ACS FOOD SCIENCE & TECHNOLOGY

Open Access

pubs.acs.org/acsfoodscitech

Article

Gryllus assimilis Dietary Wholemeal Powder Improves Glycemic Parameters and Regulates the Expression of Lipogenic Genes in Obese Mice

Published as part of ACS Food Science & Technology virtual special issue "Alternative Protein Sources for Responsible Food Consumption and Production".

Samara Cardoso de Jesus, Guilherme Henrique Mendes Ribeiro, Hebert Cleiton Ferreira Souza, Alfredo Mauricio Batista de Paula, Lucyana Conceição Farias, André Luiz Sena Guimaraes, and Sérgio Henrique Sousa Santos*

Cite This: *ACS Food Sci. Technol.* 2024, 4, 1632−1639

Read Online

ACCESS | Metrics & More | Article Recommendations

ABSTRACT: Obesity is a chronic illness that lowers quality of life; several dietary approaches have been considered as potential treatments. Due to its impact on regulating metabolism and weight, eating edible insects has become more popular among the available options. The objective of the current investigation was to assess the impact of wholemeal *Gryllus assimilis* (GA) powder as a dietary supplement on the regulation of genes in the adipose tissue and metabolic alterations in a mouse model of obesity. Several parameters were evaluated, including food intake, body weight, biochemical parameters, histological parameters, and adipose tissue mRNA expression. The main results showed that *G. assimilis* consumption modulates metabolic pathways and prevents hypertrophy in adipocytes while promoting a reduction in adipose tissue weight. In addition, glycemic parameters were improved, increasing insulin sensitivity and glucose tolerance. Thus, it can be said that eating black crickets enhanced the problems associated with obesity and effectively provided metabolic benefits. The results indicate that *G. assimilis* consumption may be a viable therapeutic strategy for preventing and treating obesity.

KEYWORDS: *entomophagy, obesity, metabolism, food supplementation, functional foods, edible insects*

1. INTRODUCTION

The idea that obesity is a metabolic change that can accelerate the development of other diseases has taken on new significance.[1] Nowadays, obesity can be defined as a chronic disease marked by excessive body weight and inflamed adipose tissues aggravated by different molecular mechanisms and producing systemic complications such as alterations in the metabolic balance and target organ damage.[2] Many facets of the community are concerned about the effects of obesity.[3] When established, obesity increases morbidity and mortality impacting numerous health issues with high costs for public care services, therefore causing an economic, social, and cultural problem.[4,5]

Among the most innovative nutritional intervention proposals capable of providing positive metabolic effects are the emerging nutritional products based on edible insects as a promising research line on improving human health.[6−8] In addition to providing essential nutrients like proteins and fats, the edible insects also contain some bioactive compounds that can improve glucose metabolism, reduce oxidative stress, modify inflammatory pathways, and improve lipid parameters.[9,10]

One of the main insects studied with promising data on metabolic damage is the edible insect named *Gryllus assimilis* (GA). The nutritional composition of this insect guarantees the source of different functional compounds of wide antioxidant and anti-inflammatory actions.[11] In addition, GA has been described as an alternative pathway for the dietary supply of proteins, amino acids, polyunsaturated fatty acids, and minerals, making it a valuable source of nutrients for the human diet.[12] However, there is a lack of studies proving the true impacts and supporting the molecular action mechanism of GA intake managing obesity and its complications.[13]

In this context, the present study aimed to evaluate the GA wholemeal powder effect on the metabolic changes caused by obesity. Biochemical, histological, and molecular parameters of the adipose tissue were evaluated in an experimental obese mice model.

Received: January 9, 2024
Revised: June 25, 2024
Accepted: June 25, 2024
Published: July 1, 2024

https://doi.org/10.1021/acsfoodscitech.4c00013
ACS Food Sci. Technol. 2024, 4, 1632−1639

2. MATERIALS AND METHODS

2.1. Animals. For the present study, 40 male Swiss mice, aged 4 to 6 weeks, and a mean body mass of 28.01 g, obtained at the State University of Montes Claros (Unimontes), were used. The choice of the mice line was based on previous studies and its heterogeneous characteristics and greater genetic variability, which approximates from human variations.[14] During the experiment, the animals were maintained on a 12-h light/dark cycle with temperature and humidity conditions (20 ± 3 °C; 40−70%), respectively, and fed *ad libitum*. This experiment followed all the ethical principles proposed for the use of animals adopted by the Ethics Committee on Animal Experimentation and Animal Welfare of the State University of Montes Claros (UNIMONTES). It was approved under protocol number 224/2021.

After the adaptation period, the animals were allocated into five groups (n = 8 each), and consequently, body weight gain was induced over 12 weeks by offering the following diets: standard (ST), AIN93-M, and high-fat diet (HFD). The diet used presented a total of kcal/g 2.18, 3.54, and 5.4 kcal per 1 g of the diet, respectively (Table 1).

Table 1. Diet Compositions[a,b,c]

ingredients	ST	AIN93-M	AIN93-M+ GA	high-fat diet	high-fat diet + GA
BHT		0.001	0.001	0.001	0.001
choline bitartrate		0.250	0.250	0.245	0.245
methionine		0.180	0.180	0.294	0.294
mix of vitamins		1.000	1.000	0.980	0.980
mix of minerals		3.500	3.500	3.430	3.430
cellulose		5.000	5.000	4.900	4.900
soy oil		4.000	0.730	6.890	3.620
casein		14.000	4.175	19.600	9.775
sucrose		10.000	10.000	1.900	14.900
maltodextrin		15.500	15.500		
maise starch		46.569	45.279	20.440	19.150
lard				18.520	18.520
gooseberry				9.800	9.800
G. assimilis powder		0.000	15.000	0.000	15.000
total		100	100	100	100

[a]Percentage values. [b]All ingredients were purchased from Rhoster LTDA (São Paulo. SP. Brazil). [c]ST: Standard diet commercial; AIN93M: rodent diet; GA: *G. assimilis* powder; HFD: High-fat diet.

