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Review Article

CURRENT PHARMACOLOGICAL STATUS OF CARDIOPROTECTIVE PLANTS AGAINST ISOPROTERENOL INDUCED MYOCARDIAL INFARCTION

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ABSTRACT

Objective: Cardiovascular diseases are the major cause of morbidity and mortality in the modern era. Myocardial infarction is a condition where there is a significant decrease or block in the blood (oxygen) supply to the part of heart, leading to degeneration of a portion of the myocardium which triggers a cascade of cellular, inflammatory and biochemical events, leading eventually to the irreversible death (necrosis) of heart muscle cells. Various therapeutic interventions, including lifestyle modification, pharmacological treatment options, and surgical techniques are available. The present review focus on the plants that have been evaluated for cardioprotective activity against isoproterenol-induced myocardial infarction.

Method: The current status of Cardioprotective plants was obtained from a literature search of electronic databases such as Google Scholar, Pubmed and Scopus up to 2017 for publications on medicinal plants used against isoproterenol-induced myocardial infarction. Isoproterenol, Isoprenaline, myocardial infarction, cardioprotective were used as keywords for the searching.

Result: A total of 117 different plant parts and their extracts have till now been published to possess cardioprotection against isoproterenol-induced myocardial infarction. Isoproterenol a beta-adrenergic receptors agonist causes severe stress in myocardium resulting in the infarct-like lesion and produced cardiotoxic effects by elevating the levels of cardiac biomarkers and causing changes in ECG. Plant-based medicines with their antioxidant, antiapoptotic, antihyperlipidemic, platelet antiaggregatory, anti-lipid peroxidation property provide substantial evidence for the management of Ischemia.

Conclusion: This review, therefore, provides a useful resource to enable a thorough assessment of the profile of plants that have cardioprotective activity against isoproterenol-induced myocardial infarction.

Keywords: Isoproterenol; Myocardial infarction; Cardioprotective

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INTRODUCTION

Cardiovascular diseases are the foremost cause of morbidity and mortality globally; more people die annually from cardiovascular diseases than from any other cause. An estimated 17.7 million people died from cardiovascular diseases in 2015, representing 31% of all global deaths. Of these deaths, an estimated 7.4 million were due to coronary heart disease and 6.7 million were due to stroke. Over three-quarters of cardiovascular disease, deaths take place in low- and middle-income countries. There are 32.4 million myocardial infarctions and strokes cases worldwide every year [1]. Myocardial infarction (i.e., heart attack) is defined pathologically as the irreversible death (necrosis) of myocardial cells secondary to prolonged lack of oxygen supply (ischemia). In concept, the imbalance between oxygen delivery and myocardial oxygen demand can be corrected by decreasing oxygen demand or by increasing delivery (by increasing coronary flow) [2]. Oxygen demand can be reduced by decreasing cardiac exertion or, according to recent studies, by shifting myocardial metabolism to substrates that involve less oxygen per unit of adenosine triphosphate (ATP) produced. Among the pharmacological agents used in the treatment of infarction are nitrovasodilators, β-adrenergic receptor antagonists, calcium channel antagonists, and antiplatelet agents. All approved agents improve the balance of myocardial oxygen supply and demand, increasing supply by dilating the coronary vasculature or decreasing demand by decreasing cardiac work [3]. The progress in the management of myocardial infarction is a result of several major trends, including improvements in risk stratification, more widespread use of an invasive strategy, implementation of care delivery systems prioritizing immediate revascularization through percutaneous coronary intervention (or fibrinolysis), advances in antiplatelet agents and anticoagulants, and greater use of secondary prevention strategies such as statins [4].

Isoprenaline or isoproterenol [1-(3, 4-dihydroxyphenyl)-2-isopropylamino ethanol hydrochloride] is a synthetic catecholamine used for the treatment of bradycardia, heart block, and rarely for asthma. It is a non-selective β-adrenoreceptor agonist and Trace amine-associated receptor 1 agonist that is the isopropylaminomethyl analog of epinephrine, which is an important controller of myocardial contractility and metabolism, thus serving as the key element of a standard model for the study of potentially beneficial effects of numerous drugs on cardiac function [5]. Isoproterenol induces cardiac necrosis by several mechanisms, including increased oxygen consumption, functional hypoxia and ischemia, coronary insufficiency, poor oxygen utilization, increased calcium overload and accumulation, altered myocardial cell metabolism, increased myocardial cyclic adenosine monophosphate levels, decreased level of high-energy phosphate stores, deranged electrolyte milieu, altered membrane permeability, intracellular acidosis, oxidative stress, and increased levels of lipid peroxides [6]. Isoproterenol induces myocardial infarction by causing alterations in hematological, biochemical, oxidative stress markers, and histopathological parameters [7].

A plethora of herbal medicines is employed routinely by patients to manage and/or treat chronic cardiovascular conditions and related complications. Interestingly, more than 2000 plants have been documented to be used in traditional systems of medicine, and some of these are providing comprehensive relief to the people suffering

from cardiovascular diseases and related complications, especially hyperlipidemia and ischemic heart disease among others [8]. The present review endeavors to overview up-to-date information on plants that have been proved to have a cardioprotective effect against isoproterenol-induced myocardial infarction.

