RADIOPHARMACEUTICALS

INTRODUCTION

- Radiopharmaceuticals are unique medicinal formulations containing radioisotopes which are used in major clinical areas for diagnosis and/or therapy.

Pharmaceutical

Traces physiology / localises in organs of interest

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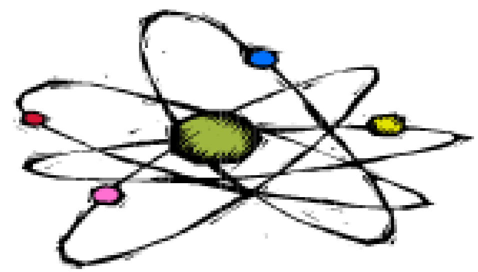
Biochemical Bonding

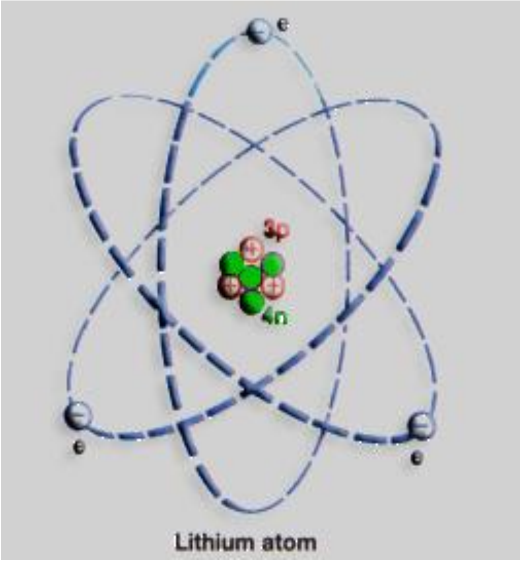


Radioactive nuclide

Emits radiation for detection or therapy

- All substances are made of **atoms**.
- These have **electrons** (e) around the outside (negativelycharged),

  and a **nucleus** in the middle.



- The nucleus consists of **protons** (positively charged) and **neutrons** (neutral).
- The **atomic number** of an atom is the number of protons in its nucleus.
- The **atomic mass** is the number of protons + neutrons in its nucleus.

- Isotopes of an atom have the same number of protons, but a different number of neutrons.

- Radiopharmaceuticals are medicinal formulations containing radioisotopes (emit particular types of ionizing radiation) which are safe for administration in humans for diagnosis or for therapy.

Composed of two parts: Radionuclide + Pharmaceutical

- Nuclide defines any species of atom characterized by a specific number of neutrons and protons within the atom.

:

Types of radioactivity

- **Radiation**: The process in which energy is released in the form of waves or particles from an unstable atom.

- **Radioactivity**: Can be described as the process in which an unstable atom releases energy and/or particles in an attempt to reach stabilization (non-radioactive form).
  - This process is referred to as radioactive decay.

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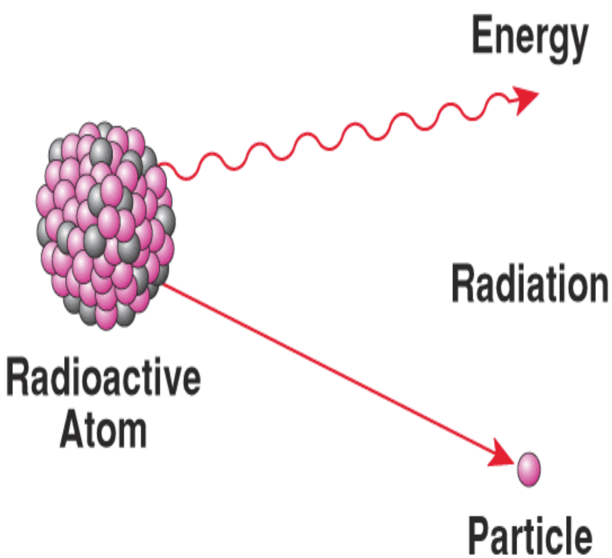
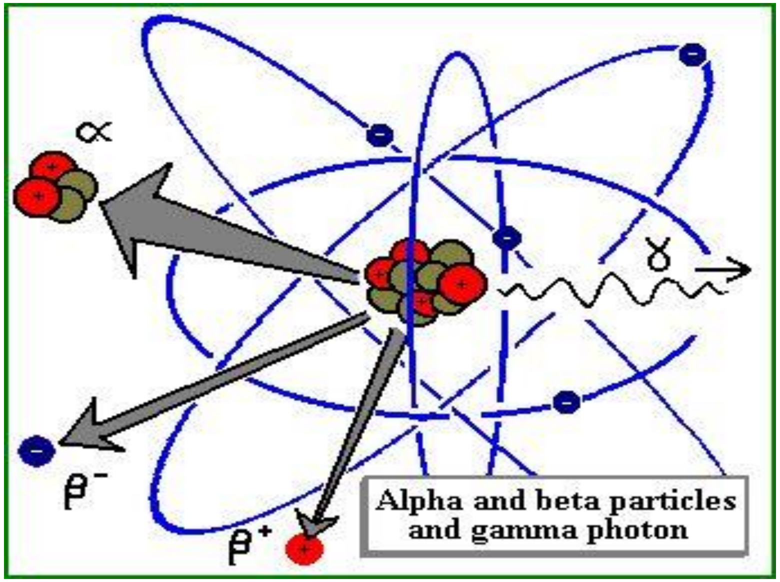