The composition of the diets followed the standardization already described in the literature, and the intake of macronutrients and micronutrients was adjusted according to the provisions of the American Institute of Nutrition (AIN93-M).[15,16] These diets were prepared every week and placed in hermetically sealed containers under refrigeration at 4 °C throughout the experiment. The food intake of mice was measured daily, and body weight was monitored weekly.

After the period of induction of weight gain and obesity, food was introduced through the wholemeal powder of the *G. assimilis* insect to the diet of the groups of interest, namely AIN93-M + GA and HFD + GA, which were considered groups of treatment. The wholemeal powder of the insect under study was purchased from the Federal University of Minas Gerais' breeding grounds.

For 4 weeks, the animals were fed with the whole meal GA powder. After intervention and therapy, the animals underwent an overnight fast before being beheaded. For a biochemical study, blood was drawn. Weighed and frozen in liquid nitrogen, the epididymal adipose tissue was kept in a super freezer at −80 °C for subsequent analysis.

2.2. Glucose Tolerance Test and Insulin Sensitivity. The glucose tolerance test (GTT) was carried out after an overnight fast of 8−12 h. For the GTT, 2 g/kg of D-glucose was administered intraperitoneally, and blood glucose levels were measured at time intervals of 0, 15, 30, 60, and 120 min after glucose administration. The insulin sensitivity test (IST) was carried out with the animals in a fed state after administration of insulin (0.75 U/kg body weight) by intraperitoneal injection at 0, 15, 30, and 60 min.[14−16] To measure glycemic levels, capillary blood was obtained from the animals' tails and measured with reactive strips in an Accu-Check Active glucometer (Roche, SP, Brazil).

2.3. Biochemical Parameters Analyses. After the decapitation, blood samples were collected for biochemical analysis. The serum was obtained after blood centrifugation (3000 rpm for 10 min at 4 °C). The following parameters were assessed: total cholesterol (TC), high-density lipoprotein (HDL), triglycerides (TG), alanine aminotransaminases (ALT), and aspartate aminotransferase (AST) using enzymatic kits (Wiener Laboratorios, Rosario, Argentina). The measurements were performed on a Wiener BT-3000 kit plus a Chemistry Analyzer (Wiener Laboratories, Rosario, Argentina).[17]

2.4. Histology. Initially, the samples of epididymal adipose tissues were fixed in a 10% formaldehyde solution, and after this step, they were placed in ethyl alcohol for dehydration, followed by diaphanization in xylene solution and solidified in paraffin.[18] The histological sections were sectioned at a size of 5 μm and placed on slides for later staining. For staining the sectioned sections, hematoxylin and eosin (H&E) dyes were used. The finalized samples were examined under an optical microscope, thus achieving the capture of images.[14]

2.5. Quantification by Real-Time qRT-PCR. To assess the mechanisms by which insect wholemeal could contribute to obesity processes, qRT-PCR analyses were performed to assess the expression of lipogenic genes ***Srebp-1α, Fas, Acc, and Fat* mRNA.** Thus, total RNA extraction from adipose tissues was performed using the Trizol reagent (Invitrogen Corp., San Diego, California). The RNA was subsequently treated with DNase and using Invitrogen 34 Corp. Amplification of cDNA samples was performed using specific primers and SYBER Green PCR reagent (Applied Biosystems) in a Quant Studio 6 flex, 384-well equipment (Applied Biosystems). Relative gene expression was expressed as the relative level of mRNA compared to the control and was calculated after normalizing to the glyceraldehyde 3-phosphate dehydrogenase (GAPDH) gene and analyzed by the 2-ΔΔCt. The CT value was presented as the mean of duplicate measurements[19] (Table 2).

2.6. Data Analysis. Statistical analysis was performed using the GraphPad Prism software (version 5.0, San Diego, California), adopting $p < 0.05$ and a 95% confidence interval. Data were obtained as mean ± standard error. The statistical significance of the values for the different groups was estimated by one-way analysis of variance (ANOVA) and two-way ANOVA (body weight and insulin/glucose tests), followed by the post-Bonferroni test for multiple analysis tests. Normality was checked by the Shapiro-Wilk test.

Table 2. Primer Sequences Used in RT-PCR Analysis in This Study

gene	forward	reverse
GAPDH	AAGAAGGTGGTGAAGCAGGCATC	CGAAGGTGGAAGAGTGGGAGTTG
ACC	GCG TCG GGT AGA TCC AGT	CTC AGT GGG GCT TAG CTC TG
FAS	GTT CAC GGA CAT GGA GCAC	GTG GCT CTT GAT GAT CAG GTC
FAT	GCTGCGGAAACTTCAGGAAAT	AGAGACGTGTCACTCCTGGACTT
SREBP-1α	GGA GCC ATG GAT TGC ACATT	AGG AAG GCT TCC AGA GAGGA

https://doi.org/10.1021/acsfoodscitech.4c00013
ACS Food Sci. Technol. 2024, 4, 1632−1639

