# Biologically active substances of edible insects and their use in agriculture, veterinary and human medicine – a review

# Biologicky aktivní látky jedlého hmyzu a jejich využití v zemědělství, veterinární a humánní medicíně - review

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## Abstract

Possibilities of edible insect use in Western countries is now increasingly debated issue. Insects in Asian, African, American and South Central American cultures are mainly nutritional components. In Europe and other developed countries, however, insect is used in different ways, and this issue is viewed from a different angle. Insects are mainly used as feed for animals, in the organic waste recycling systems, in human and veterinary medicine, material production (such as silk) etc. This review summarizes up-to-date knowledge about using edible insects in human, veterinary medicine and agriculture, especially from the viewpoint of the biological and chemical content of active substances and the possibilities of further use in these areas.

**Keywords:** antioxidants, chitin, feed, human medicine, insect, insulin, vertebrates, veterinary

## Abstract in native language (Czech republic)

Možnosti využití jedlého hmyzu v západních zemích je nyní stále více diskutovanou otázkou. Hlavní význam jedlého hmyzu v asijských, afrických, amerických (hlavně v jižních a středoamerických) kulturách je dán především nutriční hodnotou. V Evropě a dalších vyspělých zemích je však hmyz využíván, nebo v budoucnu bude využíván, různými způsoby a otázka využití jedlého hmyzu je brána z jiného úhlu pohledu. Hmyz se používá hlavně jako krmivo pro zvířata, v organických systémech

recyklace odpadů, v humánní (hypertenze, kardiovaskulární choroby) a veterinární medicíně, výroba materiálu (např. hedvábí) atd.
Možné vedlejší přínosy výzkumu z hlediska nutričních hodnot a dalšího využití jedlého hmyzu, můžou také zahrnovat vyhledávání nových sloučenin (chitin, chitosan, insulin), biotechnologií (léčba celiakie) a hledání výživového, farmaceutického (včelí jed), veterinárního, průmyslového a kosmetického potenciálu (antimikrobiální a antimykotické látky). Budoucí výzkum se bude také týkat využití extraktů z jedlého hmyzu a dalších látek prospěšných pro lidské zdraví (antioxidační enzymy). Kromě tohoto, může hmyz sloužit jako cenné krmivo, vzhledem k jejich složení, a také jako náhrada obratlovců v experimentálním testování toxických látek.
Přes zavedení mnoha chovných center a dalších systémů určených pro využití u hmyzu pro člověka, zvířata a jiné účely, bude však další vědecký výzkum zapotřebí.
Tyto otázky jsou a budou předmětem práce mnoha vědců z různých oblastí.
V mnoha ohledech se hmyz jeví jako strategická "surovina", s cílem využít tohoto potenciálu pro lidstvo. Je však nutné si uvědomit některé atributy tohoto hlediska, vzít v úvahu negativa a pracovat s pozitivy.
Tato souhrnná práce uvádí aktuální znalosti o použití jedlého hmyzu v zemědělství, humánní a veterinární medicíně a to zejména z hlediska biologického a chemického složení účinných látek a možnostech dalšího využití v těchto oblastech.

**Keywords:** antioxidanty, hmyz, humánní medicína, chitin, insulin, krmivo, obratlovci, veterinární medicína

## Introduction

Environmental cycles and human factors have altered ecosystems throughout the world. Natural resources have acquired a high value because they are important to life and the survival of human beings. Edible insects are among these resources. They have many important features and, nowadays, up to 2,086 species are consumed by 3,071 ethnic groups (Cerritos, 2011).

Insects provide critical basic tools for studying a great many aspects of biology. Human and animal protein products derived from insect cell lines are marketed for a number of purposes, including drug screening and clinical trials.

Even 3,600 years ago, insects, their parts, and toxins derived from them were used to alleviate a number of human illnesses. Nowadays, this area is a subject of many pieces of scientific research. Therefore, insect products and by-products probably account for the lion’s share of insect commercialization for future (Kampmeier and Irwin, 2009; Mlcek, et al., 2014).

## Insects as a source of chemical and bioactive substances

### Chitin

Chitin is a macromolecular compound that has a high nutritional and health value (Burton and Zaccone, 2007). As a form of low-calorie food, chitin also has a medicinal value (Chen et al., 2009). In most cases, the hard cover polysaccharide chitin of insects accounts for 5– 20% of the dry weight (Barker et al., 1998; Finke, 2002).

