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THE USE OF INVERTEBRATES IN BIOTECHNOLOGY: MEDICINAL LEECHES, SILKWORMS, BEES

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The article summarizes current trends in the biotechnological use of invertebrate animals, particularly medicinal leeches (*Hirudo medicinalis*), silkworms (*Bombyx mori*), and honey bees (*Apis mellifera*). It examines the bioactive substances produced by these organisms and analyzes their potential applications in medical, pharmaceutical, cosmetological, and bioengineering fields. Special attention is given to hirudotherapy – a method of treatment using the secretion of leech salivary glands, which contains enzymes with anticoagulant, anti-inflammatory, analgesic, and antibacterial properties. The role of hirudotherapy in microsurgery and aesthetic medicine is also highlighted.

The modern use of silk proteins–fibroin and sericin–in the development of biocompatible and biodegradable materials for tissue engineering, controlled drug release, wound healing, as well as in dental and ophthalmological practice is described. The article also emphasizes the prospects for using bioactive silk peptides in pharmaceutical and cosmetic developments.

The potential of apitherapy – a biotechnological approach based on the therapeutic properties of bee products (honey, propolis, wax, apitoxin, royal jelly) is revealed. Scientific data are provided on their antiseptic, regenerative, anti-inflammatory, and immunomodulatory effects. Their potential use in the creation of medicinal and cosmetic products is assessed.

The article presents the results of current studies confirming the effectiveness and promise of using invertebrate animals as sources of biologically active substances and technological solutions in modern biotechnology. The summarized data can serve as a foundation for further interdisciplinary research and the implementation of innovations in medical practice.

Keywords: invertebrates, biotechnology, hirudotherapy, fibroin, sericin, silkworm, bees, apitherapy, bioactive substances, medical application.

Problem statement. The development of biotechnology requires the search for new environmentally safe and highly effective sources of biologically active substances. In this context, invertebrate animals represent a promising biological resource for medical, pharmacological, and cosmetological technologies. Despite the significant amount of empirical data, the task of scientific systematization of knowledge and the development of new approaches to the practical use of these organisms in biotechnological processes remains relevant.

Analysis of recent research and publications. Modern scientific literature covers a wide range of studies dedicated to the biotechnological potential

of various invertebrate species. In particular, hirudotherapy demonstrates the effectiveness of enzymes found in the saliva of medicinal leeches (hirudin, bdellins, eglins) in the treatment of thrombosis, varicose veins, and cardiovascular diseases. In the fields of entomology and biomaterials science, the use of silk proteins – fibroin and sericin – as a basis for creating bioimplants and tissue scaffolds is actively being studied. Apitherapy research confirms the wide range of pharmacological activity of honey, propolis, bee venom, and wax. At the same time, comparative interspecies studies on the effectiveness and biosafety of using these organisms in biotechnologies remain insufficiently explored.

Objective. The aim of this work is to conduct a comprehensive analysis of modern approaches to the use of medicinal leeches, silkworms, and bees in biotechnology. The objectives of the study are: to characterize the biological features of the studied organisms that determine their biotechnological potential; to analyze the areas of practical application of these species in medicine and industry; and to identify the advantages and limitations of their use in biotechnological processes.

Research results. The integrated use of invertebrates in biotechnology opens up prospects for the creation of multifunctional biomaterials that combine the properties of various biological agents. In particular, the combined use of medicinal leech secretions, silk proteins from silkworms, and apitherapeutic products enables the development of innovative tools for tissue engineering, chronic wound treatment, and a range of dermatological disorders. For example, silk fibroin-based hydrogel matrices containing hirudin and propolis have been developed, characterized by antimicrobial, anti-inflammatory, and regenerative properties.

The synergistic effect of such biocomposites is due to the combination of the physicommechanical stability of silk proteins with the bioactivity of leech and bee components. Hirudin provides anticoagulant protection of microvessels, sericin promotes the migration of keratinocytes and fibroblasts, while propolis and honey have strong antiseptic properties, which are critically important for the healing of infected wounds. These materials can be used as biofilms, dressings, or systems for local drug delivery.

