UNIT 5

Radiopharmaceuticals:

Radiopharmaceuticals are **radioactive compounds** used for **diagnosis**, **therapy**, or **research** in nuclear medicine. These compounds contain one or more radionuclides and are administered to humans in **trace amounts**.

They combine a **radioactive isotope** with a **pharmaceutical agent** to target specific organs, tissues, or cellular receptors.

Radioactivity

Radioactivity is the phenomenon by which unstable atomic nuclei **spontaneously decay** and emit **radiation** in the form of alpha (α), beta (β), or gamma (γ) rays to attain a stable form.

Types of Radioactive Emissions

1. **Alpha (α) Particles**
    - Helium nuclei (2 protons + 2 neutrons)
    - Heavily charged and low penetrating power
    - Can be stopped by paper or skin
2. **Beta (β) Particles**
    - High-energy electrons or positrons
    - Moderate penetrating power
    - Can be stopped by aluminum sheets
3. **Gamma (γ) Rays**
    - Electromagnetic radiation
    - High penetrating power
    - Require lead or thick concrete for shielding

Units of Radioactivity

- **Curie (Ci)**: Traditional unit (1 Ci = 3.7×10^{10} disintegrations/sec)
- **Becquerel (Bq)**: SI unit (1 Bq = 1 disintegration/sec)

Half-life (t½)

The time required for a radioactive substance to lose half of its radioactivity due to decay. Each radioisotope has a unique half-life, which is critical in selecting radiopharmaceuticals.

Measurement of Radioactivity

Measurement of radioactivity is essential in nuclear medicine, pharmaceutical applications, radiotherapy, and radiation safety. Radioactivity is measured by detecting and quantifying the **emissions (α, β, or γ rays)** from radioactive substances. The instruments used depend on the type of radiation and the purpose of the measurement.

Units of Measurement

1. **Becquerel (Bq)** – SI unit
    - 1 Bq = 1 disintegration per second (dps)
2. **Curie (Ci)** – Older unit
    - 1 Ci = 3.7×10^{10} disintegrations per second
3. **Gray (Gy)** – Measures **absorbed dose**
    - 1 Gy = 1 joule/kg
    - Used to quantify energy absorbed by tissues
4. **Sievert (Sv)** – Measures **biological effect** of radiation
    - Takes into account the type of radiation and its impact on tissues

Instruments for Measuring Radioactivity

1. Geiger-Müller Counter (GM Counter)

- Detects **α, β, and γ radiation**, mostly used for β and γ
- Contains a gas-filled tube that gets ionized by radiation
- Ionization causes a measurable electric pulse
- **Used for**: Detection and general survey of radioactive contamination

2. Scintillation Counter

- Uses a **scintillator** (crystal or liquid) to emit light when struck by radiation
- Light is converted into an electrical signal by a **photomultiplier tube**
- Very sensitive and accurate
- **Used for**: Quantitative measurement of γ rays and some β emitters
- **Widely used in radiopharmaceutical analysis**

3. Ionization Chamber

- Measures the **current produced** by ion pairs in a gas-filled chamber

- Can measure high levels of radiation
- **Used for**: Calibration of radiation therapy equipment and dose measurement

4. Film Badges / Thermoluminescent Dosimeters (TLDs)

- Worn by personnel working with radioactivity
- Record cumulative radiation exposure
- **Used for**: Radiation safety monitoring

5. Well Counter (Gamma Counter)

- Specialized scintillation counter with a well-type detector
- Highly efficient for **measuring small samples**
- **Used in**: Nuclear medicine for counting radioactivity in biological samples

Selection of Instrument

Radiation Type	**Suitable Instrument**
Alpha (α)	Ionization chamber (if not shielded)
Beta (β)	GM counter, Scintillation counter
Gamma (γ)	Scintillation counter, Well counter

Applications in Pharmacy

- **Quality control** of radiopharmaceuticals
- **Dosimetry** for radiotherapy planning
- **Monitoring contamination** in manufacturing areas
- **Diagnostic imaging** studies (e.g., thyroid scans using I-131)

Technetium-99m (^{99m}Tc): Diagnostic imaging

- **Iodine-131 (^{131}I)**: Thyroid treatment
- **Cobalt-60 (^{60}Co)**: Cancer radiotherapy
- **Phosphorus-32 (^{32}P)**: Treatment of blood disorders

1. Geiger-Müller Counter (GM Counter)

Principle

Radiation ionizes the gas inside a sealed tube. The resulting ions generate a pulse of current, which is counted to indicate the presence of radiation.

