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Review Article

A Review On Radioisotopes In Cancer Therapy

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ABSTRACT

This work points out importance of medical radioisotopes in nuclear medicine based on treatment and diagnosis of cancer. Moreover, possible production methods of medical radioisotopes are evaluated, and an application for the production of two medical radioisotopes through neutron and deuteron induced reaction processes is discussed by comparing with experimental data in the literature.

INTRODUCTION

Radiopharmaceutical are radioactive isotopes which are used to diagnose [to find the traces] or work as a cancer therapy. Radioactive isotopes have unstable nucleus that decays or emit excess radiation or energy until the becomes stable. To date, researcher have discovered radioactive substances that can target various cancer like thyroid cancer, lymphoma, ovarian cancer, brain cancer or cancer which widespread to the bones. In the thyroid cancer the cause is unknown or poorly understood but may involve the genetic and environmental factors. To treat the thyroid cancer patients, undergo the medication, surgery and radiation therapy to kill the cancerous cell which left after the surgery. Radioactive substances administered in the different form such as orally [in form of pill], IV and interstitial [inserted into the cavity]. Isotopes have the same number of protons but different number of neutrons and these elements have same atomic number but differ in atomic mass. These unstable element decay by emission of energy in the form of alpha, beta (electron)/beta plus (positron) and gamma rays. Such isotopes, which emit radiation, are called radioisotopes. These radioisotopes are also known as radionuclides. These isotopes are used in various sectors like industries, agriculture, healthcare and research centres because of their characteristic nature of

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emitting radiation and their energies. Radioactive products which are used in medicine are referred to as radiopharmaceuticals. Radiopharmaceuticals differ from other medically employed drugs since they generally elicit no pharmacological response (owing to the minute quantities administered) and they contain radionuclide. They are prepared by tagging the chosen carrier component with an appropriate radioactive isotope. The carrier component of the radiopharmaceutical is a biologically active molecule used to localize the drug in a specific organ or group of organs to provide diagnostic information about those tissues such as pyrophosphate and methylene diphosphonate (MDP) compounds in skeleton bone tissues.

EVOLUTION OF RADIOISOTOPES:-

In 1898, discovery of polonium by Pierre and Marie Curie introduced the term “radioactive”. Radium was discovered by the Curie six months after the discovery of polonium with the collaboration of the chemist G. Be mont. Radium played by far a more important role than polonium. Its separation in significant amount opened the way to its medical and industrial application and also its use in laboratories. Later ‘uranic rays’ was discovered by Henri Becquerel in 1900.Overall 1800 isotopes are present, but at present only up to 200 radioisotopes are used on a regular basis, and most of them are produced artificially. Radioisotopes can be manufactured in several ways. The most common is by neutron activation in a nuclear reactor. This involves the capture of a neutron by the nucleus of an atom resulting in an excess of neutrons(neutron rich) which leads to the production of desired radioisotope .Some radioisotopes are manufactured in a cyclotron ,devised by Lawrence and Livingston in 1932 which charged particles such as protons, deuterons and alpha particles are introduced to the nucleus resulting in a deficiency of neutrons (proton rich). These particles are accelerated to high energy levels and are allowed to impinge on the target material. 11C, 13N, 18F, 123I, etc. are some of the isotopes that can be produced in a cyclotron.

Isotopes in Medicine:-

Radioisotopes are used in medicine in two different ways:

1. as radiation sources or
2. as radioactive tracers

As radiation sources their principal role is in therapy.

As radioactive tracers they are used mainly for diagnostic purposes. A radiopharmaceutical is a preparation, intended for in vivo use, containing a radionuclide in the form of an element, a simple salt or a complex and may exist in the form of a solid, liquid or gas. Radiopharmaceuticals are used for diagnosis and therapy. For diagnostic applications, a radiopharmaceutical should not be pharmacologically active in that it should not produce a physiological effect. For therapy, the radiopharmaceutical preparation contains enough radioactivity to produce the intended specific changes in tissue.

