Effect of Eight Weeks of Resistance Training with Spirulina Platensis Ingestion on the Heart Weight and Cardiac C/EBPβ Expression in Male Rats

Fatemeh Ahmadi¹, Mohsen Ghanbar Zadeh ¹*, Abdolhamid Habibi ¹ and Forouzan Karimi ²

¹Department of Exercise Physiology, Faculty of Sport Science, Shahid Chamran University of Ahvaz, Ahvaz, Iran
²Department of Immunology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

*Corresponding author: Department of Exercise Physiology, Faculty of Sport Science, Shahid Chamran University of Ahvaz, Ahvaz, Iran. Email: ghanbarzadeh213@gmail.com

Received 2019 May 13; Revised 2019 May 27; Accepted 2019 June 04.

Abstract

Background: Resistance training and Spirulina consumption could change the expression of the gene involved in hypertrophy.

Objectives: The study investigated the effect of eight weeks of resistance training with Spirulina platensis ingestion on the heart weight and cardiac CCAAT-enhancer-binding proteins beta (C/EBPβ) expression in male rats.

Methods: We divided 32 male Sprague Dally rats into four groups: control (CO; n = 8), Spirulina platensis (SP; n = 8), resistance training (RE; n = 8), and Spirulina plus resistance training (SP + RE; n = 8). The resistance training group practiced five sessions a week for eight weeks. Spirulina 200 mg/kg/day was used in the supplement group and the exercise plus Spirulina platensis group. Twenty-four hours after the last training session, the gene expression was measured using real-time PCR.

Results: The results showed that resistance training significantly increased heart weight (P = 0.001) and left ventricular weight (P = 0.001) but significantly decreased CEBP (P = 0.001). Spirulina insignificantly increased heart weight (P = 0.46), significantly increased left ventricular weight (P = 0.001), and significantly decreased CEBP (P = 0.02). On the other hand, resistance training plus Spirulina significantly increased heart weight (P = 0.001) and left ventricular weight (P = 0.001) but had no significant effect on C/EBPβ reduction (P = 0.10).

Conclusions: A combination of resistance training and Spirulina supplementation cannot have a significant effect on the important signaling factor in heart hypertrophy.

Keywords: Resistance Training, Spirulina, C/EBPβ, Rat, Heart

1. Background

The efforts of health facilities around the world to prevent heart disease with an emphasis on physical activity have led to an increased number of participants in recreational and competitive sports programs. This is because regular exercise is associated with structural (such as heart and left vernacular weight), functional, and electrical changes in the heart (1).

The main muscular adaptation in the athlete’s body is the cardiac myocytes (2). Physiological hypertrophy leads to the changed structure of the heart (e.g., heart and left vernacular weight), the increased expression of the genes functioning in heart hypertrophy, increased metabolism, and improved myocardial function. However, heart reconstruction requires the expression of many genes involved in the heart structure (3).

On the other hand, today, the use of food supplements in exercise is widely appreciated such that most athletes consume one or more supplements in some or even all the stages of the Championship. Spirulina is a blue-green alga (4) and a potential source of proteins and vitamins (5). Protein comprises 60 to 70% of the weight of Spirulina (5). Studies have shown that Spirulina can increase muscle isometric strength and the rate of muscle protein synthesis (6).

Sandho et al. (7) found that Spirulina consumption combined with exercise led to a significant increase in isometric strength compared to Spirulina consumption or exercise alone. Several complicated mechanisms have shown to be involved in the molecular basis of cardiac hypertrophy (8). Physiological heart hypertrophy develops through several signals such as growth hormones and mechanical force.

In the physiological range, growth hormones such as insulin, insulin growth factor 1, thyroid hormone, and me...
Mechanical force can induce physiological cardiac hypertrophy by activating several signals such as PI3K, Akt, AMPK, and mTOR pathways (9, 10). The inhibition of the pathways of protein degradation and/or stimulation of protein synthesis pathways can be effective in the treatment of atrophy and hypertrophy in the skeletal muscle (11). Recently, it has been reported that CCAAT-enhancer-binding proteins beta (C/EBP\(\beta\)) plays a role in exercise-induced cardiac hypertrophy (12, 13) and cardiac growth (12). C/EBP\(\beta\) decreases in cardiac hypertrophy due to exercise and suppresses the growth of the heart muscle in adults (13). Overall, research suggests that endurance exercise can lead to reduced C/EBP\(\beta\), which can help expand the physiologic hypertrophy (e.g., heart and left vernacular weight) of the heart (14).

