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Use of Radiopharmaceuticals as Nuclear Medicine for the Treatment of Diseases

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Abstract

Radiopharmaceuticals are radioactive substances that contain a bonded radionuclide with the intention of directing the radionuclide to a specific place for treatment or imaging. Radiopharmaceuticals are employed in nuclear medicine for cancer therapy as well as other therapeutic and diagnostic applications. Therefore, the primary goal of this study is to identify the key metal complexes and radioactive elements utilized in radiopharmaceutical applications. The sodium and methylenediphosphonate (MDP-99mTc) complexes, along with isotopes such as indium (111In), thallium (201Tl), gallium (67Ga, 68Ga), iodine (123I, 131I), chromium (51Cr), sulfur (35S), phosphorus (32P), and fluorine, are among the most significant radio-nuclear metal complexes used. These components have played a crucial role in enabling early medical detection, particularly with regard to cancer. Iodine-131 for thyroid conditions, lutetium-177 for prostate cancer, and yttrium-90 for targeted radiation therapy are examples of commonly used radiopharmaceuticals. Advancements in nuclear medicine have led to the development of safer and more effective radiopharmaceuticals, significantly improving patient outcomes. The field continues to evolve through ongoing research and technological advancements, offering promising treatments for conditions such as cancer, neurological disorders, and cardiovascular diseases. At present, technetium complexes account for the larger share of radiopharmaceuticals in international use. Brazil's Institute of Energy and Nuclear Research (IPEN) is a major producer, importer, and distributor of radiopharmaceuticals that supplies clinics and hospitals across the country.

Keywords: Nuclear research, diagnosis, isotopes, metal complexed, radio nuclear medicines

INTRODUCTION

Radiopharmaceuticals are used in nuclear medicine for diagnostic imaging and radiation, as well as in general medicine to help with organ diagnosis and pathological condition treatment, particularly cancer. Radiopharmaceuticals use radioactive tracers to visualize organs such as the kidneys and lungs, thyroid or heart function, bone metabolism, and blood circulation. They are administered orally, intravenously, or inhaled. Specific radiopharmaceuticals deliver a high dose of radiation to the diseased organ in order to treat cancer or an overactive thyroid gland [1].

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A radioactive component (radionuclide) that enables external scanning and a nonradioactive element, a biologically active molecule, medication, or cell (such as red and white blood cells labelled with a radionuclide) that acts as a carrier or ligand, guiding the radioactive component to a particular organ-are the two main components of radiopharmaceuticals [2].

Some conditions should be attached to the radiopharmaceuticals' assessment for therapeutic use in imaging. (1) Radionuclide decay should produce radiation in specific energy emission ranges (511 keV in the case of PET and 100–200 keV in the case of gamma cameras) and in adequate amounts for detection by tomographic devices; (2) should not emit particulate radiation (such as beta emissions), as this will increase radiation dose to the patient; (3) The half-life should be limited by a few hours; (4) The existence of another radionuclide of the same element, including its stable radioisotopes (carrier-free), will not contaminate any of the radionuclides; (5) They need to have a distinct activity, and the more suitable the carrier-free radionuclides, the higher the unique activity; (6) There should be no physiological effects or toxicity from the radiopharmaceutical; (7) It should be easy to compound and easily accessible for use; and (8) it should get to the target organ quickly and precisely, in accordance with its intended application [3]. The important difference between normal and artificial drugs is that the former are considered therapeutic, whereas the latter are not. In addition, few radiopharmaceuticals have short half-lives due to degradation of their physical radiation. As a result, radiopharmaceuticals are made just before their administration. To protect the operator and the patient, radiopharmaceuticals have to be manufactured and handled with care. Understanding the radionuclide's interactions with drugs, cells, tissues, and organs is critical for developing more effective imaging or therapeutic radiopharmaceuticals [4].

HISTORICAL BASES OF NUCLEAR MEDICINE AND RADIOACTIVITY

Wilhelm Roentgen's work in X-ray research influenced scientists like Henri Poincare, who studied the use of X-rays and fluorescence. Charles Henry was the first to test all that Poincare claimed, and he utilized zinc sulphide X-ray amplifiers to discover that it increased the sharpness of radiographs when exposed to light [5].

