The design of medicinal substances of natural origin for modeling their biological activity.

Formation of the protoarsenal of natural medicines

People discovered the first medicines by accident. Ancient people received them from the "natural pharmacy": plants (leaves, bark, flowers, fruits, roots, stems), animals and minerals.

Formation of the protoarsenal of natural medicines

Up to the present time, the value of medicines obtained in the form of tinctures, extracts and decoctions (mainly from plants) remains at a high level (in Russia, such medicines account for about 30% of the total number of medicines).

Formation of the protoarsenal of natural medicines

From the 17th to the beginning of the 20th century The modern arsenal of medicinal products was replenished mainly by accidental discoveries of herbal medicines. The first individual natural compounds with a therapeutic effect (the so-called "active principle") began to be isolated from plants only in the 19th century.

Herbal remedies

Herbal remedies can be divided into the following groups:

1. Medicinal preparations based on isolated highly purified substances from plants.
2. Medicinal preparations containing a complex of biologically active substances of plants of varying degrees of purification.
3. Medicinal plant raw materials and medicinal plant collections.
4. Biologically active food additives of plant origin, which, in turn, are divided into nutraceuticals and parapharmaceuticals.

Key terms of herbal medicines

Medicinal plant raw materials are whole medicinal plants or parts thereof, used in dried, rarely fresh form as a medicinal product or for the production of medicinal substances, phytopreparations, dosage forms and authorized for use by authorized bodies in accordance with the established procedure

Key terms of herbal medicines

Galenic preparations are medicinal products representing various extracts from medicinal plant raw materials and used internally and externally

Key terms of herbal medicines

Novogalene preparations are extracts from medicinal plant raw materials, maximally freed from ballast substances (contain the sum of biologically active substances of the plant) and suitable not only for oral and external use, but also for parenteral administration

Key terms of herbal medicines

Biologically active active food additives are concentrates of natural (identical to natural) biologically active substances intended for direct intake with food or introduction into the composition of food products

Medicinal products of bacterial origin

Medicinal products of bacterial origin are bacterial cultures or biological products of bacterial origin used for the prevention, treatment and diagnosis of infectious diseases.

Bacterial preparations include:

1) suspensions of live or killed bacteria (vaccines, diagnosticums)

Bacterial preparations include:

2) individual components of microbial cells (protective antigens, hemosensitins, allergens, pyrogenal, etc.);

Bacterial preparations include:

3) bacterial waste products released into the culture medium (native and neutralized toxins, enzymes, some antibiotics);

Bacterial preparations include:

4) serums containing antibodies to the cellular components and extracellular products of bacteria.

Medicinal products of bacterial origin

According to the intended purpose, bacterial preparations are divided into :

- Preventive (vaccines, toxoids, protective antigens, serums),
- Therapeutic (antibiotics, serums and gamma globulins, vaccines, toxoids, components of microbial cells)
- Diagnostic (agglutinating, precipitating and luminescent sera, microbial diagnosticums, toxins, allergens, erythrocytes sensitized by microbial antigens or antibodies).

Combinatorial chemistry

Combinatorial chemistry (combinatorial chemistry), a methodology of chemical (primarily organic) synthesis, which aims to synthesize a large array of similar chemical compounds (combinatorial libraries) in the fastest and most economical way, using specific approaches and technologies.

Combinatorial chemistry

In practice, combinatorial chemistry is a set of techniques and methods for combining diverse initial chemical reagents to obtain as diverse arrays of chemical products as possible by conducting tens, hundreds, and sometimes thousands of parallel chemical transformations to form a huge number of end products.

Combinatorial chemistry

Task of combinatorial chemistry :

- Quickly synthesize many substances, usually complex in structure and sufficiently pures.
- The development of new economical and high-speed technologies for parallel synthesis and parallel purification of substances is achieved in a variety of ways.

Combinatorial chemistry

In the methods of liquid-phase combinatorial chemistry, they try to use only those reactions that occur with high yields and require minimal efforts to purify substances. To achieve a greater variety of products, conventional two-component reactions are replaced by multicomponent ones.

Combinatorial chemistry

Combinatorial chemistry is used in pharmaceuticals (design of new medicines), in the search for effective catalysts (polymerization, etc.), the design of nanomaterials. Automation tools have been developed for testing combinatorial libraries, robot systems, the productivity of which reaches 100 thousand samples per day.

Combinatorial chemistry

A powerful technology of combinatorial chemistry is solid – phase synthesis – conducting reactions on a modified polymer substrate.

