UDC 613.72:577.112:612.398:616-001.16/.17(048.8) https://doi.org/10.26641/2307-0404.2024.4.319168

*N. Ayubi* [1, *], *J. C. Wibawa* [2], *C. Callixte* [3]

# THE MECHANISM OF PHYSICAL EXERCISES INCREASES HEAT SHOCK PROTEIN 70 (HSP70) (a systematic review)

*Universitas Negeri Surabaya* [1]
*Surabaya, Jawa Timur, 60213, Indonesia*
*STKIP PGRI Trenggalek* [2]
*Jl. Supriyadi str., 22, Trenggalek, Jawa Timur, 66319, Indonesia*
*University of Rwanda* [3]
*KK 737 str, Kigali, Rwanda*
*Державний університет Сурабаї* [1]
*Сурабая, Східна Ява, 60213, Індонезія*
*Педагогічний університет STKIP PGRI Trenggalek* [2]
*вул. Дж. Супріяді, 22, Тренггалек, Східна Ява, 66319, Індонезія*
*Університет Руанди* [3]
*вул. KK 737, Кігалі, Руанда*
[*]*e-mail: novadriayubi@unesa.ac.id*

***Цитування: Медичні перспективи. 2024. Т. 29, № 4. С. 14-22***
***Cited: Medicni perspektivi. 2024;29(4):14-22***

**Key words:** *HSP70, oxidative stress, physical exercises, inflammation, reactive oxygen species, catalase, superoxide dismutase*
**Ключові слова:** *HSP70, окиснювальний стрес, фізичні вправи, запалення, активні форми кисню, каталаза, супероксиддисмутаза*

**Abstract. The mechanism of physical exercises increases heat shock protein 70 (HSP70) (a systematic review). Ayubi N., Wibawa J.C., Callixte C.** *This study aimed to analyze physical exercises in increasing the expression of heat shock protein 70 (HSP70). This research is a systematic review involving searches from journal databases such as Pubmed, Web of Science, and Science Direct. Before starting the search, the study determines inclusion and exclusion criteria. The inclusion criteria were articles that discussed oxidative stress, physical exercises, and heat shock protein 70 (HSP70), and were published in the last five years (2018-2023). Meanwhile, the articles were excluded if they were published in non-reputable journals or were not indexed by Scopus and Web of Science. A total of 3211 articles from the Science Direct, Pubmed, and Web of Science databases were initially identified. Among them, ten articles met the inclusion criteria and thus were selected and analyzed for this systematic review. For standard operations, this study follows the preferred reporting items for systematic reviews and meta-analyses (PRISMA) assessment. The results showed that physical exercises played a certain role in increasing HSP70 expression as a physiological reaction to exercises. The increase in HSP70 is good as it can reduce and prevent inflammation, which reduces cell damage due to physical stress. Additionally, HSP70 increases catalase and superoxide dismutase, the processes that can reduce reactive oxygen species (ROS) caused by physical exercises. This enzyme is also important in protein optimization based on requirements. Therefore, we recommend doing physical exercises to improve health and avoid degenerative diseases.*

**Реферат. Механізм підвищення рівня білка теплового шоку 70 (HSP70) під впливом фізичних вправ (систематичний огляд). Аюбі Н., Вібава Дж.К., Каллікст К.** *Це дослідження мало на меті проаналізувати вплив фізичних вправ на підвищення експресії білка теплового шоку 70 (HSP70) та є систематичним оглядом з пошуком у базах даних журналів, таких як Pubmed, Web of Science і Science Direct. Перед початком пошуку в дослідженні визначено критерії включення та виключення. Критеріями включення були статті, в яких обговорювались окиснювальний стрес, фізичні вправи та білок теплового шоку 70 (HSP70), опубліковані за останні п'ять років (2018-2023). При цьому статті виключалися, якщо вони були опубліковані в неавторитетних журналах або не були проіндексовані Scopus і Web of Science. Спочатку було ідентифіковано 3211 статей з баз даних Science Direct, Pubmed і Web of Science. Серед них десять статей відповідали критеріям включення, тому їх було відібрано та проаналізовано для цього систематичного огляду. Для стандартних операцій це дослідження притримується переважних елементів звітності для систематичних оглядів і метааналізів (PRISMA). Результати показали, що фізичні вправи відіграли певну роль у підвищенні експресії HSP70 як фізіологічної реакції на вправи. Збільшення HSP70 добре, оскільки воно може зменшити та запобігти запаленню, що зменшує пошкодження клітин через фізичний стрес. Крім того, HSP70 підвищує рівень каталази та супероксиддисмутази – це процеси, які можуть зменшити активні форми кисню, спричинені фізичними вправами. Цей фермент також важливий для оптимізації білка на основі потреб. Тому ми рекомендуємо займатися фізичними вправами, щоб зміцнити здоров'я та уникнути дегенеративних захворювань.*

Human muscles can adapt to stress due to mechanical and physiological changes from exercises [1]. When doing exercises, the human body will produce more free radicals because the body responds to physical exercises to adapt physiologically [2]. The formation of free radicals can cause an increase in oxidative stress, which is the main cause of myocardial ischemia damage and is the beginning of disorders related to heart attacks [3]. In submaximal physical exercises, the formation of free radicals begins with muscle contraction during explosive force movements [4]. Muscle ischemia will occur during the action of an explosive force, and then the muscles will relax alternately [5]. Muscle contractions caused by this muscle movement limit blood flow. After that, ischemia-reperfusion occurs, which is a condition where the blood will flow easily, causing the release of electrons from the respiratory chain. This process ultimately produces free radicals or ROS (reactive oxidative species) [6]. An increase in ROS can basically lead to continuous inflammation and damage to the heart muscle. It can result in cell death, which will reduce the heart's capacity to pump blood [6].

