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Medicinal plants with beneficial effects on heart

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Abstract

Cardiovascular diseases (CVDs) kill 17.9 million people per year, by 2030, it is predicted that more than 22.2 million people will die annually from CVDs. Many medicinal plants possessed cardiac and anti-arrhythmic effects. The current study was designed to highlight the medicinal plants which possess beneficial effect in heart failure, protect heart from the toxicity of wide range of chemicals, and exert anti-arrhythmic activities.

Keywords: Heart Failure; Arrhythmia; Protective Effect; Medicinal Plants

1. Introduction

According to WHO, cardiovascular diseases (CVDs) kill 17.9 million people per year, by 2030, it is predicted that more than 22.2 million people will die annually from CVDs, low and middle income countries contribute 75% of the CVD deaths [1]. The herbal treatments for heart failure and ischemic heart diseases were applied traditionally since ancient times. Medicinal plant derived cardiac glycosides have long served as the main medical treatment to congestive heart failure and cardiac arrhythmia, due to their effects of increasing the force of muscle contraction while reducing heart rate[2]. Many recent reviews mention that medicinal plants possessed wide range of therapeutic effects in heart diseases [3-5]. The present study was conducted to assess the medicinal plants which possessed beneficial effect in curing heart diseases and to protecting heart from the toxicity of wide range of chemicals, to encourage the studying of clinical effectiveness, safety and to investigate the active ingredients, and their biological mechanisms.

2. Medicinal plants with cardiac effect

2.1. *Achillea santolina*

With the using of 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 [6].

2.2. *Adonis aestivalis*

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 *Adonis vernalis* 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

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blocked by the atropine. In isolated guinea pig and rabbit auricles the drug increased the threshold of electrical stimulation [7-8].

Strophanthidin aglycone is one of several cardenolides extracted from *Adonis aestivalis*. 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. They increased 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 [7, 9].

2.3. *Alhagi maurorum*

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 [10-11].

2.4. *Althaea rosea*

Alcoholic extract of the flower of *Althaea rosea* 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 [12].

2.5. *Ammi visnaga*

Ammi visnaga induced relaxation of smooth muscle, including coronary arteries, in a variety of animal species. Samidin and khellol glucoside induced positive inotropic effects on heart. A clinical trial of khellin in 38 cases of angina pectoris and in 8 cases of coronary thrombosis was performed. Continuous treatment, by the oral or intramuscular routes or by both, gave favorable results in 35 out of 38 cases of angina pectoris. Continuously administration of khellin for several weeks to eight patients after coronary thrombosis appeared favorable [13-14].

Immediately after the rapid intravenous administration of 20-30 mg of khellin to the dogs, the heart beats considerably slower. The entire effect lasts for only a short time, within a minute or two [15].

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 [16-17].

2.6. *Anchusa strigosa*

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 [18-19].

2.7. *Apium graveolens*

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* [20-21].

2.8. *Asclepias curassavica*

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) [22].

2.9. *Bacopa monnieri*

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 quinidine on heart [23-24].

2.10. *Brassica nigra*

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 [25-26].

2.11. *Caesalpinia crista*

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 [27-28].

2.12. *Calendula officinalis*

Rat hearts perfused with calendula solution at 50 mM in KHB bufferfor 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 the activation of Akt and Bcl2 and depression of TNFα [29-30].

2.13. *Calotropis procera*

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 [31-32].

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 [33].

2.14. *Carthamus tinctorius*

An animal model of myocardial ischemia injury was induced by left anterior descending coronary artery occlusion in adult rats. Pretreatment with *C. tinctorius* (ECT) (100, 200, 400, 600 mg/kg body wt.) protected the heart from ischemia injury by limiting infarct size and improving cardiac function. In the *in vitro* experiment, neonatal rat ventricular myocytes were incubated to test the direct cytoprotective effect of ECT against H2O2 exposure. Pretreatment with 100-400 microg/ml ECT prior to H2O2 exposure significantly increased cell viability. ECT also markedly attenuated H2O2-induced cardiomyocyte apoptosis. The protection is achieved by scavenging of ROS and mediating the PI3K signaling pathway [34-35].