Construction

- **Metal or glass tube** filled with an inert gas (e.g., argon)
- **Central electrode** (anode)
- **Outer metal casing** (cathode)
- **Thin mica window** to allow radiation entry
- **High voltage supply** and pulse counter

Working

- When ionizing radiation enters through the window, it ionizes the gas
- Electrons move toward the anode; positive ions toward the cathode
- This causes a momentary current pulse
- Each pulse corresponds to one radiation event and is counted

Applications

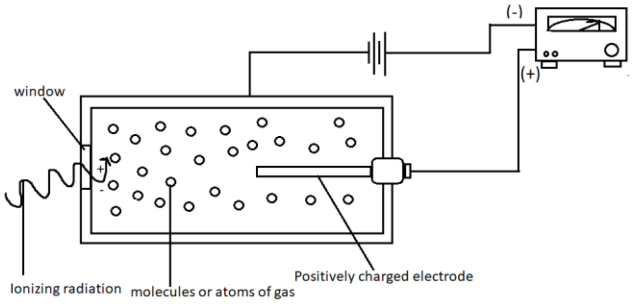
- Detecting radiation leaks in pharmaceutical labs
- Environmental monitoring of radioactive contamination
- Personal safety monitoring in nuclear facilities

Advantages

- Portable and easy to use
- Quick detection of radiation presence
- Inexpensive

Disadvantages

- Cannot distinguish between alpha, beta, and gamma rays
- Poor energy resolution
- Ineffective at high radiation intensities (dead time issues)



2. Scintillation Counter

Principle

When radiation interacts with a scintillating material, it emits light (photons). This light is detected and amplified by a photomultiplier tube to produce an electrical signal, which is counted.

Construction

- **Scintillator** (e.g., sodium iodide crystal doped with thallium)
- **Photomultiplier tube (PMT)**
- **Light-tight enclosure**
- **Electronic amplifiers and counters**

Working

- Ionizing radiation strikes the scintillator, producing flashes of light
- Light is guided to the PMT, where electrons are emitted and multiplied
- The electrical signal is amplified and counted, giving a radiation count rate

Applications

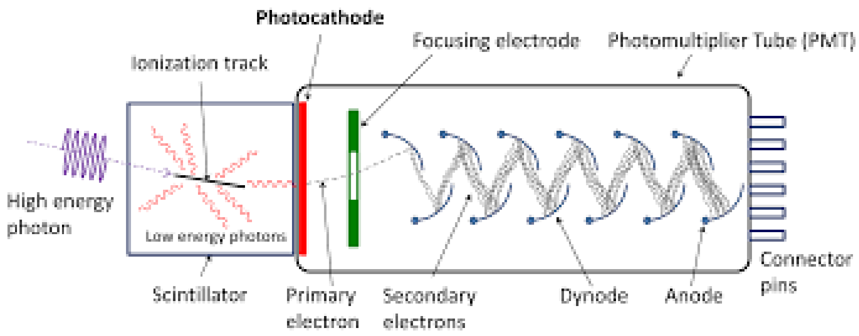
- Measurement of γ-emitters in radiopharmaceuticals
- Clinical diagnostic tests (e.g., thyroid uptake studies)
- Environmental radiation monitoring
- Research in radioisotope labeling

Advantages

- High sensitivity and accuracy
- Capable of measuring low radiation levels
- Can distinguish radiation types by energy levels

Disadvantages

- Expensive equipment
- Requires careful calibration and maintenance
- Affected by temperature and background light



Properties of α (alpha), β (beta), and γ (gamma) radiations:

Property	Alpha (α) Radiation	Beta (β) Radiation	Gamma (γ) Radiation
Nature	Helium nucleus (2 protons + 2 neutrons)	Electrons (β^-) or positrons (β^+)	Electromagnetic waves (high-energy photons)
Charge	+2	−1 (β^-) or +1 (β^+)	0
Mass	4 amu (heavy)	~1/1836 amu (very light)	0 (massless)
Penetration Power	Very low – stopped by a sheet of paper or skin	Moderate – stopped by a few mm of aluminum or plastic	Very high – requires thick lead or concrete to stop
Ionizing Power	Very high	Moderate	Low
Speed	~5–7% of speed of light	Up to 99% of speed of light	Speed of light
Deflection by Magnetic/Electric Field	Deflected (due to +ve charge)	Deflected in opposite direction (due to −ve or +ve charge)	Not deflected (neutral)
Biological Hazard (external)	Low (blocked by skin, but dangerous if inhaled/ingested)	Moderate	High (deep tissue penetration)

