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Dietary and Therapeutic Benefits of Edible Insects: A Global Perspective

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Abstract

Edible insects are gaining traction worldwide for research and development. This review synthesizes a large and well-established body of research literature on the high nutritional value and variety of pharmacological properties of edible insects. Positive benefits of insect-derived products include immune enhancement; gastrointestinal protection; antitumor, antioxidant, and anti-inflammatory capacities; antibacterial activities; blood lipid and glucose regulation; lowering of blood pressure; and decreased risk of cardiovascular diseases. However, the pharmacological mechanisms of these active components of edible insects in humans have received limited research attention. In addition, we discuss health risks (safety); application prospects; regulations and policies governing their production and consumption with a view to promote innovations, intraglobal trade, and economic development; and suggestions for future directions for further pharmacological functional studies. The aim is to review the current state of knowledge and research trends on edible insects as functional ingredients beneficial to the nutrition and health of humans and animals (livestock, aquatic species, and pets).

INTRODUCTION

For thousands of years, edible insects have been used as feed, foods, and medicines (due to their therapeutic properties) that are beneficial to humans and animals because they alleviate hunger and improve nutrition (138). This is due not only to the high nutritional value of edible insects, but also, and more importantly, to the active substances in edible insects, which have a variety of biofunctional activities (138). Based on information gathered by the Food and Agriculture Organization (FAO) of the United Nations, it is important to promote the use and development of edible insects as a solution for nutritionally deficient diets and to improve health among the rapidly growing human population (28, 112). Population surges and food insecurity have become major challenges with which the world has been grappling in the past two decades, and hunger and malnutrition are emerging as perpetual problems in highly vulnerable communities, particularly poverty-stricken regions (28). This implies that present and future dietary challenges need to be reconsidered to rectify inefficiencies and reduce nutritional deficiency, which are the major root causes of numerous other pathologies (114).

Edible insects are being considered globally among diverse scientific communities (64, 82, 113) as a promising means to bridge the nutrient gap. Between 1,600 and 2,300 species of edible insects have been reported worldwide (5, 115), and their consumption has been recommended as a strategy to enhance food and nutritional security (53, 117, 118). Edible insects are part of numerous traditional diets found in over 113 countries (95, 108), and at least 2 billion people consume insects as food and medicine (45, 115). Murugu et al. (83) reported the recommended dietary allowance of nutrient intake for cricket-derived products among different age groups. However, it is likely that these values and quantities will vary according to individual consumer preferences and the prevalence of specific species. The eggs, larvae, pupae, and adults of several species are utilized in different forms as highly nutritious food and feed sources (106), thus reducing dependency on proteins of non-insect animal and plant origin. Edible insect meals or powder have extensively been used as protein or flavor enhancers in a variety of functional food products (49, 50, 52, 59, 60). Nevertheless, edible insect consumption has been linked to different risk factors, including toxicological, biological, and allergenic responses leading to human health problems (microbial intoxication or infection and ingestion of poisons, pesticides, antinutrients, heavy metals, and parasitic foodborne diseases) (99). Factors associated with the safety of entomophagy should be investigated, as most of these risk factors are largely unknown. Besides the nutrient quality (protein, lipids, amino acids, fatty acids, vitamins, and minerals) of edible insects, which is high compared to those of plant and animal origins, they have also been shown to be healthy and environmentally beneficial (by reducing water pollution, greenhouse gas emissions, and pesticide usage) and can be sustainably produced in large quantities (48).

Apart from their dietary benefits, certain edible insects have long been used in pharmaceuticals or as medications to treat several human illnesses (92–94) because they contain useful compounds. Many insect species host a reasonable number of bioactive compounds, such as flavonoids (22, 45, 84, 114) and other active ingredients, and thus can be used in food modification and pharmaceutical development (52). This provides a broader prospect for the application of insect-based products in the healthy food and biomedical industries to meet the human demand for nutritious food and safe medicine (65, 97). In recent years, numerous studies have found that the disease-suppressive properties of extracts from edible insects can be attributed to the presence of functional ingredients. These have been demonstrated in many in vivo and in vitro studies in relation to gastrointestinal protection; antioxidant and anti-inflammatory activity; antibacterial, hepatoprotective, anticancer, and immunomodulatory effects; blood glucose and lipid regulation; hypotensive effects; and a decreased risk of cardiovascular disease (20, 22, 29, 86). In recent years, numerous studies on the pharmacological functions of edible insects have been carried out largely in vitro and in animal models; therefore, future clinical trials are needed to support the promising functional properties of edible insect–derived products, given that insect therapy is increasingly gaining traction globally (15). As a result, finding new insect-derived food and medicine alternatives to traditional sources will be critical for humanity's long-term development and to advance our knowledge in the emerging area of edible insect research globally.

Previous reviews have provided elaborate evidence on the potential health benefits of eating insects, the mode of action of whole insects or insect isolates, and their potential implications as foodstuffs or dietary supplements (135–137). More recently, Zhou et al. (138) reviewed the status of and trends in the application of insects in fish feed, with a focus on single insect species representing different varieties of silkworms: *Antheraea pernyi* (Guérin-Méneville), *Bombyx mori* Linnaeus, *Antheraea assamensis* Helfer, *Antheraea mylitta* Drury, and *Samia cynthia* (Drury). They emphasized the nutritional composition of the pupae as food and medical ingredients (pharmacological functions) and their mechanism of action. Zhou et al. (137) further broadly summarized the nutritional composition of edible insects and discussed the biological functions of edible insect–derived products and their potential benefits to human health.

This review attempts to bridge gaps in the existing large and well-established body of edible insect research literature by presenting information on the responses of humans, different livestock, and aquatic species, as well as pets, to insect-derived products and opportunities for further improvement. Furthermore, we review health risks (safety); application prospects (food and medicinal properties exhibited by different edible insect species and active compounds associated with observed bioactivities); and regulations and policies governing edible insect production and consumption with the view to promote innovations, intraglobal trade, and economic development. Suggestions for future directions for further dietary and pharmacological functional studies are included in this review.

GLOBAL RESEARCH TRENDS ON DIETARY AND THERAPEUTIC BENEFITS OF EDIBLE INSECTS

Peer-reviewed journal articles focusing on insects for food, feed, therapeutics, and other uses were reviewed. We carefully used major online databases such as Scopus, Web of Science, and Google Scholar, among others, to search for relevant publications. The key words used to demarcate edible insect species in the search included "insects as feed," "insects as food," "insects as medicine," "pharmaceutic properties of insects," "insects as functional ingredients," "insects as antimicrobial agent," "insect products for immune enhancement," "gastrointestinal protection using insect products," "antitumor properties of insects," "antioxidant activities of insects," "anti-inflammatory properties of insects," "antibacterial activities of insects," "antifungal properties of insects," "blood lipid and glucose regulation using insect-derived products," "biologically active substances (phytosterols, flavonoids, antinutrients) of edible insects," "insects as vaccine vectors," "insect-derived products for lowering of blood pressure and decreased risk of cardiovascular diseases," "processing of edible insects," "safety of edible insects," "health risks (allergens, allergic reactions, toxicology, heavy metals, etc.) of entomophagy," "application prospects of edible insects," "regulations and policies governing insect production and utilization," "entomophagy," "role of insects in food and nutritional security," "insect farming," "insect-based animal feeds," "nutritional benefits of insects for livestock, fish, and pets," "nutrient profile of insects," "insect wild harvesting, preservation, and storage," "marketing of edible insects," and "economic impacts of edible insects." Specific focus was directed to documents published on edible insects for the period of 42 years from 1980 to 2022.

Over the past decade, there has been increased research attention focusing on the exploration of edible insects for their dietary and therapeutic benefits, with higher publication outputs in Europe, Asia, and North America compared to Africa and South America (**Figure 1*a–f***). Research efforts

