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Medicinal plants for prevention and treatment of cardiovascular diseases - A review

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Abstract: There were substantial evidences that many medicinal plants decreased the risk of cardiovascular diseases. With the high prevalence of herbal medicine use worldwide, the information regarding the therapeutic use or safety of herbal remedies usually obtained from books and pamphlets, most of which base their information on traditional reputation rather than relying on existing scientific research. This review will cover the plants with vascular, hypotensive, cardiac, cardioprotective, antiarrhythmic, hypolipidemic, hemostatic, fibrinolytic and anticoagulant effects.

Keywords: *medicinal plants, cardioprotective, antiarrhythmic, hypolipidemic, hemostatic, fibrinolytic, anticoagulant*

I . INTRODUCTION:

There were substantial evidences that many medicinal plants decreased the risk of cardiovascular diseases. Previous reviews revealed that many medicinal plants affected cardiovascular function and can be utilize for therapeutic purposes. They produced wide range of cardiovascular effects included vascular, hypotensive, positive and negative inotropic, cardioprotective, antiarrhythmic, hypolipidemic, hemostatic, fibrinolytic and anticoagulant effects [1-2]. This review was designed to cover the cardiovascular effects of medicinal plants.

Plants with vascular and hypotensive effects:

Plant	The tested constituent	Activity	Ref
Adonis vernalis	tincture of *Adonis vernalis*	Tincture of *Adonis vernalis* was evaluated as hypotensive therapy. The dog blood pressure responses was varied with dose, low doses showed rise in blood pressure whereas larger doses showed fall in blood pressure.	4
Agrimonia eupatoria	different extracts	A hypotensive effect in anaesthetised cats has been documented for an agrimony extracts given by intravenous injection; blood pressure was lowered by more than 40%.	5-6
Allium sativum	raw and extracts	Experimental and clinical studies showed that garlic produced hypotensive effects. Garlic induced significant reduction in systolic and diastolic blood pressure**.**	7-12
Althaea rosea	alcoholic extract	The alcoholic extract showed a transient hypotensive effect on anesthetic cats.	13
Ammi visnaga	visnadine and visnagin	Visnadine caused nonspecific inhibition of vascular smooth muscle. It was selectively inhibited the contractile response in the rat isolated aortic ring and portal vein segment. On the other hand ,intravenous administration of visnagin decreased blood pressure with no significant changes on the heart rate.	14-16
	chloroform, and methanol extract	A chloroform, and methanol extract (1mg/ml) of the fruits inhibited the potassium chloride induced contractions of the rabbit guinea-pig aorta in vitro.	17-18
	visnadin	Visnadin, 60.0 µg/ml or 120.0 µg/ml, increased coronary blood flow in isolated guinea-pig hearts by 46% and 57% respectively.	19-20
	visnadin	Visnagin inhibited the contractile responses induced in rat aortic rings by: (a) KCl or increases of extracellullar Ca^{2+} in KCl depolarized aortic rings, its effects being more potent against low (20 mM) than high (80 mM) KCl-induced contractions, (b) noradrenaline in Ca^{2+}-containing solution and less effectively those in Ca^{2+}-free solution and (c) phorbol 12-myristate 13-acetate (PMA) in a Ca^{2+}-containing and with a lower potency in Ca^{2+}-free medium. The relaxation induced by visnagin in aorta precontracted with noradrenaline was not affected by endothelium removal. Additionally, visnagin inhibited the	21 .

		spontaneous myogenic contractions of portal veins. The results showed that visnagin inhibited vascular smooth muscle contractility by acting at multiple sites.	
	khellin	Khella seems to improve blood supply to smooth muscles and makes myocardial metabolism more efficient. It dilated the coronary vessels, and increased the capacity of the heart without increasing the heart rate.	22
Anethum graveolens	seed oil	Intravenous administration of 5–10 mg/kg body weight of 5% seed oil in saline to cats caused hypotension and increased respiration volume.	23-25
Apium graveolens	aqueous and ethanol extracts	The effects of aqueous and ethanol extracts (0.5-15 mg/kg) was investigated on the mean blood pressure of anaesthetized rabbits and contractility of isolated atria of the rats. The intravenous administration of aqueous extracts induced the least hypotensive effects (14.35±2.94%), while the ethanol extract caused the greatest fall in the blood pressure (45.79±10.86%). Hypotensive effect of the extracts was partially blocked by atropine (0.3 mg/kg).	26
Arachis hypogaea	peptides isolated from peanut	A bioactive peptides with antihypertensive effects against Angiotensin Converting Enzyme were isolated from peanut.	27
Avena sativa	fibers of oats	In addition to cholesterol lowering effect of *Avena sativa*, it improved the blood pressure when consumed with vitamin C, improved endothelial function, and exerted angiotensine converting enzyme inhibition. According to these results, the United States Food and Drug Administration in 1997 approved the heart-health benefit of food containing soluble fiber from oats.	28-30
	beta glucan from oats	In overweight patients, beta glucan from oats has been shown to decrease hypertension. Avenanthramide is an oat polyphenol that has been shown to enhance production of nitric oxide, a potent vasodilator, and to inhibit thickening of vascular smooth muscle. Both actions are preventative to developing atherosclerosis.	31-32
Bryophyllum calycinum	aqueous and methanolic leaf extracts	The effects of aqueous and methanolic leaf extracts of the herb were examined on arterial blood pressures and heart rates of normal (normotensive) and spontaneously hypertensive rats, using invasive and non-invasive techniques. Both the aqueous and methanolic leaf extracts of the plant*(* 50-800 mg/kg iv or ip) produced dose-related, significant ($P<0.05$ - 0.001) decreases in arterial blood pressures and heart rates of anaesthetized normotensive and hypertensive rats. The hypotensive effects of the leaf extracts were more pronounced in the hypertensive than in normotensive rats. The leaf extracts (0.25 - 5.0 mg/ml) also inhibited provoked electrical field stimulation (ES-provoked) , as well as potassium and receptor-mediated agonist drugs-induced contractions of the rat isolated thoraxic aortic strips in a non-specific manner.	33-35
Caesalpinia crista	aqueous leaf extract	The administration of aqueous leaf extract induced a progressive decrease of blood pressure. The hypotensive action of the extract was dose-dependent and reversible. Hypotension induced by aqueous leaf extract of *Caesalpinia crista* or acetylcholine were inhibited by atropine. On the other hand, it significantly reduced blood pressure caused by the prior administration of adrenaline.	36-37
Capparis spinosa	aqueous extract	The vaso relaxant effect of *Capparis spinosa* aqueous extract (CSAE) at a dose of 10 mg/ ml was studied on the isolated aortic rings of normal rats. Adding of CSAE during the plateau phase of contraction, induced by noradrenaline and KCl, produced a rapid relaxation. Incubation of aortic ring with CSAE during 30 min shifted the noradrenaline induced dose response curve ($p<0.001$), the maximum response ($p<0.001$) was attenuated which indicating that antagonistic effect of the α1-adrenoreceptors was non-competitive. However, endothelium remove significantly reduced the vaso relaxant effect of CSAE ($p<0.01$). Furthermore, nitric oxide inhibition reduced the vaso relaxant effect of CSAE.	38
	aqueous extract of roots, leaves, stems, flowers, fruits and kernels	The *in vitro* vasomotor effects of aqueous extract of of roots, leaves, stems, flowers, fruits and kernels were evaluated on the rings of thoracic aorta and windpipe of rat. The addition of extracts with different concentrations during the stage of contraction led by the phenylephrin for the thoracic arteries showed a light vasodilatation. Furthermore 30 min incubation with extracts at different concentrations showed a significant vasodilator effect for fruits and kernels, and vasoconstrictor effect for leaves.	39

Carthamus tinctorius	safflower yellow	Safflower yellow (SY) 1-2 g/ kg / day lowered the blood pressure of spontaneously hypertensive rats (SHR), for about 1.86-3.86 kPa. Five weeks after administration of SY, the plasma renin activity and angiotensin II level diminished in the SHR experimental groups, which indicated that the decrease of blood pressure is mediated by inactivation of renin-angiotensin system.	40 .
	hydroxysafflor yellow A	The vasodilatation effects of hydroxysafflor yellow A (HSYA) on pulmonary artery (PA) were explored by an assay of tension study on rat pulmonary artery (PA) rings. Results suggest that HSYA possessed vascular relaxation effects on rat PA by activating the KV channel in pulmonary vascular smooth muscle cells (PVSMCs).	41
	hydroxysafflor yellow A	Intravenous injection of the hydroxysafflor yellow A (HSYA) reduced left ventricular systolic pressure (LVSP), left ventricular end-diastolic pressure (LVEDP), the maximum rate of increase of left ventricular pressure (+dp/dt(max)) and heart rate (HR) in a dose-dependent manner. HSYA had no remarkable effect on the maximum rate of decrease of left ventricular pressure (-dp/dt(max)); BK(Ca) and K(ATP) blocker can weakened the inhibitory effect of HSYA on heart function and HR, but K(V) and K(ACh) blocker did not significantly weaken the HSYA effects.	42
	N-(p-coumaroyl) serotonin (CS) and N-feruloyl serotonin (FS)	The vascular effect of N-(p-coumaroyl) serotonin (CS) and N-feruloylserotonin (FS), was evaluated. Both CS and FS (each 10 to 100 μM) relaxed rat femoral arteries, which were pre-contracted by 10-5 M phenylephrine or 50 mM KCl, independently of their endothelium. Both CS and FS also concentration-dependently inhibited the increase of cytosolic free Ca2+ concentration that was induced by KCl or 5-hydroxytryptamine in cultured rat vascular smooth muscle cells (VSMCs).	43
Chamaemelum nobile	aqueous extract	Single oral administration of *C. nobile* aqueous extract (CNAE) (140 mg/kg) produced a significant reduction ($p < 0.05$) in systolic blood pressure (SBP) after 24 h of the administration. Daily oral administration of CNAE (140 mg/kg) during 3 weeks produced a significant reduction in SBP in the day 8 ($p < 0.01$) of treatment. Furthermore, CNAE produced a significant increase in urinary output and electrolytes excretion ($p < 0.01$) from the day 8 to the end of treatment. The in vitro vasorelaxant effect of *C. nobile* aqueous extract was evaluated using aortic ring isolated from Wistar rats. *C. nobile* aqueous extract at doses of 5, 10 and 20 mg/mlpossessed in vitro vasorelaxant effect. Incubation of aqueous *C. nobile* extract for 30 minutes produced a significant shift of the dose-response curve to norepinephrine (NE) (10-8 to 10-5) M ($p < 0.001$).	44
Cicer arietinum	legumin of *Cicer arietinum* and the fractions of its hydrolysate	Treatment of legumin of *Cicer arietinum* with alcalase yielded a hydrolysate that inhibited the angiotensin I converting enzyme with an IC50 of 0.18 mg/ml. Fractionation of this hydrolysate by reverse phase chromatography afforded six inhibitory peptides with IC50 values ranging from 0.011 to 0.021 mg/ml. All these peptides contain the amino acid methionine and are also rich in other hydrophobic amino acids. Hydrolysates of chickpea legumin obtained by treatment with alcalase are a good source of peptides with angiotensin-1converting enzyme inhibitory activity.	45-46
Cichorium intybus	chicoric acid and caffeic acid	The vasorelaxant activities of chicoric acid from *Cichorium intybus* along with caffeic acid were studied in isolated rat aorta strips. chicoric acid , a diester composed of (S,S)-tartaric acid and caffeic acid, showed slow relaxation activity against norepinephrine (NE)-induced contraction of rat aorta with/without endothelium. These compound did not affect contraction induced by a high concentration of potassium (60 mM K+), while it inhibited NE-induced vasocontraction in the presence of nicardipine. The results revealed that the inhibition of NE-induced vasocontraction is due to a decrease in calcium influx from the extracellular space, which enhanced by NE.	47
Cistanche tubulosa	echinacoside, a phenylethanoid glycoside isolated from *Cistanche tubulosa*	The vasorelaxant activity of echinacoside, a phenylethanoid glycoside isolated from *Cistanche tubulosa*, and its possible underlying mechanism on isolated rat thoracic aortic rings pre-contracted with phenylephrine (PE, 1 microM) and KCl (60 mM) was investigated. Echinacoside (30-300 microM) exhibited an acute relaxation in endothelium-intact rings in a concentration-dependent manner, while this relaxation was significantly inhibited in endothelium-denuded condition and in the presence	48

		of the endothelial nitric oxide synthase (eNOS) inhibitor, N(W)-nitro-L-arginine methyl ester (L-NNA, 100 microM), an unselective soluble guanylate cyclase blocker, methylene blue (10 microM) and the selective sGC inhibitor 1 H-[1, 2, 4] oxadiazolo[4,3- A]quinoxalin-1-one (ODQ, 1 microM); in addition, atropine (1 microM), a selective muscarinic receptor antagonist, partially affected the relaxation. However, the cyclooxygenase inhibitor indomethacin (5 microM) had no influence on the relaxant action. Echinacoside enhanced the cyclic guanosine monophosphate (cGMP) production in aortic rings contracted with PE. The authors concluded that echinacoside mediates the endothelium-dependent vasodilator action in rat thoracic aortic rings through nitric oxide (NO)-cGMP pathway.The methanolic extract from the dried stems of *Cistanche tubulosa* showed inhibitory effect on contractions induced by noradrenaline in isolated rat aortic strips. From the extract, new phenylethanoid oligoglycoside constituents, kankanosides F and G, and an acylated oligosugar, kankanose, were isolated together with 14 known compounds. Kankanoside F, kankanose, echinacoside, acteoside, and cistanoside F, showed vasorelaxant activity.	
Citrus species	the juice of two different citrus fruits	The effect of drinking the juice of two different citrus fruits on vascular neointima formation was studied using a cuff-induced vascular injury mouse model. Male C57BL6 mice were divided into five groups as follows: 1) Control (water) (C), 2) 10% citrus unshiu (CU) juice (CU10), 3) 40% CU juice (CU40), 4) 10% citrus iyo (CI) juice (CI10), and 5) 40% CI juice (CI40). After drinking them for 2 weeks from 8 weeks of age, cuff injury was induced by polyethylene cuff placement around the femoral artery. Neointima formation was significantly attenuated in CU40, CI10 and CI40 compared with C. However, no remarkable preventive effect was observed in CU10. The increases in levels of various inflammatory markers including cytokines such as monocyte chemotactic protein-1, interleukin-6 (IL-6), IL-1β, and tumor necrosis factor-α in response to vascular injury did not differ significantly between C, CU10 and CI10. The increases in cell proliferation and superoxide anion production were markedly attenuated in CI10, but not in CU10 compared with C. The increase in phosphorylated ERK expression was markedly attenuated both in CU10 and CI10 without significant difference between CU10 and CI10. Accumulation of immune cells did not differ between CU10 and CI10. The results indicate that drinking citrus fruit juice attenuates vascular remodeling partly via a reduction of oxidative stress.	49
	Citrus aurantifolia fruit	The cardiovascular effects of *Citrus aurantifolia* fruit were studied experimentally. The anti-hypertensive effect was tested on three experimental hypertensive models including cadmium induced hypertensive model, glucose induced hypertensive model, Egg feed diet induced hypertensive model, and normotensive model. The systolic pressure, diastolic pressure, mean blood pressure and heart rate of Spargue Daweley rats were measured by tail cuff method from the tail of rats using non-invasive blood pressure instrument and body weights were also measured. Three different doses were used for screening 0.25, 05, and 0.75g/kg, orally given and there effects on normotensive rats were observed at 2hr, 4hr and 6hr intervals. The dose of 0.75g/kg was selected because it significantly reduced the mean blood pressure, systolic blood pressure, diastolic blood pressure, and heart rate. The methanol extract of *Citrus aurantifolia*, administered at the dose of 0.75mg orally, significantly ($p<0.01$) reduced systolic blood pressure, mean blood pressure, diastolic blood pressure, heart rate and body weight of Spargue Dawely rats in both normotensive and hypertensive experimental models when compared to control groups.	50
	aqueous extract of *Citrus aurantifolia*	The effects of an aqueous extract of *Citrus aurantifolia* on arterial blood pressure and on isolated heart and aorta activities was evaluated experimentally. Rabbits were used for the study on the arterial blood pressure using a Ludwig manometer. Albino Wistar rats were used for the isolated heart and aorta activities using isolated organ bath systems. Aqueous extract of *Citrus aurantifolia* (4mg/kg-16mg/kg bw) produced a dose-dependent and significant decrease in rabbit blood pressure ($p<0.05$). This	51