The effects of safflower injection (SI) in protecting heart, on energy charge and anti-apoptosis gen bcl-2 in cardiac tissue were investigated by Rats' Langendorff isolated heart infused model. As compared with the control, SI improved the functions of cardiac contraction and dilation, increasing coronary blood flow, and strengthening the bcl-2 protein expression [36].

The effect of Flos Carthami FC (EtOH)) ethanolic extract on LPS-induced apoptosis in H9c2 cardiomyoblast cells was studied. FC (EtOH) (62.5 microg/ml) inhibited LPS-induced apoptosis by suppressing JNK1/2 activity, which resulted in the reduction of both IkappacB degradation and NF kappaB activation. In addition, FC (EtOH) led to activation of anti-apoptotic proteins, Bcl-2 and Bcl-xL, the stabilization of the mitochondria membrane and the down-regulation of extrinsic and intrinsic pro-apoptotic proteins, such as TNF alpha, active caspase-8, t-Bid, Bax, active caspases-9, and -3. The ability of *Carthamus tinctorius* to suppress JNK activity and inhibit LPS-induced TNF alpha activation and apoptosis in H9c2 cardiomyoblast cells could potentially serve as a cardio-protective agent against LPS-induced apoptosis [37-38].

The effects of safflor yellow A (SYA) was evaluated on cultured rat cardiomyocytes exposed to anoxia/reoxygenation (A/R). The A/R exposure markedly decreased the viability of cardiomyocytes, suppressed the activities of SOD, GSH, CAT, GSH-Px, and Bcl-2 protein expression. Meanwhile, the A/R exposure markedly increased the release of LDH, CK,

MDA production in the cardiomyocytes, increased the rate of apoptosis, caspase 3 activity and Bax protein expression [39].

The protective effect of safflor yellow B (SYB) was investigated against vascular endothelial cells (VECs) injury induced by angiotensin-II (Ang-II). Comparing with control group, Ang-II was able to increase Ca2+ and ROS level, decrease MMP level, inhibit complex IV activity and enhance caspase 3 activity in VECs, as a result, enhance apoptosis of VECs. SYB was able to eliminate the effect of Ang-II on VECs via regulating Ca+2, mitochondrial structure and function and inhibiting apoptosis [40].

Intravenous injection of the hydroxysafflor yellow A (HSYA) significantly reduced MAP and HR in both normotensive rats and SHR in a dose-dependent manner. HSYA reduced left ventricular systolic pressure (LVSP), left ventricular end-diastolic pressure (LVEDP), the maximum rate of increase of left ventricular pressure (+dp/dt (max)) and heart rate (HR) in a dose-dependent manner. HSYA had no remarkable effect on the maximum rate of decrease of left ventricular pressure (-dp/dt (max)); BK (Ca) and K (ATP) blocker can weakened the inhibitory effect of HSYA on heart function and HR, but K (V) and K (ACh) blocker did not significantly weaken the HSYA effects [41-42].

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 over expression 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 [43].

2.15. *Cheiranthus cheiri*

Cardiac glycosides called cheiranthosides I-XI together with two olitoriside and erysimoside were isolated from the seeds of the plant. The glycosides were evaluated for their inhibitory activity against Na^+, K^+ -ATPase by comparing with typical cardiac glycosides. Two of them, cheiranthoside III and VIII, showed high inhibiting activity which was equivalent to that of digitoxin. Cheiranthoside XI containing a rhamnopyranosyl digitoxopyranosyl moiety and a carboxyl group showed the lowest activity which was similar to that of the inactive aglycone, strophanthidin [44-45].

2.16. *Cichorium intybus*

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 [46-47].

2.17. *Citrus species*

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 [48-49].

2.18. *Corchorus aestuans*

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 [50-52].

2.19. *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 [53-57].

2.20. *Coriandrum sativum*

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 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 [58-59].

2.21. *Coronilla scorpioides*

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 [60-61].

2.22. *Coronilla varia*

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 [62-66].

2.23. *Crocus sativus*

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) 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 doxorubicin - cardiotoxicity [67].