In addition, there is potential for bioengineering the combined properties of leech peptides and bee venom to create new anti-inflammatory and analgesic agents. For example, melittin – the main component of bee venom – exhibits a synergistic effect when combined with leech-derived thrombin inhibitors in reducing swelling and pain in rheumatological practice.

Thus, the integrative use of biological resources from different invertebrate species significantly expands the possibilities of modern biomedicine, enabling the development of complex, multifactorial therapeutic platforms.

Medicinal Leeches (*Hirudo medicinalis*) are among the oldest biotherapeutic agents that continue to hold clinical relevance in modern medicine.

Their therapeutic effect is primarily based on saliva, which contains over 100 biologically active compounds, among which the key components are hirudin, bdellins, eglins, hyaluronidase, and apyrase. Hirudin is a potent thrombin inhibitor that provides an anticoagulant effect – critically important in the treatment of thromboembolic complications, coronary artery disease, and heart attacks. Other enzymes exhibit anti-inflammatory, analgesic, anti-edematous, and anti-bacterial properties.

Hirudotherapy has found application in aesthetic medicine for improving microcirculation, lymphatic drainage, and reducing swelling and inflammatory processes in the dermis. The biologically active components of leech saliva promote tissue regeneration, increase skin turgor, enhance facial complexion, and aid in the treatment of dermatological conditions such as acne, rosacea, and post-acne marks.

In microsurgery, leeches are used as an effective tool for eliminating venous congestion following tissue transplants (such as ear, finger, or lip replantation). Their ability to provide temporary venous drainage, reduce swelling, and prevent thrombosis enhances the viability of transplants. An additional advantage is the presence of analgesic components in leech saliva, which help reduce postoperative pain.

Clinical studies confirm the relevance of using hirudotherapy in reconstructive surgery, dermatology, and aesthetic medicine. A visualization of the prevalence of clinical cases involving this method across various medical fields is presented in Figure 1 [1].

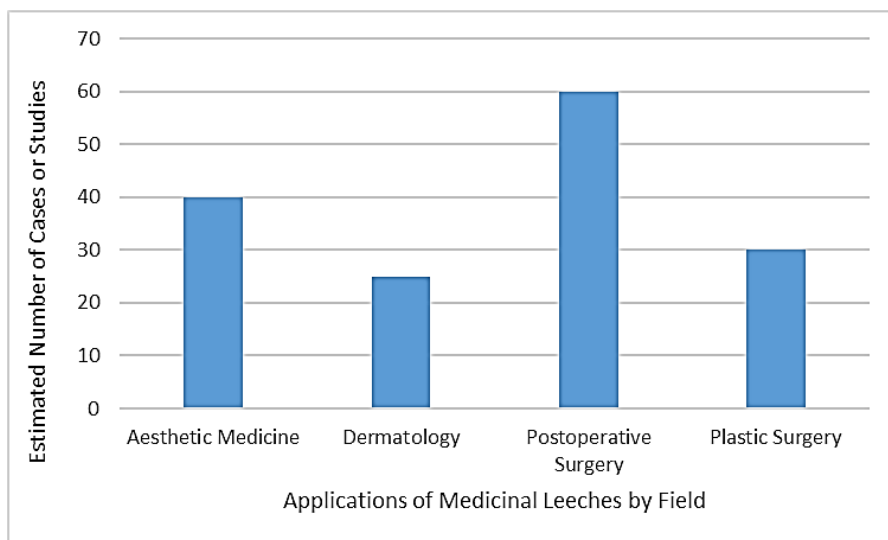


Fig. 1. Applications of Medicinal Leeches by Field

Medicinal Leeches (*Hirudo medicinalis*). In modern biomedicine, medicinal leeches (*Hirudo medicinalis*) have regained considerable attention due to their potent anticoagulant properties. They are widely used in microsurgery, particularly in limb replantation and reconstructive procedures, to restore microcirculation and prevent thrombosis. The primary bioactive component of leech saliva – hirudin – inhibits thrombin, thereby preventing blood clot formation. Although precise statistics on the clinical use of *H. medicinalis* are currently limited, numerous clinical reviews indicate a growing demand for hirudotherapy in many countries across Europe, Asia, and North America.

