

Pharmacologically Active Cardioprotective Plants at a Glance

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Cardiovascular diseases remain a leading cause of death in the developed and developing countries. The prevalence of coronary artery disease in rural as well as urban India is increasing day by day. The main reason for this increase is lifestyle changes such as sedentary jobs, improvement in socio-economic status leading to unhealthy diet rich in fats, high stress jobs and the addictions like smoking and tobacco chewing.

Great Unani philosopher, Ibn Nafees was the first to describe the circulatory system of the human body, whereas Ibn Sina, described the causes of cardiac diseases in details in his treatise namely *Risala-e-Advia Qalbiya*. He also mentioned drugs having cardioprotective as well as the cardiostimulant properties. This review deals with medicinal plants possessing cardioprotective and cardiostimulant activity. This review work explains chemical and pharmacological status of various cardioprotective plants including phytoconstituents responsible for cardioprotection, dosage, pharmacological screening model and mechanism involved in cardioprotection. Unani or local name of the drug is mention in parenthesis with the Latin name. This review will definitely help in assessing the quantum of work done on cardioprotective plants.

Keywords: Cardioprotective, Cardiostimulant, Muqawwi-e-Qalb, Unani medicine.

Introduction

Cardiovascular disease remains a leading cause of death in developed and developing countries. There is lesser prevalence in rural area being estimated to be upto 7% as compared to the urban areas where the incidence is upto 12%.

The main reason for these diseases is lifestyle changes that include sedentary jobs, unhealthy diets, stress and addictions like smoking and

tobacco chewing. These changes lead to the development of diabetes and obesity which in turn is the most important aggravating factor for cardiovascular diseases. Great Unani physician Ibn Sina (980-1037 A.D.) has described the causes, sign and symptoms of cardiovascular diseases and their management in his book *Risala-e-Advia Qalbia*. Ibn Sina was the first who mentioned that the human heart reacts to emotions such as pleasure, sorrow, fear etc. (Hameed, 1983). Feelings and emotions of a person are directly related to cardiovascular system. The Unani system of medicine takes a holistic view of the disease and targets to improve functions of an organ through protection and strengthening by organ specific tonics. In case of cardiovascular diseases not only cardioprotective drugs but also cardiotonic drugs have been described to maintain the internal (innate) immunity of the organ. It is believed that herbal drugs give comprehensive relief to the people suffering from cardiovascular diseases specially hyperlipidemia, ischemic heart disease hypertension, congestive heart failure and post myocardial infarction. Following are some medicinally important plants which have been shown to possess beneficial effects towards cardiovascular system.

1. *ACORUS CALAMUS* LINN. (WAJ TURKI)

Acorus calamus Linn. rhizome extract significantly reduces calcineurin, nitric oxide, lactate dehydrogenase, and thiobarbituric acid-reactive substance levels, glutathione, glutathione peroxidase, glutathione reductase, and glutathione-S-transferase levels and heart weight/body weight ratio (Singh *et al.*, 2011).

2. *ALLIUM CHINENSE*

Allium chinense potentially prevented cardiac injuries induced by oxidative stress injury of H9C2 cells in an experimental study (Ren *et al.*, 2010).

3. *ALLIUM SATIVUM* (SEER)

Experimental and clinical studies confirm that garlic and its various forms reduce cardiovascular risk, including abnormal plasma lipids, oxidized low density lipoproteins (LDL), abnormal platelet aggregation and a high blood pressure inhibiting the rate of progression of coronary calcification. Garlic as a dietary component appears to hold promises to reduce the risk of cardiovascular disease (Ginter *et al.*, 2010). Garlic extract appeared to be cardioprotective effect in doxorubicin-induced cardiotoxicity in rats model compared to control group by determining malondialdehyde, superoxide dismutase, catalase, xanthine oxidase levels, and creatine kinase

(Demitkava *et al.*, 2009). Freshly crushed garlic supported cardioprotective effect by phosphorylation of antiapoptotic ERK1/2 proteins, reduced Bax/Bcl-2 ratio, and reduced phosphorylation of proapoptotic p-38MAPK and JNK in comparison to processed garlic due to presence of H₂S (Mukherjee *et al.*, 2009). Garlic powder significantly decreased total cholesterol level and increased HDL levels in test group patients as compared to control group (Sobenin *et al.*, 2008). Aqueous garlic contains organosulfur compounds, S-allylcysteine and diallyl sulphide inhibit lipid peroxidation and prevent depletion in glutathione favouring cardioprotective actions (Sener *et al.*, 2007). Garlic showed cardioprotective effect by significantly reducing the ventricular tachycardia and ventricular fibrillation during 20 min occlusion of the descending branch of the left coronary artery, it also reduces the infarction size (Isensee *et al.*, 1993).

4. *ALLIUM URSINUM*

Wild garlic also showed cardioprotective effect by significantly reducing the ventricular fibrillation during 20 min occlusion of the descending branch of the left coronary artery in experimental study (Rietz *et al.*, 1993).

5. *ANETHUM GRAVEOLENS (HAAZA)*

Anethum graveolens induced cardioprotective effect by lowering lipid in high cholesterol fed diet in rats (Hajhashemi and Abbasi, 2008).

6. *ANGELICA SINENSIS*

Aqueous extract of *Angelica sinensis* significantly improved heart performance by normalization of antioxidative activity and serum AST, preventing loss of myofibrils as well as improving arrhythmias and conduction abnormalities in doxorubicin-induced cardiac toxicities in mice (Xin *et al.*, 2007).

7. *ARALIA MANDSHURICA*

Aralia mandshurica showed cardioprotective effect by preventing the appearance of ventricular arrhythmias (Arbuzov *et al.*, 2009). and increasing the cardiac resistance to the arrhythmogenic action of coronary artery occlusion (Maslov and Guzarova, 2007).

8. *ASTRAGALI RADIX*

Astragali radix prevented myocardial injury by the attenuation of

sarcoplasmic reticulum Ca²⁺-ATPase mRNA and protein expression as well as Ser (16)-phosphorylated phospholamban protein expression in isoproterenol-treated rats (Xu *et al.*, 2008).

