SYNTHESIS, BIOFUNCTIONALIZATION AND APPLICATION OF GOLD NANOPARTICLES

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ABSTRACT. Gold nanoparticles (AuNPs) have specific chemical and physical properties, which make them suitable drug carriers and allow them to be used in various fields of biology, medicine, pharmacy and environment monitoring. In the last 30 years, with the rapid development of nanotechnologies, scientists have found an increasing number of applications of AuNPs and improved methods for their synthesis and characterization. The mechanisms of their formation and growth, as well as in their biofunctionalization, for example with proteins, are of increasing interest, which allows the study of various enzyme-catalytic processes.

Key words: gold nanoparticles, biofunctionalization, sensors

СИНТЕЗ, БИОФУНКЦИОНАЛИЗИРАНЕ И ПРИЛОЖЕНИЕ НА ЗЛАТНИ НАНОЧАСТИЦИ

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РЕЗЮМЕ. Златните наночастици имат специфични химични и физични свойства, които ги правят подходящи лекарствени носители и позволяват да бъдат използвани в редица области на биологията, медицината фармацията и мониторинга на околната среда. През последните 30 години, с бързото развитие на нанотехнологиите, учените намират все по-голям брой приложения на златните наночастици и подобряват методите за тяхното получаване. Все по-голям интерес представляват и механизмите на тяхното формиране и растеж, както и в биофункционализирането им, например с протеини, което позволява изучаването на различни ензимо-каталитични процеси.

Ключови думи: златни наночастици, биофункционализиране, сензори

Introduction

Gold nanoparticles have peculiar chemical and physical properties, that make them appropriate drug carriers and allows them to be used in diverse fields of biology, medicine and pharmacy, environment protection.

Gold nanoparticles can be functionalized with a large number of organic or biological ligands for selective binding and serve to determine the presence and concentration of small molecules and biological objects (R. Pool, 1990). The color of gold nanoparticles is very sensitive to the degree of their aggregation in suspension (H. Li, L. Rothberg, J, 2004).

Methods for the synthesis of gold nanoparticles make it possible to obtain nanosized objects of different sizes, which is essential for their further use in various fields of chemistry, biology, pharmacy, medicine and environment monitoring and protection. For example, AuNPs can be used at detection of phenolic compounds, which is important because they have extremely hazardous impact and poor environmental degradation (Nusiba Mohammed Modawe Alshik Edrisab, Yusran Sulaiman, 2020).

The characterization of gold nanoparticles is an essential issue for a better understanding of their properties and nature. Among the most commonly used methods for their characterization are UV-vis spectroscopy, Transmission electron microscopy (TEM) and Atomic force microscopy (AFM). They allow us to monitor both their specific properties such as surface plasmon resonance and to obtain sufficient information about the size of individual particles, their shape and distribution. Due to the important relationship between particle size and their properties, methods for characterizing gold nanoparticles that have been synthesized are essential in conducting experiments with them.

The paper presents the most important and widely applied methods for AuNPs synthesis and analysis, as well and the AuNPs applications.

Historic preparation of AuNPs

Gold nanoparticles have been known to humans since antiquity. They were obtained probably in a purely empirical way and this can be confirmed by the found and preserved objects from different historical periods.

Among the most famous and well-preserved objects from antiquity is probably the cup of a Lycurgus. It is an exquisite object of Roman art, which was made around the 4th century AD. During its manufacture in the glass small amounts of gold and silver nanoparticles were dispersed in a certain proportion, which created an interesting optical effect - if through the glass no light passes, the cup is green, but when a ray of light passes through it, it turns red.

The first scientifically documented production of colloidal gold belonged to the English physicist M. Faraday. In 1857 he conducted a series of experiments based on the use of gold hydrosols, which were prepared by reducing aqueous solutions of chloroauric acid ($HAuCl_4$) with phosphorus dissolved in carbon disulfide (M. Faraday, 1857).

A large number of methods for the synthesis of colloidal gold have been developed - the Turkevich method, the Brust method, the Navarro method, etc., each of which allows to obtain particles with different stability. These methods can be conditionally - according to the time in which they were created, divided into classical and new (modern).

