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Research Article

Effect of Red Ginger Extract Prepared Using a Natural Deep Eutectic Solvent on Body Weight and Obesity-Related Parameters in Rats Fed an Atherogenic Diet

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Abstract

This study evaluated the anti-obesity effects of red ginger (*Zingiber officinale* var. *rubrum*) extract prepared using Natural Deep Eutectic Solvents (RGE-NADES) in rats fed an atherogenic diet (AD). *Zingiber officinale* var. *rubrum* rhizomes were extracted via ultrasound-assisted extraction using a betaine-lactic acid NADES (1:2 ratio) at a 1:30 solid-to-solvent ratio. Twenty Sprague-Dawley rats were divided into five groups (n = 4): normal control, negative control (AD), orlistat (2.16 mg/kg BW), RGE-NADES 25 mg/kg BW, and RGE-NADES 50 mg/kg BW. Treatments and diets were administered over 14 days, during which body weight, nasoanal length, and food intake were monitored. End-of-study assessments included the Lee obesity index, adiposity index, and relative organ indices. Compared with the negative control group, both RGE-NADES doses significantly reduced body weight and the Lee obesity index ($p < 0.05$), with decreases of 10.31% (25 mg/kg) and 8.68% (50 mg/kg), respectively. Food intake and adiposity index were also lower in the treatment groups, with a statistically significant reduction in adiposity index observed specifically at 25 mg/kg. Importantly, RGE-NADES administration did not produce significant differences in relative heart, liver, or kidney indices across groups ($p > 0.05$). Overall, RGE-NADES effectively mitigates body weight gain and obesity indicators in AD-fed rats over a 14-day period without adversely affecting major organ weights.

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INTRODUCTION

Obesity is a complex chronic condition characterized by excessive body fat accumulation that significantly elevates the risk of cardiovascular disease, hypertension, type 2 diabetes, and various malignancies. Its multifactorial etiology encompasses complex interactions among genetic, environmental, socioeconomic, behavioral, and psychological drivers that ultimately result in a sustained imbalance between energy intake and expenditure[1,2]. Globally, obesity rates continue to rise at an alarming rate[3]. In Indonesia, national surveillance data reflect this growing public health crisis, with adult obesity prevalence escalating from 10.5% in 2007 to 23.4% in 2023, underscoring the urgent imperative for targeted, sustainable preventive and therapeutic strategies[4,5].

Red ginger (*Zingiber officinale* var. *rubrum*) is a traditional medicinal plant rich in a diverse array of bioactive secondary metabolites with broad health-promoting potential[6]. Oral administration of *Z. officinale* var. *rubrum* extract at 200 mg/kg body weight over 14 days was previously demonstrated to induce a 22.5% body weight reduction in hypercholesterolemic

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rat models[7]. Furthermore, *Z. officinale* var. *rubrum* extracts exhibit robust antioxidant activity and effectively inhibit key metabolic enzymes implicated in the pathogenesis of obesity and associated metabolic dysregulation[8].

These biological activities are primarily attributed to key lipophilic constituents, most notably 6-gingerol and 6-shogaol[9]. Beyond their marked antioxidant and anti-inflammatory properties, these compounds directly modulate molecular pathways governing adipogenesis, lipolysis, systemic lipid metabolism, and energy expenditure[10-12]. However, conventional isolation methods rely heavily on volatile organic solvents like ethanol and hexane, which pose distinct environmental, operational, and safety challenges. Natural Deep Eutectic Solvents (NADES) have consequently gained prominence as green, biodegradable, and highly efficient extraction media for plant bioactives[13,14]. Specifically, a betaine and lactic acid NADES mixture at a 1:2 molar ratio has demonstrated superior extraction efficiency and was selected as the specialized solvent system for *Z. officinale* var. *rubrum* in this investigation[15].

Zingiber officinale var. *rubrum* extracts prepared using this system yield substantial total concentrations of gingerols and shogaols, reaching approximately 15.09 mg/g[9]. Preliminary functional studies have shown that *Z. officinale* var. *rubrum* extract in NADES (RGE-NADES) significantly improves serum lipid profiles and reduces atherogenic risk indices in hyperlipidemic models[16]. Building upon these findings, the present study comprehensively evaluated the anti-obesity efficacy of RGE-NADES in rats maintained on a high-fat atherogenic diet, specifically assessing its impact on body weight trajectories, daily food consumption, nasoanal length, Lee obesity index, adiposity index, and relative visceral organ weights (heart, liver, and kidneys).