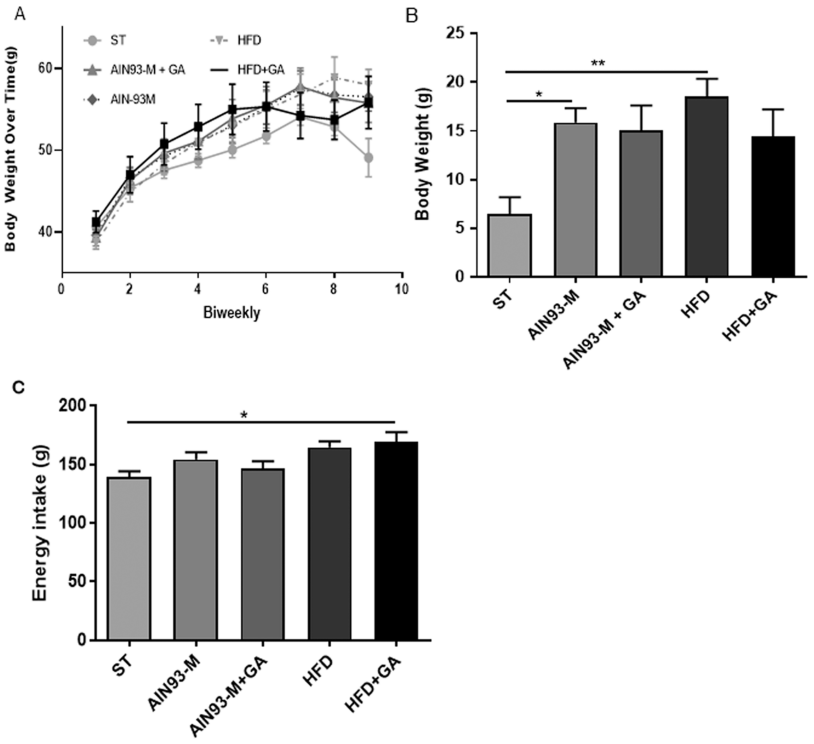

Figure 1. Body weight and energy intake of obese mice treated with *G. assimilis* whole powder. (A) Body weight gain over time (g); (B) Δbody weight (g); and (C) energy intake (g). *$p < 0.05$, **$p < 0.01$; ***$p < 0.001$. ST: palletized diet; AIN93-M: standard diet; AIN93-M + GA: standard diet addition *G. assimilis*: HFD: standard high-fat diet; HFD + GA: high-fat diet addition of *G. assimilis*.

3. RESULTS

3.1. Body Weight and Energy Intake. The consumption of wholemeal powder from the edible insect *G. assimilis* was able to promote different metabolic benefits. However, contrary to one of our hypotheses, in the analyses of body weight, no statistical differences were observed between the groups and the variable presented ($p > 0.05$) (Figure 1A,B).

Dietary control was also evaluated throughout our study and demonstrated an effect that can be corroborated by previous chaos directed at body weight. Food consumption was also assessed throughout the study. The results showed an increase in food consumption in different groups. However, the higher quantitative food intake of the HFD + GA group was considered to be higher than that of the baseline ST group ($p < 0.05$) (Figure 1C).

3.2. Biochemical Parameters and Glycemic. The glycemic data and biochemical parameters are represented in Figure 2. After the test period, the glycemic metabolic effects revealed that a high-fat diet was able to establish metabolic disorders by increasing the degree of glucose intolerance in the HFD group compared to the other groups ($p < 0.001$) and ($p < 0.05$), respectively (Figure 2A). However, the addition of cricket wholemeal powder to the diet of animals in the HFD + GA group proved to be effective in reducing the degree of glucose intolerance compared to the HF group ($p < 0.05$) (Figure 2A).

In addition, the possible effects on glycemic control can be evidenced and confirmed in our study by the effects of the hormone insulin. Thus, we observed that the cricket wholemeal powder improved insulin sensitivity in the AIN93-M + GA compared to its control AIN93-M ($p < 0.01$) (Figure 2B).

Fasting glucose also showed a statistically significant response. In the present study, we confirmed that the treated group (HFD + GA) obtained superior responses for glycemic control compared to the control fed the high-fat diet ($p < 0.05$) (Figure 2C).

The biochemical parameters of the lipid showed that cricket wholemeal powder favored the reduction of total cholesterol in the groups that received the treatment (HFD + GA) compared to the group on the HFD ($p < 0.05$) (Figure 2D). HDL concentrations were higher in the group that received wholemeal powder (HFD + GA) than in the ST group ($p < 0.01$) (Figure 2E).

Reductions in triglyceride levels were found in the group fed a high-fat diet when wholemeal powder was added ($p < 0.05$) (Figure 2F). The analysis of liver enzymatic markers revealed that the concentration of the ALT enzyme did not change between the groups in this study (Figure 2G). However, AST enzyme levels were expressed in lower concentrations in the HFD + GA group than in the ST group ($p < 0.05$) (Figure 2H).

3.3. Epididymal Adipose Tissue. The effects of supplementation of edible insect powder GA on the adipose tissue were measured and are summarized in Figure 3. Regarding adipose tissue weight, our analyses showed that the supply of edible insect powder via supplementation was able to confer a reduction in tissue weight in obese animals treated with it (HFD + GA) compared to the obese control group (HFD)($p < 0.001$) (Figure 3A).

In reinforcement of the findings of tissue effects of adiposity, our findings show that the group fed the high-fat diet in association with the whole fraction of edible insect GA presented a significant reduction in the size of the area of fat cells compared to the HFD group ($p < 0.05$) (Figure 3 B–C).

https://doi.org/10.1021/acsfoodscitech.4c00013
ACS Food Sci. Technol. 2024, 4, 1632−1639

