Radiopharmaceutical Preparations

Radiopharmaceutical isotopes are primarily emitting beta or gamma radiation, with beta radiation often in the negatron form and sometimes positrons. Specific isotopes target tissues, such as ^{131}I in the thyroid, creating "hot spots" (high concentration) or "cold spots" (low concentration). Isotopes may be tagged to molecules to guide them to specific tissues. Key considerations include:

- Selective absorption and distribution to minimize hazards.
- The ability for isotopes and their decay products to be easily eliminated from the body.
- Low toxicity beyond their inherent radioactivity.

1- Chromium-51

Chromium-51 is artificially produced via neutron bombardment of chromium-50, which emits a gamma ray in the process. It decays by K-capture to vanadium-51, releasing 0.320 MeV gamma rays. The isotope has a half-life of 27.8 days.

$$^{51}_{24}\mathrm{Cr} \xrightarrow[K\ Capture]{27.8\ days} {}^{51}_{23}\mathrm{V} + \gamma$$

Sodium Chromate Cr 51 ($Na_2{}^{51}CrO_4$) injection

It is a clear to slightly yellow solution with a pH between 7.5 and 8.5. Used diagnostically to:

- Measure red blood cell mass, volume, and survival time.
- Scan the spleen for functionality.

Chromium in its +6-oxidation state (Cr[VI]) binds to erythrocytes. Inside red blood cells, chromium is reduced to Cr(III) and attaches to the hemoglobin. After red blood cells are reinjected, their destruction over time releases chromium-51, which is excreted in urine. The rate of excretion helps determine the survival time of red blood cells.

Heat-damaged red blood cells are labeled with chromium-51 and reinjected and the spleen uptakes these cells, the concentration of radioactivity indicates spleen functionality.

2- Cyanocobalamin Co-57 and Co-60

Cobalt-57 can be produced by several methods. One of these methods involves gamma irradiation of ^{58}Ni, and another is accomplished through proton bombardment of ^{56}Fe. On the other hand, cobalt-60 is produced by bombardment of the stable cobalt-59 in a neutron reactor. Co-57 decays by K-capture and emits 0.123 Mev gamma rays. The half life of the isotope is 270 days.

$$^{57}_{27}Co \xrightarrow[K\ Capture]{270\ days} {}^{57}_{26}Fe + \gamma$$

Cyanocobalamin Co 57 or Co 60 is vitamin B_{12}, in which a portion of the molecules contains radioactive cobalt in place of the stable isotope of the metal. The radioactive forms of the vitamin are used in diagnostic procedures for pernicious anemia. The basis of the test was developed by Schilling on the premise that if vitamin B_{12} is absorbed from the gastrointestinal tract, it will be excreted in the urine. Therefore, the radioactivity from an oral dose of ^{60}Co-labeled vitamin B_{12} should be detected in the urine of the normal patient and absent or at significantly lower levels in the urine of the patient with pernicious anemia, since these patients lack intrinsic factors which are necessary for the proper intestinal absorption of vitamin B_{12}.

Cobalt-57 is preferred over cobalt-60 in diagnostic applications due to its advantages:

- Higher radiation counting efficiency.
- Reduced scattering: Unlike cobalt-60, it avoids the Compton effect, which reduces detector efficiency.
- Lower radiation exposure: Cobalt-57 has a shorter half-life, no beta radiation, and lower-energy gamma emissions, minimizing radiation

exposure to the patient, especially to the liver, which stores unexcreted vitamin B_{12} and receives the most radioactivity.

3- Iron-59

Iron-59 is a beta- and gamma-emitting isotope prepared by neutron activation of iron-58, which is a stable isotope in iron metal occurring in 0.339% abundance. The half-life of iron-59 is 45 days.

$$^{59}_{26}\mathbf{Fe} \xrightarrow{\mathbf{45\ days}} {}^{59}_{27}\mathbf{Co} + \beta^- + \gamma$$

Ferrous Citrate Fe 59 and Ferric Chloride Fe 59

Ferrous Citrate Fe 59 is normally provided in a sterile solution preserved in (benzyl alcohol) and contains an antioxidant (ascorbic acid).

The isotope is employed in diagnostic procedures relating to various aspects of iron metabolism and red blood cell formation. The preparation can be administered orally to study the absorption of iron from the G.I. tract and injected intravenously for determinations of plasma iron clearance and turnover, and the incorporation of iron into erythrocytes.