Although chitin presents problems of digestibility and assimilability in monogastric animals, it and its derivatives, particularly chitosan, possess properties that are of increasing interest in medicine, industry and agriculture. If the time should come when protein concentrates from insects are acceptable and produced on a large scale, the chitin byproduct could be of a significant value. A significant contribution of chitin can be presented for example by significantly reducing serum cholesterol, acting as a hemostatic agent for tissue repair, enhancing burn and wound healing, acting as an anticoagulant, protecting against certain pathogens in the blood and skin, serving as a nonallergenic drug carrier, providing a high tensile strength biodegradable plastic for numerous consumer goods, enhancing pollutant removal from waste-water effluent, improving washability and antistatic nature of textiles, inhibiting growth of pathogenic soil fungi and nematodes and boosting wheat, barley, oat, and pea yields as much as 20% (Goodman, 1989; Chen, et al., 2009).

**Chitin sugestibility**

For animals with lack of chitinase, this indigestible component may be important to gut function and nutrient absorption (Van Soest, 1994) and may play a role as dietetic fibers (Muzzarelli et al., 2012 ). On the contrary, chitin may be a significant energy source in diets of animals possessing chitinase (Cornelius et al., 1976). In general, chitinases can digest chitin and reduce it into assimilable components suchas N-acetyl-glucosamine (Talent and Gracy, 1996; Jolles and Muzzarelli, 1999; Gardiner, 2000). Western society does not consider insects an important food (De Foliart, 1999); however, crustaceans such as lobsters and shrimps are commonly eaten mostly after discarding the hardened chitin-rich tegument. Therefore, Western nutrition apparently does not seem to depend on chitinases (De Foliart, 1992). For instance, Renkema et al. (1997, 1998) described in plasma of patients affected by Gaucherdisease, there were elevated levels of chitotriosidase (Chit), a hydrolytic enzyme produced by macrophage cells, which exhibit optimum activity at pH 6. More recently it has been reported that Chit may also be involved in innate immune responses (Van Eijk et al., 2005). Moreover, Chit has been shown to be high in diseases such as acute malaria (Barone et al., 2003), beta-thalassemia (Barone et al., 1998, 2001), and other hemoglobinopathies, indicating that macrophage activation is responsible for Chit expression (Bouzas et al., 2003; Musumeci et al., 2005). Another chitinase, acidic mammalian chitinase (AMCase), produced by the bronchial epithelium, exhibits optimum activity in the acid pH range and has been implicated in allergic bronchial asthma (Zhu et al., 2004). Chitinases have been found in several human tissues and their role is associated with defense against parasitic infections and some allergic incidents. Since this chitinase activity was demonstrated at acidic pH, it is currently referred to acidic mammalian chitinase (AMCase). An increased activity of AMCase, detected in tropical human populations with higher rates of Entomophagy, may represent just adaptive response to alimentary habits, the result of which is the increased resistance against parasitic infections in those areas. Absence of AMCase activity in 20% of gastric juices in Europe may be due to the virtual absence of chitinous foods in Western diets (Paoletti et al., 2007, Krykbaev et al., 2010).

**Chitosan**

Chitosan is a partially deacetylated polymer obtained from the alkaline deacetylation of chitin. Chitosan exhibits a variety of physicochemical and biological properties resulting in numerous applications in fields such as wastewater treatment, agriculture, fabric and textiles, cosmetics, nutritional enhancement and food processing (Varshosaz, 2007). Recently, much attention has been given to the use of chitosan in veterinary applications, as a wound healing agent, antimicrobial agent, bandage material, skin grafting template, hemostatic agent and drug delivery vehicle (Şenel and McClure, 2004).

In addition to its lack of toxicity and allergenicity, its biocompatibility, biodegradability and bioactivity make it a very attractive substance for diverse applications as a biomaterial in the pharmaceutical and medical fields (Varshosaz, 2007). For wound healing, it is important to control any infection of a wound under dressing. Infectious organisms preferentially target wounds beneath the dressing materials and elicit serious infections that frequently require the removal of the wound dressing. For these reasons, the treatment of wounds requires the suppression of bacterial growth. Chitosan has been shown to provide inhibition of bacterial proliferation in the treatment of infected wounds (Şenel and McClure, 2004).

