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Review Article

Chitosan and Ecosomal Systems as Promising Compilation Components of Pharmaceutical Compositions

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Abstract

The content of this article analyzes the features of the use of exosomal and chitosan particles in the design of veterinary pharmaceutical compositions. Ecosomes, as well as chitosan biological particles, are under the close attention of scientists since veterinary pharmacology has insufficient information about the mechanisms of their action in the composition of various pharmaceutical compositions. At the same time, there is enough reason to believe that they are one of the most promising modern means of delivering therapeutic substances to the focus of the disease, a specific target cell. These conclusions are based on very serious grounds. The second promising nano-transport for the targeted delivery of therapeutic agents is chitosan biological systems. Chitosan and exosomal preparations, both individually and in various combinations, have been used in humanitarian medicine for a long time. However, as regards veterinary preparations created on the basis of these components, so far, they have been insufficiently studied and require in-depth studies. The purpose of the study was to analyze and systematically present information on the use of chitosan and ecosomal sources in pharmacological compositions as presented in available literature sources.

Keywords: Exosomes; Chitosan; Nano-transport; Pharmacology; Nanoparticles; Composition of therapeutic substances

Introduction

Modern veterinary pharmacology is based on the latest developments in biochemistry in the field of drugs. The flagship in this direction is the development of means for such a therapeutic effect that would allow influencing a specific system, a specific organ, or a specific cell that needs help, combined with the safety of surrounding cells, organs, and tissues. For this reason, the search for optimal means of delivering therapeutic drugs is an urgent problem. Ecosomes are a “cell in miniature”, Their cell membrane allows you to isolate their contents from other cells of the body and from the environment. All this makes it possible to preserve therapeutic agents unchanged while ensuring the biological compatibility of the ecosome and the nano-sized drugs included in it with affected cells of the body. Chitosans include biodegradable and biocompatible polymeric aminoglucopyranans, which are classified as renewable natural resources. The key factor contributing to the classification of chitosan nanoparticles as promising drugs is their ability to release the active therapeutic substance in doses directly at the site of its action. Another unique property of chitosan is the presence of specific bioactivity, due to which the polymer is able to independently act as an inhibitor of viral agents in warm-blooded animals. Of no small importance to the effectiveness of the therapeutic effect is the competent definition of not only the delivery route of the therapeutic drug but also the fullness of the component composition, the presence of synergy or antagonism between them, as well as the interaction of the body's biosystem with the chemical system of the drug. Only with a reasonable combination of the proportion of side effects and the effectiveness of the therapeutic effect is it possible to form a composition that is able to minimize the first effect and work as productively as possible in the second direction.

Main Text

Ecosome

The concept of "ecosome" in itself is not something new. Already in the last decades of the twentieth century, this term was used to refer to special membrane vesicles formed in tumors by cancer cells. A few more years later, ecosomes were found not only in tumor cells with an avalanche-like increase in numbers but also in normal cells of the body. It is quite obvious that such a discovery did not take long to lead to numerous studies aimed at studying the properties and functions of newly discovered formations. The first studies carried out by a team of authors made it possible to establish that ecosomes are able to eliminate membrane-bound proteins from the cell [20].

Further study of ecosomes led to the following important discovery, which determined the possibility of using them for applied purposes: the ability of ecosomes for intercellular communication The researchers found that the stability of the content is provided by the cellular plasma membrane, which delimits the ecosome from any components of the external environment and makes it a miniature copy of an organism's cell. The fact that almost all classes of biomolecules were included in ecosomes became quite remarkable. They contained ribonucleic and deoxyribonucleic acids, peptides, lipids, and other inclusions [53]. The ability of ecosomes to move transcellularly as well as to penetrate into all systems and organs together with blood requires much more thorough study in order to use them for a variety of applied purposes, including the transport of therapeutic agents [24].

Ecosomes are special spheres (vesicles), ranging in size from 40 to 100 nm, formed inside the cell by pressing the membrane into the endosome, followed by budding of an independent cell inclusion. In essence, these are isolated sections of the cytoplasm with a double lipid layer [5]. The presence of exosomes in the blood, saliva, and milk also occurs in urine, seminal, and cerebrospinal fluid [14].

