Radioligands for the study of brain 5-HT$_{1A}$ receptors *in vivo*–development of some new analogues of way

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„...Calculated from Pallas 2.1 for Windows (**Compudrug**). b Reference 4 . c Reference 25 . d...hydrolysis being the primary route of **metabolism**. However, the kinetic behaviour of DWAY...additional benefit of less susceptibility to **metabolism** than WAY, DWAY, or C6BPWAY. The results..."

Abstract

ABSTRACT. [*Carbonyl*-^{11}C]WAY-100635 (WAY) has proved to be a very useful radioligand for the imaging of brain 5-HT$_{1A}$ receptors in human brain *in vivo* with positron emission tomography (PET). WAY is now being applied widely for clinical research and drug development. However, WAY is rapidly cleared from plasma and is also rapidly metabolised. A comparable radioligand, with a higher and more sustained delivery to brain, is desirable since these properties might lead to better biomathematical modelling of acquired PET data. There are also needs for other types of 5-HT$_{1A}$ receptor radioligands, for example, ligands sensitive to elevated serotonin levels, ligands labelled with longer-lived fluorine-18 for distribution to "satellite" PET centres, and ligands labelled with iodine-123 for single photon emission computerised tomography (SPECT) imaging. Here we describe our progress toward these aims through the exploration of WAY analogues, including the development of [*carbonyl*-^{11}C]desmethyl-WAY (DWAY) as a promising, more brain-penetrant radioligand for PET imaging of human 5-HT$_{1A}$ receptors, and (*pyridinyl-6*-halo)-analogues as promising leads for the development of radiohalogenated ligands.
Author Keywords: WAY; Radioligands; 5-HT$_{1A}$ receptors; Brain; PET; Carbon-11; Fluorine-18

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