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RESEARCH ARTICLE

Cardioprotective effect of Hrudroga Chintamani Rasa in isoproterenol induced cardiotoxicity in male Sprague Dawley rats

Ankit P. Laddha[1,2] · Mukesh B. Chawda[1,2] · Yogesh A. Kulkarni[1,2]

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Abstract

Purpose Ayurvedic system, a traditional medicinal system has mentioned a preparation Bruhat Vata Chintamani Rasa (Suvarnayukta) for management of heart diseases. Hrudroga Chintamani Rasa (HCR) is a formulation containing Bruhat Vata Chintamani Rasa and a few additional ingredients having beneficial effects in heart diseases. The present study was designed to investigate the cardioprotective activity of the Hrudroga Chintamani Rasa in isoproterenol (ISO)-induced myocardial infarction in rats.

Methods Male Sprague Dawley rats were treated with HCR at a dose of 56.16 and 112.32 mg/kg for 30 days. Animals received ISO (85 mg/kg. *s.c.*) on 28th and 29th day at an interval of 24 h.

Result Disease control animals treated with HCR at a dose of 56.16 mg/kg and 112.32 mg/kg to rats showed a significant reduction in elevated levels of aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and creatine phosphokinase MB (CK-MB), and prevented loss of depleted antioxidant enzymes from the cardiac tissue. ISO-altered electrocardiogram pattern and haemodynamic parameters were also brought about to normal by treatment with HCR. HCR treatment also improved the levels of 5' adenosine monophosphate-activated protein kinase (AMPK) and Silent information regulator 1 (SIRT1) which have potent role in antioxidant defence mechanism. Histopathological findings also showed HCR treatment prevented cardiac tissue from damage.

Conclusion HCR treatment showed a significant cardioprotective effect in ISO-induced cardiotoxicity in rats probably because of the potent antioxidant activity.

Keywords Myocardial infarction · Ayurvedic system · Cardiovascular · Isoproterenol · Hrudroga Chintamani Rasa · Cardio toxicity

Introduction

As per the World Health Organization (WHO) report, Coronary Artery Disease (CAD) prevalence continues to rise in India and other parts of the world at a rapid rate. In Western countries, the incidence of CAD in the young population is 2–5%, whereas it is 11–16% in Asian Indians. This disease affects patients living in the most productive years of their lives [1].

Acute myocardial infarction is a severe condition of ischemic heart disease which is a key marker worldwide to the mortality caused within the population suffering from CAD [2]. It is well known that ischemic heart tissue forms oxygen-derived free radicals that are responsible for oxidative damage of membrane lipids and proteins. This abnormality develops the quantitative and qualitative alterations of the myocardium [3]. If cardiac ischemia remains for a longer duration it leads to a myocardial infarction which is nothing but the death of heart muscle tissue.

Isoproterenol (ISO) is a catecholamine derivative that has β-adrenergic agonist activity. It causes a positive inotropic and chronotropic effect which increases myocardial oxygen demand, when administered in high dose in rats and develops ischemic necrosis of myocardium. Autoxidation of ISO generates cytotoxic free radicals which causes peroxidation of phospholipids of the myocardium

✉ Yogesh A. Kulkarni
yogeshkulkarni101@yahoo.com

[1] Shobhaben Pratapbhai Patel School of Pharmacy & Technology Management, SVKM's NMIMS, V.L. Mehta Road, Vile Parle (West), Mumbai 400056, India

[2] Shree Dhootapapeshwar Limited, 135, Nanubhai Desai Road, Khetwadi, Mumbai 400 004, India

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and alters its permeability and ultimately damages the myocardium. A higher dose of catecholamine also depletes the reserved energy of cardiac muscle and develops biochemical and structural abnormality in the myocardium [4]. ISO at selected dose develops the same condition which is more relevant with the clinical condition of myocardial infarction and hence the ISO induced model was selected for the study.

Various treatment options as reactive oxygen species scavengers are now in a developing phase and will be considered as newer therapeutic interventions for ischemic diseases.

Ayurvedic medicines (herbs, minerals, and their formulations) can be beneficial in reducing the risk of heart diseases. Hrudroga Chintamani Rasa is a rational combination of widely used cardioprotective ingredients like Bruhat Vata Chintamani Rasa (Suvarnayukta), Akeek Pishti- (processed Agate gem (mineral of silica)], Abhraka Bhasma (processed mica), Poornachandrodaya Makardhwaja- ayurvedic mineral-based preparation, Arjuna stem bark (*Terminalia arjuna.* Roxb) (Chunekar, K 1500–1600 AD), Jatamansi rhizome (*Nardostachys jatamansi* D.Don*) DC*), Manjishtha stem (*Rubia cordifolia.* L) and Dashamoola Kwath (Supplementary data 1). All these ingredients work in synergy to improve cardiac functioning.