9. *ASTRAGALUS MEMBRANACEUS* (FISCH.) BGE.

Astragalus membranaceus (Fisch.) Bge., improves cardiac function by upregulation of SERCA2a expression in adriamycin injured rat hearts (Su *et al.*, 2009).

10. *AZADIRACHTA INDICA* A. JUSS. (NEEM)

Aqueous leaves extract of *Azadirachta indica* A. Juss. significantly showed cardioprotective actions by restoring the haemodynamic, biochemical and histopathological parameters in isoprenaline-induced myocardial infarction in rats (Peer *et al.*, 2008).

11. *MOMORDICA CHARANTIA* (KARELA/BITTER MELON)

Bitter melon seed exerted cardioprotective effects by down-regulating the nuclear factor-kappa-B (NF- κ B) inflammatory pathway by adipose tissue, expression of peroxisome proliferator-activated receptor gamma (PPAR- γ), nuclear factor- κ B, and interferon- γ mRNA in heart tissue of the female Zucker obese rats. (Gadang *et al.*, 2011).

12. BLACK RICE

Black rices cardioprotective effect was due to anthocyanins protection (Abdel-Moemin *et al.*, 2011).

13. *VACCINIUM CORYMBOSUM* (BLUEBERRIES)

Seven phenolic acids of blueberries demonstrated potential cardioprotective and atheroprotective effects in lipopolysaccharide-induced mRNA expression and protein levels of pro-inflammatory cytokine TNF- α and IL-6 by reducing mitogen-activated protein kinases Jun N-terminal kinase, p38, and Erk1/2 phosphorylation 7PA increased expression and protein levels of ATP-binding cassette transporter A1 (ABCA1), which facilitates cholesterol efflux and reduces cholesterol accumulation in macrophages in the rodent model (Xie *et al.*, 2011). Blueberry also protected the myocardium from ischemic damage in permanent ligation of the left descending coronary artery in experimental rats (Ahmet *et al.*, 2009).

14. *BRASSICA OLERACEA* (BROCCOLI)

Its aqueous slurry improved postischemic ventricular function, reduced myocardial infarct size, decreased cardiomyocyte apoptosis accompanied by reduced cytochrome C release and increased pro-caspase 3 activities in comparison to control group (Mukherjee and Gangopadhyay, 2008).

15. *CALENDULA OFFICINALIS* (MARIGOLD)

Calendula strengthens the concept of using natural product in degenerative diseases e.g. ischemic heart disease. It activated Akt and Bcl2 and depression of TNF alpha and showed cardioprotection by stimulating left ventricular developed pressure and aortic flow as well as by reducing myocardial infarct size and cardiomyocyte apoptosis (Ray *et al.*, 2010).

16. *CAMELLIA OLEIFERA* ABEL.

Sasanguasaponin of *Camellia oleifera* Abel. decreases the incidences of arrhythmias and improve the heart functions in ischemia-reperfusion (I/R) injury isolated rat heart (Liao *et al.*, 2009).

17. *CANNABIS* (QINNAB)

Cannabidiol reduced infarct size, myocardial inflammation, interleukin-6 levels in transient ligated left anterior descending coronary artery-induced myocardial ischemic reperfusion injury (Durst *et al.*, 2007).

18. *CARTHAMUS TINCTORIUS* L. (QURTUM)

Extract of *Carthamus tinctorius* showed cardioprotective effects by scavenging of reactive oxygen species scavenging and mediating the PI3K signaling pathway through reducing oxidative stress induced damage and apoptosis (Han *et al.*, 2009).

19. *CHRYSANTHEMUM MORIFOLIUM* RAMAT

C. morifolium attenuated the reduced ischemia/reperfusion, increased peak velocity of cell shortening/relengthening and contraction amplitude of isolated ventricular myocytes of left ventricular developed pressure, and coronary flow caused by ligation of left coronary descending artery (Jiang *et al.*, 2004).

20. CLERODENDRON COLEBROOKIANUM WALP.

Crude and organic extracts of *Clerodendron colebrookianum* Walp. significantly lowered the serum total cholesterol, triglycerides and low density lipoprotein in high-fat diet fed rats (Devi and Sharma, 2004).

21. COCUS NUCIFERA (COCONUT KERNEL/NARJEEL)

Coconut kernel significantly decreased creatinine phosphokinase, glutamate oxaloacetate transaminase and glutamate pyruvate transaminase in serum in isoproterenol-induced myocardial infarction (Mini and Rajamohan, 2002).

22. COMMIPHORA MUKUL (MUQIL)

Hydroalcoholic extract of *C. mukul* significantly improved the cardiac function and prevented myocardial ischemic impairment manifested in the form of increased heart rate, decreased arterial pressure, increased left ventricular end diastolic pressure, and altered myocardial contractility indices against cardiac dysfunction in isoproterenol-induced ischemic rats (Ojha *et al.*, 2008).

23. CORIANDRUM SATIVUM L. (KISHNEEZ)

Its extract elicited cardioprotective effect by significantly decreasing the total cholesterol, and triglycerides (Aissaoui *et al.*, 2011). Methanolic extract significantly prevented or resisted increased LPO, decreased levels of endogenous antioxidants and ATPases in the cardiac tissue together with increased plasma lipids and markers of cardiac damage Isoproterenol-induced cardiotoxicity model in male Wistar rats (Patel *et al.*, 2012).

24. VACCINIUM OXYCOCCOS (CRANBERRY)

Cranberry juice significantly showed cardioprotective indices by increasing plasma HDL-cholesterol concentration in abdominally obese men (Ruel *et al.*, 2006).

25. CRATAEGUS

Water-soluble fraction of crataegus increases coronary flow in the ischemic-reperfused heart (Nasa *et al.*, 1993).

26. CRATAEGUS OXYCANTHA (AQSI)

Alcoholic extract improved antioxidant enzymes rate of adenosine diphosphate stimulated oxygen uptake in isoproterenol-induced reduction in them (Jayalakshmi and Devaraj, 2004). Hydroalcoholic extract attenuated the elevation of the ST-segment in the ECG, diminished the incidence of ventricular fibrillations and reduced the mortality rate in ligation of the left coronary artery (Veveris *et al.*, 2004).