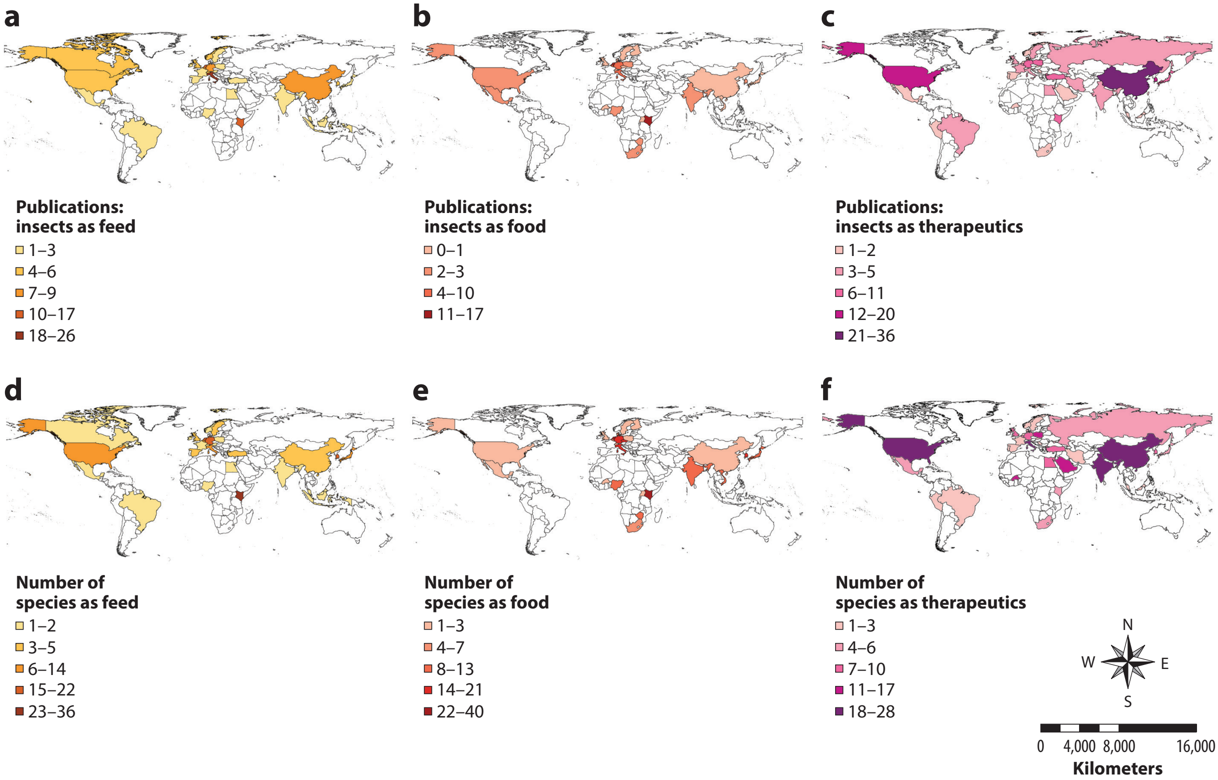

Figure 1

(*a–c*) Global distribution of research publications focusing on the exploration of the benefits of edible insects in (*a*) dietary feed, (*b*) food, and (*c*) therapeutics and (*d–f*) the number of edible insect species per country studied with regards to their application in (*d*) feed, (*e*) food, and (*f*) therapeutics.

in Asia, North America, and some parts of Europe have focused largely on the use of insects as therapeutics (**Figure 1*c***), while Africa has largely explored them as food and feed (**Figure 1*a*,*b***). A larger fraction of research publications has focused on the use of insects as therapeutics (46%) and animal feed (34%) compared to publications on the use of insects as food (20%). Generally, there was a significant increase in the number of research publications from 2013 to date, with a consistently higher number of publications on the use of insects as therapeutics compared to food and feed benefits (**Figure 2*a***). However, we notice a decline in publication outputs between 2020 and 2022, probably due to the COVID-19 pandemic, which may have disrupted research efforts across the globe. Most publications have focused on black solder flies (BSFs) (25%), mealworms (13%), crickets (12%), and bees (7%) (**Figure 2*b***). China, Kenya, and the Netherlands are the top three countries undertaking extensive research on edible insects globally (**Figure 2*c***), and most research outputs have been published in *PLOS ONE* and the *Journal of Insects as Food and Feed* (**Figure 2*d***).

DIETARY BENEFITS OF EDIBLE INSECTS

Dietary Nutrients of Edible Insects

Edible insects have high-quality and readily assimilated proteins, unsaturated fatty acids, amino acids, minerals, vitamins, and functional compounds (10, 23, 35, 43, 109, 120) (**Table 1**). Insect

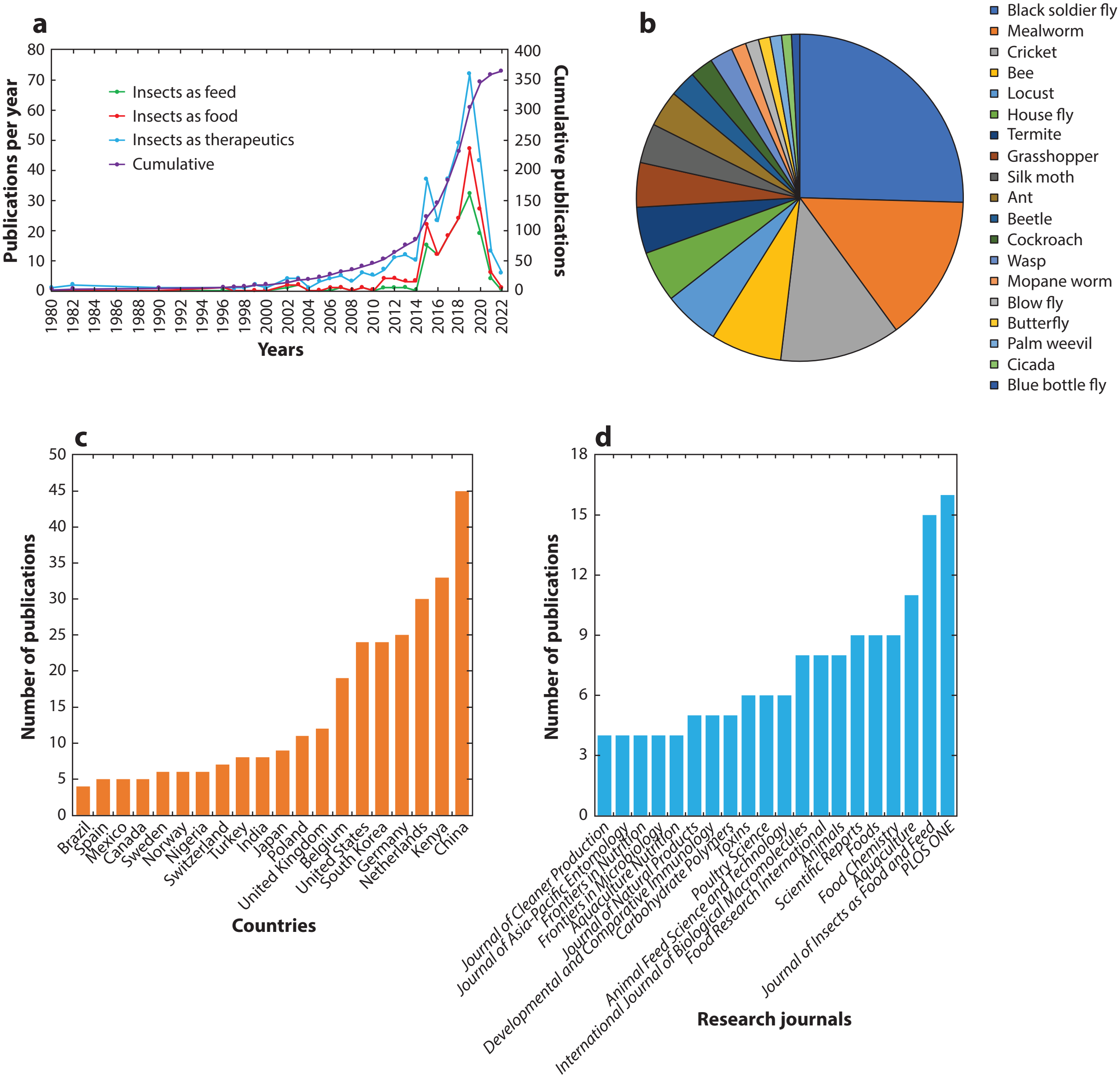

Figure 2

Distribution of publications from 1980 to 2022 on the dietary and therapeutic benefits of insects. (*a*) Trends in publications. (*b*) Top 20 researched edible insect species. (*c*) Efforts of top 20 countries in terms of research activities and (*d*) top 20 journals publishing research outputs on dietary and therapeutic uses of edible insects.

dietary composition is strongly influenced by diet, developmental life stages, species, sex, growth conditions, and processing techniques (62). The digestibility of insect proteins ranged between 76% and 96%, which is higher than values reported for many plant proteins (96). Plant proteins have a lower digestibility (75–80%) than animal proteins (90–95%), which has been attributed to the presence of antinutritional factors, indigestible cell walls, and specific protein structures in plants (49). Fat is the second-most important dietary nutrient, with an average of 10–70% fat

