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RESEARCH ARTICLE OPEN ACCESS

Protective role of resveratrol against isoproterenol-induced myocardial infarction in male rats

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Abstract
Objective: The present study aimed to evaluate the protective effect of resveratrol against isoproterenol-induced myocardial infarction in male Sprague-Dawley rats.
Methods: The study included 40 rats aged 3 to 4 months, weighing 200 to 250 grams, randomly distributed into four groups. The first group (Control) received 1 ml of distilled water. The second group (Resveratrol) received 20 mg/kg orally at a dose of 2 ml daily. The third group (Isoproterenol) received 100 mg/kg intraperitoneally (IP). The fourth group, Res + ISO, received oral resveratrol (20 mg/kg/day) for 21 days. After resveratrol, they received IP injections of 100 mg/kg of ISO on days 20 and 21 of the resveratrol regimen for 21 days.
Results: The results showed that isoproterenol caused a significant increase in markers of oxidative stress (MDA), inflammation (TNF-α), triglyceride levels, cholesterol, and cardiac enzymes (CK-MB, cTnI, LDH), along with a decrease in total antioxidant activity (T-AOC). In contrast, treatment with resveratrol resulted in a significant improvement in these markers, as elevated values decreased and antioxidant levels returned to normal, indicating the effect of resveratrol in reducing oxidative and inflammatory damage. The Res + ISO group showed intermediate results, demonstrating a clear protective role of resveratrol against the toxic effects of isoproterenol.
Conclusion: These findings suggest that resveratrol is a potential agent for preventing cardiomyopathy and enhancing heart function in situations of oxidative and inflammatory stress since it has anti-hyperlipidaemia, antioxidant, and anti-inflammatory qualities.

Keyword: Resveratrol; Isoproterenol; Oxidative stress, Inflammation, Cardiac enzymes

Plain English Summary

This study tested whether resveratrol, a natural antioxidant found in foods like grapes and peanuts, can protect the heart from damage caused by isoproterenol, a chemical that mimics a heart attack in rats. Forty rats were divided into groups and given resveratrol, isoproterenol, both, or neither. The group that received isoproterenol alone showed high levels of heart injury markers, inflammation, oxidative stress, and unhealthy fat levels in the blood. However, rats treated with resveratrol, especially those that received it before the isoproterenol, had lower levels of these harmful effects. Their hearts also showed less tissue damage under the microscope. These findings suggest that resveratrol can reduce heart damage by fighting oxidative stress and inflammation. The researchers conclude that resveratrol has the potential to support heart health, but more research is needed, especially in humans, to explore how it works and how best to use it.

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Introduction

Cardiomyocytes' adaptive response to a variety of stimuli, including pathological conditions like myocardial infarction and hypertension, as well as specific substances like the non-selective beta-agonist isoproterenol, is cardiac hypertrophy (1). ECG anomalies and elevated oxidative stress in the heart are linked to isoproterenol-induced cardiac hypertrophy. One of the main causes of cardiac hypertrophy is oxidative stress, which can then increase the expression of fibrotic and inflammatory markers (2). Higher blood triglycerides and higher levels of cholesterol salts in serum and heart tissue are the primary causes of impaired vascular function following myocardial infarction caused by isoproterenol production. Maintaining good heart conditions requires the use of natural products and nutrients that help prevent, cure, and protect cardiovascular illnesses (3).

One well-known paradigm for examining the pathogenesis of myocardial ischaemia is isoproterenol-induced myocardial infarction (MI). The adrenergic substance isoproterenol increases myocardial oxygen consumption by raising heart rate and contractility. Myocardial infarction can result from cardiac ischaemia caused by excessive cardiac stimulation. Myocytes experience anaerobic metabolism and decreased ATP generation during ischaemia and MI. This can weaken membrane integrity, resulting in calcium overload and compromised myocardial function (4).

Nowadays, more and more people are turning to natural goods and medicinal plants to treat a variety of illnesses and get rid of toxins that have built up in the body. As one of the contemporary pillars, the World Health Organisation (WHO) has emphasised the significance of its application in international conferences. Given that most plants contain active substances, it has also emphasised the significance of adopting therapeutic foods to lessen the adverse effects that may be brought on by chemical pharmaceuticals. Active compounds derived from plants may have a greater physiological impact than synthetic ones (5).

