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Role of Medicinal plants on Remedies and prevention of cardiovascular disorders in Iran-A review

Ebrahim Alinia-Ahandani[1]*, Ani Boghozian[1,] Zahra Alizadeh-Terepoei[1], Zahra Musavizadeh[2,] Habibollah Nazem [1], Mohammad Fazilati[1], Mahdi Alinia-Ahandani[3]

1- Department of Biochemistry, Payame Noor University, PO BOX 19395-3697 Tehran, I. R. Iran
2-Department of Biomedical sciences, Sapienza University of Rome, Italy
3- Health Department, Medical university of Ardebil, I. RIran
*Corresponding author: Ebrahim Alinia-Ahandani, E-mail: ebi.alinia@gmail.com

Abstract: The pointed feature of the traditional Iranian medicinal system, *Ayurveda*, is its emphasis on the maintenance of positive health effects of them. As per *Ayurveda*, Iranian medicinal plants are rich sources of substances that have several therapeutic features including cardiopro- tection. Globally, cardiovascular disorders are a leading cause of mortality. This review deals with medicinal plants which possess cardiotonic, cardioprotective and antioxidant or positive effects on heart. It also includes our studies on the antioxidant prop- erties of some of these plants such as *Agrimonia eupatoriaAllium sativum, Althaea rosea, Ammi visnaga Anethum graveolens, Arachis hypogaea, Avena sativa, Bryophyllum calycinum, Caesalpinia crista, Capparis spinose, Carthamus tinctorius, Cicer arietinum, Cichorium intybus Cistanche tubulosa, Citrus species, Cordia myxa, Coriandrum sativum, Crocus sativus, Cuminum cyminum, Cydonia oblonga, Daucus carota, Adonisa estivalis, Alhagi maurorum, Althaea rosea, Ammi visnaga, Anchusa strigose, Apium graveolens, Asclepias curassavica, Bacopa monnieri, Brassica nigra, Caesalpinia crista, Calendula officinalis, Calotropis procera, Cheiranthus cheiri, Citrus species, Corchorus aestuans, Corchorus capsularis, Coriandrum sativum, Coronilla scorpioides, Coronilla variaCrocus sativus, Cynodon dactylon, Cyperus rotundus, Dalbergia sissoo, Daucus carota, Digitalis lanata and Arachis hypogaea, Asparagus officinalis, Avena sativa, Bauhinia variegate, Bellis perennisCistanche tubulosaCitrullus colocynthisAchillea santolina, Allium cepa and etc.* possesses the highest potential and inhibit whole effects in rats besides showing significant intestinal absorption or reports in human. Other plants studied also exhibit radical scavenging effects as studied using various biochemical assays. These effects may possibly be responsible for their known beneficial remedies effects including their use in cardioprotection in Iran.

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I. INTRODUCTION

The World Health Organization (WHO) estimates that 80% of the people of developing countries rely on traditional medicines, mostly plant-derived drugs, for their primary health needs. Medicinal plants are commonly used in treating and preventing specific ailments and are considered to play a significant role in health care. Traditional medicinal systems use plants as indispensable sources of medicinal preparations. Hundreds of species are recognized as having medicinal value. Indeed, 'phytomedicines' are beginning to link traditional and modern medicines. According to the World Health Organization, the burden of chronic diseases, including coronary heart disease (CHD), cancers, diabetes and obesity contributed 59% of the 56.5 million deaths reported worldwide in 2001. With CHD ranking number one as the main contributor to morbidity and mortality worldwide, there is a significant interest in identifying plants that have cardioprotectant and cardiotonic activity, as well as the phytochemicals responsible for these activities. To date, the evidence suggests that the health benefits of complex plant constituents are even more considerable than we thought due to the large numbers of phytochemicals present in each plant. New evidence suggests that in order to understand the health benefits of plant-based supplements and foods, we will need to take into account the fact that complex mixtures of phytochemicals found in foods and other botanicals may act synergistically. These new revelations may in time dispel the "magic bullet theory", which suggests that only pure compounds are the most efficacious. There is also no doubt that the emerging new fields of nutrigenomics and pharmacogenomics will play an important role in determining the interaction of these complex substances with the genetic variability of individuals and will determine the individual response and its magnitude to phytochemicals.

II. Role of Ayurveda in Human Health

Iran is well-known for its rich traditional systems of medicine, and rich of herbs in various sites like Guilan, Mazandaran, Shahrekurd, Mashhad and etc .Many rural households in Iran, with limited access to organized health services practice home remedies, the recipes and formulae of which have been handed down from generation to generation. In Iranian systems of medicine, generally the medicines of plant origin are preferred over the medicines of animal origin, due to presence of abundant natural flora. The basic concept of disease prevention, has existed in the ancient Vedic scripture and has been practiced in Iranian traditional medicine, the *Ayurveda*, for many centuries. In *Ayurveda*, it is clearly mentioned that any patient can be cured with the help of herbs present in the sur roundings [1,2]. The two main approaches to illness in Ayurveda are preventive and curative. [2]. A harmonious balance between three humors of the body viz. 'Vayu', 'Pitta' and 'Kafa' is needed for positive health; imbalance of these may cause disease(s). A significant part of Ayurvedic therapeutics aims to promote positive health. The prescribed proce- dures include drugs along with daily routine including exercise, diet and nutirtion besides mental attitude and discipline. This is achieved by using extracts of various plant materials, the rasayanas. These enhance body's resistance and by using them, one obtains longevity, regains youth, gets sharp memory and intellect besides curing diseases [3, 4]. Iranian medicinal plants are rich sources of substances that have several therapeutic properties like cardioprotective, chemopreventive and other effects [5,6].

III- Cardiovascular Disorders

Globally, cardiovascular diseases (CVD) constitute a leading cause of mortality. Developing countries like India are also struggling to manage the impact of CVD along with the growing burden of obesity, Type II diabetes and hyper- tension [*5,7,8*]. Heart disease in Iran occurs 12 to 17 years earlier than in the West. One fifth of the deaths in India are from coronary heart disease (CHD). By the year 2020, it will account for one third of the deaths. Current projections suggest that by the year 2020, Iran will have the largest CVD burden in the world [*6,9*]. The prevalence of these dis- eases is more in urban than in rural areas [*7,12,10*]. Lower vitamin C and selenium in Indians as compared to other ethnic groups, particularly in combination, could play a part in their increased risk of CHD. Lower vitamin C in Indians is probably because of its destruction by prolonged cooking [*8*]. There are epidemiological correlations between poor plasma levels of essential antioxidants and the risk of coronary heart disease [*9,14,15,3*].

Epidemiological studies have revealed many important risk factors of environmental and genetic origin that are associated with atherosclerosis. The most important clinical complication is an acute occlusion due to blood clot forma- tion during rupture of the lesion, resulting in myocardial infarction [*10,22.45*]. One of the major initiating event in athero- sclerosis is oxidative damage to the cholesterol component of the LDL known as LDL oxidation. Oxidation of LDL contributes to atherogenesis in various ways [*11,17,19*]. An appropriate balance between processes that stimulate or in- hibit oxidative stress, LDL oxidation, and additional LDL atherogenic modifications determines the progression of atherogenesis [65,254-4].

LDL oxidation and atherogenesis can be inhibited by

antioxidants. Elevation in the activity of nutritional antioxi- dants over the damaging effects of prooxidants has the potential to attenuate atherosclerosis, which is a leading cause of mortality in several human populations. There are also epidemiological evidences and interventional studies to correlate higher level of antioxidant-rich food uptake with lower incidence of CHD [*12, 13,23,29*]. Contrary to popular belief, CHD is indeed common in the Indian subcontinent. The prevalence of CHD increased from 1% to over 8% in urban population [*14*]. Indians have among the highest prevalence of CHD and have rather unusual risk factors characterized by high triglycerides, low High Density Lipoproteins (HDL), glucose intolerance, insulin resistance, abdominal obesity and increased lipoprotein (a) levels [*15,24,26*]. Hence there is an urgent need to explore various strategies to combat the increasing risk of CVDs in the Indian subcontinent. Medic- inal plants with cardioprotective effects can play a major role in this aspect [27,28].

IV-Antioxidant Potential of Plant Extracts and Natural Compounds

A number of epidemiological studies show that diets high in fruits and vegetables, the foods rich in antioxidant com- pounds, are associated with a lower incidence of cardiovas- cular disease. Observational data in animals and humans suggest that greater intake of antioxidant vitamins are associated with the reduced risk of atherosclerotic vascular disease [67,42,41,87]. Antioxidants may at least in part prevent atherosclerosis and cardiovascular disease [68]. Hence it is pertinent to examine cardioprotective and antioxidant effects of plants used in Indian herbal preparations [88,89,92].

For ease of study, in biological systems, oxidative stress can be generated using various physical / chemical agents. Among them, ionizing radiation such as γ-rays is an important source of reactive oxygen species. The exposure of biological systems to radiation results in radiolytic cleavage of water yielding. OH, .H, e−aq etc. in presence of oxygen even O .−, H2O2, 1O2 etc. are produced. Thermal decomposition of an azo-initiator, 2.2'-Azobis (2-amidinopropane) dihydro-chloride (AAPH) in presence of oxygen gives rise to a constant source of peroxyl radicals. These free radicals especially. OH and LOO. can initiate lipid peroxidation. Cumene hydroperoxide, ascorbate-Fe2+ and peroxynitrite are some other free radical generators [12,91,92,1].

Antioxidants exhibit their effects at different levels. These include ability to bind iron that can prevent radical forma- tion, the scavenging of primary and secondary radicals and ability to inhibit free radical induced membrane damage. Among the sub-cellular organelles mitochondria are crucial targets for oxidative damage. In this paper, we have demon- strated that ROS induce significant lipid peroxidation in the model system i.e. rat liver mitochondria as measured by LOOH, an unstable intermediate, which further breaks down to stable aldehydes and react with thiobarbituric acid (TBA) to form TBARS, the final stable end product. Apart from enhancing lipid damage to membranes, oxidative damage leads to protein oxidation resulting in the formation of pro- tein hydroperoxide, protein carbonyls besides inactivation of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPX) and glutathione reductase (GR)[93,34,107].

V-Iranian Medicinal Plants

Ayurveda has identified many plants which possess cardiotonic and cardioprotective effects. Some of them are*; Agrimonia eupatoriaAllium sativum, Althaea rosea, Ammi visnagaAnethum graveolens, Arachis hypogaea, Avena sativa, Bryophyllum calycinum, Caesalpinia crista, Capparis spinose, Carthamus tinctorius, Cicer arietinum, Cichorium intybus Cistanche tubulosa, Citrus species, Cordia myxa, Coriandrum sativum, Crocus sativus, Cuminum cyminum, Cydonia oblonga, Daucus carota, Adonisa estivalis, Alhagi maurorum, Althaea rosea, Ammi visnaga, Anchusa strigose, Apium graveolens, Asclepias curassavica, Bacopa monnieri, Brassica nigra, Caesalpinia crista, Calendula officinalis, Calotropis procera, Cheiranthus cheiri, Citrus species, Corchorus aestuans, Corchorus capsularis, Coriandrum sativum, Coronilla scorpioides, Coronilla variaCrocus sativus, Cynodon dactylon, Cyperus rotundus, Dalbergia sissoo, Daucus carota, Digitalis lanata and Arachis hypogaea, Asparagus officinalis, Avena sativa, Bauhinia variegate, Bellis perennis Cistanche tubulosaCitrullus colocynthisAchillea santolinaAllium cepa and etc*. These plants exhibit potent antioxidant effects[2,3], which might be the mechanism behind their beneficial therapeutic properties. Details of Iranian medicinal plants having cardioprotective, therapeutic and antioxidant properties are given in Table 1 [*5-336*].

To elucidate the possible positive correlation between the antioxidant and cardioprotective effects, we studied some medicinal plants in detail which were brought in to the category, too.

Plants with vascular and hypotensive effects:

Plant	The tested constituent	Activity	Ref

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.	17-18-15
	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.	19-20-17
	Visnadin	Visnagin inhibited the contractile responses induced in rat aortic rings by: (a) KCl or increases of extracellular 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
Arachis hypogaea	peptides isolated from peanut	A bioactive peptides with antihypertensive effects against Angiotensin Converting Enzyme were isolated from peanut.	27-26-32
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	28-30-29

		benefit of food containing soluble fiber from oats.	
	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.	33-35-65
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.	36-37-67
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.	38-34

	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.	39-66

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.	40-68
	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.	42-69
	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
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.	45-46-49

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.	47-44
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	48-49
		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.	49-74
	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	51-75

		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.	52-55-76
	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.	53-77
	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.	54-78
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.	57-58-79
	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.	61-80
	ethanol 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.	62-81

	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.	64-1-82
Cuminum cyminum	aqueous 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.	65-67
Cydonia oblonga	ethanol leaf extracts	The effect of ethanol leaf extracts of *Cydonia oblonga* Mill. (COM) was studied on hypertension and on biomarkers	66-83

		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.	67-68-84
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 coumarin 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 well 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*	70-85

		studies.	

