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SYNTHESIS OF NANOCOMPOSITE MATERIALS BY SOL–GEL TECHNOLOGY AND THEIR SIGNIFICANCE IN MEDICINE

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Abstract: This article analyzes the theoretical and practical foundations of nanocomposite material synthesis by sol–gel technology and examines the prospects for using such materials in modern medicine. The concepts of nanotechnology and nanocomposite materials, in particular nano-scale biomaterials (nanobiomaterials), and their roles in drug delivery systems, tissue engineering, regenerative medicine and medical imaging are discussed in detail. The stages of the sol–gel process, mechanisms of stable incorporation of metal-oxide nanoparticles into oxide matrices, and the key parameters that allow control of particle size and morphology (pH, temperature, water-to-precursor ratio R, type of catalyst) are explained from a methodological point of view. Based on the analysis, it is substantiated that nanocomposites obtained via sol–gel processing has high scientific and practical potential as drug-carrier platforms, bioactive coatings, bone implants and diagnostic probes. The work provides a comparative review of research conducted by CIS and international scientific schools and presents a systematic discussion of the scientific and technological approaches required for introducing sol–gel nanocomposites into medical practice.

Keywords: sol–gel technology, nanocomposite materials, nanobiomaterials, drug delivery systems, nanoporous materials, metal–organic frameworks (MOF), bioactive coatings, regenerative medicine.

Introduction. Nanotechnology is one of the most rapidly developing areas of modern science and engineering and is based on the creation, investigation and control of structures in the size range of approximately 1–100 nm. This field emerged as a result of deep integration of physics, chemistry, biology, medicine and materials science and makes it possible to implement in practice new effects and properties that arise at the nanoscale level [3, 11, 12].

The use of nanotechnology in medicine has opened a qualitatively new stage in such areas as targeted drug delivery, early diagnostics, regenerative medicine, tissue engineering, imaging systems and the development of “smart” implants [3, 19]. Liposomes, dendrimers, polymer nanocapsules, metal and metal-oxide nanoparticles, as well as nanoporous and hybrid frameworks, make it possible to deliver drugs and biomolecules to a specific target — a pathological focus or damaged tissue — and to control their dosage and release kinetics [11, 12, 18].

Nanocomposite materials are multicomponent systems in which different phases (for example, organic–inorganic, metal–oxide, polymer–ceramic) are combined at the nanoscale. Such systems are distinguished by the fact that their properties are not just the sum of the properties of the individual components, but are determined by synergistic effects, leading to fundamentally new functional characteristics [6, 7]. Sol–gel technology is recognized as one of the most suitable and controllable methods for synthesizing oxide nanocomposites, in particular for obtaining hybrid organic–inorganic materials and functional oxide coatings [4, 5, 8, 9].

In this article, the scientific bases of obtaining nanocomposite materials by sol–gel technology, their importance as nanobiomaterials in medicine, and the conceptual and methodological approaches developed in the works of CIS and international researchers are considered and analyzed [1–3, 14–16, 19–21].

Main part. The concept of nanocomposite materials implies the coexistence of two or more phases with a nano-scale structure that are harmoniously combined with each other. The most important nanocomposites for medical applications include hybrid systems based on oxide matrices (for example, SiO_2, ZrO_2, TiO_2), polymer–ceramic composites, bioactive glass–hydroxyapatite mixtures, metal–organic frameworks (MOFs) and their combinations with biomolecules [1, 2, 13, 20]. These structures, due to their high specific surface area, controllable porosity, chemical tunability and bioactivity, occupy a special place in medical practice [3, 18, 21].

Nanobiomaterials are characterized by nanoscale structure, high reactivity and the ability to interact selectively with the biological environment. They can be used as nanoscale drug-delivery systems, coatings for modifying implant surfaces, scaffolds for tissue engineering and contrast agents for imaging [11, 12, 19]. In particular, nanoporous glass- and ceramic-based composites represent convenient platforms for drug loading and controlled release [1, 2, 13, 20].

