A radiopharmaceutical is a preparation intended for in-vivo use that contains a radionuclide in the form of a simple salt 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.

**Keywords:** Radiopharmaceutical, in-vivo, Radionuclide, Radioactive decay, Radioactive emission

**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 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. tumour 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 non invasive 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[1].

THERAPEUTIC APPLICATIONS

Therapeutic Radiopharmaceuticals are radio labelled 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 labelled 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 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[2].

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[3]. A few examples of how radioisotopes are used for therapeutic purposes are summarized below.

Non-Hodgkin’s Lymphoma Therapy

Therapeutic treatments are given using a radioisotope attached to an antibody to deliver radioactivity to specific cells are called radioimmunotherapy (RIT). Radiopharmaceuticals I-131 tositumomab and Y-90 ibritumomab and Y90epratuzunab are used to treat Non-Hodgkin’s lymphoma[3].

Treatment of Cancers and Tumours[4]

- Americium 241 used as antineoplastic.
- Californium 252 used as antineoplastic."
- Cobalt 60 used as antineoplastic.
- Gold1 94 used as antineoplasic.
- Holmium 66 (26 h) being developed for diagnosis and treatment of liver tumours.
- Iodine-125 (60 d) used in cancer brachytherapy (prostate and brain).
- Iodine 123 used as antineoplastic.
- Iodine 131 used as antineoplastic.
- Rhenium 186 (3.8 d) used for pain relief in bone cancer. Beta emitter with weak gamma for imaging.
- Iridium 192 (74 d) supplied in wire form for use as an internal radiotherapy source for cancer treatment (used then removed).
- Palladium 103 (17 d) used to make brachytherapy permanent implant seeds for early stage prostate cancer.
- Samarium 153 (47 h) Sm-153 is very effective in relieving the pain of secondary cancers lodged in the bone, sold as Quadramet. Also very effective for prostate and breast cancer.
- Strontium 89 (50 d) very effective in reducing the pain of prostate and bone cancer
- Yttrium 90 (64 h) used for cancer brachytherapy and as silicate colloid for the relieving.

Treatment of Thyroid Disease with Iodine 131

- I-131 is therapeutically used for to treat thyroid cancer, hyperthyroidism (including Graves’ disease, toxic multinodular goiter, and toxic autonomously functioning thyroid nodules), and Nontoxic
multinodular goiter. I-131 has a physical half-life of 8.1 days. It emits beta particles (average energy of 0.192 MeV, maximum energy of 0.61 MeV) to ablate any remaining tissue, as well as to treat residual thyroid cancer or metastatic thyroid cancer.

**Palliative Treatment of Bone Metastasis**
- Various radioisotopes and pharmaceuticals are used to deliver palliative treatment of bone metastases, including samarium-153 (Sm-153), strontium-89 (Sr-89) chloride, and phosphorus-32 (P-32) sodium phosphate. The two most common side effects occurring from radiopharmaceutical therapy for metastatic bone disease are initial increased bone pain (flare) and a decrease in WBC and platelet counts.

- Samarium-153 EDTMP (lexidronan): The most commonly used radioisotope for this treatment in the United States is Sm-153. Sm-153 has a physical half-life of 1.9 days and emits beta particles with an average energy of 0.23 MeV (maximum energy of 0.81 MeV). Sm-153 has a soft-tissue range of approximately 0.6mm, keeping radioactive damage to tissue localized in bone matter. Sm-153 also has a gamma ray emission of 103 keV, which allows diagnostic imaging of the radioisotope distribution to be performed. Sm-153 will localize specifically in osteoblastic sites (sites of bone proliferation). Sm-153 is administered intravenously.

- Strontium-89 chloride: Sr-89 incorporates itself into the bone similarly to calcium. Its primary area of localization is in areas of osteoblastic activity. Sr-89 has a physical half-life of 50.5 days and emits beta particles with an average energy of 0.58 MeV (maximum energy of 1.46 MeV). Sr-89 has a soft-tissue range of approximately 2.4mm, keeping radiation damage localized in the bone tissue.

- Phosphorous-32 sodium phosphate: P-32 is one of the first radioisotopes used for palliative treatment of bone metastases. It incorporates itself into the cortex of the bone as well as into the nucleic acids of growing bone matter. Its beta particle emission has an average energy of 0.70 MeV (maximum energy 1.71 MeV) and a soft tissue range of approximately 3.0mm, limiting damage to organs surrounding the skeleton. Its physical half-life is 14.3 days. P-32 can be administered orally or intravenously.

**Treatment of Arthritis**
- Erbium-169 (9.4 d): Use for relieving arthritis pain in synovial joints.
- Yttrium-90 (64 h): as silicate colloid for the relieving the pain of arthritis in larger synovial joints. Pure beta emitter.

