BIOCHEMICAL ASPECTS OF THE PRODUCTION OF PHARMACEUTICAL PREPARATIONS

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Introduction. The development of pharmacy is closely linked to the understanding of fundamental biochemical processes in the body and the development of biochemical methods for studying its vital functions and reactions to the effects of drugs. Pharmacy makes extensive use of the advances, methodology and techniques of modern biochemistry. Biochemical research is used to address drug technology issues such as the biological justification of the efficacy of various dosage forms of a therapeutic drug or combination of drugs, their efficacy of action.

The aim of the study. To study the influence of biochemical techniques and methods in the implementation of the formation of new technological processes in the production of innovative drugs.

Methods of research. This paper uses educational and scientific data on biochemical principles correlating with the field of industrial technology for the production of drugs in the conditions of modern requirements for the creation of new pharmaceuticals [1, 2].

Main results. Recent advances in enzymology and the development of enzyme immunoassays and radioimmunoassay have significantly improved biochemical methods for the standardisation and quality control of drugs. For example, immunoenzymatically and radioimmunological methods based on the analysis of antigen-antibody interaction have been successfully used to determine in blood and urine a number of natural drugs (e.g., hormones) and drugs that are foreign substances (Codeine, Morphine, Barbiturates, etc.). Both methods ensure high specificity and sensitivity of the analysis.

The development of applied areas of biochemistry, molecular and cell biology, molecular genetics, has significantly changed the way a number of drugs are obtained and has ensured the rapid development of pharmaceutical biotechnology. In pharmaceutical biotechnology, tangible advances have been made in the field of microbial synthesis of drugs, the production and use of enzymes for medical purposes and in the pharmaceutical industry, and in the field of genetically engineered biotechnology of drugs.

Enzyme preparations and their inhibitors are now widely used for the treatment and prevention of various diseases. The introduction of enzymotherapy into medical practice was ensured by progress in the development of perfect methods for the preparative isolation of highly purified enzyme preparations and their inhibitors suitable for medical purposes. Enzyme preparations are used:

- as non-specific therapeutic agents, mainly for the removal of non-viable tissue;
- as thrombolytic therapy in parenteral administration and in non-specific anti-inflammatory therapy;
- as replacement therapy to compensate for an enzyme deficiency occurring in certain diseases;

- finally, enzyme inhibitors are used, the most common being tissue protease inhibitors (Tracilol, Iniprol, Contrical, etc.). Inhibitors are used in particular for fibrinolytic bleeding.

In addition to enzymotherapy, enzymes are used as analytical reagents. In the pharmaceutical industry immobilised enzymes are often used as analytical reagents. Immobilised enzymes are included as a leading working component in automatic flow analysers and special enzyme electrodes which are used for the analysis of pharmaceuticals during their production process. Automatic detection of ethanol, urea, glucose, penicillin and some toxic substances has been established using such systems.

Immobilised enzymes are increasingly used in the pharmaceutical industry for the synthesis of pharmaceuticals. In particular, immobilised penicillinamidase is used to produce semi-synthetic penicillin's, and immobilised steroid hydroxylase and steroid dehydrogenase are used to produce the steroid hormones cortisol and prednisolone [3].

One of the areas of pharmaceutical biotechnology is the microbial synthesis of drugs. The study of numerous biochemical reactions characteristic of microorganisms ensured the isolation of secondary metabolites from bacterial and fungal cells, which were used to create hypotensive, anti-inflammatory and antiparasitic agents. It should be noted that microorganisms were the richest sources of enzyme inhibitors, potentially suitable for pharmacological purposes. Among them, Mevalonil has been obtained, which was used as the basis for the drug Miscleron, an anti-atherosclerotic drug that is a competitive inhibitor of b-hydroxy-b-methylglutaryl-CoA reductase in the liver. Among pharmacologically active compounds synthesised by microbial cells, antibiotics, as well as antifungal agents, antitumor agents and alkaloids are of particular note.

A major area of drug production is genetically engineered biotechnology, based on recombinant DNA techniques. According to the UNESCO definition, recombinant DNA is DNA molecules obtained in vitro by combining natural or synthetic DNA fragments with DNA molecules capable of replicating in a cell. The basis of the experiment is the insertion of natural or foreign DNA into a vector, which is a bacterial plasmid or a viral genome. The recombinant DNA is then inserted into the cell, most commonly into *E. coli* cell (most commonly in E. coli), where it is replicated. The bacterial cell containing the DNA multiplies to form a clone of transformed cells capable of producing specific proteins (encoded in the DNA) in large quantities, which are used as a source for the therapeutic agent. Currently, insulin, somatostatin, somatotropin, interferon, etc. are being produced using genetically engineered technology [4].

