury has also demonstrated the protective effect of GBLE on cardiac muscle and its antioxidative action in vivo. Favorable results have been obtained in double-blind, placebo-controlled, comparative trials of patients with memory disorders, obstructive arteriosclerosis, and

dementia. GBLE shows a very strong scavenging action on free radicals, and is thus considered to be useful for the treatment of diseases related to the production of free radicals, such as ischemic heart disease, cerebral infarction, chronic inflammation, and aging (Yoshikawa etal., 1999).

The cardioprotective efficacy and the total plasma antioxidant activity of a standardized Ginkgo biloba L. extract (GB) (300 mg/kg/day) or complexed with phosphatidylcholine (GB-PC; 1:2 w/w), after a 5 days oral administration was studied. On the 6th day, the total plasma antioxidant defence was determined by the TRAP and FRAPS assay. The hearts from all groups of animals were subjected to moderate ischemia (flow reduction to 1 ml/min for 20 min) and reperfusion (15 ml/min for 30 min). The recovery of left ventricular developed pressure (LVDP) at the end of reperfusion was 35-40% of the preischemic values in both control and vehicle rats, 50.2% in the GB group and 72.5% in the GB-PC pre-treated animals. CK outflow in the perfusate from the hearts of GB and GB-PC treated animals were restrained to a different extent vs. controls (by 71% GB-PC; by 22% GB); the rate of prostacyclin (6-keto-PGF1 alpha) release was far greater in GB-PC than in GB hearts. In parallel, the GB extract significantly increased the total antioxidant plasma capacity only when complexed with phospholipids. This indicated that there was an increase in bioavailability of phenolic antioxidants when suitably embedded within a lipophilic carrier. The results of this study demonstrated that complexation of Ginkgo biloba with phospholipids provided superior cardioprotection perhaps due to an increased plasma antioxidant activity (Carini et al., 2003).

The cardioprotective effects of EGb 761 on the release of nitric oxide (NO), the concentration of serum thiobarbituric acid reaction substance (TBARS), the activity of CK and the incidence of ventricular arrhythmias were investigated in an in vivo model of myocardial I/R injury. The hearts of the Wistar rats were subjected to 30 min of ischemia and 10 min of reperfusion in vivo. Different doses of EGb 761 (25, 50, 100, 200 mg/kg i.p.), SOD, l-arginine (50 mg/kg i.p.) and nitric oxide synthase inhibitor NG-nitro-l-arginine (NNA, 50 mg/kg i.p.) were administered to the I/R rats. EGb 761 (100 mg/kg) increased the signal intensity of NOFe2+(DETC)2 complex, while EGb 761 at 200 mg/kg showed an effect of decreasing the signal intensity of NOFe2+(DETC)2 complex. EGb 761 inhibited the formation of TBARS, the release of CK, and mitigated the incidence of ventricular arrhythmias in a dose dependent way. Both l-arginine and SOD increased the signal intensity of NOFe2+(DETC)2 complex and inhibited the formation of TBARS, the leakage of CK and the incidence of ventricular arrhythmia. In conclusion, EGb 761 demonstrated significant cardioprotective effects by means of adjusting the level of NO and inhibiting oxygen free radicals induced lipid peroxidation in myocardial I/R injury in vivo (Shen et al., 1999).

Ginkgo biloba extract, a containing kaempferol and quercetin esters, which are potent radical scavengers, was studied on various models of cardiac ischaemia, both in vitro and in vivo. Ginkgo biloba extract showed no significant effect on the cardiac function in vitro models of I/R injury. However, a significant decrease in the intensity of ventricular fibrillation during the reperfusion stage was observed. On normal or hypertrophied heart in vivo, Ginkgo biloba extract provided effective protection against the electrocardiographic disorders induced by ischaemia. On the different models of global or localized ischaemia (followed or not by reperfusion), a decrease of arrhythmia without change in cardiovascular parameters was regularly noted (Guillon et al., 1986).

To assess the cardioprotective and antioxidant effects of therapeutically relevant concentrations of Ginkgo biloba extract (EGb 761; 5, 50 or 200 microg/ml), its terpenoid constituents (ginkgolide A; 0.05 microg/ml and ginkgolide B; 0.05, 0.25 or 0.50 microg/ml), and a terpene-free fraction of EGb 761 (CP 205; 5 or 50 microg/ml), hemodynamic and electron spin resonance (ESR) analyses were performed on isolated ischemic and reperfused rat hearts. Hearts underwent 10 min of low-flow ischemia, 30 min of no-flow global ischemia, and 60 min of reperfusion. Test substances were added to the perfusion fluid during the last 10 min of control perfusion, low-flow ischemia and the first 10 min of reperfusion. The study results showed that in vitro exposure of hearts to EGb 761 (5 or 50 microg/ml) or to ginkgolides A and B (both at 0.05 microg/ml), or in vivo pretreatment of the rats with CP 205 delayed the onset of contracture during ischemia. A significant decline in left ventricular end-diastolic pressure was observed in the EGb 761, by ginkgolide A, and to a lesser extent by ginkgolide B, or by prior oral treatment with CP 205 treated hearts. Post-ischemic functional recovery was significantly improved by in vivo administration of CP 205, by perfusion with 5 microg/ml of EGb 761 or with both terpenoids as compared to untreated group but in vitro CP 205 was not effective. ESR analyses revealed that free radical concentrations in coronary effluents were markedly decreased by all treatments, except for the lowest concentration of ginkgolide B. The findings provide the first evidence that part of the cardioprotection afforded by EGb 761 involves a mechanism independent of direct free radical-scavenging property. These effects may partly be due to a specific action of its terpenoid constituents and the flavonoid metabolites that are formed after in vivo administration of the extract. These may act in a complementary manner to protect against myocardial I/R injury (Liebgott et al., 2000).

l) Polygonum multiflorum extract

'Dang-Gui Decoction for Enriching the Blood' (BE), is a traditional Chinese formulation consisting of Angelica sinensis and Astragalus membranaceus. It is used for stimulating red blood cell production as well as enhancing cardiovascular function. In the present study, the myocardial protection afforded by BE pretreatment against I/R injury in isolated-perfused rat hearts was studied. Polygonum multiflorum extract supplemented BE preparation (BEA) demonstrated a more complete and potent myocardial protection against IR injury. The results suggest that superior cardioprotective effects demonstrated by BEA may be linked to its ability to sustain the myocardial glutathione antioxidant status under conditions of I/R-induced oxidative stress. These beneficial effects may be because of synergistic interaction between the BE and Polygonum extract (Yim et al., 2000).

m) Panax ginseng

The protective effect of oral administration (one week) of Panax ginsengs (PG) extract (10 mg/ml in drinking water; 1.6 g/kg/day) on myocardial post-ischemic damage induced by hyperbaric oxygen (HBO) and on the loss in functionality of the endothelium in aorta ring preparations was investigated. The hearts from control rats (no-HBO and no-HBO-PG), and from rats exposed to HBO and to HBO after PG treatment were isolated and subjected to mild ischemia and then reperfused. Exposure to HBO greatly worsened the post-ischemic damage in controls. A significant rise of left ventricular end diastolic pressure (LVEDP) and coronary perfusion pressure (CPP) was observed in the control group. PG significantly attenuated the increase in LVEDP and CPP with respect to HBO-untreated rats. In HBO control rats the reduction of the vasorelaxant effect of acetylcholine on norepinephrine precontracted aortic rings, was markedly recovered by PG. A similar trend was observed in aortic rings challenged with the nitric oxide synthase inhibitor NG-monomethyl-L-arginine (56% recovery). These results strongly indicate that through an antioxidant intervention, PG prevented the myocardial I/R damage and the impairment of endothelial functionality induced by reactive oxygen species following exposure to HBO. The antioxidant activity of PG seems to be too weak (0.05-0.5 mg/ml). This suggests the indirect antioxidant action of the drug (endothelial nitric oxide synthase stimulation) also plays an important role (Maffei Facino et al., 1999).

n) Scutellaria baicalensis Georgi

Scutellaria baicalensis Georgi is a Chinese herbal medicine used to treat allergic and inflammatory diseases. The constituent flavones reported to have antioxidant properties may be responsible for the medicinal effects of S. baicalensis root. It was investigated whether S. baicalensis could confer protection in a cardiomyocyte model of ischemia and reperfusion. The intracellular fluorescent probes 2',7'-dichlorofluorescin diacetate (sensitive to H2O2 and hydroxyl radicals) and dihydroethidium (sensitive to superoxide) were used to assess intracellular reactive oxygen species, and propidium iodide was used to assess cell viability in cultured embryonic cardiomyocytes. S. baicalensis extract (SbE) significantly attenuated generation of free radicals during transient hypoxia and during exposure to the mitochondrial site III inhibitor antimycin A, as measured by fluorescent probes. Reduced oxidative stress was associated with improved survival and function. Cell death after ischemia/reperfusion decreased significantly in S. baicalensis treated cells ($p<0.001$). After antimycin A exposure, S. baicalensis decreased cell death from 49+/-6 % in untreated to 23+/-4 % in treated cells. Return of contraction occurred in S. baicalensis-treated cells but was not observed in control cells. Studies have revealed that baicalein, a major flavone component of SbE possess antioxidant property and can directly scavenge superoxide, hydrogen peroxide, and hydroxyl radicals. Collectively, these findings indicate that SbE and its constituent flavones such as baicalein can attenuate oxidant stress and protect cells from lethal oxidant damage in an I/R model (Shao et al., 1999).

o) Crataegus oxyacantha

The effect of water-soluble fraction of Crataegus (Crataegus extract) was studied on the cardiac mechanical and metabolic function in the isolated, perfused working rat heart. Ischemia for 15 min was induced by removing afterload pressure, and reperfusion of 20 min was produced by returning it to the original pressure. In the control (no drug) heart, ischemia decreased mechanical function to the lowest level, which did not recover even after the end of reperfusion. Crataegus extract (0.01 or 0.05%) was applied to the heart from 5 min before ischemia through the first 10 min after reperfusion. With the high concentration of Crataegus extract (0.05%) the mechanical function recovered during reperfusion incompletely without increasing coronary flow, but the low concentration of Crataegus extract (0.01%) did not. In the heart treated with the high concentration of Crataegus extract, the reperfusion-induced recovery of the energy metabolism was accelerated. The level of lactate during ischemia was lower than that in the control heart, though the myocardial levels of free fatty acids during I/R were not greatly affected. These results demonstrate that Crataegus extract (0.05%) has a cardioprotective effect on the ischemic-reperfused heart. However, the cardioprotective effect is not accompanied by an increase in coronary flow (Nasan et al., 1993).

The effect of the pretreatment with the powder of crataegus oxyacantha on the release of LDH during I/R was studied in an isolated rat heart model. Male Wistar rats were divided into control and crataegus

treated group. For the control group, the standard diet was mixed with a 2% crataegus powder standardized to 2.2% flavonoids. The investigations started 3 months after commencing the treatment. The hearts were isolated and a retrograde perfusion was performed at constant pressure according to the technique of Langendorff. The experimental protocol comprised of 10 min equilibration, according to the technique of Langendorff. The experimental protocol comprised of 10 min equilibration, 110 min occlusion of the left anterior descending coronary artery, and 30 min reperfusion. The coronary effluent was sampled for the LDH determination at various time points (5, 30, 90, 120 and 150 min). The LDH activity increased slightly during the ischemia, and markedly as soon as the heart was reperfused. Crataegus pretreatment resulted in significant decrease in LDL activity. The attenuation of the LDH release by crataegus pretreatment suggests preservation of the cell membrane and significant myocardial protection (Al Makdessi et al., 1996).

