

Radiopharmaceuticals

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Definition

- ▶ Compounds or substances which emit radiations and which are used in medicines are called radiopharmaceuticals.
- ▶ These are used in medicine for the following purpose-
 - (i) As a source of radiation for radiotherapy, in case of cancer.
 - (ii) As radioactive tracers for diagnostic purpose

Discovery of radioactivity

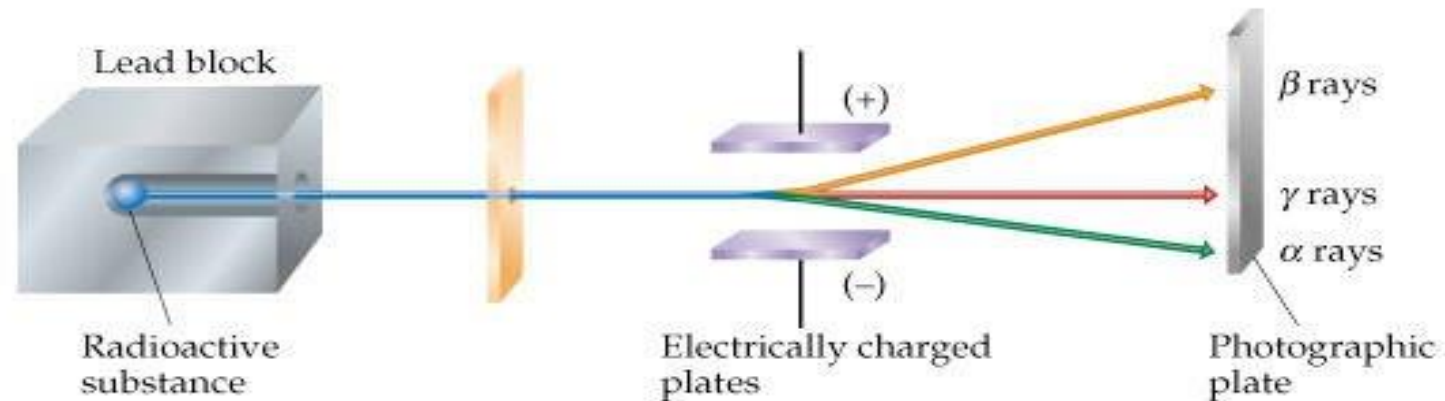
- ▶ Henry Bacquerel took up the study of phosphorescent (light emitted by substance without combustion) substances.
- ▶ Among his materials, uranium was sending out mysterious radiations. These radiations were found to effect photographic plate and ionise gases.
- ▶ The phenomenon of spontaneous emission of certain invisible radiations by elements like uranium is called **radioactivity**.
- ▶ The radiations emitted are called **radioactive radiations** and the elements which emit such radiations are called **radioactive elements**

Types of Radioactivity

- ▶ Radioactivity are of 2types-
- ▶ **(1) Natural radioactivity-** It is a substance emits radiations by itself without the help of any external agency, is said natural radioactivity.
- ▶ **(2) Artificial radioactivity-** If a substance does not emit radiations by itself but starts emitting radiations on exposure to radiations emitted by natural radioactive substance, this is called artificial radioactivity.

Nature of radiations

- ▶ Rutherford subjected the radioactive radiations under the influence of electric and magnetic fields.
- ▶ A small amount of radioactive substance is taken on a lead block. The radioactive radiations which are emitted are then passed through the slit.
- ▶ After this, these are subjected to the action of electric and magnetic fields. Finally the radiations are made to fall on a photographic plate.



Conclusion

- ▶ 1. One type of radiations were deflected from the normal path towards positively charged plate. It proves that such radiations carry -ve charged particles and named as **β -particles**.
- ▶ 2. The 2nd type of radiations were deflected towards -ve charged plate. It proves that such radiations carry +ve charged particles and named as **α -particles**.
- ▶ 3. The 3rd type of radiations were not deflected and struck the photographic plate straight and named as **γ -particles**.

