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Utilisation of Insect Gut as a Biosource for the Development of Future Biotransformation Processes

Converting wastes, organic materials and residues into valuable products

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Sustainability has been one of the main issues in the world in recent years. The decrease of resources in the world, along with the growing world population and the resulting environmental waste, present a fairly significant problem. As an alternative solution to this problem, insects are put forward as an ideal resource. Due to the enzymes and microorganisms in their intestinal microbiota, the biotransformation processes of insects are capable of converting wastes, organic materials and residues into valuable products that can be used for various industrial applications such as pharmaceuticals, cosmetics and functional foods. Some species of insects are in an advantageous position because of the simplicity of their lifecycle, the ease of their production and their ability to feed on organic materials to make valuable products. From a sustainability perspective, utilisation of the microorganisms or enzymes isolated from these microorganisms available in the microbiota of insects may allow novel insect-based biotransformation processes that promise a more sustainable world and novel green technologies.

Introduction

The chemical conversion of substances by living organisms or enzymes is called biotransformation (1). There are several different reactions involved in biotransformation processes, including oxidation, dehydration, hydrolysis, reduction and esterification. These specific reactions have high biotransformation yields (2, 3). Biotransformation processes are economical and environmentally friendly processes (4). Insects, the most successful group of animals in terms of both diversity and survival, are a sustainable alternative for biotransformation processes due to their low environmental impact and high productivity (5–9).

Insects contain a diverse and complex community of microorganisms in their guts where biotransformation takes place (6). There are a wide variety of microorganisms in the insect gut microbiota, including bacteria, viruses, fungi and archaea. Bacteria are the most abundant microorganisms in the gut microbiota (10). Most insect guts contain large gut communities of specific bacteria (5). Analysis of insect-microbiota interactions has contributed to a better understanding of insect ecology and explains its achievements in nature (11). Insect intestinal microbiota is a system inhabited by various microorganisms and enzymes that affect food digestion, defense against pathogens, host nutrition and immunity (12). The gut microbiota, an important part of the system, is affected by a range of stimuli, including diet, disease conditions, stress, pathogens, pharmaceuticals and phytochemicals (9). The insect gut microbiota is considered a highly efficient natural bioreactor. The gut microbiota has its own metabolism that can break down waste and generate products that benefit the host (13). Insects can be produced more sustainably than conventional livestock since they have higher feed conversion efficiencies, consume less water and land and emit fewer greenhouse gases (14). The cultivation of insects on various organic wastes provides an opportunity to produce bio-based products with the simultaneous utilisation of nutrient-rich animal feed, fuel, organic fertiliser, waste (15) or natural compounds.

Insects produce biomass by feeding on waste. At the same time, they can produce compounds with different bioactivities *via* the biotransformation of natural compounds through the microorganisms and enzymes in their microbiota. Insects or larvae can be used directly, or by isolating microorganisms or enzymes in the microbiota and performing bioconversions in bioreactors, high value-added products can be produced using environmentally friendly and sustainable approaches (**Figure 1**).

In this review, biotransformation processes that utilise the insect gut as a bioresource will be discussed.

Insect Gut: Structure, Functions and Symbionts

Insects' digestive systems share a common basic structure. The foregut, midgut and hindgut represent three parts of an insect's intestinal system. The foregut and hindgut are derived from embryonic ectoderm. Before digestion starts, food is deposited in the foregut and passes to the midgut. Water is absorbed by the hindgut, which is also where faecal matter is stored before being ejected from the body (16). The midgut has the highest level of digestion and absorption (17). Endothermal cells differentiate into the midgut. The midgut of some insect species is divided into two by a structure known as the peritrophic matrix or membrane (18). The midgut's peritrophic membrane provides mechanical digestion and inhibits the absorption of hazardous toxins with large molecular weights. Additionally, it prevents microorganisms from reaching the intestinal epithelium. The basic structure of the insect gut may change depending on its habitat niche and variation in feeding habits. Many of these adaptations result from the symbiotic relationships between insects and microorganisms (5).