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 [68].

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 [69].

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 [70-71].

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 $p<0.001$) [72].

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 definitely slowed the electrical conduction velocity in both atrium and ventricle [73].

2.24. *Cynodon dactylon*

The effects of hydroalcoholic extract of *Cynodon dactylon* rhizomes was evaluated on cardiac contractility in normal hearts and on 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 [74].

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 [75].

The probable antiarrhythmic effects of *Cynodon dactylon* against ischemia/ reperfusion (I/R)-induced arrhythmias were investigated in isolated rat heart. The hearts were subjected to 30min regional ischemia followed by 30min reperfusion and perfused with hydroalcoholic extract of rhizome of *Cynodon dactylon* (25, 50, 100 and 200µg/ml). During ischemia, the extract produced marked reduction in the number, duration and incidences of ventricular tachycardia (VT) at 25 and 50µg/ml ($p<0.001$ and $p<0.01$) respectively. Total number of ischemic ventricular ectopic beats (VEBs) were lowered by 25, 50, 100µg/ml ($p<0.001$, $p<0.001$ and $p<0.050$ respectively. At the reperfusion phase, *Cynodon dactylon* (25 and 50µg/ml) decreased incidence of VT from 100% (control) to 13 and 33% ($p<0.001$ and $p<0.05$) respectively. Duration and number of VT and total VF incidence were also reduced at the same concentration ($p<0.05$ for all). Perfusion of the extract (25, 50, 100µg/ml) was markedly lowered reversible VF duration from 218±99second to 0 second, 0 second and 10±5 second ($p<0.01$, $p<0.01$ and $p<0.05$) respectively. Moreover, *Cynodon dactylon* (25 and 50µg/ml) decreased number of total VEBs from 349±73 to 35±17 ($p<0.001$) and 66±26 ($p<0.01$). It was also shown that perfusion of the extract produced a marked and concentration-dependent positive inotropic effect [76-77].

2.25. *Cyperus rotundus*

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 [78-79].

2.26. *Dalbergia sissoo*

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 [80-81].

2.27. *Daucus carota*

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 [82-83].

2.28. *Digitalis lanata and Digitalis purpurea*

Cardiac glycosides, are often called digitalis or digitalis glycosides, in particular digoxin and digitoxin, have been a cornerstone of the treatment of heart diseases for more than two centuries. They possessed many cardiovascular effects: (I) Regulation of cytosolic calcium concentration: by inhibiting the Na^+/K^+-adenosine triphosphatase (ATPase) enzyme, thereby increasing cardiac contractility. (II) Increased contractility of the cardiac muscle: causing cardiac output to more closely resemble that of the normal heart. Vagal tone is also enhanced, so both heart rate and myocardial oxygen demand decrease. Digitalis slows 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 [84-90].

2.29. *Ephedra Species*

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 [91-93].

2.30. *Erodium cicutarium*

The addition of extracts of *Erodium cicutarium* extracts 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 [94-97].

2.31. *Fritillaria imperialis*

In anesthetized dogs, the alkaloidal fraction isolated from the corms of *Fritillaria imperialis* showed an appreciable fall in blood pressure due to cardiac depression and peripheral vasodilatation. Hypotensive effect is also observed in experimental hypertension. On frogs heart the alkaloidal fraction exhibited cardiotonic effect. The alkaloidal fraction also exhibited anti-arrhythmic activity resembling that of quinidlne and spasmolytic activity similar to that of papaverine [98-99].

2.32. *Haplophyllum Species*

The aqueous extract of *H. tuberculatum* significantly decreased the contractility and the heart rate but did not affect the flow rate of isolated perfused rabbit heart. The effect of the aqueous extract was not blocked by atropine. Aqueous extract caused fall in the blood pressure when administered to anaesthetized cats, muscarinic antagonist blocked the fall in blood pressure in cats. The extract also stimulated rabbit aortic strip, rat vas deferens, and rat anococcygeus muscles. These adrenergic effects were largely reduced by phentolamine [100-101].

