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НАЦІОНАЛЬНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ ІМЕНІ О.О. БОГОМОЛЬЦЯ
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Збірник містить матеріали VI Науково-практичної конференції з міжнародною участю «PLANTA+. НАУКА, ПРАКТИКА ТА ОСВІТА». У збірнику опубліковано результати наукових досліджень провідних вчених України та іноземних фахівців з питань фітохімічного аналізу, стандартизації лікарської рослинної сировини, інтродукції, ресурсознавства лікарських рослин. Висвітлено питання технології та аналізу лікарських засобів рослинного походження, дієтичних добавок, лікувально-профілактичних та косметичних засобів. представлені фармакологічні дослідження з питань безпечності та застосування у клінічній практиці лікарських засобів рослинного походження. Розглянуто проблеми модернізації навчального процесу та орієнтації на дистанційне навчання у закладах освіти.

Матеріали представляють інтерес і можуть бути корисними для широкого кола наукових та науково-педагогічних працівників наукових установ, закладів вищої освіти фармацевтичного, медичного, біологічного профілю, докторантів, аспірантів, студентів, співробітників фармацевтичних підприємств та громадських організацій.

Друкується в авторській редакції. відповідальність за достовірність наданого для видання матеріалу несуть автори одноосібно. Будь-яке відтворення тексту без згоди авторів забороняється. Матеріали пройшли антиплагіатну перевірку за допомогою програмного забезпечення Strikeplagiarism.

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MOLECULAR IMPRINTED POLYMERS (MIP's): FROM HISTORICAL ORIGINS TO MODERN SYNTHESIS STRATEGIES AND APPLICATIONS

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Keyword: MIPs, artificial antibodies, molecular recognition, NIP, highly selective, imprinting factor

Introduction. Despite their high specificity, natural antibodies have a number of significant limitations. This creates an urgent for the development of robust molecular recognition systems, particularly molecular imprinted polymers (MIPs). MIPs model biological mechanisms by synthetically forming an “artificial lock” to identify a “molecular key” while simultaneously featuring enhanced chemical and thermal stability.

Scope and objectives. To analyze the theoretical basis of the molecular imprinting process, emphasizing the "key-and-lock" principle. To compare the functional characteristics of MIPs with natural antibodies. To identify the key application areas of MIPs in highly selective binding.

Results and discussion. MIPs represent a highly specialized class of synthetic receptors developed to mimic the phenomenon of highly selective molecular recognition characteristic of natural biological systems, particularly the immune system.

The theory of molecular imprinting dates back to the 1930s, when the chemist M.V. Polyakov reported on the unusual absorption properties of silica particles. Template molecules were found to leave structural imprints in its porous particles, which could then be utilized in chromatography [1]. Subsequent research shifted the focus from silica to organic polymers.

In parallel, Linus Pauling proposed a theory in 1940 that antibody production in the body's cells occurs in the presence of an antigen, which acts as a template, dictating the antibody's geometry [1]. This mechanism explains the high specificity demonstrated by the antibody-antigen complex.

Beginning in the 1970s, G. Wulff developed polymers in which the template was covalently bound to the polymer matrix [6]. A revolutionary event in molecular imprinting was the introduction of the non-covalent method by K. Mosbach in the early 1980s. The approach utilizes the polymerization of monomers whose functional groups interact with the template molecule through non-covalent interactions. In the 1990s, researchers actively developed this principle, devising synthetic methods for creating imprinted polymers. These materials demonstrate selectivity comparable to natural antibodies, which is why they are often referred to as "artificial receptors," "antibody mimics," or "plastic antibodies" [3].

The creation of a highly selective binding site is achieved by one of two main chemical strategies, which determine both the complexity of the synthesis and the final properties.

Covalent Imprinting, a method that involves the prior chemical binding of the template to the monomer. The reactions form a stable covalent bond, after which the resulting complex, which contains unsaturated bonds, undergoes polymerization. The key advantage is ensuring the stability of the obtained structure before polymerization and allowing for flexible selection of conditions for the polymerization reaction itself. [6] There are also disadvantages to this reaction: limited applicability to many classes of template molecules, as well as a complex and lengthy process for removing the template from the polymer matrix.

