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Antioxidant Role of *Caralluma indica* Stem Extract in Isoproterenol Induced Oxidative Stress in Albino Rats

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Plants are important for human life on earth and serve as the food. Another important aspect of the plant is therapeutic use. Medicinal plants afford a best source of active compounds to find new medicines that have no adverse effects, such as those that are a very respectable source of disease treatment, that are associated with oxidative stress. Oxidative stress plays a significant role in the pathogenesis of a myocardial infarction (MI) and has been well recognized in the properties of isoproteinol-induced MI. Current research aims to investigate the role of antioxidants in the *Caralluma indica* stem extract (CISE) in isoproterenol -induced oxidative stress in albino rats. Depending on the results achieved, CISE can be a suitable candidate to reduce the oxidative stress induced by isoproterenol. CISE management shows an increase in antioxidant status in the treatment of isoproterenol as follows. The cardioprotective properties of CISE can be attributed to the antioxidant components of CISE.

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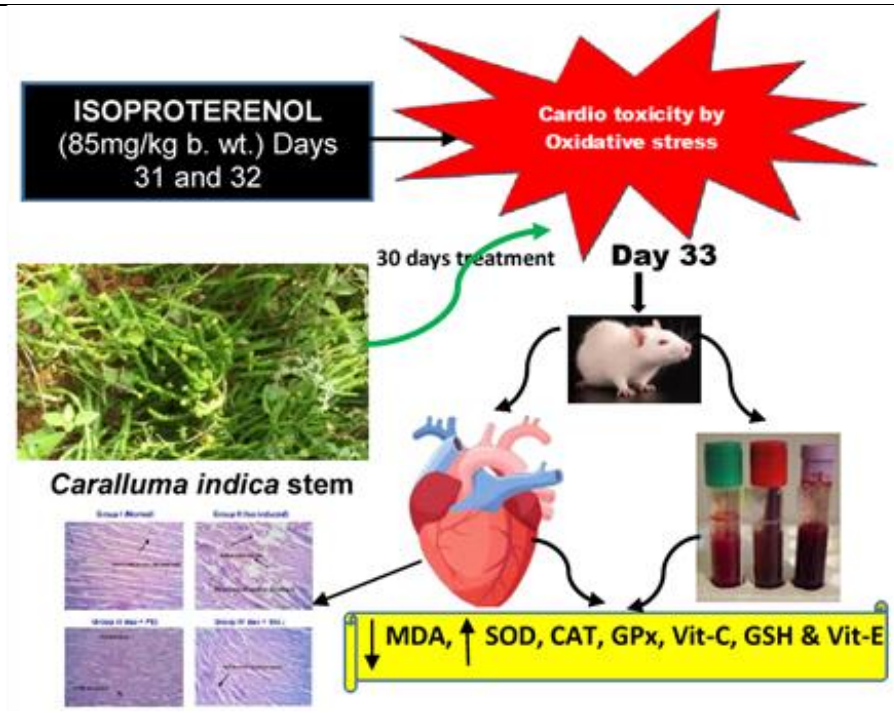

Graphical abstract of antioxidant role of Caralluma indica stem extract

Keywords: Medicinal plants; antioxidants; Caralluma indica; oxidative stress; Isoproterenol.

1. INTRODUCTION

Oxidative stress is the inequality between the production of free radicals and the defense against antioxidants in the body. Free radicals are compounds with unpaired electrons that become highly reactive molecules, that can attack stable molecules such as lipids, carbohydrates and proteins. Antioxidants interact with free radicals, neutralize them and prevent damage from oxidative stress. Therefore, they are called radical scavengers. Antioxidants are substances that significantly delay or prevent the oxidation of a substrate [1,2,3] if they are in lower concentrations than that of an oxidizable substrate. Medicinal plants are an important type of plant and can be used to treat diseases and improve human health according to modern scientific research and conventional medical practice. These plants are considered a rich source of ingredients for the synthesis and manufacture of medicinal products [4]. Plants are a major source of new phytochemicals with beneficial property [5,6,7].