Properties of α , β , γ rays

α -rays-

- These are made up of electrically charged particles, called α -particles. Each particle carries 2 units of +ve charge and has mass equal to 4 times the mass of hydrogen. Thus α -particles are doubly charged helium ion. (${}^4_2\text{He}$)
- It moves with velocity $1/10^{\text{th}}$ the velocity of light ($3.8 \times 10^8 \text{ m/s}$)
- Due to large mass, it possesses large amount of kinetic energy.
- Penetrating power is not very high. So elements which emit these do not find use in biological applications as they cannot penetrate tissues.
- When the nucleus of a radioactive element emits an α -particle, the new particle, has atomic no less by 2 units and mass no. less by 4 units as compared to parent element.
- ${}^{238}_{92}\text{U} \longrightarrow {}^{234}_{90}\text{Th} + {}^4_2\text{He}$

β-rays

- ▶ These are high speed electrons and electrically charged particles. Each particle carries a unit -ve charge and has mass equal to $1/1835^{\text{th}}$ mass of hydrogen atom.
- ▶ Velocity is same that of light.
- ▶ Due to large velocity and small mass, they have much more penetrating power than alpha particles.
- ▶ Beta particles have less ionizing power than alpha particles.
- ▶ It is of 2 types
- ▶ Electrically positive particles which are called 'positrons'
- ▶ Electrically negative particles which are called 'negatrons'
- ▶ When the nucleus of a radioactive element emits a β-ray, the new element formed has atomic no greater by 1 than the parent and atomic mass does not alter.

γ -rays

- ▶ They have no mass and carry no charge.
- ▶ These have been more penetrating than alpha and beta rays.
- ▶ These are having velocity same as the speed of light.
- ▶ They have poor ionising power.
- ▶ When gamma rays are emitted from an element, there is lowering of nuclear energy but no elemental change.

UNITS OF RADIOACTIVITY-

▶ Curie-

- ▶ The unit of radioactivity is “curie” symbolised as ‘c’. it may be defined as the quantity of any radioactive substance undergoes the same no of disintegration in unit time as 1g of radium and is equal to 3.7×10^{10} disintegration per second
- ▶ 1millicurie (mc) = 1×10^{-3} of curie = 3.7×10^7 disintegration per second
- ▶ 1 microcurie = 1×10^{-6} of curie = 3.7×10^{-4} disintegration per second

▶ Roentgen (R)-

- ▶ It is the unit of exposure.
- ▶ $1R = 2.58 \times 10^{-4} C kg^{-1}$ (C= coulomb)

▶ RAD-

- ▶ It is the unit of absorbed dose.
- ▶ $1rad = 10^{-2} J kg^{-1}$

▶ REM -

- ▶ It refers to the unit of dose equivalent. The dose in REM has been equal to the dose in RADS multiplied by quality factor and the distribution factor.

Isotopes

- ▶ These are nuclides with same atomic no. but different mass no. i.e. different no of neutrons in the nucleus.
- ▶ e.g. ${}_1\text{H}^1$, ${}_1\text{H}^2$, ${}_1\text{H}^3$
- ▶ If they are unstable, they undergo radioactive decay.
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- ▶ **Carbon-**
- ▶ Stable- ${}_6\text{C}^{12}$, ${}_6\text{C}^{13}$
- ▶ Unstable- ${}_6\text{C}^{11}$, ${}_6\text{C}^{14}$
- ▶ **Iron-**
- ▶ Stable- ${}_{26}\text{Fe}^{54}$, ${}_{26}\text{Fe}^{56}$, ${}_{26}\text{Fe}^{57}$, ${}_{26}\text{Fe}^{58}$
- ▶ Unstable- ${}_{26}\text{Fe}^{55}$, ${}_{26}\text{Fe}^{59}$
- ▶ **Phosphorous-**
- ▶ Stable- ${}_{15}\text{P}^{31}$
- ▶ Unstable- ${}_{15}\text{P}^{32}$
- ▶ **Iodine-**
- ▶ Stable- ${}_{53}\text{I}^{127}$
- ▶ Unstable- ${}_{53}\text{I}^{131}$

