SUMMARY

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Radiopharmaceuticals are preparations of adequately constant composition, radiochemical and radionuclidic purity and uniformity of physiological action for use in nuclear medicine as a diagnostic or therapeutic agent. Nearly about 80% of all radiopharmaceuticals used in nuclear medicine are ^{99m}Tc-labeled compounds. The reason for such a permanent position of technetium-99m in clinical use is its extremely favourable physical and radiation characteristics. The six hours, physical half life and the free of beta particles permit the administration of millcurie amounts of ^{99m}Tc-radioactivity without significant radiation dose to the patient. In addition, the monochromatic 140 KeV photons are readily collimated to give images of superior spatial resolution. Technetium-99m is readily available in a sterile, pyrogen free state from ^{99}Mo/^{99m}Tc generator.

The goal of this study is the organic synthesis of ortho, meta and para-amino hippuric acid iminodiacetic acid analogs and labelling them with technetium-99m to be used as renal function agents.

The factors affecting the labelling yield were studied and the labelled complexes were evaluated radiochemically and biologically. This thesis was divided into three chapters, chapter one includes the general introduction, chapter two includes the organic synthesis of three iminodiacetic acid (IDA) derivatives and characterization of the synthesized compounds, chapter three includes labelling of the synthesized AHIDA derivatives with technetium-99m and study its biological distribution.

The results obtained from this study can be summarized as follows:

Chapter I

It deals briefly the following topics:

Radionuclide produced in a reactor, in a cyclotron and radionuclide generator. Among the important radionuclides produced in a reactor is technetium-99m isotope. The chemical and nuclear properties of technetium-99m and its availability from $^{99}Mo/^{99m}Tc$ generator led to the preparation of different groups of ^{99m}Tc-radiopharmaceuticals used in diagnostic procedures in nuclear medicine.

Chapter II

Synthesis, characterization and evaluation of iminodiacetic acid derivatives ortho, meta and para-aminohippuric acid analogs as renal function agents. Several substituted amino hippuric acid iminodiacetic acid had gained much popularity in the recent years as an important class of imaging agents. A number of studies have been performed to evaluate its chemical properties and also to improve its biological behavior. Because AHIDA derivatives are not available commercially it is necessary to synthesis them locally.

The following AHIDA derivatives were synthesized:

1- ortho aminohippuric acid iminodiacetic acid

2- meta aminohippuric acid iminodiacetic acid

3-para aminohippuric acid iminodiacetic acid

The above compounds were synthesized following Burn's method which depends on the condensation reaction between nitrilotriacetic acid monoanhydride and ortho aminohippuric acid, meta aminohippuric acid and para aminohippuric acid in pyridine to give reaction yield 79%, 65% and 69% respectively. The different analytical techniques such as m.p.,

I.R, ^{1}H-NMR and mass spectroscopy were used for characterization the synthesized compounds.

Chapter III

Labeling of iminodiacetic acid derivatives of ortho, meta and para aminohippuric acid analogs as renal function agents with technetium-99m. AHIDA derivatives were labelled with technetium-99m using tin reduction method in which the chelates react with the reduced technetium-99m at pH 5.7. The percent labeling yields for all the synthesized AHIDA derivatives were found equal to 95.8%, 96.3% and 98.9% for OAHIDA, MAHIDA and PAHIDA respectively. The different parameters affecting the labeling yield were studied such as the amount of substrate Sn(II) content, the pH of reaction mixture, and reaction time. The optimum conditions for the preparations of ^{99m}Tc-ortho, meta and para-AHIDA complexes were as follow:

Exactly weigh 10 mg of o, m and p-aminnohippuric acid analogs , 0.25mg $SnCl_2.2H_2O$, pH of reaction mixture 5.7 and 15 min reaction time. The radiochemical purity and labelling yield of ^{99m}Tc-AHIDA complexes were estimated using instant thin layer chromatography (ITLC-SG) in acetonitrile : water (3:1) and saline as eluants. These ^{99m}Tc-AHIDA complexeswere found stable for 6h after labelling with ^{99m}Tc (> 95%). The biodistribution of the in-house formulated AHIDA derivatives after labelling with technetium-99m were evaluated in mice. The percent administrated dose measured in urine of mice for ^{99m}Tc-o, m and p-AHIDA complexes were equal to 60, 56 and 87 respectively after 60 min post injection. The organ distribution studies in mice confirmed that ^{99m}Tc-p-AHIDA complex has excellent renal excretion characteristics compared to the other derivatives.