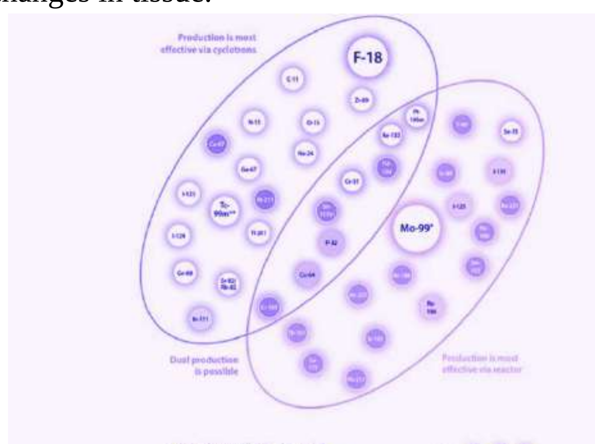

Figure 1: Production of isotopes in medicine - both cyclotrons and nuclear reactors are necessary Source: Medical isotopes.

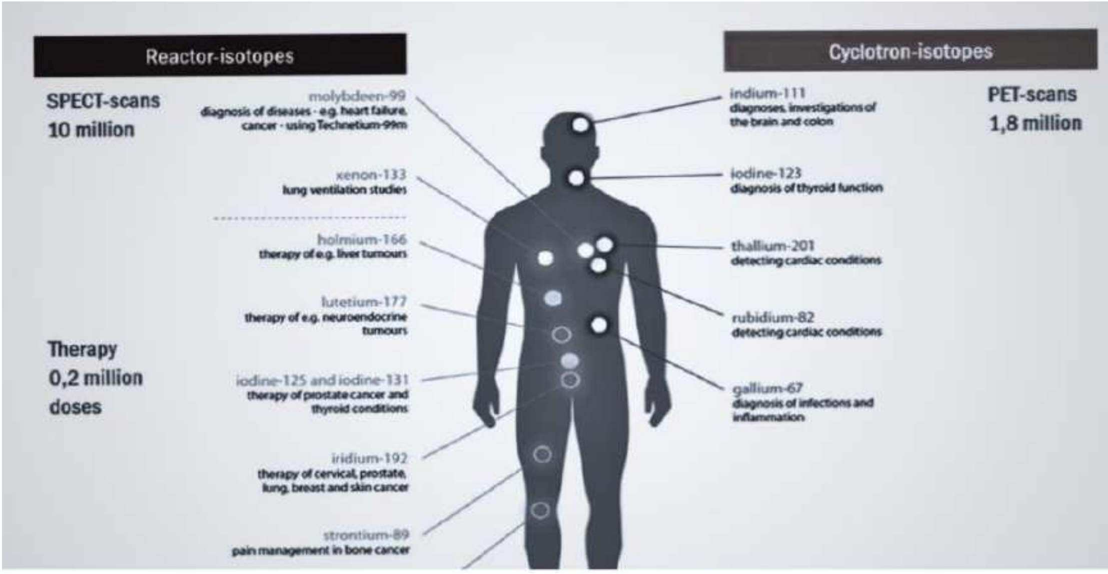

Figure 2: Number of procedures with medical isotopes

Table 53.2. Commonly used radioisotopes

Element	Isotope	Approximate half- life	Major radiation	Important Application
Carbon	14C	5600 years	Beta	Research in metabolism, carbon dating
Hydrogen	3H	12 years	Beta	Research in cell biology
Phosphorus	32P	14 day	Beta	Nucleic acid research, treatment for polycythemia
Chromium	51Cr	28 day	Gamma	RBC kinetics in diagnosis
Iodine	125I	60 day	Gamma	Radio immunoassay
Technetium	99Tc	6 hour	Gamma	Blood flow experiments; gamma imaging
Radium	226Ra	1600 years	Gamma	Interstitial implantation for treating cancer
Cobalt	60Co	5.3 years	Gamma	Teletherapy for cancer
Caesium	137Cs	30 years	Gamma	Teletherapy for cancer

