Ministry of Health of the Russian Federation
Volgograd State Medical University

Department of Pharmaceutical and Toxicological Chemistry

GENERAL PHARMACEUTICAL CHEMISTRY

SOURCES AND METHODS OF OBTAINING DRUGS

Lesson 2
IV term

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Discipline

GENERAL PHARMACEUTICAL CHEMISTRY

LESSON №2 Sources and methods of obtaining drugs.	Obtaining medicinal substances from plant and animal raw materials. Preparation of drugs based on biological synthesis. Obtaining medicinal substances from mineral raw materials and by organic synthesis

QUESTIONS FOR THE LESSON

1. What mineral sources are used to obtain medicines? Give examples.
2. What are plant sources for obtaining medicines? What are the steps involved in the isolation and purification of drugs?
3. What animal sources are used to obtain medicines? Give examples.
4. What marine sources are used to obtain medicines?
5. What are microbial drug sources? Give examples.
6. What is organic drug synthesis? What types of chemical reactions are used?
7. What types of organic synthesis are there? Give them a description.
8. What are semi-synthetic drug sources?
9. What are biosynthetic drug sources?

MINERAL SOURCES

The source of obtaining inorganic drugs is mineral raw materials. The minerals themselves or individual elements are used.

To obtain synthetic organic drugs, dry distillation products of coal, wood, oil shale, as well as various oil fractions are used.

Coal tar is a complex mixture that includes over 480 different aromatic and heterocyclic compounds. With the help of distillation columns, coal tar is subjected to separation into fractions. Then each fraction is distilled in a narrower temperature range and individual substances are isolated. Isolated individual substances serve as starting products for basic and fine organic synthesis of various compounds, including drugs.

During the dry distillation of **wood**, charcoal and two liquid fractions (wood resin) are formed. One of them contains methyl alcohol, acetone, acetic acid, other (wood tar) contains phenols, phenolic acids, fatty acids, carbohydrates and some other organic substances. Furfural, cresol, catechol esters and pyrogallol are also obtained from wood.

Examples include ferrous sulfate in iron deficiency anemia; magnesium sulfate as purgative; magnesium trisilicate, aluminum hydroxide and sodium bicarbonate as antacids for hyperacidity and peptic ulcer; zinc oxide ointment as skin protectant, in wounds and eczema; gold salts (solganal, auranofin) as anti-inflammatory and in rheumatoid arthritis; selenium as anti-dandruff.

PLANT SOURCES

Plant materials - leaves, flowers, peels, seeds, fruits, roots of plants - in themselves can be medicines. More than 12,000 chemical compounds of various classes have been found in plants. Medicinal plant materials are a source of natural biologically active substances: alkaloids, terpenes, glycosides, vitamins. Isolated as individual compounds, they are drugs.

The isolation of biologically active substances from plant and animal raw materials, their separation and purification is a difficult task.

The process of their selection consists mainly of the following steps:

1. grinding of raw materials,
2. extraction,
3. separation of the extract from the raw material,
4. removal and recovery of the solvent from the extract and feedstock,
5. isolation and purification of biologically active substances.

Typically, plants contain several biogenetically related compounds that are similar in chemical structure and properties. Therefore, the amount of biologically active substances with an admixture of other related natural compounds contained in the feedstock is most often extracted.

The bulk of vegetable raw materials are fiber, proteins, chlorophyll, resins, mucus, tannins and other substances. Therefore, it is very difficult to separate BAS from these related substances. In the chemical-pharmaceutical industry, various ***extraction*** options are still widely used for this purpose. Along with extraction, various variants of ***chromatography*** are increasingly being used. Column and ion-exchange chromatography are used to isolate, separate and purify organic compounds from impurities.

ANIMAL SOURCES

Individual substances are obtained from raw materials of animal origin - hormonal preparations, enzymes. Insulin, heparin, adrenaline, thyroxin, cod liver oil, musk, beeswax, enzymes, and antitoxins sera are some examples of drugs obtained from animal sources.

The pancreas, mucous membranes of the stomachs and small intestines of pigs, and other organs of animals can serve as raw materials for the industrial production of enzymes of animal origin.

Stages of isolation of biologically active substances from animal raw materials, their separation and purification:

1. grinding of raw materials,
2. extraction,
3. separation of the extract from the raw material,
4. removal and recovery of the solvent from the extract and feedstock,
5. isolation and purification of biologically active substances.

MARINE SOURCE

Bioactive compounds from marine flora and fauna have extensive past and present use in the prevention, treatment or cure of many diseases. Coral, sponges, fish, and marine microorganisms produce biologically potent chemicals with interesting anti-inflammatory, anti-viral, and anticancer activity. *For example* curacin A from marine cyanobacterium Lyngbya majuscule, eleutherobin from coral Eleutherobia sp., discodermolide from marine sponge Discodermia dissoluta, etc. show potent anti-tumour activity.