At the same time, the active commercial use of leeches in medicine presents ecological challenges. Natural populations of *Hirudo medicinalis* are under pressure due to overharvesting, habitat degradation, and changes in hydrological conditions, which has led to the inclusion of this species on protected lists in several regions. This highlights the urgent need to develop artificial breeding technologies for leeches to meet the needs of medicine and scientific research.

Silkworm (*Bombyx mori*). The silkworm (*Bombyx mori*) is one of the most thoroughly studied species in the field of biotechnology, primarily due to the unique properties of the silk it produces. The silk thread consists of two structural proteins – fibroin and sericin. Fibroin, which forms the fibrous core of the cocoon, is distinguished by its high mechanical strength, biocompatibility, low immunogenicity, and capacity for controlled biodegradation. These characteristics make it an extremely promising material for use in tissue engineering, the development of bioactive implants, corneal transplants, nerve conduits, and vascular prostheses [4].

Special attention should be given to fibroin-based 3D scaffolds, which are actively used as matrices for culturing osteoblasts, chondrocytes, and fibroblasts, thus promoting the regeneration of bone, cartilage, and connective tissues. Additionally, fibroin is employed as a carrier for controlled drug delivery. Micro- and nanocapsules made from this protein ensure prolonged release of active substances, including antibiotics, anticancer agents, and vaccines, enabling the development of personalized therapeutic regimens with optimized pharmacokinetic parameters.

Sericin, the other protein component of the cocoon, exhibits antioxidant, antimicrobial, and anti-inflammatory activity. It is being actively studied in cosmetology and dermatology as a promising ingredient in skincare and hair-care products. Bioactive peptides of sericin, obtained through hydrolysis, have demonstrated the ability to reduce oxidative stress, stimulate cell proliferation, and promote tissue healing (Table 1) [2].

These data highlight the multifunctionality of silk proteins and their high potential in translational medicine and pharmaceuticals. Innovative approaches to modifying fibroin and sericin allow for the optimization of their properties for targeted use, opening up prospects for the development of new biocompatible materials with tailored characteristics [4].

Table 1. Comparative Characteristics of the Biotechnological Applications of Silkworm Fibroin and Sericin (*Bombyx mori*)

Protein Component	Application Field	Form of Use	Main Functions and Effects
Fibroin	Tissue engineering	3D scaffolds, films, hydrogels	Supports cell adhesion, biocompatibility, stimulates tissue regeneration
	Surgery and transplantation	Bioimplants, vascular grafts, nerve conduits	Biodegradability, mechanical strength, no immune response
	Pharmaceuticals	Micro- and nano-capsules for drug delivery	Controlled release, stability of active substances, improved bioavailability
	Ophthalmology	Transparent films	Used as corneal transplants, sterility, transparency, biocompatibility
Sericin	Cosmetology	Creams, serums, masks	Antioxidant action, moisturizing, anti-inflammatory effects
	Dermatology	Peptide fractions, hydrogels	Wound healing support, oxidative stress protection, antimicrobial activity
	Pharmaceuticals	Protein-based bioactive complexes	Immunostimulation, drug delivery, improved stability of bioactive compounds

Figure 2 presents a comparative analysis of the use of fibroin and sericin proteins across different biotechnological fields. As shown in the diagram, fibroin is most widely used in regenerative medicine, the pharmaceutical industry, and ophthalmology, due to its excellent mechanical properties, biocompatibility, and low immunogenicity. In contrast, sericin is predominantly utilized in cosmetology, dermatology, and nanomedicine, owing to its moisturizing, antioxidant, and anti-inflammatory characteristics.