2. Objectives

The present study aimed to investigate the effect of eight weeks of resistance training with Spirulina platensis ingestion on the cardiac weight and cardiac C/EBP\(\beta\) expression in male rats. Therefore, the present study hypothesized that resistance training and Spirulina consumption have interaction effects on heart weight and cardiac C/EBP\(\beta\) expression increases in male rats.

3. Methods

3.1. Experimental Animals

The study used 32 male rats (Sprague-Dawley race; weight: 290 ± 20 g; age: 9 weeks). All the animals had free access to healthy water and standard rat food (specifically designed for rats supplied by Pars Feed Co.) and were provided with human care in accordance with the relevant instructions.

Rats were randomly divided into four groups of eight rats: (A) without resistance training, without Spirulina supplementation (control (CO) group), (B) Spirulina supplementation without resistance training (SP group), (C) Resistance training without Spirulina supplementation (RT group), (D) resistance training with Spirulina supplementation (RT + SP group).

3.2. Training Protocol: Resistance Exercise

First, an adaptation period of one week was designated. The training protocol included the climbing of a ladder with a height of one meter for eight weeks. Before the start of training, rats climbed up the ladder three times without lifting and without a rest between the repetitions to warm up. Then, rats in the training groups started to exercise on a ladder, 5 repetitions per set (one-minute rest between each repetition), three sets per day (two-minute rest between sets), and five days per week for eight weeks (30% - 100% of body weight per week) (15). The study received approval from the Jahrom University of Medical Sciences (IR.JUMS.REC.1398.011).

3.3. Spirulina Supplementation

Each day, Spirulina (200 mg/kg/day) was added to the drinking water of rats in the SP group and SP + RE group (16).

3.4. Sampling

After 24 hours of the last training session, all rats were decapitated (15) following anesthetization for about five minutes by injecting ketamine 10% (50 mg/kg body weight) and xylazine 2% (10 mg/kg body weight) to measure the parameters. Then, the heart of the animal was removed from the chest and the left ventricle was obtained. The left ventricular tissue was placed immediately in nitrogen tanks and transferred to an 80-degree freezer for the extraction of RNA (ribonucleic acid). RT-PCR was used for measuring the C/EBP\(\beta\) gene expression.

3.5. Statistical Analysis

The Kolmogorov-Smirnov test we used to examine the distribution of data in the research groups and two-way ANOVA (SPSS version 18) to examine the effect of interventions at a significance level of P < 0.05.

4. Results

The effects of Spirulina supplementation, resistance training, and Spirulina combined with resistance training on rat weight (Table 1), heart/left ventricular weight and CEBP (Table 2) are shown. The weight of rats increased during the training period in the CO, SP, RE, and SP + RE groups. The findings showed that the distribution of variables in the research groups was normal.

The exercise training had a significant effect on the CEBP reduction in rats (P = 0.001). Spirulina consumption had a significant effect on the CEBP reduction in rats (P = 0.02). However, the exercise training and Spirulina consumption had no significant interaction effects on the CEBP reduction in rats (P = 0.10) (Table 3 and Figure 1).

The results indicated that exercise training significantly increased the heart weight of rats (P = 0.001). The use of Spirulina had no significant effect on the heart weight of rats (P = 0.46). However, exercise training and Spirulina consumption had significant interaction effects.
Table 1. Comparison of the Effects of Spirulina, Resistance Exercise, and Spirulina Plus Resistance Exercise on Changes in Rat’s Weight

| Test | Groups       | CO          | SP          | RE         | SP + RE     |
|------|--------------|-------------|-------------|------------|-------------|
| Pretest, g |              | 149.75 ± 5.14 | 151.62 ± 6.82 | 147.12 ± 15.83 | 149.12 ± 13.68 |
| Posttest, g |              | 227.75 ± 6.71 | 211.12 ± 13.84 | 257.28 ± 12.22 | 242.57 ± 5.19  |

Abbreviations: CO, control; RE, resistance exercise; SP, Spirulina; SP + RE, Spirulina plus resistance exercise.

Data are presented as mean ± SD.

$b^p$ values of less than 0.05 were considered significant.

