Influence of α-Bi_2O_3 chemical prehistory on the morphology of the obtaining basic bismuth succinate

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Abstract. The antibacterial drug, basic bismuth succinate of the composition $Ñ_2Í_4(ÑÎÎBiO)_2$ is shown to obtain expediently by the interaction of bismuth oxide α-Bi_2O_3 with a succinic acid solution. Using the method of electron microscopy the influence of the chemical prehistory of obtaining the precursor, monoclinic modification of α-Bi_2O_3, on the morphological features of basic bismuth succinate synthesized from it has been investigated. The composition of $Ñ_2Í_4(ÑÎÎBiO)_2$ was confirmed by the data of X-ray phase and chemical analyses. Based on the data of grain size analysis, the particle size of the obtained samples of basic bismuth succinate was estimated and the conditions for the synthesis of fine-crystalline $C_2H_4(COOBiO)_2$, which is necessary for medical applications, were selected.

1 Introduction

Succinic (amber) acid HCOO-CH_2-CH_2-COOH and its salts succinates are widely used in medicine [1]. The basic bismuth salt of succinic acid, $C_2H_4(COOBiO)_2$, is a medicinal substance of the drugs Biquinol (Merck, Germany) and Pholcones (Cooper, France) which are used to treat angina, laryngitis and pharyngitis. In addition, it is considered promising for the treatment of infections caused by *Helicobacter pylori*, *Mycobacterium tuberculosis* and *Treponema pallidum*. In Russia this substance is not registered and we have not found any literature data on the methods of obtaining and studying the physical and chemical properties of the main bismuth succinate. As a consequence, the development of environmentally safe ways of obtaining this compound with the possibility of further practical use acquires relevant.

Bismuth compounds for engineering and medicine are usually obtained by precipitation from nitric acid solutions, while the problem of purifying bismuth salts from impurity metals has been solved [2]. However, precipitation products are easily contaminated by nitrate ions, the content of which in bismuth compounds for medicine should not exceed

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0.4%, as in the gastrointestinal tract they transform into nitrites, which have a carcinogenic effect. In this connection, it is of practical interest to develop a method for obtaining basic bismuth succinate in the absence of nitrate ions by the reaction of interaction of bismuth oxide with succinic acid solution.

In the present work the influence of the chemical prehistory of α-Bi_2O_3 on the morphological features of drug substance $C_2H_4(COOBiO)_2$ obtained in the system "α-Bi_2O_3 - succinic acid solution" is discussed in detail with the help of electron microscopy and grain size analysis in order to select the synthesis conditions of fine crystalline basic bismuth(III) succinate required for medical applications.

2 Experimental

All reagents in this work were of analytical grade and were used without further purification. Bismuth stock solution in nitric acid (450 $g \cdot l^{-1}$ Bi) was prepared from metallic bismuth grade Vi0 according to [3].

The conditions for obtaining bismuth oxide α-Bi_2O_3 samples of monoclinic modification with different chemical prehistory and residual content of nitrate ions in wt. % are presented in Table 1.

Table 1. Conditions for obtaining α-Bi_2O_3 samples with different chemical prehistory.

Sample	α-Bi_2O_3, chemical prehistory	Residual content of NO_3^- (wt. %)
1	oxidative thermolysis $[Bi_6O_4(OH)_4](NO_3)_6 \cdot H_2O$, 4 ч при 600°C	0.5
2	oxidative thermolysis $[Bi_6O_5(OH)_3](NO_3)_5 \cdot 3H_2O$, 4 ч при 600°C	0.35
3	Treatment with 2 M NaOH solution $[Bi_6O_4(OH)_4](NO_3)_6 \cdot H_2O$ or $[Bi_6O_5(OH)_3](NO_3)_5 \cdot 3H_2O$	0.14
4	Bismuth stock solution in nitric acid, treatment with 2 M NaOH solution	0.04

Basic bismuth succinate of the composition $C_2H_4(COOBiO)_2$ was obtained by interaction of bismuth oxide α-Bi_2O_3 with a succinic acid solution at molar ratio of succinate ions to bismuth equal 1.0 and process temperature 70 °C. The residual content of nitrate ions in all samples of basic bismuth succinate does not exceed 0.02%.