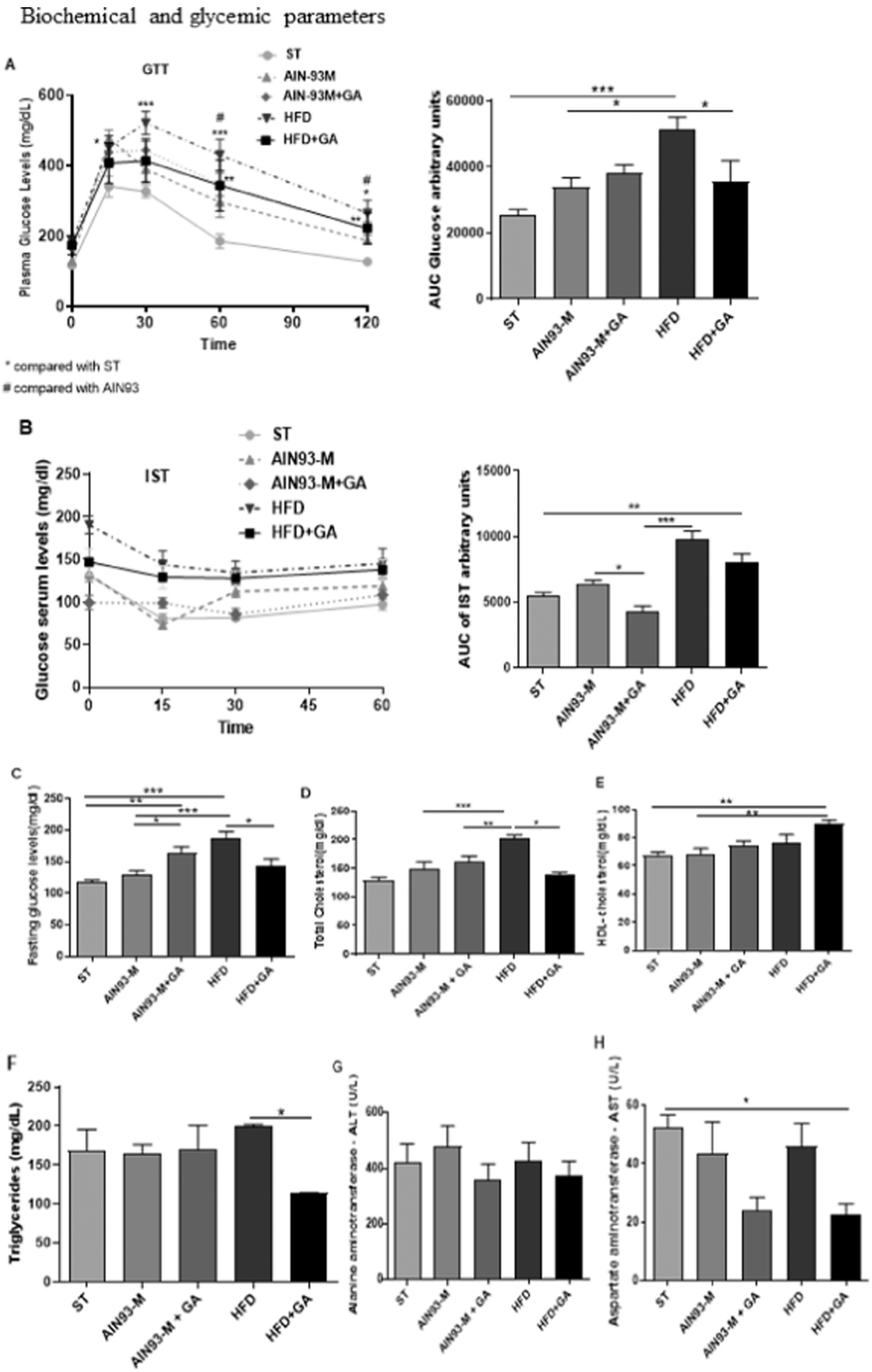

Figure 2. Biochemical and glycemic parameters of obese mice treated with *G. assimilis* whole powder: (A) glucose tolerance test (GTT) glucose levels and area under the curve; (B) insulin sensitivity test (1ST) glucose levels and area under the curve; (C) fasting blood glucose levels; (D) total cholesterol; (E) HDL cholesterol; (F) triglycerides; (G) ALT; and (H) AST. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. HDL: high-density lipoprotein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ST: palletized diet; ATN93-M: standard diet; ATN93-M + GA: standard diet addition *G. assimilis*; HFD: standard high-fat diet; FTFD + GA: high-fat diet addition of *G. assimilis*.

3.4. *Srebp-1α, Fas, Acc, and Fat* mRNA Expression. The consumption of GA edible insect wholemeal was able to promote effects at the molecular level (Figure 4). The Srebp-1α marker reduced the expression of molecular markers associated with adiposity in the group that received the edible insect wholemeal compared to the obese group ($p < 0.01$) (Figure 4 A). The low expression in the molecular pathway of fatty acid synthesis was favored by the consumption of whole insect frown ($p < 0.05$) (Figure 4B). However, the modulation in the gene expression of *Acc* could not be identified in the

https://doi.org/10.1021/acsfoodscitech.4c00013
ACS Food Sci. Technol. 2024, 4, 1632−1639

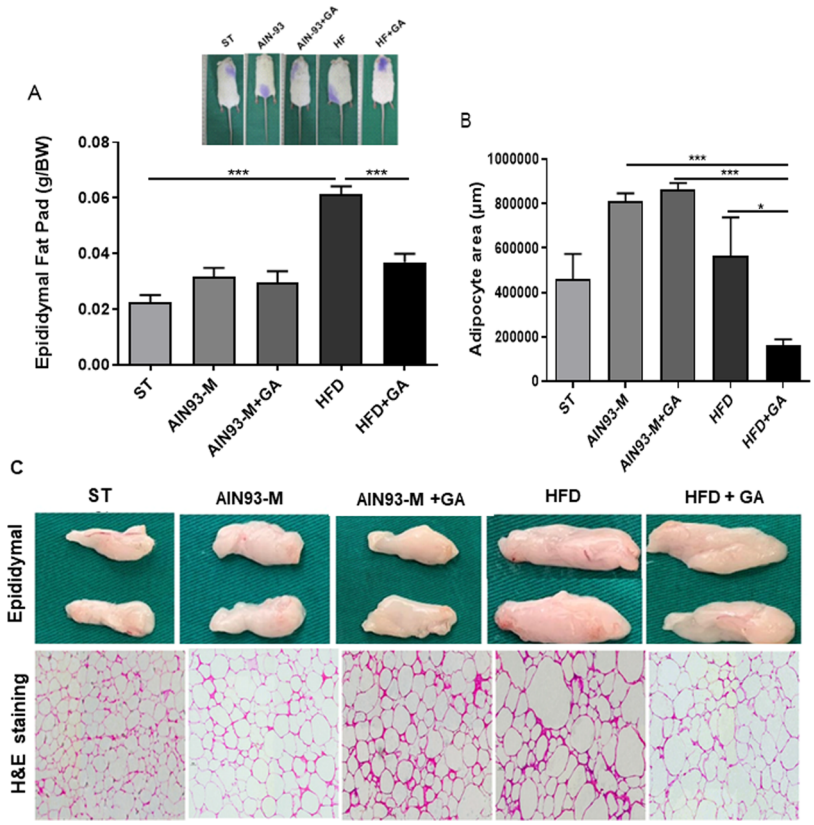

Figure 3. Epididymal adipose tissue of obese mice treated with *G. assimilis* whole powder. (A) Epididymal tissue (g/bw); (B) epididymal adipose, tissue area (μm^2); (C) histological images H&E staining. *$p < 0.05$; **$p < 0.01$; ***$p <$ Q.001: Standard diet addition *G. assimilis*; HFD: standard high-fat diet; HFD + GA: high-fat diet addition of *G. assimilis*.