Table 2. Comparison of the Effects of Spirulina, Resistance Exercise, and Spirulina plus Resistance Exercise on Changes in Rat’s Heart and Left Ventricular Weight and CEBP After the Experimental Period

| Parameters | Groups       | CO          | SP          | RE         | SP + RE     |
|------------|--------------|-------------|-------------|------------|-------------|
| Heart weight, mg |              | 0.93 ± 0.09 | 1.11 ± 0.05 | 1.42 ± 0.02 | 1.19 ± 0.07 |
| Left ventricular weight, mg |              | 0.55 ± 0.02 | 0.56 ± 0.01 | 0.89 ± 0.02 | 0.71 ± 0.01 |
| CEBP, fold change |              | 1.00 ± 0.06 | 0.86 ± 0.09 | 0.56 ± 0.13 | 0.53 ± 0.05 |

Abbreviations: CO, control; RE, resistance exercise; SP, Spirulina; SP + RE, Spirulina plus resistance exercise.

Data are presented as mean ± SD.

5. Discussion

The main findings of the study showed that the expression of C/EBPβ changed after eight weeks. Indeed, the expression of C/EBPβ significantly decreased in the resistance-training group and the Spirulina supplement group while it dropped in the resistance training plus Spirulina supplement group. The findings of some studies in the literature are consistent with the findings of the current study. For example, Bei et al. (17) showed that C/EBPβ decreased in the heart of rats after swimming training.

In addition, it was found that exercise training (P = 0.001) significantly increased the left ventricular weight of rats (P = 0.001). Spirulina consumption significantly increased the weight of the left ventricle of rats (P = 0.001). The exercise training and Spirulina consumption had significant interaction effects on the increases of the left ventricular weight of rats (P = 0.001) (Table 3 and Figure 3).

Figure 1. The effects of SP, RE, and SP + RE on the expression of C/EBPβ in cardiac muscle. CO, control; SP, Spirulina; RE, resistance exercise; SP + RE, Spirulina plus resistance exercise. Data are presented as means ± standard error of the mean. *P values of less than 0.05 were considered significant.

Figure 2. The effects of SP, RE, and SP + RE on heart weight (mg). CO, control; SP, Spirulina; RE, resistance exercise; SP + RE, Spirulina plus resistance exercise. Data are presented as means standard error of the mean. *P values of less than 0.05 were considered significant.

Figure 3. The effects of SP, RE, and SP + RE on the heart weight of rats (P = 0.001) (Table 3 and Figure 2).

on the heart weight of rats (P = 0.001) (Table 3 and Figure 2).

In addition, it was found that exercise training (P = 0.001) significantly increased the left ventricular weight of rats (P = 0.001). Spirulina consumption significantly increased the weight of the left ventricle of rats (P = 0.001). The exercise training and Spirulina consumption had significant interaction effects on the increases of the left ventricular weight of rats (P = 0.001) (Table 3 and Figure 3).
Table 3. The Results of Two-Way ANOVA on the Effects of Exercise and Spirulina on Heart Weight, Left Ventricular Weight, and CEBP in Rats

| Source of Change | Statistics |
|------------------|------------|
|                  | Mean Square | df | F     | Sig. | Partial Eta Squared |
| Heart weight, mg |             |    |       |      |                   |
| Exercise         | 0.61        | 1  | 152.60| 0.001 | 0.83 |
| Spirulina        | 0.00        | 1  | 0.55  | 0.46  | 0.02 |
| Spirulina + exercise | 0.32      | 1  | 69.09 | 0.001 | 0.71 |
| Left ventricular weight, mg |         |    |       |      |                   |
| Exercise         | 0.47        | 1  | 141.34| 0.001 | 0.98 |
| Spirulina        | 0.05        | 1  | 162.46| 0.001 | 0.85 |
| Spirulina + exercise | 0.06      | 1  | 193.76| 0.001 | 0.87 |
| CEBP (fold change) |           |    |       |      |                   |
| Exercise         | 1.18        | 1  | 143.22| 0.001 | 0.83 |
| Spirulina        | 0.04        | 1  | 5.94  | 0.02  | 0.17 |
| Spirulina + exercise | 0.02      | 1  | 2.79  | 0.10  | 0.09 |

*p values of less than 0.05 were considered significant.

Figure 3. The effects of SP, RE, and SP + RE on left ventricular weight (mg). CO, control; SP, Spirulina; RE, resistance exercise; SP + RE, Spirulina plus resistance exercise. Data are presented as mean and SD. *P values of less than 0.05 were considered significant.