While exercises causes the body to produce more ROS as a physiological response, interestingly, it also causes the body to produce more antioxidants, such as glutathione peroxidase (GSH), superoxide dismutase (SOD), and catalase. Guerrero et al. (2021) expressed that the body has compensatory mechanisms to compensate for the increase in oxidative stress caused by exercises [7]. Oxidative damage to proteins, lipids, and DNA in cells can also be caused by an imbalance in redox processes in cells [2]. Another marker of cell injury is the upregulation of HSP70 protein expression caused by oxidative stress. Therefore, generating reactive oxygen species (ROS) triggers oxidative stress to increase HSP70 expression as a response and protective measure [5].

HSP70 is a protein molecule required to repair cells and maintain homeostasis [8]. It is a protein type that increases rapidly after stress, including oxidative stress [9, 10]. When cells are frozen, HSP70 expression helps prevent cell death by enzymatically breaking down proteins involved in cell necrosis [11]. Exercises and self-care practices can impact metabolic regulation [12].

HSP70 strains are widespread, conserved, and required for all species to continue to exist [10]. It is a multifunctional protein that works with HSP90 and is responsible for the final folding and maturation of various substrate proteins and cellular degradation mechanisms in various activities related to protein quality control [13]. In addition, HSP70 protects cells from pathogenic conditions, age, and proteotoxic stress that can disrupt protein homeostasis [9].

An earlier study reported that eight weeks of interval training dramatically decreased caspase 3 gene expression in the heart muscle of mice used in a heart attack model [6]. Although moderate-intensity exercises can modulate physiological characteristics by triggering internal recalibration of many systems, high-intensity exercises can overload physiological response mechanisms, allowing the organism to adapt to internal dysfunction or survive in an aggressive external environment [14, 15].

Skeletal muscle adapts to a variety of stimuli, including growth hormones, mechanical stress, exercises, and nutrition [16, 17]. Although Heat Shock Proteins (HSP) may help avoid metabolic diseases, a detailed discussion of how HSP70 is expressed after physical exercises has not been reported in depth [18]. This study aims to fill this gap by analyzing the potential of physical exercises in increasing the expression of Heat Shock Proteins 70.

**MATERIALS AND METHODS OF RESEARCH**

This research is a systematic review involving searches from journal databases such as Pubmed, Web of Science, and Science Direct. Before starting the search, the research determined inclusion and exclusion criteria. The inclusion criteria were articles that discussed oxidative stress, physical exercises, and Heat Shock Protein 70 (HSP70), which were published in the last five years (2018-2023). Meanwhile, articles were excluded if they were published in non-reputable journals or were not indexed by Scopus and Web of Science.

The research was conducted in accordance with the principles of bioethics set out in the “Universal Declaration on Bioethics and Human Rights” (UNESCO).

The process of searching literature in this research involved several stages. Before screening, articles’ titles, abstracts, and full text were saved and stored in Mendeley software. This is to help the researchers navigate thousands of articles and screen them faster. To begin with, a total of 3,211 articles were initially identified. These articles were filtered in the second stage, yielding 1,250 based on the suitability of the title and abstract. In the third stage, these articles were verified, and 128 items were generated for further processing. At this stage, we filtered the articles based on the overall suitability. Then, in the final stage, ten articles were selected because they met the inclusion criteria predetermined earlier. They were observed and systematically analyzed using established standard operational procedures called Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The process of the literature screening using PRISMA is illustrated in Figure 1.