How to produce a radioactive nuclide ?

1. Natural radioactivity:

- Nuclear reactions occur spontaneously
  - Naturally occurring
    - very long-lived ($T^{1/2}$ -10^{9} yrs)
    - very heavy elements (uranium & radium)

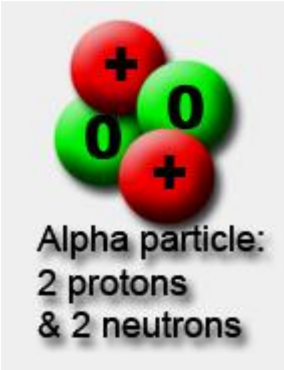
2- Artificial radioactivity:

- radioactivity produced by particle bombardment or electromagnetic irradiation
  - bombarding stable atoms with neutrons, protons
  - convert stable nucleus into unstable (radioactive)

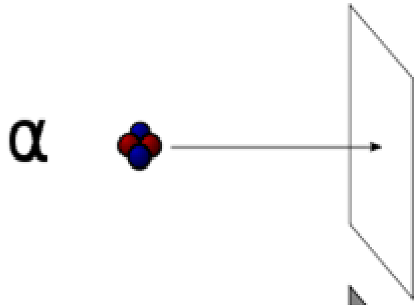
1- Alpha particle decay:

- Alpha particles are made of **2 protons and 2 neutrons**.
- We can write them as $^{4}_{2}\alpha$, or $^{4}_{2}He$, because they're

the same as a helium nucleus.



- This means that when a nucleus emits an alpha particle, its atomic number decreases by 2 and its **atomic mass decreases by 4.**
- Alpha particles are relatively **slow** and **heavy**.
- They have a **low penetrating power** - you can stop them with just a sheet of **paper**.



- Because they have a large charge, alpha particles ionize other atoms strongly.

Alpha-decay occurs in very heavy elements, for example, Uranium and Radium.

2- Beta particle decay:

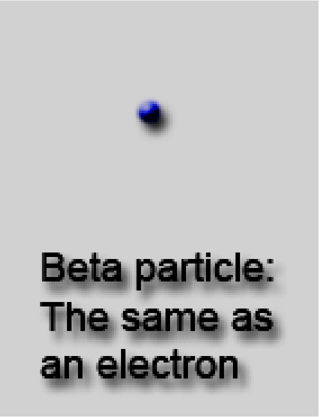
- Beta particles have a charge of **minus 1.** This means that beta particles are **the same as an electron**. We can write them as or , because they're the same as an electron.

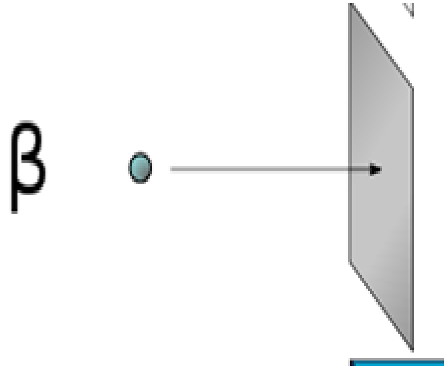
  β^- e^-

- This means that when a nucleus emits a β -particle: the **atomic mass is unchanged**

- They are **fast**, and **light**.
- Beta particles have a **medium penetrating power** - they are stopped by a sheet of **aluminium**.

