Radiopharmaceuticals: Radio activity, Measurement of radioactivity, Properties of α, β, γ radiations, Half-life, radio isotopes and study of radio isotopes - Sodium Iodide 131, Storage conditions, precautions & pharmaceutical application of radioactive substances.

- **Defination:**

- Radiopharmaceuticals, as the name suggests, are pharmaceutical formulations consisting of radioactive substances (radioisotopes and molecules labelled with radioisotopes), which are intended for use either in diagnosis or therapy or diagnosis.
- The use of radioactive material necessitates careful and safe handling of these products by trained and authorized personnel, in approved/authorized laboratory facility as per the guide lines of Atomic Energy Regulatory Board (AERB) of India.

- **Units of Radioactivity:**

- In the International System (SI), the unit of radioactivity is one nuclear transmutation per second and is expressed in **Becquerel (Bq)**, named after the scientist *Henri Bequerel.*
- The old unit of radioactivity was **Curie (Ci)**, named after the scientists *Madame Marie Curie* and *Pierre Curie*, the pioneers who studied the phenomenon of radioactivity.
- One Ci is the number of disintegrations emanating from **1 g** of **Radium-226**, and is equal to **3.7 x 10^{10} Bq**.
  - The **Becquerel (Bq)** is the SI derived unit of radioactivity. One becquerel is defined as the activity of a quantity of radioactive material in which one nucleus decays per second. The activity of a source is measured in bacquerels.
  - ✓ This is a very small unit, and multiples are often used:
    1 MBq = 1 mega Becquerel = 1,000,000 Bq; 1 GBq = 1 giga Becquerel = 1,000,000,000 Bq;
    1 TBq = 1 tera Becquerel = 1,000,000,000,000 Bq
  - ✓ The radioactivity of an environment, a material or a foodstuff is given in Becquerel's per kilogram or per liter.
  - The **gray (Gy)** is defined as the absorbed dose of radiation per unit mass of tissue. One gray is the absorption of one joule of radiation energy per kilogram of matter. The amount of radiation your cells absorb is measured in grays.
    1 Gy = 1 joule per kilogram
    Sub-multiples are often used:
    1 mGy = 1 milligray = 0.001 Gy; 1 μGy = 1 microgray = 0.000001 Gy
    1 nGy = 1 nanogray = 0.000000001 Gy
  - The **Sievert (Sv)** is a measure of the health effects of low levels of ionizing radiation on the human body. At equal doses, the effects of radioactivity on living tissue depends on the type of radiation (alpha, beta, gamma, etc.), on the organ concerned and also on the length of exposure.
    Contrary to the Becquerel, the sievert is a very large unit, and we often use sub-multiples:
    1 mSv = 1 millisievert = 0.001 Sv; 1 μSv = 1 microsievert = 0.000001 Sv

- **Half-Life Period:**

- The time in which a given quantity of a radionuclide decays to half its initial value is termed as half-life ($T_{1/2}$).
- Formulas for half-life in exponential decay.

$N(t_{1/2}) = \frac{1}{2}N_0$ as expected (this is the definition of half-life)

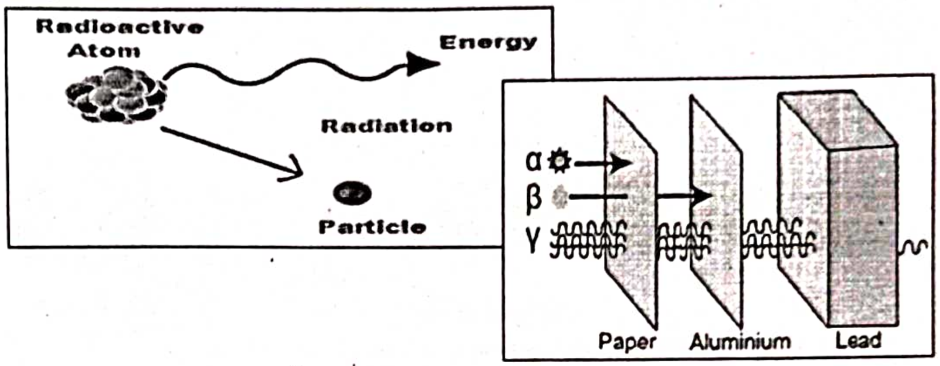
$$N(t) = N_0 \left(\frac{1}{2}\right)^{\frac{t}{t_{1/2}}}$$
$$N(t) = N_0 e^{-\frac{t}{\tau}}$$
$$N(t) = N_0 e^{-\lambda t}$$

Where:

- N_0 is the initial quantity of the substance that will decay (this quantity may be measured in grams, moles, number of atoms, etc.),
- $N(t)$ is the quantity that still remains and has not yet decayed after a time t,
- $t_{1/2}$ is the half-life of the decaying quantity,
- τ is a positive number called the mean lifetime of the decaying quantity,
- λ is a positive number called the decay constant of the decaying quantity.