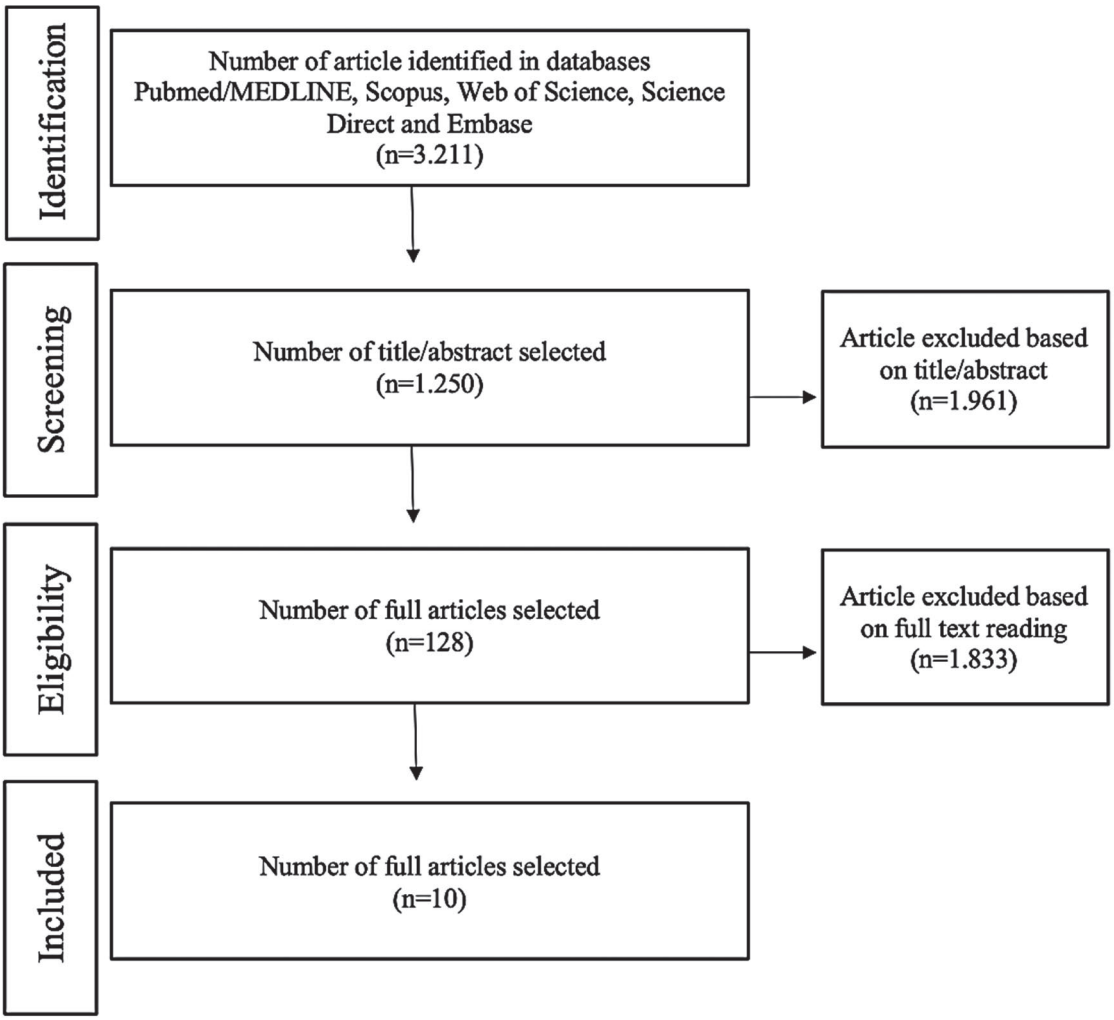


**Fig. 1. PRISMA flowchart of the article selection process**

**RESULTS AND DISCUSSION**

**Results of physical exercises that increases HSP70**

| Author | Sample Characteristics | Study Design | Intervention | Results |
|---|---|---|---|---|
| (Harahap et al., 2021) [5] | Twenty non-smokers and athletes participated in the study. They did not take any vitamins or antioxidants for two weeks before or during the program. The sample was also divided into two groups. Group B received submaximal physical exercises with dragon fruit juice, while Group A received submaximal physical exercises without antioxidants. | Experimental | The participants did physical exercises by running on a treadmill for 30 minutes at an intensity of between 80 and 85 percent of their maximum heart rate, without inclines or fast steps. Then, they cooled down for three to five minutes. The intervention was given for four weeks, in which the treadmill was used three days a week. | The study found an increase in HSP70 expression during submaximal physical exercises without antioxidants. |

| Author | Sample Characteristics | Study Design | Intervention | Results |
|---|---|---|---|---|
| (Cumming et al., 2021) [19] | A 12-week functional, control strength training, or strength training group, was randomly assigned to 38 seniors as a group. Then, 13 teenagers without any training performed strength training for eleven weeks to compare the young and old. | Experimental | Over 12 weeks, training, including hiking and aerobics, was completed with senior participants. | A greater increase in HSP70 expression was found in the older group. |
| (Pouzesh Jadidi et al., 2022) [6] | A total of 30 male Wistar rats (body weight: 200–250 grams, age: 16 weeks) were randomly divided into three groups: myocardial infarction training, MI (myocardial infarction) controls, and healthy controls. | Experimental | The samples received eight weeks of HIIT training (five sessions per week), with ten running sessions (4 minutes each) at 85–90% $VO_2$max and two-minute rest intervals at 50–60% $VO_2$max each session. | The group that received HIIT training experienced the most significant increase in HSP70 expression. |
| (Mazhari et al., 2024) [20] | Three groups of nine mice were randomly divided into control, calorie restriction, and calorie restriction combined with high-intensity interval training. | Experimental | For eight weeks, the high-intensity interval training (HIIT) used in this study involved five sessions per week on a treadmill, at an intensity of 85%–90% $VO_2$max and active rest. Throughout the training period, the treadmill incline remained zero, but the training intensity increased gradually until the eighth week by varying the treadmill speed by 0.02 m/s. Each session began with a ten-minute warm-up at a speed of five meters per second, which was performed before the main training section. | The group undergoing HIIT combined with calorie restriction experienced the greatest increase in HSP70 expression. |
| (Wang et al., 2019) [21] | Male Wistar rats weighing 270±30 g were divided into two groups, namely the control group (C) and the aerobic exercises group (AE). | Experimental | For five weeks, six days a week, mice in the AE group received treadmill aerobic physical training with increasing loads. The running speeds of the first to fifth weeks were 10, 15, 18, 21, and 21 meters per minute. Meanwhile, the training durations were 10, 20, 30, 40, and 40 minutes respectively. | There was an increase in HSP70 expression in the group given aerobic exercises intervention. |
| (Medica et al., 2021) [22] | In this study, twelve healthy horses (six females and six males) with an average body weight of 480±50 kg and an age ranging from 3 to 6 years were kept stable. | Experimental | The horses were taught according to a conventional training program, involving two high-intensity training sessions per week (2 bouts of 5 minutes at an average speed of 10 m/s) on a 1,800 m long sand track. 3600 m warm-up slow run (6.0–6.5 m/s), 1800 m run (10.5–10.7 m/s), 10-minute walk, and 1800 m sprint (8.5-8.7 m) were all part of the first training session. The second session consisted of a warm-up 3600 m slow run (6.0–6.5 m/s), an 1800 m run (10.5–10.7 m/s), a 10-minute walk, and a sprint, where all of these were part of the sand track sprint race. | The group participating in the training session experienced the most significant increase in HSP70. |

