Extract from Beetle Ulomoides dermestoides

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A biologically active extract from the darkling beetle Ulomoides dermestoides was obtained using the electro-pulse plasma dynamic extraction method. The beetle water extract contained a complex of antioxidant substances such as antioxidant enzymes and nonprotein antioxidants, as well as a complex of heat shock antistress proteins. This determines the rather high antioxidant activity of the aqueous extract of the beetle, i.e., 1 mg of dry matter/mL of the extract has an equivalent antioxidant activity to 0.2 mM Trolox (a water-soluble analog of vitamin E). It was shown that the beetle extract can lead to a 25–30% increase in the average lifespan of nematode Caenorhabditiselegans, under normal conditions, and a 12–17% increase under conditions of oxidative stress (with paraquat), and significantly inhibits the fructosylation reaction of serum albumin. Therefore, the beetle aqueous extract shows promise as a biologically active complex exhibiting antioxidant activity.

Ulomoides dermestoides | electro-pulse plasma dynamic extraction | antioxidant activity | lifespan | antiglycation activity

1. Introduction

Insects that show promise for the development of new antibiotics, immunoactive peptides, and substances for pharmaceutical use have been attracting the attention of researchers. Interest in the use of the biomass of certain insect species for the production of biologically active substances has been enhanced by the development of technologies for breeding some species in artificial conditions. In this case, it is important to identify the active components of insects and obtain evidence of their biological effects on the body.

Insects are a natural source of substances with biological activity, including antimicrobial, antiviral, anti-inflammatory, antioxidant, and anticancer effects [1]. In Central and South American traditional medicine, the darkling beetle *Ulomoides dermestoides* is used to treat inflammatory diseases and cancer. The literature has also reported on the anti-inflammatory and immunomodulatory activities of an aqueous extract of this beetle, suggesting the presence of components that are pharmacologically promising [2][3][4][5][6][7][8]. The insect is able to reproduce rapidly in artificial conditions similar to those described for the related species *Alphitobius diaperinus* [9]. This indicates the possibility of obtaining renewable biomass of the darkling beetle. However, in order to assess the possibility of its practical use, it is necessary to obtain characteristics of its composition and assess its biological activity. To maximize the extraction of useful components from biomass, it is important to use efficient extraction processes. Electro-pulse plasma dynamic extraction (EPDE) is a known extraction method that resembles a natural lightning storm, in which a high-voltage discharge is used to destroy biological objects [10]. When a high-

power electric discharge is passed, shock waves appear in the extracted mixture, creating high impulsive pressure and powerful cavitation processes. Under the action of the forces caused by a high-voltage discharge (38,000 volts) in the extracted mixture (biological raw material and extractant), shock waves are generated within milliseconds, creating a high impulse pressure. As a result, in a millisecond time interval in the confined space of the reactor, a large amount of energy is released, destroying the cellular structures—external and internal biological membranes.

It is important to note that the extraction process using the EPDE method, in contrast to the traditionally used methods, takes place without heating. This is due to the fact that when an electric discharge passes through the extracted mixture, a gas–vapor film is formed from the evaporating liquid, which protects the organic raw material from combustion. Thus, biological raw materials are not subject to thermal damage, keeping all the extracted biologically active substances in their native state. Tissue processing in this way increases the yield of cellular components into the extract while maintaining biological properties. The EPDE method made it possible to obtain an extract with antioxidant activity from the larvae of the black soldier fly *Hermetia illucens* [11].

To study the biological activity of the aqueous extract, a complex approach was used, including analyses of the proteins and nonprotein hydrophilic components of the extract, followed by an assessment of its antioxidant activity in model systems. An indispensable tool for the characterization of proteins in biological samples is liquid chromatography coupled with the tandem mass spectrometry (LC–MS/MS) technique [12][13]. A proteomic analysis approach called GeLC–MS/MS was chosen to study the aqueous extract of *U. dermestoides* [14][15][16]. The nonprotein components of the extract were investigated using ultra-high-resolution chromatography–mass spectrometry.