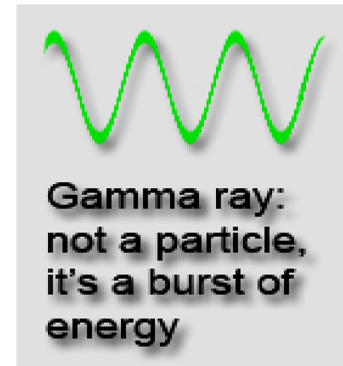
- Example of radiopharmaceutical emits , phosphorus-32
- Beta particles ionize atoms that they pass, but not as strongly as alpha particles do.





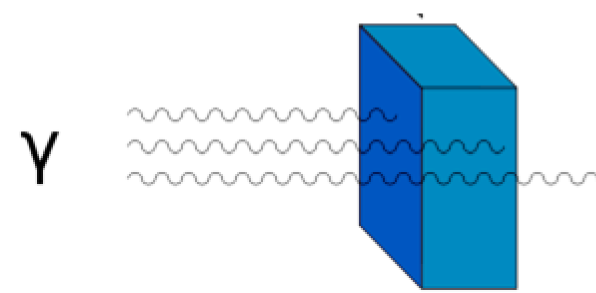
3- Gamma ray:

- Gamma rays are **waves, not particles**. This means that they have **no mass** and **no charge**.
- **in Gamma decay:**
- **atomic number unchanged**
- **atomic mass unchanged.**



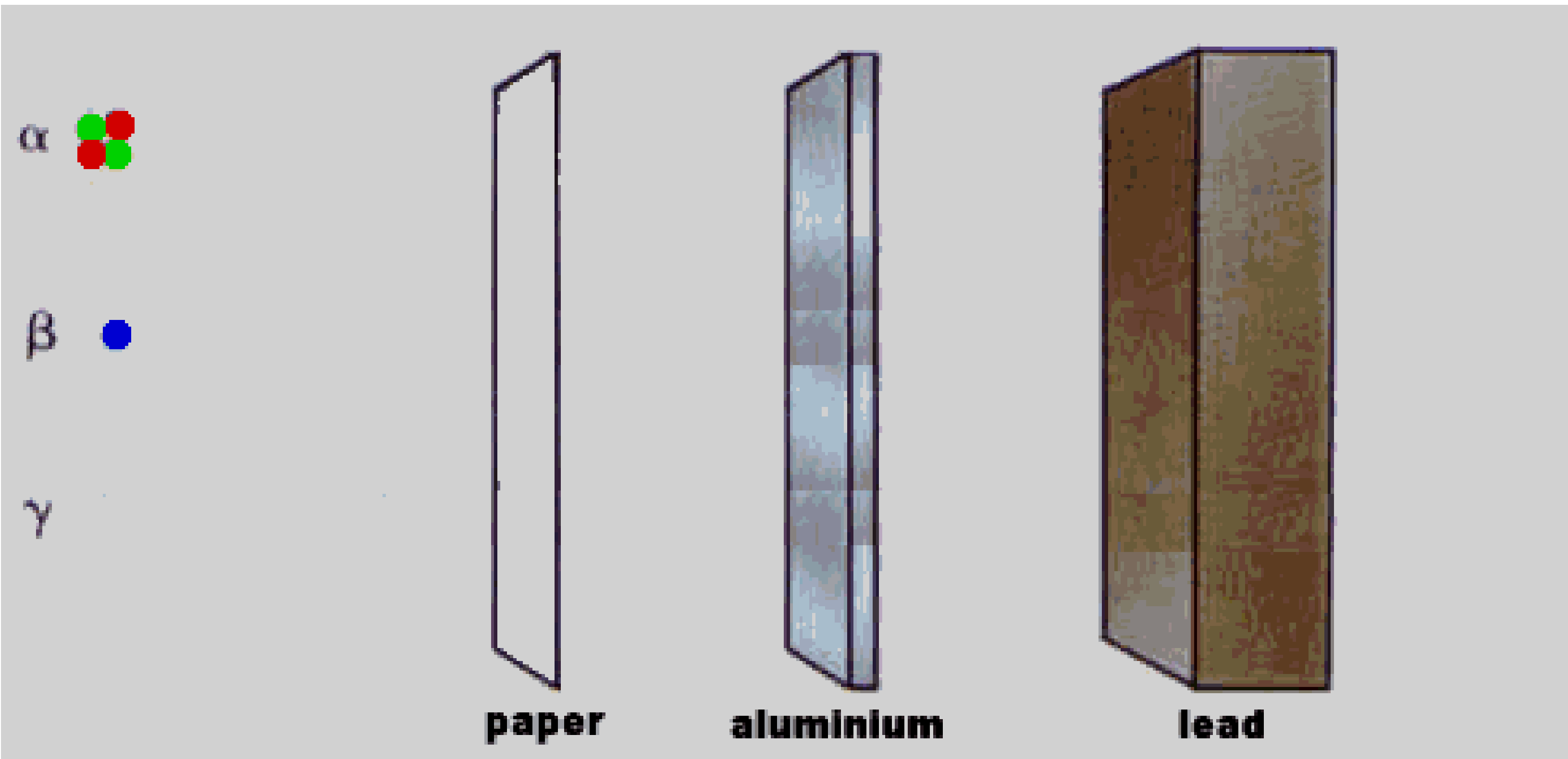
- Gamma rays have a **high penetrating power** - it takes a thick sheet of metal such as **lead** to reduce them.