Effect on Photographic Plate	Weak effect	Moderate effect	Strong effect
Range in Air	Few centimeters	Up to a few meters	Several meters to kilometers
Detection	GM counter, scintillation counter (limited due to low penetration)	GM counter, scintillation counter	Scintillation counter, ionization chamber
Example of Emitter	Radium-226, Americium-241	Carbon-14, Phosphorus-32	Cobalt-60, Technetium-99m
Use in Medicine/Pharmacy	Rarely used directly; internal therapy (e.g., brachytherapy)	Used in diagnostic imaging and therapy (β-emitters in radiopharmaceuticals)	Widely used in imaging (e.g., PET scans, gamma scans), sterilization, cancer therapy

Half-life ($t_{1/2}$)

The half-life of a radioactive substance is the **time required for half of the radioactive atoms present in a sample to decay**.

Formula:
For a first-order radioactive decay:

t1/2=0.693λ

Where:

- t1/2t_{1/2}t1/2 = half-life
- λ\lambdaλ = decay constant

Characteristics:

- Independent of initial quantity
- Unique for each radioisotope
- Used to calculate the remaining radioactivity over time

Applications in Pharmacy:

- Determining shelf-life and dosing intervals for radiopharmaceuticals
- Calculating safe disposal time for radioactive waste

- Planning timing for diagnostic scans (e.g., PET, SPECT)

Radioisotopes

Radioisotopes (or radioactive isotopes) are **unstable isotopes of elements** that **emit radiation** (α, β, or γ) as they decay to a more stable form.

Types of Radioisotopes:

1. **Natural Radioisotopes** – occur naturally (e.g., Uranium-238, Radon-222)
2. **Artificial Radioisotopes** – produced in reactors/cyclotrons (e.g., Cobalt-60, Iodine-131)

Important Radioisotopes in Pharmacy and Medicine:

Radioisotope	Radiation Type	Half-life	Application
Iodine-131	β and γ	~8 days	Thyroid treatment & imaging
Technetium-99m	γ	~6 hours	Diagnostic imaging (SPECT)
Cobalt-60	γ	~5.27 years	Radiotherapy and sterilization
Phosphorus-32	β	~14.3 days	Cancer therapy (blood disorders)
Carbon-14	β	~5730 years	Tracer in drug metabolism studies
Strontium-89	β	~50.5 days	Bone pain palliation in cancer

Applications of Radioisotopes:

- **Diagnosis:** SPECT, PET scans using Technetium-99m, Fluorine-18
- **Therapy:** Use of Iodine-131, Cobalt-60 for cancer and thyroid treatment
- **Research:** Radiolabeling in pharmacokinetics and drug development
- **Sterilization:** Gamma rays from Cobalt-60 to sterilize surgical/pharmaceutical products

Sodium Iodide I-131 (Na^+ I^{-131})

1. Nature and Composition:

- Sodium Iodide I-131 is a **radioactive isotope** of iodine.
- It is commonly administered in the form of **sodium iodide (NaI)**.
- The isotope Iodine-131 has an **atomic mass of 131** and emits **β (beta)** and **γ (gamma)** radiations.

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2. Physical and Radiological Properties:

Property	Details
Atomic Number	53 (Iodine)
Atomic Mass	131
Type of Radiation	β^- and γ
Half-life ($t_{1/2}$)	~8.02 days
Mode of Decay	Beta decay to stable Xenon-131
Radiation Energy (β^-)	Maximum 606 keV
Radiation Energy (γ)	364 keV

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3. Principle of Action:

- I-131 gets **concentrated in the thyroid gland** because the gland uses iodine to produce thyroxine (T_4) and triiodothyronine (T_3).
- The **β-radiation destroys thyroid tissue**, making it useful for hyperthyroidism and thyroid cancers.
- The **γ-radiation is useful for diagnostic imaging** (though less common than Tc-99m).

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4. Preparation:

- Iodine-131 is produced by **neutron irradiation** of **Tellurium (Te)** in a nuclear reactor.