The phase compositions of the samples were analyzed using X-ray diffraction technique (XRD) on diffractometer (Bruker D8 Advance, Germany) using Cu-Kα radiation. The chemical determination of macro amounts of Bi(III) in solutions was carried out by titration with complexon III solution in the presence of a xylenol orange indicator. Micro quantities of Bi(III) were determined photocolorimetrically with sodium iodide. The carbon and hydrogen content in the synthesized samples was determined by a modified Pregl method with gravimetric termination. Microstructure of the samples was studied by scanning electron microscopy (SEM) using Hitachi TM 1000 Scanning Electron Microscope. Grain size analysis of powders was carried out using a laser particle size analyzer Microsizer 201A (Ltd “VA Instalt”, Russia).

3 Discussion

According to the data of X-ray phase analysis (XRD) the diffractograms of all synthesis products are identical and do not contain diffraction maxima of the initial substances: α-

Bi_2O_3 and succinic acid. Data of chemical analysis confirm that the product has the composition $C_2H_4(COOBiO)_2$, the content (in wt. %): Bi - 72.9 (estimated 73.85); C - 8.30 (8.48); H - 0.65 (0.71).

The grain size analysis of basic bismuth succinate powders was carried out. The results are shown in Fig. 1.

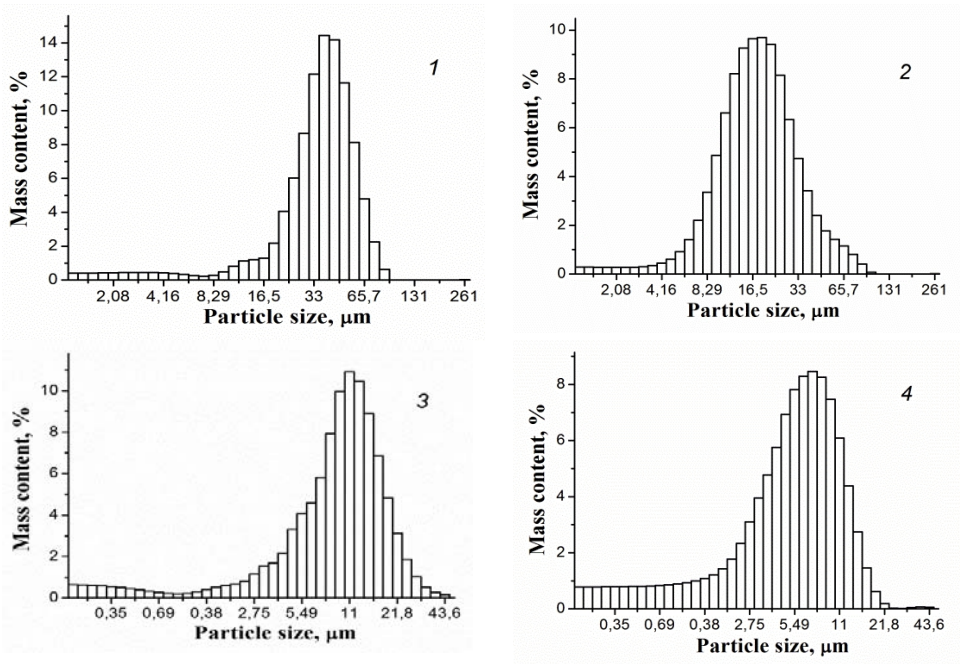

Fig. 1. Histograms of basic bismuth succinate samples synthesized from α-Bi_2O_3 samples (1-4), respectively.

According to the data of grain size analysis, the samples of basic bismuth succinate have the following average particle/aggregate size (D_{50}), μm: 40,2 (1); 18,9 (2); 10,8 (3) и 6,11 (4). Thus, the largest particle size corresponds to the basic succinate synthesized from α-Bi_2O_3 obtained by thermolysis of $[Bi_6O_4(OH)_4](NO_3)_6{\cdot}H_2O$, and the smallest - by the addition of a bismuth-containing nitric acid solution in sodium hydroxide solution.

