Pakistan Veterinary Journal

ISSN: 0253-8318 (PRINT), 2074-7764 (ONLINE)
Accessible at: www.pvj.com.pk

RESEARCH ARTICLE

Cardioprotective Potential of Gemmomodified Extract of *Terminalia arjuna* against Chemically Induced Myocardial Injury in Rabbits

Nazish Jahan*, Khalil-ur-Rahman, Shaukat Ali, M. Rafiq Asi[1] and Ajaz Akhtar[2]

Department of Chemistry and Biochemistry, University of Agriculture, Faisalabad; [1]Nuclear Institute of Agriculture & Biology, Faisalabad; [2]District Head Quarter Hospital, Faisalabad, Pakistan
*Corresponding author: nazishjahanuaf@yahoo.com

ARTICLE HISTORY

Received: October 23, 2011
Revised: December 27, 2011
Accepted: January 06, 2012

Key words:
Cardioprotective potential
Gemmomodified extract
HPLC analysis
Terminalia arjuna

ABSTRACT

The objective of this study was to determine the comparative cardioprotective potential of bark and gemmomodified extract of *Terminalia arjuna.* Cardioprotective potential was evaluated against isoproterenol induced cardiotoxicity. Both ways of treatment, curative and preventive were studied. In preventive cardioprotective potential, rabbits were pretreated with both extracts of *T. arjuna* (200 mg/kg) for three weeks and then cardiotoxicity was induced with isoproterenol. In curative way of treatment isoproterenol was given for two days and then these cardio intoxicated rabbits were treated with plant extracts. The activities of cardiac marker enzymes (CK-MB, AST, ALT, and LDH) and antioxidants enzymes (SOD, CAT) were analyzed in serum and heart tissues of different groups of experimental rabbits. Isoproterenol significantly ($P<0.001$) increased the level of enzymes. The three week prior administration and curative treatment of *T. arjuna* extracts resorted the enzymes and antioxidants level equal to normal. HPLC analysis of the extracts confirmed the presence of important flavonol and phenolic acids in both extracts. It can be concluded that gemmomodified and bark extract of *T. arjuna* has strong cardioprotective potential.

To Cite This Article: Jahan N, KU Rahman, S Ali, MR Asi and A Akhtar, 2012. Cardioprotective potential of gemmomodified extract of *Terminalia arjuna* against chemically induced myocardial injury in rabbits. Pak Vet J, 32(2): 255-259.

INTRODUCTION

Coronary heart diseases are leading cause of death in developed and industrialized countries and increasing alarmingly in developing and poor countries (Karthikeyan *et al*., 2007; Torabian *et al*., 2009; Subhashini *et al*., 2011; El-Sayed *et al*., 2011). The chemotherapeutic agents, which inhibit the free radical formation and can reduce the risk of heart diseases, have gained imperative value in the modern medicines. Herbal medicines having antioxidant properties may therefore, have protective role in cardiovascular diseases (Viswanatha *et al*., 2010).

There is increasing trend towards the application of herbal medicines to treat the cardiovascular diseases (Nandave *et al*., 2007; Hina *et al.,* 2010; Ojha *et al.,* 2011). Gemmotherapy is a subdivision of phytotherapy which utilizes glycerin macerates of fresh plants and other vegetative tissues in the growing stage. These tissues are rich in growth factors including phytohormones, auxins and gibberellins. The bioactive compounds are present in embryonic and growing tissues which start to disappear after plant maturation. The use of the buds, young leaf and rootlets makes it possible to obtain a more active medication than remedies that are prepared from the whole plant. Gemmotherapeutically treated remedies are safe, abundant in nutrients and impart positive effect on cure and recovery of human health.

Ancient physicians used the powdered bark of *T. arjuna* for alleviating the cardiovascular diseases (Gauthaman *et al*., 2001; Parveen *et al*., 2011; Oberoi *et al*., 2011) and wound healing. Many scientific studies proved its medicinal importance. Experimental studies revealed that its bark showed significant antioxidant, antidiabetic, antimutagenic (Jahan *et al.,* 2011a), anthelmintic and antimicrobial activities (Ramya *et al*., 2008; Jahan *et al.,* 2011b).