		hypotension was not prevented by atropine (2 mg/kg bw, p>0.05). Aqueous extract (4mg/kg-16mg/kg bw) was dose-dependently reduced hypertension evoked by adrenalin (30 µg/kg bw). The extract also induced both negative inotropic and chronotropic effects on the heart contractile activity. The extract induced a dose dependent relaxation of contractions produced by adrenalin or by KCl. Aqueous extract of *Citrus aurantifolia* evoked vasorelaxant effects were totally abolished by removal of the endothelium layer or by a pretreatment with L-NAME.	
	the aqueous extract of *C. medica limetta*	The antihypertensive effect of *C. medica limetta* leaves was investigated against the acute response of blood pressure to angiotensin II administration The results showed that different concentrations of the aqueous extract prevented the raise of systolic blood pressure ($p \leq 0.001$ vs. vehicle), diastolic blood pressure ($p \leq 0.0002$ vs. vehicle) and mean blood pressure ($p \leq 0.0000$ vs. vehicle); with a dose dependent effect for diastolic pressures at 125–500 mg/kg dosages. The 500 and 1000 mg/kg doses inhibited the action of Ang II in similar extent to telmisartan. Toxic signs or deaths were not observed in mice treated with a dose of 2000 mg/kg.	52
	orange (*Citrus sinensis*) juice	Four-week consumption of orange juice in healthy middle-aged, normal-weight men reduced diastolic blood pressure (DBP). However, the effects of four-week intake of natural and commercial orange (*Citrus sinensis*) juice (CSJ) on blood pressure was evaluated in healthy volunteers. 22 healthy subjects were included and randomly divided into two groups. Group A consumed commercial CSJ during the first four-week period. After a two-week washout period, they consumed natural CSJ for another four weeks. The procedure was reversed in group B. The participants were asked to drink 500 ml/day of either natural or commercial CSJ twice a day with breakfast and dinner. After drinking commercial CSJ, diastolic and systolic blood pressure were significantly decreased (5.13%; P = 0.03 and -5.91%; P = 0.003, respectively). However, consumption of natural CSJ did not have significant effects on either diastolic or systolic blood pressure. Higher flavonoid, pectin, and essential oils content of concentrated products compared to natural juice might have been responsible for this effect.	53
	water extract of *Citrus unshiu*	An attempt was made to isolate hypotensive substances from a hot water extract of *Citrus unshiu*. Six flavonoid glycosides were isolated by repeated chromatography and gel filtration after extraction with butanol and treatment with lead subacetate. Each component was intravenously injected into SHR-SP rats (1 mg/100g body weight), 3,6-di-C-glucosylapigenin and rutin were found to lower their blood pressure.	54
Cordia myxa	mucilage from both ripe and unripe *Cordia obliqua*	Mucilage from both ripe and unripe *Cordia obliqua* (RCo and URCo) decreased rabbit blood pressure and stimulated the respiratory rate. URCo was 12.37-fold more potent as a hypotensive agent than RCo. Investigation of the mode of action revealed that the hypotensive effect was more likely due to activation of parasympathetic ganglia and dilatation of peripheral blood vessels.	55-56
Coriandrum sativum	crude extract	Coriander crude extract (1-30 mg/ml) caused fall in arterial blood pressure of anesthetized animals which partially blocked by atropine. Coriander crude extract produced vasodilatation against phenylephrine and K+ (80 mM)-induced contractions in rabbit aorta and caused cardio-depressant effect in guinea-pig atria. Bioassay-directed fractionation revealed the separation of spasmogenic and spasmolytic components in the aqueous and organic fractions respectively. Furthermore, Coriander crude extract produced diuresis in rats at 1-10mg/kg.	57-58
	aqueous extracts	The water extract of coriander seed had hypotensive effects in rats. Aqueous extracts of coriander seeds inhibited the electrically- evoked contractions of spiral strips and tubular segments of isolated central ear artery of rabbit.	59-60
Crocus sativus	aqueous extracts	The effect of *Crocus sativus* on Ca^{2+} influx in isolated rat aortas was investigated by using ^{45}Ca as a radioactive tracer. Ca^{2+} uptake in isolated rat aorta rings in normal physiological status was not markedly altered by these drugs, whereas the Ca^{2+} influxes induced by norepinephrine of 1.2 mmol/l and KCl of 100 mmol/l were significantly inhibited by crocus in a concentration-dependent manner. The results showed that extracellular Ca^{2+} influx through receptor-operated Ca^{2+}channels and potential dependent Ca^{2+}channels can be blocked by crocus.	61

	ethanol extracts of petals	The effects of *Crocus sativus* petals' extract on blood pressure was evaluated on anaesthetized rats. Aqueous and ethanol extracts of *Crocus sativus* petals reduced the blood pressure in a dose-dependent manner. Administration of 50mg/100 g of aqueous extract changed the blood pressure from 133.5±3.9 to 117±2.1 (mmHg). The effects of saffron (*Crocus sativus*) stigma aqueous extract and two active constituents, crocin and safranal, were investigated on blood pressure of normotensive and desoxycorticosterone acetate-induced hypertensive rats. Three doses of crocin (50, 100 and 200 mg/kg), safranal (0.25, 0.5 and 1 mg/kg) and the aqueous extract (2.5, 5 and 10 mg/kg) were administered intravenously in different groups of normotensive and hypertensive animals and their effects on mean arterial blood pressure (MABP) and heart rate (HR) were evaluated. The aqueous extract of saffron stigma, safranal and crocin reduced the MABP in normotensive and hypertensive anaesthetized rats in a dose-dependent manner. Administrations of 10 mg/kg of aqueous extract, 1 mg/kg of safranal and 200 mg/kg of crocin caused 60 ± 8.7, 50 ±5.2 and 51 ± 3.8 mmHg reductions in MABP, respectively. Accordingly, the aqueous extract of saffron stigma had hypotensive properties which appear to be attributable, in part, to the actions of two major constitutes of this plant, crocin and safranal, and safranal was more important than crocin for lowering the blood pressure of rats.	62
	aqueous extract	The effects of saffron (*Crocus sativus*) stigma aqueous extract was studied on blood pressure of normotensive and desoxycorticosterone acetate (DOCA)-salt induced hypertensive rats. Five weeks administration of three doses saffron aqueous extract (10, 20 and 40 mg/Kg/day) and spironolactone (50 mg/Kg/ day) in different groups of normotensive and hypertensive rats (at the end of 4 weeks treatment by DOCA-salt) showed that chronic administration of saffron aqueous extract reduced the MSBP in DOCA salt treated rats in a dose dependent manner. It did not decrease the MSBP in normotensive rats. The data also showed that the antihypertensive effects of saffron did not persist.	63
	crocetin	The vasomodulatory effects of crocetin was analyzed in hypertension. Myographical experiments were performed to compare the relaxation induced by acetylcholine (ACH) on aortic rings from normotensive (Wistar) and hypertensive (SHR) rats, incubated with or without crocetin or saffron extract and L-NAME or indomethacin. Extracts were also assayed in deendothelialized rings. Crocetin enhanced the ACH relaxations in aorta from hypertensive (strongly) and normotensive rats (weakly). Crocetin plus L-NAME abolished the relaxant response in SHR but not in Wistar aorta. Crocetin plus indomethacin did not modify the indomethacin response in either SHR or Wistar aorta. Crocetin in rubbed segments did not modify the ACH responses. In contrast, saffron increased this response in rubbed segments from SHR but not Wistar rats. Accordingly, crocetin exerts healthy vasomodulatory effects in hypertension, strongly improving endothelium-dependent ACH relaxations via endothelial nitric oxide but not the cyclooxygenase pathway.	64
Cuminum cyminum	aqueous extract of seeds	The anti-hypertensive potential of standardized aqueous extract of *Cuminum cyminum* seeds and its role in arterial endothelial nitric oxide synthase expression, inflammation, and oxidative stress were evaluated in renal hypertensive rats. Renal hypertension was induced by the two-kidney one-clip (2K/1C) method in rats. Systolic blood pressure (SBP), plasma nitrate/nitrite, carotid–eNOS, renal–TNF-α, IL-6, Bax, Bcl-2, thioredoxin 1 (TRX1), and thioredoxin reductase 1 (TRXR1) mRNA expressions were studied to demonstrate the anti-hypertensive action of *Cuminum cyminum*. *Cuminum cyminum* seed was administered orally (200 mg/kg bw) for a period of 9 weeks, it improved plasma nitric oxide and decreased the systolic blood pressure in hypertensive rats. It also up-regulated the gene expression of eNOS, Bcl-2, TRX1, and TRXR1; and down-regulated Bax, TNF-α, and IL-6. The data revealed that *Cuminum cyminum* seeds augment endothelial functions and ameliorate inflammatory and oxidative stress in hypertensive rats.	65
Cydonia oblonga	ethanol leaf extracts	The effect of ethanol leaf extracts of *Cydonia oblonga* Mill. (COM) was studied on hypertension and on biomarkers	66

		associated with blood pressure control, such as angiotensin-II (AII), plasma renin activity (PRA), apelin-12 (A), endothelin (ET) and nitric oxide (NO), compared to captopril. Two-kidney one-clip (2K1C) Goldblatt model rats were divided randomly into six groups: sham, model, captopril 25 mg/kg, COM leaf extract 80, 160 and 320 mg/kg. Drugs were administered orally daily for eight weeks. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured before treatment and every 2 weeks. Blood and kidney samples were collected after the last treatment to measure AII, PRA, A, ET and NO. Renal hypertensive rats (RHR) had increased blood pressure, AII, A, PRA, ET and decreased NO. Treatment with captopril reduced blood pressure, AII, A, PRA, and ET, though not quite to normal values. COM leaf extracts significantly and dose-dependently reduced blood pressure, AII, A, RA and ET, whereas NO was increased. The effects of COM extracts on blood pressure and biomarkers were dose-dependent and at the highest dose, it produced effects similar to those of captopril.	
	fruit and leaf ethanolic extracts	The effects of *Cydonia oblonga*. (COM) fruit and leaf extracts on blood pressure and rheology were studied in renal hypertensive rats (RHR). Daily doses of 80 and 160mg/kg aqueous or ethanol extracts of COM fruit or leaves, or 25mg/kg captopril were given orally once daily for 8 weeks. Blood pressure was measured before treatment and every 2 weeks thereafter. Blood rheology was tested after 8 weeks. Model rats had higher blood pressure than sham, 8 weeks after the procedure (systolic blood pressure 193±7 vs. 138±8mmHg, $p<0.05$). Those treated with captopril had decreased blood pressure within 2 weeks but that did not return to the level found in the sham group at 8 weeks (167±7, $p<0.05$ vs. model). With the COM extracts, the effect on blood pressure was notable after 4 weeks. At 8 weeks blood pressure was similar with captopril and with 160mg ethanol leaf extract (166±4, $p<0.05$ vs. model), it was the most effective of the extracts. Model rats had higher blood viscosity and lower erythrocyte deformability than sham. Captopril had little effect on blood rheology; whereas COM extracts reduced whole blood viscosity and improved erythrocyte deformability to levels approaching those found in sham.	67
Daucus carota	ethanolic extract	Ethanolic extract of *Daucus carota* at the dose of 10–100 mg/kg caused a dose-dependent fall in systolic and diastolic arterial blood pressure in normotensive anesthetized rats. These effects were not blocked by atropine (1 mg/kg). Pretreatment with *Daucus carota* did not alter the pressor response to norepinephrine indicating that, cardiovascular effects of *Daucus carota* were independent of cholinergic or adrenergic receptors involvement. In spontaneously beating guinea-pig paired atria, *Daucus carota* induced a concentration-dependent (0.3-5 mg/ml) decrease in force and rate of atrial contractions. In rabbit thoracic aorta, *Daucus carota* caused inhibition of K^+-induced contractions at similar concentrations.	68-69
	two cumarin glycosides isolated from the aerial parts	Fractionation of aerial parts of *Daucus carota* resulted in the isolation of two cumarin glycosides coded as DC-2 and DC-3. Intravenous administration (1-10mg/kg) of these compounds caused a dose-dependent fall in arterial blood pressure in normotensive anaesthetised rats, Both compounds caused a dose-dependent (10-200 pg/ml) inhibitory effect on spontaneously beating guinea pig atria as weIl as on the Kt-induced contractions of rabbit aorta at similar concentrations *in vitro*. The results indicated that DC-2 and DC-3 acting through blockade of calcium channels, the effect which may be responsible for the blood pressure lowering effect of the compounds observed in the *in vivo* studies.	70

Plants with cardiac effect:

Plant	The tested constituent	Activity	Ref

Adonisa estivalis	strophanthidin aglycone	Strophanthidin aglycone is one of several cardenolides extracted from *Adonisa estivalis*. The direct effect elicited by these compounds is similar to other cardiac glycoside-containing plants and is due to inhibition of the sodium potassium adenosine triphosphatase enzyme system pump. Theyincrease vagal tone, which decreases the rate of sinoatrial node depolarization. In intoxication , the electro cardiographic changes seen are include bradycardia, varying levels of atrioventricular block, ventricular arrhythmias, and ventricular fibrillation.	71-72
	tincture of *Adonis vernalis*	Tincture of *Adonis vernalis* is used by homeopathic physicians in patients suffering from congestive cardiac failure. Its action was very much similar to digitalis on heart. Aqueous extract of *Adonisvernalis* was found to have cardiac stimulant action on isolated heart preparations. It showed protection against heart failure produced by excessive load and high potassium concentration. Tincture of *Adonis vernalis* was found to cause cardiac depression which was not blocked by the atropine. In isolated guinea pig and rabbit auricles the drug increased the threshold of electrical stimulation.	4, 73
Alhagi maurorum	ethanolic extract	In evaluation the effect of the ethanolic extract of *Alhagi maurorum* powdered roots in anaesthetized rats, the results revealed that the extract at a dose of 1 g/kg induced bradycardia only and not myocardial depressant. Glyceryl-n-tetracosan-17-ol- 1-oate (a new aliphatic ester isolated from the root of the plant) possessed a heart rate stimulant action and a myocardial depressant action on rat isolated heart.	74-75
Althaea rosea	Alcoholic extract of the flower	Alcoholic extract of the flower of *Althaea rosea* (L.)increased the outflow of coronary artery of isolated guinea pig's heart and markedly dilated the blood vessels in the hind-limbs of rats. The extract showed a transient hypotensive effect on anesthetic cats. It inhibited platelet aggregation induced by ADP and showed a inhibitory effect on experimental thrombosis formation.	76
Ammi visnaga	Extract, samidin and khellol	*Ammi visnaga* induced relaxation of smooth muscle, including that coronary arteries, in a variety of animal species. Samidin and khellol glucoside induced positive inotropic effects on heart. A clinical trial of khellin in 38 cases of angina pectoris and in 8 cases of coronary thrombosis was performed . Continuous treatment, by the oral or intramuscular routes or by both, gave favourable results in 35 out of 38 cases of angina pectoris. Continuously administration of khellin for several weeks to eight patients after coronary thrombosis appeared favourable.	77-78
	khellin	Immediately after the rapid intravenous administration of 20-30 mg of khellin to the	79