The prevention of several illnesses has made extensive use of medicinal plants and their derivatives. Reactive oxygen species (ROS) are one of the main causes of many major illnesses, and the active components in plant extracts, including polyphenols and others, effectively reduce ROS. Furthermore, natural antioxidants are being tested by scientists and physicians more frequently as a secure substitute for synthetic ones (6).

As a potent defence mechanism, resveratrol is one of many natural plant compounds utilised as a therapeutic and chemopreventive agent in treating several illnesses. Resveratrol has been widely researched as a therapy for cardiovascular disorders because of its anti-inflammatory and antioxidant qualities, which have been demonstrated to improve cardiovascular health (7). Although past research has shown that resveratrol has antioxidant and anti-inflammatory effects, this study takes a different approach by looking at how it affects multiple aspects at once—like oxidative stress (measured by MDA and T-AOC), inflammation (TNF-α), cholesterol and triglyceride levels, and heart injury markers (cTnI, CK-MB, LDH), all in a single model of heart attack caused by isoproterenol. This comprehensive look gives a broader understanding of how resveratrol might protect the heart, something that hasn't been fully explored before.

The main dietary sources of resveratrol, a polyphenol, are peanuts, grapes, berries, and nuts. Resveratrol's polyphenol content has anti-inflammatory and antioxidant properties and may lessen apoptosis. Resveratrol has been demonstrated to reduce headaches and stop the growth and spread of tumours. Additionally, it increases apoptosis, which stops cancer cells from growing (8, 9). Recent meta-analyses and systematic reviews further support resveratrol's cardioprotective potential, highlighting its ability to improve endothelial function, reduce infarct size, and modulate key signalling pathways such as SIRT1/AMPK and NF-κB (10, 11). These findings reinforce the rationale for investigating resveratrol as a therapeutic agent in ischemic heart disease. Therefore, by analysing physiological data, the current study sought to use resveratrol to protect the heart against isoproterenol-induced myocardial infarction in male albino rats.

Materials and Methods

Animals Used in the Study

For two months, this study was carried out in the animal house of the Department of Life Sciences at the College of Education for Pure Sciences, University of Anbar. The research comprised forty adult male albino rats of the *Sprague Dawley* type. They weighed between 200 and 300 g and were between 3 and 4 months old. After a specialist veterinarian checked the animals, they were put in metal-covered, specially designed plastic cages that were 64 by 15.5 by 30 cm and were used for growing rats. In this experiment, the animals were kept in a laboratory with proper ventilation, a temperature of 22 ± 2 °C, and a natural light and

dark time of 13:11 hours. Male rats were chosen to minimise the potential influence of hormonal fluctuations linked to the oestrous cycle in females, which could interfere with the cardiovascular responses to isoproterenol. Nevertheless, we recognise that future investigations should incorporate both sexes to assess possible differences in the cardioprotective effects of resveratrol. Animals were allocated to treatment groups through a computer-generated randomisation process. To ensure unbiased results, the researchers conducting biochemical analyses remained blinded to the group assignments, thereby reducing measurement bias. The cages were equipped with sawdust and had adequate ventilation. The cages were cleaned and disinfected regularly, the sawdust was changed three times a week, the drinking bottles (airports) were cleaned, and the water was changed every day. The animals were continuously given water and standard feed prepared ad libitum in the following proportions: (35%) wheat, (35%) yellow corn, (20%) soybeans, (10%) concentrated protein, and (1%) dry milk powder, along with antifungal and preservative ingredients. For two weeks, the rats were left to acclimatise, and it was ensured that they were disease-free.