The understanding of molecular mechanisms that specifically control physiological hypertrophy may have important implications for the treatment of heart disease (18). C/EBPβ decreases in cardiac hypertrophy due to exercise and suppresses the growth of the heart muscle (13). Research has shown that C/EBPβ reduces cardiovascular effects induced by exercise and protects the heart against pathological changes (13, 19). Other studies have shown that C/EBPβ is one of the transcriptional regulators involved in exercise responses to the heart. In a study, C/EBPβ decreased the growth of myocytes and activated genes similar to those observed in the exercise groups (13).

On the other hand, clinical studies have shown that exercise is an effective intervention for the primary and secondary prevention of cardiovascular disease although the desirable nature, intensity, and duration of exercises to maximize cardiovascular benefits are still unclear (20).

At the molecular level, exercise stimulates the physiological growth of the heart primarily by controlling cardiac hypertrophy, particularly via the signaling pathways of IGF-1-Pi3K-AKT and C/EBPβ (20). The activation of the Pi3K-AKT pathway inhibits the expression of C/EBPβ by exercise, which increases the physiological hypertrophy (13). Akt inhibits C/EBPβ. Systemic reductions in C/EBPβ heterozygote can increase cardiovascular hypertrophy and improve systolic dysfunction (13).

Maillet et al. (21) showed that C/EBPβ is one of the main regulators of adaptive or physiological response to hypertrophy. C/EBPβ inhibition induces the expression of useful and protective genes and allows for the expression of genes, which, in turn, increases the heart muscle Heart muscle mass and the number of cells in the heart. Therefore, the inhibition of C/EBPβ activity most likely restores the damaged heart tissue and cardiomyopathy of the heart.

The other finding of the present study showed that at the end of eight weeks, the weight of the heart and the left ventricle increased while the increases were lower in the Spirulina supplement group than in the other groups.
This finding is justified based on the structure and complementary nature of Spirulina, which partially suppresses weight gain; but in two groups that were involved in resistance activity, increases in the heart rate and left ventricular weight were due to the characteristics of resistance exercise that could compensate for the reduced effectiveness of Spirulina supplementation.

Eight weeks of running on a treadmill increased the weight of the left ventricle in rats in a prior study (22). Another study showed that six weeks of resistance training increased the weight of the rat’s heart (23). In another study, it was found that six weeks of running exercise did not have a significant effect on the heart weight and left ventricular mass, but in the exercise group, the weight of the heart and left ventricular mass decreased (24). Eight weeks of running on a treadmill led to an increase in heart weight in female rats (9). Eight weeks of resistance training did not significantly increase the left ventricular weight of male rats (25). Twelve weeks of resistance training significantly increased the heart’s weight (26). Eight weeks of swimming training caused a significant increase in the left ventricular weight in the training group compared to a control group (27). It has been shown that nine weeks of running on a treadmill significantly increased the heart weight of rats (28). It seems that cardiac hypertrophy develops in response to various stimuli such as pressure and volume overload. Subjects who participate in resistance exercises are mainly involved in the isometric non-aerobic exercise, which increases the thickness of the left ventricular wall (27).

5.1. Conclusions

Based on the findings of this study, it can be concluded that although resistance training or Spirulina supplementation could have a significant effect on the reduction of CEBP in the heart muscle of rats, the combination of resistance training with Spirulina supplementation could not have a significant effect on this important factor in heart hypertrophy. There were some limitations to this study, such as the lack of using different methods of measurement such as Western blot, not using different doses of Spirulina, and not measuring signaling pathway gene expression. Therefore, it is suggested that future studies investigate the effect of different doses of Spirulina on signaling pathway gene expression and employ other methods of measurement such as Western blot for protein expression.

Acknowledgments

The present study is part of a doctoral dissertation approved by the Shahid Chamran University of Ahvaz. The authors express their gratitude and appreciation to the Research and Technology Department of the University.

Footnotes

Authors’ Contribution: All authors equally contributed to the writing and revision of this paper.

Conflict of Interests: The authors declare that they have no conflicts of interest.

Ethical Approval: The present study received approval from the Jahrom University of Medical Sciences (IR.JUMS.REC.1398.011).

Funding/Support: The Shahid Chamran University of Ahvaz funded the study.

