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Original Article | Artículo Original

Desmodium gangeticum root extract attenuates isoproterenol-induced cardiac hypertrophic growth in rats

[*El extracto de raíz de* Desmodium gangeticum *atenúa el crecimiento hipertrófico cardíaco inducido por isoproterenol en ratas*]

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Abstract

Context: Desmodium gangeticum (L) DC (Fabaceae; DG), a medicinal plant that grows in tropical habitats, is widely used to treat various ailments including digestive and inflammatory disorders.

Aims: To investigate the possible cardioprotective activity of a DG root extract against isoproterenol (ISO)-induced left ventricular cardiac hypertrophy (LVH) in adult Wistar rats.

Methods: Daily intraperitoneal administration of ISO (10 mg/kg body weight, single injection) for 7 days induced LVH in rats. The LVH rats were post-treated orally with DG (100 mg/kg body weight) for a period of 30 days. Thereafter, changes in heart weight (HW) and body weight (BW), HW/BW ratio, percent of hypertrophy, collagen accumulation, activities of matrix metalloproteinase (MMP) -2 and -9, superoxide dismutase (SOD) and catalase (CAT) enzymes, and the level of an oxidative stress marker, lipid peroxide (LPO), were determined.

Results: HW/BW ratio, an indicator of hypertrophic growth, was significantly reduced in DG root post-treated LVH rats as compared with that for the non-treated LVH rats. The altered levels of ventricular LPO, collagen, MMPs-2 and -9, and antioxidant enzymes in the ISO-treated animals reverted back to near normal upon DG treatment. Further, the anti-hypertrophic activity of DG was comparable to that of the standard drug losartan (10 mg/kg).

Conclusions: The results of the present study suggest that the aqueous root extract of DG exhibited anti-hypertrophic activity *in-vivo* by inhibiting ISO-induced ROS generation and MMP activities.

Keywords: *Desmodium gangeticum;* cardiac hypertrophy; collagen; isoproterenol; losartan; MMPs.

Resumen

Contexto: Desmodium gangeticum (L) DC (Fabaceae; DG), una planta medicinal que crece en hábitats tropicales, se usa ampliamente para tratar varias dolencias, incluyendo desórdenes digestivos e inflamatorios.

Objetivos: Investigar la posible actividad cardioprotectora del extracto de raíz de DG contra la hipertrofia cardiaca ventricular izquierda (LVH) inducida por isoproterenol (ISO) en ratas Wistar adultas.

Métodos: La administración intraperitoneal diaria de ISO (10 mg/kg peso corporal, en una sola inyección) por 7 días indujo LVH en ratas. La LVH fue tratada oralmente con DG (100 mg/kg peso corporal) por un periodo de 30 días. Posteriormente, se determinaron cambios en el peso del corazón (HW) y peso corporal (BW), la relación de HW/BW, porcentaje de la hipertrofia, la acumulación de colágeno, las actividades de metaloproteinasas de matriz (MMP)-2 y -9, las enzimas superóxido dismutasa (SOD) y catalasa (CAT), y el nivel de un marcador de estrés oxidativo, lipoperóxido (LPO).

Resultados: La relación HW/BW, un indicador de crecimiento hipertrófico, se redujo significativamente en ratas tratadas con extractos de la raíz de DG después de la inducción de LVH en comparación con las ratas con LVH no tratadas. Las concentraciones alteradas de LPO ventricular, colágeno, MMP-2 y -9, y las enzimas antioxidantes en los animales tratados con ISO volvieron a valores cercanos a los normales después del tratamiento con DG. Además, la actividad anti-hipertrófica de DG fue comparable a la del fármaco de referencia losartán (10 mg/kg).

Conclusiones: Los resultados del presente estudio sugieren que el extracto acuoso de la raíz de DG presenta actividad anti-hipertrófica *in-vivo* mediante la inhibición de la generación de ROS inducida por ISO y las actividades de MMP.

Palabras Clave: Colágeno; *Desmodium gangeticum;* hipertrofia cardiaca; isoproterenol; losartán; MMPs.

