



The Effects of Fermented Buffalo Milk (Dadih) Fortified with Red Dragon Fruit and Selenium on Adiponectin and Tumor Necrosis Factor-Alpha Levels in Obese Rats

Fitri Wulandari¹, *Ninik Rustanti^{1,2}, Adriyan Pramono^{1,2}

¹Department of Nutrition Science, Faculty of Medicine, Diponegoro University, Indonesia, ²Center of Nutrition Research (CENURE), Diponegoro University, Indonesia. *Email: ninik.rustanti@fk.undip.ac.id

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Abstract: The increasing prevalence of obesity and its associated complications necessitates the exploration of functional foods as therapeutic interventions. This study aimed to analyze the effects of fermented buffalo milk (dadih) fortified with red dragon fruit (*Hylocereus polyrhizus*) and selenium on adiponectin and Tumor Necrosis Factor-Alpha (TNF- α) levels in obese rats. This experimental study employed a pretest-posttest control group design involving 20 Wistar rats divided into four groups: K1 (healthy control), K2 (obese control), P1, and P2 (obese intervention). K2, P1, and P2 were in obesity conditions induced by a high-fat-fructose diet (HFFD) for 28 days, and K1 was a healthy control group. Furthermore, dadih only and dadih fortified with red dragon fruit and selenium at 1.8 g/200 g body weight/day were administered to P1 and P2 groups, respectively. Treatment using dadih fortified with red dragon fruit and selenium significantly reduced weight gain ($p=0.000$) compared to K2 and P1. In addition, the P2 group showed increased adiponectin levels and decreased TNF- α levels ($p=0.000$) compared to the K2 and P1 groups. A strong negative correlation was found between adiponectin levels and TNF-alpha and body weight, while TNF-alpha and body weight showed a strong positive correlation. To conclude, fortifying dadih with red dragon fruit and selenium is more effective in improving the metabolic condition of obese rats compared to non-fortified dadih. This fortification significantly enhances adiponectin levels and reduces TNF-alpha levels. These findings suggest that functional food fortification could be a promising approach for managing obesity-related inflammation and metabolic disorders in humans, highlighting the potential application of dadih in dietary interventions.

Keywords: Fermented buffalo milk; inflammation in obesity; red dragon fruit; selenium

INTRODUCTION

Obesity is a growing global health concern, with prevalence increasing each year. A projection for 2030 suggests that 14% of men and 20% of women in the world's population will develop clinical obesity. Furthermore, estimates indicate that 18% of the population will have a BMI exceeding 30 kg/m², 6% will have a BMI above 35 kg/m², and 2% will have a BMI surpassing 40 kg/m² (Chandrasekaran & Weiskirchen, 2024). In Indonesia, the prevalence of obesity reached 23.4% in 2023, with higher rates observed in women (31.2%) compared to men (15.7%) (BKPK, 2023). This rise is attributed to increased consumption of fats and carbohydrates and reduced physical activity (Nabila et al., 2024). Obesity is closely linked to various metabolic disorders, including type 2 diabetes mellitus (T2DM), hypertension, cardiovascular disease (CVD), and metabolic syndrome (Metsyn). One primary mechanism connecting

Corresponding Author: Ninik Rustanti

Department of Nutrition Science, Faculty of Medicine, Diponegoro University, Jl. Prof. Mr. Sunario, Tembalang, Semarang, Indonesia, 50275.

Email: ninik.rustanti@fk.undip.ac.id

obesity to these conditions is chronic low-grade inflammation (Endalifer & Direess, 2020). Excess fat accumulation, particularly in adipose tissue, triggers the production of reactive oxygen species (ROS), leading to oxidative stress and cellular dysfunction (Varra et al., 2024). Consequently, the secretion profile of adipose tissue shifts, characterized by a reduction in anti-inflammatory adipokines such as adiponectin and an increase in pro-inflammatory adipokines like Tumor Necrosis Factor-Alpha (TNF- α) (Świątkiewicz et al., 2023). Additionally, obesity reduces gut microbiota diversity and increases intestinal permeability, allowing lipopolysaccharides (LPS) to enter the bloodstream, further promoting inflammation (Weiss & Hennet, 2017). Studies have shown that obese individuals exhibit decreased adiponectin levels and elevated TNF- α levels, collectively contributing to metabolic dysfunction and obesity-related complications (Alzamil, 2020; Zorena et al., 2020).