**DIAGNOSTIC RADIOPHARMACEUTICALS**
- Every organ in our bodies acts differently from a chemical point of view. Doctors and chemists have identified a number of chemicals which are absorbed by specific organs. The thyroid, for example, takes up iodine, the brain consumes quantities of glucose, and so on. With this knowledge, radiopharmacists are able to attach various radioisotopes to biologically active substances. Once a radioactive form of one of these substances enters the body, it is incorporated into the normal biological processes and excreted in the usual ways.
- Diagnostic radiopharmaceuticals can be used to examine blood flow to the brain, functioning of the liver, lungs, heart or kidneys, to assess bone growth, and to confirm other diagnostic procedures. Another important use is to predict the effects of surgery and assess changes since treatment.
- The amount of the radiopharmaceutical given to a patient is just sufficient to obtain the required information before its decay. The radiation dose received is medically insignificant. The patient experiences no discomfort during the test and after a short time there is no trace that the test was ever done. The non-invasive nature of this technology, together with the ability to observe an organ functioning from outside the body, makes this technique a powerful diagnostic tool.
- A radioisotope used for diagnosis must emit gamma rays of sufficient energy to escape from the body and
it must have a half-life short enough for it to decay away soon after imaging is completed.\[3\]

**Diagnostic Radiopharmaceuticals**\[5,6,7,8,9,10,11,12\]
- Ammonia N 13 Injection is a radioactive diagnostic agent for Positron Emission Tomography (PET) indicated for diagnostic PET imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease.
- Chromium 51 (28 d) as chromium chloride injection: Used to label red blood cells and quantify gastrointestinal protein loss cyanocobalamine preparation used for diagnosis of pernicious anaemia.
- Dysprosium 165 (2 h) used as an aggregated hydroxide for synovectomy treatment of arthritis.
- Floufine 18 Asfluoro2 Deoxy D-Gluocose (fdg) used for cerebrbral, myocardial and tumor glucose metabolism.
- Holmium 166 (26 h) being developed for diagnosis and treatment of liver tumours.
- Iodine 125 (60 d) as iothalamate sodium used diagnostically to evaluate the filtration rate of kidneys and to diagnose deep vein thrombosis in the leg. It is also widely used in radioimmuno assays to show the presence of hormones in minute quantities
- Iodine 131 (8 d): as sodium iodide 131 used as a diagnostic aid for studying the function of the thyroid gland and in scanning the thyroid for determining size, position and possible tumour location. Iodine 131 as sodium iodohippurate as a diagnostic for studying kidney function.
- Iron 59 (46 d) as ferric chloride solution used in studies of iron metabolism in the spleen.
- Lofetamine HCl 123 commonly known as IMP used for non invasive evaluation of local cerebral blood flow in cerebrovascular accidents.
- Oxygen15 as H215 O in equilibrium studies of tissue water content and as a tracer for regional blood flow.
- Potassium 42 (12 h) as potassium chloride injection, used for the determination of exchangeable potassium in coronary blood flow.
- Rubidium 86 as Rubidium chloride injection used for determination of myocardial blood flow.
- Selenium 75 (120 d), used in the form of selenomethionine to study the production of digestive enzymes.
- Sodium 24 (15 h) as sodium chloride injection to study sodium exchange.
- Xenon-133 (5 d) used for pulmonary (lung) ventilation studies.
- Gallium 67 (78 h) as gallium citrate used for tumour imaging and localisation of inflammatory lesions (infections).
- Indium 111 (2.8 d) used Strontium 92 (25 d) as indium111 pentetreotide used in imaging of neuroendocrine tumors. asindium 111 oxyquinoline for radiolabeling autologous leukocytes and platelets; as indium 111 cepromab penditide. It is monoclonal antibody for imaging prostate cancer.
- Strontium 89 chloride is in a class of drugs known as radioisotopes. It delivers radiation to cancer sites and ultimately decreases bone pain. The length of treatment depends on the types of drugs you are taking, how well your body responds to them, and the type of cancer you have.
- Thallium 201 (73 h) thallous chloride used for diagnosis of coronary artery disease other heart conditions such as heart muscle death and for location of low-grade lymphomas.

**Uses of Technetium-99m**
The radioisotope most widely used in medicine is technetium 99, employed in some 80% of all nuclear medicine procedures. It is an isotope of the artificially-produced element technetium and it has almost ideal characteristics for a nuclear medicine scan.

