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## INCREASED SECRETION OF IRISIN HORMONE DURING PHYSICAL EXERCISE: A SYSTEMATIC REVIEW

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**Key words:** physical exercise, irisin, health, obesity

**Ключові слова:** фізичні вправи, іризин, здоров'я, ожиріння

**Abstract.** Increased secretion of irisin hormone during physical exercise: a systematic review. **Pembayun N.S.R., Wibawa J.C., Lobo J., Ardha M.A.A., Nurhasan, Hartati S.C.Y., Komaini A., Ayubi N.** Obesity is a medical condition characterized by the accumulation of excess fat in the body, which can increase the risk of various chronic diseases such as type 2 diabetes, hypertension, and heart disease. Obesity also correlates with an increase in metabolic syndrome diseases that have a negative impact on human health. The prevalence of obesity continues to increase globally, including in developing countries, along with changes in diet and lifestyle. Genetic, environmental, and behavioral factors play an important role in the development of obesity. The impact is not only limited to physical health, but also includes psychological and social aspects. Therefore, it is important to immediately address this problem. Irisin is one of the hormones that plays a major role in reducing obesity rates. The purpose of this study was to determine how physical exercise can increase the expression of the irisin hormone. For this study, a number of journal databases were searched, such as Pubmed, Embase, Science Direct, Web of Science, and Scopus. This study considered various variables, including research on physical activity and the irisin hormone published in journals in the last five years. The analysis included only publications from reputable scientific journals that met the established inclusion criteria, namely: the studies had to involve human participants, and the interventions had to consist of physical exercise. Using databases from Pubmed, Science Direct, Embase, Web of Science, and Scopus, 104 publications were found. Approximately ten carefully selected publications discussed the need for a systematic review analysis. The standard operating procedure for the investigation was developed using – preferred reporting items for systematic reviews and meta-analyses (PRISMA). The results of the systematic review showed an increase in irisin expression during physical activity. The limitation of this review only concerned the effect of physical activity on the irisin hormone. The best dose given during physical exercise to increase irisin expression is still not fully understood, therefore it is important to conduct further studies that discuss an adequate and optimal dose of physical activity to increase irisin.

**Реферат. Підвищена секреція гормону іризину під час фізичних вправ: систематичний огляд. Пембайун Н.С.Р., Вібава Дж.К., Лобо Дж., Ардха М.А.А., Нурхасан, Хартаті С.К.Й., Комайні А., Аюбі Н.** *Ожиріння – це медичний стан, що характеризується накопиченням надлишку жиру в організмі, що може збільшити ризик розвитку різних хронічних захворювань, таких як діабет 2 типу, гіпертонія та хвороби серця. Ожиріння також корелює зі збільшенням кількості захворювань, пов'язаних з метаболічним синдромом, які негативно впливають на здоров'я людини. Поширеність ожиріння продовжує зростати в усьому світі, зокрема в країнах, що розвиваються, разом зі змінами в харчуванні та способи життя. Генетичні, екологічні та поведінкові фактори відіграють важливу роль у розвитку ожиріння. Його вплив обмежується не лише фізичним здоров'ям, але й включає психологічні та соціальні аспекти. Тому важливо негайно вирішити цю проблему. Іризин – один з гормонів, який відіграє важливу роль у зниженні рівня ожиріння. Метою цього дослідження було визначити, як фізичні вправи можуть збільшити експресію гормону іризину. Для цього дослідження було проведено пошук у низці журналних баз даних, таких як Pubmed, Embase, Science Direct, Web of Science та Scopus. У цьому дослідженні розглядалися різні змінні, включаючи дослідження фізичної активності та гормону іризину, опубліковані в журналах за останні п'ять років. Аналіз охоплював лише публікації в авторитетних наукових журналах, що відповідали визначенім критеріям включення, зокрема: дослідження мали бути проведені за участю людей, а втручання – передбачати виконання фізичних вправ. Використовуючи бази даних Pubmed, Science Direct, Embase, Web of Science та Scopus, було знайдено 104 публікації. У близько десяти ретельно відібраних публікацій обговорювалась необхідність систематичного оглядового аналізу. Стандартну операційну процедуру для дослідження було розроблено з використанням рекомендацій PRISMA (Переважні елементи звітності для систематичних оглядів та метааналізів). Результати систематичного огляду показали збільшення експресії іризину під час фізичної активності. Обмеження цього огляду стосувалися лише впливу фізичної активності на гормон іризин. Однак на сьогодні відсутні достатні дані щодо найбільш ефективних характеристик фізичних вправ (тривалості, частоти та інтенсивності) для впливу на експресію іризину, тому важливо провести подальші дослідження, які обговорюватимуть належну та оптимальну дозу фізичної активності для збільшення рівня іризину.*