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.	71-72-86
	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, 73-79-14-87
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.	74-75-89
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.	76-90
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	77-78

		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.	
	Khellin	Immediately after the rapid intravenous administration of 20-30 mg of khellin to the	79-91

		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.	80-81-93
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*.	96-82
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.	84-85-94
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.	88-100
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.	91-92-99
	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.	93-98
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	101-94

		rhamnopyranosyl digitoxopyranosyl moiety and a carboxyl group showed the lowest activity	
		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.	102-104-100 .
Corchorus aestuans	alcoholic extract and glycosides of seeds	Alcoholic extract and glycosides of seeds exhibited cardiotonic activity.	105-95
	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.	106-107-108
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.	109-96 113-105
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	114-97

		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- 116-98-110
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- 120-99
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.	121-116
	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.	122-119

	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.	123-100
	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.	124-128-16
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	125-101
		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.	127-102
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.	128-129-103
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 29th and 30th 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	digitalis glycosides	Cardiac glycosides, are often called digitalis or digitalis	131-184-142

lanata* and *Digitalis purpurea		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	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.	139-141-104
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.	142-145-150

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.	146-151

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.	78-105-147
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, 148-152
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.	149-106
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	151-169

		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	152

		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.	

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	153-172-166
		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.	173-174-165
	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	176-178

		significant inhibitory effects on PAF with IC50 value of 5.5ug/ml in rabbit platelets.	
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	179-172
		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.	180-175 181
	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	184-180 188

		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.	
	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 polyphenol ic 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.	190-178 191
	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.	192-187
	peanut consumpti on	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.	193-188
	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.	194-195-191

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	196-192 198
		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.	199-200-193
	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.	201-194
	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.	202-195
	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, 203-198-197
		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.	204-200
	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 variegate	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.	206-201 207
	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 ($p<0.05$).	208-206
	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 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.	209
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.	210-212-209

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.	213-214-212
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.	216-201-202-203
	Ethanolic Extracts	The influence of ethanolic extracts of *Brassica 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.	217-211
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.	218-208
	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	88-210

		isoproterenol group.	
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.	219-212
Capparis spinose	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.	221-210
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- 223-217
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- 225-219
	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.	227-222
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- 232-229
	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	231-227-226
		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 ($p< 0.01$).	237-230
	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 phospholipids concentration.	238-237
	Eriocitrin (eriodictyol 7-rutinoside), aflavonoid 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.	239-236
	Citrus medica peel extract	*Citrus medica* cv Diamante peel extract lowered plasma cholesterol and triglycerides in mice	240-238
Clitoria ternatea	hydroalcoholic extract	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	241-242

	of t he roots and seeds of *Clitoria ternatea*	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).	
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.	243-239
	70% methanolic extract	The hypolipidemic and antioxidant action of *Coriandrum sativum* were investigated in	244-240
		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- 246-249
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.	247-245
	Crocetin	Crocetin, was administered to rabbits to determine its effect on the development of atherosclerosis. New Zealand white rabbits were	248-244

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

		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- 250-245
	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.	252-253
	leaves extract	The anti-obesity effect of *Crotalaria juncea* leaves extract was documented in high fat induced obesity in rats.	257-254
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- 259-254
	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	260-255

		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	
		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.	261-258
	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	263-259 264
		(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	265- 266

		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.	
	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.	267-23
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.	269-268
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,	271-265

		whereas the cholesterol apparent absorption was reduced in rats fed carrot diet.	
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.	274-275-272
	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.	276-274-275

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	277-273

		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.	
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	278-284-280

		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.	287-284
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*	288-293-299
	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.	294-302-299
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.	304-305-298
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	methanolice xtracts, the acidic fractions of aerial and root parts, and three identified compounds (aristolochic	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	307-308-304

	acid I, aristolochic acid II and aristolochic acid IIIa)		

		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.	
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)	313-300-327

		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.	317-315-314
	Capsaicin	Capsaicin inhibited platelet aggregation and the activity of clotting factors VIII and IX, a property which reduce the incidence of cardiovascular diseases.	318-319-317
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 blood stasis model. Hematocrit and platelet aggregation were reduced, while prothrombin time was delayed with increasing doses of CY.	320-321
	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.	322-319
	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.	323-321
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,	326-327

		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.	
Citrus species	*Citrus limon*	*In vitro* / *in vivo* study was designed to 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.	328
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.	329-331-328
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	334-333-332

		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.	333
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- epinephrinepulmonary 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	334
		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.	334-333
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.	336-335

IV.CONCLUSION:

In this review, we focused on various aspects of past studies on importance of herbs for heart safety and disorders in Iran.With the high prevalence of herbal medicine use worldwide. the information regarding the remedical use or safety of herbal curing usually obtained from books and pamphlets, most of which base their information on traditional reputation rather than relying on existing scientific seeking. This review pointed the cardiovascular effects of the medicinal plants as proved experimentally or clinically by the previous works and opened an oversight on Iranian new usages on this platform. As we know 70 percent of all drugs orginated by herbs as well as our remedies must be based on medicinal plants,too.

REFERENCES

[1] Asadi-Samani, M., N. Kafash-Farkhad, N. Azimi, A. Fasihi, E. Alinia-Ahandani and M. Rafieian-Kopaei, 2015. Medicinal plants with hepatoprotective activity in Iranian folk medicine. Asian Pac. J. Trop. Biomed., 5: 146-157.

[2] Alinia-Ahandani, E., M. Fazilati, Z. Alizadeh and A. Boghozian, 2018. The introduction of some mushrooms as an effective source of medicines in Iran Northern. Biol. Med., Vol. 10. 10.4172/0974-8369.1000451.

[3] Shinde S, Shastry S and Agrawal S L.Cardiovascular effects of aqueous extract of *Adonis vernalis*. IX Annual conference of IPS, 76-77. http://lib.hebust.edu.cn/ywyfzsk/zsk/pharm-docum/b014.pdf

[4] Petkov V. Plants with hypotensive, antiatheromatous and coronarodilatating action. Am J Chin Med 1979; 7: 197-236.

[5] Al-Qattan KK, Alnaqeeb MA, Ali M *et al.*The antihypertensive effect of garlic (*Allium sativum*) in the rat two-kidney–one-clip Goldblatt model. Journal of Ethnopharmacology 1999; 66: 217-222.

[6] Ali M, Al-Qattan KK, Al-Enezi F *et al.* Effect of allicin from garlic powder on serum lipids and blood pressure in rats fed with a high cholesterol diet. Prostaglandins Leukotrienes and Essential Fatty Acids 2001; 62(4): 253-259.

[7] Fallon MB, Abrams GA, Abdel-Razek TT *et al.* Garlic prevents hypoxic pulmonary hypertension in rats. Am J Physiol Lung Cell Mol Physiol 1988; 275: L283-L287.

[8] Silagy CA and Neil HA. A meta-analysis of the effect of garlic on blood pressure. J Hypertens 1994; 12: 463-468.

[9] Aqel MB, Gharaibah MN and Salhab AS. Direct relaxant effects of garlic juice on smooth and cardiac muscles. J Ethnopharmacol 1991; 33: 13-19.

[10] Ahandani, E.A., M.R.A. Gawwad and A. Yavari, 2013. Extraction and preparation of psoralen from different plant part of psoralea corylifolia and psoralen increasing with some elicitors. J. Plant Biol. Res., 2: 25-37.

[11] Ahandani, E.A., 2018. Medicinal plants with disinfectant effects. J. Pharm. Sci. Res., 10: 1-1.

[12] Durate J, Perez-Vizcaino F, Torres AI, Zarzuelo A, Jimenez J and Tamargo J. Vasodilator effects of visnagin in isolated rat vascular smooth muscle. Eur J Pharmacol 1995; 286(2): 115-122.

[13] Durate J, Vallejo I, Perez – Vizcaino F, Jimenez R, Zarzuelo A and Tamargo J. Effects of visnadine on rat isolated vascular smooth muscles. Planta Med 1997; 63(3): 233-236.

[14] Durate J, Torres A I and Zarzuelo A. Cardiovacular effects of visnagin on rats. Planta Med 2000; 66(1): 35- 39.

[15] Rauwald HW, Brehm H and Odenthal KP. Screening of nine vasoactive medicinal plants for their possible calcium antagonist activity. Strategy of selection and isolation for the active principles of *Olea europaea* and *Peucedanaum ostruthium*. Phytotherapy Research 1994; 8: 135-140.

[16] Rauwald HW, Brehm H and Odenthal KP. The involvement of Ca^{2+} channel blocking mode of action in the pharmacology of *Ammi visnaga* fruits. Planta Medica 1994; 60: 101-105.

[17] Erbring H, Uebel H and Vogel G. Zur Chemie, Pharmakologie und Toxicologie von Visnadin. Arzneimittelforschung 1967; 17: 283-287.

[18] Goyal, R.K., Singh, J., and Lal, H.: Asparagus racemosus-an update. Indian J. Med. Sci., 57, 408–414, 2003.

[19] Duarte J, Pérez-Vizcaíno F, Torres AI, Zarzuelo A, Jiménez J and Tamargo J. Vasodilator effects of visnagin in isolated rat vascular smooth muscle. Eur J Pharmacol 1995; 286(2):115-122.

[20] Altinterim B. Hıltan tohumunun (Umbelliferae, *Ammi visnaga* L.) düz kaslar üzerine etkisi. Nevşehir Dergisi Üniversitesi Fen Bilimleri Enstitü 2012:60-64.

[21] Leung A Y, Foster S. Encyclopedia of common natural ingredients used in food, drugs and cosmetics. New York, John Wiley and Sons 1996.

[22] Yazdanparast R, Bahramikia S. Evaluation of

the effect of Anethum graveolens L. crude extracts on serum lipids and lipoproteins profiles in hypercholesterolaemic rats. DARU 2008; 16(2):88-94.

[23] African pharmacopoeia. Vol.1. Lagos, Organization of African Unity, Scientific Technical and Research Commission 1985.

[24] Branković, S., Kitić, D., Radenković, M., Veljković, S., Kostić, M., Miladinović, B., & Pavlović, D. Hypotensive and cardioinhibotory effects of the aqueous and ethanol extracts of celery (*Apium graveolens*, Apiaceae). Acta Medica Medianae 2010; 49(1): 13-16.

[25] Quist EE. Peanut *(Arachis hypogaea L.*) as a source of antihypertensive and antimicrobial peptides. PhD thesis, Uga Univ 2005.

[26] Sobotka W, Flis M, Antoszkiewicz Z, Lipiński K and Zduńczyk Z. Effect of oat by-product antioxidants and vitamin E on the oxidative stability of pork from pigs fed diets supplemented with linseed oil. Arch AnimNutr 2012; 66(1): 27-38.

[27] Andersson KE, Axling U, Xu J, Swärd K, Ahrné S, Molin G, Holm C and Hellstrand P. Diverse effects of oats on cholesterol metabolism in C57BL/6 mice correlate with expression of hepatic bile acid- producing enzymes. Eur J Nutr 2013; 52(7): 1755-1769.

[28] Othman RA, Moghadasian MH and Jones PJ. Cholesterol-lowering effects of oat β-glucan. Nutr Rev 2011; 69(6): 299-309.

[29] Maki KC, Galant R, Samuel P, Tesser J, Witchger MS, Ribaya-Mercado JD, Blumberg JB and Geohas J. Effects of consuming foods containing oat beta-glucan on blood pressure, carbohydrate metabolism and biomarkers of oxidative stress in men and women with elevated blood pressure. Eur J ClinNutr 2007; 61(6): 786-795.

[30] Nie L, Wise ML, Peterson DM and Meydani M. Avenanthramide, a polyphenol from oats, inhibits vascular smooth muscle cell proliferation and enhances nitric oxide production. Atherosclerosis 2006; 186(2): 260-266 .

[31] Devasagayam, T.P.A. and Sainis, K.B.: Immune system and antioxidants, especially those derived from Indian medicinal plants. Indian J. Expt. Biol., 40, 639–655, 2001.

[32] John AO. Ojewole. Antihypertensive properties of *Bryophyllum pinnatum* {(Lam) Oken} leaf extracts.
Am J Hypertens 2002; 15: 34A–34A

[33] Prasad AK, Kumar S, Iyer SV, Sudani RJ and Vaidya SK. Pharmacognostical, phytochemical and pharmacological review on *Bryophyllum pinnata.* International Journal of Pharmaceutical & Biological Archives 2012; 3(3):423-433.

