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Biologically Active Complexes Based on Natural Raw Materials: Composition and Prospects for Use

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ABSTRACT

In order to improve the absorption of biologically active chemicals and compounds with limited bioavailability, the present study examines the feasibility of mixing partly soluble arabinogalactan polysaccharides with chitosan polysaccharides. Chitosan succinate, succinic anhydrate, and arabinogalactan with covalently unbound dihydro quercitin, with weight percentages of 3.0-5.0, 2.0-4.0, 15.0-20.0, and 3.0-5.0, respectively, are all components of the physiologically active biopolymer matrix. They act as vehicles for the precise delivery of medicinal and diagnostic substances to specific cells, such as hepatocytes (parenchymal liver cells), such as enzymes, nucleic acids, vitamins, and hormones. Arabinogalactan from Siberian larch (Larix sibirica) was shown to have strong membranotropic activity in the research. Because arabinogalactan creates a binding complex with the drug being administered and engages with the cell's asialoglycoprotein receptor, it can be utilized to improve the absorption of other active components with limited bioavailability through the digestive tract. The paper also examines the effectiveness of arabinogalactan to improve the technological and functional properties of PSE-like broiler meat. The addition of arabinogalactan to sausage filling in an amount of 0.5% of the total raw materials increased the moisture-binding capacity by 5% while reducing losses during heat treatment by 6%. We can also note better peroxide and acid values during storage resulting in oxidative process inhibition and prevention of product spoilage.
The possibilities of developing a new gel complex polymer based on the polysaccharide matrix as well as its use in health-saving technologies have been considered.

Key words: *Arabinogalactan, Chitosan succinate, Biocomplex, Biologically active compounds, Areas of use*

INTRODUCTION

Long-term studies on polysaccharides from higher plants give ground for their extensive use in specialized products, including dietary supplements [1, 2]. Polysaccharides containing galactan have an immunomodulatory property. They raise the phagocytic index and stimulate the reticuloendothelial system (RES). The structural characteristics and conformation of macromolecules (the method by which aggregates form) determine biological activity. Additionally, the location of the polysaccharide within the plant cell is crucial [3].
The research aims to develop biologically active complexes based on natural raw materials and consider their prospects.

MATERIALS AND METHODS

X-ray diffraction analysis (XRD) and thermal analysis, differential scanning calorimetry (DSC), were used to reveal phase and structural transformations. Scanning electron microscopy was utilized to obtain micrographs of the test samples.

Test substance concentration in aqueous solutions was determined by HPLC on Agilent 1200 and Millichrom A-02 chromatographs.

IR spectra were analyzed to identify the arabinogalactan test sample.

To study complex formation in solutions the increase in solubility of biologically active substances was measured. Measuring 1H NMR relaxation times in aqueous and aqueous-alcohol solutions was also applied.

The molecular weight distribution (MWD) of the samples was studied by gel permeation chromatography (GPC).

RESULTS AND DISCUSSION

A biologically active supplement, arabinogalactan extracted from larch (AG), has been developed. The issued patent proves the product's novelty and originality [4].

Numerous investigations have demonstrated the potential of Siberian larch AG as a vehicle for the targeted delivery of diagnostic and therapeutic agents as well as enzymes, nucleic acids, vitamins, and hormones to specific cells, including hepatocytes or parenchymal liver cells [2, 5-7]. In model tests, AG showed strong membrane reversibility [8]. It can thus be utilized to increase the bioavailability of other physiologically active substances that are known to have limited bioavailability [1, 6, 8-11]. Arabinogalactan forms a complex with an agent being delivered and interacts with the cell’s asialoglycoprotein receptor. This interaction is explained by the branched macromolecular structure of AG and its numerous terminal galactose and arabinose groups [3]. Conjugates of AG and its degradation products with different pharmaceutical products can be extensively used [12-18].

A potential synthon that can react with both mono- and bifunctional reagents is arabinogalactan. This capacity may result in the creation of novel, commercially viable water-soluble goods. Both the polysaccharide itself and the added functional groups will affect how they behave. Products from AG chemical modification are highly sought-after by several industries. Chemical modification of AG is reported to result in lower polymer bioactivity or no bioactivity at all [19, 20]. Thus, studies on arabinogalactan modification have potential.

The combination of arabinogalactan polysaccharides and chitosan polysaccharides was examined.

Strong intermolecular complexes of active compounds can develop as a result of the structure of AG macromolecules. Within the gap the side chains create, their molecules are capable of forming intermolecular hydrogen bonds. It is easier to build supramolecular complexes with a variety of substances because of the AG macromolecule's conformational mobility, which causes the size of the gap to change [6].

Chitosan works well as an emulsifier and gelling agent. It has demonstrated the potential to combine with proteins and lipids to generate complex molecules. With other biopolymer components, hydroxyl groups with high electron densities and unshared electron pairs along the molecule generate hydrogen bonds. Chitosan serves as a core to create strong initial complexes with lipids and proteins [7].

