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The exploration and utilization of functional substances in edible insects: a review

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Abstract

Edible insects as food have been considered as a core future protein source. Not only are edible insects abundant in nutrient value, but also have numbers of functional substances, which could provide a multiple valuable benefits for humans. This review examines and summarizes the functional substances in edible insects and their special effects for people, as well as the use and prospects for these functional substances. There are many functional substances in edible insects, such as antimicrobial peptides, interferon, sex attractant hormones, cordycepin, active polysaccharides, microelement, chitin/chitosan, steroidal material, vitamin, lecithin, etc., which could provide multiple benefits for human beings. These special functional substances could help people enhance immunity, inhibit tumor, regulate intestinal function, relieve fatigue, anti oxidation, protect against colds, improve sleeping, promote the growth and development, as well as reducing blood sugar and blood pressure, among others. According to these valuable efficacies, the functional substances extracted from edible insects can be exploited mainly in three ways: edible insects are used to discover new medicines or health care products for people; and edible insects are applied in chemical, agricultural, food technology, pollutant treatment and textile sectors; as well as being consumed as animal feedstuff for livestock and other animals, which indirectly meet the different requirements for humans. Currently, edible insects have generated global interest to be developed as different forms of products and has promoted more research and development. However, pupae and larvae are still the main consumption ways in the market, which is unacceptable. to most people. It is expected that the edible insect industry would be prosperous and sustainable by integrating the power of beneficial policies and regulations, huge consumer demand and proper strategies of promotion and production.

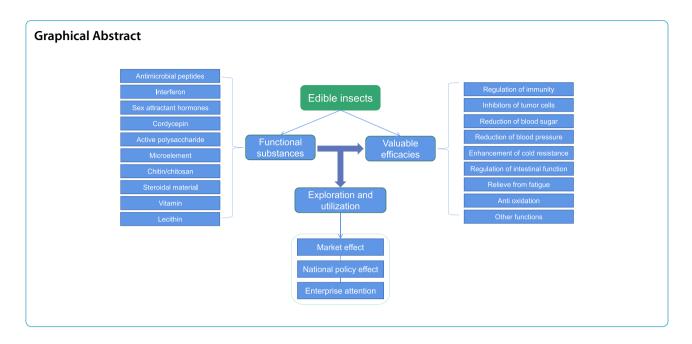
Keywords: Edible insects, Functional substances, Valuable efficacies, Development and application, Prospect

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Introduction

Population growth, urbanization, over-exploitation and depletion of natural resources, climate change and decreased availability of arable land are some of the crucial factors that may raise the food crisis, which probably result in the issue of global food security in the coming years (Legendre & Baker 2020; Verneau et al. 2021). Edible insects regarded as a potential sustainable animal protein by The Food and Agriculture Organization of the United Nations can meet the growing global demand for new protein sources (Hadi & Brightwell 2021). These species can provide the equivalent amount of animal protein as well as cattle, pigs and poultry, while they use less land and water, and produce much lower levels of greenhouse gases (Hermans et al. 2021; Lanng et al. 2021). Thus, edible insects should not be neglected in the quest to safeguard the future global food security (Brunner & Nuttavuthisit 2019; Meyer-Rochow et al. 2021).

Edible insects have been used as food since 7000 years ago. It has been recorded that over 2300 edible insects of 18 orders occur in many parts of the world, including Asia, Oceania, Africa, and North and South America (Jongema 2017; Tang et al. 2019; van Huis 2013). Generally, people consume edible insects in the original forms of pupae or larvae, which contain abundant nutrient substance, including protein, amino acids, minerals, vitamins, and easily digestible fatty acids. However, the primitive way of consumption and some traditional aspects prevent most people from trying this unique and splendid flavor (Hlongwane et al. 2020; Verneau et al. 2021). Besides, edible insects are also widely used in feed or feed additives. In order to

expand consumer market and promote the development of industry sustainably, it is necessary to change the consumption patterns for edible insects (Hermans et al. 2021).

Since times immemorial, edible insects have not only been used as an item of food, but have also played important roles in the treatment of diseases and other dysfunctions (Himan 1933; Morge 1973). Apart from being rich in nutrients, edible insects also have a lot of functional substances, including a variety of amino acids, functional lipids (i.g. polyunsaturated fatty acids, complex lipids, fat modified products, fat substitutes and so on), microelement, insect vitamin and hormone, not to mention fibre and chitin deemed to be beneficial for gut functionality. Due to these various functional substances, edible insects resources have been used by human beings for a long time as medicine and chemical materials. Extractions from insect bodies, eggs and egg shells, and insect exuvium and secretions are used commonly in traditional medicine. In modern scientific domain, insects are also an important resource for the discovery of new drug (Feng et al. 2009; Lucas et al. 2021). Currently, edible insects industry has attracted great attention from individuals, enterprises, and even governments. Many fundamental studies and market surveys have focused on artificial culture, nutritional components, and food developing and processing have been conducted (Liu et al. 2020; Legendre et al. 2020; Meyer-Rochow et al. 2021). However, more in depth investigations into the exploration and utilization of functional substances from edible insects still need to be developed.

Functional substances in edible insects

As a new source of protein, edible insects are not only abundant in nutrient value, but also have a lot of functional substances, such as antimicrobial peptides, interferon, sex attractant hormones, cordycepin (Fig. 1A), active polysaccharides, microelement, chitin/chitosan, steroidal material, vitamin, lecithin (Fig. 1B), and so on (Ghosh et al. 2016; Oduor et al. 2008; Ran & Zhao 2014). These functional substances in edible insects could offer a variety of valuable benefits to people. They can enhance immunity, inhibit tumor, relieve fatigue, anti oxidation, protect against colds, improve sleeping, promote the growth and development for humans, as well as reducing blood sugar and blood pressure, and other efficacies for humans (Mohamoud et al. 2013; Ran & Zhao 2014).

