HALLOYSITE NANOTUBES AS POTENTIAL CARRIER FOR GENTAMICIN

EWA STODOLAK-ZYCH[1]*, KATARZYNA SKÓRA[2], ALICJA RAPACZ-KMITA[1], MACIEJ MIKOŁAJCZYK[3], MARCIN GAJEK[1], MIROSŁAW M. BUĆKO[1]

[1] FACULTY OF MATERIALS SCIENCE AND CERAMICS, AGH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KRAKOW, POLAND
[2] FACULTY OF ELECTRICAL ENGINEERING, AUTOMATICS, COMPUTER SCIENCE AND BIOMEDICAL ENGINEERING, AGH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KRAKOW, POLAND
[3] THE UNIVERSITY HOSPITAL IN KRAKOW, DIVISION OF MICROBIOLOGY, KRAKOW, POLAND
*E-MAIL: STODOLAK@AGH.EDU.PL

[ENGINEERING OF BIOMATERIALS 148 (2018) 93]

Introduction

The special properties of clay minerals, their widespread availability, low cost and biocompatibility in contact with human tissues made them used as carriers in controlled drug delivery systems. One of these minerals is halloysite, which unique tubular structure makes it distinctive from all aluminosilicates. The empty lumen of halloysite nanotubes is an excellent space to locate various compounds inside, such as proteins or drugs. The main goal of the intercalation of the latter inside halloysite nanotubes is to extend their release time from minutes to even a few hours [1]. The mechanisms of the binding of ofloxacin [2], tetracycline and ciprofloxacin [3], belonging to cationic drugs, were investigated among others. The general observation from these scientific papers is that the maximum amount of bound drug is lower than it would be expected from the halloysite CEC [3]. The aim of this work was to investigate the possibilities of using halloysite nanotubes as a carrier for gentamicin. As part of the study, the effect of three parameters of preparation of the Hal-GS hybrids (temperature, mixing time and initial amount of drug) on the process of attaching the drug to halloysite nanotubes was analyzed.

Materials and Methods

Halloysite Dragonite™ HP (Hal) (Applied Minerals) and gentamicin sulfate (GS) (Amara) were used in the research. Samples were prepared at different temperatures (20, 60 and 80°C), varying the mixing time (2, 12 and 24 h) and using different amounts of the drug determined by the cation exchange capacity (CEC) of Hal. The obtained hybrids were investigated by X-ray diffraction (XRD), infrared spectroscopy (FTIR), zeta potential measurement, thermal analysis (DSC/TG), infrared spectroscopy with total internal reflection (FTIR-ATR) and X-ray photoelectron spectroscopy (XPS). Studies on the kinetics of gentamicin sulfate release were performed in buffered saline (PBS) at pH 7.4 by UV-Vis spectroscopy. Selected materials were subjected to antibacterial tests using the certified *Escherichia coli* ATCC 25922 reference strain (Gram-negative bacillus) to assess the effect of the production process and drug intercalation method on the antibacterial properties of Hal-GS hybrids.

Results and Discussion

The XRD results showed no shift of the peaks from halloysite towards higher values of the 2θ angle, which indicates the lack of the effect of incorporating GS into the interlayer spaces of halloysite nanotubes, regardless of the amount of drug in the initial suspension. Analysis of FTIR spectra did not show bands originating from newly formed chemical bonds, which confirms the attachment of drug particles on the surface of the Hal nanotubes by weak intermolecular interactions. Based on measurements of Zeta potential, it can be estimated that the amount of drug accumulated on the surface of the nanotubes depends on the amount of drug in the initial suspension. The addition of the drug changes the value of Zeta Hal potential from negative to positive. DSC/TG measurements indicate a non-thermal GS thermal stabilization in the presence of Hal. Considering the conditions of formation of Hal-GS hybrids, the highest amount of drug was found in conjugates prepared at 60ºC. The release curves (UV-Vis) indicate that the amount of released drug increases with its increasing content in Hal-GS conjugates. Lack of changes in XPS spectra of silicon, aluminum and oxygen indicates the lack of new chemical bonds. The presence of GS confirms the widening of the peak from carbon. A phenomenon of formation of asymmetric zones of bacterial growth inhibition (FIG. 1) around the Hal-GS pellets was observed. The higher GS content in the initial suspension was, the greater the bactericidal effect.

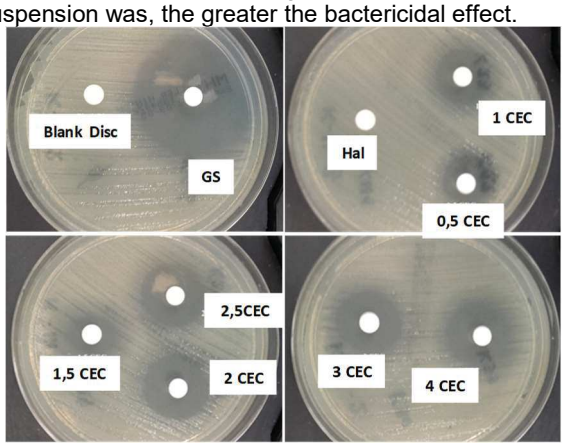

FIG. 1. Hal-GS antibacterial activity.

Conclusions

The results of physicochemical tests indicated that gentamicin sulfate binding occurs only on the surface of nanotubes. The grafting of GS onto halloysite nanotubes is most effective at 60° C with a 24 h mixing time, and the increase in temperature to 80°C causes a dramatic decrease in the efficiency of Hal-GS hybrids formation. The release process of GS from hybrids in the PBS solution proceeded very rapidly, and a maximum time of the drug release measured by spectrophotometry did not exceed 20 minutes. Moreover, the amount of gentamicin sulfate was lower than it would result from CEC measurements, because only the surface of nanotubes was grafted with the drug. The process of producing the hybrids did not affect the antibacterial properties of GS against *E. coli* bacteria. The unusual asymmetry of zones inhibiting the growth of bacteria may lead to the conclusion that the tubular structure of the carrier affects the distribution of the drug in the biological environment.

Acknowledgments

This work was performed within the framework of funding for statutory activities of AGH University of Science and Technology in Krakow, Faculty of Materials Science and Ceramics (11.11.160.617).

References

[1] N.G. Veerabadran, R.R. Price, Y.M. Lvov, Nano 2 (2007) 115-120.
[2] Q. Wang, J. Zhang *et al.*, Colloids Surf. B Biointerfaces 113 (2014) 51-58.
[3] W.T. Jiang, P.H. Chang *et al.*, Micropor. Mesopor. Mater. 220 (2016) 298-307.