Table 1 Nutritional profile of edible insect orders

Parameter	Blattodea	Coleoptera	Diptera	Epheme-roptera	Hemiptera	Homoptera	Hymenoptera	Lepidoptera	Megal-optera	Odonata	Orthoptera
Proximate composition (%) dry matter											
Crude protein	19.0–65.6	8.9–71.1	31.1–63	66.3	27.0–72.0	29–72	4.9–70.0	13.17–79.6	62.1	40–66	6.3–80.3
Crude fat	6.7–50.9	0.7–69.8	1.8–49	5.7–11.9	4.33–54.2	4–33	5.8–62.0	1.4–77.2	10.4	16.7–25.4	2.2–53.05
Crude fiber	2.2–13.1	1.5–28.1	0.0–12.4	NA	2.0–23.0	19.2	0.9–29.1	1.68–29.0	NA	10.0–13.6	1.0–22.8
Moisture	2.8–69.1	1.0–67.9	5.8–78.4	NA	4.9	29.3	3.8–59.5	2.5–85.7	NA	NA	2.6–69.2
Ash	1.9–11.3	1.0–10.9	3.9–30.9	NA	1.0–21.0	4.5–9	1.6–9.6	0.6–11.5	NA	4.2–12.9	0.34–14.0
Carbohydrates	6.1–23.2	13.1–51.6	22.9–31.6	NA	5.0–7.6	16.0	NA	8.2–40.2	NA	NA	15.1–47.2
NFE	0.8–43.3	0.0–43.6	10.6	NA	0.01–18.07	NA	0.0–77.7	1.0–66.6	NA	3.0–6.2	0.0–85.3
Energy (Kcal/ 100g)	617.4	282.3–652.3	326.9–460.3	354.0–355.0	329.0–622.0	329.0–629.0	400.1–655.0	293.3–776.9	332–366	431–520	90.1–566.0
Amino acids											
Histidine	18.1–51.4 mg/g	11.0–38.9 mg/g	10.0–30.9 mg/g	3.3%	11.4–20.6%	1.5–3.7 g/100 g	23.4–35.3 g/ 100 g	7.8–35.4 g/100 g	4.0–4.3%	2.9–7.0%	13.5–25.7%
Isoleucine	28.7–51.1 mg/g	24.0–77.5 mg/g	22.8–40.0 mg/g	5.3%	14.2–50.0%	3.8–4.1 g/100 g	42.0–53.0 g/ 100 g	21.4–108.7 g/ 100 g	4.8–5.6%	2.8–7.3%	26.4–49.5%
Leucine	56.0–78.3 mg/g	47.0–106.4 mg/g	45.3–53.0 mg/g	8.5%	19.5–80.0%	6.8–7.7 g/100 g	69.7–93.0 g/ 100 g	13.1–91.3 g/ 100 g	7.0–9.0%	4.0–7.5%	42.5–100.0%
Lysine	40.0–54.3 mg/g	18.8–64.9 mg/g	52.0–81.6 mg/g	5.5%	6.4–55.0%	5.3–5.7 g/100 g	37.4–61.7 g/ 100 g	8.8–91.0 g/100 g	6.3–7.4%	4.6–7.9%	35.7–62.3%
Methionine	7.5–36.0 mg/g	7.0–25.0 mg/g	19.0–36.6 mg/g	NA	2.7–35.9%	1.9 g/100 g	14.0–45.0 g/ 100 g	0.0–47.0 g/100 g	NA	NA	7.9–42.0%
Cysteine	3.2–20.0 mg/g	6.8–26.7 mg/g	4.0–6.6 mg/g	NA	7.2–57.1%	1.4–2.1 g/100 g	7.0–21.3 g/100 g	3.5–26.1 g/100 g	NA	NA	8.3–21.0%
Phenylalanine	30.2–43.8 mg/g	26.2–103.0 mg/g	42.0–55.8 mg/g	3.3%	10.5–62.0%	4.7–5.9 g/100 g	33.4–88.0 g/ 100 g	17.4–95.0 g/ 100 g	4.2–10.6%	2.9–12.1%	22.5–117.0%
Tyrosine	30.2–69.0 mg/g	46.4–166.0 mg/g	48.0–71.1 mg/g	6.0%	8.6–90.0%	6.8–9.0 g/100 g	37.0–71.0 g/ 100 g	13.2–76.5 g/ 100 g	5.8–9.8%	6.2–7.7%	41.0–92.8%
Threonine	27.5–36.0 mg/g	26.9–41.8 mg/g	32.0–49.0 mg/g	4.9%	16.6–45.0%	4.5–4.7 g/100 g	33.0–47.0 g/ 100 g	13.8–76.0 g/ 100 g	4.1–4.8%	3.8–5.3%	20.6–44.0%
Tryptophan	6.0–14.3 mg/g	5.1–27.1 mg/g	7.1–49.5 mg/g	NA	9.6–11.0%	0.6–1.0 g/100 g	6.0–27.4 g/100 g	0.0–41.1 g/100 g	0.7%	0.5–5.2%	5.2–24.4%
Valine	42.6–73.3 mg/g	29.3–69.0 mg/g	34.0–61.0 mg/g	5.8%	17.4–74.0%	4.0–7.4 g/100 g	52.0–82.7 g/ 100 g	17.6–102.2 g/ 100 g	5.6–7.6%	6.0–10.1%	34.4–60.0%

(Continued)

Table 1 (*Continued*)

Parameter	Blattodea	Coleoptera	Diptera	Epheme-roptera	Hemiptera	Homoptera	Hymenoptera	Lepidoptera	Megal-optera	Odonata	Orthoptera
Arginine	32.0–69.4 mg/g	24.0–81.6 mg/g	42.0–56.7 mg/g	5.8%	12.8–36.9%	4.5–4.6 g/100 g	35.2–51.0 g/100 g	3.2–66.2 g/100 g	3.9–7.2%	4.9–12.5%	31.1–78.0%
Serine	38.8–45.0 mg/g	31.3–54.6 mg/g	32.0–88.0 mg/g	4.6%	7.7–12.9%	4.2–4.9 g/100 g	3.8–53.0 g/100 g	30.9–83.0 g/100 g	4.1–7.7%	3.9–4.3%	23.9–52.0%
Proline	65.0 mg/g	47.0–102.0 mg/g	24.7–31.0 mg/g	5.7%	NA	5.4–6.7 g/100 g	56.8–75.0 g/100 g	18.9–77.0 g/100 g	4.5–4.9%	4.5–5.6%	26.6–62.0%
Alanine	52.2–61.0 mg/g	24.7–31.0 mg/g	42.0–75.8 mg/g	9.2%	13.9–38.9%	7.5–7.9 g/100 g	43.5–88.4 g/100 g	18.2–71.4 g/100 g	5.7–14.3%	5.8–7.9%	59.0–101.1%
Glycine	46.3–71.0 mg/g	47.2–84.4 mg/g	39.0–51.1 mg/g	5.0%	12.8–20.0%	4.8–6.0 g/100 g	43.6–128.6 g/100 g	14.1–60.2 g/100 g	4.8–5.1%	4.3–5.5%	30.6–75.0%
Glutamic acid	69.3–130.0 mg/g	89.0–156.0 mg/g	89.2–108.0 mg/g	15.2%	16.6–30.8%	12.4–18.8 g/100 g	112.1–180.6 g/100 g	6.1–149.0 g/100 g	12.7–17.1%	8.3–14.4%	53.0–154.0%
Aspartic acid	NA	NA	NA	8.7%	NA	8.9–9.1 g/100 g	NA	NA	9.1–11.7%	6.3–8.5%	NA
Fatty acids (%)											
SFA	32.8–52.9	3.1–95.8	29.8–35.9	NA	20.5–64.8	56.0	21.3–40.3	22.5–61.4	NA	32.3–35.0	0.6–50.6
MUFA	2.1–53.1	0.7–66.6	27.9–55.1	NA	1.2–56.8	1.2	2.0–73.1	6.2–38.0	NA	27.9–42.3	3.1–50.4
PUFA	2.6–65.3	2.8–65.3	14.4–17.0	NA	5.4–43.8	43.8	3.1–68.8	11.2–53.8	NA	17.8–27.9	4.3–58.4
Minerals (mg/100g)											
Calcium	0.1–132.0	0.0–208.0	140.0–2,010.0	NA	69.8–1,021.2	NA	15.4–108.0	7.0–391.0	NA	9.0–96.0	2.0–1,290.0
Potassium	336.0–507.3	0.2–2209.0	792.2	NA	108.0–412.5	NA	24.0–1,159.5	47.6–3,259.0	NA	135.1–268.0	41.0–2,030.0
Magnesium	0.2–47.7	6.1–280.0	130–673.4	NA	63.1–1,910.0	NA	5.2–982.0	1.0–402.2	NA	10.1–70.3	0.1–902.0
Phosphorus	1.5–136.0	1.5–1,420.0	1,100.0–1,320	NA	57.0–1,234.3	NA	106.0–936.0	45.9–1,200.0	NA	NA	0.8–21,800.0
Sodium	92.7–112.0	26.3–174.1	270.0–660.0	NA	58.6–401.1	NA	20.0–270.0	30.0–3,340.0	NA	133.9–1,410.0	1.0–1,350.0
Iron	1.0–332.0	2.3–30.9	28.6–60.4	NA	20.2–57.0	NA	5.0–118.0	1.3–64.0	NA	2.3–410.0	0.4–1,562.0
Zinc	0.1–17.6	2.3–26.5	14.7–29.8	NA	7.9–59.0	NA	5.7–32.0	4.3–25.3	NA	4.0–29.5	0.4–232.0
Manganese	0.1–1.7	0.2–1.36	1.6–21.5	NA	3.2	NA	0.3–32.3	0.3–10,163.1	NA	0.7–6	0.0–10.4
Copper	0.1–1.7	0.9–2.1	0.9–3.4	NA	4.6	NA	0.9–2.4	0.2–2.6	NA	0.2–0.4	0.5–4.6
Selenium	0.0	0.0–0.1	NA	NA	NA	NA	0.0	0.0–0.1	NA	0	0.0–0.1