Biochemical research also provides the basis for the creation of new effective dosage forms of therapeutic agents and for the development of methods to increase the bioavailability of drugs. Recently, the production and use of drugs that are immobilized enzymes on biologically compatible degradable polymers in tissues have become increasingly widespread. Such dosage forms are successfully used as antitumor, antioxidant, immunomodulatory, and fibrinolytic drugs.

The development and use of drug forms with targeted transport to the affected area, to the target tissue, is very promising. For this purpose, the binding of the drug

substance to a soluble high molecular weight polymer is used, which leads to the accumulation of the drug in the renal tubules. Binding of the medicinal substance to the system, which releases the drug in a zone with acidic pH and high temperature, typical for a focus of inflammation, is used. A magnetotransported dosage form is used. The binding of the medicament to vector molecules, for which a particular organ or cell is a natural target, hormones, enzymes, glycolipids, glycoproteins, and especially immunoglobulins (so-called antibodies against target organ antigens) is used. Finally, inclusion of drugs (including enzymes) into microcontainers (microcapsules, cell shadows, liposomes) with subsequent immobilization of vector molecules on the outer surface of the microcontainer is used, which increases the targeting of such microcontainers.

Liposomes seem to be the most promising compared to other possible –nocontainers, as they are easily metabolized in the body, and they also have a great variety of mechanisms of interaction with biological objects, as a huge variety of their composition, size and other structural and functional parameters are possible. They are easy to make, which is important. Liposomes are microscopic vesicles, whose walls are formed by bilayers of polar amphiphilic lipids: glycerophospholipids, sphingomyelins, etc. Drugs can interact with and bind to several regions of liposomes. Highly polar small molecules of dissolved drugs are incorporated into the internal water space of liposomes. Non-polar molecules are incorporated inside the phospholipid bilayer. Amphipathic drugs are bound by hydrocarbon residues of the liposome shell. Macromolecules, especially proteins, often associate with the surface of liposomes. The interaction of liposomes with cells is a complex process that is not yet well understood. It has been proved in cell culture experiments that liposomes can be adsorbed on the cell surface, incorporated into cells through endocytosis, and fused to the plasma membrane. The composition of liposomes depends on their structure (i.e. charge, size, composition) and the way they are administered (oral, intravenous or subcutaneous). To improve the selectivity and targeting of the effect of liposomes, vector molecules (for example, antigens to antibodies of certain tissues) are embedded in the lipid shell of liposomes.

Liposomes are currently used in medicine for enzyme replacement therapy (in particular, for the treatment of lysosomal diseases), cancer chemotherapy, for the treatment of some parasitic diseases, for intraarticular rheumatoid arthritis, etc. The list of drugs that are in one way or another associated with liposomes includes more than 300 names, which shows the promise of this dosage form [5].

When creating new drugs, to study their pharmacological and toxicological properties, various biochemical methods are necessarily used in experiments on normal animals and animals with experimental models of various pathologies. At the same time, it turned out that experimental studies can’t provide complete information about the new drugs, guaranteeing the absence of adverse biochemical reactions during the subsequent use of these drugs in sick people. This is due in some cases to significant differences in the sensitivity of receptors to the drug substance and to differences in the metabolism of drugs in humans and animals. The latter has led to the need for clinical and biochemical studies on human volunteers in drug trials, which allows to clarify many of the experimental biochemical data and identify the human-specific metabolic effects of the drugs.

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Biochemistry thus serves as the foundation of biopharmacy, this theoretical basis of drug technology. Biopharmacy is designed to reveal the relationship between a medicinal substance, its dosage form and its therapeutic effect.

Once a drug has entered the body, it goes through a complex process in the body in order to achieve its therapeutic effect. Initially, during the administration phase, the medicine has to be released from the dosage form in which it is enclosed (tablets, ointments, etc.) and travel all the way to the intended site of absorption. The drug is then absorbed, i.e. transported through biomembranes, subject to the laws of diffusion, filtration, and active transport. Diffusion and filtration kinetics are influenced by both pharmaceutical factors (e.g. accompanying surfactants, mechanical strength of tablets, etc.) and biochemical factors, such as state of cell membranes, enzymatic activity of cells, etc. An even greater role for biochemical factors is seen in the later stages when the drug substance is distributed in fluids and tissues, interacts with receptors, undergoes transformation and is excreted from the body.

Conclusions. Thus, the biochemical basis provided by the various branches of biological chemistry is decisive for further modelling the design of the process flow diagram for the production of innovative pharmaceuticals free of undesirable impurities and consequently with a high therapeutic effect for adequate treatment.

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