The cardioprotective effects of a standardized extract from leaves with flowers of Crataegus (WS-1442; content of oligomeric procyandins [OPC]: 18.75%) have been documented in various studies. To elucidate its cardioprotective mechanism, the active constituents involved in these effects of WS-1442 were identified. Exhausting partitioning between ethyl acetate/water and successive ultrafiltration of the aqueous layer led to the quantitative recovery of three fractions, which were tested for their in vitro radical scavenging (RS) and human neutrophil elastase (HNE) inhibitory activity. The OPCs of Crataegus extracts possess superior antioxidant activities than flavone derivatives or other constituents. In addition, the oligomeric components are more potent inhibitors of HNE. Oral administration of 20 mg/kg/d of the OPC-rich fraction to rats afforded comparative protection against I/R induced pathologies as treatment with 100 mg/kg WS-1442. These observations indicate that radical scavenging and elastase inhibitory activities could indeed be involved in the observed cardioprotective effects of WS-1442. The study emphasizes that OPCs are major orally active constituents of WS-1442. Thus, Crataegus extracts used therapeutically for cardiovascular diseases should be analyzed and standardized for their OPC-content (Chatterjee et al., 1997).

p) Panax pseudoginseng

Trilinolein, a natural plant triacylglycerol, known to have myocardial protective effects was evaluated in vivo. This study investigated if inhibition of calcium influx and alteration of SOD activity are involved the myocardial protection mechanism of trilinolein. In isolated cardiomyocytes, pretreatment with 10(-9) M trilinolein significantly reduced Ca2+ influx stimulated by hypoxia/normoxia. Pretreatment with 10(-7) M trilinolein (for 15 min) in isolated perfused rat heart subjected to 60 min global hypoxemia without reperfusion significantly reduced infarct size. SOD-mRNA assay was analysed by Northern blot. Pretreatment with 10(-7) M trilinolein to in vivo rat heart subjected to 30 min ischaemia and 10 min reperfusion, significantly reduced oxidative stress. It prevented the rise in SOD-mRNA. These results reconfirm the myocardial protection of trilinolein. Cardioprotection may be attributed to antioxidant activity and inhibition of Ca2+ influx (Chan et al., 1999-2006).

q) Withania somnifera

The cardioprotective effects and mechanisms of Withania somnifera (Ws), in the setting of I/R injury were assessed. Wistar rats were divided into three groups and received orally saline (sham, control I/R) and Ws-50 mg/kg (Ws-I/R), respectively, for 1 month. On the 31st day, in the control IR and Ws-IR group rats, left anterior descending coronary artery occlusion was undertaken for 45 min followed by 1 h reperfusion. Subsequently, all the animals were sacrificed for biochemical, immunohistochemical {Bax and Bcl-2 protein}, terminal deoxynucleotidyl transferase biotin-dUTP nick end labeling (TUNEL) positivity and histopathological studies. Post-ischemic reperfusion injury resulted in significant cardiac necrosis, apoptosis, and decline in antioxidant status and elevation in lipid peroxidation in the I/R control group as compared to sham. Ws prior-treatment favorably restored the myocardial oxidant-antioxidant balance, exerted marked anti-apoptotic effects {upregulated Bcl-2 ($p<0.001$) protein, decreased Bax ($p<0.01$) protein, and attenuated TUNEL positivity ($p<0.01$)}, and reduced myocardial damage as evidenced by histopathologic evaluation. It is speculated that the antioxidant and anti-apoptotic properties of Ws may contribute to the observed cardioprotective effects (Mohanty IR et al., 2008).

r) Bacopa monniera

Bacopa monniera(Bm), a medicinal herb commonly known as Brahmi is widely used in the Indian system of medicine. The cardioprotective effects of Bm was studied in the Langendorff model of myocardial I/R injury. Effect of Bm on cardiomyocyte apoptosis and antioxidant status following I/R injury was investigated. Forty-eight rats were randomly divided into four groups (12 in each group): sham group (no I/R injury), Bm control group (orally fed Bm at a dose of 75 mg/kg, for three weeks); I/R control group (subjected to I/R-induced myocardial injury) and Bm-treated group (same protocol as I/R control group except that rats also fed Bm). Post-ischaemic reperfusion injury resulted in significant cardiac necrosis, apoptosis, depression of heart rate, decline in antioxidant status and elevation in lipid peroxidation. Oral administration of Bm per se for three weeks to healthy rats caused augmentation of myocardial antioxidants, SOD, catalase and glutathione, along with induction of heat shock protein 72 (HSP72).

I/R induced biochemical and histopathological perturbations were significantly prevented by Bm(75 mg/kg) pre-treatment. Interestingly, Bm also restored the antioxidant network of the myocardium and reduced myocardial apoptosis, caspase 3 and Bax protein expression. Histopathological studies and myocardial creatine phosphokinase content further confirmed the cardioprotective effects of Bm (75 mg/kg) in the experimental model of I/R injury. The study provides scientific basis for the putative therapeutic effect of Bm in ischaemic heart disease (Mohanty IR et al., 2010).

s) Curcuma longa

The cardioprotective potential of Curcuma longa (Cl) in the I/R model of myocardial infarction was investigated. Wistar rats were divided into three groups and received saline orally (sham, control I/R group) and Cl 100 mg/kg (CL-100 treated group) respectively for one month. On the 31st day, rats of the control I/R and Cl treated groups were subjected to 45 min of occlusion of the LAD coronary artery and were thereafter reperfused for 1 h. I/R resulted in significant cardiac necrosis, depression in left ventricular function, decline in antioxidant status and elevation in lipid perodixation in the control I/R group as compared to sham control. Myocardial injury due to I/R was significantly prevented by Cl treated group. Cl treatment resulted in restoration of the myocardial antioxidant status and favorable modulation of hemodynamic parameters as compared to control I/R. Furthermore, I/R-induced lipid peroxidation was significantly inhibited by Cl treatment. The beneficial cardioprotective effects also translated into the functional recovery of the heart. Cardioprotective effect of Cl may be attributed to the suppression of oxidative stress and improvement in ventricular function. Histopathological examination further confirmed the protective effects of Cl on the heart (Mohanty et al., 2004). Further, the effect of Cl on myocardial apoptosis was studied in the I-R model of myocardial injury. Cl pre-treatment reduced the Bax/Bcl-2 ratio and demonstrated significant ant-apoptotic activity. The antioxidant and anti-apoptotic properties of Cl may contribute to the cardioprotective effects (Mohanty et al., 2006).

III. Congestive Cardiac Failure (Chf)

a) Corydalis yanhusuo

Corydalis yanhusuo, a Chinese medicinal plant is reported to possess significant cardioprotective effects. The main active principle, l-tetrahydropalmatine, is responsible for its pharmacological effects. The protective effects of Corydalis yanhusuo was evaluated in a rat heart failure model. Rats were orally fed with 50, 100, or 200 mg/ kg of ethanolic extract of Corydalis yanhusuo daily, from the 7th day after surgery and thereafter subjected to coronary artery ligation. The cardiac function, plasma atrial natriuretic peptide (ANP), relative heart and lung weights, infarct size and ventricular dilatation after treatment for 8 weeks were measured. Corydalis yanhusuo treatment led to a significant reduction in infarct size and improvement in cardiac function as demonstrated by lower LVEDP and elevated +/-dp/dt(max). Corydalis yanhusuo significantly reduced left ventricular (LV)/body weight ratio, lung/body weight ratio and inhibited neurohormonal activation. The study concluded that Corydalis yanhusuo exerted salutary effects on heart failure induced by myocardial infarction in rats (Wu L et al, 2007).

b) Shenqi Fuzheng

The effect of Shenqi Fuzheng injection (SFI) on the humoral immunity (IgG IgM IgA), cellular immunity (T-lymphocyte subsets), SOD activity and plasma viscosity in CHF patients were studied. Sixty patients with CHF, with heart function of NYHA grade II-IV were randomly divided into two groups. The treaded group was treated with SFI 100 ml, and the control group was treated by 10 mg nitroglycerine injection. To detect the IgG, IgM, IgA, T-lymphocyte subsets, SOD, lipid peroxidation and plasma viscosity, venous blood from cubital vein was collected before and after treatment. Results demonstrate that the heart function improved markedly in the treated group as compared to the control group ($P < 0.05$). The left ventricular ejecting fraction (LVEF) and end systolic volume (ESV) were improved in both group ($p < 0.05$, $p < 0.01$), and the improvement in the treated group was superior to the control group ($p < 0.05$). In the treated group, the CD4, SOD level and CD4/DC8 ratio increased ($p < 0.05$), whereas lipid peroxidation, IgG and IgM reduced ($p < 0.05$) significantly compared to the control group. Significant improvement in the plasma viscosity was seen in the treatment group. SFI improved the immune function of CHF patients. Shenqi Fuzheng injection (SFI) has potential as an adjuvant therapy in the treatment for CHF (Liu H et al., 2005).

c) Manshuailing

The clinical effect of manshuailing in patients with CHF was evaluated. A total of 90 heart failure patients were randomly divided into 2 groups: 45 cases in the routine treatment group (RT) received general therapy including diuretics and digitalis, and 45 cases in the Chinese herbal medicine group (CH) were treated for six weeks with the above medicine, with additional manshuailing oral liquid for six weeks. The clinical effect was summarized six weeks after treatment. Total effect rate was 82.2% and 62.2% in CHF and RT group respectively. Compared with pretreatment, heart function including stroke volume (SV), stroke volume index (SVI), cardiac index (CI), distance of inter-ventricular septal to mitral valve (EPSS) were all improved significantly in both groups ($p < 0.05$ or $p < 0.01$). The cardiac function was superior in the CH group as compared to the RT group ($p < 0.05$ or $p<$

0.01). Manshuailing oral liquid alleviated clinical symptom, decreased EPSS, and improved heart function (Yang et al., 2003).

d) Zhimu and huangqi combination

The efficacy of Zhimu in treating cardiac hypertrophy associated with CHF was evaluated. Mice cardiac hypertrophy model was established by s.c. Isoproterenol (ISO), 2 times per day for 14 days and heart-weight-index was measured. Zhimu and Huangqi were given orally alone or jointly for 14 days. Abdominal aorta banding operation was done in mice and 3 weeks after operation, they were administrated for 2 weeks, and then run-time (exercise capacity), quiet heart rate, heart rate after ISO and heart-weight-index were measured. Cardiac hypertrophy model mice were administrated for 12 days, and the mortality and dying time of mice in cold (-20 degrees C) and heat (45 degrees C) stimulative condition were observed. Zhimu could cut down the increasing of heart rate induced by ISO, decreased significantly heart-weight-index in cardiac hypertrophy mice, reduced the quiet heart rate and prolonged the run time in abdominal banding model. Zhimu combined with Huangqi improved the ISO response in abdominal banding model mice, reduce the mortality and delayed dying time of mice in stimulative condition. Zhimu combined with Huangqi slowed down heart rate, enhanced the reserve force of the heart, and improved the response capacity of cardiac hypertrophy mice in stimulative condition (Hu etal., 2003) .