		dogs, the heart beats considerably slower. The entire effect lasts for only a short time, within a minute or two.	
Anchusa strigosa	Aqueous extracts of the flowers	The extract was found to have slight inhibitory effect on the auricular contraction in bilaterally vagotomised dog but there was no effect on ventricular contraction in this animal. These results indicate that the site of action is probably blood vessel.	80-81
Apium graveolens	aqueous and ethanol extracts	Both aqueous and ethanol extracts exhibit a negative chronotropic and inotropic actions. Aqueous extract decreased the rate of contractions by 12.88±2.74% and amplitude by 8.73±0.89%. Ethanol extract inhibited the rate of atria contractions by 34.26±5.69% and amplitude by 25.40±3.61%. Pretreatment of rat atria with atropine (1 μM) partially blocked the inhibitory response induced by aqueous and ethanol extracts of *Apium graveolens*.	82
Asclepias curassavica	asclepin	Asclepin extracted from *Asclepias curassavica* showed positive inotropic activity; it was more potent, and safer than other cardiac glycosides (including digoxin). It showed longer duration of action than digoxin (96 h in cat, as opposed to the 72 h of digoxin).	83
Bacopa monnieri	ethanolic extract of whole plant	Ethanolic extract of whole plant of *Bacopa monnieri* has shown cardiac depressive activity on left ventricular contractility, heart rate and coronary flow in isolated rabbit heart and it appeared that, the activity of ethanolic *Bacopa monnieri* extract was similar to that of quinidineon heart.	84-85
Brassica nigra	mustard	Mustard stimulated the cardiac and respiratory activity in sufficient force to arouse one from an attack of fainting. Both the breathing and circulation are stimulated by its reflex action upon the respiratory center and the heart.	86-87
Caesalpinia crista	alcoholic and aqueous extract	The alcoholic and aqueous extract was evaluated for protection against isoproterenol (85 mg/kg bw) induced myocardial infarction in albino rats. Pretreatment with an ethanolic and aqueous extract at a dose of 400 mg/kg, orally for 30 days, reduced significantly ($p<0.01$) the elevated marker enzyme levels in serum and heart homogenates in isoproterenol - induced myocardial infarction. Histopathological observation revealed a marked protection by the extract in myocardial necrotic damage.	88
Calendula officinalis	calendula solution	Rat hearts perfused with calendula solution at 50 mM in KHB buffer for 15 min prior to subjecting the heart to ischemia, showed cardioprotection by stimulating left ventricular developed pressure and aortic flow as well as by reducing myocardial infarct size and cardiomyocyte apoptosis. Cardioprotection appears to be achieved by changing ischemia reperfusion-mediated death signal into a survival signal by modulating antioxidant and anti-inflammatory pathways as evidenced by	89-90

		the activation of Akt and Bcl2 and depression of TNFα.	
Calotropis procera	ethanolic latex extract	Latex was evaluated for protection against isoproterenol (20 mg/100g) induced myocardial infarction in albino rats. The pretreatment with an ethanolic latex extract at a dose of 300 mg/kg body weight orally three times a day for 30 days, reduced significantly ($p<0.01$) the elevated markers enzyme levels in serum and heart homogenates in isoproterenol induced myocardial infarction.	91-92
	ethanol, n-butanol, ethyl acetate extracts and latex	The effects of ethanol, n-butanol, and ethyl acetate (EtOAc) extracts of the aerial parts of the plant, were evaluated on isolated toad heart. Their mechanisms of action were also studied. Perfusion with 2 μg/ml ethanol, 0.2 μg/mL butanol, and 0.2 μg/mL EtOAc extracts caused a significant decrease in heart rate (bradycardia), significant increase in the force of ventricular contraction, and increase in T-wave amplitude. The different extracts and latex of *C. procera* induced negative chronotropism and positive inotropism on isolated toad heart.	93
Carthamus tinctorius	Ethanolic extract of the petals	An animal model of myocardial ischemia injury was induced by left anterior descending coronary artery occlusion in adult rats. Pretreatment with *C. tinctorius* (ECT) (100, 200, 400, 600 mg/kg body wt.) protected the heart from ischemia injury by limiting infarct size and improving cardiac function. In the *in vitro* experiment, neonatal rat ventricular myocytes were incubated to test the direct cytoprotective effect of ECT against H2O2 exposure. Pretreatment with 100-400 microg/ml ECT prior to H2O2 exposure significantly increased cell viability. ECT also markedly attenuated H2O2-induced cardiomyocyte apoptosis. The protection is achieved by scavenging of ROS and mediating the PI3K signaling pathway.	94-95
	Carthamus tinctorius injection	The effects of safflower injection (SI) in protecting heart, on energy charge and anti-apoptosis gen bcl-2 in cardiac tissue were investigated by Rats' Langendorff isolated heart infused model. As compared with the control, SI improved the functions of cardiac contraction and dilation, increasing coronary blood flow, and strengthening the bcl-2 protein expression.	96
	Flos Carthami FC(EtOH)) ethanolic extract	The effect of Flos Carthami FC(EtOH)) ethanolic extract on LPS-induced apoptosis in H9c2 cardiomyoblast cells was studied. FC(EtOH) (62.5 microg/mL) inhibited LPS-induced apoptosis by suppressing JNK1/2 activity, which resulted in the reduction of both IkappacB degradation and NF kappaB activation. In addition, FC(EtOH) led to activation of anti-apoptotic proteins, Bcl-2 and	97-98

		Bcl-xL, the stabilization of the mitochondria membrane and the down-regulation of extrinsic and intrinsic pro-apoptotic proteins, such as TNF alpha, active caspase-8, t-Bid, Bax, active caspases-9, and -3. The ability of *Carthamus tinctorius* to suppress JNK activity and inhibit LPS-induced TNF alpha activation and apoptosis in H9c2 cardiomyoblast cells could potentially serve as a cardio-protective agent against LPS-induced apoptosis.	
	safflor yellow A (SYA), a flavonoid extracted from Carthamus tinctorius	The effects of safflor yellow A (SYA) was evaluated on cultured rat cardiomyocytes exposed to anoxia/reoxygenation (A/R). The A/R exposure markedly decreased the viability of cardiomyocytes, suppressed the activities of SOD, GSH, CAT, GSH-Px, and Bcl-2 protein expression. Meanwhile, the A/R exposure markedly increased the release of LDH, CK, MDA production in the cardiomyocytes, increased the rate of apoptosis, caspase 3 activity and Bax protein expression.	99
	safflor yellow B (SYB)	The protective effect of safflor yellow B (SYB) was investigated against vascular endothelial cells (VECs) injury induced by angiotensin-II (Ang-II). Comparing with control group, Ang-II was able to increase Ca2+ and ROS level, decrease MMP level, inhibit complex IV activity and enhance caspase 3 activity in VECs, as a result, enhance apoptosis of VECs. SYB was able to eliminate the effect of Ang-II on VECs via regulating Ca+2, mitochondrial structure and function and inhibiting apoptosis.	100
	hydroxysafflor yellow A	Intravenous injection of the hydroxysafflor yellow A (HSYA) significantly reduced MAP and HR in both normotensive rats and SHR in a dose-dependent manner. HSYA reduced left ventricular systolic pressure (LVSP), left ventricular end-diastolic pressure (LVEDP), the maximum rate of increase of left ventricular pressure (+dp/dt(max)) and heart rate (HR) in a dose-dependent manner. HSYA had no remarkable effect on the maximum rate of decrease of left ventricular pressure (-dp/dt(max)); BK(Ca) and K(ATP) blocker can weakened the inhibitory effect of HSYA on heart function and HR, but K(V) and K(ACh) blocker did not significantly weaken the HSYA effects.	42
Cheiranthus cheiri	Plant glycosides (cheiranthoside III and VIII)	Cardiac glycosides called cheiranthosides I-XI together with two olitoriside and erysimoside were isolated from the seeds of the plant. The glycosides were evaluated for their inhibitory activity against Na^+,K^+ -ATPase by comparing with typical cardiac glycosides. Two of them, cheiranthoside III and VIII, showed high inhibiting activity which was equivalent to that of digitoxin. Cheiranthoside XI containing a rhamnopyranosyl digitoxopyranosyl moiety and a carboxyl group showed the lowest activity	101

		which was similar to that of the inactive aglycone, strophanthidin.	
Citrus species	ethanolic extract of *Citrus medica*	The protective effect of the ethanolic extract of Otroj, *Citrus medica* (EEOT) against isoproterenol (ISO)-induced cardiotoxicity was evaluated in rats. Rats were administered EETO (250 and 500 mg/kg) or vehicle orally for 15 days along with ISO (85 mg/kg, sc) on the 14th and 15th day. ISO induced cardiac dysfunction, increased lipid peroxidation and alteration of myocyte-injury specific marker enzymes. ISO also showed an increase in levels of plasma cholesterol, triglycerides (TG), LDL-C, and VLDL-C. Moreover, the histological investigations showed myocardial necrosis and inflammation. EETO treatment brought the above parameters towards normal level. Moreover, *in vitro* DPPH radical scavenging and β-carotene-linoleic acid tests of the EEOT exhibited a notable antioxidant activity in both assays used. In addition, histopathological examination reconfirmed the protective effects of EEOT. Accordingly *C. medica* alleviates myocardial damage in ISO-induced cardiac injury and demonstrates cardioprotective potential.	102-104.
Corchorus aestuans	alcoholic extract and glycosides of seeds	Alcoholic extract and glycosides of seeds exhibited cardiotonic activity.	105
	Cardiac glycoside isolated from the plant	Cardiac glycoside was isolated from the plant fruits and tested for cardiotonic activity using isolated frog heart perfusion technique (IFHP). A significant increase in the height of force of contraction (positive inotropic effect) and decrease in heart rate (negative chronotropic effect) was observed at smaller doses (0.4 mg). The effect increased as dose was increased. The test compound had not produced cardiac arrest even at a dose of 2 mg, compared to standard, digoxin that showed cardiac arrest at dose of 0.2 mg. Hence, as compared to standard, the tested cardiac glycoside showed wide therapeutic index.	106-108
Corchorus capsularis	Corchortoxin (strophanthidin) a cardiac aglycone isolated from the seeds of *Corchorus capsularis*	Corchortoxin (strophanthidin) was a cardiac aglycone isolated from *Corchorus capsularis* seeds, showed a cardio-tonic activity. These activities were similar to digitalis genus. However, jute seeds extract showed better activities than corchortoxin. Corchoroside A and B, which also isolated from other plants also showed digitalis like action.	109-113
Coriandrum sativum	aqueous extracts	The preventive effect of *Coriandrum sativum* (CS) on cardiac damage was evaluated by isoproterenol induced cardiotoxicity model in male rats. Rats were pretreated with methanolic extract of CS seeds at a dose of 100, 200 or 300 mg/kg orally for 30 days and they were subsequently administered (sc) with isoproterenol (85 mg/kg body weight) for the	114

		last two days. Isoproterenol treated rats showed increased LPO, decreased levels of endogenous antioxidants and ATPases in the cardiac tissue together with increased plasma lipids and markers of cardiac damage. TTC staining showed increased infarct areas while HXE staining showed myofibrillar hypertrophy and disruption. CS (200 and 300 mg/kg body weight) pretreatment significantly prevented or resisted all these changes. The results showed that methanolic extract of CS is able to prevent myocardial infarction by inhibiting myofibrillar damage. It is also postulated that, the rich polyphenolic content of CS extract was responsible for preventing oxidative damage by effectively scavenging the isoproterenol generated ROS.	
Coronilla scorpioides	Coronillin	The physiological studies have demonstrated that the coronillin was toxic to the heart, its effect on the heart is similar to digitalis. In small doses it slowed the pulse through stimulation of the inhibitory ganglia, and in larger quantity increased the tonicity and contractility of the heart, eventually leading to systolic spasm of the ventricle. This action upon the heart was accompanied by increase in the arterial pressure, followed after a time by lowering of the pressure, which apparently was the result of failure of diastole, causing the amount of blood forced out of the heart at each systole to be insufficient to fill the arteries.	115-116
Coronilla varia	glycosides, hyrcanoside and deglucohyrcanoside isolated from the seeds	The Cardiotonic and cardiotoxic effects of two cardiac glycosides, hyrcanoside and deglucohyrcanoside isolated from the seeds of *Coronilla varia* were evaluated in comparison with the effect and toxicity of digoxin and ouabain. Evaluation of the cardiotonic effect using the methods of heart (in situ) and the isolated heart (Langendorff) proved that deglucohyrcanoside was more effective than hyrcanoside and that its effect was equal to that of digoxin as well as ouabain. The efficacy of deglucohyrcanoside at least equal to that of digoxin, while the toxicity of the former was several times lower, which indicated that the glycoside a potential candidate for therapeutic use.	117-120
Crocus sativus	saffron extracts	The effect of saffron was investigated against acute myocardium damage by anthracyclines using rabbit heart model. The heart was perfused with anthracycline, i.e. 30 μM doxorubicin (Doxo) in the presence and absence of 10 μg/ml saffron extracts. Saffron perfused during electrolysis helped trap ROS and significantly improved myocardial function; however, saffron was less effective against Doxo, thus suggesting that mechanisms other than oxidative stress underlie Doxo cardiotoxicity.	121

	aqueous extract and safranal	The cardioprotective effect of *Crocus sativus* (saffron) aqueous extract and safranal, the major constituent of the essential oil of saffron was evaluated on lipid peroxidation, biochemical parameters and histopathological findings in isoproterenol (ISO)-induced myocardial infarction in Wistar rats. Saffron pretreatment (20, 40, 80 and 160 mg/kg ip) or safranal pretreatment (0.025, 0.050, 0.075 ml/kg ip) for 8 days, significantly decreased ($p<0.001$) the serum LDH and CK-MB and myocardial lipid peroxidation as compared to ISO- induced rats. Histological findings of the heart sections confirmed myocardial injury with ISO administration and preserved nearly normal tissue architecture with saffron or safranal pretreatment.	122
	Saffron	The cardioprotection effect of saffron (200, 400 and 800 mg/kg) was evaluated in isoproterenol-induced myocardial damage in rats. Saffron at all the doses exerted significant cardioprotective effect by preserving hemodynamics and left ventricular functions, maintaining structural integrity and augmenting antioxidant status. Among the different doses used, saffron at 400mg/kg exhibited maximum protective effects which could be due to maintenance of the redox status of the cell which reinforcing its role as an antioxidant.	123
	aqueous-ethanol extract	The effects of an aqueous-ethanol extract from *Crocus sativus* on heart rate and contractility were examined on isolated guinea-pig hearts. Heart rate and contractility were determined in the presence of four concentrations of the extract (0.1, 0.5, 1.0 and 5.0 mg%) and diltiazem (0.1, 1, 10 and 100 microm) in perfused heart with: (1) ordinary Krebs solution (group 1) and calcium-free Krebs solution (group 2). In group 1, three higher concentrations of diltiazem (1, 10 and 100 microm), but only the highest (5.0 mg%) and two higher concentrations (1.0 and 5.0 mg%) of the extract caused significant reduction in heart rate and contractility, respectively ($p < 0.05$ to $p < 0.001$). In group 2, the highest (100 microm), two higher concentrations (10 and 100 microm) of diltiazem ($p<0.05$ to $p<0.01$), and the highest concentration of the extract showed significant reductions in the heart rate and contractility ($p < 0.05$ to $p < 0.01$). There were significant negative correlations between concentrations of the extract and diltiazem and their effects in both groups ($p<0.01$ to $p<0.001$). The results suggested a potent inhibitory effect of aqueous-ethanol extract from *Crocus sativus* on the calcium channel of guinea-pig heart.	124
Cynodon dactylon	hydroalcoholic extract of rhizomes	The effects of hydroalcoholic extract of *Cynodon dactylon* rhizomes was evaluated on cardiac contractility in normal hearts and on	125

		cardiac functions in right-heart failure in rats. Right-heart failure was induced by intraperitoneal injection of monocrotaline (50 mg/kg). Two weeks later, the animals were treated orally with different doses of the extract for fifteen days. At the end of the experiments, cardiac functions and markers of myocardial hypertrophy were measured. The treated rats showed very less signs of fatigue, peripheral cyanosis and dyspnea. The survival rate was high in the extract treated groups (90%). Administration of *Cynodon dactylon* in monocrotaline-injected rats led to profound improvement in cardiac functions as demonstrated by decreased right ventricular end diastolic pressure (RVEDP) and elevated mean arterial pressure. RVdP/dtmax, and RVdP/dt/P as indices of myocardial contractility were also markedly ($p<0.001$) increased by the extract. The extract reduced heart and lung congestion by decreasing tissue wet/dry and wet/body weight ratios ($p<0.01$). In the isolated rat hearts, the extract produced a remarkable ($p<0.001$) positive inotropic effect concomitant with a parallel decrease in LVEDP.	
	phenolic fraction	The phenolic fraction of *Cynodon dactylon* (CDP) was evaluated for its cardio-protective activity using isolated frog's heart perfusion method. The CDP produced negative inotropic and chronotropic actions on isolated frog heart. These pharmacological effect were selectively inhibited by atropine, which indicated that these effects were mediated through muscarinic receptor.	126
Cyperus rotundus	ethanolic extract	The preventive role of ethanolic extract of *Cyperus rotundus* rhizomes (CRRE) was investigated on age associated changes in glucose and lipids in young and aged rats. CRRE was given as (500mg/kg body weight) orally for 30 days. Age associated increase in serum glucose, total cholesterol, triglycerides, LDL cholesterol, VLDL cholesterol and a decrease in HDL cholesterol was observed in aged rats compared to young rats. Administration of CRRE to aged rats prevented the age associated changes in glucose, total cholesterol, triglycerides, LDL cholesterol and VLDL cholesterol. HDL cholesterol level was found to be increased significantly in both young and aged rats after treatment with CRRE.	127