It is a universal phenomenon that different functional substances extracted from edible insects have similar efficacies for people, while a single functional substance may have multiple efficacies for humans (Eleftherianos et al. 2021; Xu et al. 2021). For example, polysaccharides have proven to have immunological regulation, antifatigue, anti-mutation, anti-virus, anti oxidation and other functions, and they exist widely in animals, plants, and microbes (Ma et al. 2014; Zhong et al. 2015). In-depth research on polysaccharides has found that polysaccharides from different sources have certain differences in structure and monosaccharide composition. Polysaccharides and sugar complexes with medicinal physiological activities have functions of regulating immune capacity, inhibiting tumor cells, lowering blood pressure and blood sugar, anti-radiation, bacteriostasis, anti-virus, anti oxidation, free radical scavenging, among others. Especially, the antitumor function of polysaccharides has attracted the attention of the medical field (Feng et al. 2014; Lin et al. 2013). On the other side, antimicrobial peptides existing in edible insects can not only enhance immunity for people, but also inhibit tumor cell proliferation (Francesco et al. 2021). For example, antimicrobial peptides extracted from (Aspongopus Chinensis Dallas)

have obvious effects of antibacterial, anticancer, analgesic, anti-fiber and anti-angiogenic for humans (Mohamoud et al. 2013; Zhao et al. 2011). Similarly, chitin also has various physiological functions (Lucas et al. 2021). According to these valuable efficacies, the functional substances extracted from edible insects and can be exploited for many valuable products for human beings, like health care products, pharmaceuticals, food additives and animal feed (Qin et al. 2011; Zhong et al. 2015). This potential of edible insects has generated global interest to develop and use insect products and has promoted research and development on edible insects.

Regulation of immunity

Insect proteins mainly include antifreeze proteins, storage proteins, heat shock proteins, antimicrobial peptides, interferon, immune globulin-like, sterol carrier protein-2, pheromone binding proteins, diapause associated proteins, insect chitinase and other functional proteins, as well as a variety of active immune substances (Hermans et al. 2021; Lanng et al. 2021). In addition, antimicrobial peptides, antimicrobial proteins, bacteriolytic proteins, insect agglutinin and polysaccharides are important components of the defense system in the host, which can balance the bodies (Table 1) (Eleftherianos et al. 2021; Xu et al. 2020).

Antimicrobial peptides, antibacterial proteins and insect lectins extracted from heolymph of silkworm pupae, flies, moths, scorpions and other insects, have been applied in the production of anti-viral and antibacterial biological agents (Das et al. 2021; Ran & Zhao 2014; Xu et al. 2020). The antimicrobial peptides extracted from *A. chinensis* have good antibacterial effects on *Escherichia coli* and *Staphylococcus aureus* (Li et al. 2015; Wu & Jin 2005). The peptides of the larvae of queen bees have biological activities that could regulate the immune system and anti-aging. The antibacterial protein from the embryonic cell of *Musca domestica* has significant inhibitory activity

Table 1 The functional substances of immunological regulation in edible insects

Functional substances	Insect species	References
Anti-microbial peptide	Bombyx mori, Castor silkworm, Hyalophra cecropia, Tobacco hornworm, Sarcophagidae, Oestris ovis, Drosophila mela- nogaster, Honeybee, Meal beetle, Locusta migratoria manilen- sis, Aspongopus chinensis	Wu & Jin 2005; Ran & Zhao 2014; Li et al. 2015; Xu et al. 2020
Antimicrobial proteins	Silkworm Chrysalis, Musca domestica, Mesobuthus tamulus, Stomoxys calcitrans,	Zhang et al. 2013; Ran & Zhao 2014; Xu et al. 2020; Das et al. 2021
Agglutinin	Silkworm Chrysalis, Bombyx mori, Antherea pernyi, Hyalophra cecropia, Spodoptera exigua, Mythimna separata, Teleogryllus commodus, Periplaneta americana, Extatosoma tiaratum, Allo- myrina dichotoma, Boettcherisca peregrina, Musca domestica	Zhao et al. 2012; Ran & Zhao 2014; Xu et al. 2020; Eleftherianos et al. 2021; Lanng et al. 2021
Bacteriolytic proteins	Antheraea pernyi, Plutella xylostella, Helicoverpa armigera, Galleria mellonella,	Altincicek & Vilcinskas 2006; York 2018; Liao et al. 2018
Polysaccharides	Ericerus pela Chavannes, Silkworm Chrysalis, Tenebrio molitor, Periplaneta americana, Heterolocha jinyinhuaphaga Chu, Eupolyphagasinensis Walker	Sun et al. 2009, b; He et al. 2008 & He 2011; Zhao et al. 2012

on melanoma cells A375, and has no inhibition activity on normal human cells (Zhang et al. 2013). All of Bombyx mori, Antherea pernyi, Hyalophra cecropia, Spodoptera exigua, Mythimna separata, Teleogryllus commodus, Periplaneta americana, Extatosoma tiaratum, Allomyrina dichotoma, Boettcherisca peregrina, Musca domestica contain lectins, which could specifically bind to some monosaccharides and oligosaccharides, and act as agglutinating cells (Table 1). They have been applied extensively in scientific research and medicine (Eleftherianos et al. 2021; Lanng et al. 2021).

Besides, lysozyme is one of the antibacterial factors isolated and purified from hemolymph of insects, also known as cell wall lysozyme. Lysozyme is an important effector in animal natural immune system. It mainly kills invading pathogens by hydrolyzing peptidoglycan in bacterial cell wall, and plays an important role in humoral immunity of insects. It is produced in a non-specific manner in a variety of organisms, including insects, and plays an important role in insects that lack an acquired immune system as an Arsenal of innate immune defenses against invading pathogens (Liao et al. 2018; York 2018). It has been proven that the expression of lysozyme in both of Helicoverpa armigera and Galleria mellonella increases at the metamorphosis time from larval to pupal (Altincicek & Vilcinskas 2006; Zhang et al. 2009). Moreover, many species of edible insects, such as Ericerus pela Chavannes, Silkworm Chrysalis, Tenebrio molitor, Periplaneta americana, among others, containing starch, cellulose, glycogen, chitin and pectin, could regulate the immunity of human beings (Sun et al. 2009, b; Zhao et al. 2012; Liu et al. 2014).

Inhibitors of tumor cells

Anti-tumor is one of the most important efficacies of functional substances extracted from edible insects, which have drawn much attention from experts in the field of life sciences and medical companies in recent years (Eleftherianos et al. 2021). There are many functional substances of tumor inhibition in edible insects, including antimicrobial peptides, interferon, sex attractant hormones, cordycepin, steroidal material, microelement, vitamin, chitin/chitosan, and so on (Table 2) (Eleftherianos et al. 2021). These substances have been developed to become the new anti-tumor and anti-viral agents and clinical trials have been in progress.

