BMC Pharmacology

Meeting abstract

P-Glycoprotein inhibition at the blood-brain barrier visualized with (*R*)-[^{11}C]verapamil μPET

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from 13th Scientific Symposium of the Austrian Pharmacological Society (APHAR). Joint Meeting with the Austrian Society of Toxicology (ASTOX) and the Hungarian Society for Experimental and Clinical Pharmacology (MFT)
Vienna, Austria. 22–24 November 2007

Published: 14 November 2007

BMC Pharmacology 2007, **7**(Suppl 2):A24 doi:10.1186/1471-2210-7-S2-A24

This abstract is available from: http://www.biomedcentral.com/1471-2210/7/S2/A24

Introduction

Inhibition of the multidrug efflux transporter P-glycoprotein (P-gp) at the blood-brain barrier (BBB) is considered a promising strategy in order to increase intracerebral penetration of therapeutics, such as antiepileptic and anticancer drugs. The aim of this study was to evaluate the usefulness of (*R*)-[^{11}C]verapamil (VPM) and small-animal positron emission tomography (μPET) to measure P-gp inhibition at the BBB following administration of the third-generation P-gp inhibitor tariquidar (TQD, Xenova, UK).

Methods

Five Wistar Unilever rats underwent paired VPM μPET scans, one baseline scan followed by i.v. administration of TQD (15 mg/kg) and a second PET scan at 2 hour after TQD administration. Arterial blood sampling was performed along with analysis of metabolism and plasma protein binding of VPM.

Results

Following TQD administration, the brain-to-plasma ratio of radioactivity was increased by a factor of 11–16 as compared to baseline scans, whereas VPM metabolism and plasma protein binding were left unaffected.

Conclusion

Our pilot data suggest that VPM PET is a sensitive tool to quantitatively visualize P-gp inhibition at the animal and human BBB.