4- Gold-198

Gold-198 is a radioactive isotope with a short half-life of 2.7 days, emitting both beta and gamma radiation. It is produced by neutron bombardment of gold-197 and used in both therapeutic and diagnostic applications.

$$^{198}_{79}\mathbf{Au} \xrightarrow{\mathbf{2.7\ days}} {}^{198}_{80}\mathbf{Hg} + \beta^- + \gamma$$

Therapeutic Uses:

Administered via intracavitary injection into the pleural or peritoneal cavities to manage:

- Pleural effusion: Accumulation of fluid in the pleural cavity.
- Ascites: Accumulation of fluid in the peritoneal cavity.

Beta radiation targets cancerous tissues within 4 mm of its placement, making it effective for localized treatment. It may also provide prophylactic benefits against tumor regrowth after surgical removal. Contraindicated in unhealed surgical wounds, exposed cavities, or ulcerative tumors to prevent complications.

Diagnostic Uses:

At lower doses, gold-198 colloidal solutions are used for liver scanning, it is taken up by Kupffer's cells (phagocytic cells in the liver) and helps assess the position, size, and shape of the liver, as well as Kupffer cell functionality. Areas without Kupffer's cells, such as tumors, abscesses, or cysts, appear as "cold spots" in scans. Gold-198 does not differentiate between types of growth, limiting its diagnostic specificity.

5- Iodine-123,125,131

Iodine I has an atomic number 53. It is a member of the halogens (Group 17 in the periodic table). It exists naturally as the diatomic molecule I_2. The iodide ion (I^-) is water-soluble and found primarily in the oceans. The important emission from iodine-131 for medical purposes are the beta$^-$ and gamma rays when this isotope decays to the metastable isotope of xenon-131 with a half-life of 8.08 days.

$$^{131}_{53}\mathbf{I} \xrightarrow{\mathbf{8.08\ days}} {}^{131}_{54}\mathbf{Xe} + \beta^- + \gamma$$

Iodine is critical to produce thyroid hormones (T3 and T4), which regulate metabolism. The thyroid gland actively absorbs iodine from the bloodstream, making it a target for both diagnostic and therapeutic applications involving iodine isotopes.

Medical Uses of Radioactive Iodine:

1. Imaging with ^{123}I: Its gamma radiation and short half-life (13 hours) make it ideal for nuclear medicine scans. Using a gamma camera, doctors can

detect iodine concentration in the thyroid, helping diagnose thyroid disorders.

2. Therapy with ^{131}I: High dose ^{131}I is used to treat hyperthyroidism and thyroid cancer. Its beta radiation destroys thyroid cells or cancerous tissue selectively. Low dose ^{131}I, however, may pose a cancer risk, as beta radiation damages DNA in healthy cells over prolonged exposure.

Potassium iodide (KI) provides protection by saturating the thyroid gland with stable iodine, preventing radioactive iodine uptake.

6- Strontium-89

Strontium Sr has an atomic number 38, which is a soft grey metal belonging to Group 2 (alkaline-earth metals). It is highly reactive with water, producing strontium hydroxide and hydrogen gas and stored under mineral oil to prevent oxidation.

Natural strontium consists of four stable isotopes: ^{84}Sr, ^{86}Sr, ^{87}Sr, ^{88}Sr with ^{88}Sr being the most abundant. ^{89}Sr is a synthetic beta-emitting radioisotope with a half-life of 50.5 days, produced via neutron activation of ^{88}Sr. It undergoes β^- decay into yttrium-89.

$$^{89}_{38}\mathbf{Sr} \xrightarrow{\mathbf{50.5\ days}} {}^{89}_{39}\mathbf{Y} + \boldsymbol{\beta}^- + \boldsymbol{\gamma}$$

Due to its similarity to calcium, ^{89}Sr is metabolized similarly, accumulating in bones, particularly in hydroxyapatite cells. Localized beta radiation is delivered, providing pain relief for bone metastases. A majority of ^{89}Sr accumulates in bone metastases, with unabsorbed amounts excreted through the kidneys or feces.

It is administered intravenously for pain management in bone metastases, commonly seen in patients with prostate, breast, or lung cancer. The effectiveness lies in its ability to deliver targeted beta radiation to cancer-affected bone tissue, alleviating pain.

A common side effect of strontium administration is low platelet count, which typically resolves within 6 months post-treatment. Other side effects may include reduced white blood cell counts.