present study among the groups treated and analyzed ($p > 0.05$) (Figure 4C). Our analyses also reinforce such metabolic effects via fatty acid transport mechanisms due to the low expression of *Fat* in the group that received the intervention by the edible insect powder investigated in comparison to the control group fed a high-fat diet ($p < 0.05$) (Figure 4D).

4. DISCUSSION

The search for new alternative food products with the potential to promote positive metabolic effects in obese patients is a promising research area. New functional food may generate benefits that can improve life quality being nutritional alternatives without side effects.[20] In this perspective, the present study evaluated the *G. assimilis* (GA) wholemeal powder modulation on the adipose tissue and metabolic effects in a murine model of obesity. The most relevant findings showed that edible GA supplementation improved the obese mice's metabolic regulation. The main data included a reduction in adipose tissue mass, ameliorating glycemic and lipid parameters, as well as improved adipose molecular responses.

According to the current data, the consumption of GA promoted a reduction in fat/obesity and promoted beneficial molecular modulations *in vivo*. Previous studies corroborate our results by demonstrating that oral administration of an ethanolic extract from edible insects promoted functional improvements via inhibition of lipogenesis mediated by a high-fat diet, endocrine regulation, and physiological benefits on fat metabolism and aging.[21−23]

The results could be explained by a number of methods, although earlier studies showed that the edible insect has a rich nutritional profile and beneficial chemicals. High nutritional value proteins, peptides, phenolic compounds, polysaccharides, and micronutrients were among the substances found. These compounds can alter metabolism by causing a marked reduction in intracellular lipid reserves, lowering inflammatory processes, and lowering the generation of reactive oxygen species. The synthesis of new fatty acids is minimized by lipid regulation.[24,25]

Adipose lipogenesis markers may be regulated by multiple cofactors. In the present study, fat storage was modified by the addition of edible insect powder to the animals' diet.[26] Therefore, our results confirm the effects of reducing adipose amount with specific suppression of the lipogenesis genes Srebp, Fas, and Fat.

There is already substantial evidence in the literature linking adipose gene regulation to obesity. Sterol regulatory element 1c (SREBP-1α), lipoprotein lipase (LPL), stearoyl-CoA desaturase-1 (SCD1), and fatty acid synthase (FAS), among other transcription factors, are linked to adipocyte differentiation mechanisms in the final stage of cell maturation and stimulate a new endogenous lipid synthesis at the molecular level, which is significantly higher in overweight and obese conditions.[27]

Lipid synthesis potentiates metabolic dysfunctions, also known as dyslipidemia, and strongly correlates with atherosclerotic processes.[28] Regarding this abnormality, the present study identified that GA wholemeal powder influenced lipid metabolism by ensuring the reduction of total cholesterol and

https://doi.org/10.1021/acsfoodscitech.4c00013
ACS Food Sci. Technol. 2024, 4, 1632−1639

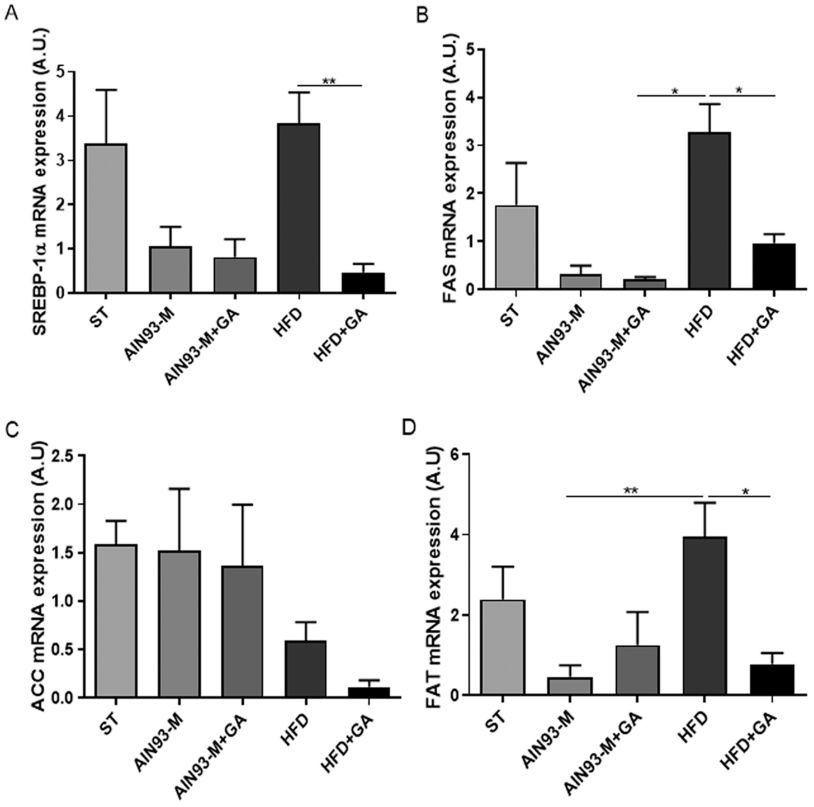

Figure 4. mKNA expression, of genes related to those of obese mice treated with *G. assimilis* whole powder: (A) SREBP-lot mRNA expression; (B) FAS mRNA expression; (C) ACC mRKA expression; (D) FAT mRKA expression; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. ST: palletized diet; ATN93-M: standard diet; ATN93-M+GA: standard diet addition *G. assimilis*; HFD: standard high-fat diet; HFD + GA: high-fat diet addition of *G. assimilis*.

triglyceride lipid fractions. Previous studies conducted in vitro have suggested that eating insects may have a hypocholesterolemic effect on lipid markers by lowering the absorption of cholesterol through the suppression of gastrointestinal enzymes when the insects are larval.[29] Thus, the potential mediator and compounds present in the insects may induce a cholesterol-lowering response, which is of great interest in developing new dietary products to improve metabolic parameters.