A potential nutritional intervention for obesity management uses *dadih*, a traditional fermented buffalo milk product from West Sumatra, Indonesia. *Dadih* is produced through spontaneous fermentation at room temperature without adding starter cultures (Arnold et al., 2021). This process involves natural lactic acid bacteria (LAB), such as *Lactococcus lactis* ssp. *lactis*, *Lactobacillus plantarum*, *Bifidobacterium*, and *Leuconostoc paramesenteroides* (Setiarto et al., 2023). Numerous studies indicate that LAB in *dadih* act as probiotics, supporting fat absorption reduction, adipocyte size reduction, gut microbiota modulation, and inhibition of pathogenic bacteria growth (Herlina & Setiarto, 2024). They also strengthen intestinal barriers, reducing permeability and LPS translocation, thus mitigating inflammation (Amelia et al., 2023; Zheng et al., 2023).

However, *dadih* is less favored due to its aroma and taste. The fortified red dragon fruit (*Hylocereus polyrhizus*), rich in antioxidants, vitamin C, betacyanin, and dietary fiber, is expected to improve the nutritional value, flavor, color, and aroma of *dadih*, making it more appealing (Aryanta, 2022; Taswin & Oktarida, 2020). The fiber in red dragon fruit may function as a prebiotic, supporting LAB growth, while its antioxidants reduce oxidative stress and neutralize ROS, thereby suppressing pro-inflammatory cytokine production (Arivalagan et al., 2021; Saenjum et al., 2021). Furthermore, selenium, an essential micronutrient with antioxidant and anti-inflammatory properties, can enhance the functional properties of *dadih*. Selenium supports glutathione peroxidase activity, protecting cells from oxidative damage, and inhibits the NF- κ B pathway, reducing pro-inflammatory cytokine production, including TNF- α (Tinkov et al., 2020; Zhao et al., 2020).

Despite extensive studies on probiotic-fermented dairy products and their impact on obesity-related inflammation, there is limited research on the potential benefits of *dadih* fortified with red dragon fruit and selenium. While red dragon fruit is known for its antioxidant and prebiotic properties, and selenium has demonstrated anti-inflammatory benefits, their combined effects in a fermented dairy matrix remain largely unexplored. This study aims to investigate the effects of *dadih* fortified with red dragon fruit and selenium on adiponectin and TNF- α levels in obese rats. By integrating traditional fermented buffalo milk with functional fortification, this research provides a novel approach to addressing obesity-related inflammation. It offers new insights into the role of functional fermented dairy products in metabolic health.

MATERIALS AND METHODS

Place and Time of Research

The milk used for *dadih* production was sourced from buffalo farmers in the Kapau region, West Sumatra. At the same time, the red dragon fruit (*Hylocereus*

polyrhizus) was obtained from local dragon fruit plantations. In this study, sodium selenite (Na_2SeO_3) was used as the source of selenium (Se) fortification (10102-18-8, Sigma-Aldrich). The experimental animals were maintained and treated in the Food and Nutrition Study Center laboratory at Gadjah Mada University in Yogyakarta. The study occurred from September to November 2024. This study has obtained Ethical Clearance approval from the Faculty of Medicine Health Research Ethics Committee of Universitas Diponegoro, Semarang, 090/EC-H/KEPK/FK-UNDIP/IX/2024.

Population and Sample

Twenty male Sprague Dawley rats aged 8–12 weeks, weighing 150–200 g, were divided into four groups. The sample size in this study followed the WHO guidelines for the minimum number of experimental animals, with five rats allocated to each treatment group (WHO, 2000). The rats were grouped as follows: the healthy control group (K1), the obese control group (K2), the obese rat's group treated with dadih at a dose of 1.8 g/200 g body weight/day (P1), and the obese rat's group treated with dadih fortified with red dragon fruit and selenium at a dose of 1.8 g/200 g body weight/day (P2).

