

# **RADIO ISOTOPES**

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# INTRODUCTION

- An Atom is composed of a positively charged nucleus that is surrounded by a cloud of negatively charged electrons.
- The number of orbital electrons is equal to the number of protons present in the nucleus , this number is known as atomic number ( Z ) .
- The sum of protons & neutrons in a given nucleus is the mass number.

$$A = Z + N \quad ( N \text{ is the number of neutrons } )$$

# DEFINATION

- Isotopes are nuclides with the same atomic number but different mass numbers .
- The spontaneous degradation of nucleus & transmission of one element to another with consequent emission of rays ( or ) particles is known as radioactivity .

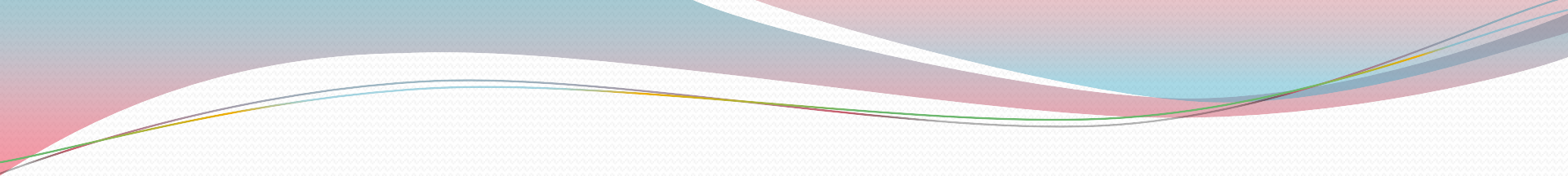
# TYPES OF RADIO ACTIVE DECAY

- 1 )Decay by negatron emission ,
- 2 )Decay by positron emission ,
- 3 )Decay by  $\alpha$  particle emission ,
- 4 )Decay by gamma rays emission ,
- 5 )Decay by X rays emission .
- Decay by Negatron emission : When Neutron is converted to a Proton by the ejection of a negatively charged  $\beta$  particle called a Negatron (  $\beta^-$  ) is emitted .

Neutron

Proton + Negatron



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- contd
- Negatron emission is very important to biochemist .
  - $^3\text{H}$  &  $^{14}\text{C}$  are  $\beta$  emitters can be used to label any organic compound .
  - $^{35}\text{S}$  used to label methionine , to study protein synthesis.
  - $^{32}\text{P}$  , a powerful tool in molecular biology & used as a nucleic acid label .
  - $\beta$  emitting isotopes are most suitable for autoradiography , particularly for cell & tissue localization experiment .

**DECAY BY POSITRON EMISSION**

• When Proton is converted to Neutron a positively charged  $\beta$  particle known as positrons ( $\beta^+$ ) is emitted .

Proton                      Neutron + Positron .

- Positrons are extremely unstable , they dissipate their energy in interaction with electrons .

# Contd

- The mass & energy of 2 particles( positron & electron ) are converted to 2  $\gamma$  (gamma) rays are emitted at 180 to each other .
- Positrons are detected by the same instrument used to detect  $\gamma$  radiation .
- Positron emission tomography used to identify active & inactive areas of brain .

## DECAY BY $\alpha$ PARTICLE EMISSION

- Isotopes of elements with high atomic numbers frequently decay by emitting  $\alpha$  particle .
- An  $\alpha$  particle is a helium nucleus contains 2 protons & 2 neutrons ( ${}^4\text{He}^{2+}$ ).
- $\alpha$  particles have high ionizing power, less penetrance & are extremely toxic .
- Isotopes that decay by  $\alpha$  particle emission are not frequently encountered in biological work .



# ELECTRON CAPTURE

- Proton captures an electron orbiting in the inner most shell .



- Proton becomes a Neutron & electromagnetic X rays is given out .

DECAY BY EMISSION OF  $\gamma$  RAYS

• These  $\gamma$  rays result from a transformation in the nucleus of an atom ( in contrast to X rays emission ) & frequently accompany  $\alpha$  &  $\beta$  particle emission .