| Author | Sample Characteristics | Study Design | Intervention | Results |
|---|---|---|---|---|
| (Goh et al., 2020) [23] | Men in good health (N = 7) who were free from respiratory, metabolic, or cardiovascular conditions were selected from the general population and participated in the study. Each subject did physical exercises in their free time, doing sport or exercises for at least half an hour, three times a week. | Experimental | The samples receive three weeks of non-stop sports training, consisting of three training days a week. Each participant warmed up in week 1 by running for five minutes on a treadmill. After that, they ran for five minutes at a speed equivalent to 80% of their maximum heart rate. After using the treadmill, there was a break for two minutes. | HSP70 levels increased after three weeks of physical exercises. |
| (Lu et al., 2023) [24] | Eight-week-old male Sprague-Dawley rats (n=45) were divided into three equal groups (n=15/group): group C was the control group, the EE group was the group that underwent total exercises, and the HIIT+EE group was the group that underwent total exercises, did a full HIIT+ workout. | Experimental | In this study, rats in Group EE ran at a speed of 0% and 25 m/min on a treadmill until exhausted. Meanwhile, rats in the HIIT + EE group ran on a treadmill for four periods of ten minutes each, with ten minutes of rest in between, at a speed of 28 m/min and a speed of 0%. This was done so the mice approached 80% of their maximum oxygen consumption. | The exercises to exhaustion (EE) group showed increased expression of HSP70. |
| (Min et al., 2020) [25] | Pre-submaximal exercises (running for 30 minutes at 70-80% maximum heart rate) and post-submaximal exercises were performed by six healthy men and 12 male professional volleyball players. | Experimental | Everyone ran for thirty consecutive minutes at submaximal heart rate (70–80% of maximum heart rate) at 20ºC and 60% humidity on the day of testing. Every day, twelve male professional volleyball players trained for at least two hours. At a temperature of 20ºC and humidity of 60%, participants ran on a treadmill for thirty minutes at a speed between 70 and 80% of their maximum heart rate. | In the training group, there was an increase in HSP70 expression. |
| (dos Santos et al., 2020) [26] | 250 Wistar mice and 86 Knockout Transgenic mice were involved in this study. | Experimental | Treadmills for rodents were used for training (Insight). Initially, the day before instruction, each animal was placed on a treadmill and allowed to walk for five minutes at a slow speed of five meters per minute. The rats were then allowed to run for forty minutes at increasing speeds: five meters per minute for the first five minutes, ten meters per minute for the fifteenth, fifteen meters per minute for the thirty-first, and seventeen meters per minute for the forty minutes. | The study foun that HSP70 levels increased most 8 hours after physical exercises intervention. |

Scholars argue that homeostatic imbalances in the body can be triggered by situations of instability caused by oxidative stress during and after exercises [27]. They also add that tissue hypoxia, a state in

which cell pressure and oxygen content are lower than normal, can act as a catalyst, leading to increased production of heat shock proteins (HSPs) [27, 28].

In this systematic review, a study was found to have an increase in HSP70 expression, especially among individuals who did physical exercises three times a week for four weeks with interventions, such as running on a treadmill for 30 minutes with an intensity of 80-85% of the maximum heart rate [5]. Another finding in this review also reported similar results on mice. The study found that mice that received five weeks of aerobic exercises on a treadmill experienced increased expression of HSP70 [21]. Like humans and mice, another study reported that healthy horses physically trained for competition have been shown to express more HSP70 when competing [22]. There are two main elements that trigger the physiological activation of the Heat Shock Response (HSR): conditions that threaten proteostasis and metabolic stress [29]. These factors may not be mutually exclusive since a metabolic balance known as "caloristasis" may determine which factors are more common [30].

The primary function of the Heat Shock Response (HSR), a highly evolutionarily conserved physiological manifestation, is to restore cellular homeostasis following a stressful event [30]. For example, the present study found that a 12-week study showed that a training program, including hiking and aerobics, could increase HSP70 expression [19]. Another study reported that eight weeks of high-intensity interval training (HIIT) with five sessions per week consisting of ten running sessions lasting four minutes each at 85-90% $VO_2$max and a two-minute rest period at 50–60% $VO_2$max per session could increase HSP70 expression in Wistar rats [6]. According to Zhang (2022), exercises, heat stress, ischemia, oxidative stress, and metabolic stress are some of the factors that cause HSP expression. The present study also found that eight weeks of high-intensity interval training (HIIT) on a treadmill with five sessions per week at an intensity of 85% to 90% $VO_2$max and active rest increased HSP70 expression [20]. These findings confirm earlier studies which reported that treadmill training for three weeks with a frequency of three times per week was proven to increase HSP70 expression [23].