Bruhat Vata Chintamani Rasa is a classical gold-containing cardioprotective formulation offering the benefits of Suvarna Bhasma (Processed Gold), Raupya Bhasma (Processed Silver), Abhrak Bhasma (Processed Mica), Loha Bhasma (Processed Iron), Pravala Bhasma (Processed Coral), Mouktik Bhasma (Processed Pearl), Rasasindoor and the herb Kumari (*Aloe barbadensis* Miller). Arjuna stem bark (*Terminalia arjuna. Roxb*) is a widely used herb in the management of cardiovascular diseases. Its effectiveness as a cardioprotective agent, preventing reperfusion ischemic injury to the heart and the potential to reduce atherogenic lipid levels are documented in experimental and clinical studies [5]. Jatamansi rhizome (*Nardostachys jatamansi (D.Don) DC*) is also documented for its cardioprotective and hypolipidemic effect in myocardial injury induced by doxorubicin in rats. Its cardioprotective action could be due to its anti-lipid peroxidative properties [6].

Manjishtha stem (*Rubia cordifolia. L*) is documented to protect the rats from cyclophosphamide-induced cardiac tissue injury by restoring the antioxidant markers [7]. Dashamoola (Roots of ten herbs) formulation alone and its combination with aspirin is reported for anti-inflammatory, analgesic, and anti-platelet effects comparable to aspirin [8].

In the present study, a herbomineral formulation Hrudroga Chintamani Rasa (HCR) tablets were tested for its activity against ISO-induced cardiotoxicity in rats.

Materials and methods

Male Sprague Dawley rats (180–220 g) were purchased from the National Institute of Biosciences, Pune, Maharashtra, India, and housed in the animal facility. The temperature of 22 ± 2 °C, relative humidity 75 ± 5%, and a 12 h light/dark cycle were maintained in an animal facility throughout the study. Animals received a basal multi-nutritional diet and purified water, ad libitum. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) (Approval Number & Date: CPCSEA/IAEC/P-35/2019, 10th August 2019). Animals were treated following the National Research Council(NRC) guidelines for the care and use of laboratory animals [9].

Chemicals and kits

Isoproterenol (ISO) was procured from Sigma (St. Louis, MO, USA). Kits for determination of serum Lactate dehydrogenase (LDH), Creatinine kinase (CK-MB), and Aspartate transaminase (AST) were obtained from Transasia Biomedicals Ltd., India. ELISA kits of 5' adenosine monophosphate-activated protein kinase (AMPK) and Silent information regulator 1 (SIRT1) were procured from Bioassay Technology Laboratory, Birmingham, United Kingdom.

Experimental design

Male Sprague Dawley rats after 7 days of acclimatization were randomly divided into four groups six animals each. Animals were treated with HCR for a period of 30 days and ISO was administered simultaneously on 28th and 30th day of treatment.

The detailed treatment regimen was as follows:

Group I (Normal control): Animals in this group received vehicle (0.5% Carboxymethyl cellulose- CMC) for 30 days.

Group II (Disease control): Animals in this group received 0.5% CMC for 30 days and additionally, received ISO (85 mg/kg. *s.c.*) on the 28th and 29th day at an interval of 24 h [10].

Group III (HCR, Low dose): Animals in this group received HCR (56.16 mg/kg *p.o.*) for 30 days and additionally, received ISO (85 mg/kg. *s.c.*) on the 28th and 29th day at an interval of 24 h.

Group IV (HCR, High dose): Animals in this group received HCR (112.32 mg/kg *p.o.*) for 30 days and additionally received ISO (85 mg/kg. *s.c.*) on the 28th and 29th day at an interval of 24 h.

Parameters assessed

Assessment of electrocardiogram

An electrocardiogram (ECG) was recorded with the help of the Power Lab data acquisition system (AD Instruments, Australia).

Assessment of haemodynamic studies

The mid-line incision was given near the chest portion and the left carotid artery was canulated for measurement of hemodynamic, left ventricular end-diastolic pressure (LVEDP), rate of ventricular contractility (+ dp/dt and –dp/dt), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MABP) [11].

Estimation of cardiac marker enzymes

Blood was withdrawn from heart by cardiac puncture and serum was separated by centrifugation at 5000 RPM for 15 min.

The marker enzymes AST, LDH, and CK-MB were assayed using Transasia Biomedical kits as per the standard protocol. The measurement was carried out on ERBA chem 7 biochemical analyzer (Germany).

Assessment of AMPK, SIRT1 and cTn-I levels

Levels of AMPK, SIRT1, and cTn- I were determined using 96 well-plate rats ELISA kits [12].

Determination of cardiac hypertrophy

Animals were sacrificed after 30 days of treatment and heart tissue was isolated and weighed. The percentage of heart to body weight ratio was taken to determine relative organ weight.

Determination of oxidative stress parameters and histopathological evaluation

Isolated heart tissues were washed with ice-cold saline. A mid-line cut was given to divide heart tissue into two equal parts. One part of heart tissue was used for the determination of oxidative stress parameters and the other part was used for histopathology [13–15][16].

Statistical analysis

Statistical analysis was carried out using Graph pad prism 5 software. One way ANOVA, Bonferroni's multiple comparison test were carried out to determine the level of significance. $P < 0.05$ were kept as the level of significance.