World Health Organization WHO, 2022 teaches people that obesity is defined as the build-up of abnormally high body fat and overweight levels. Adipose tissue is more expressed in obesity, and it is more prevalent and distributed in visceral areas [1]. Furthermore, inflammatory immune cells, white adipocytes, stem cells, and other cells frequently infiltrate adipose tissue [2]. The body mass index, or  $\text{kg}/\text{m}^2$ , is a measure of obesity in humans that is obtained by dividing the weight in kilos of a person by the square of their height in meters. Although obesity is a complicated illness that needs to be treated medically, it can be avoided by using a variety of management techniques [3]. Obesity contributes to a number of metabolic syndrome illnesses, which are becoming more prevalent worldwide each year [4].

Additionally, obesity increases the chance of other illnesses including cardiovascular disease, which deteriorates health [5]. Obesity contributes directly to incidence of cardiovascular risk factors, including dyslipidemia, type 2 diabetes, hypertension, and sleep disorders [6]. Nearly every physiological function of the body is adversely impacted by obesity, which also poses a serious risk to public health [7]. The imbalance between energy intake and expenditure is the primary cause of the rising prevalence of obesity, despite the fact that there are numerous other factors that also play a role [8].

Numerous factors, including obesity, high blood pressure, and problems with lipid and glucose metabolism, can predispose the body to metabolic syndrome diseases [9]. This metabolic syndrome increases

the risk of stroke, non-alcoholic fatty liver disease, coronary heart disease, and type 2 diabetes mellitus (T2DM), all of which can exacerbate human health issues [9]. Adipokines are proteins secreted by adipose tissue that play a crucial role in regulating glucolipid metabolism in our body. Adipokines affect a wide range of physiological processes in the body, such as appetite, energy balance, insulin metabolism, glucose metabolism, lipid metabolism, and blood pressure regulation. Among these is asprosine, which is produced by white adipose tissue adipocytes and aids in the production and release of glucose [10].

Irisin is a myokine with a molecular weight of 12 kDa and 112 amino acids. Irisin is produced by cleaving the fibronectin type III domain containing 5 (*FNDC5*) gene, which codes for a type of membrane protein mostly seen in human and mouse muscle tissue. *FNDC5* gene expression is mediated by peroxisome proliferator-activated receptor gamma (PPAR- $\gamma$ ) and peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1 $\alpha$ ) [11]. Irisin is classified as a myokine, a hormone that is believed to be actively involved in the management and prevention of metabolic syndrome and obesity. There is a clear association between high levels of irisin and a decrease in cardiometabolic illnesses by having anti-inflammatory properties [12]. A characteristic of brown adipose tissue, irisin increases uncoupling protein 1 (UCP1) gene expression in white adipose tissue and promotes fatty acid oxidation and thermogenesis. Therefore, by increasing thermogenesis, energy expenditure, and glucose

homeostasis, irisin promotes the conversion of white adipose tissue into brown adipose tissue, which aids in weight loss [13].

