Review Article **Open Access**

Tenebrio molitor-derived ingredients in obesity management: The new frontier of nutrition and health

Pietro Ragozzino-Paulino,* Maria Lucia Cocato, Jorge Eduardo de Souza Sarkis

Center of Lasers and Applications, Nuclear and Energy Research Institute, São Paulo, SP, Brazil

***Corresponding Author:** P. Ragozzino-Paulino, Center of Lasers and Applications, Nuclear and Energy Research Institute, Setor E5 - CLA (Lasers e Aplicações), Av. Prof. Almeida Prado, 2242 - Butantã, São Paulo - SP, 05508-000, Brazil

Submission date: August 21st, 2025; **Acceptance Date:** October 13th, 2025, **Publication Date:** October 24th, 2025

Please cite this article as: Ragozzino-Paulino P., Cocato M. L., Sarkis J. E. de S. *Tenebrio molitor*-derived ingredients in obesity management: The new frontier of nutrition and health. *Dietary Supplements and Nutraceuticals* 2025; 4(10): 70-86. DOI: https://doi.org/10.31989/dsn.v4i10.1751

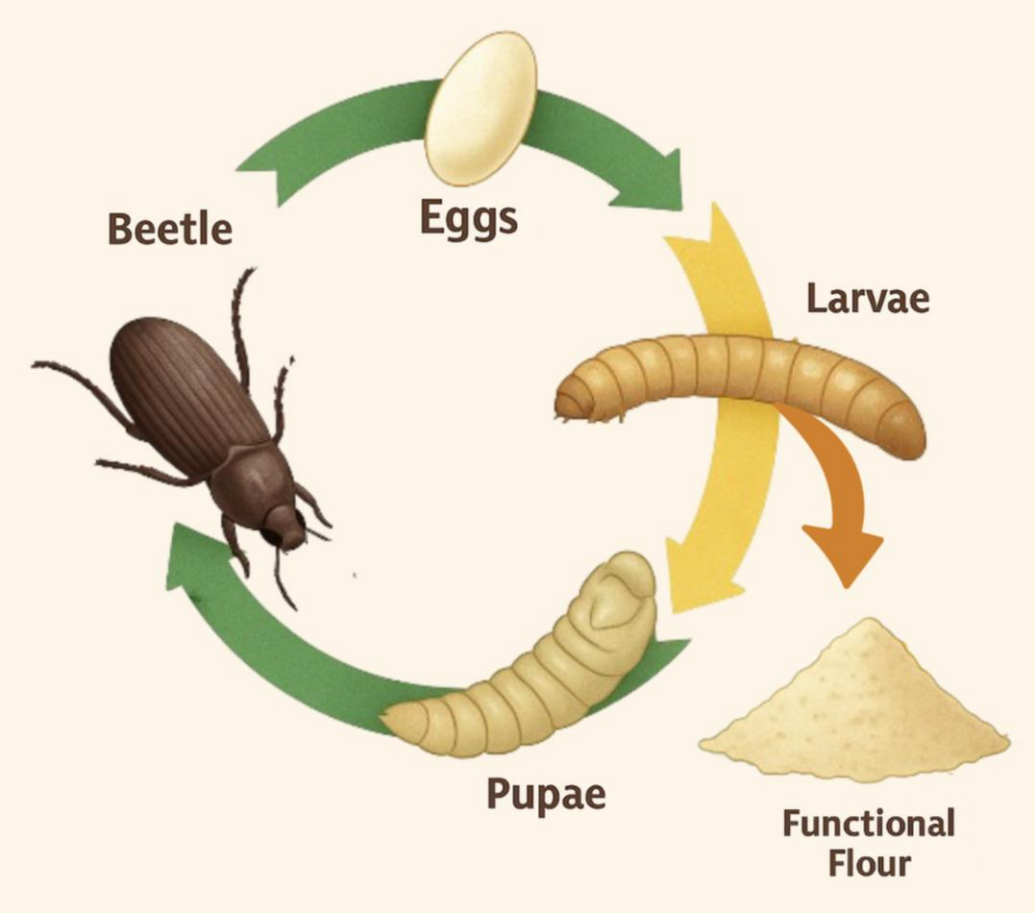
ABSTRACT

Pharmacological strategies for obesity management have advanced rapidly with GLP-1 and dual GLP-1/GIP agonists. Despite their clinical efficacy, these treatments remain costly, require ongoing use, and can cause adverse events—highlighting the need for complementary, safe, and sustainable options. *Tenebrio molitor* (yellow mealworm) has been investigated as a source of bioactive peptides and lipids with preclinical signals relevant to obesity (metabolic and inflammatory pathways) and microbiota modulation. This perspective consolidates species-specific mechanistic pathways for *T. molitor* and synthesizes them into a single translational framework with implications for nutraceutical development. Evidence from in vitro and in vivo animal models indicates that derivatives—including whole/defatted flours, protein hydrolysates, lipid extracts, and oil fractions—can suppress adipogenesis, improve lipid handling, attenuate inflammatory signaling, regulate appetite, and induce beneficial gut-microbiota shifts; collectively, these effects align with modulation of PPARα/AMPK/MAPK signaling, reduced low-grade inflammation, and engagement of gut–brain axis satiety mechanisms. Human trials with standardized *T. molitor* formulations remain limited, reinforcing the need for randomized studies with defined compositions and metabolic endpoints. Translational use also requires consideration of allergenicity (arthropod pan-allergens) and heterogeneous regulatory frameworks, emphasizing labeling and ingredient specification.

Novelty: This perspective delivers a species-specific, mechanism-first framework for *Tenebrio molitor* that unites scientific, technological, and regulatory dimensions. It provides the first integrated mechanistic map linking ingredient

classes (flours, hydrolysates, fermented extracts, oils) to pathways and metabolic outcomes, paired with a curated evidence table and concise, practice-oriented safety and regulatory guidance. By stating explicit study-selection criteria and emphasizing standardization of derivatives, dosage/delivery, and long-term safety, the paper advances functional food science with a clear translational scaffold for nutraceutical development and future targeted-outcome evaluations.

Keywords: *Tenebrio molitor*; bioactive peptides; nutraceuticals; protein hydrolysates; lipid extracts; PPARα; AMPK; MAPK; gut–brain axis; functional food science.



Graphical Abstract: Life cycle of *T. molitor.*
Created by the authors.

INTRODUCTION

Obesity remains a global public health crisis, with over 1.9 billion adults classified as overweight or obese in 2022 according to the World Health Organization (WHO) [1]. The condition is a major driver of morbidity and mortality worldwide, contributing to cardiovascular disease, type 2 diabetes, certain cancers, and reduced quality of life. Despite recent pharmacological advances, such as glucagon-like peptide-1 (GLP-1) receptor agonists and dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) receptor agonists, including semaglutide and tirzepatide, important challenges

remain. These drugs, while effective in promoting weight loss and improving metabolic health, are often costly, require long-term administration, and can be associated with gastrointestinal disturbances, gallbladder disease, and other adverse events. Moreover, discontinuation frequently leads to weight regain, highlighting the need for complementary, food-based, multi-target interventions that can be integrated into preventive and therapeutic strategies.

In this context, insects have emerged as promising and underexplored resources. Having coexisted with vertebrates for over 480 million years, insects represent a vast reservoir of bioactive molecules with both nutritional and pharmacological potential. Among the more than 2,000 edible insect species identified globally, *Tenebrio molitor* (yellow mealworm) stands out for its high nutrient density, ecological efficiency, and expanding recognition as a source of bioactive compounds capable of modulating metabolic health [2]. Within the framework of functional food science, functional foods are understood as natural or processed foods containing biologically active compounds that, in defined, effective, and non-toxic amounts, provide clinically supported health benefits via specific biomarkers [3]. In this sense, edible insects have increasingly been discussed as functional foods supplying bioactive peptides and other compounds relevant to metabolic and immune regulation, while underscoring the need for further clinical trials [4].