[34] Datté YJ, Traoré A, Offoumou AM. Anti-hypertensive effect of aqueous extract of *Caesalpinia bonduc*)Caesalpiniaceae) on arterial blood pressure in guinea-pig. Revue Med Pharm Afr 1997; 11: 79- 88 .

[35] Jadhav, H.R. and Bhutani, K.K.: Antioxidant properties of Indian medicinal plants. Phytother. Res., 16, 771–773, 2002.

[36] Heber, D.: Herbs and atherosclerosis. Curr. Atheroscler. Rep.,3, 93–96, 2001.Zeggwagh NA, Michel JB and Eddouks M. Cardiovascular effect of *Capparis spinosa* aqueous extract. Part VI: *In vitro* vasorelaxant effect. American Journal of Pharmacology and Toxicology 2007; 2(3): 135-139.

[37] Benzidane N, Imane K, Abderrahmane B, Noureddine C, Seddik K, Xavier N, and Lekhmici A. *In vitro* vasomotor effects of *Capparis spinosa* aqueous extracts. The 3rd International Symposium on the Medicinal Plants, Their Cultuvation and Aspects of Uses, BeitZaman Hotel & Resort, Petra – Jordan, November 21-23/ 2012.

[38] Liu F, Wei Y, Yang XZ, Li FG, Hu J and Cheng RF. Hypotensive effects of safflower yellow in spontaneously hypertensive rats and influence on plasma renin activity and angiotensin II level. Yao Xue Xue Bao 1992; 27(10): 785-787

[39] Bai Y, Lu P, Han C, Yu C, Chen M, He F and Yi D, Wu L. Hydroxysafflor yellow A (HSYA) from flowers of *Carthamus tinctorius* L. and its vasodilatation effects on pulmonary artery. Molecules 2012; 17(12): 14918-14927.

[40] Nie PH, Zhang L, Zhang WH, Rong WF and Zhi JM. The effects of hydroxysafflor yellow A on blood pressure and cardiac function. J Ethnopharmacol 2012; 139(3): 746-750.

[41] Takimoto T, Suzuki K, Arisaka H, Murata T, Ozaki H and Koyama N. Effect of N-(p-coumaroyl)serotonin and N-feruloylserotonin, major anti-atherogenic polyphenols in safflower seed, on vasodilation, proliferation and migration of vascular smooth muscle cells. Mol Nutr Food Res 2011; 55(10): 1561-1571.

[42] Zeggwagh NA, Michel JB and Eddouks M. Vascular effects of aqueous extract of Chamaemelum nobile: in vitro pharmacological studies in rats. Clin Exp Hypertens 2013; 35(3): 200-206.

[43] Pedroche J, Vioque J, Millan F, Alaiz M, Gir J and Yust MM. Production of ACE inhibitory peptides by digestion of chickpea legumin with alcalase. Food Chemistry 2003; 81: 363-369.

[44] Al-Snafi AE. The medical Importance of *Cicer arietinum* - A review. IOSR Journal of Pharmacy 2016; 6(3): 29-40.

[45] Sakurai N, Iizuka T, Nakayama S, Funayama H, Noguchi M and Nagai M. Vasorelaxant activity of caffeic acid derivatives from *Cichorium intybus* and *Equisetum arvense*. Yakugaku Zasshi 2003; 123(7):593-598.

[46] Yoshikawa M, Matsuda H, Morikawa T, Xie H, Nakamura S and Muraoka O. Phenylethanoid oligoglycosides and acylated oligosugars with vasorelaxant activity from *Cistanche tubulosa*. Bioorg Med Chem 2006; 14(22):7468-7475.

[47] Ohnishi A, Asayama R, Mogi M, Nakaoka H, Kan-No H, Tsukuda K, Chisaka T, Wang XL, Bai HY, Shan BS, Kukida M, Iwanami J and Horiuchi M. Drinking citrus fruit juice inhibits vascular remodeling in cuff-induced vascular injury mouse model. PLoS One 2015; 10(2):e0117616.

[48] Akhtar SS. Evaluation of Cardiovascular Effects of *Citrus aurantifolia* (Linn.) Fruit. Social Science Research Network 2013, http://ssrn.com/abstract=2279447

[49] Souza A, Lamidi M, Ibrahim B, Samseny A, Mounanga MB and M'Batchi. B. Antihypertensive effect of an aqueous extract of *Citrus aurantifolia* (Rutaceae) (Christm.) Swingle, on the arterial blood pressure of mammal. International Research of Pharmacy and Pharmacology 2011; 1(7): 142-148.

[50] Perez YY, Jimenez-Ferrer E, Alonso D, Botello-Amaro CA and Zamilpa A. *Citrus limetta* leaves extract antagonizes the hypertensive effect of angiotensin II. Journal of Ethnopharmacology 2010; 128(3): 610- 614.

[51] Asgary S and Keshvari M. Effects of *Citrus sinensis* juice on blood pressure. ARYA Atheroscler 2013; 9(1): 98-101.

[52] Kumamoto H, Matsubara Y, Izuka Y, Okamoto K, Yokoi K. Structure and hypotensive effect of flavonoid glycosides in orange (*Citrus sinensis* OSBECK) peelings. Agric Biol Chemistry 1986; 50: 781- 783.

[53] Abuo-Shaaban RR, Angari AA, El-Tahir KE, Al-KhamisKI and Mirghani OM. Comparative hypotensive and respiratory stimulation effects of ripe and unripe fruit mucilage of *Cordia myxa* and *Cordia obliqua* in guineapigs and rabbits. Phytotherapy Res 1989; 3(4): 126-131.

[54] Al-Snafi AE. The Pharmacological and therapeutic importance of *Cordia myxa*- A review. IOSR Journal of Pharmacy 2016; 6(6): 47-57.

[55] Jabeen Q, Bashir S, Lyoussi B and Gilani AH. Coriander fruit exhibits gut modulatory, blood pressure lowering and diuretic activities. J Ethnopharmacol 2009;122(1):123-130.

[56] Upadhyay, S.N.: Immunomodulation. Narosa Publishing House, New Delhi, 1997.

[57] Medhin DG, Bakos P and Hadházy P. Inhibitory effects of extracts of *Lupinus termis* and *Coriandrum sativum* on electrically induced contraction of the rabbit ear artery. Acta Pharm Hung 1986; 56(3): 109- 113.

[58] Medhin DG, Hadhazy P, Bakos P and VerzarPetri G.Hypotensive effects of *Lupinus termis* and *Coriandrum sativum* in anesthetized rats: preliminary study. Acta Pharmaceutica Hungarica 1986; 56(2): 59-63.

[59] Liu N, Yang Y, Mo S, Liao J and Jin J.Calcium antagonistic effects of Chinese crude drugs: Preliminary investigation and evaluation by 45Ca. Applied Radiation and Isotopes 2005; 63:151-155.

[60] Imenshahidi M, Hosseinzadeh H and Javadpour Y. Hypotensive effect of aqueous saffron extract (*Crocus sativus* L.) and its constituents, safranal and crocin, in normotensive and hypertensive rats. Phytother Res 2010; 24(7): 990-994.

[61] Imenshahidi M, Razavi BM, Faal A, Gholampoor A, Mousavi SM and Hosseinzadeh H. The effect of chronic administration of saffron (*Crocus sativus*) stigma aqueous extract on systolic blood pressure in rats. Jundishapur J Nat Pharm Prod 2013; 8(4): 175-179.

[62] Mancini A, Serrano-Díaz J, Nava E, D'Alessandro AM, Alonso GL, Carmona M and Llorens S. Crocetin, a carotenoid derived from saffron (*Crocus sativus* L.), improves acetylcholine-induced vascular relaxation in hypertension. J Vasc Res 2014; 51(5): 393-404.

[63] Kalaivani P, Saranya RB, Ramakrishnan G, Ranju V, Sathiya S, Gayathri V, Thiyagarajan LK, Venkhatesh JR, Babu CS and Thanikachalam S. *Cuminum cyminum*, a dietary spice, attenuates hypertension via endothelial nitric oxide synthase and NO pathway in renovascular hypertensive rats. Clin Exp Hypertens 2013; 35(7): 534-542.

[64] Zhou WT, Abdurahman A, Abdusalam E, Yiming W, Abliz P, Aji Q, Issak M, Iskandar G, Moore N and Umar A. Effect of *Cydonia oblonga* Mill. leaf extracts or captopril on blood pressure and related biomarkers in renal hypertensive rats. J Ethnopharmacol 2014; 153(3): 635-640.

[65] Zhou W, Abdusalam E, Abliz P, Reyim N, Tian S, Aji Q, Issak M, Iskandar G, Moore N and

Umar A. Effect of *Cydonia oblonga* Mill fruit and leaf extracts on blood pressure and blood rheology in renal hypertensive rats. J Ethnopharmacol 2014; 152(3): 464-469.

[66] Gilani A, Shaheen F and Saeed SA. Cardiovascular action of Daucus carota. Archives of Pharmacal Research 1994; 17(3):150-153·

[67] Lele, R.D.: Ayurveda and Modern Medicine. Bharatiya Vidya Bhavan, Mumbai, 2001.

[68] Gilani AH, Shaheeri F, Saeed SA, Bibi S, Irfanullah, Sadiq M and Faiz S. Hypotensive action of coumarin glycosides from *Daucus carota*. Phytomedicine 2000; 7(5):423-426.

[69] Joubert J P J. Cardiac glycosides. In: Toxicants of plant origin, Glycosides, ed. Cheeke PR, CRC Press, Boca Raton 1989: 61-96.

[70] [19] Noguchi, N. and Niki, E.: Phenolic antioxidants: a rationale for design and evaluation of novel antioxidant drug for atherosclerosis. Free Rad. Biol. Med., 28, 1538–1546, 2000. Philippine Medicinal Plants, Family, Asclepiadacea, Bulak-damo, *Asclepias curassavica* Linn. http://www.stuartxchange.com/Bulak-damo.html.

[71] Marashdah MS and AL-Hazimi HM. Pharmacological activity of ethanolic extract of *Alhagi maurorum*

roots. Arabian Journal of Chemistry 2010; 3(1): 39-42.

[72] Scartezzini, P. and Speroni, E.: Review on some plants of Indian traditional medicine with antioxidant activity. J. Ethnopharmacol., 71, 23–43, 2000.

[73] Ahandani, E.A., H.D. Ramandi, J. Sarmad, M.A. Samani, A. Yavari and R.A. Ahandani, 2014. Evaluation of morphological diversity among somepersian walnut accessions (*Juglans regia* L.) in Guilan, Northern Iran. Int. J. Plant Biol. Res., Vol. 2. .

[74] Quart SKJ. Hıltan tohumunun (*Umbelliferae, Ammi visnaga* L.) düz kaslar üzerine etkisi. Nevşehir Üniversitesi Fen Bilimleri Enstitü Dergisi 2012; 2: 60-64.

[75] Galal EE, Kandil A and Latif MA. Evaluation of cardiac inotropism of *Ammi visnaga* principles by the intra-ventricular technique. Journal of Drug Research of Egypt 1975; 7: 45-57.

[76] Anrep GV, Barsoum GS, Kenawy MR, and Misrahy G.*Ammi visnaga* in the treatment of angina syndrome. Gazette of the Faculty of Medicine Cairo 1975; 13: 39.

[77] Mahipal SK, Garg BD and Ahmad A. Hypotensive Action of Flowers of *Anchusa strigosa* (Gaozeban). IX Annual Conferencev of IPS, 79. http://lib.hebust.edu.cn/ywyfzsk/zsk/pharm-docum/b014.pdf

[78] Ahandani, E.A., 2018. Milk-increasing medicinal plants. J. Pharm. Sci. Res., 10: 4-4.

[79] Mahran GH *et al.* Investigation of diuretic drug plants. 1-Phytochemical screening and pharmacological evaluation of *Anethum graveolens* L., *Apium graveolens* L., *Daucus carota* L. and *Eruca sativa* Mill. Phytotherapy Research1991; 5: 169-172.

[80] Al-Snafi AE. Chemical constituents and pharmacological effects of *Asclepias curassavica* – A review. Asian Journal of Pharmaceutical Research 2015; 5(2): 83-87.

[81] Rashid S, Lodhi F, Ahmad M and Usmanghani K. Cardiovascular effects of *Bacopa monnieri* (L.) pennel extract in rabbits. Pak J Pharm Sci 1990; 3(2): 57-62.