It is common for functional substances to have different effects on humans. Antimicrobial peptides and polysaccharides existing in edible insects can not only enhance immunity for people, but also inhibit tumor cell proliferation (Eleftherianos et al. 2021; Xu et al. 2021). Currently, over 200 kinds of antibacterial peptides from insects have been identified (Xu et al. 2021). Back in the last century, Jia et al. (1997) found that the peptides from silkworm had the activity of tumor inhibition, which could even kill cancer cells. During the same period, Japanese also found that insect protein could offer antibacterial and anticancer effects on people. In the modern times, Xia et al. (2014) found that the combination of cecropin-XJ from silkworm and chemotherapeutic drugs could significantly inhibit the proliferation of Eca109 cells and induce apoptosis of E-CA109 cells. All of the cantharidin from Meloidae of Coleoptera, the dichostatin from Dynastidae of Coleoptera, and the isoxanthopterin from butterflies of Lepidoptera have proven to have anticancer activity components. At present, many related products have the market. In addition, polysaccharides with medicinal physiological activities can effectively

Table 2 The functional substances of tumor inhibition in edible insects

Functional substances	Insect species	References
Anti-microbial peptide	Bombyx mori, Castor silkworm, Hyalophra cecropia, Tobacco hornworm, Sarcophagidae, Oestris ovis, Drosophila mela- nogaster, Honeybee, Meal beetle, Locusta migratoria manilen- sis, Meloidae, Dynastidae, butterflies	Wu & Jin 2005; Ran & Zhao 2014; Li et al. 2015
Polysaccharides	Ericerus pela Chavannes, Silkworm Chrysalis, Tenebrio molitor, Periplaneta americana, Heterolocha jinyinhuaphaga Chu, Eupolyphagasinensis Walker	Sun, Feng, et al. 2009; He et al. 2008 & He 2011; Zhao et al. 2012
Interferon	Termitidae and Rhinotermitidae	Jiang 1999; Zhang & Hu 2000; Oloomi et al. 2018
Sex attractant hormones	Termitidae and Rhinotermitidae	Zhang & Hu 2000
Steroidal materia	Termitidae and Rhinotermitidae, Blattodea	Ran & Zhao 2014
Cordycepin	Cordyceps sinensis	Chen et al. 2013; Nxumalo et al. 2020
Trace elements	Polyrhachis vicina Roger, Anomala corpulenta, Motschulsky, Polyrhachis lamellidens, Periplaneta americana, Rhynchophorus phoenicis, Tenebrio molitor, Zophobas morio, Drosophila melanogaster, Hermetia illucens, Musca domestica, Bombyx mori, Acheta domesticus, Ruspolia differens, Sphenarium histrio, Sphenarium purpurascens, Imbrasia truncata, Euschistus egglestoni, Apis mellifera, Oecophylla virescens, Polybia occidentalis, Bee brood, Macrotermes nigeriensis, Anaphe venata, Usta terpsichore, Boopedon flaviventris	Liu & Wei 2002; Wang et al. 2004; Józefiak et al. 2016; Kulma et al. 2016; Arunthirumeni et al. 2021
Vitamin	Tenebrio molitor, Gryllus assimilis, Locusta migratoria, Shelfordella lateralis,	Douglas 2017; Schmidt et al. 2018; Liu et al. 2019; Zhang et al. 2020
Chitin/chitosan	Tenebrio molitor, Heliothis zea, Hypera postica, Drosophila melanogaster, Atta cephalotes isthmicola, Dendrolimus houi Lajonquiere, Dendrolimus punctata tehchangensis Tsai et Liu, Dendrolimus punctata wenshanensis Tsai et Liu	Merzendorfer, 2006; Merzendorfer & Zimoch 2003; Hahn et al. 2020; Lucas et al. 2021
Others	Aspongopus chinensis	Tan et al. 2013; Yang et al. 2017

Others - some valuable edible insects are of great value to human health, but these important effects have not been identified in relation to the specific substance

prevented the growth and development of cancer cells, which has heightened the attention of the medical field (Sun, Feng, et al. 2009; Zhao et al. 2012).

Interferon is a special protein released by reticular tissue cells and white blood cells, which could inhibit tumor by preventing virus synthesis and kill the cancer cells, and can be used to prevent and treat breast cancer, uterine cancer, and esophageal cancer (Jiang 1999; Oloomi et al. 2018; Zhang & Hu 2000). It is mostly found in the adults of Termitidae and Rhinotermitidae of Isoptera, and Formicidae of Hymenoptera, as well as the pupae of Saturniidae of Lepidoptera. In addition, the sex attractant hormones from the adults of Termitidae and Rhinotermitidae of Isoptera, and Formicidae of Hymenoptera could also be the cure for breast, uterine, and esophageal cancers (Zhang & Hu 2000).

Some species of edible insects like the adults of Termitidae and Rhinotermitidae of Isoptera and cockroach (*Blattodea*) adults cannot synthesize steroids by themselves, and need to obtain these substances from outside sources, such that some herbivorous insects can use phytosteroids from host plants. Cockroach is one of three kinds of animals in the world that would never get cancer,

and the steroidal material extract from them can improve the immunity, promote the growth of granulation, and have anticancer effect in humans (Ran & Zhao 2014; Sohn & Kim 2012). In addition, *Cordyceps sinensis* is the pathological product made of Hepialidae larvae of Lepidoptera (Chen et al. 2013). It has a significant anti-cancer effect by inhibiting cell division and nucleic acid metabolism, and has been used to cure esophagus cancer, liver cancer, osteocarcinoma, and prostate cancer (Nxumalo et al. 2020).

Edible insects are also rich in trace elements, especially iron (Fe), manganese (Mn), zinc (Zn) and copper (Cu), e.g. black ants (*Polyrhachis vicina* Roger), bronze beetle (*Anomala corpulenta* Motschulsky) and red-pecked spiny ants (*Polyrhachis lamellidens*) (Liu & Wei 2002; Tang et al. 2019; Wang et al. 2004), etc. As we know, Fe prevents stomach cancer, esophageal cancer and liver cancer; Mn is an important antioxidant with anti-tumor effects; Zn can promotes the immunity of humans and therefore enhance the anti-tumor function; Cu can also prevent the development of tumors (Józefiak et al. 2016; Kulma et al. 2016). More important, some edible insects contain microactive elements, such as selenium (Se).

