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LIPID NANOTECHNOLOGY IN MODERN BIOMEDICINE

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Introduction. Research and development of nanotechnological delivery of therapeutic molecules is a driving force in the context of disease treatment and prevention. This is due to the limited delivery of traditional drug forms, which depends on their physicochemical properties. Lipid nanoparticles enable the use of proteins, nucleic acids, and other molecules for the prevention of diseases or the treatment of pathologies in the human body. The synergy between medicine and nanotechnology today determines the direction of high-tech healthcare development, transforming the concept of treatment at the molecular level. The unique properties of nanomaterials open up broad prospects for the diagnosis and treatment of diseases, where the treatment process becomes more accurate, less invasive, and more effective. Nanomaterials have distinct size-dependent properties in the range of 1 – 100 nm, where quantum phenomena occur. The International Organization for Standardization defines nanoparticles as nano-objects whose external dimensions are all on the nanoscale, where the length of the longest and shortest axes of the nano-object does not differ significantly. The size of a nanoparticle can range from 1 to 100 nm [1]. Depending on their composition, all nanoparticles are usually divided into three classes: organic, inorganic, and carbon-based nanoparticles [1; 2]. The organic category includes nanoparticles consisting of proteins, carbohydrates, lipids, polymers, or any other organic compounds. They are non-toxic and biocompatible. Today, organic nanoparticles are mainly used in the biomedical field for targeted

drug delivery and cancer treatment [1].

The main material. Over the past decade, lipid-based nanoparticles have become particularly important among organic nanoparticles. These are nanoscale particles that consist mainly of lipids and are used as carriers (substrates) for drug delivery. The term “drug delivery” refers to a specially designed mechanism for introducing a pharmacological agent with the aim of controlled release of compounds and improving their pharmacokinetic properties. The development of delivery systems for therapeutic molecules is primarily determined by the need to preserve their properties, target specific areas, and minimize negative effects on the human body. Traditional drug forms (tablets, solutions, gels, etc.) without nanotechnology cannot always meet the above-mentioned needs of modern medicine. In particular, anticancer drugs must be delivered directly to target cells, and the mRNA molecule must be protected from spontaneous hydrolysis and ribonuclease cleavage, which requires the development of innovative delivery systems. Lipid nanoparticles are capable of transporting therapeutic molecules, such as drugs, biopolymers, and other bioactive molecules, to specific cells or tissues in the organism. The use of lipid nanoparticles is an effective strategy for transporting drugs through dense biological barriers, in particular the hematoencephalic and hemato-ophthalmic barriers [2].

The main types of lipid nanoparticles include liposomes, solid lipid nanoparticles, and nanostructured lipid carriers [2, p. 13].

Liposomes are the first generation of lipid nanoparticles. Externally, they appear as spherical, disc-shaped, or ellipsoidal vesicles ranging in size from 10 to 1000 nm. Liposomes consist of one or more phospholipid bilayers with stabilizers, separated by gaps filled with liquid. Sometimes these particles are coated with polyethylene glycol to avoid an immune response from the organism. The structure of liposomes allows hydrophilic substances to be captured inside, while hydrophobic and lipophilic substances can be placed directly in the lipid layer [3]. In addition, this type of lipid nanoparticle can also carry other macromolecules, such as nucleic acids and proteins, making them an extremely versatile platform for drug delivery [4, p. 604]. For example, it is known that more than 40% of low molecular weight

drugs for cancer therapy have low water solubility, so the advantages of drug delivery systems capable of encapsulating the necessary compounds and increasing their solubility were immediately apparent. The first liposomal drug approved by the Food and Drug Administration was Doxil, a lipid nanoparticle form of the antitumor agent doxorubicin, which is used to treat ovarian cancer. Another liposomal drug aimed at treating cancer (for ovarian cancer, breast cancer, multiple myeloma, and sarcoma) is DaunoXome [5].