Handling and storage of radioactive materials

- ▶ Great care has to be taken in handling and storage of radioactive materials for protecting people and personnel who handle it from harmful radiations which the radioactive material emits.
- ▶ Certain precautions have to be taken while working with detectors, tracer experiment, radioassays manufacturing or handling of radioactive materials.
- ▶ Radioactive materials must be stored in an area not frequently visited by people. Shielding may be required. Thick glass or Perspex containers (solid transparent plastic made of polymethyl methacrylate) usually provide sufficient shielding. In order to protect from the gamma radiations, lead shielding has to be used. The storage area must be regularly checked for the radioactivity.

- ▶ The working areas should not be contaminated with radioactive materials. If radioactive liquid has to be handled, it must be carried in trays having absorbent tissue paper so that any leakage will get absorbed by paper. Rubber gloves have to be used when working with radioactive liquids. Pipettes operated by mouth should never be employed. The waste radioactive material has to be stored till the activity becomes low before its disposal.
- ▶ The following precautions have to be kept in mind while handling and storage of radioactive substances-
- ▶ One should not touch radioactive emitter with hand but it should be handled by means of forceps or suitable instruments.
- ▶ Smoking, eating and drinking activities should not be done in the laboratory where the radioactive materials are handled.
- ▶ Sufficient protective clothing or shielding have to be used while handling the materials.
- ▶ Radioactive materials have to be stored in suitable labelled containers, shielded by lead bricks and preferably in a remote corner.
- ▶ Areas where radioactive materials have been stored or used should be monitored, that is tested for radioactivity regularly.
- ▶ Disposal of radioactive materials should be carried out with great care.
- ▶ Precise requirements are prescribed by the Department of Atomic Energy (DAE) for the establishment of a radio-isotope facility in a hospital or pharmacy.

Application of radioisotopes

Radioisotopes find use in medicine in 4 different ways.

- ▶ Radiation source in therapy
- ▶ Radioactive tracers for diagnostic purposes
- ▶ Research
- ▶ Sterilisation

1. Radiation source in therapy

- ▶ The therapeutically used radioisotopes have been found to depend mainly on their ability to ionize atoms. The energy of alpha, beta and gamma rays is expressed in MeV.
- ▶ The radiation of shortwave length (gamma rays) are having high penetrating power than long wavelength (beta rays).
- ▶ The greater the MeV of the rays the more destructive it becomes to the surrounding tissues.
- ▶ Radioisotopes may be used internally or externally. If the radioisotopes are used externally, the dose could be terminated by removal of the source.
- ▶ If they are given internally, the dose cannot be stopped by removal of the source.

- ▶ **Gold (^{198}Au)** finds use in the treatment of abdominal and pleural effusions (buildup of fluid in the pleural space, area between the layers of tissue that line the lungs and chest cavity cells associated with malignant tumors) it is given in the form of a colloidal gold suspension.
- ▶ ^{198}Au also finds use in the treatment of carcinoma of uterus and urinary bladder.
- ▶ **Sodium phosphate (^{32}P)** finds use in the therapy of **polycythemia vera** (rare type of blood cancer in which your body produces too many blood cells, carry oxygen throughout the body. Too many RBC thickens blood and flows more slowly, clumps and clots inside blood vessel causes stroke and even death) to decrease the rate of formation of leukemia.
- ▶ **Cobalt labelled cyanocobalamins (vitamin B_{12})** finds use in the diagnosis of pernicious anaemia (decrease in RBC).
- ▶ The labelled isotope of cobalt **Co-57, Co-58, Co-60** and **sodium iodide (^{131}I)** preparations find use in the treatment of thyroid disorders.