e) Crataegus oxyacantha (aubepine)

Crataegus oxyacantha (Aubepine, Hawthorn), was used by European herbalist in the first century A. D. Until the 19th century, its true potential for treatment of heart disease was not fully explored. The leaves, flowers, and berries of hawthorn contain a variety of bioflavonoid-like complexes that appear to be primarily responsible for the cardiac actions of the plant. Bioflavonoids found in C. oxyacantha include oligomeric procyanidins (OPCc), vitexin, quercetin, and hyperoside. These ingredients are responsible for its beneficial cardiovascular effects (Ju LY et al., 2005). A placebo controlled, randomized, parallel group, multicentre trial was conducted to assess the efficacy and safety of a standardized extract of fresh berries of Crataegus oxyacantha L. and monogyna Jacq. (Crataegisan) in patients with grade NYHA class II cardiac failure. A total of 143 patients (72 men, 71 women, mean age of 64.8 (8.0 years) were recruited and treated with 3 times 30 drops of the extract (n = 69) or placebo (n = 74) for 8 weeks. The primary endpoint included the evaluation of change in exercise tolerance determined with bicycle exercise testing; secondary variables included the blood pressure-heart rate product (BHP). Subjective cardiac symptoms at rest and at higher levels of exertion were assessed by the patient on a categorical rating scale. The difference between the treatment groups was 8.3 watts in favor of the standardized extract of fresh Crataegus berries ($p = 0.045$). Although, the results were not statistically significant, changes in BHP at 50 watts and at comparable maximum load were in favour of Crataegus extract. The subjective assessment of cardiac symptoms at rest and at higher levels of exertion did not change significantly and the patient and investigator overall assessment of efficacy were similar for the two groups. The medication was well tolerated and had a high level of patient acceptability. These results are clinically significant as the symptoms of dyspnoea and fatigue do not correct until a significantly higher wattage has been reached in the bicycle exercise test. The study concluded that NYHA II patients showed improvement in their heart failure condition under long term therapy with the standardized extract of fresh Crataegus berries (Degenring et al., 2003).

f) Berberine

Berberine, is an alkaloid from Hydrastis canadensis L., a Chinese herb Huanglian. It is widely used in traditional Chinese medicine as an antimicrobial for the treatment of dysentery and infectious diarrhea. Berberine and its derivatives, tetrahydroberberine and 8-oxoberberine have significant beneficial cardiovascular effects. Berberine has positive inotropic, negative chronotropic, antiarrhythmic, and vasodilator properties. Both derivatives of berberine have antiarrhythmic activity. Cardiovascular effects of berberine and its derivatives are attributed to the blockade of K+ channels (delayed rectifier and K(ATP)) and stimulation of Na+ -Ca(2+) exchanger and prolongation of the duration of ventricular action potential. Its vasodilator activity has been attributed to multiple cellular mechanisms. The cardiovascular effects of berberine suggest its possible clinical usefulness in the treatment of heart failure (Lau et al, 2001).

g) Digitalis purpurea

Digoxin has been commonly used to treat patients with CHF, over the past 200 years. William Withering was able to identify Digitalis purpurea as the essential ingredient in a prescription dispensed by a herbalist, and systematically proceeded to show its value in patients with cardiac failure (Krikler, 1985). He identified the cardinal symptoms of digitalis intoxication and worked out effective rules for the prescription of an infusion of digitalis.

Use of digitalis for the treatment of patients with CHF and sinus rhythm remains controversial. To ascertain the proper therapeutic role of digitalis, the published clinical evidence of digitalis was critically appraised. A search of the English literature from 1960 to 1982 identified 736 articles, of which 16 specifically addressed the clinical evaluation of digitalis therapy for patients with CHF and sinus rhythm. Only two double-blind, placebo-controlled trials provided clinically useful information. One study showed that digoxin therapy

could be withdrawn successfully in elderly patients with stable CHF. The other showed that patients with chronic heart failure and an S3 gallop benefited from digoxin therapy (Wray et al., 1985; Mulrow et al., 1984).

Clinical trials have demonstrated the benefits of the use of digoxin on exercise tolerance, ejection fraction, and neurohormone production. The Digoxin Investigators Group trial has recently provided strong evidence for the long-term benefits of digoxin on morbidity for patients with heart failure (Demers et al., 1999).

h) Red Ginseng

The beneficial effect of red ginseng in CCF was evaluated and compared with Ginseng. Forty-five patients with class IV cardiac function were divided into three groups of fifteen patients each: group I (digoxin group), group II (Red Ginseng group) and group III (Red Ginseng plus digoxin group). After treatment, the improvement in the hemodynamic and biochemical indexes in Red Ginseng group and Red Ginseng plus digoxin group were greater than those of digoxin group, and group Red Ginseng plus digoxin group was the most significant amongst all. The results suggested that Red Ginseng and digoxin act synergistically in the treatment of CCF. Red Ginseng is an effective and safe adjuvant for effective management of CHF (Ding et al., 1995).

i) Terminalia Arjuna

The beneficial effect of Terminalia Arjuna, an Indian medicinal plant, in CCF was studied in a double blind cross over study. Terminalia Arjuna was administered to twelve patients with refractory chronic CHF (Class IV NYHA), related to idiopathic dilated cardiomyopathy (10 patients); previous myocardial infarction (one patient) and peripartum cardiomyopathy (one patient). Terminalia Arjuna bark extract (500 mg 8-hourly) or placebo was administered for 2 weeks each, separated by 2 weeks washout period. The clinical, laboratory and echocardiographic evaluation was carried out at baseline and at the end of Terminalia Arjuna and placebo therapy. Thereafter, the results were compared. Terminalia Arjuna, compared to placebo, was associated with improvement in symptoms and signs of heart failure, improvement in NYHA Class (Class III vs. Class IV), decrease in echo-left ventricular end diastolic and end systolic volume ($P < 0.005$) indices, increase in left ventricular stroke volume index $P < 0.05$) and increase in left ventricular ejection fractions ($P < 0.005$). Further, on long term evaluation in an open design Phase II study, participants continued Terminalia Arjuna in fixed dosage (500 mg 8-hourly) in addition to flexible diuretic, vasodilator and digitalis dosage for 20-28 months (mean 24 months) on outpatient basis. Patients showed continued improvement in symptoms, signs, effort tolerance and NYHA Class, with improvement in quality of life (Bharani et al., 1995).

j) Sini decoction

The study was conducted to investigate the protective effects of Sini decoction (SND) on Adriamycin-induced heart failure and also elucidate its cardioprotective mechanism. SD rats were randomly divided into three groups: control group, heart failure model group and SND group. Adriamycin was injected in the rats of Adriamycin model group and SND group by caudal vein. After injection, the rats in SND group were given SND (3.75 g/kg) per day, per orally. Three weeks later, protein expressions of Bid and Bcl-xl were detected by immunohistochemistry; mRNA expression ratio of Bcl-xl/Bcl-xs was detected by RT-PCR and apoptosis rate was determined by flow cytometry. The protein expression of Bcl-xl and mRNA ratio of Bcl-xl/Bcl-xs decreased, while the protein expression of Bid and apoptosis rate significantly increased in the SND treatment group as compared with the control group. SND could decrease cell apoptosis, increase the protein expression of Bcl-xl, increase bcl-xl/bcl-xs mRNA ratio and decrease Bid protein expression. Bcl-xl plays an important role in ADR-induced heart failure in rats. The mechanism of SND cardioprotection may be related to modulation of key regulatory proteins of apoptosis, Bcl-xl and Bid (Zhao et al., 2009).

k) Wenxin Keli

The effect of Wenxin Keli treatment on ISO induced heart failure was studied in rats. Sixty six-week old male Wistar rats were randomized to six groups. The rats of control group received distilled water every day. Wenxin Keli (9 mg/kg) was administered for 2 weeks every day. The rats in Wenxin Keli and control group received two subcutaneous injections (85 mg/kg of ISO, separated by a 24 hour interval). The rats in valsartan and ISO group received two subcutaneous injections (85 mg/kg) of ISO, and received valsartan 30 mg/kg for 2 weeks every day. Echocardiogram measurement in rats was carried out after 4 weeks and 10 weeks feeding. In the In the ISO group, echocardiogram indicated that left ventricular internal diameter at diastolic phase (LVIDd), left ventricular internal diameter at systolic phase (LVIDs), LV percent fractional shortening (FS) and LV ejection fraction (EF) were reduced. Treatment with valsartan for 4 weeks significantly increased FS and EF as compared with the ISO group. However, treatment with Wenxin Keli for 10 weeks did not significantly change the LVIDs, FS, EF compared to the ISO group. 10 weeks of treatment with valsartan and Wenxin Keli resulted in significant improvement in the hemodynamic parameters: LVEDP, left ventricular systolic pressure (LVSP), and dp/dt(max). It was concluded that Wenxin Keli significantly improves the ISO induced cardiac dysfunction (Zhou et al., 2007).

IV. Hypertension

a) Asttragalus complanatus

The effects of total flavonoid fraction of Asttragalus complanatus on blood pressure in conscious spontaneously hypertensive rats (SHR) and hemodynamics in anesthetized SHR was investigated. It was observed that the total flavonoid fraction of Asttragalus complanatus (100, 200 mg/kg) decreased the blood pressure of conscious SHR significantly (decreasing 7.1%, $P < 0.05$ and 9.3%, $p < 0.01$ respectively) and total peripheral resistance (decreasing 20%, $P < 0.05$). However, there was no significant change in heart rate and cardiac output. It was concluded that the total flavonoid fraction of Asttragalus complanatus possesses significant antihypertensive effects by virtue of decreasing the total peripheral resistance (Xue et al., 2002).

b) Allium sativum

Allium sativum commonly referred to as garlic, possess a number of beneficial cardioprotective effects. The active ingredient allicin is responsible for its therapeutic effects. Qidwai et al, 2000 conducted a study to find out whether individuals with blood pressure (BP) on the lower side consume more garlic in their diets. A questionnaire was developed and was administered to 101 adult subjects, presenting to the Family Practice Centre of a hospital in the city of Karachi, Pakistan. It was estimated that average garlic use was 134 grams per case per month. Subjects with BP on the lower side were found to consume more garlic in their diets ($p < 0.05$). This study demonstrates that individuals whose blood pressures (BP) are on the lower side are likely to consume more garlic in their diets.

The effect of garlic on pulmonary pressures in rats subjected to alveolar hypoxia and on vasoconstriction in isolated pulmonary arterial rings was also studied (Fallon et al., 1998). Garlic gavage (100 mg/kg wt) for 5 days resulted in complete inhibition of acute hypoxic pulmonary vasoconstriction compared with the control group. These studies document that garlic blocks hypoxic pulmonary hypertension in vivo and demonstrates a combination of endothelium-dependent and -independent mechanisms responsible for the effect in pulmonary arterial rings. Meta-analysis concluded that garlic possess significant hypotensive effects only in patients with increased systolic pressure (Reinhart et al., 2008). Compared to placebo, garlic preparations were found to be superior in reducing BP in individuals (Ried et al, 2008). The beneficial cardioprotective action of garlic in essential hypertension (HTN) was studied. The antihypertensive effect of garlic was observed in 20 patients with HTN receiving garlic pearls preparation for a period of two months (Dhawan and Jain, 2008).

c) Apium graveolens

Apium graveolens, commonly known as celery, according to Chinese theory is known to be effective for HTN associated with liver disease. In Mainland China, celery was useful in reducing HTN in 14 out of 16 patients. The juice was mixed with equal amount of honey and about 8 ounces were taken orally three times each day for up to one week. It significantly reduced systolic and diastolic BP. The difference of BP in human beings before and after treatment was found to be significant ($p<0.05$), indicating that seeds of A. graveolens possess significant hypotensive effect. Fresh celery juice can be mixed with vinegar to relieve dizziness and headache and shoulder pain associated with HTN. It is also effective in HTN associated with pregnancy and climacteric (Gharooni and Sarkarati, 2000).

d) Artemisia vulgaris L.