Results

Effect of HCR electrocardiogram

A significant increase in PR interval, QT interval, and ST-segment was reported in disease control animals when compared with of normal control animals ($p < 0.001$). HCR treatment at a low dose significantly reduced the elevated PR interval, QT interval, and ST-segment ($p < 0.05$). HCR at high dose significantly reduced the elevated PR interval ($p < 0.01$), QT interval ($p < 0.01$) and ST-segment ($p < 0.001$). A significant reduction in QRS duration was observed in disease control animals when compared to normal control animals ($p < 0.001$). Treatment with HCR at low and high

Table 1 Effect of HCR on electrocardiogram

Treatment Groups / Parameters	Normal Control	Disease Control (ISO 85 mg/kg)	ISO + HCR (Low Dose)	ISO + HCR (High Dose)
PR Interval (Sec)	0.02826 ± 0.0033	0.05273 ± 0.0038$^{###}$	0.03808 ± 0.0023*	0.0354 ± 0.0032**
QT Interval (Sec)	0.05176 ± 0.0033	0.1079 ± 0.0084$^{###}$	0.07767 ± 0.0097*	0.06607 ± 0.0069**
QRS Duration (Sec)	0.06748 ± 0.0068	0.01893 ± 0.0011$^{###}$	0.05028 ± 0.0030*	0.05521 ± 0.0088**
ST Segment (mV)	0.06765 ± 0.0182	0.2171 ± 0.0188$^{###}$	0.166 ± 0.011*	0.1053 ± 0.009***

Values are expressed as Mean ± S.E.M. (n = 6). ***p < 0.001,**p < 0.01 and *p < 0.05 when compared with disease control, $^{###}$p < 0.001 compared with normal control

doses showed a significant increase in QRS duration when compared to disease control animals ($p < 0.05$ and $p < 0.01$) (Table 1).

Effect of HCR on haemodynamic parameters

Disease control animals also showed a significant reduction in SBP, DBP and MABP ($p < 0.001$). Treatment with HCR at low dose significantly improved ($p < 0.05$) the reduced SBP, DBP and MABP when compared with disease control animals. HCR treatment at high dose significantly improved the reduced SBP ($p < 0.05$), DBP ($p < 0.01$) and MABP ($p < 0.05$) when compared with disease control animals (Fig. 1).

Left ventricular end diastolic pressure (LVEDP) was also found to be elevated in disease control animals when compared with normal control animals ($p < 0.001$). HCR treatment at low and high dose significantly attenuated the elevated LVEDP ($p < 0.01$ and $p < 0.001$). Significantly reduced + dp/dt and –dp/dt was observed in disease control animals when compared with normal animals ($p < 0.001$). Treatment with HCR at low dose significantly improved the + dp/dt and –dp/dt when compared with disease control animals ($p < 0.05$). Treatment with HCR at high dose significantly improved the + dp/dt and –dp/dt when compared with disease control animals ($p < 0.01$ and $p < 0.001$). (Fig. 2).

Effect of HCR on biochemical parameters

Serum levels of AST, LDH and CK-MB were found to be significantly increased in disease control animals when compared to normal control animals ($p < 0.001$). Treatment with HCR at a high dose significantly reduced the elevated levels of serum AST and CK-MB ($p < 0.01$ and $p < 0.001$) when compared with disease control animals. HCR at low and high doses significantly reduced ($p < 0.05$ and $p < 0.01$) the level of LDH when compared with disease control animals. (Fig. 3).

Effect of HCR on AMPK and SIRT1 level

Disease control animals showed significantly reduced serum levels of AMPK and SIRT1 when compared with normal control animals ($p < 0.001$ and $p < 0.01$). Treatment with HCR at low dose did not affect the level of AMPK and SIRT1significantly. Treatment with HCR at a high dose prevented the loss of AMPK and SIRT1 when compared with disease control animals ($p < 0.05$) (Fig. 4).

Effect of HCR on cTn-I level

Serum level of cTn-I was significantly increased in disease control animals when compared with normal control animals ($p < 0.001$). HCR treatment at low and high doses showed a reduction in the level of CTn-I significantly ($p < 0.001$) when compared with the disease control group (Fig. 5).