In 1896; it was after that Henri Becquerel placed uranium salts on photographic plates and produced clear radiographs in the absence of light. In 1905, Marie and Pierre Curie insisted on radium's use in the treatment of cancer. The Curies' ground-breaking research has rightfully been referred to as the origins of contemporary nuclear medicine. Ernest Lawrence built the first cyclotron in 1931, which produced stable and radioactive isotopes by directing accelerated alpha particles, including protons, deuterons, and helium ions, towards the nucleus. Decades later, the cyclotron produced 223 isotopes which are now widely used in therapeutic and biological research [6].

By building the cyclotron in 1930, Ernest Lawrence and Milton Livingstone made it possible to artificially synthesise new radioactive elements, albeit in trace amounts. During World War II, radionuclides found their first medical application in the United States with the reactor producing the global primary supplies. Hal Anger invented the image-scintillation chamber in 1958, making it unnecessary for the detector to move. It had higher geometric resolution, enabling several projections of the same radiotherapy distribution. Computers, on the other hand, were still incapable of receiving the information and converting it into visuals. As a result, the information was transmitted to the cathode ray tube, where it was captured on photographic plates or films. Modern scintillation cameras are of the Anger type [7]. Nuclear medicine really took off as a diagnostic approach to medicine after 99mTc was chosen by Paul Harper and his colleagues as a marker. This radionuclide emits 140 keV gamma-type photons and radiation and is produced through radioactive decay via isotopic transition with a biological half-life of about 6 h, which is appropriate for imaging intervals that are important for diagnosis [8]. In 99Mo/99mTc generators, it is a byproduct of the parent element 99Mo's decay. In the 1950s, the first radiopharmaceutical formulations were created and manufactured. Abbott Laboratories was the first to manufacture radiopharmaceuticals for medical use, and 131Iodine was the first isotope to be produced commercially.

NUCLEAR MEDICINE AND RADIOPHARMACEUTICALS

Radiopharmaceuticals are classified into two types: radionuclides with a half-life (radioactive decay period) of less than 2 h and radioactive substances with a half-life greater than 2 h [9]. Radioactive particle detection can be done with nuclear medicine cameras. The type of radiation emitted determines the type of camera: PET cameras can identify a pair of gamma rays emitted after positron decay, while SPECT cameras capture nuclides that decay by generating single gamma rays [10].

Nuclear Medicine Techniques

Nuclear medicine diagnostics use radioactive isotopes and tracers to produce gamma radiation from within the body. A camera, which consists of a large rectangular array of detectors scintillation, then combines these points into an image of the radiation's emission. This image is digitized, magnified, and displayed on a screen to show anomalies [11].

SPECT, PET, CT-PET (for improved spatial visualization), micro-PET (for ultra-high resolution), and micro-CAT are other nuclear medicine techniques. These methods are used to look into biochemical dysfunctions that may be early warning signs of many diseases, as well as their causes and connections to a variety of diseases, from mental disorders to cardiovascular disease and cancer [6, 12].

The pair of gamma rays created when a positron interacts with an electron in tissues is detected by the positron emission tomography (PET) imaging technology. When the electron and proton annihilate one other, two gamma rays are created that are moving in opposite directions. PET works by producing scintillation signals from the energy generated by gamma rays. While ^{18}Fluorine is useful for PET, technetium is the typical radionuclide for gamma cameras [11, 10]. X-ray CT uses computer-generated three-dimensional images with significantly improved resolution and detail of the body's internal structures and organs [6].

Radionuclides in Medicine

Radionuclides play an important role in diagnostic and therapeutic treatments in many nuclear science applications, particularly in the medical field. According to the World Nuclear Association, in developed nations, which collectively account for over 25% of the world's population, one out of every 50 patients receives treatment using nuclear medicine. Approximately 10% of these treatments are radionuclide therapy [11].