2.33. *Hibiscus rosa-sinensis*

The cardioprotective effects of dried pulverized flower of *Hibiscus rosa sinensis* (150-200 g/kg, bw, orally) on isoproterenol induced myocardial injury was studied in rats. There was significant increase in the baseline contents of thiobarbituric acid reactive substances with both doses of *Hibiscus rosa- sinensis*. In the 250 mg/kg treated group, there was significant increase in superoxide dismutase, reduced glutathione, and catalase levels but not in the 125 and 500 mg/kg treated groups. Accordingly, *Hibiscus rosa sinensis* (250 mg/kg) augments endogenous antioxidant compounds of rat heart and also prevents the myocardium from isoproterenol induced myocardial injury [102].

The cardioprotective effects of *Hibiscus rosa-sinensis* (HRS) (applied at concentration of 90, 180, and 360 µg/ml for 15 minutes) were investigated in Langendorff- perfused rat hearts prior to 25-min global ischemia/120-min reperfusion (I/R).Only a moderate increase in LVDP (21% and 55%) and a tendency to increase CF was observed at HRS 180 and 360.HRS at 180 and 360 significantly improved post-ischemic recovery of LVDP, it dose-dependently reduced the numbers of ectopic beats and duration of ventricular tachycardia. HRS significantly reduced the infarct size at all concentrations in a dose-dependent manner [103-104].

2.34. *Hibiscus sabdariffa*

The hypolipidemic and antiatherosclerotic effects of *Hibiscus sabdariffa* extract (HSE) were investigated in rabbits with experimental atherosclerosis. Rabbits were fed with a normal diet, high cholesterol (1.3%), lard oil (3%) diet (HCD) with or without 0.5 or 1% HSE for 10 weeks. The levels of triglyceride, cholesterol, and low-density lipoprotein cholesterol (LDL-C) were decreased in the serum of rabbits fed HCD plus HSE than in the serum of rabbits fed HCD. Feeding HSE (0.5 and 1% in the diet) to rabbits significantly reduced severe atherosclerosis in the aorta. Histopathological examination showed that HSE reduced foam cell formation and inhibited smooth muscle cell migration and calcification in the blood vessel of rabbits. These results suggest that HSE inhibits serum lipids and shows an antiatherosclerotic activity [105-106].

2.35. *Hyoscyamus Species*

The cardioprotective activity of the crude powder of the *Hyoscyamus niger* was studied in rats (100mg/100g bw). Many biochemical parameters like TGL, Ck-MB and LPO were evaluated to assess the cardioprotective effect of *Hyoscyamus niger* crude powder in isoproterenol induced myocardial injury. The oral administration of crude powder of *Hyoscyamus niger*water suspension against isoproterenol for 30 days, protected rats from the cardiac damage induced by lipid peroxidation and activation of antioxidant enzymes. It protected from cardiac necrosis as evidenced by the inhibitory activity of CK-Mb and TGL [107-108].

2.36. *Juglans regia*

Regular consumption of nuts has been associated with a reduced risk of both fatal coronary heart disease and non-fatal myocardial infarction. The epidemiological

Studies showed that people who consumed nuts five or more times a week had a 50% reduced risk of coronary heart disease relative to those who never consumed nuts. A reduction in cardiovascular risk was also recorded in a cohort of women from the Nurses' Health Study [109-112].

2.37. *Lagerstroemia speciosa*

The cardio-protective effect of *Lagerstroemia speciosa* leave extract (containing 1 % corosolic acid) was evaluated in isoproterenol-induced myocardial injury in mice. Extract pretreatment augmented myocardial antioxidant status and attenuated myocardial oxidative stress. Myocardial apoptosis as well as MMPs activities was significantly prevented by the extract pretreatment in isoproterenol-induced myocardial injury in mice. Furthermore, extract pretreatment enhanced the nuclear protein expression of Nrf2 [113].