T. arjuna is a versatile traditional medicinal plant. Some studies are available on preventive cardioprotective effect of bark extract. But no significant study is available on cardioprotective potential of gemmomodified extract which is also a rich source of bioactive compounds. In literature, many studies about preventive cardioprotective

mode of medicinal plants are available but research reports about curative mode are rare. The present study was therefore planned to evaluate the cardioprotective potential of *T. arjuna* extracts through both (preventive and curative) mode of treatments and to identify its important flavonoid and phenolic contents by HPLC.

MATERIALS AND METHODS

Extract preparation: *T. arjuna* was collected from University of Agriculture, Faisalabad Pakistan. The bark powder (30 g) was refluxed with methanol. After completion of time extract was filtered and methanol was evaporated under reduced pressure. Paste of plant material (100 g), which was freshly harvested from plants during their growing stage was macerated with one liter mixture of glycerin and methanol in a ratio of 1:2 and shake vigorously. After one month macerate was filtered and solvent was removed with rotary evaporator and crude extract was stored.

HPLC analysis of phenolic compounds: The analytical HPLC system used for separation of flavonol was consisted of UV-visible detector (λ max 360 nm) Hypersil-ODS column (4.6 x 250 mm, I.d., 5-*u*m) at ambient temperature. The mobile phase consisted of solvent A (3% aq. trifluoroacetic acid) and solvent B (acetonitrile and methanol (80:20 v/v), was run with isocratic elution at flow rate of 1mL/min. The column and detector (λ max 280 nm) used for phenolic acid separation were similar to that used in flavonol analysis (Sultana and Anwar, 2008).

Experimental protocol: Cardioprotective potential of *T. arjuna* was evaluated in chemically induced myocardial infarction in animal model. Male albino rabbits weighing 1-1.5 kg were kept under standard conditions of environment. Animals were allowed free access to standard diet and water. Rabbits were kept for one week acclimatization period and then divided into six groups, each comprised of five animals (Table 1).

Table 1: Treatment protocol in different experimental groups of rabbits

Groups	Detail
I	Normal controls; animals were given standard diet only
II	ISO control group; rabbits were injected with ISO (85 mg/Kg b.wt.) for two consecutive days
III	Baseline group: rabbits were treated with 200 mg/kg b.wt. *T. arjuna* extracts once daily by oral gavage for three weeks.
IV	Preventive group: rabbits were pretreated with *T. arjuna* 200 mg/kg b.wt. once daily by oral gavage for three weeks and then ISO (85 mg/kg) was injected for two days.
V	Curative groups: rabbits were injected with ISO (85 mg/kg) for two days to induce cardiotoxicity. Then these cardio intoxicated rabbits were treated with 200 mg/kg b.wt of plant extracts (gemmomodified and bark) once daily for four days and blood samples were collected daily.
VI	Standard drug curative group: rabbits were injected with ISO (85 mg/kg) for two days to induce cardiotoxicity. Then these cardio intoxicated rabbits were treated with combination of two standard drugs including Propranolol (5 mg) and gemfibrazole (50 mg) once daily for four days and blood samples were collected daily.

ISO= Isoproterenol

Biochemical assessment: At the end of experimental period the blood samples were taken and serum was separated for analysis of different enzymes related to myocardial infarction such as lactate dehydrogenase (LDH), creatine kinase-MB fraction (CK-MB), aspartate transaminase (AST), alanine transaminase (ALT). All the analyses were performed with commercially available kits using chemistry analyzer. Animals were slaughtered and the heart tissues were removed for the analysis of antioxidant enzymes like superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT).

Statistical Analysis: Each sample was analyzed in triplicate and data were expressed as mean±SD. Data was analyzed using analysis of variance (ANOVA) in SPSS 15 software. Tukey Multiple Comparison test was used for comparison of means of different treatments ($P<0.001$).