Dalbergia sissoo	alcoholic leaf extract	The effect of alcoholic extract of *Dalbergia sissoo* leaf (DSE) (30, 100 and 300 mg/kg of body weight) was studied in isoproterenol (ISP)-induced myocardial injury in rats. Rats pretreated with DSE (30, 100 and 300 mg/kg of body weight) showed significant ($p < 0.05$-0.001) improvement in the relative heart weight, myocardial infarcted areas, heart rate and mean arterial pressure in ISP-induced myocardial injury. DSE showed significant ($p < 0.05$-0.001) improvement in serum LDH, CK-MB, cholesterol, LDL and triglyceride levels at all the dose levels. However, DSE pretreatment had no significant effect on serum HDL level. Pretreatment with DSE (30, 100 and 300 mg/kg body weight) showed significant ($p < 0.001$) reduction in MDA level in comparison with myocardial injured rats. Furthermore, antioxidant potential was also improved in terms of improved activities of reduced glutathione, superoxide dismutase and catalase with the DSE pretreatment. Histopathology also showed significant improvement in heart tissue.	128-129
Daucus carota	aqueous extract of tubers	Aqueous extract of *Daucus carota* tubers were investigated for inotropic and cardioprotective effects by measuring various biochemical parameters at the test doses of 250 and 500 mg/kg. Isoproterenol (5.25 mg/kg and 8.5 mg/kg) was administered subcutaneously on 29^{th} and 30^{th} day respectively in order to induce myocardial infarction. Cardiac tonicity was estimated by evaluating Na^+K^+ATPase, Mg^{2+}ATPase and Ca^{2+}ATPase levels in heart. The levels of Na^+K^+ATPase and Mg^{2+}ATPase were decreased and that of Ca^{2+}ATPase was increased in extract-treated group significantly ($p<0.001$). Cardioprotection was assessed by estimating serum aspartate transaminase, alanine transaminase, lipid peroxidase, and lactate dehydrogenase levels and cardiac total protein and lipid peroxidase, and lactate dehydrogenase. The levels altered by isoproterenol were restored significantly by the administration of the extract.	130
Digitalis lanata **and** ***Digitalis purpurea***	digitalis glycosides	Cardiac glycosides, are often called digitalis or digitalis glycosides, in particular digoxin and digitoxin, have been a cornerstone of the treatment of heart diseases for more than two centuries. They possessed many cardiovascular effects: (I)Regulation of cytosolic calcium concentration: by inhibiting the Na^+/K^+-adenosine triphosphatase (ATPase) enzyme, thereby increasing cardiac contractility. (II) Increased contractility of the cardiac muscle: causing cardiac output to more closely resemble that of the normal heart. Vagal tone is also enhanced, so both heart rate and myocardial oxygen demand decrease. Digitalis slows	131-138

		conduction velocity through the AV node, making it useful for atrial fibrillation. (III) Electrophysiological effects: the major effect on cardiac rhythm of digitalis preparations is believed to be due to inhibition of the sodium pump. However, cells in various parts of the heart show differing sensitivities to digitalis, and both direct and neurally mediated effects are now known to occur. Indeed, at therapeutic levels of digitalis, these drugs decrease automaticity and increase maximum diastolic potential, effects that can be blocked by atropine, whereas higher (toxic) concentrations decrease diastolic potentials and increase automaticity. Similarly, the toxic arrhythmogenic effects of the cardiac glycosides are due to a combination of direct effects on the myocardium and neurally mediated increases in autonomic activity.	
Ephedra alata* and *Epedra foliata	Ephedrine	The arterial pressure, raised and vagal slowing occurred after administration of ephedrine to experimental animals. It appeared that ephedrine activates the same adrenergic receptors as epinephrine but is less potent and has a longer duration of action. The pressor response to ephedrine is due in part to peripheral constriction and in part to myocardial stimulation. In humans, ephedrine increases the arterial pressure both by peripheral vasoconstriction and by cardiac stimulation. The heart rate is usually increased, as is the pulse pressure, both suggesting an increased cardiac output. However, the hypotension that commonly occurs during surgery under spinal anesthesia is practically always prevented by ephedrine. As a conclusion, it appeared that ephedrine activates the same adrenergic receptors as epinephrine but is less potent and has a longer duration of action. In complete heart block with Stokes–Adams syncope, ephedrine proved of value to increase ventricular rate and prevent ventricular asystole, an initial dose of about 8 mg of ephedrine sulfate orally may be tried, then the dose increased to 25 mg three or four times daily. Syncope due to ventricular tachycardia can also be prevented in some cases with ephedrine.	139-141
Erodium cicutarium	organic extracts	The addition of extracts of *Erodium cicutarium* to the Kreb's solution perfusing isolated heart from rabbit, they produced a negative ionotropic action. Organic extracts (hexane and methanol) having a greater activity on smooth and cardiac muscles than water extracts.	142-145

Plants with anti-arrhythmic effects:

Plant	The tested constituent	Activity.	Ref
Achillea santolina	methanol extract	On isolated heart of rats as an experimental model to determine the effect of the methanol extract of *Achillea santolina* on the electro physiological properties, the methanolic extract of *Achillea santolina* induced significant depression of WBCL, AVCT and ERP and non-significant increase in the time constant of recovery (t.rec). It may be considered a potential drug for anti-arrhythmic effect for suppression or treating supraventricular tachyarrhythmia.	146
Ammi visnaga	visnadin, dihydrosamidin, khellin and samidin	In coronary vasospasm and myocardial ischaemia induced in dogs by daily intramuscular injections of vasopressin, visnadin, dihydrosamidin, khellin and samidin effectively normalized the electrocardiogram when given in a dose of 4.7 mg/kg bw per day intramuscularly for 7 days.	78, 147
Carthamus tinctorius	*Carthamus tinctorius* aqueous injection	*Carthamus tinctorius* injection(CTI) (2.5 and 0.625 g/kg) significantly inhibited the typical ECG S-T segment elevation, reduced concentration of IL-6 and TNF-α in serum, suppressed overexpression of Bax protein and also inhibited the reduction of BCl-2 expression and markedly depressed the Bax/Bcl-2 ratio in isoprenaline-induced acute myocardial ischemia (AMI) . These findings demonstrate that CTI is cardioprotective against AMI in rats and is likely to related to decrease inflammatory response mediated by TNF-α and IL-6, down-regulate protein level of Bax and up-regulate that of Bcl-2 in the heart tissue.	95, 148
Cichorium intybus	roots extracts of different varieties of the plant	Pharmacological study of eight varieties of *Cichorium intybus* on isolated toad's heart showed that the eight varieties have a quinidine like action, but with variable potency.	149
Crocus sativus	hydroalcohol extract	The effects of aqueous-ethanolic extract from Crocus sativus (0.1, 0.5, 1.0 and 5.0 mg%) were investigated on heart rate and contractility of guinea-pig isolated heart. Only highest and two larger concentrations of the extract caused significant reduction in heart rate and heart contractility respectively ($p<0.05$ to $P<0.01$). There were significant negative correlation between concentrations of the extract and diltiazem and their effect on heart rate and contractility in both groups ($p<0.01$ to $p<0.001$).	150
	saffron	High dose (200 mg/kg) of saffron significantly increased the PR interval, P duration, QT interval ($p<0.01$), QRS interval, QTcn (normalized corrected QT) ($p<0.001$), and JT interval ($p<0.05$) of ECG compared to the control group. In addition, the two other doses only significantly prolonged the QT, QTcn and JT intervals of ECG versus the control group. The SAF200 group also showed a notable increase in RR interval which only was significant compared to the SAF50. There was no significant difference among ST height and T amplitude ranges of different groups. Accordingly, the results revealed that high dose of saffron	151

		definitely slowed the electrical conduction velocity in both atrium and ventricle.	
Cynodon dactylon	hydroalcoholic extract of rhizome	The probable antiarrhythmic effects of *Cynodon dactylon* against ischemia/ reperfusion (I/R)-induced arrhythmias were investigated in isolated rat heart. The hearts were subjected to 30min regional ischemia followed by 30min reperfusion and perfused with hydroalcoholic extract of rhizome of *Cynodon dactylon* (25, 50, 100 and 200µg/ml). During ischemia, the extract produced marked reduction in the number, duration and incidences of ventricular tachycardia (VT) at 25 and 50µg/ml ($p<0.001$ and $p<0.01$) respectively. Total number of ischemic ventricular ectopic beats (VEBs) were lowered by 25, 50, 100µg/ml ($p<0.001$, $p<0.001$ and $p<0.050$ respectively. At the reperfusion phase, *Cynodon dactylon* (25 and 50µg/ml) decreased incidence of VT from 100% (control) to 13 and 33% ($p<0.001$ and $p<0.05$) respectively. Duration and number of VT and total VF incidence were also reduced at the same concentration ($p<0.05$ for all). Perfusion of the extract (25, 50, 100µg/ml) was markedly lowered reversible VF duration from 218±99second to 0 second, 0 second and 10±5 second ($p<0.01$, $p<0.01$ and $p<0.05$) respectively. Moreover, *Cynodon dactylon* (25 and 50µg/ml) decreased number of total VEBs from 349±73 to 35±17 ($p<0.001$) and 66±26 ($p<0.01$). it was also shown that perfusion of the extract produced a marked and concentration-dependent positive inotropic effect.	152

Plants with hypolipidemic effects:

Plant	The tested constituent	Activity	Ref
Allium species	Garlic (1–4% in diet), different extracts	Garlic (1–4% in diet) and garlic protein administration in hypercholesterolemic rats induced by a high-cholesterol diet, significantly reduced serum cholesterol, triglyceride and LDL cholesterol. Long term feeding of garlic and garlic preparations on experimental atherosclerosis induced by a high-cholesterol diet in rabbits cause statistically significant reduction in serum lipids and atheromatous lesions. Water soluble extract of garlic inhibited the biosynthesis of cholesterol in hepatocytes. Garlic derived components are capable of mbining with the sulphydryl (-SH) group. Reduced conversion of acetate into cholesterol has been observed both *in vivo* and *in vitro* . Eating of 10 g fresh garlic per day for 2 months significantly decreases (15%-28.5%) serum cholesterol levels among hypercholesterolemic patients. Garlic oil caused a steady decrease in LDL and VLDL levels with concomitant increase in HDL levels. Intake of enteric-coated garlic	153-172

		powder (equal to 400 mg garlic, 1mg allicin) twice daily in hyperlipidemic patients has significantly reduced total cholesterol, LDL-cholesterol and triglyceride and increased HDL-cholesterol. The level of cholesterol, triglyceride, phospholipids and ß- lipoproteins were significantly declined in the individuals consuming 10-50 g of garlic /week. These results indicate that routine consumption of garlic in the diet has a beneficial effect in maintaining the serum lipids at low or normal levels. In a placebo-controlled trial of patients with stage II peripheral arterial occlusive disease, garlic powder supplements , 800 mg daily were associated with a significant increase in walking distance by 46 meters; the improvement started after the fifth week of treatment. Patients treated with 900 mg daily of standardized garlic powder showed 9-18% reduction in plaque volume, a 4% decrease in LDL levels, an 8% increase in HDL concentrations, and a 7% decrease in blood pressure.	
Aloe vera	*Aloe vera* gel	*Aloe vera* gel lowered triacylglyceride levels in liver and plasma. Histological examinations of periepididymal fat pad showed that *Aloe vera* gel reduced the average size of adipocytes.	173-174
	Aloe vera in diet	Five thousand patients of atheromatous heart disease, presented as angina pectoris, were studied over a period of five years. After adding the (Husk of Isabgol) and *(Aloe vera*) to the diet, a marked reduction in total serum cholesterol, serum triglycerides, increased HDL, decreased fasting and postprandial blood sugar level in diabetic patients were noted. Simultaneously the clinical profile of these patients showed reduction in the frequency of anginal attacks.	175
Alpinia galangal	ethanolic extract and constituents	Ethanolic extract of *A. galanga* 20mg/day for 4 weeks in rats exerted hypolipidemic activity, with a significant increase in the serum levels of high density lipoproteins (HDL) in rats. *A. galanga* constituents exerted platelet activating factor (PAF) antagonists. Methanolic extract showed significant inhibitory effects on PAF with IC50 value of 5.5ug/ml in rabbit platelets.	176-178
Ammi visnaga	khellin	A clinical study was carried out on 20 non-obese, normolipaemic male subjects to determine the effects of orally administered 50 mg khellin four times daily for 4 weeks on the plasma lipids. Plasma total cholesterol and triglyceride remained unchanged, but high-density-lipoprotein cholesterol concentration was significantly elevated during the treatment and till one week after cessation of treatment. In a comparison with glyceryl trinitrate, khellin (3 ml containing 150 mg of	179

		khellin, alcoholic extract standardized to contain 50 mg/ml) was used in twelve patients for prevention of angina of effort and the electrocardiographic changes that may accompany it . Khellin was less potent but longer acting than glyceryl trinitrate , and it did not cause any unpleasant side effects.	
Anethum graveolens	crude extract	The crude extract of *Anethum graveolens* showed anti-hyper cholesterolaemic and anti-hyperlipidaemic activities. The crude extracts of *A. graveolens* L. besides having strong anti-hyperlipidaemic effects, it improved the biological antioxidant status by reducing lipid peroxidation in liver and modulating the activities of antioxidant enzymes in rats fed with high fat.	180-181
	defatted ethanolic extract	Treatment of hyperlipidaemic rats with defatted ethanolic *Anethum graveolens* extract (single daily dose of 1 ml, equivalent to 500 mg of the plant powder) and high-fat diet for up to 10 and/or 30 days reversed the serum lipid levels compared to rats which were fed only high-fat diet. In addition, it induced significant increase in HMG-CoA/mevalonate ratio as compared to rats which were fed high-fat diet after treatment with defatted ethanolic *Anethum graveolens L*. extract for 30 days.	182-183
Apium graveolens	different extracts of different parts and 3-N-butylphthalide islated from the plant	Many experimental studies showed that *Apium graveolens* significant lowered serum total cholesterol , triglycerides , LDL and VLDL and increased HDL level. *Apium graveolens* also reduced the formation of arterial plaques in experimental studies. However, the mechanisms suggested for lipid lowering action of *Apium graveolens* including inhibition of hepatic cholesterol biosynthesis, increasing faecal bile acid excretion and enhancing plasma lecithin: cholesterol acyltransferase activity and reduction of lipid absorption in the intestine. Some authors mentioned that blood lipids lowering effects was attributed to the compound 3n butylphthalideor (3nB) isolated from *Apium graveolens*, but, the active extract free from 3-n-butylphthalide has been reported to have lipid-lowering action. Instead, thin layer chromatography indicated that polar compounds with sugar or amino acid side chains(s) could be the hypocholesterolaemic constituents of celery extract.	184-188
	ethanolic extract of seeds	In evaluation of the protective effects of ethanolic extract of *Apium graveolens* on ritonavir (a protease inhibitor) - induced dyslipidemia. It appeared that concurrent treatment with high dose of ethanolic extract of *Apium graveolens* (150mg/kg) in mice with ritonavir, showed significant improvement in blood lipid profile. However, using of low	189

