

DEDICATION

**To my husband
Abdalkareem, for his
support, and
encouragement.**

ACKNOWLEDGEMENT

I am greatly indebted to my supervisor Dr Adam K. Sam for endless encouragement and invaluable support which make this study possible.

I would like also to thank the staff of nuclear medicine in the Radiation & Isotope Center of Khartoum for their help and support.

I am sincerely indebted to Mr. Mohammed Mohammed Omer, Mr. Mohammed Elnima & Mr. Abdalmonim Mahgoub, College of Medical Radiological Sciences, Sudan University of Science & Technology.

ABSTRACT

Indium-111 is a common radioisotope in Nuclear Medicine; it ranks second radioisotope after ^{99m}Tc , and it is used to prepare a number of radiopharmaceuticals for a number of diagnostic applications. Because of non-availability of textbooks or monographs on ^{111}In -radiopharmaceuticals in our University and hospital libraries in Sudan, this research has been conducted as an attempt to avail a comprehensive review containing the relevant and most needed knowledge that related to the usage of ^{111}In in Nuclear Medicine from Internet and Journals in the field of NM and pharmacy. Currently, ^{111}In is yet to be introduced in our centers in Sudan as an indicator nuclide. However, there is a great need for using this important radioisotope. This study presents a comprehensive coverage on indium chemistry, physical properties, production and decay, as well as preparation, quality control procedures, administration, pharmacokinetics (biodistribution, mechanism of localization and clearance routes), indications, contraindications, side effects and radiation dosimetry of indium radiopharmaceuticals; namely Indium-111 chloride, ^{111}In -pentetate (DTPA), ^{111}In -oxyquinoline (oxine), ^{111}In -capromab pendetide (ProstaScint), ^{111}In - Imciromab pentetate (Myoscint), ^{111}In -Pentetreotide (Octreoscan) and ^{111}In -Satumomab pendetide (OncoScint).

الخلاصة

يعتبر الانديوم-111 من أكثر النظائر المشعة المستخدمة في الطب النووي، وهو يأتي في المرتبة الثانية بعد التكنيشيوم-99m من حيث الاستخدام. ويستخدم في وسم عدد من المواد الصيدلانية للاستعمالات التشخيصية.

نسبة لعدم توفر المراجع او المقالات عن هذا النظير ومواده الصيدلانية في مكتبت الجامعة والمستشفى في السودان، في هذا البحث نحاول بلستعرض شامل يحتوي على المعلومات المطلوبة والمتعلقة باستخدام الانديوم-111 ومواده الصيدلانية في الطب النووي من خلال شبكة المعلومات (الانترنت) والمجلات العلمية.

عموما، الانديوم-111 لم يتم ادخاله بعد في مراكزنا في السودان كعنصر لسلسي. ومع ذلك هناك حاجة كبيرة لاستخدام هذا العنصر الهام الذي يكشف الكثير من الامرض. هذا البحث قدم عرض شامل عن الانديوم ومواده الصيدلانية مثل خصائصه الكيميائية والفيزيائية، طرق انتاجه وتحلله، تحضيره، اجراءت ضبط الجودة، كيفية تعاطيها، (توزيعها داخل الجسم، طريقة تحديدها للعضو المراد تصويره، وطرق تخلى الجسم منها) دواعيها، موانعها، اثارها الجانبية، قياس الجرعة الممتصة من الانديوم-111 ومواده الصيدلانية الاتية اسمائها:

Indium-111 chloride, ^{111}In - pentetate (DTPA),
 ^{111}In -oxyquinoline (oxine), ^{111}In -capromab pendetide
(ProstaScint), ^{111}In -Imciromab pentetate (Myoscint),
 ^{111}In -Pentetreotide (Octreoscan) and ^{111}In -Satumomab
pendetide (OncoScint).