MATERIALS AND METHODS

Materials

The chemical reagents and biological materials utilized in this study comprised betaine, lactic acid, *Z. officinale* var. *rubrum*, distilled water, carboxymethyl cellulose sodium (CMC-Na), cholesterol, cholic acid, goat fat, cotton, and carbon dioxide gas. Male Sprague-Dawley rats served as animal models and were maintained on standard feed pellets. Analytical and processing procedures were carried out using Pyrex® laboratory glassware, an analytical balance (LabPro®), a hotplate magnetic stirrer (Thermo Scientific®), a sonicating bath (Branson 2800®), a centrifuge (Cole-Parmer®), a drying oven (Memmert®), a muffle furnace (Daihan Scientific®), and micropipettes (Eppendorf Research Plus®). Additional general labware included aluminum foil, porcelain dishes, silica crucibles, cold plates, rulers, and measuring tapes. Animal maintenance, dosing, and tissue harvesting were conducted using rat housing cages, oral gastric gavage probes, 1 mL disposable syringes (OneMed®), a dissecting instrument set (Golo Cross®), surgical tweezers, and disposable scalpels.

Methods

Preparation and extraction of plant materials

Zingiber officinale var. *rubrum* rhizomes were procured from PT. Palapa Muda Perkasa, Depok, West Java, Indonesia, and authenticated under specimen identification number 996/IPH.11.02/f.1.1/I/2023. The dried powder was transferred to an Erlenmeyer flask and mixed with a NADES system composed of betaine and lactic acid at a 1:2 molar ratio at a solid-to-solvent ratio of 1:30 (w/v). Two distinct RGE-NADES stock preparations were formulated for experimental administration. For the lower-dose regimen, 65 mg of *Z. officinale* var. *rubrum* powder was combined with 5 mL of NADES to achieve an initial concentration of 13 mg/mL. For the higher-dose regimen, 130 mg of *Z. officinale* var. *rubrum* powder was combined with 5 mL of NADES, yielding an initial concentration of 26 mg/mL. The suspensions were subjected to ultrasound-assisted extraction at 42°C for 25 min and subsequently centrifuged at 3200 rpm. The resulting clear supernatants were harvested and stored in sealed glass vials. The RGE-NADES extracts were administered via oral gavage at target doses of 25 and 50 mg/kg body weight, following a procedure adapted from Yulianita *et al*[16].

Qualitative phytochemical screening

Qualitative phytochemical screening of the RGE-NADES extract was conducted to identify alkaloids, flavonoids, phenolics, glycosides, and saponins, following standard protocols described by Hanani[17]. Alkaloids were detected using Mayer's and Dragendorff's reagents; flavonoids were evaluated using magnesium ribbon and concentrated hydrochloric acid; phenolics

were tested using ferric chloride solution; and glycosides were screened using glacial acetic acid, ferric chloride, and concentrated sulfuric acid. Saponins were confirmed through persistent foam formation. Steroids and triterpenoids were evaluated using the Liebermann–Burchard reagent following the method of Dahanayake *et al*[18].

Experimental design

The animal protocol was approved by the Ethics Committee of Animal Research, Faculty of Mathematics and Natural Sciences, Pharmacy Study Program, Universitas Pakuan (Approval No. 004/KEPHP-UNPAK/02-2024). Male Sprague-Dawley rats weighing 150–200 g (coefficient of variation: 10.21%) were acclimatized for 7 days under standardized laboratory conditions, including a 12-h light/dark cycle, relative humidity of 73–79%, and ambient temperature of 25 ± 2 °C. Following acclimatization, the animals were randomly assigned to five experimental groups (n = 4 per group): Group 1 (normal control), receiving a standard rodent chow diet and vehicle NADES; Group 2 (negative control), receiving an atherogenic diet and vehicle NADES; Group 3 (positive control), receiving an atherogenic diet (AD) and orlistat; Group 4, receiving an atherogenic diet and RGE-NADES at 25 mg/kg body weight; and Group 5, receiving an atherogenic diet and RGE-NADES at 50 mg/kg body weight.

The RGE-NADES extract was administered by oral gavage using the direct supernatant without additional organic solvents. Dosing volumes were dynamically calibrated to individual daily body weights to deliver precise treatments of 25 and 50 mg/kg body weight. All groups except the normal control received an AD comprising 2% cholesterol, 5% goat fat, 0.2% cholic acid, and standard rodent chow, to a total of 100%. The AD was supplied as pellets at 20 g/day/rat for 14 consecutive days. Treatments were administered daily by oral gavage 2 h following diet presentation.