APPLICATIONS OF RADIOISOTOPES :-

Radioisotopes can also be used, typically in higher doses than as a tracer, as treatment. Radiation therapy is the use of high-energy radiation to damage the DNA of cancer cells, which kills them or keeps them from dividing (Figure \(\PageIndex{3}\)). A cancer patient may receive external beam radiation therapy delivered by a machine outside the body, or internal radiation therapy (brachytherapy) from a radioactive substance that has been introduced into the body. Note that chemotherapy is similar to internal radiation therapy in that the cancer treatment is injected into the body, but differs in that chemotherapy uses chemical rather than radioactive substances to kill the cancer cells. Isotopes are atoms of the same element that have different numbers of neutrons. The most common isotope of carbon is carbon-12, which has six protons and six neutrons. Another common isotope of carbon is carbon-14, which has six protons and eight neutrons. Carbon-14 is unstable and decays over time. The rate of decay is known, so scientists can use it to calculate the age of something that contains carbon-14. For example, if a scientist found a sample of wood that contained carbon-14, they could use the rate of decay to calculate how long ago the tree died. Isotopes of an element will have identical chemical reactions. Hence when a radiolabelled compound is administered, these molecules are metabolized by the body similar to normal molecules. This is called Tracer technique. Almost all biochemical research will utilise such tracer methods. A few examples are given below.

i. Almost all the pathways described in earlier chapters were studied by using tracers. For example, 14 C-labelled aceto acetic acid is shown to be incorporated into palmitic acid. Suppose labelled "A" is administered to an animal. After a few minutes, liver contains labelled "B" and after one hour, labelled "C" is seen in liver. Thus, we can say that the pathway is A to B to C.
ii. The turnover rate of a substance in the body, that is, the rate of synthesis and breakdown could also be studied by tracer techniques. For example, if 131 I-labelled immunoglobulin is injected, the quantity of the labelled molecules in the circulation will be proportional to the catabolism of the Ig. By such methods, it is shown that the half-life of IgG is 15 days, of albumin is about 21 days.
iii. 32P is useful to trace the nucleic acid synthesis in vivo and in vitro. It is therefore employed in genetic research. 3H-labelled thymidine is incorporated in the newly synthesized DNA and therefore used in assessing cell division kinetics. 51Cr is taken up by living cells and the label is liberated when the cell is lysed. Therefore, it is used in vitro to quantitate the cell lysis by immunological or pathological mechanisms.
iv. The total body content of a particular substance (also designated as the "pool" of the substance) can be quantitated by the isotope dilution technique. To cite an example, 1 ml of 131 I-labelled albumin is seen to have 1 million dps. This is injected intravenously to a man. The radioactivity will be uniformly mixed in the total blood volume. After 10-15 minutes, a blood sample is withdrawn. One ml of blood is shown to have a radioactivity with 200 dps. The volume injected and removed is the same 1 ml, but the original count is now diluted 5,000 times. Thus, the intravascular space is 5,000 times more than the volume injected. Therefore, the blood volume is 5,000 ml.
v. Similarly extracellular volume (intravascular + interstitial spaces) is determined by 24 Na-labelled NaCl, and the total body water by means of 3 H-labelled water. From such experiments it is shown that intracellular compartment is 40%, interstitial compartment is 16% and intravascular volume is 4% of the total body weight.

BIOLOGICAL EFFECTS OF RADIATION:-

1. Direct Effects on Cancer Tissues The radiation damages DNA molecules. No effects are visible immediately. But the damage is observed during the next mitosis. Since new DNA cannot be synthesized, cells die at the attempt of the next division. Chromosome breakage is often noticed. Radiation produces large quantities of free radicals in tissues. The catastrophic effects of free radicals on different biological compounds (including DNA) are described in Chapter 20.
2. Indirect Effects on Cancer Tissues Damage to local blood supply cuts off the nutrition and causes local necrosis and cell death.
3. Effects of Radiation on Normal Tissues In 1904, Madam Curie went for a lecture-

demonstration class, keeping a few mg of impure radium ore in her breast pocket. Within 1 hour, this caused severe dermatitis. That was the first indication of a health hazard by radioactivity. Madam Curie succumbed to radiation-induced leukaemia in 1934