The lifecycle of an endopterygote (Holometabola) insect consists of three stages: larval stage, pupal

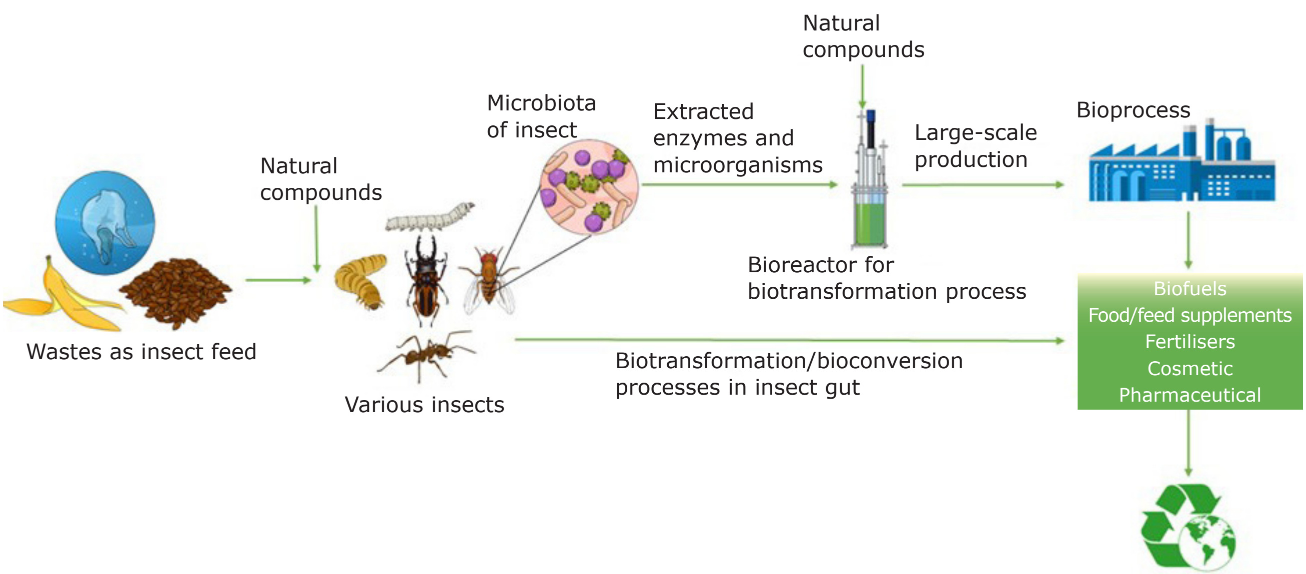

Fig. 1. Production of sustainable products using insects and use of insects as biosources in bioprocesses

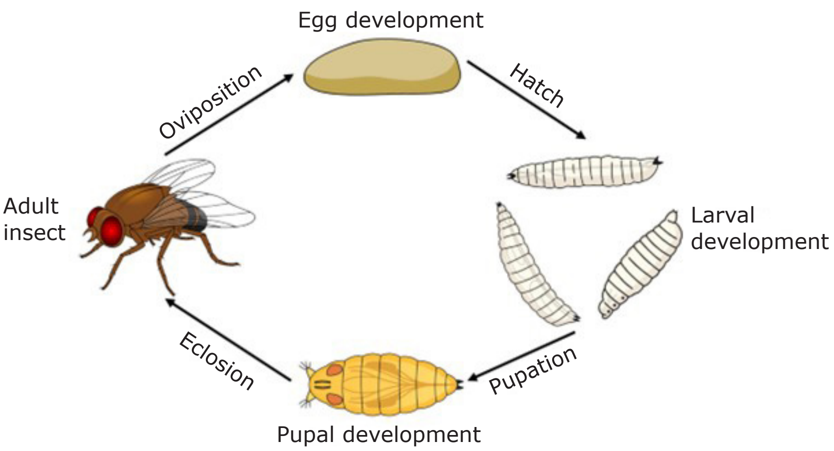

Fig. 2. The lifecycle of an endopterygote insect

stage and adult stage (**Figure 2**) (19). Since they have different structures at each stage, the gut microbiota also varies. For example, when the larvae turn into pupae, they change their intestine walls and almost all of the microbiota can be altered (20). Therefore, insects have an unstable gut microbiota until they reach adulthood.

