



Lecithin Provide Alleviation Effect on Impairments of Mitochondrial Adaptations Induced by Pharmacological H1/H2 Blockade

Trinh Quynh Dieu¹, Tran Nguyen Hoang Vy¹, Le Thi My Huyen¹,
 Nguyen Thi Kim Xuyen¹, Mai Huynh Nhu², Do Van Thanh Nhan³, Pham Duc Toan⁴

10.18805/IJAR.BF-2084

ABSTRACT

Background: Histamine signaling plays a pivotal role in the post-exercise muscular responses. Blockage of H1/H2 receptor could result in the down-regulation of post-exercise muscle strength. Lecithin is a well-known supplement to improve exercise training effectiveness. In this study, we investigated the effects of lecithin on H1/H2 antagonists-induced changes in motor performance of mice.

Methods: The study was performed on *Swiss albino* mice brought from Pasteur Institute in Ho Chi Minh City, Vietnam. Mice were divided into 4 groups: Control, lecithin, model and treatment and were underwent a rotarod exercise training procedure. During training processes, mice were given fexofenadine and cimetidine for blocking histamine receptors. Treatment with lecithin were applied during administration of antihistamine drugs. After that, the post-exercise muscle strength between groups were evaluated via behavioral test including Rotarod Test, Wire Hanging Test and Grip strength test. The changes of biological markers were evaluated in the serum and the muscular tissue of mice via commercial ELISA assay kit.

Result: We found that lecithin could ameliorate the detrimental effects of H1/H2 antagonists. In addition, we also revealed the mechanism under this protective effect implicated on the effect of lecithin on mitochondrial adaptation process during exercise training. Administration with antihistamines induced increase in SOD, GPx activity and reduced GSH/GSSG ratio. Treatment with lecithin potentiated this the compensative response of antioxidant enzyme SOD and GPx. Moreover, lecithin also counteracted the effects of antihistamines that decreased GSH/GSSG ratio. In conclusion, our results suggested that lecithin is potentially useful to be taken as a supplement during exercise training and its biological effects, at least in part, related to the regulation of redox balance in muscular tissue during training processes.

Key words: Antihistamines, Glutathione peroxidase, Lecithin, Mitochondrial adaptations, Superoxide dismutase.

INTRODUCTION

Exercise training helps to prevent and mitigate diseases including cardiovascular, metabolic, psychiatric, pulmonary and cancer diseases (Li *et al.*, 2023; Pedersen and Saltin, 2015). Exercise training exerts health beneficial effects through modulating metabolic communication between cells and tissues in the human body and stimulating mitochondrial adaptations (Murphy *et al.*, 2020). Although physicians have still questioned that exercise can be considered as medicine and prescribed for patients or not (Cairney *et al.*, 2018), the role of exercise training in treatment protocol is indisputable. As the *exercise-is-medicine* concept has been developing (Li *et al.*, 2023; Thompson *et al.*, 2020), understanding pharmacological medication and exercise interaction is important to promote positive health outcomes and minimize "side effects" of exercise training in treatment regimen for patients.

Histamine signaling pathways have been reported to be important in modulating exercise training responses. Histamine exert its biological effects as an agonist of four widely expressed heterotrimeric guanine nucleotide-binding protein-coupled histamine receptors (H1, H2, H3, H4) in the skeletal muscle cells. Activation of H1 and H2

¹Faculty of Applied Sciences, Ton Duc Thang University, Ho Chi Minh City, Vietnam.

²School of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam.

³Faculty of Pharmacy, Ton Duc Thang University, Ho Chi Minh City, Vietnam.

⁴Research Group in Pharmaceutical and Biomedical Sciences, Faculty of Pharmacy, Ton Duc Thang University, Ho Chi Minh City, Vietnam.

Corresponding Author: Pham Duc Toan, Research Group in Pharmaceutical and Biomedical Sciences, Faculty of Pharmacy, Ton Duc Thang University, Ho Chi Minh City, Vietnam.

Email: phamductoan@tdtu.edu.vn

ORCID: 0009-0004-1847-3794, 0009-0005-5947-7975, 0009-0001-9267-3215, 0009-0005-5715-0127, 0000-0001-6668-3930, 0000-0001-5656-6677, 0000-0001-5794-6882

How to cite this article: Dieu, T.Q., Vy, T.N.H., Huyen, L.T.M., Xuyen, N.T.K., Nhu, M.H., Nhan, D.V.T. and Toan, P.D. (2025). Lecithin Provide Alleviation Effect on Impairments of Mitochondrial Adaptations Induced by Pharmacological H1/H2 Blockade. *Indian Journal of Animal Research*. 1-9. doi: 10.18805/IJAR.BF-2084.

Submitted: 18-10-2025 **Accepted:** 23-12-2025 **Online:** 16-01-2026

histamine receptor profoundly influence human physiological responses to exercise. Pharmacological effects of antihistamines have also been reviewed previously and suggested that these medications can be applied in certain case to investigate the modification of genes responding to exercise (Luttrell and Halliwill, 2017). Those findings about the role of histamine reveal that it is plausible to utilize pharmacological inhibition of histamine signaling pathway to study mechanism under a compound on muscular responses after a training process.