Dadih Preparation

The dadih fortified red dragon fruit and selenium were prepared in Agam Regency, Kapau area of West Sumatra. The production of dadih with added red dragon fruit and selenium involved several steps. First, the red dragon fruit pulp was blended into a smooth puree. Second, the 1000 ml buffalo milk was heated to 72°C for 15 seconds and then cooled to 30 °C. Then, the milk was mixed with 10% pureed red dragon fruit and 0.4 ppm selenium (Na_2SeO_3), stirring until evenly combined. The selenium dosage was based on a previous study on buffalo milk yogurt, which concluded that selenium addition up to 0.4 ppm (40 mcg/1000 ml of milk) could be used in yogurt production without adverse effects on organoleptic properties (color, taste, and texture) compared to other concentrations (0.2 and 0.6 ppm) (Osman et al., 2020). The mixture was poured into bamboo containers and sealed with banana leaves (Figure 1) to facilitate the traditional fermentation process. Fermentation was carried out at room temperature for two days. The finished dadih, both the non-fortified and fortified versions, was then stored at -18°C to preserve its quality for future use (Figure 2).



Figure 1. Fortified dadih during spontaneous fermentation

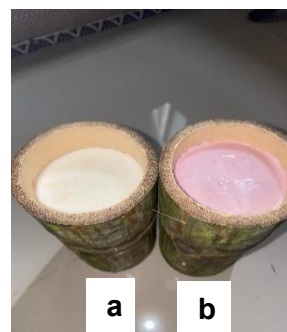


Figure 2. Fortified dadih after fermentation (a: Non-fortified dadih; b: Fortified dadih)

Animal Treatment

Twenty male Wistar rats were acclimatized for seven days under controlled environmental conditions with a room temperature of 23°C and a 12-hour light-dark cycle. The rat cages were cleaned daily, and body weights were recorded weekly from the acclimatization period until the end of the study. During the acclimatization period,

all rats were provided with standard feed and water *ad libitum*, which was continued throughout the study at a daily allowance of 20 g/day. The standard feed, Comfeed II, contained 15% crude protein, 3-7% crude fat, 12% moisture, 6% crude fiber, 7% ash, 0.9-1.1% calcium, 0.6-0.9% phosphorus, and vitamins.

Induction of obesity in the test rats by administering a high-fat fructose Diet (HFFD) orally for 28 days. The composition of the HFFD included 2 mL/200 g body weight/day of lard, 1 mL/200 g body weight/day of quail egg yolk, and 1 mL/200 g body weight/day of pure fructose. These components were homogenized into a single solution and administered via oral gavage. Obesity in the rats was determined using the Lee index, with rats classified as obese if their Lee index exceeded 300 after HFFD induction. The Lee index was calculated as follows: $\{\text{Body weight (g)}^{(1/3)} / \text{Naso-anal length (cm)}\} \times 10^3$. The body weight of rats was measured using a digital analytical balance with a precision of 0.01 g to ensure accuracy.

Subsequently, intervention groups were treated for 28 days. The P1 group received dadih only at a dose of 1.8 g/200 g body weight/day, while the P2 group was given dadih fortified with red dragon fruit and selenium at the same dose of 1.8 g/200 g body weight/day. The dosage used in this study was based on the recommended dosage of fermented milk for humans weighing 70 kg, which is 100–200 mL per day (Pei et al., 2017). Therefore, the dadih dosage was calculated using the body weight conversion factor from a 70 kg human to a 200 g rat, which is 0.018. The dadih dosage for rats = conversion factor \times human dosage of dadih = $0.018 \times 100 \text{ g} = 1.8 \text{ g/200 g}$ body weight of rats.