Now it has been recognized that Se is the first trace element with anti-cancer effect and can remove free radicals of carcinogenic factors in the body, inhibit the activity of carcinogens, accelerate detoxification, destroy carcinogens, and prevent the division and growth of cancer cells (Arunthirumeni et al. 2021). A lot of edible insects contain trace elements (Fe, Mn, Zn, Cu and Se) as listed in Table 2.

Likewise, vitamin A (V_A) , vitamin C (V_C) and vitamin E (V_F) from edible insects also have antineoplastic activity for people (Jiang 1999). V_A prevents the canceration of epithelial tissues, inhibits the growth of cancer cells and promotes immunity. It has been proven that Vc could prevent cancer and restrain the invasion and diffusion of cancer cells, remove the carcinogenic toxins, and improve airframe immunity, as well as promoting the interferon synthesis. V_F has the anti oxidation effect, and can prevent aging (Liu et al. 2019; Zhang et al. 2020). However, insects generally cannot synthesize eight B vitamins that function as co-enzymes in various enzymatic reactions. Most insects derive their B vitamin requirements from the diet, microbial symbionts, or a combination of these complementary sources (Douglas 2017). Schmidt et al. (2018) gave the first validated report on the content of vitamin B12 (V_B12) in edible insects. The levels of V_B12 in mealworm larvae (Tenebrio molitor), cricket (Gryllus assimilis), grasshopper (Locusta migratoria) and cockroach (Shelfordella lateralis) were 1.08, 2.88, 0.84, and $13.2 \,\mu\text{g}/100 \,\text{g}$ dry weight, respectively.

Insects can be proposed as an alternative protein and other nutrients for human consumption. In addition to having an amino acid profile that can be compared with other food sources, they also have a considerable amount of fiber in their composition, present in the form of chitin in their exoskeletons (Wu et al. 2020). Chitin and its deacetylated form, chitosan are among the six life elements (i.e. protein, lipids, sugars, vitamins, mineral elements, chitin) in the European and American academic circles, and are important functional factors. Chitin is abundant in nature, and is a huge renewable resource (Merzendorfer 2006). The content of chitin in insect body surface is up to 18% (Hahn et al. 2020; Merzendorfer & Zimoch 2003). It can promote the peristalsis of digestive tract, absorb toxic substances, reduce the abdominal pressure and intestinal pressure, and prevent the occurrence of colorectal cancer (Lucas et al. 2021). Besides, γ-linolenic acid extracted from Clanis bilineata tingtauica Mell is proved to inhibit the growth of human neuroblastic cancer cells, induce the reversal of their surface type, restrain the DNA synthesis of colon cancer (Ma et al. 1993). Moreover, asparaginase from insects could prevent the proliferation of cancer cells. 10-Methoxyoleic acid from royal jelly, abundant flavonoids, terpenes, enzymes and organic acids from propolis show a synergistic effect on inhibiting cancer cells.

Furthermore, some edible insects are of great value to human health, but these important effects have not been identified in relation to any specific substance. The hemolymph of *A. chinensis* inhibit the proliferation of breast cancer and gastric cancer cells, which might be related to the presence of fumaric acid, 3,4-dihydroxybenzoic acid, adenosine, uridine and palmitic acid, among others (Tan et al. 2013; Yang et al. 2017; Zhao et al. 2011). Besides, the decoction got from *A. chinensis* can cause a dosedependent inhibition on the proliferation and migration of MDA-MB-453 and 4 T1 cells (Tian et al. 2020).

Reduction of blood sugar

There are a variety of hypoglycemic active substances in insects and their products, such as proteins, peptides, polysaccharides, unsaturated fatty acids, alkaloids, and flavonoids, among others (Chen & Liao 2013; Liu et al. 2007). It is reported that the hydrolysate and fibroin of silkworm is an ideal blood sugar regulator (Park et al. 2011; Wang et al. 2012). Ants are rich in protein, known as the treasure house of micro animal nutrition. They can regulate the endocrine dysfunction, enhance the metabolisms of carbohydrate, protein and fat. At present, the health care products of ant power capsules have been used to prevent diabetes syndrome in China. The formula of the capsule contains ants, yam, black sesame, fried jujube kernel, which can stabilize blood sugar (Li 2009).

In addition, grubs, honey, silkworm pupae contain a large number of polysaccharides with the effect of lowering blood sugar (He 2011, He et al. 2008; Zhao et al. 2012). Removing the acetyl group, chitin would convert into soluble chitosan, chitosan. Oligosaccharides (also known as chito-oligosaccharides) obtained by enzymolysis or acid hydrolysis of chitosan also have hypoglycemic effects on humans (Gao et al. 2012; Hahn et al. 2020).

Insect fat is rich in unsaturated fatty acids, which is listed in Table 3 (Elmadfa & Kornsteiner 2009; Finke 2013). Linoleic acid can improve glucose tolerance, has insulin effects, and reduces the incidence of cardio-vascular and retinal complications in diabetic patients (Muramatsu et al. 2010; Belluco et al. 2013). Increasing the intake of α -linolenic acid can significantly improve the insulin sensitivity of middle-aged people with normal body mass, slower the apoptosis of human umbilical vein endothelial cells induced by hyperglycemia (Józefiak et al. 2016; Zhang et al. 2007).