The Experiment Design

The animals were split up into four groups based on comparable weights. Ten animals were allocated to each group: Group 1 (Control): Distilled water (1 mL/kg) was administered orally. Group 2 (Resveratrol): Given 2 ml of resveratrol daily for 28 days at a level of 20 mg/kg. Group 3: Protein-based subcutaneous injection of isoproterenol (100 mg/kg) for two days in a row. Group 4 (Isoproterenol + Resveratrol): This group received combined treatment (Res+ISO), which was administered daily oral resveratrol for 21 days. Besides, isoproterenol was administered only on days 20 and 21, with a 48-hour interval between doses, to assess the protective effect of resveratrol against acute cardiotoxicity induced by isoproterenol. Resveratrol was prepared in a 1% carboxymethyl cellulose (CMC) solution for oral delivery, whereas isoproterenol was dissolved in 0.9% sterile saline for intraperitoneal injection.

Based on previous preclinical research, a dose of 20 mg/kg of resveratrol was selected due to its demonstrated effectiveness in reducing oxidative damage to the heart without causing adverse effects (7, 12). Conversely, the 100 mg/kg dose of isoproterenol was chosen to reliably induce myocardial infarction, as it consistently triggers substantial oxidative stress and cardiac injury in rodent models (4, 13).

Collection of blood samples

Following 24 hours of starvation, the animals were anaesthetised the following day using a 0.1 ml/100 g intraperitoneal dose of ketamine/xylazine. A sterile, disposable 5-mL syringe was used to take blood straight from the heart. White tubes containing the blood were centrifuged for 15 minutes at 3,000 rpm. Before biochemical testing was done, the serum was separated using micropipettes and preserved in white plastic tubes at -20°C. Data regarding each sample was documented. After being removed, each animal's heart was cleaned in 0.9% normal saline.

Assay of Oxidative Stress and Antioxidants

The level of (T-AOC and MDA) in serum was estimated using a ready-made test kit provided by the American company Elabscience, using the colourimetric method on a spectrophotometer.

Commercial kits were used with the following catalogue numbers:

MDA (Elabscience, E-BC-K025-S)
T-AOC (Elabscience, E-BC-K771-S)
TNF-α ELISA (Elabscience, E-EL-H0109)
cTnI (Ichroma, CR1002)
CK-MB (Biolabo, 80017)

Measurement of the level of Tumour Necrosis Factor Alpha (TNF-α) in the blood serum

Using an ELISA Microplate Reader and a pre-made test kit from the American company Elabscience (www.elabscience.com, **No:** E-EL-H0109), serum TNF-α levels were determined using the Sandwich ELISA technique.

Risk Factors

The concentration of triglycerides and cholesterol in the blood serum was estimated using the analysis kit provided by the French company Biolabo (14).

Heart function test

A kit from Ichroma (Geodudanji 1-gil, Dongnae-myeon, Chuncheon-si, Gangwon-do, Republic of Korea) was used to quantify the concentration of serum troponin (cTnI). A kit from Biolabo France was used to measure the levels of CK-MB (15). By adopting the Friedman et al., 1997 approach (16), which involves converting pyruvate to lactate in the presence of NADH, the activity of lactate dehydrogenase (LDH) was discovered.

Statistical Analysis

Statistical analyses were conducted using one-way ANOVA, followed by Tukey's post hoc test to assist multiple comparisons. The assumption of normality was verified through Shapiro-Wilk tests, while the homogeneity of variances was assessed with Brown-Forsythe tests. A significance level of $p < 0.05$ was adopted for all analyses. Results are expressed as mean ± standard deviation (SD), with different superscript letters (a, b, c) indicating groups that differ considerably from one another (17).

Results

Estimation of oxidation balance and antioxidants in blood serum

Figure 1 shows that isoproterenol (ISO) and Resveratrol (RES) affect oxidative stress and antioxidants. Male rats injected with (ISO) nmol/ml (16.66 ± 0.847) had a highly significant increase in MDA activity at the level ($P \leq 0.05$) when compared to the control group (7.617±0.984). In contrast, the second group dosed with Resveratrol nmol/ml (5.770±0.988) showed a significant decrease, and the fourth group of rats dosed with Resveratrol and injected with (ISO) nmol/ml (8.175±1.036) showed a significant decrease.