Blood Sampling

According to the manufacturer's instructions, Adiponectin and TNF- α levels were measured using an ELISA kit (EliKine™, China). The measurement utilized rat blood serum samples collected on day 36 for the pre-test and day 64 for the post-test through the retro-orbital plexus, with a total volume of 2 mL. Also, 100 μ l of standard and serum of each sample were transferred into well plates, which were sealed with a cover and incubated at room temperature for 2 h. After incubation, the wells were aspirated and washed by filling them with washing buffer (250 μ l), repeating the process twice for three washes. 100 μ l of diluted Mouse IL-6 detected antibodies was added to the well and incubated at room temperature for 1 h. Thereafter, the wells were aspirated and washed by filling them with washing buffer (250 μ l), repeating the process twice for three washes. Similarly, 100 μ l of the working dilution of Streptavidin-HRP was added to each well. In addition, the plate was sealed with a cover and incubated at room temperature for 30 min in the dark. The wells were aspirated and washed by filling them with washing buffer (250 μ l), repeating the process twice for three washes. 100 μ l of HRP substrate (TMB) was added and sealed with a cover.

Furthermore, it was incubated at room temperature for 15 min in the dark. Finally, 50 μ l of stop solution was added, and the color turned yellow immediately. The absorbance of the samples was measured using an ELISA reader (ZENIX Microplate Reader) at 450 nm.

Data Analysis and Processing

Data with a normal distribution were presented as mean \pm standard deviation (SD), otherwise manifested as a median (min-max). The statistical difference was analyzed using One-Way ANOVA, followed by the Bonferroni post hoc test. Kruskal-Wallis test, followed by the Mann-Whitney U-test, was used as the alternative. Correlations between variables were assessed using Pearson correlation analysis. All statistical evaluations were performed using SPSS 26.0 for the Windows version.

Likewise, the differences and correlations were considered significant at p value < 0.05 and 95% confidence intervals, and the r -value determined its strength.

RESULTS AND DISCUSSION

Table 1 presents the changes in rat body weight during the study. The K2, P1, and P2 groups experienced an increase in body weight during the HFFD period.

Table 1. The Effect of Fortified Dadih with Red Dragon Fruit and Selenium on Body Weight (BW), Adiponectin, and TNF- α Levels

Groups	K1	K2	P1	P2	p ¹
BW after HFFD (gr)					
Pre	189.2 \pm 3.34	188.8 \pm 2.77	189.2 \pm 2.58	186.0 \pm 3.39	0.313
Post	219.2 \pm 3.42 ^a	281.2 \pm 2.58 ^b	281.4 \pm 3.36 ^b	278.4 \pm 3.36 ^b	0.000*
Δ	30 (29-31) ^a	92 (91-94) ^b	92 (91-93) ^b	92(92-93) ^b	0.010*
p	0.000*	0.000*	0.000*	0.000*	
BW of intervention(gr)					
Pre	219.2 \pm 3,42 ^a	281.2 \pm 2.58 ^b	281.4 \pm 3.36 ^b	278.4 \pm 3.36 ^b	0.000*
Post	249.4 \pm 3.84 ^a	364.4 \pm 3.50 ^b	329.8 \pm 2.58 ^c	316.6 \pm 2.40 ^d	0.000*
Δ	30.2 \pm 1.30 ^a	83.2 \pm 1.09 ^b	48.4 \pm 1.14 ^c	38.2 \pm 1.09 ^d	0.000*
p	0.000*	0.000*	0.000*	0.000*	
Adiponectin (pg / ml)					
Pre	27.96 \pm 1.31 ^a	11.87 \pm 1.00 ^b	11.71 \pm 0.65 ^b	11.87 \pm 0.86 ^b	0.000*
Post	27.29 \pm 1.19 ^a	11.21 \pm 0.80 ^b	17.46 \pm 2.34 ^c	23.96 \pm 1.00 ^d	0.000*
Δ	-0.83 (-0,84-(-0,41) ^a	-0.83 (-0.84-(-0.41) ^a	4.17 (3.75-10.41) ^b	11.67 (10.84-13.33) ^c	0.001*
p	0.003*	0.003*	0.011*	0.000*	
TNF-α (pg/ml)					
Pre	6.40 \pm 0.24 ^a	19.22 \pm 0.36 ^b	19.32 \pm 0.35 ^b	19.50 \pm 0.55 ^b	0.000*
Post	6.30 \pm 0.27 ^a	19.37 \pm 0.40 ^b	8.75 \pm 0.38 ^c	6.42 \pm 0.19 ^{ad}	0.000*
Δ	-0.12 (-0.13-0.00) ^a	0.13 (0.12-0.25) ^b	10.50 (-11.00-(-10.37) ^c	-13.00 (-13.88-(-12.50) ^d	0.000*
p	0.016*	0.004*	0.000*	0.000*	