Artemisia vulgaris L. dried leaves were extracted in distilled water and chloroform. Two partition fractions from the aqueous extracts and four partition fractions from the chloroform extracts were tested on male Sprague-Dawley rats using both the in situ mesenteric circulation and the isolated perfused mesentery. Administration of 10% w/v solutions of water extract fractions FGN 63-1 and FGN 63-2 of A. vulgaris in the isolated perfused rat mesentery model was highly effective in reversing the hypertensive action induced by norepinephrine with no significant effect on heart rate in either the normotensive or hypertensive states (Tigno et al, 2000).

e) Ajmaloon

Ajmaloon, an herbal drug, was studied in anesthetized rabbits and monkeys for its effect on the arterial BP, heart rate and baroreceptor-heart rate reflex. Intravenously administered Ajmaloon produced a dose-dependent hypotensive response in both the species without any significant effect on the heart rate. In Ajmaloon treated animals, loss of tachycardia response to fall in arterial pressure indicated that the drug suppresses normally existing sympathetic excitatory influence in response to hypotension. Even after intravenous administration of 100 mg/kg Ajmaloon (a dose much higher than the prescribed highest oral dose for humans), Baroreflex regulatory heart rate response to hypertension remained intact. Intact baroreflex regulation of arterial BP in response to hypertension in Ajmaloon treated group suggests that Ajmaloon does not interfere with the normal BP regulatory mechanism through arterial baroreceptors during hypertension. Study concluded that Ajmaloon possess significant hypotensive effect (Fahim et al, 2005).

f) Bidens pilosa Linn

The hypotensive effect of Bidens pilosa Linn (Asteraceae) leaves was evaluated in SHR, salt-loading hypertensive rats (SLHR) and normotensive Wistar rats, using the indirect (tail-cuff) method. Acute changes in urine volume and urinary excretion of Na+ and K+ were also studied. It was found that the hypotensive effect of the extract was more remarkable in hypertensive than in normotensive rats. Although not statistically significant, the urinary excretion of Na+ was decreased by 36% in SHR and the excretion of K+ increased by 35% in normotensive rats. These results suggest that the extract has significant hypotensive effect by virtue of its vasodilatory property (Dimo et al., 1999)

g) Cecropia obtusifolia (Moraceae)

The antihypertensive efficacy of the leaf extract of Cecropia obtusifolia was evaluated. Cecropia obtusifolia leaf extract demonstrated significant antihypertensive when administrated intravenously to conscious spontaneous hypertensive rats. Forty-five minutes after injection, the maximum fall in arterial pressure (-23.5% relative to pre-injection values) was seen. At the end of the 180 min observation period, recovery was not complete. The extract was administered to pre-hypertensive SHR and normotensive rats. The fall in BP was more conspicuous in the two SHR groups and was not accompanied by changes in cardiac frequency in any group (Salas et al, 1888).

h) Crataegus pinnatifida

Crataegus pinnatifida, commonly known as hawthorn's decoction has been used in China for treatment of HTN for thousands of years. The active ingredients that contribute to hawthorn's beneficial effects on heart are flavonoids and oligomeric procyanidins. In experiments with anesthetized rabbits, intravenous administration of the extract preparation lowered the BP for up to 3 hours (Bensky and Gamble, 1990). Grataegic acid was identified as the hypotensive principle. Mechanisms of action of Crataegus involve a broad-based influence on the cardiovascular system. The hypotensive activity is mediated via vasorelaxation resulting from nitrous oxide stimulation, significant antioxidant activity, and a tonic action on cardiac myocytes (Schüssler et al, 1995).

i) Carica papaya (L.)

The hypotensive action of crude ethanolic extract from the unripened fruit of Carica papaya was evaluated and compared with hydrallazine. Both hydrallazine (200 microg/100 g i. v) and Carica papaya extract (20 mg/kg. i.v) produced a significant depression of mean arterial pressure (MAP) in all groups ($p < 0.01$ vs controls). The hypotensive effect of the extract was more profound. It produced about 28% more depression of MAP than hydrallazine in the hypertensive groups. The extract (10 microg/mL) produced relaxation of vascular muscle tone in vitro studies using isolated rabbit arterial (aorta, renal and vertebral) strips. These effects were however, attenuated by phentolamine (0.5-1.5 microg/mL). Based on the study results it is concluded that the fruit juice of C. papaya produces significant hypotension attributed to mainly the inhibition of alpha-adrenoceptor activity (Eno et al, 2000).

j) Casimiroa edulis

Casimiroa edulis seed is reported to possess hypotensive activity. The methanolic extract of Casimiroa edulis contains many active ingredients: synephrine acetonide, N-monomethyl histamine, N,N-dimethyl histamine, proline, N-methylproline, gamma-aminobutyric acid and casimiroedine. These components were isolated. Their antihypertensive activity was tested in experimental animals. In anesthetized rats, both histamine derivatives produced transient hypotension mediated via H1-histaminergic receptors and in the case of N,N-dimethyl histamine, via nitric oxide release. Synephrine acetonide produced transient hypertension and tachycardia, mediated via alpha and beta-adrenergic receptors, respectively. N-methyproline, proline and gamma-aminobutyric acid elicited pronounced and prolonged hypotension. Casimiroedine did not significantly affect on the BP of anesthetized rats. However, it was capable of lowering blood pressure persistently in anesthetized guinea pigs. It was concluded that several active components of C. edulisis are responsible for its hypotensive effects. Histamine derivatives acting on H1-receptors are responsible for its immediate effect. More prolonged hypotension is attributed to the mixture of amino acids through an unknown mechanism, as well as by casimiroedine, possibly by activation of H3-receptors (Magos et al, 1999).

k) Cecropia lyratiloba

The effect of methanol extract (ME) of Cecropia lyratiloba and its flavonoid fraction (FF) on the contractility of cardiac, vascular and tracheal smooth muscles was evaluated. Adrenaline-induced contractions of the aorta were inhibited by both ME and FF in a concentration-dependent manner. The flavonoids isolated from FF, namely iso-orientin and a mixture of orientin and isovitexin, were also tested in the aorta. Results show that this flavonoid is not responsible for the vasorelaxant effects of ME and FF. The vascular relaxation of FF was abolished in the presence of N(omega)-nitro-L-arginine methyl ester, an inhibitor of nitric oxide synthase. It was concluded that the endothelium-dependent vasodilation induced by FF is mediated by the release of nitric oxide (NO). The vascular relaxation demonstrated by ME and FF validate its traditional use for treatment of arterial hypertension (Ramos et al 2006).

l) Panax ginseng

Panax ginseng is well known to enhance the release of NO from endothelial cells of the rat aorta and to reduce BP in experimental animals. To further confirm the efficacy of the Panax ginseng extract, clinical studies were conducted. The effects of water extract of Korea red ginseng (KRG) on NO concentration levels in the exhaled breath, BP, and heart rate of human volunteers was studied. It was also investigated whether NO level in exhaled breath was increased by KRG extract, and if any correlation between BP and heart rate. A single administration of KRG water extract (500 mg/50 kg) increased NO levels in exhaled breath, and concomitantly decreased mean blood pressure and heart rate of twelve healthy, non-smoking male volunteers. The correlation value between NO levels and heart rate ($r = 0.94$), and the correlation value between NO levels and heart rate ($r = 0.84$) were found to be significant ($P < 0.01$). Linear regression analysis shows the clear conversed correlation between NO levels and BP as well as heart rate. The results support the claim that KRG may be useful for the treatment of HTN and pulmonary vascular obstruction (Han et al, 2005)

Han et al, 1998, evaluated the changes in diurnal blood pressure pattern (24 hour ambulatory blood pressure monitoring) after 8 weeks of red ginseng medication (4.5 g/day). Study was conducted among 26 subjects with essential hypertension. Their 24 hour mean systolic blood pressure decreased significantly ($p = 0.03$) while diastolic blood pressure showed only a slight decline ($p = 0.17$). The decrease in pressures were observed at daytime (8 A.M.-6 P.M.) and dawn (5 A.M.-7 A.M.). 8 subjects were probably of white coat hypertension, as no significant change in BP was observed. Based on the results, it was concluded that red ginseng might be useful as a relatively safe medication adjuvant to current antihypertensive medications.

m) Ginkgo biloba

The acute effect of ginkgo (Ginkgo biloba L.) ethanolic extracts on arterial BP, and heart rate in anesthetized normotensive rats was examined and compared. The left carotid artery was used for the measurement of arterial BP. The intravenous administration of the extracts produced a statistically significant dose-dependent and reversible hypotensive and bradycardic effects (Brankovic et al, 2011). The effects of Ginkgo biloba extract (GBE) on the development of hypertension, platelet activation and renal dysfunction in deoxycorticosterone acetate (DOCA)-salt hypertensive rats was also studied (Umegaki et al, 2000). Both DOCA-salt hypertensive rats and normotensive rats were fed a 2% GBE diet for 20 days. The tail-cuff and telemetry methods were used for the measurement of BP. Rats fed a 2% GBE diet did not develop significant hypertension. In addition, an increase in heart weight, an indicator of sustained high BP, was inhibited significantly by feeding of the GBE diet. Feeding of the GBE diet also decreased 5-hydroxytryptamine content in platelets, a marker of platelet activation in vivo associated with hypertension. The telemetry study demonstrated that BP and heart rate showed a clear circadian rhythm and the antihypertensive effect of GBE was prominent in the daytime, a resting period for rats. This anti-hypertensive effect of GBE was not detected in normotensive rats (Umegaki et al, 2000).

n) Guazuma ulmifolia

The hypotensive effect of procyanidin fraction (PCF) obtained from acetone extract of Guazuma ulmifolia bark was studied. 10 mg/kg PCF dose was orally administered to sugar-fed hypertensive rats. PCF significantly decreased both the systolic arterial pressure and the heart rate, whereas the same doses administered intravenously induced arterial hypotension. Hypotensive effect was attenuated by NG-nitro-L-arginine methylester (L-NAME) pretreatment. The PCF reduced the contraction induced by norepinephrine (1x10(-7) M) in isolated aortic rings of normotensive and sugar-fed hypertensive rats. Vascular endothelium removal or L-NAME (30 microM) pretreatment inhibited the relaxant activity of PCF. Procyanidin oligomers consisting mainly of tetramers and trimers are the active ingredients of PCF responsible for its hypotensice effects. Guazuma ulmifolia bark possesses long-lasting antihypertensive and vasorelaxing properties. These beneficial effects can be linked to the endothelium related factors; involving nitric oxide (Magos et al, 2008).