		dose of ethanolic extract of *Apium graveolens* (75mg/kg) showed no significant effects.	
Arachis hypogaea	soluble polyphenolic extract	The effect of water soluble polyphenolic extract of peanut skin (PE) was investigated for its hypolipidemic properties and improvement of lipid homoeostasis in rats. 300mg/kg body weight of (PE) significantly reduced body weight and epididymal fat. Plasma and liver triglyceride (TG) and cholesterol (TC) levels were also significantly reduced, and the faecal secretion of TG and TC was greatly increased upon PE administration. Liver mRNA expression of enzymes involved in fatty acid synthesis, such as fatty acid synthase (FAS), sterol receptor element binding protein (SREBP)-1c, acetyl-CoA carboxylase (ACC1) and lipid uptake genes, such as PPARγ, were decreased, while PPARα was up-regulated by administration of PE.	190-191
	water-soluble peanut skin polyphenol fraction	Feeding a high-cholesterol diet with a water-soluble peanut skin polyphenol fraction to rats reduced their plasma cholesterol level, with an increase in fecal cholesterol excretion. The hypocholesterolemic effect was greater with the lower-molecular-weight rather than higher- molecular-weight polyphenol fraction. This effect attributed to some oligomeric polyphenols which reduced the solubility of dietary cholesterol in intestinal bile acid-emulsified micelles.	192
	peanut consumption	The effects of peanut (*Arachis hypogaea*) consumption on oxidant-antioxidant status and lipid profile in Streptozotocin (STZ) induced diabetic rats was investigated. Rats were given standard rat chow supplemented with 0.63 g % peanut for 12 weeks. The supplementation with peanut in the diabetic group led to significantly higher HDL-C levels and lower atherogenic index (AI) levels compared to diabetic group. Peanut consumption increased GSH levels significantly both in control and diabetic groups.	193
	peanet stilbenoids	Most of peanet stilbenoids inhibited intracellular generation of reactive oxygen species (ROS) in PMA inducedHL-60 cells. Three stilbenids compounds produced a strongest antioxidant effect. Twelve compounds demonstrated significantly high antioxidant properties which were comparable to those of Trolox. Although, the majority of stilbenoids demonstrated moderate cytoxicity toward HL-60 cells, but the antioxidant effect was observed at much lower concentrations which confirmed that the antioxidant effect was not related to cytotoxic effect.	194-195
Asparagus officinalis	butanol extract	The hypolipidemic effect of *n*-butanol extract from asparagus by-products was evaluated in mice fed a high-fat diet. Asparagus butanol	196-198

		extract significantly decreased the levels of body weight gain, serum total cholesterol and low density lipoprotein cholesterol; it dramatically increased the high density lipoprotein level when administered at three different doses (40, 80 or 160 mg/kg body weight) for 8 weeks in hyperlipidemic mice. In addition, asparagus butanol extract decreased the levels of alanine transaminase, aspartate transaminase and alkaline phosphatase in serum. Superoxide dismutase activity and the total antioxidation capacity were evidently increased; in addition, the malondialdehyde level and the distribution of lipid droplets were reduced in liver cells of asparagus butanol extract- treated mice.	
Avena sativa	Oat β-glucan	Oat β-glucan exerted cholesterol-lowering properties. The consumption of oat meal and oat bran reduced total plasma cholesterol and LDL-cholesterol levels. This effect attributed to β-glucan, it interfered with the reabsorption of bile acid in the gut and reduces cholesterol levels The oat bran has been found to be the only fiber source that significantly lowered total and low density-lipoprotein cholesterol levels in mild hypercholesterolemics.	199-200
	oat bran	C57BL/6 NCrl mice responded to oat bran with 19 ± 1 % ($P < 0.001$) lower plasma cholesterol, 40 ± 5% ($P < 0.01$) higher excretion of bile acids and increased expression of the bile acid-producing hepatic enzymes CYP7A1 and CYP8B1, but none of these effects were found in control C57BL/6JBomTac mice.	201
	oat β-glucan	To explored the dose-dependent effect of oat cereal β-glucan on improving metabolic indexes of obesity mice, C57-Bl mice were randomized to chow diet (N) group and high fat diet group and other three doses of oat β-glucan groups (low β-glucan, medium β-glucan, and high β-glucan). Energy intake, glucose, lipids, and appetite related hormones were tested. Dose-dependent relation was observed on oat β-glucan doses and body weight change, average energy intake, total cholesterol, HDL cholesterol, plasma neural peptide Y, arcuate neural peptide Y mRNA, and arcuate neural peptide Y receptor 2 mRNA level. Oat β-glucan helped to increase plasma peptide Y-Y and intestine peptide Y-Y expression in obesity mice.	202
	oat β-glucan	The United States Food and Drug Administration (FDA) approved a health claim for β-glucan soluble fiber from oats for reducing plasma cholesterol levels and risk of heart disease in 1997. Similarly, in 2004 the United Kingdom Joint Health Claims Initiative (JHCI) allowed a cholesterol-lowering health claim for oat β-glucan.	30, 203

		Studies conducted during the past 13 years support the suggestion that intake of oat β-glucan at daily doses, of at least 3 g, reduced plasma total and low-density lipoprotein (LDL) cholesterol levels by 5-10% in normo cholesterolemic or hyper cholesterolemic subjects. Studies also showed that oat consumption is associated with 5% reductions in total cholesterol levels.	
	oat β-glucan	A clinical trial was carried out to confirm the anti- obesity effect of oat. Subjects with BMI ≥27 and aged 18-65, were randomly divided into a control (n=18) and an oat-treated (n=16) group, taking a placebo or beta glucan-containing oat cereal, respectively, for 12 weeks. The result showed that consumption of oat reduced body weight, BMI, body fat and the waist-to-hip ratio. Profiles of hepatic function, including AST and ALT showed decrements in patients with oat consumption. Nevertheless, anatomic changes were not observed by ultrasonic image analysis. Ingestion of oat was well tolerated and there was no adverse effect during the trial.	204
	oat consumption	The effect of oat consumption on serum lipid profiles in Thai hypercholesterolemic adults was studied. Following daily oat consumption, total cholesterol and LDL-cholesterol levels were significantly lower than baseline levels and lower than the levels observed with rice consumption. Oat consumption reduced total cholesterol by 5% and LDL-cholesterol by 10% from baseline levels. In addition, mean and percent changes were significantly different from the levels after consuming rice porridge ($p < 0.05$).	205
Bauhinia variegata	ethanolic and aqueous extracts of roots	The ethanolic and aqueous extracts of the root of *B. variegata* (200 and 400 mg/kg body weight) in rats, showed significant reduction ($P \geq 0.01$) in cholesterol and significant reduction ($P \geq 0.01$) in triglyceride level. The VLDL level was also significantly ($P \geq 0.05$) reduced, with a significant increase in HDL.	206-207
	fractions of total methanol extract of leaves	The anti-hyperlipidemic activity of fractions of total methanol extract of leaves of *Bauhinia variegata* was investigated against Triton WR-1339 induced hyperlipidemia in rats. Fractions were administered at a dose of 100mg/kg orally. Butanol fraction showed significant reduction ($p<0.05$) in serum cholesterol, triglyceride, LDL, VLDL and increase in HDL level in comparison with standard drug fenofibrate ($p<0.05$).	208
	methanolic extract of stem and root barks	The antiobesity effect of methanolic extract of stem and root barks of *Bauhinia variegata* was examined in female rats fed with hypercaloric diet. The methanolic plant extract (200 and 400 mg/kg) exhibited a significant	209

		hypolipidemic effect with a reduction in the feed intake and body weight. Treatment of obese animals with the methanolic extract of *B. variegate* exhibited an increased brain serotonin level and high density lipoprotein with a concomitant decrease in total cholesterol, triglycerides and low density lipoprotein. Thus the antiobesity activity of methanolic extract of *B. variegata* could be attributed to tendency of the extract to reduce lipid profile and elicit the brain serotonin level.	
Bellis perennis	methanolic extract and its saponin fraction (methanol-eluted fraction) of the flowers	The methanolic extract and its saponin fraction (methanol-eluted fraction) of the flowers of *Bellis perennis* were found to suppress serum triglyceride elevation in olive oil-treated mice. Among these saponins, perennisosides I and II showed inhibitory effects on serum triglyceride elevation at doses of 25-50 mg/kg orally. As a result of hypolipidemic effect of saponin constituents isolated from the flowers of *Bellis perennis*, it also can be utilize as preventive drug in ischemic diseases and as an anti-obese remedy.	210-212
Benincasa hispida	ash gourd (*Benincasa hispida*)	Salad prepared by using 100gm of ash gourd (*Benincasa hispida*) and one gram of curry leaves (10 curry leaves) and five grams of skimmed milk powder (made into curd) and pepper and salt are added for taste. This salad was freshly prepared every day and given to hyperlipidemic diabetic patients in mid morning for a period of three months to find out the therapeutic effect of supplementation of ash gourd and curry leaves. Supplementation of ash gourd and curry leaves had significant hypoglycemic and hypolidemic effect and it reduced the blood glucose level (both fasting and post prandial), within the period of three months.	213-214
Brassica rapa	ethanol extract of root	The effect of different doses ethanol extract of root on blood lipid changes was studied in hypercholesterolemic rabbits. Extract was given in as 100, 200, 400 mg / kg body weight of the rabbits. The results showed that the turnip root extract can prevent the occurrence of atherosclerotic in hypercholesterolemic rabbits which may be due to flavonoids and vitamins contents.	215
	Caulilexin C , indoleacetonitrile and arvelexin isolated from the root	Caulilexin C , indoleacetonitrile and arvelexin isolated from the root of *Brassica rapa* (at a concentration of 100 µg/ml) showed an inhibitory activity on human Acyl CoA: cholesterol transferase 1 (hACAT1) by 54.6±6.0%, 69.2±4.7% and 68.6±3.7%, and on human Acyl CoA: cholesterol transferase 2 (hACAT2) by 4.8±13.4%, 45.6±4.8% and 39.5±4.3%, respectively.	216
	ethanolic	The influence of ethanolic extracts of *Brassica*	217

	extracts	*campestris* spp. rapa roots (EBR) on obesity was examined in imprinting control region (ICR) mice fed a high-fat diet (HFD) and in 3T3-L1 adipocytes. The molecular mechanism of the anti-obesity effect of EBR was investigated in 3T3-L1 adipocytes as well as in HFD-fed ICR mice. In the obese mouse model, both weight gain and epididymal fat accumulation were highly suppressed by the daily oral administration of 50 mg/kg EBR for 8 weeks, whereas the overall amount of food intake was not affected. EBR treatment induced the expression in white adipocytes of lipolysis-related genes, including beta3-adrenergic receptor (beta3-AR), hormone-sensitive lipase (HSL), adipose triglyceride lipase, and uncoupling protein 2. Furthermore, the activation of cyclic AMP-dependent protein kinase, HSL, and extracellular signal-regulated kinase was induced in EBR-treated 3T3-L1 cells. The lipolytic effect of EBR involved beta3-AR modulation, as inferred from the inhibition by the beta3-AR antagonist propranolol. Accordingly, EBR may have potential as a safe and effective anti-obesity agent via the inhibition of adipocyte lipid accumulation and the stimulation of beta3-AR-dependent lipolysis.	
Caesalpinia crista	methanol extract	The methanol extract significantly ($P<0.05$) decreased the levels of lipid peroxidation and significantly ($P<0.05$) increased the levels of GSH, superoxide dismutase and catalase, when administered at the doses of 50, 100, and 200 mg/kg body weight per day for 14 days in mice.	218
	Aqueous extract	Aqueous extract in isoproterenol treated rats significantly decreased plasma total cholesterol, TC (87.45 ±1.5), triglycerides TG (91.59±2.12), LDL (67.79±1.80), VLDL (12.46±0.68), along with a significant increased in HDL level (18.67±0.72) when compared to untreated isoproterenol group. Ethanolic extract of *Caesalpinia Crista* + isoproterenol treated group showed decrease lipoproteins level except HDL of plasma. *Caesalpinia crista* aqueous extract treated group showed significantly decrement plasma TC (81.23±1.99), TG (73.82±1.34), LDL (60.34±1.56), VLDL (10.53±0.54), along with a significant ($P<0.01$) increased in HDL level (19.38±1.25) when compared to untreated isoproterenol group.	88
Calotropis procera	root extracts	Serum lipid profile was measured in the diabetic rats. The extracts were significantly ($p<0.001$) decreased total cholesterol, triglycerides, phospholipids, LDL and VLDL cholesterol and significantly ($p<0.001$) increased HDL cholesterol.	219
Capparis spinosa	different extracts	Leaves and flowers of *Capparis spinosa* were	220-

	of different parts	rich in either polyphenols or flavonoids, while roots are the poor ones. All extracts have anti lipid peroxidation and antioxidant effects with a dominance of flowers and leaves especially in the methanolic extracts (82.78 ± 2.64 and 80.94 ±1.57 respectively). Seeds exerted the acceptable effects followed by bud than roots.	221
Capsicum annuum* and *Capsicum frutescens	aqueous extract	The anti-obesity effects of water extracts of seven *Capsicum annuum* L. varieties, Putgochu (Pca), Oyee gochu (Oca), Kwari putgochu (Kca), Green pepper (Gca), Yellow paprika (Yca), Red paprika (Rca) and Cheongyang gochu (Cca), were examined through the evaluation of lipoprotein lipase (LPL) mRNA expression level in 3T3-L1 cells (mouse pre-adipocytes). After capsaicin elimination by chloroform defatting, freeze-dried powder of Cca was treated to 3T3-L1 cells and anti-obesity effects were examined by determining the LPL mRNA level using the RT-PCR method. Of the primary fractions, only proven fractions underwent secondary and tertiary re-fractionating to determine anti-obesity effects. From seven different *Capsicum annuum*, there was a significant decrease of the LPL mRNA expression level of 50.9% in Cca treatment compared to the control group. A significant decrease of the LPL mRNA expression level was shown in primary fractions (Fr) 5 (36.2% decrease) and 6 (30.5% decrease) of the Cca water extracts. Due to the impurities checked by UPLC chromatography, Fr 5 and 6 were re-fractionated to determine the LPL mRNA expression level. Treatment of Fr 6-6 (35.8% decrease) and Fr 5-6 (35.3% decrease) showed a significant decrease in the LPL mRNA expression level. When analyzed using UPLC, major compounds of Fr 6-6 and Fr 5-6 were very similar. Subsequently, Fr 6-6 and Fr 5-6 were re-fractionated to isolate the major peak for structure elucidation. Treatment of Fr 5-6-1 (26.6% decrease) and Fr 6-6-1 (29.7% decrease) showed a significant decrease in the LPL mRNA expression level.	222-223
Carum carvi	aqueous extract	The hypolipidemic effect of aqueous extract of *Carum carvi* seeds (60 mg/kg of body weight for eight weeks) was investigated in diet induced hyperlipidemia in rats. Carum carvi and simvastatin significantly decreased lipids levels in rats. Carum carvi extract reduced lipid levels more effectively than the simvastatin. Carum carvi constituents, especially flavonoids and carvone have strong anti-oxidant activity which might be involved in hypolipidemia.	224-225
	aqueous extract of the seeds	Oral administration of caraway to rats, 1g/kg body weight, daily caused a significant decrease in blood glucose level (p=0.001) and	226