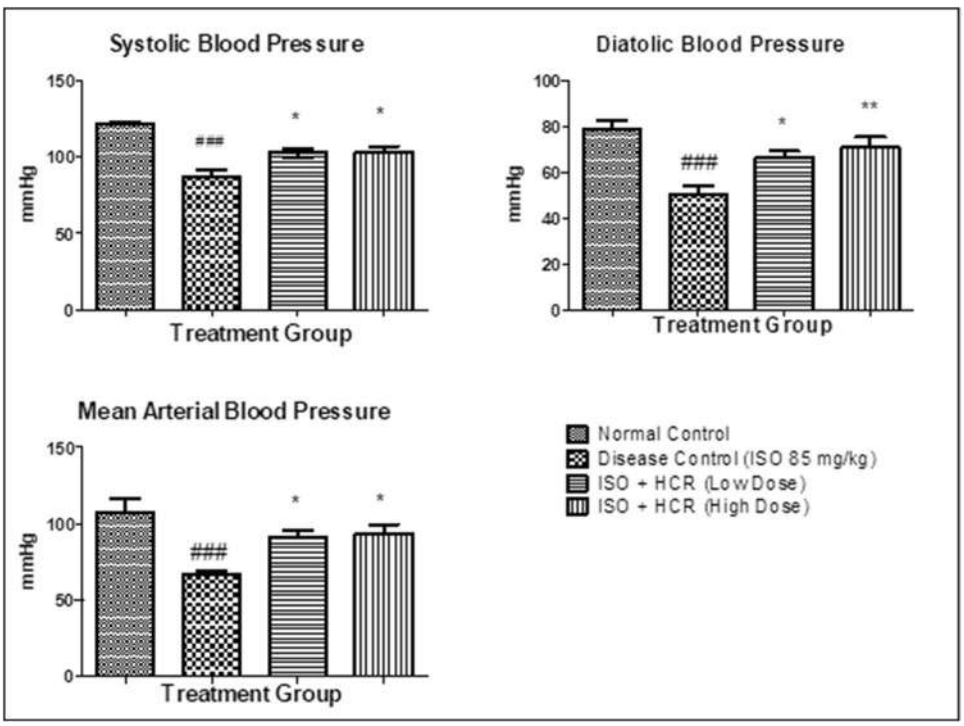

Fig. 1 Effect of HCR on systolic blood pressure, diastolic pressure and mean arterial blood pressure. All values are expressed as Mean ± S.E.M. (n = 6). **$p < 0.01$ and *$p < 0.05$ when compared with disease control. ###$p < 0.001$ compared with normal control

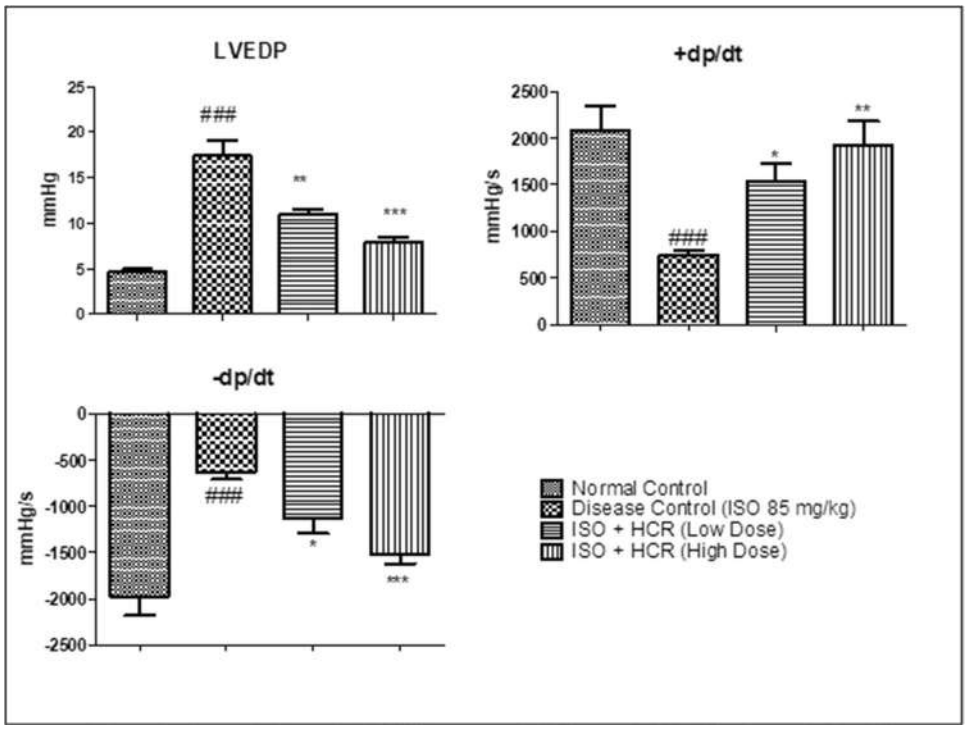

Fig. 2 Effect of HCR on left ventricular end-diastolic pressure (LVEDP) and rate of ventricular contractility (+dp/dt and –dp/dt). All values are expressed as Mean ± S.E.M. (n = 6). ***p < 0.001, **p < 0.01 and *p < 0.05 when compared with disease control. ###p < 0.001 compared with normal control