o) Hibiscus sabdariffa

The antihypertensive effect of the plant extract of Hibiscus sabdariffa was evaluated. It was observed that in experimentally induced hypertensive rats, an intravenous administration of 20 mg/kg aqueous extract of dry H. sabdariffa calyx produced a significant fall in the BP. The hypotensive effects of the crude extract of H. sabdariffa may be mediated through direct vasorelaxant effects of acetylcholine and histamine. Earlier report showed that the petal crude extract of same plant produced a direct relaxant effect on the aortic smooth muscle of rats (Herrera-Arellano et al., 2004). The chronic administration of aqueous extract of HS has been reported to reverse cardiac hypertrophy in reno-vascular hypertensive rats. A clinical trial of the plant extract has shown reliable evidence of antihypertensive effect. A standardized dose of H. sabdariffa (9.6 mg per day) given to 39 patients and captopril, 50 mg per day, given to the same number of patients did not show significant difference relative to hypotensive effects, antihypertensive effectiveness and tolerability (Odigie et al., 2003).

p) Herniaria glabra

The antihypertensive effects of Herniaria glabra saponins was studied and compared with that of furosemide. Spontaneously hypertensive rats were treated with Herniaria glabra saponins at a dosage of 200mg/Kg of body weight. Treatment with Herniaria glabra saponins led to significant decline in both systolic and diastolic blood pressures after 1 month. However, no significant change in heart rate was observed. It was concluded that H. glabra saponins lowered blood pressure by multifactorial mechanism (Rhiouani et al, 2001).

q) Olea. africana (Oleaceae)

The effects of crude extract of the root and stem of Olea africana on MAP and heart rate in normo and hypertensive rats was studied in experimental rats. An immediate and dose dependent fall in MAP and heart rate in anaesthetised normotensive rats was produced by intravenous administration of aqueous and ethanolic extracts of Olea Africana. The efficacy of the aqueous extract was more superior to the ethanolic extract. Orally administered aqueous extract produced lowering of MAP and HR in DOCA-salt hypertensive rats (Osim et al, 1999).

r) Rauwolfia serpentina

Reserpine, was the purified alkaloid of Rauwolfia serpentina. It was the first potent drug widely used for the long-term treatment of hypertension. In Europe, Georg Eberhard Rumpf first reported about rauwolfia in his Herbarium amboinense, 1755. The first modern paper about therapeutic applications of the whole root of rauwolfia was published in 1931 in the Indian Medical Journal by Sen and Bose, and many papers dealing with botanics, chemistry and pharmacology then appeared in Indian and European periodics. In 1949, Vakil published the first report of the antihypertensive effect of rauwolfia in the British Heart Journal. In the Ciba laboratories in Basel, Switzerland, Mueller, Schlittler and Bein analyzed various rauwolfia alkaloids and published in 1952 the first complete report about their chemistry and pharmacology. In the same year, reserpine was introduced under the name Serpasil for the treatment of hypertension, tachycardia and thyreotoxicosis (Jerie et al, 2007).

In a carefully controlled series of 39 severe cases of hypertension (38 with essential hypertension and 1 with nephritic hypertension) treated for 6 to 20 months with rauwolfia preparations, a fall in BP in 67% of cases was observed. In most cases there was a proportionate fall in both systolic and diastolic BP, but in several the fall in the diastolic appeared to be relatively greater than in the systolic. The fall was slight (10-20 mm. Hg diastolic) in 21 % but appreciable or marked in 46% (greater than 20 mm. Hg diastolic), and in four patients the diastolic BP fell to below 100 mm. Hg (S. Locket, 1955).

s) Terminalia superba

Terminalia superba, is used in traditional Cameroonian medicine as an antihypertensive remedy. Tom et al., 2010 investigated the hypotensive efficacy of the aqueous extract of Terminalia superba. Rats were orally administered 10% D-glucose for 3 weeks to induce hypertension. The antihypertensive effects were studied after oral administration of the extract (50 and 100 mg/kg/day) or nifedipine (10 mg/kg/day) for 3 weeks. BP and heart rate were measured along with the antioxidant parameters in the heart, aorta, liver and kidney at the end of the experiment. Intravenous administration of the aqueous extract of Terminalia superba induced a significant hypotensive response without any significant change in HR. The oral administration of the extract significantly prevented the rise in BP in glucose-hypertensive rats. Treatment with plant extract resulted in withdrawal of sympathetic tone and an improvement in the antioxidant status as it significantly reduced the oxidative stress associated with hypertension. The present study demonstrates that the aqueous extract of the stem bark of Terminalia superba exhibits significant hypotensive effects that are, at least in part, related to a withdrawal of sympathetic tone and to an improvement of the antioxidant status (Tom et al., 2010).

t) Xingnao Qingxuan

Zhou et al., 1999 studied the effect of Xingnao Qingxuan capsules (XQC) in decreasing BP of normal and anesthetized cats. Oral administration of XQC, 2.8 g/kg produced a decrease in BP of normal cats. XQC 1.4, 2.8 and 5.6 g/kg once a day for 14 days, produced a dose-dependent reduction of BP in SHR. Although after 3-4 days of administration the BP returned to the baseline values but the change was not statistically significant. With oral administration of 2.8 and 5.6 g/kg XQC, the incubation period of eyeball tremor induced by chloroform by dropping into the ear was prolonged by 14.4% and 13.0%, and the keeping time shortened by about 33.3% and 23.3% respectively. Brain basic arterial spasm induced by KCl or 5-HT in dog was relaxed significantly by XQC in vitro experiment. Results demonstrate that XQC reduces blood pressure resisting dizziness (Zhou et al., 1999).

u) Stephania tetrandra S Moore

The hypotensive effect of the extract of Radix Stephaniae Tetrandrae (RST), the root of a Chinese hero Stephania tetrandra S Moore was evaluated experimentally. Results were compared to those of tetrandrine (Tet), active component of RST (Wong et al., 2000). The RST extract inhibited Ca2+ influx into the myocyte and reduced protein release during reperfusion. RST extract suppressed elevation of arterial blood pressure in DOCA-salt hypertensive rats. The results suggest that the efficacy of the RST extract cannot be accounted for by Tet alone. Some of the

effects may be due to an interaction between the components of the extract. The RST extract produced similar hypotensive effects as verapamil, a prototype Ca2+ channel antagonist widely used in the treatment of hypertension.

v) Solanum sisymbriifolium

S. sisymbriifolium Lam., root, a perennial herb, has been used as a traditional medicine in Paraguay. It possesses diuretic and antihypertensive properties. The hypotensive effect of the crude hydroalcoholic extract from root was investigated both in normotensive and hypertensive rats. The intravenous administration of the extract (50 and 100 mg/kg) produced a significant decrease in BP in anesthetized DOCA hypertensive rats. Oral administration of the extract (10, 50, 100, and 250 mg/kg) produced a dose-dependent hypotensive effect in conscious hypertensive animals. In anesthetized normotensive rats, the extract (50 and 100 mg/kg, i.v) induced hypotension in a dose-dependent manner. When administered orally (10, 50, 100, 250, 500, and 1000 mg/kg) to conscious normotensive rats, no significant effect on BP was produced by the extract. In another study, the active ingredient nuatigenosido was isolated from the extract. Nuatigenosido at 100 g/kg and 1 mg/kg i.v lowered BP in rats and at 10−6 and 10−5 M augmented the contractile force in the right atrium of a bullfrog. Nuatigenosido at 10-7 M increased the overshoot amplitude in frog atrial myocytes, the action potential duration was shortened, the calcium current was increased, and the delayed outward potassium current was increased. The study concluded that nuatigenosido may play an important role in the therapeutic effects of this herb (Ibarrola et al., 2003).

w) Uncaria rhynchophylla

U. rhynchophylla has been used in traditional oriental medicine to lower BP and relieve various neurological symptoms. The indole alkaloid called hirsutine acts on calcium chaneels and is responsible for its hypotensive activity. The effects of hirsutine on cytosolic Ca2+ level ([Ca2+]cyt) were studied by using fura-2- Ca2+ fluorescence in smooth muscle of the isolated rat aorta. Noradrenaline and high K+ solution produced a sustained increase in [Ca2+]cyt. Application of hirsutine after the increases in [Ca2+]cyt induced by noradrenaline and high K+ notably decreased [Ca2+]cyt. Results suggest that hirsutine inhibits Ca2+ influx through voltage-dependent Ca2+ channel. Furthermore, hirsutine had profound effect on intracellular Ca2+ stores. It significantly reduced the caffeine-induced contraction under the Ca2+ -free nutrient condition in the rat aorta. During Ca2+ loading when hirsutine was added it augmented the contractile response to caffeine. It was concluded that hirsutine reduces intracellular Ca2+ level through its effect on the Ca2+ store as well as through its effect on the voltage-dependent Ca2+ channel. In another study, the methanolic extract of the hooks of an Uncaria species was found to have a potent and long-lasting hypotensive effect in rats. Further studies of the extract resulted in the isolation of 3-indole alkaloid, glycoside, cadambine, dihydrocadambine, and isodihydrocadambine. The active ingredients dihydrocadambine, and isodihydrocadambine were found to possess significant hypotensive property, whereas cadambine was inactive (Endo et al., 1983).

x) Zingiber officinale

Zingiber officinale (Zo.Cr), commonly known as Ginger is used in Asian cooking. It is known to improve the blood circulation. In anesthetized rats, the crude extract of Zo.Cr induced a dose-dependent (0.3-3 mg/kg) fall in the arterial BP. In guinea pig paired atria, Zo.Cr exhibited a cardiodepressant activity on the rate and force of spontaneous contractions. In rabbit thoracic aorta preparation, Zo.Cr inhibited the phenyl ephrine-induced vascular contraction at a dose ten times higher than that required against K+ (80 mM)-induced contraction. Similar to the effect of verapamil, Zo.Cr shifted the Ca2+ dose-response curves to the right, confirming the Ca2+ channel-blocking activity. The results suggest that the hypotensive effect of Zo.Cr is mediated via blockade of voltage-dependent calcium channels. Chronic administration of Pet ether extract (PE) (50 mg/kg/day; po), toluene fraction (10 mg/kg/day; po) of ginger rhizome, and Korean ginseng extract (KGE) (30 mg/kg/day; po) significantly reduced the BP in DOCA salt-induced hypertensive rats. The PE (50 mg/kg/day; po) and KGE (30 mg/kg/day; po) produced significant hypotensive effects in fructose-induced hypertensive rats. It was also speculated that the hypotensive mechanism of action may partly be attributed to serotonin antagonism. Few clinical trials using low dose Zo.Cr have been undertaken with inconclusive results (Nicoll and Henein, 2009).

y) Zygophyllum coccineum

Gibbons and Oriowo, 2001, studied the effects of an aqueous extract of Zygophyllum coccineum L. on rat BP and on the mesenteric vascular bed. The extract dose-dependently reduced BP and heart rate in normotensive and spontaneously SHRs. It also reduced BP in pithed SHRs. In vitro, the extract had no effect on basal perfusion pressure of the mesenteric vascular bed. However, when the perfusion pressure was raised with noradrenaline or potassium chloride, the extract produced a dose-dependent reduction in perfusion pressure. It was concluded that extracts of Z. coccineum possess significant hypotensive activity which may be attributed to membrane hyperpolarization (Gibbons and Oriowo, 2001).

z) Withania somnifera and Terminalia Arjuna combination

In Ayurveda, medicinal plants, Withania somnifera (Ws) and Terminalia Arjuna (Arjuna) have been described to be beneficial for cardiac ailments. Ashwagandha is categorised as Rasayana, known to promote health and longevity and Arjuna primarily for treatment of heart ailments (coronary artery disease, heart failure, hypercholesterolemia, anginal pain and can be considered as a useful drug for coronary artery disease, hypertension and ischemic cardiomyopathy). The present investigation assessed the effects of Ws and Arjuna individually and as a combination on maximum velocity, average absolute and relative power, balance, maximum oxygen consumption (VO2 max) and blood pressure in humans. Ws and Arjuna were administered in the form of capsules (dosage 500mg/day). Thirty participants were assigned to experimental group of which 10 received standardized root extracts of Ws, 10 received standardized bark extract of Arjuna and the rest of the 10 received standardized root extract of both Ws and Arjuna. Ten participants received placebo (capsules filled with flour). All the subjects continued the regimen for 8 weeks. All variables were assessed before and after the course of drug administration. The results showed that Ws increased velocity, power and VO2 max whereas Arjuna increased VO2 max and lowered resting systolic blood pressure. When given in combination, the improvement was seen in all parameters except diastolic blood pressure. Ws were found to be useful for treating generalized weakness, improving speed and lower limb muscular strength and neuro-muscular co-ordination. Arjuna was found to be beneficial in improving cardio-vascular endurance and lowering systolic blood pressure (Sandhu et al., 2010).