Research has shown that Heat shock factor 1 (HSF1), heat shock protein 1 (HspBP1), and HSP70-ATPase are some factors that activate HSP70 [31]. Although the biological significance of HspBP1 is not well understood, it is involved in the group of chaperones that activate HSP70 [32]. Within the cell membrane, HSP70 (iHSP70), which is initially located within the cell, is transferred to the circulation via mechanisms such as cell membrane apoptosis or ATP-binding transporters [33]. This HSP is known as eHSP70, or extracellular HSP70. iHSP70 exerts anti-inflammatory effects through the pancreatic reticulum. In contrast, eHSP70 can reduce pro-inflammatory cytokines and is associated with insulin resistance in type 2 diabetes [34]. Therefore, it is recommended to use the ratio of eHSP70 to iHSP70 as a further testing biomarker [34].

The correlation between insulin resistance, type 2 diabetes, and HSP70 is thought to increase with T2DM, and HSP70 targets may be modulated by interventions such as physical exercises [35]. In addition, a study revealed that in patients with advanced diabetes, HSP70 increased in vascular endothelial cells during the inflammatory phase, and there was a significant relationship between serum HSP70 levels and systolic blood pressure in newly diagnosed hypertensive patients [36]. As mentioned previously, cells are known to secret HSP70 when under stress [34]. In conclusion, low levels of iHSP70 impair the capacity of cells to prevent NFκB translocation, which is critical for reducing inflammation [37].

HSP70, a significant molecular chaperone, can confer substrate selection specificity on the autophagy pathway in response to stress, a process known as selective chaperone-assisted autophagy that may have a mediating role in upstream processes to regulate this process [38]. In addition to its assistance in substrate breakdown via the autophagy pathway, HSP70 is also involved in protein refolding and disaggregation. It is likely that increasing HSP70 suppresses degradation caused by autophagy after being given priority to maintain appropriate protein structure and restore cellular homeostasis [39]. Through its interaction with selective autophagy, upregulation of the HSP70 chaperone complex in response to exercises-induced myofibril damage may promote repair and limit apoptosis [24].

As mentioned earlier, the body will increase oxidative stress when doing physical exercises to respond to the physical stress that occurs by increasing ROS (reactive oxygen species) [2]. Research findings in this systematic review showed that mice that received the intervention of jogging on a treadmill until exhausted at a speed of 0% and 25 m/min had higher HSP70 expression [24]. Although a small amount of heat shock proteins (HSPs) are produced constitutively, most are molecular chaperones that are usually overexpressed by cells in response to stimuli that can denature these stress proteins, such as heat, starvation, oxidative stress, viral infection, ischemia, exercises, and bacterial infections [40]. This HSF1 response will provide a signal to express HSP70 [41]. SOD and CAT levels may increase in response to increased HSP70

expression. They act as a physiological mechanism to increase endogenous antioxidants, which will impact the actual reduction in ROS [42, 43]. The results of another study reported that individuals who ran for thirty consecutive minutes at submaximal heart rate (70–80% of maximum heart rate) in 20 ºC weather with 60% humidity experienced increased expression of HSP70 [25]. It has been demonstrated that HSP70 regulates inflammation both inside and outside cells [36]. HSP70 interacts with transcription factors, including inflammation-causing factors, such as nuclear factor-kappaB (NF-kB), which consists of p65 and p50 heterodimers. The results of a study report that HSP70 can reduce NF-kB activity [44]. Additionally, reduced ROS generation and decreased tumor necrosis factor-alpha (TNF-α) release have been associated with increased iNOS in inflammatory and heat-stressed cells [44]. These findings and their intercorrelations are illustrated in Figure 2 below.