27. CRATAEVA NURVALA (BARNA)

Lupeol, a pentacyclic triterpene, isolated from *C. nurvala* stem bark reduced lactate dehydrogenase and creatine phosphokinase in serum against cyclophosphamide-induced cardiotoxicity (Sudharsan *et al.*, 2005).

28. CROCUS SATIVUS L. (ZAFRAN)

Crocin, a pharmacologically active constituent of *C. sativus* L. showed cardioprotective effect in histopathological and ultrastructural examinations in isoproterenol-induced cardiac toxicity through modulation of oxidative stress (Goyal *et al.*, 2010).

29. CURCUMA LONGA (ZARD CHOB)

C. longa significantly reduced myocardial infarction developed after ischemia-reperfusion induced myocardial injuries (Mohanty *et al.*, 2004).

30. CYMBOPOGON CITRATES (LEMON GRASS/GANDANA)

Cymbopogon citrates extract significantly decreased cardiac markers in serum and increases the same in heart homogenate in Wistar albino rats (Gayathri *et al.*, 2011).

31. CYNODON DACTYLON (DOOB/NAJM)

Aqueous extract showed the cardioprotective activity by lowering the cholesterol; low density lipoprotein and triglyceride levels and increasing the high density lipoprotein levels in streptozotocin-induced diabetic rats (Singh *et al.*, 2007).

32. DENDROPANAX MORBIFERA LEVEILLE

Its essential oil demonstrated significant lipid-lowering effects and

emerged as a promising agent that should be considered safe, and effective natural cardioprotective agents (Chung *et al.*, 2009).

33. *ELEUTHEROCOCCUS SENTICOSUS*

Eleutherococcus senticosus extract prevented the stress-induced damages by isoproterenol in rat heart (Maslov and Guzarova, 2007).

34. *EMBELIA RIBES BURM (BAOBARANG)*

Aqueous extract showed cardioprotective activity by enhancing the antioxidant defense against isoproterenol-induced myocardial infarction in rats (Bhandari *et al.*, 2008).

35. *EMBLICA OFFICINALIS (AMLA)*

Emblicanin-A and B significantly showed the antioxidant and cardioprotective activity by decreasing cardiac superoxide dismutase, catalase and glutathione peroxidase in ischemia-reperfusion-induced oxidative stress in rat heart (Bhattacharya *et al.*, 2002).

36. *ERIGERON BREVISCAPUS*

A flavonoid, breviscapine, extracted from *Erigeron breviscapus* significantly reduced ST-segment elevation and infarction size in dog hearts subjected to myocardial infarction caused by left coronary artery ligation and lactate dehydrogenase (LDH) leakage, changes of intracellular free Ca²⁺ levels, apoptosis and necrosis (Li *et al.*, 2004).

37. *EURYALE FEROX (TALMAKHANA)*

The hearts of the makhana treated rats were resistant to ischemic reperfusion injury as evidenced by their improved post-ischemic ventricular function and reduced myocardial infarct size in isolated rat hearts preperfused for 15 min with Krebs Henseleit bicarbonate buffer and makhana-treated hearts had increased amounts of thioredoxin-1 (Trx-1) and thioredoxin-related protein-32 (TRP32) compared to the control hearts (Das *et al.*, 2006).

38. *FRUCTUS CHORSPONDIATIS*

Total flavonoids of *Fructus chorspondiatis* suppressed the variation of J points in electrocardiogram and inhibited the upregulated serum level

of creatine kinase, creatine kinase-MB, and lactate dehydrogenase in isoproterenol-induced myocardial ischemia in rats (Ao *et al.*, 2007).

39. *GINKGO BILOBA*

Phytosomes of *Ginkgo biloba* significantly lowered the lipid peroxidation, and restored antioxidant activities (Panda and Naik, 2009). Elevated glutathione, superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase in isoproterenol-induced oxidative damage in rats (Panda and Naik, 2008). Extract significantly increased distal left anterior descending coronary artery blood flow in maximal diastolic peak velocity, and diastolic time velocity integral compared with the control group patients (Wu *et al.*, 2007). It also restrained the creatine kinase outflow in the perfusate from the hearts and release of prostacyclin in hearts (Carini *et al.*, 2001). Ginkgolides A and B showed cardioprotection against myocardial ischemia-reperfusion injury and improved myocardial functional (Liebgott *et al.*, 2000; Fitzl *et al.*, 1999; Pietri *et al.*, 1997).

40. *PANAX GINSENG* (GINSENG)

Ginseng treatment protects the heart from myocardial ischemia and reperfusion (I/R) injury via upregulation of eNOS expression. (Wu *et al.*, 2011). Ginsenosides decreased the heart rate both *in vivo* and *in vitro* also inhibited contractility of isolated heart and atrium and exhibited negative inotropic effect in the experiments with isolated cardiomyocytes. Ginsenosides shortened duration of the action potential and decreased the amplitude of slow action potential in cardiac cells. There is evidence that ginsenosides inhibit Ca²⁺ channels. Triterpenoid saponins of ginseng improved the cardiac tolerance to ischemic and reperfusion damage both *in vivo* and *in vitro* and also increased cardiac resistance to the toxic action of isoproterenol and adriamycin. Ginsenosides prevented the appearance of ischemic/reperfusion arrhythmias and decreased the incidence of arrhythmias induced by epinephrine, protein kinases, NO synthase, K(ATP) channels, and Ca²⁺ channels (Maslov and Konkovskaia, 2009).

41. *GLEDITSIA SINENSIS* LAM.

Echinocystic acid, a pentacyclic triterpene from the fruits of *Gleditsia sinensis* Lam., showed cardioprotective effect by preventing the ST-segment depression induced by isoproterenol or vasopressin in a dose-dependent manner (Wu *et al.*, 2009).

42. GLYCYRRHIZA URALENSIS

Glycyrrhiza uralensis extract significantly decreased the levels of serum LDH and creatine kinase isoenzyme (CK-MB), improved heart morphology and increased glutathione peroxidase ((GSH-P)(X)) activity and glutathione (GSH) level in doxorubicin-induced cardiotoxicity (Zhang *et al.*, 2011).

