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A Review on Rediopharmaceutical for Therapeutic and Dignostic

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ABSTRACT: A radiopharmaceutical is a preparation intended for in-vivo use that contains a radionuclide in the form of a simple sal or a complex. It may exist as a solid, liquid, gas or a pseudo gas. The chemical and physical identity and a form of a radiopharmaceutical are very important because in each case, once administered the radiopharmaceutical is intended to target certain tissues, binding sites, biochemical pathways. A radiopharmaceutical can be used for either diagnostic or therapeutic purposes depending on its specific physicochemical and radiation properties. The characteristic of radioactive decay is what makes radioisotopes useful in their medical applications; however, different applications will take advantage of radioactive emissions in different ways. Radioactive materials are regularly used to treat medical conditions, diagnosis pathology, visualize and measure physiological functions, and localize structures and pathways. This review describes both the therapeutic as well as diagnostic uses of radiopharmaceuticals.

I. INTRODUCTION

By definition a radiopharmaceutical is a radioactive pharmaceutical agent that is used for diagnostic or therapeutic procedures. Over the past three decades the discipline of nuclear. 9 "RADIOPHARMACEUTICAL FOR THERAPEUTIC AND DIAGNOSTIC APLLICATION" pharmacy or radio- pharmacy has become highly specialized and contributed positively to the practice of nuclear medicine. Nuclear pharmacy the first specialty in pharmacy recognized in 1978 by the Board of the Pharmaceutical specialties focuses on the safe and effective use of radioactive drugs or radiopharmaceuticals. The application of radiopharmaceuticals is divided into two major areas, diagnostic and therapeutic the diagnostic side is well established. While the therapeutic side of nuclear medicine is evolving e.g. more than 100 radiopharmaceutical products are available with the largest proportion of these having application in cardiology (e.g. myocardial perfusion,) oncology (e.g. tumor imaging and localization) and neurology (e.g. cerebral perfusion) diagnostically they are also used for infection imaging and nephrology. Historically nuclear medicine has been well established as a therapeutic modality for thyroid cancer, Graves's disease, hyperthyroidism and bone pain palliation associated with skeletal metastasis. However, recent radiopharmaceuticals e.g. iodine-131 or iodine 125 labelled MIBG (m-iodobenzyl guanidine) are being used to treat pheochromocytoma and neuroblastoma and radiolabeled somatostatin analogues are used for the treatment of neuro endocrine tumors e.g. neuroblastoma. A radiopharmaceutical consists of drug component and a radioactive component. Most radio nuclides contain a component that emits gamma radiation. Substances that have the same number of protons but have varying numbers of neutrons are called radio nuclides. Radio nuclides may be stable or unstable those that are unstable are radioactive because their nuclei undergo rearrangement while changing to a stable state and energy is given off. An important distinction between radiopharmaceuticals and traditional drugs is lack of pharmacological activity on the part of radiopharmaceuticals. For intensive purposes radiopharmaceuticals have been used as tracers of physiologic processes. There huge advantage is that their radioactivity allows noninvasive external monitoring or targeted therapeutic irradiation with very little effect on the biologic processes in the body indeed radiopharmaceuticals have an excellent safety record and their incidence of adverse effects is extremely low. Radiopharmaceuticals play an important role in the field of medicine. The global radiopharmaceutical applications market is expected to grow from $ 4.9 billion in 2010 and to $ 7.9 billion in 2011, at a CAGR of 9.25% from 2010 to 2015. There is a significant increase in the global demand of radiopharmaceuticals, with the increasing incidences of cardiac, neurological and cancer disease. Radiopharmaceuticals, as the name

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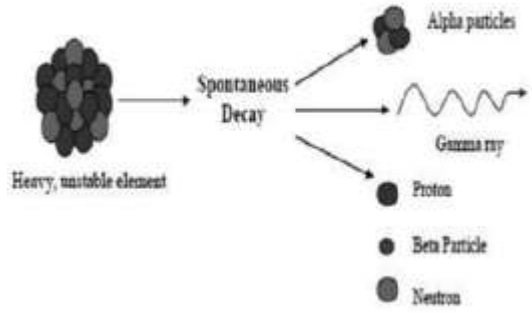
suggests, are pharmaceutical formulations consisting of radioactive substances (radioisotopes and molecules labelled with radioisotopes), which are intended for use either in diagnosis or therapy or diagnosis. Radiopharmaceuticals are essential components of nuclear medicine practice. A modality where radiopharmaceuticals are administered to patients for diagnosing, managing and treating number of diseases. A variety of radiopharmaceuticals are being developed which have different targeting mechanisms, routes and forms of administration. Some are given in the simple salt form, or attached to more complex molecules. It has been used extensively in the field of nuclear medicine as non-invasive diagnostic imaging agents to provide both functional and structural information about organs and diseased tissues. They may be given to the patient in several ways, e.g. orally, parenterally, or placed into the eye or the bladder Radiopharmaceuticals are used for diagnosis or therapeutic treatment of human diseases; hence nearly 95% of radiopharmaceuticals are used for diagnostic purposes, while the rest is used for therapy. Radiopharmaceuticals usually have no pharmacologic effects, as they are used in tracer quantities. There is no dose-response relationship in this case, which thus differs significantly from conventional drugs.