Turkevich created one of the most famous syntheses of gold nanoparticles. His method is based on citrate reduction of carbon tetrachloric acid in an aqueous medium (J. Turkevich et al., 1951). Citrate anions have both the role of reducing and stabilizing agent. This type of colloidal gold production was first developed by Hauser and Lynn and later modified by Turkevich (Hauser and Lynn, 1940). Figure 1 shows a scheme of citrate synthesis.

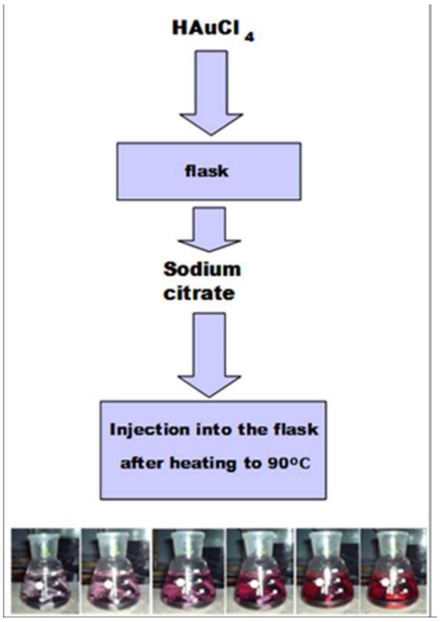

Fig. 1 Scheme of Au nanoparticle synthesis by the citrate method.

The Turkievich method is a relatively simple synthesis in which 10 ml of a $HAuCl_4$ solution containing 5 mg of Au is carefully added to 85 ml of boiling distilled water (100 ° C). When the mixture is refluxed, 5 ml of 1% sodium citrate solution are added. The reaction mixture was stirred continuously with a magnetic stirrer. The synthesis is completed after about 30 min. It produces spherical nanoparticles of gold that have an average diameter of about 20 nm.

Nowadays preparation of AuNPs

Due to the scientific interest in obtaining gold nanoparticles, the methods for their synthesis are numerous. These methods can differ both in the synthesis procedure itself and in the average size of the obtained gold nanoparticles, as well as in the possibilities of the method itself to obtain particles similar in size and shape in their entire volume. Many ideas for the synthesis of gold nanoparticles can be mentioned, and to illustrate the basic principles by which such suspensions are obtained, we can consider the following procedures:

Golden sol of Faraday

This method is based on the interaction between a solution of $HAuCl_4$, a saturated solution of white phosphorus in diethyl ether and a solution of KOH. The color of the solution changes, first to brown, then gray, purple and red. In this synthesis, the average diameter of the nanoparticles is 5 nm.(J. Perez-Juste et al, 2005).

Donau golden sol

This synthesis consists in passing gaseous CO_2 through a solution of $HAuCl_4$. The solution turns purple. The diameter of the nanoparticles is about 20 nm.(J. Perez-Juste et al, 2005, 2005).

Acetylene gold sol

In this method, a solution of $HAuCl_4$ is treated with an aqueous solution of acetylene. A pink color appears in about 20 seconds, and in 2 minutes the solution turns dark red. The diameter of the nanoparticles is about 29 nm.(J. Perez-Juste et al, 2005)

Golden sol with citric acid.

This approach consists of preparing a $HAuCl_4$ solution and then heating it to boiling. A solution of citric acid is added to it, a dark blue to red color is observed. The diameter of the nanoparticles is about 50 nm.

The fungal gold nanoparticles synthesis

An excellent example of eco-friendly synthesis of gold nanoparticles is the fungal gold nanoparticles synthesis. Its essence is that AuNPs with 20 nm diameter were synthesized on the fungal surface and the cytoplasmic membrane of the fungal mycelium (Kalishwaralal Kalimuthu et al., 2020).

Marine alga synthesis

In this approach, the synthesis is carried out by algal cells with absorption at around 540 nm.The average size of gold nanoparticles is about 15 nm (Kalishwaralal Kalimuthu et al., 2020).

Bacteria synthesis

It is known that just a few groups of bacteria can selectively reduce metal ions. In this approach it is observed intracellular synthesis of AuNPs. Different morphologies – cubic, hexagonal, and spherical – with particles size in the range in the range of 5–200 nm were reported by using sulfate-reducing bacteria (Kalishwaralal Kalimuthu et al., 2020).