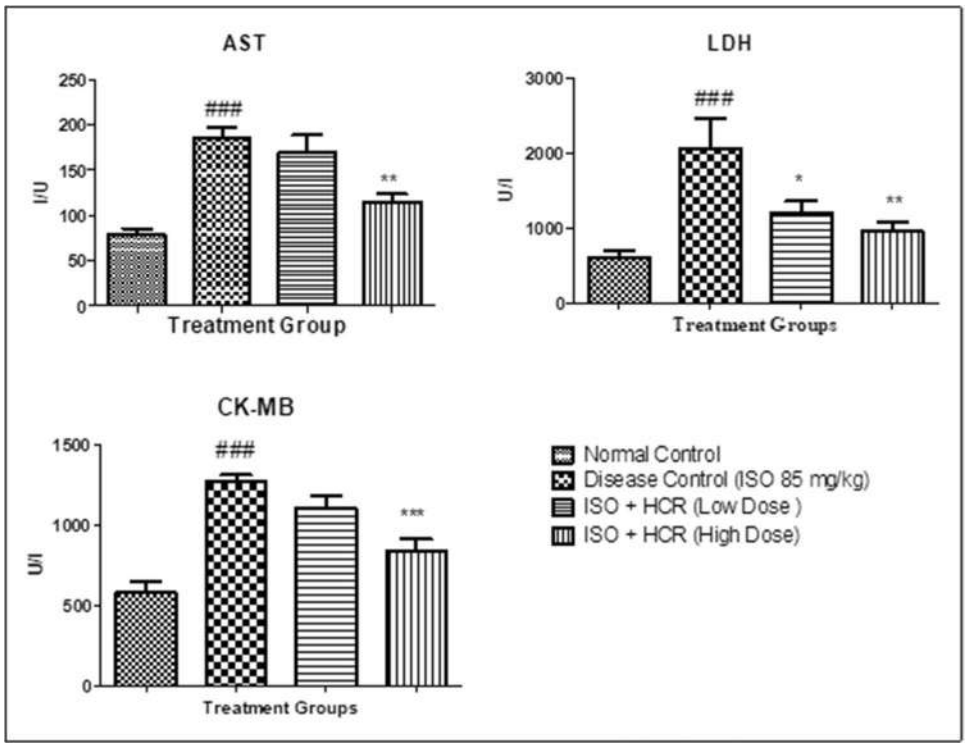

Fig. 3 Effect of HCR on biochemical parameters. All values are expressed as Mean ± S.E.M. (n = 6). ***p < 0.001, **p < 0.01 and *p < 0.05 when compared with disease control. ###p < 0.001 compared with normal control

Effect of HCR on cardiac hypertrophy

Percent heart to bodyweight ratio of disease control animals was found to be significantly increased when compared with normal control animals. HCR treatment at low and high doses significantly ($p < 0.05$ and $p < 0.001$) prevented the rise in percentage heart to body weight ratio. (Supplementary data 1).

Effect of HCR on oxidative stress parameters

Disease control animals showed a significant reduction ($p < 0.001$) in levels of antioxidant enzyme-like glutathione (GSH), Superoxide dismutases (SOD), Catalase (CAT) and a significant increase ($p < 0.001$) in the level of MDA in the heart tissue when compared with normal control animals. Treatment with HCR at selected doses significantly

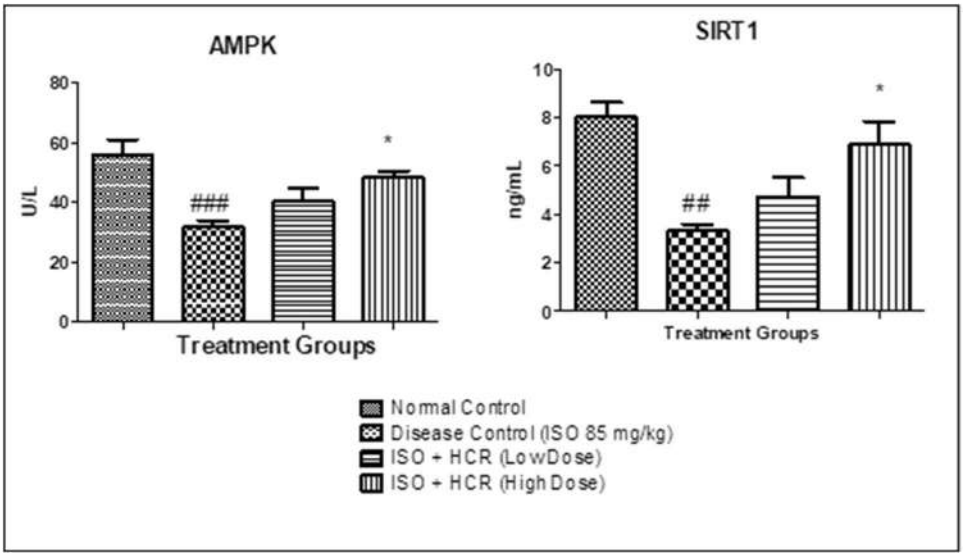

Fig. 4 Effect of HCR on 5' adenosine monophosphate-activated protein kinase (AMPK) and Silent information regulator 1 (SIRT1) levels. All values are expressed as Mean ± S.E.M. (n = 6). *$p < 0.05$ when compared with disease control. ###$p < 0.001$ and ##$p < 0.01$ compared with normal control

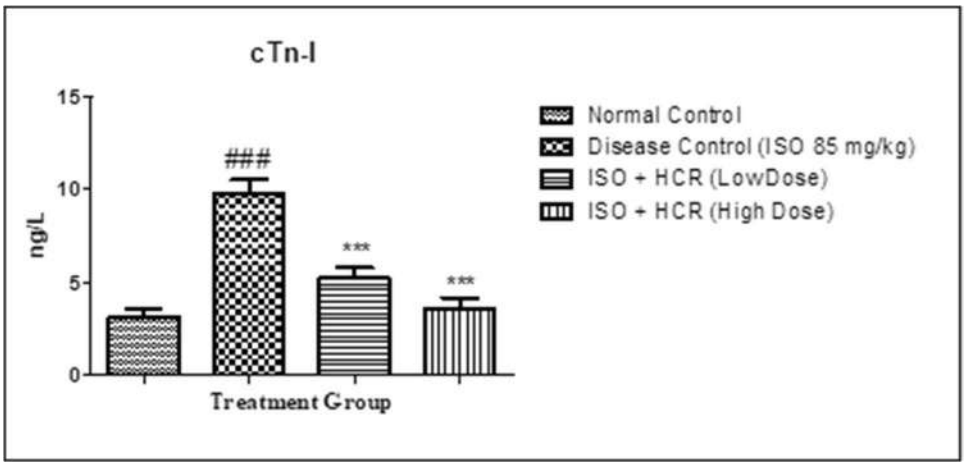

Fig. 5 Effect of HCR on cardiac troponin (cTn-I) level. All values are expressed as Mean ± S.E.M. (n = 6). *$p < 0.05$ when compared with disease control. ###$p < 0.001$ and ##$p < 0.01$ compared with normal control