This perspective proposes a conceptual shift: *T. molitor* should not be regarded merely as an alternative protein source, but as a platform for developing nutraceutical ingredients—food-derived preparations intended to modulate validated health-related biomarkers under safe, defined conditions of use. Its derivatives, including whole flours, protein hydrolysates, oil fractions, and bioactive extracts, have demonstrated the capacity to suppress adipogenesis, attenuate systemic inflammation, modulate gut microbiota, and engage molecular pathways commonly targeted by anti-obesity drugs [5-6]. Consistent with the functional food paradigm, such bioactive-rich matrices typically act through multi-pathway mechanisms (e.g., antioxidant, anti-inflammatory, lipid/glucose modulation) and are evaluated through biomarker-based outcomes under specified conditions of use [7]. In line with a biomarker-centric evaluation typical of functional food science, obesity-related domains of interest include serum triglycerides and cholesterol, insulin sensitivity indices (e.g., HOMA-IR), hepatic steatosis measures, inflammatory mediators, and microbiome-derived metabolites. In parallel, recent reports illustrate microbiome-modulating nutraceutical strategies that improve dysbiosis indices alongside glycemic and lipid markers over multi-week interventions, reinforcing the translation pathway from composition to biomarker change that is mapped for *T. molitor* in this synthesis [8]. Standardized human trials evaluating *T. molitor* derivatives remain unavailable, representing a key translation gap to be addressed by future studies.

By situating *T. molitor* within the framework of modern functional foods and dietary supplements and recognizing its potential to complement current pharmacotherapies, this article aims to stimulate interdisciplinary research and innovation. As the global burden of obesity demands safe, accessible, and multi-targeted solutions, *T. molitor*-derived ingredients emerge as compelling candidates in the next generation of nutritional interventions.

Research strategy: Literature searches were performed in PubMed, Scopus, and Web of Science focusing on 2015–2025, prioritizing studies from the last 4–5 years.

Foundational sources before 2015 were considered only for conceptual or methodological context (e.g., pathway definitions, assay standards). Boolean strategies combined taxonomic, ingredient, and mechanism terms (e.g., "*Tenebrio molitor*", "mealworm", "hydrolysate", "oil", "fermented", "PPAR", "AMPK", "MAPK", "NF-κB", "SCFA", "obesity", "adipogenesis"). Inclusion criteria were primary preclinical in vitro/in vivo studies that explicitly used *T. molitor* derivatives and reported obesity-relevant outcomes and/or mechanistic readouts, with ingredient type/processing described when available. Exclusions comprised reviews/opinions, studies on other species without a *T. molitor* arm, models/outcomes not pertinent to metabolic health, and clinical reports lacking ingredient characterization. Records were screened by title/abstract and full text, with data charted on model, ingredient class/processing, dose/duration, mechanisms, and metabolic endpoints. No meta-analysis was attempted due to heterogeneity in models; instead, findings were synthesized by pathway domain and mapped to ingredient classes, as summarized in Figure 2 and Table 1.

Obesity management: gaps in current therapeutic approaches: Since 1975, the global prevalence of obesity—defined as a body mass index (BMI) ≥ 30 kg/m²—has more than tripled, reflecting profound changes in dietary patterns, physical activity, and the food environment [1]. Beyond excessive adiposity, obesity is a chronic, progressive disease characterized by systemic metabolic dysfunction, including low-grade inflammation, insulin resistance, hepatic steatosis, and impaired appetite regulation mediated by hormones such as leptin and ghrelin [9]. Pharmacological agents such as liraglutide, semaglutide, and tirzepatide have achieved unprecedented efficacy in reducing body weight and improving glycemic control by acting on both central and peripheral metabolic pathways [10]. Yet, their benefits are counterbalanced by important limitations: treatment discontinuation often leads to weight regain and gastrointestinal side effects, and high costs restrict access for the majority of the global population.

These constraints highlight the need for complementary approaches that combine multitarget metabolic efficacy with long-term safety, affordability, and accessibility. Food-derived bioactive compounds, capable of simultaneously modulating lipid metabolism, inflammation, appetite, and gut microbiota, represent a promising avenue for reshaping obesity interventions through nutritional pharmacology. These clinical realities underscore the bidirectional links between obesity and type 2 diabetes and the need for integrated strategies that address both conditions [11].

***T. molitor* as a biofunctional matrix: composition, digestion, and metabolic activity:** *T. molitor* larvae contain approximately 45–60% protein (dry basis) with high digestibility and a balanced profile of essential amino acids [12-13]. They are also rich in unsaturated fatty acids—primarily oleic, linoleic, and palmitoleic acids—along with vitamins (e.g., B12, riboflavin), minerals (e.g., iron, zinc), and chitin, a polysaccharide with fiber-like and immunomodulatory properties [12]. The oil fraction exhibits a favorable polyunsaturated-to-saturated fatty acid ratio and contains antioxidant compounds such as tocopherols and phenolics, which contribute to oxidative stability and may support cardiovascular and metabolic health [14].

Upon enzymatic digestion, either through gastrointestinal processes or targeted hydrolysis with proteases such as pepsin, trypsin, or chymotrypsin, protein-rich derivatives of *T. molitor* (such as defatted flour and protein isolates) release bioactive peptides, typically 2–20 amino acids in length. These peptides have demonstrated antioxidant, antihypertensive, anti-inflammatory, and anti-obesity activities in vitro and in vivo [12,15–19]. Hydrolysates obtained using food-grade

enzymes (e.g., alcalase, subtilisin) have shown potent inhibition of dipeptidyl peptidase-IV (DPP-IV) and angiotensin-converting enzyme (ACE), as well as iron-chelating and free radical-scavenging properties, supporting their potential for metabolic modulation [14-15].

Fermentation of *T. molitor*–based ingredients, particularly defatted flours and protein extracts, with lactic acid bacteria can enhance peptide bioavailability, stability, and immunoregulatory activity, while also increasing antioxidant potential [18,20–22]. This bioprocess promotes the release of amino acids and short-chain peptides, alongside the generation of microbial metabolites that may beneficially influence gut microbiota composition and function.

In 3T3-L1 adipocyte models, ethanolic extracts and protein hydrolysates from *T. molitor* downregulate adipogenic transcription factors (PPARγ, C/EBPα) and activate AMPK and MAPK signaling, leading to reduced lipid accumulation without cytotoxic effects [17]. Animal studies reinforce these findings: supplementation with *T. molitor*–based flours, hydrolysates, or oil fractions reduces weight gain, visceral fat, hepatic lipid content, and systemic inflammation in diet-induced obesity models. These effects are associated with upregulation of mitochondrial regulators such as FABPpm and PGC-1α, suggesting enhanced fatty-acid oxidation and energy metabolism [18,20,23–26]. Altogether, these results position *T. molitor* as a biofunctional platform capable of modulating multiple metabolic pathways through naturally derived compounds, bridging nutritional and pharmacological mechanisms in the context of obesity management.

Multitarget molecular mechanisms underlying the metabolic activity of *T. molitor*: Bioactive compounds from *T. molitor* modulate multiple pathways relevant to obesity pathophysiology, including adipogenesis, lipid metabolism, inflammation, neuroendocrine signaling, and gut microbial composition (Table 1). Figure 2 consolidates the principal signaling routes engaged across preclinical models. These processes mirror key pharmacologic targets and reinforce the potential of *T. molitor*–based ingredients as food-derived modulators of metabolic function.