Initial body weight and nasoanal length were recorded prior to intervention (Day 0) and at the completion of the treatment period (Day 14). Food intake was monitored daily throughout the trial and calculated as the difference between the mass of food supplied and the mass of unconsumed residual food. At the conclusion of the 14-day intervention, animals were humanely sacrificed, and abdominal adipose tissue, along with visceral organs, were carefully excised and weighed using an analytical balance.

Obesity-related parameters

The Lee obesity index was calculated using final body weight and nasoanal length measurements, as described by Lee[19]. The adiposity index and relative visceral organ mass indices (heart, liver, and kidneys) were determined following established procedures[20] using **Equations 1-3**.

$$Lee\ index = \frac{Cube\ root\ of\ body\ weight}{Nasoanal\ length\ (cm)} \times 1000 \quad [1]$$

$$Adiposity\ index\ (\%) = \frac{Total\ abdominal\ fat\ weight\ (g)}{Body\ weight\ (g)} \times 100\% \quad [2]$$

$$Relative\ organ\ index\ (\%) = \frac{Organ\ weight\ (g)}{Body\ weight\ (g)} \times 100\% \quad [3]$$

Data analysis

Statistical analyses were performed using IBM SPSS Statistics software (version 27.0). Quantitative data are expressed as mean ± standard deviation. Normality of distribution and homogeneity of variance across experimental groups were evaluated using the Shapiro–Wilk test and Levene's test, respectively. Inter-group statistical comparisons were conducted using one-way analysis of variance (ANOVA), followed by Tukey's honestly significant difference (HSD) post hoc test for multiple pairwise comparisons. Differences were considered statistically significant at $p < 0.05$.

RESULTS AND DISCUSSION

The *Z. officinale* var. *rubrum* extract prepared using RGE-NADES was obtained as a dark brown liquid extract. The extraction procedure used ultrasound-assisted extraction with betaine and lactic acid as NADES at a 1:2 molar ratio. Ultrasound-assisted extraction accelerates cavitation-driven mass transfer and significantly enhances the recovery of thermolabile plant

bioactive compounds[21]. This specific NADES composition has been shown to be highly effective at extracting gingerols and shogaols from *Z. officinale* var. *rubrum*, yielding a reported cumulative bioactive concentration of approximately 15.09 mg/g[9].

Qualitative phytochemical screening confirmed the presence of alkaloids, flavonoids, tannins, and saponins in RGE-NADES. These findings align with previous literature describing the primary secondary metabolite profile of *Z. officinale* var. *rubrum* rhizomes[22]. The identified phytochemical classes likely drive the extract's biological activity through synergistic antioxidant, anti-inflammatory, and lipid-modulating pathways. The non-detection of specific phytochemical classes in qualitative assays should be interpreted with caution, as chemical detection remains sensitive to sample preparation methods, geographic variation in plants, and test detection thresholds.

Table I presents the body weight trajectories and daily food consumption across the experimental cohorts during the 14-day treatment period. At baseline (Day 0), body weight did not differ significantly among the groups ($p > 0.05$). Following the 14-day intervention, the negative control group exhibited the greatest body weight gain (46.98 ± 5.05%), which was significantly higher than that of all other experimental groups ($p < 0.05$). The normal control group showed a modest physiological weight gain of 6.40 ± 1.66%, which was significantly different from all high-fat diet groups ($p < 0.05$). In contrast, active treatment with orlistat, RGE-NADES 25 mg/kg, and RGE-NADES 50 mg/kg induced net body weight reductions of -11.47 ± 2.68%, -10.31 ± 2.35%, and -8.68 ± 1.03%, respectively. No statistically significant differences in weight reduction were observed among these three treatment groups ($p > 0.05$). Daily food intake varied significantly among the experimental groups ($p < 0.05$). The negative control group consumed the highest daily food mass (12.14 ± 0.15 g/day), whereas food consumption was markedly lower in animals receiving orlistat (1.80 ± 0.30 g/day), RGE-NADES 25 mg/kg (4.18 ± 0.48 g/day), and RGE-NADES 50 mg/kg (2.77 ± 0.60 g/day).

Table I. Effect of RGE-NADES on body weight and daily food intake.

