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α-Lipoic acid protects against γ-rays-induced cardiac injury in rats

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α-LIPOIC acid is found in some mammalian and plant tissues. It has antioxidant and anti-inflammatory effects. The objective of this study was to test the hypothesis that oral administration of α-lipoic acid causes protection against cardiac injury in γ-irradiated rats.

A group of rats was exposed to a single session of 6 Gy γ-rays and compared with three other groups: a control group (received vehicle only), an α-lipoic acid-treated group (received 100 mg/kg body weight orally for 10 days), and a combined treatment group (received 6 Gy γ-radiation along with α-lipoic acid for 10 days).

The effect of radiation was indicated by an increase in the activity of lactate dehydrogenase (LDH), creatin Kinase MB (CK-MB), myeloperoxidase (MPO), xanthine oxidase (XO), malondialdehydes (MDA), protein carbonyl (PC), and cytokine IL-6 (IL-6) and a significant decrease in the activity of superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase (CAT), ferric reducing ability (FRA) and reduced glutathione (GSH) concentrations.

α-Lipoic acid supplementation to γ-rays group ameliorates all parameter alterations occurred in blood and rat cardiac tissues, suggesting the existence of a compensatory increase of antioxidant defences.

It could be postulated that α-lipoic, as a functional dietary supplement, could exert a modulator role in the radiation-induced cardiac injury through its antioxidant and anti-inflammatory properties.

Keywords: α-Lipoic acid, γ-rays, myocardium, rats

Introduction

Acute exposure to γ-radiation (6 Gy) results in cardiac injury in rats and triggers cardiac inflammation (Karam et al., 2024). Gamma-ray-induced cardiac disease is a common complication of thoracic radiotherapy (Liu et al., 2025). In rats, ionising radiation is associated with oxidative stress and impaired immune function (Aziz et al., 2024; Hussien and Rashed, 2023). Moreover, gamma rays enhance lipid peroxidation in rat cells (Moselhy et al., 2025). Oxidative stress, reactive oxygen species (ROS), and hypoxia contribute to cardiac dysfunction and acute myocardial ischaemia injury (Jiang et al., 2025).

α-Lipoic acid is a naturally occurring molecule found in certain mammalian and plant tissues.

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It mitigates pro-oxidant and pro-inflammatory activities and modulates both nitrogen and ROS species (Pingali et al., 2024). Supplementation with α-lipoic acid may offer protection against immune dysfunction and cardiac injury in mice (Wang et al., 2023). Additionally, it functions as a free radical scavenger and metal-chelating compound (Pang et al., 2024). α-Lipoic acid also alleviates toxins associated with oxidative stress-related diseases (Zhao et al., 2025).

α-Lipoic acid has proven effective in reducing the extent of myocardial injury (Wang et al., 2025[b]). In both rats and mice, it demonstrates a safe and protective role against myocardial ischaemia-reperfusion injury (Oskuye et al., 2024; Wang et al., 2025[b]).

α-Lipoic acid provides protection against myocardial ischaemia-reperfusion injury by directly interacting with lipid peroxidation products (Sztolsztener et al., 2022), detoxifying aldehydes generated from oxidised lipids (Khan et al., 2022). Furthermore, its cardioprotective efficacy following myocardial infarction in humans has been demonstrated (Jermendy et al., 2023). In animal studies, α-lipoic acid has also shown effective therapeutic potential in treating myocardial perfusion injury in rats and mice (Xie et al., 2023; Wang et al., 2025[b]). In addition, α-lipoic acid prevents γ-ray-induced testicular injury by restoring normal testicular function, ultimately leading to the recovery of spermatogenesis in rats (Said et al., 2020). Moreover, it protects against γ-ray-induced brain injury in rats by reactivating antioxidant and anti-inflammatory mechanisms (Xu et al., 2023).

It has been postulated that α-lipoic acid administration may offer protection against streptozotocin/high-fat diet-induced diabetic nephropathy (Helmy et al., 2024). Furthermore, α-lipoic acid exhibits a protective effect against ultraviolet-A/B-induced skin damage (Tülüce et al., 2024). It may also provide a novel preventive approach due to its potent antioxidant and anti-inflammatory properties, alongside its favourable safety profile in the lungs of irradiated rats (Seyedpour et al., 2024). Additionally, α-lipoic acid mitigates radiotherapy-induced liver tissue damage (Gezer et al., 2023), and its pretreatment has been shown to alleviate ionising radiation-induced oxidative stress and apoptosis in rat brain tissue (Xu et al., 2023).

