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11. Radiopharmacy.

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11.04 Labelling of vasoactive intestinal peptide (vip) with 131-iodine. Preliminary biological distribution studies in animal.

Objective: The application of radiolabelled peptides for the imaging and therapy of cancer has been extensively pursued during the past decade. Various tumor cells express significantly higher amounts of Vasoactive Intestinal Peptide (VIP) receptors that provided the basis for the clinical use of radiolabelled VIP for *in vivo* localization of tumors. In this work, we described the production of radioiodinated VIP and preliminary distribution studies in mice.

Methods: The labelling procedure employed human VIP (25 ug, Sigma) dissolved in 20 uL of 0.2M phosphate buffer pH 7.5, [131-I]NaI solution (3.7-7.4 MBq/10uL), 6 ug of Iodogen as oxidant agent, introduced as a suspension and 5uL of KI (0.10 ng). The iodination was allowed to proceed for 30 minutes at room temperature with gentle stirring. Labelling procedure was also developed using 5 uL Chloramine T (1.0 mg/mL) and after few minutes of reaction at room temperature, the reaction was terminated by the addition of 5 uL of sodium methabisulfite solution (2.0 mg/mL). Radiochemical purity was determined by horizontal zone electrophoresis (Amershan) on Whatman 1 MM paper, 0.1M barbital buffer, pH 8.6, using a field of 295 V for 40 minutes. Aliquots of the reaction mixture were injected into a HPLC system (column RP C18, 10 um, 4.2 x 50 mm, Waters) eluted isocratically with 73% aqueous TFA (trifluoroacetic acid 1% solution) and 27% acetonitrile with a flow rate of 0.5 mL/minute. Biodistribution studies were carried out for both VIP preparations on normal Swiss mice. In both animal groups, blood samples were collected by an orbital bleed 1, 4 and 24 hours after radiopharmaceutical administration (18 uCi/100 uL of 131-I-VIP) and the animals were sacrificed, the tissues of interest removed, washed, weighted and counted for 131-I activity using a gamma counter (N = 6 animals for each time). The percent injected dose/organ was calculated by comparing the activity in each tissue to injection standards of suitable count rate.

Results and Conclusions: Radioiodinated VIP could be obtained with high radiochemical yield: 99% for labelling condition using Iodogen and 97% when using Chloramine T as oxidant agent. The proposed isocratic HPLC system possibilited the separation of labelled VIP in high specific activity, necessary for receptor-mediated diagnostic procedures with radiopharmaceuticals. Nevertheless, preliminary biological distribution studies were carried out without VIP purification. Results of biological distribution studies showed fast blood clearance and predominant uptake on liver, stomach and intestines in the first hour. Thyroid uptake was low in the first hour and increased with time but not significantly, showing a good *in vivo* stability of the compound labelled using Iodogen and Chloramine T as oxidant agents.

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