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INTRODUCTION

Left ventricular cardiac hypertrophy (LVH) has been identified as an independent risk factor for heart failure, which is the primary cause of mortality worldwide (Lip et al., 2000; Gradman & Alfayoumi, 2006). Abnormal thickening of the ventricular chamber wall and diastolic dysfunction are clinical symptoms of the hypertrophied heart (Frohlich, 1991). However, the underlying molecular mechanism, that activates hypertrophic growth in the heart, is not well understood.

Extracellular matrix (ECM) collagen plays a major role in maintaining the architecture and preserving the contractile function of the myocardium (Porter et al., 2009; Mann et al., 2011). Abnormal collagen accumulation in the heart contributes to myocardial stiffness and ventricular dysfunction (Swan, 1994). It has been reported that a large amount of collagen is secreted into the intercellular and perivascular spaces of the myocardium during the process of LVH and remodeling (Huang et al., 2012). Matrix metalloproteinase -2 and -9 reportedly play an important role in balancing extracellular matrix production and degradation in the myocardium (Nagase et al., 2006). Unbalanced activation of them has been identified as a cause for the increased accumulation of collagen in the intercellular and perivascular spaces of the hypertrophied myocardium (Heineke & Molkentin, 2006).

Synthetic drugs such as angiotensin-converting enzyme inhibitors (captopril and enalapril) (Wing et al., 2003), an AT1 receptor blocker (losartan) (Shibasaki et al., 2002), β-blockers (e.g., propranolol) (Ostman-Smith, 1995), diuretics (e.g., Thiazidea) (Shah et al., 2004), etc. are effective in attenuating the LVH and heart failure. However, in recent years, researchers have shown considerable interest in treating diseases with extracts of medicinal plants because of their low toxicity and potential pharmacological properties (Rates, 2001). Medicinal plants have been used in the Indian system of medicine (siddha and ayurvedha) to treat various diseases, including infectious and non-infectious ones.

Desmodium gangeticum (Fabaceae family) is a small medicinal shrub abundantly found in tropical countries such as India, China, Africa, and Australia (Kurian et al., 2010). The root portion of this plant is used as the main ingredient in famous ayurvedic preparations such as *"Dashmoola," "Dashmularistha," "Dashmula-kwath," "Chitrak haritika," "Dashmoola kadha," "Dashmoola ark," "Dhanvantar tailum"* and *"Brah-ma rasayan"* (Niranjan & Tewari, 2008).

This medicinal herb is used to treat various ailments such as digestive, inflammatory, and cardiovascular disorders (Chopra et al., 1956). Three pterocarpinoids, namely gangetin, gangetinin, and desmodin were identified as the major chemical constituents present in the root of DG (Purushothaman et al., 1971). Gangetin has been reported to have anti-inflammatory and analgesic activities (Kurian & Paddikkala, 2009). Moreover, *in-vitro* studies have shown that DG root extracts possess strong antioxidant, anti-hypertrophic, and anti-inflammatory activities (Sankar et al., 2013). Hence, the present study was designed to investigate the possible *in-vivo* anti-hypertrophic activity of a DG root extract against ISO-induced cardiac hypertrophy.

MATERIALS AND METHODS

Chemicals

Isoproterenol hydrochloride (catalogue no. I5627) and Direct red 80 (catalogue no. 365548) were purchased from Sigma, St. Louis, MO, USA. Gelatin came from CDH Laboratories, New Delhi, India. All other chemicals used were of analytical grade.

Plant material

DG specimens were collected in the month of September 2011 from in and around the Thanjavur district, Tamilnadu. The herbarium specimen of the plant were deposited at CAS in Botany herbarium (Voucher specimen, CASBUM 1006), University of Madras and the identity of the plants was confirmed by Dr. N. Mathivanan, Associate Professor, Centre for Advanced Studies in Botany, University of Madras, Chennai, Tamil Nadu, India.