The physicochemical and functional traits of edible insects are linked to their functional qualities, which can be used to emphasize the presence of essential lipids, protein particles, and micronutrients like vitamins and minerals—basic components of the animal class.[30] The current study's findings demonstrated how using GA wholemeal powder may enhance insulin sensitivity and improve glycemic management. Wholemeal insects are thought to have the ability to decrease the intestinal epithelium's absorption of glucose during the postabsorptive phase, thereby lowering plasma glycemic levels.[31] Linked to these benefits, other characteristics can strengthen the potential parameter for insect-based food product use. Previous studies showed increased satiety and reduction in food intake followed by edible insect use,[32] despite no differences observed in the present data, which can be related to the type of insect, treatment period, and processing differences.

Edible crickets have innovative potential as an alternative food source of proteins and bioactive peptides. Hydrolyzed peptides from edible insects may act through different physiological mechanisms. A recent published work identified that GAs addition to the diet may ensure an antihypertensive effect with angiotensin-converting enzyme of type 2 (ACE2) modulation, improving the renin-angiotensin system (RAS) balance, and the Mas receptor (MasR) expression.[33] The peptides YKPRP, PHGAP, and VGPPQ were able to interact with the residues of the enzyme active site for hypertension control via ACE inhibition.[34,35] In addition, the histidine, arginine, and lysine amino acid sequences present in these insects act as free radical scavengers to reduce oxidative damage and improve chronic diseases associated with obesity.[35,36] Consequently, the edible GA cricket has novel possibilities as a substitute protein and bioactive peptide dietary source.

The results of this study show that consuming wholemeal powder made from GA could enhance the metabolic profile of obese mice by lowering body fat and enhancing glycemic and lipid control through the modulation of adipose lipogenic genes. The discovery of novel insect-functional foods is a promising avenue for improving obesity and related disorders. Further research on the metabolic effects of GA in other organs and metabolic disorders may be possible, as suggested by the current results.

AUTHOR INFORMATION

Corresponding Author

Sérgio Henrique Sousa Santos − *Postgraduate Program in Health Science, State University of Montes Claros (UNIMONTES), Montes Claros 39401-089, Brazil; Institute of Agricultural Sciences, Postgraduate Program in Food and Health, Federal University of Minas Gerais*

https://doi.org/10.1021/acsfoodscitech.4c00013
ACS Food Sci. Technol. 2024, 4, 1632−1639

(UFMG), Montes Claros 39404-547, Brazil; orcid.org/0000-0002-7788-5447; Phone: +55 (38)2101 7922; Email: sergiosousas@hotmail.com

Authors

Samara Cardoso de Jesus − *Postgraduate Program in Health Science, State University of Montes Claros (UNIMONTES), Montes Claros 39401-089, Brazil;* orcid.org/0000-0001-8076-2766

Guilherme Henrique Mendes Ribeiro − *Postgraduate Program in Food Science, Faculty of Food Engineering, State University of Campinas (UNICAMP), Campinas 13083-862, Brazil; Institute of Agricultural Sciences, Postgraduate Program in Food and Health, Federal University of Minas Gerais (UFMG), Montes Claros 39404-547, Brazil*

Hebert Cleiton Ferreira Souza − *Postgraduate Program in Health Science, State University of Montes Claros (UNIMONTES), Montes Claros 39401-089, Brazil*

Alfredo Mauricio Batista de Paula − *Postgraduate Program in Health Science, State University of Montes Claros (UNIMONTES), Montes Claros 39401-089, Brazil*

Lucyana Conceição Farias − *Postgraduate Program in Health Science, State University of Montes Claros (UNIMONTES), Montes Claros 39401-089, Brazil*

André Luiz Sena Guimaraes − *Postgraduate Program in Health Science, State University of Montes Claros (UNIMONTES), Montes Claros 39401-089, Brazil*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsfoodscitech.4c00013

Funding

The Article Processing Charge for the publication of this research was funded by the Coordination for the Improvement of Higher Education Personnel - CAPES (ROR identifier: 00x0ma614).

Funding

This work was partially supported by the Coordination for the Improvement of Higher Education Personnel − CAPES-Brazil, the National Council for Scientific Development − CNPQ, and the Foundation for Research Support of the State of Minas Gerais − FAPEMIG.

Notes

The authors declare no competing financial interest.

This experiment followed all the ethical principles proposed for the use of animals adopted by the Ethics Committee on Animal Experimentation and Animal Welfare of the State University of Montes Claros (UNIMONTES). It was approved under protocol number n°224/2021.

■ ACKNOWLEDGMENTS

S.C.J., study design, data analysis, and drafting of the article, G.H.M.R., and H.C.F.S. contributed data analysis and acquisition of data; S.H.S.S. reviewed it critically for the important intellectual contribution of the content presented and the submitted content. All authors read and agreed to the published version of the manuscript. The TOC Graphic was created with BioRender.com.