43. CAMELLIA SINENSIS (GREEN TEA)

Green tea extract significantly ameliorated the aspartate transaminase (AST), lactate dehydrogenase (LDH) and creatine kinase (CPK) in streptozotocin-induced diabetes rats and significant increase in collagen linked Maillard-type fluorescence and decrease in collagen solubility in the myocardium of diabetic rats as compared to control. The ameliorating myocardial collagen characteristics may provide a therapeutic option in the treatment of cardiovascular complications of diabetes (Babu *et al.*, 2007).

44. CORYLUS AVELLANA LINN. (HAZELNUT)

Hazelnut provided cardioprotective effect in doxorubicin-induced cardiotoxicity in rats model by determining malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), xanthine oxidase (XO) levels, and creatine kinase (CK) (Demitkava *et al.*, 2009).

45. HEMIDESMUS INDICUS (L.) R.Br. (USHBA)

Hemidesmus indicus (L.) R.Br. showed cardioprotective activity by improving functional recovery in reperfusion arrhythmias, and decreasing infarct size (TTC staining) (Khandelwal *et al.*, 2011).

46. HERBA LEONURI

Extract of *Herba leonuri* demonstrated antioxidant activity by reducing superoxide dismutase and glutathione peroxidase, especially in the acute phase of acute myocardial infarction in rats (Sun *et al.*, 2005).

47. Hibiscus rosa-sinensis L. (Gurhal)

Hibiscus rosa-sinensis L. showed cardioprotective activity by improving functional recovery in reperfusion arrhythmias, and decreasing infarct size (Khandelwal *et al.*, 2011). Dried flower significant increases

superoxide dismutase, reduced glutathione, and catalase levels, myocardial thiobarbituric acid reactive substances *in vivo* myocardial ischemic reperfusion injury in isoproterenol-induced myocardial necrosis (Gauthaman *et al.*, 2006).

48. *HIBISCUS SABDARIFFA*

Aqueous extract of petals of *Hibiscus sabdariffa* reduced systolic blood pressure, heart rate in renovascular hypertension induced by left renal artery clamping (Odigie *et al.*, 2003). Crude hydroalcoholic extract showed angioprotective activity *in vivo* by appreciable enzyme-inhibiting activity towards the Angiotensin I converting enzyme (Jonadet *et al.*, 1990).

49. *HIPPOPHAEA RHAMNOIDES* (UQAAS/ABUQANAS)

Seed oil significantly showed anti-atherogenic and cardioprotective activity by decline LDL-cholesterol, total cholesterol, triglycerides, also decreased accumulation of cholesterol on aorta in high cholesterol diet feed albino rabbits (Basu *et al.*, 2007).

50. *HYDROCOTYLE ASIATICA* L. (MANDOK BRAHMI)

Alcoholic extract of *Hydrocotyle asiatica* Linn. limited ischemia-reperfusion-induced myocardial injury (Pragada *et al.*, 2004).

51. *ILEX PARAGUARIENSIS*

Ilex paraguariensis extract attenuates the myocardial dysfunction provoked by ischemia and reperfusion (Schinella *et al.*, 2005).

52. *INULA RACEMOSA* (RASAN)

Hydroalcoholic extract significantly decrease mean arterial pressure, heart rate, contractility, relaxation along with increased left ventricular end diastolic pressure, endogenous myocardial enzymatic and non-enzymatic antioxidants and prevented the leakage of myocytes specific marker enzymes creatine phosphokinase-MB and lactate dehydrogenase from the heart in isoproterenol induced myocardial infarction in rats (Ojha *et al.*, 2011; Ojha *et al.*, 2010). Alcohol extract showed anti-atherogenic cardioprotective and anti-obesity effect in high-fat diet taking guinea-pigs (Mangathayaru *et al.*, 2009).

53. KAEMPFERIA PARVIFLORA

Ethanol extract exerted vasorelaxation action in isolated rat aorta and inhibited superoxide radical generation induced by xanthine. It also attenuated the ventricular dysfunction caused by 20 min global ischaemia and 30 min reperfusion (I/R) in rat isolated hearts (Malakul *et al.*, 2011).

54. KIWI FRUIT

Consumption of two or three kiwi fruits per day reduced platelet aggregation response to collagen and ADP as well as lowered blood triglycerides levels (Duttaroy and Jorgensen, 2004).

55. LAGENARIA SICERARIA STAND. (KADU DARAAZ)

Methanolic extract of fruits exhibited antihyperlipidemic effect and has valid scientific basis for consuming it in the treatment of coronary artery diseases (Ghule *et al.*, 2009).

56. LEUZEA CARTHAMOIDES

Extract prevented the development of stress-induced damage in rat heart by elevating the level of beta-endorphin and increases the level of opioid peptides (Maslov and Guzarova, 2007).

57. LIGUSTICUM WALLICHII FRANCHAT

Tetramethylpyrazine, an active ingredient of *Ligusticum wallichii* Franchat showed cardioprotective effect by significantly suppressing the occurrence of ventricular fibrillation, After 45 min of ischemia and 1 hr of reperfusion, and reduction in infarct size induced HO-1 expression in ischemic myocardium (Chen *et al.*, 2006).

58. LIMONIUM WRIGHTII

Aqueous extracts significantly attenuated ischemic contracture during ischemia and improved myocardial dysfunction after reperfusion having cardioprotective effects against myocardial ischemia-reperfusion injury in isolated rat hearts (Yamashiro *et al.*, 2003).

59. LYCIUM BARBARUM (CHIRCHITTA)

Elicited a typical cardioprotective effect, loss of myofibrils and

improved the heart function normalizing oxidative activity and serum aspartate aminotransferase and creatine kinase, as well as improving arrhythmias and conduction abnormalities in doxorubicin-induced cardiotoxicity in rats (Xin *et al.*, 2007).