The symbiotic relationships of organisms are an indispensable part of nature. Microorganisms live with a vast variety of other organisms, especially animals and plants (21). Many resident symbionts live in the gut of insects. The diversity and evolutionary success of insects are due to their beneficial gut symbionts (20).

The majority of insect species have used symbiotic relationships to improve their metabolic processes. Symbionts play important roles in the digestive system, fertility, development and growth of their hosts (21, 22). They also help in detoxifying the host and providing pathogen resistance. However, symbiotic relationships can also stimulate the hosts' immune response (23).

Insects provide food and a safe environment for symbionts. Symbionts, on the other hand, contribute to the nutrition of the host by providing the enzymes, vitamins or sterols necessary for digestion. The host's digestive products may change depending on the symbionts' features (24). Insect gut symbionts can contain many types of microorganisms such as bacteria, archaea and viruses (25).

Insects may execute a variety of biotransformations with the help of these microorganisms that they are normally unable to do. Intestinal microorganisms have developed the ability to degrade a wide range of materials, including lignocellulose and even plastic (26–28).

The insect gut microbiota can enhance the host's nutrient absorption and digestive efficiency by providing enzymatic functions. For example, *Bombyx mori* is an insect used in silk production and for medicinal purposes in China. A component of the intestinal microbiota of *B. mori* is *Enterococcus mundtii*, which can effectively convert lactic acid under highly alkaline conditions (29). For the production of bioplastics, lactic acid is an essential metabolite and demand for it is rising steadily (30). Insect species capable of biotransformation such as *B. mori* can be used in the pretreatment of biomass to produce valuable compounds.

Insect gut microbiota is influenced by many factors, including gender, environment, diet, gut physiology and pH, availability of oxygen in the gut and stages of development (5, 31, 32). Yellow mealworms' guts predominantly contain Firmicutes, Proteobacteria, Tenericutes, Bacteroidetes and Actinobacteria. According to a study, Streptococcaceae, Spiroplasmataceae, Clostridiaceae, Enterobacteriaceae and Lactobacillaceae species were detected in the intestines of yellow mealworms after they were fed with polylactic acid for 24 days. It has been proven that gut symbionts in the microbiota can change with diet (33).

Insect Species Currently Used for Biotransformation

Some insect species are used industrially in biotransformation processes for today's waste. The most common insect species is *Hermetia illucens* which is usually known as the black soldier fly (31). Black soldier fly larvae (BSFL) (Diptera, Stratiomyidae) mostly inhabit temperate regions of America but today they are spread throughout Europe, North and South America, Asia and other warm regions around the world (33, 34). There are five stages in the *H. illucens* lifecycle. These phases include eggs, larvae, pupae or pupa and adult phases respectively. Most of its lifecycle is spent in the larvae and pupa stages (35).

BSFL presents a highly effective process for the bioconversion of food waste. Fertilisers, food waste, industrial waste or animal waste can easily be processed by BSFL (15, 36). So large volumes of waste can be converted into high nutrient-value products (37). Another important characteristic of BSFL is that they are easy to produce and fast breeding. Using the larvae of this species has provided a more sustainable process to reduce the ecological footprint of organic waste (38). The BSFL gut microbiota can change depending on the substrates they feed on. So, changing the BSFL microbiota helps turn the substrates into industrially usable and valuable compounds (39).

BSFL can degrade antibiotics inside fertilisers due to bacteria in their microbiota. A study has shown that biodegradation of tetracycline antibiotics is affected by bacteria and fungi found in the microbiota. Proteobacteria and Firmicutes constituted approximately 99% of the flora in the gut microbiota before BSFL larvae consumed the tetracycline-containing fertiliser material. Eight days after the tetracycline consumption, microflora analyses showed that while Bacteroidetes species increased, Proteobacteria and Firmicutes decreased in numbers. This increase shows a variation in the degradation of tetracycline. Other bioconversion products were obtained such as biodegradation, hydrolysis and inactivation products (40).