Nutrition is an very important key to achieve exercise training goals. Increase lecithin in the dietary have been showed that it might be beneficial in optimizing exercising performance (Jäger *et al.*, 2007). Lecithin plays many important functions which regulate effectiveness of training process such as maintaining structural and stability of cell membranes, normalizing choline and lactic acid concentration and supporting mitochondrial function (Jäger *et al.*, 2007; Wang *et al.*, 2025). However, study about the effects of lecithin on exercise and muscular function is limited. Decrease of lecithin levels has previously been reported to be mediated via histamine receptor signaling (Rao, 2000). Lysolecithin, which is synthesized via phospholipase A treatment, was shown to caused rapid degranulation of mast cells and resulted in the release of histamine (Rothschild, 1965). In this study, we evaluated the effects of lecithin on post-exercise muscle strenght impairment caused by H1 and H2 antagonists and clarify the involvement of mitochondrial adaptations in the mechanism under the these effects.

MATERIALS AND METHODS

Animals

Swiss *albino* mice were purchased from Pasteur Institute in Ho Chi Minh City, Vietnam. The male mice used for the experiments were 8-week-old. The average body weight of the mice was about 24 g. All mice were fed *ad libitum* in an air-conditioned room at 23±1°C and 55±5% relative humidity with a standard 12 h light and 12 h dark cycle. Feed composition was followed the standard feeding rodent (Ramzi *et al.*, 2025). All experiments were conducted in the year 2025 and were approved by The Animal Research Ethics Committee of Ton Duc Thang University (TDTU-AEC). Decision No. 07/HĐTVĐĐ.

Drug treatment

Fexofenadine (Sanofi), cimetidine (Mekophar Chemical Pharmaceutical Joint-Stock Co.) and Lecithin from soybean (Sigma-Aldrich) were suspended in 0.5% CMC-Na. Mice were divided into 4 groups, six mice per group (n=6):

Control: Mice were administrated with vehicle (0.5% CMC-Na).

Lecithin: Mice were administrated with only lecithin.

Model: Mice were administrated with fexofenadine and cimetidine.

Treatment: Mice were administrated with lecithin, fexofenadine and cimetidine.

Mice received fexofenadine (540 mg/kg, p.o./day) and cimetidine (40 mg/kg, p.o./day) for 14 consecutive days (Van der Stede *et al.*, 2025). Lecithin (200 mg/kg, p.o./day) (Wang *et al.*, 2025), was administrated once a day for 14 consecutive days during treatment of antihistamine drugs. The doses employed in the present study were determined according to references and preliminary tests.

Rotarod exercise training

Rotarod exercise training was conducted following previous study with modifications (Herrera *et al.*, 2024). All experimental animals partaken in rotarod exercise training. The exercise training occurred between the hours of 8:00 a.m. and 05:00 p.m. and was performed on a The Rota Rod (Panlab, Spain). Before each individual training session, the rotarod was thoroughly cleaned with 70% ethanol. Mice underwent rotarod exercise training within 5 min for 14 consecutive days. The intensity of the training session was gradually increase by increasing the rotational speed (in RPMs) from 3, 5, 10, 15, 20, 25, to 30 RPMs every 2 days of training. At the 15th day, motor performance were assessed via rotarod test, wire hanging test and grip strength test.

Rotarod test

The test was performed via an accelerating paradigm, starting from a rate of 3 rpm to a maximum speed of 30 rpm, then the rotation speed was kept constant at 30 rpm for a maximum of 300s. The duration for which the animal could maintain balance on the rotating drum was measured as the latency to fall, with a maximal cutoff time of 300s (Hur *et al.*, 2020).

Wire hanging test

The wire hanging test detects neuromuscular abnormalities of muscle strength. For this test, a wire cage lid is used with duct tape around the edges to prevent the mouse from walking off the rim. The animal is placed on the top of the cage lid. The lid is then slightly shaken to force the mouse to grip the wire. Afterwards, the lid is slowly turned upside down. The lid is held at a height of approximately 0.5 - 0.6 m above a soft underlay, high enough to prevent the mouse from jumping down, but not high enough to cause harm in the event of a fall. The time until the animal falls is measured. A 90 or 300 seconds cut-off time is used depending on the model (Tam *et al.*, 2015).

Grip strength test

Mice are placed on the grip strength apparatus in a way that they can grab a small grid with their fore paws. Then, the experimenter slowly pulls the mice away from the grid until it releases the handle. The maximum strength of the animal's grip is recorded. Each animal undergoes three trials per testing session (Nazari *et al.*, 2023).

Sample collection

Serum and gastrocnemius muscles were harvested. The gastrocnemius muscles were frozen in liquid nitrogen (LN)

and stored at -80°C to determine molecular and biochemical parameters further. Serum samples was stored at -20°C prior using for further biochemical testing.

Evaluation of cholesterol levels and triglyceride levels

Mouse serum cholesterol and triglyceride levels were evaluated using the Erba cholesterol test kit (Cat No: BLT00080, Germany) and the Erba triglyceride test kit (Cat No: BLT00057, Germany). Results are calculated automatically by Semi Automated Biochemistry Analyzer.

Evaluation of total superoxide dismutase (T-SOD), superoxide dismutase 1 (SOD-1) and superoxide dismutase 2 (SOD-2) activity levels

The evaluation of T-SOD, SOD-1 and SOD-2 activity levels was performed using the Elabscience® CuZn/Mn Superoxide Dismutase (CuZnSOD/Mn-SOD) Activity Assay Kit (Cat No: E-BC-K022-M, China). Briefly, the gastrocnemius muscles were homogenized using dounce homogenizer at 4°C . After that, they were centrifuged at $10000\times g$ for 10 min at 4°C and collected supernatant for detection. The principle of the assay is that superoxide anion produced by xanthine oxidase system reacts with hydroxylamine and finally converted to a purplish-red substance after chromogenic reaction. The amount of purplish-red substance is measured by optical density (OD) at 550 nm. The SOD in the sample has a specific inhibitory effect on superoxide anion, can reduce the content of purplish-red substance and then was calculated by the formula in the assay kit manual. The T-SOD activity is the sum of SOD-1 and SOD-2 activity, a specific pretreatment method can be used to eliminate the activity of SOD-2, leaving only the activity of SOD-1 to be measured.