Table 2 Effect of HCR on oxidative stress parameters

Group	GSH (μMol/mg tissue protein)	SOD (IU/mg of protein)	CAT (μM of H202 decompose/min/mg of protein)	MDA (μMol/mg of protein)
Normal Control	41.62 ± 5.597	0.2249 ± 0.02626	0.1603 ± 0.01431	1.314 ± 0.2669
Disease Control (ISO- 85 mg/kg)	8.519 ± 1.090###	0.08932 ± 0.009076###	0.04310 ± 0.008809###	6.790 ± 0.9959###
ISO + HCR (Low Dose)	27.42 ± 4.621*	0.1778 ± 0.01156**	0.09279 ± 0.009730*	3.327 ± 0.4417**
ISO + HCR (High Dose)	29.45 ± 6.127*	0.1797 ± 0.01265**	0.1391 ± 0.01355***	1.578 ± 0.4962***

All values are expressed as Mean ± S.E.M. (n = 6). ***$p < 0.001$, **$p < 0.01$, *$p < 0.05$ when compared with disease control. ### $p < 0.001$ compared to normal control

prevented the loss of GSH, SOD, and CAT when compared with disease control animals. Whereas, HCR treatment at low and high doses significantly reduced ($p < 0.01$ and $p < 0.001$) the formation of malondialdehyde (MDA) in heart tissue when compared with disease control animals (Table 2).

Effect of HCR in cardiac tissue histology

H&E staining of cardiac tissue in disease control animals showed a significant increase in tissue necrosis (N), degeneration (D), angiogenesis (A), and lymphocytic infiltration (L) in the myocardium when compared with normal control animals. Treatment with HCR at a high dose reduced the severity of the damage to the myocardium (Fig. 6). Masson Trichrome staining of cardiac tissue in disease control animals showed markedly increased deposition of collagen (C) in cardiac muscle as compared to normal control animals. Treatment with HCR at a high dose inhibited the deposition of collagen in cardiac muscle (Fig. 7). HCR treatment at high dose showed better improvement in histopathology of heart tissue when compared to that of HCR low dose.

Discussion

Administration of β-adrenergic agonist, ISO at high dose is a well accepted animal model for induction of myocardial infarction in rats. ISO has been known to exert abnormality in both inotropic and chronotropic cardiac functions which lead to necrosis and cell infiltration because of inflammation, cardiac hypertrophy, and fibrosis.

Ayurvedic medicines in the form of herbs, minerals, and their formulations are advocated by practitioners in the management of ischemic heart disease (IHD). Hrudroga Chintamani Rasa (HCR) is a proprietary cardioprotective formulation offering the benefits of Bruhat Vata Chintamani Rasa (Suvarnayukta), Akeek Pishti, Abhraka Bhasma, Poornachandrodaya Makardhwaja, Arjuna (*Terminalia arjuna, Roxb*), Jatamansi (*Nardostachys jatamansi, (D.Don) DC*), Manjishtha (*Rubia cordifolia.L*) and Dashamoola Kwath. Standardization of herbal formulation has not been carried out in the present study which is a plan in the next phase of the study. Also, we have not used any positive control group. As HCR is a herbomineral formulation which showed cardioprotective effect via various mechanisms, the effect of HCR with any standard drug would be difficult to compare.

All these ingredients are known to have a beneficial effect on the cardiovascular system. The prime ingredient of HCR, Bruhat Vata Chintamani Rasa is a widely used, leading classical herbomineral cardioprotective formulation. It is reported for its cardioprotective/antiarrhythmic activity in an experimental model of ouabain-induced arrhythmia. The herbal components such as Arjuna (*Terminalia arjuna*), Jatamansi (*Nardostachys jatamansi*), Manjishtha (*Rubia cordifolia*) and Dashamoola Kwath in HCR are also documented for beneficial actions on the cardiovascular system[17–19].