[82] Al-Snafi AE. The pharmacology of *Bacopa monniera*. A review. International Journal of Pharma Sciences and Research 2013; 4(12): 154-159.

[83] Felter HW. Monographs extracted from: The eclectic materia medica, pharmacology and therapeutics 1922. Michael Moore Bisbee (ed), Southwest School of Botanical Medicine, Arizona, 2001, 412-415.

[84] Al-Snafi AE. The pharmacological importance of *Brassica nigra* and *Brassica rapa* grown in Iraq. J of Pharm Biology 2015; 5(4): 240-253.

[85] Kumar SR and Kumar SA. Cardio protective effect of *Caesalpinia crista* Linn. on isoproterenol induced myocardial necrosis in rats. International Journal of Research in Pharmacy and Science 2013; 3(1): 119- 130.

[86] Ray D, Mukherjee S, Falchi M, Bertelli A and Das DK. Amelioration of myocardial ischemic reperfusion injury with *Calendula officinalis*. Curr Pharm Biotechnol 2010; 11(8): 849-854.

[87] Heber, D.: Herbs and atherosclerosis. Curr. Atheroscler. Rep.,3, 93–96, 2001.

[88] Mueen Ahmed KK, Rana AC and Dixit VK. Effect of *Calotropis procera* latex on isoproterenol induced myocardial infarction in albino rats. Phytomedicine 2004; 11: 327–330.

[89] Al-Snafi AE. The constituents and pharmacological properties of *Calotropis procera* - An Overview. International Journal of Pharmacy Review & Research 2015; 5(3): 259-275.

[90] Moustafa AM, Ahmed SH, Nabil ZI, Hussein AA and Omran MA. Extraction and phytochemical investigation of *Calotropis procera*: effect of plant extracts on the activity

of diverse muscles. Pharm Biol 2010; 48(10): 1080-1090.

[91] Han SY, Li HX, Ma X, Zhang K, Ma ZZ and Tu PF. Protective effects of purified safflower extract on myocardial ischemia *in vivo* and *in vitro*. Phytomedicine 2009; 16(8): 694-702.

[92] Wan L, Chen J, Li L, Xiong W and Zhou L. Protective effects of *Carthamus tinctorius* injection on isoprenaline-induced myocardial injury in rats. Pharmaceutical Biology 2009; 49(11): 1204-1209.

[93] Zhang SQ and Jiang LD. Effect of safflower injection on cardiac energy charge and anti-apoptosis gene bcl-2 in rats' heart. Zhongguo Zhong Xi Yi Jie He Za Zhi 2004; 24(5): 442-444.

[94] Hotta Y, Nagatsu A, Liu W, Muto T, Narumiya C, Lu X, Yajima M, Ishikawa N, Miyazeki K, Kawai N, Mizukami H and Sakakibara J. Protective effects of antioxidative serotonin derivatives isolated from safflower against postischemic myocardial dysfunction. Mol Cell Biochem 2002; 238(1-2): 151-162.

[95] Tien YC, Lin JY, Lai CH, Kuo CH, Lin WY, Tsai CH, Tsai FJ, Cheng YC, Peng WH and Huang CY. *Carthamus tinctorius* L. prevents LPS-induced TNFalpha signaling activation and cell apoptosis through JNK1/2-NFkappaB pathway inhibition in H9c2 cardiomyoblast cells. J Ethnopharmacol 2010; 130(3): 505-513.

[96] Duan JL, Wang JW, Guan Y, Yin Y, Wei G, Cui J, Zhou D, Zhu YR, Quan W, Xi MM, Wen AD. Safflor yellow A protects neonatal rat cardiomyocytes against anoxia/reoxygenation injury in vitro. Acta Pharmacol Sin 2013; 34(4): 487-495.

[97] Wang CY, Zhang SP, Xu Y, Yang M, Jiang WG and Luan HY. Effect of safflor yellow B on vascular endothelial cells injury induced by angiotensin-II. Yao Xue Xue Bao 2012; 47(6): 811-815.

[98] Lei Z H, Kuniyasu A, Tai BS, Nakayama H and Nohara T. Na+,K+-ATPase inhibiting activity of cardiac glycosides from Erysimum cheiranthoides. Planta Med 2001; 67(4): 369-370.

[99] Al-Yahya MA, Mothana RA, Al-Said MS, El-Tahir KE, Al-103-Sohaibani M and Rafatullah S. *Citrus medica* "Otroj": Attenuates oxidative stress and cardiac dysrhythmia in isoproterenol-induced cardiomyopathy in rats. Nutrients 2013; 5: 4269-4283.

[100] Ahandani, E.A., 2018. Medicinal plants effective on pregnancy, infections during pregnancy, and fetal infections. J. Pharm. Sci. Res., 10: 3-3.

[101] S. Asha and G. Taju; CARDIOPROTECTIVE EFFECT OF TERMINALIA ARJUNA ON CAFFEINE INDUCED CORONARY HEART DISEASE; International Journal of Pharmaceutical Sciences and Research ; 2012; Vol. 3(1): 150-153. Assessed on 19/01/16 at 8pm.

[102] Shridhar Dwivedi: Terminalia arjuna Wight & Arn.—A useful drug for cardiovascular disorders: Journal of Ethnopharmacology; vol 114; issue 2; 1 november: 2007: page 114-129.assesed on 19/01/16 at 7.20pm.

[103] Patel RP and Patel M. Cardiotonic activity of isolated cardiac glycoside from fruit of Linn. Int Res J Pharm 2013; 3(7): 239-242.

[104] Dhanalakshmi R and Manavalan R. In silico docking approach for antiathero-seclerosis of and admet prediction. Asian J Pharm Clin Res 2015; 8(2): 350-353.

[105] Al-Snafi AE. The constituents and pharmacology of *Corchorus aestuans*: A review. The Pharmaceutical and Chemical Journal 2016; 3(4):208-214

[106] Helen, A., Rajasree, C.R., Krishnakumar, K., Augusti, K.T., and Vijayammal, P.L.: Antioxidant role of oils isolated from garlic (Allium sativum Linn) and onion (Allium cepa Linn) on nicotine-induced lipid peroxidation. Vet. Hum. Toxicol., 41, 316–319, 1999.

[107] Karrer P and Banergee P. Corchortoxinm a cardiac agent from jute seeds. Helv Chim Acta 1949; 32:2385-2392.

[108] Negm S, EI-Shabrawy O, Arbid M and Radwan AS. Toxicological study of the different organs of *Corchorus olitorius* L. plant with special reference to their cardiac glycosides content. Zeitsc Ernaehrungsw 1980; 19(1): 28-32.

[109] Rao EV, Rao DV, Pavanaram SK, von Euw J and Reichstein T. Structure of Corchoroside β-Glycosides and aglycones. Helv Chim Acta 1971; 54(7): 1960-1968.

[110] Rao MR Liu TP and Meng ZJ. Comparative studies on the cardiotonic action of corchoroside A, ouabain and strophanthin K on the heart-lung preparation of guinea pig and cat. Yao Xue Xue Bao 1979; 14(5): 257-266.

[111] Patel DK, Desai SN, Gandhi HP, Devkar RV and Ramachandran AV. Cardio protective effect of *Coriandrum sativum* L. on isoproterenol induced myocardial necrosis in rats. Food Chem Toxicol 2012; 50(9):3120-3125.

[112] United States Dispensatory- 1918: 183-184. The Southwest School of Botanical Medicine

http://www.swsbm.com
[113] Agarwal, S.S. and Singh, V.K.: Immunomodulators: A re- view of studies on Indian medicinal plants and synthetic peptides. Part I: Medicinal Plants. Proc. Indian Natl. Sci. Acad. B., 65, 179–204, 1999.
[114] Slavík J, Zácková P, Michlová J, Opletal L and Sovová M. Phytotherapeutic aspects of diseases of the circulatory system. III. Cardiotonic and cardiotoxic effects of hyrcanoside and deglucohyrcanoside isolated from *Coronilla varia* L. Ceska Slov Farm 1994; 43(6):298-302.
[115] Zácková P, Sovová M, Horáková M and Opletalová V. Study of *Coronilla varia* L. III. Pharmacological evaluation of its effects on heart function. Cesk Farm 1982; 31(6):242-246.
[116] Gersl V. Effects of *Coronilla varia* Linné extract and lanatoside C in rabbits with experimental acute heart overloading *in vivo*. Sb Ved Pr Lek Fak Karlovy Univerzity Hradci Kralove 1980; 23(4): 445-457.
[117] Biletskyi I. Cardiac glycosides from *Coroilla varia*. Farm Zh 1964; 19: 22-25.
[118] Chahine N, Hanna J, Makhlouf H, Duca L, Martiny L and Chahine R. Protective effect of saffron extract against doxorubicin cardiotoxicity in isolated rabbit heart. Pharm Biol 2013; 51(12):1564-1571.
[119] Mehdizadeh R, Parizadeh MR, Khooei AR, Mehri S and Hosseinzadeh H. Cardioprotective effect of saffron extract and safranal in isoproterenol-induced myocardial infarction in wistar rats. Iran J Basic Med Sci 2013; 16(1): 56-63.
[120] Sachdeva J, Tanwar V, Golechha M, Siddiqui KM, Nag TC, Ray R, Kumari S and Arya DS. *Crocus sativus* L. (saffron) attenuates isoproterenol-induced myocardial injury via preserving cardiac functions and strengthening antioxidant defense system. Exp Toxicol Pathol 2012; 64(6): 557-564.
[121] Boskabady MH, Shafei MN, Shakiba A and Sefidi HS. Effect of aqueous-ethanol extract from *Crocus sativus* (saffron) on guinea-pig isolated heart. Phytother Res 2008; 22(3): 330-334.
[122] Garjani A, Afrooziyan A, Nazemiyeh H, Najafi M, Kharazmkia A and Maleki-Dizaji N. Protective effects of hydroalcoholic extract from rhizomes of *Cynodon dactylon* (L) Pers on compensated right heart failure in rats. BMC Complement Altern Med 2009; 9: 28-36.
[123] Shabi MM, Raj David C, Sasikala C, Gayathri K and Joseph J. Negative inotropic and chronotropic effects of phenolic fraction from *Cynodon dactylon* (Linn) on isolated perfused frog heart. Journal of Scientific Research 2012; 4(3): 657-663.
[124] Nagulendran KR, Mahesh R and Begum VH, Preventive role of *Cyperus rotundus* rhizomes extract on age associated changes in glucose and lipids, Pharmacologyonline 2007; 2: 318-325.
[125] Kasa JK, Singh TU, Parida S, Addison MP, Darzi SA, Choudhury S, Kandasamy K, Singh V, Dash JR, Shanker K and Mishra SK. Assessment of Indian Rosewood (Dalbergia sissoo) Standardized Leaf Extract on Isoproterenol-InducedMyocardial Injury in Rats. Cardiovasc Toxicol 2015;15(3):250-260.
[126] Bridget B. Kelly; Institute of Medicine; Fuster, Valentin (2010). Promoting Cardiovascular Health in the Developing World: A Critical Challenge to Achieve Global Health. Washington, D.C: National Academies Press. ISBN 0-309-14774-3.
[127] Muralidharan P, Balamurugan G and Kumar P. Inotropic and Cardioprotective Effects of *Daucus carota* Linn. on isoproterenol-induced myocardial infarction. Bangladesh Journal of Pharmacology 2008; 3: 74- 79.
[128] Whalen K, Finkel R and Panavelil TA. Lippincott illustrated reviews: pharmacology, 6th Ed. Wolters Kluwer 2015: 263-265.
[129] Kaplan JH. Biochemistry of Na, K- ATPase. Annu Rev Biochem 2002; 71: 511–535.
[130] Smith TW. The fundamental mechanism of inotropic action of digitalis. Therapie 1989; 44: 431-435.
[131] Jorgensen PL, Hakansson KO and Karlish SJ. Structure and mechanism of Na, K-ATPase: functional sites and their interactions. Annu Rev Physiol 2003; 65: 817–849.
[132] Mason DT and Braunwald E. Studies on digitalis, X: effects of ouabain on forearm vascular resistance and venous tone in normal subjects and in patients in heart failure. J Clin Invest 1964; 43:532–543.
[133] Hauptman PJ and Kelly RA. Cardiovascular drugs, Digitalis. *Circulation* 1999; 99: 1265-1270.
[134] Sharma P C, Yelne M B, Dennis T. J., Data base of medicinal plants used in Ayurveda; vol III; New Delhi, Central Council for Research in Ayurveda and Siddha; Reprint 2005; pg- 230-233.
[135] Billore K V, Yelne M B, Dennis T. J., Chaudhari B.G. Data base of medicinal plants used in Ayurveda; vol VI; New Delhi, Central