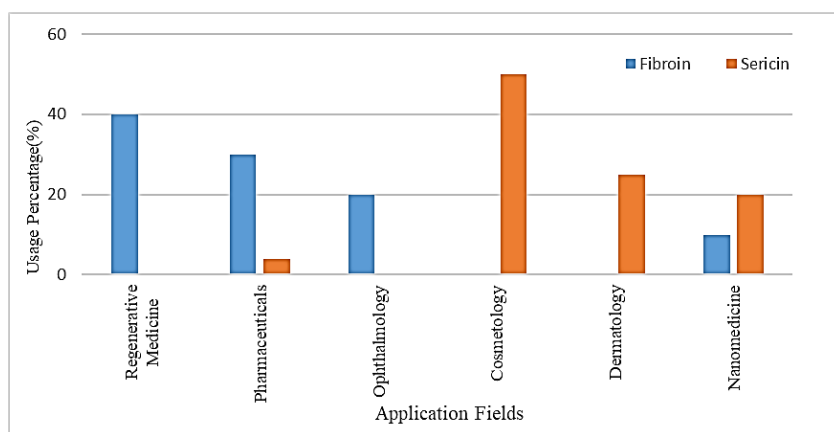


Fig. 2. Comparison of Fibroin and Sericin Applications in Biotechnology

Silkworms (*Bombyx mori*) remain the primary biological source of natural silk, which is important not only for the textile industry but also for modern biotechnological advancements. According to 2023 data, China is the leading producer of silkworm cocoons, accounting for approximately 834,000 metric tons or about 80 % of global production. India ranks second, contributing around 16 % of the global volume. The development of sericulture holds significant socio-economic importance, promoting employment in rural areas and reducing urbanization by lowering migration rates to cities [7].

Bees (*Apis mellifera*) also play a significant role in biotechnological research and practical applications, particularly in medicine, pharmaceuticals, and cosmetology. Beekeeping products are characterized by a unique biochemical composition and a wide range of biological activities – antimicrobial, anti-inflammatory, antioxidant, and immunomodulatory.

Honey, due to its natural antiseptic properties, is widely used in the treatment of wounds, burns, and trophic ulcers. Its antimicrobial activity is attributed to the presence of the enzyme glucose oxidase, which produces hydrogen peroxide, as well as its low pH (3.2–4.5), which inhibits the growth of pathogenic microorganisms. Additionally, polyphenols and flavonoids in honey provide antioxidant effects, promoting tissue regeneration.

Propolis, or bee glue, exhibits a broad spectrum of antimicrobial activity, effectively acting against pathogens such as *Staphylococcus aureus* and *Escherichia coli*. Its high flavonoid content ensures anti-inflammatory, analgesic, and antiviral properties. Propolis is actively used in the production of pharmaceutical preparations for the treatment of inflammatory conditions of the oral cavity and throat.

Beeswax is mainly used as a base for pharmaceutical ointments, creams, and suppositories due to its emollient properties, which help retain moisture in the skin and form a protective barrier.

Royal jelly is a highly bioactive product that stimulates cell proliferation, enhances metabolic processes, and strengthens the immune system. Its biochemical composition includes amino acids, B vitamins, enzymes, and fatty acids, which underpins its use in the production of immunomodulatory, tonic, and restorative preparations.

Bee venom is used in apitherapy – a branch of alternative medicine that employs it for treating musculoskeletal disorders, including arthritis, radiculitis, and osteochondrosis. The main biologically active components of bee venom are melittin, which has strong anti-inflammatory properties, and apamin, which enhances nerve conductivity (Figure 3).

The graph presents the number of primary biomedical application areas for five key beekeeping products: honey, propolis, beeswax, royal jelly, and bee venom. According to the data presented, the most versatile in the field of bio-

medicine are honey, propolis, royal jelly, and bee venom – each of these products has at least three main applications, including antimicrobial activity, immunomodulatory effects, and the ability to promote tissue regeneration. Beeswax, by contrast, is primarily used in the pharmaceutical and cosmetic industries as an auxiliary component [10].

