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Protective effect of taurine on myocardial antioxidant status in isoprenaline-induced myocardial infarction in rats

K. S. Shiny, S. Hari Senthil Kumar, K. H. Sabeena Farvin, R. Anandan and K. Devadasan

Abstract

We have examined the protective effect of taurine on the myocardial antioxidant defense system in isoprenaline (isoproterenol)-induced myocardial infarction in rats, an animal model of myocardial infarction in man. Levels of diagnostic marker enzymes in plasma, lipid peroxides and reduced glutathione, and the activity of glutathione-dependent antioxidant enzymes and antiperoxidative enzymes in the heart tissue were determined. Intraperitoneal administration of taurine significantly prevented the isoprenaline-induced increases in the levels of alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, and creatine phosphokinase in the plasma of rats. Taurine exerted an antioxidant effect against isoprenaline-induced myocardial infarction by preventing the accumulation of lipid peroxides and by maintaining the level of reduced glutathione and the activity of glutathione peroxidase, glutathione-S-transferase, catalase and superoxide dismutase at near normality. The results indicated that the cardioprotective potential of taurine was probably due to the increase of the activity of the free radical enzymes, or to a counteraction of free radicals by its antioxidant nature, or to a strengthening of myocardial membrane by its membrane stabilizing property.

Introduction

Despite improved clinical care, heightened public awareness, and widespread use of health innovations, myocardial infarction remains a leading cause of death. It is estimated that by the year A.D. 2020, up to three quarters of deaths in developing countries will result from non-communicable diseases and that myocardial infarction will top the list of killers (Gupta & Gupta 1998). With changing life style in developing countries like India, particularly in urban areas, myocardial infarction is making an increasingly important contribution to mortality statistics of such countries (Farvin et al 2004). In India, the number of patients being hospitalized for heart attack has increased over the past 35 years, with male patients showing a striking increase (Krishnaswami 1998).

Taurine (2-aminoethanesulfonic acid), a non-protein sulfur containing amino acid, is the most abundant free amino acid and has been shown to play several essential roles in the human body (Lombardini 1996). It is widely distributed in very high concentrations in brain, heart, kidney, lens, and reproductive organs (Huxtable 1992). It is involved in various important biological and physiological functions, which include cell membrane stabilization (Heller-Stilb et al 2002), antioxidation (Atmaca 2004), detoxification (Birdsall 1998), osmoregulation (Timbrell et al 1995), neuromodulation, and brain (Renteria et al 2004) and retinal development (Wright et al 1986). Taurine accounts for more than 50% of the total amino acid pool in the mammalian heart (Lombardini 1996). Earlier studies (Keith et al 2001; Warskulat et al 2004) demonstrated that pathology develops in the myocardium if an animal is depleted of taurine stores either through a taurine-deficient diet or use of taurine transport antagonists. Pion et al (1987) were the first to explain the role of dietary taurine deficiency associated with a dilated cardiomyopathy observed in experimental animals. Other studies by Keith et al (2001) and Lake et al (1994) have explored the relationship between

Biochemistry and Nutrition Division, Central Institute of Fisheries Technology, Matsyapuri (PO) Cochin-682029, India

K. S. Shiny, S. Hari Senthil Kumar, K. H. Sabeena Farvin, R. Anandan, K. Devadasan

Correspondence: R. Anandan, Scientist Sr. Scale, Biochemistry and Nutrition Division, Central Institute of Fisheries Technology, Cochin-682029, India. E-mail: kranandan@email.com

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taurine deficiency and cardiac contractility, loss of cardiac myofibrils, and arrhythmogenesis. Though there is considerable evidence concerning the pharmacological significance of taurine in maintaining the integrity of an organism, the protective effect of taurine on myocardial antioxidant status in experimentally-induced myocardial infarction in rats has not been explored in detail.