Studies about trace elements show that Mn, Zn, calcium (Ca), Fe, Cu, chromium (Cr), nickel (Ni), Se and others are related to human blood glucose metabolism

Table 3 The functional substances of reducing blood sugar in edible insects

Functional substances	Insect species	References
Polypeptides	Cryptotympana, Clanis bilineata tsingtauica, Tenebrio molitor, Locusta migratoria manilensis, Gryllidae, Apis mellifera	Salazar-Olivo, & Paz-Gonz, lez, V. 2005; Sun, Zhang, et al. 2009;
Polysaccharides	Ericerus pela Chavannes, Silkworm Chrysalis, Tenebrio molitor, Periplaneta americana, Heterolocha jinyinhuaphaga Chu, Eupolyphagasinensis Walker	Sun, Feng, et al. 2009; He et al. 2008 & He 2011; Zhao et al. 2012
Chitin/chitosan	Tenebrio molitor, Heliothis zea, Hypera postica, Drosophila melanogaster, Atta cephalotes isthmicola, Dendrolimus houi Lajonquiere, Dendrolimus punctata tehchangensis Tsai et Liu, Dendrolimus punctata wenshanensis Tsai et Liu	Merzendorfer 2006; Merzendorfer & Zimoch 2003; Hahn et al. 2020; Lucas et al. 2021
Unsaturated fatty acid	Bombyx mori, Antheraea pernyi, Philosamia cynthia ricini, Chondracris rosea, Gampsocleis gratiosa, Gryllidae, Musca domestica L., Tenebrio molitor, Clanis bilineata tsingtauica, Locusta migratoria manilensis, Acrida cinerea, Dendrolimus superans (Butler), Cryllus testaceus wallker, Orgyiaericae Ger- mar, Heliothis assulta, Argyrogramma agnata (Staudinger), Agrius convolvuli	Elmadfa & Kornsteiner 2009; Mariod et al. 2011; Belluco et al. 2013; Finke 2013; Rumpold & Schluter 2013; Józefiak et al. 2016
Cordycepin	Cordyceps sinensis	Chen et al. 2013; Nxumalo et al. 2020
Trace elements	Polyrhachis vicina Roger, Anomala corpulenta, Motschulsky, Polyrhachis lamellidens, Periplaneta americana, Rhynchophorus phoenicis, Tenebrio molitor, Zophobas morio, Drosophila melanogaster, Hermetia illucens, Musca domestica, Bombyx mori, Acheta domesticus, Ruspolia differens, Sphenarium histrio, Sphenarium purpurascens, Imbrasia truncata, Euschistus egglestoni, Apis mellifera, Oecophylla virescens, Polybia occidentalis, Bee brood, Macrotermes nigeriensis, Anaphe venata, Usta terpsichore, Boopedon flaviventris	Liu & Wei 2002; Wang et al. 2004; Józefiak et al. 2016; Kulma et al. 2016; Arunthirumeni et al. 2021
Vitamin	Tenebrio molitor, Gryllus assimilis, Locusta migratoria, Shelfordella lateralis,	Douglas 2017; Schmidt et al. 2018; Liu et al. 2019; Zhang et al. 2020
Others	Bombyx mori, Tenebrio molitor, Drosophila melanogaster, Hermetia illucens, Musca domestica	Liu et al. 2007; Park et al. 2011; Zhao et al. 2012; Chen & Liao 2013

Others - including alkaloids, fibroin, flavonoid, insect hormones, and other functional substances of reducing blood sugar in edible insects

and have hypoglycemic effects on people (Józefiak et al. 2016; Kulma et al. 2016). Cr can improve glucose tolerance. Ca can affect the secretion and release of insulin. Zn maintains the structure and function of insulin. Mn participates in the function regulation of pancreatic cells and can improve glucose metabolism index. Ni is the coenzyme of insulin (Arunthirumeni et al. 2021). Besides, vitamin D is a typical anti-diabetic vitamin, which is present at 10 times higher concentration in bee larvae than in fish liver oil.

The most frequent report about alkaloids with hypoglycemic activity in insects and their products is *Bombyx mori*, and the product 1-deoxynojirimycin (DNJ). DNJ and its derivatives can effectively inhibit sucrase, maltase, isomaltase, trehalase and lactase on small intestinal microvilli, but do not inhibit α -amylase, thus delaying the absorption of carbohydrate in food, which can be used in the treatment of diabetes and obesity, without causing sugar absorption disorders and other side effects (Kong et al. 2008; Liu et al. 2012). Moreover, flavonoids can reduce blood glucose by stimulating insulin release, increasing insulin sensitivity, inhibiting

 $\alpha\text{-glucosidase,}$ increasing the benefit of peripheral sugars, and promoting the use of hyperoxygenation. As well as insect hormones, such as ecdysone, which has hypoglycemic effect and can be used to improve the clinical symptoms of diabetic patients.

Reduction of blood pressure

Hypertension is well known as one of the major risk factors for cardiovascular diseases which annually affect millions of people. The angiotensin converting enzyme (ACE) plays a key role in blood pressure regulation. Indeed, hypertension treatment by synthetic ACE inhibitors is effective (Dai 2012). However, their use can cause serious side effects, such as hypotension, cough, reduced renal function and angioedema. Thus, research has focused on natural ACE inhibitory peptides sources such as foodstuffs and edible insects. In the last decades, ACE inhibitory activity has been detected in protein hydrolysates from insect species belonging to the orders of Coleoptera, Diptera, Hymenoptera, Lepidoptera and also Orthoptera. Further investigations led to identifying

Table 4 The functional substances of reducing blood pressure in edible insects

Functional substances	Insect species	References
Angiotensin converting enzyme	Bombyx mori, Tenebrio molitor, Spodoptera littoralis, Oecophylla smaragdina	Dai 2012; Cito et al. 2017
α-linolenic acid	Eligma narcissus Gramer, Clanis bilineata tsingtauica Mell, Tenebrio molitor, Zophobas atratus, Metabolus tumidifrons Fairm, Dastarcus longulus Sharp, Lycorma delictula White, Erthesina fullo Thunberg, Periplaneta americana, Lucilia sericata	Kong & Xiong 2006; Li 2006; Vercruysse et al. 2009
Chitin/chitosan	Tenebrio molitor, Heliothis zea, Hypera postica, Drosophila melanogaster, Atta cephalotes isthmicola, Dendrolimus houi Lajonquiere, Dendrolimus punctata tehchangensis Tsai et Liu, Dendrolimus punctata wenshanensis Tsai et Liu	Merzendorfer, 2006; Merzendorfer & Zimoch 2003; Hahn et al. 2020; Lucas et al. 2021
Others	Oxya chinensis	Hadi & Brightwell 2021; Hermans et al. 2021

Others - including lysine combinding with methionine, and other functional substances of reducing blood pressure in edible insects

specific ACE inhibitory peptides from *Bombyx mori, Tenebrio molitor, Spodoptera littoralis* and *Oecophylla smaragdina* (Table 4) (Cito et al. 2017; Dai 2012).