- **Properties of α, β, γ radiations:**

- All substances are made of atoms. These have **electrons** (e) around the outside, and a nucleus in the middle. The nucleus consists of **protons** (p) and **neutrons** (n), and is extremely small. (Atoms are almost entirely made of empty space!).
- In some types of atom, the nucleus is unstable, and will decay into a more stable atom. This radioactive decay is completely spontaneous.
- When an unstable nucleus decays, there are three ways that it can do so. It may give out:-
  - an alpha particle (α)
  - a beta particle (β)
  - a gamma ray (γ)



✓ **Alpha particles**

- Alpha particle radiation consists of two neutrons and two protons, as they are charged they are affected by both electric and magnetic fields.
- The speed of the α -particle depends very much on the source, but typically are about 10% of the speed of light.
- The capacity of the α -particle to penetrate materials is not very great, it usually penetrates no more than a few centimetres in air and is absorbed by a relatively small thickness of paper or human skin. However, because of their speed and size, they are capable of ionising a large number of atoms over a very short range of penetration.
- This makes them relatively harmless for most sources that are about a metre or more away, as the radiation is easily absorbed by the air.
- But if the radiation sources are close to sensitive organs α -particle radiation is extremely dangerous.

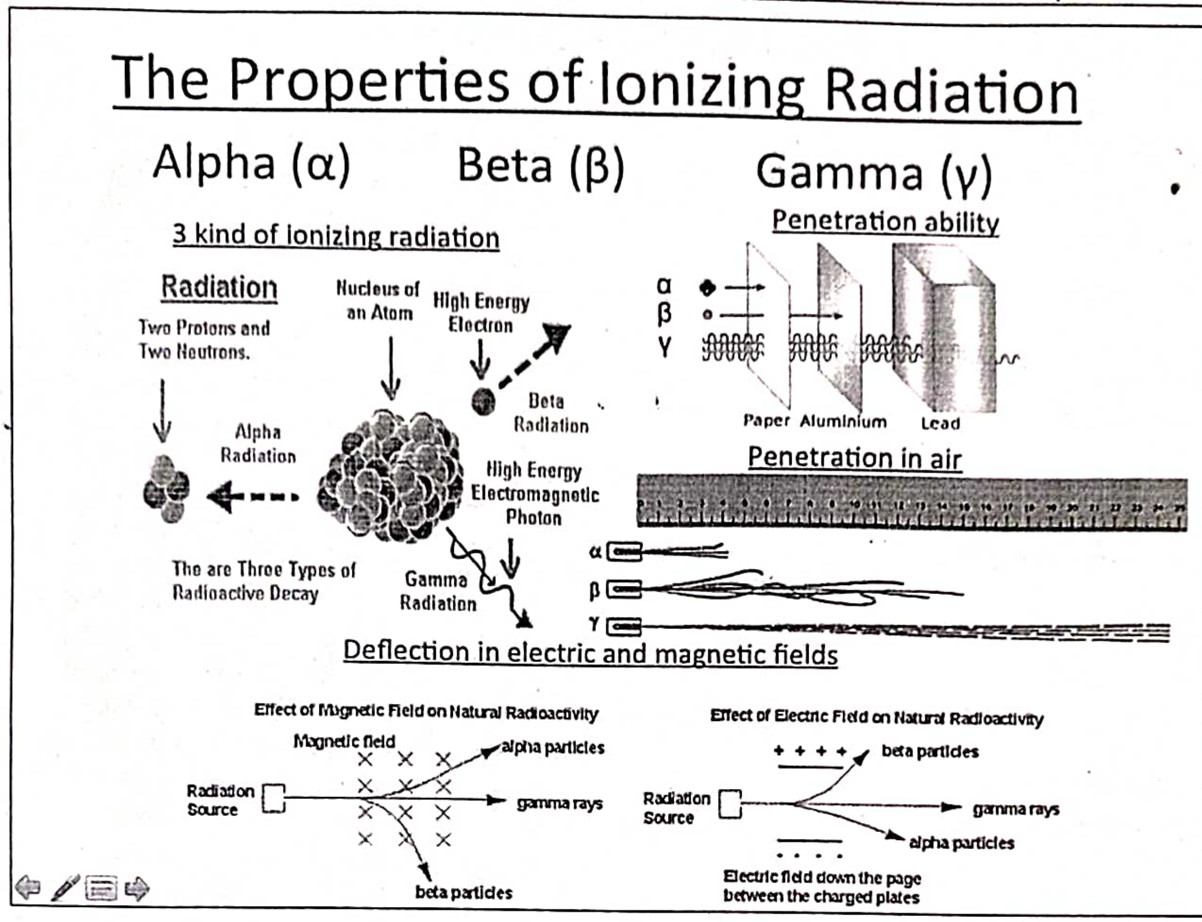
✓ **Beta particles**

- Beta-particle radiation consists of fast moving electrons. Every β -particle carries either one negative or one positive electronic charge ($\pm 1.6 \times 10^{-19}$ coulomb: -e, +e). They are affected by electric and magnetic fields.
- The speed depends on the source, but it can be up to 90% of the speed of light.
- β particles can penetrate up to 1 m of air. They are stopped by a few millimetres of aluminium or perspex.
- Their ionising capacity is much less than that of α -radiation. They are very dangerous if ingested.

✓ **Gamma rays**

- Gamma radiation does not consist of charged particles, it is a form of very short wavelength electromagnetic energy. They travel at the speed of light (3×10^8 m/s).
- Gamma radiation is very difficult to stop, it takes up to 30mm of lead. Although the ionising capacity of γ radiation is considerably smaller than that of beta-radiation, their high penetration power means that they are dangerous even at a distance.
- They can penetrate our bodies and hit sensitive organs. They are particularly dangerous if ingested or inhaled.

Property	α ray	β ray	γ ray
Nature	Positive charged particles, 2He 4 nucleus	Negatively charged particles (electrons).	Uncharged γ~0.01a, electromagnetic radiation
Charge	+2e	–e	0