RESULTS

HPLC analysis of polyphenols: HPLC analysis demonstrated that *T. arjuna* bark and gemmomodified extract contained the highest amount of myricetin followed by quercetin and kaempferol (Table 2)**.** *T. arjuna* bark extract exhibited good concentration of phenolic acids. Bark extract contained highest amount of ferulic acid followed by p-coumaric acid, gallic acid, chlorogenic acid, caffeic acid and catechin. In gemmomodified extract ferulic acid, gallic acid, caffeic acid, chlorogenic acid and catechin were identified (Table 2).

Table 2: Flavonol and phenolic acid contents of *Terminalia arjuna* (µg/g) of dry or fresh weight of plant quantified by HPLC

Flavonol/phenolic acids	Bark extract	Gemmomodified extract
Gallic acid	93.76±0.5	82.96±0.9
Catechin	4.6±0.9	2.10±0.8
Chlorogenic acid	48.25± 0.5	43.56±0.2
Caffeic acid	8.93±0.4	27±0.8
Ferulic acid	210±0.9	175.50±0.9
p- coumaric acid	105±0.8	N.D
Myricetin	817±0.25	503±0.05
Quercetin	66.5±1.00	60±0.9
Kaempferol	7.6±2.5	1.8±0.9

Preventive cardioprotective activity: The present study demonstrated the cardioprotective potential of polyphenolic rich extract of *Terminalia arjuna* in terms of curative and preventive modes of treatments.

Isoproterenol (ISO) significantly ($P<0.001$) increased the level of serum cardiac marker enzymes like CK-MB, LDH, AST, ALT in isoproterenol-induced group as compared to normal control group indicating myocardial infarction in rabbits. Prior administration of plant extracts (200 mg/kg b.wt.) significantly decreased the ISO-induced elevated level of cardiac marker enzymes (Table 3).

Group of rabbits treated with the bark extract brought ISO-induced elevated enzyme level close to the normal. Gemmomodified extract of *T. arjuna* also demonstrated significant ($P<0.001$) decline in enzyme level when compared to ISO control group. Treatment of *T. arjuna* bark extract showed greater effect in comparison of gemmomodified extract. This decline in enzyme level could be due to the action of *T. arjuna* extracts on

Table 3: Preventive effect of bark and gemmomodified extracts of *Terminalia arjuna* on cardiac markers and antioxidant enzymes in rabbits.

Parameter	Control (normal)	ISO control	Gemmo+ISO	Bark+ISO	BSL -200mg
CK-MB(IU/L)	142.100±1.241	292.980±2.477*	157.460±0.699**	146.400±0.970**	143.900±2.339
LDH(IU/L)	253.340±9.418	512.420±0.507*	287.480±1.36**	271.580±0.90**	251.240±0.702
AST(IU/L)	34.080±0.60	73.300±2.401*	41.66±0.643**	38.040 ±094**	31.560±1.918
ALT(IU/L)	36.440±0.767	82.580±1.869*	40.720±.4.9**	44.80±1.206**	36.900±1.086
SOD ($IUmg^{-1}$ protein)	11.022±1.045	4.160±0.541*	9.836±9.29**	10.0±1.086**	11.22±0.849
CAT ($IUmg^{-1}$ protein)	34.82±0.487	14.820±1.004*	31.40±1.67**	32.4±0.897**	38.680±0.841
GPX ($IUmg^{-1}$ protein)	1.54±0.183	0.626±0.877*	1.424±2.07**	1.470±2.0**	1.642±2.588

Results are expressed as mean±SD for 5 rabbits in each group. *Significantly different from control group (P<0.001). **Significantly different from ISO control group (P<0.001). Control; received normal diet and water. ISO control; received two doses of 85 mg/kg isoproterenol. Groups gemmo + ISO and bark+ISO received 200mg extracts doses for three weeks and then two doses of 85 mg/kg ISO was given. BSL groups received only plant extracts doses.