Low doses of *Lagerstroemia speciosa* extracts inhibited the interactions between nuclear factors and target DNA elements mimicking sequences recognized by the nuclear factor kappaB (NF-kappaB). Aqueous extracts of the leaves of *Lagerstroemia speciosa* completely blocked the activation of NF-kappaB by tumor necrosis factor (TNF) in rat cardiomyocyte H9c2 cells in a dose- and time- dependent manner. Diabetes leads to cardiomyocyte hypertrophy in association with an upregulation of vasoactive factors and activation of nuclear factor (NF)-kappaB and activating protein-1. These effects possessed by the extract explained its inhibitory effect on diabetes-induced cardiomyocyte hypertrophy [114-116].

2.38. *Lantana camara*

The cardiovascular activity of ethanolic extract of *Lantana camara leaves* was evaluated in different experimental models. The ethanolic extract of *Lantana camara leaves* produced negative inotropic and negative chronotropic effect, antagonised by atropine on isolated frog heart. The ethanolic extract caused dose dependent ($p<0.05$) decrease in the mean arterial blood pressure in anesthetic chick. Salt treated rats displayed significant ($p<0.05$) increase in blood level of SGOT, SGPT, creatinine and sodium, decrease in potassium levels in comparison with normal rats. Treatment with ethanolic extract (200 and 400 mg/kg) significantly balanced the ionic levels such as lower the sodium and elevate the potassium levels. Creatinine levels were significantly ($p<0.05$) reduced by ethanolic extract [117-118].

2.39. *Lathyrus sativus*

The cardioprotective effect of *Lathyrus sativus* seed flour was studied in myocardial infarction induced byisoproterenol (ISP) in rats. *Lathyrus sativus* seed flour was incorporated in the rat's diet (30, 50 and 75%). The results showed that *Lathyrus* countered the adverse effects of ISP induced myocardial infarction to major extent suggesting its vasodilatation and inhibition of platelet aggregation and antioxidant potential owing to replenishment of antioxidant defenses and decreasing the ischemic injury due to presence of phenols and homoarginine [119-120].

2.40. *Leontice leontopetalum*

The effects of (−) oblongine chloride, on blood pressure, heart rate and blood flow were studied in anaesthetized guinea-pig. Oblongine chloride caused a doses ranging (0.5 to 30 mg/kg, iv) reduction of systolic and diastolic blood pressure. These effects were associated with an increase in heart rate. Propranolol (5 mg/kg) failed to block the effects of oblongine chloride on systolic and diastolic blood pressure but significantly reduced the increase in heart rate observed with low doses (0.5–6 mg/kg) of oblongine chloride. Oblongine chloride also caused doses ranging (0.05 to 0.5 mg/kg) increase in blood flow. Larger doses (1.5, 4.5, 15 and 30 mg/kg) caused an initial decrease followed by an increase of blood flow. The net effect of cumulative doses was an increase in blood flow over the control value. Accordingly, oblongine chloride possessed potential haemodynamic effects, which were not mediated by β-adrenergic receptor stimulation [121-122].

2.41. *Lepidium sativum*

The ethanolic extract of the seeds of *Lepidium sativum* caused marked increase in the rate and force of auricular and ventricular movements of open chest cat heart preparation. The cardiac stimulatory effect was also observed on isolated rabbit auricles [123-125].

2.42. *Linum usitatissimum*

The beneficial effects of the methanolic extracts of seeds and oil of seeds of *Linum usitatissimum* were evaluated in congestive heart failure. The methanolic extract of seeds of *Linum usitatissimum* showed significantly increased in positive inotropic effect (force of contraction 48.8±1.53 mm) as compared to control group (force of contraction 17.5±0.76 mm). Both methanolic extracts of seeds and oil of seeds of *Linum usitatissimum* showed significant decreased

QT interval in doxorubicin-induced congestive heart failure. The histopathologic study indicated that methanolic extract treated animals showed the least damage to the architecture of myocardial membrane. The methanolic extract of seeds of *Linum usitatissimum* increased urine output (5.66±0.16 ml and 6.58±0.15 ml respectively) significantly in Lipschitz model as compared to diseased control group (4.58±0.15 ml) [126].