		alleviated their body weight loss ($p = 0.037$). Furthermore, it caused significant decrease in total cholesterol ($p = 0.036$), and low-density lipoprotein cholesterol levels ($p = 0.001$) compared with the diabetic control rats, and with no significant changes in triglyceride and high-density lipoprotein cholesterol levels were recorded.	
	aqueous extract	The effect of single and repeated oral administration of the aqueous extract of Carum carvi fruits at a dose of (20mg/kg) on lipid metabolism was studied in normal and streptozotocin-induced diabetic rats (STZ). After a single oral administration, Carum carvi extract produced a significant decrease on triglycerides levels in normal rats ($p<0.05$). In STZ diabetic rats, cholesterol levels were decreased significantly 6h after Carum carvi treatment ($p<0.05$). On the other hand, repeated oral administration of Carum carvi extract exhibited a significant hypo-triglyceridemic and hypo-cholesterolemic activities in both normal ($p<0.01$) and STZ diabetic rats ($p<0.001$), 15 days after Carum carvi treatment.	227
Carthamus tinctorius	dichloromethane extract	The effect of the extracts from safflower was investigated on cholesterol metabolism in high cholesterol fed rats. After treatment for 14 and 30 days, a significant reduction in total cholesterol and total cholesterol/HDL-cholesterol and a significant induction in HDL-cholesterol were observed in the hypercholesterolemic rats treated with the dichloromethane extract. Higher expression of SRBI and ABCA1 in the liver of the control group was observed after 4 weeks whereas no significant difference in the expression level of SRBI and ABCA1 was found in groups treated with extract after 2 and 4 weeks. The authors suggested that the expression of SRBI and ABCA1 mRNA may not be regulated by the crude extract of safflower, which may not in part explain the decrease in HDL-cholesterol and gene encoding enzymes of the cholesterol biosynthetic pathway.	228-229
	defatted safflower seed extract	The inhibitory effects of defatted safflower seed extract (SSE) and serotonin derivatives (N-p-coumaroyl serotonin and N-feruloyl serotonin, CS+FS), were evaluated on hypercholesterolemia and atherosclerosis, using Pulse wave velocity (PWV) in Kurosawa and Kusanagi-hypercholesterolemic rabbits. The atherosclerotic lesioned area in the aorta was significantly reduced in the SSE and CS+FS groups, without significant changes in serum cholesterol and triglyceride levels among the three groups after supplementation. Local PWV (LPWV) in the middle thoracic and distal abdominal aortas	230

		was significantly smaller in the SSE and CS+FS groups than in the control group. PWV in the entire aorta was also significantly lower in the SSE and CS+FS groups, compared with that in the control group. Pressure-strain elastic modulus, an index of wall distensibility, was significantly lower in the middle thoracic and middle abdominal aortas in the SSE and CS+FS groups than in the control group. Wall thickness was also significantly smaller in the middle thoracic aorta in the SSE and CS+FS groups compared with that in the control group.	
Casuarina equisetifolia	*Casuarina equisetifolia* bark	The effect of *Casuarina equisetifolia* bark incorporated into rat feed at 10-40% on the lipid profiles and blood sugar of albino rats was investigated. The parameters studied were triacylglycerol (TGL), total cholesterol (TC), total lipid (TL), phospholipids (PHOS), high-density lipoprotein (HDL) and random blood sugar (RBS). There was no significant change ($P>0.05$) in the TGL levels of all the rats, including the control, as they all range between 0.18-0.22(mg/dl). The effects on TC and TL were irregular as they did not display any dose dependence. The mean plasma PHOS levels did not change significantly ($P>0.05$) between the control and the rats fed on 10% feed (0.19± 0.00 vs 0.18± 0.00 mg/dl), but was significantly lowered ($P<0.05$) at 20-40% feed content. The mean HDL level rose, although insignificantly ($P>0.05$) with the percentage contents of the bark in the feeds; by implication, the low-density lipoprotein (LDL) was decreasing with the increase in the bark contents of the feeds. The RBS also decreased as the percentage bark contents of the feeds increased, indication that it could have anti-diabetic properties.	231-232
	bark extracts	The effect of extracts of *Casuarina equisetifolia* bark on serum lipid profile, total cholesterol, triglycerides, low density, very low density and high density lipoprotein was evaluated in the diabetic and non diabetic rats. There was significant reduction in total cholesterol, LDL cholesterol, VLDL cholesterol and improvement in HDL cholesterol in diabetic rats.	233
Cistanche tubulosa	aqueous ethanol extract (CTE) of the roots	The hypocholesterolemic effect of the aqueous ethanol extract (CTE) of the roots of *Cistanche tubulosa* was evaluated in mice using gene chip and RT-PCR analysis of the livers of mice given CTE (400 mg/kg) for 14 days. The administration of CTE (400 mg/kg) for 14 days significantly suppressed serum cholesterol elevation in high cholesterol diet-fed mice. The mRNA expressions of VLDL receptor and cytochrome P450 SCC were	234

		significantly enhanced. In addition, acteoside, a major constituent of CTE, was found to enhance the mRNA expressions of apolipoprotein B, VLDL receptor, and cytochrome P450 SCC in HepG2 hepatocytes. According to these results, the authors concluded that CTE affected the mRNA expressions of molecules related to cholesterol transport and metabolism and exhibited hypocholesterolemic activity in diet-induced hypercholesterolemia mice. Acteoside was involved in the hypocholesterolemic activity of CTE.	
Citrullus colocynthis	powdered seeds	The hypolipidemic effect of *Citrullus colocynthis* was studied clinically. One hundred dislipidemic patients were randomly divided into two treated and placebo groups. They were treated daily with powdered seeds of *Citrullus colocynthis* (300 mg) and placebo for 6 weeks. A daily intake of 300 mg/ day of powdered seeds of *Citrullus colocynthis* can lower the triglyceride and cholesterol concentration significantly in nondiabetic hyperlipidemic patients.	235-236
	Citrus aurantifolia peel essential oil	The effect of *Citrus aurantifolia* peel essential oil was studied on serum triglyceride and cholesterols in Wistar rats. Thirty Wistar rats were divided into 5 groups: control, sham, and 3 experimental groups. The animals were treated in 2 phases: first, except for control group, which received normal saline, the rest of the groups were fed with a high cholesterol regimen to induce hyperlipidemia; then, the 3 experimental groups were treated with *Citrus aurantifolia* peel essential oil in 3 different doses: 25, 50, and 100 µl/kg. The sham group demonstrated a significant rise in mean serum triglyceride, cholesterol, and LDL level in comparison with the control group ($p<0.05$). The results of experimental groups treated with peel essential oil in 50 and 100 µl/kg doses demonstrated a significant reduction in triglyceride, cholesterol, and LDL ($p< 0.01$).	237
	Citrus aurantifolia juice	The effect of *Citrus aurantifolia* on hepatic lipidomics was studied in female albino rats, it was found that the fresh juice of lime had different effects on cholesterol, riacylglycerol and phospholipid concentrations of the liver. The low concentration of lime juice (30µl) did not showed considerable effect on cholesterol concentration of the liver. Increase in cholesterol concentration was observed only after applying a concentration of 60 µl. Beyond this concentration, cholesterol concentration was decreased. Therefore, it was demonstrated that peak stimulation for lime juice is 60µl. Similar effect also occur for triacylglycerol concentration. However, it caused dose-dependent increase in	238

		phospholipids concentration.	
	Eriocitrin (eriodictyol 7-rutinoside), a flavonoid of lemon	Eriocitrin (eriodictyol 7-rutinoside), a powerful antioxidative flavonoid in lemon with lipid-lowering effects was evaluated in a rat model of high-fat diet to investigate its mechanism of action. A feeding experiments was conducted in zebrafish with diet-induced obesity. Oral administration of eriocitrin (32 mg/kg/day for 28 days) improved dyslipidaemia and decreased lipid droplets in the liver. DNA microarray analysis revealed that eriocitrin increased mRNA of mitochondrial biogenesis genes, such as mitochondria transcription factor, nuclear respiratory factor 1, cytochrome c oxidase subunit 4, and ATP synthase. In HepG2 cells, eriocitrin also induced the corresponding orthologues, and reduced lipid accumulation under conditions of lipid loading. Eriocitrin increased mitochondrial size and mtDNA content, which resulted in ATP production in HepG2 cells and zebrafish.	239
	Citrus medica peel extract	*Citrus medica* cv Diamante peel extract lowered plasma cholesterol and triglycerides in mice	240
Clitoria ternatea	hydroalcoholic extract of the roots and seeds of *Clitoria ternatea*	The anti-hyperlipidemic effect of *Clitoria ternatea* L. was studied in experimentally induced hyperlipidemia in rats. The poloxamer 407-induced acute hyperlipidemia and diet-induced hyperlipidemia models were used in this investigation. Oral administration of the hydroalcoholic extract of the roots and seeds of *Clitoria ternatea* resulted in a significant ($p < 0.05$) reduction of serum total cholesterol, triglycerides, very low-density lipoprotein cholesterol, and low-density lipoprotein cholesterol levels. The atherogenic index and the HDL/LDL ratio were also normalized after treatment in diet-induced hyperlipidemic rats. The effects were compared with atorvastatin (50 mg/kg, po) and gemfibrozil (50 mg/kg, po).	241-242
Coriandrum sativum	fresh leaves extracts	The antilipidemic activity of fresh leaves of *Coriandrum sativum* was studied against salbutamol induced cardiac injury in rabbits. Salbutamol administered rabbits (50mg/kg) showed elevated level of serum lipids (LDL-cholesterol, triglyceride) and decreased level of HDL-cholesterol and antioxidant enzymes (SOD, CAT). Both the pre- and post treatment of plant extract (100mg/kg) for three weeks exerted significant antilipidemic effect against salbutamol-induced myocardial infarction by lowering the level of serum LDL-cholesterol, triglycerides and peroxidase and increasing the level of HDL-cholesterol and antioxidant enzymes.	243
	70% methanolic extract	The hypolipidemic and antioxidant action of *Coriandrum sativum* were investigated in	244

		cholesterol-fed rabbits. Cholesterol feeding (500 mg/ kg bw/day) for 120 days caused a significant increase in serum total cholesterol, phospholipid, triglyceride, LDL-cholesterol and VLDL-cholesterol levels, whereas HDL ratio was decreased significantly when compared with control group. The changes in the antioxidant parameters were accompanied by an increase in hepatic lipid peroxidation and reduction in glutathione (GSH) and catalase activity. The level of lipid peroxidation was reduced whereas GSH content and catalase activity were elevated after the treatment with 70% methanolic extract of *Coriandrum sativum* at a dose of 500 mg/kg bw/day. Reduced serum lipid profile and elevated HDL ratio was observed after administration of *Coriandrum sativum*. *Coriandrum sativum* extract feeding increased the faecal excretion of cholesterol and phospholipids. Histological studies showed less cholesterol deposits in the aorta of high cholesterol diet animals given *Coriandrum sativum* compared to the high cholesterol diet untreated animals.	
	seeds	*Coriandrum sativum* seeds were incorporated into diet, and the effect of the of coriander seeds on the metabolism of lipids was studied in rats fed with high fat diet and added cholesterol. The seeds had a significant hypolipidemic action. In the experimental group of rats (tissue) the level of total cholesterol and triglycerides increased significantly. There was significant increase in beta-hydroxy, beta-methyl glutaryl CoA reductase and plasma lecithin cholesterol acyl transferase activity were noted in the experimental group. The level of low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol were decreased, while that of high density lipoprotein (HDL) cholesterol was increased compared to the control group.	245-246
Crocus sativus	crocin	Serum triglycerides, total-, LDL-, cholesterol, fecal excretion of fat and cholesterol were significantely inhibited by crocin (100 mg/kg/day) compared to the control group.	247
	Crocetin	Crocetin, was administered to rabbits to determine its effect on the development of atherosclerosis. New Zealand white rabbits were given three different diets for eight weeks: a standard diet, a high lipid diet (HLD), or a high lipid + crocetin diet. The HLD group developed hypercholesterolemia and atherosclerosis, while the crocetin-supplemented group decreased the negative health effects of a high lipid diet. However, the results did not show a significant difference in the plasma lipid levels (total, low	248

		density lipoprotein (LDL), and high density lipoprotein (HDL) cholesterol) between the HLD and crocetin groups but showed significant decrease in the aorta cholesterol deposits, atheroma, foam cells, and atherosclerotic lesions. The authors suggested that nuclear factor kappa B (NF-κB) activation in the aorta was suppressed by crocetin which in turn decreased the vascular cell adhesion molecule-1 (VCAM-1) expression.	
	crocetin	Administration of a monthly intramuscular injection of crocetin reduced serum cholesterol concentrations by 50%, and the severity of atherosclerosis by 30% in rabbits fed an atherosclerosis-inducing diet. Crocin exerted antiatherosclerotic effects through decreasing the level of Ox-LDL that plays an important role in the initiation and progression of atherosclerosis.	249-250
	fifty milligrams saffron in 100 ml of milk	Fifty milligrams of saffron dissolved in 100 ml of milk was administered twice a day to human subjects, the significant decrease in lipoprotein oxidation susceptibility in patients with coronary artery disease (CAD) indicated the potential of saffron as an antioxidant.	251
	extract of saffron stigma	Healthy, mildly overweight women (N = 60) participated in a randomized, placebo-controlled, double-blind study to evaluated the efficacy of satiereal supplementation (Inoreal Ltd, Plerin, France), a novel extract of saffron stigma, on body weight changes over an 8-week period. They took twice capsule of satiereal (176.5 mg extract per day or a matching placebo. Caloric intake was left unrestricted during the study. At baseline, both groups were homogeneous for age, body weight, and snacking frequency. Satiereal caused a significantly greater body weight reduction than placebo after 8 weeks ($p<0.01$). The mean snacking frequency was significantly decreased in the satiereal group as compared with the placebo group ($P < .05$). Other anthropometric dimensions and vital signs remained almost unchanged in both groups. No subject withdrawal attributable to a product effect was reported throughout the trial, suggesting a good tolerability to satiereal.	252
Crotalaria juncea	ethanolic extract	The antihypercholesterolemic effects of 50 and 100 mg/kg bw per day of an ethanolic extract of *Crotalaria juncea* Linn (whole plant) were investigated in rats fed high-fat diet by evaluating food consumption, weight gain, fecal fat excretion, serum and liver lipids, and biochemical profiles as well as by histopathological studies. The results were compared to animals fed with the standard diet and animals fed with a high-fat diet and atorvastatin (10 mg/kg bw). The animal group	253-254