Preparation of root extract

Collected fresh root samples were carefully washed with deionised water and immediately allowed to air dry. The dried roots were finely powdered by using a commercial blender. The root sample (1 kg) was extracted with 1000 mL of water in a successive manner in Soxhlet apparatus for 48 h, after which it was filtered and the aqueous portion condensed. The final condensed portion was weighed (8 g) and stored at -20°C for further use.

Animals

Adult male albino rats of the Wistar strain, weighing around 120 to 150 g, were used for the study. All animals were purchased from Tamil Nadu Veterinary and Animal Science University, Chennai, India. The rats were maintained in individual polypropylene cages under standard temperature (25 ± 2°C) and 12 h light/dark photoperiod. The animal were acclimatized for a week before the start of the experiment and fed a commercial pellet diet (Hindustan Lever Ltd., Bangalore, India) and given free access to water.

Ethics statement

The experiments were designed and conducted according to the norms of the Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA), Ministry of Social Justices and Empowerment, Government of India. The protocol for conducting this study was approved by Institutional Animal Ethics Committee guidelines (IAEC No. 02/02/2011).

Experimental design

A total of 30 animals were divided into 5 groups, each comprising 6 animals. Group I was untreated and served as the control; Group II rats received ISO (10 mg/kg BW; intraperitoneal injection daily for 7 days); Group III rats received ISO and post-treatment with oral administration (gavage syringe feeding) of DG (100 mg/kg daily for a period of 30 days); Group IV received ISO and post-treatment with LOS (10 mg/kg orally for 30 days), which served as a positive control; and Group V rats received the DG extract alone. Body weight was recorded during the experimental period. At the end of experimental period (i.e., on the day 38th) the animals were subjected to ketamine anesthesia (90 mg/kg body weight, Intramuscular injection) and were sacrificed by cervical decapitation. The collected blood and heart samples were placed at -20°C for further examination.

Heart weight, body weight and HW/BW ratio

The HW/BW ratio is considered as a sensitive indicator of hypertrophic growth. Hence, the whole heart was harvested from the 5 different experimental groups of rats. The residual blood was removed with the help of filter papers. The weight of the each heart was then recorded, after which the HW/BW ratio was calculated.

Preparation of left ventricular tissue homogenate and biochemical parameters

The excised left ventricular tissue was washed several times in ice-cold saline, and 50 mg of it was subsequently homogenized in Tris-buffer, pH 7.4. The resultant homogenate was centrifuged at 20 000 rpm for 5 min at 4°C (Urata et al., 1990). The tissue debris was separated, and the homogenate was stored at -20°C until further use. Protein quantification was carried out with Bradford reagent (BIO-RAD Laboratories, Inc). The left ventricular homogenate was used to determine the levels of cardiac collagen (Mukherjee & Sen, 1990) and lipid peroxidation (Ohkawa et al., 1979).

Gelatin zymography analysis of matrix metalloproteinase-2 and -9

The levels of MMP-2 and -9 were examined by gelatin zymography (Vellaichamy et al., 2005). The frozen LV tissue was homogenized in ice-cold MMP extraction buffer (10 mM cacodylic acid, 150 mM NaCl, 0.01 mM $ZnCl_2$, 20m M $CaCl_2$, 2 mM NaN_3 and 0.1% Triton X-100; pH 5.0). The extracted MMPs (20 µg of protein) were separated on an 8% native-PAGE gel containing substrate (10 mg/mL of gelatin). The gel was then sequentially washed with 2.5% Triton X-100 for 1 h, incubated at 37°C in developing buffer for 12-18 h, stained with 0.25% Coommassie Brilliant Blue R250, and

distained until the clear gelatin lytic bands appeared.

Sirius red staining of cardiac collagen

For determination of the collagen content, 5-micrometer-thick sections of ventricle were prepared, attached to glass slides, and stained with 0.1% picrosirius red (10 mg of Sirius red in 10 mL of aqueous picric acid solution). With the use of light microscope, these sections were analyzed morphometrically. Fibrillar collagen deposition appeared red in color (Pick et al., 1989).