The cardioprotective and positive inotropic actions of methanolic extract of seeds and oil of seeds of *Linum usitatissimum* were evaluated in doxorubicin (15mg/kg, ip within 3 weeks) to induce congestive heart failure in Wistar rat. ECG recording, cardiac biomarkers like CPK-MB, LDH and SGOT and cytosolic Ca^{2+} level were estimated. Both methanolic extracts of seeds and oil of seeds of *Linum usitatissimum* showed significant increase in cytosolic Ca^{2+} level with significantly decreased QT interval as well as cardiac bio-markers [127].

The cardioprotective activity of flax lignan concentrate was evaluated in isoprenalin induced cardiotoxicity in rats. Isoprenalin intoxicated group showed cardiotoxicity, manifested by increased levels of marker enzymes and increased heart rate. Flax lignan concentrate treatment reversed these biochemical changes significantly compared with isoprenalin group. The cardiotoxic effect of isoprenalin was less in flax lignan concentrate pretreated animals. Furthermore, haemodynamic, biochemical alteration and histopathological results confirmed the cardioprotective protective effect of flax lignan concentrate in isoprenalin induced cardiotoxicity [128].

2.43. *Luffa acutangula*

The protective effects of hydroalcoholic extract of *Luffa acutangula* on doxorubicin induced cardio and nephrotoxicity were investigated in mice using various parameters such as serum biomarkers, antioxidants in target organs and histoarchitecture alterations. Pretreatment with hydroalcoholic extract reversed significantly the elevated serum alanine amino transferase, lactate dehydrogenase and creatinine phosphokinase in heart and kidney in doxorubicin treated mice. Hydroalcoholic extract treatment also inhibited the elevated malondialdehyde and restored the depleted glutathione, catalase, superoxide dismutase in heart and kidney tissue. The altered histoarchitecture of heart and kidney tissue due to doxorubicin treatment were also improved with hydroalcoholic extract. The protective activity observed with hydroalcoholic extract on doxorubicin induced cardio and nephrotoxicity in mice was related to antioxidant property of the plant extract [129-130].

2.44. *Lycium barbarum*

The effect *Lycium barbarum* polysaccharides (LBPs, 300 μg/ml, for 24 h) was studied in hypoxia-injured H9c2 cells. LBPs exhibited *in vitro* and *in vivo* cardioprotective activities via down-regulating miR-122. LBPs increased cell viability, down-regulated p53, p21 and p16 protein expressions, improved migration, and repressed apoptosis in hypoxia-injured H9c2 cells. The miR-122 was highly expressed in response to hypoxia, and was down-regulated by addition of LBPs. LBPs-induced the activation of MEK/ERK and AMPK signaling pathways were attenuated by miR-122 overexpression, and were accelerated by miR-122 suppression. *In vivo* investigation revealed that, LBPs decreased infarct size and improved cardiac function via down-regulation of miR-122 in MI rats [131].

The cardioprotective effect and molecular mechanism of *Lycium barbarum* polysaccharides (LBPs)was studied in mice. LBPs significantly reduced the expression of myocardial miR-1. LBPs improved the abnormal ECG and indexes of cardiac functions in P-V loop detection in transgenic (Tg) mice with miR-1 overexpression. LBPs recovered morphological changes in sarcomeric assembly, intercalated disc and gap junction and reversed the reductions of CaM and cMLCK, the proteins targeted by miR-1. Similar trends were also obtained in their downstream effectors including the phosphorylation of MLC2v and both total level and phosphorylation of CaMKII and cMyBP-C [132].

Lycium barbarum polysaccharides significantly decreased the myocardium LD level, increased Na^{+}-K^{+}-ATPase and Ca^{2+}-ATPase activities in heart ischemia reperfusion (IR)rats. *Lycium barbarum* polysaccharides markedly decreased myocardium Bax positiverate and myocardial cell apoptosis and increased Bcl-2 positive rate in a dose- dependent manner [133].