Council for Research in Ayurveda and Siddha; Reprint 2005; pg- 157-159.
[136] Infra specific taxon details: Ephedra alata subsp alenda (Stapf) Trab., urn:lsid:catalogue oflife.org:taxon:9704b927-e478-11e5-86e7-bc764e092680:col20160426 [28 April 2016].
[137] Abula T, Rao SA, Mengistu A, Worku S, Legesse E and Aberra M. Pharmacology. University of Gondar 2004: 46.
[138] Devasagayam, T.P.A. and Sainis, K.B.: Immune system and antioxidants, especially those derived from Indian medicinal plants. Indian J. Expt. Biol., 40, 639–655, 2001.
[139] Devasagayam, T.P.A., Tilak, J.C., Boloor, K.K., Sane, K.S., Ghaskadbi, S., and Lele, R.D.: Free radicals and antioxidants in human health: current status and future prospects. J. Asso. Physi. India, Oct., 794–804, 2004.
[140] Lis-Balchina MT and Hartb SL. A Pharmacological appraisal of the folk medicinal usage of *Pelargonium grossularioides* and *Erodium cicutarium*. Journal of Herbs, Spices & Medicinal Plants1994; 2(3): 41-48.
[141] Lis-Balchina M and Guittonneaub GG. Preliminary investigations on the presence of alkaloids in the genus Erodium L'Her. (Geraniaceae). Acta Botanica Gallica: Botany Letters 1995; 142(1): 31-35.
[142] Al-Snafi AE. A review on *Erodium cicutarium*: A potential medicinal plant. Indo Am J P Sci 2017; 4(01): 110-116.
[1] Ong, A.S.H. and Packer, L.: *Lipid-soluble Antioxidants: Biochemistry and Clinical Applications*. Basel: Birkhauser Verlag, 1992.
[143] Rauwald HW, Brehm H and Odenthal KP. The involvement of Ca^{2+} channel blocking mode of action in the pharmacology of Ammi visnaga fruits. Planta Medica 1994; 60: 101-105.
[144] Kong D, Zhang WZ, XiaoL and Yuan D. Safflower yellow injection combined with conventional therapy in treating unstable angina pectoris: a meta-analysis. Journal of Traditional Chinese Medicine 2013; 33(5): 553-561.
[145] Balbaa SI, Zaki AY, Abdel-Wahab SM, El-Denshary ESM and Motazz-Bellah M. Preliminary phytochemical and pharmacological investigations of the roots of different varieties of *Cichorium intybus*. Planta Med 1973; 24(6): 133-144.
[146] Boskabady MH, Shafei MN, Shakiba A and Sefidi HS. Effect of aqueous-ethanol extract from *Crocus sativus*(saffron) on guinea-pig isolated heart. Iranian Congress of Physiology and Pharmacology 2007,18, http://en.seminars.sid.ir/ViewPaper.aspx?ID=760
[147] Joukar S . Electrocardiogram alterations following one- week consumption of *Crocus sativus* L.(Saffron). EXCLI Journal 2012; 11: 480-486.
[148] Najafi M, Nazemiyeh H, Ghavimi H, Gharakhani A and Garjani A. Effects of hydroalcoholic extract of *Cynodon dactylon* (L) pers on ischemia/reperfusion-induced arrhythmias. DARU 2008; 16 (4): 233-238.
[149] Jain RC. Effect of garlic on serum lipids, coagulability and fibrinolytic activity of blood. Am J Clin Nutr 1977; 30: 1380-1381.
[150] Bordia A, Verma SK, Vyas AK *et al.* Effect of essential oil of onion and garlic on experimental atherosclerosis in rabbits. Atherosclerosis 1997; 26: 379-386.
[151] Chang ML W, Johnson MA. Effect of garlic on carbohydrate metabolism and lipid synthesis in rats. J Nutr 1980; 110: 931-936.
[152] Kamanna VS, Chandrasekhara N. Hypocholesteromic activity of different fractions of garlic. Ind J Medical Res 1984; 79: 580-583.
[153] Mand JK, Gupta PP, Soni GL *et al.* Effect of garlic on experimental atherosclerosis in rabbits. Ind Heart J 1985; 37: 183-188.
[154] Betz E, and Weidler R. Die Wirkung von Knoblauchextrakt auf die atheerogenese bei kaninchen. In: Betz E, editor. Die anwendung aktueller methoden in der arteriosklerose. Forschung 1989: 304-311.
[155] Rajasree CR, Rajmohan T and Agusti KT. Biochemical effects of garlic on lipid metabolism in alcohol fed rats. Ind J Exp Biol 1999; 37: 243-247.
[156] Mathew BC and Daniel RS. Hypolipidemic effect of garlic protein substituted for caseinin diet of rats compared to those of garlic oil. Ind J Exp Biol 1996; 34: 337-340.
[157] Qureshi AA, Din ZZ, Abuirameileh N *et al.* Suppression of avian hepatic lipid metabolism by solvent extracts of garlic: impact on serum lipids. J Nutr 1983; 113: 1746-1755.
[158] Kamanna VS and Chandrasekhara N. Effect of garlic on serum lipoproteins cholesterol levels in albino rats rendered hypercholesteremic by feeding cholesterol. Lipids 1982; 17: 483-488.
[159] Chi MS. Effect of garlic products on lipid metabolism in cholesterol-fed rats. Proc Soc Exp Biol Med 1982; 171: 174-178.
[160] Chi MS, Koh ET and Stewart TJ. Effect of garlic on lipid metabolism in rats fed cholesterol or lard. J Nutr 1982; 112: 241-248.
[161] Gebhardt R. Multiple inhibitory effects of

garlic extracts on cholesterol biosynthesis in hepatocytes. Lipids 1993; 28: 613-619.
[162] Saxena KK, Gupta B, Kulshreshtha VK *et al.* Effect of garlic treatment on isoprenaline-induced myocordial necrosis in albino rats. Indian J Physiol Pharmacol 1980; 24: 233-236.
[163] Bordia A. Effect of garlic and blood lipids in patients with coronary heart disease. Am J Clin Nutr 1981; 34: 2100-2103.
[164] Kojuri J, Vosoughi AR and Akrami M. Effects of *Anethum graveolens* and garlic on lipid profile in hyperlipidemic patients. Lipids Health Dis 2007; 6: 5.
[165] Sainani GS, Desai DB, Gorhe NH *et al.* Effect of dietary garlic and onion on serum lipid profile in jain community. Indian J Med Res 1979; 69: 776-780.
[166] Kiesewetter H, Jung F, Jung EM *et al*. Effects of garlic coated tablets in peripheral arterial occlusive disease. Clin Investig 1993; 71: 383-386.
[167] Siegel G, Walter A, Engel S *et al.* Pleiotropic effects of garlic. Wien Med Wochenschr 1999; 149: 217- 224.
[168] Bhushan S, Sharma SP, Singh SP *et al.* Study of the hypocholesterolemic effect of onion (*Allium cepa*) on normal human beings. Indian Med Gaz 1979; 16: 249-251.
[169] Kim K, Kim H, Kwon J, Lee S, Kong H, Im SA, Lee YH, Lee YR, Oh ST, Jo T H, Park YI, Lee CK and Kim K. Hypoglycemic and hypolipidemic effects of processed *Aloe vera* gel in a mouse model of noninsulin- dependent diabetes mellitus. Phytomedicine 2009; 16(9): 856-863.
[170] Lusis, A.J.: Atherosclerosis. Nature, 407, 233–241, 2000.Stocker, R.: The ambivalence of vitamin E in atherogenesis.Trends Biochem. Sci., 24, 219–223, 1999.
[171] Agarwal OP. Prevention of atheromatous heart disease. Angiolog1985; 36(8). Presented at the 31st Annual Meeting, American College of Angiology and 26th Annual Meeting, International College of Angiology 1984.
[172] Al-Snafi AE. The pharmacological activities of *Alpinia galangal* - A review. International Journal for Pharmaceutical Research Scholars 2014; 3(1-1): 607-614.
[173] Achuthan CR and Padikkala J. Hypolipidemic effect of *Alpinia galangal* (Rasna) and *Kaempferia galangal* Kachoori). Indian J Clin Biochem 1997; 12(1): 55-58.
[174] Jantan I, Rafi AA, and Jali J. Platelet-activating factor (PAF) receptor-binding antagonist activity of Malaysian medicinal plants. Phytomedicine 2005; 12(6): 88-92.
[175] Harvengt C and Desager J P. HDL-cholesterol increase in normolipaemic subjects on khellin: a pilot study. International Journal of Clinical Pharmacology Research 1983; 3: 363-366.
[176] Yazdanparast R and Bahramikia S. Improvement of liver antioxidant status in hyper- cholesterolamic rats treated with *A. graveolens* extracts. Pharmacologyonline 2007; 3: 88-94.
[177] Yazdanparast R and Alavi M. Antihyperlipidaemic and anti-hypercholesterolaemic effects of *Anethum graveolens* leaves after the removal of furocoumarins. Cytobios 2001; 105: 185-191.
[178] Yazdanparast R., and Bahramikia S. Evaluation of the effect of *Anethum graveolens* L. crude extracts on serum lipids and lipoproteins profiles in hypercholesterolaemic rats. DARU 2008; 16(2): 88-94.
[179] Al-Snafi AE. The pharmacological importance of *Anethum graveolens*- A review. International Journal of Pharmacy and Pharmaceutical Sciences 2014; 6(4): 11-13.
[180] Tsi D, Das NP and Tan BK. Effects of celery (*A. graveolens*) extract on lipid parameters of rats fed a high fat diet. Planta Med 1995; 6: 18-21.
[181] Tsi D and Tan BK. Effects of celery extract and 3-N-butylphthalide on lipid levels in genetically hypercholesterolaemic (RICO) rats. Clin Exp Pharmacol Physiol 1996; 23(3): 214-217.
[182] Tsi D and Tsi BKH. The mechanism underlying the hypocholesterolemic activity of aqueous celery extract, its butanol and aqueous fractions in genetically hypocholesterolemic rats. J Life Sci 2000; 66: 755-767.
[183] Kamal M, Adel MA, Ahmad D and Talal A. Hypolipidemic effects of seed extract of celery (*Apium graveolens*) in rats. Phcog Mag 2009; 5: 301-305.
[184] Le QT and Elliott WJ. Dose response relationship of blood pressure and serum cholesterol to 3-n- butylphthalide, a component of celery oil. Clin Res 1991; 39: 750A.
[185] Ahmed, QS, and Sayedda K . Effect of celery (*Apium graveolens*) seeds extract on protease inhibitor (Ritonavir) induced dyslipidemia. NJIRM 2012; 3(1): 52-56.
[186] Bansode RR, Randolph P, Hurley S, and Ahmedna M. Evaluation of hypolipidemic effects of peanut skin-derived polyphenols in rats on Western-diet. Food Chem 2012; 135(3): 1659-1666.
[187] Packer, L. and Ong, A.S.H.: Biological

Oxidants and Anti- oxidants: Molecular Mechanisms and Health Effects. Cham- paign: AOCS Press, 1998.

[188] Tamura T, Inoue N, Shimizu-Ibuka A, Tadaishi M, Takita T, Arai S, and Mura K. Serum cholesterol reduction by feeding a high-cholesterol diet containing a lower-molecular-weight polyphenol fraction from peanut skin. Biosci Biotechnol Biochem 2012; 76(4): 834-837.

[189] Emekli-Alturfan E, Kasikci E and Yarat, A. Peanut (*Arachis hypogaea*) consumption improves Glutathione and HDL-cholesterol levels in experimental diabetes. Phytotherapy Research 2008; 22(2): 180-184.

[190] Sobolev VS, Khan SI, Tabanca N, Wedge DE, Manly SP, Cutler SJ, Coy MR, Becnel JJ, Neff SA and Gloer JB. Biological Activity of Peanut (*Arachis hypogaea*) Phytoalexins and selected natural and synthetic stilbenoids. J Agric Food Chem 2011; 59: 1673–1682.

[191] Lappano R, Rosano C, Madeo A, Albanito L, Plastina P, Gabriele B, Forti L, Stivala LA, Iacopetta D, Dolce V, Ando S, Pezzi V and Maggiolini M. Structure-activity relationships of resveratrol and derivatives in breast cancer cells. Mol Nutr Food Res 2009; 53: 845– 858.

[192] Zhu X, Zhang W, Pang X, Wang J, Zhao J and Qu W. Hypolipidemic Effect of *n*-Butanol Extract from
Asparagus officinalis L. in mice fed a high-fat diet. Phytother Res 2011; 25(8): 1119-1124.