2. Radioactive tracers for diagnostic purposes-

- ▶ **Labelled cyanocobalamin** finds use for measuring the glomerular filtration rate.
- ▶ **Ferric citrate (^{59}Fe) injection** finds use for the haematological disorders.
(Problems in RBC, platelet and blood vessels)
- ▶ **Colloidal gold (^{198}Au) injection** has been used for studying blood circulation in the liver.
- ▶ **Sodium iodide (^{131}I) injection** finds use to diagnose the functioning of thyroid gland.
- ▶ **Iodinate (^{131}I) human serum albumin injection** finds use to investigate the cardiovascular functions.
- ▶ **Sodium iodohippurate I-131 injection** use in the study of renal functions.
- ▶ **Sodium rose Bengal I-131 injection** finds use as a diagnostic agent to test liver functions.

3. Research

- ▶ Excellent biological and medicinal studies have been carried out with radioactive isotopes as tracers.
- ▶ $^{14}\text{C}_6$, $^3\text{H}_1$ are most commonly used for this purpose.

4. Sterilisation

- ▶ Some strong radiation source has been used for sterilising pharmaceuticals in their final packed containers and surgical instruments in hospitals.
- ▶ The radiation does not harm or destroy most pharmaceuticals. No heat or chemicals get involved for sterilisation.
- ▶ Thermolabile substances such as vitamins, hormones, antibiotics etc. can be safely sterilised.
- ▶ $^{60}\text{Co}_{27}$ or **Cesium-137** may be used for sterilising surgical instruments. It also finds use for sterilising pharmaceuticals.

Other applications

- ▶ **Calcium (Ca-44 and Ca-45)** - used to study the bone structure and in the treatment of carcinoma of bone.
- ▶ **Carbon-14** - medical and pharmaceutical research
- ▶ **Strontium-90** - radiotherapy of superficial carcinoma
- ▶ **Cobalt-60**- sterilisation of surgical materials
- ▶ **Nitrogen (N-13 and N-15)** - investigation of amino acids and protein metabolism and studies of nitrogen fixation by plants.
- ▶ **Oxygen (O-17 & O-18)**- Use in studies of organic reactions and photosynthesis

Use of ^{131}I in treatment-

- ▶ Inhibition of release of thyroid hormone by iodide forms the basis for its use in hyperthyroidism.
- ▶ All isotopes of iodine are rapidly taken up in the thyroid follicles. Radioactive ^{131}I is available as solution of Na^{131}I . It is administered orally in form of aqueous solution or in capsule form. Its half-life is 8.04days.
- ▶ The absorption of this leads to the highly localised destruction of the thyroid follicles due to beta particles. This property promoted it to use this in surgical removal of the gland.
- ▶ Advantage of radio iodine therapy include simplicity of the procedure, the avoidance of surgical risks and complications.

Sodium iodide I-131

- ▶ Sodium iodide I-131 solution is a solution which is suitable either for oral or i.v administration. The solutions are clear and colourless, but over a period of time both the solution and glass may darken due to the effects of radiation. The p^H of both solutions is between 7.5-9.0.
- ▶ For injection, a suitable preservative such as benzyl alcohol is added. A reducing agent such as sodium thiosulphate is added to the solution to prevent the oxidation of sodium iodide in aqueous solutions.
- ▶ Its half-life has been 8.08 days. The solution has to be prepared in single dose or multiple dose containers that have been previously treated to prevent adsorption. So as to avoid adsorption on the walls of containers including laboratory vessels, the containers should be first of all rinsed with a solution having 0.8% sodium bisulfate and 0.25% sodium iodide and then water.
- ▶ Sodium iodide I-131 has been the most common isotope and a diagnostic aid for studying the functioning of the thyroid gland, and in scanning the thyroid for determining size, position, and possible tumor location. It is mainly used in hypothyroidism, thyroid carcinoma, and severe cardiac disease.
- ▶ Diagnostic preparations having sodium iodide I-131 or I-125 are available in capsule or solution form under the name **Isotope⁰**. Other names have been **Radiocaps⁰ - 131 (capsule)** and **Tracervial⁰ - 1311**.