Superoxide dismutase (SOD) activity assay

The SOD enzyme assay was carried out by using the native polyacrylamide gel electrophoresis (PAGE) method described by Beauchamp & Fridovich (1971). Protein samples (30 µg/lane) were separated on a 10% native-PAGE gel. The gel was then soaked in a riboflavin-NBT solution (2-5 mL) at room temperature for 15 min in the dark (riboflavin being light sensitive). After incubation the riboflavin-NBT solution was removed, and 2-5 mL of 0.1% TEMED was added, followed by 15 min incubation at room temperature in the dark. Remove the staining solution the keep the gel in light which induces superoxide synthesis.

Catalase (CAT) activity assay

The CAT enzyme activity was examined by using the native polyacrylamide gel electrophoresis (PAGE) method of Woodbury et al. (1971). Protein samples (30 µg/lane) were first separated on a 10% native-PAGE gel. The gel was then rinsed with distilled water and subsequently immersed in 0.003% H_2O_2 for 10-15 minutes. Thereafter, the gel was stained with 2% potassium ferric cyanide and 2% ferric chloride solution

Statistical analysis

All the values were expressed as the mean ± SEM for the 6 rats in each group. All data were analyzed by using SPSS/11.5 software. Hypothesis testing included one-way analysis of variance (ANOVA) followed by the least significant test (LSD). The probability value of $p<0.05$ was considered significant.

RESULTS

Effect of DG on heart weight, body weight, HW/BW ratio and percent of hypertrophy in control and experimental groups of rats

Table 1 presents the data obtained for the heart weight, body weight, HW/BW ratio and percent of hypertrophy in the control and experimental groups of rats. Significant increases in heart weight ($p<0.01$) and percent of hypertrophy (23%) were observed in the ISO-induced LVH rats (Group II) as compared with the values of the control rats (Group I). Both ISO+DG (Group III) and ISO+LOS (Group IV) rats showed a marked reduction in the heart weight, HW/BW ratio, and percent of hypertrophy as compared with the ISO-induced rats (Group II). The group treated with DG alone (Group V) did not show any significant alteration in body weight, heart weight or HW/BW ratio.

Effect of DG on ventricular collagen levels in control and experimental groups of rat hearts

Figure 1A presents the ventricular tissue collagen levels in the control and experimental groups of rats. The ventricular collagen level was significantly increased (295 ± 3.31 vs. 214 ± 2.4; $p<0.01$) in the ISO-induced LVH rats (Group II) as compared with the level in the control rats. However, this increased level was significantly decreased in both ISO+DG (Group III)- and ISO+LOS (Group IV)-treated groups. The DG alone (Group V)- treated rats did not show any significant changes from the control ventricular collagen level. Figure 1B (a) shows the results of picro Sirius red staining of collagen in the control and experimental rat heart sections. The ISO-induced (Group II) rat heart section showed increased collagen deposition compared with the control level (Figure 1B [b]). However, a significant reduction in collagen deposition was noted in both Group III and Group IV (Figure 1B [c] and [d]), respectively.

Table 1. Effect of *Desmodium gangeticum* aqueous root extract (DG) on body weight, heart weight, heart weight/body weight (HW/BW) ratio, and percent of hypertrophy in control (CON) and experimental groups of rats.

Group	Body weight (g)	Heart weight (g)	HW/BW ratio (g/g)	Percent hypertrophy (%)
CON	232 ± 3.39	0.467 ± 0.04	0.201 ± 0.039	-
ISO	220 ± 3.48*	0.578 ± 0.06**	0.262 ± 0.031*	23
ISO+DG	226 ± 3.89$^{\#\#}$	0.501 ± 0.06$^{\#}$	0.227 ± 0.025$^{\#}$	11
ISO+LOS	229 ± 3.67†	0.489 ± 0.05††	0.213 ± 0.037†	5.6
DG	231 ± 3.67^{NS}	0.479 ± 0.06 ^{NS}	0.207 ± 0.030 ^{NS}	-

Values are expressed as the mean ± SEM (n=6). Body weight, heart weight, and heart weight/body weight ratio, and percent of hypertrophy for each group are shown. Data are expressed as the mean ± SD. Values are given statistically significant at, CON vs. isoproterenol (ISO) **p<0.01, *p<0.05; ISO vs. ISO+DG ##p<0.01, #p<0.05; ISO vs. ISO+losartan (LOS) ††p<0.05, †p<0.05 and ^{NS}p>0.05 (Non significant).

