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Development of *in situ* ionic-sensitive nasal gels of amoxicillin-loaded albumin nanoparticle applying QbD-based optimization for improved local delivery

Sandra Aulia Mardikasari[1,2], Gábor Katona[1]*, Mária Budai-Szűcs[1], Bence Sipos[1], László Orosz[4], Katalin Burián[4], László Rovó[3], Ildikó Csóka[1]

[1] Institute of Pharmaceutical Technology and Regulatory Affairs, Faculty of Pharmacy, University of Szeged, Szeged, Hungary

[2] Faculty of Pharmacy, Hasanuddin University, Makassar, Indonesia

[3] Department of Oto-Rhino-Laryngology and Head-Neck Surgery, University of Szeged, Szeged, Hungary

[4] Department of Medical Microbiology, Albert Szent-Györgyi Health Center and Albert Szent-Györgyi Medical School, University of Szeged, Szeged, Hungary

A high dose of orally administered amoxicillin (AMT) is recommended as the first-line treatment regimen for acute bacterial rhinosinusitis (ABR), even though it possesses poor oral bioavailability and frequently causes systemic adverse effects. Accordingly, nasal administration of AMT may become a viable strategy to overcome these drawbacks and to treat ABR locally effectively. Within the framework of Quality by Design (QbD) methodology, the current study aimed to develop an appropriate carrier system for improved local nasal delivery of AMT by combining albumin nanoparticles with gellan gum, a stimuli-responsive polymer. Application of albumin nanoparticles in combination with ionic-sensitive *in situ* gelling polymers for local nasal therapy means a novel strategy by hindering the nasal absorption of the drug and further prolonging its release in the nasal cavity. The obtained formulations were investigated for their mucoadhesive properties, *in vitro* drug release, and antibacterial activities. As a result, the formulation of 0.3 *%w/v* gellan gum concentration was chosen as the optimal *in situ* gelling system. Interestingly, the growth of five common nasal pathogens in ABR was effectively inhibited by each formulation. In brief, the development of albumin-based nanoparticles combined with ionic-sensitive *in situ* gelling polymer shows promise as nanocarrier systems for administering AMT for local delivery in the nasal cavity.

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