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RADIOPHARMACEUTICAL IN NUCLEAR PHARMACY & MEDICINE AND THEIR THERAPEUTICS APPLICATION IN **HEALTH CARE SYSTEM**

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ABSTRACT

Radiopharmaceuticals, as the name proposes, are drug details comprising of radioactive substances, which are planned for utilize either in determination or treatment or finding. As of late, notwithstanding, there has been a critical development of this part of atomic medication with the presentation of various new radionuclides and radiopharmaceuticals for the treatment of metastatic bone torment, neuroendocrine and different tumors. This survey zeroed in on the creation of radiopharmaceuticals, their applications, marking, bundling and capacity. Radiopharmaceuticals are radioactive mixtures which have a bound radionuclide in their design, whose intention is

coordinating the radionuclide to an area to be dealt with or to get pictures. Atomic medication is the clinical forte that utilizes radiopharmaceuticals, which has introduced itself as an immensely valuable partner for medication aiding different findings and therapies, particularly for disease. The overall target of this work is to distinguish the principle radionuclides and metal buildings as of now utilized as radiopharmaceuticals.

KEYWORDS: Radiopharmaceuticals, radioactive, nuclear medicine, diagnosis.

INTRODUCTION

Radiopharmaceuticals serve an essential function in field of medicine. From 2010 to 2015, the worldwide radiopharmaceutical applications market is anticipated to expand at a CAGR of 9.25 percent, from \$ 4.9 billion in 2010 to \$ 7.9 billion in 2011. With the rising rates of cardiac, neurological, and cancer illness, there is a considerable growth in global demand for radiopharmaceuticals.^[1]

Radiopharmaceuticals are radioactive chemicals that are employed in the diagnosis and treatment of medical conditions. Nuclear pharmacy, which deals with the safe and effective administration of radioactive substances, was first recognized as a specialty in pharmacy by the board of pharmaceutical specialties in 1978. More than 100 radioactive substances are utilized for therapeutic purposes, such as tumor localization, hyperthyroidism, toxic diffuse goiter, skeletal metastasis-related bone pain, and cerebral perfusion. [2] These radioactive medicines are also utilized in the diagnosis of infections and renal disease.

Radiopharmaceuticals are employed in diagnostic imaging and radiotherapy in nuclear medicine, and they are extremely important in medicine in general for assisting in organ diagnostics and treating pathological diseases, particularly cancer. In the imaging modality, radiopharmaceuticals are given orally, intravenously, or inhaled to allow viewing of different organs, such as kidneys, lungs, thyroid and heart functions, bone metabolism, and blood circulation, using their radioactive tracers. A high dosage of radiation is administered by specialized radiopharmaceuticals targeting the diseased organ in a treatment modality aimed at treating cancer or an overworking thyroid gland.

A radioactive element (radionuclide) that allows external scanning is connected to a nonradioactive element, a physiologically active chemical, medication, or cell that serves as a carrier or ligand, allowing the radionuclide to be delivered to a specific organ.

The majority of radiopharmaceuticals (about 95%) are utilized for diagnostic purposes, with the remainder being utilized in treatment. There is no pharmacological effect in radiopharmaceuticals, unlike conventional medicines. Radiopharmaceuticals offer a noninvasive, low-side-effect method of targeting therapeutic radiations. Radioactive medicines are also non-invasive imaging tools that provide information on the structure and function of sick organs or tissue in the event of diagnosis. [4-5]

History and Growth of Radiopharmaceuticals and Nuclear Medicine

Radiopharmaceuticals are pharmaceutical formulations that contain radioisotopes that are safe to use in humans for diagnosis or therapy. Although radiotracers were explored as a medicinal medication soon after radioactivity was discovered, the first substantial uses didn't come until much later, when cyclotrons for particle acceleration to generate radioisotopes were available. Nuclear reactors gained the capacity to manufacture greater amounts of radioisotopes as a result. For example, radioiodine (iodine-131) was initially used to treat thyroid cancer in 1946, and it is still the most effective treatment for hyperthyroidism and thyroid cancer today. [6]

Henri Becquerel put uranium salts on photographic plates in 1896, resulting in radiographs that were marked without the need of light. Marie and Pierre Curie were the first to propose the use of radium as a cancer therapy in 1905. The work of the Curies is often seen as the beginning of modern nuclear medicine. Ernest Lawrence constructed the first cyclotron in 1931, which accelerated alpha particles like protons, deuterons, or helium ions to piercing the nucleus and producing stable and radioactive isotopes. Lawrence's cyclotron had generated 223 radioactive isotopes a decade later, many of which are today very useful for medical research and biological investigations.