SOLID –PHASE SYNTHESIS

In this case, a complex molecule is immobilized ("built up") onto the polymer surface during a sequence of reactions, and then, at the final stage, cleaves off the solid substrate due to chemical transformations.

SOLID –PHASE SYNTHESIS

Therefore, reactions can be carried out with a large excess of the reagent, washingthe latter from the polymer with the target substance and reducing the synthesis to the principlea "tea bag".

SOLID –PHASE SYNTHESIS

A new technologyis the replacement of solid polymers with perfluorinated liquids miscible with water and standard solvents). Forimmobilization (transfer of the substance to the perfluorinated phase), an extended perfluoroalkyl fragment is attached to the molecule of the initial reagent. This allows synthesis in emulsions with subsequentseparation of liquid phases.

Combinatorial chemistry

A combined method of combinatorial chemistry is the use of solid-phase reagents (oxidizer, acid, base are immobilized on a polymer). The excess of the solid reagent is introduced in to the solutions of the substances, and then separated by filtration.

Combinatorial chemistry

Another technique is the use of so-called **scavengers** -a modified polymer is added to the solution, which selectively removes unnecessary reagent taken in excess from the reaction mixture. Programmable proms are increasingly being used. robots that perform a sequence of routine monotonous procedures for the isolation and purification of substances (automatic synthesizers).

Combinatorial chemistry

The effectiveness of the use of combinatorial chemistry has been proven by the examples of the discovery of new drugs and catalysts.The sources of molecules for testing for biological properties can be both products of chemical synthesis and natural compounds having molecules with a very unusual and complex structure.

Combinatorial chemistry

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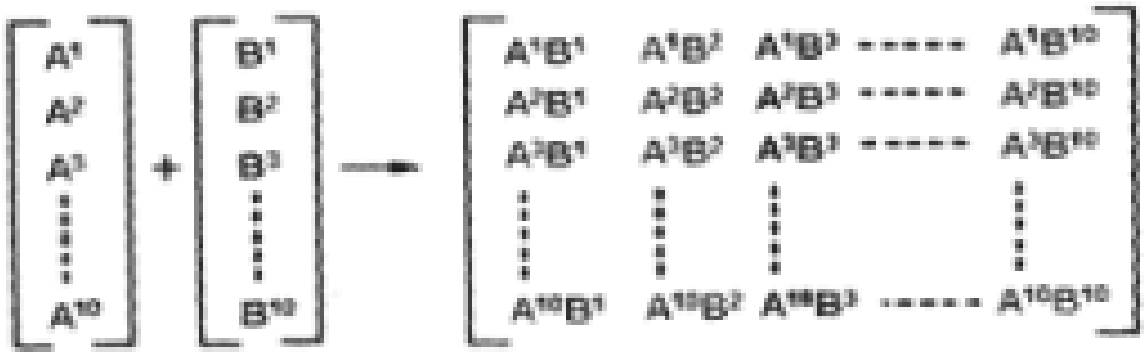
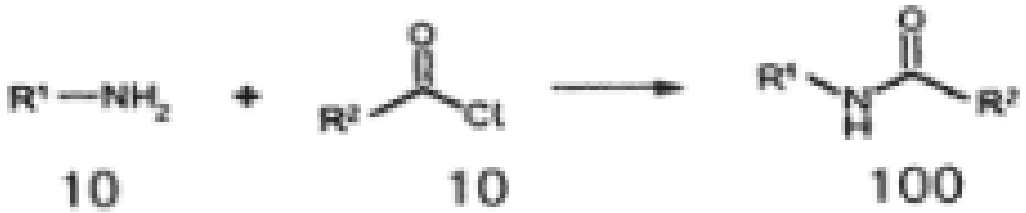
Combinatorial chemistry

In principle, all reactions can be carried out in one flask, after which a mixture of one hundred products will be obtained. This situation, unthinkable for classical synthesis and traditional biological tests, turned out to be quite common for combinatorial chemistry. After all, another revolution are feature of HTC technology is that it is possible to test no teach compound individually, but a mixture of substances.

Combinatorial chemistry





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reactants reactants products

Combinatorial chemistry

There is another way. The synthesis of the library can be carried out separately in one hundred micro-samples. They are inserted into a special reaction unit with a large number of sockets, and solutions of starting substances are introduced using multi-position pipettes. The block is closed with a common lid, and all reactions take place simultaneously under the same conditions (if necessary, the block is heated and shaken by a special mechanism). The result is one hundred individual compounds that will be used for testing or for subsequent parallel synthesis.