Solid lipid nanoparticles were first introduced in 1991 as an alternative drug carrier designed to address the disadvantages of liposomes. They can ensure the stability of the nanosuspension for a longer period of time compared to liposomal delivery systems [6, p. 1]. This type of lipid nanoparticle consists of a solid lipid matrix containing drug molecules and a layer of surface-active substance (surfactant) to stabilize the solid lipid nanoparticles in the aqueous phase [7, p. 953]. Solid lipids in solid lipid nanoparticles are saturated fats that act as binding agents for therapeutic molecules in the lipid matrix and remain solid at room temperature and body temperature. In turn, surfactants act as a barrier on the outside of the nanoparticles. Currently, there are three models of solid lipid nanoparticles: a homogeneous matrix model, a drug-enriched shell model, and a drug-enriched core model [6, p. 5]. Each of these forms affects the prolonged release of molecules from the lipid matrix of nanoparticles when they enter the body, which can be used for various therapeutic purposes. Solid lipid nanoparticles modified with polyethylene glycol are particularly effective in this context [6, p. 6]. Solid lipid nanoparticles can also encapsulate both hydrophobic and hydrophilic substances even more effectively than liposomes, transport peptides and proteins, and penetrate the blood-brain barrier [7, p. 953; 5, p. 16]. Moreover, thanks to the formation of a complex of solid lipid nanoparticles with pharmaceutical agents, the drugs demonstrate higher efficacy than when administered in free form [7, p. 962 – 964]. For example, in 2022, a gel was developed from solid lipid nanoparticles in combination with Raloxifene, a drug used to treat osteoporosis in postmenopausal women. The high drug encapsulation (95%) enhanced drug bioavailability by three and 6-fold compared to conventional gel and

drug suspension, resulting in reduced levels of alkaline phosphate and calcium, suggesting that the developed nano gel was suitable for osteoporosis treatment [6, p. 6]. A particularly interesting area of application for solid lipid nanoparticles is the treatment of cancer. Thanks to the successful encapsulation of these drugs with anti-cancer properties in the drug delivery system, the volume of distribution can be significantly reduced and the concentration of the drug in the tumor area increased [6, p. 7]. This is promising in the context of systemic toxicity of chemotherapy, its fast elimination from the body, and chemoresistance. This is evidenced by studies on the use of solid lipid nanoparticles in the treatment of cancer of the breast, large intestine, lungs, prostate, and brain [6, p. 8 – 9].

Nanostructured lipid carriers – second-generation lipid nanoparticles (introduced in 1999), developed to overcome the disadvantages characteristic of solid lipid nanoparticles – consist of a lipid matrix, therapeutic molecules, and a surfactant. However, unlike its prototype, which contains solid lipids arranged in a highly organized manner, the core of nanostructured lipid carriers consists of a mixture of liquid and solid lipids that form a disordered matrix. This allows more drugs to be placed in the core of nanostructured lipid carriers and improves stability [8, p. 447]. Typically, nanostructured lipid carriers are divided into three types: imperfect crystal type, Multiple types (or oil-in-fat-in-water O/F/W carrier), and Amorphous (or non-crystalline type) – formed as a result of different contents of solid and liquid lipids [8, p. 447 – 448]. NLC have the inherent ability to deliver drugs safely and effectively through different routes (oral route, transdermal route, nasal route, parenteral route, ophthalmic route). Numerous studies also confirm the improved action of therapeutic molecules in combination with nanostructured lipid carriers and even indicate the possibility of treating diseases that require penetration through the physiological barriers of the brain and eyes [8, p. 451 – 455]. These nanocarriers are also being investigated in the context of delivering genetic material for gene therapy, as they are less cytotoxic than ionized nanocarriers [8, p. 455]. Nanostructured lipid carriers have good prospects in the context of cancer therapy, various neurodegenerative and infectious diseases, as well as genetic diseases that cannot be

treated using traditional delivery systems [8, p. 457].

Cationic lipid nanoparticles – this type of nanoparticle is a new development and is actively used in modern medicine for the delivery of nucleic acids. Studies of mRNA-LNP structures show that mRNA is located in the LNP core together with ionized cationic lipids and water. Currently, the leading mRNA COVID-19 (Pfizer/BioNTech and Moderna) vaccines are all utilizing LNP technology. This illustrates the successes achieved with this type of nanoparticle to stabilize mRNA and successfully deliver it into cells [9, p. 4].

Lipid nanoparticle-based mRNA vaccines have undergone clinical trials against various infectious diseases, and mRNA vaccines show significant potential in the immunotherapy of melanoma, as well as cancer of the ovaries, breast, and other types of malignant neoplasms.

Conclusions. Due to their unique properties, liposomes are used in medicine for cancer treatment, antimicrobial and gene therapy. Despite the successful clinical implementation of lipid nanoparticles, their therapeutic potential requires further study and optimization. The development of nanotechnological delivery systems is imperative to overcome the limitations of traditional drug forms and minimize side effects. Due to their high biodegradability, low immunogenicity, and unique structure, lipid nanoparticles are becoming the foundation for the creation of a new generation of drugs capable of significantly improving the effectiveness of therapy for complex pathologies.

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