Teichoic acids, phosphates, and carboxyl groups on microbial membranes are particularly attracted to the positively charged molecules in chitosan due to its sorbent characteristics. Pathogens are more susceptible to various antibiotic drugs because membrane fixation paralyzes their function, particularly the movement of ions and beneficial chemicals. It's crucial to know that chitosan mixes with any living tissue, has mucoadhesive qualities, degrades, and opens tight cell junctions. All these factors significantly improve drug delivery through the mucosal membrane [21].

The non-specific mechanism of antimicrobial activity helps effectively fight against infections that are especially resistant to antibiotics: salmonella, E. coli, staphylococcus, gram-positive cocci, Pseudomonas aeruginosa, and Candida fungi.

Glucosamine and succinate, the conjugate bases of the acid, are produced in the body when protonated chitosan degrades with the aid of lysozyme. Deacetylated chitin and succinic acid are dissolved in chitosan succinate to form a salt. Additionally, it is biodegradable, biocompatible, and hypoallergenic. Chitosan gains two crucial traits as a result of deacetylation, which influence its characteristics and field of application.

When the pH reaches 7, the deacetylated and substituted groups in chitosan succinate become positively charged, making chitosan gel a polycation that binds to negatively charged molecules.

Two polysaccharides, chitinous (chitosan succinate) and vegetal (arabinogalactan), are mechanochemically activated to produce the biopolymer matrix.

Solids may be ground into molecules by mechanochemical activation, with the crushed particles forming aggregates. We can see more molecular mixing of materials if mechanochemical stimulation continues. Chemical reactions occur with the production of a solid phase that is defined by various molecular interactions, depending on the nature of the ingredients. When substances are heated or hydrated, the desired results are produced.

There are two steps involved in creating a polysaccharide matrix.

Chitin that has been deacetylated to a degree greater than or equal to 75% and a molecular weight between 1 and 30 kDa is used in the first stage to produce chitosan succinate. With succinic anhydride, it is mechanically crosslinked. All chitosan amino groups are quantitatively acylated as a result of mechanical activation, which is supported by conductometric titration. The dissolution of dicarboxylic acid anhydrides in an organic solvent is not necessary for a solid-state reaction; this should be emphasized.

The molecular modification of arabinogalactan took place during the second stage, which involved combining the mechanically produced chitosan succinate with it. The major components were mechanically and chemically processed in the rotary rolling mill VM-1, which had a fluoroplastic liner on the drum. In water, the resulting fine powder was dissolved. After being neutralized with an aqueous alkaline solution, the mixture was dried by spraying or vacuuming [8].

With its many spherical cavities ranging in size from 1.0 to 5000.0 nm, the polymer matrix takes on a flexible structure of chitosan particles and resembles a cross-linked net-structured polymer.

The biopolymer matrix includes chitosan succinate, succinic anhydrate, and arabinogalactan containing covalently unbound dihydro quercitin.

To determine the improved solubility of hydrophobic pharmaceuticals in water, optical spectroscopy was used to examine the complexing capacity of a supramolecular compound including chitosan succinate, succinic anhydrate, and arabigalactan.

Two poorly water-soluble compounds, carvedilol and zeaxanthin, were studied.

Among the carotenoid pigments, zeaxanthin is a frequent antioxidant. The retina's macular zone contains two carotenoids, this one being one of them. The retina can be oxidized and damaged by free radicals, which it can neutralize. This property helps prevent the development of cataracts and age-related macular degeneration. However, its low water solubility limits its use in the food industry and pharmacology.

Our studies discovered that complex formation resulted in more than a thousandfold increase in zeaxanthin water solubility. In our research, the concentration of the complex consisting of zeaxanthin and biopolymer matrix in the proportion of 1:10 was 40 micromoles or 22 mg/L. The reported solubility increase (1000 times) is the minimum estimation as the intrinsic solubility of the complex is beyond the instrumental sensitivity.

Carvedilol is an antianginal, antioxidant, anti-hypertensive, and vasodilator drug. It is poorly soluble in water and its bioavailability is about 25%.

According to the study, the polymer matrix complex formation improves the aqueous solubility of carvedilol by a factor of 40. There were 50 micromoles, or 20 mg/L, of the carvediol-biopolymer matrix combination at a concentration of 1:10. Calculated from the observed carvedilol extinction coefficient at the wavelength of 332 nm, the absolute solubility value is 4760 l mol-1 cm-1.

The research shows the effectiveness of AG in improving the technological and functional properties of PSE-like broiler meat when the dietary supplement is added to sausage filling in the amount of 0.5% of the main raw material. The moisture-binding capacity increased by 5%, and heat treatment losses reduced by 6%. The sausage consistency and color improved, with the score increasing by 4%. Peroxide and acid values during storage were also reduced, indicating oxidative process inhibition and product spoilage prevention.

The study's findings provide additional evidence that the produced polysaccharide matrix exhibits strong biological activity both on its own and in combination with other compounds. We created a bioactive biopolymer matrix with the following composition: chitosan succinate 3.0-5.0, succinic anhydrate 2.0-4.0, arabinogalactan 15.0-20.0, and dihydroquercetin 3.0-5.0 (wt%). This matrix can serve as a carrier for a wide range of biologically active substances (vitamins, minerals, amino acids) and be extensively used in the food and processing industries.