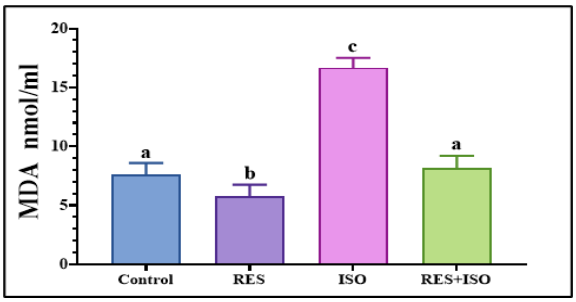

Figure 1: The effect of resveratrol on the level of oxidative stress (MDA) in the blood serum of male rats treated with isoproterenol

Figure (2) shows isoproterenol (ISO) and Resveratrol (RES) affect oxidative stress and antioxidants in this study, we observe a significant increase in antioxidant effectiveness at the level ($P \leq 0.05$) in male white rats orally dosed with Resveratrol µmol/ml (56.81±3.330) compared to the control group µmol/ml (49.29±3.000). Conversely, the third group injected with ISO showed a significant decrease in antioxidant effectiveness, with results of µmol/ml (31.96±2.760). In contrast, the fourth group of rats orally dosed with Resveratrol and injected with ISO showed a significant increase in antioxidant effectiveness, with results of µmol/ml (48.52±2.778).

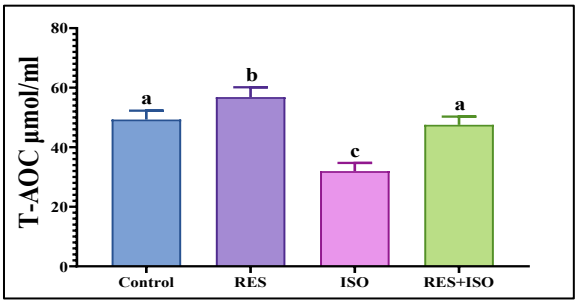

Figure 2: The effect of resveratrol on the level of the antioxidant (T-AOC) in the blood serum of male rats treated with isoproterenol
Values are expressed as mean ± SE; n=10 for each treatment group; means in each column with different superscript letters are significantly different ($p<0.05$)

Effect of resveratrol on the level of TNF-α in the serum of male rats treated with isoproterenol

Figure (3) shows a significant increase in the level of (TNF-α) activity at the level ($P \leq 0.05$) in the G3 of male rats injected with (ISO), where the ratio reached (56.02±3.763) pg/ml compared to the control group (33.47±2.554) pg/ml. On the other hand, a significant decrease is observed in the G2 group dosed with resveratrol, where the results were (33.03±3.597) pg/ml, while a significant decrease is observed in the G4 group dosed orally

with Resveratrol and injected with (ISO) where the results were (37.63±3.084) pg/ml.

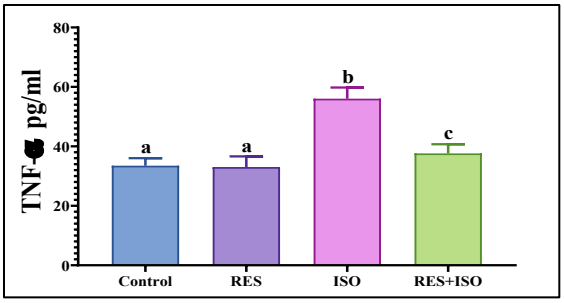

Figure 3: The effect of resveratrol on the level of tumour necrosis factor alpha (TNF-α) in the blood serum of male rats treated with isoproterenol
Values are expressed as mean ±SE; n=10 for each treatment group; means in each column with different superscript letters are significantly different (p<0.05)

Biochemical Assay: Results of the level of cholesterol and triglycerides in the blood serum of male rats

Figures (4,5) show that the results showed a significant decrease at the level (P ≤ 0.05) for both Cholesterol and triglycerides in the group 2 of male rats that were orally dosed with Resveratrol, where the results were mg/dl (69.00±7.967) and mg/dl (33.74±6.967), respectively, compared with the control group mg/dl (6.829±80.34) and mg/dl (56.12±9.370), respectively. While in the group 3 that was intravenously injected with (ISO), a significant increase was observed at the level (P≤ 0.05) for both Cholesterol and Triglycerides, where the results were mg/dl (129.60±6.393), mg/dl (152.0±10.81), respectively, compared to the group 4 that was orally dosed with Resveratrol and intravenously injected with (ISO) where a significant decrease was observed for both Cholesterol and Triglycerides and the results were mg/dl (69.25±7.745) and mg/dl (57.67±7.633) respectively.