(*Continued*)

Table 1 (*Continued*)

Parameter	Blattodea	Coleoptera	Diptera	Epheme-roptera	Hemiptera	Homoptera	Hymenoptera	Lepidoptera	Megal-optera	Odonata	Orthoptera
Vitamins (mg/100g)											
Vitamin A/ retinol	2.6–2.9	0.0–12.5	0	NA	0.2	NA	0.0–12.4	0.0–3.4	NA	0.1	0.0–67.0
Vitamin B1	0.7	0.2–3.4	1.5	NA	0.3–1.0	NA	0.1–0.6	0.2–4.0	NA	0.1	0.1–3.4
Vitamin B2/ riboflavin	1.5–2.0	0.1–2.6	2.3	NA	0.3–0.9	NA	0.2–20.3	0.1–5.5	NA	1.3	0.0–11.1
Vitamin B3/ niacin	2.7	0.4–14.8	11.1	NA	0.7–2.6	NA	0.3–6.3	1.0–15.2	NA	NA	1.2–12.6
Vitamin 5/ pantothenic acid	NA	3.7–6.9	NA	NA	NA	NA	NA	4.9–12.5	NA	NA	7.5–11.5
Vitamin B6/ pyridoxine	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.2
Vitamin B7	NA	0	NA	NA	NA	NA	0.0	0.0–0.1	NA	NA	0
Vitamin B9/ folic acid	NA	0.2–0.4	NA	NA	NA	NA	0.5	0.0–0.4	NA	NA	0.2–0.9
Vitamin B12	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.0–10.0
Vitamin C	3.0–23.8	3.1–45.7	NA	NA	NA	NA	0.0–36.1	2.0–46.3	NA	NA	0.0–25.5
Vitamin E	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1.3–30.0

Data taken from References 62, 91, and 137. Abbreviations: MUFA, monounsaturated fatty acid; NA, not applicable; NFE, nitrogen free extract; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

content (96). The high lysine and threonine contents in *Acheta domesticus* Linnaeus and *Gryllus bimaculatus* De Geer imply that both species could be considered as excellent ingredients for supplementing cereal-based diets (rice, wheat, maize, and to a lesser extent sorghum and millet), which are generally low in these essential amino acids, around the world (34, 111).

Insect Meal in Livestock Nutrition

Insect-based additives have been applied to livestock feed due to their health-promoting properties (47) and positive effect on the growth performance, gastrointestinal tract microbiota, and immune response of livestock (75). For example, broiler chickens fed insect-based diets had decreased levels of bacteria (*Escherichia coli* and *Salmonella* spp.) in the gut, which might be attributed to the rich diversity of the >326 antimicrobial peptides (AMPs) in insects (47). Full-fatted mealworm meal diets fed to broilers led to significant improvement in growth performance (body weight gain) and feed intake (75). These positive effects are associated with shifts toward beneficial microbials in the gut, particularly in the ceca (63). Similarly, application of full-fatted BSF larva meal in young turkey diets led to efficient anti-inflammatory, immune stimulatory, and antioxidant impacts in birds (134). Furthermore, the positive role of lauric acid concentration of BSF (*Hermetia illucens* Linnaeus) larvae in preventing bacterial infections has been reported (110); BSF larvae exhibit strong activities against *Enterobacteriaceae*, *Campylobacter jejuni*, *E. coli*, and *Clostridium perfringens* (116), which are together responsible for severe economic losses in poultry flocks worldwide (56). Antiviral and antiparasitic modes of action of insect-based diets have also been reported (7, 55).

However, given the wide spectra of responses by birds to various inclusion levels of insect-based meal in diets, further investigations are needed on the impact of productivity and gut microbiome modulations. Fat is the second-most important nutrient and is present in insect meals at a level that is comparable to protein (54, 55); thus, insect meals can potentially substitute for environmentally unfriendly and frequently used feed materials (palm or soybean oils) in poultry nutrition. A major challenge in the use of insect fat in poultry diets is the poor fatty acid profile of the meals, which can be improved through various diet composition and extraction techniques. Metabolizable energy values of insect fat in chickens (broilers and layers) and turkeys have been reported to be comparable to those of soya bean oil (41, 58, 105). According to Kierończyk et al. (57), meat from broiler chickens fed mealworm fat exhibited similar atherogenic and thrombogenic indexes to those obtained from the meat tissue belonging to birds fed diets with plant-origin oils (6, 54). There are no reported risks of using insect fat as an energy source in poultry diets (25, 33, 40). However, more studies emphasizing the potential adverse effects of insect fat on consumer preferences and palatability of meat products is needed.

A wide spectrum of different developmental stages of insect species in the orders Diptera, Anoplura, Lepidoptera, Coleoptera, Orthoptera, Hymenoptera, and Trichoptera (98) is commonly consumed by domestic pigs, as well as wild boar (pigs), *Sus scrofa* Linnaeus, to compensate for protein deficiencies during nutrient scarcity (50, 133). Insects are rich in iron; thus, they can play a key role in microelement supplementation in piglet diets and have been effectively implemented at the nursing, weaning, grower, and finisher phases (132) of pigs, leading to positive effects on body weight gain, feed intake, and feed conversion ratio (3, 132, 133). The growth performance of pigs fed diets with various inclusion levels of insect-based (BSF larva and mealworm) meal or dietary fat is consistent with reports for pigs fed diets with most commonly used protein and energy sources (fishmeal, soybean meal, corn and soybean oils) (12, 61, 79, 133).

Positive impacts on the immune response of weaning piglets fed a diet with full-fatted BSF larva meal have been observed, resulting in decreased proinflammatory and improved anti-inflammatory factors (3, 11, 127, 129–131). Upregulation in gastrointestinal barrier genes has been documented in finishing pigs fed a diet with BSF larva meal (132). This is not a surprise, as BSF larva meals are known to be rich in products such as chitin, lauric acid, and AMPs (128). Additionally, inclusion of BSF larva meal in pig diet increases neutral mucin production, limiting the access of pathogenic bacteria (*Streptococcus* sp.) to the epithelium in the small intestine (132) but promoting *Lactobacillus* and *Bifidobacterium* populations. AMP complexes (lactoferrin, defensin, plectasin, and cecropin) in *H. illucens* larva meals have been reported to positively improve growth performance, intestinal morphology, and fecal microbiota; reduce diarrhea; and increase the survival rate of weaning piglets (2, 18, 19, 124). Given the biologically active components of insect meal and the positive effects of its inclusion in pig diets at all stages of development, it is necessary to widely promote the use of these eco-friendly products in small- to large-scale practical commercial pig production systems.

Chia et al. (17) and Altmann et al. (2) confirmed that the inclusion of insect (*H. illucens*) larva meal improved the quality of pork meat [particularly by increasing polyunsaturated fatty acids (PUFAs) and reducing saturated fatty acids and monounsaturated fatty acids], as well as overall odor and juiciness of the pork tissues. Chia et al. (17) further highlighted significant improvement in fasted and carcass weight, as well as increased fat content in loin muscle, for pigs fed insect-derived diets. Macro- and microelement concentrations of finishing pig tissues were increased, which implies that insect-based diets resulted in increased loin eye area, marbling scores, inosine monophosphate concentration, and intramuscular fat content in the longissimus dorsi muscles (14). Both low and high inclusion levels of insect (*H. illucens*) meals in pig diets resulted in considerable economic efficiency (17, 18). However, to increase the efficiency of insect-based pig diets, detailed nutrient requirements and insect biomass processing techniques for economically important species would be needed in the future.

Insect Meal in Aquaculture Nutrition

In aquaculture, BSF (*H. illucens*), yellow mealworm (*Tenebrio molitor* Linnaeus), earthworm (*Perionyx excavatus* Perrier), mopane worm (*Imbrasia belina* Westwood), superworm (*Zophobas atratus* Fabricius), silkworm (*Bombyx mori* Linnaeus), cricket (*G. bimaculatus*), and common housefly (*Musca domestica* Linnaeus) larvae have been widely used (full-fat or defatted) to substitute fish meal and/or fish oils (78) in aquafeed formulations for over 15 aquatic species, yielding remarkable results in terms of improved growth parameters and immune defense against some diseases (78). However, the results reported to date regarding insect meal incorporation levels in aquafeeds have varied depending on factors such as fish species, growth stage, feed formulation, insect biomass processing method, and dietary administration period. Despite the significant research efforts to substitute fishmeal in fish feed, very limited studies have successfully established the optimal requirement levels of dietary insect meals in aquafeed; 27.6% of *H. illucens* larva meal (corresponding to 75% of fishmeal substitution) is considered the maximum range of inclusion of insect meal without adverse effects (78). Potential adverse effects observed to date with the inclusion of insect meal in aquafeed include decreased growth performance; poor feed utilization; safety issues; and poor fish flesh quality, particularly in terms of essential fatty acid profiles (78). Furthermore, the texture properties of fish fed insect-derived products should not be overlooked. For example, studies have shown that mealworm (*T. molitor*) and housefly (*M. domestica*) maggot meal incorporation in diets of yellow croaker (*Larimichthys crocea* Richardson) and Nile tilapia (*Oreochromis niloticus* Linnaeus) led to significantly increased muscle hardness, reduced thaw loss, and lower shear force in fillets (119), all of which are important for consumers. Therefore, the texture of and heavy metals and mycotoxins (safety) in fish fillets from fish fed insect-derived products, which are rarely investigated, should be examined in future studies. Additionally, studies comparing insect meal requirement levels between freshwater and marine fish species are warranted.