The preparation of radioisotopes was one of the primary aims for the construction of nuclear research reactors. Medical applications were seen to be the most important of the radioisotope applications. The majority of medium and high flux research reactors are now routinely utilized to generate radioisotopes for medical and industrial purposes. Molybdenum-99 (for the synthesis of technetium-99m), iodine-131, phosphorus-32, chromium-51, strontium-89, samarium-153, rhenium-186, and lutetium-177 are the most widely utilized reactor generated isotopes in medical applications.^[7]

Radiopharmaceuticals

Any medical or pharmaceutical product that contains one or more radionuclides intended for human use in diagnosis or therapy is referred to as radiopharmaceutical.

Radiopharmaceuticals are radioactive compounds that release radiations as they breakdown. Radioactive nuclides are similar to regular nuclides in that they have the same number of protons but differ in the number of neutrons. Radiation in the form of alpha, beta, and gamma can be released. Curie, which equals 3.71010 decomposition per second, is used to provide radiopharmaceutical doses to patients. [8]

The nuclide is an elemental species characterized by its mass number 'A,' (the total of the number of protons and neutrons in its nucleus), the atomic number 'Z,' as well as the number of protons in a neutral nucleus, and its state of nuclear energy. Nuclides with an atomic number "Z" but differing mass numbers "A" constitute an element isotope. They have the same position on the periodic table and comparable chemical characteristics.^[9]

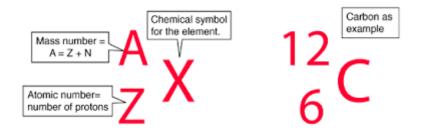


Fig 1: Chemical element and its mass and atomic number.

Radionuclide: Nuclides having an unstable arrangement of protons and neutrons that spontaneously convert to either a stable or another unstable arrangement of protons and neutrons with a constant statistical probability through radiation emission. These are referred to as radionuclides and are considered to be radioactive.

Radioactivity: Radioactivity is the emission of radiation caused by the spontaneous change or disintegration of a radionuclide. The word radioactivity, on the other hand, is used to describe the physical quantity (activity or intensity) of this event. The number of nuclear disintegrations or transformations per unit time defines a preparation's radioactivity.

They emit radiation in the form of alpha and beta particles, which are directed towards the afflicted areas. They're often used in modest doses for imaging examinations, but they may also be used to give higher doses of radiation.

Units of Radioactivity

One nuclear transmutation per second is the SI unit of radioactivity, which is measured in Becquerel (Bq), after the physicist Henri Bequerel. Curie (Ci) was the previous unit of radioactivity, named after radiation pioneers Madame Marie Curie and Pierre Curie. One Ci equals 3.7 x 10 10 Bq and represents the number of disintegrations produced by 1 g of Radium-226.

The division of radiopharmaceuticals into four categories

- 1. Radiopharmaceutical preparation: It's a radionuclide-containing preparation that's ready for people to utilize. The radionuclide must be present in order for the preparation to be useful in diagnosis or treatment.
- 2. Radionuclide generator: It is the method that permits the separation of a daughter radionuclide (with a short half-life) from a parent radionuclide (with a long half-life) by elution or other means for subsequent use in the manufacture of a radiopharmaceutical preparation.
- 3. Radiopharmaceutical precursor: It's a ligand or chemical molecule utilized in the radiopharmaceutical preparation's production. It might be an inert chemical molecule or a radiolabeled intermediary used to prepare radiopharmaceutical formulations before delivery.
- **4. Kit for radiopharmaceutical preparation:** In general, a vial holding the nonradio nuclide components of a radiopharmaceutical preparation, generally in the form of a sterilized, approved product to which the relevant radionuclide is added or diluted before medical use. The kit is usually a multidose vial, and the radiopharmaceutical preparation may require extra procedures such as boiling, heating, filtering, and buffering. Kitderived radiopharmaceuticals are typically meant to be used within 12 hours following manufacture.[10]

Radionuclide production

One of the following procedures can be used to produce the radionuclides intended for use in radiopharmaceutical preparations.

