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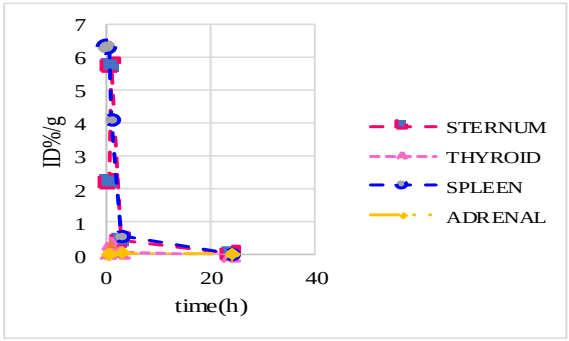
Human absorbed Dose estimation of ^{99m}Tc-MAX based on biodistribution data in mice



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Abstract

In this work, the absorbed dose evaluated from human organs for the novel ^{99m}Tc-MAX agent based on balb/c mice biodistribution data. The designed ligand with chelating properties was synthesized by the reaction between the two substances Chloroacetamide and xanthate. Then, the labeling process was performed successfully with ^{99m}Tc by 93% radiochemical purity in the laboratory. biodistribution of the labeled complex in balb/c mice up to 24 hours post-injection was examined and therefore the human absorbed dose of ^{99m}Tc-MAX was calculable by the radiation dose assessment resource methodology. The liver is that the vital organ with a dose of 0.0011 mGy/MBq. According to these results. The novel ^{99m}Tc-MAX agent can be a potentially effective imaging agent for the hepatic system.

Keywords: Dosimetry, Biodistribution, ^{99m}Tc, Methoxy Amido Xanthate (MAX)

Introduction

Diagnostic radiology, the imaging modalities using ionizing radiation, produces images of anatomical internal structures of human organs and physiological (functional) biological systems and helps significantly improve patient management and care in screening and diagnosis, assessing treatment response, and predicting [1]. Radioisotopes are an essential part of medical diagnostic procedures. In combination with imaging devices that register the gamma rays emitted from within, they can be used for imaging to study the dynamic processes taking place in various parts of the body [2, 3]. Radiopharmaceuticals consist generally out of three functional elements: (1) a vector molecule (or carrier) that shows high selectivity and affinity for a target; (2) a radionuclide; and (3) a linker or chelator to attach the former to the latter Fig.1 [4].

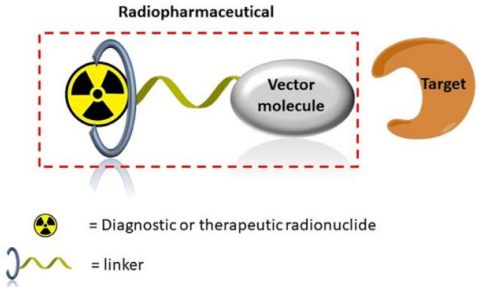

Figure1. Schematic design of a radiopharmaceutical

^{99m}Tc can be incorporated into numerous vector molecules via complexation chemistry employing a kit-based radiolabeling method. Meanwhile, the importance of preparing and characteristic ^{99m}Tc-based labeled compounds, taking under consideration its ideal properties, this radionuclide used for over 80% of diagnostic nuclear medicine cases. It is important to note that many ^{99m}Tc-labeled compounds used in nuclear medicine are produced by chelating agents [4-6]. Methoxy Amido Xanthate (MAX) ligand is a novel chelating agent that was designed and synthesized for the first time and its labeling rate was evaluated with ^{99m}Tc. Since the application of novel labeling agents is based on the ability to transmit specific radiation to a specific organ of the body, estimating the absorbed dose of such compounds is an important part of the development and use of novel agents. In line with our earlier investigation [7-10], the current research was applied to estimation of absorbed dose of ^{99m}Tc-MAX labeled compound in the organs of male balb/c mice in order to Recognition of its ability as a novel imaging agent.

Experimental

Preparation of the materials

Synthesis of MAX was performed according to the previously reported [11]. ^{99m}Tc-MAX was prepared at the optimized conditions (room temprature, 1-4 mg

chelating agent, 18 mg/10µl ascorbic acid, 10µl $SnCl_2.2H_2O$, $^{99m}TcO_4^-$ radionuclide was obtained with specific activity of 22mCi/50µl from $^{99}Mo/^{99m}Tc$). The radiochemical purity of ^{99m}Tc-MAX was determined by ITLC (wathman as a solid phase and saline, acetone:methanol (50:50), phosporic acid 15% as a mobile phase). Stability of the product was determined through storing the final solution at 22°C and in presence of freshly prepared human blood serum at 37°C for 4h for *in vitro* and *in vivo* stabilities respectively. After 4 hours, the radiochemical purity was estimated to be about 90%. As well as in the presence of human blood serum (37°C). Biodistribution studies were performed by injection of 450µCi of ^{99m}Tc-MAX to male mice via the tail vain after 0.5, 1, 3 and 24 hours post injection.
The mices were sacrificed (three mice for each time interval) and some of their tissues dissected and counted for calculating the %ID/g according to equation 1:

$$ID\%/g = (A_{tissue} / M_{tissue})/A_{total})\times 100 \quad (1)$$

The absorbed dose dependent on the amount of radioactivity in the source tissue and the time length of the radiopharmaceuticals internalized into the source tissue.
Accumulation activity for each animal organ was calculated based on Equation (2):

$$\tilde{A} = \int_{t_1}^{\infty} A(t)dt \quad (2)$$

Then, with the method proposed by Sparks et al., It was generalized to accumulated activity in humans:

$$\tilde{A}_{humanorgan} = \tilde{A}_{animal\ organ} \frac{\frac{Organ\ mass_{human}}{Body\ mass_{human}}}{\frac{Organ\ mass_{animal}}{Body\ mass_{animal}}} \quad (3)$$