Numerous studies have shown that the medicinal properties of plants are due to the presence of bioactive agents in their extracts [8,9]. Therefore medicinal plants and extracts from natural substances were regarded as alternative therapy for various diseases [10]. Eating antioxidant foods and fruits plays an important role in increasing the body's natural resistance to oxidative stress [11.12]. The plants also contain many other antioxidant nutrients, including alkaloids, phenols, and flavonoids. These polyphenolic compounds are extensively examined and documented as free radical quenchers [13]. The plant is stated to have many secondary compounds with antioxidant activity with a varied kind of therapeutic applications. The selected medicinal plant, namely the *Caralluma indica* tribe, belongs to the Apocynaceae family. and is widespread in Tamil Nadu, Andhra Pradesh and Karnataka. No pharmacological studies have been performed on the *Caralluma indica* stem. Therefore, this study aimed to investigate the antioxidant effects of *Caralluma indica* stem extract (CISE) in isoprotenol-induced oxidative stress in albino rats.

2. MATERIALS AND METHODS

2.1 Animals

The study used male albino rats, a Wister strain weighing approximately 180 to 220 g. They were

healthy animals bought by Sri Venkateswara in Bangalore, India. The animals were housed in a spacious polypropylene cage with a rice shell. The animal chambers were well ventilated and kept under experimental standard conditions (temperature 27±2ºC, light 12 hours / dark cycle) throughout the test period. All animals received a standard pellet-based diet (Gold Mohur, Mumbai, India) and a water-based *ad libitum*. It adapted to its surroundings 1 week before experimental use. The experiment was conducted in accordance with the guidelines of the Committee (ethical number: CPCSEA / 265) for the control and monitoring of animal testing (CPCSEA) in New Delhi, India.

2.2 Chemicals

Nitroblutetetrazolium (NBT), ethylenediaminetetraacetic acid (EDTA), trichloroacetic acid (TCA), thiobarbituric acid (TBA), 1-chloro-2,4-dithirobenzene (CDNB), 5,5'-dithio-bis (2-nitrobenzoic acid), and L-ascorbic acid were obtained from Sigma Chemical Company (St. Louis, Missouri, USA). All other chemicals used were of analytical quality and were obtained from the Glaxo Institute in Mumbai, India, and from the Sisco Research Institute in Mumbai, India.

2.3 Plant Material

The *Caralluma indica* tribe was harvested in November 2017 from the Kathattiipattii of Sengipatti, Thanjavur district, Tamil Nadu, India. The stems have been identified and certified by doctor John Britto. The voucher sample (from RSV01) were deposited in St. Herbarium. Rapinat Herbarium, St. Josephs College, Tiruchirappalli, Tamil Nadu, India.

2.4 Preparation of Alcoholic Extract

The *Caralluma indica* stems were first washed numerous times with distilled water to remove traces of contamination from the stems. The unhealthy and damaged parts of the stems were then removed. A healthy stem was distributed on plain paper and dried in the shade for about 10 days at room temperature. Cut the collected stems into small pieces and make a fine powder with a grinding mixture. Powder extracted with ethanol extract for 24 hours. After 24 hours, the supernatant was transferred into china dish. Upper layer was completely removed by keeping Chine dish on a 45°C water bath. The extract is then concentrated until the solvent is completely removed. After the solvent has been completely removed, a semi-solid extract is obtained. CISE was kept in the refrigerator and used for other experiments. The therapeutic dose as 250 mg/kg was used for subsequent studies as reported by [14].

2.5 Experimental Design

After a week of acclimatization, the animals were randomly divided into four groups, each with six rats. In group I (normally controlled), normal animals have 1 ml /kg B.W. of saline solution with standard food and water to maintain their libido throughout the test. was administered. Group II (Negative control), the rats were orally fed normal saline once daily for 30 days and in addition, received isoproterenol (ISO) (85mg/kg body weight) on the 31 and 32 day at an interval of 24 h. In group III (manipulation of extracts), the rats were treated with CISE (250 mg/kg body weight, SC) plus isoproterenol 85 mg / in 31 and 32 days every 24 hours. Group IV rats (positive control) were treated with atorvastatin (10 mg/kg) and isoprotenol 85 mg/kg body weight for 30 days. 31 And 32 days every 24 hours. ISO (85 mg) is dissolved in ordinary saline solution (1 ml) and in rats (85 mg/s. C) was injected subcutaneously /kg to induce experimental myocardial infarction for 2 days at 24-hour intervals.

2.6 Collection of Samples

After completing the second ISO injection of (24 hours during the test period, the animal was anesthetized with thiopentone sodium (50 mg/kg). With or without EDTA, the blood was taken as an anticoagulant. Plasma was separated to estimate various biochemical parameters. The heart tissue was removed, washed with ice saline and weighed. Their known weight has been used for the preparation of homogenates and for various biochemical analyses.