Table of Contents

Dedication	I
Acknowledgment	II

Abstract (English)	III
Abstract (Arabic)	IV
Table of contents	V
List of Tables	VIII
List of Figers	IX
Abbreviations	X
CHAPTER ONE	
Introduction	1
CHAPTER TWO	
2.1 Introduction	4
2.2 Aqueous chemistry of Indium	7
2.3 The uses of Indium in organic chemistry	8
2.4 Production and decay of ^{111}In	11
CHAPTER THREE	
3.1 Introduction	16
3.2 Biologic test	17
3.2.1 Sterility	17
3.2.1.1 Colony culture	18
3.2.1.2 Radiorespirometry	18
3.2.2 Pyrogenicity	18
3.2.2.1 United State Pharmacopeia (USP) test	19
3.2.2.2 Limulus Amebocyte Lysate (LAL) test	19
3.2.3 Toxicity	20
3.2.4 Biodistribution	20
3.3 Physicochemical test	20
3.3.1 Physical Appearance	21
3.3.2 Particle size	21
3.3.3 pH	22
3.3.4 Radionuclidic Purity	22
3.3.4.1 Gamma scintillation spectroscopy	23
3.3.4.2 Radionuclidic Purity of ^{111}In	24
3.3.5 Radiochemical Purity	25
3.3.5.1 Chromatography	25
3.3.5.2 Gel Filtration	29
3.3.5.3 Electrophoresis	29
3.3.6 Chemical Purity	28
Chapter Four	
4.1 Introduction	30
4.2 Indium-111 chloride	30
4.2.1 Chemistry	30
4.2.2 Quality Control	32
4.2.3 External radiation	33
4.2.4 Emergency over view	33

4.2.5	Pharmacokinetics	34
2.2.6	Indication, Usage and Precaution	34
4.2.7	Radiation Dosimetry	36
4.3	Indium-111 pentetreotide	36
4.3.1	Chemistry	36
4.3.2	Quality Control	40
4.3.3	Pharmacokinetics	40
4.3.4	Administration	41
4.3.5	Biodistribution	42
4.3.6	Indication and Usage	42
4.3.7	Adverse reaction	45
4.3.8	Disposal consideration	45
4.3.9	Radiation Dosimetry	46
4.4	ProstaScint (Capromab pendetide)	47
4.4.1	Chemistry	47
4.4.2	External Radiation	48
4.4.3	Pharmacodynamics	48
4.4.4	Indication and Usage	49
4.4.5	Imaging precautions	51
4.4.6	Distribution	51
4.4.7	Information for Patients	53
4.4.8	Heterologous Protein Administration	53
4.4.9	Drug Interaction	54
4.4.10	Drug /Laboratory Test Interactions	54
4.4.11	Adverse Reactions	55
4.4.12	Administration	56
4.4.13	Elimination	56
4.4.14	Image Acquisition and Interpretation	56
4.4.15	Radiation Dosimetry	58
4.5	Myoscint (Imciromab pentetate)	60
4.5.1	Chemistry	60
4.5.2	Pharmacokinetics	60
4.5.3	Pharmacodynamics	61
4.5.4	Administration	62
4.5.5	Localization of myocardial infarction	62
4.5.6	Indication and Usage	64
4.5.7	Information for Patients	65
4.5.8	Drug Interaction	66
4.5.9	Image Acquisition and Interpretation	67
4.5.10	Radiation Dosimetry	69
4.6	Indium-111oxyquinoline (oxine)	71
4.6.1	Chemistry	71
4.6.2	Procedure for labeling Leukocyte with In-111 oxyquinoline	71

4.6.3	Quality Control	75
4.6.4	Pharmacokinetics	75
4.6.5	Administration	75
4.6.6	Indication, Usage and Precautions	77
4.6.7	Adverse Reaction	80
4.6.8	Radiation Dosimetry	80
4.7	Indium-111 pentetate (DTPA)	83
4.7.1	Chemistry	83
4.7.2	Preparation	84
4.7.3	Pharmacokinetics	85
4.7.4	Indication, Usage and Precautions	86
4.7.5	Paediatric Use	87
4.7.6	Adverse Reaction	88
4.7.7	Administration	88
4.7.8	Radiation Dosimetry	88
4.8	OncoScint (Satumomab pentetide)	90
4.8.1	Chemistry and Pharmacokinetics	90
4.8.2	Quality Control	91
4.8.3	Biodistribution	92
4.8.4	Indication	93
4.8.5	Side Effects	96
	Conclusion	98
	Recommendations	99