[193] Zhu X, Zhang W, Zhao J, Wang J and Qu W. Hypolipidaemic and hepatoprotective effects of ethanolic and aqueous extracts from *Asparagus officinalis Asparagus officinalis* L. by products in mice fed a high- fat diet. Journal of the Science of Food and Agriculture 2010; 90(7):1129-1135.

[194] Archana, P., Tandan, S.K., Chandra, S., and Lal, J.: Anti-pyretic and analgesic activities of Caesalpinia bonducella seed kernel extract. Phytother. Res., 19, 376–381, 2005.

[195] Saltzman E, Das S K and Lichtenstein A H. An oat-containing hypocaloric diet reduces systolic blood pressure and improves lipid profile beyond effects of weight loss in men and women. J Nutr 2001; 131: 1465–1470.

[196] Manonmani, G., Bhavapriya, V., Kalpana, S., Govindasamy, S., and Apparanantham, T.: Antioxidant activity of Cassia fistula (Linn.) flowers in alloxan induced diabetic rats. J. Ethnopharmacol., 97, 39–42, 2005.

[197] Sobotka W, Flis M, Antoszkiewicz Z, Lipiński K and Zduńczyk Z. Effect of oat by-product antioxidants and vitamin E on the oxidative stability of pork from pigs fed diets supplemented with linseed oil. Arch Anim Nutr 2012; 66(1): 27-38.

[198] Lin N, Li Y, Tang L, Shi J and Chen Y. In vivo effect of oat cereal β-glucan on metabolic indexes and satiety-related hormones in diet-induced obesity C57-Bl mice. Mol Nutr Food Res 2013; 57(7): 1291- 1294.

[199] El Khoury D, Cuda C, Luhovyy BL, and Anderson GH. Beta glucan: health benefits in obesity and metabolic syndrome. Journal of Nutrition and Metabolism 2012; Article ID 851362,
http://dx.doi.org/10.1155/2012/851362

[200] Chang HC, Huang CN, Yeh DM, Wang SJ, Peng CH and Wang CJ. Oat prevents obesity and abdominal fat distribution, and improves liver function in humans. Plant Foods Hum Nutr 2013; 68(1): 18-23.

[201] Thongoun P, Pavadhgul P, Bumrungpert A, Satitvipawee P, Harjani Y and Kurilich A. Effect of oat consumption on lipid profiles in hypercholesterolemic adults. J Med Assoc Thai 2013; 96 (5): S25-S32.

[202] Reddy MV, Reddy MK, Gunasekar D, Caux C and Bodo B. A flavanone and a dihydro dibenzoxepin from *Bauhinia variegata*. Phytochemistry 2003; 64: 879-882.

[203] Subramanian, M., Sreejayan, N., Rao, M.N.A., Devasagayam,

[204] T.P.A., and Singh, B.B.: Diminution of singlet oxygen in- duced DNA damage by curcumin and related antioxidants. Mutat. Res., 311, 249–255, 1994.

[205] Kumar D, Parcha V, Maithani A and Dhulia I. Effect and evaluation of antihyperlipidemic activity of fractions of total methanol extract of *Bauhinia variegata (Linn.)* leaves on Triton WR-1339 (Tyloxapol) induced hyperlipidemic rats. Int J Res Pharm Sci 2011; 2(4): 493-497.

[206] Balamurugan G and Muralidharan P. Antiobesity effect of *Bauhinia variegata* bark extract on female rats fed on hypercaloric diet. Bangladesh J Pharmacol 2010; 5: 8-12.

[207] Morikawa T, Li X, Nishida E, Nakamura S, Ninomiya K, Matsuda H, Ody Y, Muraoka O and Yoshikawa M. Perennisosides I-VII, acylated triterpene saponins with antihyperlipidemic activities from the flowers of *Bellis perennis.* J Nat Prod 2008; 71: 828-835.

[208] Morikawa T, Muraoka O and Yoshikawa M. Pharmaceutical food science: search for anti-obese constituents from medicinal foods-anti-hyperlipidemic saponin constituents from the flowers of *Bellis perennis*. Yakugaku Zasshi

2010; 130(5): 673-678.
[209] Harrison, D., Griendling, K.K., Landmesser, U., Hornig, B., and Drexler, H.: Role of oxidative stress in atherosclerosis. Am. J. Cardiol., 91, 7A–11A, 2003.
[210] Amirthaveni M and Priya V. Hypoglycemic and hypolipidemic effect of ash gourd (*Benincasa hispida)*
and curry leaves (*Murraya koenigii*). International Journal of Current Research 2011; 3(8): 37-42.
[211] Shanmugasundaram, K.R., Srinivas, K., Sundaram, P., Satyaraj, D., Muthu, R., Padma, P., Maheswari, R.U., Veeraraghavan, V., Sharada, V., and Amudha, B.: Lipid peroxidation, antioxidant defenses and rod-cell membrane changes in relation to coronary risk index and symptomatic coronary heart disease. J. Cardiovasc. Risk, 2, 551–561, 1996.
[212] Mirzaie H, Johari H, Najafian M and Kargar H. Effect of ethanol extract of root turnip (*Brassica rapa*) on changes in blood factors HDL, LDL, triglycerides and total cholesterol in hypercholesterolemic rabbits. Advances in Environmental Biology 2012; 6(10): 2796-2801.
[213] Bang MH, Lee DY, Oh YJ, Han MW, Yang HJ, Chung HG, Jeong TS, Lee KT, Choi MS and Baek NI. Development of biologically active compounds from edible plant sources XXII. Isolation of indoles from the roots of *Brassica campestris* ssp *rapa* and their hACAT inhibitory activity. J Korean Soc Appl Biol Chem 2008; 51(1): 65-69.
[214] An S, Han JI, Kim MJ, Park JS, Han JM, Baek NI, Chung HG, Choi MS, Lee KT and Jeong TS. Ethanolic extracts of *Brassica campestris* spp. rapa roots prevent high-fat diet-induced obesity via beta3- adrenergic regulation of white adipocyte lipolytic activity. J Med Food 2010; 13(2): 406-414.
[215] Gupta M, Mazumder UK, Sambath KR, Thangavel S, and Vamsi M L M. Antitumor activity and antioxidant status of *Caesalpinia bonducella* against Ehrlich ascites carcinoma in Swiss albino mice. J Pharmacol Sci 2004; 94: 177-184.
[216] Bhaskar VH and Ajay SS. Antihyperglycemic and antihyperlipidaemic activities of root extracts of *Calotropis procera* (Ait.) R.Br on streptozotocin. Jordan Journal of Biological Sciences 2009; 2(4): 177- 180.
[217] Lekhmici A, Benzidane N, Imane K, Noureddine C, Seddik K, and Abderrahmane B. Comparison between Polyphenol contents and antioxidant activities of different parts of *Capparis spinosa* L. The 3rd International Symposium on the Medicinal Plants, Their Cultuvation and Aspects of uses, Beit Zaman Hotel & Resort, Petra, 2012.
[218] Dwivedi, S. and Agarwal, P.: Antianginal and cardioprotec-tive effects of Terminalia arjuna, an indigenous drug, in coro- nary artery disease. J. Assoc. Physicians India, 42, 287–289, 1994.
[219] Baek J, Lee J, Kim K, Kim T, Kim D, Kim C, Tsutomu K, Ochir S, Lee K, Ho Park C, Lee Y and Choe
M. Inhibitory effects of *Capsicum annuum* L. water extracts on lipoprotein lipase activity in 3T3-L1 cells. Nutrition Research and Practice 2013; 7(2): 96-102.
[220] Ahmed, R.S., Seth, V., and Banerjee, B.D.: Influence of dietary ginger (Zingiber officinalis Rosc) on antioxidant de- fense system in rat: Comparison with ascorbic acid. Indian J. Exp. Biol., 38, 604–606, 1997.
[221] Saghir MR, Sadiq S, Nayak S and Tahir MU. Hypolipidemic effect of aqueous extract of *Carum carvi*
(black Zeera) seeds in diet induced hyperlipidemic rats. Pak J Pharm Sci 2012; 25(2): 333-337.
[222] Alam, M.I. and Gomes, A.: Viper venom-induced inflamma- tion and inhibition of free radical formation by pure com- pound (2-hydroxy-4-methoxy benzoic acid) isolated and pu- rified from anantamul (Hemidesmus indicus R. BR) root ex- tract. Toxicon., 36, 207–215, 1998.
[223] Haidari F, Seyed-Sadjadi N, Taha-Jalali M and Mohammed-Shahi M. The effect of oral administration of *Carum carvi* on weight, serum glucose, and lipid profile in streptozotocin-induced diabetic rats. Saudi Med J 2011; 32(7): 695-700.
[224] Lemhadri A, Hajji L, Michel JB and Eddouks M. Cholesterol and triglycerides lowering activities of caraway fruits in normal and streptozotocin diabetic rats. J Ethnopharmacol 2006; 106(3): 321-326.
[225] Arpornsuwan T, Changsri K, Roytrakul S and Punjanon T. The effects of the extracts from *Carthamus tinctorius* L. on gene expression related to cholesterol metabolism in rats. Songklanakarin J Sci Technol 2010; 32(2): 129-136.
[226] Gupta, R., Singhal, S., Goyle, A., and Sharma, V.N.: Antiox- idant and hypocholesterolemic effects of Terminalia arjuna tree bark powder: a randomized placebo-controlled trial. J. Asso. Physicians India, 49, 231–235, 2001.
[227] Katsuda S, Suzuki K, Koyama N, Takahashi M, Miyake M, Hazama A and Takazawa K.

Safflower seed polyphenols (N-(p-coumaroyl)serotonin and N-feruloylserotonin) ameliorate atherosclerosis and distensibility of the aortic wall in Kurosawa and Kusanagi-hypercholesterolemic (KHC) rabbits. Hypertens Res 2009; 32(11): 944-949.

[228] Sunday AG, Ifeanyi OE and Eucharia UC. The effects of casuarina bark on lipid profile and random blood sugar level in albino rats. Journal of Dental and Medical Sciences 2014; 13(4): 11-15.

[229] Gupta, S.K., Sharma, M., Kishore, K., and Arya, D.S.: Ocimum sanctum provides cardiac protection in isoproterenol induced myocardial infirction in rats. J. Mol. Cell. Cardiol., 33, A42, 2001Sriram N. Antidiabetic and antihyperlipidemic activity of bark of *Casuarina equisetifolia* on streptozocin induced diabetic rats. International Journal of Pharmacy Review and Research 2011; 1(1): 4-8.

[230] Shimoda H, Tanaka J, Takahara Y, Takemoto K, Shan SJ and Su MH. The hypocholesterolemic effects of *Cistanche tubulosa* extract, a Chinese traditional crude medicine, in mice. Am J Chin Med 2009; 37(6): 1125-1138.

[231] Rahbar AR and Nabipour I. The hypolipidemic effect of *Citrullus colocynthis* on patients with hyperlipidemia. Pak J Biol Sci 2010; 13(24):1202-1207.

[232] Gao, D., Tawa, R., Masaki, H., Okano, Y., and Sakurai, H.:Protective effects of baicalein against cell damage by reac- tive oxygen species. Chem. Pharm. Bull. Tokyo, 46, 1383–1387, 1998.

[233] Yaghmaie P, Parivar K and Haftsavar M. Effects of *Citrus aurantifolia* peel essential oil on serum cholesterol levels in Wistar rats. Journal of Paramedical Sciences (JPS) 2011; 2(1):29-32.

[234] Akinboyewa OM. Effect of *Citrus aurantifolia* on hepatic lipidomics in female albino rats. BSc thesis, Department of Biochemistry, College of Natural Sciences, Federal University of Agriculture, Abeokuta 2012.

[235] Hiramitsu M, Shimada Y, Kuroyanagi J, Inoue T, Katagiri T, Zang L, Nishimura Y, Nishimura N and Tanaka T. Eriocitrin ameliorates diet-induced hepatic steatosis with activation of mitochondrial biogenesis. Sci Rep 2014; 4: 3708.

[236] Menichini F, Tundis R, Loizzo MR, Bonesi M, Liu B, Jones P, Persaud SJ, Mastellone V, Lombardi P, Houghton PJ, Avallone L and Menichini F. *C. medica* cv Diamante peel chemical composition and influence on glucose homeostasis and metabolic parameters. Food Chemistry 2011; 124(3): 1083-1089.

[237] Solanki YB and Jain SM. Antihyperlipidemic activity of *Clitoria ternatea* and *Vigna mungo* in rats. Pharmaceutical Biology 2010; 48(8): 915-923.

[238] Shieh, D.E., Liu, L.T., and Lin, C.C.: Antioxidant and free radical scavenging effects of baicalein, baicalin and wogo- nin. Anticancer Res., 20, 2861–2866, 2000.