2.7 Biochemical Estimations

"Malondialdehyde was estimated by the Beuge thiobarbiturate assay method" [15]. The superoxide dismutase activity is analyzed according to the method of Kakkar et al. [16]. "The activity of catalase was determined by the method of Beers and Sizer" [17]. The activity of glutathione peroxidase was determined using the estimation of Rotruck et al. [18]. The ascorbic acid content was determined using Omaye et al.

[19]. Tocopherol according to the method of Baker et al. [20] analyzed. Histological examination of the heart, carried out according to the method of Ochei and Kolkhatkar, [21].

2.8 Statistical Analysis

In vivo values were presented as the mean SD of ± for six rats in each group, and the statistical difference in significance between the mean values was determined by a unidirectional analysis of variance (ANOVA) followed by an analysis of the Duncan multiplicity test. A statistical analysis was used, which was carried out by the Graph Pad Instat software based on Ms Windows (Graph Pad software from San Diego, California, USA) 3. The value of $P < 0.05$ was considered statistically significant.

3. RESULTS

Myocardial infarction (MI), known as heart attack, is one of the most common cardiovascular diseases. Certain medications or mechanical means are used, Natural products such as herbal or spice based MI treatments are becoming more popular than drugs or mechanical agents day after day due to their pharmacological effects with little or no side effects. In this study, we examined the relationship between CISE biopotency and the antioxidant enzyme defense system.

3.1 Effect of *Caralluma indica* on Plasma Antioxidant

Tables 1 and 1 showed the effect of CISE on the defense against plasma antioxidants in the control and tested rats. Measuring antioxidant activity in plasma may be a good approach to studying the integrated effects of many antioxidants. The active antioxidant activity in the ISO treatment group was administered with CISE (or a dose of 250 mg per 1 kg body weight). The CISE treatment group has restored plasma antioxidant enzymes such as superoxide dismutase (SOD), to the, catalase (CAT) and glutathione peroxidase (GPx) as well as non-enzymatic antioxidant enzymes such as glutathione (GSH), vitamin C and vitamin E. Malondialdehyde (MDA) showed and increased a significant reduction in glutathione (GSH) content in plasma from the ISO treatment group. Restored antioxidant defense was observed significantly ($p < 0.05$), which was close to the norm in animals treated with atorvastatin and controlled by group I. These results suggest that oxidative stress has disappeared due to the effects of CISE.

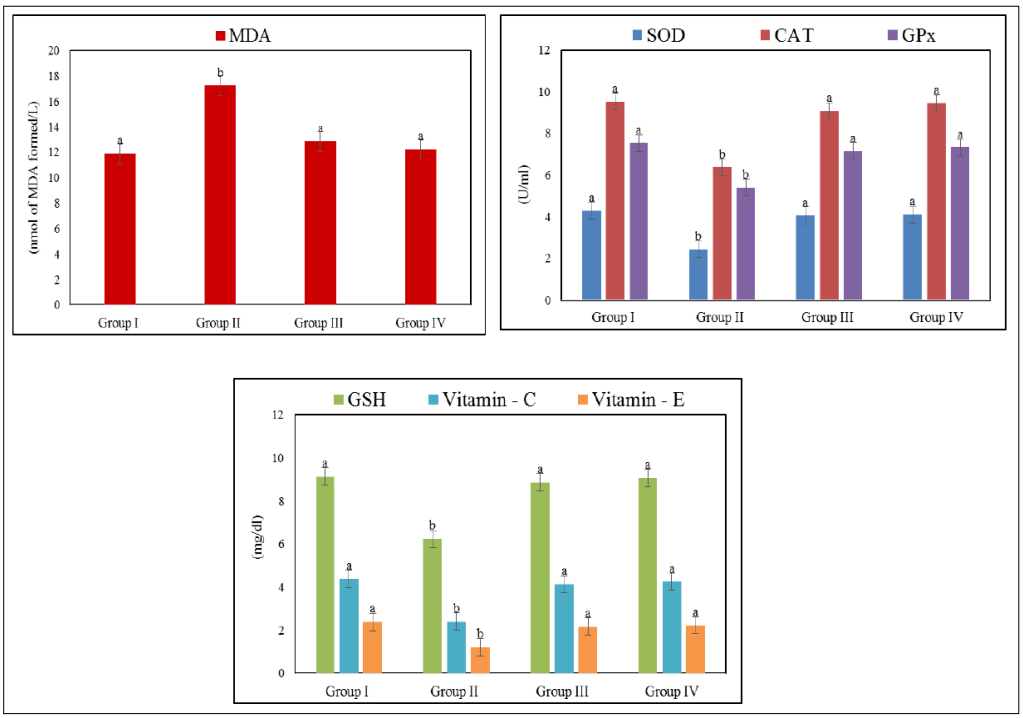

Fig. 1. Effect of *Caralluma indica* on plasma antioxidant defence of control and experimental rats