The use of *aquatic organisms (marine organisms)* for obtaining drugs has great prospects. Hydrobionts contain nitrogen-containing aliphatic substances, halogen-containing compounds of the aromatic series (benzene derivatives), heterocyclic derivatives, polyenoic acids, terpenoids, etc.

MICROBIAL SOURCES

Several life-saving drugs have been historically derived from microorganisms. *Examples* include penicillin produced by Penicillium chrysogenum, streptomycin from Streptomyces griseus, chloramphenicol from Streptomyces venezuelae, neomycin from Streptomyces fradiae, bacitracin from Bacillus subtilis etc. Xanthan (polysaccharide gum secreted by Xanthomonas campestris), dextran (polysaccharide of glucose synthesized by lactic acid bacteria Leuconostoc mesenteroides, Streptococcus mutans, Lactobacillus brevis), curdian (β-1,3-glucan polymer, product of Agrobacterium biobar and Alcaligenes faecalis), pullulan (a polysaccharide polymer of maltotriose units produced from starch by the fungus Aureobasidium pullulans) etc. are all examples of drugs from microbial sources.

SYNTHETIC/CHEMICAL DERIVATIVE

A synthetic drug is produced using chemical synthesis, which rearranges chemical derivatives to form a new compound. At present, majority of drugs used in clinical practice are exclusively prepared synthetically in pharmaceutical and chemical laboratories.

One of the earliest synthetic drugs was sulphonamide, which began with the synthesis of prontosil dye. *Other examples* include acetylsalicylic acid (aspirin or

ASA), oral antidiabetics, antihistamines, thiazide diuretics, chloroquine, chlorpromazine, general and local anesthetics, paracetamol, phenytoin, etc.

Synthetically manufactured drugs generally have higher yields that are significantly associated with quality, purity, and low cost.

The synthesis of an organic compound with a predetermined structure is carried out from relatively simple and available compounds produced by the chemical industry. They form the future molecule.

Obtaining an organic drug is a complex process, often consisting of 10-20 stages or more. It includes many technological operations based on chemical, physical and physicochemical methods.

The chemical reactions used to synthesize organic drugs can be classified into three main groups:

- substitution reactions,
- substituent transformation reactions,
- oxidation-reduction reactions.

Substitution reactions. These reactions are based on the substitution of hydrogen atoms in the aliphatic chain, aromatic, heterocyclic ring or functional group with various substituents.

Substituent transformation reactions. This group of reactions is based on the chemical transformations of the substituents present in the molecule of the intermediate product to give it new properties or change its reactivity.

Oxidation-reduction reactions. Reduction and oxidation are a single process, as a result of which one group of atoms is reduced, while acquiring electrons, and another group of atoms is oxidized. In redox reactions, not only the degree of oxidation changes but also the composition of the molecule.

Types of organic synthesis

There are basic organic synthesis and fine organic synthesis.

Basic organic synthesis is the industrial large-scale production of organic compounds. The basic organic synthesis is characterized by a small number of stages. It is carried out at large industrial complexes. The products of the basic organic synthesis are used in various branches of the chemical industry, including the chemical and pharmaceutical industry. Some of them are used as drugs, but mainly they are the starting products of the synthesis of organic drugs.

Fine organic synthesis is low-tonnage. As a result of production, organic substances of a complex structure are obtained. Fine organic synthesis is carried out from the products of the main organic synthesis. Fine organic synthesis is characterized by a multistage nature, high energy and labor costs, and sophisticated equipment. A large number of steps lead to the formation of various by-products of the synthesis. Therefore, it requires step-by-step quality control and additional purification from impurities and production waste.

Since modern drugs have a complex chemical structure, fine organic synthesis is the only synthetic way to obtain alkaloids, hormones, antibiotics, their analogues, as well as other organic drugs.

SEMI-SYNTHETIC SOURCES

Semi-synthetic drugs are neither completely natural nor completely synthetic. They are a hybrid and are generally made by chemically modifying substances that are available from a natural source to improve their potency, efficacy and/or reduce side effects. Sometimes, semi-synthetic processes are used to prepare drugs when the natural sources may yield impure compounds or when the synthesis of drugs (complex molecules) may be difficult, expensive, and commercially unviable.

In semi-synthetic drugs, the nucleus of the drug obtained from a natural source is kept intact but the chemical structure is altered. *Examples* of semi-synthetic medicine include heroin from morphine, bromoscopolamine from scopolamine, homatropine from atropine, ampicillin from penicillin, etc.

BIOSYNTHETIC SOURCES (GENETICALLY ENGINEERED DRUGS)

This is relatively a new field that is being developed by mixing discoveries from molecular biology, recombinant DNA technology, DNA alteration, gene splicing, immunology, and immune pharmacology. Drugs developed using living organisms with the help of biotechnology or genetic engineering are known as biologics, biopharmaceuticals, recombinant DNA expressed products, bioengineered, or genetically engineered drugs. *Examples* include recombinant Hepatitis B vaccine, recombinant insulin, and others.

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