Table 4: Curative effect of bark and gemmomodified extracts of *Terminalia arjuna* on cardiac markers and antioxidant enzymes in rabbits

Parameter	Days	Control	ISO Treated	ISO + Standard drug	ISO+(Bark)200mg	ISO+(gemmo)200mg
CK-MB(IU/L)	1	152.080±1.326	291.48±1.38*	270.40±1.140*	284.82±2.532	281.36±1.532
	2	151.760±1.081	282.66±1.75*	220.06±0.932*	234.58±2.23*	220.58±2.13*
	3	151.400±1.140	250.80±0.83*	181.30±1.204*	191.04±0.953*	181.08±0.253*
	4	151.400±1.140	210.84±0.94*	163.52±2.626*	169.82±1.308**	164.82±0.308**
LDH (IU/L)	1	250.640±0.462	533.24±2.528*	500.720±0.817	520.800±0.837	516.060±1.539
	2	251.440±0.336	513.86±1.936*	480.320±6.902*	497.300±3.867*	497.580±1.477*
	3	250.980±0.968	491.70±1.988*	409.600±2.074*	431.100±0.742*	426.860±0.773*
	4	249.820±1.076	481.1±0.894*	300.500±0.524*	306.260±3.505*	314.960±1.335*
AST(IU/L)	1	33.240±1.762	91.900±0.894*	77.900±2.014*	83.860±2.190	77.860±0.830*
	2	35.160±1.674	90.180±1.182*	66.520±1.672*	73.640±2.182*	69.940±0.862*
	3	32.900±1.386	80.540±0.677*	53.580±1.668*	59.700±0.711*	46.660±1.038*
	4	33.160±0.551	84.380±1.105*	41.000±0.771*	45.320±0.779*	41.260±0.830*
ALT(IU/L)	1	36.920±0.937	82.080±1.992*	76.480±1.377	81.40±0.897	78.40±0.397
	2	36.320±1.232	81.520±1.201*	71.080±0.958*	74.920±0.798	70.920±0.298
	3	35.880±1.244	75.300±1.808*	61.660±1.108*	66.500±1.15*	64.500±1.0%*
	4	36.660±1.057	78.360±1.036*	55.660±3.532**	48.260±1.93*	42.260±1.03*

Results are expressed as mean±SD for 5 rabbits in each group.*Significantly different from normal control group P<0.001) **Significantly different from ISO control group (P<0.001). Control received normal diet and water. ISO control; received 85 mg/kg b.wt. isoproterenol. Group ISO+ P (gemmo&bark) 200; received the ISO for two days and then gemmomodified and bark extract dose were given to these rabbits for four days Standard drug group; received the ISO for two days and then standard drug was given to these rabbits for four days.

maintaining membrane integrity therefore constrained the leakage of enzymes.

Myocardial antioxidant enzymes activities like SOD, CAT and peroxidase were significantly (P<0.001) lower in isoproterenol-treated group than in control group. Pretreatment with *T. arjuna* followed by ISO administration significantly (P<0.001) protected the rabbits against ISO-induced changes in SOD, CAT and GPx level. Treatment of rabbits with gemmomodified extract of *T. arjuna* at the dose of 200 mg/kg b.wt. restored the antioxidant enzyme level near to the normal. *T. arjuna* bark extract also significantly restored antioxidant enzyme level as compared to ISO control group. However, this effect was slightly less than gemmomodified extract. In baseline groups level of cardiac and antioxidant enzymes was normal.

Curative cardioprotective activity: Curative cardio-protective effect is important parameter for the evaluation of cardioprotective activity of medicinal plants. In curative cardioprotective activity, cardiotoxicity (ischemia and myocardial infarction) was induced in rabbits and then plant extract (200 mg/kg b.wt) was fed orally to ischemic/ myocardial infarcted rabbits once daily for four days.