The purpose of this article is studying the efficacy of α-lipoic acid on cardiac injury induced in whole body gamma-irradiated rats.

Material and Methods

Experimental animals

Thiry-two male Wister Rats 9-10 weeks old, weighing 335± 11g were used. They were bought from the Holding Company for Biological Products and Vaccines (VACSERA, Helwan, Cairo, Egypt). The experimental animals were kept in suitable cages and controlled environmental situation, constant temperature (24-28 °C), constant light cycle (light from 6.00_{AM} to 6.00_{PM}). and humidity (50-70%). Rats were supplied normal balanced rat-pellets as well as water *ad-libitum*. The animals were kept and used in agreement with the animal ethics. All experiments were conformed to the procedure and guides for the care and use of laboratory animals published earlier, National Institutes of Health, No. 85–23, revised 1996.

Radiation technique

Irradiation was performed with a Canadian gamma cell-40, (^{137}Cs) at the NCRRT, Cairo, Egypt. Animals were exposed to one session of γ-rays at a dose rate 0.37 Gy/ minute. The selected γ-rays dose (6Gy) was enough to induce distinct biochemical alteration and pathological lesion (Mekkawy et al., 2024; Tawfik et al.., 2019).

Animal groups and treatment schedules

Rats were divided into four groups, each group 8rats. Control group: Rats were received 1ml bi-distilled water daily (as a vehicle) / for ten following days via stomach-tubes. α-lipoic acid group: Rats were received α-lipoic acid (Sigma-Aldrich, USA) suspended in 1ml of the vehicle (100mg/ kg/ day for 10days) via stomach-tubes, according to Abdel-Aziz et al. (2021) and Andreeva et al. (2020). γ-rays group: Rats were exposed to acute whole body γ-rays (6Gy-one single dose) then after half an hour, rats received the vehicle daily/ for ten days via stomach-tubes. γ-rays+ α-lipoic acid group: Rats were exposed to γ-rays (6Gy) then were received via stomach-tubes α-lipoic acid (100mg) half an hour post-irradiation and continued for ten days.

Rats in all groups were killed 24hours after the end of the experiment period. The blood plasma and sera were prepared from collected whole blood samples from rat hearts. The hearts were quickly removed. The heart muscles were kept on ice; they were then trimmed from fat and connective tissue and instantly frozen at -80 °C.

Biochemical measures in blood and cardiac tissue

Lactate dehydrogenase (LDH) and creatin Kinase MB (CK-MB) activities were estimated in serum as an induces for cardiac cells damage induced by gamma-radiation. LDH (E.C.1.1.1.27) and CK-MB (Catalog Number: 239 002) activities were determined at absorbances of 340 nm using kinetic methods distributed by Spectrum-diagnosis, Cairo, Egypt. The cardiac tissue myeloperoxidase (MPO); A044-1-1 was estimated according to the patent kit of Jianchen, Nanjing, China. The xanthine oxidase (XO) was estimated according to Bergmeyer et al. (1983). The malondialdehydes (MDA) assessed as described by Buege and Aust (I987). The quantification of protein carbonyl (PC) was assessed according to Levine et al. (1990) technique. The plasma ferric reducing ability (FRA) level was assessed as Bustamante et al. (1998) described. The serum level of cytokine IL-6 (IL-6) was estimated by using kit (Catalog Number: CSB-E04640r) obtained from CUSABIO Technology Biotech Company, China. The cardiac superoxide dismutase (SOD), glutathione peroxidase (GPx) and Catalase (CAT) activities were measured according to Lawrence and Burk (2012), Kakkar et al. (1984), Titov and Osipoc (2017), and reduced glutathione (GSH) content was estimated according to Cigala et al. (2012). The amount of total heart protein was performed according Lowry et al. (1951) method.