Evaluation of glutathione peroxidase (GPx) activity levels

GPx activity level was quantified via a spectrophotometric assay previously described (Sharma *et al.*, 2021). The assay, which uses 2.0 mM reduced glutathione and 0.25 mM cumene hydroperoxide as substrates, monitors the rate of NADPH oxidation at 340 nm. The reaction mixture, with a total volume of 1 mL, contained 50 mM potassium phosphate buffer (pH 7.5), 1 mM EDTA, 1 mM NaN_3 , 0.2 mM NADPH, 1 E.U./mL glutathione-reductase, 1 mM reduced glutathione and either 1.5 mM cumene hydroperoxide or 0.25 mM H_2O_2 . A 0.1 mL aliquot of the enzyme source was added to 0.8 mL of the mixture and pre-incubated for 5 minutes at room temperature before the reaction was initiated by the addition of 0.1 mL of peroxide solution. Blanks, in which the enzyme source was replaced with distilled water, were used to correct for background absorbance. The rate of reaction was calculated using the molar extinction coefficient for NADPH ($6.22\text{ mM}^{-1}\text{cm}^{-1}$). GPx activity was normalized to protein concentration and expressed as nmol NADPH oxidized/min/mg protein at 25°C . Protein was quantified using the BCA protein assay with bovine serum albumin as the standard.

Evaluation of reduced glutathione (GSH), oxidized glutathione (GSSG) level and GSH/GSSG ratio

The evaluation of GSH, GSSG levels and GSH/GSSG ratio was performed using the Elabscience® Total Glutathione (T-GSH)/Oxidized Glutathione (GSSG) Colorimetric Assay Kit (Cat No: E-BC-K097-S, China). The principle of the assay is that glutathione reductase converts GSSG into GSH. After that, GSH reacts with a 5,5'-dithiobis-(2-nitrobenzoic acid) (DTNB) and produces yellow 1,3,5-trinitrobenzene (TNB).

The total amount of glutathione (GSH and GSSG) can be determined by the amount of yellow TNB produced *via* measuring the absorbance at 412 nm wavelength. The amount of GSSG was measure by removing all of the GSH from the sample before performing the same reaction.

Statistical analysis

Statistical analyses were performed using GraphPad Prism 8.0.2 (GraphPad Software, La Jolla, CA, U.S.A.) with one-way ANOVA followed by Tukey's multiple comparison test. $p < 0.05$ was considered as statistically significant. Data was presented as the $\text{MEAN} \pm \text{S.E.M.}$ of values obtained from 06 mice per group ($n=6$) and checked for normality by Kolmogorov-Smirnov test.

RESULTS AND DISCUSSION

Effects of lecithin on the changes of motor performance induced by administration with fexofenadine and cimetidine

To clarify whether lecithin reduced motor performance of mice after administration with fexofenadine and cimetidine, we examined whether lecithin attenuated antihistamines-induced changes in latency to fall in rotarod and wire hanging test. We also examined the forelimb grip strength using the grip strength test. As shown in Fig 1A and Fig 1B, administration with fexofenadine and cimetidine significantly decreased the latency to fall in the rotarod and wire hanging test. Treatment with lecithin significantly attenuated the reduction in latency to fall of mice on the rotarod drum (Fig 1A) as well as on the wire (Fig 1B) in comparison with Model group. In addition, Fig 1C demonstrated that fexofenadine and cimetidine significantly decrease fore limb grip strength of mice and that treatment with lecithin could counteracted the decrease of animal's grip strength induce by antihistamine drugs administration. These results suggested that fexofenadine and cimetidine decreased post-exercise muscle strenght of mice in comparison with the control group and that lecithin alleviated this phenomenon.

Effects of lecithin on the changes of serum cholesterol and triglyceride levels induced by fexofenadine and cimetidine

To examine whether antihistamines altered lipid metabolism, we evaluated cholesterol and triglyceride levels in mouse serum. Fig 2A and Fig 2B demonstrated that administration with antihistamines and lecithin did not induce significant changes in cholesterol and triglyceride levels. The lack of change in lipid profile suggests lipid

metabolism is not involved in the down-regulation of post-exercise muscle strenght induced by antihistamines.

Effects of lecithin on the changes of muscular SOD activity levels induced by fexofenadine and cimetidine

Clinical studies indicated that exercise training-induced increase in mitochondrial SOD expression (Van der Stede

et al., 2025). Therefore, in this study, we examined whether our animal model can mimics this phenomenon. As demonstrated in Fig 3A, after administrating with antihistamines, T-SOD activity significantly increased. Treatment with lecithin enhanced the increase of T-SOD activity after antihistamines administration. To determine which SOD isoforms was contributed into T-SOD changes,