Cardiotoxicity was induced in experimental rabbits by injection of isoproterenol at the dose of 85 mg/kg b.wt. Isoproterenol significantly increased (P<0.001) the level of diagnostic cardiac markers in serum of the rabbits as compared to the rabbits of normal control group indicating cardiac insufficiency, ischemia and myocardial infarction (Table 4).

Treatment of myocardial infarcted rabbits with *T. arjuna* extracts significantly (P<0.001) reduced the ISO-induced rise in cardiac marker enzymes after four treatments (one dose daily). Both bark and gemmomodified extracts of *T. arjuna* (200 mg/kg b.wt) decreased the ISO-induced elevated enzyme level close to normal. These results are comparable with the effect of standard drug. Combination of two standard drugs Propranolol and gemfibrazole is used to compare the activity of medicinal plants.

DISCUSSION

The present study demonstrated both important curative and preventive modes of cardioprotective activity. It explained the cardioprotective potential of bark and gemmomodified extract of *T. arjuna* in widely used ISO-induced model of myocardial infarction in rabbits. ISO, a synthetic catechol amine, is β- adrenergic receptor agonist. In high dose, it has ability to destruct myocardium and cause cardiotoxicity due to cytosolic Ca^{2+} overload. As a result of this myocardium destruction, cytosolic enzymes (CK-MB, LDH, AST, and ALT) are secreted into blood and serve as diagnostic markers of cardiotoxicity. Pathophysiological changes including cell necrosis, contractile failure, ventricular arrhythmias and subcellular changes after ISO administration (85 mg/kg) are comparable to those taking place in human myocardial ischemia/infarction (Nandave

et al., 2007; Panda and Niak, 2008; Ojha *et al.,* 2011; Subhashini *et al*., 2011).

ISO treated rabbits showed significant increase in the levels of diagnostic marker enzymes including CK-MB, LDH, AST, and ALT at the dose of 85 mg/kg. The high levels of enzymes are an indicator of the severity of ISO-induced myocardial cell necrosis. The myocardial cell necrosis can be due to increase in lipid peroxidation. These finding are in agreement with earlier reports (Karthikeyan *et al*., 2007).

Activities of antioxidant enzymes including SOD, CAT, and peroxidase were significantly lower in cardiac tissues of ISO treated group. Limited activity of endogenous antioxidant enzymes might be due to less availability of their substrates. These enzymes provide protection from peroxidative damage in oxidative stress as antioxidant enzyme consumption is increased due to high lipid peroxidation. Production of highly reactive free radical species inhibited the activities of antioxidant enzymes (Karthikeyan *et al*., 2007).

Treatment of different groups of rabbits with extracts (200 mg/Kg b.wt.) significantly blocked the ISO-induced secretion of all cardiac diagnostic marker enzymes (CK-MB, LDH, AST, ALT). The decline in enzymes levels could be due to potential of extracts for repairing and maintenance of the membrane due to antioxidant polyphenols, thereby preventing the secretion of enzymes.

The rabbits treated with 200 mg/kg b.wt. of plant extracts showed significant restoration in activities of antioxidant enzymes (SOD, CAT and GPx) when compared with ISO-induced group. The rise in endogenous antioxidant enzyme level might be a cellular adaptive mechanism which led to the increased synthesis of these enzymes and attributed to free radical scavenging potential of antioxidant polyphenols in medicinal plants (Karthikeyan *et al*., 2007).

T. arjuna is very important medicinal plant and results of this study has exposed that both bark and gemmomodified extracts protected the myocardial tissues of experimental animals from ISO-induced myocardial changes by regulating the levels of serum diagnostic marker enzymes and activities of antioxidant enzymes. Preventive (prior administration for 3 weeks) and curative treatment of *T. arjuna* bark and gemmomodified extract significantly protected from ISO induced myocardial infarction. It had strong restoration effect on antioxidant enzymes (SOD, CAT peroxidase). Recent studies suggested that free radical formation, and oxidative stress associated with occurrence of deficiency in antioxidant enzymes might be the major causative factor for the development of heart failure after myocardial infarction (Karthikeyan *et al*., 2007; Ojha *et al.,* 2011).