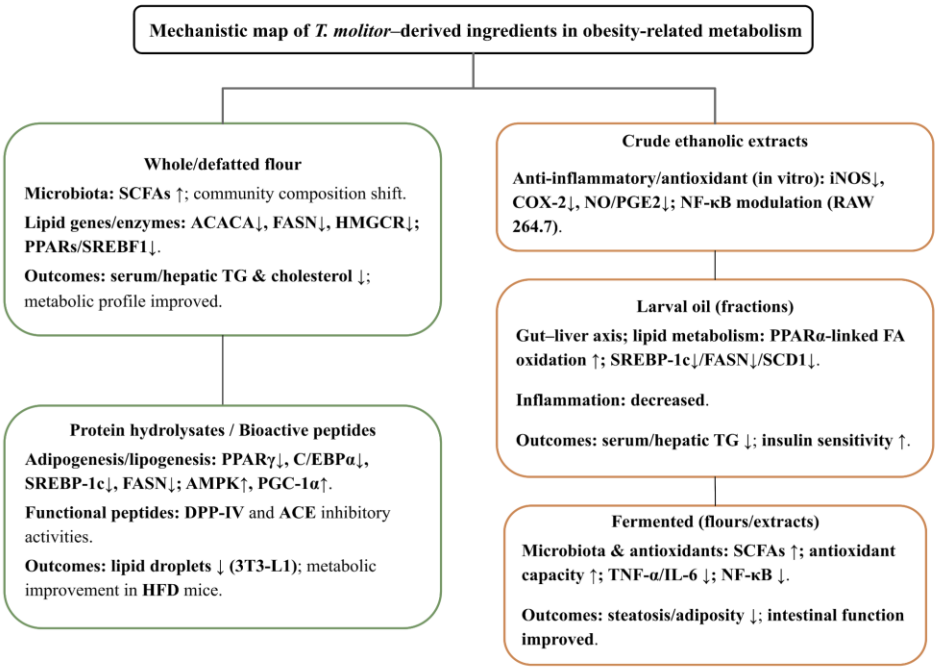


Figure 1. Mechanistic map of *T. molitor*–derived ingredients in obesity-related metabolism.

Abbreviations: 3T3-L1, mouse preadipocyte cell line; ACE, angiotensin-converting enzyme; ACACA, acetyl-CoA carboxylase alpha; AMPK, AMP-activated protein kinase; C/EBPα, CCAAT/enhancer-binding protein alpha; COX-2, cyclooxygenase-2; DPP-IV, dipeptidyl peptidase-IV; FASN, fatty acid synthase; HFD, high-fat diet; HMGCR, 3-hydroxy-3-methylglutaryl-CoA reductase; IL-6, interleukin-6; iNOS, inducible nitric oxide synthase; NF-κB, nuclear factor kappa B; NO, nitric oxide; PGE2, prostaglandin E2; PGC-1α, peroxisome proliferator-activated receptor gamma coactivator-1 alpha; PPARγ, peroxisome proliferator-activated receptor gamma; PPARs, peroxisome proliferator-activated receptors (α/γ/δ); RAW 264.7, murine macrophage cell line; SCFAs, short-chain fatty acids; SCD1, stearoyl-CoA desaturase-1; SREBF1, sterol regulatory element-binding transcription factor 1; SREBP-1c, sterol regulatory element-binding protein-1c (SREBF1 isoform); TG, triglycerides; TNF-α, tumor necrosis factor-alpha. Symbols: ↑ indicates upregulation or increase; ↓ indicates downregulation or decrease. Created by the authors.

Adipogenesis and lipid metabolism*:* Peptides and lipid fractions derived from *T. molitor* act on multiple nodes of lipid metabolism, showing a convergence of effects on both adipocyte differentiation and lipid turnover. In 3T3-L1 adipocytes, protein hydrolysates and ethanolic extracts suppress the expression of peroxisome proliferator-activated receptor gamma (PPARγ) and CCAAT/enhancer-binding protein alpha (C/EBPα)—key transcription factors in adipogenesis—while simultaneously activating AMP-activated protein kinase (AMPK) and mitogen-activated protein kinase (MAPK) signaling cascades [17]. Downstream, these actions are consistent with phosphorylation and inactivation of acetyl-CoA carboxylase (ACC), increased fatty-acid oxidation capacity, and reduced intracellular lipid droplet accumulation without compromising viability [13,29]. These observations are consistent with the convergent routes summarized in Figure 2.

In vivo experiments, these bioactive fractions exert synergistic effects. Supplementation with *T. molitor* fermentation extracts as a protein substitute in high-fat diet (HFD)–induced obese mice not only reduces body weight gain, visceral adiposity, and hepatic steatosis, but also reprograms hepatic proteomic profiles toward improved lipid handling, downregulating enzymes involved in lipogenesis (e.g., fatty acid synthase, stearoyl-CoA desaturase-1) and upregulating mitochondrial biogenesis markers such as peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1α) and fatty acid-binding protein, plasma membrane (FABPpm) [23,30-31].

Recent studies also suggest that insect-derived peptides may inhibit lipogenesis indirectly through hormonal modulation, including reduced circulating leptin and improved leptin sensitivity, as well as lowered fasting insulin levels—parameters associated with improved metabolic flexibility [23,31].

Additionally, *T. molitor* oil is enriched in oleic and linoleic acids and contains tocopherols and phenolics [32]. These features are consistent with activation of PPAR-linked fatty-acid oxidation and improvements in plasma lipids by inference from PUFA biology, but direct mechanistic confirmation with *T. molitor* oil remains limited. Available animal data show improved lipid profiles with oil [22,26] and reduced hepatic steatosis with fermented preparations [23], supporting a lipid-lowering effect while warranting targeted studies on PPARα signaling in this specific matrix. Collectively, these findings support a multitarget mechanism whereby *T. molitor* components attenuate lipid accumulation and promote oxidative metabolism (Figure 2).

Inflammatory and immunological modulation: Bioactive fractions from *T. molitor* exhibit anti-inflammatory effects through multiple cellular and molecular targets. In vitro, ethanolic extracts and protein hydrolysates suppress key pro-inflammatory mediators—IL-6, TNF-α, iNOS and COX-2—in adipose-tissue models and RAW 264.7 macrophages, alongside NF-κB inhibition [16]; in vivo, defatted *T. molitor* fermentation extract attenuates hepatic/systemic inflammation with NF-κB inhibition and favorable remodeling of the gut–liver–immune axis [33].

A deeper mechanistic layer emerges when considering AMPK-mediated immunometabolic regulation. AMPK acts as a metabolic sensor that, upon activation, can drive macrophage polarization toward the anti-inflammatory M2 phenotype and restrain inflammatory signaling cascades [28]. In parallel, activation of PPARα by lipid components—such as oleic and linoleic acids found in *T. molitor*—promotes fatty-acid oxidation and contributes to systemic anti-inflammatory effects through suppression of cytokine release [34]. In an in vivo model of chronic alcohol–induced systemic inflammation, *T. molitor* fermentation extract (MWF-1) improved hepatic steatosis, reduced pro-inflammatory cytokine expression, and beneficially remodeled gut microbiota—suggesting an axis connecting the gut, liver, and immune system [33]. In aged obese mice, oil-rich fractions of *T. molitor* produced broader benefits: beyond reducing visceral fat and serum triglycerides, they restored immune homeostasis by increasing B-cell populations and normalizing cytokine levels (IFN-γ, TNF-α, IL-2, IL-6) to values observed in young controls [22]. These effects align with the NF-κB/PPARα/AMPK crosstalk (Figure 2) and with contemporary views of PPARs as key transcriptional regulators at the interface of metabolism and inflammation [27].

Neuroendocrine and appetite regulation: Although *T. molitor* does not synthesize hormones, bioactive peptides derived from its protein hydrolysates and extracts appear to influence hypothalamic and peripheral signaling pathways involved in appetite control. In murine models, intracerebroventricular administration of *T. molitor* extracts suppressed the expression of orexigenic neuropeptides, including neuropeptide Y (NPY) and agouti-related peptide (AgRP), through activation of mTOR/MAPK signaling cascades, resulting in reduced food intake and attenuation of body weight gain in high-fat-diet–induced obese mice [31]. Beyond central mechanisms, protein hydrolysates from *T. molitor* have shown in vitro inhibition of key metabolic enzymes, such as dipeptidyl peptidase-IV (DPP-IV) and α-glucosidase, both of which play roles in postprandial glucose regulation and may indirectly influence satiety signaling [15]. These findings suggest that *T. molitor*–derived peptides could exert dual anorexigenic actions centrally via neuropeptide modulation and peripherally through improved glycemic control (Figure 2). Additionally, oil fractions of *T. molitor*, characterized by a high content of oleic and linoleic acids, have been associated with improvements in lipid metabolism and reductions in systemic inflammation, factors that may indirectly enhance satiety hormone sensitivity, including leptin and insulin signaling, thereby supporting long-term energy balance [14].