Intraperitoneal administration of isoprenaline (isoproterenol; L-β-(3,4-dihydroxyphenyl)-α-isopropylaminoethanol hydrochloride), a β-adrenergic agonist, produces acute irreversible myocardial injury in rats that morphologically resembles myocardial infarction in man (Ravichandran et al 1990; Geng et al 2004). It induces myocardial necrosis by a multiple-step mechanism (Chagoya de Sanchez et al 1997). Peroxidation of endogenous lipids has been shown to be a major factor in the cardiotoxic action of isoprenaline (Kumar et al 2001; Chattopadhyay et al 2003). Isoprenaline-induced myocardial infarction is generally attributed to the formation of the highly reactive hydroxyl radical ($OH^{\bullet}$), stimulator of lipid peroxidation and source for the destruction and damage to cell membranes (Farvin et al 2004). Alterations in tissue defense systems including chemical scavengers or antioxidant molecules and the antioxidant enzymes catalase, superoxide dismutase, glutathione peroxidase, and glutathione-S-transferase have been reported in isoprenaline-induced myocardial infarction (Sharma et al 2001; Saravanan & Prakash 2004).

In this study, an attempt has been made to assess the preventive effects of taurine against isoprenaline-induced myocardial infarction in rats by virtue of its hypolipidaemic (Takenaga et al 2000), antioxidant (Rodriguez-Martinez et al 2004) and membrane stabilizing properties (Birdsall 1998).

Materials and Methods

Chemicals

Taurine, adrenaline (epinephrine), tetramethoxypropane and isoprenaline were obtained from Sigma Chemical Company (St Louis, MO). All the other chemicals used were of analytical grade.

Animals

Wistar strain male albino rats (100–120 g) were housed individually in polyurethane cages under standard environmental conditions and allowed free access to food and water. The experiment was carried out according to the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), New Delhi, India, and approved by the Institutional Animal Ethics Committee.

Induction of myocardial infarction

Myocardial infarction was induced in experimental rats by injecting isoprenaline (11 mg (dissolved in physiological saline)/100 g/day), intraperitoneally for two days (Anandan et al 2003).

Experimental protocol

The rats were divided into four groups of six rats and housed individually in polyurethane cages. Group 1 served as the control. Group 2 animals were intraperitoneally (i.p.) injected with taurine (100 mg kg^{-1}/day, dissolved in physiological saline) for 15 days. Group 3 rats were injected intraperitoneally with isoprenaline (11 mg (dissolved in physiological saline)/100 g/day), for two days for the induction of myocardial infarction. Group 4 animals were injected with taurine at the above dosage for 15 days and then injected intraperitoneally with isoprenaline (11 mg/100 g/day) for two days.

At the end of the experimental period, i.e. 24 h after the last injection of isoprenaline, the rats were killed. Blood was collected using heparin as the anticoagulant. The plasma was separated and then used for the determination of alanine aminotransferase [EC 2.6.1.2] (ALT) (Mohur & Cook 1957), aspartate aminotransferase [EC 2.6.1.1] (AST) (Mohur & Cook 1957), lactate dehydrogenase [EC 1.1.1.27] (LDH) (King 1965) and creatine phosphokinase [EC 2.7.3.2] (CPK) (Okinaka et al 1961). The heart tissue was excised immediately and washed with chilled isotonic saline. The heart tissue homogenates prepared in ice-cold 0.1 M Tris-HCl buffer, pH 7.2, were used for the determination of lipid peroxides (LPO) (Ohkawa et al 1979), reduced glutathione (GSH) (Ellman 1959), glutathione peroxidase (GPx) [EC 1.11.1.9] (Pagila & Valentine 1967), glutathione-S-transferase (GST) [EC 2.5.1.18] (Habig et al 1974), catalase [EC 1.11.1.6] (Takahara et al 1960) and superoxide dismutase (SOD) [EC 1.15.1.1] (Misra & Fridovich 1972). The protein content was estimated by the method of Lowry et al (1951).

Statistics

Results are expressed as mean $\pm$ s.d. Multiple comparisons of the significant analysis of variance were performed by Tukey's multiple comparison test. A P-value < 0.05 was considered as statistically significant. All data were analysed with the aid of a statistical package program, SPSS 10.0 for Windows.

