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THEORETICAL INSIGHTS  
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## LIPOSOMAL AND MICELLAR DRUG DELIVERY SYSTEMS: THERAPEUTIC PROSPECTS AND LIMITATIONS

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**Annotation:** This study reveals the current state and prospects of the application of micellar and liposomal drug forms as tools for targeted transport. It analyzes the transition from the free distribution of substances in the body to the concept of targeted delivery using nanotechnologies, specifically PEGylation and the use of bioconjugated nanocarriers.

**Relevance.** Nanotechnologies in the form of micellar and liposomal drug formulations, including PEGylated ones, are promising in modern therapeutic practice. Nanoparticles can be used to administer medicines into the body via inhalation, transdermal, injectable, oral, and other routes. The use of bioconjugated nanoparticles and other modified nanocarriers enables increased selectivity of action against tumour cells and promotes the release and accumulation of drugs at the required sites [1–3]. These systems have the potential to address problems such as low solubility, poor bioavailability, excessively rapid clearance, high systemic toxicity, and limited tissue selectivity.

**Key words:** liposomes, micelles, nanotechnologies, drug delivery systems.

**Aim of the study.** To clarify the mechanisms and therapeutic potential of the transition from the free distribution of agents to the concept of targeted delivery using nanotechnologies.

**Materials and methods.** A review and analysis of contemporary national and international scientific sources on the properties, mechanisms of action, and therapeutic potential of liposomal and micellar drug delivery systems was conducted.

**Results and discussion.** Micelles are aggregates of amphiphilic molecules with a hydrophobic core and a hydrophilic shell and are mainly intended for the solubilization of poorly soluble drugs. Liposomes are bilayer phospholipid structures with a hydrophilic core and a lipophilic membrane. Accordingly, they can transport both hydrophilic and lipophilic agents. Their advantage lies in their affinity for cell biomembranes, whereas their disadvantage is recognition by the reticuloendothelial system, which leads to opsonisation by blood proteins, complement activation, and phagocytosis. One of the ways to avoid this is PEGylation technology, i.e., modification of the carrier surface with polyethylene glycol (PEG). In addition to its barrier function, PEG chains can be conjugated to ligands to increase delivery specificity, however, current studies indicate that anti-PEG antibodies can be produced. Hyaluronic acid and polysarcosine are considered promising alternatives for steric stabilisation. Such modifications can prolong drug circulation in the bloodstream and ensure a stable therapeutic concentration [4–6].

In Ukraine, liposomal preparations based on natural phospholipids, such as Lipin, Lipoflavon, Lioliv, and Lipodoks, have been developed and studied – they have shown therapeutic potential in cardiology, pulmonology, oncology, ophthalmology, and hepatology, both in liposomes per se with their own reparative activity due to phospholipids and in liposomes with incorporated pharmacologically active derivatives [7].

Of particular interest are micellar delivery systems for cytostatic agents, particularly doxorubicin, using copolymers and PEGylation technology [3], as well as liposomal formulations of irinotecan and oxaliplatin [8]. The efficacy of liposomal irinotecan has been confirmed by international clinical studies [9], whereas liposomal oxaliplatin is still under investigation [8].

The influence of lipid composition on nanocarrier stability is also being studied, and it has been shown that specific combinations of phosphatidylcholine and cholesterol can optimise the rigidity of the liposomal membrane and its pharmaceutical properties [10].

The use of the EPR effect, which means enhanced permeability and retention in tumour tissue, is considered promising, although its manifestation is heterogeneous. Increased permeability of tumour vessels allows the use of cardiotoxic drugs, such as anthracyclines, in liposomal form, which do not cross the tight junctions of the myocardial capillary endothelium but do cross the pores of tumour vessels [11].

**Conclusions:** The implementation of micellar and liposomal formulations contributes to more selective (targeted) drug delivery, thereby increasing bioavailability and reducing systemic toxicity, particularly the cardiotoxicity of

anthracyclines, due to their selective accumulation in the tumour, partly via the EPR effect. Domestic phospholipid preparations demonstrate therapeutic potential as both delivery systems and membrane repair agents, underscoring the expediency of their further application and study in medicine. Promising directions include PEGylation, the use of immunologically inert stabilisers (polysarcosine, hyaluronic acid), optimising lipid composition to create stable oral nanoformulations, and considering the limitations of passive accumulation in tumours.

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## НАРКОЛЕПСІЯ ТА КАТАПЛЕКСІЯ: РОЛЬ ОРЕКСИНУ

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**Анотація.** У роботі представлено сучасний огляд ролі орексинової (гіпокретинової) системи в патогенезі нарколепсії та катаплексії. Проаналізовано фізіологічні функції орексину в регуляції циклу «сон–неспанья», механізми селективної втрати орексин-продукуючих нейронів гіпоталамуса, а також генетичні та імунологічні чинники розвитку нарколепсії 1 типу. Окрему увагу приділено нейрофізіологічним механізмам катаплексії як прояву REM-атонії в стані неспанья. Узагальнено дані експериментальних моделей та сучасні підходи до терапії, зокрема застосування агоністів орексинових рецепторів. Показано, що дефіцит орексину є ключовою ланкою патогенезу захворювання та перспективною мішенню для патогенетичного лікування.

**Ключові слова.** нарколепсія, катаплексія, орексин, гіпокретин, REM-сон, аутоімунний процес, гіпоталамус, орексинові рецептори, сон–неспанья, нейродегенерація.

**Актуальність .** Нарколепсія є хронічним неврологічним розладом, що суттєво впливає на якість життя пацієнтів, їх когнітивну функцію та соціальну адаптацію. Особливу клінічну значущість має нарколепсія 1 типу з катаплексією, яка пов'язана з дефіцитом орексину. Незважаючи на значний прогрес у розумінні патогенезу, механізми розвитку захворювання та ефективні методи етіотропної терапії залишаються недостатньо вивченими, що обумовлює актуальність даного дослідження.

**Мета роботи –** Комплексний аналіз сучасних уявлень про роль орексинової системи у розвитку нарколепсії та катаплексії на основі клінічних, нейробіологічних, генетичних і експериментальних досліджень.