Table 1. Effect of CISE on plasma antioxidant defence of control and experimental rats

Parameters	Group I	Group II	Group III	Group IV
MDA (nmol of MDA formed/L)	11.90 ± 0.55^{a}	17.24 ± 0.74^{b}	12.85 ± 0.77^{a}	12.25 ± 0.60^{a}
GSH (mg/dl)	9.13 ± 0.24^{a}	6.24 ± 0.27^{b}	8.86 ± 0.33^{a}	9.07 ± 0.36^{a}
SOD (U/ml)	4.29 ± 0.21^{a}	2.44 ± 0.31^{b}	4.06 ± 0.17^{a}	4.11 ± 0.23^{a}
CAT (U/ml)	9.52 ± 0.24^{a}	$6s.38 \pm 0.30^{b}$	9.07 ± 0.50^{a}	9.44 ± 0.30^{a}
GPx (U/ml)	7.52 ± 0.26^{a}	5.40 ± 0.29^{b}	7.14 ± 0.30^{a}	7.32 ± 0.23^{a}
Vit-C (mg/dl)	4.38 ± 0.22^{a}	2.40 ± 0.24^{b}	4.13 ± 0.13^{a}	4.25 ± 0.17^{a}
Vit-E (mg/dl)	2.38 ± 0.18^{a}	1.21 ± 0.16^{b}	2.17 ± 0.07^{a}	2.22 ± 0.14^{a}

Values are expressed as Mean ± SD for six rats

Mean values with diverse superscripts letters in the same row were considered statistically significance (P<0.05), while those with the similar superscript character were not significance (P>0.05) when compared to each other.

3.2 Effect of CISE on Heart Antioxidant

The ISO treatment group was administered to ICES (or 250 mg per kg body weight) and cardiac antioxidants (Table 2 and Fig. 2). The MDA concentration was significantly higher in the hearts of ISO-treated rats compared with ordinary control animals, including, that these ingredients reach almost normal values in the heart of rats treated with ISO + CISE. Conversely, the GSH, vitamin C and E content in the centre of the group II animals decreased significantly compared with the controls. However, group III animals have been found to, as the content of GSH, vitamin C and E normalizes almost after treatment with CISE. The activity of SOD, CAT and GPx showed a significant decrease in the rats treated with ISO compared with the usual control. In rats treated with ISO + CISE, the activity of these enzymes was almost normalized.