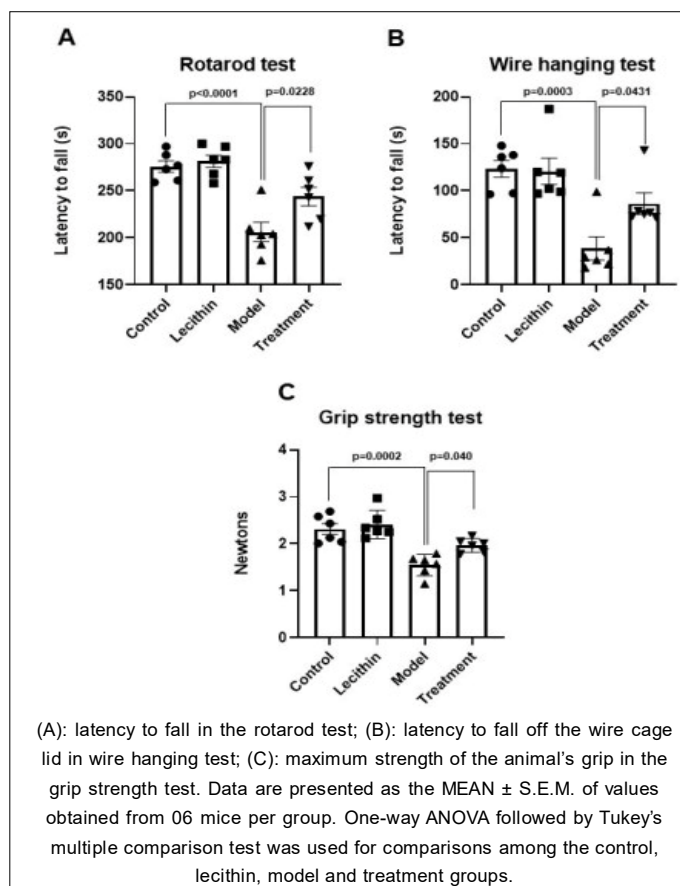


Fig 1: Effects of lecithin on the changes of motor performance induced by administration with fexofenadine and cimetidine.

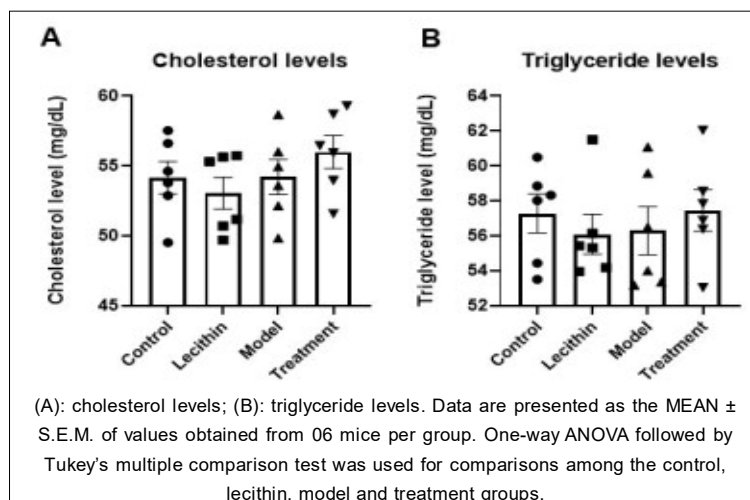


Fig 2: Effects of lecithin on the changes of cholesterol and triglyceride induced by administration with fexofenadine and cimetidine.

we evaluated SOD-1 and SOD-2 levels. As depicted in Fig 3B, SOD-1 activity did not changes between experimental animal groups. In the other hand, SOD-2 activity significantly increased after antihistamines administration. Treatment with lecithin also potentiated the increase of SOD-2 activity after antihistamines administration (Fig 3C). A similar pattern was seen for T-SOD and SOD-2 activity combined with the unchanged result of SOD-1 activity suggested that SOD-2 was the main contributing factors of antihistamines-induced changes in T-SOD activity. These results was consistent with the clinical study and suggested that lecithin could modulate post-exercise muscle strenght of mice via SOD-2 activity alterations (Van der Stede *et al.*, 2025).

Effects of lecithin on the changes of muscular GPx activities induced by fexofenadine and cimetidine

Since SOD-2 and GPx are two related antioxidant enzymes, we continued our study by evaluating the changes of muscular GPx activity. As demonstrated in Fig 4A, GPx activity was increased after administration with antihistamines. This increase was further enhanced by lecithin treatment.

Effects of lecithin on the changes of muscular GSH/GSSG ratios induced by fexofenadine and cimetidine

We also examined the metabolism of GSH and GSSG to ensure the role of GPx in the protective effects of lecithin against antihistamines-induced post-exercise muscle strenght impairments. Fig 4B and Fig 4D indicated that administration with antihistamines decreased GSH

(39.1%) and GSH/GSSG ratio (83.7%) while increasing GSSG (55.6%) (Fig. 4C). Treatment with lecithin counteracted the effects of antihistamine on GSH and GSSG metabolism in the muscular tissues. These results suggested that lecithin mitigated the impairment of GSH/GSSG antioxidant system induced by administration with antihistamines.

Pharmacological blockage of H1/H2 receptor could lead to impairment of microvascular and mitochondrial adaptations to interval training and profoundly reduce post-exercise muscle perfusion in humans (Van der Stede *et al.*, 2025). Animal models also showed that blockage of H1 receptor result in inhibition of arterioles dilation and capillary permeability and thus down-regulate the oxygen and nutrients supply and the removal of waste products (Nijjima-Yaoita *et al.*, 2012). Lecithin is well-known for providing health benefits (Onaolapo *et al.*, 2024). In the present study, we have showed that treatment with antihistamines H1/H2 induced post-exercise muscle strength of mice through behavioral tests. In addition, our results suggested lecithin exerted the protective effects against antihistamines H1/H2 on post-exercise muscle strength. Because lecithin is well-known for their role in cardiovascular benefit that it could redesign cholesterol homeostasis and lipoprotein metabolism (LeBlanc *et al.*, 2003; Onaolapo *et al.*, 2024), we evaluated the effects of lecithin on changes of cholesterol and triglyceride metabolism of mice after antihistamins administration. Unexpectedly, antihistamines H1/H2 did not alter neither cholesterol nor triglyceride levels of mice. Therefore, our