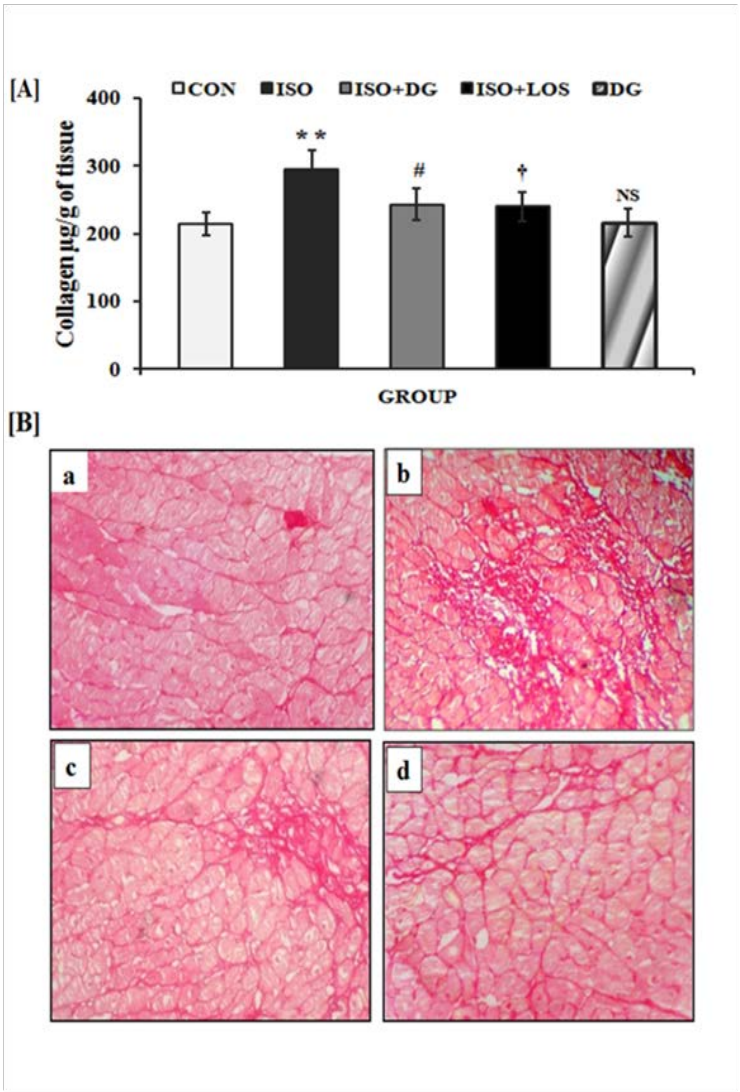

Figure 1. Collagen level and Picro-Sirius red staining of control (CON) and experimental groups of rat hearts treated with *Desmodium gangeticum* aqueous root extract (DG): **(A)** Ventricular tissue collagen levels in normal, isoproterenol (ISO)-infused, ISO+DG-, ISO+losartan (LOS)-, and DG alone-treated rat hearts. Data are presented as the means ± SEM (n=6) per group. Values are given statistical significance at **p<0.01 for CON vs. ISO; at $^{\#}$p<0.05 for ISO vs. LOS+DG; and at †p<0.05 for ISO vs. ISO+LOS. CON vs. DG, ^{NS}p>0.05 (Non significant). **(B)** Assessment of collagen architecture by Picro-sirius red staining of ventricular section from control and experimental groups of rats. Tissue sections were stained with picric acid and Sirius red (Direct red 80). Collagen appears red in color when viewed under a light microscope at 20× magnification. **(a)** Control section showing scarce deposited collagen; **(b)** ISO-induced group shows increased collagen deposition; **c** and **d**, Ventricular sections from DG **(c)** and LOS **(d)** treated rats shows comparatively less collagen deposition then the section from the ISO-induced group.

