QPS, LLC
Delaware Technology Park
3 Innovation Way, Suite 240
Newark, DE 19711

QUALITY • PERFORMANCE • SERVICE

WEB www.qps-usa.com
TEL (302) 369-5601
FAX (302) 369-5602

CONFERENCE

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A comparison of Brain Distribution of IgG and AZT After Intranasal and Intracranial Administration in Rats

AUTHORS

E. Solon, A. Lordi, H. Shen, and Z. Lam
QPS, LLC, DE, USA

ABSTRACT

Direct intracranial infusion (IC) and intranasal (IN) administration of large molecule biotherapeutics have been proposed routes of administration to overcome the inhibition of brain penetration by the BBB. IC dosing *via* an indwelling cannula placed into a specific brain region using sterotaxic positioning provides a means to slowly infuse compounds into brain tissue at very slow rates and over periods of time up to week in duration. The objective of IN dosing is to administer the test article(s) into the nares of test animals with the intention of establishing uptake into the olfactory nerves for delivery to the brain.

This study examines and compares the capability of IC and IN dosing to achieve brain penetration and distribution of human ^{125}I-IgG and the small molecule ^{14}C-AZT into the different brain regions of rats using quantitative autoradiography image analysis and bioanalysis of whole-brain homogenates to determine tissue concentrations of parent material. In this study, 4 Groups (Gp) of male Sprague Dawley rats were used (total of 40 rats). Gp 1 rats were given a 1-h IC infusion of ^{125}I-IgG; Gp 2 rats were given a single IN dose of ^{125}I-IgG; Gp 3 rats were given a 1-h IC dose of ^{14}C-AZT; and Gp 4 rats were given a single IN dose of 14C-AZT. Four rats per time point per group were euthanized at 1 h and 8 h post-dose for Gps 1-3, and at 0.25 h, 0.5 h, 1 h, and 8 h post-dose for Group 4. One rat per time point, per Gp was frozen and analyzed by QWBA to examine brain distribution, and the brains from the remaining 3 rats per time point, per Gp were removed, flash frozen, and homogenized for determination of the concentration of test article in each sample.

This presentation will compare and discuss the results of IN and IC dosing and how it relates to brain penetration of biopharmaceutics and small molecule pharmaceuticals.