Irisin levels are significantly lowered in obese and cardiometabolic disease patients, which, if left unchecked, will harm human health [14]. Exercise is the most significant factor in stimulating irisin. But the kind, degree, and length of exercise can all impact irisin levels [15]. Due to its ability to enhance primary metabolic and cardiovascular risk factors, reduce fat mass, encourage weight loss, and increase cardiorespiratory fitness, exercise is advised as the initial line of treatment for obesity. Myocytes function as secretory organs during muscle contraction, releasing substances which are called myokines [16].

The vast majority of relevant studies have shown that irisin regulates human metabolism [17]. High intensity interval training significantly increases the expression of irisin in humans, according to earlier research [18]. The exact method by which physical activity increases irisin expression is still under debate. Therefore, the purpose of this study is to discuss in depth how physical activity can increase irisin expression.

## MATERIALS AND METHODS OF RESEARCH

To determine how physical exercise affects the hormone irisin in humans, this study was conducted by evaluating academic literature. This study used a systematic literature review method. A systematic literature review is a research method used to identify, evaluate, and synthesize all research evidence relevant to a specific research question. A systematic literature review aims to provide clear and comprehensive answers to research questions in a systematic and structured manner. Search databases such as PubMed, Science Direct, and Web of Science were used to find scientific papers. The search terms used were physical exercise and the hormone irisin. Article selection was based on the following inclusion criteria: English language proficiency, experimental research and studies, and year of publication (Table 1). Furthermore, articles that did not meet the inclusion criteria, including research samples that did not involve humans, non-experimental studies, and parameters other than the hormone irisin, were excluded from our analysis and subjected to exclusion criteria.

Table 1

### Inclusion criteria

| Web search engines | Pubmed, Science Direct, and Web of Science                |
|--------------------|---|
| Publishing period  | 2019-2025   |
| Key word           | Physical exercise and irisin hormone                      |
| Language           | English   |
| Type of article    | Original research article                                 |
| Full Text          | Articles matched the purpose and/or topic of the research |

Investigations on physical activity and hormone irisin published in the last five years provided the inclusion criteria for this investigation. Publications excluded from our study included papers published in journals that were not reputable and those that did not meet the inclusion criteria such as studies on animals and if intervention was not physical exercise. The research was conducted in accordance with the principles of bioethics set out in the WMA Declaration of Helsinki – “Ethical principles for medical research involving human participants” and “Universal Declaration on Bioethics and Human Rights” (UNESCO).

Full texts, abstracts, and titles of verified and approved publications were added to the Mendeley database. The keywords used were physical exercise

and irisin hormone. The search period was from February to March 2025. A total of 104 papers were included in the first part of the study using Pubmed, Embase, Science Direct, Scopus, and Web of Science databases. A total of 57 entries were assessed in the second round based on how closely their titles and abstracts followed the guidelines. A total of 22 entries were verified for further processing in the third stage. Next, we made a screening decision based on whether the topic met the inclusion criteria for further discussion or not. Ten papers that met the inclusion criteria for this systematic review were selected and carefully examined after a thorough study. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) review of standard operating procedures was supported by this study.