References

1. Curtis GL, Chughtai M, Khlopas A, Newman JM, Khan R, Shaffiy S, et al. Impact of physical activity in cardiovascular and musculoskeletal health: Can motion be medicine? J Clin Med Res. 2017;9(5):375-81. doi: 10.14740/jocmr3001w. [PubMed: 28392856]. [PubMed Central: PMC5380069].
2. Barauna VG, Rosa KT, Irrigoyen MC, de Oliveira EM. Effects of resistance training on ventricular function and hypertrophy in a rat model. Clin Med Res. 2007;5(2):114-20. doi: 10.3121/cmr.2007.707. [PubMed: 17607046]. [PubMed Central: PMC1905918].
3. Bernardo BC, Weeks KL, Pretorius I, McMullen JR. Molecular distinction between physiological and pathological cardiac hypertrophy: Experimental findings and therapeutic strategies. Pharmacol Ther. 2010;128(4):191-227. doi: 10.1016/j.pharmthera.2010.04.005. [PubMed: 20438756].
4. Karkos PD, Leong SC, Karkos CD, Sivaji N, Assimakopoulos DA. Spirulina in clinical practice: Evidence-based human applications. Evid Based Complement Alternat Med. 2011;2011:531053. doi: 10.1093/ecam/nen058. [PubMed: 18955364]. [PubMed Central: PMC3165777].
5. Belay A, Ota Y, Miyakawa K, Shimamatsu H. Current knowledge on potential health benefits of Spirulina. J Appl Physiol. 1993;75(2):323-41. doi: 10.1152/jappl.1993.75.2.323.
6. Voltarelli F, Araújo M, Moura L, Garcia A, Mendes C, Silva S, et al. Nutrition recovery with Spirulina diet improves body growth and muscle protein of protein-restricted rats. Int J Nutr Metab. 2013;22-30.
7. Sandhu JS, Dheera B, Shweta S. Efficacy of spirulina supplementation on isometric strength and isometric endurance of quadriceps in trained and untrained individuals - a comparative study. IJnosina J Med Biomed Sci. 2010;2(2):79. doi: 10.4103/1947-489X.210974.
8. Shimizu I, Minamino T. Physiological and pathological cardiac hypertrophy. J Mol Cell Cardiol. 2006;77:245-62. doi: 10.1016/j.yjmcc.2016.06.001. [PubMed: 27262074].
9. Kemi OJ, Ceci M, Wisloff U, Grimaldi S, Gallo P, Smith GL, et al. Activation or inactivation of cardiac Akt/mTOR signaling diversifies physiological from pathological hypertrophy. J Cell Physiol. 2008;214(2):316-21. doi: 10.1002/jcp.21897. [PubMed: 17941081].
10. Lyon RC, Zanella F, Omens JH, Sheikh F. Mechanotransduction in cardiac hypertrophy and failure. Circ Res. 2015;116(8):1462-76. doi: 10.1161/CIRCRESAHA.116.304937. [PubMed: 25858069]. [PubMed Central: PMC4394185].
11. Glass DJ. Skeletal muscle hypertrophy and atrophy signaling pathways. Int J Biochem Cell Biol. 2005;37(10):1974-84. doi: 10.1016/j.biocel.2005.04.018. [PubMed: 16087388].
12. Huang GN, Thatcher JE, McAnally J, Kong Y, Qi X, Tan W, et al. C/EBP transcription factors mediate epicardial activation during heart development and injury. Science. 2012;338(6114):599-603. doi: 10.1126/science.1229765. [PubMed: 23160954]. [PubMed Central: PMC3681494].

13. Bostrom P, Mann N, Wu J, Quintero PA, Plovie ER, Panakova D, et al. C/EBPbeta controls exercise-induced cardiac growth and protects against pathological cardiac remodeling. Cell. 2010;143(7):1072-83. doi: 10.1016/j.cell.2010.11.036. [PubMed: 21183071]. [PubMed Central: PMC3035164].

14. Wackerhage H. Molecular exercise physiology: An introduction. London: Routledge; 2014.

15. Dehghan F, Hajiaghaalipour F, Yusof A, Muniandy S, Hosseini SA, Heydari S, et al. Saffron with resistance exercise improves diabetic parameters through the GLUT4/AMPK pathway in-vitro and in-vivo. Sci Rep. 2016;6:25139. doi: 10.1038/srep25139. [PubMed: 27122001]. [PubMed Central: PMC4848502].