Statistical analysis

The obtained data were expressed as mean ± standard error (SE). Statistical analysis was performed using one-way analysis of variance (ANOVA), followed by Duncan's post hoc test to determine significant differences among the experimental groups. The normality of data distribution was assessed using the Shapiro-Wilk test. Statistical analyses were conducted using SPSS software. A *p*-value of less than 0.05 was considered statistically significant.

Results

All experimental investigations and statistical tests were carried out blindly. All Groups were given code numbers. No one knows the group of rats during analysis.

The activities of LDH and CK-MB were significantly elevated in the γ-rays group, reaching 1.4- and 2.0-fold increases, respectively, compared to the control, and 1.6- and 2.0-fold increases, respectively, compared to the α-lipoic acid-treated group. However, these enzyme activities were significantly reduced in the γ-rays+ α-lipoic acid group compared to the γ-rays group and were nearly restored to control levels (Table 1).

MPO and XO activities were significantly increased in the γ-rays group by 4.3- and 2.4-fold, respectively, compared to the control, and by 4.2- and 2.4-fold, respectively, compared to the α-lipoic acid group. α-Lipoic acid supplementation reduced both MPO and XO activities in the γ-rays+ α-lipoic acid group, restoring them to near-control levels (Table 1).

In the γ-rays group, MDA, PC, and IL-6 concentrations significantly increased by approximately 2.4-, 2.0-, and 1.7-fold, respectively, when compared to both the control and α-lipoic acid groups. These levels significantly declined in the γ-rays+ α-lipoic acid group, approaching values similar to the control (Table 2).

TABLE 1. Serum lactate dehydrogenase (LDH) and creatin kinase MB (CK-MB) and cardiac myeloperoxidase (MPO) and xanthin oxidase (XO) levels after α-lipoic acid/ or γ-rays exposure in different rat groups.

Groups	LDH	CK-MB	MPO	XO
	U/ ml	U/ ml	U/ 100 mg tissue	U/ mg protein
Control	271.21± 8.332	148.21± 4.114	5.12± 0.128	0.66±0.014
α-lipoic acid	266.82± 8.123	146.32± 3.521	5.23± 0.132	0.67± 0.022
γ-rays	438.22± 14.651[a,b]	294.24± 10.444[a,b]	22.14± 0.705[a,b]	1.58± .036[a,b]
γ-rays+ α-lipoic acid	308.13± 8.253[c]	162.12± 4.925[c]	8.32± 0.205[c]	0.81± 0.021[c]

[a] significant difference when comparing with control group.

b significant difference when comparing with α-lipoic acid-treated group.

[c] significant difference when comparing with γ-rays (6Gy) exposure group.

In the α-lipoic acid group, FRA levels significantly increased compared to the control (1.6-fold). In contrast, the γ-rays group showed a significant reduction in FRA compared to both the control (−40.7%) and α-lipoic acid-treated (−61.9%) groups. In the γ-rays + α-lipoic acid group, FRA levels significantly increased relative to both the control (1.5-fold) and γ-rays groups (2.5-fold), with no significant difference observed between the α-lipoic acid-treated and γ-rays + α-lipoic acid groups (Table 2).

In the γ-rays group, all oxidative stress markers; SOD, GPx, and CAT activities, along with GSH content were significantly decreased compared to the control group (by −35.0%, −54.1%, −62.2%, and −55.2%, respectively) and the α-lipoic acid-treated group (by −32.6%, −44.3%, −62.7%, and −54.6%, respectively).

In the γ-rays+ α-lipoic acid group, SOD and GPx activities were significantly elevated compared to the γ-rays group (by 1.4-fold, respectively), and their levels were nearly restored to those of the control. However, although CAT activity and GSH content were also significantly increased compared to the γ-rays group, they remained significantly lower than those in the control group (by −23.0% and −13.9%, respectively) and the α-lipoic acid-treated group (by −24.0% and −12.9%, respectively).

Discussion

In recent years, gamma radiation has emerged as a contributing factor to cardiac injury during radiotherapy protocols (Liu et al., 2025). Concurrently, potent antioxidants such as α-lipoic acid have garnered attention for their cardioprotective potential in radiation-induced injuries (Adhab et al., 2025; Wang et al., 2025[b]). The present study aimed to evaluate the protective efficacy of α-lipoic acid against γ-radiation-induced cardiac damage in rats. Owing to its

TABLE 2. Cardiac malondialdehydes (MDA) and protein carbonyl (PC), plasma ferric reducing ability (FRA) and serum level of cytokine IL-6 (IL-6) levels after α-lipoic acid/ or γ-rays exposure in different rat groups.

