

Synthesis of Tinidazole-Based Nanocomposites and Evaluation of Their Physicochemical Properties

***Avramenko V.V.¹, Vakuliuk P.V.¹, Furtat I.M.¹, Pryshchepa O.²,
Melnykov V.M.¹, Murlanova T.V.^{1,3}, Pomastowski P.², Smarsly B.³***

1 National University of Kyiv-Mohyla Academy, Kyiv, Ukraine

E-mail: viktoriaa.avramenko@ukma.edu.ua

2 Centre for Modern Interdisciplinary Technologies, Nicolaus Copernicus University in Torun, Poland

3 Institute of Physical Chemistry, Justus Liebig University, Giessen, Germany

The synthesis of nanocomposites (NC) with antimicrobial activity for the creation of targeted delivery systems for active substances allows overcoming the shortcomings of traditional agents and expanding their application in clinical practice [1]. The study used tinidazole, an antiprotozoal drug with antibacterial activity. In particular, it is effective against *Fusobacterium spp.*, *Bacteroides spp.*, *Clostridium spp.*, *Peptococcus spp.*, and *Veillonella spp.* At the same time, its use in clinical practice is primarily limited by its low water solubility. Therefore, the creation of controlled-release NCs is aimed at increasing therapeutic efficacy, reducing the risk of side effects, and improving the solubility of tinidazole.

The aim of the study was to obtain NCs based on nanosilica capable of improving the properties of tinidazole and increasing the safety of its use. In the nanocomposite system, silica acts as an inorganic carrier, ensuring effective immobilization of tinidazole on its surface. The effect of NC synthesis conditions on their physicochemical properties was compared by varying the synthesis conditions, namely: from aqueous solutions, from alcoholic solutions, or by a mechanochemical method. The interaction between the inorganic carrier and the antimicrobial drug in the NC was confirmed by infrared spectroscopy. Each of the spectra contained characteristic absorption bands. The structural characteristics of NCs were evaluated by the physical adsorption of nitrogen. It was shown that native silica has a specific surface area of 221 m²/g and an average pore diameter of 40 nm. After modification of the carrier with tinidazole, the specific surface area decreased to 206 m²/g and 212 m²/g for NC obtained from aqueous and alcoholic solutions, and to 136 m²/g when using the mechanochemical method. With a decrease in the surface area of NCs obtained from solutions, a decrease in the average pore diameter to 25 nm was observed. With the mechanochemical method, the average pore diameter remained unchanged. The release of tinidazole from NCs in phosphate buffer was determined by HPLC. The nanocomposites obtained by the mechanochemical method showed the highest drug release (98 %) with a

low RSD (1.1 %), indicating their stability and efficiency. NCs obtained from aqueous and alcoholic solutions were characterized by moderate release (95 % and 94 %, respectively) at low dosages. For them, the RSD was 3.6 % and 2.8 %, respectively.

The results obtained allow establishing a relationship between the synthesis method, the structural characteristics of nanocomposites, and the efficiency of immobilization of the active substance.

Acknowledgements: Viktoriia Avramenko, Iryna Furtat and Polina Vakuliuk were internship grant holders in the frame of Solidarni z Ukraїnā programe financially supported by NAWA agency.