بسم الله الرحمن الرحيم

شبكة المعلومـــــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

﴿ قـــسـم ﴾

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
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15 – 25c and relative humidity 20-40 %

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بالرسالة صفحات

لم ترد بالأصـــل

STUDIES ON THE LABELLING OF SOME ORGANIC COMPOUNDS WITH TECHNETIUM – 99m FOR RENAL IMMAGING

Thesis

Submitted by

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to

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2001

Book


بسم الله الرحمن الرحيم
قالوا
سبحانك لا علم لنا إلا ما علمتنا
إنك أنت العليم الحكيم
صدق الله العظيم
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To :

my mothers (mother & taunt)
my brothers, my husband,
my sons (Aiya, Ahmed and Yara)
and my friends.

Aim of the work

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Radiopharmaceuticals have wide spread applications for diagnosis and therapy in nuclear medicine. Among the various types of radiopharmaceuticals used for kidney function studies are the technetium-99m labeled aminohippuric acid derivatives. ^{131}I-ortho-iodohippuric acid is the gold standard for kidney function studies. It has disadvantages of imparting a relatively high absorbed radiation ($t_{1/2}$= 8.03 d, γ = 340 KeV, β^-= 0.61 MeV) dose to the patient at low diagnostic doses. Although ^{123}I-ortho-iodohippuric acid lowers the radiation dose ($t_{1/2}$= 13.2 h, γ = 159 KeV) to the patient. It is not available at a reasonable coast for routine use. Technetium-99m has ideal physical and nuclear properties for many applications in nuclear medicine, by its virtue of its short half life and favorable radiation characteristics ($t_{1/2}$= 6.02, γ = 140 KeV). It is difficult to label ortho-aminohippuric acid by technetium-99m due to the lack of donor atoms or chelating groups to bind ^{99m}Tc.

To prepare ^{99m}Tc aminohippuric acid derivatives for renal function studies, chelating moiety, iminodiacetic acid (IDA) can be attached to aminohippuric acid molecule to bind with ^{99m}Tc.

The aim of the present work is to synthesize the aminohippuric acid derivatives:-

(1)ortho aminohippuric acid iminodiacetic acid

(2)meta aminohippuric acid iminodiacetic acid

(3)para aminohippuric acid iminodiacetic acid

The synthesised compounds will be characterized using different analytical techniques (elemental analysis, IR, ^{1}H-NMR and mass spectroscopy) and then labelled with technetium-99m by direct labeling

method. The thesis also aims to study the factors affecting the percent labeling yield of AHIDA derivatives with technetium-99m. These factors include, the amount of AHIDA derivatives, the Sn(II) content, pH, and the reaction time. The ^{99m}Tc-AHIDA complexes will be evaluated biologically in the experimental animals (mice).

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.,