ORIGINAL ARTICLE

Annals of Nuclear Medicine Vol. 10, No. 1, 19–32, 1996

Both total chain length and position of dimethyl-branching effect the myocardial uptake and retention of radioiodinated analogues of 15-(p-iodophenyl)-3,3-dimethylpentadecanoic acid (DMIPP)

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Introduction of geminal dimethyl-branching into the 3-position of 15-(p-iodophenyl)pentadecanoic acid (IPPA) significantly delays myocardial clearance in rats and dogs following intravenous administration. Several new analogues of DMIPP have been synthesized and evaluated in fasted rats. The effects of both the position of dimethyl-branching and the total chain-length of 3,3-dimethyl analogues on heart uptake and clearance kinetics have been studied. In the first series of compounds, two methyl groups were introduced into the 3-, 4-, 6-, or 9-position. Tissue distribution studies of the 15-(p-[I-125]iodophenyl)-analogues demonstrated that the position of dimethyl-branching is an important factor affecting both myocardial specificity and retention. The [I-125]labeled 3,3- and 4,4-DMIPP analogues showed higher myocardial uptake and faster blood clearance than the 6,6- and 9,9-DMIPP analogues [heart, % dose/gm (heart : blood), 30 min: 3,3-DMIPP = 5.06 (12 : 1); 4,4-DMIPP = 8.03 (16.7 : 1); 6,6-DMIPP = 2.26 (3.1 : 1); 9,9-DMIPP = 3.06 (2.77)]. In the second series, the effects of total fatty acid chain length were evaluated with 3,3-dimethyl-substituted analogues with C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, and C_{19} chain lengths. The C_{14} and C_{15} chain length analogues showed the best properties [global heart uptake (heart : blood ratios): 30 min: C_{11}, 0.70 (0.82); C_{12}, 1.25 (0.68); C_{13}, 0.47 (0.90); C_{14}, 1.63 (3.54); C_{15}, 5.06 (12); C_{19}, 1.29 (0.82). These detailed studies have demonstrated that both total chain length and the position of geminal dimethyl-branching are important structural parameters which affect myocardial specificity and retention of ω-(p-iodophenyl)-substituted fatty acid analogues and that 3,3-DMIPP and 4,4-DMIPP are the best candidates with optimal properties for further study.

Key words: cardiac SPECT, cardiodine, DMIPP, iodine-123, methyl-branched fatty acids