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Approaches to the Stabilization of Titanium-Containing Nanopowder for Biomedical Research

Demetska O* and Beliuha O

Kundiiev Institute of Occupational Health of National Academy of Medical Sciences of Ukraine, Ukraine

***Corresponding author:** Oleksandra Demetska, Kundiiev Institute of Occupational Health of National Academy of Medical Sciences of Ukraine, St. Saksagansky 75, Kyiv, Ukraine, Tel: +380506378108; Email: dalexandra@ukr.net

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Abstract

The paper is devoted to the stabilization of nanopowders for use in biomedical research. Conducting biomedical research on nanopowders has a lot of obstacles and complications related to the aggregate state of matter: a significant number of new materials are presented in the form of nanopowders, which actualizes the issue of obtaining stable hydrosols of nanopowders for experimental studies *in vitro* and *in vivo* and the choice of stabilizers that do not affect on the toxicity and biological properties of the starting material. The dispersibility of hydrosols of nanopowders of titanium-containing nanomaterials (TiO_2, TiO_2-Ag (4%) in various environments was analyzed and the feasibility of using certain stabilizers for a series of screening scientific studies was substantiated.

Keywords: Titanium-Containing Nanopowders; Stabilization; Dispersion; Biomedical Research

Introduction

The toxicological behavior of nanomaterials in direct contact with cells depends on their chemical composition, concentrations, solubility, shape, area and charge. Effects may depend on how long the nanoparticles remain intact and how they can accumulate in the biosystem. Impurities formed during the production of nanomaterials also can affect their toxicity [1].

At the same time, as at the beginning of the development of nanotechnology, the development and introduction of new materials is significantly ahead of biomedical research on the potential dangerous effects of nanomaterials on living organisms and environmental objects. In turn, conducting these studies has a number of obstacles and complications related to the aggregate state of the substance: a significant number of new materials are presented in the form of nanopowders, which actualizes the issue of obtaining stable hydrosols of nanopowders for experimental studies *in vitro* methods and the choice of stabilizers that do not affect on the toxicity and biological properties of the starting material.

The toxicity of the composition is determined not only by the toxicity of the active substance (for example, metal nanoparticles), but also by stabilizing or other auxiliary components that can affect the biological activity of the resulting solution, as well as cause an increase in its toxicity. In particular, a method of stabilizing silver nanoparticles with sodium citrate is known, the disadvantage of which is a wide size distribution of the obtained nanoparticles, low stability during storage, as well as contamination of the final sol with citrate anion oxidation products, in particular, acetone dicarboxylic and itaconic acids [2]. There is also a known method of stabilizing nanocrystalline cerium dioxide with citric and polyacrylic acid, which are added directly during synthesis and are adsorbed on the surface of cerium dioxide nanoparticles and prevent their agglomeration during the

synthesis process [3]. The disadvantage of this method is its complexity and time-consuming nature.

As is known, applications of nanostructured titanium dioxide (TiO_2) can now be found in a wide range of fields, including electronic materials, energy, environment, medicine, catalysts, etc. [4,5]. Usually, titanium-containing nanomaterials are presented in the form of nanopowders, which actualizes the issue of converting them into stable hydrosols for in vitro and in vivo studies and, accordingly, the search for an adequate stabilizer. To stabilize nanomaterials in solutions, organic and inorganic compounds are used to obtain colloidal solutions of varying degrees of stability (polythiocyanohydroquinone, low molecular weight polyvinylpyrrolidone, human serum albumin, polysaccharides, sodium citrate, etc.) [6].

Therefore, the aim of the work was to analyze the dispersibility of hydrosols of nanopowders of doped titanium-containing nanomaterials in various environments and to justify the feasibility of certain stabilizers for a series of screening studies of potential in vitro hazards.

Materials and Methods

The dispersion of the silver-doped titanium dioxide complex (TiO_2-Ag nanocomposite, mass fraction of Ag~4%) and titanium dioxide nanopowder (TiO_2) synthesized by the thermal decomposition method in various media/stabilizers was evaluated. The size of the particles was determined by the method of dynamic light scattering using the Analysette 12 DynaSizer device (Fritsch, Germany).

Results and Discussion

The possibility of using nanoparticles of polyhydroxyl compounds (primarily carbohydrates) as a stabilizer has been revealed [7,8]. Glucose-citrate buffer (glucose (4 g), sodium citrate (1 g) in 100 ml of distilled water) is used in an express method for determining the toxicity of nanomaterials in vitro solutions using bovine spermatozoa as a test object for thawing sperm, and also as a control solution. Therefore, under the conditions of using bovine spermatozoa as a test object, stabilization of metal nanopowders with a glucose-citrate buffer (4:1 ratio of glucose and sodium citrate) is the optimal solution, as it allows obtaining stable hydrosols (Table 1).

Stabilizer/medium	Time, hours	Hydrodynamic diameter, nm
Glucose-citrate buffer (glucose : sodium citrate: 4:1)	1	48,65
Glucose-citrate buffer (glucose : sodium citrate: 4:1)	24	53,37
Glucose-citrate buffer (glucose : sodium citrate: 4:1)	48	52,12
Glucose-citrate buffer (glucose : sodium citrate: 4:4)	1	134,93
Glucose-citrate buffer (glucose : sodium citrate: 4:4)	24	195,04
Glucose-citrate buffer (glucose : sodium citrate: 4:4)	48	234,49

Table 1: Dispersion of TiO_2-Ag(4%) nanocomposite in glucose-citrate buffer over time.

