13èmes Journées du Cancéropôle Grand Sud-Ouest
Poitiers du 15-17 novembre 2017

Acute toxicology and biodistribution preclinical studies of new ^{188}Rhenium and ^{99m}Technetium bearing-nitro-Imidazolic probe (NGT_1).

Hafid BELHADJ-TAHAR, Nouredine SADEG, Guanghua YANG
- Nanomedicine Research and Expertise Group (AFPreMed), 31100 Toulouse.
Mail: contact@afpremed.org

Introduction:

Radiopharmaceuticals are used in two main fields of medicine: scintigraphic diagnosis and targeted anti-cancer therapy. Radiopharmaceuticals for diagnostic use gamma photon emitting radioisotopes (Technetium-99m, Zirconium-89, Gallium-67), whereas particle emitters (Rhenium-188, Yttrium-90) are reserved for therapy. It should be noted that we are currently seeing a renewed interest in radiopharmaceuticals due to their application in the field of nanomedicine, which aims to improve the specificity and therefore the effectiveness of the targeted therapy in a decisive way. In this context, we recently launched a research project on the synthesis and development of technetium and rhenium-bearing immidazole probes for the targeting of hypoxic tumors. In this paper we report the results of preclinical studies concerning the acute toxicology and the biodistribution in rats of an imidazole probe (NGT_1): 1-Nitro-1H-Imidazole-Methyl-1,2,3-Triazol-Methyl-Di- (2-Pycolyl) Amine.

Methods :

The probe was synthesized according to the protocol described by Yang et al[1] (fig 2). The In vivo studies were carried out in accordance with the guidelines of Decree No. 87-848 of 19 October 1987 on experiments in animals.
The labeled 99mTc-NGT1 probe solution dosed at 0.087mCi / µL (3.34MBq / µL) was prepared by reacting 330 µL of 1.725 mM NGT_1 in physiological solution with radioactive carbonyl-technetium (28.86 mCi) and heated at 60 ° C for 1 hour and then filtered via a 0.22 µm filter. Eight Wistar RjHan: Wi rats were divided into 2 groups:
- Group 1: 6 rats receiving 0.1 ml of the labeled solution of ^{99m}Tc-NGT_1 into IV.
- Group 2: 2 control rats receiving 0.1 ml of the saline solution into IV.
The animals were observed for 1 day after the administration and then the biodistribution was obtained by measuring the radioactivity present in each organ; as well as the anatomopathological examination was carried out.

Results:

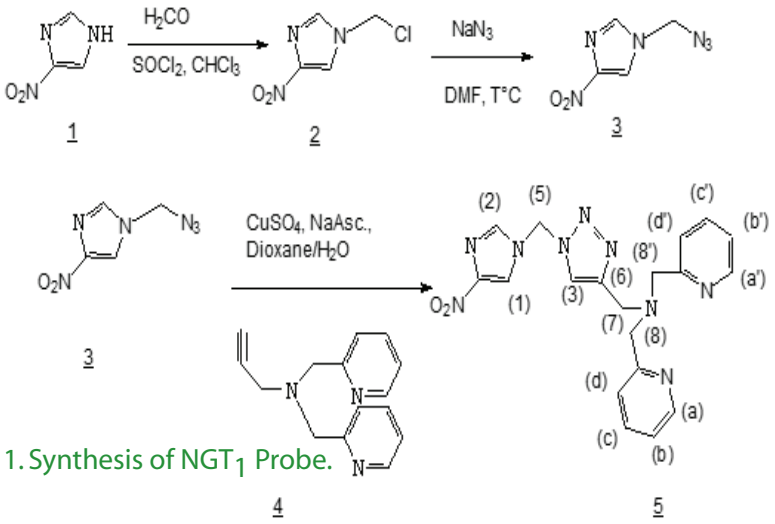

Fig. 1. Synthesis of NGT_1 Probe.

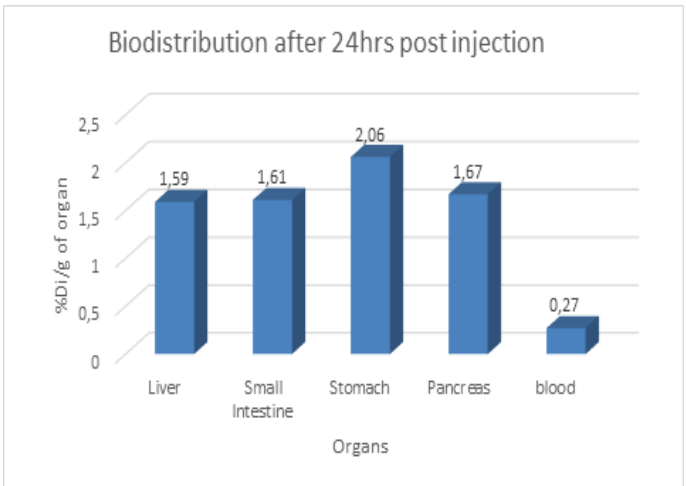

Fig. 2. Biodistribution Study

No mortality nor symptoms were observed. No anotomopathological abnormality was observed on the different organs. The labeled probe showed a very large distribution volume that was estimated at 167L.Kg^{-1}. As shown in Fig. 2, the digestive tract was particularly targeted by NGT_1 (Liver: 1.59% Di/g, Small Intestine 1.61% Di/g, Stomach 2.06 % Di/g and Pancreas 1.67% Di/g where % Di/g is % injected dose by gram of studied organ).

Conclusion: This Nitro-Imidazole probe (NGT1) seems to be suitable to targetting therapy according to its biodistribution and innocuity characteristics.

1- Yang G, Sadeg N and Belhadj-Tahar H. Drug Des 2017, 6:1