2. Current Discussions on Extract from Beetle Ulomoides dermestoides

Natural antioxidants can be essential for solving health problems, lifespan, and improving quality of life. However, insect antioxidants are much less studied than plant antioxidants. Some insect species contain very high concentrations of antioxidants, even when compared to classic herbal products such as olive oil or orange juice. For example, it has been shown that Trolox equivalent antioxidant capacity (TEAC) of extracts of some edible insects (grasshopper, silkworm, cricket) is five times higher than the TEAC of fresh orange juice. Simultaneously, the extracts of grasshopper and cricket exhibited high Ferric reducing antioxidant power, twice as high as that for freshly orange juice [8]. It is also known for the high antioxidant and anti-inflammatory activity of hydrolysates of edible insects—cricket *Gryllodes sigillatus*, mealworm *Tenebrio molitor*, and locust *Schistocerca gregaria* [6].

In this work, we have found that the aqueous extract of the *U. dermestoides* beetle obtained by the EPDE method is a strong quencher of the chemiluminescence of luminol, which indicates the content of antioxidants in the extract. The high antioxidant activity of the aqueous extract of the *U. dermestoides* beetle is due to the protein and nonprotein antioxidants contained in it. The antioxidant proteins included superoxide dismutase (SOD), one of the most important enzymes of the body's antioxidant system. Heat shock proteins with molecular weights of 60, 70,

and 83 kDa [17] likely play an important role in the biological activity of the extract under conditions of oxidative stress, protecting biological systems from damaging effects under stress, including oxidative stress. The presence of a poorly studied vitellogenin-like protein in an amount exceeding the SOD content was also noted. Vitellogenin is an insect antioxidant that may affect longevity [18]. According to the literature, studies of the molecular mechanisms of Vg function in worker bees have shown that Vg protects tissues from oxidative damage, which usually occurs during aging in cells or tissues of various species [19].

The aqueous extract also contains nonprotein substances with anti-infective properties, such as phenolic compounds and ethyl p-hydroquinone, as well as methyl esters of widespread octadecenoic (oleic) and hexadecanoic fatty acids. Octadecenoic acid is a monounsaturated fatty acid that refers to the group of omega-9 unsaturated fatty acids and is one of the most important acids contained in lipids involved in the construction of biological membranes.

The aqueous extract of the beetle showed an inhibitory effect on the Maillard reaction. The Maillard reaction (or nonenzymatic glycation) is a complex reaction process between the aldehyde (or ketone) groups of reducing sugars and the amino groups of proteins, as a result of which—under conditions of hyperglycemia—the so-called advanced glycation end products (AGEs) are formed. It is known that AGE products of glycation, such as advanced lipoxidation end products (ALEs), are extremely toxic to cells [20]. The formation and accumulation of AGE products in various cells and tissues leads to damage to extracellular and intracellular structures and disruption of their functions and is one of the main reasons for the development of diabetic complications [21]. The accumulation of AGE products occurs in aging, diabetes, arthritis, atherosclerosis, chronic renal failure, nephropathy, neuropathy, Alzheimer’s disease, etc. [20][22]. The ability of beetle extracts to suppress the process of nonenzymatic glycation may be associated with both the presence of antioxidants in their composition and amine-containing substances that can compete with the amino groups of proteins in reaction with carbonyls. It is well known that antioxidants can inhibit the development of the Maillard reaction [23]. This discovered property of the considered aqueous beetle extract to inhibit the glycation process may be used in pharmacological practice, in the treatment and prevention of diseases associated with aging and diabetes.

The discovered components of the *U. dermestoides* extract have multiple biological activities, the totality of which also manifested through experiments with the free-living soil nematode *C. elegans*. The water extract of the beetle had a dose-dependent effect on the lifespan of the nematode, both under normal conditions (i.e., in the control without oxidative stress) and under OS conditions. In the presence of 10% extract, nematodes looked healthy and remained active much longer than nematodes from other groups: the MLS in the control without OS was 36 h, while, in the presence of the extract, the MLS was more than 48 h (minimum predicted value). Oxidative stress reduced the MLS of control nematodes up to 24 h. However, with the simultaneous introduction of 10% of the extract, the MLS increased up to 28 h (more than 16%). Dilution of the extract (reducing the injection dose to 2.5%) reduced the effect of the extract on the MLS, where no biological activity was observed at a dose of 1%. It can be assumed that the presence of antioxidants in the *U. dermestoides* extract was associated with the effect of increasing the lifespan of the nematode *C. elegans*, both under normal conditions and under oxidative stress.

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