Groups	MDA	PC	FRA	IL-6
	µmol/ mg tissue	nmol/ mg tissue	mM/ L	Pg/ ml
Control	2.4± 0.08	0.54± 0.018	0.86± 0.021	44.12± 1.103
α-lipoic acid	2.3± 0.08	0.54± 0.019	1.34± 0.043[a]	43.59± 1.092
γ-rays	5.8± 0.28[a,b]	1.09± 0.045[a,b]	0.51± 0.013[a,b]	73.57± 2.355[a,b]
α-lipoic acid+ γ-rays	2.6± 0.12[c]	0.64± 0.021[c]	1.30± 0.034[a,c]	52.12± 1.274[c]

[a] significant difference when comparing with control group.
[b] significant difference when comparing with α-lipoic acid-treated group.
[c] significant difference when comparing with γ-rays (6Gy) exposure group.

TABLE 3. Cardiac superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) activities, and reduced glutathione (GSH) content after α-lipoic acid/ or γ-rays exposure in different rat groups.

Groups	SOD	GPx	CAT	GSH
	µg/ g tissue	nmol/ g tissue	U/ g tissue	µmol/ g tissue
Control	66.64± 1.465	28.54± 0.684	169.92± 4.594	1.65± 0.092
α-lipoic acid	64.21± 1.577	29.54± 0.738	172.21± 4.471	1.63± 0.044
γ-rays	43.27± 1.298[a,b]	13.09± 0.425[a,b]	64.15± 1.924[a,b]	0.74± 0.022[a,b]
α-lipoic acid+ γ-rays	62.45± 1.686[c]	24.64± 0.641[c]	130.92± 3.272[a,b,c]	1.42± 0.035[a,b,c]

[a] significant difference when comparing with control group.
[b] significant difference when comparing with α-lipoic acid-treated group.
[c] significant difference when comparing with γ-rays (6Gy) exposure group.

established antioxidant and anti-inflammatory properties, α-lipoic acid is proposed to mitigate oxidative and inflammatory stress linked to cardiac dysfunction (Oskuye et al., 2024; Wang et al., 2025[a]). Given that γ-rays exposure induces oxidative stress and inflammation, this experimental model was utilised to simulate distinct cardiac injury (Karam et al., 2024).

Our findings revealed that γ-radiation exposure resulted in significant myocardial damage, as indicated by elevated levels of cardiac enzymes (LDH, CK-MB), pro-inflammatory markers (MPO, XO, MDA, PC, IL-6), and a notable decrease in endogenous antioxidants (SOD, GPx, CAT, FRA, GSH). However, co-administration of α-lipoic acid significantly ameliorated these alterations, supporting its role as a potential radioprotective agent for cardiac tissues.

Oxidative stress and the accumulation of inflammatory markers significantly increase the risk of cardiac damage (Naderi et al., 2025). γ-rays exposure results in extensive injury to cardiac tissue, in line with previous studies (Ahmed et al., 2021; Karam et al., 2024; Thabet et al., 2022). In the present study, α-lipoic acid conferred notable protection to cardiac tissues, mitigating the deleterious effects of γ-rays. This supports earlier findings that α-lipoic acid reduces heart injury in rodent models (Nascimento et al., 2024; Oskuye et al., 2024).

FRA levels were significantly higher in the α-lipoic acid group compared to the control. The beneficial effects of α-lipoic acid may be attributed to its multifaceted ability to modulate antioxidant and pro-oxidant metabolism (Skibska et al., 2006). Due to its dithiol structure, α-lipoic acid can scavenge various ROS, including hydroxyl radicals, superoxide anions, alkoxyl radicals, and peroxyl radicals, thereby interrupting the propagation of lipid peroxidation (Biewenga et al., 1997). Beyond its direct scavenging activity, α-lipoic acid participates in the regeneration of several endogenous antioxidants such as vitamin C, vitamin E, coenzyme Q10, and ubiquinone (Gotz et al., 1994; Kozlov et al., 1999; Moini et al., 2002). Additionally, α-lipoic acid can indirectly elevate GSH levels by enhancing cysteine uptake, a rate-limiting step in GSH biosynthesis (Ruiter et al., 1981). This increase in thiol antioxidants contributes to an overall enhancement of total antioxidant capacity.

