Characterization of [^{99m}Tc]Duramycin as a SPECT Imaging Agent for Early Assessment of Tumour Apoptosis

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Materials and methods

In vivo metabolite analysis

In vivo plasma stability of [^{99m}Tc]duramycin was evaluated as previously described [1]. Briefly, mice were i.v. injected with 37 MBq purified [^{99m}Tc]duramycin. Four and 24 h p.i. (n=3 for each time point) mixed blood was drawn by cardiac puncture, and the mice were euthanized by cervical dislocation. The blood was collected in EDTA-coated tubes and the plasma fraction was obtained by centrifugation (4000 g for 7 min). The plasma (200 µl) was mixed with an equal amount of cold acetonitrile to enable sample deproteination and counted for radioactivity using an automatic γ-counter. After vortexing and centrifuging for 4 min at 4000 g, the supernatant was separated from the pellet and both fractions were γ-counted to calculate the amount of radioactivity extracted in acetonitrile. To study radiometabolite formation, 100 µl of the supernatant were analyzed by RP-HPLC using the method described before. Eluate fractions of 0.5 min were collected and counted for radioactivity in the γ-counter.

Results

In vivo metabolite analysis

Adult normal CD1-/- nude mice were used to examine the metabolic stability of [^{99m}Tc]duramycin. According to the radio-HPLC analysis of the plasma samples, the majority of the injected radiotracer remains unchanged after 4 and 24 h p.i. (Figs. 1b and c, respectively). One minor polar impurity was detected eluting at 3 min. As it was also visible in the reference radiochromatogram (Fig. 1a), it was not related to in vivo metabolisation of [^{99m}Tc]duramycin. Radiometabolites eluting with a longer retention time (18.5 – 30 min) could also be detected.

Their presence might be the result of a complex formation between [^{99m}Tc]duramycin and blood lipoproteins, which are known to contain PE [2].

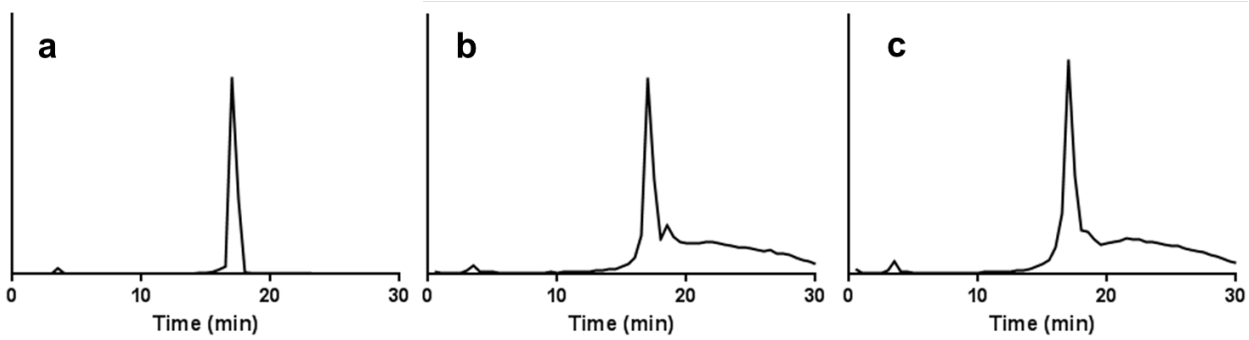

Fig. 1. Representative radio-HPLC chromatograms of [^{99m}Tc]duramycin reference (a), plasma at 4 h (b) and 24 h (c) after injection

References

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