60. *LYCOPERSICON ESCULENTUM* (TAMATAR)

Lycopene, lutein, and zeaxanthin of *Lycopersicon esculentum* exhibited better cardiac performance, reduced myocardial infarct size, decreased number of apoptotic cardiomyocytes, and reduced oxidative stress (Morelli *et al.*, 2006). Consumption of tomato reduces cardiovascular diseases risk and reduction of low-density lipoprotein, cholesterol, homocysteine, platelet aggregation, and blood pressure (Willcox *et al.*, 2003).

61. *MAGNOLIA OFFICINALIS*

Magnolol, an active component of *Magnolia officinalis* show potent inhibitory effects on cell proliferation in cultured vascular smooth muscle cells in the presence of TNF-alpha (Kim *et al.*, 2007).

62. *MORINGA OLEIFERA* (SAHANJNA)

Hydroalcoholic extract of leaf showed antioxidant, antiperoxidative, and myocardial preservative properties by prevented isoproterenol-induced myocardial damage in rats (Nandave *et al.*, 2009).

63. *MORUS ALBA* (SHAHTOOT)

Morus alba showed cardioprotective effect against doxorubicin-induced cardiotoxicity (Wattanapitayakul *et al.*, 2006).

64. *NASTURTIUM OFFICINALE* R.Br. (QURATUL AIN/JARJIR)

Hydroalcoholic extract lowered serum total cholesterol, triglyceride, low density lipoprotein, serum aspartate aminotransferase and alanine aminotransferase and raised the high density lipoprotein cholesterol in high-fat diet fed rats (Bahramikia and Yazdanparast, 2008).

65. *NERIUM OLEANDER* LINN.

Hydroethanolic extract of flower elicited cardioprotective activity against isoproterenol-induced myocardial toxicity in experimental rats

prevented the elevation of marker enzymes such as lactate dehydrogenase (LDH), \hat{I}^3 -glutamyl transferase (GGT), creatine kinase (CK-MB and creatine phosphokinase [CPK]), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) in plasma. (Gayathri *et al.*, 2011).

66. *OCIMUM SANCTUM* (RAIHAAN)

Fixed oil of *Ocimum sanctum* normalized the high serum levels of LDH and CK-MB oil in rats fed with a high fat (HF) diet profile expressed cardioprotective actions (Suanarunsawat *et al.*, 2011). Extract also significantly decreased lipid peroxidation and restored antioxidant activities in isoproterenol induced myocardial necrosis in rats (Panda and N., 2009). Hydroalcoholic extract significantly reduced glutathione, superoxide dismutase and LDH levels, lipid peroxidation thiobarbituric acid reactive substances levels in isoproterenol-induced myocardial infarction in rats (Sharma *et al.*, 2001).

67. *PANAX GINSENG*

Panax ginseng showed cardioprotective effect by decreasing the incidence of ventricular fibrillation during ischemia (Arbuzov *et al.*, 2009).

68. *PANAX NOTOGINSENG*

Panax notoginseng saponins significantly improved ventricular contractile function lowerd levels of serum lactate dehydrogenase, creatine kinase and creatine kinase isoenzyme in hearts (Liu *et al.*, 2008).

69. *PANAX QUINQUEFOLIUS*

Extract significantly decreased oxygen free radicals, and cell death exposed to H₂O₂ against oxidant-mediated injury (Shao *et al.*, 2004).

70. *PASSIFLORA ALATA* DRYANDER

The leaf extract showed significant decline in cardiac TBARS levels on carbon tetrachloride-treated rats (Rudnicki *et al.*, 2007).

71. *PHYLLANTHUS EMBLICA* (AMLA)

Ethanollic extracts showed cardioprotective effect against doxorubicin-induced-cardiotoxicity (Wattanapitayakul *et al.*, 2006).

72. *PHYLLANTHUS URINARIA* L.

Ethanol extract showed cardioprotective activity against doxorubicin-induced cardiotoxicity (Chularojmontri *et al.*, 2005).

73. *PICRORRHIZA KURROA* (KUTKI)

Ethanol extract significantly showed cardioprotective activity in isoproterenol-induced myocardial infarction in rats (2001).

74. *PIPER ROSTRATUM* ROXB.

Ethanol extracts showed cardioprotective effect against doxorubicin-induced cardiotoxicity (Wattanapitayakul *et al.*, 2006).

75. *PISTACIA LENTISCUS* (ILK AL BUTM)

Chios mastic gum of plant *Pistacia lentiscus* significantly inhibited vascular cell adhesion molecule-1 (VCAM-1) and Intercellular Adhesion Molecule (ICAM-1) expression in TNF-alpha-stimulated Human Aortic Endothelial Cells (HAEC). This showed its cardioprotective effect (Loizou *et al.*, 2009). *Pistacia lentiscus* var. chia powder showed cardioprotective activity by exhibiting decline in serum total cholesterol, LDL, total cholesterol/HDL ratio, lipoprotein (a), apolipoprotein A-1, apolipoprotein B (apoB/apoA-1 ratio did not change), SGOT, SGPT and gamma-GT levels (Triantafyllou *et al.*, 2007).

76. *PRUNELLA VULGARIS*

Prunella vulgaris ethylacetate fraction showed cytoprotectivities in doxorubicin-treated rat cardiomyocytes (Psotova *et al.*, 2005).

77. *PRUNUS AMYGDALUS* (ALMOND/BADAAM SHIREEN)

Almonds have been reported to have a consistent LDL-C-lowering effect in healthy individuals, and in individuals with high cholesterol and diabetes, in both controlled and free-living settings. Almonds are low in saturated fatty acids, rich in unsaturated fatty acids, and contain fiber, phytosterols, and plant protein. The nutrients present in almonds may regulate enzymes involved in de novo cholesterol synthesis and bile acid production. Research is needed to understand all mechanisms by which almonds reduce cardiovascular disease risk (Berryman *et al.*, 2011).

78. PRUNUS CERASUS (AALOO BALU)

Kernel extract from *Prunus cerasus* seed significantly improved the postischemic recovery of cardiac function (coronary flow, aortic flow, and left ventricular developed pressure) during reperfusion induced damage in isolated rat hearts (Bak *et al.*, 2006).