Chitin in insect meals has been reported to provide beneficial effects on fish by shaping the gut microbial community and boosting the innate immune response when incorporated at moderate quantities ranging from 25 to 50 mg/kg (78). According to Xiang et al. (125), inclusion of combined dietary insect oils in aquafeed significantly improves the antioxidant capacity in the liver of juvenile mirror carp (*Cyprinus carpio* Linnaeus). BSF oil showed better results compared to mealworm and silkworm pupa oils. Replacing fishmeal with dietary mealworm meal in the diets of juvenile Pacific white shrimp and yellow catfish led to improved survival rates when fish were challenged with pathogenic bacteria (*Vibrio parahaemolyticus* and *Edwardsiella ictalurid*, respectively) (78). The health status (hematology and immunity) of juvenile mandarin fish (*Siniperca scherzeri* Steindachner) and Nile tilapia (*O. niloticus*) was improved when they were fed a diet with mealworm and BSF meal, respectively (78). The survival rate of red seabream (*Pargus major* Giinther) subjected to dietary mealworm meal was improved over controls after the fish were challenged with a bacterial clinical pathogen (*Edwardsiella tarda*) (44). The immune defense in fish fed diet with insect-based meal against diseases can be attributed to the presence of bioactive peptides in insect-derived products (66, 123, 126). However, further investigation is required to characterize the bioactive peptides present in insect meals. Additionally, information on the combined effects of multiple insect meals in aquaculture will be crucial.

An increase in dietary ratios of omega-3 to omega-6 PUFAs in fish fillets from sea-water Atlantic salmon (*Salmo salar* Linnaeus) and European perch (*Perca fluvatilis* Linnaeus) when fed diets with BSF (*H. illucens*) larva, house cricket (*A. domestica*), and superworm (*Z. morio*) meal as a substitute for fish meal has been reported (78). The omega-3 to omega-6 ratio has been implicated in controlling markers of the metabolic syndrome, including insulin sensitivity, inflammation, lipid profiles, and adiposity.

Positive perceptions of fish fillets from fish fed insect-derived products (78) have been widely reported, with consumer gender and age playing a significant role. Despite these promising results, important research gaps still exist. Most of the studies using insects as ingredients in aquafeed have focused on adult fish species, leaving a significant gap with regards to ontogenetic stages like embryos and fingerlings. Data on the effects of insect-based aquafeed on different fish species under different culture systems are lacking. The role of bioactive compounds (fatty acids, chitin, and AMPs) from insects in the growth and physiology of fish is largely unknown. Finally, studies on fish fillet safety and quality for human consumption are imperative.

Insect Meal in Human Nutrition

Globally, insects have been reported to be consumed in at least 11 European countries, 14 Oceanian countries, 23 American countries, 29 Asian countries, and over 45 African countries (85). The most commonly consumed insect orders in the world are described in **Table 1**. Orders such as Hymenoptera, Coleoptera, Lepidoptera, Homoptera, Hemiptera, and Orthoptera have been evaluated in human nutrition as an energy source (91). In many studies, consumers have demonstrated interest in new-generation food products that incorporate insects as functional ingredients in an unrecognizable form. For example, insects can be incorporated in the forms of flours or powder or minced to enrich various common, ready-to-eat, and familiar food products like energy drinks, buns, bread, yogurt, burgers, cookies, chips, biscuits, crackers, and corn tortillas (55). This increases the nutritional value of these foods while also influencing the sensory attributes of the end-products. The high levels of acceptability of these products have been partially attributed to the high fat content, which positively influences the flavor and texture (55). These value-added products occupy a promising market niche to be targeted through the development of food technologies and innovations. Another critical area of interest is the development of techniques to partially or totally extract functional food ingredients (chitin, oleic acid, proteins, and bioactive peptides) (55) for industrial applications. Snacks using insect products are increasing in popularity in the global market and are attractive to early adopters (55). The market for edible insects is rapidly expanding, posing challenges for quality control and safety; thus, future research needs to consider potential safety issues such as allergic reactions, clinical pathogenic microorganisms, pesticide residues, excessive levels of heavy metals, parasites, harmful toxins, and antinutrient aspects (36) that can threaten human and animal health.

Food fortification with insect-derived products has been documented to increase levels of protein, fat, fiber, provitamin A, riboflavin, vitamin C, minerals (iron, zinc, magnesium, and calcium), saturated fats, caproic acid, arachidic acid, lauric acid, myristic acid, monounsaturated fatty acids, polyunsaturated acids, and essential amino acids; energy values; thickness; and percentages of unsaturated fatty acids rich in omega-6 and omega-9 (55). Protein digestibility has been observed to be significantly higher in insect-enriched food products than in products using other protein sources (55). Given that the nutrient quality of the above-described insect-based food products generally met the reference values for both children and adults according to the standards of the FAO and World Health Organization (WHO) (55), the adoption and utilization of these products could play a critical role in decreasing the incidence of malnutrition and anemia among the growing population. Therefore, further studies should focus on making edible insect–enriched food products more appealing to consumers by modifying food formulations or masking some off-flavors, as well as determining optimal conditions for pre- (rearing) and postprocessing of edible insects.

Insect Meal in Pet Food

The growing demand and increased availability of insect protein in the market have resulted in the expansion and diversification of hypoallergenic commercial pet food products (9). Domestic cats and dogs have widely been reported to consume insects (9). Mealworm (*T. molitor*) and BSF (*H. illucens*) larvae are mostly considered novel insect ingredients that can be used as protein sources in pet foods. Besides the palatability of insect biomass, insects also serve as an attractant in the pet food industry. Differences between sexes have been observed, with female dogs having more preference for Turkestan cockroach (*Shelfordella lateralis* Walker), while males favored mealworm (*T. molitor*) larvae (9). Cats preferred BSF larva meal, while dogs favored mealworm larva products (69). Inclusion of *H. illucens* larva meals in dog diets linearly improved the apparent total tract digestibility and crude protein and favorably impacted immune and antioxidative status (68). Feedings of defatted mealworm meal–based diets to dogs resulted in reduced cutaneous lesions and skin barrier dysfunction (100, 101), improved lesion scores, and improved hair and coat quality in dogs with atopic dermatitis. Interestingly, BSF larva meal in diets fed to older dogs significantly lowered serum cholesterol levels (24).

Future studies are needed to expand our knowledge base on the long-term effects of insect-based diets on pet nutrient digestibility coefficients, growth, feed intake, blood hematology, biochemistry, immunological response traits, oxidative stress, and gut microbial diversity. There are also limited data on the hypoallergenic properties of various inclusion levels of insect-based meal in companion animal diets. Despite the many advantages of insect-based meals in pet food, analyses of the impact of tropomyosin, arginine kinase, and other allergens in diets fed to companion animals are lacking and warranted. Clinical skin symptoms observed in dogs allergic to insect-based pet food may range from mild symptoms of hypersensitivity, like itching in the mouth and erythematous dermatitis of the face, ear canals, armpits, groin, and paws, to severe, systemic, and often fatal reactions, such as anaphylactic shock (100, 101).

THERAPEUTIC PROPERTIES OF EDIBLE INSECT–DERIVED PRODUCTS

In recent years, mainstream research organizations and private sector companies have extended their research efforts toward investigating natural products derived from insects using cutting-edge molecular and biochemical processes to identify therapeutics; these efforts have given rise to the term "drugs from bugs." However, this area of drug discovery has received little attention in terms of bioprospecting for novel natural products (29). This can be attributed to the lack of a systematic and targeted approach to the study and prioritization of novel areas in the edible insects research agenda. Edible insects have produced several valuable natural products that have been widely used in non-Western medicine (29). **Table 2** provides a summary of the medicinal properties exhibited by different edible insect species and associated active compounds and extracts that have been identified, highlighting their respective bioactivities. The specific structures of these active compounds, as described in **Table 2**, are illustrated in **Supplemental Figure 1**. Some compounds from edible insects have been described to exhibit bioactivities with various activity ranges, as shown in **Table 3**.