[239] Kousar S, Jahan N, Khalil-ur-Rehman and Nosheen S. Antilipidemic activity of *Coriandrum sativum.*
Bioscience Research 2011; 8(1): 8-14.

[240] Joshi SC, Sharma N and Sharma P. Antioxidant and lipid lowering effect of *Coriandrum sativum* in cholesterol fed rabbits. Int J Pharm Pharm Sci 2012; 4(3):231-234.

[241] Dhanapakiam P, Joseph JM, Ramaswamy VK, Moorthi M and Kumar AS. Coriandor seeds have a cholesterol-lowering action. J Environ Biol 2008; 29(1):53-56.

[242] Chithra V and Leelamma S. Hypolipidemic effect of coriander seeds (*Coriandrum sativum*): mechanism of action. Plant Foods Hum Nutr 1997; 51(2):167-172.

[243] Sheng L, Qian Z, Zheng S and Xi L. Mechanism of hypolipidemic effect of crocin in rats: crocin inhibits pancreatic lipase. Eur J Pharmacol 2006; 543: 116-122.

[244] Zheng S, Qian Z, Tang F and Sheng L. Suppression of vascular cell adhesion molecule-1 expression by crocetin contributes to attenuation of atherosclerosis in hypercholesterolemic rabbits. Biochem Pharmacol 2005; 70: 1192-1199.

[245] Gainer JW and Chisolm GM. Oxygen diffusion and atherosclerosis. Atherosclerosis 1974; 19:135-138.

[246] He S, Qian Z, Tang F, Wen N, Xu G and Sheng L. Effect of crocin on experimental atherosclerosis in quails and its mechanisms. Life Sciences 2005; 77: 907–921.

[247] Verma SK and Bordia A. Antioxidant property of saffron in man. Indian J Med Sci 1998; 52: 205-207.

[248] Gout B, Bourges C and Paineau-Dubreuil S. Satiereal, a *Crocus sativus* L extract, reduces snacking and increases satiety in a randomizedplacebo-controlled study of mildly overweight, healthy women. Nutr Res 2010; 30(5): 305-313.

[249] Kumar DS, David B, Harani A and Vijay B. Role of an ethanolic extract of *Crotalaria*

juncea L. on high- fat diet-induced hypercholesterolemia. Sci Pharm 2014; 82(2): 393-409.

[250] Al-Snafi AE. The contents and pharmacology of *Crotalaria juncea*- A review. IOSR Journal of Pharmacy 2016; 6(6): 77-86.

[251] Harikumar K, Niveditha B, Kumar MRB, Monica K and Gajendra B. Anti-hyperlipidemic activity of alcoholic and methanolic extracts of *Crotolaria juncea* in Triton-WR 1339 induced hyperlipidemia. International Journal of Phytopharmacology 2012; 3(3): 256-262.

[252] Prasad J, Singh VK, Shrivastava A, Chaturvedi U, Bhatia G, Arya KR, Awasthi SK and Narender T. Antidyslipidemic and antioxidant activity of an unusual amino acid (2-amino-5-hydroxyhexanoic acid) isolated from the seeds of *Crotalaria juncea*. Phytomedicine 2013; 21(1):15-19.

[253] Sreedhar KS. Evaluation of Anti-obesity activities of *Crotalaria juncea* L. in albino rats. MSc thesis, Gautham College of Pharmacy 2011.

[254] Shirke SS and Jagtap AJ. Effects of methanolic extract of *Cuminum cyminum* on total serum cholesterol in ovariectomized rats. Indian J Pharmacol 2009; 41(2): 91-93.

[255] Bharani A., Ganguli, A., Mathur, L.K., Jamra, Y., and Raman, P.G.: Efficacy of Terminalia arjuna in chronic stable angina: a double-blind, placebo-controlled, crossover study comparing Terminalia arjuna with isosorbide mononitrate. Indian Heart J. 54: 170–175, 2002.

[256] Zare R, Heshmati F, Fallahzadeh H and Nadjarzadeh A. Effect of cumin powder on body composition and lipid profile in overweight and obese women. Complement Ther Clin Pract 2014; 20(4): 297-301.

[257] Samani KG and Farrokhi E. Effects of cumin extract on oxLDL, paraoxanase 1 activity, FBS, total cholesterol, triglycerides, HDL-C, LDL-C, Apo A1, and Apo B in in the patients with hypercholesterolemia. Int J Health Sci (Qassim) 2014; 8(1):39-43.

[258] Taghizadeh M, Memarzadeh MR, Asemi Z and Esmaillzadeh A. Effect of the *Cuminum cyminum* L intake on weight loss, metabolic profiles and biomarkers of oxidative stress in overweight subjects: A randomized double-blind placebo-controlled clinical trial. Ann Nutr Metab 2015; 66(2-3):117-124.

A. Karkabo unas S, Kiortsis DN, Zelovitis J, Skafida P, Demetzos C, Malamas M, Elisaf M and Evangelou Effects of *Cupressus sempervirens* cone extract on lipid parameters in Wistar rats. *In Vivo* 2003;17(1):101-103.

[259] Manikandan, P., Sumitra, M., Aishwarya, S., Murali Manohar, B., Lokanadam, B., and Puvanakrishnan, R.: Cur- cumin modulates free radical quenching in myocardial is-chaemia in rats. Int. J. Biochem. Cell Biol., 36, 1967–1980, Abliz A, Aji Q, Abdusalam E, Sun X, Abdurahman A, Zhou W, Moore N and Umar A. Effect of *Cydonia oblonga* Mill leaf extract on serum lipids and liver function in a rat model of hyperlipidaemia. J Ethnopharmaco 2014; 151(2): 970-944.

[260] Karthikeyan, K., Sarala Bai, B.R., Gauthaman, K., Sathish, K.S., and Niranjali Devaraj, S.: Cardioprotective effect of the alcoholic extract of Terminalia arjuna bark in an in vivo model of myocardial ischemic reperfusion injury. Life Sci., 73, 2727–2739, 2003.

[261] Khademi F. The efficay of quince leave extract on atherosclerotic plaques induced by atherogenic diet in coronary and aorta, hyperlipidemia and liver in rabbit. MSc thesis, Tabriz University of Medical Sciences, Tabriz, Iran 2009.

[262] Chandratre RS, Chandarana S and Mengi SA. Lipid lowering activity of alcoholic extract of *Cyperus rotundus.* IJRPC 2011; 1(4): 1042-1045.

[263] Lemaure B, Touché A, Zbinden I, Moulin J, Courtois D, Macé K and Darimont C. Administration of *Cyperus rotundus* tubers extract prevents weight gain in obese Zucker rats. Phytother Res 2007; 21: 724- 730.

[264] Poudyal H, Panchal S and Brown L. Comparison of purple carrot Juice and β-carotene in a high- carbohydrate, high-fat diet-fed rat model of the metabolic syndrome. British Journal of Nutrition 2010; 104: 1322-1332.

[265] Nicolle C, Cardinault N, Aprikian O, Busserolles J, Grolier P, Rock E, Demigné C, Mazur A, Scalbert A, Amouroux P and Rémésy C. Effect of carrot intake on cholesterol metabolism and on antioxidant status in cholesterol-fed rat. European Journal of Nutrition 2003; 42: 254-261.

[266] Ramakrishna V, Rani PJ and Rao PR. Hypocholesterolemic effect of diet supplemented with Indian bean (Dolichos lablab L. var lignosus) seeds. Nutrition & Food Science 2007; 37(6): 452- 456.

[267] Oszmianski, J. and Lee, C.Y.: Isolation and HPLC determina-tion of phenolic compounds in red grapes. Am. J. Enol. Vitic.,39, 259–262, 1990.

[268] Pavani M, Ramadurg B and Varshitha C. Anti-

obesity activities of hydroalcoholic extract of *Echinochloa crusgalli* (L.) P. Beauv grains in albino rats. Research Journal of Pharmacology and Pharmacodynamics 2014; 6(1): 13-20.

[269] Deby-Dupont, G., Mouithys-Mickalad, A., Serteyn, D.,Lamy, M., and Deby, C.: Resveratrol and curcumin reduce the respiratory burst of Chlamydia-primed THP-1 cells. Bio- chem. Biophys. Res. Comm., 333, 21–27, 2005.

[270] Al-Awwadi NAJ. Effects of *Achillea Santolina* extracts and fractions on human platelet aggregation *in vitro* and on rat arteriovenous shunt thrombosis *in vivo*. Thi-Qar Medical Journal 2010; 4(3): 131-141.

[271] Breu W, Dorsch W. *Allium cepa* L. (Onion): Chemistry, analysis and pharmacology. In: Wagner H, Farnsworth NR, eds. Economic and medicinal plants research 1994; 6: 115-147.

[272] Srivastava KC. Aqueous extracts of onion, garlic and ginger inhibit platelet aggregation and alter arachidonic acid metabolism. Biomedica biochimica acta 1984; 43: S335-S346.

[273] Chauhan LS *et al.* Effect of onion, garlic and clofibrate on coagulation and fibrinolytic activity of blood in cholesterol fed rabbits. Indian Medical Journal 1982; 76: 126-127.

[274] Augusti KT. Therapeutic values of onion (*Allium cepa* L.) and garlic (*Allium sativum* L.). Indian J Exp Biol 1996; 34(7):634-640.

[275] Makheja AN, Vanderhoek JY, Bailey JM. Inhibition of platelet aggregation and thromboxane synthesis by onion and garlic. Lancet 1979; 1: 781.

[276] Ariga T and Oshiba S. Effects of the essential oil components of garlic cloves on rabbit platelet aggregation. Igaku to seibutsugak 1981; 102: 169-174.

[277] Vanderhoek JY, Makheja AN and Bailey JM. Inhibition of fatty acid oxygenases by onion and garlic oils. Evidence for the mechanism by which these oils inhibit platelet aggregation. Biochemical Pharmacology 1980; 29: 3169-3173.

[278] Dorsch W, Ettl M, Hein G *et al.* Anti-asthmatic effects of onions: Inhibition of platelet-activating factor- induced bronchial construction by onion oils. Int Arch Allergy Appl Immunol 1987; 82: 535–536.

[279] Dorsch W, Wagner H, Bayer T *et al.* Antiasthmatic effects of onions: Alk(en)ylsulfinothic acid alk(en)ylesters inhibit histamine release, leukotriene and thromboxane biosynthesis in vitro and counteract PAF- and allergen-induced bronchial obstruction *in vivo*. Biochem Pharmacol 1987; 37: 4479–4485.

[280] Ross I A. Medicinal Plants of the world: Chemical Constituents, Traditional and Modern Medicinal Uses, Humana Press, Totowa 2001.

[281] Mohammad SF and Woodward SC. Characterization of a potent inhibitor of platelet aggregation and release reaction isolated from *Allium sativum* (garlic). Thromb Res 1986; 44: 793-796.

[282] Mohammad SF, Brown S, Chuang HYK *et al.* Isolation, characterization, identification and synthesis of an inhibitor of platelet function from *Allium sativum*. Fed Proc 1980; 39: 543A.

[283] Srivastava KC and Justesen U. Isolation and effect of some garlic components on platelet aggregation and metabolism of arachidonic acid in human blood platelets. Wien Klin Wochenschr 1989; 8: 293-299.

[284] Makheja AN and Bailey JM. Antiplatelet constituents of garlic and onion. Agents and actions 1990; 29: 360-363.

[285] WHO monographs on selected medicinal plants, WHO Library Cataloguing in Publication Data, 2007.

[286] Srivastava KC. Effect of aqueous extract of onion, garlic and ginger on platelet aggregation and metabolism of arachidonic acid in blood vascular system: *in vitro* study. Prostaglandins Leukot Med 1984; 13: 227-235.

[287] Kiesewetter H, Jung F, Wolf S *et al.* Effect of garlic on thrombocyte aggregation, microcirculation, and other risk factors. International Journal of Clinical pharmacology 1981; 29: 151-155.

[288] Bordia AK, Joshi HK, Sanadhya YK and Bhu N. Effect of essential oil of garlic on serum fibrinolytic activity in patients with coronary heart disease. Atherosclerosis 1977; 28: 155-159.

[289] Harenberg J, Giese C, and Zimmermann R. Effect of dried garlic on blood coagulation, fibrinolysis, platelet aggregation and serum cholesterol levels in patient with hyperlipoproteinemia. Atherosclerosis 1988; 74: 247-249.

[290] Jung F, Wolf S, Kisewetter H *et al.* Wirkung von knoblauch auf die fließfahigkeit des Blutes, Ergebnisse placebokontrolllierter Pilotstudien an gesunden Probanden. Natur und Ganzheitsmed 1989; 7: 216-221.