79. PSIDIUM GUAJAVA L. (AMROOD)

Aqueous extracts of *Psidium guajava* L. significantly attenuated ischemic contracture during ischemia and improved myocardial dysfunction after reperfusion favouring cardioprotective effects against myocardial ischemia-reperfusion injury in isolated rat hearts (Yamashiro *et al.*, 2003).

80. PUNICA GRANATUM L. (RUMMAN)

The whole fruit extract of (pomegranate) *Punica granatum* L. decreased QT and increased in heart rate compared to the doxorubicin group. Significant decrease in CK-MB, LDH and no such significant decrease in AST were observed as compared to the doxorubicin group. There was a significant increase in the levels of GSH, whereas inhibition of LPO and increase in SOD concentration was not significant in the WFEP group compared to the doxorubicin group. Histopathological study of the WFEP-treated group showed slight protection against myocardial toxicity induced by doxorubicin. These results indicate that WFEP has cardioprotective effect against doxorubicin-induced cardiotoxicity in rats (Hassanpour *et al.*, 2011). Pomegranate juice showed significant antiatherogenic, antioxidant, antihypertensive, and anti-inflammatory effects in immune-deficient mice and intima media thickness in cardiac patients on medications (Basu and Penugonda, 2009).

81. RADIX GINSENG

Radix Ginseng demonstrated cardioprotective effect on protein S-nitrosylation in rats myocardial with ischemia/reperfusion injury by decreasing the serum levels of CK and LDH as well as increased the serum levels of nitric oxide and the expression of endothelial nitric oxide synthase in myocardial tissue (Feng *et al.*, 2008).

82. RHODIOLA ROSEA LINN.

Salidroside, a phenylpropanoid glycoside isolated from *Rhodiola*

rosea L, significantly attenuated hypoxia-induced cell viability loss, cell necrosis and apoptosis by increasing HIF-1 α expression and subsequently up-regulating VEGF levels (Zhang *et al.*, 2009). Salidroside extracted from *Rhodiola rosea* L. showed cardioprotective effects on oxygen-glucose deprivation (OGD)-induced cardiomyocyte death and ischemic injury evoked by acute myocardial infarction (AMI) in rats. It has a potential to be a promising drug for preventing and treating myocardial ischemic diseases (Zhong *et al.*, 2010).

83. RHODOBRYUM ROSEUM

Hydroalcoholic extract of *Rhodobryum roseum* showed significant cardioprotective effect by lowering the levels of serum marker enzymes, lipid peroxidation (MDA) in isoproterenol-induced myocardial injury in rats and cardiac myocytes against oxidative stress-triggered damage (Hu *et al.*, 2009). *Rhodiola rosea* extract decreased the infarction size/risk area ratio during the coronary artery occlusion and reperfusion in vivo in isoproterenol and the arrhythmogenic action of epinephrine in rats (Maslov and Lishmanov, 2007).

84. RHUS CORIARIA L. (SUMAAQ)

Hydrolysable gallotannins from leaves of *Rhus coriaria* L. demonstrated cardiovascular protective effect due to an interplay of different factors including: coronary endothelium cyclo-oxygenase pathway activation, TNF- α inhibition, endothelial nitric oxide synthase activation, and free radical and reactive oxygen species scavenging (Beretta *et al.*, 2009).

85. SALACIA OBLONGA

Water extract of *Salacia oblonga* showed cardioprotective activity by less cardiac hypertrophy by decrease in weights of the hearts and left ventricles and reduced cardiomyocyte cross-sectional areas (Huang *et al.*, 2008).

86. SALVIA MILTIORRHIZA

Water-soluble active component of Danshen from *Salvia miltiorrhiza* significantly decreased heart weight/body weight (HW/BW) and left ventricular weight/body weight (LVW/BW) ratios. This was further confirmed by using ECG, decreased the serum and myocardium levels of creatine kinase, lactate dehydrogenase, and malondialdehyde (CK, LDH,

and MDA) and increased serum activity of superoxide dismutase (SOD). These results showed that it prevented cardiac I/R injury and improved cardiac function in a rat model of hypertrophy (Tang *et al.*, 2010). Salvianolic acid (SAL) and tanshinone (TAN) from Danshen delay the development of ischemia by decreasing infarct size and improving systolic function post MI, contributing to the cardioprotective effect. TAN acts at an early stage after ischemic injury mainly by inhibition of intracellular calcium and cell adhesion pathways whereas SAL acts mainly by down-regulating apoptosis (Wang *et al.*, 2011). Tanshinone IIA extracted from danshen exhibits cardio-protective effects by preventing cardiac fibroblast proliferation by interfering with the generation of ROS and involves the activation of the eNOS-NO pathway (Chan *et al.*, 2011). Tanshinone IIA a major active component of *Salvia miltiorrhiza* Bunge showed cardio-protective capacity in myocardial ischemia in vivo study in rat model induced by permanent left anterior descending coronary artery (LAD) ligation. Tanshinone IIA attenuates the MI pathological changes and improves heart function, and reduces expression of MCP-1, TGF-beta (1) and macrophage infiltration. It also decreases the expression of TNF-alpha and activation of nuclear transcription factor-kappa B (NF-kappaB) (Ren *et al.*, 2010). Purified *Salvia miltiorrhiza* extract showed cardio-protective effects by Gene expression levels of the pro-apoptotic genes Asp53, Bax, and Fas in vascular smooth muscle cell line in vitro study (Husna *et al.*, 2007). Purified extract showed significant postischemic contractile function recovery in compare to control in myocardial ischemia/reperfusion injury in isolated rat hearts with Krebs-Henseleit solution maintained at 37 degrees C and continuously gassed with 95% oxygen and 5% carbon di oxide (Chang *et al.*, 2006). Extract of *Salvia miltiorrhiza* significantly reduces size of infarct size, lowers ratios of heart weight to the body weight as well as the left and right ventricular weights to body weight and also normalizes the antioxidant defense enzymes in myocardial infarcted rats (Ji *et al.*, 2003).