Group	Day 0 Body Weight (g)	Day 14 Body Weight (g)	Body Weight Change (%)	Food Intake (g/day)
Normal control	219.50 ± 3.70^{a}	233.50 ± 2.38^{b}	6.40 ± 1.66^{b}	7.57 ± 0.38^{d}
AD + NADES (negative control)	219.75 ± 6.99^{a}	322.75 ± 3.50^{c}	46.98 ± 5.05^{c}	12.14 ± 0.15^{e}
AD + orlistat 2.16 mg/kg	220.00 ± 1.83^{a}	194.75 ± 5.32^{a}	-11.47 ± 2.68^{a}	1.80 ± 0.30^{a}
AD + RGE-NADES 25 mg/kg	220.25 ± 2.50^{a}	197.50 ± 3.42^{a}	-10.31 ± 2.35^{a}	4.18 ± 0.48^{c}
AD + RGE-NADES 50 mg/kg	222.00 ± 2.71^{a}	202.75 ± 4.57^{a}	-8.68 ± 1.03^{a}	2.77 ± 0.60^{b}

Note: Values are expressed as mean ± SD (n = 4). Values within the same column sharing different superscript letters indicate statistically significant differences ($p < 0.05$). Body weight change was calculated as (Day 14 - Day 0 / Day 0) x 100.

Table II details rat nasoanal length at baseline and at the conclusion of the 14-day study. At Day 0, animals in the orlistat group displayed a significantly greater baseline nasoanal length than those in the normal and negative control groups ($p < 0.05$). Conversely, baseline nasoanal lengths in the RGE-NADES cohorts did not differ significantly from the control groups ($p > 0.05$). On Day 14, mean nasal lengths ranged from 21.77 ± 0.47 cm to 23.88 ± 1.28 cm. Neither the RGE-NADES dose cohort nor the control groups differed significantly at Day 14 ($p > 0.05$). Overall, only minor, non-significant fluctuations in nasoanal growth were observed throughout the 14-day intervention period. The Lee obesity index is an established metric for assessing rodent adiposity, with values exceeding 310 indicating an obese phenotype[19].

Table II. Effect of RGE-NADES on nasoanal length during the 14-day treatment period.

Group	Day 0 Nasoanal Length (cm)	Day 14 Nasoanal Length (cm)	Nasoanal Length Change (%)
Normal control	21.85 ± 0.60^{a}	22.23 ± 0.53^{ab}	+1.74
AD + NADES (negative control)	22.13 ± 0.62^{a}	21.77 ± 0.47^{a}	-1.63
AD + orlistat 2.16 mg/kg	24.48 ± 1.34^{b}	23.88 ± 1.28^{b}	-2.45
AD + RGE-NADES 25 mg/kg	23.28 ± 1.14^{ab}	22.78 ± 1.06^{ab}	-2.15
AD + RGE-NADES 50 mg/kg	22.65 ± 0.79^{ab}	22.25 ± 0.84^{ab}	-1.77

Note: Values are expressed as mean ± SD (n = 4). Values within the same column sharing different superscript letters indicate statistically significant differences ($p < 0.05$). Nasoanal length change was calculated as (Day 14 - Day 0 / Day 0) x 100.

Figure 1 illustrates the Lee obesity index across groups on Day 14. The negative control group exhibited the highest Lee index (315.28), which was significantly higher than that of the normal control group (207.38; $p < 0.05$). Orlistat administration reduced the Lee index to 237.78. Marked reductions were likewise recorded in the RGE-NADES treatment groups, reaching 257.04 at 25 mg/kg and 263.45 at 50 mg/kg. Both RGE-NADES doses maintained significantly lower Lee index values than the negative control group ($p < 0.05$).

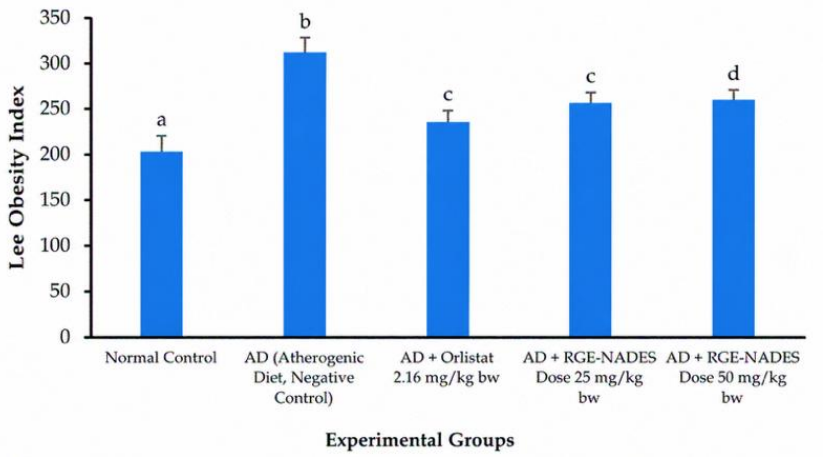


Figure 1. The Lee obesity index of rats on day 14 of treatment with RGE-NADES. Bars labeled with different lowercase letters represent statistically significant differences ($p \leq 0.05$).