We examined the possibility of creating a new biopolymer – a gel complex based on arabinogalactan polysaccharides, chitosan succinate, and dihydro quercitin, cross-linked with antler extract concentrate, antler deer dry blood and plant extracts.

The composition of antler extract concentrate, a complex adaptogen, is presented in **Table 1**.

Table 1. Content of biologically active micronutrients in antler concentrate

Indicators	Value
Total amino acids (mg/g)	676.2
Free amino acids (mg/g)	179.8
Collagen (mg/g)	462.5
Vitamins (mg/100 g)	708.9
Macroelements (mcg/g)	18600
Microelements (mcg/g)	52.08
Testosterone (pg/g)	1559
Dehydroepiandrosterone (DHEA), ng/g	4.28
Estradiol, pg/g	89.0
Insulin-like growth factor 1 (IGF-1), ng/g	57.2
Epidermal growth factor (EGF), pg/g	19.8
Nerve growth factor (NGF), ng/g	86.8
Transforming growth factor alpha (TGF-α), ng/g	186.0
Transforming growth factor beta (TGF-β), ng/g	61.5
Ciliary neurotrophic growth factor (NGF3, CNTF), ng/g	94.8
Bone morphogenetic protein (BMP-4), ng/g	237.1

The biologically active components of antler extracts have a hypotensive and lipotropic effect, exhibit a gonadotropic activity and antimutagenic effect, demonstrate immunostimulating properties, enhance metabolism, act as a pronounced reparative agent, improve the thyroid gland function, and can be considered a toxicant. Antler product intake can increase the nonspecific body resistance to adverse environments, compensate for nutrient deficiency, and obtain a safe mechanism of regulating and supporting the body's organs and systems functions, thus improving health, reducing morbidity, and prolonging working life.

Dihydroquercitin is an active antioxidant that possesses capillary protective, anti-inflammatory, and hepatoprotective properties. Due to these properties, dihydro quercitin is widely used in the manufacturing of specialized products and medicines.

Chitin and chitosan are natural polymers obtained from the shells of commercial crustaceans and other sources. They have numerous useful properties and are in demand in the food industry, medicine, and agriculture. Drugs containing chitosan are developed for various purposes, such as vaccine carriers, drug-releasing hydrogels, membranes, and mesh materials.

Chitin is one of the three most common polysaccharides besides cellulose and starch.

Antler extracts also contain protein, hormones, cytokines, and growth factors. When cells communicate with one another using signal proteins sent through the intercellular fluid, growth factors play a signaling role. These proteins include the cytokines themselves as well as growth factors, which are substantial, bodily-produced molecules with at least 100 amino acids.

The synthesis of growth factors and their functional activity decreases with age.

Growth factors are capable of modifying cell division and differentiation by normalizing these processes, i.e. decreasing them at an increased level of proliferation and stimulating them at a reduced level. Growth factors also have a long-term effect on target cell receptors. Like hormones, growth factors affect many cells of the body – they stimulate or inhibit mitogenesis, chemotaxis, and differentiation (maturation) of cells. Cells are known to divide under the action of insulin-like (IGF) and epidermal (EGF) growth factors and mature with the help of transforming growth factor (TGF).

Growth factors push back the "planned old age" of a cell and rejuvenate tissues and the entire body: they restart genes turned off with old age or diseases, prolonging the cell life; stimulate cell division; and improve cell metabolism. They activate a child's growth, especially the musculoskeletal system development, which is particularly important in adolescence. According to clinical trials, growth factors ease symptoms of digestive tract diseases and can be used for treating acute intestinal diseases. Their contribution to preventing hyperplastic process development (mastopathy, uterine fibroids, and endometriosis) and slowing down progressive cancer is still under study. Nerve growth factor (NGF) plays an important part in the nervous system development and functioning and damaged neuronal structures regeneration. Transforming factor (TGF2) is angiogenic and is involved in cell proliferation and regulation of tumor cell growth. Testosterone and dihydrotestosterone are formed in peripheral tissues during the metabolism of dehydroepiandrosterone (DHEA). Epidermal factor (EGF) controls and stimulates the proliferation of epidermal and epithelial cell structures, including fibroblasts, renal epithelial cells, glial cells, and granulosa cells. The ciliary neurotrophic factor (CNTF) is regarded as a key differentiation factor for developing neurons and glial cells. Bone morphogenetic protein (BMP-4) has a pronounced therapeutic effect in arthritis and bone tissue regeneration. Insulin-like growth factor (IGF) performs endocrine, autocrine, and paracrine regulation of the growth processes, and tissue cell development and differentiation. The effect of growth factors should be considered in connection with other stimulants, primarily hormones, including hormones of biologically active antler products.

CONCLUSION

In our research, we combined the polymer matrix with the concentrated antler extract and other excipients, when the agents being cross-linked were exposed to electromagnetic fields. In this case, the composition was suspended with an antler extract concentrate.

The obtained gel complex is non-toxic, demonstrates high biological activity, and can be used as a health and beauty product, in composition for antler baths, and other health-saving technologies.

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