87. *SCHIZANDRA CHINENSIS*

An aqueous extract of *Schizandra chinensis* restored endothelial function in rats that underwent balloon-induced carotid artery injury, and it reduced serum cholesterol levels in OVX rats exhibited similar cardioprotective effects, thereby suggesting that ScEx is a potential candidate to replace estradiol in the prevention and treatment of cardiovascular diseases (Kim *et al.*, 2011). Schisandrin B from *Schizandra chinensis* showed cardioprotective effect by improving Hsp25 and Hsp70 expression in rat hearts pre-treatment against ischemia-reperfusion (I-R) injury (Chiu *et al.*, 2004).

88. SCUTELLARIA BAICALENSIS GEORGI

Extract of the dry root of *Scutellaria baicalensis* Georgi containing high content of flavonoids and phenolic significantly reduces myocardial infarct size and marked increase in the activity of catalase in liver and additionally enhances acetylcholine induce vasorelaxation. It was supposed that extract exerted its cardioprotection by stimulating the catalase activity and improving vascular elasticity (Chan *et al.*, 2011).

89. SEMECARPUS ANACARDIUM L. (BALADUR)

Ethanol extract of *S. anacardium* demonstrated cardioprotective effect against isoproterenol-induced myocardial damage in rats, female Sprague-Dawley rats were pre-treated with propranolol. The influence of prophylactic treatment was analysed by quantification of biomarkers and antioxidants, electrocardiographic parameters and histopathological observations. The activities of lactate dehydrogenase and creatinine phosphokinase-MB were reduced in serum and raised in heart tissue with concurrent elevation in superoxide dismutase and catalase activities as well as reduction in thiobarbituric acid reactive species levels significantly in compared to isoproterenol (Chakraborty and Asdaq, 2011).

90. SESBANIA GRANDIFLORA (AGASTI)

Aqueous suspension of *Sesbania grandiflora* restored the antioxidant status and retained the levels of micronutrients in cigarette smoke-induced oxidative damage in rats by its antioxidant potential (Ramesh *et al.*, 2008).

91. SOLANUM MELONGENA L

In an experiment the role of raw and grilled *Solanum melongena* L. (egg plants) on cardioprotection using an isolated perfusion heart model were examined and left ventricular function was monitored, and myocardial infarct size and cardiomyocyte apoptosis were assessed. It was found that as containing potent cardioprotective compounds judging by their ability to increase left ventricular function, and reduced myocardial infarct size and cardiomyocyte apoptosis (Das *et al.*, 2011).

92. TERMINALIA ARJUNA (ARJUN)

Terminalia arjuna bark extract showed cardioprotective effects in isoproterenol-induced chronic heart failure in rats, in maximal rate of

rise and fall of left ventricular pressure [LV (dP/dt)(max) and LV (dP/dt)(min)], cardiac contractility index [LV (dP/dt)(max)/LVP], cardiac output and rise in LV end-diastolic pressure. CHF rats showed a significant increase in serum creatine kinase isoenzyme-MB (CK-MB) and malondialdehyde levels, as well as fall in the activities of superoxide dismutase, reduced glutathione, prophylactic and therapeutic beneficial effect on protection of heart against ISO-induced CHF possibly through maintaining endogenous antioxidant enzyme activities, inhibiting lipid peroxidation and cytokine levels (Parveen *et al.*, 2011). Ethanol extract of the bark of *Terminalia arjuna* showed cardioprotective action against sodium fluoride (NaF)-induced oxidative stress in murine heart in mice by alteration in antioxidant enzymes superoxide dismutase, catalase, and glutathione S-transferase), levels of cellular metabolites, reduced glutathione, and oxidized glutathione, levels of lipid peroxidation end products, and protein carbonyl in comparison to control group (Sinha *et al.*, 2008). Butanolic fraction of *Terminalia arjuna* bark increases the cardiac antioxidant enzymes, decreases in serum creatine kinase-MB levels and reduction in lipid peroxidation in doxorubicin-induced cardiotoxicity in rats as compared to Dox-treated animals (Singh *et al.*, 2008). Arjunolic acid showed cardioprotection by decreasing the levels of superoxide dismutase, catalase, glutathione peroxidase, ceruloplasmin, alpha-tocopherol, glutathione in isoproterenol induced myocardial necrosis in rats (Sumitra *et al.*, 2001). Bark powder of *Terminalia arjuna* is fairly effective in patients with symptoms of stable angina pectoris and limited role in unstable angina (Dwivedi and Agarwal, 1994). Alcoholic extract of *Terminalia arjuna* bark shows significant decrease in myocardial thiobarbituric acid reactive substances and significant rise in the levels of glutathione, superoxide dismutase and catalase isoproterenol induced myocardial ischemic reperfusion injury in rats (Karthikeyan *et al.*, 2003).

93. *TERMINALIA CHEBULA* (HALELA)

Ethanol extract of fruits of *Terminalia chebula* significantly prevented cardiotoxicity by reducing glutathione peroxidase, glutathione reductase, glutathione-S-transferase, superoxide dismutase and catalase in the heart tissue in isoproterenol-induced oxidative stress in rats (Suchalatha *et al.*, 2005). Ethanol extract of *Terminalia chebula* fruits ameliorate the effect of isoproterenol on lipid peroxide formation significantly in the serum and heart (Suchalatha and Shyamala Devi, 2004).

94. *TINOSPORA CORDIFOLIA* (GILO)

Alcoholic extract of *Tinospora cordifolia* reduced infarct size and

lipid peroxide levels of serum and heart tissue in surgically-induced myocardial ischemia in an in vivo rat model (Rao *et al.*, 2005).

95. UNCARIA RHYNCHOPHYLLA

Hirsutine isolated from the methanolic extracts of *Uncaria rhynchophylla*. It significantly increased the viability of cardiomyocytes injured by hypoxia due to its antioxidant activity in neonatal rats (Wu *et al.*, 2011).

