

# Novel Ionic Hyaluronic Acid-vancomycin Complexes for Inhalation †

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† Presented at The Sixth International Meeting of Pharmaceutical Sciences (RICiFa), November 10-12, 2021, Córdoba, Argentina

Received: 26.04.2022; Revised: 4.05.2022; Accepted: 6.05.2022; Published: 8.05.2022

**Abstract:** Polyelectrolyte-Drug complexes are interesting alternatives to improve drug performance. Vancomycin (VAN) is an antimicrobial drug used in the treatment of methicillin-resistant *S.aureus* lung infections in patients with cystic fibrosis. VAN is generally administered by intravenous route with high toxicity and side effects associated, which could be improved by pulmonary route. Nowadays, there aren't effective and secure inhalable formulations containing VAN. This work is focused on the preparation and characterization of novel ionic complexes between hyaluronic acid (HA), a biocompatible bioadhesive polymer, and VAN. Isosmotic HA-VAN complexes were easily prepared in an aqueous dispersion with different proportions of VAN. The pH was adjusted close to 7. Dispersions containing  $\leq 50\%$  of VAN were physically stable for at least a week. All dispersions exhibited negative Z potential ( $-20 \pm 4$  mV), and pseudoplastic flow and could be nebulized appropriately. FT-IR and thermal analysis confirmed ionic interaction between HA and VAN. Freeze-dried complexes were easily redispersed in water by simple mixing. Microbiology assay of complexes against reference strains of methicillin-resistant and methicillin-sensitive *S.aureus* showed no changes in the antimicrobial activity of VAN. Release profiles of HA-VAN showed extended release of VAN with anomalous non-fickian transport. In summary, HA-VAN systems exhibited interesting properties for the development of inhaled formulations.

**Keywords:** cystic fibrosis; Vancomycin; polyelectrolyte-drug complexes; drug delivery systems; pharmaceutical technology.

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## Funding

This research was funded by SECyT of the Universidad Nacional de Córdoba (Grant number: Consolidar-1, 05/C539-33620180101234CB) and Technological Link Projects "Universities Adding Value". MINISTRY OF EDUCATION AND SPORTS, SECRETARIAT OF UNIVERSITY POLICIES (RESOL-2016-2373-E-APN-SECPU#ME).

## Acknowledgments

Authors thanks to Química Luar SRL for supplying the VAN.

## **Conflicts of Interest**

The authors declare no conflict of interest.