Non-Covalent Imprinting, a method that forms the prepolymerization complex through self-assembly due to various non-covalent interactions between the template and the functional monomer. Advantages include rapid complex formation and the possibility of simultaneous use of different types of non-covalent interactions. Also, the non-covalent bond guarantees the ease and simplicity of removing the template from the matrix [4]. The main disadvantage lies in the limited stability of the prepolymerization complex. Its stability is negatively affected by the presence of other reagents and the general polymerization conditions .

There is another method known as the intermediate or semi-covalent approach, which represents a hybrid strategy designed to combine the two aforementioned methods to minimize their respective disadvantages. It involves the formation of a "template-functional monomer" complex based on stable covalent bonds during the polymerization stage. However, subsequent rebinding occurs through non-covalent interactions after the template has been removed. The removal of the template is typically achieved under harsh conditions, most commonly through hydrolysis .

The manufacturing of MIPs utilizes diverse synthetic methods, ranging from classical bulk polymerization to modern approaches aimed at optimizing the morphological and functional properties of the polymer.

Bulk polymerization is a traditional technique that results in the formation of rigid polymeric monoliths. To obtain material suitable for analytical purposes, the monoliths require obligatory mechanical grinding followed by sieving to achieve the necessary particle size [3] .

Newer dispersive methods include precipitation, suspension, emulsion, and surface polymerization.

MIPs are created using Molecular Imprinting Technology (MIT), which models biological mechanisms (such as enzyme-substrate interaction) to synthetically create an "artificial lock" for the identification of a "molecular key".

The process of MIP preparation typically consists of three main stages:

- complex formation: preassembly of the template molecule and the functional monomer takes place. The template interacts with the monomer through various types of bonds, forming a "host-guest" complex;
- polymerization: A cross-linking agent and an initiator are added, and a highly cross-linked polymer is created using specific initiation methods;
- release: Templates are removed from the polymer, leaving behind cavities that ensure specific and conformational recognition of the target molecules [5].

