GOLD IN MEDICAL AND BIOLOGICAL RESEARCHES, MEDICINE AND PHARMACY

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Briefly shows the role of gold (Au) in medicine, the content of trace elements in the environment and the importance for the body. The use of Au and its compounds in biomedical research, pharmacology, radiation therapy and modern electronics is considered.

The use of Au in various fields of biomedicine is explained by high chemical stability, rather low toxicity, relative simplicity of synthesis and modification of the obtained products, economic and environmental safety, rapid excretion of the ^{198}Au radionuclide from the body, and selectivity of action.

In the 20s of the last century, researchers found that gold chlorides have a bactericidal effect. Some gold preparations exhibit antibacterial effects, in particular against Helicobacter pylori, as well as antifungal activity. Gold compounds such as aurothioglucose, sodium aurothiomalate, triethylphosphine have also been tried to treat syphilis, alcoholism, morphine addiction, nephritis, anemia, neurasthenia, and premature aging. A more effective and less toxic compound was gold sodium thiosulfate $AuNaS_2O_3$, which has been successfully used to treat lupus. Since the middle of the last century, complex compounds of gold with organic ligands have been used in medical practice, for example, cryzolgan, trifol, auranofin, aurothioprol, etc. Later, a more active and less toxic drug, cryzanol $(Au\text{-}S\text{-}CH_2\text{-}CHOH\text{-}CH_2SO_3)_2Ca$, used for the treatment of tuberculosis, lupus, leprosy. Auro therapy is today one of the most effective methods of treating rheumatoid arthritis. By the interaction of tetrachloroaurate acid $H[AuCl_4]$ with glycine, histidine and tryptophan, substances with high antimicrobial activity are obtained.

The mechanism of therapeutic and toxic effects is associated with inhibition of thiol enzymes, which is confirmed by studies on the interaction of Au compounds with blood proteins, enzymes, immunoglobulins and hormones. It is based on the ability of Au to inhibit macrophages and, as a result, inhibit the development of subsequent pathological immune reactions of the body.

Modern medicine uses various forms of gold. For the diagnosis and treatment of cancer, colloidal solutions containing the ions of the synthetic radioactive isotope ^{198}Au are used. An isotope is synthesized by neutron irradiation of natural ^{197}Au. The half-life of ^{198}Au is 2.8 days. The presence of β- and γ-radiation contributes to the creation of high tissue doses and the determination of isotope dislocation sites. Colloidal solutions of radioactive nanogold selectively accumulate in the cells of the reticuloendothelial system and connective tissue, which allows them to be used for the diagnosis and treatment of cancer tumors.

Currently, interest in the use of Au nanoparticles (NPs) in biomedical research has increased due to the intensive development of nanotechnology. Nanotechnologies make it possible to synthesize Au NPs of various shapes and sizes, modify them with molecules of biologically active substances, and use them for early diagnosis and treatment of many diseases. The beginning of the use of Au NPs in medicine is the work in which antibodies conjugated with colloidal gold were used for direct visualization of Salmonella surface antigens. Now this direction has developed into an independent industry, including the use of Au NPs in biomedical research, diagnostics, biosensors, photothermal and photodynamic therapy, as well as in targeted delivery of drugs and genetic materials.

The structure and use of Au NPs can be divided into two groups. The first group includes conjugates of NPs with oligonucleotides, peptides, polyethylene glycol, etc. These structures are used for targeted delivery and controlled release of drugs, local tumor hypothermia, optical imaging, and the creation of biosensors. The second group includes hollow NPs with a dielectric or magnetic core and a gold shell. These structures are used to encapsulate drugs. Modified Au NPs have low immunogenicity and high biocompatibility.

NPs are synthesized by two methods: dispersion and condensation. The disadvantage of the dispersion method is the formation of particles that are inhomogeneous in size. The condensation method makes it possible to obtain Au nanoparticles uniform in size with a diameter of 8-120 nm by chemical reduction of gold ions with various reducing agents: sodium citrate or borohydride, ascorbic and isoascorbic acids, EDTA, an alkaline solution of hydrogen peroxide, potassium thiocyanate, etc. The rate of NP formation depends on the concentration of reagents and the chemical nature of the reductant, and the NP size depends on the nucleation rate and condensation rate. The use of microorganisms, plant, animal and human cells for the synthesis of Au NPs has become a new direction in biotechnology. Plants contain biologically active substances, such as flavonoids, polyphenols, organic acids, terpenes, alkaloids, reductases, which act as reducing agents and as stabilizing and insulating agents. Au NPs synthesized using “green” chemistry have various sizes and shapes: spheres, rods, cubes, triangles.

In biomedicine, modern methods are being developed for introducing gold nanocapsules into the tumor tissue, followed by heating them with IR rays, as a result of which cancer cells die and healthy ones are not damaged.

Of great importance for biomedicine are the developed methods for the synthesis of gold NPs, as well as the simplicity and reliability of methods for modifying their surface by attaching oligonucleotides, peptides, polyethylene glycol and other biologically active components to them. Modified Au NPs circulate longer in the bloodstream and are less affected by cellular components of the immune system. Today it is generally accepted that gold NP conjugates are excellent labels for diagnosing cancer, Alzheimer's, AIDS, hepatitis, tuberculosis, diabetes mellitus and other diseases.