- Gamma rays do not directly ionize other atoms, although they may cause atoms to emit other particles which will then cause ionization.



- We don't find pure gamma sources - gamma rays are emitted alongside alpha or beta particles.

Alpha particles are easy to stop, gamma rays are hard to stop.



Mode of radioactive decay:

Type of Radiation	Alpha particle	Beta particle	Gamma ray
Symbol	$^{4}_{2}\alpha$ or $^{4}_{2}He$	β^{-}	γ
Charge	+2	-1	0
Speed	slow	fast	Very fast
Ionising ability	high	medium	0
Penetrating power	low	medium	high
Stopped by:	paper	aluminium	lead

Radiation measurement

- The basic unit for quantifying radioactivity (i.e. describes the rate at which the nuclei decay).

Curie (Ci):

- **Curie** (Ci), named for the famed scientist Marie Curie

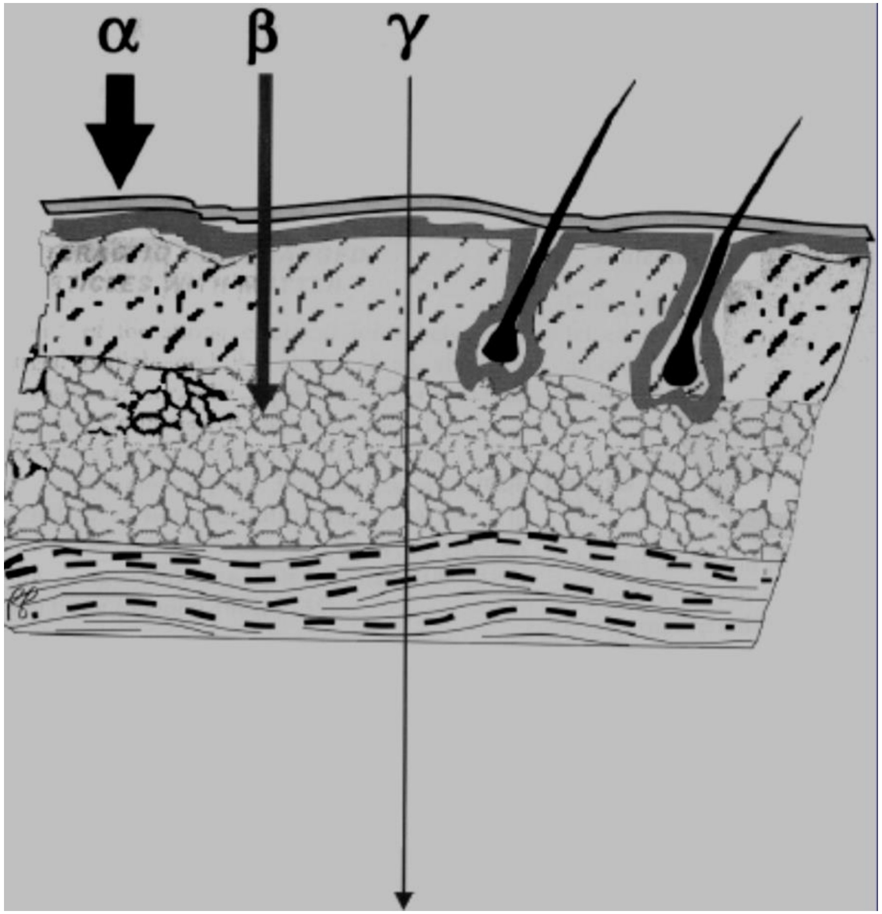
$$\text{Curie} = 3.7 \times 10^{10} \text{ disintegration per second (dps)}$$