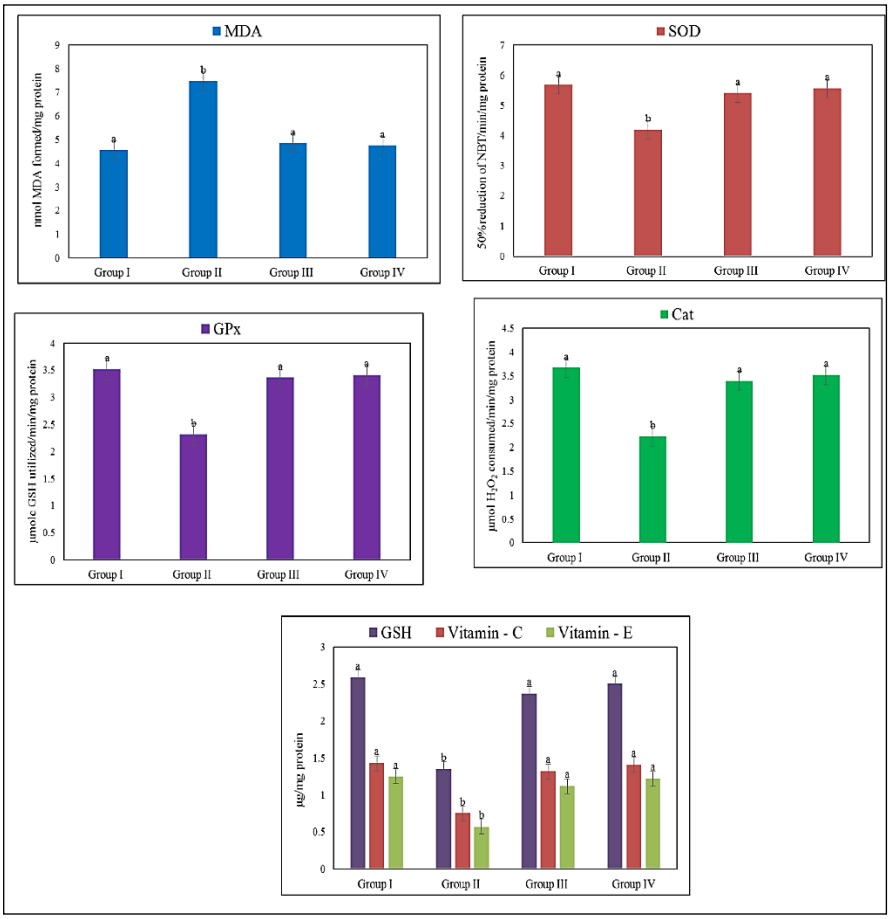

Fig. 2. Effect of *Caralluma indica* on heart antioxidant defence of control and experimental rats

Table 2. Effect of *Caralluma indica* on heart antioxidant defence of control and experimental rats

Parameters	Group I	Group II	Group III	Group IV
MDA	4.56 ± 0.38^{a}	7.47 ± 0.36^{b}	4.85 ± 0.24^{a}	4.74 ± 0.30^{a}
GSH	2.59 ± 0.26^{a}	1.35 ± 0.15^{b}	2.37 ± 0.25^{a}	2.50 ± 0.24^{a}
SOD	5.68 ± 0.22^{a}	4.20 ± 0.29^{b}	5.41 ± 0.22^{a}	5.56 ± 0.19^{a}
Cat	3.67 ± 0.16^{a}	2.23 ± 0.22^{b}	3.40 ± 0.25^{a}	3.52 ± 0.20^{a}
GPx	3.52 ± 0.28^{a}	2.31 ± 0.21^{b}	3.36 ± 0.18^{a}	3.41 ± 0.16^{a}
Vit C	1.43 ± 0.14^{a}	0.75 ± 0.07^{b}	1.32 ± 0.16^{a}	1.41 ± 0.13^{a}
Vit E	1.25 ± 0.12^{a}	0.57 ± 0.13^{b}	1.12 ± 0.14^{a}	1.22 ± 0.16^{a}

Values are expressed as Mean ± SD for six rats

Mean values with diverse superscripts letters in the same row were considered statistically significance (P<0.05), while those with the similar superscript character were not significance (P>0.05) when compared to each other. MDA: nmol MDA formed/mg protein; SOD: 50% reduction of NBT/min/mg protein; Catalase: μmol H_2O_2 consumed/min/mg protein. Glutathione peroxidase: μmole GSH utilized/min/mg protein; Reduced Glutathione: μg/mg protein; Vitamin C: μg/mg protein; Vitamin E: μg/mg protein.

3.3 Effect of CISE on Heart Histology

Histopathology can be used to assess the health of the organ. Such an approach has the advantage of being able to detect other diseases such as exposure to chemical pollutants and changes in toxic effects due to other idiopathic lesions that may affect the health of rats. Histological sections of the cardiac tissue in normal control rats showed a normal structure. The rats that underwent ISO treatment caused severe heart damage, as evidenced by pathological changes in the structure of the heart. The heart muscle portion of the rats pretreated with CISE showed persistent damage (Plate 1). The histopathology of myocardial tissue also confirms the vital capacity of CISE.