In this study, plasma FRA served as an indicator of the oxidant/antioxidant balance. The total antioxidant capacity of plasma, assessed via FRA, was markedly reduced following γ-radiation-induced damage (Gupta et al., 2008; Verma et al., 2010). However, α-lipoic acid administration effectively restored antioxidant status, protecting against lipid peroxidation in the red skeletal muscle of insulin-resistant rats (Dajnowicz-Brzezik et al., 2025).

The proinflammatory cytokine IL-6 adversely affects the structure of cardiomyocytes and contributes to heart muscle injury. Serum levels of IL-6 were measured to assess the acute inflammatory response following whole-body γ-rays exposure in rats (Moselhy et al., 2025).

The CK-MB is predominantly found in cardiac muscle, comprising up to 42% of total CK. Elevated CK-MB levels in the bloodstream are indicative of cardiac muscle injury (Zhang et al., 2025).

The current data demonstrate that oxidative stress significantly depletes SOD, leading to increased lipid peroxidation and elevated MDA concentrations. Similarly, other studies have shown that GSH levels may result from increased ROS production in cells and tissues (Li et al., 2025). In this study, early administration of α-lipoic acid effectively counteracted γ-ray-induced lipid peroxidation and provided significant protection against endotoxin-induced oxidative stress in rats (Skibska et al., 2006).

Numerous studies have demonstrated the therapeutic potential of α-lipoic acid in various disorders associated with oxidative stress (Hosny et al., 2024; Nascimento et al., 2024; Oskuye et al., 2024). Moreover, α-lipoic acid has been shown to reduce IL-6 levels in several tissues, notably in cardiac tissue of rats (Khoder et al., 2022; Nemati et al., 2024). In the present study, α-lipoic acid significantly restored CK-MB, MDA, IL-6, and SOD levels to values close to controls and effectively maintained GSH concentrations.

The observed elevation of LDH and CK-MB in irradiated rats indicates cardiac dysfunction, as these enzymes are released into circulation during heart injury. Treatment with α-lipoic acid effectively normalized these enzyme levels (Hosny et al., 2024; Oskuye et al., 2024).

Increases in MPO and XO activities in damaged cardiac muscle corroborate previous findings (Hamed et al., 2024; Lu et al., 2025).

Administration of α-lipoic acid mitigated γ-ray-induced oxidative injury by significantly enhancing antioxidant enzyme activities and restoring them near control levels (Petronilho et al., 2016).

Exposure to γ-rays elevates ROS, resulting in increased H_2O_2, MDA, and PC levels (Rosen et al., 2020). α-Lipoic acid has shown protective effects against oxidative stress in patients with cardiac injuries and normalized PC levels close to baseline (Ratchford et al., 2019; Wedan et al., 2024). Furthermore, antioxidant enzymes GPx and CAT were reduced in irradiated rat hearts (Abdel-Magied et al., 2020), whereas α-lipoic acid treatment modulated these enzymes, alleviating γ-ray-induced damage (Kosoko et al., 2017).

Overall, α-lipoic acid may safeguard rat hearts from γ-ray-induced oxidative and inflammatory changes by preserving biomacromolecules and maintaining their native functional integrity under oxidative stress.

Conclusion

The present study demonstrated that oral administration of α-lipoic acid significantly mitigated the biochemical alterations induced by γ-radiation in rat cardiac tissue. Radiation exposure resulted in oxidative stress, inflammation, and elevated cardiac injury markers, while α-lipoic acid supplementation effectively restored antioxidant enzyme activities and reduced oxidative and inflammatory biomarkers. These findings suggest that α-lipoic acid offers a protective effect against radiation-induced cardiac injury, likely through its antioxidant and anti-inflammatory mechanisms. Therefore, α-lipoic acid holds potential as a functional dietary supplement for reducing cardiac damage in contexts of radiation exposure. Further studies in humans are recommended to validate these results and explore clinical applicability.