These methods make it possible to obtain particles of different sizes, and in the volume of the solution these particles can be both relatively similar in shape and not so homogeneous. Due to the search for solutions that have the largest possible number of identical particles in their volume (size and shape), the synthesis methods that are chosen to prepare AuNPs used as sensors for enzyme activity or in the development of drug carriers should be able to a large extent to ensure the production of homogeneous particles. This provides a good opportunity to study different biological systems, as well as to create good physicochemical models to explain the behavior and formation of gold nanoparticles, their behavior on different boundary surfaces or in the bulk phase.

AuNPs application

The advantages of nanoparticles that distinguish them from bulk materials are mainly in their specific chemical and physical properties. For example, gold nanoparticles have a specific characteristic absorption maximum at 520 nm, which is due to their surface plasmon resonance, and this provides an excellent opportunity for them to be functionalized with proteins, such as antibodies, proteins attached to them, and the like. This facts are widely used in medicine as a therapeutic agent in targeted drug delivery systems.

The aggregation of Au nanoparticles with certain dimensions (d > 3.5 nm) is a result of the interaction between the surface plasmons of individual nanoparticles, as a result of which a change in their color from red to blue is observed (S. Srivastava et al., 2005). This color change of Au nanoparticles leads to their successful application as absorption-based colorimetric sensors for an analyte that causes aggregation of Au nanoparticles (R. R. Liu et al., 2007). This type of use of gold nanoparticles as sensors starts a new and distinct scientific field in which they can find opportunities for research and be used to solve various biological, analytical, biochemical and medical problems.

Gold nanoparticles are objects that can be functionalized with a wide range of organic or biological ligands for selective binding and serve to determine the presence and concentration of small molecules and biological objects. They can be used as drug carriers or in monitoring the catalytic activity of enzyme-catalytic chemical reactions.

The preparation of stable suspensions of protein-modified gold nanoparticles is a prerequisite for their use as an analytical procedure for colorimetric analysis. In recent years, colorimetric studies based on surface plasmon resonance of metal nanoparticles have received special attention due to their simplicity, sensitivity and low cost. Spherical gold nanoparticles are used to detect biomolecules on the principle of aggregation-induced red to blue color change. The ability of gold nanoparticles to retain biomolecules is a major advantage for their use as biosensors.

In recent decades, the development of medicine has been directly linked to the search for new chemical approaches for the diagnosis and treatment of various diseases. Attaching molecules of a particular protein to the surface of various nanostructured materials, as well as nanosized objects (quantum dots, nanoparticles, etc.) is an efficient way to improve their stability and a good opportunity to create particles for targeted delivery of drug carriers, as well as other functional properties. Therefore, biofunctionalized protein nanomaterials are widely used in modern pharmaceutical technologies for the transport of dosage forms, as well as for biocatalysis.

Nanoscale objects that are close to the dimension of biological units, as well as their easy synthesis, relatively large surface area and easy functionalization make them particularly interesting for achieving various biological goals, such as tissue engineering and regenerative medicine.

Gold nanoparticles can be used effectively for environmental monitoring. Gold nanoparticles- Biphenyl-4,4'-dithiol and AuNPs- p-Terphenyl-4,4''-dithiol with size 6–8 nm were deposited onto quartz fibres and used as adsorbent materials for the detection of total gaseous mercury, both indoor for adsorption studies, at defined concentrations and outdoor, at the vapour mercury concentration of the environmental countryside (Andrea Bearzottia et al., 2018).

Conclusion

Gold nanoparticles have been known to humans since ancient times and their specific properties have attracted their attention. With the development of chemistry, various methods for their synthesis gradually began to appear, and in the last three decades their study has become an increasingly interesting issue for science. This is due to their properties, which make them excellent drug carriers, allow them to be used in the diagnosis of various diseases, as well as various other applications in the natural sciences and the environment protection. Their biofunctionalization is an important step for the implementation of these tasks and is carried out by covering the surface of gold nanoparticles with various proteins.

This makes gold nanoparticles an increasingly evolving field of research that will be increasingly used mainly in pharmacy and medicine, but also in biology and the environmental monitoring.

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