

Modified Acetamidobenzoxazolone Based Biomarker for Translocator Protein Mapping during Neuroinflammation

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Abstract : The 18-kDa translocator protein (TSPO) previously called as peripheral benzodiazepine receptor, is proven biomarker for variety of neuroinflammation. TSPO is tryptophane rich five transmembranal protein found on outer mitochondrial membrane of steroid synthesising and immunomodulatory cells. In case of neuronal damage or inflammation the expression level of TSPO get upregulated as an immunomodulatory response. By utilizing Benzoxazolone as a basic scaffold, series of TSPO ligands have been designed followed by their screening through in silico studies. Synthesis has been planned by employing convergent methodology in six high yielding steps. For the synthesized ligands the 'in vitro' assay was performed to determine the binding affinity in term of K_i . On ischemic rat brain, autoradiography studies were also carried to check the specificity and affinity of the designed radiolabelled ligand for TSPO. Screening was performed on the basis of GScore of CADD based schrodinger software. All the modified and better prospective compound were successfully carried out and characterized by spectroscopic techniques (FTIR, NMR and HRMS). In vitro binding assay showed best binding affinity $K_i = 6.1 + 0.3$ for TSPO over central benzodiazepine receptor (CBR) $K_i > 200$. ARG studies indicated higher uptake of two analogues on the lesion side compared with that on the non-lesion side of ischemic rat brains. Displacement experiments with unlabelled ligand had minimized the difference in uptake between the two sides which indicates the specificity of the ligand towards TSPO receptor.

Keywords : TSPO, PET, imaging, Acetamidobenzoxazolone

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