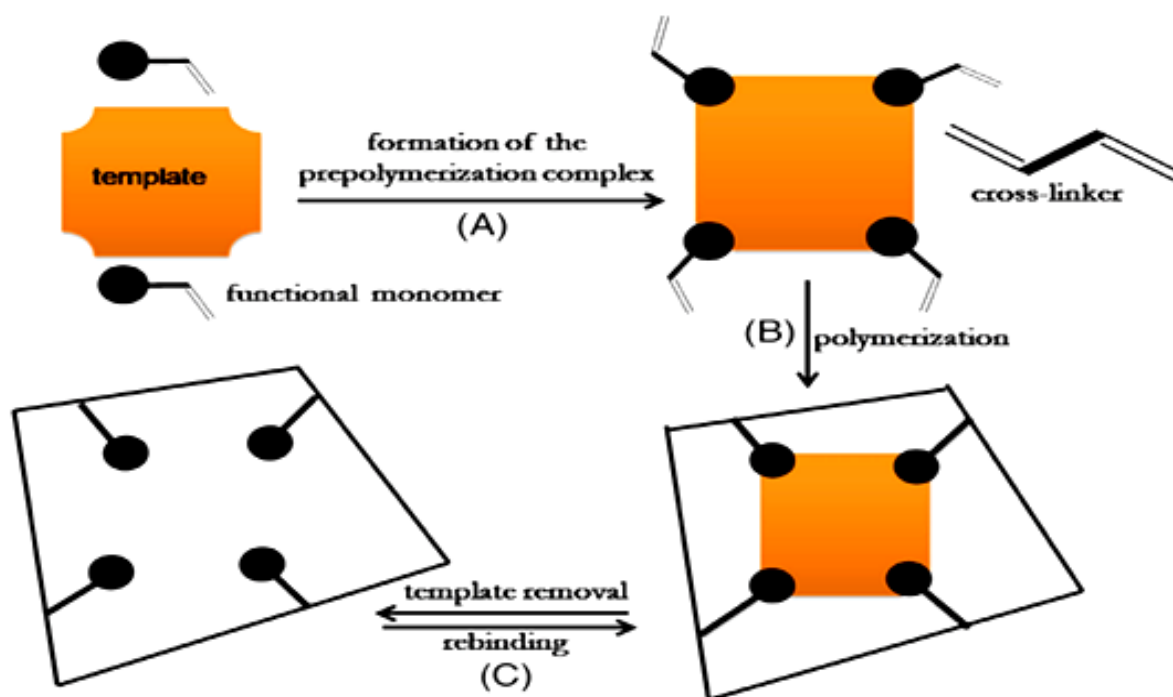


Fig.1. The Principle of Molecular imprinting [5]

It is assumed that cavities are formed within the polymer matrix that are complementary to the removed template. Due to this, the target molecule – the analyte (template) – can rebind to these cavities with high selectivity, similar to that observed in natural receptors [3, 4].

To assess the success of the imprinting process – specifically, the magnitude of the imprinting effect and to confirm the selectivity of the cavities in the MIP matrix (the fact of creating "molecular memory") – a control polymer, known as the Non-Imprinted Polymer (NIP), is mandatorily used.

The NIP is prepared according to the same scheme as the MIP (Fig. 1), but without the addition of the template molecule. Although the template is absent, the NIP also undergoes the "template removal" stage.

The use of NIP is necessary for calculating two key performance indicators: imprinting factor and selectivity [4].

These materials are already being used successfully. In the last few years, interest has grown in the potential application of MIPs in drug delivery technology. For controlled and prolonged release, the drug substance is introduced into the cavities formed in the polymer matrix during the imprinting process. The interactions between the drug compound and the matrix modify the release profile, extending it. Drugs are delivered continuously over a period of time [4]. The release of drug substances from various MIP forms, including nanoparticles, hydrogels, or composite cellulose membranes, is being studied. Ocular delivery (contact lenses): the authors demonstrated the prospect of using MIPs in ophthalmology. A polymer was obtained in the form of a hydrogel and integrated into a contact lens for the prolonged release of the drug into the conjunctival sac. The MIP-based system significantly outperforms conventional eye drops. Other applications include chromatographic separation of

related compounds and the detection of falsifications in food products, purification of biological and chemical reagents, environmental separation and analysis [3]

MIP sensors are applied in liquid samples with a focus on biomarkers, including the detection of amino acids, pesticides, pathogens, explosives, and environmental pollutants, pharmaceutical and prohibited drugs, and biomedical marker molecules. A significant number of MIP sensors have been specifically developed for the detection of biomarkers associated with the diagnosis of carcinomas, the identification of active infections, and the detection of organ-specific diseases. The goal of these developments is to create synthetic diagnostic tools that can replace existing tests based on natural receptors, such as the Enzyme-Linked Immunosorbent Assay (ELISA).[2]

However, it is worth noting that despite the immense potential and successful laboratory trials, many MIP applications are still at the laboratory or prototype stage. This highlights a significant perspective for further research aimed at scaling these technologies for industrial and clinical use

Conclusions. MIPs are a key technology that utilizes the principle of molecular memory to create accessible, selective, and chemically stable materials. The application sphere of MIPs, which are essentially "artificial antibodies," is extremely broad and extends far beyond sensory technologies. Thanks to the wide involvement of scientific knowledge and intellectual capital in the development of MIPs, their future prospects are very promising. It is expected that such a significant investment in scientific expertise will undoubtedly lead to new, major advancements in the field.

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The background of the page is a blurred, grayscale photograph of a laboratory or scientific setting. In the lower right corner, a glass container holds a plant with dark leaves. The rest of the image is out of focus, showing various shapes and light reflections.

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