Gut microbiota modulation: Processing and fermentation of *T. molitor*–based pastes or defatted flours significantly alter their nutritional profile and bioactive compound composition, influencing interactions with the gut microbiota. Fermentation with lactic acid bacteria enhances the release of free amino acids and bioactive peptides, while increasing antioxidant activity—properties demonstrated both in vitro and in vivo in non-obese models [20,36]. These changes can promote the growth of beneficial bacterial taxa, including

lactic acid bacteria, which are associated with improved intestinal barrier function and metabolic homeostasis [37-38].

In human gut microbiota fermentation models, *T. molitor* flour provides fermentable substrates such as chitin and proteins that modulate microbial composition and activity, leading to increased production of short-chain fatty acids (SCFAs)—particularly acetate and butyrate—which are known to regulate inflammatory responses and energy metabolism [39]. Similarly, dietary inclusion of *T. molitor* meal in animal models has been shown to alter cecal microbiota composition, increasing bacterial diversity and favoring SCFA-producing taxa [24,40]. In obesity-related contexts, fermented *T. molitor* wholemeal and flour have demonstrated the ability to modulate gut microbial profiles in parallel with downregulation of adipose-tissue lipogenesis genes, suggesting a link between gut microbiota shifts and metabolic improvements [25]. In models of chronic alcohol-induced systemic inflammation, defatted fermented *T. molitor* extract modified both hepatic and intestinal parameters, reducing inflammatory cytokines and reshaping the gut microbial community [16]. Collectively, these findings indicate a microbiota-centric contribution to the metabolic benefits of *T. molitor* (Figure 2).

Table 1. Molecular pathways modulated by *T. molitor*-derived ingredients.

***T. molitor* derivative**	**Biological Process**	**Molecular Targets**	**Reported Effects**	**References**
Protein hydrolysates / ethanolic extracts	Adipogenesis; lipid metabolism	PPARγ ↓; C/EBPα ↓; AMPK ↑; (context-specific MAPK modulation); PGC-1α ↑; FABPpm ↑; PPARδ ↑	Marked reduction of lipid droplets in 3T3-L1 cells; anti-adipogenic activity without cytotoxicity; peptide fractions with antioxidant and ACE/DPP-IV-modulating actions; improved body weight, fat mass, hepatic steatosis and plasma lipids in HFD mice.	Seo et al. [17]; Song et al. [5]; Rivero-Pino et al. [15]
Oil fractions (larval oil)	Lipid metabolism; gut–liver axis; inflammation	PPARα ↑; SREBP-1c ↓; FASN ↓; SCD1 ↓	↓ Serum triglycerides; ↑ reduced hepatic steatosis; improved lipid profile; modulated PUFA ratios; antioxidant constituents (e.g., tocopherols) supporting oxidative stability of the oil	Mun et al. [22]; Martínez-Pineda et al. [32]
Fermented extracts / fermented flours	Gut microbiota; inflammation; antioxidant activity	↑ antioxidant capacity; cytokines TNF-α ↓, IL-6 ↓; ↑ SCFA production (human fecal in-vitro fermentation); shifts in microbiota composition	Enhanced antioxidant properties after LAB fermentation; attenuation of steatosis and inflammatory markers in HFD mice; modulation of intestinal microbiota (rats, alcohol model); increased SCFA and favorable microbial changes in vitro	Kim et al. [20]; Ham et al. [23]; Choi et al. [33]; de Carvalho et al. [39]
Whole / defatted meal or flour	Systemic lipid metabolism; gut microbiota	ACACA/FASN/HMGCR ↓; FASN ↓, G6PD ↓; PPARγ ↓; SCFA ↑ (human fecal in-vitro fermentation)	Serum and hepatic triglycerides and cholesterol ↓; improved metabolic profile in obese rodents; cecal microbiota modulation in pigs and broilers; SCFA ↑ (in vitro).	Meyer et al. [24,41]; Biasato et al. [42]; de Carvalho et al. [39]; Gessner et al. [13]; Ham et al. [23]; Kang et al. [30]
Crude ethanolic extracts (e.g., exoskeleton)	Anti-inflammatory; antioxidant activity	iNOS ↓; COX-2 ↓; NO/PGE2 ↓ in RAW 264.7; NF-κB pathway modulation in vivo	Anti-inflammatory effects in RAW 264.7; improved hepatic/inflammatory markers in rodents	Yu et al. [16]; Choi et al. [33]; Navarro del Hierro et al. [43]

T. molitor derivative	Biological Process	Molecular Targets	Reported Effects	References
Whole proteins / oral extract administration	Neuroendocrine appetite regulation	mTOR/AMPK signaling (peripheral); hypothalamic NPY ↓ and AgRP ↓ (ICV)	Reduced food intake and body-weight gain after neuroendocrine / metabolic modulation	Seo et al. [17,35]
Saccharomyces-fermented defatted *T. molitor* larvae extract	Gut microbiota; antioxidant activity	↑ DPPH scavenging; ↑ FRAP activity; ↑ phenolic/flavonoid content	Increased antioxidant potential; supports sustainable protein-ingredient production	Kang et al. [44]
Concurrent hydrolysis–fermentation by *Lactobacillus plantarum* KCCM13068P	Inflammation; gut health	TNF-α ↓; IL-6 ↓; NO ↓ in RAW 264.7;	Attenuated inflammation in RAW 264.7; alleviated constipation in loperamide-induced mice	Jo et al. [21]

Abbreviations: 3T3-L1, mouse preadipocyte cell line; ACACA, acetyl-CoA carboxylase alpha; ACE, angiotensin-converting enzyme; AgRP, agouti-related peptide; AMPK, AMP-activated protein kinase; C/EBPα, CCAAT/enhancer-binding protein alpha; COX-2, cyclooxygenase-2; DPP-IV, dipeptidyl peptidase-IV; DPPH, 2,2-diphenyl-1-picrylhydrazyl; FABPpm, plasma membrane fatty acid-binding protein; FASN, fatty acid synthase; FRAP, ferric reducing antioxidant power; G6PD, glucose-6-phosphate dehydrogenase; HFD, high-fat diet; HMGCR, 3-hydroxy-3-methylglutaryl-CoA reductase; ICV, intracerebroventricular; IL-6, interleukin-6; iNOS, inducible nitric oxide synthase; MAPK, mitogen-activated protein kinase; mTOR, mechanistic target of rapamycin; NF-κB, nuclear factor kappa B; NO, nitric oxide; NPY, neuropeptide Y; PGE2, prostaglandin E2; PGC-1α, peroxisome proliferator-activated receptor gamma coactivator-1 alpha; PPARα, peroxisome proliferator-activated receptor alpha; PPARδ (PPARβ/δ), peroxisome proliferator-activated receptor delta; PPARγ, peroxisome proliferator-activated receptor gamma; PUFA, polyunsaturated fatty acids; RAW 264.7, murine macrophage cell line; SCD1, stearoyl-CoA desaturase-1; SCFA, short-chain fatty acids; SREBP-1c, sterol regulatory element-binding protein-1c; TNF-α, tumor necrosis factor-alpha. **Symbols:** ↑ indicates upregulation or increase; ↓ indicates downregulation or decrease.

Bridging nutrition with pharmacology: the case for *T. molitor*-derived ingredients: The boundary between food and pharmacology is increasingly blurred. Bioactive peptides generated by gastrointestinal digestion or targeted hydrolysis of *T. molitor* proteins modulate pathways relevant to metabolic syndrome, including lipid metabolism, inflammatory signaling, and glycemic control, in preclinical models [12,16-17,36]. In vitro, mealworm protein hydrolysates produced with food-grade proteases inhibit dipeptidyl peptidase-IV (DPP-IV) and angiotensin-converting enzyme (ACE), and display antioxidant/metal-chelating activities that support redox balance and vascular function [15]. These peptide-level actions align with pharmacological targets in metabolic syndrome while originating from a food matrix.