THE PHARMACOLOGICAL STATUS OF SOME CARDIOPROTECTIVE PLANTS AGAINST ISOPROTERENOL-INDUCED MYOCARDIAL INFARCTION

1. *Acalypha indica* leaf methanolic extract restored inflammatory marker (lactate dehydrogenase), cardiac markers (C-reactive protein, troponin-T, and creatine kinase-muscle/brain [MB]), and lipid peroxidase activity to normal levels in isoproterenol-induced myocardial infarction in rats [9].
2. Hydroalcoholic extract of *Achyranthes aspera* restored the isoproterenol-induced myocardial necrosis altered serum levels of cardiac injury markers (creatine kinase-MB, lactate dehydrogenase, alkaline phosphatase, aspartate transaminase and alanine transaminase, and total proteins), antioxidant defense status (catalase, superoxide dismutase, glutathione, and lipid hydroperoxide) in the heart to the normal [10].
3. The administration of water extract of rhizomes of *Acorus gramineus* in male pigs possesses significant cardioprotective potential against isoproterenol-induced myocardial infarction as it significantly attenuated increased cardiac injury markers, such as cardiac troponin T, tumor necrosis factor (TNF)-α, and myeloperoxidase activity, and cardiac marker enzymes, and prevented the depletion of antioxidant parameters [11].
4. The treatment of Male Albino rats with Baobab fruit pulp (*Adansonia digitata*) showed significant cardioprotective activity by bringing all the parameters such as cardiac markers (creatine kinase MB, lactate dehydrogenase, and aspartate aminotransferase), some antioxidant enzymes, interleukin (IL)-1 β, monocyte chemoattractant protein-1, myeloperoxidase, collagen-1, galectin-3, and serum corticosterone to near normal level in isoproterenol administered model rat [12].
5. Cardiopreventive effects of an aqueous *Aegle marmelos* leaf extract in isoproterenol-induced myocardial infarction in rats is by significantly decreasing creatine kinase and lactate dehydrogenase and by increasing the heart rate. *A. marmelos* pretreatment increased the activity of Na+–K+ ATPase and decreased the activity of Ca+2 ATPase in the heart and aorta simultaneously along with decreasing the levels of cholesterol and triglycerides and increasing phospholipids in the heart and aorta [13].
6. The aqueous extract of *Allium cepa* bulb significantly recovered the altered parameters (troponin-I, creatine kinase-MB, glutamate-pyruvate transaminase, heart rate, R-R interval, and oxidative stress markers) in isoprenaline-induced myocardial injury in Wistar albino rats [14].
7. The garlic (*Allium sativum*) oil elicited a significant cardioprotective activity by lowering the levels of serum marker enzymes (aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, and creatine phosphokinase) and lipid peroxidation and elevated the levels of glutathione. The cardioprotective effects of garlic oil in isoproterenol-induced oxidative damage may be due to an augmentation of the endogenous antioxidants and inhibition of lipid peroxidation of the membrane [15].
8. The ethanolic extract of *Alstonia scholaris* (Family, *Apocynaceae*) significantly decreased the serum biomarkers creatine kinase-MB and lactate dehydrogenase and restoration of biochemical and histopathological alterations of heart tissue [16].
9. *Amaranthus viridis* oral treatment for 45 days elicited a significant cardioprotective activity by lowering the levels of serum marker enzymes, cardiac troponin, glutathione disulfide and lipid peroxidation, and elevated the levels of antioxidant enzymes and glutathione [17].
10. The hydroalcoholic extract of *Ananas comosus* possess cardioprotective activity against isoproterenol-induced myocardial infarction in rats by decreasing the elevated the cholesterol, low-density lipoprotein, very low-density lipoprotein, triglycerides, alanine aminotransferase and aspartate aminotransferase levels and increasing high-density lipoprotein and total protein in plasma along with reducing infracted zone with inflammatory cells, lipid droplets, myocardial necrosis, and vacuolization of myofibrils [18].
11. The ethanol leaf extract of *Andrographis paniculata* exhibited the cardioprotective effect in rats showing potent antioxidant properties (increased antioxidant enzymes such as superoxide dismutase, glutathione peroxidase, glutathione S-transferase, and glutathione, and reduced oxidative stress markers such as Myeloperoxidase) as well as improving the hemodynamic changes in the rats [19].
12. Pretreatment with the aqueous leaf extract of *Artemisia afra* prevented the elevation of serum marker enzymes, namely, lactate dehydrogenase, aspartate transaminase, alanine transaminase, and ALP (Alkaline phosphatase) in isoproterenol-induced myocardial injured rats. The extract also attenuated lipid peroxidation in the heart and improved the imbalance in glutathione reductase, glutathione peroxides, superoxide dismutase, glutathione, and lipid profile caused by isoproterenol [20].
13. Cardiac hemodynamics, heart coefficient and marker enzymes in serum showed that *Astragali radix* prevented isoproterenol-induced myocardial damage. *A. radix* also improved the antioxidant status by decreasing the lipid peroxidative product Myeloperoxidase and increasing the activity of the antioxidant enzyme superoxide dismutase. The observed depressions in sarcoplasmic reticulum calcium ATPase messenger ribonucleic acid and protein expression as well as ser(16)-phosphorylated phospholamban protein expression in isoproterenol-treated rats were attenuated by *A. radix* treatment [21].
14. The hydroalcoholic *Averrhoa carambola* fruit extract maintains near normal levels of cardiac biomarker enzymes (cardiac troponin-T, creatinine kinase, and lactate dehydrogenase) and antioxidant enzymes (glutathione, MPO, catalase, and superoxide dismutase). The infarcted hearts treated with extract showed a reduction in necrosis, infiltration of leukocyte and inflammation conferring its cardioprotective effect [22].
15. Aqueous leaf extract of *Azadirachta indica* exhibits cardioprotective effect by significantly restoring hemodynamic (mean arterial blood pressure, systolic arterial blood pressure, diastolic arterial blood pressure, and heart rate), biochemical cardiac marker enzymes (lactate dehydrogenase and serum glutamate oxaloacetic transaminase [SGOT]), and histopathological parameters in isoprenaline-induced myocardial necrosis in rats [23].
16. The ethanolic extract of *Azolla microphylla* alleviates myocardial damage of isoproterenol which significantly diminution in cardiac antioxidant enzyme activities, increased lipid peroxidation and alteration in cardiac marker enzymes apart from increasing levels of serum lipid profiles and pro-inflammatory cytokines (IL-6 and IL-8) accompanied with a significant reduction in the anti-inflammatory cytokine levels (IL-10). Treated rats improved energy metabolism of cardiac mitochondria by upregulating and downregulating expressions of Bcl-2 and Bax/iNOS proteins [24].
17. The standardized hydroalcoholic lyophilized extract of *Bacopa monnieri* produced maximum cardioprotection as evidenced by significant restoration of endogenous antioxidants (superoxide dismutase, catalase, glutathione peroxidase, and reduced glutathione), myocyte-specific injury markers (myocardial lactate dehydrogenase and creatine kinase-MB isoenzyme), and decrease in lipid peroxidation marker Myeloperoxidase (MPO) [25].
18. Dose-dependent cardioprotection was observed in the ethanolic extract of *Bixa orellana* as it significantly decreased the serum cardiac marker enzymes, lipid, and MPO levels as well as increased the enzymatic and non-enzymatic antioxidants [26].
19. Anthocyanin-rich red *Brassica oleracea* L. cabbage extract alleviated isoproterenol-induced myocardial infarction by attenuating heart: Body weight ratio, decreasing circulating levels of creatine kinase-MB, improving levels of enzymatic antioxidants (superoxide dismutase and catalase), and favorable modulations of apoptotic markers (bax and bcl-2) [27].

20. The methanol extract of *Buddleja asiatica*, ameliorated the biochemical (creatine kinase-myoglobin, SGOT, lactate dehydrogenase, serum glutamate pyruvate transaminase [SGPT], and total protein) and antioxidant parameters (catalase, superoxide dismutase, reduced glutathione, glutathione peroxidase, glutathione reductase, and MPO) levels significantly in isoproterenol-induced oxidative stress thereby offering significant cardioprotection [28].
21. The alcoholic and aqueous extract of *Caesalpinia crista* Linn (*Caesalpiniaceae*) attenuated the heart damage induced by isoproterenol was indicated by elevated levels of the marker enzymes such as creatine kinase-isoenzyme, lactate dehydrogenase, SGOT, and SGPT in serum with increased lipid peroxide and reduced glutathione content in heart homogenates. Histopathological observation also revealed marked protection by the extract in myocardial necrotic damage [29].
22. Marigold extract *Calendula officinalis* augmented the myocardial antioxidant enzyme level, preserved histoarchitecture and improved cardiac performance by changing marker level following isoproterenol administration [30].
23. Black tea extract (*Camellia sinensis*) reduced the levels of glutathione, thiobarbituric acid reactive substances, superoxide dismutase, catalase, lactate dehydrogenase, and SGOT isoproterenol-induced myocardial infarction in Wistar Albino rats as well as protected the heart by reducing in the infarct size [31].