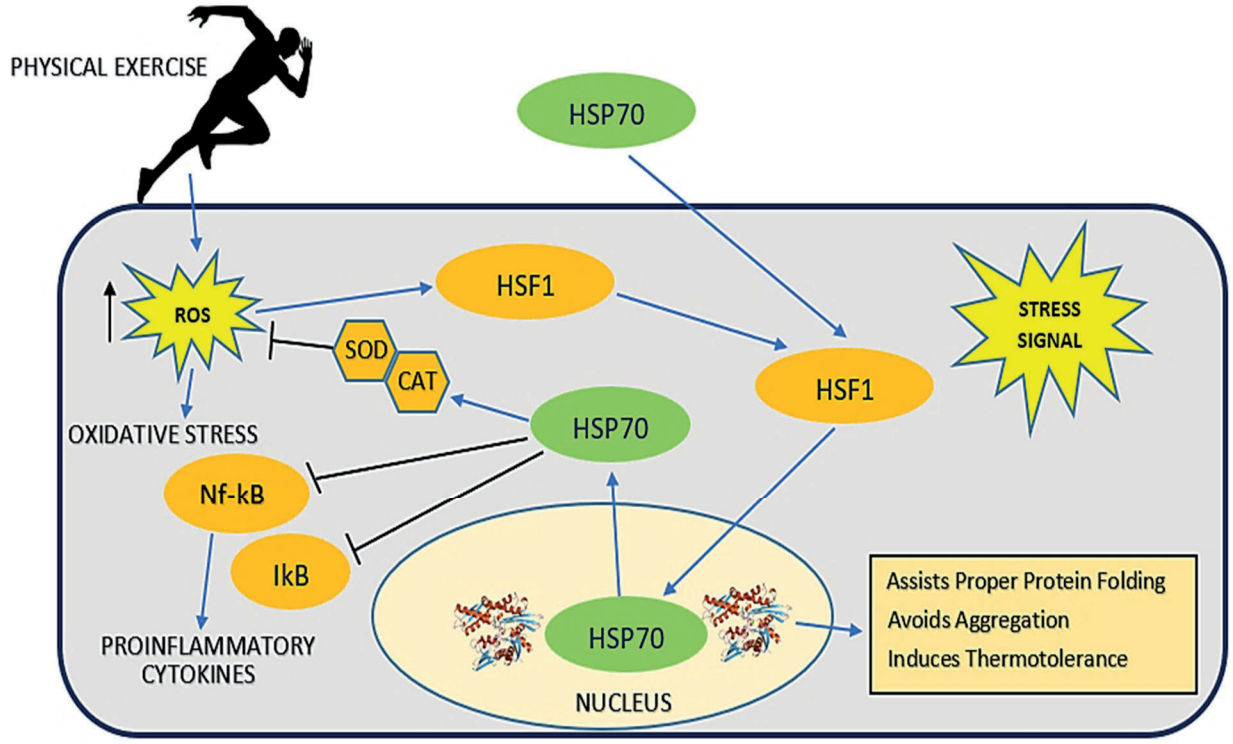


**Fig. 2. Mechanism of physical exercises increases heat shock protein 70 (HSP70)**

**CONCLUSIONS**

1. This study concluded that physical exercises plays a role in increasing the expression of Heat Shock Protein 70. It functions as a physiological response to physical exercises.
2. Heat Shock Protein 70 can reduce and prevent inflammation, which can further reduce cell damage due to physical stress.
3. In addition, Heat Shock Protein 70 increases catalase and superoxide dismutase, two processes that can reduce reactive oxygen species caused by physical exercises. Heat Shock Protein 70 is also important in protein optimization based on needs. Although these findings seem promising, this study still has limitations because it only discusses how Heat Shock Protein 70 is expressed during physical exercises.
4. Therefore, further research is needed to investigate the expression of other Heat Shock Proteins, which are closely related to cellular processes that occur during physical exercises. In this way, everyone is aware of the many cellular processes that occur, especially those related to heat shock proteins. In addition, this study recommends that people do physical exercises and maintain a healthy lifestyle to improve their health and prevent degenerative diseases.

**Contributors:**

Ayubi N. – conceptualization, validation, formal analysis, resources, writing – original draft, writing – review & editing, visualization, project administration, funding;

Wibawa J.C. – methodology, software, validation, investigation, resources, data curation, supervision, writing – original draft, writing – review & editing;

Callixte C. – validation, resources, writing – review & editing.

**Funding.** This research received no external funding.

**Conflict of interests.** The authors declare no conflict of interest.

**Acknowledgments.** The authors would like to thank the support from Universitas Negeri Surabaya, STKIP PGRI Trenggalek, and University of Rwanda

## REFERENCES

1. Marinho DA, Ferraz R, Toubekis AG, Neiva HP. Editorial: Musculoskeletal Adaptations to Training and Sports Performance: Connecting Theory and Practice. Front Physiol. 2022 Mar 3;13:866895.
doi: https://doi.org/10.3389/fphys.2022.866895

2. Wibawa JC, Arifin MZ, Herawati L. Ascorbic Acid Drink after Submaximal Physical Activity can Maintain the Superoxide Dismutase Levels in East Java Student Regiment. Indian J Forensic Med Toxicol. 2021;15(3):3383-92.
doi: https://doi.org/10.37506/ijfmt.v15i3.15824

3. Baghaiee B, Bayatmakoo R, Karimi P, Pescatello LS. Moderate Aerobic Training Inhibits Middle-Aged Induced Cardiac Calcineurin-NFAT Signaling by Improving TGF-ß, NPR-A, SERCA2, and TRPC6 in Wistar Rats. Cell J. 2021;23(7):756-62.
doi: https://doi.org/10.22074/cellj.2021.7531

4. El Assar M, Álvarez-Bustos A, Sosa P, Angulo J, Rodríguez-Mañas L. Effect of Physical Activity/Exercises on Oxidative Stress and Inflammation in Muscle and Vascular Aging. Int J Mol Sci. 2022;23(15):8713.
doi: https://doi.org/10.3390/ijms23158713

5. Harahap NS, Amelia R, Sibuea A, Manalu N, Novita N. HSP70 (heat shock protein 70) expression and antioxidant as a protective againts oxidative stress triggered by sub-maximal physical activity. IOP Conf Ser Earth Environ Sci. 2021;713(1):012051.
doi: https://doi.org/10.1088/1755-1315/713/1/012051

6. Pouzesh Jadidi, Seifi-Skishahr F, Bolboli L, Ghoroughchi AP. Effect of high intensity interval training on cardiomyocytes HSP70 and Caspase-3 gene expression levels in myocardial infarction male rat model. Journal of Applied Health Studies in Sport Physiology. 2022;9(2):1-11.
doi: https://doi.org/10.22049/JAHSSP.2021.27521.1407

7. Guerrero C, Collado-Boira E, Martinez-Navarro I, et al. Impact of plasma oxidative stress markers on post-race recovery in ultramarathon runners: A sex and age perspective overview. Antioxidants. 2021;10(3):1-12.
doi: https://doi.org/10.3390/antiox10030355