Beyond peptides, *T. molitor* oils provide complementary effects. Recent characterizations report a fatty-acid profile enriched in oleic and linoleic acids alongside tocopherols and phenolics contribute to antioxidant capacity and oxidative stability [28]. In animal models, *T. molitor* oil and fermented extracts improve plasma lipids, reduce hepatic steatosis, and blunt low-

grade inflammation [22-23]; PPAR-linked pathways are implicated but require confirmation specifically for the mealworm oil matrix. Fermented preparations produced with selected lactic acid bacteria further enhance peptide bioavailability and antioxidant activity and generate postbiotic metabolites that may benefit gut and systemic immunity [20,25,36].

Importantly, whole and partially defatted flours deliver a composite matrix—proteins and peptides, bioactive lipids, chitin, vitamins, and minerals—that can act synergistically on adipogenesis, lipid handling, and immunomodulation [19,38,45]. When benchmarked against established protein sources, *T. molitor* derivatives—whether hydrolysates, oils, fermented extracts, or whole meals—have shown comparable or, in some cases, greater efficacy in preclinical models in suppressing adipogenesis, improving lipid metabolism, and dampening inflammatory responses across in vitro and in vivo systems [13,20,23,35,45]. From a translational standpoint, these ingredients are already compatible with multiple delivery formats (e.g., powders for beverages, protein-enriched snacks, encapsulated extracts), facilitating their integration into preventive nutrition and adjunctive metabolic care. Coupled with the well-documented environmental advantages of insect farming, substantially lower feed, water, and greenhouse-gas footprints than conventional livestock. This strengthens the case for *T. molitor* as a scalable, low-impact biofunctional platform [46].

Safety and regulatory considerations: *T. molitor* has been assessed by EFSA and authorized in the EU under Commission Implementing Regulation (EU) 2022/169 for frozen, dried, and powder forms of yellow mealworm larvae, with allergy labeling required—particularly for individuals allergic to crustaceans or dust mites [47–49]. Authors, manufacturers, and practitioners should verify the most current implementing acts and product-specific conditions of use before commercialization; subsequent EU acts/opinions have also addressed additional forms (e.g., UV-treated powder) within the novel food framework, reinforcing labeling and conditions of use [50]. Outside the EU, requirements are jurisdiction-specific: Singapore maintains a positive list of insect species permitted for human consumption that explicitly includes *T. molitor* (life stage specified) with sourcing/processing controls [51]; in Australia, guidance indicates *T. molitor* may be produced/imported for human consumption under the FSANZ/novel foods framework, with GMP/HACCP and labeling compliance [52]; in Canada, Health Canada conducts case-by-case novel food assessments, publishing no-objection decisions at the product/formulation level rather than blanket species approvals [53]. Where insect-specific contaminant limits are not yet defined, general EU limits for contaminants in food (e.g., Regulation (EU) 2023/915) can serve as interim benchmarks [54].

Regarding allergenicity, EFSA concluded that authorized forms are safe under specified conditions of use but require allergy warnings because of potential IgE cross-reactivity—notably via tropomyosin and arginine kinase—in individuals sensitized to crustaceans or dust mites [48-49]. Recent IgE-based studies further support an association between mealworm sensitization and shrimp/house-dust-mite allergy, reinforcing precautionary labeling for at-risk consumers [55]. In occupational settings (rearing/processing), respiratory sensitization to insect proteins is frequent, justifying preventive controls (engineering/administrative controls and PPE) and B2B allergen statements along the supply chain [52]. Notably, common processing steps (e.g., heating) may not eliminate allergenic risk because some pan-allergens are heat-stable; therefore, allergen labeling remains indicated even after thermal processing or fermentation [48,49,57]. Where local regulations allow, manufacturers should also maintain a batch-level

allergen risk assessment (including environmental monitoring in facilities handling crustaceans/dust mites) to inform periodic label review and post-market surveillance [48-49,56].

With respect to stability, primary data indicates good microbiological robustness of powders and lyophilized materials under controlled water activity (aw) and protective packaging, while overall stability remains matrix-dependent and linked to processing parameters (blanching, drying) and storage conditions. Rather than a universal duration claim, stability should be supported by matrix-specific evidence with explicit aw/packaging details, as shown by Yan et al. and Ribeiro et al. (process routes; effects of blanching/storage/drying; microbiological and physicochemical quality) [58-59].

Finally, overall safety hinges on process controls. Standardization of rearing substrates, processing steps, and routine contaminant monitoring (heavy metals, mycotoxins) should be described in methods and reflected in labeling [25,45,60–63]. *T. molitor* can bioaccumulate Cd, Pb, As from contaminated substrates, making feed-source quality a critical control point [60–62]. Mycotoxin monitoring is likewise essential, as mold-contaminated feed can lead to carry-over (e.g., aflatoxins, ochratoxin A) into final products [58-59]. Controlled trials show that larvae reared on different feed streams (industrial feed waste vs. farm by-products) can present distinct heavy-metal and microbial profiles, underscoring the need for validated substrate specifications and surveillance [54,63].

Translational potential and research priorities: To fully understand the potential of *T. molitor*–derived bioactives in obesity management, future research should address converging priorities that bridge promising preclinical results to validated human applications:

- Comprehensive peptidomic and lipidomic profiling. Essential to resolve structure–function relationships underlying anti-adipogenic, anti-inflammatory, and microbiota-modulating effects. Priority actions include batch-to-batch comparability, identification/quantification of sentinel peptides and lipid signatures (e.g., oleic/linoleic–rich fractions), and linking composition to PPAR/AMPK/MAPK and gut–brain axis readouts.
- Human clinical evidence—gap and priorities. To date, no randomized controlled trials in humans have tested *T. molitor* derivatives for obesity-related endpoints. Phase II RCTs should use standardized derivatives (defined hydrolysate or oil), validated dosing, and well-defined target populations (overweight/obesity with metabolic dysfunction). Prespecify primary endpoints (e.g., DXA fat mass, HOMA-IR) and secondary outcomes (fasting lipids, hepatic fat by imaging where feasible, hs-CRP/cytokines, tolerability). Include gut microbiome/SCFA profiling, allergen screening, and robust safety monitoring. Designs of 8–12 weeks to establish signal, followed by ≥24-week studies for weight maintenance and durability, would directly address this evidence gap.
- Long-term safety evaluations. Go beyond acute toxicity and allergenicity to address potential bioaccumulation of contaminants, interactions with anti-obesity pharmacotherapies, and effects in vulnerable populations (e.g., immune impairment). Incorporate exposure modeling, monitoring metals/mycotoxins, and post-market surveillance frameworks aligned with labeling.
- Development and standardization of *T. molitor* derivatives. Advance functional flours, concentrated protein/peptide extracts, refined oils, and fermented products with consistent bioactive content, oxidative stability, and sensory

acceptability. Harmonize processing, storage, and shelf-life protocols (including aw and packaging specs) and report critical quality attributes that predict biological activity.

- Cross-sector collaboration. Coordinate nutrition scientists, entomologists, food technologists, clinicians, and regulators to set composition/quality standards, validate health claims, and align safety criteria across jurisdictions. Shared reference materials and open analytical methods will accelerate reproducibility and scale-up.

By integrating omics-based discovery, clinical validation, and regulatory harmonization, *T. molitor* can progress from a promising functional ingredient to a scientifically credible nutraceutical platform for obesity prevention and management.

CONCLUSION

There is increasing interest in the interface between nutrition and pharmacology. *T. molitor* hydrolysates, oil fractions, and fermented or enzymatically derived extracts are biologically complex matrices with potential multi-target activity when produced under rigorously controlled hygienic, microbiological, and processing standards. Emerging preclinical and translational evidence indicates the capacity to attenuate weight gain, improve lipid metabolism, modulate gut microbiota composition, and reduce systemic inflammation through a naturally digested matrix of synergistic bioactive compounds. Nevertheless, findings remain heterogeneous across models and preparations, underscoring the need for standardized characterization and replication.