Effect of DG on MMP-2 and -9 activities in control and experimental rats

Figure 2 (A and B) presents the activity of MMP-2 and -9 and densitometric results, respectively, for the control and experimental groups of rats. Figure 2A shows that the clear white bands, representing enzyme activity, were notably reduced in size in the ISO+DG (Group III)- and ISO+LOS (Group IV)-treated rats. The ISO-induced LVH rat (Group II) heart showed 4-fold and 3-fold increases $p<0.01$ in the activities of MMP-9 and MMP-2, respectively, as compared with the control levels. The group treated with the DG extract alone did not show any alteration from the control.

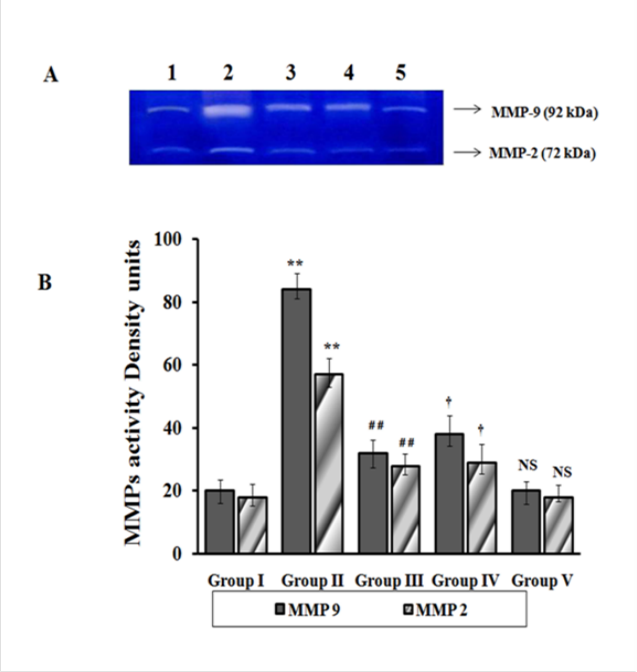

Figure 2. Activities of MMP-2 (72 kDa) and MMP-9 (92 kDa) in the five different groups of rats. **(A)** Zymograms showing enzyme activities. Lane 1, Control; lane 2, ISO-infused; lane 3, ISO + DG; lane 4, ISO + LOS; lane 5, DG alone treated group. **(B)** Results of the densitometic analysis of MMP-2 and MMP-9 activities. Data are presented as the mean ± SEM (n=6) per group. Values are given statistical significance at $^{**}p<0.01$ for CON vs. ISO; at $^{\#\#}p<0.01$ for ISO vs. ISO+DG; and at $^{\dagger}p<0.05$ for ISO vs. ISO+LOS. CON vs. DG, $^{NS}p>0.05$ (Non significant). CON: control; DG: *Desmodium gangeticum* aqueous root extract; ISO: isoproterenol; LOS: losartan.

Effect of DG on SOD, CAT activity and LPO level in control and experimental groups of rats

Figure 3 A and B show native PAGE gels of left ventricular SOD and CAT activities, respectively. Rats with ISO-induced LVH (Group II) showed significant decreases ($p<0.01$ and $p<0.05$) in their ventricular SOD and CAT activities, respectively, as evidenced by the decreased band intensity as compared with that for the control rats (Group I). In contrast, significant increases in SOD and CAT activities (increased band density) were observed in the ISO+DG (Group III)- and ISO+LOS (Group IV)-treated groups when compared with these activities in the ISO-induced LVH hearts (Group II). Rats treated with DG alone (Group V) did not show any abnormalities in either enzyme activity. The level of LPO, an oxidative stress marker, is presented in Figure 3E. ISO-induced LVH rats (Group II) showed a significant ($p<0.05$) increase in their cardiac LPO level, whereas ISO+DG (Group III)- and LOS (Group IV)-treated ones showed significantly decreased levels of ventricular LPO. Group V rats (DG alone) did not show any changes from normal in their SOD or CAT activity or in their LPO level.