DEFINATIONS AND TERMINOLOGY



Radiopharmaceutical refers to any medicinal or pharmaceutical product, which when ready for use contains one or more radionuclides (radioactive isotopes) intended for human use either for diagnosis or therapy. Nuclide is an elemental species characterized by its mass number 'A', (the sum of the number of protons and neutrons in its nucleus), its atomic number 'Z' (number of protons which is also same as number of electrons in a neutral atom) and also by its nuclear energy state Isotopes of an element are nuclides with the same atomic number 'Z' but different mass numbers 'A'. They occupy the same place in the periodic table and have similar chemical properties. Radionuclide: Nuclides containing an unstable arrangement of protons and neutrons that transform spontaneously to either a stable or another unstable combination of protons and neutrons with a constant statistical probability by emission of radiation. These are said to be radioactive and are called radionuclides. Radioactivity: The phenomenon of emission of radiation owing to the spontaneous transformation or disintegration of the radionuclide is known as 'Radioactivity'. However, the term radioactivity is also used to12CRadionuclide: Nuclides containing an unstable arrangement of protons and neutrons that transform spontaneously to either a stable or another unstable combination of protons and neutrons with a constant statistical probability by emission of radiation. These are said to be radioactive and are called radionuclides. Express the physical quantity (activity or strength) of this phenomenon. The radioactivity of a preparation is the number of nuclear disintegrations or transformations per unit time. They put out radiation, mostly in the form of alpha and beta particles that target the affected areas. They're most often used in small amounts for imaging tests, but larger doses can be used to deliver radiation

THERAPEUTIC APPLICATIONS

Therapeutic Radiopharmaceuticals are radio labeled molecules designed to deliver therapeutic doses of ionizing radiation to specific diseased sites. Therapeutic applications of radiopharmaceuticals have emerged from the concept that certain radio nuclides possessing particulate emission such as alpha and beta radiations or low-energy low-range electrons (Auger electrons) possess the ability to destroy diseased tissues. The dual facets of these agents constitute either curative or palliative measures in treatment modalities. Contrary to the usual requirement that intravenous injections be true solutions, some radiopharmaceuticals are deliberately particulate to achieve site-specific localization of radioactivity in the body. These specialized dosage forms permit imaging of, for example, the principal organs of the reticulo-endothelial system (liver, spleen, and bone marrow) with radio labeled colloidal particles, the cardiac blood pool with radiolabeled red blood cells, and lung perfusion with albumin aggregates. Radioisotopes may be used internally or externally. If the radioisotopes are used externally or as implants in sealed capsules in a tissue, the dose could be terminated by removal of the sources. If

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they are given internally as unsealed source, the dose cannot be stopped by removal of the source. The total dose in therapeutic applications may be calculated on the basis of effective half- life of the isotope, concentration of the isotope and the type and energy of radiation emitted In therapeutic uses, the deleterious effect of high-energy radiation on human cells is used. Therapeutic radioisotopes are generally longer lived than those in diagnostic use and possess higher energies. 14 “radiopharmaceutical for therapeutic and diagnostic apllication" A few examples of how radioisotopes are used for therapeutic purposes are summarizedbelow.

TABLE No. I: RADIOPHARMACEUTICALS AND ITS PRIMARY USE

RADIOPHARMACEUTICAL	PRIMARY USE
Fluorine-18 FDG	Positron emission tomography imaging
Gallium-67	Soft-tissue tumour and inflammatory process imaging
Indium-111 pentetate (DTPA)	Imaging of cerebral spinal fluid (CSF)kinetics
Indium-111 capromab pendetide	Monoclonal antibody for imaging prostate cancer
Indium-111 imciromab pentetate	Monoclonal antibody for diagnosis of myocardial Necrosis
Indium-111 pentetreotide	Imaging of neuroendocrine tumours
Indium-111 satumomab pendetide	Imaging of metastatic disease associated with colorectal and ovarian cancer
I-123 sodium iodide	Thyroid imaging & uptake
I-125 iothalamate	Measurement of glomerular filtration
I-125 human serum albumin (RISA)	Plasma volume determinations