- Emission of  $\gamma$  radiation leads to leads to no change in atomic number or mass .
- $\gamma$  radiation has low ionizing power but high penetration .

# HALF LIFE OF RADIOISOTOPES

- Half life of radio isotope is the time period required for radionuclide to decay to one half the amount originally present .
- $t_{1/2} = 0.693/\lambda$ .
- $\lambda$  is decay constant , a characteristic of a given isotope decaying in unit time .

# UNITS OF RADIOACTIVITY

- Becquerel is the unit of radioactivity is defined as one disintegration per second (1 d. p. s. ).
- Frequently used units are curie , defined as the quantity of radioactive material in which the number of nuclear disintegrations per second is same as the 1gm of radium (  $3.7 \times 10^{10}$  Bq ).
- Specific activity is defined as disintegration rate per unit mass of radioactive atoms.

# Detection & Measurement of Radioactivity

- Various methods for measuring radioactivity
- 1) Autoradiography ,
- 2) gas ionization detectors &
- 3) fluorescent scintillation , are the basis to detect & measure radioactivity in clinical laboratory .

# AUTORADIOGRAPHY

- In autoradiography a photographic emulsion is used to visualize molecules labeled with a radioactive element .
- The emulsion consists of a large number of silver halide crystals embedded in a solid phase such as gelatin .

# Contd

- As energy from radioactive material dissipated in the emulsion , the silver halide becomes negatively charged & is reduced to metallic silver.
- Photographic developers are designed to show these silver grains as blackening of the film , & fixers remove any remaining silver halide .

## contd

- Techniques of autoradiography have become more important in molecular biology .
- Weak  $\beta$  – emitting isotopes (  $^3\text{H}$  ,  $^{14}\text{C}$  ,  $^{35}\text{S}$  ) are most suitable for autoradiography , particularly for cell & tissue localization experiments .
- Low energy of negatrons & short ionizing track of isotope will result in discrete image .



# contd

- $\beta$  emitting radioisotopes are used when radioactivity associated with subcellular organelles is being located .
- $^3\text{H}$  is the best radioisotope , since it's all energy will get dissipated in the emulsion .
- Electron microscopy can then be used to locate the image in the developed film .

# contd

- For location of DNA bands in electrophoretic gel,  $^{32}\text{P}$  labeled nucleic acid probes are useful .
- After hybridization ,hydrolysis & separation of DNA fragments by electrophoresis , a photographic plate is applied to to the covered gel & allowed to incubate .

# Choice of emulsion & film

- X ray films are generally suitable for macroscopic samples such as whole body, electrophoretographs , chromatographs .
- When light (or) electron microscopic , detection of image ( cellular , subcellular localization of radioactivity ) very sensitive films are necessary .

# contd

- Time of exposure & film processing depends upon the isotope , sample type , level of activity , film type & purpose of the experiment.
- In Direct autoradiography , the X ray film or emulsion is placed as close as possible to the sample .

# Fluorography

- Fluorography is used to cut short the time of exposure .
- A fluorescent material such as ( PPO or sodium silicate ) is infiltrated into the gel .
- Negatrons emitted will excite fluorescent material & emit light , which will react with the film .

# Intensifying screens

- When  $^{32}\text{P}$  labeled or  $\gamma$ -isotope labeled samples are used because of more penetrating nature of  $\gamma$  rays poor image is formed .
- Intensifying screens helpful in giving a good image .
- Solid phosphorus is applied on the other side of the film from the sample .

# Other methods for amplifying image

- Sensitivity of film is increased by preflashing .
- Preflashing involves millisecond light flash prior to sample is being brought to juxtaposition with the film .
- Low temperature exposure will provide higher sensitivity.