Results

Table 1 shows the levels of diagnostic marker enzymes (AST, ALT, LDH and CPK) in plasma of normal and of experimental rats. Injection of isoprenaline caused significant elevation in the levels of these marker enzymes in the plasma of group 3 rats as compared with group 1 normal controls. Prior treatment with taurine significantly ($P < 0.001$) prevented the isoprenaline-induced elevation in the levels of diagnostic marker enzymes in plasma of group 4 animals as compared with group 3 rats.

A significant rise in the level of lipid peroxidation was observed in the heart tissue of group 3 isoprenaline-administered rats as compared with controls (Table 2). This was paralleled by a significant decline in the level of reduced glutathione and the activity of glutathione-

Table 1 Levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and creatine phosphokinase (CPK) in plasma of normal and experimental rats

Diagnostic marker	Group 1 (control)	Group 2 (administered taurine)	Group 3 (administered isoprenaline)	Group 4 (administered taurine and isoprenaline)
ALT	95.8 ± 7.1	90.3 ± 6.5	$408 \pm 35.3^{a,b}$	103 ± 7.5^{c}
AST	132 ± 9.4	127 ± 8.1	$376 \pm 28.7^{a,b}$	145 ± 8.7^{c}
LDH	169 ± 14.8	165 ± 12.4	$412 \pm 36.1^{a,b}$	188 ± 14.2^{c}
CPK	118 ± 7.2	115 ± 7.6	$343 \pm 18.5^{a,b}$	$142 \pm 8.9^{c,d,e}$

Results are mean ± s.d. of six animals. Values expressed: ALT, AST, and LDH, μmol pyruvate liberated $h^{-1} L^{-1}$; CPK, μmol creatine liberated $h^{-1} L^{-1}$. [a] $P < 0.001$ significantly different compared with group 1 control; [b] $P < 0.001$ significantly different compared with group 2 taurine-administered animals; [c] $P < 0.001$ significantly different compared with group 3 isoprenaline-induced myocardial infarcted rats; [d] $P < 0.05$ significantly different compared with group 1; [e] $P < 0.05$ significantly different compared with group 2.

Table 2 Levels of lipid peroxides (LPO) and reduced glutathione (GSH), and the activity of glutathione peroxidase (GPx), glutathione-S-transferase (GST), catalase and superoxide dismutase (SOD) in the heart tissue of normal and experimental rats

Diagnostic marker	Group 1 (control)	Group 2 (administered taurine)	Group 3 (administered isoprenaline)	Group 4 (administered taurine and isoprenaline)
LPO	0.95 ± 0.04	0.92 ± 0.04	$2.79 \pm 0.15^{a,b}$	1.05 ± 0.18^{c}
GSH	5.17 ± 0.27	5.99 ± 0.35^{f}	$2.12 \pm 0.15^{a,b}$	$5.34 \pm 0.25^{c,e}$
GPx	3.15 ± 0.29	3.27 ± 0.24	$1.45 \pm 0.16^{a,b}$	2.98 ± 0.26^{c}
GST	1193 ± 84	1218 ± 91	$827 \pm 71^{a,b}$	$1105 \pm 88^{c,e}$
Catalase	10.4 ± 0.76	9.98 ± 0.84	$3.76 \pm 0.18^{a,b}$	$9.02 \pm 0.55^{c,d,e}$
SOD	3.73 ± 0.24	3.85 ± 0.32	$1.01 \pm 0.05^{a,b}$	$3.51 \pm 0.21^{c,e}$