DIAGNOSTIC NUCLEAR IMAGING AGENTS

99mTc-Labelled.Radiopharmaceuticals

Many 99mTc-containing radiopharmaceuticals have become available for clinical use, including perfusion agents for the heart [99mTc-MIBI (Cardiolite®)] and the brain [99mTc-ECD (Neurolite®) and 99mTc- HMPAO (Ceretec®)], as well as an agent that images renal function (99mTc-MAG3)25. In this section we discuss some ofthe 99mTc-labelled radiopharmaceuticals. 99mTc-HMPAO (99mTc-hexamethyl-propylene amine oxime) 99mTc-HMPAO is a lipophilic compound with the ability to cross the BBB and to accumulate in the brain proportional to blood flow. The mechanism of 99mTc-HMPAO retention in tissues is related to its conversion from a lipophilic form to hydrophilic derivatives. The cellular content of glutathione, a reducing agent present in the CNS, appears to be one of the determinants of 99mTc-HMPAO retention through the conversion mechanisms. Other factors appear to mediate the flow-independent accumulation of99mTc-HMPAO, including changes in redox state of cells, metabolic alterations, and formation of a complex with proteins in subcellular organelles. The nature of the cells in which 99mTcHMPAO conversion and its subsequent retention take place is still undetermined. In vitro studies performed in brain slices do not allow the establishment of a cellular localization of 99mTcHMPAO retention. Studies in neuronally-enriched cultures show a moderate degree of retention in this cell type. Astrocytes, another important cell type in the CNS, outnumber neurons by a factor of five to ten; they possess specialized processes called end-feet which almost entirely cover the surface of intraparenchymal capillaries. This feature suggests that astrocytes could represent a privileged site of 99mTc-HMPAO uptake and retention as it penetrates within the brain parenchyma.

Indium Labelled Radiopharmaceuticals:

[Indium-111-(111In)-DTPA] Octreotide Peptides have fast clearance, rapid tissue penetration and low antigenicity and can be produced easily. For evaluation of tumour receptor expression, different radiolabelled peptide analogues, such as somatostatin, cholecystokinin, gastrin, bombesin, substance-p, vasoactive intestinal peptide and neuropeptide analogues have been introduced. The most commonly used receptor-targeting agents are the variety of analogues of somatostatin36. [Indium-111-(111In)-DTPA] octreotide was the first radiolabelled peptide approved by FDA for use in tumour imaging. Octreotide is an 8-amino acid analogue of somatostatin, which binds on specific receptors constituted by membrane glycoproteins. Beyond diagnostic applications, octreotide may be useful in peptide receptor radionuclide therapy using high activities of 111In37.

Labelling and Packaging Labelling : The label on the container should state: • The name of the product and the name of the radionuclide; • Any product identification code; • The name of the manufacturer; • An identification number (batch number); SHRI BHAGWAN COLLEGE OFPHARMACY aurangabad. 33 “radiopharmaceutical for therapeutic and diagnostic APLLICATION" • For liquid preparations, the total radioactivity in the container, or the radioactive concentration per milli litre, at a stated date and, if necessary, hour, and the volume of liquid in container; • For solid preparations, such as freeze-dried preparations, the total radioactivity at a stated date and, if necessary, hour; • For capsules, the radioactivity of each capsule at a stated date and,

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if necessary, hour and the number of capsules in the container; • In addition, the label on the package should state: qualitative and quantitative composition; • The route of administration; • The expiry date; • Any special storage conditions. Information on batch coding should be provided to the authorities. Packaging The suitability of packaging material for the product and for the labelling procedure to be carried out should be described. It may be necessary to describe special radiation shielding. Package leaflets Package leaflets play a particularly important role for semi manufactured Products such as preparation kits and should include: • The name of the product and a description of its use; • A list of the contents of the **STORAGE :** Store in an airtight container in a place that is sufficiently shielded to protect personnel from exposure to primary or secondary emissions and that complies with national and international regulations concerning the storage of radioactive substances. During storage, containers may darken due to irradiation. Such darkening does not necessarily involve deterioration of the preparations. Radiopharmaceutical preparations are intended for use within a short time and the end of the period of validity must be clearly stated. Radiopharmaceuticals intended for parentral use should be stored in such a manner so that pharmaceutical purity of the product is maintained.

II. SUMMART & CONCLUSION :

Nowadays there are different types of radiopharmaceuticals are available and having an important role in diagnosis of disease. Recently, however, there has been a significant growth of this branch of nuclear medicine with the introduction of a number of new radionuclides and radiopharmaceuticals for the treatment of metastatic bone pain, neuroendocrine and other tumours. Today the field of radionuclide therapy is going through an extremely interesting and exciting phase and is poised for greater growth and development in the coming years

SOME OF THE ADVANAGES FROM THE ABOVE RESULTS

a)Eliminated Mechanical Linkages
b)It can make Engine clean , efficient and responsive
c)ECU can control the valve velocity acceleration and deceleration of valve
d)Reduction in size and weight
e)Fuel economy Increases
f)Power and Torque increase

kit; • The name and the address of the manufacturer of the kit; • Identification and quality requirements concerning the radiolabelling materials that can be used to prepare the radiopharmaceutical; • Directions for preparing the radiopharmaceutical including range of activity and volume and a statement of the storage requirements for the prepared radiopharmaceutical; • A statement of the useful life of the prepared radiopharmaceutical; • Indications and contra-indications in respect of the prepared radiopharmaceutical; • Warnings and precautions in respect of the components and the prepared radiopharmaceutical including radiation safety.aspects.

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