■ ABBREVIATIONS

GA: *Gryllus assimilis*
mRNA: messenger RNA
ST: standard
AIN93-M: American Institute of Nutrition −93 Maintenance
HFD: high-fat diet
TTG: glucose tolerance tests
IST: insulin sensitivity tests
TC: total cholesterol
HDL: high-density lipoprotein
TG: triglycerides
AST: alanine aminotransaminases
ALT: aspartate aminotransferase
H&E: hematoxylin and eosin
RT-qPCR: real-time quantitative reverse transcription
ACE: angiotensin-converting enzyme
RAS: renin-angiotensin system
MasR: Mas receptor

■ REFERENCES

(1) Bray, G. A.; Kim, K. K.; Wilding, J. P. H. Obesity: A Chronic Relapsing Progressive Disease Process. A Position Statement of the World Obesity Federation. *Obes. Rev.* **2017**, *18* (7), 715−723.

(2) De Lorenzo, A.; Romano, L.; Di Renzo, L.; Di Lorenzo, N.; Cenname, G.; Gualtieri, P. Obesity: A Preventable, Treatable, but Relapsing Disease. *Nutrition* **2020**, *71*, No. 110615.

(3) Wang, Y. C.; McPherson, K.; Marsh, T.; Gortmaker, S. L.; Brown, M. Health And Economic Burden of the Projected Obesity Trends in the USA and the UK. *Lancet* **2011**, *378* (9793), 815−825.

(4) Malkin, J. D.; Baid, D.; Alsukait, R. F.; Alghaith, T.; Alluhidan, M.; Alabdulkarim, H.; et al. The Economic Burden of Overweight and Obesity in Saudi Arabia. *PLoS One* **2022**, *17* (3), No. e0264993.

(5) Goettler, A.; Grosse, A.; Sonntag, D. Productivity Loss Due to Overweight Obesity: A Systematic Review of Indirect Costs. *BMJ Open* **2017**, *7* (10), No. e014632.

(6) Caldas, B. V.; Guimarães, V. H. D.; Ribeiro, G. H. M.; dos Santos, T. A. X.; Nobre, D. A.; de Castro, R. J. S.; da Costa, D. V.; et al. Effect of Dietary Supplementation with Tenebrio Molitor Wholemeal and Fermented Powder Modulating Adipose Lipogenesis Gene Expression in Obese Mice. *J. Insects Food Feed* **2023**, *9* (5), 625−635.

(7) Liceaga, A. M.; Aguilar-Toalá, M. E.; Vallejo-Cordoba, B.; González-Córdova, A. F.; Hernández-Mendoza, A. Insects as an Alternative Protein Source. *Annu. Rev. Food Sci. Technol.* **2022**, *13*, 19−34.

(8) Oliveira, J. R.; Cota, J.; Carvalho, B. M.; de Oliveira Costa, T.; da Costa, D. V.; Santos, S. H. S. Diet Supplementation with Madagascar Cockroach Wholemeal Powder (*Gromphadorhina portentosa*) Improved Malnourished Mice Metabolism and Ameliorated Liver Inflammatory Markers. *Recent Pat. Food, Nutr. Agric.*. **2021**, *12* (2), 112−122.

(9) Vanqa, N.; Mshayisa, V. V.; Basitere, M. Proximate, Physicochemical, Techno-Functional and Antioxidant Properties of Three Edible Insect (*Gonimbrasia belina*, *Hermetia illucens* And *Macrotermes subhylanus*) Wholemeal Powders. *Foods* **2022**, *11* (7), No. 976.

(10) Zielińska, E.; Baraniak, B.; Karaś, M. Antioxidant and Anti-Inflammatory Activities of Hydrolysates and Peptide Fractions Obtained by Enzymatic Hydrolysis of Selected Heat-Treated Edible Insects. *Nutrients* **2017**, *9*, No. 970.

(11) Araújo, R. R. S.; dos Santos Benfica, T. A. R.; Ferraz, V. P.; Santos, E. M. Nutritional Composition of Insects *Gryllus Assimilis* and *Zophobas Morio*: Potential Foods Harvested in Brazil. *J. Food Compos. Anal.* **2019**, *76*, 22−26.

(12) Nowakowski, A. C.; Miller, A. C.; Miller, M. E.; Xiao, H.; Wu, X. Potential Health Benefits of Edible Insects. *Crit. Rev. Food Sci. Nutr.* **2022**, *62* (13), 3499−3508.

(13) Quinteros, M. F.; Martínez, J.; Barrionuevo, A.; Rojas, M.; Carrillo, W. Functional, Antioxidant, and Anti-Inflammatory Proper-