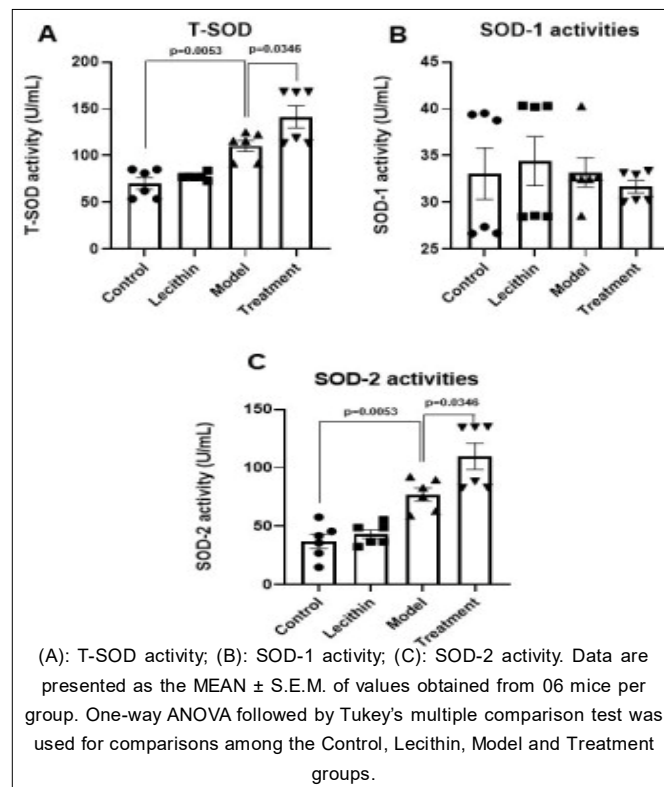


Fig 3: Effects of lecithin on the changes of muscular SOD activity induced by administration with fexofenadine and cimetidine.

results suggested that H1/H2 receptor signaling did not regulate lipid metabolism during exercise training.

As mitochondrial adaptations could be impaired by H1/H2 blockage in human (Van der Stede *et al.*, 2025), we investigated SOD activities in the muscular tissue of mice. Interestingly, our data indicated that SOD-2 (mitochondrial SOD) but not SOD-1 (cytosolic SOD) activity significantly increased after administration with antihistamines. In the previous clinical study, Van der Stede *et al.* (2025) reported that post-training SOD-2 expression was higher in participants of the placebo groups in comparison with H1/H2 blockade-treated group. Our data showed a contrary outcome that blockage of H1/H2 receptor induced increase in post-training SOD-2 activity. This may be due to the differences in mitochondrial adaptations between mouse and human. In muscle cells, mitochondria merge together to produce energy more efficiently. This process, called mitochondrial fusion, is triggered by aerobic exercise, which improves how well the mitochondria function (Hood *et al.*, 2019). Exercise training consumes a lot of energy and produces reactive oxygen species (ROS). ROS are mainly produced by mitochondria in muscle cells (Zhou *et al.*, 2024). In fact, an appropriate ROS concentration is necessary for muscle growth during training. ROS may induce the stimulation to the mitochondrial biogenesis resulting from exercise training which is important for the muscle adaptive process. However, excessive ROS production can cause negative effects on post-exercise results (Davies *et al.*, 1982; Zhou *et al.*, 2024). Smitha

(Bhaskar *et al.*, 2020) reported that SOD-2 is able to increase mitochondrial fusion in a manner independent of its role as an antioxidant (Bhaskar *et al.*, 2020). Therefore, in the previous clinical research, H1/H2-dependent regulation of training adaptations might occur in a condition in which ROS was not excessively produced. In that case, administration with antihistamines subsided SOD-2 level and induced reductions in training-induced effects on mitochondrial capacity via antioxidative-independent intracellular signaling pathways. In contrast, in this study, blockage of histamine H1/H2 might cause excessive oxidative stress and muscular tissue damage due to species-specific differences in ROS threshold and mitochondrial dynamics. Blockage of histamine receptors can induce excessive ROS production via disrupting the enhancement of post-exercise blood flow and vasodilation (Ely *et al.*, 2016, 2020; Sieck *et al.*, 2025; Trinity *et al.*, 2016). Therefore, we hypothesized that the elevation of SOD-2 was the consequence of the compensation response of mouse mitochondria when ROS excessively increased. During exercise, the body relies on a network of antioxidant enzymes and substances such as superoxide dismutase, glutathione peroxidase, catalase, thioredoxin, peroxiredoxin and thioredoxin reductase to maintain a crucial redox balance in humans and animals (Demirhan *et al.*, 2025; Le Moal *et al.*, 2017; Powers *et al.*, 2011). For that reason, we evaluated the expression of GPx and GSH/GSSG levels to validate our hypothesis. GPx activity was upregulated after administering with antihistamines. However, the GSH