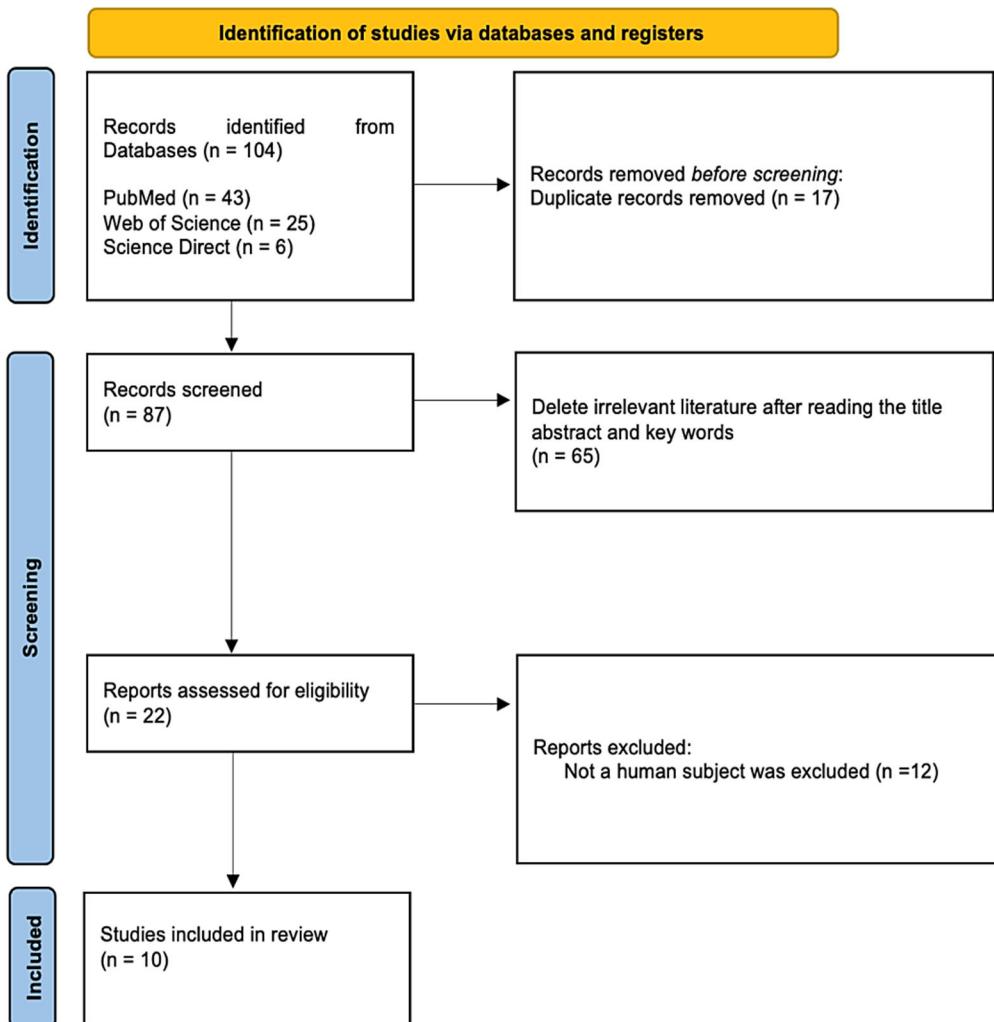


Fig. 1. PRISMA flowchart of the article selection process

## RESULTS AND DISCUSSION

This study set was to ascertain how the process of physical activity increases the levels of hormone irisin in humans. The results of a study compared young and middle-aged people who have been given physical exercise interventions using ergocycles until they experience fatigue. The data showed that physical exercise increased irisin levels in both groups, but the young people group had higher irisin levels than the middle-aged people [19]. Other data compared patients with diabetes who did high-intensity interval training with moderate-intensity continuous training. The findings demonstrate that irisin levels are higher following high intensity interval training than following moderate intensity continuous exercise [20] (Table 2).

HIIT has the ability to significantly enhance human health. This is known from several research

data with high-intensity physical exercise interventions that have higher irisin levels than moderate-intensity exercise. This is also reinforced by the report Enteshary et al., 2019 that the comparison between physical exercise with high intensity has higher irisin levels than physical exercise with a combination. 60 patients with diabetes mellitus were divided into 2 groups in an experimental test between a control group without exercise and a group with physical exercise intervention 3-5 per week for 12 weeks. The results demonstrated that among individuals with diabetes mellitus, physical activity also had a positive effect on raising irisin levels [22]. It can also make recommendations for non-pharmacological therapeutic efforts in an endeavor to enhance human health.