Measurement of radioactivity

For measuring the radiations of alpha, beta, gamma particles, many techniques involving detection and counting of individual particles or photons have been available.

- ▶ Ionisation chamber
- ▶ Proportional counter
- ▶ Geiger- Muller counter
- ▶ Scintillation counter

Ionisation chamber

- ▶ An ionisation chamber consists of chambers filled with gas and fitted with two electrodes kept at different electrical potentials (50-100volts for each centimetre of distance between the two electrodes) and a measuring device to indicate the flow of electric current.
- ▶ Radiation brings about ionization of gas molecules or ions which cause emission of electrons which in turn reveals the change in electric current.

Proportional counters

- ▶ These are the modified ionization chambers in which an applied potential ionization of primary electrons causes production of more free electrons which get carried to the anode.
- ▶ As for each primary electron liberated, much more additional electrons get liberated, the current pulse through electric circuit is amplified.
- ▶ The voltage range over which the gas ionization occurs is called the proportional counters.

Geiger- Muller counters (GM-counters)

Introduction

- ▶ Geiger Muller counter is an instrument used for detecting and measuring ionizing radiations (radiation that carries enough energy to liberate electrons from atom or molecules, thereby ionizing them)
- ▶ It detects ionizing radiations such as α -particles, β -particles, γ -particles using the ionization effect produced in a G-M tube.

Geiger- Muller counters (GM-counters)