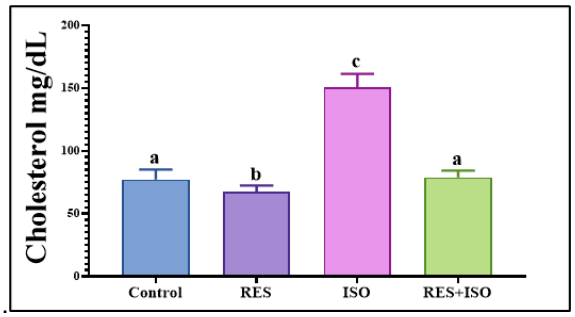

Figure 4: The effect of resveratrol on the activity of cholesterol in the blood serum of male rats treated with isoproterenol

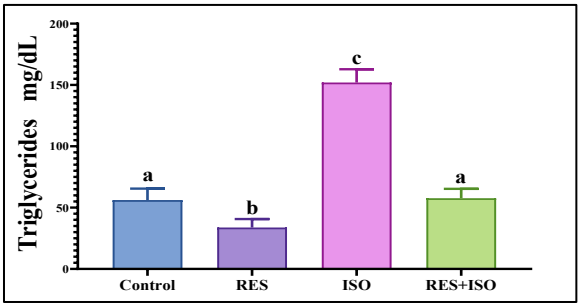

Figure 5: The effect of resveratrol on the activity of Triglycerides in the blood serum of male rats treated with Isoproterenol

Effect of resveratrol on cardiac functions in the blood serum of male rats treated with isoproterenol
Table (1) shows the results from the serum of male white rats for the concentration of the following enzymes: cTNL) (CK-MB) (LDH). The results showed a significant decrease at the level (P ≤ 0.05) for the group 2 orally dosed with Resveratrol compared with the control group, while the group 3 intravenously injected with (ISO) had a significant increase at the level (P ≤ 0.05) compared with the group 4 orally dosed with Resveratrol and injected with (ISO).

Table 1: Effect of resveratrol on heart functions in the blood serum of male rats treated with isoproterenol

		Control	RES	ISO	ISO+RES
cTnl ng/ml	**Mean**	**0.284 [a]**	**0.258 [a]**	**1.076 [b]**	**0.352 [ac]**
	± SD	**± 0.067**	**± 0.071**	**± 0.069**	**± 0.077**
CK-MB U/L	**Mean**	**137.6 [a]**	**121.9 [a]**	**315.6 [b]**	**143.4 [ac]**
	± SD	**± 15.45**	**± 12.49**	**± 20.89**	**± 19.15**
LDH U/L	**Mean**	**176.7 [a]**	**100.5 [b]**	**446.9 [c]**	**206.3 [a]**
	± SD	**±27.21**	**±21.80**	**±28.99**	**±21.38**

Mean values within a column not sharing a common superscript letter (a, b, and c) were significantly different, p < 0.05

Discussion

Cardiomyopathy prevention remains a significant health concern. Treatment with bioactive antioxidants is thought to be a viable strategy to stop pathological alterations and preserve heart function since oxidative stress is a major contributor to the pathophysiology of cardiac damage. When ISO is administered, laboratory rats' hearts experience necrotic damage and oxidative stress. Oxidative stress and the pathophysiology of myocardial infarction (MI) are caused by the production of reactive oxygen species (ROS) and/or the depletion of antioxidants (4, 18). In ISO-induced myocardial infarction, elevated ROS levels cause endothelial dysfunction, cardiomyocyte damage, mitochondrial dysfunction, inhibition of several enzymes that impact metabolism, production of inflammatory cytokines, and enhanced apoptosis (19).

