SYNTHESIS AND INVESTIGATION OF AGAR-AGAR GELS FILLED BY HALLOYSITE NANOTUBES FOR MEDICAL USE

N.P. Suprun[1], A.V. Brichka[2] and S.Ya. Brichka[1]

[1]*Kyiv National University of Technologies & Design, N.-Danchenko srt. 2, 01011 Kyiv, Ukraine*
[2]*Chuiko Institute of Surface Chemistry, NAS of Ukraine, General Naumov srt. 17, 03164 Kyiv, Ukraine*
suprun.knutd@ukr.net

Abstract: *Was received a series of agar-agar hydrogels filled with aluminosilicate nanotubes and investigated their morphology and physicochemical characteristics.*

Keywords: *halloysite nanotubes, gel, agar-agar, synthesis, wound dressing.*

1 INTRODUCTION

Gels are gelatinous bodies that consist of a three-dimensional polymer frame and liquid. They represent a wide range of various functional materials which take an intermediate position between liquids and solid bodies. Gels are sometimes remarkable for unique mechanical, optical and electrical properties that determine their wide application in industry and daily life. A structured system gives to gels mechanical properties of firm bodies: absence of flowability, ability to maintain a form, strength, ability for elastic deformation. Recently great attention is paid to biopolymer-based gels which differ from synthetic polymers in the absence of toxicity, biocompatibility with living systems, favorable biological decomposition and availability. Among biopolymers polysaccharides are most extensively used. Hydrogels based on natural components with "smart" properties are of considerable interest to researchers, since they are in demand in medicine as therapeutic transport systems for burn therapy, as sanitizing.

Nanocomposite hydrogels are novel macromolecular biomaterials, which are three-dimensional cross-linked polymer meshes filled with nanoparticles or nanomaterials such as flat clays and discrete inorganic nanoparticles. Such systems are used extensively for up-to-date biomedicine in the field of somatic tissues engineering, for creation of medicine delivery systems and also as biosensors [1-3]. Adding of fillers gives to gels excellent mechanical properties that help in its turn to overcome certain restrictions which usual polymer hydrogels have [4-6]. Nanomedicine uses possibilities and objects of nanotechnologies for diagnostics and treatment of diseases or for improvement of biological functions of organism. In nanomedical biotechnology nanocrystal materials, which halloysitic aluminosilicate nanotubes belong to, are basic. Chemical compounds of a tubular form provoke interest in experts owing to new possibilities of synthesis of materials with the properties distinct from lamellar and other morphological forms. By using of nanotubes with a certain diameter and length it is possible to control functional characteristics of a desirable end-product. Along with a big variety of synthetic nanotubes there are natural halloysite aluminosilicate nanotubes which are notable for high dispersity and uniformity of distribution as a filling agent in gels, respectively [7].

Halloysite nanotubes are material of natural origin and a commercial product obtained from halloysite. Halloysite is described by chemical formula $Al_2Si_2O_5(OH)_4nH_2O$, where n changes from 0 to 2, at this water located between the layers of the crystal firm body. Halloysite nanotubes are not subject to biodegradation and are biocompatible that predetermines extensive possibilities of their use in medicine, cosmetology, and veterinary science. Polymer hydrogels on the basis of natural components and halloysite nanotubes with “smart” properties provoke significant interest in researchers as they are required in medicine as therapeutic systems with transport, barrier, absorbing properties for wound healing at therapy of burn traumas, as sanitary moisture absorptive materials (blood, urine, sweat, etc.), [8-14].

We consider that a phenomenon of energetically strong adsorption of molecules on nanotubes that enables to slow down the release of functionally significant substances from the material can be used at development of nanofilled gel wound coverings of agar-agar/halloysite nanotubes type.

The purpose of the work is to receive and investigate a series of agar-agar hydrogels for definition of the influence of nano-sized filling agent on their physicochemical characteristics.

2 EXPERIMENTAL PART

Hydrogels have been synthesized as follows: to 20 ml of distilled water heated to 60-70°C was added 200 mg of agar-agar, then kept for 15 minutes for biopolymer swelling, and then in a water bath the final dissolution of agar-agar was done. After this to the obtained solution was added 1, 2 and 3 mg of halloysite nanotubes, respectively, distributing them by stirring in a whole volume of the obtained mixture. The obtained nanocomposite was kept in the refrigerator at 6°C during 30 min for hydrogel formation. The content of nanotubes in relation to agar-agar has made 0.5-1.5%. To estimate the quality of obtained materials the system of general organoleptic indices has been used, which include appearance, taste, smell, consistence, color.