Adiposity and relative organ mass indices were analyzed to evaluate tissue-specific alterations in response to high-fat atherogenic diet feeding and RGE-NADES intervention (**Table III**). The adiposity index was significantly elevated in the negative control group (1.32 ± 0.124) compared with the normal control group (0.43 ± 0.108; $p < 0.05$). Both orlistat and RGE-NADES at 25 mg/kg significantly attenuated adiposity accumulation relative to the negative control group, yielding values of 0.68 ± 0.047 and 0.86 ± 0.168, respectively ($p < 0.05$). Although the 50 mg/kg RGE-NADES cohort had a numerically lower adiposity index (1.06 ± 0.100) than the negative control, the difference was not statistically significant ($p > 0.05$). Relative heart, liver, and kidney weight indices showed no statistically significant differences across any experimental groups ($p > 0.05$).

Table III. Effect of RGE-NADES on adiposity and relative organ indices.

Group	Adiposity Index	Heart Index	Liver Index	Kidney Index
Normal control	0.43 ± 0.108[a]	0.35 ± 0.058	4.09 ± 0.490	1.02 ± 0.125
AD + NADES (negative control)	1.32 ± 0.124[d]	0.36 ± 0.049	4.10 ± 0.087	1.11 ± 0.092
AD + orlistat 2.16 mg/kg	0.68 ± 0.047[b]	0.37 ± 0.046	3.70 ± 0.387	0.94 ± 0.152
AD + RGE-NADES 25 mg/kg	0.86 ± 0.168[c]	0.36 ± 0.026	3.87 ± 0.582	0.98 ± 0.131
AD + RGE-NADES 50 mg/kg	1.06 ± 0.100[d]	0.36 ± 0.045	4.24 ± 0.295	1.06 ± 0.153

Note: Values are presented as mean ± SD (n = 4). Superscript letters within the same column denote significant differences ($p < 0.05$). Relative organ indices did not differ significantly across groups ($p > 0.05$).

The induction of obesity via high-fat atherogenic diet feeding was successfully established, as demonstrated by the negative control group displaying significantly elevated hyperphagia, body weight, Lee obesity index, and abdominal adiposity index compared with normal controls. Furthermore, the Lee index in the negative control group exceeded the threshold of 310, confirming diet-induced obesity in rats[19,20]. Treatment with RGE-NADES effectively counteracted this metabolic phenotype, suppressing food intake and body weight gain relative to untreated atherogenic controls. Both RGE-NADES doses significantly reduced the Lee obesity index, while abdominal fat accumulation was suppressed in both treatment cohorts, with the 25 mg/kg dose demonstrating statistically significant adiposity suppression compared with the negative control group.

These results indicate that administration of RGE-NADES at 25 and 50 mg/kg effectively mitigates weight gain and visceral fat accumulation in rats maintained on an atherogenic diet. In our previous investigation, this identical RGE-NADES extract demonstrated potent hypolipidemic and cardioprotective effects in an atherogenic model[16]. The current study expands these findings by establishing its direct anti-obesity efficacy. Nirvana *et al*. previously reported that conventional ethanol extracts of *Z. officinale* var. *rubrum* reduced body weight in hypercholesterolemic rats at a dose of 200 mg/kg[7]. Notably, RGE-NADES elicited comparable anti-obesity responses at substantially lower dosages (25 and 50 mg/kg). While variations in extraction vehicles and study protocols preclude direct quantitative comparisons, these findings suggest that green eutectic solvents may enhance the bioactivity or bioaccessibility of constituents of *Z. officinale* var. *rubrum*.

The negative control group exhibited the highest food consumption, whereas both orlistat and RGE-NADES treatments were associated with decreased hyperphagia. This pattern aligns with observations by Amin *et al*.[23], who reported that high-fat diet consumption promotes hyperphagia, whereas pharmaceutical interventions like orlistat suppress overall food intake. Although orlistat primarily acts by inhibiting intestinal lipase to block dietary lipid absorption, the concurrent appetite suppression observed in this study likely contributed to the overall reduction in body mass.