**Antimicrobial and antifungal peptides**

Antimicrobial peptides seem to be ubiquitous and multipotent components of innate immune defense used both by prokaryotic and eukaryotic organisms.

During the last 25 years a large number of these peptides has been isolated mainly from insects, amphibians, mammals, plants and bacterial species, e.g. citropin 1.1 and protegrin 1 (Kamysz and Turecka, 2005) or betasheet peptides (defensins isolated from insects and also from mammalian tissues) (Duclohier, 2010).

Antimicrobial peptides are pivotal elements of the innate immune defense against bacterial and fungal infections. Within the impressive list of antimicrobial peptides available at present, more than half have been characterized in arthropods. Cysteine-rich antimicrobial peptides represent the most diverse and widely distributed family among arthropods and, to a larger extent, among invertebrates. (Dimarcq et al., 1998; Rossi et al., 2008). According to the species, the fat body can respond to the bacterial infection by the synthesis of either a large panel of antimicrobial substances. E.g.: *Apis mellifera* produces short-chain proline-rich peptides such as apidaecin Ia, Ib, II, III and long-chain proline-rich peptides such as abaecin. *B. mori* produces lebocin 1, 2, 3 (Bulet *et al*., 1999), orcecropin, attacin, lysozyme and moricin (Ponnuvel *et al*., 2007). *Tenebrio molitor* produces tenecin 4 (Chae et al., 2011) and *Galleria mellonella* eight antimicrobial peptides (Cytryńska et al., 2007; Mak et al., 2010).

Insect metalloproteinase inhibitor and antimicrobial peptides from *Galleria mellonella* may provide promising templates for the rational design of new drugs since evidence is available that the combination of antibiotics with inhibitors of pathogen-associated proteolytic enzymes yields synergistic therapeutic effects (Vilcinskas, 2011).

Generally, insect antimicrobial peptides have wide activity spectrum and are not cytotoxic. They rapidly kill microorganisms and other harmful invaders (bacteria, fungi, and protozoa) (Schröder, 1999), they have a mode of action that should restrict the selection of resistant strains. Insects can thus eliminate the alarming problem of bacterial resistance to drugs and the rising emergence of opportunistic pathogens, especially in immunosuppressed hosts (Bulet et al., 1999).

The potential value of AMPs for clinical purposes includes their use as single anti-microbial agents, as synergistic agents to existing antibiotics, as immunostimulatory agents, and as endotoxin neutralizing agents (Rossi et al., 2008).

The major b-1,3-glucanase from *Tenebrio molitor* efficiently lyses fungal cells, suggesting a role in making available walls and cell contents to digestion and in protecting the midgut from pathogen infections (Genta *et al*., 2009). Tenecin 3, an antifungal protein isolated from the insect *Tenebrio molitor* larvae, inhibits growth of the fungus *Candida albicans* (Kim et al., 1998).

**Insulin**

The oral administration of disease-specific auto antigens can induce oral immune tolerance and prevent or delay the onset of autoimmune disease symptoms. Gong et al. (2005) describe the construction of an edible vaccine consisting of a fusion protein composed of cholera toxin B subunit (CTB) and insulin that is produced in silkworm larvae at levels of up to 0.3 mg/ml of haemolymph. The silkworm bioreactor produced this fusion protein vaccine as the pentameric CTB–insulin form, which retained the GM1- ganglioside binding affinity and the native antigenicity of CTB and insulin. Non-obese diabetic mice fed haemolymph containing microgram quantities of the CTB–insulin vision protein showed a prominent reduction in pancreatic islet inflammation and a delay in the development of symptoms of clinical diabetes. Gong et al. (2005) also presents hypothesis that oral tolerance may be a feasible and useful therapeutic strategy for the treatment of autoimmune diseases. The oral administration of silkworm-expressed CTB–INS fusion protein may be a novel and practical approach for the prevention of type 1diabetes in human beings (Gong et al., 2005).