IV. Hypolipidemics

a) Bougainvillea spectabilis

The active ingredient, D-pinitol (3-O-methyl-chiroinositol), of the traditional antidiabetic plant, Bougainvillea spectabilis, has significant antidiabetic effects. This study was undertaken to evaluate the effect of D-pinitol on lipids and lipoproteins in streptozotocin (STZ)-induced diabetic Wistar rats. Type II diabetic was induced by a single intraperitoneal injection of 40 mg/kg STZ. In diabetic rats, a significant increase in blood glucose, total cholesterol, triglycerides, free fatty acids, phospholipids in the liver, kidney, heart, and brain was observed. In diabetic rats, a significant increase in the levels of low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) cholesterol and a decrease in the high-density lipoprotein (HDL) were seen in diabetic rats. Oral administration of D-pinitol to STZ-induced diabetic rats showed significant ($p < 0.05$) decrease in the levels of blood glucose and total cholesterol, triglycerides, free fatty acids, and phospholipids in serum, liver, kidney, heart, and brain. Treatment with D-pinitol significantly ($p < 0.05$) lowered LDL and VLDL cholesterol levels and significantly ($p < 0.05$) increased HDL cholesterol levels in the serum of diabetic rats. Thus, the present study clearly demonstrates the antihyperlipidemic effect of D-pinitol in STZ-induced type II diabetic rats (Geethan et al., 2008).

b) Daming capsule

The hypolipidemic effect of darning as well as the mechanism of its hypolipidemic effect was elucidated. The expression of connexin43 in the myocardium before and after using the capsule was studied. Forty Wistar rats were randomly divided into 5 groups: control group, hyperlipemia model group and Daming capsule treatment (200, 100, 50 mg/kg) groups. The indexes of total cholesterol (TC), TG, LDL, HDL and non-esterified free fatty acid (NEFA) in the serum were measured via vena caudalis. The myocardial total RNA was extracted by Trizol method. RT-PCR, immunostaining and microconfoul was used to study the expression of connexin 43. The concentrations of TC, TG, LDL and NEFA in hyperlipemic serum were significantly increased ($P < 0.05$), while that of HDL decreased ($P < 0.05$). Daming capsule treatment decreased the concentration of the preceding four indexes. The concentration of HDL was increased up to baseline levels. No significant difference was found in the ECG of the three groups. The mRNA expressions of connexin43 in hyperlipemia group was weakened ($P < 0.05$), while that of the drug group was enhanced ($P < 0.05$) as compared with the normal group. The study demonstrates that changes in Cx43is responsible for the hypolipidemic activity of Darning capsule (Xing et al., 2007).

c) 'Trikatu'

'Trikatu' is an indigenous preparation containing Piper longum (fruit), Piper nigrum (fruit) and Zingiber officinale (rhizome) dry powder. To ascertain its efficacy as a hypolipidaemic agent, Trikatu' was fed to normal and cholesterol fed male Rattus norvegicus. Its effects on body weight, blood and tissue (aortic, cardiac and hepatic) lipids--total, free and esterified cholesterol, LDL and HDL cholesterol, TG and phospholipids—and the atherogenic index were measured. 'Trikatu' reduced triglycerides and LDL cholesterol and increased HDL cholesterol. Hence Trikatu' can reduce the risk of hyperlipidaemia and atherosclerosis. It was concluded that 'Trikatu' possess significant hypolipidaemic activity and it reduces the atherosclerosis associated with a high fat diet (Sivakumar and Sivakumar, 2004).

d) Garlic

Bordia et al., 1981 were the first to evaluate the hypolipidemic activity of garlic. A clinical study using garlic was conducted on two groups of individuals.

Group A consisted of 20 healthy volunteers who were fed garlic for 6 months and then followed for another 2 months without garlic. Administration of garlic significantly lowered the serum cholesterol and TG while raising the HDL. Group B consisted of 62 patients with coronary heart disease with elevated serum cholesterol. They were randomly divided into two subgroups: B1 was fed garlic for 10 months while B2 served as a control. Results demonstrated that garlic intake decreased the serum cholesterol ($p < 0.05$), TG ($p < 0.05$) LDL ($p < 0.05$) while increasing the HDL fraction ($p < 0.001$). These changes in lipid profile were statistically significant at the end of 8 months and persisted for the next 2 months of follow-up. This study demonstrates that the essential oil of garlic has distinct hypolipidemic action in both healthy individuals and patients of coronary heart disease (Bordia et al., 1981).

Hyperlipidemia and oxidative stress may be involved in coronary heart disease and the progression of renal damage in Nephrotic syndrome (NS) patients. Studies have documented that hypolipidemic and antioxidant properties of Garlic may be responsible for its beneficial effects. In the present study the effect of a 2% garlic diet on acute and chronic experimental NS induced by puromycin aminonucleoside (PAN) was studied. Acute NS was induced by a single injection of PAN to rats and sacrificed after 10 days. Chronic NS was induced by repeated injections of PAN to rats and sacrificed 84 days after the first injection. Results indicate that garlic treatment was unable to modify proteinuria in either acute or chronic NS, and hypercholesterolemia and hypertriglyceridemia in acute NS. However, garlic intake diminished significantly total-cholesterol, LDL-cholesterol and TG, but not HDL-cholesterol in chronic NS. Garlic significantly prevented the oxidative stress (in vivo renal H_2O_2 production and the diminished renal Cu, Zn-SOD and catalase activities in acute NS). Results demonstrate that garlic treatment ameliorates hyperlipidemia and renal damage in chronic NS (Pedraza-Chaverrí et al., 2000).

e) Red ginseng

Red ginseng is the steamed and dried root of Panax ginseng. Active ingredient (ginseng saponin) isolated from red ginseng was studied in a cyclophosphamide (CPM)-induced hyperlipidemia model in fasted rabbits. In this model, chylomicrons and VLDL accumulation occurs as a result of release of lipoprotein lipase from the heart. Oral administration of ginseng saponins at a dose of 0.01 g/kg for 4 weeks reversed the increase in serum TG and concomitant increase in cholesterol produced by CPM treatment. In addition, ginseng saponins treatment led to a recovery in post heparin plasma lipoprotein lipase activity and heparin-releasable heart lipoprotein lipase activity, which were markedly reduced by CPM treatment. In rats given 15% glycerol/15% fructose solution, postheparin plasma lipoprotein lipase activity declined to two third of normal rats, whereas ginseng saponins reversed it to normal levels. This study demonstrates that ginseng saponins sustained lipoprotein lipase activity at a normal level. It maintained the lipoprotein lipase activity and produced significant hypolipidemic activity (Inoue et al., 1999).

f) Tinospora cordifolia

Tinospora cordifolia is an indigenous plant widely used in Ayurvedic medicine in India. The present study was undertaken to evaluate the hypolipidaemic effect of an aqueous extract of Tinospora cordifolia roots. A significant reduction in serum and tissue cholesterol, phospholipids and free fatty acids was seen in alloxan diabetic rats after administration of the extract of T. cordifolia roots (2.5 and 5.0 g/kg body weight) for 6 weeks. The root extract at a dose of 5.0 g/kg body weight showed significant hypolipidaemic effect (Stanely Mainzen et al., 1999).

g) T. arjuna

The effect of orally administered indigenous drugs Terminalia arjuna, T. belerica and T. chebula were investigated on experimental atherosclerosis. Rabbits were fed a cholesterol-rich diet to induce atherosclerosis. The three drugs (Terminalia arjuna, T. belerica and T. chebula) were orally fed along with cholesterol to these rabbits. At the end of the experimental period, the plasma lipid profile and lipid peroxidation were assessed. Atherosclerotic lesions of the aorta were examined histologically. T. arjuna significantly inhibited rabbit atheroma formation. The results indicate that T. arjuna has significant hypolipidemic activity (Shaila et al., 1998).

h) Ocimum sanctum

Ocimum sanctum is commonly known as Tulsi. In the present study, 1% Tulsi leaf powder was fed to normal and diabetic rats for a period of one month to explore the effect on fasting blood sugar, uric acid, total amino acids, and the lipid profile in serum and tissue lipids. The results indicated a significant reduction in fasting blood sugar, uric acid, total amino acids, TC, TG, phospholipids and total lipids. In liver, total cholesterol, triglyceride and total lipids were significantly lowered. Total lipids were significantly reduced in kidney. In heart, a significant fall in total cholesterol and phospholipids was observed. Study observations confirm the hypoglycemic and hypolipidemic effect of Tulsi in diabetic rats (Rai et al., 1997).

i) Curcuma longa and Nardostachys jatamansi

The hypolipidemic activity of Curcuma longa and Nardostachys jatamansi was studied in triton-induced hyperlipidaemic rats. Oral feeding of fifty per cent ethanolic extract of Curcuma longa and Nardostachys jatamans resulted in elevation of HDL-cholesterol/total cholesterol ratio. The extracts also caused a significant reduction in the ratio of total

cholesterol/phospholipids. The cholesterol and triglyceride lowering activity of Curcuma longa was superior as compared to N. jatamansi in triton-induced hyperlipidaemic rats. It was concluded that Curcuma longa possesses significant hypolipidemic activity and has protective action against heart disease and atherogenecity (Dixit et al., 1988).

V. Conclusion

The renewed interest in the search for new drugs from natural sources, especially from plant sources for the treatment of cardiovascular conditions, has gained global attention during the last two decades. Development of such indigenous herbal products with potential cardioprotective effects may be a boon in developing countries like India and South East Asian Nations as the synthetic drugs are comparatively costly and therefore patients belonging to weaker sections of the society may be non-complaint in therapy on long term basis. India is blessed with natural resources, primarily due to the rich biodiversity they harbor, which may be sources of new drugs with potential novel structures. However, of this rich biodiversity, only a small portion has been studied for its medicinal potential. Thus, a major opportunity exists in our natural resources for identifying and selecting efficacious, inexpensive and safer approaches for cardioprotection.