Note: Normally distributed data are written as mean \pm SD and median (Min-Max) if otherwise. Δ : changes between pre and post-value; p: paired t-tests were used to evaluate pre-post treatment values; p¹: values between all groups were analyzed

using ANOVA if data are normally distributed and Kruskal Wallis if data are not normally distributed.; *: There is a significant difference ($p < 0.05$); a,b,c,d: The similar letter shows no significance based on the Post Hoc Bonferroni/Mann-Whitney test.

The weight gain in rats fed with HFFD was higher than in the K1 group that received standard feed ($p = 0.000$). Statistical differences were observed in the changes (Δ) in body weight of the rats before and after the intervention across the groups ($p = 0.000$). Significant differences were found between the P1 and P2 groups compared to K2 ($p = 0.000$). Significant differences were also observed between the P1 and P2 groups ($p = 0.000$), indicating that fortified dadih was more effective in mitigating weight gain in obese rats.

In Table 1, the paired t-test of adiponectin and TNF- α levels before and after intervention shows significant difference in each group, and the one-way ANOVA test also shows significant difference. However, Figures 3 illustrate the differences in adiponectin and TNF- α levels before and after the intervention.

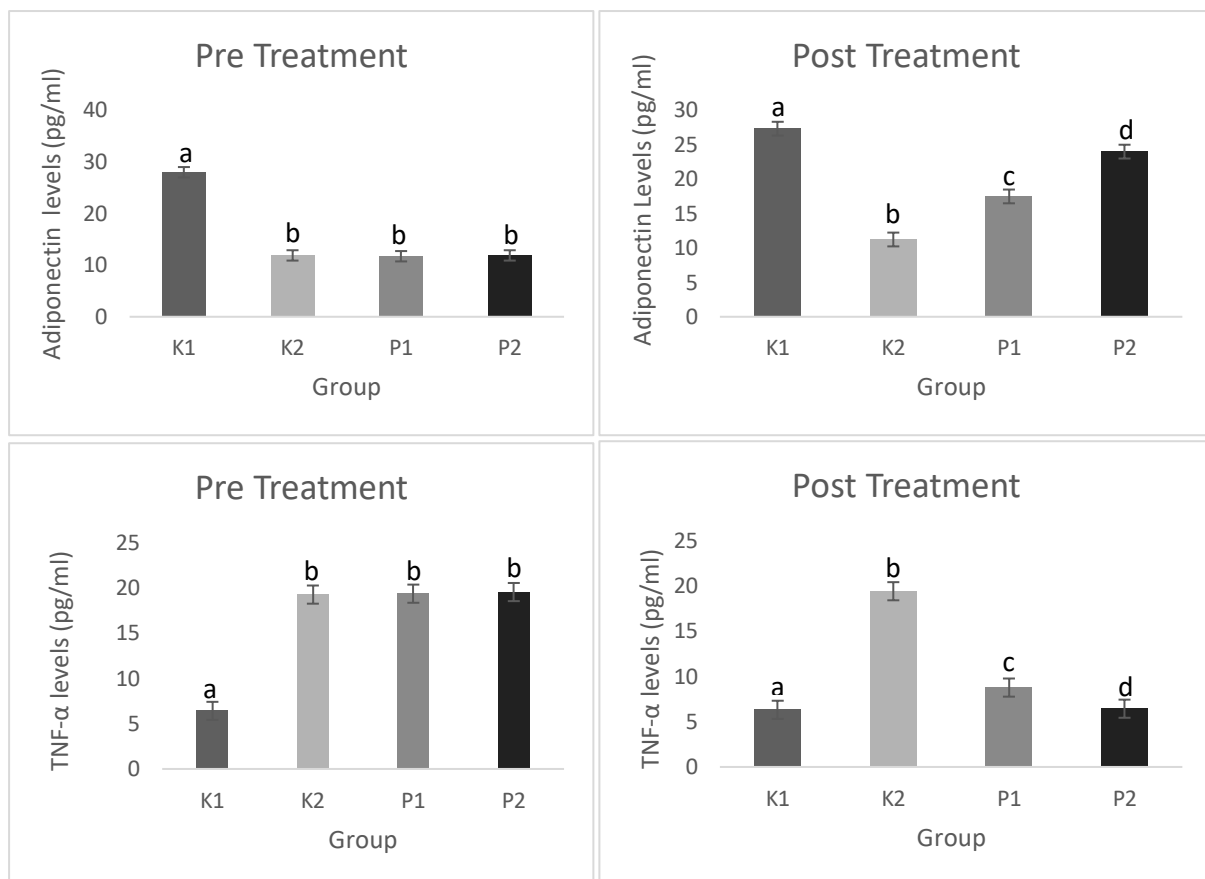


Figure 3. Effects of fortified dadih on adiponectin and TNF- α levels

Note: The bars are expressed as mean \pm SD. Bars with different letters differ significantly ($p < 0.0001$).

The post-intervention correlation analysis revealed a strong correlation among all variables (Table 2). Adiponectin levels exhibited a strong negative correlation with TNF- α . Similarly, a comparable negative correlation was observed between adiponectin levels and body weight. Furthermore, a strong positive correlation existed between body weight and TNF- α levels.

Table 2. Correlation Between Adiponectin Levels, TNF- α Levels, and Body Weight After Fortified Dadih with Red Dragon Fruit and Selenium Intervention

	TNF- α		Body Weigh	
	r	p	r	p
Adiponectin	-0,831	0,000*	-0,860	0,000*
Body Weigh	0,690	0,000*	-	-

Twenty rats were analyzed, and statistical significance was calculated by Pearson test *Value are statistically significant at $p < 0,05$