# GAS FILLED DETECTORS

- Detectors filled with gases or gas mixtures are designed to capture & measure the ions produced by radiation within the detector ( excitation & ionization produces a pulse of current ).
- Gas filled detectors used to measure radioactivity include
  - 1) Ionisation chamber
  - 2) Proportional counter
  - 3) Geiger Muller counter
- Geiger muller counter is used in clinical laboratory  
.



# SCINTILLATION COUNTING

- In scintillation process the radiation causes excitation & ionization of fluorescent material , the absorbed energy produces a flash of light.
- The principal types of scintillation detectors found in clinical laboratory are 1) sodium iodide crystal scintillation detector .  
2) the organic liquid scintillation detector.

# APPLICATIONS OF RADIOISOTOPES IN BIOLOGICAL SCIENCES

- Radioisotopes are frequently used for tracing metabolic path ways .
- Mixing radiolabeled substrates & samples of the experimental material & collecting samples at various times , extract & separate the products by chromatography.
- Radioactivity detectors can be attached to gas liquid chromatography or HPLC columns to monitor radioactivity coming off the column during separation

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# uses

- It is possible to predict the fate of individual carbon atoms of ( $^{14}\text{C}$ ) acetate through TCA cycle.
- Methods have been developed to isolate intermediates of the cycle & to ascertain the distribution of carbon atoms within each intermediate( this is called as specific labeling pattern ) .

# USES

- Radioisotopes are used in ascertaining the turnover times for particular compounds .
- Group of rats injected with radio labeled amino acid left for 24 hours allowing to assimilate into proteins.
- The rats are killed at suitable time intervals & radioactivity in organs or tissue of interest is determined .

# uses

- Radioisotopes are widely used in study of the mechanism & rate of absorption , accumulation & translocation of inorganic & organic compounds in the animal .
- Radiolabeled drugs are useful in pharmokinetic studies ( site of accumulation , rate of accumulation , rate of metabolism & metabolic products ) .

# ANALYTICAL APPLICATIONS OF RADIOISOTOPES

- Virtually any enzyme reaction can be assayed using radioactive tracer methods.
- Radioisotopes have been used in study of 1) The mechanism of enzyme action & 2) In studies of ligand binding to membrane receptors.

# contd

- Isotope dilution analysis : when a known amount of radioactive tracer is introduced into an unknown volume , after thorough mixing , the concentration of radio tracer is estimated .

$$V = N / n$$

V = volume to be measured

N = total number of counts injected

n = number of counts per ml

# Contd

- By isotope dilution analysis plasma volume , total body water , E.C.F volume , RBC cell volume , total exchangeable sodium can be measured .
- $^{131}\text{I}$  labeled human serum albumin useful in diagnosing protein losing enteropathy .
- $^{51}\text{Cr}$  labeled RBC are given intra venously if there is any GI blood loss radioactivity can be measured .



# Contd

- Radio immuno assays are useful in analysis of hormones , growth factors , tumour markers , cytokines , bacterial antigens ,vitamin D & various biological molecules .
- In RIA either antigen or antibody is radiolabeled .
- Radiolabelling must not interfere in the binding of antigen & antibody , has to be compared with unlabeled ones .

# Radioisotopes used in Diagnostic purposes

- Radio active iodine uptake & imaging reveals the functional status of thyroid tissue , including nodules , the whole thyroid gland & metastatic foci .
- $^{131}\text{I}$  is used for thyroid cancer imaging & management .
- $^{123}\text{I}$  I is used for thyroid scan .

# contd

- Schilling test : used to detect the malabsorption of vitamin B<sub>12</sub> .
- Measurement of urinary radio labeled B<sub>12</sub> following a saturation dose of non labeled stable B<sub>12</sub>
- 1000µg of non labeled B<sub>12</sub> is given IM.
- 1µg of labeled B<sub>12</sub> is given orally.
- Less than 5% excretion of radio labeled dose indicates malabsorption of Vit B<sub>12</sub>.