Protective effect of *Camellia sinensis* floral extract was examined against isoproterenol-induced myocardial infarction in male albino rats. The oral administration of aqueous extract of *C. auriculata* afforded protection against isoproterenol-induced alterations in cholesterol, low-density lipoprotein, high-density lipoprotein, triglyceride, protein, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, catalase, and glutathione peroxidase. The protective effect was further supported by the histological observations. The results clearly demonstrate that *C. auriculata* flowers have a potent cardioprotective effect [32].

25. *Centella asiatica* showed a significant cardioprotective activity by lowering the levels of serum marker enzymes (lactate dehydrogenase and creatine kinase) and lipid peroxidation (MPO) as well as elevated the levels of antioxidant enzymes (reduced glutathione, superoxide dismutase, and catalase) against myocardial infarction induced by isoproterenol [33].
26. Ethanolic extract of root of *Chonemorpha fragrans* strongly protected the myocardium against isoproterenol-induced infarction and elicits cardioprotective effects which could be related to antioxidant activities. Animals treated with root extract of *C. fragrans* showed a significant decrease in triglycerides, aspartate aminotransferase, ALP, antioxidant enzymes, namely, superoxide dismutase, lipid hydroperoxide, and increase in high-density lipoprotein cholesterol [34].
27. Isoproterenol-induced cardiac dysfunction, which was characterized by a significant increase in the heart weight/body weight ratio, serum calcineurin, nitric oxide, lactate dehydrogenase, and thiobarbituric acid reactive substance levels, as well as a significant decrease in serum-reduced glutathione, cardiac glutathione peroxidase, glutathione reductase, and glutathione-S-transferase levels, which were significantly improved by *Cissampelos pareira* root extract treatment [35].
28. The ethanol extracts of *Citrus macroptera* peel and pulp attenuated the isoproterenol-induced severe myocardial injuries associated with oxidative stress, as confirmed by elevated lipid peroxidation and decreased cellular reduced glutathione and antiperoxidative enzymes, including glutathione peroxidase, glutathione reductase, and glutathione-S-transferase. Pretreatment with *C. macroptera* peel and pulp extracts, significantly improved biochemical parameters, i.e., cardiac Troponin I, cardiac marker enzymes, lipid profile, and oxidative stress markers [36].
29. Ethanolic extract of *Citrus medica* L. brought increased lipid peroxidation and alteration of myocyte-injury specific marker enzymes, levels of plasma cholesterol, triglycerides, low-density lipoprotein cholesterol, and very low-density lipoprotein cholesterol parameters toward a normal level which were increased in isoproterenol-induced cardiac dysfunction [37].
30. The level of marker enzyme in serum lactate dehydrogenase, creatine kinase-MB fraction, aspartate transaminase, alanine transaminase, Troponin-I were significantly decreased in rats pretreated with *Coleus forskohlii*. The disruptions of several subcellular elements including myonecrosis, myophagocytosis and lymphocytic infiltration, edema, loss of myofibrils, swelling of mitochondria, vacuolization of the cytoplasm, formation of lysosomal bodies and dilation of the sarcotubule and dilation of the sarcotubular system brought by isoproterenol were restored to normal with extract treatment [38].
31. *Commiphora mukul* was commonly known as guggul significantly reversed the decrease in myocardial antioxidants; superoxide dismutase, catalase, glutathione peroxidase, reduced glutathione, along with enhanced lipid peroxidation; MPO levels in heart against isoprenaline-induced myocardial necrosis in rats. In addition, to improving myocardial antioxidant status, *C. mukul* also prevented the leakage of myocyte injury marker enzymes creatine phosphokinase-MB and lactate dehydrogenase from the heart. Further, histopathological examination showed the lessening of necrosis, edema, and inflammation following *C. mukul* pretreatment [39].
32. *Cordia sebestena* to leaf extract significantly decreased the elevated levels of cardiac marker enzymes such as creatine kinase-MB, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase and ALP in serum, and serum lipid profiles such as high-density lipoprotein, low-density lipoprotein, very low-density lipoprotein, triglycerides, and cholesterol in isoproterenol-induced myocardial infarction in rats [40].
33. *Coriandrum sativum* significantly resisted showed increased lipid hydroperoxide, decreased levels of endogenous antioxidants and ATPases in the cardiac tissue together with increased plasma lipids and markers of cardiac damage in showed increased lipid hydroperoxide, decreased levels of endogenous antioxidants and ATPases in the cardiac tissue together with increased plasma lipids and markers of cardiac damage. The methanolic extract of *C. sativum* is able to prevent myocardial infarction by inhibiting myofibrillar damage [41].
34. Saffron (dried stigmas of *Crocus sativus* L.), exerts cardioprotection in isoproterenol-induced myocardial damage by preserving hemodynamics and left ventricular functions, maintaining structural integrity and augmenting antioxidant status [42].
35. Methanolic extract of *Croton sparsiflorus* showed the significant cardioprotective effect by lowering the serum levels of various biochemical parameters such as creatine phosphokinase, lactate dehydrogenase, and transaminases in the isoproterenol-induced cardiotoxicity model [43].
36. The ethanolic extract of *Cucumis trigonus* fruit decrease in serum enzyme levels and the electrocardiogram (ECG) (increase heart rate, reduced R-wave amplitude, and ST-segment elevation) changes brought to the near normal values which were significantly increased when treated with isoproterenol. Animals treated with *C. trigonus* demonstrated marked improvement in isoproterenol-induced alterations such as vacuolar changes, edema, capillary dilatation, and leukocyte infiltration [44].
37. Hydroalcoholic extract of *Curcuma longa* rhizome significantly reversed myonecrosis caused by isoproterenol through augmentation of endogenous antioxidants (glutathione, thiobarbituric acid reactive substances, catalase, glutathione peroxidase, and superoxide dismutase), maintenance of the myocardial antioxidant status and significant restoration of the altered hemodynamic parameters (systolic, diastolic and mean arterial pressure, heart rate, left ventricular end-diastolic pressure, and left ventricular peak positive (+) dP/dt (rate of pressure development) and negative (−) dP/dt (rate of pressure decline)) [45].
38. The levels of cardiac enzymes such as aspartate transaminase, alanine transaminase, creatinine kinase-myoglobulin, lactate dehydrogenase, and the gold marker Troponin-I altered by isoproterenol were found

to be restored significantly by ethanolic extract of *Cyperus rotundus* on isoprenaline-induced myocardial infarction [46].