8. Belenichev IF, Aliyeva OG, Popazova OO, Bukhtiyarova NV. Involvement of heat shock proteins HSP70 in the mechanisms of endogenous neuroprotection: the prospect of using HSP70 modulators. Front Cell Neurosci. 2023;17:1131683.
doi: https://doi.org/10.3389/fncel.2023.1131683

9. Zhang H, Gong W, Wu S, Perrett S. Hsp70 in Redox Homeostasis. Cells. 2022;11(5):1-18.
doi: https://doi.org/10.3390/cells11050829

10. Rebeaud ME, Mallik S, Goloubinoff P, Tawfik DS. On the evolution of chaperones and cochaperones and the expansion of proteomes across the Tree of Life. Proc Natl Acad Sci USA. 2021;118(21):e2020885118.
doi: https://doi.org/10.1073/pnas.2020885118

11. Du S, Liu Y, Yuan Y, et al. Advances in the study of HSP70 inhibitors to enhance the sensitivity of tumor cells to radiotherapy. Front Cell Dev Biol. 2022;10:1-16.
doi: https://doi.org/10.3389/fcell.2022.942828

12. Tang S, Geng Y, Lin Q. The role of mitophagy in metabolic diseases and its exercises intervention. Front Physiol. 2024;15:1-20.
doi: https://doi.org/10.3389/fphys.2024.1339128

13. Rosenzweig R, Nillegoda NB, Mayer MP, Bukau B. The Hsp70 chaperone network. Nat Rev Mol Cell Biol. 2019;20(11):665-80.
doi: https://doi.org/10.1038/s41580-019-0133-3

14. Marmett B, Carvalho RB, Dorneles GP, Nunes RB, Rhoden CR. Should I stay or should I go: Can air pollution reduce the health benefits of physical exercises? Med Hypotheses. 2020;144:109993.
doi: https://doi.org/10.1016/j.mehy.2020.109993

15. Costa-Beber LC, Heck TG, Fiorin PBG, Ludwig MS. HSP70 as a biomarker of the thin threshold between benefit and injury due to physical exercises when exposed to air pollution. Cell Stress Chaperones. 2021;26(6):889-915.
doi: https://doi.org/10.1007/s12192-021-01241-1

16. Yoshihara T, Dobashi S, Naito H. Effects of preconditioning with heat stress on acute exercises-induced intracellular signaling in male rat gastrocnemius muscle. Physiol Rep. 2024;12(1):1-15.
doi: https://doi.org/10.14814/phy2.15913

17. Akbulut T, Cinar V, Aydin S, Yardim M. The Role of Different Exercises in Irisin, Heat Shock Protein 70 and Some Biochemical Parameters. J Med Biochem. 2022;41(2):149-55.
doi: https://doi.org/10.5937/jomb0-31551

18. de Lemos Muller CH, Schroeder HT, Rodrigues-Krause J, Krause M. Extra and intra cellular HSP70 levels in adults with and without metabolic disorders: a systematic review and meta-analysis. Cell Stress Chaperones. 2023;28(6):761-71.
doi: https://doi.org/10.1007/s12192-023-01368-3

19. Cumming KT, Kvamme NH, Schaad L, Ugelstad I, Raastad T. Muscular HSP70 content is higher in elderly compared to young, but is normalized after 12 weeks of strength training. Eur J Appl Physiol. 2021;121(6):1689-99.
doi: https://doi.org/10.1007/s00421-021-04633-4

20. Mazhari M, Matinhomaee H, Fatolahi H. The Effect of high-intensity interval training with caloric restriction on gene expression of apoptosis indices HSP70 and HSP60 in the myocardium of male rats. J Shahrekord Univ Med Sci. 2024;26(1):14-9.
doi: https://doi.org/10.34172/jsums.839

21. Wang D, Ripley-Gonzalez JW, Hu Y. Aerobic Physical Training Protects the Rat Brain Against Exercises-Heat Related Oxidative Damage through the Increased Expression of HSP70. Neurophysiology. 2019;51(2):66-71. doi: https://doi.org/10.1007/s11062-019-09794-9

22. Medica P, Cravana C, Rp G, Marino A, Am F. Serum Heat Shock Protein (HSP70) Changes In Horses After An Acute Exercises. Annals of Veterinary Science. 2021:1-9. doi: https://doi.org/10.31829/2691-5502/avs2021-4(1)-002

23. Goh J, Hofmann P, Aw NH, et al. Concurrent high-intensity aerobic and resistance exercises modulates systemic release of alarmins (HMGB1, S100A8/A9, HSP70) and inflammatory biomarkers in healthy young men: a pilot study. Transl Med Commun. 2020;5(1):4. doi: https://doi.org/10.1186/s41231-020-00056-z

24. Lu J, Zhang LM, Liu JJ, et al. High-intensity interval training alleviates exhaustive exercises-induced HSP70-assisted selective autophagy in skeletal muscle. J Physiol Sci. 2023;73(1):32. doi: https://doi.org/10.1186/s12576-023-00884-2

25. Min HJ, Min SJ, Kang H, Kim KS. Differential nasal expression of heat shock proteins 27 and 70 by aerobic exercises: A preliminary study. Int J Med Sci. 2020;17(5):640-6. doi: https://doi.org/10.7150/ijms.39631