Musca domestica (Linnaeus) (Diptera: Muscidae) is another type of insect used industrially. Their ability to live in a temperate climate, their short lifecycles, their rapid reproduction and their high adaptability have allowed them to expand widely around the world. *M. domestica* larvae (MDL) feed on organic waste such as animal waste and food waste and produce a variety of biotransformation products. Some factors that influence the effectiveness of the biotransformation process affect the growth and development of the larvae. These factors include substrate temperatures, pH values and humidity levels. However, when optimal conditions have been achieved, MDLs are extremely important insects for the bioconversion of food wastes (41). When MDL is fed with food waste and organic fertiliser, MDL can convert the waste into biomass with high protein and oil content and this biomass can be used in biodiesel production (42). Cheng *et al*. have used restaurant waste (cereals and dish waste) as a substrate for MDL to obtain biomass (43).

In addition to these species, different insect varieties can convert organic wastes into biomass. For instance, the Codling moth (*Cydia pomonella* L.) (Lepidoptera, Tortricidae) can use organic waste and convert it into biomass. Cambodian field crickets (*Teleogryllus testaceus*) are another species that is used as a bioconverter insect (44). *T. testaceus* can produce biomass by using organic waste such as spent grain, field weeds and cassava plant tops (45). Currently used insect species, their biotransformation products and intestinal microbiota properties are summarised in **Table I**.

Current Biotransformation Products of Insects

Due to global needs, insect species with high nutritional value are now produced in large amounts. Industrial methods must be used to produce food and animal feed. The most common insect species are beetles (Coleoptera), followed by caterpillars (18%), bees, wasps, ants (14%) and grasshoppers (Orthoptera) (13%). Orthoptera species can have up to 77% (on a dry basis) of their weight in protein, while Lepidoptera species can have up to 77% (on a dry basis) of their weight in oil (6). In addition to being high in copper, iron and magnesium content, edible insect species are also high in unsaturated fatty acids and amino acids. The use of insects as a soy protein substitute in animal feed and aquaculture production is supported by a quantity of research (60–62).

In the bioconversion of wastes, biogas, biodiesel and biomass products can be obtained using BSFL (63). In particular, biomass produced by BSFL fed with different diets can be used as a raw material for biogas formation due to its high oil and protein content. By extracting the oil content, the use of BSF constitutes an alternative to the classical biodiesel production processes. In a study using corncob, biogas was produced by anaerobic fermentation. Subsequently, BSFL fed with organic matter residues were transformed into biomass. The oil obtained from the biomass was used in the production of biodiesel (50).

The biomass produced as a result of the alteration in the intestinal microbiota when BSFL bacteria are fed with various substrates contains various amounts of protein and fat depending on the substrate. Examples of foods used and studied for

Table I Currently Used Insect Species, Their Biotransformation Products and Intestinal Microbiota Properties

Name of the species	Source	Substrate	Process time, days	Biotransformation products	Intestinal microbiota	References
Tenebrio molitor	China	Bran-fed, 100% PLA fed, PLA bran mixtures in different concentration levels	24	Frass	*Lactococcus* sp., *Spiroplasma*	(46)
Waxworms *(Plodia interpunctella)*	NM[a]	PE films	60	PE depolymerisation compounds that have a low molecular weight, water-soluble compounds	*Bacillus* sp. *YP1, Enterobacter asburiae YT1*	(47)
***Tenebrio molitor* (Yellow mealworm)**	China	PS stratiform	30	Depolymerisation products of long-chain PS films, depolymerisation metabolites, CO_2, biomass and fecula	Bacteria strains that are located in the TML gut, the extracellular enzyme in the TML gut	(25)
Tenebrio molitor	China	5 different crop residues	32	Lignin, hemicellulase, cellulase	Bacteria strains that are located in the TML gut	(48)
Odontotaenius disjunctus	USA	Wood	NM	Glucose, xylose	*Novosphingobium*, *Lactococcus*	(49)
Hermetia illucens	China	Corncub	8	Biogas, biomass	NM	(50)
Hermetia illucens	China	Rapeseed straw, chicken manure	15	Biodiesel	NM	(51)
Hermetia illucens	China	Fresh manure, daily manure	21	Biodiesel	NM	(52)
Hermetia illucens	NM	Rubber seeds	12	Biomass	NM	(53)
Hermetia illucens	Indonesia	Cassava peels	20–54	Biomass	NM	(54)
Hermetia illucens	China	Wheat bran which is contained TC in different concentration levels	8	Biodegradation, hydrolysis and inactivation products	Bacteroidetes	(40)
Musca Domestica	China	Restaurant waste	NM	Biomass, organic fertiliser, biodiesel	NM	(42)
Musca Domestica	China	Cereal waste, dish waste	30–50	Biomass	NM	(43)
Chrysomya megacephala	China	Fresh swine manure	5–6	Biomass	NM	(55)
Bombyx mori	China	Mulberry leaves	NM	Chlorophyll, sodium copper chlorophyll, pectin, carotene, triacontanol, solanesol	NM	(56–59)