39. The levels Na+K+ATPase, Mg2+ATPase, and Ca2+ATPase in heart; serum aspartate transaminase, alanine transaminase, lipid peroxidase, and lactate dehydrogenase levels and cardiac total protein and lipid peroxidase, and lactate dehydrogenase altered by isoproterenol were restored significantly by the administration of the *Daucus carota* extract [47].
40. *Desmodium gangeticum* root extract pretreatment reverted back the altered levels of heart weight, body weight, heart weight / body weight ratio, percent of hypertrophy, collagen accumulation, activities of matrix metalloproteinase-2 and-9, superoxide dismutase and catalase enzymes, and the level of an oxidative stress marker, lipid peroxide to near normal in isoproterenol-induced left ventricular cardiac hypertrophy [48].
41. Isoproterenol-induced rats when pretreated with the flavonoid-rich fraction of *Dioscorea bulbifera* amelioration of the lipid peroxidation and enhancement the antioxidant status as evidenced by the increase in the reduced glutathione content and the activity of antioxidant enzymes was observed. Moreover, the tricarboxylic acid cycle enzymes such isocitrate dehydrogenase, succinate dehydrogenase, malate dehydrogenase, and α-ketoglutarate dehydrogenase, which were found decreased in the isoproterenol-induced rats showed enhanced activity in *D. bulbifera* pretreated rats. The activity of NADH dehydrogenase and cytochrome-C-oxidase the enzymes, which transfer the electron in the electron transport chain was also increased significantly in *D. bulbifera* pretreated rats thereby suggesting its cardioprotective effect [49].
42. Cardamom (*Elettaria cardamomum*) treatment reversed the isoproterenol-induced myocardial injury which caused cardiac dysfunction demonstrated by declined arterial pressure indices, heart rate, contractility, and relaxation along with increased preload; decrease in endogenous antioxidants, superoxide dismutase, catalase, glutathione peroxidase, depletion of cardiomyocytes enzymes, creatine kinase-MB, lactate dehydrogenase, and increase in lipid peroxidation. All these changes in cardiac and left ventricular function as well as endogenous antioxidants, lipid peroxidation, and myocyte enzymes were ameliorated when pretreated with cardamom [50].
43. Aqueous extract of fruits of *Embelia ribes* showed substantial cardioprotective property in a rat model having acute myocardial infarction, induced by isoproterenol by significantly increasing the heart rate, systolic blood pressure, decreasing levels of serum lactate dehydrogenase, serum creatine kinase and myocardial lipid peroxides and significantly decreasing the myocardial endogenous antioxidants (glutathione, superoxide dismutase, and catalase) levels along with reversing the myocardial injury caused by isoproterenol [51].
44. *Emblica officinalis* exhibited significant cardioprotective activity by reversing the isoproterenol-induced cardiotoxicity in rats by increasing mean arterial pressure, heart rate, contractility, and relaxation along with decreased left ventricular end diastolic pressure, increased antioxidant enzymes, superoxide dismutase, catalase and glutathione peroxidase and myocyte-injury-specific marker enzymes, creatine phosphokinase-MB, and lactate dehydrogenase in heart along with restoration of reduced glutathione and decreasing thiobarbituric acid reactive substances beside histopathological salvage of myocardium. The cardioprotective potential of *E. officinalis* is attributed to its potent antioxidant and free radical scavenging activity [52].
45. The hydroalcoholic extract of fruit pulp of *Eugenia jambolana* showed significant cardiopreventive effects on isoproterenol-induced myocardial damage in rats by decreasing oxidative stress parameters, markers of inflammation, cardiac damage markers, and apoptotic markers along with improving cardiac architecture [53].
46. Hydroethanolic *Euphorbia hirta* leaf extract was found to diminish the effect of isoproterenol on the levels of total cholesterol, triglycerides, and low-density lipoprotein with a parallel rise in the level of high-density lipoprotein. The necrosis of myofibrils with inflammatory mononuclear collections and edema caused by isoproterenol was reversed by the administration of extract [54].
47. *Evolvulus alsinoides* administration causes myocardial adaptation by augmenting endogenous antioxidants and protects rat hearts from oxidative stress associated with isoproterenol-induced myocardial injury [55].
48. The aqueous extract of *Garcinia indica* fruit rinds showed a significant reduction in creatine kinase MB fraction, creatine kinase-N-acetylcysteine, lactate dehydrogenase levels, and increase in superoxide dismutase and catalase levels when compared to isoproterenol-induced myocardial damage rats. The cardioprotective effect was also confirmed by histopathology of hearts which showed less necrosis in extract treated rats [56].
49. *Garcinia pedunculata* aqueous fruit extract significantly ameliorated the effect of isoprenaline by reducing the activity of creatine kinase-MB and the levels of ALP, SGPT, respectively. A severe necrotic lesion in the myocardial tissue which was seen with isoprenaline administration was brought to nearly normal cytoarchitecture [57].
50. The methanolic extract of *Gardenia gummifera* root protected the serum levels of cardiac marker enzymes (lactate dehydrogenase, aspartate aminotransferase, and creatine kinase-MB), serum iron and iron binding capacity, uric acid, and ceruloplasmin; antioxidants (catalase, glutathione peroxidase, glutathione reductase, glutathione-S-transferase, and reduced glutathione) and lipid peroxidation (MPO) levels/parameters to fall from the normal levels [58].
51. *Ginkgo biloba* phytosomes and *Ocimum sanctum* extract significant restored isoproterenol depleted activities and levels of endogenous antioxidants (superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and glutathione) heart homogenate. A significant decrease in isoproterenol-induced serum marker enzyme (aspartate aminotransferase, lactate dehydrogenase, and creatine phosphokinase) elevations and a significant attenuation of the isoproterenol elevated myocardial lipid peroxidation marker MPO demonstrates significant cardiac protection of *G. biloba* phytosomes and *O. sanctum* extract [59].
52. Administration of plant extract of *Hybanthus enneaspermus* reduced the oxidative stress by decreased lipid peroxidation and reduced glutathione and also normalized the levels of cardiac marker enzymes such as creatine kinase, lactate dehydrogenase; SGOT, SGPT, and cardiac specify protein Troponin I in myocardial infarction induced by isoproterenol. *H. enneaspermus* treated animals showed a lesser degree of cellular infiltration in histopathological studies [60].
53. The hydroalcoholic leaf extract of *Indigofera tinctoria* Linn. showed decrease in the levels of serum marker enzymes by increase in cardiac total protein; and increased antioxidant levels such as superoxide dismutase, reduced glutathione, and glutathione peroxidase with decreased thiobarbituric acid reactive substances levels in both serum and heart tissue, thereby possessing cardioprotective effect by ameliorating the myocardial infarction induced by isoproterenol [61].
54. *Inula racemosa* root hydroalcoholic extract improved cardiac function by increasing the heart rate, mean arterial pressure, contractility, and relaxation along with decreasing left ventricular end diastolic pressure and also significantly restored the reduced form of glutathione and endogenous antioxidant enzymes superoxide dismutase, catalase, and glutathione peroxidase from the heart, which were depleted after isoproterenol administration. It protects the heart from isoproterenol-induced myocardial injury by reducing oxidative stress and modulating hemodynamic and ventricular functions of the heart [62].
55. The cardioprotective role of *Justicia tranquebareinsis* leaf extract on isoproterenol-induced myocardial infarction in Wistar albino rats is due to decrease in levels of cholesterol, triglycerides, phospholipids, and lipoproteins as well as myocardial marker enzymes [63].
56. The standardized aqueous and 80% ethanol extracts of *Labisia pumila var*. alata showed significant protective effects as pretreated rats showed a significant decrease in cardiac enzyme activities, i.e., cardiac Troponin I, creatine kinase MB isoenzyme, lactate dehydrogenase, alanine transaminase, and aspartate transaminase