Mass	6.6466×10^{-27} kg	9.109×10^{-31} kg	0
Natural Sources	By natural radioisotopes e.g. $^{92}U_{236}$	By radioisotopes e.g. $^{29}Co_{68}$	Excited nuclei formed as a result of α, β decay



- **Measurement of Radioactivity**

- For measuring radioactivity, three types of devices are available:
  1. Gas-filled tube counters e.g. the Geiger Muller Counter
  2. Scintillation Counters
  3. Semi-conductor Detectors

The Geiger Counter:

A potential difference just below that required to produce a discharge is applied to the tube (1000 V). Any atoms of the gas struck by the γ-rays entering the tube are ionized, causing a discharge. Discharges are monitored and counted by electronic circuitry and the output is reported as counts/sec or Rontgens/hr or mR/hr.

Scintillation Counters:

Crystals of certain substances e.g. cesium fluoride, cadmium tungstate, anthracine and sodium iodide emit small flashes of light when bombarded by γ-rays. The most commonly used phosphor in scintillation counters is NaI with a minute quantity of thallium added. In the instrument, the crystal is positioned against a photocell which in turn is linked to a recording unit. The number of flashes produced per unit time is proportional to the intensity of radiation. Small portable scintillation counters are available.

Semi-Conductor Detectors:

A semi-conductor is a substance whose electrical conductivity is between that of a metal and an insulator. It is noted that Ge(Li) semi-conductors ate excellent detectors of γ-rays with a resolution ten times higher than NaI (Th) scintillometers. The main disadvantage of these is a lower efficiency for higher energy x-rays. Besides, Ge(Li) semiconductors need to be cooled by liquid nitrogen & are hence cumbersome and not suitable as field instruments.

- **Pharmaceutical Application Of Radioactive Substances**

- *Treatment of Cancers and Tumours*
  - Americium 241 used as antineoplastic.
  - Californium 252 used as antineoplastic."
  - Cobalt 60 used as antineoplastic.
  - Gold 94 used as antineoplasatic.
  - Holmium 66 (26 h) being developed for diagnosis and treatment of liver tumours.
  - Iodine-125 (60 d) used in cancer brachytherapy (prostate and brain).
- *Treatment of Thyroid Disease with Iodine 131*
  - **Iodine-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.
- *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.
- *Treatment of Arthritis*
  - **Erbium-169:** Use for relieving arthritis pain in synovial joints
- *Diagnostic Radiopharmaceuticals*
  - **Ammonia** N 13 Injection used for diagnostic coronary artery disease.
  - **Chromium 51** used for diagnosis of pernicious anaemia.
  - **Holmium** 166 used for diagnosis and treatment of liver tumours.
  - **Iodine 125** used diagnostically to evaluate the filtration rate of kidneys.