# Contd

- Technetium 99 m (  $^{99m}\text{Tc}$  ) pertechnetate: it is trapped by the thyroid gland but not organified , it can give a reasonable thyroid image even if patient is taking thyroid replacement therapy .
- $^{99m}\text{Tc}$  – MIBI ( 2 – methoxy 2 – methyl propyl isonitrile ) used in preoperative localization of parathyroid gland .

# contd

- Thallium 201 facilitates detection of  $^{131}\text{I}$  negative metastatic thyroid cancer lesions in total body scan .
- Iodo cholesterol  $^{131}\text{I}$  labeled 6 iodo methyl -19 norcholesterol , NP-59 used in adrenocortical imaging in cushing disease, cortisol producing adenoma ,  
primary aldosteronism .

# contd

- MIBG (  $^{131}\text{I}$  or  $^{123}\text{I}$  –meta iodo benzyl guanidine )scan is useful in adrenomedullary imaging in pheochromocytoma , neural crest tumors , carcinoid , medullary carcinoma thyroid .
- Isotope bone scan is extremely useful in pagets disease of bone .

# contd

- Indium 111 octreotide scan a somatostatin analogue used to show :  
neural crest tumors,  
pheochromocytoma ,  
carcinoid ,  
paraganglioma &  
medullary carcinoma thyroid .

## Contd

- Fluorodeoxy glucose PET helpful in detection of  $^{131}\text{I}$  negative thyroid carcinoma ,& MIBG negative pheochromocytoma .
- Strontium 89 & Samarium 153 are two radionuclides that are preferentially taken in bone , particularly sites of new bone formation, capable of controlling bone metastasis .



# contd

- Xenon 133 is useful in lung function tests & is useful in diagnosing malfunctions of lung ventilation .
- (<sup>133</sup> I) iodohippuric acid used in diagnosis of kidney infections , kidney blockages or imbalance of function between two kidneys .

# Contd

- $^{51}\text{Cr}$  -EDTA ,  $^{99\text{m}}\text{Tc}$ -DTPA &  $^{125}\text{I}$  - iothalamate have clearance closest to inulin . ( useful in measurement of GFR )
- $^{99\text{m}}\text{Tc}$ -DTPA has the advantage that it can also be used for gamma camera imaging .

# Therapeutic uses of radioisotopes

- Radioisotopes have role in management of malignancies .
- Tumour tissues are attacked by beam of radiation .
- $^{131}\text{I}$  is used for treatment of thyroid cancer .
- Teletherapy :  $^{60}\text{Co}$  is the source of radiation , radiation occurs from a distant source .
- Radioactive material is impregnated into body in form of beads or needles or either as surface applicants .

## contd

- $^{60}\text{Co}$  or radium rods are used in treatment of cervical cancer .
- $^{32}\text{P}$  surface applicators have role in Rx of squamous cell carcinoma , superficial angiomas , mycosis fungoides .
- Boron 10 neutron irradiation has been recently used in the treatment of the inoperable & rapidly fatal brain tumour like glioblastoma multiforme

# Contd

- $^{48}\text{Au}$  ( gold ) is used for treatment of malignant pleural & peritoneal effusions.
- Yttrium<sup>90</sup> synovectomy is useful in management of arthrites in hemophelics .

# Radiation hazards

- Immediate effects :
  - 1 ) Bone marrow syndrome,
  - 2 ) Gastrointestinal track syndrome,
  - 3 ) Central nervous system syndrome .
- Bone marrow syndrome : severe damage to hematopoietic system , leads to pancytopenia occurs with exposure of 200-1000 rads.

## contd

- Gastro intestinal syndrome : Severe damage to mucosal epithelium . Exposure of 1000 – 5000 rads is the cause .
- Central nervous system syndrome : Blood brain barrier is lost . Exposure of 5000 – 10000 rads is the cause .
- Delayed effects : carcinogenesis by damaging DNA

# Radiation safety & protection

- The most popular triad of radiation protection is time ,distance & shield (TDS).
- Minimum possible time should spent near the radiation zone .
- Handling of radioactive material should be done from maximum possible distance .
- Person should be shielded by lead .





**THANK YOU**