and rises in the activity of oxidase enzymes, i.e., glutathione peroxide, catalase, and superoxide dismutase were observed. Histopathological examination showed an improvement in membrane cell integrity in pretreated rats [64].

57. *Lagenaria siceraria* fruit juice showed protective effect against altered biochemical changes such as significant increase in the levels of serum uric acid, tissue Na+ and Ca++ ions, and membrane-bound Ca+2-ATPase activity; decrease in the levels of serum protein, tissue K+ ion, Vitamin E level, and the activities of Na+/K+-ATPase and mg+2-ATPase in isoproterenol-induced myocardial infarction [65].
58. *Lavandula angustifolia* essential oil amended ECG pattern by suppressing ST-segment elevation and increasing R-amplitude. Oil treatment decreased heart to body weight ratio and the elevated myeloperoxidase and MPO in heart tissues suggesting its protective role of myocardium against isoproterenol-induced myocardial infarction [66].
59. The of ethanolic fruit extract of *Limonia acidissima* significantly decreased the cardiac marker enzyme (creatinine phosphokinase and lactate dehydrogenase) and increased the antioxidant enzymes (superoxide dismutase and catalase) signifying it is cardioprotective effect against the acute cardiac damage induced by isoproterenol in rats [67].
60. The flaxseed oil (*Linum usitatissimum*) showed an important inhibition of angiotensin-converting enzyme. It reversed the isoproterenol-induced changes such as ST-segment elevation, increase in the serum levels of Troponin T and cardiac injury markers (creatine kinase-MB, lactate dehydrogenase, ALP, aspartate transaminase, and alanine transaminase). Flaxseed oil also preserved the structural and functional integrity of the myocardial membrane, as evident from the reduction in the activities of cardiac dysfunction markers [68].
61. The methanolic extract of *Marrubium vulgare* significantly amended the ECG changes (ST-segment elevation and suppressed R-amplitude) by isoproterenol injection. The extract strongly increased left ventricular contractility and decreased the left ventricular end-diastolic pressure, and suppressed markedly the elevation of MPO levels both in serum and in myocardium suggesting that the protective effect could be related to antioxidant activities [69].
62. The ethanolic extract of *Medicago sativa* stem pretreatment reversed the lipid profile level, liver marker enzymes (SGPT and SGOT), cardiac marker enzymes (creatine kinase-MB and lactate dehydrogenase), and antioxidants (superoxide dismutase, catalase, glutathione peroxidase, and lipid peroxidase) to near normal than isoproterenol induced rats [70].
63. The polysaccharide extract of *Momordica charantia* pretreatment significantly inhibited increases in heart weight, the heart-weight to body-weight ratio, and infarction size, and ameliorated the increased serum levels of aspartate transaminase, creatine kinase, lactate dehydrogenase, total cholesterol, triglycerides, very low-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol. In addition, *M. charantia* enhanced the activity of superoxide dismutase, catalase, and non-protein sulfhydryls, and decreased the level of lipid peroxidation. It downregulated the expression of pro-inflammatory cytokines (TNF alpha, IL-6, and IL-10), inflammatory markers (nitric oxide, myeloperoxidase, and inducible nitric oxide synthase), and apoptotic markers (caspase-3 and Bax), and upregulated Bcl-2 expression. Pretreatment with *M. charantia* reduced myonecrosis, edema, and inflammatory cell infiltration, and restored cardiomyocytes architecture. This myocardial protective effect of *M. charantia* against isoproterenol-induced myocardial infarction could be related to the enhancement of the antioxidant defense system through the nuclear factor kappa B pathways, and to anti-apoptosis through regulation of Bax, caspase-3, and Bcl-2 [71].
64. The pretreatment with ethanolic extract of *Momordica cymbalaria* prevented the elevation of serum marker enzymes, lactate dehydrogenase, creatinine kinase-MB fraction, aspartate transaminase, alanine transaminase, ALPs, and alterations in the oxidative stress markers such as lipid peroxidase activity, glutathione activity, catalase, and superoxide dismutase cause by isoproterenol myocardial infarction in rats [72].
65. Lyophilized hydroalcoholic extract of *Moringa oleifera* leaf exhibited significant cardioprotective effect by reducing effects on isoproterenol-induced hemodynamic perturbations. Chronic *M. oleifera* treatment resulted in significantly favorable modulation of the biochemical enzymes and prevented the deleterious histopathological and ultrastructural perturbations caused by isoproterenol. The cardioprotective effect may be attributed to its antioxidant, antiperoxidative, and myocardial preservative properties [73].
66. The ethyl acetate soluble fraction of *Morus alba* L. significantly reduced ST segment, heart rate, arterial pressure, pressure rate index, heart weight, lactate dehydrogenase, creatine kinase-MB, and SGOT, whereas the levels of antioxidant enzymes were increased significantly. It reduced the pressor response to catecholamines (isoprenaline) and also showed protection from hypertrophy and degenerative changes in myocardial muscles [74].
67. The aqueous extract of *Muntingia calabura* L. significantly prevented isoproterenol-induced elevation in the levels of the diagnostic marker enzymes (aspartate transaminase and alanine transaminase, lactate dehydrogenase, and creatine phosphokinase). The cardioprotective effect of the *M. calabura* leaf extract is probably related to its ability to strengthen the myocardial membrane by its membrane-stabilizing action [75].
68. *Nelumbo nucifera* leaf extract prevents free radical-mediated myocardial damage and thereby eliminating the acute fatal complications by protecting the membrane damage against isoproterenol-induced infarction. *N. nucifera* leaf extract pretreatment also shows the inhibition of necrosis and reduced inflammation in isoproterenol-induced rats. The free radical scavenging, antioxidant, lipid lowering, and membrane stabilizing properties of leaf extract could be responsible for these effects on histology of the myocardium [76].
69. *Nepeta deflersiana* ethanolic extract pretreatment prevented the depletion of endogenous antioxidants (catalase, superoxide dismutase, non-protein thiol, and nitric oxide) and myocyte injury marker enzymes and inhibited lipid peroxidation MPO. It also downregulated the expression of pro-inflammatory cytokines (TNFα, IL-6, and IL-10) and apoptotic markers (caspase-3 and Bax) and upregulated the anti-apoptotic protein Bcl2. Extract reduced myonecrosis, edema, and infiltration of inflammatory cells and restored the architecture of cardiomyocytes thereby displaying strong antioxidant, cardioprotective, anti-inflammatory, and anti-apoptotic potential against myocardial damage induced by isoproterenol [77].
70. The hydroethanolic extract of *Nerium oleander* Linn. prevented the elevation of marker enzymes such as lactate dehydrogenase, γ-glutamyl transferase, creatine kinase (creatine kinase-MB and creatine phosphokinase), aspartate aminotransferase, alanine aminotransferase, and ALP in plasma when administered before isoproterenol challenge. It significantly attenuated the lipid peroxidation by maintaining the levels of enzymatic (superoxide dismutase and glutathione peroxidase) and non-enzymatic antioxidants (reduced glutathione and nitrite), which was also confirmed histologically [78].
71. Along with very low-density lipoprotein, triglycerides, cholesterol, and free fatty acids, the levels of marker enzymes in serum such as aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, creatine kinase, and tissue lipid profile of triglycerides, cholesterol, and free fatty acids were significantly decreased, whereas the levels of creatine kinase-MB and high-density lipoprotein, low-density lipoprotein in serum and tissue lipid profile of phospholipids were significantly increased in rats pretreated with *Nigella sativa* seeds [79].
72. The ethanolic extract of aerial parts of *Ocimum basilicum* (basil) significantly suppressed the elevation of MPO levels, suppressed ST-segment elevation and severe myocardial necrosis and fibrosis with a sharp reduction in left ventricular contractility and a marked