In addition, there is high levels of linolenic acid in edible insects, and it is an effective way of ingesting α -linolenic acid to prevent the synthesis of fatty acids and glycyrrhizin, and accelerate the β oxidation of fatty acids. Linolenic acid has the function of reducing triacylglycerides, prolonging coagulation time and anti-thrombosis, and it exists widely in lepidopterous larvae, such as *Clanis bilineata tsingtauica* Mell, *Tenebrio molitor*, *Zophobas atratus* (Table 4) (Kong & Xiong 2006; Li 2006; Vercruysse et al. 2009). Furthermore, the epidermis of *Tenebrio molitor* larvae is rich in chitin and chitosan, which can reduce blood pressure and blood lipid and promote cholesterol metabolism (Hahn et al. 2020; Lucas et al. 2021).

As we know, insects are high in protein, the dry body protein content of many insects is even up to 50%, and the amino acid composition is reasonable, so it is a high quality animal protein. Apart from synthesizing protein, some amino acids with important physiological regulatory function also participate in some special metabolic reactions. It is proven that lysine combinding with methionine could inhibit severe hypertension, and histidine could dilate blood vessels and lower the blood pressure (Hadi & Brightwell 2021; Hermans et al. 2021).

Enhancement of cold resistance

Eating edible insects enhance the ability of people against cold mainly rely on the antifreeze proteins. Antifreeze proteins are proteins or glycoproteins that have affinity with ice crystals and can bind to ice crystals and inhibit the growth of ice crystals. The first insect antifreeze proteins were isolated from *Tenebrio moliter* 50 years ago, and they have higher heat stagnation activity than antifreeze proteins in fish and plants, which could protect

the body from cold damage (Mao & Zhang 2009; Ramsay 1964). As food additives, the antifreeze proteins of the insects could improve the quality of frozen food and improve food quality. The DNAP Company of the United States adds insect antifreeze proteins to ice cream and ice milk, which removes the ice residues and improves the food quality and taste. In the regions where influenza vaccination is not available, taking ant products could protect the children, the old and infirm from cold (Melanie et al. 2002; Zhong et al. 2010). The elderly people, who have taken ant products for long-term avoided catching flu when the surrounding people were suffering from it.

Regulation of intestinal function

Chitosan is the product of deacetylated chitin, as already mentioned before. The chitosan ingested from edible insects would not be digested and absorbed as it belongs to a kind of dietary fiber, with part of the health care function of dietary fiber, such as promoting digestive tract peristalsis, adsorption of toxic substances, reducing abdominal pressure and intestinal pressure as well as prevention of colorectal cancer (Liu & Wei 2002; D' Antonio et al. 2021; Lucas et al. 2021). It is proven that intake of chitosan is conducive to the growth of short-chain fatty acids in the intestine, that would decrease pH and inhibit the growth of putrefying bacteria in the intestine. Meanwhile, ammonia, phenol, indole and other putrefying substances in feces are also significantly reduced, which are promoters of liver cancer and skin cancer (Sharbidre et al. 2021).

Relieve from fatigue

The functions of edible insects are related to the specific substances, e.g. anti-microbial peptides, polysaccharides, interferon, sex attractant hormones, steroidal material, cordycepin, trace elements, vitamins, chitin/chitosan,

unsaturated fatty acid, and antifreeze proteins, among others. Nevertheless, there are also some edible insects, the extraction from which could relieve fatigue, but their specific functional substances have not been identified. Oxya chinensis Thunberg is rich in protein, which can quickly supplement lysine and methionine to synthesize carnitine, and the alcohol extract from the adult can significantly improve fatigue resistance of mice. Zhang et al. (2008) found that the extracted bioactive peptides from male silkworm moth could enhance the anti-fatigue capability of mice. Li et al. (2015) found that extraction solution of A. chinensis acting on mice with kidney-Yang deficiency could significantly reduce the content of serum lactic acid and serum urea, and this in traditional Chinese medicine has been known to have remarkable anti-fatigue effects.

Anti oxidation

Similarly, the extraction solution from some edible insects has anti oxidation effect in humans. It is reported that enzymes in insects, such as superoxide dismutase (SOD) and peroxidase (POD), and non-enzyme anti oxidation such as ascorbic acid and carotene, can remove the excessive reactive oxygen species (ROS) in the body system (Lopez-martinez et al. 2008). Studies on the antioxidant activities of the water soluble protein, acid soluble protein, mellow soluble protein and alkaline soluble protein from barley pest (Zophobs morio L.) showed that the water soluble protein had the strongest reducing activity and scavenging power for superoxide anion, while the acid soluble protein had the strongest scavenging power for hydroxyl (Guo et al. 2011). The ethanol extracts of all seven edible insects (i.e. Lucilia sericata, Cryptotympana atrata Fabricius, Silkworm chrysalis, Vespa magnifica Smith, Ctdorophor separabus Gressitt, Locusts/Grass hoppers, Chilo sp., Sinictinogomphus clavatus Fabricius) from Yunnan Province in China have good scavenging effects on ABTS radical (Ma et al. 2021).

Other functions

There are other functions of edible insects for humans health. Ant products have sedative and hypnotic functions, and it has been found that ant products can lead people to deep sleep process, which can greatly improve the sleeping quality of those who have long-suffering neurasthenia insomnia (Li et al. 2015). Also, the drone larvae could increase the body length of young animals, and could promote the height of humans, that means some functional substances in edible insects could promote the growth and development of people. Apitoxin derived from bees and wasps can be used to treat diseases such as rheumatism and rheumatoid arthritis, gout, and other diseases. The fat in *T. molitor* larvae can relieve

symptoms and cure skin diseases, and improve the antiwrinkle ability of skin (Mao & Zhang 2009). The larvae of *C. bilineata* has special curative effect on stomach cold disease, coronary heart disease and malnutrition. Derivatives of glutamate can prevent memory disorders and instinctive renal hypertension and mental retardation. Some functional substances in edible insects also have an effect of anti-radiation, improving osteoporosis, nutritional anemia and memory, as well as clearing and nourishing throat (Eleftherianos et al. 2021).