Intriguingly, the therapeutic response to RGE-NADES did not follow a linear dose-dependent pattern. The 25 mg/kg dose produced a greater relative body weight reduction than the 50 mg/kg dose (-10.31% vs. -8.68 %). Similarly, while the 50 mg/kg dose reduced the adiposity index compared with negative controls (1.06 vs. 1.32), the change did not reach statistical significance ($p > 0.05$). This non-linear dose-response curve is a recognized phenomenon in botanical pharmacology, in which higher phytochemical concentrations may activate counter-regulatory metabolic pathways or saturate receptor kinetics[24].

The betaine-lactic acid (1:2) NADES mixture efficiently extracts the major bioactive gingerols and shogaols from *Z. officinale* var. *rubrum* rhizomes[9]. These compounds drive anti-obesity effects by directly regulating systemic lipid metabolism[10,25-28]. Purified 6-gingerol decreases adiposity in diet-induced obese models, whereas 6-shogaol suppresses adipocyte differentiation and stimulates lipolysis in 3T3-L1 preadipocytes[26,27]. Together, these cellular mechanisms limit triacylglycerol accumulation in adipose tissue, thereby reducing overall adiposity and body weight. Additionally, both 6-gingerol and 6-shogaol upregulate adiponectin expression in mature adipocytes[25]. The intrinsic antioxidant and anti-inflammatory activities of *Z. officinale* var. *rubrum* further support these metabolic benefits by dampening adipose tissue inflammation and cellular oxidative stress[8,10,11]. Although molecular biomarkers were not directly quantified in this trial, these established pathways offer a compelling explanation for the anti-obesity effects observed in RGE-NADES-treated animals[29].

The application of NADES as an extraction vehicle provides a green pharmaceutical alternative to toxic organic solvents. Because the negative control group received the atherogenic diet paired with vehicle NADES, whereas the treatment groups received RGE-NADES, the observed physiological improvements can be attributed specifically to the extracted *Z. officinale* var. *rubrum* bioactives rather than to the eutectic vehicle itself. As biodegradable extraction media, NADES formulations offer clear environmental and processing advantages over conventional organic solvents[13,14]. Although this study did not include a parallel conventional-solvent arm, future head-to-head evaluations comparing RGE-NADES with standard ethanolic extracts will further clarify the specific therapeutic advantages of green eutectic extraction media.

This study has several limitations that warrant consideration. A conventional organic solvent extraction control was not included, preventing direct isolation of the specific efficacy enhancement provided by the NADES matrix relative to standard extracts. Additionally, the intervention period was limited to 14 days, and systemic metabolic biomarkers (such as lipid profiles, adipokines, and inflammatory cytokines) were not measured. These parameters restrict long-term safety evaluations and mechanistic conclusions. Future research should compare different extraction solvents, extend the treatment duration, and incorporate comprehensive biochemical, histopathological, and molecular analyses.

CONCLUSION

In conclusion, *Z. officinale* var. *rubrum* extract prepared using a betaine-to-lactic acid (1:2 molar ratio) RGE-NADES effectively attenuates body weight gain and key obesity-related physiological parameters in rats subjected to a high-fat, atherogenic diet. Both tested dosage regimens (25 and 50 mg/kg body weight) produced statistically significant reductions in the Lee obesity index compared to the untreated negative control group, with the 25 mg/kg dose specifically demonstrating a significant reduction in the overall adiposity index. These findings underscore the promising therapeutic potential of RGE-NADES as a green, bio-enhanced natural formulation for combating diet-induced obesity and metabolic dysfunction.

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DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

DECLARATION OF AI TOOL USAGE

During the preparation of this manuscript, the authors utilized Grammarly Edu solely to improve narrative flow, refine sentence structure in the Introduction and Methods sections, and perform grammar and spelling checks. All suggestions were critically evaluated, fact-checked against primary sources, and substantially edited by the authors. The tool was not used to generate original scientific content, collect experimental data, or perform statistical analyses. The authors remain fully accountable for the content, accuracy, and original contributions of this published work.

REFERENCES

1. Ahmed SK, Mohammed RA. Obesity: Prevalence, causes, consequences, management, preventive strategies and future research directions. Metabol Open. 2025;27:100375. DOI: 10.1016/j.metop.2025.100375; PMID: 41041606; PMCID: PMC12486175.

2. Młynarska E, Bojdo K, Bulicz A, Frankenstein H, Gąsior M, Kustosik N, et al. Obesity as a Multifactorial Chronic Disease: Molecular Mechanisms, Systemic Impact, and Emerging Digital Interventions. Curr Issues Mol Biol. 2025;47(10):787. DOI: 10.3390/cimb47100787; PMID: 41150735; PMCID: PMC12564886.