Results are mean ± s.d. of six animals. Values expressed: LPO, nmol malondialdehyde (mg protein)$^{-1}$; GSH, μmol (g wet tissue)$^{-1}$; GPx, nmol GSH oxidized min^{-1} (mg protein)$^{-1}$; GST, μmol 1-chloro-2,4-dinitrobenzene conjugate formed min^{-1} (mg protein)$^{-1}$; catalase, nmol H_2O_2 decomposed min^{-1} (mg protein)$^{-1}$; SOD, one unit of the SOD activity is the amount of protein required to give 50% inhibition of adrenaline autoxidation. [a] $P < 0.001$ significantly different compared with group 1 control; [b] $P < 0.001$ significantly different compared with group 2 taurine-administered animals; [c] $P < 0.001$ significantly different compared with group 3 isoprenaline-induced myocardial infarcted rats; [d] $P < 0.05$ significantly different compared with group 1; [e] $P < 0.05$ significantly different compared with group 2; [f] $P < 0.001$ significantly different compared with group 1.

dependent antioxidant enzymes (GPx and GST) and anti-peroxidative enzymes (SOD and catalase) (Table 2). Administration of taurine significantly prevented all the isoprenaline-induced alterations in the tissue antioxidant system and maintained the rats at near normal status. The normal rats receiving taurine alone (group 2) did not show any significant change when compared with the normal rats, showing that taurine itself did not have any adverse effects.

Discussion

The significant rise noticed in the levels of AST, ALT, LDH and CPK in plasma of group 3 isoprenaline-administered rats as compared with group 1 normal controls was indicative of the severity of isoprenaline-induced myocardial infarction. This was in line with an earlier study (Suchalatha & Shyamala Devi 2004), which indicated that increased susceptibility of myocardial cell membrane to the isoprenaline-mediated peroxidative damage might lead to an increased release of these diagnostic marker enzymes into the systemic circulation. In this study, administration of taurine resulted in a significant reduction in the levels of these marker enzymes towards near normality as compared with group 3 isoprenaline-administered rats, indicating the cytoprotective effect of taurine (Schaffer et al 2003). It probably did so by its membrane stabilizing action (Redmond et al 1998). Timbrell et al (1995) had reported that taurine exerted membrane stabilization against carbon tetrachloride, hydrazine and 1,4-naphthoquinone-induced necrotic damages by modulating intracellular calcium levels and osmoregulation.

Biological membranes are sensitive to lipid peroxidation induced by reactive oxygen species. The oxidation of polyunsaturated fatty acids in biological membranes may cause impairment of membrane function, decrease in membrane fluidity, inactivation of membrane receptors and enzymes, increase of non-specific permeability to ions and disruption of membrane structure. In this investigation, the level of lipid peroxides in the heart tissue of group 3 isoprenaline-administered rats was significantly ($P < 0.001$) higher compared with group 1. This was in agreement with Nirmala & Puvanakrishnan (1996), who indicated that a lack of antioxidant defense might lead to an increase in lipid peroxidation and subsequent deleterious effects on the myocardial membrane in the isoprenaline-induced myocardial infarction condition. The rats pretreated with taurine showed a significant ($P < 0.001$) decrease in the level of lipid peroxidation in the heart tissue. This was probably achieved by means of its antioxidant nature (Rodriguez-Martinez 2004) against lipid peroxidation induced by isoprenaline. The unpaired electron present in the hydroxyl radicals generated by isoprenaline might have been trapped and subsequently dismuted by taurine. Obrosova et al (2001) reported that supplementation of taurine counteracted oxidative stress through the ascorbate system of antioxidant defenses in experimental diabetic nephropathy.

The glutathione antioxidant system plays a fundamental role in cellular defense against reactive free radicals and other oxidant species (Meister & Anderson 1983). The cellular tripeptide GSH exerts protective antioxidant influence through a complex enzyme system including GPx and GST. In this study, a significant reduction in

the activity of glutathione dependent antioxidant enzymes and antiperoxidative enzymes were observed in the heart tissue of group 3 isoprenaline-administered rats as compared with group 1 control animals. Also, the level of GSH was significantly reduced in isoprenaline-induced myocardial infarction. Decline in the activity of GPx in the heart tissue of infarction-induced rats made the myocardial cells more sensitive to oxidative damage, leading to a change in the cell composition and function.