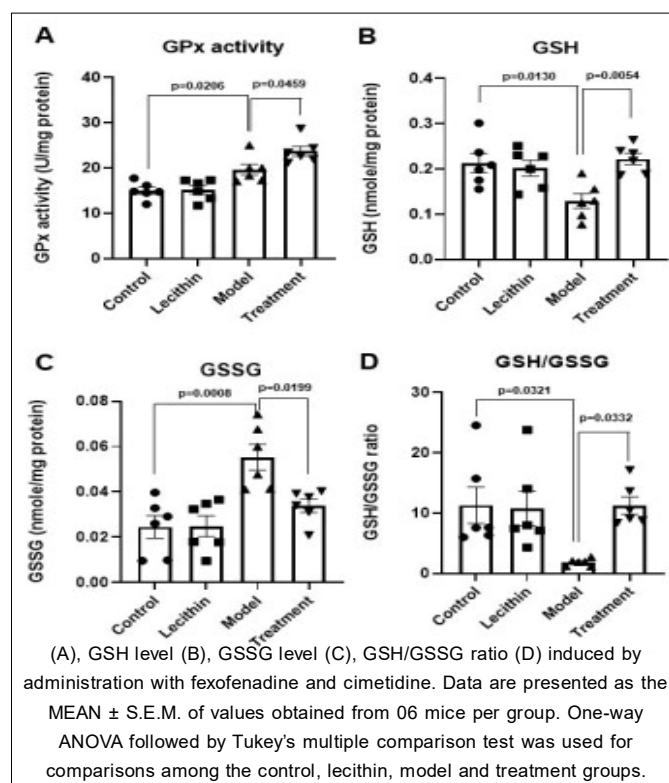


Fig 4: Effects of lecithin on the changes of muscular GPx activity.

and GSH/GSSG was downregulated. Working together, SOD and GPx form an enzymatic defense system that protects cells from oxidative damage by converting dangerous superoxide radicals into harmless water (Demirhan *et al.*, 2025; Irak *et al.*, 2021). SOD initially converts ROS into H₂O₂. Using reduced glutathione (GSH) as a substrate, GPx detoxifies hydrogen peroxide by converting it to water while oxidizing the GSH to GSSG (Muhee *et al.*, 2023). As GSH/GSSG was downregulated, our results suggested that the increase of SOD-2 and GPx was the compensation responses and related closely but not independently with the increase of ROS formation during exercise training.

Additionally, we found in this study that lecithin potentiated SOD-2 and GPx activity response after the administration with H1/H2 antagonists. Carrying on the previous explanations, our results showed that lecithin induced increase of SOD-2 and GPx activity. Moreover, treatment with lecithin also ameliorated antihistamines-induced impairments in GSH, GSSG level and GSH/GSSG ratio. Therefore, it is plausible that lecithin protected against post-exercise muscle strength downregulation induced by blockage of H1/H2 receptor via restoring redox balance managing by synergy between SOD and GPx activity. Recent research have demonstrated that lecithin supplementation significantly enhanced antioxidant capacity by increasing SOD and CAT activities (Qiu *et al.*, 2026). Lecithin can also counteract oxidative damages to muscle induced by blockage of H1/H2 receptors through its action on cardiovascular health, post-exercise blood flow and vasodilation improvement (Onalapo *et al.*, 2024). Although these studies are consistent with our data that the mechanism under protective effects of lecithin on muscular tissue rely on modulating H1/H2 blockage-induced excessive ROS formation, they can not explain the reason why SOD-2 but not SOD-1 was potentiated by treatment with lecithin. During exercise training, mitochondrial content and quality is robustly changed. ROS can trigger PGC-1 α signaling and induce mitochondrial fusion which enhance post-exercise muscle strength. In the other hand, reduction in PGC-1 α signaling could promotes impairments in mitochondrial integrity, further induce mitochondrial fission and ROS-induced mitophagy, which impair post-exercise muscle strength (Memme *et al.*, 2021). Seidman *et al.* (2002) reported that lecithin activated mitochondrial membrane-located enzymes including SOD and GPx which protected mitochondrial membrane from damage by ROS (Seidman *et al.*, 2002).

CONCLUSION

Taken together, in our study, it is plausible that excessive ROS formation induced by blockage of H1/H2 receptors during exercise activated compensation responses in mitochondria which is enhancement of SOD-2 and GPx activity. Lecithin protected against these impairments via promoting antioxidant compensation responses and

restoring mitochondrial fusion signaling. Lecithinized superoxide dismutase and calcium peroxide/carrageenan/soybean lecithin-derived polypyrrole phototherapeutic microparticles are proved to be promising therapy to elevate mitochondrial enzymatic activities. Consequently, our finding about the role of lecithin on mitochondrial adaptation could provide intimation for expending therapeutic application of these biomaterials.

ACKNOWLEDGEMENT

The present study was supported by Research Group in Pharmaceutical and Biomedical Sciences, Faculty of Pharmacy, Ton Duc Thang University, Ho Chi Minh City, Vietnam.

Disclaimers

The views and conclusions expressed in this article are solely those of the authors and do not necessarily represent the views of their affiliated institutions. The authors are responsible for the accuracy and completeness of the information provided, but do not accept any liability for any direct or indirect losses resulting from the use of this content.

Informed consent

All animal procedures for experiments were approved by the The Animal Research Ethics Committee of Ton Duc Thang University (TDTU-AEC).

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article. No funding or sponsorship influenced the design of the study, data collection, analysis, decision to publish, or preparation of the manuscript.