While pharmacological agents such as semaglutide and tirzepatide have transformed obesity treatment, *T. molitor*–derived bioactives should be considered as complementary nutritional modulators that may operate within pathways relevant to metabolic regulation. Realizing any translational value will require comprehensive peptide and lipidomic profiling, dose–formulation optimization, tissue-specific mechanistic investigations, and adequately powered randomized clinical trials to evaluate efficacy and safety in diverse populations, including long-term follow-up and assessment of real-world use.

Given the scalability and sustainability of insect farming, further investigation is warranted to define appropriate conditions of use, target populations, and regulatory pathways, alongside consistent reporting of composition, processing parameters, and quality controls. A cautious, evidence-led approach is essential to determine where *T. molitor* derivatives fit within nutrition-based strategies for obesity management. Thus, the task ahead is not to justify use but to optimize it through standardized derivatives, validated dosing, and defined target populations to deliver clinically meaningful benefits with established safety.

List of Abbreviations: ACE: Angiotensin-converting enzyme; ACACA: Acetyl-CoA carboxylase alpha; AgRP: Agouti-related peptide; AMPK: AMP-activated protein kinase; BMI: Body mass index; C/EBPα: CCAAT/enhancer-binding protein alpha; COX-2: Cyclooxygenase-2; DPP-IV: Dipeptidyl peptidase-IV; FABPpm: Plasma membrane fatty acid-binding protein; FASN: Fatty acid synthase; GIP: Glucose-dependent insulinotropic polypeptide; GLP-1: Glucagon-like peptide-1; HDL: High-density lipoprotein; HFD: High-fat diet; HMGCR: 3-hydroxy-3-methylglutaryl-CoA reductase; IL-6: Interleukin-6; iNOS: Inducible nitric oxide synthase; LDL: Low-density lipoprotein; MAPK: Mitogen-activated protein kinase; mTOR: Mechanistic target of rapamycin; NF-κB: Nuclear factor kappa B; NO: Nitric oxide; NPY: Neuropeptide Y; PGE2: Prostaglandin E2; PGC-1α: Peroxisome proliferator-activated receptor

gamma coactivator-1 alpha; PPARα: Peroxisome proliferator-activated receptor alpha; PPARδ: Peroxisome proliferator-activated receptor delta; PPARγ: Peroxisome proliferator-activated receptor gamma; PUFA: Polyunsaturated fatty acids; SCD1: Stearoyl-CoA desaturase-1; SCFA: Short-chain fatty acids; SREBP-1c: Sterol regulatory element-binding protein-1c; *T. molitor: Tenebrio molitor*; TNF-α: Tumor necrosis factor-alpha; WHO: World Health Organization.

Authors' Contribution: All authors contributed equally to the manuscript.

Competing Interests: The authors declare no competing interests.

Acknowledgments: The Nuclear and Energy Research Institute (IPEN) and the FINEP PROTINA project (nº 01.23.0776.00) by fellowship.

REFERENCES

1. World Health Organization (WHO). Obesity and overweight. 2023.https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.Retrieved on October 20th,2025
2. Zhang G, Wang Y, Liang Z, Guo J, Wu B. Nutritional value and advances of mealworm (*Tenebrio molitor*) as a sustainable functional ingredient in bakery products: A key step toward sustainable diets. Future Foods. 2025; 12:100716. DOI: https://doi.org/10.1016/j.fufo.2025.100716.
3. Martirosyan D. Functional Food Science and Bioactive Compounds. *Bioactive Compounds in Health and Disease*. 2025;8(6):218–229. DOI: https://doi.org/10.31989/bchd.v8i6.1667.
4. Iriti M, Vallone L, Vitalini S. Edible insects – a new trend in functional food science. *Functional Food Science*. 2022;2(7):157–162. DOI: https://doi.org/10.31989/ffs.v2i7.93.
5. Song Y, Gu H, Jo JM, Shin M, Kim SY, Gam DH, Imamura S, Kim JW. Production of functional peptide with anti-obesity effect from defatted *Tenebrio molitor* larvae using proteolytic enzyme. Biotechnology and Bioprocess Engineering. 2020; 25:374–383. DOI: https://doi.org/10.1007/s12257-019-0329-6.
6. Costa LFE. Larvas de *Tenebrio molitor* como modelo in vivo para estudos de obesidade: uma abordagem inicial. Natal (BR): Universidade Federal do Rio Grande do Norte; 2024. 45
7. Soumya NP, Mini S, Sivan SK, Mondal S. Bioactive compounds in functional foods and their role as therapeutics. *Bioactive Compounds in Health and Disease*. 2021;4(3):24–39. DOI: https://doi.org/10.31989/bchd.v4i3.786.
8. Natale F, Fusco C, Limatola M, Cante L, Alfieri R, Mollo N, et al. Gut Microbiome modulation in patients treated with an enriched nutraceutical composition: A multi target strategy. *Functional Foods in Health and Disease*. 2024;14(12):883–897. DOI: https://doi.org/10.31989/ffhd.v14i12.1437.
9. Chandrasekaran P, Weiskirchen R. The role of obesity in type 2 diabetes mellitus—An overview. International Journal of Molecular Sciences. 2024;25(3):1882. DOI: https://doi.org/10.3390/ijms25031882.
10. Blüher M, Aras M, Aronne LJ, Batterham RL, Giorgino F, Ji L, Pietiläinen KH, Schnell O, Tonchevska E, Wilding JPH. New insights into the treatment of obesity. Diabetes, Obesity and Metabolism. 2023;25(8):2058–2072. DOI: https://doi.org/10.1111/dom.15077.
11. Ruze R, Liu T, Zou X, Song J, Chen Y, Xu R, Yin X, Xu Q. Obesity and type 2 diabetes mellitus: connections in epidemiology, pathogenesis, and treatments. Frontiers in Endocrinology. 2023; 14:1161521. DOI: https://doi.org/10.3389/fendo.2023.1161521.
12. Stephan MP, de Souza Sarkis JE, da Rosa JS, Cocato ML. *Tenebrio molitor*: investigating the scientific foundations and proteomic and peptidomic potential. Food and Nutrition Sciences. 2025; 16:427–435. DOI: https://doi.org/10.4236/fns.2025.164024.
13. Gessner DK, Schwarz A, Meyer S, Wen G, Most E, Zorn H, Ringseis R, Eder K. Insect meal as alternative protein source exerts pronounced lipid-lowering effects in hyperlipidemic obese Zucker rats. The Journal of Nutrition. 2019; 149:566–577. DOI: https://doi.org/10.1093/jn/nxy256.
14. Martínez-Pineda B, Yagüe-Ruiz C, Hernández-Hernández O, García-González A, Pineda-Quiroga C, Rojas-Carvajal M, Torres A, Sánchez-Muros MJ, Barroso FG. Nutritional composition, antioxidant activity and oxidative stability of *Tenebrio molitor* larval oil: Potential as a functional lipid ingredient. Food Chemistry. 2024; 430:137096. DOI: https://doi.org/10.1016/j.foodchem.2024.137096.
15. Rivero-Pino F, Espejo-Carpio FJ, Guadix EM, Guadix A. Antioxidant and antihypertensive properties of peptide

fractions from protein hydrolysates of *Tenebrio molitor*. Food & Function. 2020; 11:4376–4386. DOI: https://doi.org/10.1039/D0FO00660H.

