Improving Intranasal Drug Delivery to the Olfactory Region Using Magnetophoretic Guidance

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Abstract

Background: Although direct nose-to-brain drug delivery has multiple advantages, its application is limited by the extremely low delivery efficiency (<1%) [1,2, 3] using conventional devices to the olfactory region where drugs can enter the brain. It is critical to search for more effective methods to deliver drugs to the olfactory region.

Methods: In this study, we introduced a delivery method that utilized magnetophoretic forces to steer ferromagnetic drug particles to the olfactory region. The feasibility of this method was numerically evaluated in both idealized 2-D and anatomically accurate 3-D nose models [4,5] using COMSOL Multiphysics® software. The influences of particle relative permeability, particle diameter, and drug release position on the olfactory delivery were also studied.

Results: Results showed that the particle diameter was a critical factor in controlling the motion of nasally inhaled ferromagnetic drug particles. The optimal particle size was found to be around 20 μm to ensure effective magnetophoretic guidance to the olfactory region while avoiding wall loss in the anterior nose. In both 2-D and 3-D cases, magnetophoretic -guided delivery achieved significantly better olfactory dosages than without magnetophoretic guidance. Furthermore, releasing drugs into the upper half of the nostril (i.e., partial release) led to olfactory dosages two times higher than releasing drugs over the entire area of the nostril. By combining the advantages of pointed drug release and appropriate magnetophoretic guidance, clinical significant olfactory dosages could be achieved in contrast to the extremely low olfactory dosage (< 1%) with conventional inhaler devices.

Conclusion: Controlled guidance is challenging because the magnetophoretic force and viscous drag scale differently with particle size. A high sensitivity of olfactory dosage was observed in relation to different pointed release positions, indicating the importance of precise particle guidance for effective olfactory delivery. Results of this study have important implications in developing novel delivery devices with magnetophoretic steering for the treatment of neurological disorders.

Keywords: direct nose-brain delivery; magnetophoretic guidance; medical devices; neurological medicines; respiratory physiology

Reference

1. XA Si, J Xi J, J Kim, Y Zhou Y, and H Zhong, "Modeling of release position and ventilation effects on olfactory aerosol drug delivery. Respir Physiol Neurobiol," 186: 22-32, 2013.
2. XA Si and R Gaide, “The Computational Simulation of Electrophoretic Focusing and Navigation for Intranasal Target Drug Delivery with Comsol”, Proceedings of the 2013 COMSOL Conference, Boston, MA, 2013.
3. J Xi, XA Si, and R Gaide, “Electrophoretic Particle Guidance Significantly Enhances Olfactory Drug Delivery: A Feasibility Study”, PLoS ONE, 9(1): e86953, 2014.
4. J Xi, X Si, Y Zhou, J Kim, and A Berlinski “Growth of Nasal-Laryngeal Airways in Children and Their Implications in Breathing and Inhaled Aerosol Dynamic,” Respiratory Care, 59(2): 263-273, 2014.
5. J Xi, and PW Longest, “Characterization of Submicrometer Aerosol Deposition in Extrathoracic Airways during nasal Exhalation,” Aerosol Science and Technology, 43:808-827, 2009.