i. Effects on Skin Radiation will produce epilation, however hair may grow after 3 months. Sweat glands may be permanently damaged. There may be erythema and sometimes blisters. This is called acute radiodermatitis. Chronic radiodermatitis is seen after a few months of radiotherapy. There will be atrophy of skin, hypopigmentation, fibrosis, loss of elasticity, etc.
ii. 3-B. Effects on Mucous Membrane the gastrointestinal mucosa is very sensitive to radiation. These include nausea, vomiting, diarrhea and in severe cases ulceration and bleeding. Late sequelae such as adhesions, fibrosis, stenosis and obstruction may appear many months after radiotherapy.
iii. 3-C. Effects on Blood Cells Bone marrow and lymphoid tissues are highly radiosensitive because of the higher rate of cell division in these organs. Leukopenia and thrombocytopenia is an accepted side effect of radiotherapy. If WBC count is below 2,000/cu mm and platelet count is below 80,000/cu.mm, the therapy is temporarily stopped till recovery is affected.
iv. 3-D. Effects on Reproductive Organs Gonads (ovary and testis) are highly radiosensitive. Complete sterility is effected at 1000 rads. Even low doses of radiation, too low to have any obvious effect on mitosis, can still affect the genes, so as to produce genetic alterations in the offspring. This is especially important when radiation is given in pelvic region.
v. 3-E. Radiation Sickness Dose above 700 rads given, as whole-body irradiation, is usually fatal. Even 150 rads to the whole body will cause severe illness. In clinical practice, this is avoided by shielding the tissues in such a way that the beam is focussed to the cancer tissues only.
vi. 3-F. Carcinogenic Potential During the period 1900-1910, people were working with X-rays without any precautions. This caused non-healing ulcers in many of them. During 1910s and 20s, lip cancer was common among painters of watch dial with radioactive stain. Gradually, along with the increasing knowledge on radiation hazard, stringent safeguard for radiation protection was introduced.

Acute Radiation Syndrome (ARS) This may occur in accidents in nuclear reactors (e.g., Chernobyl accident) or the use of nuclear weapons in war (Hiroshima and Nagasaki). 15 to 25 rads will alter the blood count in exposed people, whereas the threshold for death in an individual is 150 rads. Other high dose effects are skin burns, hair loss, sterility and cataracts. Skin burns result from erythema, desquamation and blisters. Hair loss can occur after 500 rads. Cataracts (200 rads) are produced by neutrons because of the high-water content in the lens.

Radiation Protection :-

There is always some amount of background radiation, of about 150 m Rem/year. Out of this, about 50% is from the cosmic rays, about 30% from terrestrial environment and 20% from internal environment (e.g. decay of 40K). Granite and brick walls will increase external background. At higher elevation, cosmic rays are more. At an altitude of 2000 m, (e.g., Gangtok, Sikkim state), the background irradiation is 20% more. In some coastal areas (e.g.; Kerala state) natural deposits of radioactive thorium is seen, where background is 20-30% high. One diagnostic X-ray exposure may cause 75 millirem. Maximum Permissible Dose the MPD of radiation for whole body among radiation workers, (doctors, technicians) is 5 mRem/year, and for general population is 0.5 mRem/year. Small doses (less than 10 cGy) of radiation may be good to living systems, while large doses are harmful; this is called Hormesis.

Radiation Monitoring and Precautions Doctors, nurses, radiographers and research workers using the radioactive substances should wear a badge containing a piece of film. If radiation is reaching the film, it is blackened, and hence exposure could be detected. The following precautions will reduce the radiation hazards:

a. Keep the source farther away.
b. Shield the radioactive sources; cover them with lead bricks.
c. Handling is done by remote devices. Use lead-rubber gloves and aprons.
d. Radioactive materials are to be handled with speed. The shorter the time spent near the source, the lower the dose received.

Advantages of radioisotope imaging :-

- Target tissue function is investigated.
- All similar target tissues can be imaged during one
- investigation. For example, whole skeleton can be imaged in one bone scan.
- It can display blood flow.
- Assessment of physiologic or functional change in
- tissues, because of disease process.
- Computer analysis and enhancement of results are available.

Disadvantages radioisotope imaging :-

- Poor image resolution—often only minimal information is obtained on target tissue anatomy.
- The radiation dose to the whole body can be
- relatively high.
- Images are not usually disease-specific.
- Difficult to localize exact anatomical site of source of emissions.

CONCLUSION :-

Imaging technologies have become increasingly sophisticated in recent years. Nuclear medicine and molecular imaging, which provides the only means of assessing physiologic changes that is a direct result of biochemical alterations at cellular and molecular levels, and in combination with traditional anatomic imaging such as computed tomography scan and magnetic resonance imaging (MRI) scan, provide precise localization of functional abnormalities. These imaging techniques are based on the radiotracer method, and allow the measurement of tissue function in vivo and provide an early marker of disease through measurement of biochemical change. Many elements which found on earth exists in different atomic configurations used in medicine are referred to as radiopharmaceuticals which are useful to get diagnostic and therapeutic information about those tissues.

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