16. Yu J-M, Jang J-Y, Kim H-J, Cho U-H, Kim D-I, Kwon O-J, Cho Y-J, An B-J. Antioxidant capacity and RAW 264.7 macrophage anti-inflammatory effect of *Tenebrio molitor*. Korean Journal of Food Preservation. 2016;23(6):890–898. DOI: https://doi.org/10.11002/kjfp.2016.23.6.890.
17. Seo M, Goo TW, Chung MY, Baek M, Hwang JS, Kim MA, Yun EY. *Tenebrio molitor* larvae inhibit adipogenesis through AMPK and MAPKs signaling in 3T3-L1 adipocytes and obesity in high-fat diet–induced obese mice. International Journal of Molecular Sciences. 2017;18(3):518. DOI: https://doi.org/10.3390/ijms18030518.
18. Park BM, Lim HJ, Lee BJ. Anti-obesity effects of *Tenebrio molitor* larvae powder in high-fat diet–induced obese mice. Journal of Nutrition and Health. 2021;54(4):342–354. DOI: https://doi.org/10.4163/jnh.2021.54.4.342.
19. Kang Y, Oba PM, Gaulke CA, Sánchez-Sánchez L, Swanson KS. Dietary inclusion of yellow mealworms (*Tenebrio molitor*) and lesser mealworms (*Alphitobius diaperinus*) modifies intestinal microbiota populations of diet-induced obesity mice. Journal of Nutrition. 2023;153(11):3220–3236. DOI: https://doi.org/10.1016/j.tjnut.2023.09.007.
20. Kim SH, Jang JS, Kim EH, Lee WH, Yu YH, Kim HJ, Huh CK. Physicochemical fermentation characteristics and changes in antioxidant activity of mealworms (*Tenebrio molitor*) during fermentation with lactic acid bacteria: Application and selection of commercial lactic acid bacteria starters. Applied Food Research. 2025;5(1):100811. DOI: https://doi.org/10.1016/j.afres.2025.100811.
21. Jo H-S, Song D-B, Lee S-H, Lee K-S, Yang J, Hong S-M. Concurrent hydrolysis–fermentation of *Tenebrio molitor* protein by *Lactobacillus plantarum* KCCM13068P attenuates inflammation in RAW 264.7 macrophages and constipation in loperamide-induced mice. Foods. 2025;14(11):1886. DOI: https://doi.org/10.3390/foods14111886.
22. Mun SK, Jang CJ, Jo S, Park SH, Sim HB, Ramos SC, Kim H, Choi YJ, Park DH, Park KW, Jeong BG, Kim DH, Kang KY, Kim JJ. Anti-obesity and immunomodulatory effects of oil and fermented extract dried from *Tenebrio molitor* larvae on aged obese mice. Animal Cells and Systems. 2024;28(1):340–352. DOI: https://doi.org/10.1080/19768354.2024.2374547.
23. Ham JR, Choi R-Y, Lee Y, Lee M-K. Effects of edible insect *Tenebrio molitor* larva fermentation extract as a substitute protein on hepatosteatogenesis and proteomic changes in obese mice induced by high-fat diet. International Journal of Molecular Sciences. 2021;22(7):3615. DOI: https://doi.org/10.3390/ijms22073615.
24. Meyer S, Schäfer L, Röhrig J, Maheshwari G, Most E, Zorn H, Ringseis R, Eder K, Gessner DK. Supplementation of sulfur-containing amino acids or essential amino acids does not reverse the hepatic lipid-lowering effect of a protein-rich insect meal in obese Zucker rats. Nutrients. 2020; 12:987. DOI: https://doi.org/10.3390/nu12040987.
25. Caldas BV, Guimarães VHD, Ribeiro GHM, dos Santos TAX, Nobre DA, de Castro RJS, Vieira LGM, Santos SHS. Effect of dietary supplementation with *Tenebrio molitor* wholemeal and fermented flour modulating adipose lipogenesis gene expression in obese mice. Journal of Insects as Food and Feed. 2023;9(5):625–636. DOI: https://doi.org/10.3920/JIFF2022.0145.
26. Mun SK, Ramos SC, Kang KY, et al. Lipid metabolism modulation by *Tenebrio molitor* oil supplementation in obese mouse models. Food Research International. 2025; 180:113223. DOI: https://doi.org/10.1016/j.foodres.2025.113223.
27. Vázquez-Carrera M, Wahli W. PPARs as key transcription regulators at the crossroads of metabolism and inflammation. *Int J Mol Sci*. 2024;25(8):4467. DOI: https://doi.org/10.3390/ijms25084467.
28. Cui Y, Chen J, Zhang Z, Shi H, Sun W. The role of AMPK in macrophage metabolism, function and polarization. Journal of Translational Medicine. 2023; 21:892. DOI: https://doi.org/10.1186/s12967-023-04772-6.
29. Xue W, Zhang B, Wu B, Xiao H, Li Z, Li R, Xu X, Li T. Signaling pathways in obesity: mechanisms and therapeutic interventions. Signal Transduction and Targeted Therapy. 2022; 7:298. DOI: https://doi.org/10.1038/s41392-022-01149-x.
30. Kang Y, Applegate CC, He F, Oba PM, Vieson MD, Sánchez-Sánchez L, Swanson KS. Yellow mealworm (*Tenebrio molitor*) and lesser mealworm (*Alphitobius diaperinus*) proteins slowed weight gain and improved metabolism of diet-induced obesity mice. Journal of Nutrition. 2023;153(8):2237–2248. DOI: https://doi.org/10.1016/j.tjnut.2023.06.014.
31. Tarahi M, Aghababaei F, McClements DJ, Pignitter M, Hadidi M. Bioactive peptides derived from insect proteins: preparation, biological activities, potential applications, and safety issues. Food Chemistry. 2025;465(Pt 1):142113. DOI: https://doi.org/10.1016/j.foodchem.2024.142113.
32. Martínez-Pineda M, Juan T, Antoniewska-Krzeska A, Vercet

A, Abenoza M, Yagüe-Ruiz C, Rutkowska J. Exploring the potential of yellow mealworm (*Tenebrio molitor*) oil as a nutraceutical ingredient. Foods. 2024;13(23):3867. DOI: https://doi.org/10.3390/foods13233867.