The significant decrease noted in the activity of GST, another scavenging enzyme involved in the removal of toxic metabolites by glutathione conjugation reactions, in the heart tissue of group 3 myocardial infarction-induced rats might have been due to the reduced availability of GSH. This was in accordance with Sathish et al (2002), who indicated that GSH- and GSH-dependent enzyme systems might be directly related to the pathogenic mechanism of isoprenaline-induced myocardial infarction. Significant reduction observed in the activity of antiperoxidative enzymes SOD and catalase in the heart tissue of group 3 rats might have led to the formation of O^{2-} and H_2O_2, which in turn formed hydroxyl radical ($OH^{\bullet}$) and brought about a number of reactions harmful to the myocardial cell membranes. Similar observations were reported by Farvin et al (2004) and Gupta et al (2004).

This investigation has shown that prior treatment with taurine significantly prevented the isoprenaline-induced reduction in the level of GSH and the activity of catalase, SOD, GPx and GST in the heart tissue of group 4 rats as compared with group 3 rats. It probably did so either by increasing the level of GSH or by counteraction of isoprenaline-generated free radicals by its antioxidant nature. Hwang et al (2000) indicated that the level of thiobarbituric acid reactive substances was reduced and the level of GSH was elevated in the liver when the rats were fed with a taurine supplement.

Conclusion

Pretreatment with taurine prevented isoprenaline-induced myocardial infarction in rats. The overall cardioprotective effect of taurine was probably due to its membrane stabilizing action, or to a counteraction of free radicals by its antioxidant nature, or to its ability to maintain near to the normal status the activity of the free radical scavenging enzymes and the level of reduced glutathione, which protected the myocardial membrane against peroxidative damage by decreasing lipid peroxidation and strengthening the myocardial membrane.

References

Anandan, R., Asha, K. K., Ammu, K., Suseela, M., Viswanathan Nair, P. G. (2003) Effects of peroxidised PUFA on tissue defense system in experimentally induced myocardial infarction in rats. In: Surendran, P. K., Mathew, P. T., Thampuran, N., Nambiar, N., Joseph, J., Boopendranath, Laksmanan, P. T., Viswanathan Nair, P. G. (eds) *Seafood safety*. Society of Fisheries Technologists (India), Cochin, pp 330–335

Atmaca, G. (2004) Antioxidant effects of sulfur-containing amino acids. *Yonsei Med. J.* **45**: 776–788

Birdsall, T. C. (1998) Therapeutic applications of taurine. *Altern. Med. Rev.* **3**: 128–136

Chagoya de Sanchez, V., Hernandez-Munoz, R., Lopez-Barrera, F., Yanez, L., Vidrio, S., Suarez, J., Cota-Garza, M. D., Aranda-Fraustro, A., Cruz, D. (1997) Sequential changes of energy metabolism and mitochondrial function in myocardial infarction induced by isoproterenol in rats: a long-term and integrative study. *Can. J. Physiol. Pharmacol.* **75**: 1300–1311

Chattopadhyay, A., Biswas, S., Bandyopadhyay, D., Sarkar, C., Datta, A. G. (2003) Effect of isoproterenol on lipid peroxidation and antioxidant enzymes of myocardial tissue of mice and protection by quinidine. *Mol. Cell. Biochem.* **245**: 43–49

Ellman, G. L. (1959) Tissue sulfhydryl groups. *Arch. Biochem. Biophys.* **82**: 70–71

Farvin, K. H. S., Anandan, R., Kumar, S. H. S., Shiny, K. S., Sankar, T. V., Thankappan, T. K. (2004) Effect of squalene on tissue defence system in isoproterenol-induced myocardial infarction in rats. *Pharmacol. Res.* **50**: 231–236

Geng, B., Chang, L., Pan, C., Qi, Y., Zhao, J., Pang, Y., Du, J., Tang, C. (2004) Endogenous hydrogen sulfide regulation of myocardial injury induced by isoproterenol. *Biochem. Biophys. Res. Commun.* **318**: 756–763

