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IN VIVO EVALUATION OF NANOSTRUCTURED LIPID LABELLED WITH TC-99M

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BACKGROUND-AIM

This study describes the preparation, characterization, and first biologic evaluation in rats of radiolabelled nanostructured lipid carriers (NLC) especially designed for in vivo tomographic study. A technological study was conducted in order to associate ^{99m}Tc within the matrix of NLC. At this aim ^{99m}Tc complexes containing a terminal Tc≡N multiple bond ([^{99m}Tc]N-DBODC$_2$) have been encapsulated.

METHODS

[^{99m}Tc]N-DBODC$_2$ was produced through the two-step synthesis. In the first step, generator-eluted [^{99m}Tc][TcO_4]$^-$ was mixed with SDH as a donor of nitride nitrogen atoms (N^{3-}), in the presence of Sn^{2+} ions as reducing agent. The resulting mixture, containing nitride technetium intermediate complexes, was allowed to stand at room temperature for 30 min. The preparation was completed by adding the bis(dithiocarbamato) ligand (DBODC) in phosphate buffer. NLC were produced by stirring and ultrasonication methods based on different modalities. NLC morphology and dimensional distribution have been investigated by Cryogenic Transmission Electron Microscopy, x-ray, Photon Correlation Spectroscopy and Sedimentation Field Flow Fractionation. In vivo tomographic images of the rat body obtained by use of a small-animal SPECT scanner enabled to investigate NLC biodistribution after intraperitoneal (i.p.), intravenous (i.v.), intranasal (i.n.) and oral administration.

RESULTS

The [^{99m}Tc]N-DBODC$_2$ is a neutral symmetrical complex possesses a square pyramidal geometry with an apical ^{99m}Tc≡N multiple bond and the two dithiocarbamate ligands spanning the residual four positions on the square plane through the four sulfur atoms of the two >CS_2 groups. The loading of the radioactive tracer was achieved during NLC production by adding the ethanolic solution of [^{99m}Tc]N-DBODC$_2$ solution into the melted lipids. The encapsulation of the ^{99m}Tc complex into NLCs was highly satisfactory both in term of RCP and encapsulation efficiency. The administration of ^{99m}Tc-NLC in rats by different routes enabled to evaluate the biodistribution of NLC by the YAP-(S)-PET small animal scanner, collecting high-quality scintigraphic images.

CONCLUSION

The images clearly indicate the presence of radioactivity in liver and intestine after i.p., i.v. and per os administration, the absence of radioactivity in the brain even following i.n. administration and the absence of radioactivity in myocardial tissue. This latest result indicates that ^{99m}Tc is firmly associated to NLC, confirming the suitability of ^{99m}Tc-NLC production protocol, moreover the radioactivity presence after 6 hours from administration of ^{99m}Tc-NLCs corroborates their potential as controlled release nanosystems.