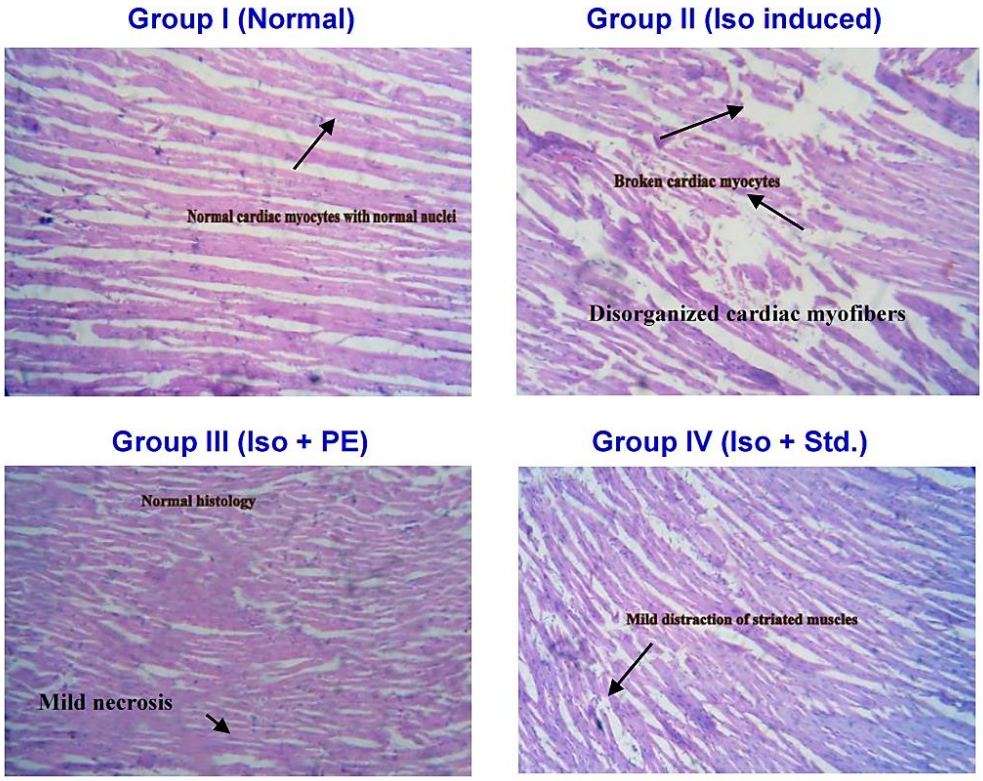

Plate 1. Histological observation of heart tissue in control and experimental rats (40x)

Iso: Isoproterenol; PE: Plant extract; Std.: Atorvastain

Group I: The normal structure of the heart with a regular arrangement with clear bands of myocardial fibers without histological changes. Group II: Isoprotenol-induced rats showed degeneration of the heart, destruction of myocardial fibers, pronounced necrosis of the ventricular areas and an area of invasive edema. Group III: Pretreatment of ICES (250 mg/kg showed that the infarct area decreased with mild necrosis, and, the inflammatory cells with edema and cardiac fibers in the heart muscle of the rats were within the normal range. Group IV: Atorvastatin (10 mg /kg) pretreatment /kg) showed that the heart had an almost normal appearance, with slight changes in constipation and necrosis.

4. DISCUSSION

Oxidative stress shows an important role in the pathophysiology of myocardial infarction (MI). “Oxidative stress is the effects of which are well documented by the IM induced by isoproterenol” [22]. “Oxidative stress affects heart function through the reduced activity of antioxidant enzymes such as catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GPX)” [23]. “Reactive oxygen species (ROS) induce lipid peroxidation, promote malondialdehyde (MDA) formation, and contribute to the release of proapoptotic factors from mitochondria” [24]. “It has been confirmed that isoprenaline (ISO), a non-selective synthetic agonist of beta-adrenergic receptors, induces MI at high doses (85 – 340 mg/kg) in the rat” [25,26] which causes an imbalance between the production of free radicals and antioxidants and antioxidants. ISO-induced IM is documented in numerous studies in laboratory animals with properties similar to those of humans.

In recent years, there has been an increasing emphasis on plant research around the world, and there has been a lot of evidence gathered to demonstrate the immense potential of medicinal plants used in various traditional systems [27]. More than 20,000 plants have been studied in the last 5 years. Two important facts that are focused on research on medicinal plants are dietary supplements. Research on plants that are part of our normal diet has been compiled independently of activity Second research on phytochemical research related to pharmacological activity [28]. Current research to study the phytochemical analysis of CISE in relation to biological activity in the field of view.

4.1 Effect of CISE on Plasma and Heart Antioxidants

Oxidative stress can be exerted by ISO metabolites, which react with molecular oxygen to produce superoxidanions and other ROS, which can interfere with the antioxidant enzymes of cells [29]. Endogenous and exogenous defense against antioxidant enzymes plays an important role in neutralizing tissue damage caused by oxygen free radicals. SOD, Catalase and GPx are the most important enzymes for capturing free radicals that are involved in the first line of cellular defense against oxidative damage, oxygen [30], and, remove both O_2 [and hydrogen peroxide (H_2O_2) before interacting to form more reactive hydroxyl radicals.