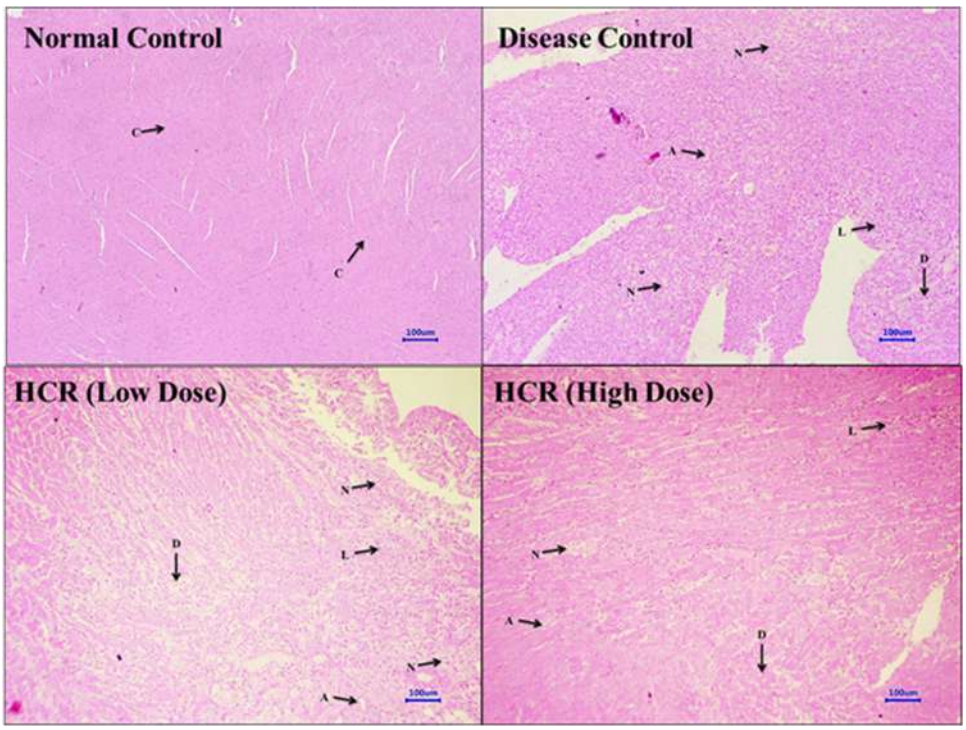

Fig. 6 Effect of HCR on cardiac histopathology (H& E Staining, 100X) *N* Tissue necrosis, *D* Degeneration, *A* Angiogenesis, *L* Lymphocytic infiltration, *C* Collagen cardiac muscle

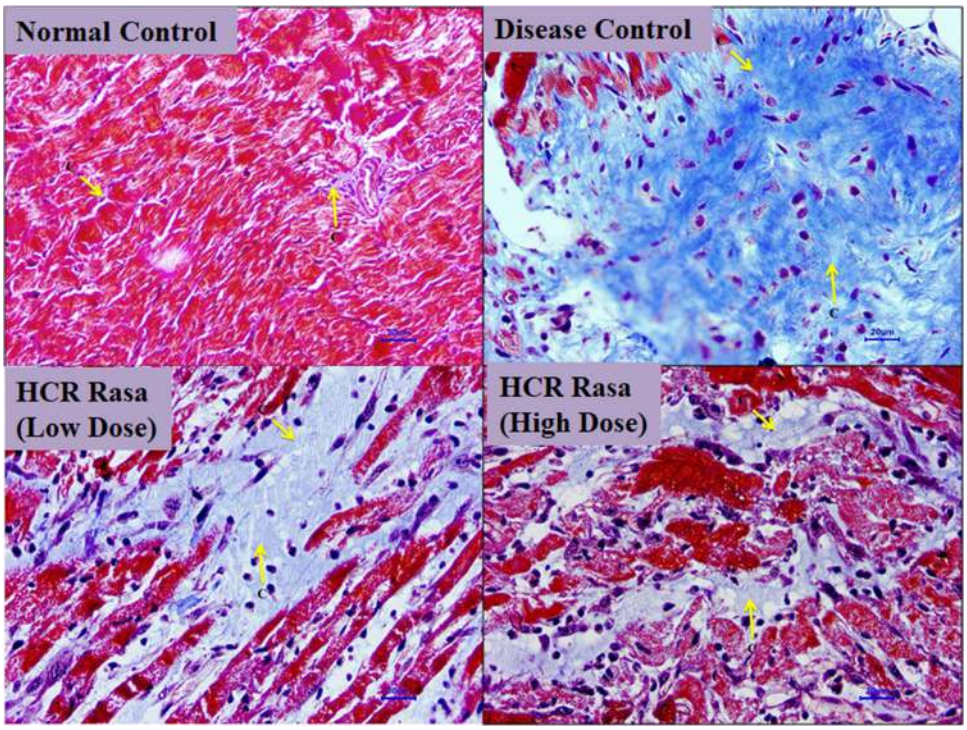

Fig. 7 Effect of HCR on cardiac histopathology (Masson-Trichrome Staining, 400X)

ISO administration developed alteration in biochemical and histological parameters in the animals which resembles those observed in human myocardial infarction [20]. Hence, ISO-induced cardiotoxicity in a rat model was used in this study for a better understanding of the pathogenesis of ischemic heart disease and the role of HCR in the prevention of the progression of ischemic heart diseases.

ECG abnormalities are the primary and the most important criteria used for the definitive diagnosis of cardiotoxicity. ISO treatment showed alterations in ECG pattern when compared to normal animals that could be because of the loss of cell membrane integrity in damaged cardiomyocytes due to free radical damage [21]. PR interval represents conduction time between atrial depolarization to the ventricular depolarization. Whereas, QT interval indicates the time between ventricular depolarisation to ventricular repolarisation. Both the intervals are prolonged in case of myocardial infarction, ischemia, and abnormality in the conduction system [22]. ISO treated animals showed significant elevation in PR and QT intervals. Treatment with HCR significantly shortened the PR and QT intervals. The ST segment is an isoelectric section of ECG which represents the time when ventricular contractile fibers are depolarized during the plateau phase of the action potential [23]. ISO develops myocardial infarction which causes an elevation in ST-segment. Treatment with HCR prevented the elevation in ST segment. QRS duration represents how fast ventricles depolarize. ISO-treated animals showed fast ventricular depolarization which is because of the positive inotropic effect that results in a decrease in QRS duration [24]. Treatment with HCR prevented rapid depolarization and showed a significant increase in QRS duration.