increase in left ventricular end-diastolic pressure induced by isoproterenol [80].

73. Pretreatment of hydroalcoholic extract of *Ocimum canum* significantly reduced glutathione, aspartate aminotransferase, alanine aminotransferase, creatine phosphokinase, Troponin T, catalase, superoxide dismutase, and lactate dehydrogenase levels and inhibited the lipid peroxidation as observed by the reduced thiobarbituric acid reactive substances levels demonstrate cardioprotective effect against isoproterenol [81].
74. Egyptian sweet marjoram (*Origanum majorana*) leaf powder and marjoram leaf aqueous extract significantly reduced erythrocytosis, granulocytosis, thrombocytosis, shortened clotting time, decrease in relative heart weight, myocardial oxidative stress and the leakage of heart enzymes (creatine phosphokinase, creatine phosphokinase-MB isoenzyme, lactate dehydrogenase, and aminotransferase) in isoproterenol treated rats through reactivating non-enzymatic (reduced glutathione) and enzymatic (catalase, glutathione peroxidase, glutathione S-transferase, and superoxide dismutase) antioxidant defense system and inhibiting the production of nitric oxide and lipid peroxidation in heart tissues [82].
75. Aqueous extract of *Oxalis corniculata* exhibits protective potential against isoproterenol-induced myocardial infarction in rats by decreasing in the activity of cardiac injury marker enzymes such as creatine phosphokinase and lactate dehydrogenase; lipogenic enzyme, glucose-6-phosphate dehydrogenase, and lipid peroxidation products (thiobarbituric acid reactive substances and conjugated dienes) and the concentration of serum lipids. *O. corniculata* exhibits significant antioxidant and radical scavenging activity against 2,2-diphenyl picrylhydrazyl, superoxide, and nitric oxide radicals and was found to be protecting the myocardium against ischemic insult by its antioxidative and antihyperlipidemic activities [83].
76. Red ginseng (*Panax ginseng*) has been shown to possess various ginsenosides that possess cardioprotective potential against isoproterenol-induced myocardial infarction by significantly attenuating isoproterenol-induced cardiac dysfunctions by improving ventricular hemodynamic functions and reducing ST segment and QRS complex intervals along with increasing myocardial injury parameters such as antioxidants [84].
77. The ethanolic leaf extract of *Pandanus odoratissimus* significantly decreased the cardiac marker enzyme creatinine phosphokinase and lactate dehydrogenase and increased the levels of creatinine phosphokinase and lactate dehydrogenase of superoxide dismutase and catalase exhibiting cardioprotective activity against isoproterenol-induced cardiac damage [85].
78. The hydroalcoholic extract of stem bark of *Parkia biglobosa* ameliorated positively biochemical alterations, prevented oxidative stress and histological and morphological changes induced by isoproterenol [86].
79. Ajwa, a special variety of Saudi Arabian dates (*Phoenix dactylifera* L.) is a rich source of nutrients, fibers, and bioactive molecules. While previous studies have shown the therapeutic value of dates phytoconstituents in liver and kidney diseases, etc., its cardioprotective potential remains elusive. We, therefore, investigated the cardioprotective effect of lyophilized Ajwa extract *ex vivo* as well as *in vivo*. Oral administration of extract prevented the depletion of endogenous antioxidants (catalase, superoxide dismutase, non-protein thiol, and nitric oxide) and myocyte injury marker enzymes, and inhibited lipid peroxidation (MPO, myeloperoxidase). As well as downregulated the expressions of pro-inflammatory cytokines (IL-6, IL-10, and TNFα) and apoptotic markers (caspase-3 and Bax), and upregulated the anti-apoptotic protein Bcl2. Extract pretreatment reduced myonecrosis, edema, and infiltration of inflammatory cells and restored the cardiomyocytes architecture [87].
80. The ethanol extract of *Picrorhiza kurroa* rhizomes and roots significantly prevented the isoproterenol-induced myocardial infarction by modulating the changed lipid metabolism in serum and heart tissue to normal [88].
81. *Piper betle* extract favorably modulated hemodynamic (systolic, diastolic, and mean arterial pressure) and ventricular function parameters apart from restoring superoxide dismutase, catalase, glutathione peroxidase, reduced glutathione, and myocyte injury marker enzymes; creatine phosphokinase-MB isoenzyme and lactate dehydrogenase along with reducing the leakage of creatine phosphokinase-MB isoenzyme and lactate dehydrogenase and decreasing lipid peroxidation in the heart against isoproterenol-induced myocardial infarction in rats [89].
82. The methanolic extract of *Piper longum* pretreatment days significantly prevents the damage induced by isoproterenol by decreasing levels of serum myocardial markers creatine kinase-MB and lactate dehydrogenase and histopathological examination evinced by decreased vascular and fatty degeneration, granular disintegration and hyaline necrosis of muscle fibers [90].
83. The methanol extract of *Polygonum glabrum* showed greater cardioprotection by restoring the cardiac marker enzymes (creatine kinase, lactate dehydrogenase, SGOT, SGPT, and total protein) and attenuated the level of plasma lipid profiles plasma total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, and very low-density lipoprotein along with an increase in high-density lipoprotein. In addition, level of myocardial antioxidants significantly increased along with a reduction in the content of MPO against isoproterenol induced myocardial necrosis [91].
84. Pretreatment with the hydroalcoholic leaf extract of *Pongamia pinnata* significantly attenuated the transaminases (aspartate transaminase and alanine transaminase), lactate dehydrogenase and creatine phosphokinase activities thereby offering protection in experimental cardiotoxicity induced by isoproterenol [92].
85. *Punica granatum* seed juice extract attenuates cardiotoxic effects of isoproterenol by reversing thrombus formation, contraction band necrosis and inflammation of myocardium along with restoration of heart rate, pressure rate index, and ECG values to normal. A significant increase in the levels of superoxide dismutase and catalase activity and increased vascular reactivity to various catecholamines and a significant decrease in the levels of cardiac marker enzymes-lactate dehydrogenase and creatine kinase indicate a substantial therapeutic value in the prophylactic treatment of myocardial infarction [93].
86. Alcoholic extract of the stem part of *Rhus tripartita* male genotype significantly mitigated isoproterenol triggered upregulation of cardiac-specific markers of injury creatine kinase and lactate dehydrogenase. Extract treatment significantly attenuated the isoproterenol-induced increase in myocardial MPO, serum cholesterol, and triglycerides as well alterations in serum lipoproteins and decrease in non-protein sulfhydryl in cardiac tissue. Pretreatment with extract enhanced the survival fraction of cardiac cells exposed to oxidative stress [94].
87. *Rhodobryum roseum* elicited a significant cardioprotective effect by augmentation of the endogenous antioxidants and inhibition of lipid peroxidation of the membranes. Significant myocardial necrosis, increase serum marker enzymes (lactate dehydrogenase, glutamate oxaloacetic transaminase, and creatine kinase) by isoproterenol were reversed by pretreatment with ethanolic extract of *R. roseum* [95].
88. Pretreatment with ethanolic extract of *Rhododendron arboretum* prevented the increase in serum and tissue lipid peroxidation, serum cardiac marker enzymes such as lactate dehydrogenase aspartate transaminase and alanine transaminase and the decrease in both enzymatic and non-enzymatic antioxidants in isoproterenol-treated rats [96].
89. Polysaccharide from *Salvia miltiorrhiza* showed the extensive cardioprotective effect on isoproterenol-induced myocardial infarction in rats. Pretreatment with polysaccharide for 30 days significantly increased the body weight, decreased the heart weight, attenuated the serum levels of creatine kinase, creatine phosphokinase-MB, dehydrogenase, alkaline phosphate, aspartate transaminase, alanine transaminase, total cholesterol, triglyceride, and low-density lipoprotein cholesterol, along with the increased concentration of high-density lipoprotein cholesterol. In addition, it also enhanced myocardial superoxide dismutase, catalase, and glutathione peroxidase activities and elevated myocardial reduced