		administered with the ethanolic extract for 35 days showed decreased levels of TC, LDL, VLDL, TG, HDL+VLDL, VLDL+LDL, LDL/TC, AI, SGOT, SGPT, and elevated levels of HDL, HDL/TC, significantly ($p<0.01$ and $p<0.05$) in a dose-dependent manner.	
	methanol extract	The antihyperlipidemic activity of alcoholic and methanol extract of leaves of *Crotolaria juncea* (CJ) was investigated against Triton induced hyperlipidemia in mice. CJ was administered at a dose of 100 and 200mg/kg (po) to Triton induced hyperlipidemic mice. Atorvastatin was used as reference standard. CJ showed a significant decrease in the levels of serum total cholesterol, triglyceride, LDL, VLDL and significant increase in the level of serum HDL at the dose of 100 and 200mg/kg (po) against Triton induced hyperlipidemia in mice.	255
	amino acid, 2-amino-5-hydroxyhexanoic acid isolated from the seeds	The amino acid, 2-amino-5-hydroxyhexanoic acid isolated from the seeds of *Crotalaria juncea*, showed dose dependent lipid lowering activity in the *in vivo* experiments and also showed good *in vitro* antioxidant activity. The cyclized compound, 3-amino-6-methyl tetra hydro -2H-pyran-2-one showed better lipid lowering and antioxidant profile than the parent compound.	256
	leaves extract	The anti-obesity effect of *Crotalaria juncea* leaves extract was documented in high fat induced obesity in rats.	257
Cuminum cyminum	methanolic extract	The hypocholesterolemic effect of methanolic extract of *Cuminum cyminum* (MCC) was evaluated in ovariectomized (OVX) rats. MCC 1000 mg/kg and estradiol benzoate equivalent to 0.15 mg/kg of estradiol were administered to OVX rats per orally for 10 weeks. The results indicated that estradiol as well as MCC protected OVX rats against increased cholesterol levels due to ovariectomy, MCC was better than estradiol.	258-259
	cumin powder	The effect of cumin powder on body composition and lipid profile was studied in overweight and obese women in a randomized clinical trial. 88 overweight/ obese women were randomly assigned into two groups. The experimental group was given 3 g/day cumin powder with yogurt at two meals for 3 months. The same amount of yogurt without cumin powder was prescribed for the control group. All patients received nutrition counseling for weight loss in a similar manner. Anthropometric and biochemical parameters were determined before and after the intervention. Cumin powder reduced serum levels of fasting cholesterol, triglyceride, and LDL and increased HDL. Weight, BMI, waist circumference, and fat	260

		mass were also significantly reduced. However, it exerted no effect on FBS and fat-free mass.	
	cumin extract	The effects of cumin extract supplementation on oxLDL, paraoxanase 1 activity, FBS, total cholesterol, triglycerides, High density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), apo lipoprotein A1 (Apo A1), and apolipoprotein B (Apo B) were studied in the patients with hypercholesterolemia. The results demonstrated that there was a significant decrease in the level of oxLDL after receiving cumin. Paraoxonase and arylesterase activities increased in serum after taking cumin extract. Paraoxanase 1 (PON1) played a protective role against the oxidative modification of plasma lipoproteins and hydrolyzes lipid peroxides in human atherosclerotic lesions.	261
	Cumin capsule	The effects of *Cuminum cyminum* intake on weight loss and metabolic profiles among overweight subjects was studied by a randomized double-blind placebo-controlled clinical trial which conducted among 78 overweight subjects (male, n = 18; female, n = 60) aged 18-60 years old. Participants were randomly assigned into three groups to receive: (1) *Cuminum cyminum* capsule (n = 26); (2) orlistat 120 capsule (n = 26) and (3) placebo (n = 26) three times a day for 8 weeks. Anthropometric measures and fasting blood samples were taken at baseline and after 8 weeks of intervention. Consumption of the *Cuminum cyminum* and orlistat120 resulted in a similar significant decrease in weight (-1.1 ± 1.2 and -0.9 ± 1.5 compared with placebo 0.2 ± 1.5 kg, respectively, p = 0.002) and BMI (-0.4 ± 0.5 and -0.4 ± 0.6 compared with placebo 0.1 ± 0.6 kg/m(2), respectively, p = 0.003). In addition, *Cuminum cyminum* L., compared with orlistat and placebo, led to a significant reduction in serum insulin levels (-1.4 ± 4.5 vs. 1.3 ± 3.3 and 0.3 ± 2.2 μIU/ml, respectively, p = 0.02), HOMA-B (-5.4 ± 18.9 vs. 5.8 ± 13.3 and 1.0 ± 11.0, respectively, p = 0.02) and a significant rise in QUICKI (0.01 ± 0.01 vs. -0.005 ± 0.01 and -0.004 ± 0.01, respectively, p = 0.02).	262
Cupressus sempervirens	cone extract	The effects of *Cupressus sempervirens* cone extract (CSE) on the lipid profile was studied in Wistar rats. The oral administration of the extract resulted in a substantial decrease of serum total cholesterol, which was significant even after 6 weeks of treatment. Moreover, these animals exhibited lower total cholesterol levels compared to the controls after the initiation of treatment ($p<0.001$). The administration of the extract also led to a substantial reduction in serum triglycerides	263-264

		($p<0.05$) , comparing 0 week to 6-24 weeks. However no significant differences in triglyceride levels were observed between CSE animals and controls during the entire study period. No significant changes in HDL-cholesterol level.	
Cydonia oblonga	leaf extracts	The hypolipidemic effect of *Cydonia oblonga* was studied in a rat model. low-, medium- and high-dose *Cydonia oblonga* leaf extracts (COM) were given orally for 56 days. The normal controls were fed a normal diet, all other groups a high fat diet. COM dose-dependently reduced TC, TG, LDL-C and MDA, inhibited the activity of ALT, AST and LPS, increased HDL-C content, increased the activity of SOD, GSH-PX, LPL and HL, and reduced liver steatosis in hyperlipidaemia rats, significant at medium and high doses. The effect of COM was similar to that of simvastatin except for increased lipoprotein lipase and hepatic lipase which were reduced by COM but not by simvastatin.	265-266
	total flavonoids of *Cydonia oblonga*	The effects of *Cydonia oblonga* Miller (COM) total flavonoids (TF) from leaves and fruit on the blood lipid and antioxidant potentials were studied using hyperlipidaemic rat models. Compared with the hyperlipidaemic model group, TF significantly reduced serum TC, TG, LDL-C ($p<0.01$), ALT and AST ($p<0.01$ or $p<0.05$) and increased HDL-C ($p<0.05$ or $p<0.01$). TF also reduced MDA ($p<0.01$ or $p<0.01$). The effects of hydromethanolic extract of quince leaf was investigated on the lipid profile of rabbits fed with cholestrol enriched diet (2% w/w for two months). Animals were treated as follow: no treatment (NT), atrovastatin (AT) (0.5 mg/kg/day) and quince extract (QE) (dried extract, 50 mg/kg/day) treatment, and then fed with normal diet for three months. Significant increases ($p<0.05$) in the mean values of cholestrol I, triglyceride, low density lipoprotein, aspartate aminotransferase, alanine transaminase, creatinine, and alkaline phosphatase with a significant decrease ($p<0.05$) in high density lipoprotein level, were recorded after receiving cholestrol enriched diet in comparison with the control group.	267
Cyperus rotundus	Rhizomes extracts	Hypolipidaemic activity of *Cyperus rotundus* rhizomes was evaluated in high fat diet induced hyperlipidaemic rats (70, 140 and 280 mg/kg bw). The results demonstrated statically significant reduction in serum lipid profile. Treatment with different doses of extract exerted statistically significant ($p<0.05$) reduction in serum total cholesterol, LDL, TG levels at the end of 15 days of intervention.	268

	tubers extract	The biological efficacy of *Cyperus rotundus* tubers extract was studied on weight control in obese Zucker rats. Administration of 45 or 220 mg/kg/day of *Cyperus rotundus* tubers hexane extract for 60 days in Zucker rats induced a significant reduction in weight gain without affecting food consumption or inducing toxicity. *In vitro*, 250 microg/ml of this extract was able to stimulate lipolysis in 3T3-F442 adipocytes suggesting that this medicinal plant contained activators of beta-adrenoreceptors (AR). The binding assay performed on the rat beta3-AR isoform, known to induce thermogenesis, demonstrated that *Cyperus rotundus* tubers extract can consistently and effectively bind to this receptor. The data suggest that the effect on weight gain exerted by *Cyperus rotundus* tubers extract may be mediated, at least partially, through the activation of the beta3-AR.	269
Daucus carota	purple carrot juice	High-carbohydrate, high-fat diet-fed rats developed hypertension, cardiac fibrosis, increased cardiac stiffness, endothelial dysfunction, impaired glucose tolerance, increased abdominal fat deposition, altered plasma lipid profile, liver fibrosis and increased plasma liver enzymes together with increased plasma markers of oxidative stress and inflammation as well as increased inflammatory cell infiltration. Purple carrot juice reversed all these parameters.	270
	diet with carrot (15% dry matter)	The effects of a 3-week supplementation of the diet with carrot (15% dry matter) in lipid metabolism was studied in rats. A significant decrease of cholesterol level in liver (–44%; p= 0.0007) was observed together with a reduction of the level of liver triglycerides (–40%; P= 0.0005). Fecal total steroids excretion increased by 30% upon feeding the carrot diet as compared to the control. The secretion of bile acids was maintained, whereas the cholesterol apparent absorption was reduced in rats fed carrot diet.	271
Dolichos lablab	supplementation of the diet with dried powder of soaked bean	The hypocholesterolemic effect of germinated Indian bean (*Dolichos lablab* L. var lignosus) was studied in hypercholesterolemic rats. Supplementation of the diet with dried powder of soaked bean almost brought the plasma cholesterol to 72.5 ± 0.75 from 178 ± 1.85 compared with that of the control (61.5 ± 0.70), although the liver cholesterol was still three times higher compared with the control. The 24h germinated Indian bean cotyledons could effectively counteract the effects of added cholesterol on liver and plasma by their high fiber content coupled with enormous increase in ascorbic acid levels.	272-273

Echinochloa crusgalli	hydroalcoholic extracts of grains	The anti-obesity effect of hydroalcoholic extracts of *Echinochloa crusgalli* grains was evaluated in high fat diet induced obesity in albino rats. Obesity was induced by administration of high fat diet for 4 weeks, the obtained obese rats were treated with hydroalcoholic extracts of *Echinochloa crusgalli* grains in a dose of 200, 400 and 600 mg/kg, bw orally for next 4 weeks. *Echinochloa crusgalli* caused significant decrease in body weights, adipose tissue weight, SGOT and SGPT levels, blood glucose levels, LDL-C, VLDL-C, total cholesterol, triglyceride levels, atherogenic index, with a significant increase in HDL-C levels compared with high fat diet control.	274-275
	methanolic extract	The curative effect of *Echinochloa crusgalli* extract as antihypercholesterolemic therapy was evaluated by performing in vivo studies and and identifying its effects by on food consumption, weight gain, fecal fat excretion, serum lipid &biochemical profiles. The animal group administered methanolic extract of the plant has shown decreased levels of TC, LDL, VLDL, TG, HDL+VLDL, VLDL+LDL, LDL/TC, AI, SGOT, SGPT and elevated levels of HDL, HDL/TC in a dose dependent manner significantly ($p<0.01$ & $p<0.05$). Body weight and food intake in treated groups were significantly lower than that in model control.	276

Plants with hemostatic, fibrinolytic or anticoagulant effects

Plant	The tested constituent	Activity	Ref
Achillea santolina	Crude extract	*Achillea santolina* crude extract induced dose-dependently inhibition in *in vitro* ADP and collagen-induced human platelet aggregation (maximal inhibition was 34.4 - 2.9% and 78.3 ± 2.5 % respectively). This effect was mostly exerted by diethylester extract**.** Chloroform and ethyl acetate extracts had about half the effect, and water extract was devoid of antiaggregant effect. However, when *Achillea Santolina* extracts given to rats for 10 days (10 mg/kg/day), they produced insignificant decline in the thrombus weight.	277
Allium cepa	raw onions and the essential oil	Both raw onions and the essential oil increased fibrinolysis in rabbits and humans. An increase in coagulation time was also observed in rabbits. *Allium cepa* inhibited platelet aggregation *in vitro* and *in vivo*. An aqueous extract of *Allium cepa* inhibited diphosphate, epinephrine, arachidonic acid, adenosine, and collagen induced platelet aggregation *in vitro*. Essential oil, a butanol and chloroform extract inhibited platelet aggregation in rabbits. Chloroform, ethanol, butanol extract and the	278-284

		essential oil 10–60µg/ml inhibited aggregation of human platelets *in vitro* by decreasing thromboxane synthesis.	
	Sulfur compounds of onion oil	Sulfur compounds of onion oil inhibited the formation of thromboxanes and the action of platelet activating factor (PAF).	285-286
	bulb juice	The bulb juice exerted fibrinoloytic effects in rabbits. The essential oil administered by gastric intubation to the rabbits at a dose of 2.0 gm/kg for 3 months, decreased fribrinolytic activity. Butanol extract and ethanol soluble fractions of the bulb (20.0 microliters) inhibited ADP-induced aggregation of platelets in human and rabbit via inhibition of thromboxane synthesis. The essential oil, at concentrations of 10 to30 mcg/ml, produced strong antiplatelet in human adults vs ADP-induced aggregation.	287.
Allium sativum	Aqueous, chloroform, and methanol extract	Garlic inhibited platelet aggregation in both *in vitro* and *in vivo* studies. A water, chloroform, or methanol extract of the drug inhibited collagen-, ADP-, arachidonic acid-, epinephrine-, and thrombin-induced platelet aggregation *in vitro*	288-293
	garlic, ether extract and garlic juice and its constituents	Experimental animals and clinical studies showed that garlic, ether extract and garlic juice and its constituents decreased cholesterol and fibrinogen, increased tissue plasminogen activator activity, increase fibrinolytic activity and blood coagulation time, and decrease in thrombocyte aggregation in blood.	294-302
Althaea rosea	Alcoholic extract	The extract inhibited platelet aggregation induced by ADP and showed a inhibitory effect on experimental thrombosis formation.	303
Apium graveolens	apigenin	Apigenin from *Apium graveolens* exhibited potent antiplatelet activity in vitro, inhibiting the aggregation of rabbit platelet induced by collagen, ADP, arachidonic acid and platelet aggregation factor, but not that induced by thrombin or ionophore A23187.	304-305
Arachis hypogaea	crude	There is a haemostatic principle in the peanut flour, which is said to improve the condition of haemophiliacs. It contained a protease inhibitor which act on the fibrinolytic system, primarily as an antiplasmin.	306
Aristolochia maurorum	methanolic extracts, the acidic fractions of aerial and root parts, and three identified compounds (aristolochic acid I , aristolochic acid II and aristolochic acid IIIa)	The methanolic extracts, the acidic fractions of aerial and root parts, and the three identified compounds (aristolochic acid I , aristolochic acid II and aristolochic acid IIIa) were evaluated using an automatic platelet aggregometer and coagulation tracer (APACT 2). Pure compounds and aristolochic acid standard were tested at two concentrations, 0.20 and 0.40 mg/mL on both phase I (adhesion of platelet) and phase II (platelet aggregation), while the methanolic extracts and the acidic fractions were tested at 4.4 mg/mL. Methanolic extracts of aerial and roots parts, in addition to acidic fractions, showed 100% activity at 4.4 mg/ mL. Also, 100% inhibition of platelet	307-308