REFERENCES

- Bhaskar, S., Sheshadri, P., Joseph, J.P., Potdar, C., Prasanna, J. and Kumar, A. (2020). Mitochondrial superoxide dismutase specifies early neural commitment by modulating mitochondrial dynamics. *IScience*. **23**(10). doi: 10.1016/j.isci.2020.101564.
- Cairney, J., McGannon, K.R. and Atkinson, M. (2018). Exercise is medicine: Critical considerations in the qualitative research landscape. *Qualitative Research in Sport, Exercise and Health*. **10**(4): 391-399. doi: 10.1080/2159676X.2018.1476010.
- Davies, K.J.A., Quintanilha, A.T., Brooks, G.A. and Packer, L. (1982). Free radicals and tissue damage produced by exercise. *Biochemical and Biophysical Research Communications*. **107**(4): 1198-1205. doi: 10.1016/S0006-291X(82)80124-1.
- Demirhan, I., Kurutas, E.B. and Oner, E. (2025). Network Pharmacology-based Investigation and Experimental Discovery of *Resveratrol*'s Mechanism of Liver Ischemia Reperfusion-Induced Oxidative Stress Damage. *Indian Journal of Animal Research*. **59**(1): 101-107. doi: 10.18805/IJAR.BF-1649.
- Ely, M.R., Ratchford, S.M., La Salle, D.T., Trinity, J.D., Wray, D.W. and Halliwill, J.R. (2020). Effect of histamine-receptor antagonism on leg blood flow during exercise. *Journal of Applied Physiology*. **128**(6): 1626-1634. doi: 10.1152/jappphysiol.00689.2019.

- Ely, M.R., Romero, S.A., Sieck, D.C., Mangum, J.E., Luttrell, M.J. and Halliwill, J.R. (2016). A single dose of histamine-receptor antagonists before downhill running alters markers of muscle damage and delayed-onset muscle soreness. *Journal of Applied Physiology*. **122**(3): 631-641. doi: 10.1152/jappphysiol.00518.2016.
- Herrera, J.J., McAllister, C.M., Szczesniak, D., Goddard, R.C. and Day, S.M. (2024). High-intensity exercise training using a rotarod instrument (RotaHIT) significantly improves exercise capacity in mice. *Physiological Reports*. **12**(9): e15997. doi: 10.14814/phy2.15997.
- Hood, D.A., Memme, J.M., Oliveira, A.N. and Triolo, M. (2019). Maintenance of skeletal muscle mitochondria in health, exercise and aging. *Annual Review of Physiology*. **81**(1): 19-41. doi: 10.1146/annurev-physiol-020518-114310.
- Hur, K.H., Kim, S.E., Lee, B.R., Ko, Y.H., Seo, J.Y., Kim, S.K., Ma, S.X., Kim, Y.J., Jeong, Y. et al. (2020). 25C-NBF, a new psychoactive substance, has addictive and neurotoxic potential in rodents. *Archives of Toxicology*. **94**(7): 2505-2516. doi: 10.1007/s00204-020-02740-3.
- Irak, K., Mert, H., Mert, N., Aysin, N., Söğütü, I. D. and Comba, A. (2021). Evaluation of various biochemical parameters in the serum and tissues of lambs with white muscle disease. *Indian Journal of Animal Research*. **55**(11): 1293-1297. doi: 10.18805/IJAR.B-1372.
- Jäger, R., Purpura, M. and Kingsley, M. (2007). Phospholipids and sports performance. *Journal of the International Society of Sports Nutrition*. **4**(1): 5. doi: 10.1186/1550-2783-4-5.
- Le Moal, E., Pialoux, V., Juban, G., Groussard, C., Zouhal, H., Chazaud, B. and Mounier, R. (2017). Redox control of skeletal muscle regeneration. *Antioxidants and Redox Signaling*. **27**(5): 276-310. doi: 10.1089/ars.2016.6782.
- LeBlanc, M.J., Brunet, S., Bouchard, G., Lamireau, T., Yousef, I.M., Gavino, V., Lévy, E. and Tuchweber, B. (2003). Effects of dietary soybean lecithin on plasma lipid transport and hepatic cholesterol metabolism in rats. *The Journal of Nutritional Biochemistry*. **14**(1): 40-48. doi: 10.1016/S0955-2863(02)00253-X.
- Li, J., Qiu, H. and Li, J. (2023). Exercise is medicine. *Frontiers in Aging Neuroscience*. **15**. doi: 10.3389/fnagi.2023.1129221.
- Luttrell, M.J. and Halliwill, J.R. (2017). The intriguing role of histamine in exercise responses. *Exercise and Sport Sciences Reviews*. **45**(1). doi: 10.1249/JES.0000000000000093.
- Memme, J.M., Erlich, A.T., Phukan, G. and Hood, D.A. (2021). Exercise and mitochondrial health. *The Journal of Physiology*. **599**(3): 803-817. doi: 10.1113/JP278853.
- Muhee, A., Malik, H.U., Bhat, R.A., Akhoun, Z.A., Khan, A.M., Nabi, S.U., Hussain, S.A., Beigh, S.A. and Shaheen, M. (2023). Amelioration of oxidative stress through supplementation of self-formulated anti-oxidant mixture for early recovery and prophylaxis of bovine mastitis in Kashmir valley. *Indian Journal of Animal Research*. **57**(6): 762-769. doi: 10.18805/IJAR.B-4339.
- Nazari, S.E., Tarnava, A., Khalili-Tanha, N., Darroudi, M., Khalili-Tanha, G., Avan, A., Khazaei, M. and LeBaron, T.W. (2023). Therapeutic potential of hydrogen-rich water on muscle atrophy caused by immobilization in a mouse model. In *Pharmaceuticals*. **16**(10). doi: 10.3390/ph16101436.
- Murphy, R.M., Watt, M.J. and Febbraio, M.A. (2020). Metabolic communication during exercise. *Nature Metabolism*. **2**(9): 805-816. doi: 10.1038/s42255-020-0258-x.
- Nijima-Yaoita, F., Tsuchiya, M., Ohtsu, H., Yanai, K., Sugawara, S., Endo, Y. and Tadano, T. (2012). Roles of Histamine in Exercise-Induced Fatigue: Favouring Endurance and Protecting against Exhaustion. *Biological and Pharmaceutical Bulletin*. **35**(1): 91-97. doi: 10.1248/bpb.35.91.
- Onaolapo, M.C., Alabi, O.D., Akano, O.P., Olateju, B. S., Okeleji, L.O., Adeyemi, W.J. and Ajayi, A.F. (2024). Lecithin and cardiovascular health: A comprehensive review. *The Egyptian Heart Journal*. **76**(1): 92. doi: 10.1186/s43044-024-00523-0.
- Pedersen, B.K. and Saltin, B. (2015). Exercise as medicine - evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scandinavian Journal of Medicine and Science in Sports*. **25**(S3): 1-72. doi: 10.1111/sms.12581.
- Powers, S.K., Ji, L.L., Kavazis, A.N. and Jackson, M.J. (2011). Reactive oxygen species: Impact on skeletal muscle. *Comprehensive Physiology*. **1**(2): 941-969. doi: 10.1002/j.2040-4603.2011.tb00348.x.
- Qiu, Z., Xu, Q., Chong, C.M. and de Cruz, C.R. (2026). Lecithin-enriched diet improves growth performance, lipid metabolism and disease resistance in giant river prawn (*Macrobrachium rosenbergii*). *Aquaculture*. **611**: 743016. doi: 10.1016/j.aquaculture.2025.743016.
- Ramzi, A., Ammari, A. and Ahmad, A. (2025). Evaluation of large animal feed as an alternative to laboratory rat diets along with the addition of raisins as a nutritional supplement and its impact on growth and fertility on male rat. *Indian Journal of Animal Research*. **59**(7): 1160-1166. doi: 10.18805/IJAR.BF-1925.
- Rao, G.J. (2000). Histamine induced decrease of lecithin levels in broncho-alveolar lavage fluid of rats is mediated by H2 receptor. *Asian Pacific Journal of Allergy and Immunology*. **18**(3): 169.
- Rothschild, A.M. (1965). Histamine release by bee venom phospholipase a and mellitin in the rat. *British Journal of Pharmacology and Chemotherapy*. **25**(1): 59-66. doi: 10.1111/j.1476-5381.1965.tb01756.x.
- Seidman, M.D., Khan, M.J., Tang, W.X. and Quirk, W.S. (2002). Influence of lecithin on mitochondrial DNA and Age-related hearing loss. *Otolaryngology-Head and Neck Surgery*. **127**(3): 138-144. doi: 10.1067/mhn.2002.127627.
- Sharma, N., Shin, E.J., Pham, D.T., Sharma, G., Dang, D.K., Duong, C.X., Kang, S.W., Nah, S.Y., Jang, C.G., Lei, X.G., Nabeshima, T., Bing, G., Jeong, J.H. and Kim, H.C. (2021). GPx-1-encoded adenoviral vector attenuates dopaminergic impairments induced by methamphetamine in GPx-1 knockout mice through modulation of NF- κ B transcription factor. *Food and Chemical Toxicology*. **154**: 112313. doi: 10.1016/j.fct.2021.112313.
- Sieck, D.C., Kobak, S.H., Larson, E.A., Dreyer, H.C., Fogarty, M.J., Sieck, G.C., Minson, C.T. and Halliwill, J.R. (2025). Histamine is a molecular transducer of adaptation to endurance exercise training in humans. *Journal of Applied Physiology*. **138**(6): 1398-1410. doi: 10.1152/jappphysiol.00687.2024.