The cardioprotective potential of *T. arjuna* is attributed to the presence of potent antioxidant compounds and their free radical scavenging activity. Cardioprotective potential of *T. arjuna* extracts in terms of curative and preventive mode can be correlated with polyphenolic fraction and antioxidant activity.

HPLC analysis revealed the presence of most important flavonol (quercetin, myricetin, kaempferol), flavanole (catechin) and phenolic acids (gallic acid, *P.* coumaric, ferulic acid) in significantly higher concentrations. Many studies supported the cardioprotective effect of plant polyphenols (Alyane *et al*., 2008). Flavonoids can show their cardioprotective potential by various mechanisms. The intake of flavonoids may stop endothelial dysfunction by increasing the vasorelaxation process leading to reduction of arterial pressure (Narayana *et al*., 2001; Kurosawa *et al*., 2005). Flavonoids may directly scavenge some radical species and also help in uptake of oxdatively modified low density lipoprotein (LDL) through scavenger receptors. Scientific studies have revealed that quercetin an important flavonol suppressed the LDL oxidation and exerted significant vasorelaxation (Burns *et al*., 2000). Polyphenols may enhance cardiovascular health through regulation of platelet activity. Selected flavonoids such as quercetin kaempferol and myricetin inhibited platelet aggregation (Keevil *et al*., 2000).

Some studies are reported about cardioprotective (Gauthaman *et al*., 2001), hypocholesterolemic and antioxidant effect of *T. arjuna* bark (Jahan *et al*., 2011a). But no pervious data is available on cardioprotective effect of gemmomodified extracts (young buds and shoots). It is first time reported in this study that gemmomodified extract showed cardioprotective effect close to bark extract. It could be used as new cardioprotective agent. Other aspect of this study (curative effect or post-myocardial infarction treatment) of plant is also first time reported in this study and no previous reference was available on this aspect. Both gemmomodified and methanolic bark extracts offered a great potential to cure the myocardial infarction induced by consecutive doses of ISO.

Antioxidant constituents of *T. arjuna* is mainly responsible for its superlative cardioprotective activity. Bark of *T. arjuna* has also reported rich in co-enzyme Q which is highly effective to prevent heart disease. All these facts confirmed strong cardioprotective potential of gemmomodified and bark extracts of *T. arjuna.*

REFERENCES

Alyane M, L Benguedouar, W Kebsa, HN Boussenane, H Rouibah and M Lahouel, 2008. Cardioprotective effects and mechanism of action of polyphenols extracted from propolis against doxorubicin toxicity. Pak J Pharm Sci, 21: 201-209.

Burns J, PT Gardner, JO Neil, S Crawford, I Morecroft, DB McPhail, C Lister, D Matthews, MR MacLean, ME Lean, GC Duthie and A Crozier, 2000. Relationship among antioxidant activity, vasodilatation capacity and phenolic content of red wines. J Agric Food Chem, 48: 220-230.

El-Sayed EM, ASA El-azeem, AA Afify, MH Shabana and HH Ahmed, 2011. Cardioprotective effects of *Curcuma longa* L. extracts against doxorubicin-induced cardiotoxicity in rats. J Medicinal Plant Res, 5: 4049-4058.

Gauthaman K, M Maulik, R Kumari, SC Manchanda, AK Dinda and SK Maulik, 2001. Effect of chronic treatment with bark of *Terminalia arjuna*: a study on the isolated ischemic reperfused rat heart. J Ethnopharmacol, 75: 197-201.

Hina S, K Rehman, ZH Dogar, N Jahan, M Hameed, ZI Khan, K Ahmad, K Mukhtar and EE Valeem, 2010. Cardioprotective effect of gemmotherapeutically treated *withania somnifera* against chemically induced myocardial injury. Pak J Bot, 42: 1487-1499.

Jahan N, KU Rehman, S Ali and IA Bhatti, 2011a. Antimicrobial potential of gemmo-maodified extracts of *Terminalia arjuna* and *Euophorbia tirucalli.* Int J Agric Biol, 13: 1001-1005.