The surface morphology of materials were examined by scanning electron microscopy MIRA3 LMU, Tescan with a resolution of ±1 nm and with an Oxford X-MAX 80 mm^2 energy dispersive spectroscopic chemical analysis system with an instrument uncertainty of ±1%. The IR spectra of the materials were measured at room temperature on an IR Affinity-1, Shimadzu spectrometer in the 4000-550 cm^{-1} region using an ATRV attachment with an instrument uncertainty of ±1 cm^{-1}.

3 RESULTS AND DISCUSSION

Images of samples of agar-agar gel synthesized according to the above technique are represented at Figure 1A. A yellow color is caused by significant (about 1 cm) thickness of gel samples, and increase of intensity is connected with the increase in content of halloysite nanotubes filling agent from 0.5 to 1.5%. By touch the strength of hydrogels grows along with the increase of halloysite concentration. At hydrogels drying, filling agent concentration and agglomeration occurs on certain sites (Figure 1B).

The electronic images of frozen gels indicate a developed surface (Figure 2). There are macropores that can serve as the places of adsorption, for example, of physiological fluid that is released from wounds [10]. At the same time, the active substances localized in the nanotubes of the gels are prolonged to be released to the damaged areas of the skin.

To confirm the presence and to determine the distribution of aluminosilicate nanotubes in agar-agar gels the chemical element analysis of chosen gel areas, which are indicated in the Figure 3, has been carried out. Lower image clearness of aluminosilicate nanotubes can obviously testify to the fact that they are coated with a polymer layer. The usual agar-agar composition contains carbohydrates (to 70%) with nitrogen and sulfur atoms protein compounds (1-2%) and significant number of calcium ions etc. So, basic agar elements are carbon, oxygen and calcium. When filling the gel with nanotubes in the energy-dispersive analysis spectra the signals of silicon and aluminum atoms as well as oxygen, in addition, shall appear.

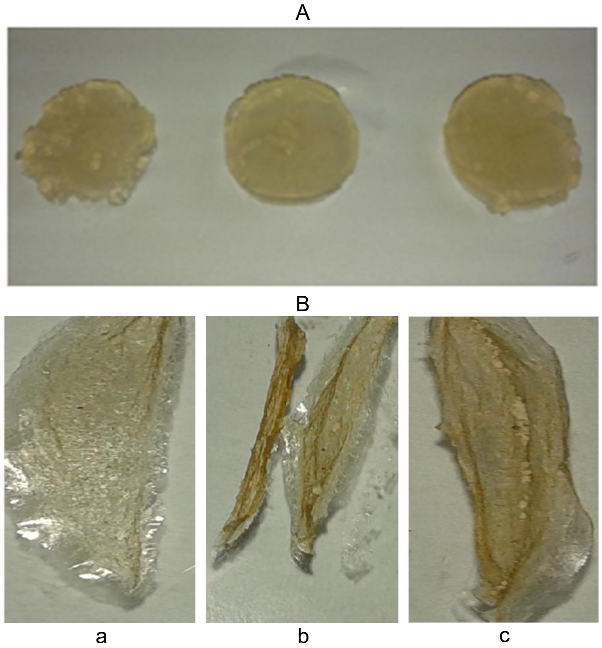

Figure 1 A - Optical photo of agar-agar hydrogels B - their dried samples, containing nanotubes: 0.5% (a), 1% (b) and 1.5% (c)

