SHREE H. N. SHUKLA INSTITUTE OF PHARMACEUTICAL EDUCATION AND RESEARCH

B.PHARM

(SEMESTER –I)

SUBJECT NAME: PHARMACEUTICAL INORGANIC CHEMISTRY

SUBJECT CODE: BP104TP

UNIT 5: RADIOPHARMACEUTICALS

Content: Radioactivity, Measurement of radioactivity, Properties of alpha, Beta & Gamma radiations, Half life, Radioisotopes and study of radioisotopes-Sodium Iodide^{131}, Storage conditions, Precautions & Pharmaceutical application of radioactive substances.

Definition:

- 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 C**i is the number of disintegrations emanating from 1 g of Radium-226, and is equal to 3.7 x 1010 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.
- Rountagen (1R) = 2.54 x 10^{-8} C Kg^{-1}.
- Rutherford (1 Rd) = 10^6 DPS.

Half-Life Period:

The time in which a given quantity of a radionuclide decays to half its initial value is termed as half-life (T1/2).

Formula of Half life period:

$T_{1/2}$ = 0.693/lamda

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:- o an alpha particle (α) o a beta particle (β) o 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. -particle depends very much on the source, but typically are about 10% of the speed of light. α
- The speed of the -particle to penetrate materials is not very great, it usually penetrates no more than a few α.
- The capacity of the 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. -particle radiation is extremely dangerous.
- But if the radiation sources are close to sensitive organs.

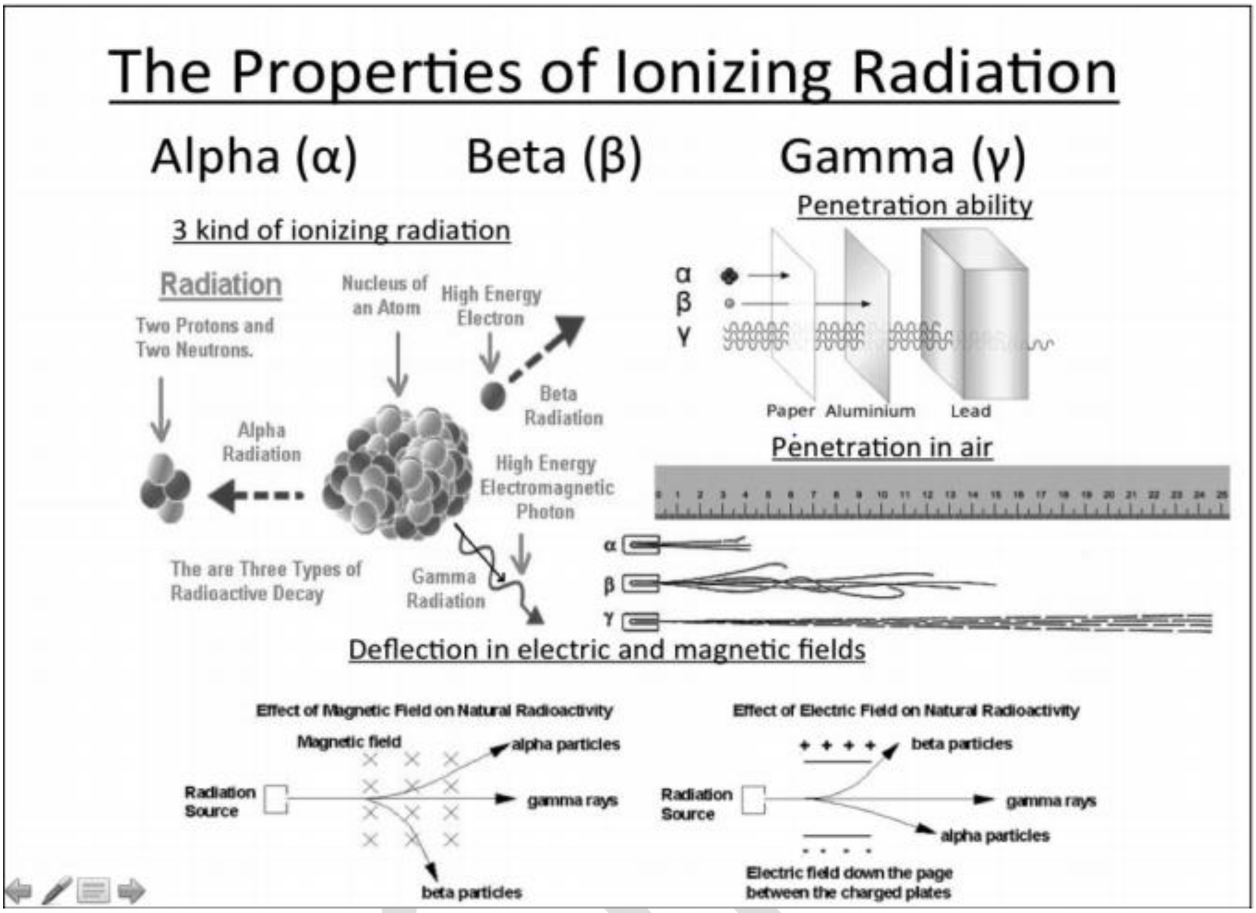
Beta particles

- Particle carries either one negative or one positive β Beta-particle radiation consists of fast moving electrons. Every 1.6 × 10-19 coulomb: -e, +e). They are affected by electric and magnetic fields. ±electronic charge.
- The speed depends on the source, but it can be up to 90% of the speed of light. particles can penetrate up to 1 m of air. They are stopped by a few millimetres of aluminium or perspex β -radiation. They are very dangerous if ingested.
- Their ionising capacity is much less than that of alpha particle, 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 × 108 m/s). radiation isγ
- Gamma radiation is very difficult to stop, it takes up to 30mm of lead. Although the ionising capacity of 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

1.) **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.