Electron microscopy data also made it possible to trace a significant influence of the chemical prehistory of α-Bi_2O_3 precursor preparation on the morphology of synthesized bismuth succinate samples. The results of electron microscopy investigations of bismuth basic succinate powders are in good agreement with data of grain size analysis. Fig. 2 shows microphotographs of bismuth oxide samples (the most characteristic samples 1 and 4 were chosen), as well as samples of basic succinate obtained from them.

Sample 1 (Fig. 1a) obtained by thermal decomposition of compound $[Bi_6O_4(OH)_4](NO_3)_6{\cdot}H_2O$ well preserved the appearance and size of clusters of short prismatic crystals of initial compound and represents the melted prismatic aggregates with size in the basic plane 10-30 μm, and 10-20 μm in thickness. The particles of basic bismuth succinate obtained from it (Fig. 1b) also retain prismatic appearance of original crystals, slightly increasing in size due to formation on their surface spherical particles of the final product with size up to 6-8 μm. The treatment of bismuth stock solution in nitric acid with sodium hydroxide solution is accompanied by the formation of fine-crystalline bismuth oxide powder (sample 4), which are aggregated needle-like crystals up to 10 μm long and 1-1.5 μm thick (Fig. 1c). Sample 3 has a similar morphology. Their treatment with succinic

acid leads to the formation of aggregates of basic bismuth succinate from 5 to 20 μm in size, which consist of spherical formations of 1-3 μm, built of thin needle-like particles 1-2 μm long and 0.1-0.2 μm thick (Fig. 1d).

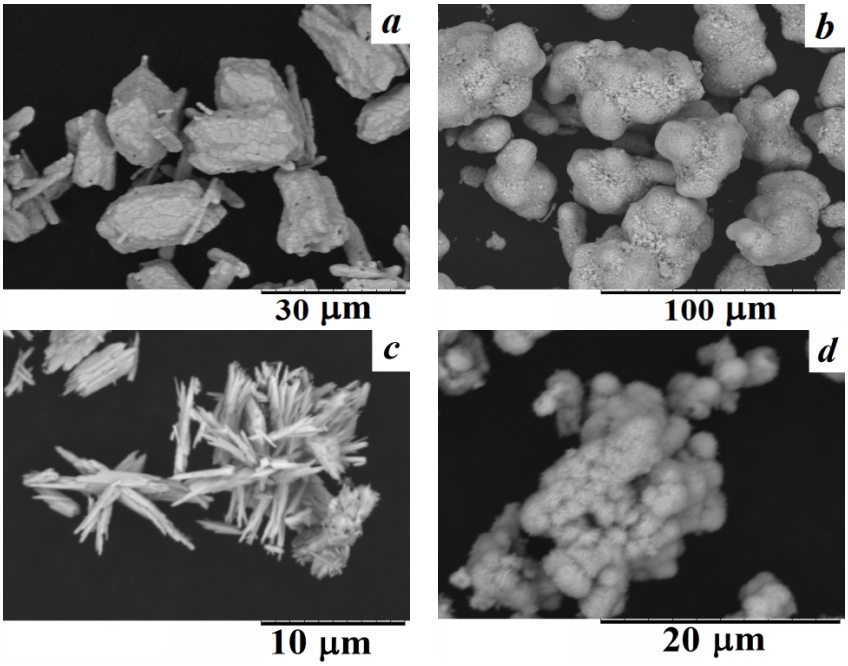

Fig. 2. Micrographs of α-Bi_2O_3 samples obtained by thermolysis of $[Bi_6O_4(OH)_4](NO_3)_6 \cdot H_2O$ (*a*) and after treatment of bismuth stock solution in nitric acid with 2 M NaOH solution (*c*), and samples of basic bismuth succinate synthesized from them (*b*, *d*).

Thus, the performed studies indicate that the morphology and particle size of bismuth basic succinate powders significantly depend on the chemical prehistory of the α-Bi_2O_3 precursor samples. It is shown that the fine crystalline powder of basic bismuth succinate can be synthesized from bismuth oxide precipitated from nitric acid solution by alkaline hydrolysis, as a result of its interaction with succinic acid solution. It is advisable to use the methods of electron microscopy and grain size analysis for morphological control of bismuth compounds used as medicinal substances.

The work is supported by Topical Plan of NSTU, project TP-HHT-1_21 and by State Assignment of ISSCM SB RAS, project 121032500064-8.

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