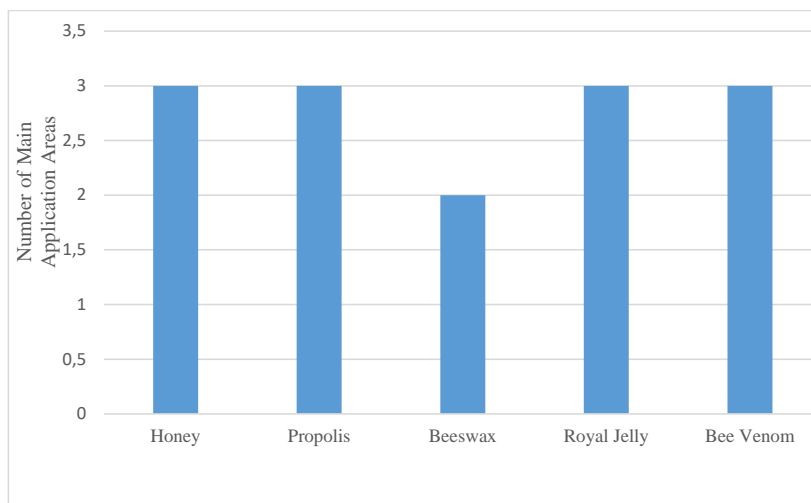


Fig. 3. Applications of Beekeeping Products in Biomedicine

Bees (*Apis mellifera*) play a critically important role in agriculture and biotechnology through the pollination of crops and the production of biologically active products such as honey, wax, propolis, royal jelly, and venom. According to estimates from the Food and Agriculture Organization of the United Nations (FAO), the economic value of pollination services provided by bees amounts to hundreds of billions of US dollars annually. In addition, beekeeping products are widely used in medicine, cosmetology, and pharmaceuticals, further confirming their biotechnological significance. As of 2022, there were approximately 80 million bee colonies worldwide, producing around 1.6 million tons of honey annually, nearly half of which was exported. This underscores the crucial role of beekeeping in the global economy. In Ukraine, according to FAO data, annual honey production ranges from 66,000 to 73,000 tons, with around 400,000 registered beekeepers.

Thus, invertebrate animals represent promising subjects for biotechnological research and practical applications due to the high bioactivity of the substances they produce, their relative ease of maintenance, and their environmental safety. Their natural potential enables wide applications in medical, pharmaceutical, and cosmetic technologies. As the analysis shows, medicinal

leeches, silkworms, and bees are of significant importance for the advancement of regenerative medicine, apitherapy, tissue engineering, and the development of bioactive materials [9].

Medicinal leeches are used in microsurgery due to their ability to secrete hirudin – a natural thrombin inhibitor that prevents blood clotting and promotes tissue preservation following transplantation. In addition, hirudotherapy is gradually finding application in aesthetic medicine, particularly in rejuvenation procedures, which highlights the need for further research into its efficacy, mechanisms of action, and long-term clinical outcomes.

Silkworms (*Bombyx mori*) serve as a source of the protein's fibroin and sericin, which are used in the development of biodegradable implants, scaffolds for tissue engineering, and cosmetic and pharmaceutical products. Thanks to favorable molecular characteristics – including biocompatibility, thermal stability, and modifiability – silk proteins offer new prospects for the creation of personalized drug delivery systems with enhanced efficacy and reduced side effects.

Beekeeping products exhibit complex effects on the human body. Their antibacterial, immunomodulatory, anti-inflammatory, and wound-healing properties form the basis for the development of innovative medical and cosmetic products. In particular, honey and propolis are widely used in antibacterial ointments, gels, and wound dressings, while bee venom is applied in the treatment of rheumatic conditions, including arthritis.