glutathione level, along with a decrease in thiobarbituric acid reactive substances concentration. It produces a cardioprotective effect through enhancement of endogenous antioxidants and antihyperlipidemic activity [97].

90. The aqueous extract of root of *Saussurea lappa* produced significant dose-dependent cardioprotective activity against isoproterenol-induced myocardial injury by reversing the increased serum concentration of lactate dehydrogenase, creatinine kinase, and aspartate transaminase increased myocardial thiobarbituric acid reactive substances level and decreased myocardial glutathione level due to myocardial damage produced by isoproterenol [98].
91. Pretreatment with the ethanolic extract of fruits of *Sechium edule* significantly reduce the levels of serum transaminases, alkaline phosphates, lactate dehydrogenase, creatinine kinase, total cholesterol, triglycerides, low-density lipoprotein cholesterol, very low-density lipoprotein cholesterol, and increase the levels of high-density lipoprotein cholesterol in isoproterenol-induced myocardial necrosis in rats [99].
92. *Sida rhomboidea* extract displays cardioprotective effect by decreasing heart weight, plasma lipid profile, plasma marker enzymes of cardiac damage, cardiac lipid peroxidation, Ca+2 ATPase and significantly increasing plasma high-density lipoprotein, cardiac endogenous enzymatic and non-enzymatic antioxidants, Na+–K+ ATPase and Mg+2 ATPase against isoproterenol induced myocardial necrosis in rats [100].
93. The hydroalcoholic extract of *Semecarpus anacardium* nuts ameliorates the myocardial damage induced by isoproterenol by elevation in superoxide dismutase activity with a simultaneous increase in catalase and thiobarbituric acid reactive substances activity along with a change in biomarkers and antioxidants levels to normal [101].
94. Lycopene isolated from *Solanum lycopersicum* significantly prevented the isoproterenol-induced ECG, hemodynamic (i.e., systolic, diastolic, and mean arterial pressure), biochemical (C-reactive protein, myeloperoxidase, nitrite levels, and caspase-3 protease activity), electrolytes (Na+, K+, and Ca2+), and apoptotic (increase in DNA fragmentation) changes thereby exhibiting significant cardioprotective effect [102].
95. Hydroalcoholic extract of *Solanum nigrum* Linn. reduced the creatine kinase-MB, lactate dehydrogenase, SGOT, SGPT, cholesterol, triglycerides, and Troponin-T to normal values. Treatment with extract significantly reduced the effects of isoproterenol-induced myocardial infarction by attenuating superoxide dismutase, catalase, and glutathione levels [103].
96. Ethanolic extract of *Solanum surattense* was found to be most effective in the reduction of cardiac biomarkers such as creatine kinase-MB and lactate dehydrogenase and restoration of membrane-bound Na+/K+ATPase, tissue antioxidant enzymes such as superoxide dismutase, catalase and glutathione, and histopathological alterations against isoproterenol-induced biochemical alterations [104].
97. Prior treatment with a hydroethanolic extract of *Solanum torvum* significantly decreased the levels of cholesterol, triglycerides, low-density lipoprotein, and increased the levels of high-density lipoprotein in isoproterenol-induced myocardial infarcted rats [105].
98. The hydroethanolic leaf extract of *Solanum xanthocarpum* possesses potent cardioprotective activity as it significantly decreases in the levels of total cholesterol, triglycerides, low-density lipoprotein, and an increase in high-density lipoprotein in isoproterenol-induced rats [106].
99. The 70% ethanolic extract of bark of *Spathodea campanulata* P. Beauv protected myocardium from isoproterenol-induced myocardial functional and structural injury through normalization levels of diagnostic marker enzymes such as serum aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, creatine phosphokinase, triglycerides, total cholesterol, low-density lipoproteins and high-density lipoproteins, and by restoring the glutathione and lipid peroxidation levels. The extract showed remarkable improvement of the cardiac architecture by reversing the focal lesions, fragmentation of muscle fibers and retrogressive lesions over the isoproterenol-treated groups [107].
100. Alterations to markers of myocardial injury and indices of antioxidant capacity by isoproterenol intoxication were significantly corrected on pretreatment with *Spondias mombin*. A significant decrease in the inflammatory index, serum lactate dehydrogenase activity and cholesterol level whereas increase in tissue catalase and superoxide dismutase activities, as well as glutathione level, was noted in extract treated group. Disruption in the structure of cardiac myofibrils by isoproterenol intoxication was reduced by treatment with *S. mombin* [108].
101. Aqueous fruit extract, alcoholic fruit extract, aqueous seed extract, and alcoholic seed extract of *Tamarindus indica* exhibited cardioprotective activity against isoproterenol hydrochloride-induced myocardial infarction in rats by reversing the increase in serum marker enzymes, an increase in the percent infarction area increase in heart weight and a decrease in body weight along with the decrease in endogenous enzyme levels. Pretreatment and cotreatment with the various extracts decreased the heart rate, ST segment elevation, and QT interval, while an increased RR interval was observed against infract induced control [109].
102. The 70% ethanolic extract of *Tecoma stans* prevented fall in antioxidants such as lipid peroxidation, superoxide dismutase, reduced glutathione, and catalase and retarded elevation of cardiac damage markers such as alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, creatinine kinase, total cholesterol, triglycerides, low-density lipoproteins, and high-density lipoproteins in isoproterenol-treated rats, significantly [110].