These are:
- It has a half-life of six hours which is long enough to examine metabolic processes yet short enough to minimise the radiation dose to the patient.
- Technetium-99m decays by a process called "isomeric"; which emits gamma rays and low energy electrons. Since there is no high energy beta emission the radiation dose to the patient is low.
- The low energy gamma rays it emits easily escape the human body and are accurately detected by a
gamma camera. Once again the radiation dose to the patient is minimised.

- The chemistry of technetium is so versatile it can form tracers by being incorporated into a range of biologically-active substances to ensure that it concentrates in the tissue or organ of interest.
- Sodium pertechnetate used for Brain imaging, Cerebral angiography; thyroid imaging; salivary gland imaging; placenta localization; blood pool imaging; gastric mucosa imaging; cardiac function studies; renal blood flow studies. Urinary bladder imaging. nasolacrimal drainage system imaging.
- Sodium pertechnetate labelled red blood cells used for determine of red blood cell volume, short-term survival studies. In vitro compatibility studies.
- Tc-albumin used for blood pool imaging, cardiovascular studies, placenta localization, determine of blood or plasma volumes.
- Tc-albumin (aggregated) used for Liver imaging.
- Tc-aciptide used for Acute venous thrombosis imaging.
- Tc-arctumomab used for tumour detection for colorectal cancer.
- Tc-bicsate used for Brain imaging.
- Tc-butedronate (DPD used for Brain imaging. 
- Tc-depreotide used for Tumour detection for lung cancer.
- Tc-disofenin (DISIDA) used for stic Hepatobiliary imaging.
- Tc-oxidronate (HDP) used for Bone imaging.
- Tc-pentetate (DTPA) used for Brain imaging, renal imaging, assess renal and brain perfusion, estimation of glomerular filtration rate, Lung ventilation studies. 
- Tc-polyphosphates used for Bone imaging, myocardial imaging, blood pool imaging, detection of gastrointestinal bleeding. 
- Tc-pyrophosphate used for Bone imaging, cardiac imaging, blood pool imaging, detection of gastrointestinal bleeding.
- Tc-sestamibi (HEXAMIBI) used for myocardial perfusion imaging.
- Tc-succimer used for renal imaging.
- Tc-sulesomab used for detection of infections and inflammation.

OTHER USES OF RADIOPHARMACEUTICALS

Radiosynoviorthesis or radiosynovectomy is a technique wherein a radiopharmaceutical is delivered into the affected synovial compartment (the interior of joints that is lubricated by fluid) of patients suffering from joint pain, as in the case of rheumatoid arthritis. Beta-emitting radiolabelled colloids are widely used for this purpose. Several radiopharmaceuticals have been developed usingphosphorus-32, yttrium-90, samarium-153, holmium-166, erbium-169, lutetium-177, rhenium-186 etc. and some of them are registered for human use. The radiation properties of each therapeutic isotope determine their respective use and applicability for the joint size.

Radiopharmaceuticals for Positron Emission Tomography Imaging

The evolution of PET as a clinically useful imaging modality has its origin in the synthesis of fluorine-18 fluorodeoxyglucose (18F-FDG) in 1976 at the Brookhaven National Laboratory. Fluorine-18 is the positron emitting radioisotope. The initial application of 18F-FDG was for mapping glucose-metabolism in the brain in the understanding and monitoring neurological diseases. While it is also useful for studying myocardial viability, due to the greater utilisation of glucose by the proliferating cells, the major use of 18F-FDG subsequently emerged in the
detection, staging and treatment follow-up of various types of cancers. Currently PET studies using 18F-FDG account for 10% of all imaging performed using radiopharmaceuticals. A number of other fluorine-18 labelled radiopharmaceuticals are being developed and a few of them are under clinical investigations[1]. Increasing clinical demand for 18F-FDG has triggered technological advances in various fields such as accelerator technology, radiochemistry, automated processing modules, detector systems, and imaging software. A typical cyclotron-PET centre nowadays includes a dedicated medical cyclotron together with automated radiochemistry modules and a number of PET or PET-CT units. Daily large scale production of 18F-FDG in the early morning hours for extensive and rapid distribution to medical centres is becoming common practice in several countries.

Generator produced PET Radiopharmaceuticals

The PET isotope gallium-98 can be obtained from germanium-68 – gallium-68 generator. The parent germanium-68 prepared using 30-60 MeV energy and high current cyclotron has a long half life(271 days) and hence the generator can be transported over very long distances and useful for periods of up to one year. In addition to infection imaging, gallium-68 is finding use in cancer imaging when labelled with peptides. The ultra short-lived rubidium-82 (a half-life of 75 seconds), available from astronium-82 – rubidium-82 generator, and useful for PET imaging of blood flow to myocardium, has high potential in managing heart patients.

CONCLUSIONS
Radiopharmaceuticals in medical research care and treatment today are being used to help millions of patients throughout the world.

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