“Malondialdehyde (MDA) is a major aldehyde that results from the peroxidation of polyunsaturated fatty acids in the biomembrane. MDA, a secondary product of lipid peroxidation, is used as an indicator of tissue damage caused by a series of chain reactions” [31]. “Ray and Husain study of lipid peroxidation has attracted much attention in recent years due to its role in the disease process. Membrane lipids are particularly sensitive to lipid peroxidation due to the presence of polyunsaturated fatty acids. It is involved in the pathogenesis of many diseases and clinical conditions. These include atherosclerosis, cancer, etc. Experimental and clinical data suggest that aldehyde products of lipid peroxidation also act as bioactive molecules under physiological and pathological conditions. It is now widely recognized that lipid peroxidation and its products play an important role in liver, kidney, heart and brain toxicity” [32].

MDA is one of the indicators of oxidative stress. In this context a marked increase in the concentration of MDA was observed in plasma and heart of ISO treated rats when compared to control rats. ISO administration caused a marked elevation in LPO, which was expressed as MDA content, in line with previous reports [29,33]. Pretreatment with CISE significantly decreased the levels of MDA in plasma and heart of ISO treated rats. Present study agreement with researcher [34] study who reported the decreased MDA content on treatment with *Trichopus zeylanicus* against myocardial ischemia induced by isoproterenol in rats.

Superoxidants and hydroxyl radicals are known to significantly damage the surrounding tissues

and organs. Natural or synthetic compounds with antioxidant properties can help reduce liver damage in whole or in part. Therefore, the removal of superoxides and hydroxyl radicals is probably one of the most effective defense mechanisms against various diseases. Mercury promotes the formation of reactive oxygen species (ROS) such as hydrogen peroxide [35]. ISO results in a significant decrease in the activity of antioxidant serum and cardiac enzymes in myocardial rats. SOD and CAT activity. The two enzymes used to remove superoxide or. The contribution to hydroxylyone was significantly lower in ISO-treated rats than in control rats. The reduced activity of SOD and CAT leads to the accumulation of these highly reactive free radicals, this leads to adverse effects such as loss of cell membrane integrity and membrane function [36]. The restoration of SOD and CAT activity observed in our study on CISE treatment may affect the direct stimulatory effect of CISE on SOD and CAT and the activity to remove radicals free from CISE Extract.

Glutathione peroxidase is common in almost all tissues. The main intracellular distribution is in the cytosols and mitochondria as well as in the extracellular fluoride. In this study, the GPx activity of rats treated with ISO was reduced compared to controlled rats. The observed reduction in GPx activity indicates increased H2O2 production and lower GSH levels in ISO-treated rats. Pretreatment with CISE in rats treated with ISO restored the activity of the GPx activity. Restored activity of GPx may increase the level of GSH in rats treated with ISO. The reduction in the activity of the SOD, CAT and GPx enzymes is consistent with the results of previous studies [37,38].

“Glutathione is a ubiquitous thiol that contains tripeptide and plays a central role in cell biology. It is involved in cellular defense against xenobiotics and natural harmful compounds such as free radicals and hydrogen peroxide. Glutathione status is a sensitive indicator of the functionality and viability of the cells. GSH depletion is associated with many conditions, including cancer, neurodegenerative diseases, kidney and cardiovascular diseases. The kidneys are exposed to various cytotoxic agents before these agents are eliminated in the urine. Therefore, the concentration of GSH in kidney cells is important” [39]. In this study, a significant decrease in GSH concentration was observed in plasma and heart of ISO-treated rats compared to control rats. Pretreatment with CISE significantly increased GSH levels in plasma and in the hearts of ISO-treated rats.

“Organisms have developed complex antioxidant systems to fight off the reactive species of oxygen. These antioxidant systems include enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. Polymers such as albumin, celluloplasmin, ferritin and various small molecules, including ascorbic acid, alpha-tocopherol, glutathione, methionine, etc, uric acid and reduction of bilirubin” [40]. “Antioxidants are defined as “all substances that significantly slow or prevent oxidation of a substrate if they are present in low concentrations compared to substances in an oxidizable substrate. When ROS/RNS occurs, its effects are rejected by the antioxidant lines of complex and coordinated defense systems. This includes enzymatic and non- antioxidants that check ROS/RNS levels and repair oxidative cellular damage” [41].

