

Transnasal drug delivery into the brain for new CNS active molecules: PK modeling of drug distribution after intranasal, intravenous and intracerebral administration of imatinib

○ Nobuko Hada and Sveinbjörn Gizurarson
(Faculty of Pharmacy, University of Iceland)

Developing the effective methods for drug delivery into the brain is one of the major challenges today. More than 99% of the worldwide development effort for CNS drugs is devoted to the drug discovery and chemical modification of CNS active molecules, while less than 1% is devoted to CNS drug delivery. The result is that the majority of new drugs that emerge from CNS drug discovery programs will not be effective pharmaceuticals because many of them cannot easily cross the BBB *in vivo*. Nasal delivery has been suggested as an alternative administration route to target drugs directly inside the brain, since the evidence in support of direct transport of viruses, bacteria and parasites into the brain, has been shown. Despite a large number of interesting results and data available, it is still under debate whether this kind of direct nose-to-brain delivery route exists or not.

The objective of this study is to characterize nose-to-brain transport and brain distribution of imatinib after intranasal (*i.n.*), intravenous (*i.v.*) and intracerebral (*i.c.*) administration using pharmacokinetic model. Imatinib is a new anticancer agent, which has shown ability to inhibit the production of β -amyloid or its accumulation in the brain in Alzheimer's disease. However, it cannot be transported into the brain easily because of P-glycoprotein that limits its distribution and accumulation inside the brain. Therefore this study is important for the future CNS drug discovery and delivery, since it may open doors to a wide range of new CNS active molecules that previously have been discarded because they lack CNS access.