16. Liping L, Qian LA, Yiquan W, Guorong Y. Spirulina platensis extract supplementation attenuates oxidative stress in acute exhaustive exercise: A pilot study. Int J Phys Sci. 2011;6(12):2901-6.

17. Bei Y, Fu S, Chen X, Chen M, Zhou Q, Yu P, et al. Cardiac cell proliferation is not necessary for exercise-induced cardiac growth but required for its protection against ischaemia/reperfusion injury. J Cell Mol Med. 2017;21(8):2648-55. doi: 10.1111/jcmm.13078. [PubMed: 28304153]. [PubMed Central: PMC4542991].

18. Redondo-Angulo I, Mas-Statucharska A, Sitges M, Giralt M, Vilarroya F, Planavila A. C/EBPbeta is required in pregnancy-induced cardiac hypertrophy. Int J Cardiol. 2016;210:189-99. doi: 10.1016/j.icard.2015.10.005. [PubMed: 26470093].

19. Zou J, Li H, Chen X, Zeng S, Ye J, Zhou C, et al. C/EBPbeta knockdown protects cardiomyocytes from hypertrophy via inhibition of p65-NFkappaB. Mol Cell Endocrinol. 2014;390(1-2):38-25. doi: 10.1016/j.mce.2014.03.007. [PubMed: 24700426].

20. Wei X, Liu X, Rosenzweig A. What do we know about the cardiac benefits of exercise? Trends Cardiovasc Med. 2015;25(6):529-36. doi: 10.1016/j.tcm.2014.12.004. [PubMed: 25646311]. [PubMed Central: PMC4490514].

21. Maillet M, van Berlo JH, Molkentin JD. Molecular basis of physiological heart growth: Fundamental concepts and new players. Nat Rev Mol Cell Biol. 2013;14(1):38-48. doi: 10.1038/nrm3495. [PubMed: 23258295]. [PubMed Central: PMC446212].

22. Reyes DRA, Gomes MJ, Rosa CM, Pagan LU, Zanati SG, Damatto RL, et al. Exercise during transition from compensated left ventricular hypertrophy to heart failure in aortic stenosis rats. J Cell Mol Med. 2019;23(3):1235-45. doi: 10.1111/jcmm.14025. [PubMed: 30457099]. [PubMed Central: PMC6349654].

23. Jourkesh M, Soori R, Earnest CP, Mirheidari I, Ravasi AA, Stannard SR, et al. Effects of six weeks of resistance-endurance training on microRNA-29 expression in the heart of ovariectomised rats. Prz Menopauzalny. 2018;17(4):355-60. doi: 10.5114/pm.2018.81737. [PubMed: 30766462]. [PubMed Central: PMC6372852].

24. Libonati JR. Cardiac remodeling and function following exercise and angiotensin II receptor antagonism. Eur J Appl Physiol. 2012;112(8):3449-54. doi: 10.1007/s00421-011-2263-y. [PubMed: 22143841].

25. Melo SF, Barauna VG, Junior MA, Bozi LH, Drummond IR, Natali AJ, et al. Resistance training regulates cardiac function through modulation of miRNA-214. Int J Mol Sci. 2015;16(4):6855-67. doi: 10.3390/ijms16046855. [PubMed: 25822872]. [PubMed Central: PMC4424992].

26. Soufi FG, Saber MM, Ghiassi R, Alipour M. Role of 12-week resistance training in preserving the heart against ischemia-reperfusion-induced injury. J Regen Med. 2018;12(2):140-5. doi: 10.1007/s12268-018-0226-8. [PubMed: 2143819].

27. Medeiros A, Oliveira EM, Gianolla R, Casarini DE, Negrao CE, Brum PC. Swimming training increases cardiac vagal activity and induces cardiac hypertrophy in rats. Braz J Med Biol Res. 2004;37(12):1999-1. doi: 10.1590/S0100-879X20040012000018. [PubMed: 15554099].

28. Hrmanka R, Raksapharm S, Kijtawornrat S, Ngamcharoeng C, Vephalaktr T. Role of cardiac mast cells in exercise training-mediated cardiac remodeling in angiotensin II-infused ovariectomized rats. Life Sci. 2019;219:209-18. doi: 10.1016/j.lfs.2019.01.018. [PubMed: 30658099].