Table 2

## Results of physical exercise on increasing irisin hormone secretion

| Author                        | Sample Characteristics  | Study Design | Intervention  | Results  |
|-------------------------------|---|--------------|---|--|
| (Tommasini et al., 2024) [19] | In this study, 34 healthy males were split into two groups: the young adult group (n=22) and the middle aged adult group (n=12)   | Experimental | Physical exercise using an ergocycle until fatigue occurs   | Following the physical exercise intervention, irisin levels increased in both groups. In contrast to middle-aged individuals, the young adult group showed higher amounts of irisin  |
| (Dünnewald et al., 2019) [20] | In this study, 14 individuals with diabetes mellitus were split into two groups: continuous-moderate training (CMT; n=6) and high-intensity interval training (HIIT; n=8) | Experimental | For four weeks, patients used a bicycle ergometer to complete a structured, supervised training program three times a week. A 7-minute warm-up cycle at 70% of maximal heart rate preceded the 42-minute HIT training, which consisted of 5 4-minute intervals at 90-95% of HRmax. The exercise was done by the CMT group at a moderate intensity of 70% of Hrmax for a total of 50.3 minutes   | In the group receiving HIT intervention, there was a noteworthy rise in irisin levels  |
| (Enteshary et al., 2019) [21] | In this study, 26 women with diabetes mellitus were split into three groups: control, combined moderate-intensity exercise, and combined high-intensity training          | Experimental | Eight weeks of mixed exercise – aerobic and weight training – five sessions a week made up the training regimen. For eight weeks, the moderate-intensity combined exercise group walked at a heart rate between 55% and 69% of their maximum heart rate (HRmax). For five days, the combined high-intensity exercise group 75 minutes of aerobic activity, which included walking or running between 70% and 89% of HRmax and between 14 and 16 RPE. Aerobic exercise was done for fifteen minutes throughout each training session. For eight weeks, two days a week of resistance training with colored resistance bands were conducted | Both the high and moderate intensity groups of the physical exercise intervention showed an increase in irisin levels. On the other hand, the group receiving the high intensity intervention experienced the largest statistical rise |
| (Yang et al., 2020) [22]      | This study had 60 diabetes mellitus patients who were split into two groups: 30 patients in the control group and 30 patients in the physical activity group              | Experimental | They did aerobic exercise 3-5 times a week for 12 weeks   | In the group that received physical activity intervention, there was a noteworthy rise in irisin levels  |

Continuation of the Table 2

| Author                       | Sample Characteristics  | Study Design | Intervention   | Results  |
|------------------------------|---|--------------|--|--|
| (Sari et al., 2024) [23]     | 28 obese women participated in this study and were divided into 3 groups, namely the control group, the group (TRG) which was given a time-restricted feeding intervention and time-restricted feeding and exercise (TREXG) for 2 weeks | Experimental | In the group performing the combined aerobic exercise, the exercise was performed on a treadmill at a moderate intensity of 60-70% of HRmax. The exercise was performed 30 minutes before breaking the fast for 40 minutes (a 5-minute warm-up at 50-60% HRmax) for 2 weeks  | There was a significant increase in irisin levels in the exercise group  |
| (Amanat et al., 2020) [24]   | 60 research respondents were divided into 4 groups, namely aerobic, resistance, combination training and control groups   | Experimental | All groups underwent training according to their respective groups during the 12-week intervention   | There was a significant increase in irisin levels in the combined exercise and aerobic exercise groups           |
| (Batumi, 2020) [25]          | Twenty volunteers took part in the trial and were split into two groups: ten for the control group and ten for the HIT physical activity therapy group  | Experimental | For eight weeks, the members of the experimental group underwent three sessions a week of high-intensity interval training (HIT) at 90% of their heart rate reserve for 45 to 60 minutes each  | The group receiving the HIT physical activity intervention had a statistically significant rise in irisin levels |
| (Colpitts et al., 2022) [18] | In this study, twenty-five youngsters were split into two groups: eleven children were fat and the remaining fourteen were healthy  | Experimental | While the HIIT cycling session comprised two minutes of riding at 85%-90% HR reserve after five minutes of cycling at 50% HR reserve, the MCI cycling session featured 35 minutes of cycling at 50% HR reserve. The HIIT cycling program consisted of five intervals conducted over a total of 35 minutes of cycling | The group receiving the HIT physical activity intervention had a noticeably greater rise in irisin levels        |
| (Dündar, 2019) [26]          | In this study, 19 male handball players took the pretest and posttest   | Experimental | Training in handball lasts thirty minutes. The first ten minutes of training have been dedicated to stretching and warm-up. Thirty minutes of intensive game training was preceded by fifty minutes of general physical training. After the workout, low-intensity stretching has been done                          | Following the physical activity intervention, there was a notable rise in irisin levels                          |
| (Planella et al., 2019) [27] | 43 participants were divided into 3 groups, namely the control group, resistance exercise, resistance exercise + nutrition  | Experimental | Resistance training was performed for 45 minutes per session, 2x a week for 16 weeks   | There was a significant increase in irisin levels in the group given resistance exercise intervention            |