- Tam, C.S., Power, J.E., Markovic, T.P., Yee, C., Morsch, M., McLennan, S.V and Twigg, S.M. (2015). The effects of high-fat feeding on physical function and skeletal muscle extracellular matrix. *Nutrition and Diabetes*. **5(12)**: e187-e187. doi: 10.1038/nutd.2015.39.
- Thompson, R., Sallis, W., Robert, J., Elizabeth, J., Carrie, A., Stuhr, Robyn, M. and Trilk, Jennifer, L. (2020). Exercise Is Medicine. *American Journal of Lifestyle Medicine*. **14(5)**: 511-523. doi: 10.1177/1559827620912192.
- Trinity, J.D., Broxterman, R.M. and Richardson, R.S. (2016). Regulation of exercise blood flow: Role of free radicals. *Free Radical Biology and Medicine*. **98**: 90-102. doi: 10.1016/j.freeradbiomed. 2016.01.017.
- Van der Stede, T., Blancaert, L., Stassen, F., Everaert, I., Van Thienen, R., Vervaet, C., Gliemann, L., Hellsten, Y. and Derave, W. (2025). Histamine H1 and H2 receptors are essential transducers of the integrative exercise training response in humans. *Science Advances*. **7(16)**: eabf2856. doi: 10.1126/sciadv.abf2856.
- Wang, X., Li, D., Li, X. Y., Lu, W., Ding, H., Qi, C., Wang, X., Shen, J., Chi, Y., Li, T., Dunk, M. M., An, Y., Huang, H., Yu, K., Xu, W., Xiao, R. and Xi, Y. (2025). Lecithin alleviates memory deficits and muscle attenuation in chinese older adults and SAMP8 Mice. *Advanced Science*. **12(30)**: 2405222. doi: 10.1002/advs.202405222.
- Zhou, Y., Zhang, X., Baker, J.S., Davison, G.W. and Yan, X. (2024). Redox signaling and skeletal muscle adaptation during aerobic exercise. *IScience*. **27(5)**: 109643. doi: 10.1016/j.isci.2024.109643.