26. dos Santos RS, Veras FP, Ferreira DW, et al. Involvement of the Hsp70/TLR4/IL-6 and TNF-α pathways in delayed-onset muscle soreness. J Neurochem. 2020;155(1):29-44. doi: https://doi.org/10.1111/jnc.15006

27. Krüger K, Reichel T, Zeilinger C. Role of heat shock proteins 70/90 in exercises physiology and exercises immunology and their diagnostic potential in sports. J Appl Physiol. 2019;126(4):916-27.
doi: https://doi.org/10.1152/japplphysiol.01052.2018

28. Aas SN, Hamarsland H, Cumming KT, et al. The impact of age and frailty on skeletal muscle autophagy markers and specific strength: A cross-sectional comparison. Exp Gerontol. 2019;125:110687.
doi: https://doi.org/10.1016/j.exger.2019.110687

29. Hu C, Yang J, Qi Z, et al. Heat shock proteins: Biological functions, pathological roles, and therapeutic opportunities. MedComm. 2022;3(3):1-39.
doi: https://doi.org/10.1002/mco2.161

30. Schroeder HT, de Lemos Muller CH, Heck TG, Krause M, de Bittencourt PIH. The Dance of Proteostasis and Metabolism: Unveiling the Caloristatic Controlling Switch. Cell Stress Chaperones. 2024;29(1):175-200. doi: https://doi.org/10.1016/j.cstres.2024.02.002

31. Mahboubi H, Moujaber O, Kodiha M, Stochaj U. The Co-Chaperone HspBP1 Is a Novel Component of Stress Granules that Regulates Their Formation. Cells. 2020;9(4):825. doi: https://doi.org/10.3390/cells9040825

32. Youn CK, Lee JH, Hariharasudhan G, et al. HspBP1 is a dual function regulatory protein that controls both DNA repair and apoptosis in breast cancer cells. Cell Death Dis. 2022;13(4):1-14.
doi: https://doi.org/10.1038/s41419-022-04766-0

33. Murao A, Aziz M, Wang H, et al. Release mechanisms of major DAMPs. Apoptosis. 2021;26(3-4):152-62. doi: https://doi.org/10.1007/s10495-021-01663-3

34. Nagai M, Kaji H. Thermal Effect on Heat Shock Protein 70 Family to Prevent Atherosclerotic Cardiovascular Disease. Biomolecules. 2023;13(5):1-15.
doi: https://doi.org/10.3390/biom13050867

35. Lissarassa YPS, Vincensi CF, Costa-Beber LC, et al. Chronic heat treatment positively impacts metabolic profile of ovariectomized rats: association with heat shock response pathways. Cell Stress Chaperones. 2020;25(3):467-79. doi: https://doi.org/10.1007/s12192-020-01087-z

36. Zhou L, Fang L, Tamm M, Stolz D, Roth M. Extracellular Heat Shock Protein 70 Increases the Glucocorticoid Receptor and Dual-Specificity Phosphatase 1 via Toll-like Receptor 4 and Attenuates Inflammation in Airway Epithelial Cells. Int J Mol Sci. 2023;24(14):11700. doi: https://doi.org/10.3390/ijms241411700

37. Mulyani WRW, Sanjiwani MID, Sandra, et al. Chaperone-based therapeutic target innovation: Heat shock protein 70 (HSP70) for type 2 diabetes mellitus. Diabetes, Metab Syndr Obes. 2020;13:559-68.
doi: https://doi.org/10.2147/DMSO.S232133

38. Tedesco B, Vendredy L, Timmerman V, Poletti A. The chaperone-assisted selective autophagy complex dynamics and dysfunctions. Autophagy. 2023;19(6):1619-41. doi: https://doi.org/10.1080/15548627.2022.2160564

39. Tedeschi V, Vinciguerra A, Sisalli MJ, Pignataro G, Secondo A. Pharmacological inhibition of lysosomal two-pore channel 2 (TPC2) confers neuroprotection in stroke via autophagy regulation. Neurobiol Dis. 2023;178:106020. doi: https://doi.org/10.1016/j.nbd.2023.106020

40. Ikwegbue PC, Masamba P, Oyinloye BE, Kappo AP. Roles of heat shock proteins in apoptosis, oxidative stress, human inflammatory diseases, and cancer. Pharmaceuticals. 2018;11(1):1-18.
doi: https://doi.org/10.3390/ph11010002

41. Garde R, Dea A, Herwig MF, PincusD. Feedback control of the heat shock response by spatiotemporal regulation of Hsp70. J Cell Biol. 2024 Dec 2;223(12):e202401082. doi: https://doi.org/10.1083/jcb.202401082

42. Lubkowska A, Dudzińska W, Pluta W. Antioxidant Enzyme Activity and Serum HSP70 Concentrations in Relation to Insulin Resistance and Lipid Profile in Lean and Overweight Young Men. Antioxidants. 2023;12(3):655. doi: https://doi.org/10.3390/antiox12030655

43. Szerlauth A, Madácsy T, Samu GF, et al. Reduction of intracellular oxidative stress with a copper-incorporated layered double hydroxide. Chem Commun. 2024;60(10):1325-8.
doi: https://doi.org/10.1039/d3cc05762c

44. Rakic J, Jantz T, Davis R, et al. Brain Injury Brain Injury. Arch Phys Med Rehabil. 2020;95(10):e62-e63. doi: https://doi.org/10.1016/j.apmr.2014.07.194

Стаття надійшла до редакції 08.07.2024;
затверджена до публікації 03.10.2024