PREPARATION AND PRE-CLINICAL INVESTIGATION OF L-α-METHYLTYROSINE LABELED WITH IODINE -131 OR IODINE-123 (IMT-131I, IMT-123I)

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The amino acid α-methylotyrosine (IMT) radiolabeled with the iodine-131 or iodine-123 has been used in the diagnostics of recurrent brain tumors, in the planning of re-operation and/or external radiotherapy. The mechanism of IMT uptake is connected with the active transport of this amino acid to the rapidly proliferating tumor cells. From the clinical point of view the IMT-^{123}I is the radiopharmaceutical of choice due to the favorable physical characteristics of iodine-123. However, taking into account the high cost of imported iodine-123, the diagnostic investigations using IMT-^{131}I still present considerable clinical value.

The aim of our work was to indicate that both radiopharmaceuticals IMT-^{131}I and IMT-^{123}I can be prepared in a reproducible manner, retaining high in vitro and in vivo stability and thus can be a subject of preliminary clinical investigation.

For radiolabeling of IMT-$^{123/131}$I the electrophilic substitution reaction has been applied in the presence of iodogen. The walls of the reaction vial were covered with a film of iodogen and then 300μg of L-α-methylotyrosine dissolved in the boric buffer (pH 8.0) was added followed by iodine-131 or iodine-123 (111-3700 MBq) in carbonate buffer (pH =8.5). The reaction was carried out during 10 minutes. Then the reaction mixture was transferred on the Sephadex DEAE A-25 column and the column eluted with water. Purified radiolabel was collected in the first 5 fractions (1 ml each). For quality control of the labelling yield and radiochemical purity of the iodinated compounds the methods of HPLC and electrophoresis were employed. The investigations of biological distribution were carried out on Swiss mice and the abnormal toxicity test was performed according to Polish Pharmacopoeia VI.

Altogether 18 batches of IMT-^{131}I and 6 batches of IMT-^{123}I were prepared. The radiolabeling yield of IMT-^{123}I was at the level of 85-92%, and for IMT-^{131}I at the level of 92-98%. The radiochemical purity of both iodinated compounds was in the range of 99.5-99.9%. The shelf life of IMT-^{123}I was determined to be 10 hours from the date and hour of calibration of iodine-123, which is a consequence of its half-life (13.27 h). The shelf life of IMT-^{131}I was confirmed to be 7 days, when stored at $+4^0$C - $+8^o$C.

The preparation is not harmful in the dose of 4200MBq/70kg.

The final parameters of the two radiopharmaceuticals have been formulated:

Pharmaceutical form - $^{123/131}$I- IMT solution in 0.9% NaCl for injection,

Specific activity -10 - 36.6 mCi/mg (370-1357 MBq/mg)

Radioactive concentration > 95%, radionuclide purity > 98%

Both radiopharmaceuticals $^{123/131}$I-IMT fulfill the requirements of pre-clinical phase.