DISCUSSION

The results obtained from this study demonstrate that treatment with the aqueous DG root extract effectively prevented the ISO-induced experimental cardiac hypertrophy and fibrosis in adult male rats.

The heart weight/body weight ratio (HW/BW) is considered to be a sensitive indicator of hypertrophic growth (Warren et al., 2003). In the present study, DG treatment effectively prevented the hypertrophic growth and fibrosis as evidenced by the near normal level of HW/BW ratio in the DG post-treated rats. This anti-hypertrophic effect of the DG root extract was comparable to that of losartan treatment. Losartan is a well-known AT_1 receptor blocker, and is prescribed as a drug for the treatment of hypertensive and cardiomyopathic patients (Strauss & Hall, 2006). Our results (*in-vivo)* coincide well with those of the recent *in-*

vitro study carried out by Sankar et al. (2013), who suggested that DG root extract inhibits ISO-induced cardiomyoblast hypertrophic growth by inhibiting ROS generation.

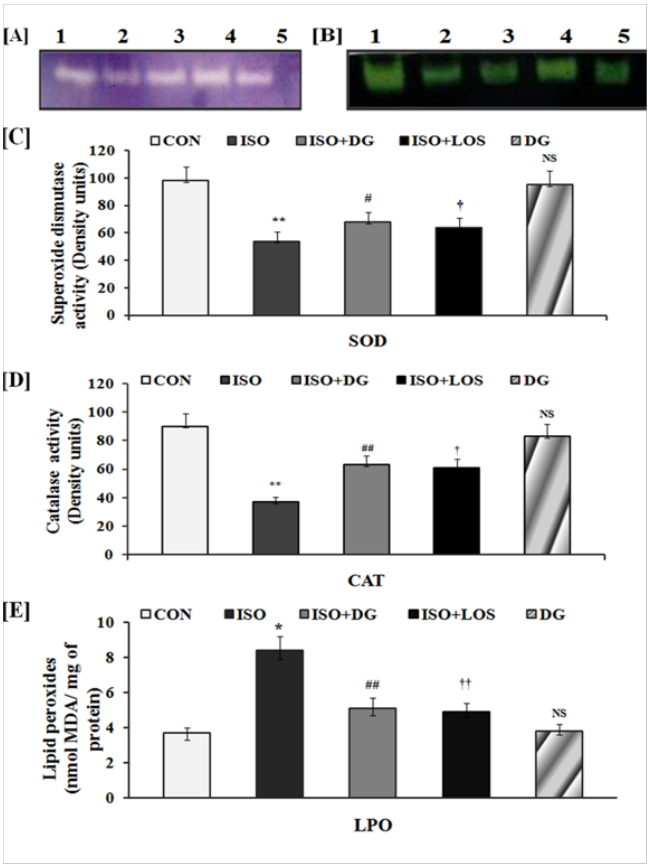

Figure 3. Effect of *Desmodium gangeticum* aqueous root extract (DG) on superoxide dismutase (SOD) and catalase (CAT) activities and on lipid peroxidation (LPO) level in the control (CON) and experimental groups of rats. A and B: Native polyacrylamide gel stained for SOD **(A)** or CAT **(B)** activity in the various groups of hearts. Lanes: 1, control; 2, isoproterenol (ISO) infused; 3, ISO + losartan (LOS); 4, ISO + DG; 5, DG alone. Data are presented as the mean ± SEM (n=6) per group. Values are statistical significance at $^{**}p<0.01$ for CON vs. ISO; at $^{\#\#}p<0.01$ or $^{\#}p<0.05$ for ISO vs. ISO+DG; and at $^{\dagger}p<0.05$ for ISO vs. ISO+LOS. CON vs. DG, $^{NS}p>0.05$ (Non significant). C and D: Results of densitometric analysis of SOD **(C)** and CAT **(D)** bands. **(E)** Lipid peroxidation activity of the 5 different groups. The levels of LPO are expressed as nmol of MDA/mg of protein. Values are given statistical significance at $^{*}p<0.05$ for CON vs. ISO; at $^{\#\#}p<0.01$ for ISO vs. ISO+DG; and at $^{\dagger\dagger}p<0.01$ for ISO vs. ISO+LOS. CON vs DG, $^{NS}p>0.05$ (Non significant).

Increased collagen deposition in the ventricular tissue is considered to be a sensitive indicator of fibrosis development (D'Armiento, 2002). Moreover, increased levels of MMP-2 and -9 activities were observed in the left ventricular tissue of ISO-infused hypertrophied rats, indicating that an ECM remodeling process had been activated in their hearts. MMPs have been shown to play a critical role as modulators of the myocardial ECM in cardiac pathologies including heart failure and ischemia-reperfusion injury (Chow et al., 2007). A positive correlation has been reported between the increased levels of activeted ventricular MMPs and collagen degradation of the ECM (Ko et al., 2005). It has been suggested that collagen sub fragments degraded by selective MMPs such as MMP-2, MMP-9, and MMP-13 promote collagen synthesis by disrupting the balance between synthesis and degradation, resulting in collagen accumulation and cardiac fibrosis (Evans et al., 2012).