Gupta, R., Gupta, V. P. (1998) Lessons for prevention of coronary heart disease epidemiological study in western India. *Curr. Sci.* **74**: 1074–1077

Gupta, S. K., Mohanty, I., Talwar, K. K., Dinda, A., Joshi, S., Bansal, P., Saxena, A., Arya, D. S. (2004) Cardioprotection from ischemia and reperfusion injury by Withania somnifera: a hemodynamic, biochemical and histopathological assessment. *Mol. Cell. Biochem.* **260**: 39–47

Habig, W. H., Pabst, M. J., Jackoby, W. B. C. (1974) Glutathione-S-transferases: the first enzymatic step in enzymatic stepping mercapturic acid formation. *J. Biol. Chem.* **249**: 7130–7139

Heller-Stilb, B., Van Roeyen, C., Rascher, K., Hartwig, H. G., Huth, A., Seeliger, M. W., Warskulat, U., Haussinger, D. (2002) Disruption of the taurine transporter gene (*taut*) leads to retinal degeneration in mice. *FASEB J.* **16**: 231–233

Huxtable, R. J. (1992) Physiological actions of taurine. *Physiol Rev.* **72**: 101–163

Hwang, D. F., Hour, J. L., Cheng, H. M. (2000) Effect of taurine on toxicity of oxidized fish oil in rats. *Food Chem. Toxicol.* **38**: 585–591

Keith, M. E., Ball, A., Jeejeebhoy, K. N., Kurian, R., Butany, J., Dawood, F., Wen, W. H., Madapallimattam, A., Sole, M. J. (2001) Conditioned nutritional deficiencies in the cardiomyopathic hamster heart. *Can. J. Cardiol.* **17**: 449–458

King, J. (1965) Lactate dehydrogenase. In: Van, D. (ed.) *Practical clinical enzymology*. Nostrand Co., London, pp 83–93

Krishnaswami, S. (1998) Observations on serial changes in coronary artery disease in Indians. *Curr. Sci.* **74**: 1064–1068

Kumar, S. H. S., Anandan, R., Devaki, T., Kumar, M. S. (2001) Cardioprotective effects of *Picrorhiza kurroa* against isoproterenol-induced myocardial stress in rats. *Fitoterapia* **72**: 402–405

Lake, K. (1994) Alterations of ventricular contractility and myofibril loss in taurine-deficient hearts. *Adv. Exp. Med. Biol.* **359**: 335–342

Lombardini, J. B. (1996) Taurine depletion in the intact animal stimulates *in vitro* phosphorylation of a ~44-kDa protein pre-

sent in the mitochondrial fraction of the rat heart. *J. Mol. Cell. Cardiol.* **28**: 1957–1961

Lowry, O. H., Rosebrough, N. J., Farr, A. L., Randall, R. J. (1951) Protein measurement with Folin phenol reagent. *J. Biol. Chem.* **193**: 265–275

Meister, A., Anderson, M. E. (1983) Glutathione. *Annu. Rev Biochem.* **52**: 711–760

Misra, H. P., Fridovich, T. (1972) The role of superoxide ion in the auto-oxidation of epinephrine and a simple assay for superoxide dismutase. *J. Biol. Chem.* **247**: 3170–3175

Mohur, A., Cook, I. J. Y. (1957) Simple methods for measuring serum levels of glutamic-oxalo acetic and glutamic-pyruvic transaminase in routine laboratories. *J. Clin. Pathol.* **10**: 394–399

Nirmala, C., Puvanakrishnan, R. (1996) Protective role of curcumin against isoproterenol induced myocardial infarction in rats. *Mol. Cell. Biochem.* **159**: 85–93

Obrosova, I. G., Fathallah, L., Stevens, M. J. (2001) Taurine counteracts oxidative stress and nerve growth factor deficit in early experimental diabetic neuropathy. *Exp. Neurol.* **172**: 211–219

Ohkawa, H., Onishi, N., Yagi, K. (1979) Assay for lipid peroxides in animal tissue by thiobarbituric acid reaction. *Anal. Biochem.* **95**: 351–358