3. Lin X, Li H. Obesity: Epidemiology, Pathophysiology, and Therapeutics. Front Endocrinol. 2021;12:706978. DOI: 10.3389/fendo.2021.706978; PMID: 34552557; PMCID: PMC8450866.

4. Badan Penelitian dan Pengembangan Kesehatan Kementerian Kesehatan Republik Indonesia. Laporan Nasional Riset Kesehatan Dasar (Riskesdas) 2007. Jakarta: Departemen Kesehatan Republik Indonesia; 2008. Available from: http://www.badankebijakan.kemkes.go.id/repositori/id/eprint/4378

5. Badan Kebijakan Pembangunan Kesehatan, Kementerian Kesehatan Republik Indonesia. Laporan Tematik Survei Kesehatan Indonesia (SKI) Tahun 2023: Potret Indonesia Sehat. Jakarta: Kementerian Kesehatan RI; 2024. Available from: https://www.badankebijakan.kemkes.go.id/hasil-ski-2023/

6. Zhang S, Kou X, Zhao H, Mak KK, Balijepalli MK, Pichika MR. Zingiber officinale var. rubrum: Red Ginger's Medicinal Uses. Molecules. 2022;27(3):775. DOI: 10.3390/molecules27030775; PMID: 35164040; PMCID: PMC8840670.

7. Nirvana SJ, Widiyani T, Budiharjo A. Antihypercholesterolemia activities of red ginger extract (Zingiber officinale Roxb. var rubrum) on Wistar rats. IOP Conf Ser Mater Sci Eng. 2020;858(1):012025. DOI: 10.1088/1757-899X/858/1/012025.

8. Rampengan DDCH, Syahputra RA, Halim P, Kumalawati DA, Ramadhan RN, Surya R, et al. Red ginger confers antioxidant activity, inhibits lipid and sugar metabolic enzymes, and downregulates miR-21/132 expression. J Agric Food Res. 2024;18:101526. DOI: 10.1016/j.jafr.2024.101526.

9. Yulianita Y, Mun'im A, Yanuar A, Saputri FC. Analysis of gingerol and shogaol compounds from red ginger (Zingiber officinale var. Rubrum) extract using several combinations of natural deep eutectic solvents. Int J Appl Pharm. 2024;16(special 3):51–5. DOI: 10.22159/ijap.2024.v16s3.09.

10. Shaukat MN, Nazir A, Fallico B. Ginger Bioactives: A Comprehensive Review of Health Benefits and Potential Food Applications. Antioxidants. 2023;12(11):2015. DOI: 10.3390/antiox12112015; PMID: 38001868; PMCID: PMC10669910.

11. Saravanan G, Ponmurugan P, Deepa MA, Senthilkumar B. Anti-obesity action of gingerol: effect on lipid profile, insulin, leptin, amylase and lipase in male obese rats induced by a high-fat diet. J Sci Food Agric. 2014;94(14):2972-7. DOI: 10.1002/jsfa.6642; PMID: 24615565.

12. Dugasani S, Pichika MR, Nadarajah VD, Balijepalli MK, Tandra S, Korlakunta JN. Comparative antioxidant and anti-inflammatory effects of [6]-gingerol, [8]-gingerol, [10]-gingerol and [6]-shogaol. J Ethnopharmacol. 2010;127(2):515-20. DOI: 10.1016/j.jep.2009.10.004; PMID: 19833188.

13. Huang MM, Yiin CL, Lock SSM, Chin BLF, Othman I, Zauzi NSA, et al. Natural deep eutectic solvents (NADES) for sustainable extraction of bioactive compounds from medicinal plants: Recent advances, challenges, and future directions. J Mol Liq. 2025;425:127202. DOI: 10.1016/j.molliq.2025.127202.

14. Hikmawanti NPE, Ramadon D, Jantan I, Mun'im A. Natural Deep Eutectic Solvents (NADES): Phytochemical Extraction Performance Enhancer for Pharmaceutical and Nutraceutical Product Development. Plants. 2021;10(10):2091. DOI: 10.3390/plants10102091; PMID: 34685899; PMCID: PMC8538609.

15. Yulianita Y, Rusli Z, Monica HR. Screening and optimization method of natural deep eutectic solvent extracts from Phyllanthus niruri by ultrasonic-assisted extraction. Res J Pharm Technol. 2023;16(11):5213–7. DOI: 10.52711/0974-360X.2023.00845.