$$\text{Millicurie } (mC_i) = 3.7 \times 10^{7} \text{ dps}$$

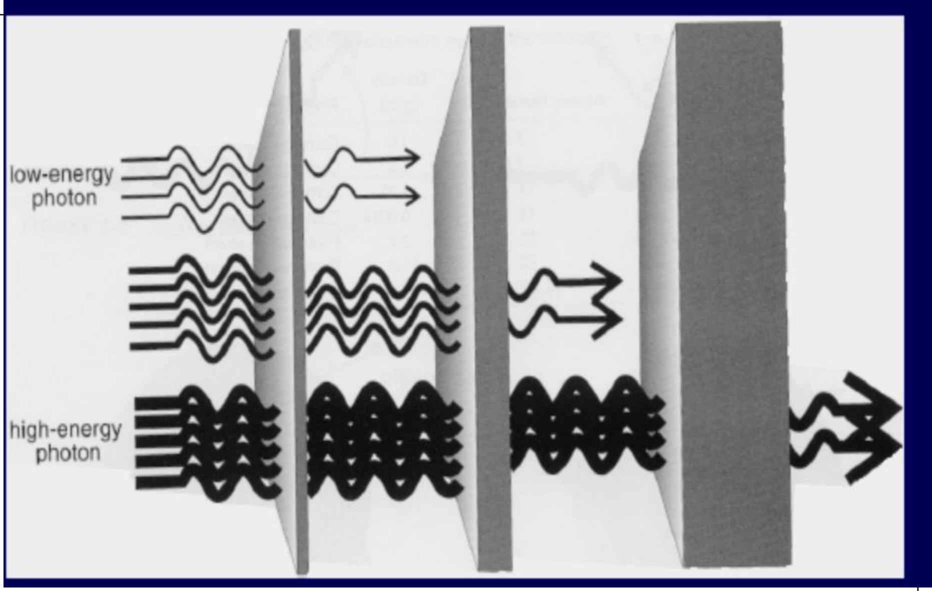
$$\text{Microcurie } (uC_i) = 3.7 \times 10^{4} \text{ dps}$$

Becquerel (Bq):

A unit of radioactivity. **One becquerel is equal to 1 disintegration per second.**



α
β
γ



low-energy
photon
high-energy
photon

Radiopharmaceuticals can be divided into:

1. **Radiopharmaceutical preparation:** A radiopharmaceutical preparation is a medicinal product in a ready-to-use form suitable for human use that contains a radionuclide.

2. **Radionuclide generator:** A system in which a daughter radionuclide (short half-life) is separated by elution or by other means from a parent radionuclide (long half-life) and later used for production of a radiopharmaceutical preparation.

3. **Radiopharmaceutical precursor**: A radionuclide produced for the **radiolabelling process** (Process of attaching a radionuclide to a non-radioactive molecule) with a resultant radiopharmaceutical preparation.

4. **Kit for radiopharmaceutical preparation:** In general a vial containing the **non-radionuclide components** of a radiopharmaceutical preparation, usually in the form of a sterilized, validated product to which the appropriate radionuclide is added

Radionuclide production

- **Charged particle bombardment:** Radionuclide may be produced by bombarding target materials with charged particles in particle accelerators such as cyclotrons.

- **Neutron bombardment:** Radionuclide may be produced by bombarding target materials with neutrons in nuclear reactors.

- **Radionuclide generator systems:** Radionuclide of short half-life may be produced by means of a radionuclide generator system involving separation of the daughter radionuclide from a long-lived parent by chemical or physical separation.