**Angiotensin converting enzyme (ACE)**

Hypertension is one of the most common chronic diseases in the developed world and is a major risk factor for coronary artery disease, congestive heart failure, stroke, and renal disease. Cardiovascular diseases are still one of the main causes of premature death in Western countries (Duprez et al., 2002). In these days, high blood pressure is mainly treated with lifestyle changes and pharmacological antihypertensive treatment (Hermansen, 2000). Synthetic ACE inhibitors such as captopril are often used as a remedy against hypertension, but they can cause serious side effects such as cough and angioedema (Antonios and MacGregor, 1995).

ACE inhibitory peptides present as natural components in both animal and vegetable proteins provide valuable alternatives to synthetic drugs (Takano, 1998). It is known that enzymatic hydrolysis of food proteins result in the creation of peptides that may exhibit different biological activity. These protein fragments are known as bioactive peptides (Meisel, 1997). As far as all the bioactive peptides are concerned, I-converting enzyme-inhibitory peptides (ACEIP) are of a particular importance due to their ability to reduce blood pressure (Quiros et al., 2007).

Silkworm pupae and other kinds of insect proteins are a good source of high quality protein. (Vercruysse et al., 2005; Wang et al., 2008).The hydrolyzates catalyzed by acidic protease exerted the highest inhibitory activity on ACE. Published studies show that hydrolyzates of silkworm protein contain ACE activity inhibitors, which could be a potential source of ACE inhibitor drugs (Wang et al., 2008).

### Antioxidant enzymes

Low molecular weight antioxidants play a decisive role in protecting tissues and extracellular fluids from oxidative stress, and compounds such as ascorbate, glutathione, and a-tocopherol could vary among grasshopper species independent of the activities of antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT), ascorbate peroxidase (APOX), and glutathione transferase peroxidase (GSTPX). SOD is secreted into the midgut lumen in insects, with activities two- to fourfold higher than those found in midgut tissues. Luminal SOD and CAT activities are due to enzymes secreted by the midgut, whereas luminal APOX and GSTPX activities are due to ingested plant antioxidant enzymes and may function as acquired defense in grasshoppers. Most notably, grasshoppers have higher SOD activities than caterpillars, but completely lack APOX in their midgut tissues (Barbehenn, 2002).

### Celiac disease treatment

Digestion in *Tenebrio molitor* larvae occurs in the midgut, where there is a sharp pH gradient from 5.6 in the anterior midgut (AM) to 7.9 in the posterior midgut (PM). Accordingly, digestive enzymes are compartmentalized to the AM or PM. Enzymes in the AM are soluble and have acidic or neutral pH optima, while PM enzymes have alkaline pH optima. The possibility of the use of two endopeptidases from the AM – cathepsin L and postproline cleaving peptidase – in the treatment of celiac disease is discussed by Elpidina and Goptar (2007). *Tenebrio molitor* contains a wide spectrum of digestive proteinases operating in the midgut with a sharp pH gradient from acid to alkaline values. Two digestive peptidases from the acidic AM, cysteine cathepsin L and post-proline cleaving peptidase, readily hydrolyze the bonds formed by the major amino acids of cereal gluten, proline and glutamine, and presumably have a potential for oral administration to treat celiac disease.

### Honeybee venom

The venom of honeybees has been used to ameliorate inflammatory and autoimmune conditions such as multiple sclerosis, arthritis, rheumatism, chronic pain, neurological diseases, asthma, and dermatological conditions (Kampmeier and Irwin, 2009).

## Substituting vertebrates in experimental testing of toxic substances

The substitution of insects for laboratory animals in toxicity testing is likely to become a reality in the framework of prescreening. Haematotoxicological studies of newly developed chemicals, such as food components, drugs, etc. performed on insects can offer advantages in, for example, environmental toxicology. Although the differences between human physiology and morphology and those of insects are great, the basic functions of insect haemocytes and mammalian leukocytes appear not to have changed during evolution. The use of insects in haematotoxicity assays represents a preclinical testing strategy, which will lower costs, accelerate screening and offer ethical benefits (Berger, 2009). The larvae of the greater wax moth *Galleria mellonella* prosper in use as surrogate alternative model hosts for human pathogens and as a whole-animal-high-throughput-system for in vivo testing of antibiotics or mutant-libraries of pathogens (Vilcinskas, 2011).