  ${}_{52}^{130}Te + {}_{0}^{1}n \rightarrow {}_{52}^{131}Te \rightarrow {}_{53}^{131}I + \beta^-$

- The I-131 is separated and combined with sodium to prepare injectable or oral sodium iodide I-131 solutions.

5. Formulations:

- Oral capsules or solutions (NaI-131)
- Intravenous injection (for diagnostic imaging or therapy)

6. Applications:

A. Therapeutic Use:

- **Hyperthyroidism (Graves' disease, toxic nodular goitre):** The β-radiation selectively destroys overactive thyroid cells.
- **Thyroid cancer (post-thyroidectomy):** Ablation of residual thyroid tissue or metastasis.

B. Diagnostic Use:

- Limited use in thyroid **uptake studies** (mostly replaced by Tc-99m now due to shorter half-life and safer profile)

7. Advantages:

- Selective uptake by thyroid tissue
- Minimally invasive treatment for thyroid conditions
- Effective for both therapy and diagnosis

8. Disadvantages:

- Radiation exposure risks (requires patient isolation)
- Long half-life necessitates strict radiation safety protocols
- Can cause hypothyroidism (destruction of normal thyroid tissue)

9. Storage and Handling:

- Stored in **shielded lead containers**
- Must be handled in **licensed nuclear medicine facilities**
- Requires **radiation monitoring badges**, proper waste disposal, and documentation

1. Storage Conditions of Radioactive Substances

Proper storage is critical to ensure the **safety of healthcare workers, the public, and the environment**. Storage guidelines are based on the type and energy of radiation emitted.

Key storage conditions:

- **Shielded Containers:** Use of **lead-lined** or **concrete-shielded containers** to absorb radiation, especially for gamma and high-energy beta emitters.

- **Labeling:** All radioactive materials must be **clearly labeled** with the **radioactive symbol**, isotope name, activity, and date.
- **Dedicated Area:** Stored in **designated, restricted-access areas** that are properly ventilated and away from populated zones.
- **Environmental Controls:**
    - Controlled **temperature** and **humidity**
    - Prevent contamination of air or surfaces (use of sealed vials or double containment)
- **Separation of Isotopes:** Radioisotopes with different energy levels or decay types are stored **separately** to avoid cross-contamination and exposure.
- **Radiation Monitoring Devices:** Area should be equipped with **Geiger-Müller counters** or **ionization chambers** for monitoring radiation levels.

2. Precautions for Handling Radioactive Substances

A. Personal Safety Measures:

- **Time:** Minimize the **time** of exposure.
- **Distance:** Maximize the **distance** from the radiation source.
- **Shielding:** Use appropriate **protective barriers** (lead aprons, tongs, gloves).
- **Personal Dosimeters:** Workers must wear **TLD badges** or **film badges** to monitor radiation dose.
- **PPE:** Use of **lab coats**, **eye protection**, and **gloves**.

B. Operational Safety:

- **Avoid Inhalation/Ingestion:** Work in **fume hoods** when handling volatile radioactive compounds.
- **Spill Control:** Trained staff must manage **radioactive spills** using absorbents and shielding.
- **Waste Disposal:** Dispose of radioactive waste as per **Atomic Energy Regulatory Board (AERB)** or **IAEA** guidelines—classified as **low, intermediate, or high-level waste**.

C. Documentation and Licensing:

- Institutions must have proper **licensing** to use and store radioisotopes.
- Maintain **records of inventory, usage, disposal**, and radiation monitoring.

3. Pharmaceutical Applications of Radioactive Substances

A. Diagnostic Applications (using low-dose isotopes):

- **Nuclear imaging** (SPECT and PET scans)
  - Example: Technetium-99m, Fluorine-18
- **Thyroid function tests:**
  - Sodium Iodide I-131 or I-123
- **Organ perfusion studies:**
  - For lungs, brain, liver, and kidneys

B. Therapeutic Applications (using higher-dose isotopes):

- **Cancer treatment:**
  - Cobalt-60 (external beam radiotherapy)
  - Iodine-131 (thyroid cancer)
  - Yttrium-90 (radioimmunotherapy)
- **Blood disorders:**
  - Phosphorus-32 used in polycythemia vera
- **Pain palliation in bone metastasis:**
  - Strontium-89 or Samarium-153

C. Research and Development:

- **Radiolabeled compounds** for pharmacokinetic studies
- **Tracer techniques** in drug development and absorption studies