Supplemental Material >

Effects of Insect-Derived Products on Wound Healing

Several studies have clearly demonstrated that honeybee (*Apis mellifera* Linnaeus)-derived products (honey and royal jelly protein 1) are good remedies for treating burns and ulcers (30, 73, 74, 80). Honey combined with beeswax has been used to treat several dermatologic disorders, such as psoriasis, atopic dermatitis, tinea, pityriasis versicolor, and diaper dermatitis (80). The accelerated wound healing processes described above can be attributed to the ability of active compounds in the products to promote the growth of epithelial tissues and granulation, protection of wounds from infections, activation of keratinocytes, and reduction of wound edema (anti-inflammatory properties) (46, 80). However, the species-specific metabolites of honey and beeswax involved in these therapeutic properties have not been well elucidated. Contrarily, haemangin from edible grasshoppers (*Haemaphysalis longicornis* Neumann) has been reported to disrupt the formation of new blood vessels and tissue repairs, thus significantly reducing or delaying wound healing (46). Furthermore, three species of blow flies have been commonly used in treating wounds in humans and animals: the illustrious greenbottle fly, *Lucilia illustris* (Meigen); black blow fly, *Phormia regina* (Meigen); and common green bottle fly, *Lucilia sericata* (Meigen), the species of choice. Maggot therapy continues to attract interest in the treatment of chronic, infected, and pressure ulcers; venous stasis ulcers; diabetic foot ulcers; severe burns; bed sores; and traumatic, necrotic, sloughy, and nonhealing postsurgical wounds (103). This involves the deliberate utilization of live, medical-grade fly larvae for the process of wound healing, disinfection (killing bacteria), faster wound debridement, granulation tissue development, wound surface reduction, and treatment of surgical contraindications (88). Furthermore, as maggots move about the wound feeding, they also secrete calcium carbonate, ammonia, and allantoin (a substance that promotes wound healing), making the milieu more alkaline and less conducive to bacterial growth (103). These maggots can be applied either in loose (confinement) or bagged (containment) dressings (103). Maggot therapy is not frequently used in medicine, but concerns over the prevalence of antibiotic-resistant bacteria suggest that it is an option that merits further consideration (88). Other advantages of maggot therapy include its simplicity, safety, effectiveness, and relatively low cost (88). Efforts are underway to isolate the active constituents in the maggots' secretions, but to date, no isolation has been found to equal the efficacy of the live larvae.

Chitosan and chitin extracted from many different insects have been exploited; chitosan and chitin from BSF have been reported to be capable of significantly inhibiting bacterial growth and

Table 2 Summary of the medicinal properties exhibited by different edible insect species and the active compounds and extracts associated with the observed bioactivities

Insect(s)	Family	Therapeutic uses	Materials, compounds, and proteins responsible for the observed activities and usage	Future research needs
Galleria mellonella Linnaeus (greater wax moth)	Pyralidae	IMPI discovered from this insect can retard *Pseudomonas aeruginosa* virulence through inhibition of PE virulence factors	IMPI	Identification of the antimicrobial peptides and small molecules that inhibit metalloproteinase
Hermetia illucens (black soldier fly)	Stratiomyidae	Antibacterial and antifungal activities: Trx-stomoxynZH1 (fused with thioredoxin in *Escherichia coli*) inhibits *Staphylococcus aureus*, *E. coli*, *Rhizoctonia solani*, and *Sclerotinia sclerotiorum*	StomoxynZH1 (an AMP)	Isolation of the antibacterial and antifungal peptides and small molecules for characterization Screen for cytotoxicity
Hydropsyche angustipennis (caddisfly)	Phryganeidae (Trichoptera)	Biomaterial for tissue engineering	Cocoons	Biotechnological approach to utilizing the material in a broad range of activities
Musca domestica (house fly)	Muscidae	Inhibits LPS-induced atherosclerosis	Protein enriched extracts	Isolation and identification of the bioactive small molecules corresponding to the observed activities
		Antibacterial activity and antitumor activities	Extracts of native and inoculated third-instar larvae	
		Induces apoptosis	Cecropin	
		Antioxidant, antifungal, and antiviral properties	Chitosan	
Vespa tropica (wasp)	Vespidae	Broad-spectrum antimicrobial activity and weak hemolytic activity toward erythrocytes	Mastoparan and vespid chemotactic peptides	Carry out cytotoxic activity
Mylabris caragnae (blister beetle)	Meloidae	Anticancer properties; inhibitor of PP1 and PP2A, which results in DNA damage and apoptosis	Monoterpene; canthardin and derivatives	Isolation of the AMPs from the hemolymph for antibacterial screening
Apis mellifera (honey bee)	Apidae	Wound healing	5.8k DNA component	Investigate the bioactive compounds produced by substances other than the propolis
		Wound healing	MRJP1	
		Antimicrobial activity	Royalisin antibacterial peptide	
		Anti-inflammatory activity (antiallergen)	MRJP3 of royal jelly	
		Antibacterial activity against *P. aeruginosa*	Honey and royal jelly	

(*Continued*)

Table 2 (*Continued*)

Insect(s)	Family	Therapeutic uses	Materials, compounds, and proteins responsible for the observed activities and usage	Future research needs
		Suppression of VEGF-induced angiogenesis	Royal jelly, bee pollen, and Chinese red propolis	
		Antitumor activity (human pancreatic cancer cell line tested)	Cytotoxic propolis compounds (see **Table 3**)	
		Antitumor activity: induction of apoptotic cell death in A549 lung cancer cells; inhibition of C33A cervix cancer cells through enhancement of death receptor expression and induction of apoptotic cell deaths; antiaging effects, i.e., decreasing total wrinkle area, total wrinkle count, and wrinkle depth; antifibrinolytic and antimicrobial activities (*Apis cerana*)	Bee venom	
		Antitumor, antibacterial (Lyme disease), and anti-HIV activity	Melittin, a constituent of bee venom	
		Anti-arthritis and anticancer activity	Apamin and melittin, constituents of bee venom	
		Treatment of Parkinson's disease	Apamin	
		Anti-COVID-19 activity	Bee products (honey, propolis, bee venom)	
Tetramorium bicarinatum (guinea ant)	Formicidae	Antimicrobial activity	Bicarinalin, an AMP constituent of venom	Isolate and identify the bioactive small molecules and other AMPs
Tenebrio molitor (mealworm beetle)	Tenebrionidae	Antioxidant and anti-inflammatory activities	Peptides (proteins)	Discovery of the natural products corresponding to the observed activities
Gryllodes sigillatus (house cricket)	Gryllidae			
Schistocerca gregaria (desert locust)	Acrididae			

(*Continued*)

Table 2 (*Continued*)

Insect(s)	Family	Therapeutic uses	Materials, compounds, and proteins responsible for the observed activities and usage	Future research needs
Spodoptera litura (cutworm)	Noctuidae	Antibacterial activity	Cecropin-like antibacterial peptide	Screen for antifungal, antiviral, and antibacterial activity against *ESKAPE* pathogens of its extracts
Tabanus bovinus (pale giant horse-fly)	Tabanidae	Anti-angiogenic activities	Crude whole-body extracts	Screen for antimicrobial activities and cytotoxicity of different larval-stage extracts of the insect
Bombyx mori (silk worm)	Bombycidae	Antimicrobial properties	Silk fiber	Identify the components that give the silk fiber its antimicrobial properties
		Protection against CCl_4-induced liver damage and radical scavenging activity	35kDNA protein purified from fecal matter	
Calliphora vicina (blow fly)	Celliphoridae	Antitumor and antiviral activities	Alloferon 1 and 2 peptides	Target different peptides from tissues other than the blood
Calosoma sycophanta (forest caterpillar hunter)	Carabidae	Antimicrobial properties	Pygidial gland secretion	Characterize the small molecules from whole-body extract
Carabus intricatus (blue ground beetle)	Carabidae	Antimicrobial properties	Pygidial gland secretion	Isolate the microbiota interacting with the beetle to identify their symbiotic relationship
Catharsius molossus (dung beetle)	Scarabaeidae	Anticancer properties	Glycosaminoglycans	Screen for antimicrobial activities
Eupolyphaga sinensis (Chinese cockroach)	Blattodea	Anticancer properties	EPS72, a 72kDNA protein	Purify other therapeutically significant proteins and their identification Extract their oil and test for antimicrobial activity
Clanis bilineata (velvet hawkmoth)	Sphingidae	Radical scavenging activity	Water-soluble chitosan (CBLSWSC)	Target the antimicrobial peptides and cytotoxicity
		Antioxidant activity	Oil extracted from larval-stage whole body	

(*Continued*)

Table 2 (*Continued*)