33. Choi RY, Ham JR, Ryu HS, Lee SS, Miguel MA, Paik M, Ji M, Park KW, Kang KY, Lee HI, et al. Defatted *Tenebrio molitor* larva fermentation extract modifies steatosis, inflammation and intestinal microflora in chronic alcohol-fed rats. Nutrients. 2020; 12:1426. DOI: https://doi.org/10.3390/nu12051426.
34. Hu P, Li K, Peng X, Kan Y, Li H, Zhu Y, et al. Nuclear receptor PPARα as a therapeutic target in diseases associated with lipid metabolism disorders. Nutrients. 2023;15(22):4772. DOI: https://doi.org/10.3390/nu15224772.
35. Seo M, Kim J, Moon SS, Hwang JS, Kim MA. Intraventricular administration of *Tenebrio molitor* larvae extract regulates food intake and body weight in mice with high-fat diet–induced obesity. Nutrition Research. 2017; 44:18–26. DOI: https://doi.org/10.1016/j.nutres.2017.05.011.
36. Borremans A, Bußler S, S Sagu T, Rawel HM, Schlüter O, Van Campenhout L. Functional properties of powders produced from either or not fermented mealworm (*Tenebrio molitor*) paste. bioRxiv. 2020. DOI: https://doi.org/10.1101/2020.04.17.042556.
37. Ferrazzano GF, D'Ambrosio F, Caruso S, Gatto R, Caruso S. Bioactive peptides derived from edible insects: Effects on human health and possible applications in dentistry. Nutrients. 2023;15(21):4611. DOI: https://doi.org/10.3390/nu15214611.
38. Kipkoech C. Beyond proteins—edible insects as a source of dietary fiber. Polysaccharides. 2023; 4:116–128. DOI: https://doi.org/10.3390/polysaccharides4020009.
39. de Carvalho NM, Walton GE, Poveda CG, Silva SN, Amorim M, Madureira AR, Pintado ME, Gibson GR, Jauregi P. Study of in vitro digestion of *Tenebrio molitor* flour for evaluation of its impact on the human gut microbiota. Journal of Functional Foods. 2019; 59:101–109. DOI: https://doi.org/10.1016/j.jff.2019.05.024.
40. Mahayri TM, Atallah E, Fliegerová KO, Mrázek J, Piccolo G, Bovera F, Moniello G. Inclusion of *Tenebrio molitor* larvae meal in the diet of Barbary partridge (*Alectoris barbara*) improves caecal bacterial diversity and composition. Scientific Reports. 2024; 14:29600. DOI: https://doi.org/10.1038/s41598-024-80341-1.
41. Meyer S, Gessner DK, Maheshwari G, Röhrig J, Friedhoff T, Most E, Zorn H, Ringseis R, Eder K. *Tenebrio molitor* larvae meal affects the cecal microbiota of growing pigs. Animals (Basel). 2020;10(7):1151. DOI: https://doi.org/10.3390/ani10071151.
42. Biasato I, Ferrocino I, Grego E, Dabbou S, Gai F, Gasco L, Cocolin L, Capucchio MT, Schiavone A. Gut microbiota and mucin composition in female broiler chickens fed diets including yellow mealworm (*Tenebrio molitor*). Animals. 2019;9(5):213. DOI: https://doi.org/10.3390/ani9050213.
43. Navarro del Hierro J, Cantero-Bahillo E, Fernández-Felipe MT, García-Risco MR, Fornari T, Rada P, et al. Effects of a mealworm (*Tenebrio molitor*) extract on metabolic-syndrome-related pathologies: in vitro insulin sensitivity, inflammatory response, hypolipidemic activity and oxidative stress. Insects. 2022;13(10):896. DOI: https://doi.org/10.3390/insects13100896.
44. Kang K-Y, Jeong B-G, Kim J-H, Park K-W. Enhanced antioxidant properties of *Saccharomyces*-fermented defatted *Tenebrio molitor* larvae extract: a sustainable alternative protein source. Fermentation. 2025;11(5):272. DOI: https://doi.org/10.3390/fermentation11050272.
45. Psarianos M, Fasseas C, Skaltsounis AL, Liadakis G, Zografos AL, Zervos I, Gkinali AA. Bioactive compounds in edible insects: aspects of cultivation, processing and nutrition. Comprehensive Reviews in Food Science and Food Safety. 2025;24(1):45–89. DOI: https://doi.org/10.1111/1541-4337.13111.
46. Food and Agriculture Organization of the United Nations (FAO). Edible insects: future prospects for food and feed security. Rome: FAO; 2013. Available from: https://www.fao.org/3/i3253e/i3253e.pdf.
47. European Commission. Commission Implementing Regulation (EU) 2022/169 of 8 February 2022 authorising the placing on the market of frozen, dried and powder forms of *Tenebrio molitor* larvae as a novel food under Regulation (EU) 2015/2283, and amending Implementing Regulation (EU) 2017/2470. Official Journal of the European Union. 2022; L 27:9–17. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX%3A32022R0169. Retrieved on October 20th,2025
48. EFSA NDA Panel, Turck D, Castenmiller J, De Henauw S, Hirsch-Ernst KI, Kearney J, et al. Scientific opinion on the safety of dried yellow mealworm (*Tenebrio molitor* larva) as a novel food pursuant to Regulation (EU) 2015/2283. EFSA Journal. 2021;19(1): e06343.

DOI: https://doi.org/10.2903/j.efsa.2021.6343.

49. Broekman HCHP, Knulst AC, de Jong G, Gaspari M, den Hartog Jager CF, Houben GF, Verhoeckx KCM. Is mealworm or shrimp allergy indicative for food allergy to insects? Molecular Nutrition & Food Research. 2017;61(9):1601061. DOI: https://doi.org/10.1002/mnfr.201601061.
50. European Commission. Commission Implementing Regulation (EU) 2025/89 of 20 January 2025 authorising the placing on the market of UV-treated powder of whole *Tenebrio molitor* larvae (yellow mealworm) as a novel food and amending Implementing Regulation (EU) 2017/2470. Official Journal of the European Union. 2025; L (21.01.2025):1–7. Available from: http://data.europa.eu/eli/reg_impl/2025/89/oj.
51. Singapore Food Agency. List of insect species assessed to be safe for human consumption (as of 13 May 2025). Singapore: SFA; 2025. https://www.sfa.gov.sg/docs/default-source/regulatory-standards-frameworks-and-guidelines/list-of-insects-assessed-to-be-safe-for-human-consumption.pdf. Retrieved on October 20th,2025
52. Food Standards Australia New Zealand (FSANZ). Record of views formed in response to inquiries: novel foods including edible insects (e.g., *Tenebrio molitor*). Canberra: FSANZ; 2023 Dec. Available from: https://www.foodstandards.gov.au/sites/default/files/2023-12/Record-of-Views-updated-Dec-2023.pdf.
53. Health Canada. Completed safety assessments of novel foods (no-objection decisions). Ottawa: Government of Canada; 2025. https://www.canada.ca/en/health-canada/services/food-nutrition/genetically-modified-foods-other-novel-foods/approved-products.html. Retrieved on October 20th,2025
54. European Commission. Maximum levels for certain contaminants in food — Regulation (EU) 2023/915 (summary). https://eur-lex.europa.eu/EN/legal-content/summary/maximum-levels-for-certain-contaminants-in-food.html. Retrieved on October 20th,2025
55. Emilia M, Choina M, Gromek W, Wykrota J, Kozłowska D, Swadźba J, et al. IgE-based analysis of sensitization and cross-reactivity to yellow mealworm and edible insect allergens before their widespread dietary introduction. Scientific Reports. 2025; 15:1466. DOI: https://doi.org/10.1038/s41598-024-83645-4.
56. Ganseman E, Goossens J, Blanter M, Jonckheere A-C, Bergmans N, Vanbrabant L, et al. Frequent allergic sensitization to farmed edible insects in exposed employees. Journal of Allergy and Clinical Immunology: In Practice. 2023;11(12):3732–3741.e10. DOI: https://doi.org/10.1016/j.jaip.2023.07.039.
57. Lamberti C, Nebbia S, Cirrincione S, Brussino L, Giorgis V, Romito A, et al. Thermal processing of insect allergens and IgE cross-recognition in Italian patients allergic to shrimp, house dust mite and mealworm. Food Research International. 2021; 148:110567. DOI: https://doi.org/10.1016/j.foodres.2021.110567.
58. Yan X, Laurent S, Hue I, Cabon S, Grua-Priol J, Jury V, Federighi M, Boué G. Quality of *Tenebrio molitor* powders: effects of four processes on microbiological quality and physicochemical factors. Foods. 2023;12(3):572. DOI: https://doi.org/10.3390/foods12030572.
59. Ribeiro JC, Marques JP, Fernandes TR, Pintado ME, Carvalho SMP, Cunha LM. Effect of blanching, storage and drying conditions on the macro-composition, color and safety of mealworm *Tenebrio molitor* larvae. LWT. 2024; 191:115646. DOI: https://doi.org/10.1016/j.lwt.2023.115646.
60. Ruiz A, Morales-Ramos J, Rojas M, Dossey A. Edible insects as functional foods: bioactive compounds, health benefits, safety concerns, allergenicity, and regulatory considerations. Trends in Food Science & Technology. 2025; 142:115–134. DOI: https://doi.org/10.1016/j.tifs.2024.12.002.
61. van der Fels-Klerx HJ, Camenzuli L, van der Lee MK, Oonincx DGAB. Uptake of cadmium, lead and arsenic by *Tenebrio molitor* and *Hermetia illucens* from contaminated substrates. PLOS ONE. 2016;11(11):e0166186. DOI: https://doi.org/10.1371/journal.pone.0166186.
62. Schrögel P, Wätjen W. Insects for food and feed—safety aspects related to mycotoxins and metals. Foods. 2019;8(8):288. DOI: https://doi.org/10.3390/foods8080288.
63. Jankauskienė A, Aleknavičius D, Antanaitis Š, Kiseliovienė S, Wedi P, Šumskienė M, Juknienė I, Gaižauskaitė Ž, Kabašinskienė A. The impact of farm and industrial feed waste on the safety parameters of *Tenebrio molitor* larvae. Processes. 2024;12(1):37. DOI: https://doi.org/10.3390/pr12010037.