Jahan N, K Rehman, S Ali and IA Bhatti, 2011b. Antioxidant activity of gemmotherapeutically treated indigenous medicinal plants. Asian J Chem, 23: 3461-3470.

Karthikeyan K, BR Bai, and SN Devaraj, 2007. Cardioprotective effect of grape seed proanthocyanidins on isoproterenol-induced myocardial injury in rats. Int J Cardiol, 115: 326-333.

Keevil JG, HE Osman, JD Reed and JD Folts, 2000. Grape Juice, but not orange Juice or grapefruit Juice, inhibits human platelet aggregation. J Nutr, 130: 53-56.

Kurosawa T, F Itoh, A Nozaki, Y Nakano, S Katsuda, N Osakabe, H Tsubone, K Kondo, H Itakura, 2005. Suppressive effects of cacao liquor polyphenols (CLP) on LDL oxidation and the development of atherosclerosis in Kurosawa and Kusanagi-hypercholesterolemic rabbits. Atherosclerosis, 179: 237-246.

Nandave M, SK Ojha, S Joshi, S Kumari, and SA Dharamvir, 2007. Cardioprotective effect of *Bocapa monneira* against isoproterenol induced myocardial necrosis in rats. Int J Pharm, 3: 385-392.

Narayana KR, MS Reddy, MR Chaluvadi and DR Krishna, 2001. Bioflavonoids classification, pharmacological, biochemical effects and therapeutic potential. Indian J Pharmcol, 33: 2-16.

Oberoi L, T Akiyama, KH Lee and SJ Liu, 2011. The aqueous extract, not organic extracts, of *Terminalia arjuna* bark exerts cardiotonic effect on adult ventricular myocytes. Phytomedicine, 18: 259-265.

Ojha S, S Bharti, AK Sharma, N Rani, J Bhatia, S Kumari and DS Arya, 2011. Effect of *Inula racemosa* root extract on cardiac function and oxidative stress against isoproterenol induced myocardial infarction. Indian J Biochem Biophys, 48: 22-28.

Panda VS and SR Niak, 2008. Cardioprotective activity of *Ginkgo biloba* phytosomes in isoproterenol induced myocardial necrosis in rats: A biochemical and histoarchitectural evaluation. Exp Toxicol Pathol, 60: 397-404.

Parveen A, R Babbar, S Agarwal, A Kotwani and M Fahim, 2011. Mechanistic Clues in the cardioprotective effect of *Terminalia arjuna* bark extract in isoproterenol-induced chronic heart failure in rats. Cardiovascular Toxicol, 11: 48-57.

Ramya S, T Kalaivani, C Rajasekaran, P Jepachanderamohan, N Alaguchamy, M Kalayansundaram and R Jayakumararaj, 2008. Antimicrobial activity of aqueous extracts of bark, root, leaves and fruits of *Terminalia arjuna* Wight & Arn. Ethnobot Leafs, 12: 1192-1197.

Sultana B and F Anwar, 2008. Flavonols (kaempeferol, quercetin, myricetin) contents of selected fruits, vegetables and medicinal plants. Food Chem, 108: 879-884.

Subhashini N, G Nagarajan, O Shahinsha, K Leelanvitha, S Kavimani, 2011. Cardioprotective effect of *Garcinia combogia* on isoproterenol induced myocardial infarction in rats. Pharma Prof, 1: 91-100.

Torabian S, E Haddad, S Rajaram, J Banta and J Sabate, 2009. Acute effect of nut consumption on plasma total polyphenols, antioxidant capacity and lipid peroxidation. J Hum Nut and Diet, 22: 64-71.

Viswanatha GLS, SK Vaidya, C Ramesh, N Krishnadas and S Rangappa, 2010. Antioxidant and antimutagenic activities of bark extract of *Terminalia arjuna*. Asian Pac J Trop Med, 3: 965-970.