Absorbed dose calculations were performed according to MIRD method:

$$D_{r_k} = \sum \tilde{A_h} \times S(r_k \leftarrow r_h) \quad (4)$$

$D(r_k)$ stated in (mGy) is the radiation absorbed dose to a target organ, r_k, from a source organs, r_h and the $S(r_k \leftarrow r_h)$ expressed in [mGy/(MBq s^{-1})], is the specific absorbed fraction of energy for the target organ. In this study the S-values for ^{99m}Tc are taken from the OLINDA/EXM software.

Results and discussion

According to the labeling results, H_3PO_4 was the suitable mobile phase for separating the reaction components and determining the radiochemical purity 93%. The biodistribution of ^{99m}Tc-MAX in some different organs of balb/c mice up to 24 h after injection is given in Fig. 2.

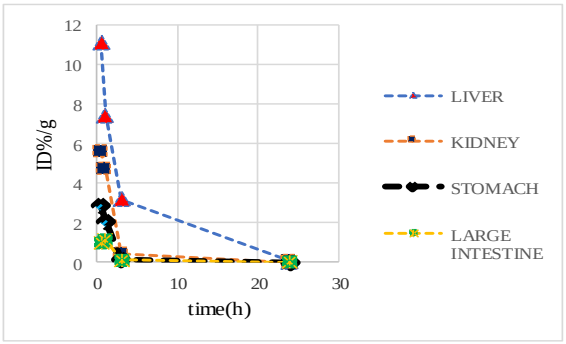

Figure 2. non-decay Corrected diagrams for each organ of balb/c mice after injection of 450µCi of ^{99m}Tc-MAX

The most common accumulation of radiopharmaceutical occurs in the liver and then the kidneys, lungs, spleen and bones. Also The absorbed dose in human organs after injection of the labeled complex is presented in Table 1. The highest absorbed dose of ^{99m}Tc-MAX was observed in the liver with 0.0011mGy / MBq.

Table (1): Absorption dose in different organs of the human body based on data from balb/c mice

organs	Dose(mGy/MBq)	±SD
Liver	1.10E-03	3.6E-05
Kidney	6.60E-05	7.36E-07
Spleen	1.20E-04	1.02E-06
Bone	6.70E-05	1.63E-06
Lung	5.70E-05	1.35E-06

Conclusions

Dosimetry is an important a part of nuclear medicine to assessment bio-distribution and pharmacokinetics of adminestrated radiopharmaceuticals. In fact, the method can be effective in reducing the dose received by the animal and its generalization to the human body based on the stated characteristics. during this study, the MIRD dosimetry technique was used for the evaluation of the novel ^{99m}Tc-MAX on balb/c mice. as expected, the best-absorbed dose of ^{99m}Tc-MAX was determined within the liver with 0.0011 mGy/MBq. according to the received very important organs absorbed dose, ^{99m}Tc-MAX can be effective in diagnosing diseases of the reticuloendothelial system and lymph nodes.

References

[1] T. Beyer et al. *What scans we will read: imaging instrumentation trends in clinical oncology*. Cancer Imaging. 20, 38 (2020).
[2] S. Dorbala et al. *Single Photon Emission Computed Tomography (SPECT) Myocardial Perfusion Imaging Guidelines: Instrumentation, Acquisition, Processing,*

and Interpretation. Journal of Nuclear Cardiology. 25, 1784 (2018).
[3] PL. Tilkemeier et al. *ASNC Imaging Guidelines for Nuclear Cardiology Procedures: Standardized reporting of nuclear cardiology procedures.* J Nuc Cardiol. 24, 2064 (2017).
[4] M. Morais et al. *Site-specific chelator-antibody conjugation for PET and SPECT imaging with radiometals.* Drug Discov Today Technol. 30, 91 (2018).
[5] A. Boschi et al. *A Picture of Modern Tc-99m Radiopharmaceuticals: Production, Chemistry, and Applications in Molecular Imaging*. Appl. Sci. 9, 2526 (2019).
[6] D. Papagiannopoulou, Technetium-99m radiochemistry for pharmaceutical applications. 60, 502 (2017).
[7] E. Sattarzadeh et al. *^{68}Ga-radiolabeled magnetic nanoparticles for PET–MRI imaging.* Journal of Radioanalytical and Nuclear Chemistry. 317, 1333 (2018).
[8] ES. Khameneh et al. *Preparation of dual-modality yttrium-90 radiolabeled nanoparticles for therapeutic investigation.* Radiochimica Acta. 106, 897 (2018).
[9] H. Tayeri et al. *Optimized production, quality control and biological assessment of ^{68}Ga-bleomycin as a possible PET imaging agent.* International Journal of Radiation Research. 18, 235 (2020).
[10] S. Kakaei et al. *Targeted Drug Delivery of Teniposide by Magnetic Nanocarrier.* Current Nanoscience. 16, 608 (2020).
[11] S. Kakaei et al. *Preparation and application of Fe_3O_4@Acetamidoxanthate as a unique nanosorbent in heavy metal removing*. Main Group Chemistry Preprint. 1-11 (2021).