103. The ethanol and aqueous extracts of *Terminalia arjuna* bark significantly restored the level of total cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein and myocardial and serum of lactate dehydrogenase, creatine kinase, and aspartate aminotransferases which were altered by isoproterenol induction [111].
104. Cardioprotective effect of ethanolic extract of *Terminalia chebula* fruits in isoproterenol-induced myocardial damage in rats is due to decrease in the level of lipid peroxides and myocardial marker enzymes in the serum and heart [112].
105. Ethanolic extract of *Terminalia pallida* fruits reversed the significant increase in total cholesterol, triglycerides, low-density lipoprotein cholesterol, and very low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and MPO and a significant decrease in high-density lipoprotein-C, cardiac marker enzymes-creatine kinase, lactate dehydrogenase, alanine transaminase, aspartate transaminase and reduced antioxidants-catalase, glutathione peroxidase, sodium potassium, calcium, and magnesium ATPs caused by isoproterenol [113].
106. The ethanolic extract of *Terminalia belerica* extract has efficiently protected the myocardium against isoprenaline-induced myocardial infarction by ameliorating the enzymes creatine kinase, lactate dehydrogenase, alanine aminotransferase, and aspartate aminotransferase to normal [114].
107. The methanolic extract of *Tinospora cordifolia* significantly restored the altered levels of heart, heart weight/body weight ratio, and cardiac enzymes such as aspartate transaminase, alanine transaminase, creatinine kinase, lactate dehydrogenase, and Troponin-I in myocardial infarction caused by isoproterenol [115].
108. Hydroalcoholic lyophilized extracts of *Tribulus terrestris* upregulated heat shock protein 70; increased basal superoxide dismutase, catalase activity and caused a marked fall in basal thiobarbituric acid reactive substances levels. The significant augmentation of myocardial glutathione content and glutathione peroxidase activity following isoproterenol-induced myocardial injury fortified the cardioprotective activity of *T. terrestris* [116].
109. 70% ethanolic extract of *Trichopus zeylanicus* leaves offered cardioprotection by alterations and restoration of the cardiac markers such as aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, and creatine phosphokinase to normal levels against isoproterenol-induced myocardial ischemia [117].

110. The ethanolic extract of *Trigonella foenum-graecum* significantly decreased blood glucose, bilirubin, total cholesterol, triglyceride and low-density lipoprotein level, myocardial lactate dehydrogenase, creatine kinase total, and creatine kinase-MB levels; and the high-density lipoprotein level was returned back to normal in isoproterenol-induced myocardial infarction. Marked myocytic necrosis with moderate infiltration of lymphocytes and macrophages was reversed by *T. foenum-graecum* pretreatment [118].
111. Ethanolic extract of *Urtica parviflora* reversed the effects of isoproterenol-induced myocardial infarction in rats by effectively controlling serum low-density lipoprotein levels and reducing cardiac complication by decreasing the levels of serum cholesterol, alanine transaminase, aspartate aminotransferase, ALP and increasing the levels of superoxide dismutase, catalase, and reduced glutathione [119].
112. The methanolic extract of *Ventilago maderspatana* pretreatment has shown cardioprotective activity significantly by reducing the concentration of cardiac injury marker enzymes (creatine kinase-MB, Lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, and ALP) and serum lipids (total cholesterol levels, low-density lipoprotein, high-density lipoprotein, and triglycerides) against isoproterenol-induced myocardial infarction [120].
113. The prior administration of *Vitex negundo* leaf ethanolic extract is effective in minimizing all the deleterious and myocardial infarction related effects induced by isoproterenol, with its capacity to fortify the myocardial cell membrane and heart tissue architecture, and also by normalizing biochemical and molecular parameters such as cardiac marker enzymes (creatine kinase-heat specific, creatine kinase, lactate dehydrogenase and gamma glutamyl transferase, aspartate transaminase, and alanine transaminase), antioxidant enzymes (reduced glutathione, glutathione s-transferase, and glutathione peroxidase), and signaling molecules (p21 activated kinase 1 and nuclear factor-kB) [121].
114. Ethanolic extract of seeds of *Vitis vinifera* significantly prevented the isoproterenol-induced elevation in the levels of diagnostic marker enzymes (aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase) and lipid peroxidation in plasma, indicating the cardioprotective activity [122].
115. Significant cardioprotective effects were observed on protein, urea, creatinine, serum lipid profile, cardiac marker enzymes, and antioxidants, when treated with hydroethanolic extract of *Wedelia, Chinensis* against isoproterenol-induced myocardial infarction in rat [123].
116. *Withania somnifera* leaf extract preserves the integrity of myocardial cell membrane by maintaining the activities of cardiac Troponin I levels and serum lipid profiles, as well as the activities of marker enzymes of isoproterenol-induced myocardial infarction. Cardioprotective activity may be due to antilipoperoxidative and antioxidant effects [124].
117. Gingerols and shogaols present in *Zingiber officinale* showed decrease in all the cardiac enzyme activities, i.e., cardiac Troponin I, creatine kinase-MB isoenzyme, lactate dehydrogenase, alanine transaminase, and aspartate transaminase against isoproterenol-induced myocardial infarction along with significant rises in the activity of glutathione peroxide, catalase, and superoxide dismutase apart from improvement in membrane cell integrity [125].

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