Lipid peroxidation has been implicated in the cardiac damage brought on by ISO injection in several investigations. Mice had severe oxidative stress due to a combination of high MDA levels and inadequate antioxidant levels (20) (Figure 1). Mice with myocardial infarction have higher levels of oxidative stress because of increased production of reactive oxygen species (ROS), which are produced due to metabolic disturbances. These ROS are highly toxic to myocardial cells and can cause myocardial necrosis and death, as well as ATP depletion reactions, lipid peroxidation of cell membranes, partial damage, and loss of elasticity (21).

Because of their high polyunsaturated fatty acid content, cell membranes are the most susceptible to free radical reactions. These acids contain double bonds, which are the primary target of free radicals. Lipid peroxidation results in the production of MDA. Many bodily tissues are impacted by oxidative damage, which is caused by a reduction in antioxidants and an increase in lipid peroxidation brought on by free radical reactions (22).

According to a study, animals exposed to ISO had higher levels of malondialdehyde (MDA), which causes greater lipid peroxidation and tissue damage. This, in turn, causes serious and deadly damage to the membranes of the heart cells. This results in cellular oxidative damage and tissue degradation, including cardiac tissue (13). It is important to note that under pathological conditions, free radical activity rises above the capacity of antioxidants to eliminate or neutralise them. This results in elevated lipid peroxidation and malondialdehyde levels, which in turn cause oxidative stress, which in turn causes myocardial cell membranes to lose their elasticity and activates the genes that cause mutations, stimulates the growth of cancerous tumours, and so on (23).

The antioxidant activity of resveratrol was demonstrated by the considerable reduction of oxidative stress markers and the rise of total antioxidant levels in the blood of rats treated with ISO. These findings demonstrate that resveratrol therapy lowers lipid peroxidation and hyperlipidaemia while improving antioxidant status. Notably, resveratrol administration markedly raised antioxidant levels, suggesting that it may improve the body's antioxidant defences. The antioxidant activity of resveratrol against isoproterenol-induced oxidative cardiotoxicity in rats was also demonstrated by the notable rise in antioxidants in the serum of rats treated with resveratrol as opposed to the group treated with isoproterenol (24). Furthermore, resveratrol demonstrated free

radical scavenging properties as a pure polyphenol (25).

These results indicate that resveratrol possesses a potent antioxidant capacity responsible for protecting the heart from oxidative stress. These changes lead us to conclude that the increased antioxidant levels were a result of the decreased MDA. These changes are a result of resveratrol's action, which inhibited the formation of free radicals in the heart muscle and thus contributed to the protection of cell membranes from oxidative stress. Polyphenolic compounds such as resveratrol act as antioxidants, which allows them to act as reducing agents, hydrogen donors, and single oxygen atom removal agents, thus inhibiting the accumulation of free radicals and reducing oxidative damage to heart muscle tissue.

Male albino rats given isoproterenol had higher serum concentrations of triglycerides and cholesterol than the control group. This is in line with a study that found isoproterenol causes negative effects by raising lipid profile levels (26). In addition to decreasing insulin sensitivity, isoproterenol treatment inhibits the production of fatty acids, triglycerides, and hepatic cholesterol in rats. By altering the concentration of the intestinal monolayer structure, it also increases the absorption of cholesterol via the gut (27).

However, the oxidative stress that results from the injection of isoproterenol may be the cause of the rise in triglycerides in the blood of rats. This could lead to a decrease in insulin secretion because free radicals destroy pancreatic beta cells, and insulin deficiency decreases the efficiency of the enzyme lipoprotein lipase, which breaks down triglycerides into fatty acids and glycerol. The liver produces more very low-density lipoprotein (VLDL) when insulin insufficiency triggers the process of lipolysis in adipose tissue, which releases free fatty acids for utilisation as an energy source (28). Because cholesterol is accumulated on the inner walls of the arteries, it damages the cells lining the arteries as well as other tissue cells. Elevated blood cholesterol levels and free radicals enhance the body's vulnerability to oxidation (29).