In drug delivery systems, nanocomposite carriers make it possible to direct therapeutic molecules exclusively to diseased tissues, prolong their circulation time in the body, reduce toxicity and significantly decrease adverse side effects [11, 12, 18]. In oncology, nanoscale carriers deliver chemotherapeutic agents selectively to tumor tissue, thereby maximizing the preservation of healthy cells. Thus, nanocomposite systems play an important role in the implementation of the concept of targeted therapy [11, 12, 19, 21].

Sol–gel technology is a flexible method that allows one to design nanocomposites according to these requirements. By changing the process parameters, it becomes possible to finely control particle size, degree of porosity, surface functional groups and the distribution of the metal-oxide phase [4–6, 8–10].

Methodology. The present article is analytical and theoretical in nature and was developed on the basis of the following methodological approaches:

– systematic analysis of research, monographs and review articles by international and CIS scholars in the fields of nanotechnology and nanobiomaterials [3–7, 11–13, 19];

– comparative study of the chemical and physical foundations of the sol–gel process and fundamental sources on the synthesis of metal-oxide nanocomposites [8, 9, 10, 14–16, 20];

– analysis of experimental results related to the use of nanocomposite materials in drug delivery, tissue engineering, implantology and imaging in medicine [1–3, 11, 12, 18, 21];

– identification of challenges and limitations in the introduction of sol–gel-based nanocomposites into medical practice and conceptual generalization of promising directions [13, 15, 16, 19–21].

In the analysis, the results of studies by Baxriyev and Rakhmonov devoted to the synthesis of SiO_2–SnO_x–CuO_γ hybrid nanocomposites by sol–gel technology and in-depth investigation of their physicochemical properties were partially used as a methodological basis [1]. The works of Nasimov, Mirzayev and co-authors on nanomaterials based on semiconductor metal oxides immobilized with organic dyes were also examined [2]. To assess the role of nanotechnology in medicine, the review papers of Eshkaraev and Pulatova [3], as well as review contributions by CIS scientists such as Zubkova, Silakov, Zharasova and others, were used [3, 19].

Analysis.

Sol–gel process and formation of nanocomposite structures

The sol–gel process usually starts from a solution of metal alkoxides or inorganic salts in a liquid phase. As a result of hydrolysis and polycondensation reactions, a connected oxide network is formed. Initially, a molecularly homogeneous solution is converted into a colloidal sol, and then the particles link together to form a macroscopic gel structure [4, 5, 6, 9].

The process includes the following stages: preparation of the precursor solution; hydrolysis; condensation and sol formation; gelation; drying of the gel and, if necessary, thermal treatment. At each stage, parameters such as pH, temperature, water-to-alkoxide molar ratio ($R = H_2O/Si$ or H_2O/M), nature and concentration of the catalyst and type of solvent can be optimized depending on the desired structure and properties [4–6, 8–10, 14].

The pH value is a central parameter in sol–gel systems; it determines the rate of hydrolysis and condensation, particle size, degree of branching and the formation of the porous structure. Very low pH values can lead to rapid condensation, increased internal stresses and loss of structural homogeneity. Conversely, relatively high pH slows down hydrolysis, delays the transition to the gel state and reduces the stability of the sol [5, 6, 9, 15]. Therefore, a narrow optimal pH range is selected to obtain high-quality nanocomposite materials.

Metal-oxide nanoparticles can be introduced into the sol–gel system using two main approaches: addition of the precursor to the initial solution (in situ formation) or mixing of pre-synthesized nanoparticles into the sol [1, 2, 8, 20]. In the first approach, the metal-oxide phase is more deeply integrated into the gel matrix; in the second, the dominant role is played by bonding through functional groups on the particle surface. In both cases, to maintain dispersity and limit aggregation, it is necessary to choose an appropriate stirring regime, stabilizers and limited concentrations [1, 2, 13, 20].

