Synthesis and Preliminary Evaluation of a 2-Oxoquinoline Carboxylic Acid Derivative for PET Imaging the Cannabinoid Type 2 Receptor

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Cannabinoid receptor subtype 2 (CB2) has been shown to be up-regulated in activated microglia and therefore plays an important role in neuroinflammatory and neurodegenerative diseases such as multiple sclerosis, amyotrophic lateral sclerosis and Alzheimer’s disease. The CB2 receptor is therefore considered as a very promising target for therapeutic approaches as well as for imaging. A promising 2-oxoquinoline derivative designated KP23 was synthesized and radiolabeled and its potential as a ligand for PET imaging the CB2 receptor was evaluated. [11C]KP23 was obtained in 10%-25% radiochemical yield (decay corrected) and 99% radiochemical purity. It showed high stability in phosphate buffer, rat and mouse plasma. In vitro autoradiography of rat and mouse spleen slices, as spleen expresses a high physiological expression of CB2 receptors, demonstrated that [11C]KP23 exhibits specific binding towards CB2. High spleen uptake of [11C]KP23 was observed in dynamic in vivo PET studies with Wistar rats. In conclusion, [11C]KP23 showed promising in vitro and in vivo characteristics. Further evaluation with diseased animal model which has higher CB2 expression levels in the brain is warranted.