The protective effect of *Lycium barbarum* polysaccharides (LBP, 200 mg/kg, for 10 days) against acute doxorubicin (DOX)- induced cardiotoxicity was studied in rats. DOX induced significantly myocardial damage in rats, which were characterized as conduction abnormalities, decreased heart-to-body weight ratio, increased serum CK, and myofibrillar disarrangement. It also increased MDA and decreased SOD and GSH-Px activity in cardiac tissues. Pretreatment with LBP significantly reduced DOX- induced oxidative injury in cardiac tissue, it significantly attenuated DOX-induced cardiac myofibrillar disarrangement and decreasing the levels of serum CK and improving conduction abnormalities caused by DOX. It also significantly increased SOD and GSH-Px activity and decreased the MDA level of heart tissues damaged by DOX exposure in rats [134].

The protective effect of water extract of *Lycium barbarum* (LB, 25mg/kg) against acute doxorubicin (DOX)-induced cardiotoxicity was studied in rats. The DOX group showed higher mortality (38%). It caused myocardial injury manifested by arrhythmias and conduction abnormalities in ECG (increased QT and ST intervals and ST elevation),decreased heart antioxidant activity, increased serum CK and AST, and induced myocardial lesions. Pretreatment with water extract significantly prevented the loss of myofibrils and improved the heart function of the DOX-treated rats. It lowered mortality (13%), normalized antioxidative activity and serum AST and CK, as well as improving arrhythmias and conduction abnormalities [135].

2.45. *Mangifera indica*

The cardioprotective effect of mangiferin was studied in the isoproterenol- induced myocardial infarction in rats. Mangiferin ameliorated the effect of isoproterenol-induced pathological changes, reduced the lipid peroxide formation and retained the myocardial marker enzyme activities at near normal level [136-137].

2.46. *Marrubium vulgare*

The cardioprotective effects of aqueous fraction of *Marrubium vulgare* hydroalcoholic extract were studied in ischaemic- reperfused isolated rat hearts. 40 µg/ml of *Marrubium vulgare* aqueous fraction significantly decreased infarct size in comparison to control group. All doses considerably reduced the total ventricular ectopic beats during 30 min of ischaemia. The extract at dose of 40 µg/ml noticeably decreased the arrhythmias during the first 30 min of reperfusion. The aqueous fraction scavenged DPPH radical with RC_{50} value of 47 µg/ml. The total phenolic and flavonoids content of the fraction was 6.05 g gallic acid equivalent and 36.13 mg quercetin equivalent per 100 g of dry plant material [138].

A severe myocardial necrosis and edematous along with a sharp reduction in the arterial blood pressure, left ventricular contractility (LVdP/dt (max or min)), but a marked increase in the left ventricular end-diastolic pressure (LVEDP) were seen in the isoproterenol group. All pathological changes induced by isoproterenol were significantly improved by the *Marrubium vulgare* extract treatment. The authors concluded that the therapeutic effects of *Marrubium vulgare* attributed to its antioxidant activities [139].

A subcutaneous injection of isoproterenol to rats (100 mg/kg/day) for 2 consecutive days caused ST-segment elevation in ECG, left ventricular dysfunction, intensive myocardial fibrosis with a profound increase in myocardial myeloperoxidase (MPO) activity and serum levels of TNF- α. All doses of the *Marrubium vulgare* extract significantly amended the ECG pattern and improved the left ventricular systolic pressure, contractility and relaxation ($P<0.001$). Interstitial fibrosis was significantly attenuated in treated groups compared with control MI group. Treatment with the extract also reduced serum levels of TNF- α (at least 40.35%) and myocardial MPO activity (at least 30.47%) [140-141].

2.47. *Medicago sativa*

The cardioprotective effect of ethanolic extract of *Medicago sativa* stem was evaluated in isoproterenol induced myocardial infarction in rats. Isoproterenol group showed increased serum levels of liver and cardiac markers andlipid profile with decreased HDL-C level. The pretreatment with the extract reversed the lipid profile level and cardiac and liver enzyme levels to near normal level [142-143].

2.48. *Melissa officinalis*

The effect of the aqueous extracts of leaves of *Melissa officinalis* upon contractile force and heart rate was investigated on rat isolated heart. The aqueous extract provoked significant heart rate reduction and did not alter the contractile force. The negative contractile force effect may occurred due to cardiac muscarinic receptors stimulation induced by the extract [144].

