

**TITLE:** EVALUATION OF THE ANTIBACTERIAL ACTIVITY OF TOBRAMYCIN ENCAPSULATED IN CHITOSAN-COATED ZEIN NANOPARTICLES AGAINST *Pseudomonas aeruginosa* STRAINS CLINICAL RESISTANT

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**ABSTRACT:**

Multidrug-resistant *Pseudomonas aeruginosa* is one of the most common causes of nosocomial infections, especially in immunocompromised patients, including infections in the lungs of patients with cystic fibrosis, in skin wounds, in the urinary system, causing prolonged hospital stay and high rates of morbidity and mortality. To treat this type of infection, aminoglycosides such as tobramycin (TOB) can be used, however, the use of this drug becomes limited, due to the impossibility of crossing the intestinal barrier and high toxicity. To overcome these limitations, encapsulating TOB in chitosan-coated zein nanoparticles becomes a promising alternative in the use of oral particles for controlled release of antimicrobials in the treatment of infections caused by *P. aeruginosa*. Thus, this study aimed to evaluate the antibacterial activity of chitosan-coated zein nanoparticles encapsulating TOB (TOB-ZNP-CH). TOB-ZNP-CH were prepared by the nanoprecipitation method and characterized by measuring the particle size ( $\emptyset$ ), polydispersity index (PDI), zeta potential ( $\xi$ ), pH and encapsulation efficiency (EE%). The determination of the minimum inhibitory concentration (MIC) of TOB and TOB-ZNP-CH against clinical isolates of *P. aeruginosa* (PA 19, PA 56, and PA 69) was performed by the broth microdilution method according to the Clinical and Laboratory Standards Institute. The minimum bactericidal concentration (MBC) was determined from the well in which the MIC showed no bacterial growth, whose aliquot was seeded on Müller Hinton agar and incubated at  $35 \pm 2$  °C for 24h. After this period, the CBM was determined as the lowest concentration at which there is no microbial growth. TOB-ZNP-CH presented  $\emptyset$  of 317.7 nm, PDI of 0.274,  $\xi$  of  $+45.1 \pm 0.7$  mV, pH 4.5 and EE% of 63.38%. The MIC of TOB against PA 19, PA 56, and PA 69 were 6.25  $\mu\text{g/mL}$ , 12.5  $\mu\text{g/mL}$ , and 6.25  $\mu\text{g/mL}$ , and for TOB-ZNP-CH were 1.56  $\mu\text{g/mL}$ , 3.12  $\mu\text{g/mL}$  and 1.56  $\mu\text{g/mL}$ , respectively. The MBC of TOB against PA 19, PA 56, and PA 69 were 12.5  $\mu\text{g/mL}$ , 50  $\mu\text{g/mL}$ , and 25  $\mu\text{g/mL}$ , and for TOB-ZNP-CH were 3.12  $\mu\text{g/mL}$ , 12.5  $\mu\text{g/mL}$ , and 6.25  $\mu\text{g/mL}$ , respectively. Tobramycin encapsulated in chitosan-coated zein nanoparticles has greater antibacterial activity when compared to the free drug, demonstrating therapeutic potential for the treatment of infections caused by multidrug-resistant *P. aeruginosa* strains.

**Keywords:** Bacterial Resistance, Gram-negative, Infection, Nanocarriers.

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