[a]NM: Not mentioned

the BSFL diet are rapeseed straw, rubber seeds, chicken manure, fresh manure, dairy manure, cassava peel, wheat bran and corncob (50–54). In addition, insects have the potential to utilise organic byproducts such as food waste or lignocellulosic waste from bioethanol production.

Silkworms carry out the biotransformation of the nutrients or natural compounds they take in through nutrition *via* the microorganisms in the digestive system and the enzymes they secrete. Silkworm faeces obtained at the end of biotransformation can be evaluated as raw materials for various products such as chlorophyll, sodium copper chlorophyllin, pectin, phytol, carotene and triacontanol used in the pharmaceutical and food industry (14, 64). Silkworm faeces contains solanesol, a very important precursor in cardiac drugs (**Table I**). Silkworm is considered a potential medicinal insect due to the wide use of its byproducts and waste. It provides up to 40% recovery in the silk industry through the use of waste (65). It may be possible to isolate the microorganisms in the silkworm microbiota and the enzymes they secrete, thus designing new biological production processes and discovering new molecules with novel bioactivity (66).

Potential Applications of Insect Gut Enzymes and Symbionts

Insect gut microorganisms frequently enrich nutrient-poor diets and support the digestion of hard-to-digest dietary components. Insects can be used for their chitin (for medicinal purposes), proteins, lipids, minerals and vitamins as well as valuable enzyme systems for other bioconversion processes. Additionally, they can be a source of antimicrobial peptides, plant protection techniques and alternative antibiotics (6).

The degradation of plant biomass is a challenge for industrial bioprocesses, and the potential of the intestinal microbiome of insects has been studied (10). To produce bioethanol, the lignocellulosic material that makes up plant biomass must be transformed into fermentable sugar or glucose. Termites (Isoptera), beetles (Coleoptera) and cockroaches (Blattodea) are among the insects that consume lignocellulosic biomass.

Termites use their jaws to mechanically grind lignocellulosic material. Additionally, they may break down 74–99% of cellulosic material. Lignocellulose is digested by the termites' own enzymes and enzymes in the termite gut's symbiotic microbiota. This symbiotic ecosystem that degrades lignocellulose is called a 'minute intestinal bioreactor'. Digestion can take from a few hours to 24 h. Termites can rapidly and effectively consume biomass. However, the amount of production is not sufficient for commercial use. Therefore, greater amounts of termite β-glucosidase must be produced by molecular techniques for bioethanol production. The termite laccase enzyme (*Reticulitermes flavipes*), which helps in the digestion of lignocellulose, may also be used to produce biofuel (6, 67).

Cellulase gene transcripts involved in the digestion of lignocellulosic biomass by termites have been identified. As a result of the studies, three xylanase genes from intestinal tract samples of Lepidoptera species and one from termites were discovered. Termite enzymes and microbial symbionts must work together for the complete digestion of lignocellulosic material (9, 68). *Odontotaenius disjuncts* is an insect which contains symbiotic bacteria and enzymes in its intestinal system. By using this microbiotic environment they can easily degrade the lignocellulosic plant cell wall and produce various biotransformation compounds. *Turicibacter, Clostridium* and *Novosphingobium* contain glucose hydrolases, which can break down cellulose and xylazine. While lignin is broken up by phenol laccase and iron-manganese superoxide dismutase enzymes in the midgut region, Erysipelothrix, *Parabacteroides* and *Lactococcus* can degrade the biotransformation products such as glucose and xylose in energy production processes (49). It is also known that root borer (*Derobrachus hovorei*), green grasshopper (*Omocestus viridulus* L.) and caterpillar (*Spilosoma virginica*) can also turn plant materials into glucose due to their microbiota (69).