Irisin increases the expression of uncoupling protein 1 (UCP1), which causes fat to brown [28]. By upregulating the expression of mitochondrial transcription factors and peroxisome proliferator-activated

receptor-alpha (PPARA), it can promote mitochondrial biogenesis [28]. During physical exercise, the physiological response of ROS will increase [29]. Physical exercise activates oxidative pathways in

muscles, thereby enhancing skeletal muscle contraction mechanisms to meet energy demands [30]. In addition to being the primary organ for contraction and movement, skeletal muscle is crucial for the oxidation of fatty acids [31]. Lipids provide the majority of the energy required for maintaining homeostasis and physical activity during rest and moderately intense exercise [32]. A crucial function

in fat metabolism is played by peroxisome proliferator-activated receptor-gamma coactivator alpha (PGC-1 $\alpha$ ), whose expression is elevated during physical activity due to increased muscular contraction [33]. For example, exercise-induced activation of PGC-1 $\alpha$ , which increases mitochondrial metabolism and biogenesis [34] (Fig. 2).

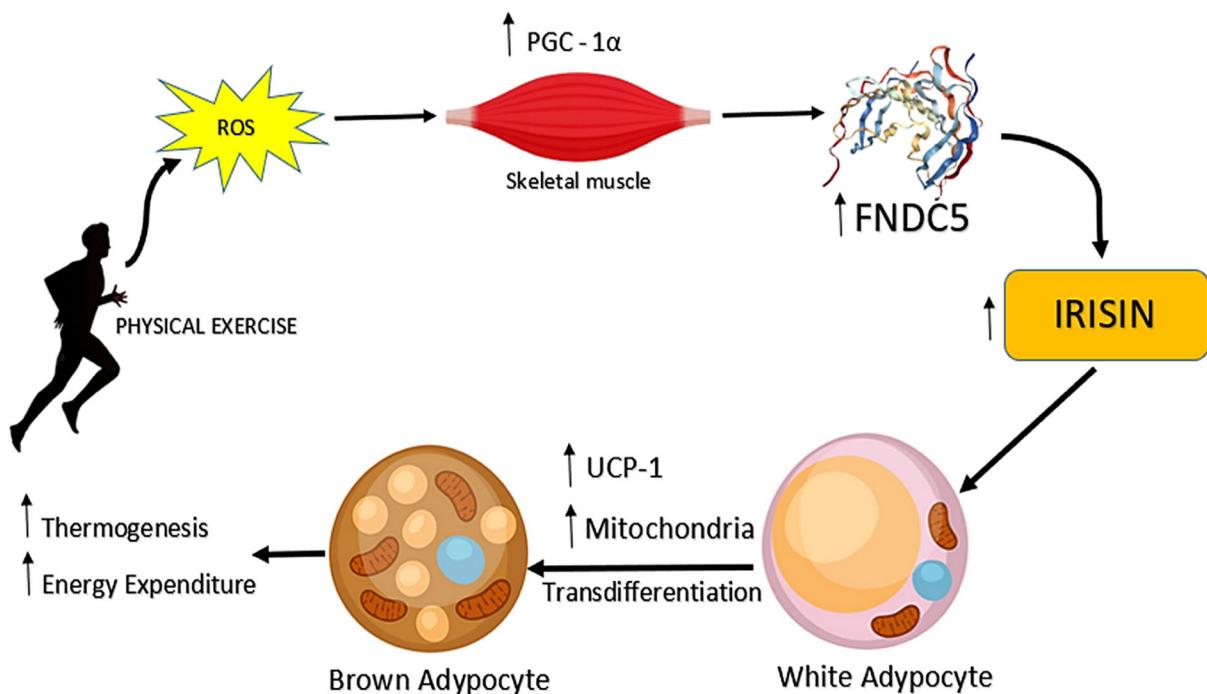


Fig. 2. The mechanisms of physical exercise in increasing secretion of irisin hormone

Two decades ago, a new gene was identified by two independent groups, widely distributed in the heart, skeletal muscle, brain, and other tissues in mice [35]. A decade later, the gene was named fibronectin type III domain-containing protein 5 (FNDC5). This gene is one of the most important target genes of peroxisome proliferator-activated receptor  $\gamma$  coactivator 1 $\alpha$  (PGC1 $\alpha$ ), a transcriptional coactivator frequently produced in active skeletal muscle [35]. PGC-1 $\alpha$  overexpression may be the mechanism driving and controlling the production of these proteins in the hippocampus, and it may also control FNDC5/BDNF [36]. Exercise causes PGC-1 $\alpha$  and FNDC5 to become active, which increases the expression of irisin as a physiological reaction to exercise [37]. Skeletal muscle and visceral and subcutaneous adipose tissue are the main sources of adiponectin irisin [38]. Irisin is also a myokine that plays a role in controlling energy balance, maintaining glucose balance, and preventing metabolic

syndrome [23]. Then irisin circulates in the blood to the target cells it will affect, thus, increasing the metabolic rate in the body.