The weight gain during the HFFD period was attributed to the higher proportion of fat and fructose. Consumption of high-energy foods such as fats and sugars significantly contributes to obesity (Setyaningrum et al., 2021). Previous studies have also shown that HFFD can significantly increase body weight by up to 40% (Rosas-Villegas et al., 2017). Fortified dadih with red dragon fruit and selenium has been shown to reduce weight gain in obese rats due to its content of lactic acid bacteria (LAB). LAB is known to have the ability to modulate lipid metabolism by inhibiting lipid absorption through the suppression of pancreatic lipase enzyme activity, which plays a role in breaking down triglycerides into free fatty acids (Kinariwala et al., 2020). In the present study, we found that fortified dadih with red dragon fruit and selenium ameliorated the increased body weight of the HFD-fed mice, which corresponds with the results that were reported by Mu et al. (2020) that diet-induced obese mice treated with probiotics (*Lactobacillus plantarum* KFY02) showed ameliorated body weight gain. Several studies have demonstrated that LAB and selenium can mitigate weight gain and fat mass accumulation (Kim et al., 2017). Similar research on the administration of *Lactobacillus reuteri* MG5149 reported a reduction in weight gain in obese mice (Choi et al., 2021). Selenium has also been reported to be associated with obesity, as some studies indicate its concentration is lower in obese individuals (Tinkov et al., 2020).

Obesity can cause gut dysbiosis, characterized by an increased Firmicutes-to-Bacteroidetes (F/B) ratio and elevated levels of Gram-negative lipopolysaccharide (LPS)-containing Proteobacteria, which trigger inflammatory responses indicated by the reduced expression of antiinflammatory cytokine adiponectin levels and increased expression of proinflammatory cytokine TNF- α levels (Thiennimitr et al., 2018). This process occurs because LPS acts as a ligand for Toll-like Receptor 4 (TLR4). Activation of TLR4 by LPS stimulates the NF κ B pathway, a transcription factor that plays a key role in the inflammatory response, producing proinflammatory cytokines (Cuevas-Sierra et al., 2019; Lim & Kim, 2017). The rats experienced after HFFD administered for 28 days demonstrated obesity with a Lee index >300 , as well as lower adiponectin levels and higher TNF- α levels in all obese groups compared to normal rats. HFFD-induced inflammation disrupted adipokine homeostasis, including adiponectin. Hypertrophic and dysfunctional adipose tissue in obesity is characterized by macrophage infiltration and adipocytes secreting proinflammatory cytokines such as TNF- α , IL-1, and IL-6. The consistent elevation of various inflammatory markers has been strongly associated with an increased risk of obesity-related diseases, including cardiovascular disease and Type 2 Diabetes Mellitus (Wang et al., 2021).