In the future, the biotechnological potential of invertebrates may be significantly expanded through the integration of natural bioactive substances with advanced technologies – including nanotechnology, genetic engineering, and tissue bioengineering. However, the large-scale implementation of such technologies requires additional interdisciplinary research, including preclinical and clinical trials, safety assessments, and the development of regulatory frameworks for quality control. At the same time, the preservation of invertebrate biodiversity and the implementation of sustainable practices remain critical in light of ethical and ecological considerations in the development of biotechnology [8].

Ukraine possesses significant potential for the development of biotechnologies based on the use of invertebrate animals – medicinal leeches, silkworms, and honey bees. National traditions of hirudotherapy, active beekeeping practices, and the presence of scientific centers focused on innovative biomaterials create favorable conditions for the transfer of knowledge into practical applications (Table 2) [10].

For example, the enterprise «Hirudocenter» (Kharkiv) is one of the leading institutions in Ukraine in the cultivation of medicinal leeches and the production of biopharmaceuticals based on them. The company's products are supplied to both medical institutions and the cosmetology industry, demonstrating the commercial potential of hirudobiotechnologies.

Table 2. Key Areas of Invertebrate Biotechnology in Ukraine

Field	Institution/Enterprise	Main Activity	Sector Status
Hirudotherapy	Hirudocenter (Kharkiv)	Breeding of medicinal leeches, production of biopharmaceuticals	Active
Apitherapy	Institute of Beekeeping (Kyiv)	Research on bee products, development of therapeutic agents	Active
Apitherapy	LLC "Ecoproduct"	Production of phytopharmaceuticals from honey and propolis	Commercialized
Sericulture	Institute of Animal Science, NAAS	Silkworm research, base for experimental production	Limited

In the field of apitherapy and beekeeping product processing, the P. I. Prokopovych Institute of Beekeeping (Kyiv) plays an active role. It conducts research on honey, propolis, royal jelly, and bee venom, and develops new therapeutic and preventive preparations. Companies such as LLC «Ecoproduct» manufacture phytopharmaceuticals from bee products for both the domestic market and export.

Regarding sericulture, although the industry has declined in Ukraine, scientific institutions remain that could serve as a foundation for its revival (Table 3). For instance, the Institute of Animal Science of the National Academy of Agrarian Sciences of Ukraine has experience working with silkworms and possesses the infrastructure necessary for experimental production. Combined with modern biotechnologies, this could form the basis for the production of bioimplants, filters, and drug delivery carriers based on silk fibroin [7].

Table 3. Biotechnological Potential of Invertebrate-Derived Products

Source	Product Type	Biomedical Application	Development Level in Ukraine
Medicinal leeches	Extracts, leeches as agents	Anticoagulants, anti-inflammatory agents	Advanced
Honey bees	Propolis, royal jelly, venom	Immunomodulators, wound healing products	Advanced
Silkworms	Silk fibroin	Bioimplants, drug carriers, regenerative medicine	Pilot stage

It is also advisable to intensify efforts to integrate national projects into the European research space (for example, through programs such as Horizon Europe or COST Action). This would enable the attraction of investments, the implementation of modern quality control methods, and the adoption of international bioethical standards.

At the same time, ensuring environmental sustainability is essential – particularly the protection of wild populations of *Hirudo medicinalis*, the regulated harvesting of raw materials, the certification of apiaries, and the development of a national strategy for the sustainable biotechnological use of invertebrates. This strategy should integrate scientific, educational, environmental, and economic policies (Table 4).

Table 4. Examples of International Experience in the Field of Invertebrate Biotechnology

Country	Application Type	Example/Company	Innovations
Germany	Medicinal leeches	BioPharma LEECH	Certified breeding (Class IIb)
Japan	Silk fibroin	Research centers	Bioelectronics, 3D printing
China	Silk proteins	Silk Engineering R&D Institutes	Medical implants, nerve conduits
France	Apitherapy, propolis	Apimab Laboratoires	Pharmaceutical products from bee-derived substances
Slovenia, Italy	Organic beekeeping	Certified apiaries	Export to EU and Asia

Ukraine, given its well-developed beekeeping sector, established scientific schools, accessible raw materials, and skilled professionals, has the potential to take a prominent position in this segment of the global bioeconomy. Expanding collaboration with international research programs, implementing EU certification schemes (e.g., GMP, ISO 13485 for medical devices), and supporting startups in the field of biomedical materials could transform the biotechnological processing of invertebrates from a niche area into a strong sector of the national innovation economy.