- **Nuclear fission:** Fissionability is a characteristic of nuclides having a large atomic number. Fission of Uranium-235 by neutrons within a nuclear reactor is the most frequent reaction. Iodine-131 and Xenon-133 are two more radionuclides that may be made this way. To avoid radioactive contaminants, the radionuclides produced using this process must be closely monitored.[11]
- **Charged particle bombardment:** The radionuclide is created in this approach by blasting the non-radionuclide with charged particles using cyclotrons.
- **Neutron bombardment:** The radionuclides are created by hitting non-radionuclides with neutrons in a nuclear reactor. The feasibility of producing iodin-131 from tellurium-130 dioxide under neutron activation was investigated.

• **Radionuclide generator systems:** The radionuclide generator system is used to separate the daughter radionuclide (short half-life) from the parent radionuclide (long half-life) via physical or chemical techniques.

Radiopharmaceuticals Labelling and Packaging

Labelling

The container label should indicate

- The name of the radionuclide and the product
- Any identifying code for a product
- The name of the producer
- An identity number (batch number)
- The total radioactivity in the container, or the radioactive concentration per milliliter, at a
 specified date and, if necessary, hour, and the amount of liquid in the container for liquid
 preparations.
- The total radioactivity at a specified date and, if necessary, hour for solid preparations such as freeze-dried preparations.
- The radioactivity of each capsule at a specified date and, if required, hour, as well as the quantity of capsules in the container for capsules.
- Furthermore, the qualitative and quantitative content should be stated on the product label.
- The administration routes.
- The date of expiration
- Any specific requirements for storage. [12]

Packaging

It is necessary to specify the packing material's appropriateness for the product and the labelling method to be performed. It's possible that specific radiation shielding will be required.^[13]

Package Leaflet

The following information should be included in the kits' or product's package leaflets:

- The radioactive substance's name and application.
- The name of all ingredients in the product.
- The manufacturer's name and address for the kits.

- The process for making radiopharmaceuticals from kits, as well as the shelf life of the finished product.
- The pharmacological and toxicological effects of the produced radiopharmaceutical, as well as the route of elimination from the body
- The amount of radioactive material in the radiopharmaceutical that has been produced.
- The precautions that the patient and nuclear pharmacist should take throughout the product's administration and preparation.
- The measures that should be followed while discarding the container and its contents that are no longer in use.
- The dosage of radiopharmaceuticals that have been produced that is recommended.^[14]

Storage of Radiopharmaceuticals

Store in an airtight container at a location that is adequately protected to prevent personnel exposure to main or secondary emissions and conforms with national and international standards on radioactive material storage. Irradiation during storage may cause containers to discolor. The darkening of the preparations does not always imply that they are deteriorating. The end of the term of validity for radiopharmaceutical preparations must be clearly specified because they are designed for usage within a limited time. Radiopharmaceuticals for parenteral use should be kept in such a way that the product's pharmaceutical purity is preserved.[15]

Nuclear Medicine and Radiopharmaceuticals

Pharmaceutical formulations that include radioactive and radiolabel substances for diagnostic or therapeutic reasons are known as radiopharmaceuticals.

According to the Society of Nuclear Medicine, 20 million nuclear medicine operations are performed in the United States each year.

These operations are carried out with the use of prepared radiopharmaceuticals and imaging equipment in order to diagnose a disease or to treat a specific target. [16]

Merits and Demerits of Nuclear Medicine

Merits of Nuclear Medicine

- Nuclear medicine examinations give information that is often unavailable through conventional imaging techniques. Details on the function and architecture of bodily structures might be included in this material.
- For many illnesses, nuclear medicine provides the most important diagnostic or therapeutic information.
- A nuclear medicine scan is less costly than exploratory surgery and may provide more precise information.
- Nuclear medicine has the ability to diagnose disease at an early stage, frequently before symptoms or anomalies may be discovered by traditional diagnostic procedures.
- PET scans may remove the need for surgical biopsy or determine the optimal biopsy location by identifying whether lesions are likely benign or malignant.
 PET scans may give extra information that can be utilized in the planning of radiation

Demerits of Nuclear Medicine

therapy.[17-18]

- Nuclear medicine isn't advised for women who are pregnant or nursing.
- In certain situations, nuclear medicine might produce an allergic response.
- In some situations, certain considerations should be made before beginning nuclear medicine.
- Nuclear medicine has a high price tag.
- Nuclear medicine has side effects.
- It is possible that nuclear medicine will take a long time to complete. It is possible that nuclear medicine will take a long time to complete. [18]

Application of Radiopharmaceuticals

The use of radiopharmaceuticals in diagnostics

Radiation used for diagnostic purposes must have enough energy to penetrate through tissues and reach the detecting equipment from within the body. The functions of the organs in the body vary. Throughout the investigation, the doctors determined the chemical compounds that each organ can ingest and absorb. The thyroid gland, for example, preferentially absorbs iodine, whereas the brain absorbs glucose and the bones absorb calcium. This concept is employed in radiopharmaceuticals, where the radioisotope is selectively up taken by certain

organs after entering the body. A diagnostic radionuclide with a short half-life and decay through gamma radiation emission is suitable.^[19] Technetium-99 m is the perfect diagnostic radionuclide because it has a short half-life (6 hours), decays solely via gamma radiation, and is easily spotted by a gamma camera.