There is a paucity of scientific data on herbal medicines as few systemically designed studies on herbal medicines are currently available and their risk-versus-benefit ratios are not clearly elucidated. These medicinal plants need to be investigated scientifically and rigorously to define their role in prevention and treatment of cardiovascular conditions and to stimulate future pharmaceutical development of therapeutically beneficial herbal drugs. At the same time, legal surveillance of herbal medicine use with low safety margins, adverse cardiovascular reactions and drug interactions should be instituted.

References Références Referencias

1. Endo K, Oshima Y, Kikuchi H, Koshihara Y, Hikino H. Hypotensive principles of uncaria hooks1. *Planta Med.* 1983;49:188–90.
2. Al Makdessi S, Sweidan H, Müllner S, Jacob R. Myocardial protection by pretreatment with Crataegus oxyacantha: an assessment by means of the release of lactate dehydrogenase by the ischemic and reperfused Langendorff heart. Arzneimittelforschung. 1996 Jan;46(1):25-7.
3. Bensky D, Gamble A. USA: Eastland Press; 1990. Chinese Herbal Medicine.
4. Bharani A, Ganguly A, Bhargava KD. Salutary effect of Terminalia Arjuna in patients with severe refractory heart failure. Int J Cardiol. 1995 May;49(3):191-9.
5. Bordia A. Effect of garlic on blood lipids in patients with coronary heart disease.
6. Brankovic S, Radenkovic M, Kitic D, Veljkovic S, Ivetic V, Pavlovic D, Miladinovic B. Comparison of the hypotensive and bradycardic activity of ginkgo, garlic, and onion extracts. Clin Exp Hypertens. 2011;33(2):95-9. Epub 2011 Jan 26.
7. Carini M, Aldini G, Rossoni G, Morazzoni P, Facino RM. Complexation of Ginkgo biloba extract with phosphatidylcholine improves cardioprotective activity and increases the plasma antioxidant capacity in the rat. Basic Res Cardiol. 2003 Feb;98(1):59-68.
8. Chan P, Hong CY, Tomlinson B, Chang NC, Chen JP, Lee ST, Cheng JT. Myocardial protective effect of trilinolein: an antioxidant isolated from the medicinal plant Panax pseudoginseng. Life Sci. 1997;61(20):1999-2006.
9. Chatterjee SS, Koch E, Jaggy H, Krzeminski T. In vitro and in vivo studies on the cardioprotective action of oligomeric procyanidins in a Crataegus extract of leaves and blooms. Arzneimittelforschung. 1997 Jul;47(7):821-5.
10. Cheng H, Liu W, Ai X. Protective effect of curcumin on myocardial ischemia reperfusion injury in Rats. Zhong Yao Cai. 2005 Oct;28(10):920-2.
11. Degenring FH, Suter A, Weber M, Saller R. A randomised double blind placebo controlled clinical trial of a standardized extract of fresh Crataegus berries (Crataegisan) in the treatment of patients with congestive heart failure NYHA II. Phytomedicine. 2003;10(5):363-9.
12. Degenring FH, Suter A, Weber M, Saller R. A randomised double blind placebo controlled clinical trial of a standardized extract of fresh Crataegus berries (Crataegisan) in the treatment of patients with congestive heart failure NYHA II. Phytomedicine. 2003;10(5):363-9.
13. Demers C, McKelvie RS, Yusuf S. The role of digitalis in the treatment of heart failure. 14. Coron Artery Dis. 1999 Sep;10(6):353-60.
14. Dhawan V, Jain S. Garlic supplementation prevents oxidative DNA damage in essential hypertension. *Mol Cell Biochem*. 2005;275:85–94.
15. Dimo T, Nguelefack TB, Kamtchouing P, Dongo E, Rakotonirina A, Rakotonirina SV. Hypotensive effects of a methanol extract of Bidens pilosa Linn on hypertensive rats. C R Acad Sci III. 1999 Apr;322(4):323-9.
16. Ding DZ, Shen TK, Cui YZ. Effects of red ginseng on the congestive heart failure and its mechanism. Zhongguo Zhong Xi Yi Jie He Za Zhi. 1995 Jun;15(6):325-7.
17. Dixit VP, Jain P, Joshi SC. Hypolipidaemic effects of Curcuma longa L and Nardostachys jatamansi, DC in triton-induced hyperlipidaemic rats. Indian J Physiol Pharmacol. 1988 Oct-Dec;32(4):299-304.

18. Eno AE, Owo OI, Itam EH, Konya RS. Blood pressure depression by the fruit juice of Carica papaya (L.) in renal and DOCA-induced hypertension in the rat. Phytother Res. 2000 Jun;14(4):235-9.
19. Fahim M, Khan MS, Hameed HA. Effect of Ajmaloon on the baroreceptor-heart rate reflex in anaesthetized rabbits and monkeys. Indian J Physiol Pharmacol. 1995 Apr;39(2):101-5.
20. Fallon MB, Abrams GA, Abdel-Razek TT, Dai J, Chen SJ, Chen YF, Luo B, Oparil S, Ku DD. Garlic prevents hypoxic pulmonary hypertension in rats. Am J Physiol. 1998 Aug;275(2 Pt 1):L283-7.
21. Gao W, Liang RX, Xiao YQ, Yang HJ. Protective effect of the pretreatment with Chuanxiong-phthalide A on the vascular endothelial cells impaired by the ischemia and reperfusion in isolated rats hearts. Zhongguo Zhong Yao Za Zhi. 2005 Sep;30(18):1448-51.
22. Geethan PK, Prince PS. Antihyperlipidemic effect of D-pinitol on streptozotocin-induced diabetic Wistar rats. J Biochem Mol Toxicol. 2008 Jul-Aug;22(4):220-4.
23. Gharooni M, Sarkarati AR. Application of *Apium graveolens* in treatment of hypertension. T*ehran Univ* Med J. 2000;58:67–9.
24. Gibbons S, Oriowo MA. Antihypertensive effect of an aqueous extract of Zygophyllum coccineum L. in rats. Phytother Res. 2001 Aug;15(5):452-5.
25. Guillon JM, Rochette L, Baranes J. Effects of Ginkgo biloba extract on 2 models of experimental myocardial ischemia. Presse Med. 1986 Sep 25;15(31):1516-9.
26. Han K, Shin IC, Choi KJ, Yun YP, Hong JT, Oh KW. Korea red ginseng water extract increases nitric oxide concentrations in exhaled breath. Nitric Oxide. 2005 May;12(3):159-62.
27. Han KH, Choe SC, Kim HS, Sohn DW, Nam KY, Oh BH, Lee MM, Park YB, Choi YS, Seo JD, Lee YW. Effect of red ginseng on blood pressure in patients with essential hypertension and white coat hypertension. Am J Chin Med. 1998;26(2):199-209.
28. Han SY, Li HX, Ma X, Zhang K, Ma ZZ, Tu PF. Protective effects of purified safflower extract on myocardial ischemia in vivo and in vitro. Phytomedicine. 2009 Aug;16(8):694-702. Epub 2009 Apr 24.
29. Han X, Liu JX, Ma XB, Wang YH. Effects of shuangshen tongguan (SSTG) on TNF-alpha, ICAM-1 during myocardial ischemia-reperfusion injury. Zhongguo Zhong Yao Za Zhi. 2004 Nov;29(11):1073-5.
30. Herrera-Arellano A, Flores-Romero S, Chávez-Soto MA, Tortoriello J. Effectiveness and tolerability of a standardized extract from Hibiscus sabdariffa in patients with mild to moderate hypertension: A controlled and randomized clinical trial. Phytomedicine. 2004;11:375–82.
31. Hu YC, Hou JY. Effect of zhimu and huangqi on cardiac hypertrophy and response to stimulation in mice. Zhongguo Zhong Yao Za Zhi. 2003 Apr;28(4):369-74.
32. Ibarrola DA, Montalbetti Y, Heinichen O, Alvarenga N, Figueredo A, Ferro EA. Isolation of hypotensive compounds from *Solanum sisymbriifolium* Lam. *J Ethnopharmacol.* 2000;70:301–7.
33. Ibarrola IP, Ettarh RR, Adigun SA. Chronic administration of aqueous extract of *Hibiscus sabdariffa* attenuates hypertension and reverses cardiac hypertrophy in 2K-1C hypertensive rats. J Ethnopharmacol. 2003;86:181–5.
34. Inoue M, Wu CZ, Dou DQ, Chen YJ, Ogihara Y. Lipoprotein lipase activation by red ginseng saponins in hyperlipidemia model animals. Phytomedicine. 1999 Oct;6(4):257-65.
35. Jerie P. Milestones of cardiovascular therapy: IV, Reserpine. Cas Lak Cesk. 2007;146:573–7.
36. Ju LY. Crataegus oxyacantha (aubepine) in the use as herb medicine in France. 8. Zhongguo Zhong Yao Za Zhi. 2005 Apr;30(8):634-40.
37. Kou YY, Zha XD, Li YF, Ge RL. The antioxidative effect of Sanwei Tanxiang powder on rats' hearts against myocardial ischemia and reperfusion injury. Zhong Yao Cai. 2008 Jul;31(7):1013-5.
38. Krikler DM. The foxglove, "The old woman from Shropshire" and William Withering. . J Am Coll Cardiol. 1985 May;5(5 Suppl A):3A-9A.
39. Lai ZF, Shao Z, Chen YZ, He M, Huang Q, Nishi K. Effects of sasanquasaponin on ischemia and reperfusion injury in mouse hearts. J Pharmacol Sci. 2004 Mar;94(3):313-24.
40. Lau CW, Yao XQ, Chen ZY, Ko WH, Huang Y. Cardiovascular actions of berberine. Cardiovasc Drug Rev. 2001 Fall;19(3):234-44.
41. Liebgott T, Miollan M, Berchadsky Y, Drieu K, Culcasi M, Pietri S. Complementary cardioprotective effects of flavonoid metabolites and terpenoid constituents of Ginkgo biloba extract (EGb 761) during ischemia and reperfusion. Basic Res Cardiol. 2000 Oct;95(5):368-77.
42. Liu H, Wu X, Zhang Y, Lian W. Effect of Shenqi Fuzheng injection (SFI) on immune function in patients with congestive heart failure. Zhong Yao Cai. 2005 Sep; 28(9):854-856.
43. Maffei Facino R, Carini M, Aldini G, Berti F, Rossoni G. Panax ginseng administration in the rat prevents myocardial ischemia-reperfusion damage induced by hyperbaric oxygen: evidence for an antioxidant intervention. Planta Med. 1999 Oct;65(7):614-9.
44. Magos GA, Mateos JC, Páez E, Fernández G, Lobato C, Márquez C, Enríquez RG. Hypotensive and vasorelaxant effects of the procyanidin fraction