Okinaka, S., Kumagai, H., Ebashi, E., Sugaita, M., Momoi, Y., Toyokura, Y. (1961) Serum creatine phosphokinase activity in progressive muscular dystrophy and neuromuscular disease. *Arch. Neurol.* **4**: 520–526

Pagila, D. E., Valentine, W. N. (1967) Studies on the glutathione characterization of erythrocyte glutathione peroxidase. *J. Lab. Clin. Med.* **70**: 158–169

Pion, P. D., Kittleson, M. D., Rogers, Q. R., Morris, J. G. (1987) Myocardial failure in cats associated with low plasma taurine: a reversible cardiomyopathy. *Science* **237**: 764–768

Ravichandran, L. V., Puvanakrishnan, R., Joseph, K. T. (1990) Alterations in the heart lysosomal stability in isoproterenol induced myocardial infarction in rats. *Biochem. Int.* **22**: 387–396

Redmond, H. P., Stapleton, P. P., Neary, P., Bouchier-Hayes, D. (1998) Immunonutrition: the role of taurine. *Nutrition* **14**: 599–604

Renteria, R. C., Johnson, J., Copenhagen, D. R. (2004) Need rods? Get glycine receptors and taurine. *Neuron* **41**: 839–841

Rodriguez-Martinez, E., Rugerio-Vargas, C., Rodriguez, A.I., Borgonio-Perez, G., Rivas-Arancibia, S. (2004) Antioxidant effects of taurine, vitamin C, and vitamin E on oxidative damage in hippocampus caused by the administration of 3-nitropropionic acid in rats. *Int. J. Neurosci.* **114**: 1133–1145

Saravanan, G., Prakash, J. (2004) Effect of garlic *(Allium sativum)* on lipid peroxidation in experimental myocardial infarction in rats. *J. Ethnopharmacol.* **94**: 155–158

Sathish, V., Vimal, V., Ebenezar, K. K., Devaki, T. (2002) Synergistic effect of nicorandil and amlodipine on mitochondrial function during isoproterenol-induced myocardial infarction in rats. *J. Pharm. Pharmacol.* **54**: 133–137

Schaffer, S., Azuma, J., Takahashi, K., Mozaffari, M. (2003) Why is taurine cytoprotective? *Adv. Exp. Med. Biol.* **526**: 307–321

Sharma, M., Kishore, K., Gupta, S. K., Joshi, S., Arya, D. S. (2001) Cardioprotective potential of *Ocimum sanctum* in isoproterenol induced myocardial infarction in rats. *Mol. Cell. Biochem.* **225**: 75–83

Suchalatha, S., Shyamala Devi, C. S. (2004) Protective effect of *Terminalia chebula* against experimental myocardial injury induced by isoproterenol. *Indian J. Exp. Biol.* **42**: 174–178

Takahara, S., Hamilton, B. H., Nell, J. V., Kobra, T. Y, Ogawa, Y., Nishimura, E. T. (1960) Hypocatalasemia: a new genetic carried state. *J. Clin. Invest.* **29**: 610–619

Takenaga, T., Imada, K., Otomo, S. (2000) Hypolipidemic effect of taurine in golden Syrian hamsters. *Adv. Exp. Med. Biol.* **483**: 187–192

Timbrell, J. A., Seabra, V., Waterfield, C. J. (1995) The in vivo and in vitro protective properties of taurine. *Gen. Pharmacol.* **26**: 453–462

Warskulat, U., Flogel, U., Jacoby, C., Hartwig, H. G., Thewissen, M., Merx, M. W., Molojavyi, A., Heller-Stilb, B., Schrader, J., Haussinger, D. (2004) Taurine transporter knockout depletes muscle taurine levels and results in severe skeletal muscle impairment but leaves cardiac function uncompromised. *FASEB J.* **18**: 577–579

Wright, C. E., Tallan, H. H., Lin, Y. Y., Gaull, G. E. (1986) Taurine: biological update. *Annu. Rev. Biochem.* **55**: 427–453