On the other hand, for studies of antibacterial activity and phytotoxicity, bovine spermatozoa cannot be used as a test object. Also, it will obviously be impractical to use glucose-citrate buffer as a stabilizer, which is a favorable environment for spermatozoa, but not for microorganisms and plants.

Studies of the dispersion of titanium-containing nanomaterials have shown that the size of particles can vary significantly in different stabilizers (Table 2; Figures 1 & 2).

Nanomaterial	Stabilizer	Concentration of nanomaterial, % wt.	Hydrodynamic diameter, nm
TiO_2	Glucose-citrate buffer (5%)	0,3	46,84
TiO_2	Sodium citrate (0.38%)	0,3	35,3
TiO_2	Polysucrose 400 (5%)	0,3	128,86
TiO_2 -Ag(4%)	Glucose-citrate buffer (5%)	0,3	43,9
TiO_2 -Ag(4%)	Physiological solution (0.9%)	0,25	41,01
TiO_2 -Ag(4%)	Physiological solution (0.9%)	0,5	48,32
TiO_2 -Ag(4%)	Polysucrose 400 (5%)	0,3	328,8

Table 2: Dispersion of titanium-containing nanomaterials in various stabilizers.

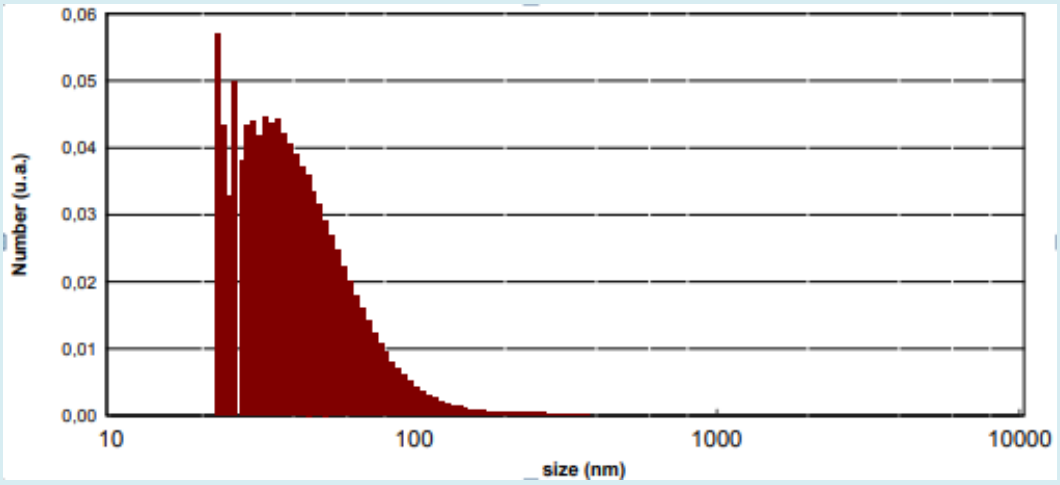

Figure 1: Distribution of TiO_2-Ag(4%) particles by size in glucose-citrate buffer (4:1).

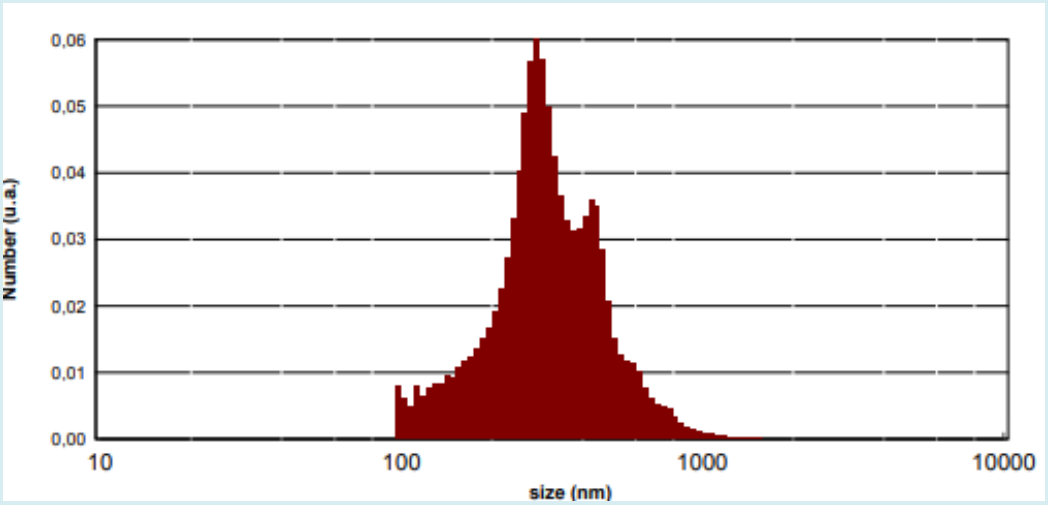

Figure 2: Distribution of TiO_2-Ag (4%) particles by size in Polysucrose 400.

The obtained results must be taken into account when planning and conducting biomedical research using certain test objects and model systems.

Conclusions

Stabilization of titanium-containing nanopowders with a glucose-citrate buffer makes it possible to obtain relatively stable hydrosols that can be used in screening studies using bovine spermatozoa as a test object. For studies of phyto- and antibacterial toxicity of nanomaterials, it is advisable to use nanopowders in physiological solution, which can be applied during the first day. The use of a sterile solution of Polysucrose 400 as a stabilizer of powdered titanium-containing nanomaterials is impractical due to rapid agglomeration of nanoparticles.

Conducting further research on acceptable stabilization of nanopowders is necessary.

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