The findings of this study indicate that obese rats given dadih fortified with red dragon fruit and selenium experienced significant improvements in metabolic markers after a 28-day intervention. The intervention increased adiponectin levels and reduced TNF- α levels compared to the HFFD control group. These effects can be attributed to the bioactive compounds in the fortified dadih, including probiotics, selenium,

flavonoids, and anthocyanins from red dragon fruit. These compounds possess antiinflammatory and antioxidative effects, which help regulate adipokine levels and improve inflammatory markers (Takahashi et al., 2020; Zheng et al., 2023). The mechanism of probiotics in increasing adiponectin levels and reducing TNF- α levels during 28 days of dadih-fortified intervention in rats with obesity is that the lactic acid bacteria (LAB) present in dadih can suppress fat absorption in the intestine by inhibiting pancreatic lipase activity and binding bile acids (Mohkam et al., 2023). This mechanism reduces fat emulsification and absorption, leading to decreased adipocyte size, reduced inflammation, and increased adiponectin secretion (Wang et al., 2020). Previous studies have demonstrated that supplementation with *Lactobacillus reuteri* JBD301 significantly lowers free fatty acid (FFA) concentrations in the small intestine, reducing fat absorption and enhancing fat excretion through feces. This effect has been practical in both animal models and human clinical trials, showing significant weight loss compared to placebo groups (Mohkam et al., 2023). Additionally, treatment with *Lactobacillus rhamnosus* GG (LGG) has been shown to increase adiponectin levels and reduce weight gain in mice with metabolic syndrome by decreasing adipocyte size, enhancing lipolysis, and lowering inflammation through reduced proinflammatory cytokines (Liu et al., 2020).

The reduction in TNF- α observed in the treatment groups is likely attributed to the antiinflammatory properties of LAB, which inhibit the phosphorylation of I κ B α and block NF- κ B activation, thus reducing proinflammatory cytokine production (López-Almada et al., 2024). In previous studies, various LAB strains in dadih have been shown to reduce proinflammatory cytokines, such as *Lactobacillus rhamnosus* 2016SWU. In experimental models, 05.0601 (Lr-0601) significantly lowered inflammatory markers, including TNF- α (Bu et al., 2024). Meta-analyses have also confirmed that probiotic supplementation significantly reduces serum concentrations of proinflammatory cytokines such as hs-CRP, TNF- α , IL-6, IL-12, and IL-4 (Milajerdi et al., 2020). Moreover, LAB increases gut microbiota diversity and decreases lipopolysaccharide (LPS) production, which is crucial as LPS triggers systemic inflammation that lowers adiponectin levels (Choi et al., 2019). LAB also produces antimicrobial compounds such as bacteriocins that inhibit pathogenic bacteria in the gut, preventing increased gut permeability and LPS translocation into circulation (Hernández-González et al., 2021; Shen et al., 2022).

Treatment group P2, which combined dadih with dragon fruit and selenium, demonstrated better results than P1, which lacked these additional components. The synergistic combination of probiotics, antioxidants, and selenium effectively reduced oxidative stress and systemic inflammation. Dragon fruit in this intervention contributes additional benefits through its antioxidant content, such as vitamin C, betalains, and flavonoids, and inhibits NF- κ B transcription factors, reducing the production of inflammatory cytokines like IL-1 β and TNF- α ; these factors are directly linked to decreased adiponectin levels (Arivalagan et al., 2021; Bhadauria et al., 2024). Furthermore, the oligosaccharides in dragon fruit stimulate the growth of beneficial bacteria like *Lactobacillus* and *Bifidobacterium*, enhancing the probiotic effect (Nishikito et al., 2023). Selenium, as an essential trace element, supports the activity of glutathione peroxidase (GPx), reducing oxidative stress in adipose tissue and improving adipogenesis, which enhances adipocyte functionality in producing adiponectin (Tinkov et al., 2020). GPx also inhibits NF- κ B activation, reducing TNF- α production (Xiao et al., 2021). Studies have shown that sodium selenite supplementation effectively increases the probiotic efficacy in reducing body fat by decreasing the expression of lipogenesis-related genes (e.g., FAS, LPL, PPAR γ ,