Insect(s)	Family	Therapeutic uses	Materials, compounds, and proteins responsible for the observed activities and usage	Future research needs
Chrysomya megacephala (Oriental latrine fly)	Calliphoridae	Antibacterial activity	Whole-body extracts	Screen for broad-spectrum bioactivities including cytotoxicity
Hyalophora cecropia (giant silk moth)	Saturnidae	Antibacterial activity	Cecropins (AMPs)	Screen for activity from the whole extracts of different developmental stages
Bruchidius dorsalis (specialist seed predator)	Bruchidae	Radical scavenging activity	Dorsamin As (see **Table 3**)	Screen for antimicrobial activity and cytotoxicity
Pergidae sp. (saw fly larvae)	Pergidae	Antimicrobial activity (*B. subtilis*)	Macrocarpal and grandinol	Investigate anticancer properties
Tetramorium sp. (red ants)	Formicidae	Antibacterial activity (*B. subtilis*)	Coumarins and amide	Expand the activity screening to anticancer, antifungal, and antiviral properties
Nasutitermes corniger (termites)	Termitidae	Ethanolic extracts modulate antibiotic activity of antibiotics (ampicillin, erythromycin, amoxicillin, levofloxacin, cephalotin, and gentamicin)	Ethanolic extracts	Vary the solvent polarity and identify the compounds responsible for the activities
Solenopsis invicta and *Solenopsis germinata* (fire ants)	Formicidae	Antiangiogenic properties; a venom alkaloid inhibits QS in *P. aeruginosa*	Solenopsin	Investigate antimicrobial properties
Byasa polyeuctes termessa (papilionid butterfly)	Papilionidae	Anticancer properties	Papilistatin	Investigate antimicrobial properties
Brachystola magna (Texas grasshopper)	Romaleidae	Antiproliferative properties	Pancratistatin, narciclasine, and ungeremine	Investigate antimicrobial properties

(*Continued*)

Table 2 (*Continued*)

Insect(s)	Family	Therapeutic uses	Materials, compounds, and proteins responsible for the observed activities and usage	Future research needs
Blaps japanensis and *Blaps rynchopetera*	Tenebrionidae	Treatment of rheumatism, cancer, and inflammatory-related disorders; evaluated for the inhibitory activities against COX-2, ROCK1/2, and JAK3 kinases	Whole-body 80% ethanol extract yielded pipajiains A–E, F, and G	Antimicrobial activity profiling and protein analyses
		Anticancer properties	Pipajiains H–J, a new unusual sulfone group containing phenolic derivatives and amide derivatives; pipajiamides A–C; an imidazole pipajiaine A; and pipajiaine B	
		Inhibitory effects toward COX-2	Blapsols A–D	
		Cytotoxic properties	Defensive secretion of *B. rynchopetera* yielded many bioactive compounds (**Table 3**)	
Holotrichia diomphalia (Bates)	Scarabaeidae	Anti-asthmatic effects through inhibition of the GATA-3/Th2 signaling pathway	Ethanol extract	Identify the specific small molecules with antimicrobial activity
		Not determined	Ethyl acetate extract yielded 3,5-dimethoxy-4-hydroxylbenzoic acid (56), salicylic acid, 4-hydroxybenzoic acid, 3-hydroxy4-methoxybenzoic acid, 4-hydroxyphenylpropionic acid, and 4-hydroxyphenylpropionic methyl ester	

Data taken from References 81, 135, and 136. Abbreviations: AMP, antimicrobial peptide; HIV, human immunodeficiency virus; IMPI, insect metalloproteinase inhibitor; LPS, lipopolysaccharide; MJRP, major royal jelly protein; PE, *Pseudomoas* elastase; PP, phosphoprotein phosphatase; QS, quorum sensing; VEGF, vascular endothelial growth factor.

Table 3 Compound names and their corresponding activity quoted

Name	Activity	
	Preferential cytotoxicity PC_{50} (μM)	Preferential cytotoxicity PC_{100} (μM)
(22*Z*,24*E*)-3-oxocycloart-22,24-dien-26-oic acid	4.3	6.3
(24*E*)-3-oxo-27,28-dihydroxycycloart-24-en-26-oic acid	>100	>100
Mangiferonic acid	>100	>100
28-Hydroxymangiferonic acid	>100	>100
27-Hydroxymangiferonic acid	38.5	50
(24E)-3-oxo-23-hydroxycycloart-24-en-26-oic acid	28.0	50
(24E)-3β- hydroxycycloart-24-en-26-al	>100	>100
Isomangiferolic acid	13.7	25
Mangiferolic acid	>100	>100
(24*E*)-3α,27-dihydroxycycloart-24-en-26-oic acid	15.5	25
(24*E*)-3α,27-dihydroxycycloart-24-en-26-oic acid	>100	>100
(24*E*)-3α,22-dihydroxycycloart-24-en-26-oic acid	13.4	25
(24*E*)-3β,23-dihydroxycycloart-24-en-26-oic acid	>100	>100
(2*S*)-5,7- dihydroxy-4′-methoxy-8,3-diprenylflavanone	7.9	12.5
(2*S*)-5,7,4′- trihydroxy-8,3′-diprenylflavanone	19.8	25
(2*S*)-5,7-dihydroxy-4′-methoxy-8-prenylflavanone	36.7	50
(2*S*)-5,7,4′-trihydroxy-8-prenylfla-vanone	39.4	50
Dorsamin-A763	SC_{50} (50% scavenging concentration) 12.1 ± 0.9	
Dorsamin-A737	SC_{50} 13.8 ± 0.4	
Dorsamin-A765	SC_{50} 11.0 ± 0.4	
Dorsamin-A739	SC_{50} 9.7 ± 0.6	
Dorsamin-A767	SC_{50} 10.5± 0.8	
Marcocarpal	Inhibition zone (8mm)	
Grandinol	Inhibition zone (7mm)	
3-[p-Phenyletheneyl]-4-aldehyl-coumarin	MIC against *Bacillus subtilis* = 25 μg/ml	
8-Methyl-11-hydroxyl-12-isopropanol-furancoumarin	MIC = 25 μg/ml	
20-Carbonyl-3-*N*-lactam, spiro 50 S-[4,5]ring 4-O-60,70-pyranoidene[3,4] pyranen-coumarin	MIC = 25 μg/ml	
N-(2-hydroxyl)-benzamide	MIC = 15 μg/ml	
N-phenyl-3,4,5-trihydroxyl-benzamide	MIC = 25 μg/ml	
Papilistatin	GI_{50}s of 0.093–3.5 μg/ml (against a panel of six human and the murine P388 leukemia cancer cell lines)	
Pancratistatin	50% effective dose (ED_{50} expressed in μg/ml) P388 leukemia cell line yielded ED_{50} 0.048 μg/ml	
Narciclasine	ED_{50} 0.018 μg/ml	
Ungeremine	ED_{50} 1.2 μg/ml	

Abbreviation: MIC, minimum inhibitory concentration.

accelerating wound healing in animals by reducing wounded areas, accelerating reepithelialization, stimulating cellular proliferation, preventing inflammation, and decreasing the healing time of cutaneous wounds (1). Efforts to advance comprehensive knowledge in this field of insect chitin and chitosan will be important.

Edible Insects as Sources of Antimicrobial Agents

AMPs are mainly found in the fat bodies and hemolymph of edible insects, particularly those with strong adaptability to harsh environments. According to Yi et al. (128), over 150 edible insect species have been shown to produce a wide range of substances with antibacterial properties, including proteins and peptides, insect oils, chitosan, honey, and chitin (138). Mudalungu et al. (82) provided an overview of antimicrobial compounds from edible insects and their associated microbiota. The most famous and effective antimicrobial peptides include defensin-like peptides, cecropin, and jellein, all of which have a broad range of activities against fungi, gram-negative and gram-positive bacteria, and yeasts (138) (**Table 2**). The combination of these antimicrobial peptides has been widely used to treat gram-negative bacterial pathogens that have become resistant to common antibiotics (90). It is noteworthy that AMPs vary with insect species, but the largest numbers of AMPs, over 50, have been reported for the invasive harlequin ladybird *Harmonia axyridis* and *H. illucens* (82). Feeding of *H. illucens* to fish and poultry and edible crickets to humans have been reported to alter intestinal flora and increase intestinal probiotics, thus improving gut health and reducing inflammation (104). The spectrum of activity of these peptides has been understudied, but it is clear that there is the potential to discover many compounds that can serve as or inspire new antibiotics. Recently, the interest of researchers has moved toward the antimicrobial properties of beeswax, demonstrating its effectiveness against several clinical pathogens: *Staphylococcus aureus*, *Salmonella enterica*, *Candida albicans*, and *Aspergillus niger*. These inhibitory effects can be further enhanced synergistically with other natural products such as honey (80). Other beneficial effects of edible insect–derived products and specific associated molecules are presented in **Table 2**, with their respective bioactivities highlighted. Their structures and activity range are indicated in **Supplemental Figure 1** and **Table 3**, respectively.

Supplemental Material >

Anticancer, Anti-Inflammatory, and Antioxidant Properties of Edible Insects

Active ingredients of edible insects with the capacity to inhibit the abnormal proliferation and growth of cancer cells have been well documented by Zhou et al. (138). These functional substances in edible insects are the most sought after by researchers and include active proteins, vitamins, chitosan, active peptides, and trace elements, among other substances (138). Advanced studies have also demonstrated that melittin, which is the main component of honeybee venom, has a variety of biological effects (i.e., applications against inflammation, pain, and asthma, among others) (51), although research has largely focused on its antitumor effects and its role in cancer treatment (31). Theories and research about the composition of edible insect venom, which is mainly of protein and peptide origin, have been driven toward the creation of antivenoms, bioinsecticides, and pharmaceutical agents (37). To date, venom research has focused on the world's deadliest animals, ignoring less dangerous arthropods, especially Hymenoptera, which represent an underexplored source of venom secretions (102). Furthermore, proteotranscriptomic studies of the Hymenopterans have revealed an extraordinary pool of toxins that are involved in various biological processes, including pain, paralysis, allergic reactions, and antimicrobial activities (102). The use of honeybee toxins, insect fats, sugars, and other secondary metabolites in cancer therapy has also been considered (138). The studies discussed above show that edible insects are a viable source of anticancer active ingredients whereby highly active, less toxic, and effective antitumor drugs can be developed, thereby promoting human and animal health.