## The use of insects as a food for animals

Insects may also be a very valuable food source for many types of pet and farm animals, not only for insects' own nutritional composition (e.g. Ramos-Elorduy et al., 2002; Wang et al., 2007; Hwangbo et al., 2009), but can also be used for transportation of other needed nutrients and micronutrients to the recipients (St-Hilaire et al., 2007). Knowing the weight of the insects and the amount of food in its gastrointestinal tract might allow zoo nutritionists and veterinarians to use insects to deliver a wide range of other compounds, such as carotenoids and pharmaceuticals (e.g. anthelmintics) to captive insectivores (Finke, 2003). Insect protein is readily available with protein quality values similar to, or slightly higher than fish meat or soybean meal. Experiments with house fly larvae (*Musca domestica)*, soldier fly larvae (*Hermetia illucens*), house crickets (*Gryllus assimilis*), yellow mealworms (*Tenebrio molitor*) and various species of lepidopteran larvae as feed have resulted in a good growth of rats, chickens and several species of fish (Capinera, 2008). Experiments with mealworms fed with chicken starter and then fed to growing chicks resulted in higher levels of vitamin D in chicks, and Ca in these mealworms was 76% as bioavailable as the Ca in oyster shell (Klasing et al., 2000). Broiler chicken feeding diets containing 10 to 15% maggots, grew up in chicken dropping after biodegradation can improve the carcass quality and growth performance of broiler chickens (Hwangbo et al., 2009). Maggot meal (magmeal) can be used as a good alternative protein source in tilapia diets – feeding *Oreochromis niloticus* fingerling with magmeal diets did not cause any form of physiological stress (Ogunji et al., 2008). Also soldier fly larvae may be valuable feedstuff in a commercial fish production for channel catfish and tilapia (Bondari and Sheppard, 1981) or rainbow trout (Sealey et al., 2011). Possibilities of using Diptera larvae for fish feeding also improved the results of the taste tests which indicated, that fish fed soldier fly larvae are acceptable to the consumer (Bondari and Sheppard, 1981). Main analyzes of the most used insect-feed are summarized in the Table 1.

Table 1. Main analysis of the most used insect-feed (Alegbeleye et al., 2012; Barker et al., 1998; Finke, 2002; Hwangbo et al., 2009; Klasing et al., 2000; Longvah et al., 2011; Ogunji et al., 2008; Ojewola et al., 2005; Rao, 1994; Sealey et al., 2011; St-Hilaire et al., 2007)

| Parameter | Unit | Black soldier fly larvae (*Hermetia illucens*), dehydrated | Housefly maggot meal | Locust or grasshopper meal | House cricket (*Acheta domesticus*), fresh | Mealworm (*Tenebrio molitor*), fresh | Silkworm pupae meal, non-defatted, dried |
|---|---|---|---|---|---|---|---|
| Dry matter | % as fed | 91.3 | 92.4 | 91.7 | 28.4 | 42.2 | 91.4 |
| Crude protein | %DM | 42.1 | 50.4 | 57.3 | 63.3 | 52.8 | 60.7 |
| Crude fibre | %DM | 7.0 | 5.7 | 8.5 | - | - | 3.9 |
| NDF | %DM | - | - | - | 18.3 | 12.0 | - |
| ADF | %DM | - | 13.8 | - | 10.0 | 6.5 | - |
| Ash | %DM | 20.6 | 10.1 | 6.6 | 5.6 | 3.1 | 5.8 |
| Gross energy | MJ/kg DM | 22.1 | 22.9 | 21.8 | - | 26.8 | 25.8 |

DM: dry matter; NDF: neutral detergent fiber; ADF: Acid detergent fiber

## Conclusions

Potential side benefits from research on the nutritive value and other uses of edible insects could also include prospecting for new compounds, biotechnology, nutritional, pharmaceutical, veterinary, industrial and cosmetic potential from edible insects and the use of edible insect extracts and other substances for human health. In addition, insects can serve as a valuable animal feed, due to their composition and also as the substituting of vertebrates in the experimental testing of toxic substances.

Despite the establishment of many breeding centers and other systems designed for the use of insects by humans, animals and other purposes, however, further scientific research will be required. These issues are, and will be the subject of work of many scientists from different areas.

In many aspects insects appear to be strategic “raw material” and with good management they have the potential to provide much good to humankind. However, it is necessary to be aware of certain attributes of this phenomenon, take into account the negatives and work with positives.

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