SREBP1) and increasing lipolysis-related gene expression (Nido et al., 2016). Combining these components with fermented milk products appears to be more effective in increasing adiponectin and lowering TNF- α levels, aligning with previous findings on the antiinflammatory effects of the combination of probiotics and natural ingredients (Plaza-Díaz et al., 2017).

The findings of this study indicate a significant and strong negative correlation between adiponectin levels and TNF- α ($p=0.000$, $r=-0.883$), as well as between adiponectin levels and body weight ($p=0.000$, $r=-0.938$). These results highlight the interconnected relationship between adiponectin, inflammation, and body weight status. Adiponectin functions as an antiinflammatory cytokine, particularly in suppressing the activity of TNF- α , a key proinflammatory cytokine (Mihalopoulos et al., 2020). However, adiponectin synthesis can be inhibited by proinflammatory cytokines such as TNF- α and IL-6, often reducing adiponectin levels in obese individuals (Varra et al., 2024). Low adiponectin levels impair lipid metabolism regulation, resulting in fat accumulation, increased body weight, and heightened inflammation (Dutheil et al., 2018; Zorena et al., 2020).

Conversely, a significant positive correlation was observed between TNF- α levels and body weight ($p=0.000$, $r=0.877$), indicating that increased body weight directly elevates TNF- α production. In obesity, the expansion of adipose tissue, particularly visceral fat, becomes a primary source of TNF- α (Kawai et al., 2021). This cytokine promotes insulin resistance by disrupting signaling pathways, impairing glucose uptake, and altering lipid metabolism. These disruptions further exacerbate visceral fat accumulation and chronic inflammation, creating a feedback loop that perpetuates weight gain and metabolic disturbances (Akash et al., 2018; Alzamil, 2020). Previous research consistently shows elevated TNF- α levels in obese individuals compared to those with normal weight, linking TNF- α to obesity-related complications such as type 2 diabetes and cardiovascular diseases (Quarta et al., 2022). Weight-loss interventions, including dietary and physical activity strategies, can reduce TNF- α levels. Moderate-intensity endurance exercise, for instance, has been shown to acutely decrease TNF- α levels in obese individuals, while pharmacological treatments like orlistat effectively reduce both body weight and TNF- α levels (Adi Bramasta et al., 2023; Munir et al., 2024). These findings underscore the importance of addressing inflammation and body weight in managing obesity and its associated risks.

This study has several limitations, including a relatively small sample size and the absence of long-term follow-up. The short intervention period did not allow for the evaluation of the sustained effects of fortified dadih with red dragon fruit and selenium on inflammation and body weight. Furthermore, as this study was conducted on animal models, clinical trials are necessary to confirm its efficacy and safety in humans.

CONCLUSION

The study findings indicate that fortified dadih with red dragon fruit and selenium is more effective in increasing adiponectin levels and reducing TNF- α levels in obese rats compared to non-fortified dadih. The strong negative correlation between adiponectin levels and both TNF- α and body weight suggests that increasing adiponectin levels while reducing TNF- α may play a crucial role in regulating body weight and inflammation in obesity. Further research is needed to explore the potential of fortified dadih with dragon fruit and selenium as a therapeutic intervention to improve adiponectin levels and reduce TNF- α in individuals with obesity. This fortified product could also be developed into functional foods or nutraceuticals with high

economic value, promoting its broader application in managing obesity and related inflammatory conditions.

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CONFLICT OF INTEREST

There is no conflict of interest related to this research and publication.

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