[291] Jung F, Jung EM, Pundir G and Kiesewetter H. Effect of different garlic preparations on the fluidity of blood, fibrinolytic activity and peripheral microcirculation in comparison with

placebo. Planta Med 1990; 56: 668.
[292] Lawson LD. Bioactive organosulfur compound of garlic and garlic products: role in reducing blood lipids. In: Kinghorn AD, Balandrin MF, editors. Human medicinal agents from plants. Washington. American Chemical Society 1993: 306-330.
[293] MacDonald JA, Marchand ME and Langler RF. Improving upon the *in vitro* biological activity of antithrombotic disulfide. Blood Coagul Fibrinolysis 2004; 15: 447-450.
[294] Srivastava KC. Evidence for the mechanism by which garlic inhibits platelet aggregation. Prostaglandins Leukot Med 1986; 22: 313-321.
[295] Srivastava KC and Tyagi OD. Effects of a garlic derived principle (ajoene) on aggregation and arachidonic acid metabolism in human blood platelets. Prostaglandins Leukot Essent Fatty Acids, 1986; 49: 587-595.
[296] Farnsworth NR, Fong HHS, Mahady GB. Folium Ginkgo. WHO Monographs on Selected Medicinal Plants, Geneva, Switzerland, World Health Organization, Traditional Medicine Programme, 1999. [The WHO monograph for Folium Ginkgo assesses the quality, safety and efficacy of Ginkgo biloba; this is an official WHO publication].
[297] Teng CM *et al.* Inhibition of platelet aggregation by apigenin from *Apium graveolens*. Asia Pasific J Pharmacol 1989;1: 85-89.
[298] DeFeudis FV (ed). (1998) In: Ginkgo biloba extract (EGb 761). From chemistry to clinic. Wiesbaden, Ullstein Medical.
[299] Khare CP . Indian herbal remedies. Springer – Verlag, Berlin, Heidelberg, New York, 2004.
[300] Wu T, Ou L, and Teng C. Aristolochic acids, aristolactam alkaloids and amides from *Aristolochia kankauensis*. Phytochemistry 1994; 36: 1063-1068.
[301] Goun E, Cunningham G, Solodnikov S, Krasnykch O, and Miles H. Antithrombin activity of some constituents from *Origanum vulgare*. Fitoterapia 2002; 73: 692-694.
[302] Liggieri C, Arribére MC, Trejo SA, Canals F, Avilés FX and Priolo NS. Purification and biochemical characterization of asclepain CI from the latex of *Asclepias curassavica* L. Protein J 2004; 23(6): 403- 411.
[303] Karpagam N, Viswanathan S and Prabhu S. Biochemical and In silico clotting activity of latex from Asclepias curassavica L. Int J Pharm Bio Sci 2013; 4(4): (B) 542 - 552.
[304] Shivaprasad HV, Riyaz M, Venkatesh Kumar R, Dharmappa KK, Tarannum S, Siddesha JM, Rajesh R and Vishwanath BS. Cysteine proteases from the Asclepiadaceae plants latex exhibited thrombin and plasmin like activities. J Thromb Thrombolysis 2009; 28(3): 304-308.
[305] Shivaprasad HV, Rajesh R, Nanda BL, Dharmappa KK and Vishwanath BS. Thrombin like activity of
Asclepias curassavica L. latex: Action of cysteine proteases. J Ethnopharmacology 2009; 123: 106–109.
[306] Ercisli S. Clinical justification of ethnomedicinal use of *Brassica rapa* in cardiovascular diseases. Exp Clin Cardiol 2014; 20(7): 764-783.
[307] Ramos MV, Viana CA, Silva AF, Freitas CD, Figueiredo IS, Oliveira RS, Alencar NM, Lima-Filho JV and Kumar VL. Proteins derived from latex of *C.* procera maintain coagulation homeostasis in septic mice and exhibit thrombin- and plasmin-like activities. Naunyn Schmiedebergs Arch Pharmacol 1999; 385(5): 455-463.
[308] Ross JA, Kasum CM. (2002) Dietary flavonoids: Bioavailability, metabolic effects and safety. Annu Rev Nutr 22:19-34 [This review describes the chemistry, biological effects and safety of dietary flavonoids].Khare CP. Indian medicinal plants – An illustrated dictionary. Springer Science and Business Media, LLC, 2007.
[309] Sheikh Anwar M, Khan IN, Sarkar MI, Barua S, Kamal ATM and Hosen SM Z. Thrombolytic and cytotoxic effect of different herbal extracts. IJPSR 2011; 2(12): 3118-3121.
[310] Adams MJ, Ahuja KD and Geraghty DP. Effect of capsaicin and dihydrocapsaicin on *in vitro* blood coagulation and platelet aggregation. Thromb Res 2009; 124: 721-723.
[311] Hogaboam CM, Wallace JL. Inhibition of platelet aggregation by capsaicin. An effect unrelated to actions on sensory afferent neurons. Eur J Pharmacol 1991; 202: 1991, 129-131.
[312] Li HX, Han SY, Wang XW, Ma X, Zhang K, Wang L, Ma ZZ and Tu PF. Effect of the carthamins yellow from *Carthamus tinctorius* L. on hemorheological disorders of blood stasis in rats. Food Chem Toxicol 2009; 47(8): 1797-1802.
[313] Farnsworth NR, Fong HHS, Mahady GB. (2004) Gummi Gugguli, WHO Monographs on Selected Medicinal Plants, Volume III, WHO Traditional Medicine Programme, Geneva, Switzerland.
[314] Huang D, Lu Y, Luo X, Shi L, Zhang J, Shen J, Bao M, Song L, Wei C, Li H and Li Z. Effect of safflower yellow on platelet activating factor

mediated platelet activation in patients with coronary heart disease. Bangladesh J Pharmacol 2012; 7: 140-144.

[315] Wang HF, Li XD, Chen YM, Yuan LB and Foye WO. Radiation-protective and platelet aggregation inhibitory effects of five traditional Chinese drugs and acetylsalicylic acid following high dose γ- irradiation. Journal of Ethnopharmacology 1991; 34: 215-219.

[316] Liwei G, Fei Y, Tianshan W, Guoxiang M and Yang P. Hemostatic effect of Flos *Celosiae cristatae* and its mechanism, 1996.

[317] Sen, C.K. and Bagachi, D.: Regulation of inducible adhesion molecule expression in human endothelial cells by grape seed proantocyanidin extract. Mol. Cell. Biochem., 216, 1–7, 2001.

[318] Buring, J.E. and Hennekens, C.H.: Antioxidant vitamins and cardiovascular disease. Nutr. Rev., 55, S53–S60, 1997.

[319] Schumacher E, Vigh E, Molnár V, Kenyeres P, Fehér G, Késmárky G, Tóth K and Garai J. Thrombosis preventive potential of chicory coffee consumption: a clinical study. Phytother Res. 2011; 25(5):744-748.

[320] Park, Y.K., Park, E., Kim, J.S., and Kang, M.H.: Daily grape juice consumption reduces oxidative DNA damage and plas- ma free radical levels in healthy Koreans. Mutation Res., 529, 77–86, 2003.

[321] Riaz A, Khan RA, Mirza T, Mustansir T and Ahmed M. *In vitro*/ *in vivo* effect of *Citrus limon* (L. Burm. f.) juice on blood parameters, coagulation and anticoagulation factors in rabbits. Pak J Pharm Sci 2014;27(4):907-915.

[322] Al-Aghawani W, Al-Madi S and Al-Lahham A. The vasodilator effects of *Convolvulus arvensis* in rabbit isolated aortic rings. Arabic Journal of Pharmaceutical Sciences 2009; 9(3): 39-48.

[323] Al-Snafi AE. The chemical constituents and pharmacological effects of *Convolvulus arvensis* and *Convolvulus scammonia*- A review. IOSR Journal of Pharmacy 2016; 6(6): 64-75.

[324] Al-Aghawani W and Al-Madi S. Study the vasodilator effect at molecular level of *Convolvulus arvensis*
in isolated aortic rings. Damascus Journal of health Sciences 2010; 26(1): 601-620.

[325] Nishio T, Okugawa H, Kato A, Hashimoto Y, Matsumoto K and Fujioka A. Effect of crocus (*Crocus sativus* L, Iridaceae) on blood coagulation and fibrinolysis. Shoyakugaku Zasshi 1987; 41: 271–276.

[326] Farnsworth NR, Fong HHS, Mahady GB. (2004) Crocus sativum. WHO Monographs on Selected Medicinal Plants, Volume III, WHO Traditional Medicine Programme, Geneva, Switzerland. [This WHO monograph on Crocus sativum describes the quality, safety and efficacy of this medicinal plant. This is an official WHO publication].Jessie SW and Krishnakantha TP. Inhibition of human platelet aggregation and membrane lipid peroxidation by food spice, saffron. Mol Cell Biochem 2005; 278(1-2):59-63.

[327] Srivastava KC. Extracts from two frequently consumed spices-cumin (*Cuminum cyminum*) and turmeric (*Curcuma longa*)- inhibit platelet aggregation and alter eicosanoid biosynthesis in human blood platelets. Prostaglandins Leukot Essent Fatty Acids 1989; 37(1):57-64.

[328] Zhou W, Abdurahman A, Umar A, Iskander G, Abdusalam E, Berké B, Bégaud B and Moore N. Effects of *Cydonia oblonga* Miller extracts on blood hemostasis, coagulation and fibrinolysis in mice, and experimental thrombosis in rats. J Ethnopharmacol 2014; 154(1):163-169.

[329] Hugar L and Ramesh H. Evaluation of hemostatic effect of *Cynodon dactylon* Pers in albino rats. Journal of Evolution of Medical and Dental Sciences 2014; 3(11): 2711-2713.

[330] Kopp P. (1998) Resveratrol, a phytoestrogen found in red wine. A possible explanation for the conundrum of the French Paradox? Eur J. Endocrinol. 138:619-620. [This article describes the active constituents of red wine and their benefits in heart disease and provides partial explanation of the French Paradox]. Seo EJ, Lee DU, Kwak JH, Lee SM, Kim YS and Jung YS. Antiplatelet effects of *Cyperus rotundus* and its component (+)-nootkatone. Journal of Ethnopharmacology 2011; 135: 48-54.

[331] Xue JX, Jiang Y and Yan YQ. Effects of the combination of *Astragalus membranaceus* (Fisch.) Bge. (AM), tail of *Angelica sinensis* (Oliv.) Diels. (TAS), *Cyperus rotundus* L. (CR), *Ligusticum chuanxiong* Hort. (LC) and *Paeonia veitchii* Lynch (PV) on the hemorrheological changes in normal rats. Zhongguo Zhong Yao Za Zhi 1993; 18(10): 621-623.

[332] Mahady GB, Schriever C, Pendland S.L. (2003) Red wine, resveratrol, Chlamydia pneumoniae and the French connection. Atherosclerosis, 171(2):379-80. [This reference describes the experimental effects of red wine and resveratrol on Chlamydia pneumonia infections and correlates these data

with atherosclerosis and the French Paradox]Mekhfi H, El Haouari M, Legssyer A, Bnouham M, Aziz M, Atmani F, Remmal A and Ziyyat A. Platelet anti-aggregant property of some Moroccan medicinal plants. J Ethnopharmacol 2004;94(2- 3):317-322.

[333] Mahady GB. (2001) Ginkgo biloba: A review of quality, safety and efficacy. Nutr. Clin Care, 4:140-147. [This article is a review of the overall safety and efficacy of Gingko products for the treatment of dementia].Saluk-Juszczak J, Olas B, Pawlaczyk, Gancarz R, Wachowicz B. Effects of the extract from Conyza canadensis on human blood platelet aggregation. Gen Physiol Biophys. 2007; 26(2):150-152.

[334] Mahady G.B. (2003) Ginkgo biloba for the prevention and treatment of cardiovascular disease: a review of the literature. J. Cardiovascul Nursing, 16(4):21-32. [This article reviews all of the data supporting the use of ginkgo for the prevention and treatment of cardiovascular disease]. Pawlaczyk I, Czerchawski L, Kuliczkowski W, Karolko B, Pilecki W, Witkiewicz W and Gancarz R. Anticoagulant and anti-platelet activity of polyphenolic-polysaccharide preparation isolated from the medicinal plant Erigeron canadensis L. Thrombosis Research 2011; 127(4): 328-340.

[335] Olas B, Saluk-Juszczak J and Pawlaczyk I. Antioxidant and antiaggregatory effects of an extract from *Conyza canadensis* on blood platelets *in vitro*. Platelets 2006; 17(6): 354-360.

1/22/2023