核化学与放射化学 2009 31 (4): 212-216 ISSN: 0253-9950 CN: 11-2045/TL

研究报告

Re/$^{99}Tc^{m}(CO)_3$-EPBI与A$\beta_{(1\sim40)}$结合能力的测定及生物分布

杨洋;刘莹;韩美娇;张家新;韩梅;王科志;朱霖

放射性药物教育部重点实验室，北京师范大学 化学学院，北京100875

收稿日期 修回日期 网络版发布日期:

摘要 为发展锝-99m标记的阿尔茨海默病（Alzheimer's disease, AD）早期诊断显像药物，在荧光测定法基础上，建立了体外荧光法测定羰基铼配合物与Aβ$_{（1\sim40）}$ 淀粉样纤维结合的解离常数K_d的方法。同时，合成了配体2-(1-乙基苯并咪唑)吡啶（EPBI）及其铼的配合物Re(CO)$_3$Cl(EPBI)，测定后者与体外缠结Aβ$_{（1\sim40）}$ 结合的解离常数K_d；采用直接标记法制备EPBI的[$^{99}Tc^{m}$(CO)$_3$]$^+$配合物，并研究配合物[$^{99}Tc^{m}$ (CO)$_3$]$^+$-EPBI的理化性质及生物分布。结果表明，Re(CO)$_3$Cl(EPBI)与Aβ$_{（1\sim40）}$结合的解离常数K_d=13.3 μmol/L；正常小鼠体内生物分布研究表明，化合物[$^{99}Tc^{m}$ (CO)$_3$]$^+$ EPBI的脑初始（2 min内）摄取值为(0.63±0.17)%ID/g（n=3），在脑内清除较快，120 min时，摄取值为(0.27±0.03)%ID/g（n=3）。

关键词 阿尔茨海默病 荧光 Re/[$^{99}Tc^{m}$ (CO)$_3$]$^+$-EPBI K_d Aβ$_{（1\sim40）}$ 生物分布

分类号

Binding Affinity of Re(CO)$_3$Cl(EPBI) for Aβ$_{（1\sim40）}$ Aggregates and Evaluation of [$^{99}Tc^{m}(CO)_3]^+$-EPBI

YANG Yang, LIU Ying, HAN Mei-jiao, ZHANG Jia-xin, HAN Mei, WANG Ke-zhi, ZHU Lin

Key Laboratory of Radiopharmaceuticals, Beijing Normal University, Beijing 100875, China

Abstract The aim of this paper was to develop potential technetium 99m-labeled diagnostic imaging agents specific for the detection of Aβ plaques. Based on previously obtained Aβ plaque-specific biphenyls containing a benzimidazol group, $^{99}Tc^{m}$ and Re-benzimidazol derivatives, [$^{99}Tc^{m}(CO)_3]^+$-EPBI and Re(CO)$_3$Cl(EPBI), were prepared. The latter showed binding affinities towards Aβ$_{（1\sim40）}$ aggregates in *vitro* (K_d=13.3 μmol/L) by fluorophotometry. 2-(1-Ethylbenzimidazol-2-yl)pyridine（EPBI） and Re(CO)$_3$Cl(EPBI) were synthesized. Binding affinity of Re(CO)$_3$Cl(EPBI) for Aβ$_{（1\sim40）}$ aggregates was determined. [$^{99}Tc^{m}(CO)_3]^+$-EPBI was prepared and analyzed by HPLC and paper eletrophoresis. Its biodistribution in mice was obtained. The K_d value of Re(CO)$_3$Cl(EPBI) is 13.3 μmol/L. Biodistribution of [$^{99}Tc^{m}(CO)_3]^+$-EPBI in mice shows brain penetration (0.63±0.17) %ID/g （n=3） at 2 min after iv injection in mice and rapid washout from normal brains (0.27±0.03) %ID/g （n=3） at 120 min. It may provide a new strategy to design the early diagnosis radiopharmaceuticals of AD labeled by [$^{99}Tc^{m}(CO)_3]^+$ core according to the result.

Key words Alzheimer's disease fluorescence Re/[$^{99}Tc^{m}$ (CO)$_3$]$^+$-EPBI K_d Aβ$_{（1\sim40）}$ biodistribution

DOI

通讯作者