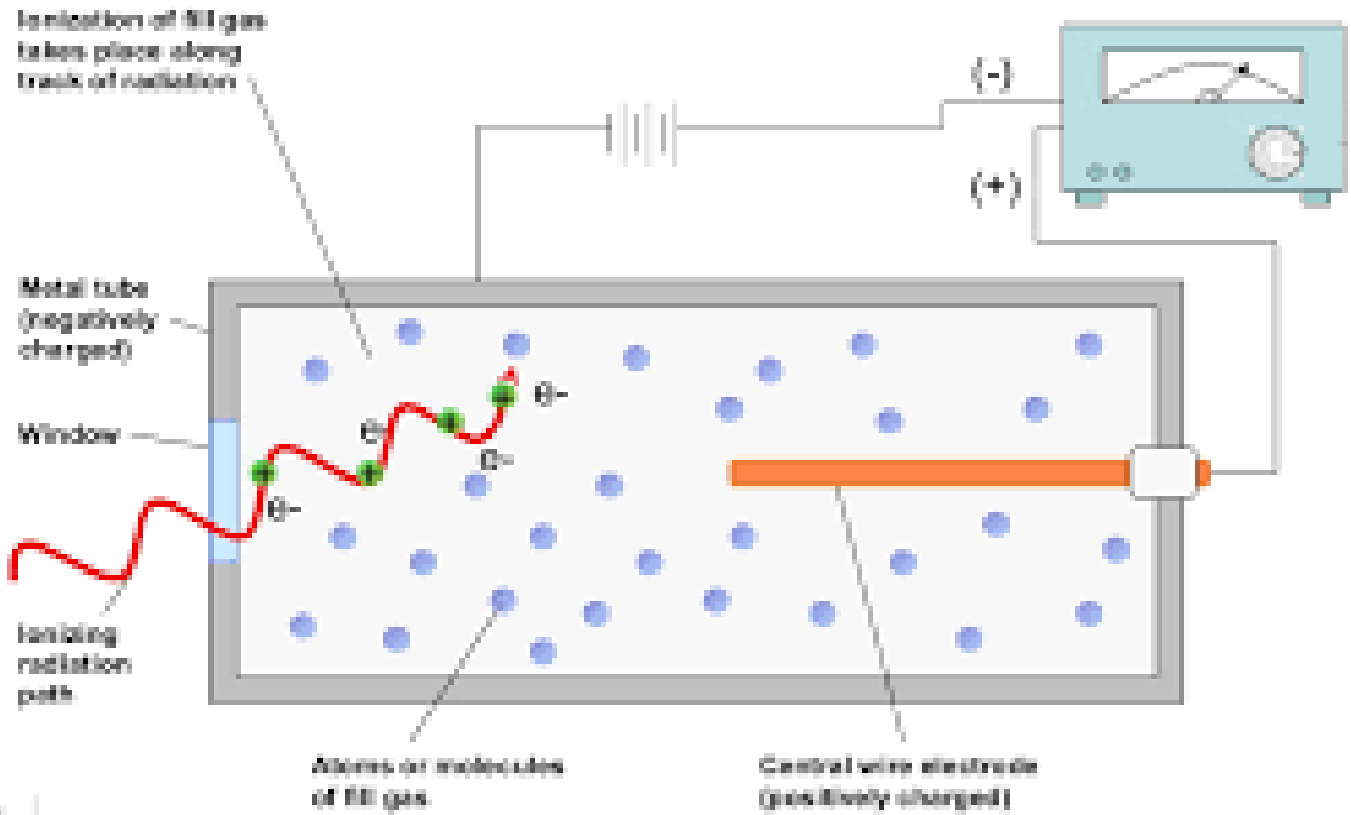
Construction

- ▶ It consists of a GM tube and processing electronics, which displays the results.
- ▶ A GM-counter consists of a cylinder of stainless steel or glass coated with silver on the inner side which acts as cathode. Coaxially inside the tube, a mounted fine wire works as an anode. The cylinder space is filled with a special gas mixture of ionising gas such as helium, neon or argon at low pressure, to which a high voltage is applied and also contains a small proportion of quenching vapour.
- ▶ The functions of quenching vapour are (i) to prevent the false pulses that may be produced due to positive ions reaching the cathode and (ii) to absorb the photons emitted by exciting atoms and molecules returning to their ground state. Chlorine, bromine, ethyl alcohol and ethyl formate are commonly used quenching agents.
- ▶ The tube briefly conducts electrical charge when a particle or photon of incident radiation makes the gas conductive by ionization. The ionization is amplified with the tube to produce an easily measured detection pulse, which is fed to the processing and display electronics.

Geiger- Muller counters (GM-counters)

Principle

- ▶ Free electrons causes electrical conduction by causing more ionization. The mica window works to enter alpha, beta and gamma rays but can't return. It is also called one way window.
- ▶ Radiation strikes with the mixture of gas and ionization occurs (knock out electrons). The free electrons attracts towards the anode. This electrons when strike with other atoms also ionize.
- ▶ When electrons reach the anode, the scale meter counts the pulse and when the positive ion attracts towards the cathode, positive ion takes more time to reach the cathode. This time is called dead time. (10^{-4} s).
- ▶ At that time, how many electrons reach the anode, but scale meter can't count before the positive ions reaches the cathode. The positive ions strike the cathode causes secondary electrons emission and that electrons come to anode and the count becomes wrong. Quenching gas is used here to prevent this.



Geiger- Muller counters (GM-counters)

Working

- ▶ A Geiger- Muller unit is regarded as an electrical switch, in which each pulse may make the current to pass to scaler to counting unit for recording the no. of pulses.
- ▶ In order to operate the GM-counter, a source of high voltage, together with a low-gain amplifier and sealing unit for registering the pulses are needed.
- ▶ When the voltage on the counter gets raised, no registration of pulses will be observed until a certain voltage gets reached.
- ▶ The counting rate increases rapidly to the threshold and at 150-200volts or more, the counting rate becomes constant.
- ▶ At the same time size of individual pulses get increased with the voltage, so that at higher voltage there has been a tendency for spurious discharges to get initiated.