The applied use of ecosome:

The established biological role of ecosomes has opened up broad prospects for their use for prophylactic and therapeutic purposes. Currently, the use of Eccles as a basis for the manufacture of vaccines, immunity modulators, and angiogenesis is quite widespread. However, the use of ecosomes as a vehicle for the targeted delivery of therapeutic agents requires further study [39]. Despite this, many researchers admit that a better delivery method has not been developed to date. The advantages of ecosomes in the form of the absence of toxic effects are distinguished. According to researchers, the presence of ecosomes in almost all studied biological fluids indicates their compatibility with any organs, tissues, or cells, and various receptors on the lipid membrane allow targeted delivery of drugs, thereby minimizing the likelihood and severity of possible side effects. It is also noteworthy that the composition of surface receptors can be corrected, thereby changing the "address" of delivery [22].

As undoubted additional advantages of delivering ecosomes, distinguish their ability to penetrate cell membranes together with the therapeutic agent inside, the ability to ensure the constancy of the transferred substance, and the ability to contain a sufficiently large volume of the drug [67]. We have already established that exosomes combine the advantages of two delivery methods at once: cell-mediated and synthetic delivery systems. Currently, a method for treating patients has already been developed and used in the laboratory, in which leukocytes are isolated from the body of a sick patient by means of therapeutic apheresis, artificially propagated, and cultivated, after which a therapeutic agent is loaded onto existing exosomes and injected into the peripheral bloodstream of the patient [22].

The technique has proven itself positively, but there is a significant drawback that researchers are trying to overcome: the difficulty of using it on an industrial scale. It is quite obvious that the number of ecosomes produced by a cell is not unlimited, and the more they can be obtained, the more opportunities the pharmaceutical industry has to use ecosomes in its production of drugs. In addition, with an increase in the number of ecosomes obtained from each cell, their cost decreases, which, in the end, will lead to a decrease in the cost of treatment [47].

In this aspect, the key point is the correct selection of recipient cells. To date, the most productive cell type in this respect is mesenchymal stem cells. They are the most suitable for the production of ecosomes on an industrial scale, and the use of special bioreactors can help in this [9,16]. The possibility of using ecosomes in humanitarian medicine has been confirmed by clinical trials. By intranasal administration of preparations based on ecosomal systems to experimental animals, a significant increase in the number of ecosomes in the brain is achieved. Thanks to the use of exosomal systems with catalase, it became possible to use specialized treatment regimens for such serious diseases as degenerative and inflammatory processes in the brain and spinal cord. Using models of Parkinson's disease in vitro and in vivo, it was found that ExoCAT actively interacts with neuronal outgrowths, thereby contributing to the manifestation of the neuroprotection effect [26,46,48,57,63].

Very impressive results have also been obtained in the experimental treatment of cancer cells. Thus, the paclitaxel drug, developed experimentally using ecosomal systems, was studied on cells with multiple resistances to a wide variety of drugs. The scheme of the study included the introduction of ecosomes extracted from leukocytes of laboratory mice loaded with the therapeutic agent paclitaxel into diseased cells cultured in Petri dishes. Empirically, it was found that to destroy a cancer cell, a dose of an experimental drug is required, which is fifty times less than currently used anticancer drugs [29,52].

Chitosan

Speaking about the second promising means of targeted delivery of therapeutic agents, it is necessary to note the chitosan biological systems. The linear polysararides of chitosan and chitin, which are fairly widespread in nature, differ from each other only in the amount of 2-amino-2-deoxy-β-D-glucose (glucosamine) and its N-acetylated derivative in the pyranose form and linked by 1–4 glycosidic bonds. Natural chitin can be deacetylated by placing it in a harsh, alkaline environment. This process also leads to its partial depolymerization. It is possible to carry out the reaction under milder conditions, for example, by lowering the temperature or adding certain enzymes. In this case, the resulting chitosan has a much higher molecular weight. Despite numerous ongoing experiments, a single scientific definition has not yet been formulated that would make it possible to distinguish between chitin and chitosan by the number of N-acetyl groups in the substance [12,21,23,28]. The applied aspect of the use of chitosan systems requires a clear understanding of the characteristics of the drug. This is important, regardless of the scope of their use. (Transport direction, immunology, biosystems, etc.). The main parameters include:

¬ degree of deacetylation.

¬ molecular mass.

¬ polydispersity index.

Speaking about the last indicator, it should be noted that it is a calculated value, determined by the formula Ip = Mw / Mn.

where Mw is the average molecular weight.

Mn - number of average molecular weights.