2.)**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.

3.) **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 nitrogenand are hence cumbersome and not suitable as field instruments.

Pharmaceutical Application Of Radioactive Substances

- **Treatment of Cancers and Tumours**

o **Americium 241** used as antineoplastic.

o **Californium 252** used as antineoplastic.

o **Cobalt 60** used as antineoplastic.

o **Gold 94** used as antineoplasatic.

o **Holmium 66** (26 h) being developed for diagnosis and treatment of liver tumours.

o **Iodine-125** (60 d) used in cancer brachytherapy (prostate and brain). - Treatment of Thyroid Disease with Iodine 131.

o **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

o 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:

o **Erbium-169**: Use for relieving arthritis pain in synovial joints - Diagnostic Radiopharmaceuticals

o **Ammonia N 13** Injection used for diagnostic coronary artery disease.

o **Chromium 51** used for diagnosis of pernicious anaemia.

o **Holmium 166** used for diagnosis and treatment of liver tumours. o 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 to be Taken in Handling of Radiopharmaceuticals:

Great care has to be taken in handling storage of radioactive material for protecting people and personnel who handle it:
i) The working areas should not get contaminated with radioactive material.
ii) If the radioactive liquid has to be handled, it must be carried in trays having absorbent tissue paper so that any spillage will get absorbed by paper.
iii) Rubber gloves have to be used when working with radioactive liquids.
iv) Pipettes operated by mouth should never be employed. Before making use of glass apparatus, it must be ensured that they have been inactive. The waste radioactive materials have to be stored till the activity becomes low before its disposal.
v) Smoking, eating, drinking activities are prohibited in the area of radioactive work.
vi) The radioactive emitter should be handled with forceps and never by hand.
vii) Sufficient shielding device should be used.
viii) Radioactive materials have to be stored in suitable labeled containers, shielding by bricks and preferably in a remote corner.
ix) Great care has to be applied for disposal of radioactive materials.
x) A regular monitoring of radioactivity be done in area where radioactive material is stored.

Sodium Iodide (I^{131})

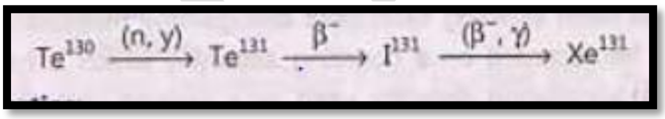
Synonym: Radioactive iodine.

Out of all the isotopes of iodine, I^{131} is most commonly used. It is used as an aqueous solution of sodium iodide having sodium thiosulphate in addition as a reducing agent.

Method of Preparation:

Most I^{131} is prepared in nuclear reactor by neutron-irridation of a neutral Tellurium target. Irridation of natural tellurium produces almost entirely I^{131} as the only radionuclide with a half life longer than hours.

Ultimately in 8.02 days it gets converted into Xenon-131 (stable isotope).



Properties:

It forms a colorless solution.

I^{131} have half life of 8.4 days and emits beta and gamma radiations.

Its solution is having pH range of 7 to 10.

Hyperthyroidism Treatment by I^{131}:

- Iodine inhibits the release of thyroid hormones and forms the basis for its use in hyperthyroidism. All the isotopes of iodine are rapidly taken up by thyroid follicles.
- Radioactive iodine available as NaI^{131} solution and is administered orally.

Sodium iodide-131 solution and capsule:

- Sodium iodide are suitable both for oral or i.v administration
- The solution is clear and colourless but as a time pass both solution and glass get darken due to the effect of radiation.
- The pH of solutions varies between 7.5-9.0
- For injection, as suitable preservative such as benzyl alcohol is added. A reducing agent such as sodium thiosulphate is also added to the solution, to prevent the oxidation of sodium iodide in aq. solution.
- Potassium salt, iodide and iodate have been acting as a carrier for iodide ions and for iodate ions present in the sodium iodide solution.
- Sodium iodide capsules are prepared by evaporating an alcoholic solution of sodium radio-iodide directly on the walls of capsule or on inrt capsule filling material.

Radioactive Identification:

- The spectrum of I^{131} has been complex but the most abundant type of photon is having energy of 0.365 MeV.It is possible to determine the energy in a spectrometer by detecting gamma radiation with a scintillation counter which having a thallium activated,
- The gamma ray scintillation spectrum of Sodium iodide solution has been found to be identical to that of specimen of I^{131} of known purity, which is exhibits major photoelectric peak, having energy of 0.365 MeV.

Assay:

- It is possible to determine its activity, using suitable counting equipment by comparision with a standardized I-131 solution or by measurement of an instrument calibrated with the aid of such solutions.
- Iodine-131 has been emiting both gamma and beta particles in its decay process.Radioactivity has to be recordedon a counting assembly which is having either a Geiger-Muller counter or scintillation detector used as a sensing unit and an electronic sealing device,

Packaging and Storage conditions:

- The solution has to be prepared in single dose or multiple dose containers that have ben previously treated to prevent absorption.
- So as to be avoid absorption of radionuclides on a wall of the container including laboratory vesse;s,it has been recommended that container used to handle solution iodide-131 solution,should be first of all rinsed with a solution having approximately 0.8% of sodium bisulphate and 0.25% of sodium iodide and then water until last rinsing has been neutral to litmus.

Uses:

1.) Radioactive iodine is mainly used for the diagnosis of disorder of thyroid function.

2.) It is also used in treatment of hyperthyroidism.
3.) Radioactive iodine is also used in the treatment of Grave's disease (toxic diffused goiter).
4.) It is also used in radiotherapy of thyroid cancer.
5.) It is also used in the treatment of thyrotoxicosis.