Conclusion.

1. Invertebrate animals, particularly medicinal leeches, silkworms (*Bombyx mori*), and honey bees (*Apis mellifera*), demonstrate high biotechnological potential due to the synthesis of unique biologically active substances and materials with pronounced therapeutic properties.

2. Medicinal leeches are a source of hirudin – a powerful natural anticoagulant used in microsurgery, regenerative, and aesthetic medicine. Their use requires further scientific research on efficacy and safety.

3. Silk proteins – fibroin and sericin – have broad applications in tissue engineering, pharmaceuticals, and cosmetology due to their biocompatibility, biodegradability, and modifiability. They also offer prospects for the development of personalized drug delivery systems.

4. Beekeeping products (honey, propolis, wax, royal jelly, and bee venom) are utilized in biomedical technologies thanks to their antibacterial, anti-inflammatory, immunomodulatory, and regenerative properties. They play a vital role in pharmaceuticals, cosmetology, and apitherapy.

5. The global significance of beekeeping is confirmed by its economic contribution through crop pollination and the wide use of beekeeping products. Ukraine ranks among the leading honey producers, which is of strategic importance to the national economy.

6. The further development of invertebrate-based biotechnologies involves integration with nanotechnology, genetic engineering, and tissue bioengineering. At the same time, it is crucial to ensure ethical regulation, environmental sustainability, and a scientifically grounded regulatory framework for quality control.

ВИКОРИСТАННЯ БЕЗХРЕБЕТНИХ У БІОТЕХНОЛОГІЯХ: МЕДИЧНІ П'ЯВКИ, ШОВКОПРЯД, БДЖОЛИ

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У статті здійснено узагальнення сучасних напрямів біотехнологічного використання безхребетних тварин, зокрема медичних п'явок (*Hirudo medicinalis*), шовкопрядів (*Bombyx mori*) та медоносних бджіл (*Apis mellifera*). Розглянуто біоактивні речовини, які продукуються цими організмами, та проаналізовано можливості їх застосування у медичній, фармацевтичній, косметологічній і біоінженерній сферах. Особливу увагу приділено гірудотерапії – методу лікування з використанням секрету слинних залоз п'явок, що містить ферменти з антикоагулянтною, протизапальною, анальгезивною та антибактеріальною активністю. Окреслено також роль гірудотерапії в мікрохірургії та естетичній медицині.

Описано сучасне застосування шовкових білків – фіброїну і серицину – у створенні біосумісних, біодеградабельних матеріалів для тканинної інженерії, контролю вивільнення лікарських засобів, засобів загоєння ран, а також у стоматологічній та офтальмологічній практиці. Звернено увагу на перспективи використання біоактивних пептидів шовку у фармацевтичних і косметичних розробках.

Розкрито потенціал апітерапії – біотехнологічного напрямку, що ґрунтується на лікувальних властивостях продуктів бджільництва (меду, прополісу, воску, апітоксину, маточного молочка). Наведено наукові дані щодо їх антисептичних, регенеративних, протизапальних та імуномодулювальних ефектів. Оцінено можливості їх використання у створенні лікарських препаратів і косметичних засобів.

Представлено результати актуальних досліджень, які підтверджують ефективність та перспективність використання безхребетних тварин як джерела біологічно активних речовин і технологічних рішень у сучасній біотехнології. Узагальнені дані можуть слугувати підґрунтям для подальших міждисциплінарних розробок і впровадження інновацій у медичну практику.

Ключові слова: безхребетні, біотехнології, гірудотерапія, фіброїн, серицин, шовкопряд, бджоли, апітерапія, біоактивні речовини, медичне застосування.

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