Antimicrobial peptides are produced by insects and the microorganisms that live as symbionts in their intestines. Peptides with antibacterial or antifungal effects were found when active metabolites in the intestines of several insects were examined. Peptides isolated from the blood of an experimentally infected *Calliphora vicina* showed antitumour and antiviral activity in mouse trials. It has been reported that the peptide Lucimycin, which was isolated from the common green bottle fly *Lucilia sericata*, exhibits antifungal activity against oomycete species belonging to the genus *Phytophthora* sp. (70). Although there are peptides obtained from insects that have antibacterial, antifungal, anticancer and antiviral activities, their commercial usage is limited by their poor bioactivity, low stability, possible toxicity, high cost and challenges with mass production (71).

Pheromones, allomones and kairomones are examples of semibiochemicals that are either generated by the insect itself or by symbiotic microbes. *Meloidae* and *Oedemeridae* insect groups generate cantharidin as a defense and it has anticancer and antitumour effects. Due to its toxic side effects, its application has been restricted. Pederin, a semibiochemical that was extracted from an insect of the genus *Paederus*, inhibits protein production and has anticancer properties (72).

Insect gut proteases are an alternative source of microbial proteases. Fast catalytic activity and chemostability are the two most significant characteristics of insect proteases. These characteristics make it possible to use in sectors including food, leather and textiles. Production of detergent frequently makes use of alkaline proteases. *Spilosoma obliqua* alkaline protease has activity between pH 9 and pH 11 and between 30°C and 60°C. This protease can be used as a cleaning agent for contact lenses and as an addition to detergent (73). By combining the pure serine protease from the gut of the silkworm pupa with detergent, its stain-removing ability was demonstrated. This enzyme is active within the range pH 9 to pH 11 and between 45°C and 60°C. This serine protease exhibits chemoresistance in solvents such as xylene, DMSO and toluene. For this reason, it can be used in synthetic reactions in the pharmaceutical industry (74). It has been reported that *Periplaneta americana* proteases (pH 8 and 60°C) and *Helicoverpa armigera* proteases (pH 10 and 50°C) have been purified for use in detergent production, medical and chemical synthesis (75, 76).

Coeliac is an autoimmune disease that occurs in the small intestine. In humans, abnormalities in the metabolism of prolamins (gluten) in grains such as wheat, rye and barley cause coeliac disease. Individuals with genetic susceptibility show antiinflammatory activity against gluten and prolamin-derived Pro and Gln (77, 78). *Tenebrio molitor* typically consumes substrates that contain gluten. When fed on various naturally gluten-containing substrates, *T. molitor* larvae were found to produce an end product with less than 20 ppm of gluten (79). The cysteine protease and prolyl endopeptidase of *T. molitor* can break down foods containing gluten. For the hydrolysis of prolamins, the *T. molitor* post-proline-degrading peptidase performs best at an acidic pH. With its acidic nature, it has excellent stability in the human stomach and has the potential to treat coeliac disease. Studies are ongoing for dietary supplementation or oral administration of these proteases (67, 80).

Environmental Aspects

Food waste is produced worldwide each year, posing a major risk to the environment and causing great concern in many countries (13). Methods such as storage and incineration can produce large volumes of leachate, odour, dioxins and greenhouse gases (81–84). Insects can feed on waste produced by humans. Bioconverting insects convert large amounts of organic waste into biomass rich in proteins and lipids. BSF, a bioconverting species, is a promising and sustainable source of bioactive compounds, lipids and proteins in the biotransformation of organic wastes in the gut microbiota (41, 85–87).