Nanobiomaterials and sol–gel nanocomposites

When nanobiomaterials are used in medicine, not only mechanical or chemical stability is important, but also biocompatibility, toxicological safety, harmlessness of degradation products and absence of undesired immune responses [3, 11, 21]. Silicate-based materials obtained by sol–gel processing (bioactive glasses, silica–hydroxyapatite composites, nanoporous scaffolds) have been shown in many studies to integrate well with bone tissue and exhibit osteogenic activity [13, 20].

From the viewpoint of drug delivery systems, sol–gel nanocomposites provide the possibility of loading drug molecules via adsorption or covalent binding, due to their nanoporous structure and tunable surface functional groups. Furthermore, they make it possible to organize stimuli-sensitive release of drugs, for example in response to changes in pH, temperature or composition of the biological medium [1–3, 11, 18]. Metal–organic frameworks (MOFs) and silica-based nanoporous materials are considered particularly promising systems for such purposes [13, 18, 21].

In tissue engineering, three-dimensional porous scaffolds prepared by sol–gel methods create a favorable microenvironment for cell adhesion, proliferation and differentiation.

Composite scaffolds based on hydroxyapatite, silica and polymer components have been successfully tested in the regeneration of bone and cartilage tissues. In this regard, the works of CIS scientists on the study of sorption, mechanical and bioactive properties of hydroxyapatite-based compositions prepared by sol–gel methods deserve special attention [20].

Results.

On the basis of the above analysis, the following conceptual results can be highlighted:

1. Sol–gel technology is a highly flexible and controllable method for synthesizing nanocomposite materials, especially oxide and hybrid organic–inorganic systems. By varying process parameters, it is possible to finely tune nanoscale structure and porosity [4–10, 14–16].

2. Nanoporous silica, bioactive glass and metal-oxide nanocomposites obtained by sol–gel processing has high potential for use as drug-carrier platforms, coatings for implant surfaces, scaffolds for bone tissue and diagnostic probes [1–3, 11–13, 20].

3. In drug-delivery systems, nanocomposite carriers ensure targeted release of therapeutic agents, reduce the total dose and systemic adverse effects of drugs and significantly increase the efficiency of treatment. These aspects are widely covered both in international literature and in the works of CIS researchers [3, 11, 12, 18, 19, 21].

4. CIS scientists have conducted a number of studies on the creation of micro- and nanocomposites, sensor materials, bioactive compositions and medically oriented nanostructures based on sol–gel technology. These studies form an important scientific platform for the development of nanobiomedicine in Uzbekistan and the region as a whole [3, 8, 9, 19–21].

5. For the wide application of sol–gel nanocomposites in medicine, it is necessary to continue detailed comprehensive research on their toxicological properties, long-term biostability, biodegradation mechanisms, pathways of elimination from the body and possible immunological responses [11, 12, 18, 21].

Conclusion. In improving the quality of medical treatment, early and accurate diagnosis, rehabilitation and prevention, nanomaterials — in particular nanocomposites created using sol–gel technology — play an increasingly important role. In this article, based on the concepts of nanotechnology and nanobiomaterials, the medical significance of sol–gel nanocomposites has been analyzed from a scientific and theoretical standpoint.

The analysis shows that sol–gel technology makes it possible to obtain multifunctional nanocomposite materials with controllable porosity, biocompatibility and, when required, bioactivity. Such materials are regarded as promising platforms for drug-delivery systems, tissue engineering, implantology and medical imaging.

For the broad introduction of sol–gel nanocomposites into clinical practice, it is advisable to deepen research in the following directions: toxicology and safety of nanoparticles, long-term in vivo monitoring, creation of “smart” (stimuli-responsive) drug carriers, development of raw materials and technologies adapted to local conditions and resolution of issues related to standardization and regulation.

Thus, the synthesis of nanocomposite materials by sol–gel technology and their application in medicine is becoming one of the key scientific and technological directions for the development of nanobiomedicine in Uzbekistan and throughout the CIS region.

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