Table 1: The use of radionuclides in diagnostics.

Radionuclide	Diagnostic use
Technetium-99 m	Used in diagnosing of cardiac amyloidosis
Chromium-51	Used in diagnosis of pernicious anemia
Fluorine-18	Used in positron emission tomography to assess alternations in glucose
	metabolism in brain and cancer
Holmium-166	Used in the diagnosis of liver cancer
Iodine-125	Used in diagnosis and evaluation of the glomerular filtration rate of
	kidneys
Gallium-67	Used in tumors imaging
Potassium-42	Used in determination of exchangeable potassium in coronary blood
	flow
Rubidium-86	Used in determination of myocardial blood flow
Iodine-131	Used in studying the function of the thyroid gland
Selenium-75	Used to study the production of digestive enzymes
Sodium-24	Used to study sodium exchange
Xenon-133	Used to study the pulmonary ventilation

Radiopharmaceutical Therapeutic Applications

Radionuclide treatment, which involves using radiopharmaceuticals that are tagged with beta emitting radionuclides, is becoming more popular in nuclear medicine. In addition to thyroid cancer management, radionuclide therapy is used for bone pain palliation, which improves the quality of life of cancer patients suffering from pain from bone metastases, as well as for the treatment of joint discomfort, such as rheumatoid arthritis. Though therapeutic radiopharmaceuticals are currently sold at a lower rate than diagnostic products, this is expected to change dramatically in the next 5-6 years as several new products for the treatment of lymphoma, colon cancer, lung cancer, prostate cancer, bone cancer, and other persistent cancers are expected to hit the market. The availability of radionuclides with high purity and appropriate specific activity, as well as the development of sophisticated molecular carriers, all contribute to the effective use of radionuclide treatment.^[20]

Radiopharmaceuticals for the relief of bone pain

Patients with advanced breast, lung, and prostate cancer develop bone metastasis, and therapeutic radiopharmaceuticals containing radionuclides such as strontium-89, samarium-153, and rhenium-186/188 are used to effectively relieve discomfort from skeletal metastases.

The International Atomic Energy Agency (IAEA) has launched a programmed to develop and test lutetium-177-based radiopharmaceuticals for the treatment of bone pain. In low/medium flux research reactors, which are accessible in various countries, it may be produced in considerable quantities for bone pain palliation. Lutetium-177 has a long half-life, which benefits production and testicular function. [21]

Primary cancer therapy using radiopharmaceuticals

Targeted radionuclide treatment includes the use of radiopharmaceuticals to deliver cytotoxic (cell-damaging) doses of radiation to a disease location, with the goal of delivering the absorbed radiation dosage to malignant tissues more selectively. Tumor biology, recombinant antibody technology, solid phase peptide synthesis, and radiopharmaceuticals chemistry have all led to new radiotherapeutic drugs being investigated. For targeted treatment, radiolabeled peptides are being developed as molecular vectors. Peptide molecules can be labelled with therapeutic radionuclides and used to kill receptor-expressing tumors, a technique known as peptide reprogramming. In most situations, comparing treatment efficacy in patients is not possible, thus developing laboratory methodologies for reliable and fast comparative evaluation of potential therapeutic radiopharmaceuticals is critical. [22-23]

Radioactive compounds are used in sterilizing

Radiation sterilizes the thermo-labile compounds. This is when radioisotopes come in handy. [24-25] Hormones, vitamins, medicines, surgical dressings, and disposable syringes are among the thermosensitive compounds. Cobalt-60 is a radioisotope that decays by gamma radiation and is used to sterilize thermo-labile material. [26-27]

CONCLUSION

There are now several types of radiopharmaceuticals accessible and have an essential role to play in illness diagnostics. Nevertheless, the radionuclide and radiopharmaceuticals for treatments for metastasis of bone pain, neuroendocrine, and the other tumors have recently been expanding significantly in that area of nuclear medicine. The radionuclide treatment industry now through a very fascinating and exciting period and is set to expand and expand in future years.

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