Many active components of some edible insects have been reported to have anti-inflammatory activities; these components are predominantly protein based (hydrolyzed peptides) (138). Heat treatment and enzymatic digestion of insect peptides have been reported to enhance their anti-inflammatory and immunosuppressive activities in animals (138). It can be concluded that the use of edible insect active ingredients as drug molecules for the treatment of various inflammation-related diseases is promising. In the meantime, however, the toxicological characteristics and targets of these active substances need to be further elucidated to develop functional foods or pharmaceuticals with beneficial effects on human and animal health in the near future. These findings demonstrate the possibilities of developing antioxidant-enabled products from edible insects (21) to protect against oxidative stress, which is often associated with diseases such as cancer, heart disease, and arthritis, as well as aging (89).

A variety of active ingredients in edible insects have been reported to possess antioxidant activities of different intensities (138), particularly when obtained through various enzymatic treatments (138). Water-soluble and fat-soluble extracts from edible insects have been reported to have five and three times more antioxidant activities, respectively, than plant-based sources (26). However, much of this work has been carried out in vitro and in animal models, and clinical trials are needed to support the antioxidant properties of insect products for human health.

Other Active Ingredients of Edible Insects with Pharmacological Benefits

Emerging new dimensions in edible insect research are now emphasizing insects as potential sources of therapeutic sterols. Cheseto et al. (16) unraveled over 34 sterols in desert locust (*Schistocerca gregaria* Forskål) with varied concentrations in different insect body parts. Five of these sterols were unique to the insects, and three had health benefits in humans. This study showed that the desert locust ingests phytosterols from a vegetative diet and amplifies (20–40-fold) and metabolizes them into derivatives with potential salutary benefits (16). The impact of processing techniques on total sterol concentrations in edible grasshoppers (*Ruspolia differens* Serville) has also been reported (87). Mudalungu et al. (81) further described 19 different sterol types from nine edible insect species. Bioactivity of the sterol extracts from *H. illucens* and desert locust (*S. gregaria*) showed significantly higher inhibition levels in response to methicillin-susceptible *S. aureus* 25923 and *E. coli* 25922. This evidence shows that edible insects are rich sources of phytosterols, known to exert cardiovascular protective effects mainly via their cholesterol-lowering ability, modulation of endothelial function, and antioxidant capacity (76, 87). Other benefits include anti-inflammatory (70), anticancer (121), and immune regulatory effects (13). Furthermore, some of the major sterols identified in edible insects are key ingredients in the cutaneous synthesis of vitamin D in humans; the roles of this vitamin range from maintaining healthy bones to fighting cancers, autoimmune diseases, infectious diseases, and cardiovascular diseases (13, 121). Because of the high phytosterol content in edible insects, studies suggest that utilizing insect meal as human food could be advantageous, as it could help reduce high levels of serum cholesterol. The recent recognition that new natural insect-derived product scaffolds are urgently needed to tackle life-threatening pathogenic infections has been prompted by the health threats posed by multidrug resistance.

Another important area in the study of edible insects that has received limited research attention is investigation into methods of propagating antibodies and vaccinating their hosts (for a study in rabbits, see 103). One of the most interesting applications of edible insects in medicine is the production of vaccines and other useful proteins using baculovirus (a DNA virus) as a vaccine expression and delivery vector to prepare antigen or subunit vaccines (71). The baculovirus is capable of infecting more than 600 insect species, which implies that it can be inoculated in any of the insect larvae, and after a period of incubation, the vaccine or protein could be harvested from the insect hemolymph (72). In addition to the protein expression and display, baculovirus has emerged as a promising gene delivery vector for cancer gene therapy and regenerative medicine, as well as an RNA interference mediator (71). Baculovirus will likely grow in popularity as a therapeutic vaccine and gene delivery vector in the future.

Safety Quality of Edible Insects

Although this review focuses on edible insects as sources of food and medicine, safety remains the cornerstone of promoting their use in food or health products. Allergenic reactions to and toxicological safety of edible insects have been extensively reported, with over 26 protein-based allergens (e.g., hyaluronidase, phospholipase A, microtubulin, arginine kinase, and proto-myosin) found to date (23, 95). Key allergic reactions include hives, breathing difficulties, redness of and itchy skin, asthma, gastrointestinal issues, dizziness, tachycardia, and in severe cases shocks or fainting (48, 122). These allergenic properties of edible insects significantly limit their use; therefore, employing approaches that reduce the presence of allergens in insect-based products would be crucial (138). According to the findings of the investigations discussed above, heat, enzymatic digestion, acidic and alkaline protease digestion, high pressure, ultrasound, gastrointestinal protease, fermentation, hydrolysis, microwave treatments, and acid–base treatments are potential strategies to significantly reduce or eliminate the cross-reactivity and allergenicity of edible insect proteins or peptides (39) to safeguard insect food and medicine. Bertola & Mutinelli (8) reported over 70 virus species in edible insects, 36 of which can cause insect death or human disease. Unfortunately, at present, virus infection of edible insects cannot be completely eradicated. Therefore, preventive measures remain the option of choice globally (8). Unknowingly ingesting processed insect-based products contaminated with viruses (*Vibrio*, *Streptococcus*, *Staphylococcus*, and *Clostridium*) can cause serious food-borne infections and poisoning threatening both humans and animal health (27). Previous studies have revealed the occurrence of pesticide residues and heavy metals in edible insects, often consumed by humans and animals (32, 42); safe and controllable insect farming would be the best option to avoid such risk. This will not only increase the safety of edible insect use, but also help the nascent industry.

Legislation and Regulation Status of Edible Insects

It is noteworthy that the laws governing edible insects across the world contrast with one another, and each country develops its own legislation, thus creating safety concerns. Given the inconsistency in the regulations, it is challenging to market edible insects internationally due to the diversity of restrictions in different countries (67). Azmir et al. (4) reported that the lack of clear legislation on edible insect farming, consumption, and commercialization in a majority of the countries has severely hampered the development of insect-based enterprises and their potential to benefit human and animal health. Many countries around the world are making intentional efforts toward regulating and developing standards on insect-derived products, particularly in the European Union (Belgium, the Netherlands, the Kingdom of Denmark, Finland), the United Kingdom, Africa (Kenya, Uganda, Rwanda, Tanzania, and recently Ethiopia), the United States, Central and South America, Asia, Canada, and Australia (38, 77, 107). Currently, the International Centre of Insect Physiology and Ecology (*icipe*) and the African Organization for Standardisation (ARSO) have established a strategic partnership to promote the development and harmonization of standards and conformity assessments for edible insect–derived products in Africa as the availability and accessibility of insect farming and consumption and the development of high-value-added products continue to grow.

CONCLUSIONS

We conclude that edible insects are an excellent nature-based source of nutrient-dense biomass suitable for human food, animal feeds, and medicine. They contain substantial amounts and varieties of biologically active compounds that can be exploited in the development of specific medications for the diagnosis, treatment, and prevention of human and animal diseases. Despite the economic benefits of edible insects' utilization in global medicine, limited research attention has been paid to their application in human-based interventions to establish whether their functional activities in humans are similar to those observed in animal models. However, the edible insect sector is rapidly growing and gaining global attention from diverse research institutions, governments, and the private sector in recent years. Despite the innovations and interest in the field, uptake and adoption of insect-based technologies for expansion as food, feed, or medicine would need additional support from international and national laws and policy makers. In addition, research attention should focus on conducting detailed inventories to identify, discover, and diversify edible insect species with both nutritional and therapeutic characteristics. Research endeavors should be directed toward the safety and stability of edible insect–derived products and the development of nontoxic and safe food and feed products. A detailed understanding of the processing techniques available to significantly reduce allergens in various edible insect species is crucial, particularly in relation to cross-reactivity and allergenicity. Edible insects could represent the future of food and feed research, as well as of medicine, and significantly contribute to improved nutrition and health in humans and animals. Evaluation and application of edible insects as biofunctional ingredients for dietary nutrient bioavailability and therapeutic enhancement should be given more attention and critically explored and studied. As discussed in this review, many biological compounds have been reported in edible insects with wound healing, antimicrobial, anticancer, anti-inflammatory, and antioxidant properties. This provides a broader prospect for the application of edible insects, with promising opportunities for use in the healthy food and biomedical industries to meet the human and animal demand for nutritious food and safe medicine. However, these multifaceted elements of edible insect species must be carefully considered in the establishment of future regulations at the national and international levels.

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