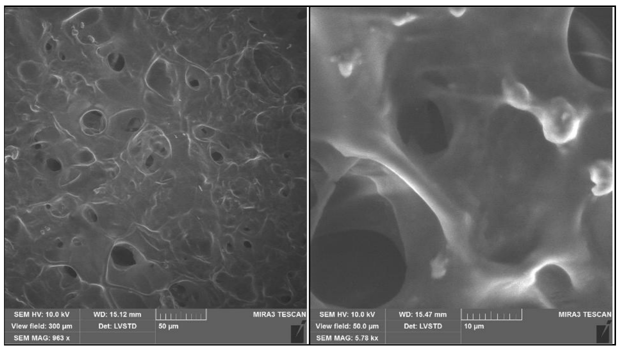

Figure 2 SEM images of frozen gels

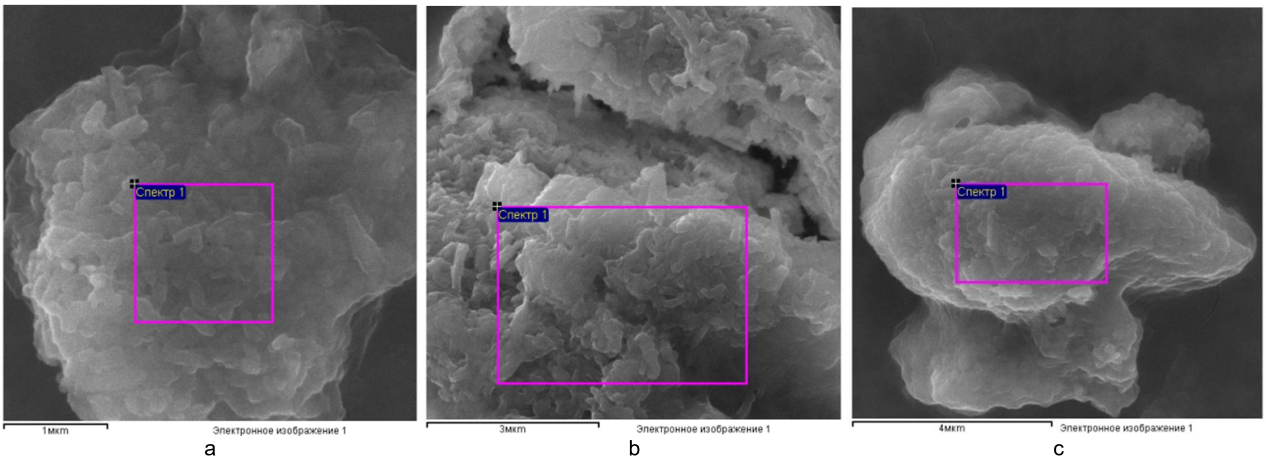

Figure 3 SEM images of dried gels containing nanotubes 0.5% (a), 1% (b), 1.5% (c) and the selected area for energy-dispersive chemical analysis

Quantitative composition of elements fixed in the spectra of filled hydrogels is given in Table 1. Significant carbon content in samples (25.85 - 37.31%) relates to agar-agar organic carbon. Silicon and aluminum elements correspond to halloysite nanotubes, and their ratio about 1:1 corresponds to stoichiometric ratio in halloysite [11].

Table 1 The results of the energy-dispersive chemical analysis of the dried gels in selected areas

Nanotube content [%]	Element content [%] at.					
	C	O	Si	Al	Ca	P
0.5	25.85	53.66	9.26	10.45	0.36	0.42
1	35.46	44.80	10.43	9.32	-	-
1.5	37.31	46.50	7.91	8.06	0.22	-

So, halloysite aluminosilicate nanotubes are distributed uniformly in the agar-agar hydrogel matrix. Oxygen is a part of organic component and aluminosilicate nanotubes, the structure of which form layers of silicon-oxygen tetrahedrons and aluminium hydroxide octahedrons. Revealed calcium and phosphorus may relate to gel former impurities and natural nanotubes.

IR spectroscopy is traditionally widely used for the study and characterization of complex natural heteropolysaccharides galactans particular group of agar-agar. In the IR spectra of freshly hydrogels (Figure 4) observed intense broad absorption bands of water and hydroxyl groups of components in the gel stretching vibration at 3700-3000 cm^{-1}. The presence of water is also evident intense band of deformation vibrations around 1740 cm^{-1}.

Skeleton fluctuations 1043.49 cm^{-1} and less intensive lower than 990 cm^{-1} are revealed. They relate to C-C and C-O polymer links. Divergences in peak maxima can obviously be related to error of samples preparation. Outlet nanotubes have absorption bands at … 907...52 cm^{-1}.

In our opinion, these bands have not been showed in IR spectra of composite hydrogels because of low content of nanotubes in hydrogels and possible nonuniform distribution of nanotubes on local sites in the gel mass. Indirect argument of the presence of aluminosilicate nanotubes with the increasing content in hydrogels is reduction in absorption band intensities with the increase in content of nanotubes.