List of Tables

Table 2.1	Chemical properties of Indium	5
Table 2.2	Physical properties of Indium	6

Table 2.3	Decay properties of ¹¹¹ In	12
Table 2.4	¹¹¹ In radiation attenuation of lead shielding	13
Table 2.5	The decay table of ¹¹¹ In	14
Table 2.6	The remaining fraction of ¹¹¹ In activity in pre and post calibration day	15
Table 4.1	Specifications of ¹¹¹ In-chloride	31
Table 4.2	Absorbed radiation dose estimates for paediatric patients from ¹¹¹ In –chloride	36
Table 4.3	Absorbed radiation dose estimates for Adults from ¹¹¹ In-chloride	36
Table 4.4	Specification of ¹¹¹ In-Pentetreotide	37
Table 4.5	The estimated radiation dose to the average adult (70kg) from intravenous administration of Octreoscan	46
Table 4.6	Estimated absorbed radiation dose to the average adult patient from intravenous injection of ProstaScint labeled with 5mCi of ¹¹¹ In	59
Table 4.7	Radiation dosimetry of Indium-111 MYOSCINT	70
Table 4.8	Radiation dose estimate in a 70kg human for 18.5 MBq, 500 μ Ci at expiry of ¹¹¹ In (99.25%) oxyquinoline labeled leukocytes with Indium-114m/114 (0.25%)	81
Table 4.9	Contribution of impurities Indium-114m/114 to radiation dose estimate in a 70kg human from ¹¹¹ In-oxyquinoline	81
Table 4.10	Estimate of total dose in mGy and Rads in respective organs from ¹¹¹ In –oxyquinoline	82
Table 4.11	Estimated absorbed radiation dose from 18.5 MBq ¹¹¹ In -pentetate	89

List of figures

Figure 2.1	Indium-111 Decay scheme	12
Figure 3.1	Thin Layer Chromatographic strip	27
Figure 4.1	Structural formula of Pentetreotide	38
Figure 4.2	Structure of ¹¹¹ Indium- DTPA	84
Figure 4.3	ITLC-Silca Gel strip	92

Abbreviations

Ag	: Silver
ALI	: Annual limit of intake
AMI	: acute myocardial infarction
Cd	: Cadmium
CPM	: counts per minute
CPS	: counts per second
CSF	: Cerebrospinal Fluid
CT	: Computed Tomography
DTPA	: diethylenetriamine pentaacetic acid
ECG	: electrocardiographic
FDA	: Food and Drug Administration
HAMA	: human anti-mouse antibodies
HPLC	: high performance liquid chromatography
In	: Indium
ITLC	: Instant Thin Layer Chromatography

Kg	: kilogram
LAL	: Limulus Amebocyte Lysate
LPP	: Leukocyte Poor Plasma
LRP	: Leukocyte Rich Plasma
MABs	: Murine monoclonal antibodies
MBq	: mega Becquerel
mCi	: millicurie
mGy	: milligray
MI	: myocardial infarction
MoAb	: monoclonal antibody
MRI	:Magnetic Resonance Imaging
mSv	: millisevert
n	: neutron
NM	: Nuclear Medicine
NRC	: Nuclear Regulatory Commission
P	: proton
PSA	: Prostate Specific Antigen
PSMA	: Prostate Specific Membrane Antigen
QA	: Quality Assurance
QC	: Quality Control
rad	: Radiation Absorbed Dose
RCP	: Radiochemical Purity
rem	: Radiation Equivalent to Man
RIA	: Radioimmunoassay
RICK	: Radiation and Isotope Center -Khartoum
SPECT	: Single Photon Emission Computed Tomography
99mTc	: Technetium-99m (m-metastable)
TPN	: Total Parenteral nutrition
UA	: unstable angina pectoris
USP	: united state pharmacopeia
WBC	: White Blood Cells
Zn	: Zinc
μCi	: microcuries