Use of functional substances

Many pharmaceutical functions of edible insects have been described above. Humans use functional substances from edible insects mainly in three ways: edible insects are used to discover new medicines or health care products for people; or are applied in chemical, agricultural, food technology, pollutant treatment and textile sectors; and being consumed as feedstuff for livestock and other animals, which indirectly meet the different requirements for humans.

Since more than 2000 years ago, edible insects have been an important resource in traditional Chinese medicine. Many edible insects, such as adults of dragonflies, scarab larva, egg cases of mantis, nymph exuvium of cicadas, shell lac secreted by lac insects, white wax secreted by white wax scales, toxins of bees and wasps, and Cordyceps sinensis, were developed into insectderived medicines. Usually, insect-derived drugs are not used alone. They are used with other herbs often in traditional prescriptions and experiential formulas. It is estimated that insect-derived drugs can be found in more than 1700 prescriptions or formulas of traditional Chinese medical science, which is easy for people to understand the therapeutic importance of functional substances from edible insects in traditional Chinese medical science (Feng et al. 2009).

Besides, functional substances isolated from edible insects, such as anti-microbial peptides, have demonstrated outstanding therapeutic functions also in the modern medicine (Li et al. 2015; Xu et al. 2020). Many studies focused on insects anti-bacterial peptides relating to gene expression and regulation, peptide characters and biological activities have shown that the anti-tumor mechanism of insect antimicrobial peptides is similar to its antibacterial mechanism, which can be divided into the mechanism of cell membrane destruction and noncell membrane destruction. In addition, the same insect antimicrobial peptides can inhibit or even kill tumor cells in a variety of ways, but have no obvious toxic and side effects on normal eukaryotic cells. Insect antimicrobial peptides have great potential in the field of tumor

treatment compared with the indiscriminate killing of traditional chemotherapy drugs (Ran & Zhao 2014; Xu et al. 2020). In addition, the epidermis of *T. moliter* larvae is rich in chitin and chitosan, and can be also used to make artificial skin to fight bacteria, stop bleeding and activate cells. The fat in mealworm larvae has the similar effect on skin diseases (Mao & Zhang 2009).

Additionally, the development of edible insects related health care products can be summarized in the following categories: beauty, weight loss, enhance immunity, antiaging, regulating blood lipid, blood glucose and blood pressure, fatigue resistance, radiation, hypoxia function, regulating intestinal flora, anti-tumor, improve osteoporosis, improve nutritional anemia, promote the growth and development, improve memory, sleep quality and clear and nourish throat, etc. For example, bees, ants, silkworm pupae, bamboo insects, wasps, locusts and crickets, and many other insects have become factory production of pure natural food raw materials. At present, the health care products of ant power capsules have been used to prevent diabetes syndrome in China. The formula of the capsule contains ants, yam, black sesame, fried jujube kernel, which can stabilize blood sugar (Li et al., 2015). Besides, Insect tea, as a traditional drink and Chinese medicine, has the function of reducing and eliminating fever, detoxifying, strengthening the stomach, and helping digestion. It has good effects on diarrhea, epistaxis, gingival bleeding and hemorrhoid bleeding, and is a functional food with a good antioxidant effect that has value for future development and utilization.

Secondly, edible insects are also popularly applied in chemical, agricultural, food technology, pollutant treatment and textile sectors. As food additives, the antifreeze proteins of insects could improve the quality of frozen food and food quality. The DNAP Company of the United States adds insect antifreeze proteins to ice cream and ice milk, which removes the ice residues and improves both the quality and taste. In the regions where influenza vaccination is not available, taking ant products could protect the children, the old and infirm from the colds (Melanie et al. 2002; Zhong et al. 2010). The elderly people, who have taken the ant products for long-term avoid catching flu when the surrounding people are suffering from the flu. Besides, chitin is one of the major components of the cell wall of some micro-organisms and exoskeleton of certain invertebrates. Recent studies show the potential application of chitin and its derivatives from edible insects in chemical, medical, agricultural, food pollutant treatment and textile sectors (Lucas et al. 2021; Sharbidre et al. 2021).

Furthermore, some species of insects, such as mealworms, locusts and grasshoppers, are usually farmed as feedstuff for livestock and other animals. The functional substances of edible insects can help animals improve intestinal function, which could greatly promote their growth and development and improve nutritional quality. Insect feed conversion efficiency is higher than traditional livestock, because most insects are omnivorous, they can use organic waste and take up less space in the rearing process. The protein content in larvae, pupae and adults of *T. molitor* is 51, 57 and 61%, respectively. It is not only an excellent concentrated feed for livestock and poultry, but also a good feed for scorpion, snake and entertainment pedes.

Market effects

Humans have been eating edible insects for a long time. In times when food was scarce, edible insects were used as a major food supplement for people. However, people consumed edible insects mainly in the original forms of pupae or larvae, the primitive way of consumption and some traditional aspects stop most people from trying edible insects (Hlongwane et al. 2020; Verneau et al. 2021). The industry still faces numerous challenges as there is a significant consumer hate factor in the commercialization process and uncertainty in which consumer markets would be interested in consuming edible insect food products (Brunner & Nuttavuthisit 2019; Legendre & Baker 2020).

With the development of social economy and civilization, people's living standard has greatly improved. At one time, eating edible insects was considered a primitive life style. In recent years, people pay more attention to healthy diet, and look for new healthy food. Edible insects, regarded as a potential sustainable animal protein, have widely attracted the attention of consumers. It is noteworthy that consumer acceptance studies suggest that vegetarians might be more open to the consumption of insects than to other food of animal origin (Tan et al. 2015; Wilkinson et al. 2018). In order to expand consumer market and promote the development of industry sustainably, it is necessary to change the consumption patterns for edible insects, thereby enhancing its acceptability as a food item for humans.

Enterprise attention

With consumer demand in the market, enterprises are realizing the huge potential of the edible insect industry. Due to media attention, a significant growth in entrepreneurial activities about edible insects is witnessed in the world (Legendre et al. 2020). They began to participate in edible insects farming, food product development, functional ingredient extraction and utilization. Moreover, because of the strong funding from local governments, enterprises are working with universities or research institutions to jointly declare the industrial

research projects on edible insects. In view of the original consumption mode of edible insects, enterprises should actively study the consumption mode of structural upgrading, and develop new products from edible insects (Verneau et al. 2021).