The activities of LDH and CK-MB, as well as elevated troponin T levels, are sensitive markers of increasing myocardial damage. Changes in the functional integrity of the plasma membrane and/or cellular permeability are reflected in the levels of these cellular enzymes in serum or plasma (30). According to the current study, rats given isoproterenol had considerably higher blood levels of troponin T and both enzyme activities, which suggests that the cardiac membrane's integrity has changed. Necrosis of the heart's cells and the release of these enzymes into the bloodstream were the symptoms of these consequences (Table 1). One known mechanism for cellular necrosis, including cardiac fibre necrosis, is increased oxidative stress. The breakdown of the endoplasmic reticulum and the majority of the cell membranes as a result of oxidative stress brought on by lipid peroxidation and the rise in free radical levels brought on by ISO exposure may be the cause of the increase in the aforementioned enzymes in the ISO-treated group (31).

The injection of resveratrol in the current study markedly reduced the high levels of these cardiac markers towards normal levels, indicating that resveratrol is a useful and cardioprotective therapy. Histological analysis of the heart supported this conclusion, showing that resveratrol may stop the damage that isoproterenol caused to the heart. This is probably because of its capacity to decrease lipid peroxidation-induced damage and increase oxygen radical scavenging activity. These findings imply that resveratrol may have the ability to shield the heart against oxidative stress and related illnesses.

The myocardium's structural alterations during ISO injection-induced ischaemic heart disease, which results in fibrosis of the afflicted region, might be the reason of the elevated CK-MB enzyme activity. Serum levels of cardiac proteins, such as the CK-MB enzyme, rise in tandem with these structural changes. When the cardiac fibres, contractile proteins, and sarcoplasmic reticulum dissolve, these proteins may be released from the cardiac fibres into the blood. The permeability of the membranes of the damaged cardiac cells changes, increasing the level of these proteins (32).

Furthermore, recent research has shown that diagnosing acute myocardial infarction and predicting the risk of subsequent myocardial infarction depend more on measuring troponin T (cTnI), a low-molecular-weight contractile protein that is not typically present in serum but is released when myocardial necrosis occurs (33). This study found that the group that received resveratrol pre-treatment had significantly lower levels of these enzymes, which may have contributed to a protective effect in maintaining the integrity of cardiac cell membranes. Resveratrol's antioxidant and anti-inflammatory properties can help prevent cardiovascular diseases, such as myocardial infarction, and lower the risk of heart disease-related death and heart attack by protecting cardiac cell membranes from oxidative damage caused by ISO. This prevents the release of enzymes, which lowers their levels in the blood. Additionally, by decreasing blood pressure, cholesterol, and the

risk of blood clots, resveratrol improves heart health (12).

Increased reactive oxygen species (ROS) and myocarditis, which is typified by the release of several cytokines, including TNF-α, can result from isoproterenol therapy. According to earlier research, isoproterenol-induced myocarditis resulted in markedly increased levels of proinflammatory cytokines and ROS (10). Research on the possible therapeutic use of anti-inflammatory drugs in myocarditis and associated consequences has been centred on data indicating that inflammatory processes play a role in the pathophysiology of cardiomyopathy. Consequently, because of its antioxidant qualities, resveratrol has been proposed to regulate cellular activity during inflammation. The present investigation showed that resveratrol reduced TNF-α in rats with isoproterenol-induced myocarditis. According to several recent experimental studies, polyphenols have anti-inflammatory properties when oxidative stress is elevated. The rise of tumour necrosis factor alpha (TNF-alpha) levels during LPS-induced acute respiratory distress syndrome in rats was proven to be reduced by resveratrol administration (11). Furthermore, TNF-α gene expression was eliminated by resveratrol (34). According to these findings, resveratrol could be a useful dietary supplement that helps reduce myocardial inflammation in conditions where there is an excess of oxidative stress. Our findings align with Shanmugasundaram et al. (26), showing resveratrol's dose-dependent reduction in cardiac enzymes, but contrast with Liu et al. (7), who reported superior TNF-α suppression at higher doses (50 mg/kg). This discrepancy suggests dose-response relationships warrant further investigation. Notably, our lipid profile improvements exceed those in similar isoproterenol models using other polyphenols (13), highlighting resveratrol's unique anti-hyperlipidaemic potential.

