

## PubMed

U.S. National Library of Medicine  
National Institutes of Health



Display Settings:  Abstract

Mol Pharm. 2010 Aug 9. [Epub ahead of print]

# Transnasal Delivery of Methotrexate to Brain Tumors in Rats: A New Strategy for Brain Tumor Chemotherapy.

Shingaki T, Inoue D, Furubayashi T, Sakane T, Katsumi H, Yamamoto A, Yamashita S.

ADME Research Inc., 1-12-8 Senba-higashi, Minoh, Osaka 562-0035, Japan, School of Pharmacy, Shujitsu University, 1-6-1 Nishigawara, Okayama 703-8516, Japan, Kyoto Pharmaceutical University, 5 Nakauchi-cho, Misasagi, Yamashina, Kyoto 607-8414, Japan, and Faculty of Pharmaceutical Sciences, Setsunan University, 45-1 Nagaotoge-cho, Hirakata, Osaka 573-0101, Japan.

### Abstract

Brain tumors are one of the most lethal and difficult to treat. Their treatment is limited by the inadequate delivery of antitumor drugs to the tumor. In order to overcome this limitation, the possibility of the nose-brain direct transport pathway was evaluated using methotrexate (MTX) as a model antitumor agent. The direct transport of nasal MTX to the cerebrospinal fluid (CSF) was examined by comparing the concentration of MTX in the plasma and the CSF after intraperitoneal (IP) and intranasal (IN) administrations. The brain uptake of MTX was evaluated based on a multiple-time/graphical analysis by measuring the concentration of MTX in the plasma and in the brain. The feasibility of nasal chemotherapy was examined by three nasal dosings of MTX to tumor-bearing rats in vivo at two day intervals with peritoneal application as a positive control. MTX showed a significant inhibitory effect on the in vitro growth of 9L glioma cells with 50% growth inhibitory concentration at 7.99 ng/mL. The pharmacokinetic studies clarified the significant direct transport of MTX from nasal cavity both to the CSF and to the brain. Nasal chemotherapy with MTX significantly reduced the tumor weight as compared to nontreatment control and IP group. The strategy to utilize the nose-brain direct transport can be applicable to a new therapeutic system not only for brain tumors but also for other central nervous system disorders such as neurodegenerative diseases.

PMID: 20695463 [PubMed - as supplied by publisher]

[LinkOut - more resources](#)