On the other side, companies play a key role in the development of edible insect industry, which can conduct some marketing strategies to lead to consumers' perception change of eating insects. The appropriate marketing strategies will improve knowledge of consumers about edible insects and their nutritional benefits that could also lower their levels of food neophobia and improve willingness to consume insects. For example, promoting insect-based functional foods as a platform for certain health-related properties is a promising option. Furthermore, it will help to boost consumers' knowledge and interest in entomophagy by proper labelling and documentation of insect products. The scientific guidelines explained by the European Food Security Authority are worth studying to prepare a manual for insects consumed in developing countries, either on a regional or national basis to assure food and nutritional security.

National policy effects

Governments also play key roles in the development of edible insects industry. In the past, governments paid more attention on traditional foods, including agricultural cultivation or animal husbandry, harvest and product processing, rather than the consumption of edible insects. This is one of the reasons why edible insects developed not so rapidly, although they are a promising new source of protein.

Recently, with further research and in-depth understanding of the development of edible insects and their products, local governments have begun to keep eyes on edible insect industry, including edible insects farming, intensive processing, as well as some related research. Currently, research on edible insects emerge one after another. In addition, governments have increased funding for research projects about edible insects, including basic theoretical research, and industrial research projects, which mainly are hosted by universities and research institutes. On the other hand, the governments have focused more on projects related to edible insect industry, which are closely related to livelihood economy, and more and more companies are now joining in the application of these projects.

According to the promulgation of relevant policies of "rural revitalization" in China, the edible insect industry is expected to receive more support and funding. Now, some edible insect industries, such as *B. mori* and *C. bilineata tsingtauica* have developed into a local characteristic economic industry in some places. These industies could not only attract migrant workers to return

to start up businesses, but also provide local farmers (mainly left-behind elderly people) with nearby employment opportunities, thus, promote the development of local rural economy. Furthermore, the combination of edible insects and vegetables (including broccoli, morchella, etc.) could effectively utilize land resources, solve problems such as pest damage and land continuous cropping obstacles, and also promote the development of edible insect industry. In future, edible insect industry combined with picking bases (such as vineyards and strawberry gardens) would be considered carefully to develop rural leisure tourism industry.

Prospects

In recent years, research on using edible insects as human food and feed has accelerated further with the recognition of insect nutritional benefits and the potential of insects to ensure food security (Meyer-Rochow & Jung 2020). However, pupae and larvae are the main consumption ways in the market, which is unacceptable to most people. Developing edible insect products is still at an early stage, though some products have successfully been introduced to the market. Now, it is expected that the industry would be prosperous by further understanding, development and utilization of functional substances from edible insect, the development of new insect products, the combining of policy and market forces, and the optimization of resources of enterprises and research institutes.

Edible insects will be the main resource for discovering new medicines or health care products in the future as research on functional substances increases (Feng et al. 2018). New technical methods and research models should be exploited to screen and test medicinal insects and insect-derived compounds in order to discover how they can treat human diseases. On the other side, although a lot of medicinal insects have been recorded and researched in China, many insects that are used as medicines by local and minority groups have not been recorded and studied. These folk medicinal insects still await investigation and study. There is also confusion in scientific names and common names of some edible insects. It is essential to name and identify more medicinal insects to meet the needs of screening insect-derived compounds and drugs.

It is important to keep cautious when developing new products of edible insects. Traditions should be followed to gain the public perception and acceptance. Comprehensive and intensive studies of the insects would be needed to ensure the food security and avoid potential risk. Currently, factors responsible for functional substances of edible insects have not been explored sufficiently. To know how the chemical composition, handling and storage methods, contamination with micro-organisms, the

insects' diet, feeding schedules, host plants and the seasons affect food insect marketability would be of considerable benefit in selecting the most suitable species. Besides, in order to ensure the security of the proteins from edible insects, it is important to strengthen the research on the toxicology and hygiene of insect proteins, which could provide the basis for the development and utilization of insect protein products. We highlight the importance of different processing methods, the risks of contamination and allergies and relate such factors to consumer choice as well as general acceptability of edible insects and insect-containing products as an alternative to conventional food items. Both farming and processing should be standardized to ensure the quality of insect products.

Furthermore, regulations and legislation along with proper farming procedures, storage and hygiene would benefit consumers by way of healthier insects. Frameworks shared by different countries exist in Europe, but are lacking for most developing countries. Meyer-Rochow et al. (2021) suggested that a regulatory legal framework is required to guarantee that manufacturing practices, quality management, hazard analysis and other issues related to content and quality of edible insects are meeting acceptable standards.

Conclusion

Edible insects regarded as a potential sustainable protein can meet the growing global demand for new protein sources, which is the key to safeguarding the future global food security. As we know, edible insects are abundant in nutrients, including protein, amino acids, minerals, vitamins, and easily digestible fatty acids. Meanwhile, edible insects also have a multitude of functional substances, such as antimicrobial peptides, interferon, sex attractant hormones cordycepin, active polysaccharides, microelements, chitin/chitosan, steroidal material, vitamins, lecithin, etc., which could provide a multiple set of benefits for human beings. These special functional substances could help people enhance immunity, inhibit tumor, regulate intestinal function, relieve fatigue, anti-oxidation, protect against colds, improve sleeping, promote the growth and development, as well as reducing blood sugar and blood pressure, etc. However, people consumed edible insects in the original forms of pupae or larvae generally, this primitive way of consumption prevents most people from trying this unique and splendid flavor. For the sustainable development of the edible insect industry, further scale up for the exploration and utilization of functional substances in edible insects is needed. Edible insect industry would certainly be prosperous by combining with the power of beneficial government policies and strong financial support, huge market consumer demand, appropriate publicity and promotion by enterprises.

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Authors' contributions

The study was primarily designated by Lei Qian and Huaijian Liao. The references were collected mainly by Pan Deng and Ye Cao, the manuscript was drafted by Lei Qian and Pan Deng, then modified by Fajun Chen and Hongwu Sun. All authors read and approved the final manuscript.

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The authors declare that they have no competing interests.

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