Radiation is used in nuclear medicine to gather data on a patient's organs for therapeutic purposes. The information is often used for prompt diagnosis. The image shows a clear view of the thyroid, bones, heart, liver, kidneys, and many other organs, pointing out any abnormalities in their activities [12–17]. Over 10,000 hospitals are currently using radionuclides around the world, and almost 90% of these procedures are diagnostic in nature. The most widely used radionuclide for diagnostic purposes is 99mTc. It performs more than 40 million nuclear medicine tests per year, accounting for 80% of all nuclear medicine tests worldwide.

An essential part of diagnostic tests are radionuclides. The processes that take place in different sections of the body can be studied when employed in conjunction with equipment that captures images from gamma rays that are emitted [16, 18]. When a patient receives a dose of radioactive material for diagnosis, its location within the organ can be viewed as either a two-dimensional image or, in the case of tomography, a three-dimensional image. These are tracers that emit gamma or positron rays that bind to specific chemicals and contain short-lived isotopes and can hence be used to measure different physiological processes.

Radiopharmaceuticals for diagnosis in human body

Scientists and medical professionals claim that some organs absorb a lot of substances. Iodine is absorbed by the thyroid, while glucose is absorbed by the brain. Using diagnostic radiopharmaceuticals, blood flow to the kidneys, liver, heart, lungs, and brain can be monitored [19]. Cancer cells can be killed or weakened by particle radiation (radiotherapy). It refers to the radiation's radionuclide donor and is present in specific organs. It is also used for diagnosis.

Beta radiation frequently destroys cancer cells. For example, 177Lutetium (177Lu) is created when 176ytterbium (176Yb) is exposed to radiation, and it is immediately converted back to 177Lu. 90Yttrium (90Y) is used to treat cancer, especially liver cancer and non-Hodgkin lymphoma. 32P, 153Sm, and 131Iodine (131I) are also used in radiotherapy. In rare instances, 131Cesium (131Cs), 103palladium (103Pd), and 223radium (223Ra) are used [11].

Production of Radionuclides

Medicine does not use naturally existing heavy hazardous elements like uranium and radium that are radioactive and have a lengthy half-life (more than 1,000 years). In nuclear medicine, radionuclides are created via nuclear fission or neutron bombardment [4].

IPEN is, therefore, Brazil's leading manufacturer of radiopharmaceuticals based in São Paulo. About 80% of nuclear medicine operations in Brazil use the 99m technetium generator, which is supplied exclusively by IPEN. Furthermore, 38 radiopharmaceuticals developed by IPEN are utilized in several Brazilian states [13]. The 2017 CNEN management report provides an overview of the major producers of radiopharmaceuticals in Brazil. They are principally the Northeast Regional Centre for Nuclear Sciences (CRCN-NE) in Recife, the Nuclear Technological Development Centre (CDTN) in Belo Horizonte, the Nuclear and Energy Research Institute (IPEN) in São Paulo, and the Nuclear Engineering Institute (IEN) in Rio de Janeiro. The Laboratory of Poços de Caldas (LAPOC) and the Institute of Radiation Protection and Dosimetry (IRD), located in Rio de-Janeiro, do not produce radiopharmaceuticals and focus instead on research and the provision of specialized services to laboratories, businesses, and industries [13].

CONCLUSION

There are numerous uses for radio nuclides in nuclear energy. Globally, radio nuclides are playing an increasingly important role in medical diagnosis and treatment. In 2018, radionuclides were employed in around 10,000 hospitals, with 90% of operations being diagnostic. By 2017, Brazil had around 440 nuclear medicine hospitals and diagnostic centres, according to the Institute of Energy and Nuclear Research. These were distributed in such a way that 55% were located in the Southeast, 19% in the North-eastern, and 15% in the Southern region. 72 PET units were installed. Approximately 1,800,000 people were aided. Nuclear reactors produce around 40 radionuclides; while cyclotrons produce approximately 20. With 67.3% of all CNEN income in 2017, technetium-99m is the most utilised diagnostic radionuclide among them. In addition to 99mTc, in Brazil in 2017, 131I (13.7%), 67Ga (2.9%), 177Lu-Dotatate (2.9%), and 18F-FDG (1.1%) were the most used radioisotopes. SPECT and PET have historically been the mainstay of nuclear medicine therapy, but with more accurate applications such as X-ray CT and three-dimensional imaging now coming out.

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