ties of Cricket Protein Concentrate (*Gryllus Assimilis*). *Biology* **2022**, *11* (5), No. 776.
(14) Rice, M. C.; O'Brien, S. J. Genetic Variance of Laboratory Outbred Swiss Mice. *Nature* **1980**, *283* (5743), 157−161.
(15) Guimarães, V. H. D.; de Faria Lelis, D.; Oliveira, L. P.; Borém, L. M. A.; Guimarães, F. A. D.; Farias, L. C.; de Paula, A. M. B.; Guimarães, A. L. S.; Santos, S. H. S. Comparative Study of Dietary Fat: Lard And Sugar as a Better Obesity and Metabolic Syndrome Mice Model. *Arch. Physiol. Biochem.* **2023**, *129* (2), 49−459.
(16) Reeves, P. G.; Nielsen, F. H.; Fahey, G. C. AIN-93 Purified Diets for Laboratory Rodents: Final Report of the American Institute of Nutrition ad hoc Writing Committee on the Reformulation of the Ain-76a Rodent Diet. *J. Nutr.* **1993**, *123* (11), 1939−1951.
(17) Santos, S. H. S.; Fernandes, L. R.; Pereira, C. S.; Guimaraes, A. L. S.; de Paula, A. M. B.; Campagnole-Santos, M. J.; Alvarez-Leite, J. I.; Bader, M.; Santos, R. A. S. Increased Circulating Angiotensin-(1−7) Protects White Adipose Tissue Against Development of a Proinflammatory State Stimulated by a High-Fat Diet. *Regul. Pept.* **2012**, *178* (1−3), 64−70.
(18) Santos, S. H. S.; Braga, J. F.; Mario, E. G.; Pôrto, L. C. J.; da Glória Rodrigues-Machado, M.; Murari, A.; Botion, L. M.; Alenina, N.; Bader, M.; Santos, R. A. S. Improved Lipid and Glucose Metabolism in Transgenic Rats with Increased Circulating Angiotensin-(1−7). *Arterioscler., Thromb., Vasc. Biol.* **2010**, *30* (5), 953−961.
(19) Andrade, J. M. O.; Paraíso, A. F.; de Oliveira, M. V. M.; Martins, A. M. E.; Neto, J. F.; Guimarães, A. L. S.; de Paula, A. M. B.; Qureshi, M.; Santos, H. S. S. Resveratrol Attenuates Hepatic Steatosis in High-Fat Fed Mice by Decreasing Lipogenesis and Inflammation. *Nutrition* **2014**, *30* (7−8), 915−919.
(20) Fu, C.; Jiang, Y.; Guo, J.; Su, Z. Natural Products with Anti-obesity Effects and Different Mechanisms of Action. *J. Agric. Food Chem.* **2016**, *64* (51), 9571−9585.
(21) Seo, M.; Goo, T. W.; Chung, M. Y.; et al. Tenebrio molitor Larvae Inhibit Adipogenesis through AMPK and MAPKs Signaling in 3T3-L1 Adipocytes and Obesity in High-Fat Diet-Induced Obese Mice. *Int. J. Mol. Sci.* **2017**, *18* (3), No. 518.
(22) Park, J. H.; Nam, Y. Y.; Park, S. Y.; Kim, J. K.; Choe, N. H.; Lee, J. Y.; Oh, Y.; Suh, J. G. Silk Fibroin has a Protective Effect Against High Glucose Induced Apoptosis in HIT-T15 Cells. *J. Biochem. Mol. Toxicol.* **2011**, *25* (4), 238−243.
(23) Wang, H. Y.; Wang, Y. J.; Zhou, L. X.; Zhu, L.; Zhang, Y. Q. Isolation and Bioactivities of a Non-Sericin Component from Cocoon Shell Silk Sericin of the Silkworm *Bombyx Mori*. *Food Funct.* **2012**, *3* (2), 150−158.
(24) Ghosh, S.; Jung, S.; Meyer-Rochow, V. B. Nutritional Value and Chemical Composition of Larvae, Pupae and Adults of Worker Honey Bee Apis Mellifera Ligustica as a Sustainable Food Source. *J. Asia-Pac. Entomol.* **2016**, *19*, 487−495.
(25) Oduor-Odete, P. M.; Struszczyk, M. H.; Peter, M. G. Characterization of Chitosan from Blowfly Larvae and Some Crustacean Species from Kenyan Marine Waters Prepared Under Different Conditions. *Western Indian Ocean J. Mar. Sci.* **2007**, *4* (20), 129−142.
(26) Nguyen, P.; Kim, K.-Y.; Kim, A-Y.; Kim, N.-S.; Kweon, H.; Ji, S.-D.; Koh, Y. H. Increased Healthspan and Resistance to Parkinson's Disease in Drosophila by Boiled and Freeze-Dried Mature SilkWorm Larval Powder. *J. Asia-Pac. Entomol.* **2016**, *19* (2), 551−561.
(27) Rosen, E. D.; MacDougald, O. A. Adipocyte Differentiation from the Inside Out. *Nat. Rev. Mol. Cell Biol.* **2006**, *7* (12), 885−896.
(28) Lin, X.; Li, H. Obesity: Epidemiology, Pathophysiology and Therapeutics. *Front. Endocrinol* **2021**, *12*, No. 706978.
(29) Oliver, A. F. N.; Navarro, A. M.; Navarro, M. Á. M.; Hernández, M. L. Long-Term Effect of a Structured Health Education Programme for Diabetic Patients. *Med. Fam. Semergen* **2019**, *45* (4), e22−e23.
(30) Gravel, A.; Doyen, A. The use of Edible Insect Proteins in Food: Challenges and Issues Related to Their Functional Properties. *Innovative Food Sci. Emerging Technol.* **2020**, *59*, No. 102272.
(31) Finke, M. D. Estimate of Chitin in Raw Whole Insects. *Zoo Biol.* **2007**, *26* (2), 105−115.
(32) Skotnicka, M.; Mazurek, A.; Karwowska, K.; Folwarski, M. Satiety of Edible Insect-Based Food Products as a Component of Body Weight Control. *Nutrients* **2022**, *14* (10), No. 2147.
(33) Ribeiro, G. H. M.; Guimarães, V. H. D.; da Silva Teixeira, H. A.; Farias, L. C.; Guimarães, A. L. S.; de Paula, A. M. B.; Santos, H. S. S. Dietary Supplementation with Black Cricket (*Gryllus assimilis*) Reverses Protein-Energy Malnutrition and Modulates Renin-Angiotensin System Expression in Adipose Tissue. *Food Res. Int.* **2024**, *189*, No. 114570.
(34) Oliveira, F.; Ribeiro, L.; Liceaga, A. M. Identification and Characterization of Edible Cricket Peptides In The In Vitro Inhibition of Hypertensive and Glycemic and Their Anti-Inflammatory Activity in RAW 264.7 Macrophage Cells. *Nutrients* **2020**, *12*, No. 3588.
(35) Fashakin, O. O.; Tangjaidee, P.; Unban, K.; Klangpetch, W.; Khumsap, T.; Sringarm, K.; Rawdkuen, S.; Phongthai, S. Isolation and Identification of Antioxidant Peptides Derived from Cricket (*Gryllus bimaculatus*) Protein Fractions. *Insects* **2023**, *14* (8), No. 674.
(36) Nino, M. C.; Reddivari, L.; Osorio, C.; Kaplan, I.; Liceaga, A. M. Insects as a Source of Phenolic Compounds and Potential Health Benefits. *J. Insects Food Feed* **2021**, *7*, 1077−1087.

https://doi.org/10.1021/acsfoodscitech.4c00013
ACS Food Sci. Technol. 2024, 4, 1632−1639