Translating these findings requires addressing resveratrol's poor bioavailability (~1% in humans). Recent formulations like nanoparticle-encapsulated resveratrol (24) achieve 5-fold higher plasma concentrations, while combination with piperine enhances absorption by 200% (12). Such advances could overcome current clinical limitations, though safety profiles in chronic use remain to be established

Study limitations

While this study demonstrates resveratrol's cardioprotective effects, certain limitations should be noted. The absence of mechanistic data (e.g., Western blot analysis of SIRT1/AMPK pathways or qPCR of inflammatory markers) prevents deeper molecular insights. Additionally, using only male rats precludes evaluation of potential sex-specific responses. Future studies should incorporate these molecular analyses and both sexes to fully characterise resveratrol's protective mechanisms

Conclusion

According to the study's findings, resveratrol shows promising cardioprotective effects against the damaging effects of isoproterenol. Reduced levels of oxidative stress and inflammatory indicators, better cardiac enzymes and lipid parameters, and increased antioxidant activity overall were the results of this action. These results show that resveratrol contributes to the prevention or treatment of oxidative stress-related cardiomyopathy through a variety of mechanisms, such as its anti-inflammatory, antioxidant, and anti-hyperlipidaemic qualities. To validate this compound's effectiveness and its mode of action on a larger scale, the study suggests more clinical and experimental research.

This study shows that resveratrol has strong protective effects on the heart in a rat model of heart attack caused by isoproterenol. It helps reduce oxidative stress, inflammation, and abnormal fat levels, while also helping to restore the balance of heart enzymes. These results not only support what we already know about its antioxidant qualities but also suggest that resveratrol can influence other damaging processes during sudden heart damage. That said, some important questions still need answers. Future research should focus on understanding exactly how resveratrol works at the molecular level, especially how it interacts with pathways like SIRT1, AMPK, and Nrf2, by studying specific proteins and gene activity. Finding the right dosage will be essential, so dose-response studies are needed. It's also important to explore whether effects differ between males and females to better understand sex-specific responses. Most importantly, making resveratrol more effective in the body, for example through new delivery methods like nanoparticles or combining it with absorption boosters, will be key for using it in humans. While animal studies keep adding evidence of its benefits, moving to human trials is essential to test how well it works and how safe it is over the long term. Until we have those results, resveratrol remains a promising but unproven option that could someday support heart health as an additional therapy.

List of Abbreviations
ISO: Isoproterenol
RES: Resveratrol
MI: Myocardial Infarction
ROS: Reactive Oxygen Species
MDA: Malondialdehyde
T-AOC: Total Antioxidant Capacity
TNF-α: Tumour Necrosis Factor Alpha
cTnI: Cardiac Troponin I
CK-MB: Creatine Kinase–Myocardial Band
LDH: Lactate Dehydrogenase
ATP: Adenosine Triphosphate
ELISA: Enzyme-Linked Immunosorbent Assay
SD: Standard Deviation
SE: Standard Error
ANOVA: Analysis of Variance
VLDL: Very Low-Density Lipoprotein
WHO: World Health Organisation

Declarations
Ethics approval and consent to participate
All experimental procedures received prior approval from the Institutional Animal Care and Use Committee of the College of Education for Pure Sciences, University of Anbar (Approval No. 242, 2024/02/26). They were carried out in strict accordance with the NIH Guide for the Care and Use of Laboratory Animals. We took every possible measure to reduce animal suffering, including administering anaesthesia during blood collection and performing humane euthanasia.

Consent for Publication
All the authors gave consent for the publication of the work under the Creative Commons Attribution Non-Commercial 4.0 license.

Availability of Data
Data for this work is available from the authors and may be provided upon reasonable request.

Conflicts of Interest
None.

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None.

Authors' contributions
MZA: Conceptualisation, methodology, investigation, data curation, and writing, original draft preparation.
AHL: Supervision, formal analysis, validation, writing, review and editing.
Both authors read and approved the final version of the manuscript.

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Nil.

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