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Manganese-doped Mesoporous Silica Nanopowder for Pharmaceutical Applications

Zlygosteva O. A.[1], Sokovnin S. Yu.[1,2], and Il'ves V. G.[2]

[1]Ural Federal University Named after the First President of Russia B. N. Yeltsin (UrFU), 19 Mira, Yekaterinburg, Russia
[2]Institute of Electrophysics, Ural Branch of the Russian Academy of Sciences (RAS), 106 Amundsen, Yekaterinburg, Russia

Abstract

The purpose of the research was to produce and analyze properties of manganese-doped mesoporous silica nanopowder (NP) for biomedical applications. SiO_2-MnO_2 NP were produced by pulsed electron evaporation demonstrated high porosity amorphous structure, magnetic properties increased with addition of dopant. The toxicity experiments on cells showed that SiO_2-MnO_2 NP exerted low toxicity. Loading experiments showed qualitative interaction of antibiotic "Amoxicillin" with NP surface. According to obtained properties, produced SiO_2-MnO_2mesoporous NP is potential material for creating targeted drug delivering system.

Keywords: mesoporous silica nanopowder, doped with manganese dioxide, targeted drug delivery.

Corresponding Author:
Zlygosteva O.A.
zlygosteva13@mail.ru

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1. Introduction

The modern trends in the development of biomedical sphere can be characterized by a transition to the nano world. Nanopowders (NP), due to their sizes commensurate with tissue and cellular structures, are already used in diagnostics as a contrast agent for signal enhancement in MRI, in therapy as an agent for hyperthermia, in tissue engineering and prosthetics, as well as in pharmaceuticals. One of the developing modern fields of NP applications is targeted drug delivery in human body [1, 2].

Promising material for the creation of the delivery system is SiO_2-MnO_2mesoporous NP. Silica is a natural compound used in food and cosmetic industry, dopant manganese dioxide can be used for signal enhancement in MRI [3], making the system possible to visualize.

The advantages of such systems include targeting the specific locations in the organism and reduction of drug concentration at nontarget locations to minimize severe side effects [4].

2. Materials and methods

SiO_2-MnO_2 mesoporous NP with different dopant mass concentration prepared by means of evaporation by a pulsed electron beam in low-pressure gas (4 Pa) on NANOBIM-2 installation [5]. The target was made of silica NP (Aerosil 90) and manganese dioxide powder (GOST 4470-79). NP was deposited on large-surface glass noncooled substrates in the powder collection chamber to prevent the crystallizer material from being absorbed into the NP.

Analysis of produced NP properties were carried out using following analytical methods: X-ray diffraction (XRD) was made on XRD 7000 diffractometer, Brunauer-Emmett-Teller (BET) method was used to define the specific surface area (Sssa) and porosity on Micromeritics TriStar 3000 installation, magnetic characteristics were measured on Cryogenic CFS-9T-CVTI vibration magnetometer.

In vitro cytotoxicity was carried out on the primary culture of human dermal fibroblasts using a cytometer. Drug loading experiments was conducted using spectrophotometry method.

3. Results and discussion

According to BET analysis, produced SiO_2-MnO_2 NP are highly porous with high pore volume (Table 1). The Sssa has risen with increasing of dopant concentration. The interaction of drug and NP during encapsulation is superficial. The porosity and Sssa determine the loading capacity of NP [4], so for toxicity and loading experiments SiO_2-3%MnO_2 NP was chosen as this sample has the highest values of defining parameters.

Table 1: BET-BJH-analysis of SiO_2-MnO_2 NP.