Exercise is still the trigger for a significant increase in irisin [39]. Irisin release modulated by PGC1- $\alpha$  increases UCP-1 [40]. The length of physical activity is another factor contributing to variability. The same group of overweight women with metabolic syndrome was the subject of two investigations, and the results indicated that blood irisin levels increased in 12 weeks but not in 8 weeks following physical activity [41]. HIIT training appears to be more successful than traditional exercise in improving cardiovascular fitness and reducing body fat percentage in obese adults [42].

It can be concluded that physical exercise is proven to increase the expression of irisin. Based on the analysis, it is known that high intensity turns out to have a better impact on increasing the expression of irisin, but this increase needs to be explored further

to provide insights related to the optimal dose and duration that is good in running high-intensity training. Of course, writing this article, the author realizes that there are still limitations in the done review. The author only focuses on how physical exercise can increase the expression of irisin. Further exploration is needed regarding how physical exercise can improve other parameters related to improving human health, especially preventing metabolic syndrome triggered by obesity. The right dose and duration of exercise also still need to be discussed further to be able to provide insight for readers related to the importance of routine and regular exercise as a non-pharmacological therapeutic effort that has the aim of improving public health status.

### CONCLUSIONS

1. Exercise has been shown to effectively increase the expression of the hormone irisin in humans.
2. From the systematic review that has been done, it seems that high-intensity physical exercise has an effect on increasing the expression of irisin significantly.

3. However, further exploration is still needed regarding the optimal dose of duration, frequency, and intensity of exercise in providing an optimal effect on increasing the expression of irisin. Exercise is the best non-pharmacological therapeutic effort, especially for people with diabetes and metabolic syndrome.

### Contributors:

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Wibawa J.C. – conceptualization, writing – original draft;

Lobo J. – data curation, visualization;

Ardha M.A.A. – data curation, visualization;

Nurhasan – data curation, visualization;

Hartati S.C.Y. – data curation, visualization;

Komaini A. – data curation, visualization;

Ayubi N. – methodology, formal analysis.

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