“Cyclic non-enzymatic antioxidants such as vitamin E and vitamin C are scavengers of free radicals. Their synergy in the elimination of oxygen-related free radicals of origin is well documented” [42]. Vitamin E reacts with lipid peroxyl radicals, which act as chain terminators for lipid peroxidation, and vitamin C helps to maintain the level of vitamin E at optimal concentrations. Serum levels of vitamin E and vitamin E in this study were significantly reduced in ISO-treated rats compared to controls in plasma and heart. This reduced content of vitamin C and vitamin E indicates its use to cleanse free radicals produced by ISO metabolism. CISE pretreatment significantly increased the vitamin C and vitamin E content in plasma and heart of ISO-treated rats.

The improvement of antioxidant systems for enzymes (SOD, CAT, GPx) and non-enzymes (GSH, vitamin C, E) in plasma and heart corresponds to several reported [43,44,45]. The standardized extract of lyophilized hydroalcohol from *Bacopa monnieri* produced maximum cardiac protection, as shown by the significant recovery of endogenous antioxidants (superoxide dismutase, catalase, etc, glutathione peroxidase and glutathione reduction) by [46.47]. Cardioprotective activity of the *Commiphora mukul*. was examined. *Commiphora mukul*. , known as Guggul, has significantly reversed the reduction of myocardial antioxidants. superoxide dismutase, catalase, glutathione peroxidase, glutathione reduction and enhanced lipid peroxidation.

We tested the integer variable, i.e. Decrease in glutathione, vitamin C and vitamin E in SOD, CAT, GPX, plasma and heart showed a significant decrease in ISO treatment. CISE treatment, however, resets the values to near normal values, indicating a bioelectric potential of CISE to combat oxidative stress. Our research has also shown that CISE contains important antioxidant properties, mainly due to the content of flavonoids and phenols. This indicates that lipid peroxidation, oxidative stress and damage induced by ISO-treated rats were deactivated due to the effects of CISE.

4.2 Effect of CISE on Heart Histology

Histology is an transdisciplinary scientific discipline that uses microscopy and dyeing techniques to focus on the structure and function of normal and diseased tissues in animals. It examines comparative forms of tissues, changes in tissues and organs during embryonic development, evolutionary changes in the structure and function of tissues of different types. In clinical medicine, histology is used as a diagnostic tool to understand and treat the pathological development of body tissues [48]. This study examines histological changes in the controlled heart, ISO-treated rats, and CISE-treated rats.

According to the hematoxylin-eosin (HE) staining of the cardiac tissue, normal histology of the scratched cardiac tissue, branched appearance and continuity with neighboring myofibrils were observed in the control group. Rats in group II-ISO showed pathological changes in the heart, such as cardiac degeneration, disturbed myocardial fibers, etc, pronounced necrosis in the ventricular region and an invasive area with edema. The heart had an almost normal appearance with minor changes in constipation and necrosis in rats treated with the standard drug atorvastatin. The same scheme was obtained in rats treated with a CISE 250 mg/kg ethanol extract. Thus, this study showed that CISE ethanol extract can protect the heart from myocardial infarction. Histological observation of the cardiac part corresponds to biochemical changes. Current research agreement with the researcher [49]. Who reported that histological changes in the heart due to treatment with isoproterenol and *Croton* species induced the Wister-Albino rat, which had a myocardial infarction. A similar result was observed for other researcher also [50].

5. CONCLUSION

Markers of oxidative stress in the form of MDA (malondialdehydes) were examined in plasma and cardiac control rats as well as in test rats. A significant reduction in MDA levels was observed during pretreatment with the *Caralluma* Indica stem extract (CISE). The results showed that the oxidative stress induced by ISO was deactivated by the CISE. We tested the integer variable, i.e. Decrease in glutathione, vitamin C and vitamin E in SOD, CAT, GPX, plasma and heart showed a significant decrease in ISO treatment. CISE treatment, however, resets the values to near normal values, indicating a bioefficacy potential of CISE to combat oxidative stress. Restoration of histological changes in cardiac tissue in rats treated with ISO during CISE treatment which support the biochemical parameters. Therefore, the continue to confirm the cardioprotective potentiality of CISE extract. Overall, CISE showed a rich source of plant substances and had potential antioxidants, activity, and restoration of histological changes with ISO. This study is the first scientific report, which represents the antioxidant property of CISE and thus offers scientific validity for the old consumption of South Indian society.

ETHICAL APPROVAL

The experiment was conducted in accordance with the guidelines of the Committee (ethical number: CPCSEA / 265) for the control and monitoring of animal testing (CPCSEA) in New Delhi, India.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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