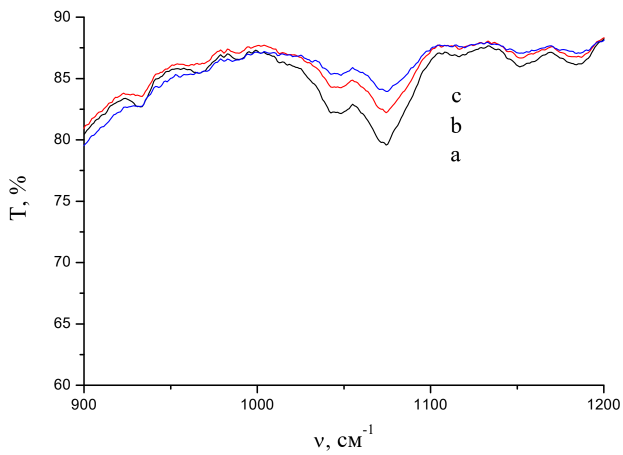

Figure 4 IR spectra of hydrogel sat 1200-900 cm^{-1} containing nanotubes 0.5 (a), 1 (b) and 1.5% (c)

4 CONCLUSION

Nanocomposite hydrogels on the basis of natural materials - agar-agar polysaccharide and halloysite aluminosilicate nanotubes have been synthesized. By organoleptic and physicochemical parameters gels are suitable for the use in biotechnology and medicine for creation of medical aseptic bandages, drain sorbents and wound dressing. Chemical analysis of nanocomposites corresponds to element content of gel components, in particular halloysitic nanotubes. Absorption bands of synthesized hydrogels are shown in IR spectra.

5 REFERENCES

1. Chang C.W., Spreeuwel A.V., Zhang C., Varghese S.: PEG/clay nanocomposite hydrogel: a mechanically robust tissue engineering scaffold, Soft Matter. 6(20), 2010, pp. 5157-5164
2. Satarkar N.S., Hilt J.Z.: Magnetic hydrogel nanocomposites for remote-controlled pulsatile drug release, J. Controlled Release130(3), 2008, pp.246-251
3. Gant R.M., Abraham A.A., Hou Y., Cummins B.M., Grunlan M.A.: Design of a self-cleaning thermoresponsive nanocomposite hydrogel membrane for implantable biosensors, Acta Biomater. 6, 2010, pp. 2903-2910
4. Martin J.E., Patil A.J., Butler M.F., Mann S.: Guest-molecule-directed assembly of meso structured nanocomposite polymer/organoclay hydrogels, Adv.Funct. Mater. 1(4), 2011, pp. 674-681
5. Xu K., et al: Polyampholytes superabsorbent nanocomposites with excellent gel strength, Compos. Sci. Technol. 67, 2007, pp.3480-3486
6. Haraguchi K, Takehisa T.: Nanocomposite hydrogels: a unique organic inorganic network structure with extraordinary mechanical, optical, and swelling/de-swelling properties, Adv. Mater. 14, 2002, pp.1120-1124
7. Brichka S.Ya.: Aluminosilicate nanotubes application, Material science of nanostructures 4, 2012, pp. 40-60
8. Cavallaro G, Gianguzza A, Lazzara G., Milioto S, Piazzese D. Alginate gel beads filled with halloysite nanotubes, Applied Clay Science, 72 2013, pp.132-137
9. Christine Shu Ching Chiewa, Phaik Eong Poh, Pooria Pasbakhsh, Beng Ti Tey, Hak Koon Yeoh, Eng Seng Chan: Physicochemical characterization of halloysite/alginate bionanocomposite hydrogel, Applied Clay Science 101, 2014, pp. 444–454
10. Jiaxing Tu, Zheng Cao, Yihan Jing Changjiang Fan a, Chao Zhang, Liqiong Liao, Lijian Li: Halloysite nanotube nanocomposite hydrogels with tunable mechanical properties and drug release behavior, Composites Science and Technology 85, 2013, pp.126-130
11. Lvov Y.M., Shchukin D.G., Möhwald H, Price R.R.: Halloysite clay nanotubes for controlled release of protective agents, ACS Nano 2, 2008, pp.814-820
12. Levis S.R., Deasy P.B.: Characterisation of halloysite for use as a microtubular drug delivery system, Int. J. Pharm. 243(1-2), 2002, pp.125-134
13. Brichka S.Ya.:Chemistry of halloysite and imogolite nanotubes, Kyiv, Ukraine: Publishing House "Kiy", 2016, 258 pp
14. Brichka S.Ya: Natural aluminosilicate nanotubes: structure and properties, Material science of nanostructures 2, 2009, pp. 40-53