96. VITIS VINIFERA (KISHMISH/ANGOOR)

Resveratrol and proanthocyanidins are responsible for cardioprotective abilities of grapes and its wines (Bertelli and Das, 2009). Proanthocyanidins showed cardioprotective effect in doxorubicin-induced cardiotoxicity in rats model compared to control group by determining malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), xanthine oxidase (XO) levels, and creatine kinase (CK) (Demitkava *et al.*, 2009). Myricetin from *Vitis vinifera* showed cardioprotective effect by significant increase in heart rate and ST elevation in ECG, and a significant increase in the levels of cardiac marker enzymes - lactate dehydrogenase, creatine kinase and aspartate aminotransferase (AST) in serum in isoproterenol-induced myocardial infarction in Wistar rats (Tiwari *et al.*, 2009). Flesh and skin of the grapes could protect the hearts from ischemic reperfusion injury as evidenced by improved postischemic ventricular recovery and reduced myocardial infarct size in isolated perfused hearts were made ischemic for 30 min followed by 2 hrs of reperfusion in the working mode (Falchi *et al.*, 2006). Flavans, anthocyanins, quercetin, myricetin, kaempferol, and resveratrol induced cardioprotective effect in pre and postmenopausal women by lowering plasma lipids and reducing oxidative stress (Zern *et al.*, 2005). Grape seed proanthocyanidin extract significantly inhibited doxorubicin-induced cardiotoxicity, demonstrated by reduced serum creatine kinase activity, DNA damage and histopathological changes in the cardiac tissue of mice and improves cardiac function including post-ischemic left ventricular function, reduces myocardial infarct size, reduce ventricular fibrillation and tachycardia, decrease the amount of reactive oxygen species (ROS) reduce malondialdehyde formation in the heart perfusate (Bagchi *et al.*, 2003). Alcohol-free hydroalcoholic extract from skins of a vinifera grape significantly reduces systolic and diastolic pressure in Wistar rats with desoxycorticosterone acetate-salt and N(G)-nitro-L-arginine methyl ester (L-NAME) induced experimental hypertension (Soares De Moura *et al.*, 2002). A fraction oligomeric procyanidins isolated from *Vitis vinifera* reduced left ventricular end-diastolic pressure during ischemia, decreased

coronary perfusion pressure, improved cardiac mechanical performance upon reperfusion, increased the release of 6-Keto-prostaglandin F₁alpha into the perfusate in both the preischemic and the reperfusion periods and suppressed rhythm irregularity (Berti *et al.*, 2003). Grape extract induced significant cardioprotection evidenced by improved postischemic ventricular recovery and reduced amount of myocardial infarction in ischemic for 30 min followed by 2 h of reperfusion (Cui *et al.*, 2002). Grape extract reduced myocardial ischemia reperfusion injury by functioning as in vivo antioxidant (Cui *et al.*, 2002). Grape seed proanthocyanidins showed cardioprotective effects against reperfusion after ischemia in isolated rat hearts. (Pataki *et al.*, 2002). Grape seed proanthocyanidins significantly reduced the appearance of apoptotic cardiomyocytes in the ischemic/reperfused hearts (Sato *et al.*, 2001). Grape seed proanthocyanidins possess cardioprotective effect against ischemia reperfusion injury (Sato *et al.*, 1999).

97. WALNUTS AND FLAX

Alpha-linolenic acid (ALA) from walnuts and flax were evaluated for cardiovascular responses to acute stress, flow-mediated dilation (FMD) of the brachial artery, and blood concentrations of endothelin-1 and arginine-vasopressin (AVP). The ALA and LA diets significantly reduced diastolic blood pressure and total peripheral resistance, and this effect was evident at rest and during stress. FMD increased on the diet containing additional ALA. The AVP also increased by 20%, and endothelin-1 was unchanged. These results showed novel mechanisms of the cardioprotective effects of walnuts and flax (West *et al.*, 2010). Consumption of 1 oz (~28.35 g) of English walnuts per day may decrease cardiovascular risk (Fitschen *et al.*, 2011).

98. WITHANIA SOMNIFERA (ASGAND)

Withania somnifera showed significant cardioprotective activity by antioxidant and antiapoptotic effects in ischemia and reperfusion (IR) injury in rats (Mohanty *et al.*, 2008). *Withania somnifera* significantly reduced myocardial injury by reducing glutathione, superoxide dismutase, catalase, creatine phosphokinase and increases malondialdehyde in serum and tissue (Gupta *et al.*, 2004). Hydro-alcoholic extract exerts a strong cardioprotective effect in the experimental model of isoprenaline-induced myonecrosis in rats by augmentation of endogenous antioxidants, maintenance of the myocardial antioxidant status and significant restoration of most of the altered haemodynamic parameters (Mohanty *et al.*, 2004). Ashwagandha showed adaptogenic, cardiotropic, cardioprotective and anticoagulant activity in rats and frogs (Dhuley *et al.*, 2000).

99. ZINGIBER OFFICINALE (ZANJABIL)

Ethanollic extract of rhizomes of *Zingiber officinale* significantly increased the levels of endogenous myocardial antioxidants (catalase, superoxide dismutase and tissue glutathione), decreased the levels of serum marker enzymes (lactate dehydrogenase, creatine kinase, aspartate transaminase and alanine transaminase) and increased myocardial lipid peroxides in isoproterenol induced oxidative myocardial necrosis in rats (Ansari *et al.*, 2006).

Conclusion

Unani System of Medicine is an age old, time tested system of medicine which owes its origin to Greece dating back 5000 years. In view of the increasing number of cardiac diseases a number of herbal drugs have demonstrated their cardio protective activity and these drugs are mentioned in Unani classical literature as cardio protective especially in *Risala Advia Qalbiya* written by Avicenna. The above review gives information about single drugs which have shown cardio protective activity in experimental models and these can be used in cardiac and associated diseases. The review also gives information about plants mentioned in *Risala Advia Qalbiya* and other Unani classical texts used for cardio protection as *Muqawwi-e-Qalb*. This effort may be helpful for scientific community of Unani scholars and allied researchers, to gather information about the drugs mentioned in Unani Medicine as cardio protective. Carrying out such attempts will be helpful in exploring the scope of Unani medicine and it will lead to better healthcare professionals.

In a nutshell it can be said that Unani system of Medicine has immense potential in the field of organ protective tonics. All the plant drugs which have been discussed in this paper have cardio protective action which have been proved with scientific studies. This was only an attempt to assess the value of the drugs which were mentioned by Avicenna in Unani classical text on the basis of modern scientific investigations.

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