The effect of *Melissa officinalis* aqueous extract (50, 100, 200 and 400 mg/ml/kg, ip)in cardiac conduction and susceptibility to reperfusion-induced lethal ventricular arrhythmias was investigated in rats. Pulse rate, corrected QT (QTc) and QRS intervals increased in the *Melissa officinalis.* During the reperfusion period, the decrease in ventricular fibrillations was statistically significant compared with control group. The score of arrhythmia severity also decreased [145].

The cardioprotective effect of standardized extract of *Melissa officinalis* (250, 500 and 750 mg/kg bw, once daily for 10 consecutive days) was studied against doxorubicin (DOX)- induced cardiotoxicity in rats. The extract protected against DOX-induced leakage of cardiac enzymes and histopathological changes. It ameliorated DOX-induced oxidative stress as evidenced by decreasing lipid peroxidation, protein oxidation and total oxidant capacity depletion and by increasing

antioxidant capacity. Furthermore, pretreatment with the extract inhibited the inflammatory responses to DOX by decreasing the expressions of nuclear factor kappa-B, tumor necrosis factor-alpha, cyclooxygenase-2 and the activity of myeloperoxidase. The extract also ameliorated DOX-induced apoptotic tissue damage in heart of rats [146].

A double blind randomized placebo-controlled clinical trial was carried out to evaluate the efficacy and safety of lyophilized aqueous extract of *Melissa officinalis*leaves (500 mg twice a day, for 14 day)on adults suffering from benign palpitations. *Melissa officinalis* leaves extract reduced the frequency of palpitation episodes and significantly reduced the number of anxious patients in comparison to the placebo. The extract showed no serious side effects [147].

A randomized, double-blind, placebo-controlled clinical trial was performed to investigate the effects of oral administration of powdered *Melissa officinalis* (3 g/day, for eight weeks)on biomarkers of oxidative stress, inflammation, and lipid profile in patients with chronic stable angina. The mean serum concentrations of triglycerides, total-cholesterol, LDL-cholesterol, malondialdehyde, and high sensitive C-reactive protein were lower in the treated group compared with placebo ($P<0.01$). Moreover, the mean serum concentration of paraxonase 1 (PNO1) and HDL-c were higher ($p<0.001$) in the treated compared with the control group [148].

2.49. *Mentha longifolia*

The antianginal effect of *Mentha longifolia* extract was studied in experimental model of angina. Aerial parts extract was given to rats three days before angina. *Mentha longifolia* extract significantly alleviated the sustained decline in cardiac contractility after vasopressin exposure, it also significantly decreased heart rate. However, the extract didn't affect the impaired cardiac dilation after vasopressin. *Mentha longifolia* also produced more increase in systolic and diastolic durations after vasopressin exposure compared with untreated animals, and alleviated the ST height changes during vasopressin injection [149].

2.50. *Momordica charantia*

The protective effects of *Momordica charantia* on ischemic diabetic myocardium was investigated in rats. Rats were treated for six weeks with 400 mg/kg bw *Momordica charantia* extract. The extract enhanced cardiac function, suppressed post-ischemic/reperfused infarct size extent and modulated serum cholesterol [150].

The protective effect of *Momordica charantia* fruit extract was investigated in hyperglycaemia-induced cardiac fibrosis. Diabetes was induced in rats by Streptozotocin (STZ). Administration of fruit extract (1.5 g/kg body weight) in diabetic rats for 28 days exerted significant increase in the body weight and decrease in the fasting blood glucose level. Significant increase in cardiac tissues superoxide dismutase (SOD), glutathione contents (GSH), and catalase (CAT) was observed following extract treatment. Hydroxyproline content was significantly reduced and the associated morphological damages reverted to normal. The extract also decreased expression of type III and type IV collagens [151]

3. Conclusion

The current study discussed the efficacy of medicinal plants in the treatment of heart diseases and in protection of heart from the toxicity of wide range of chemicals, to encourage the studying of clinical effectiveness, mode of action, bioactive ingredients, pharmacokinetic characteristics and safety.

Compliance with ethical standards

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