Radio activity

- Decay process is spontaneous
- Decay Constant (λ)
  - change in number of atoms over a time period
- Time required for a radionuclide to decay to 50% of its initial activity level (T1/2)
  - Tc-99m has a $T_{1/2}$ of 6 hours

Decay Equation

$$A_t = A_0 \, e^{-\lambda t}$$

- A_t = radioactivity in (mCi) at time
- A_0 = radioactivity in (mCi) at time = 0
- Decay constant = $-\lambda = -0.693/T1/2$
- Decay factor = $e^{-\lambda t}$
- Can calculate activity or decay of a radionuclide

FORMULATION OF RADIOPHARMACEUTICAL PREPARATION

1- Sterilization:

- Radiopharmaceutical preparations intended for parenteral administration are sterilized by a suitable method.

- Terminal sterilization by autoclaving is recommended for heat stable products

- For heat labile products, the filteration method is recommended.

2- Addition of antimicrobial preservatives:

- Radiopharmaceutical injections are commonly supplied in multidose containers.

- Parenteral preparations should contain a suitable antimicrobial preservatives.

- stored at a temperature between 2° and 8°C and

- the contents used within 7 days.

- Radiopharmaceutical injections for which the shelf-life is greater than one day and do not contain an antimicrobial preservative should be supplied in single-dose containers.

Properties of an Ideal Diagnostic Radioisotope:

- Easy Availability:

– Readily Available, Easily Produced & Inexpensive:

- Target to Non target Ratio:

– It should be high to: maximize the efficacy of diagnosis minimize the radiation dose to the patient

- Effective Half-life**:**

– It should be short enough to minimize the radiation dose to patients and long enough to perform the procedure. Ideally1.5 times the duration of the diagnostic procedure.

Example: For a Bone Scan which is a 4-h procedure 99mTc- phosphate compounds with an effective half-life of 6 h are the ideal radiopharmaceuticals

- **Patient Safety**:
  - Should exhibit no toxicity to the patient.

- **Preparation and Quality Control**:
  - Should be simple with little manipulation.
  - No complicated equipment
  - No time consuming steps

Radiopharmaceutical quality control:

1- Identity tests

- The radionuclide is generally identified by its half-life or by the nature and energy of its radiation or by both.

2- **Radionuclidic purity**

- Fraction of the total radioactivity present as the desired radionuclide The gamma-ray spectrum, should not be significantly different from that of a standardized solution of the radionuclide.

Radiopharmaceutical quality control:

4- **Chemical Purity**

- Chemical purity refers to the proportion of the preparation that is in the specified chemical form regardless of the presence of radioactivity. determined by methods of analysis.

5- **pH**

6- Sterility

7- Bacterial endotoxins/ pyrogens

8- Labelling

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;
- the preparation is for diagnostic or for therapeutic use;
- the route of administration;
- the total radioactivity present
- the expiry date
- the batch (lot) number
- for solutions, the total volume;
- any special storage requirements with respect to temperature and light;
- the name and concentration of any added microbial preservative

Storage

- Radiopharmaceuticals should be kept in well-closed containers and stored in an area assigned for the purpose.
  - the maximum radiation dose rate to which persons may be exposed is reduced to an acceptable level
- parenteral radiopharmaceuticals should be kept in a glass vial, ampoule or syringe
  - sufficiently transparent to permit the visual inspection of the contents.

Applications of radiopharmaceuticals:

1. Treatment of disease: (therapeutic radiopharmaceuticals)

- They are radiolabelled molecules designed to **deliver therapeutic doses of ionizing radiation** to specific diseased sites.

- Chromic phosphate P32 for lung, ovarian, uterine, and prostate cancers
- Sodium iodide I -131 for thyroid cancer
- Samarium Sm- 153 for cancerous bone tissue
- Sodium phosphate P 32 for cancerous bone tissue and other types of cancers
- Strontium chloride Sr- 89 for cancerous bone tissue

2- an aid in the diagnosis of disease: (diagnostic radiopharmaceuticals)

- The radiopharmaceutical accumulated in an organ of interest emit gamma radiation which are used for imaging of the organs with the help of an external imaging device called gamma camera.

- Radiopharmaceuticals used in tracer techniques for measuring physiological parameters (e.g. ^{51} **Cr-EDTA** for measuring glomerular filtration rate).

- Radiopharmaceuticals for diagnostic imaging (e.g.^{99m} **TC-methylene di phosphonate (MDP)** used in bone scanning).