from Guazuma ulmifolia bark in normotensive and hypertensive rats.. J Ethnopharmacol. 2008 Apr 17;117(1):58-68. Epub 2008 Jan 20.
45. Magos GA, Vidrio H, Reynolds WF, Enríquez RG. Pharmacology of Casimiroa edulis IV. Hypotensive effects of compounds isolated from methanolic extracts in rats and guinea pigs.J Ethnopharmacol. 1999 Jan;64(1):35-44.
46. Mamtani R, Mamtani R. Ayurveda and yoga in cardiovascular diseases. Cardiol Rev. 2005 May-Jun;13(3):155-62. Review
47. Mohanty I, Arya DS, Gupta SK. Effect of Curcuma longa and Ocimum sanctum on myocardial apoptosis in experimentally induced myocardial ischemic-reperfusion injury. BMC Complement Altern Med. 2006 Feb 19;6:3.
48. Mohanty I, Arya DS, Gupta SK. Effect of Curcuma longa and Ocimum sanctum on myocardial apoptosis in experimentally induced myocardial ischemic-reperfusion injury. BMC Complement Altern Med. 2006 Feb 19;6:3.
49. Mohanty I, Singh Arya D, Dinda A, Joshi S, Talwar KK, Gupta SK.. Protective effects of Curcuma longa on ischemia-reperfusion induced myocardial injuries and their mechanisms. Life Sci. 2004 Aug 20;75(14):1701-11.
50. Mohanty IR, Arya DS, Gupta SK. Withania somnifera provides cardioprotection and attenuates ischemia-reperfusion induced apoptosis. Clin Nutr. 2008 Aug;27(4):635-42. Epub 2008 Jul 11.
51. Mohanty IR, Maheshwari U, Joseph D, Deshmukh Y. Bacopa monniera protects rat heart against ischaemia-reperfusion injury: role of key apoptotic regulatory proteins and enzymes. J Pharm Pharmacol. 2010 Sep;62(9):1175-84.
52. Mulrow CD, Feussner JR, Velez R. Reevaluation of digitalis efficacy. New light on an old leaf. Ann Intern Med. 1984 Jul;101(1):113-7.
53. Nasa Y, Hashizume H, Hoque AN, Abiko Y. Protective effect of crataegus extract on the cardiac mechanical dysfunction in isolated perfused working rat heart. Arzneimittelforschung. 1993 Sep;43(9):945-9.
54. Nicoll R, Henein MY. Ginger (*Zingiber officinale Roscoe*): A hot remedy for cardiovascular disease? *Int J Cardiol*. 2009;131:408–9.
55. Osim EE, Mbajiorgu EF, Mukarati G, Vaz RF, Makufa B, Munjeri O, Musabayane CT. Hypotensive effect of crude extract Olea. africana (Oleaceae) in normo and hypertensive rats. Cent Afr J Med. 1999 Oct;45(10):269-74.
56. Pedraza-Chaverrí J, Medina-Campos ON, Granados-Silvestre MA, Maldonado PD, Olivares-Corichi IM, Hernández-Pando R. Garlic ameliorates hyperlipidemia in chronic aminonucleoside nephrosis. Mol Cell Biochem. 2000 Aug;211(1-2):69-77.
57. Qidwai W, Qureshi R, Hasan SN, Azam SI. Effect of dietary garlic (Allium Sativum) on the blood pressure in humans—a pilot study. J Pak Med Assoc. 2000 Jun;50(6):204-7.
58. Rai V, Iyer U, Mani UV. Effect of Tulasi (Ocimum sanctum) leaf powder supplementation on blood sugar levels, serum lipids and tissue lipids in diabetic rats. Plant Foods Hum Nutr. 1997;50(1):9-16.
59. Ramos Almeida R, Montani Raimundo J, Rodrigues Oliveira R, Coelho Kaplan MA, Gattass CR, Sudo RT, Zapata-Sudo G. Activity of Cecropia lyratiloba extract on contractility of cardiac and smooth muscles in Wistar rats. Clin Exp Pharmacol Physiol. 2006 Jan-Feb;33(1-2):109-13.
60. Reinhart KM, Coleman CI, Teevan C, Vachhani P, White CM. Effects of garlic on blood pressure in patients with and without systolic hypertension: A meta-analysis. *Ann Pharmacother*. 2008;42:1766–71.
61. Rhiouani H, Lyoussi B, Settaf A, Cherrah Y, Hassar M. Antihypertensive effect of Herniaria glabra saponins in the spontaneously hypertensive rat. Ann Pharm Fr. 2001 May;59(3):211-4.
62. Ried K, Frank OR, Stocks NP, Fakler P, Sullivan T. Effect of garlic on blood pressure: A systematic review and meta-analysis. *BMC Cardiovasc Disord*. 2008;8:13.
63. S. Locket. Oral preparations of Rauwolfia Serpentina in treatment of essential hypertension. British Medical Journal. 1955; 809-815.
64. Salas I, Brenes JR, Morales OM. Antihypertensive effect of Cecropia obtusifolia (Moraceae) leaf extract on rats. Rev Biol Trop. 1987 Jun;35(1):127-30.
65. Sandhu JS, Shah B, Shenoy S, Chauhan S, Lavekar GS, Padhi MM. Effects of Withania somnifera (Ashwagandha) and Terminalia arjuna (Arjuna) on physical performance and cardiorespiratory endurance in healthy young adults. Int J Ayurveda Res. 2010 Jul;1(3):144-9
66. Schüssler M, H lzl J, Fricke U. Myocardial effects of flavonoids from *Crataegus* species. *Arzneimittelfo--rschung*. 1995;45:842–5.
67. Schüssler M, Hlzl J, Fricke U. Myocardial effects of flavonoids from *Crataegus* species. *Arzneimittelfors--chung*. 1995;45:842–5.
68. Shaila HP, Udupa SL, Udupa AL. Hypolipidemic activity of three indigenous drugs in experimentally induced atherosclerosis. Int J Cardiol. 1998 Dec 1;67(2):119-24.
69. Shao ZH, Li CQ, Vanden Hoek TL, Becker LB, Schumacker PT, Wu JA, Attele AS, Yuan CS. Extract from Scutellaria baicalensis Georgi attenuates oxidant stress in cardiomyocytes. J Mol Cell Cardiol. 1999 Oct;31(10):1885-95
70. Shen J, Wang J, Zhao B, Hou J, Gao T, Xin W. Effects of EGb 761 on nitric oxide and oxygen free

radicals, myocardial damage and arrhythmia in ischemia-reperfusion injury in vivo. Biochim Biophys Acta. 1998 Apr 28;1406(3):228-36.
71. Sivakumar V, Sivakumar S. Effect of an indigenous herbal compound preparation 'Trikatu' on the lipid profiles of atherogenic diet and standard diet fed Rattus norvegicus. Phytother Res. 2004 Dec;18(12):976-81.
72. Stanely Mainzen Prince P, Menon VP, Gunasekaran G. Hypolipidaemic action of Tinospora cordifolia roots in alloxan diabetic rats. J Ethnopharmacol. 1999 Jan;64(1):53-7.
73. Sui DY, Qu SC, Yu XF, Chen YP, Ma XY. Protective effect of ASS on myocardial ischemia-reperfusion injury in rats. Zhongguo Zhong Yao Za Zhi. 2004 Jan;29(1):71-4.
74. Tigno XT, de Guzman F, Flora AM. Phytochemical analysis and hemodynamic actions of Artemisia vulgaris L. Clin Hemorheol Microcirc. 2000;23(2-4):167-75.
75. Tom EN, Demougeot C, Mtopi OB, Dimo T, Djomeni PD, Bilanda DC, Girard C, Berthelot A. The aqueous extract of Terminalia superba (Combretaceae) prevents glucose-induced hypertension in rats. J Ethnopharmacol. 2011 Jan 27;133(2):828-33. Epub 2010 Nov 11.
76. Umegaki K, Shinozuka K, Watarai K, Takenaka H, Yoshimura M, Daohua P, Esashi T. Ginkgo biloba extract attenuates the development of hypertension in deoxycorticosterone acetate-salt hypertensive rats. Clin Exp Pharmacol Physiol. 2000 Apr;27(4):277-82.
77. Wong TM, Wu S, Yu XC, Li HY. Cardiovascular actions of Radix Stephaniae Tetrandrae: a comparison with its main component, tetrandrine. Acta Pharmacol Sin. 2000 Dec;21(12):1083-8.
78. Wray S, Eisner DA, Allen DG. Two hundred years of the foxglove. Med Hist Suppl. 1985;(5):132-50.
79. Wu L, Ling H, Li L, Jiang L, He M. Beneficial effects of the extract from Corydalis yanhusuo in rats with heart failure following myocardial infarction. J Pharm Pharmacol. 2007 May;59(5):695-701.
80. Xing Y, Yue P, Sun LH, Zhao WX, Wang Y, Zhang Y, Liu X, Lu YJ, Yang BF. Effect of Daming capsule on expression of connexin43 isoforms in hyperlipemic rat's cardiac muscle. 3. Zhongguo Zhong Yao Za Zhi. 2007 Jul;32(14):1440-5.
81. Xue B, Li JX, Chen LB.Agathosma betulina. Depressive effect of total flavonoid fraction of Asttragalus complanatus R. Brand its influence upon hemodynamics in SHR. Zhongguo Zhong Yao Za Zhi. 2002 Nov;27(11):855-8.
82. Yamashiro S, Noguchi K, Matsuzaki T, Miyagi K, Nakasone J, Sakanashi M, Sakanashi M, Kukita I, Aniya Y, Sakanashi M. Cardioprotective effects of extracts from Psidium guajava L and Limonium wrightii, Okinawan medicinal plants, against ischemia-reperfusion injury in perfused rat hearts. Pharmacology. 2003 Mar;67(3):128-35.
83. Yang DY, Wu XL, Xu H, Duan XZ, Wang SW, Lu ZZ. A clinical study on manshuailing oral liquid in treating elder patients with congestive heart failure of type heart and kidney yang deficiency. Zhongguo Zhong Yao Za Zhi. 2003 Nov;28(11):1091-3.
84. Yang YC, Lu FH, Wu JS, Wu CH, Chang CJ. The protective effect of habitual tea consumption on hypertension. *Arch Intern Med*. 2004;164:1534–40.
85. Yim TK, Wu WK, Pak WF, Mak DH, Liang SM, Ko KM.Myocardial protection against ischaemia-reperfusion injury by a Polygonum multiflorum extract supplemented 'Dang-Gui decoction for enriching blood', a compound formulation, ex vivo. Phytother Res. 2000 May;14(3):195-9.
86. Yoshikawa T, Naito Y, Kondo M. Ginkgo biloba leaf extract: review of biological actions and clinical applications. Antioxid Redox Signal. 1999 Winter;1(4):469-80.
87. Zhao DY, Zhao MQ, Wu WK. Study on activity and mechanism of Sini Decoction anti-mitochondrial oxidation injury caused by myocardial ischemia/reperfusion. Zhong Yao Cai. 2008 Nov;31(11):1681-5.
88. Zhao MQ, Wu WK, Zhao DY, Duan XF, Liu Y. Protective effects of sini decoction on adriamycin-induced heart failure and its mechanism. Zhong Yao Cai. 2009 Dec;32(12):1860-3.
89. Zhou F, Hu SJ, Mu Y. Protection effect of Wenxin Keli on isoproterenol induced heart failure in rats. Zhongguo Zhong Yao Za Zhi. 2007 Aug;32(16):1676-9.
90. Zhou JY, Fan Y, Kong JL, Wu DZ, Hu ZB. Effects of components isolated from Astragalus membranaceus Bunge on cardiac function injured by myocardial ischemia reperfusion in rats. Zhongguo Zhong Yao Za Zhi. 2000 May;25(5):300-2.
91. Zhou Y, Hu X, Zhao Z, He X, Peng Q, Peng X, Huang L, Sun B, Cao R. Antihypertensive study of xingnao qingxuan recipe. Zhongguo Zhong Yao Za Zhi. 1999 Aug;24(8):483-8, 511-2.