In the present study, an increased level of collagen accumulation was observed in the ISO-induced LVH rat hearts, confirming the development of cardiac fibrosis. The increased level of MMP-9 activity in the ISO-infused rat hearts would seem to be associated with the development of cardiac hypertrophy and ventricular remodeling. The rats post-treated with DG showed decreased ventricular levels of MMP-2 and MMP-9, suggesting that the DG root extract possessed antifibrotic activity. Phytochemical analysis of DG root extracts has revealed that they contain several natural antioxidants and active compounds, such as gangetin, gangetinin, and desmodin (Rastogi et al., 2011). These active compounds are reported to have strong antioxidant and anti-inflammatory properties. Moreover, the natural flavonoids in them, such as myricetin reportedly to have MMP inhibitory activity (Ko et al., 2005). Thus, the observed decresed level of collagen accumulation in the DG extract-treated rats could have been be due to natural antioxidants and active compounds such as gangetin, gangetinin, and desmodin in the extract. Similar to our observation, Kurian et al. (2005) have reported that DG root extracts are effective in protecting against ISO-induced myocardial infarction and damage.

It has been demonstrated that stimulation of beta adrenergic receptors leads to excessive generation of reactive oxygen species (ROS) in

the myocardium (Sies, 1997). An increased oxidative stress during and following myocardial damage induced by ISO has been recorded (Gutteridge, 1982). The observed increased level of LPO in the ISO-treated group was probably due to the formation of free radicals and also to alterations in the level of antioxidants, leading to oxidative stress (Sies, 1997). The increased level of lipid peroxidation caused by ISO may have affected the mitochondrial and cytoplasmic membranes, causing more oxidative damage in the heart, with consequent release of LPO into the circulation (Chattopadhyay et al., 2003).

The decreased level of CAT activity in the ISO-treated rats may have been due to excessive generation of O_2^-. In the present study, treatment with DG extract was as effective as that with losartan in restoring the altered CAT enzyme level back to near normal. Our results are in agreement with those of Kurian and Paddikkala (2009).

Thus, the presently observed cardioprotective effect of the DG root extract was probably due to the presence of antioxidant and anti-inflammatory active compounds (Kurian & Paddikkala, 2009).

CONCLUSIONS

The results of the present study suggest that the aqueous root extracted of DG exhibited anti-hypertrophic activity by inhibiting ISO-induced ROS generation and MMP activities.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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