16. Yulianita, Herlina N, Handayani MTR, Al Aziz NM, Safitri A, Pamungkas RR. Cardioprotective effects of red ginger extracted using natural deep eutectic solvent on lipid profile in atherosclerotic rats. J Jamu Indones. 2025;10(3):158–63. DOI: 10.29244/jji.v10i3.410.

17. Hanani E. Análisis Fitokimia. Jakarta: EGC; 2015.

18. Dahanayake JM, Perera PK, Galappatty P, Perera HDSM, Arawwawala LDAM. Comparative Phytochemical Analysis and Antioxidant Activities of Tamalakyadi Decoction with Its Modified Dosage Forms. Evid Based Complement Alternat Med. 2019;2019:6037137. DOI: 10.1155/2019/6037137; PMID: 31186663; PMCID: PMC6521515.

19. Lee MO. Determination of the surface area of the white rat with its application to the expression of metabolic results. Am J Physiol. 1929;89(1):24–33. DOI: 10.1152/ajplegacy.1929.89.1.24.

20. Arika WM, Kibiti CM, Njagi JM, Ngugi MP. Anti-obesity effects of dichloromethane leaf extract of Gnidia glauca in high fat diet-induced obese rats. Heliyon. 2019;5(11):e02800. DOI: 10.1016/j.heliyon.2019.e02800; PMID: 31844729; PMCID: PMC6895710.

21. Rahman H, Prambudi SN, Endranaka W. Application of Ultrasonic Assisted Extraction Method for Extraction of 6-Gingerol in Zingiber officinale Var. Rubrum. In: Makul N, ed. Current Overview on Science and Technology Research Vol. 6. Kolkata: Book Publisher International; 2022. p. 71–82. DOI: 10.9734/bpi/costr/v6/8010F.

22. Srikandi S, Humaeroh M, Sutamihardja R. Kandungan gingerol dan shogaol dari ekstrak jahe merah (Zingiber officinale Roscoe) dengan metode maserasi bertingkat. Al Kimiya J Ilmu Kimia Terapan. 2020;7(2):75–81. DOI: 10.15575/ak.v7i2.6545.

23. Amin HM, Tawfek NS, El-Hussein BKA, El-Ghany MSA. Anti-obesity potential of orlistat and amphetamine in rats fed on a high-fat diet. Middle East J Appl Sci. 2015;5(2):453-61.

24. Jodynis-Liebert J, Kujawska M. Biphasic Dose-Response Induced by Phytochemicals: Experimental Evidence. J Clin Med. 2020;9(3):718. DOI: 10.3390/jcm9030718; PMID: 32155852; PMCID: PMC7141213.

25. Isa Y, Miyakawa Y, Yanagisawa M, Goto T, Kang MS, Kawada T, et al. 6-Shogaol and 6-gingerol, the pungent of ginger, inhibit TNF-alpha mediated downregulation of adiponectin expression via different mechanisms in 3T3-L1 adipocytes. Biochem Biophys Res Commun. 2008;373(3):429-34. DOI: 10.1016/j.bbrc.2008.06.046; PMID: 18577375.

26. Hong KH, Um MY, Ahn J, Ha TY. 6-Gingerol Ameliorates Adiposity and Inflammation in Adipose Tissue in High Fat Diet-Induced Obese Mice: Association with Regulating of Adipokines. Nutrients. 2023;15(15):3457. DOI: 10.3390/nu15153457; PMID: 37571394; PMCID: PMC10421254.

27. Suk S, Seo SG, Yu JG, Yang H, Jeong E, Jang YJ, et al. A bioactive constituent of ginger, 6-shogaol, prevents adipogenesis and stimulates lipolysis in 3t3-l1 adipocytes. J Food Biochem. 2016;40(1):84–90. DOI: 10.1111/jfbc.12191.

28. Crichton M, Davidson AR, Innerarity C, Marx W, Lohning A, Isenring E, et al. Orally consumed ginger and human health: an umbrella review. Am J Clin Nutr. 2022;115(6):1511-27. DOI: 10.1093/ajcn/nqac035; PMID: 35147170; PMCID: PMC9170469.

29. Suk S, Kwon GT, Lee E, Jang WJ, Yang H, Kim JH, et al. Gingerenone A, a polyphenol present in ginger, suppresses obesity and adipose tissue inflammation in high-fat diet-fed mice. Mol Nutr Food Res. 2017;61(10):10.1002/mnfr.201700139. DOI: 10.1002/mnfr.201700139; PMID: 28556482; PMCID: PMC5947313.