The use of chitosan systems as a transport for carrying therapeutic agents in both humanitarian and veterinary medicine requires a number of other parameters to be controlled, such as bacterial and endotoxin purity, the proportion of residual protein, heavy metals, allergens, yeasts, radionuclides, etc [2,50,54]. In the absence of the above harmful impurities, chitosan systems have mucoadhesiveness, biocompatibility, and the ability to biodegrade to safe components, which makes them indispensable for the pharmaceutical industry [10,36].

Studies of the bactericidal and bacteriostatic properties of chitosan made it possible to establish that the spectrum of its antimicrobial activity is quite wide [17,64,66]. Due to these properties, chitosan and its derivatives are increasingly used in tissue engineering, in the design of cleaning systems, in the development of packaging preparations, in pharmacology, in the creation of membranes, biosensors, antioxidants, and so on [33,56,65].

The applied use of chitosan:

The applied use of chitosan systems today includes more than seventy directions. Most often, chitosan is used in agriculture, in the pharmaceutical industry, and in cosmetology [25,35,41].

Agriculture: Chitosan systems are widely used as therapeutic and prophylactic agents for diseases of the gastrointestinal tract of animals since they have the ability to maintain the integrity of the composition until it enters the intestine and are not affected by gastric juice [15,40,41]. Chitosan components are an integral part of some feed products used in feeding animals and birds. An indisputable advantage is the ability to adsorb radionuclides and salts of heavy metals on itself, which reduces the contamination of livestock products [51,55,58]. The agronomic direction of agriculture also uses chitosan systems, in particular, to increase the shelf life of vegetable products, fruits, and berries [37,43,61]. Another area of activity for chitosan in agriculture is its use as a preservative with antioxidant properties, thereby extending the shelf life of meat and meat products [6,38,49].

Cosmetology: In the cosmetic industry, chitosans are used in the production of creams, ointments, and hair care products as moisturizers, to form stable emulsions and gels [3,19,25].

Pharmaceutical and medical activities: Most authors agree that the most active use of chitosan systems in modern conditions is observed in this area of the national economy [22]. The use of chitosan as an adjuvant for vaccines is described, and one of the new uses of chitosan is the targeted delivery of therapeutic drugs followed by prolonged diffuse release from the polymer shell [31]. Targeted delivery and prolonged release are impossible without the use of chitosan as a polymeric excipient and substance [13]. A number of authors point to the possibility of using chitosan as a tool for tissue engineering of some internal organs. Due to the strength of chitosan and its ability to gradually biodegrade, it is not only a fixative of the mechanical "backbone" for cartilage, skin, bone, and nervous liver tissues but also cultivates new cells at the molecular and cellular level and provides them with migration [22,31].

Describes the properties of chitosan as a hemostatic agent, and the mechanism of interaction of chitosan with blood cells, including platelets, makes it possible to single out hemostatic dressings from chitosan as having undeniable advantages over other similar means of desmurgy [11,27,42,62]. Hypoallergenicity is another property of chitosan, which makes it widely used as a suture material [44]. As an active agent in chitosan biological systems, peptides, nucleic acids, growth factors, vitamins, and anti-inflammatory agents [4,13,30,45].

As an active agent in chitosan biological systems, peptides, nucleic acids, growth factors, vitamins, anti-inflammatory, antibacterial, antitumor, and other drugs can be included. Know the use of chitosan for prolonged release of medicinal compounds such as paclitaxel, proteins, small fragments of RNA, and antigens [8,32,60]. Also, research is being conducted to test various ways of introducing microparticles into the body (orally, buccally, inhalation, internosally, intramuscularly, and transdermally); most attention is paid to non-invasive methods [1,24,59,68]. Chitosan is most widely used as feed additives for animals and as biologically active additives with an immunostimulating effect [18,51,55,58]. Chitosan derivatives for parenteral therapeutic action in humanitarian medicine are both at the stage of clinical trials and at the stage of registration of new drugs. A similar situation develops with the use of targeted delivery of therapeutic agents using ecosomal systems [7].

Conclusion

Veterinary pharmaceuticals, in our opinion, pay insufficient attention to these two undoubtedly very promising components of chitosan and ecosomal systems, especially in their combination. The use of chitosan solely as an adjuvant in animal vaccines and feed additives does not allow it to reach its full potential. For this reason, there is a need for a detailed study of the toxic and therapeutic effects of ecosomal and chitosan systems on the bodies of laboratory animals, depending on the route of their administration, as well as the development of new composite selective preparations based on them.

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Conflict of Interest

No conflict of interest.

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