- **Storage of Radioactive Substances**

- Radiopharmaceuticals should be kept in well-closed containers and stored in an area assigned for the purpose. The storage conditions should be such that the maximum radiation dose rate to which persons may be exposed is reduced to an acceptable level.
- Care should be taken to comply with national regulations for protection against ionizing radiation.
- Radiopharmaceutical preparations that are intended for parenteral use should be kept in a glass vial, ampoule or syringe that is sufficiently transparent to permit the visual inspection of the contents. Glass containers may darken under the effect of radiation.

- **Precautions For Handling Radioactive Substances**

✓ The following guidelines provide information on the safe handling of radioactive substances. They are based on the relevant legislation and on the Code of Practice for Handling Radioactive Substances.

- The radioactive substances used should comply with the following characteristics:
    - Radiotoxicity must be as low as possible.
    - Short-living isotopes are preferred to long-living ones
    - The amounts used must be kept to a minimum.
- Never work alone in a radioactive lab, especially not outside normal working hours. Always make sure to have someone nearby in case of emergency.
- Take all precautions to prevent radioactive contamination:
    - Always separate radioactive activities from non-radioactive activities.
    - As far as possible, limit the area where radioactive substances are used and mark the area, e.g. by using containers with absorbent paper.
    - Apply a radiation symbol to any containers and items that have come into contact with radioactive substances.
    - Never bring documents such as notes into the radioactive zone.
- When handling radioactive materials, always wear the appropriate protective clothing:
    - Wear a lab coat. If there is a risk of serious contamination, wear disposable clothing. Store your lab coat away from your regular clothes.
    - Always wear gloves when handling radioactive substances. Regularly check the radiation level of these gloves. Never touch anything with potentially contaminated gloves; use paper tissues instead.
    - Wear shoe covers in rooms where the floor may be contaminated.
    - Keep personal items such as handbags, etc., outside the lab.
- Use appropriate radiation shields. Return the stock solution to storage immediately after removing the amount needed.
- To avoid internal contamination, strict hygiene is essential when handling radioactive materials
    - Eating, smoking, drinking, and applying cosmetics are prohibited in radioactive labs.
    - Never pipette by mouth. Use pipetting devices instead.
    - Wash your hands thoroughly when you leave the lab.
- Regularly check the radiation level of your working area and all objects used, or at least at the end of each working day. Replace contaminated absorption paper. Decontaminate contaminated objects.
- Dispose of all radioactive waste in the appropriate containers. Limit the amount of waste to a bare minimum. Separate short-living and long-living radioactive waste.

Constant quantities:

- The *half-life*: ($t_{1/2}$) is the time taken for the activity of a given amount of a radioactive substance to decay to half of its initial value; see List of nuclides.
- The *decay constant*: (λ) "lambda" the inverse of the mean lifetime, sometimes referred to as simply *decay rate*.
- The *mean lifetime*: (τ) "tau" the average lifetime (1/e life) of a radioactive particle before decay.

- **Labelling of Radioactive Substances**

- Every radiopharmaceutical preparation must comply with the labelling requirements established under Good Manufacturing Practice.
- The label on the primary container should include:
  - A statement that the product is radioactive or the international symbol for radioactivity
  - The name of the radiopharmaceutical preparation;
  - Where appropriate, that the preparation is for diagnostic or for therapeutic use;
  - The route of administration;
  - The total radioactivity present at a stated date and, where necessary, time; for solutions, a statement of the radioactivity in a suitable volume (for example, in MBq per ml of the solution) may be given instead;
  - The expiry date and, where necessary, time;
  - The batch (lot) number assigned by the manufacturer;
  - For solutions, the total volume.
- The label on the outer package should include:
  - A statement that the product is radioactive *or* the international symbol for radioactivity
  - The name of the radiopharmaceutical preparation;
  - Where appropriate, that the preparation is for diagnostic or for therapeutic use;
  - The route of administration;
  - The total radioactivity present at a stated date and, where necessary, time; for solutions, a statement of the radioactivity in a suitable volume (for example, in MBq per ml of the solution) may be given instead;
  - The expiry date and, where necessary, time;
  - The batch (lot) number assigned by the manufacturer;
  - For solutions, the total volume;
  - Any special storage requirements with respect to temperature and light;
  - Where applicable, the name and concentration of any added microbial preservatives or, where necessary, that no antimicrobial preservative has been added.

		
The trefoil symbol used to indicate ionising radiation.	2007 ISO radioactivity danger symbol intended for IAEA Category 1, 2 and 3 sources defined as dangerous sources capable of death or serious injury	The dangerous goods transport classification sign for radioactive materials