Reduction in arterial pressure i.e. SBP, DBP and MABP are indications of abnormal sympathetic and parasympathetic inputs to the heart [25]. Deterioration in myocardial contractility followed by ISO treatment is responsible for the reduction in MABP which is a marker of after-load. Similarly, deterioration in myocardial relaxation after ISO treatment is responsible for an increase in LVEDP which is a key marker for pre-load [26]. Treatment with HCR prevented the myocardial necrosis by ISO and improved the decreased SBP, DBP, MABP and significantly decreased ISO induced increased LVEDP.

The myocardium contains a large number of lysosomal marker enzymes like AST, LDH and CK-MB. These markers are important which help in assessing the degree of necrosis to the myocardium. Free radicals generated by ISO cause lipid peroxidation of membrane-bound polyunsaturated fatty acids and alter the structure and function of the myocardium [27]. Disease control animals showed a significant increase in serum levels of AST, LDH and CK-MB due to damage to the myocardium. HCR treatment protected the myocardium from damage by its anti-oxidant property and decreased levels of AST, LDH and CK-MB.

AMP-activated protein kinase (AMPK) is an enzyme that regulates many physiological processes in the body. It also plays a major role in cardiac energy metabolism. For efficient working healthy heart (cardiomyocytes) require

large energy supply (ATP), which comes from fatty acid oxidation and glucose oxidation. Under stress AMPK in the heart increases glucose uptake as a cardioprotective and adaptive response of the heart and it can also increase fatty acid oxidation. This ultimately increases the ATP production to ameliorate the imbalance between energy supply and demand to the heart [28]. AMPK activation is also reported to have a protective role in the process of cardiac fibrosis [29].

Sirtuin 1 (SIRT1) protein, is a member of Silent Information Regulator 2 (Sir2) protein family and has a role in regulating cellular health. Evidence suggests that SIRT1 is involved in fibrotic diseases like liver, cardiac and renal fibrosis [30]. Study by Jie and co-workers has reported that upregulated SIRT1 expression inhibits the formation and development of cardiac fibrosis in a rats [31]. In our study, significantly reduced levels of AMPK and SIRT1 were observed in disease control animals. Treatment with HCR prevented a reduction in levels of AMPK and SIRT1 indicating protection to the myocardium from fibrotic damage.

Cardiac troponin is a low molecular protein associated with the myofibrillary contractile apparatus of the cardiac tissue and is considered as a highly sensitive and most specific marker for myocardial injury. The level of troponin (cTn-I) is usually nil in normal condition and elevated in myocardial necrosis. In the present study, a significantly increased level of serum cTn-I was observed in disease control animals. HCR treatment prevented the severity of myocardium damage and showed a reducetion in level of cTn-I [32].

Oxidative damage to the myocardium by ISO also affects the antioxidant enzyme status in the myocardium. GSH is the most abundant antioxidant present in the body. Together with SOD and CAT, GSH protects the myocardium from superoxide, alkoxy radicals and H_2O_2 damage. ISO also causes polyunsaturated lipid peroxidation and forms MDA which is a reactive aldehyde and considered as electrophile species that develops toxic stress to the cardiomyocytes [33]. HCR treatment prevented myocardium from oxidative damage by improving the levels of GSH, SOD and CAT and also prevented formation of reactive aldehyde in myocardium via its antioxidant mechanism.

Administration of ISO induced histological changes like myocardial degeneration, lymphocytic infiltration, tissue fibrosis and necrosis. This damage was controlled by HCR treatment probably because of its membrane-stabilizing and anti-inflammatory effect. This finding provides additional evidence of the cardioprotective effect of HCR.

Bruhat Vata Chintamani Rasa, Akeek Pishti, Abhraka Bhasma, Poornachandrodaya Makardhwaja, *Terminalia arjuna*, *Nardostachys jatamansi*, *Rubia cordifolia* and *Dashamoola Kwatha* are important components of Hrudroga Chintamani Rasa formulation.

Bruhat Vata Chintamani Rasa possesses a antiischemic action and is used in the management of heart and brain disorders. Akik pishti and Abhrak Bhasma are widely used in various cardiac disorders. . *Terminalia arjuna, Nardostachys jatamansi, Rubia cordifolia* and *Dashamoola Kwatha* are well-known herbs for their antioxidant and antiapoptotic activity.

Hrudroga Chintamani Rasa containing all these offers cardioprotection in isoprenaline or isoproterenol (ISO) induced cardiotoxicity / cardiac damage.

Supplementary information The online version contains supplementary material available at https://doi.org/10.1007/s40200-022-01012-4.

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Author contributions AL and YK performed the experiment, analyzed the data, and wrote the manuscript. YK and MC conceived and designed the experiments.

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Data availability All data generated or analyzed during this study are included in this article [and/or] its supplementary material files. Further enquiries can be directed to the corresponding author.

Declarations

Ethical approval The experimental protocol was approved by the Institutional Animal Ethics Committee (Approval Number & Date: CPCSEA/IAEC/P-35/2019, 10th August 2019).

Conflict of interest The author(s) declared the following potential conflict of interest with respect to the research, authorship, and/or publication of this article: One of the co-author is from Shree Dhootapapeshwar Limited, which has funded the study. The first and corresponding author declare no conflict of interest.

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