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Evaluation of acute intravenous toxicity in rats and local tolerance in rabbits of a formulation for the preparation of ^{68}Ga -DOTATOC (^{68}Ga -Edotreotide or ^{68}Ga -DOTA0-Tyr3-Octreotide)

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^{68}Ga -DOTATOC is a radio-labelled somatostatin analogue, considered a promising PET diagnostic agent forsstr2-positive tumors. A lyophilized DOTATOC kit (containing 1,10-phenanthroline, gentisic acid, formic acid and mannitol) for reconstitution with ^{68}Ga solution was developed and tested in single dose toxicity study in rats and in local tolerance study in rabbits. Single dose toxicity study in rats of the treatment group (5M+5F) received a single intravenous injection (2 mL/kg) of a formulation containing increased DOTATOC, 1,10-phenanthroline and gentisic acid concentration (to achieve 2 mg/kg, 0.25 mg/kg and 0.3 mg/kg dose, respectively). Control animals (5M+5F) were treated with the corresponding placebo (buffering agents only). Observation period was 14 days. No significant changes compared to the control group were noted in terms of clinical signs, body weight, hematology, coagulation, clinical chemistry, urinalysis, organ weight and macroscopic/microscopic observations, showing that the formulation is safe and well tolerated. Local tolerance in rabbits was human DOTATOC formulation (treated group, 6F) or placebo solution (control group, 6F), both at final pH of 3.5 ± 0.3 , were injected into the marginal vein of the right ear, 0.5 mL/site. Sterile saline was administered into the left ear of both groups (negative control). Assessment of reaction was 1 hour after dosing and daily thereafter. The first 3 animals in each group were sacrificed at D1 post-dosing. The remaining animals were sacrificed at D7. Histopathology of injection sites indicated mild to moderate perivascular region inflammation in animals treated with either DOTATOC or placebo. The observed effects are most likely ascribable to the acidic pH of the injected solutions.

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