Wastes from livestock contain a high proportion of pathogens and antibiotic-resistance genes (ARGs). The biotransformation of livestock manure using larvae of the beetle *Protaetia brevitarsis* is a useful method for both value creation and waste reduction. Insect cultivation on different organic wastes offers the chance to biotransform organic wastes in the intestinal microbiota into value-added goods like animal feed, fuel and organic fertilisers. The transformation of organic waste into biofertilisers is a key function of saprophagous fauna like the edible eastern beetle (*P. brevitarsis*) (14). Biodiesel produced by gut microbiota from insects has proven to be a sustainable raw material (88–90). The current industrial biotransformation of lignocellulose requires the application of high temperature and acidic or basic conditions to decompose lignin, reduce crystallinity, increase pore volume and solubilise cellulose and hemicellulose. This is called pretreatment (91, 92). However, this process is expensive, inefficient and environmentally unsustainable (91, 93, 94). The gut symbiotic microbiota of insects are able to digest lignocellulose and the enzymes or bacteria that digest lignocellulose are instrumental in the development of a low-cost biofuel. The gut microbiota of these species are considered high-throughput natural bioreactors (95).

The difficulty of recycling plastics, the accumulation of large amounts of waste plastic in the environment and its harmful effects on human health cause serious environmental problems (96–99). By using microorganisms in the gut microbiota of insects to develop easily degradable plastic materials, the negative effects caused by plastics can be mitigated (100). In the gut microflora of insects, there are microbial communities that have the potential to biodegrade and biotransform plastic in contaminated environments (46, 101, 102). *T. molitor* (Yellow mealworm), which is found in the family Tenebrionidae and the order Coleoptera, is an industrially widely used insect that can decompose organic waste. In recent years, *T. molitor* has gained more interest due to its ability to biodegrade plastic wastes such as polystyrene (PS), polyethylene (PE) and polypropylene (PP). They can be fed on different organic wastes such as wheat bran and oats (103). In a study by Yang *et al*., *T. molitor* larvae (TML) were fed with styrofoam which is a product made from PS. Due to their microbiotas, they excreted faeces within 12–24 h. The bacteria and extracellular enzymes found in the TML microbiota degraded the PS. When the new faeces were examined, the long-chain PS molecules were degraded and the metabolites were stored in the TML intestine. The process also resulted in CO_2, biomass and fecula. Based on the chemical and physical transformations and properties of the fecula, it was shown that TML can successfully degrade PS (25).

Downstream processes for the purification of bacterial polyhydroxyalkanoates (PHA) are costly and not environmentally friendly. Mealworm (*T. molitor*) can produce polyhydroxyalkanoate granules by rupturing freeze-dried *Cupriavidus necator* cells that produce polyhydroxyalkanoate. The use of *T. molitor* in downstream processes for PHA production offers a more environmentally friendly purification method by reducing costs and minimising the use of solvents (104).

Conclusion

The intestinal microbiota of insects can be used to develop biotechnological applications thanks to their metabolic and physiological diversity. Today, there are applications where insects are used in the production of food, feed, chemicals and enzymes for the biological conversion of organic residues. Studies on cellulose and xylan hydrolysis, plastic degradation, vitamin production, nitrogen fixation, production of phenolic compounds and production of antimicrobial compounds or signal compounds with microorganisms and enzymes isolated from insect microbiota are available in the literature. It has been proven that symbiotic microorganisms in the insect gut can be produced microbially by gene transfer methods without culturing. The activity of the gut microbial community is determined in part by physiological conditions. Biotransformation products with desired properties can be obtained by manipulations that can be made in the insect gut. In future studies, the insect intestinal metabolism should be clarified for the use of insects as bioreactors. It seems possible in the near future to use both the biotransformation products produced by insects in their bodies and the enzymes and microorganisms that are isolated and reproduced from the intestinal microbiota in order to dispose of wastes and convert them into valuable products.

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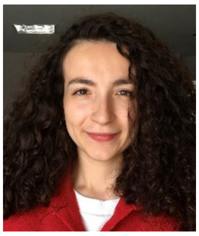

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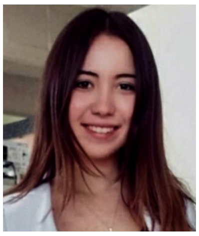

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