Recommendation

Further research needs to be carried out on animals and humans to provide additional understanding on the effects of α-lipoic acid in *vivo*.

Limitations

The study was conducted on rats, which may not fully replicate human physiological responses. Therefore, the findings may not be directly translatable to clinical applications in humans without further investigation. Only one dose of γ-radiation (6 Gy) was used. This dose was chosen because it had previously shown biochemical effects on the heart of rats. The study does not address the effects of different doses or repeated exposure, which are often encountered in radiotherapy or environmental exposure. The study duration (10 days of treatment) limits the ability to assess long-term effects of α-lipoic acid on cardiac tissue or its sustained protective action against radiation-induced damage. Although biochemical markers were measured, the study did not include detailed histological or morphological analysis of cardiac tissues to confirm tissue-level structural protection. The study used a fixed dose (100 mg/kg) without investigating dose-response relationships or evaluating the safety toxicity profile of varying doses. The focus was on oxidative stress and inflammation markers, without assessment of other relevant pathways like apoptosis, fibrosis, or endothelial dysfunction that may also play roles in radiation-induced cardiac injury. The study did not evaluate actual cardiac function (e.g., ECG, echocardiography) to support the biochemical findings with functional evidence. If only male rats were used, gender-specific responses to both radiation and α-lipoic acid might have been overlooked.

Addressing these limitations in future studies would enhance the robustness and applicability of the findings.

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حمض ألفا ليبويك يحمي عضلة قلب الجرذ من الإصابة الناجمة عن أشعة جاما

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1قسم البحوث الصحية الإشعاعية ، المركز القومي لبحوث وتكنولوجيا الإشعاع ، ص. ب. 29 مدينة نصر ، القاهرة ، و2قسم الوقاية من الاشعاع ، مركز بحوث الأمان النووي والأشعاعي ، ص. ب. ٧٥٥١ مدينة نصر ، هيئة الطاقة الذرية المصرية ، القاهرة ، جمهورية مصر العربية.

يتواجد حمض ألفا ليبويك في أنسجة الثدييات والنباتات، ويتميز بتأثيرات مضادة للأكسدة والالتهابات. هدفت هذه الدراسة إلى تقييم قدرة حمض ألفا ليبويك، الذي تجرعته الجرذان عن طريق الفم، على الحماية من إصابة عضلة القلب الناجمة عن التعرض لجرعة ٦ جراي من أشعة جاما.

تم تعريض مجموعة من الجرذان لجلسة واحدة من إشعة جاما بجرعة 6 جراي، وتم مقارنة نتائج هذه المجموعة بنتائج المجموعة الضابطة، والمجموعة المعالجة بحمض ألفا ليبويك (جرعة ١٠٠ مجم/ كجم من وزن الجرذان لمدة ١٠ أيام) عن طريق أنبوب الفم، والمجموعة التي تعرضت لأشعة جاما وتم تجريعها بالحمض يوميًا لمدة ١٠ أيام.

أدى التعرض لأشعة جاما إلى زيادة في مستويات لاكتات ديهيدروجينيز (LDH) ، وميلوبيروكسيديز (MPO)، وأوكسيد الزانثين (XO) ، ومالونداي ألديهيد (MDA) ، وبروتين الكربونيل (PC) ، وكرياتين فوسفوكيناز – MB (CK–MB) ،

والإنترلوكين– (IL–6) ٦، وانخفاض ملحوظ في نشاط سوبر أكسيد ديسميوتاز (SOD) ، والجلوتاثيون بيروكسيديز(GPx) ، والكاتلاز (CAT) ، ومقياس القدرة المضادة للأكسدة الكلية (FRAP) ، والجلوتاثيون المختزل (GSH) .

أدى تجريع الجرذان بحمض ألفا ليبويك بعد التعرض لأشعة جاما إلى تحسن في جميع المؤشرات المقاسة في أنسجة القلب والدم، مما يشير إلى حماية واستعادة لأنظمة الدفاع البيولوجية المضادة للأكسدة.

الخلاصة: يمكن استخدام حمض ألفا ليبويك كمكمل غذائي ووقائي للتخفيف من إصابة عضلة قلب الجرذ الناجمة عن التعرض لأشعة جاما، ويعزى تأثيره إلى خصائصه المضادة للأكسدة والالتهابات.