Dopant concentration, %	Pore size, nm	Sssa, m^2/g	Pore volume, cm^3/g
0,1	20,6	75,78	0,36
3	26,4	134,18	0,88
5	20,8	176,35	0,52

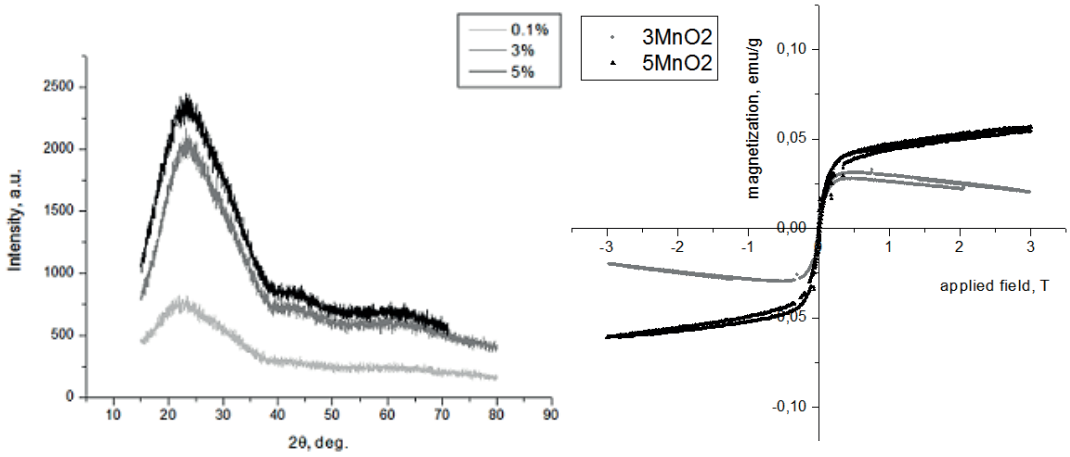
The XRD analysis demonstrated that produced SiO_2-MnO_2 mesoporous NP are completely amorphous (no Bragg peaks) (Figure 1a).

The requirements for potential drug delivery systems include both loading a large volume of drug and effectively targeting the locations in the organism. This possibility

exists using magnetic NP. By means of magnetic measurements, it is established that SiO_2 – MnO_2 mesoporous NP showed ferromagnetic behavior (Figure 1b). The increasing of ferromagnetic response, which could be caused by structural defectiveness, was observed with the increasing of manganese dioxide dopant concentration. Due to the magnetic properties of SiO_2-MnO_2 NP, using an exogenous stimulus (external high-gradient magnetic field) is the possible way of drug delivering [6].

The additional requirement for drug delivery system is an absence of cytotoxic effect. Therefore, primary cytotoxicity experiments were conducted using a cytometer [7]. The calculated cytotoxicity index of SiO_2-3%MnO_2 NP suspensions was 40% (36% control), so it can be concluded that the cytotoxic effect of suspensions on the cell culture is low, even at high concentration (500 μg / ml) of SiO_2-3% MnO_2 NP.

The qualitative analysis of sonicated NP suspensions with the addition of drug using a spectrophotometer showed that optical density of suspensions with drug "Amoxicillin" has increased by 15% in comparison with increasing by 200% of pure solution of drug. Less increasing could be associated with better drug surface interaction or with drug encapsulation into the pores. The sedimentation stability of suspensions sonicated after the adding of drug has increased due to the surfactant property of drug [8].



a b

Figure 1: XRD patterns of SiO_2-MnO_2 NP (a), magnetization curve of SiO_2-MnO_2 NP in magnetic field ± 3 T (b).

4. Conclusions

To sum up, SiO_2-MnO_2 amorphous mesoporous NP, produced by means of evaporation by a pulsed electron beam, has high porosity determining the loading capacity. NP has magnetic properties for effective delivery by magnetic field.

Due to the presence of manganese as a contrast agent for signal enhancement in MRI produced system could be visualized during the delivery process.

Basic toxicity experiments in vitro showed that SiO_2-MnO_2 NP exerted low toxicity. The qualitative loading experiment of anti-inflammatory drug "Amoxicillin" into NP pores showed the encapsulation and drug interaction with the surface of NP.

Thus, produced SiO_2-MnO_2 mesoporous NP is a perspective material for pharmaceutical applications especially for the developing targeted drug delivery systems.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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