		aggregation has been noted with aristolochic acid standard and a mixture consisting of 38% aristolochic acid I and 58% aristolochic acid II. At 0.40 mg/mL, aristolochic acid I and II exhibited 100% inhibition of platelet aggregation. 0.20 mg/ml aristolochic acid I selectively inhibited phase II with 100% activity and phase I with 39.5% inhibition while aristolochic acid II selectively inhibited phase I (adhesion) with 100% inhibition, and with less affinity towards phase II, inducing 75.8% inhibition. At 0.20 mg/ml, aristolochic acid IIIa exhibited 100% inhibition of the both phases. At 0.40 mg/ml aristolochic acid IIIa showed 85.3% and 100% inhibition of phase I and phase II, respectively. Both aristolochic acids, I and II, possessed good antithrombin activity.	
Asclepias curassavica	Cysteine proteases	Cysteine proteases from *Asclepias curassavica* latex exhibited strong pro-coagulant action.	309-311
	latex enzyme fraction of *Asclepias curassavica*	The latex enzyme fraction of *Asclepias curassavica* exhibited strong proteolytic activity when compared to trypsin and exerted pro-coagulant action by reducing plasma clotting time from 195 to 58s whereas trypsin reduced clotting time marginally from 195 to 155s. The pro-coagulant activity of this enzyme fraction was exerted by selectively hydrolyzing A alpha and B beta subunits of fibrinogen to form fibrin clot when pure fibrinogen was used as substrate as assessed by fibrinogen-agarose plate method and fibrinogen polymerization assay. The electrophoretic pattern of latex enzyme fraction-induced fibrin clot was very much similar to that of thrombin-induced fibrin clot and mimic thrombin like action. The proteolytic activity including thrombin like activity of *Asclepias curassavica* latex enzyme fraction was completely inhibited by iodoaceticacid.	310, 312
Brassica rapa	crude extract and fractions	Crude extract and fractions of *Brassica rapa* was screened against human platelet aggregation induced by two different aggregating agents and further delineated their underlying signal transduction pathways. Furthermore, *Brassica rapa* was screened for the presence of calcium channel blocking potential. The results showed that *Brassica rapa* blocked calcium channel opening as indicated by its effects on KCl-induced contraction in guinea pig ileum and this activity was distributed into various fraction of *Brassica rapa* except ethyl acetate fraction which did not show any significant calcium channel blocking activity. Platelet aggregation induced by arachidonic acid (AA), platelet activating factor (PAF) and agonists of protein kinase C (PKC) and inositol triphosphate (IP3)	313

		was inhibited by various fractions of *Brassica rapa* with different potencies, suggesting that phyto compounds responsible for these effects are differentially concentrated in various fractions.	
Calotropis procera	proteins derived from the latex	The proteins derived from the latex (LP) of Calotropis procera were evaluated for their efficacy in maintaining coagulation homeostasis in sepsis. Intraperitoneal injection of LP markedly reduced the procoagulation and thrombocytopenia observed in mice infected with Salmonella; while in normal mice, LP produced a procoagulant effect. In order to understand its mechanism of action, the LP was subjected to ion-exchange chromatography, and the three subfractions (LPPI, LPPII, and LPPIII) thus obtained were tested for their proteolytic effect and thrombin- and plasmin-like activities *in vitro*. Of the three subfractions tested, LPPII and LPPIII exhibited proteolytic effect on azocasein and exhibited procoagulant effect on human plasma in a concentration-dependent manner. Like trypsin and plasmin, these subfractions produced both fibrinogeno - lytic and fibrinolytic effects that were mediated through the hydrolysis of the Aα, Bβ, and γ chains of fibrinogen and α-polymer and γ-dimer of fibrin clot, respectively.	314
Canna indica	fower extracts	The hemostatic effect of *Canna indica* was evaluated in mice. The bleeding time (BT), clotting time (CT) and the permeability of abdominal capillary were measured respectively. The results showed that *Canna indica* significantly reduce the BT, CT and the permeability of abdominal capillary.	315
Capparis spinosa	stachydrine	When stachydrine was given to dogs, rabbits and rats, it quickened the coagulation of blood.	316
Capsicum annuum* and *Capsicum frutescens	ethanol extract	An *in-vitro* thrombolytic model was used to check the clot lysis effect of *Capsicum frutescens. A* combination of honey and *Capsicum frutescens* was also investigated along with streptokinase as a positive control and water as a negative control. By using an *in vitro* thrombolytic model *Capsicum frutescens* and a combination of honey and *Capsicum frutescens* showed 57.40% and 44.54% clot lysis effect respectively.	317
	capsaicin	Capsaicin inhibited platelet aggregation and the activity of clotting factors VIII and IX, a property which reduce the incidence of cardiovascular diseases.	318-319
Carthamus tinctorius	carthamins yellow	The effects of The carthamins yellow (CY) was studied on a blood stasis model, which was obtained by placing rats in ice-cold water during the time interval between two injections of epinephrine. The results demonstrated that CY significantly decreased the whole blood viscosity, plasma viscosity, and erythrocyte aggregation index, which were increased in the	320-321

		blood stasis model. Hematocrit and platelet aggregation were reduced, while prothrombin time was delayed with increasing doses of CY.	
	Safflower yellow	Safflower yellow inhibited the PAF induced washed platelet aggregation and 5-HT release in a dose dependent manner. When the PAF was 2.0×10-9 mol/l, the inhibition rate of platelet aggregation was 26.2%, 41.3%, 58.1%, 81.2%, and the inhibition rate of 5-HT release was 3.7%, 11.9%, 29.9% and 54.4% after treatment with safflower yellow at 0.21, 0.42, 0.85 and 1.69 g/l, respectively. Accordingly, safflower yellow can inhibit the PAF induced platelet aggregation, 5-HT release by platelets and elevation of free calcium in platelets.	322
	aqueous extract of the flowers	Intraperitoneal administration of 30 mg of an aqueous extract of the flowers to mice reduced platelet aggregation induced by adenosine diphosphate (ADP) by 65% in γ -irradiated animals.	323
Celosia cristata	decoction of Flos *Celosiae cristatae*	Five days after mice were given decoction of Flos *Celosiae cristatae* with the dosage of 17g/kg,they were compared with a control group. It emerged that the bleeding time(BT) was shortened greatly (P0.01). Seven days after rabbits were given the same decoction with the dosage of 1.7g/kg, it was found that the coagulation time (CT), prothrombin time (PT) and plasma recovery (PRT) were shortened (P0.05) ,and the euglobulin lysis time (ELT) was markedly shortened(P0.01)in comparison with control.	324-325
Cichorium intybus	Caffeine-free chicory coffee rich source of plant phenolics	Caffeine-free chicory coffee is a rich source of plant phenolics, including caffeic acid, which inhibits *in vitro* platelet aggregation, and also phenylpyruvate tautomerase enzymatic activity of the proinflammatory cytokine, macrophage migration inhibitory factor (MIF). The benefits of chicory coffee consumption were assessed on 27 healthy volunteers, who consumed 300 ml chicory coffee every day for 1 week. The dietary intervention produced variable effects on platelet aggregation, depending on the inducer used for the aggregation test. Whole blood and plasma viscosity were both significantly decreased, along with serum MIF levels, after 1 week of chicory coffee consumption. Moreover, significant improvements were seen in red blood cell deformability. No changes in hematocrit, fibrinogen level or red blood cell counts were detected. The full spectrum of these effects is unlikely to be attributable to a single compound present in chicory coffee, nevertheless, the phenolics, including caffeic acid, are expected to play a substantial role.	326-327
Citrus species	*Citrus limon*	*In vitro* / *in vivo* study was designed to	328

		determine the effect of *Citrus limon* on blood parameters, coagulation and anticoagulation factors. *In vitro* tests revealed highly significant increase in thrombin time and activated partial thromboplastin time by *Citrus limon*, whereas fibrinogen concentration was significantly reduced in comparison to control, however prothrombin time was not affected significantly. *In vivo* testing of *Citrus limon* was carried out at three different doses (0.2, 0.4 and 0.6ml/kg) in healthy rabbits. Significant changes were observed in hematological parameters such as erythrocytes, hemoglobin and mean corpuscular hemoglobin concentration. Bleeding time and thrombin time were significantly prolonged and there was increase in protein C and thrombin antithrombin complex levels. These results may be due to inactivation of thrombin because it significantly decreased fibrinogen concentration and inhibited platelet aggregation. *Citrus limon* showed maximal anticoagulant effect at 0.4ml/kg, which suggest that *Citrus limon* possessed an anti-thrombin component and could prevent thrombosis and playing a cardio- protective role.	
Convolvulus arvensis	ethanolic and aqueous extract	Ethanolic and aqueous extract of *Convolvulus arvensis* induced vasodilatation in rabbit isolated aortic rings. The molecular level (K^+ and Ca^{+2} channels and α1 receptors) of vasodilator action of both ethanolic and aqueous extract of *Convolvulus arvensis* was studied in isolated and phenylephrine-precontracted rabbit aortic rings. The role of potassium channels was determine by using two potassium channels blockers [glibenclamide and tetraethyl ammonium (TEA)], the aortic rings were contracted by using high K^+ Krebs solution in order to test the role of voltage gated calcium channels (VGCC). The concentration- response curves of phenylephrine in rings were carried out before and after added the two extracts in different doses to examine the role of α1 receptors. The results showed that calcium-dependent K channels (BKCa) has a partial role in the relaxing effect of the ethanolic extract, while the K^+ channels did not exhibit role in case of aqueous extract. With the using of high K^+ Krebs, both extracts exhibited relaxant effect due to reducing the entry of calcium ions from outside.	329-331
Crocus sativus	hot aqueous extract	A hot aqueous extract of *Crocus sativus* 10–100 mg/ml, prolonged partial thromboplastin and prothrombin times, and inhibited platelet aggregation in human platelets induced by adenosine diphosphate and collagen *in vitro*.	332-333
	aqueous extract	The inhibitory activity of saffron extract was studied on human platelets. Platelet aggregation	334

		and lipid peroxidation were evaluated with platelet rich plasma (PRP) and platelet membranes obtained from blood of healthy human volunteers. Human platelets were subjected to stimulation with a variety of agonists like ADP (61 microM), epinephrine (76 microM), collagen (11 microg/ml), calcium ionophore A 23187 (6 microM) and ristocetin (1.25 microg/ml) in the presence and absence of saffron extract. The inhibitory effect was dose dependent with concentrations varying between 0.16 to 0.80 mg and time dependent. A significant decrease was observed in malondialdehyde (MDA) formed, one of the end products of arachidonic acid metabolism and of serotonin released from dense granules of platelets at respective IC50. Lipid peroxidation in platelet membranes induced by iron-ascorbic acid system was inhibited by saffron extract significantly with IC50 of 0.33 mg. Hence, it may be said that aqueous extract of saffron may have component(s), which protect platelets from aggregation and lipid peroxidation.	
Cuminum cyminum	ethereal extract	Extract of cumin inhibited arachidonate-induced platelet aggregation. It also inhibited thromboxane B2 production from exogenous (14C) arachidonic acid (AA) in washed platelets, in addition, a simultaneous increase in the formation of lipoxygenase-derived products was also observed.	335
Cydonia oblonga	*Cydonia oblonga* Miller (COM) extracts	The effects of *Cydonia oblonga* Miller (COM) extracts was investigated on models and markers of thrombosis and related biomarkers in mice. 20, 40, 80 mg/kg/day COM aqueous extracts or 5mg/kg/day aspirin, were given orally for 14 days and were compared to untreated controls regarding bleeding and clotting times, using the tail cutting and glass slide methods and for death rates in collagen-epinephrine pulmonary thrombosis, thrombolysis *in vitro* and euglobulin lysis time (ELT). Common carotid artery $FeCl_3$-induced thrombus and inferior vena cava thrombosis occlusion time, plasma concentrations of thromboxane B2 (TXB2) and 6-keto-prostaglandine F1α (6-keto-PGF1α) were measured. Compared to controls, COM extracts dose-dependently prolonged bleeding by 2.17, 2.78 and 3.63 times, compared with aspirin 2.58, and the clotting time by 1.44, 2.47 and 2.48 times, compared with aspirin 1.91. COM reduced pulmonary embolus mortality by 27, 40 and 53%, compared with 47% for aspirin. COM dose-dependently increased thrombolysis by 45, 55 and 63%, compared with 56% for aspirin, and shortened ELT to 71, 61 and 43%, compared with 43% for aspirin. In rats, venous occlusion time was prolonged. Arterial and	336

		venous thrombus weights were dose-dependently reduced in COM groups. TXB2 decreased and 6-keto-PGF1α increased with COM and aspirin, with an association between 6-keto-PGF1α/TXB2 and arterial or venous thrombus weight for all products, and for occlusion time with COM but not for aspirin.	
Cynodon dactylon	leaves juice extract	The haemostatic activity of *Cynodon dactylon* was studied in albino rats. The Bleeding Time (BT) in control group was 160.5±8.3 second and in test group 96.8±10.3 second. The Clotting Time (CT) in control group was 507.6 ±18.2 second and in test group 319.3±27.1 second.	337-338
Cyperus rotundus	Ethanolic extract	The antiplatelet activities of *Cyperus rotundus* ethanolic extract (CRE) and eight of its constituent compounds were evaluated by examining their effects on rat platelet aggregations *in vitro* and ex vivo, and on mice tail bleeding times. During the *in vitro* platelet aggregation study, CRE showed significant and concentration dependent inhibitory effects on collagen-, thrombin-, and/or arachidonic acid (AA)-induced platelet aggregation. Of its eight components, (+)-nootkatone was found to have the most potent inhibitory effect on collagen-, thrombin-, and AA-induced platelet aggregation. In addition, CRE- and (+)-nootkatone-treated mice exhibited significantly prolonged bleeding times. Furthermore, (+)-nootkatone had a significant inhibitory effect on rat platelet aggregation ex vivo. In studying the effect of *Cyperus rotundus* on the hemorrheological changes in normal rats, *Cyperus rotundus* can improve all hemorrheological indexes, such as the whole blood specific viscosity, the plasma specific viscosity, erythrocyte electrophoresis, etc.	339-341
Equisetum arvense	aqueous extracts	The extract of *Equisetum arvense* produced a dose-dependent inhibition of thrombin and ADP-induced platelet aggregation. The effect of the plant could be related in part to the polyphenolic compounds present in the extract suggesting their involvement in the treatment or prevention of platelet aggregation complications linked to cardiovascular diseases.	342-343
Erigeron canadensis	different parts of extract	The effects of different parts of extract of the plant on platelet aggregation in vitro were investigated. Aqueous extract young or old plants, glycoconjugate part, polysaccharide part and aglycon part at the concentrations above 0.75 mg/ml strongly inhibited platelet aggregation induced by collagen (2 microg/ml) in dose-dependent manner. Polysaccharide part isolated from plant extract had the strongest inhibitory effect on aggregation stimulated by collagen and seems to be responsible for antiaggregatory properties.	344-345

	phenolic-polysaccharide	The phenolic-polysaccharide preparation from *Erigeron canadensis* demonstrated in vivo anticoagulant activity, and the effect was neutralized by protamine sulfate. It had also anti-platelet activity, limited to the cyclooxygenase pathway, induced by arachidonic acid. The plant preparation was fractionated to determine the fraction of the highest anticoagulant activity. The influences of the plant preparation as well as its most active fraction on thrombin and factor Xa inactivation by antithrombin, and on thrombin inhibition by heparin cofactor II, were compared. Both inhibited thrombin as well as factor Xa amidolytic activities in the presence of antithrombin, but much higher concentrations were required to obtain the same effects for unfractionated heparin. The mechanisms of anticoagulant activity were based on interactions with heparin cofactor II, to inactivate thrombin.	346
	polysaccharide extract	The protective effects of the polysaccharide extract from the plant on platelet proteins against nitrative and oxidative damage induced by $ONOO^-$ were studied . The oxidative damage of platelet proteins induced by peroxynitrite and protectory effects of this extract by estimation of the level of carbonyl groups and nitrotyrosine (a marker of platelet protein nitration) were investigated. The cytochrome c reduction method was used to test the ability of this extract to change O_2 generation in platelets. Moreover, the effects of the extract on blood platelet aggregation induced by ADP was also investigated. The extract of the plant distinctly reduced oxidation and nitration of proteins in blood platelets treated with $ONOO^-$ (0.1 mM) and O_2 production in these cells. The extract also inhibited platelet aggregation. The ability of the extract to decrease O_2 generation in blood platelets supports the importance of free radicals in platelet functions, including aggregation process.	347

II. CONCLUSION:

With the high prevalence of herbal medicine use worldwide. the information regarding the therapeutic use or safety of herbal remedies usually obtained from books and pamphlets, most of which base their information on traditional reputation rather than relying on existing scientific research. This review highlights the cardiovascular effects of the medicinal plants as proved experimentally or clinically by the previous works.

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