7- Boron Neutron Capture Therapy (BNCT)

Boron has two stable isotopes, ^{10}B and ^{11}B, and 14 radioisotopes with very short half-lives. ^{11}B is the most abundant isotope and represents 80% of natural boron, whilst ^{10}B (~20%) finds a significant clinical application in the so-called boron neutron capture therapy (BNCT).

BNCT is a noninvasive treatment option for malignant tumors, especially brain tumors and head and neck cancers and is currently under clinical trials. The patient is injected with a nonradioactive ^{10}B-containing compound that acts as a neutron-capturing agent and shows high selectivity to cancer tissues. Once the compound has reached the tumor, the patient is exposed to a beam of low-energy neutrons, the so-called epithermal neutrons. These neutrons lose their energy once they penetrate the skin, but they can still interact with the neutron-capturing agent and initiate a nuclear reaction.

This reaction of ^{10}B with a neutron results in the conversion to the nonradioactive isotope ^{7}Li and low-energy gamma radiation together with the emission of α-radiation ($^{4}_{2}He^{2+}$ particles). α-Radiation is of short range and bombards the local tumor tissue from within the tumor cells, which means there is minimum exposure to healthy tissue.

$$\mathbf{^{10}B + n_{th} \rightarrow [^{11}B] \rightarrow {}^{4}He + {}^{7}Li + \gamma}$$

8- ^{99m}Technetium

Technetium has the chemical symbol Tc and atomic number 43. It is the lightest element that has no stable isotope. It is a silvery-grey transition metal. ^{99m}Tc (also referred to as technetium-99m) is the metastable isomer of ^{99}Tc, which is a gamma-emitting nuclide routinely used in diagnostic medicine. It has a short half-

life of around 6h,which is ideal for diagnostic applications (but not for therapeutic applications) as it helps to keep the radiation exposure to the patient low.

$$^{99m}_{43}\mathbf{Tc} \xrightarrow{\boldsymbol{6\ hours}} {}^{99}_{43}\mathbf{Tc} + \boldsymbol{\gamma}$$

One challenge of using radioactive material is to safely manufacture the products and deliver them to the clinical setting. Products containing radionuclides with a short half-life cannot be delivered as the finished product because of their rapid decay. Therefore, they are delivered to the clinical setting as radionuclides with a long half-life and the desired radionuclide is then generated and formulated at the moment of use. ^{99m}Tc and its compounds are generated in situ for use as an imaging agent using a so-called ^{99m}Tc generator. The generator is loaded with molybdenum-99 (^{99}Mo), which is often referred to as the commercially available transportable source of ^{99m}Tc. The general idea is that the generator contains a long-lasting 'parent' compound, which decays and produces the 'daughter' radionuclide. In the case of the ^{99m}Tc generator, it contains molybdate ($^{99m}MoO_4^{2-}$) absorbed on an alumina column. $^{99m}MoO_4^{2-}$ decays to $^{99m}TcO4^{-}$, which can be removed as $Na^{99m}TcO_4$ when the column is washed with a NaCl solution.

$$^{99}_{42}\mathbf{Mo} \rightarrow {}^{99m}_{43}\mathbf{Tc} + \boldsymbol{\nu_e} + \boldsymbol{\beta^-}$$

Different molecules containing ^{99m}Tc target specific organs:

- ^{99m}Tc-aerosol: Lung ventilation imaging.
- ^{99m}Tc-albumin: Cardiac function.
- ^{99m}Tc-medronate: Skeletal imaging.
- ^{99m}Tc-succimer: Kidney imaging.
- Cardiolite (^{99m}Tc-sestamibi): Heart and parathyroid imaging.
- ^{99m}Tc-exametazime: Brain imaging for conditions like stroke, dementia, and trauma.

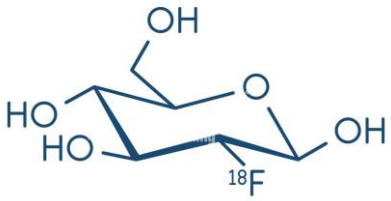
9- ^{18}Fluoride: PET scan

Fluorine has the chemical symbol F and atomic number 9 and is the most electronegative element. It belongs to group 17 of the periodic table, the so-called halogens.

There are 18 isotopes known for fluorine, but only (^{19}F) is stable. Most of the radioactive isotopes have a very short half-life, mostly <1min. Only radioisotope ^{18}F has a longer half-life of around 110 min and is clinically used. ^{18}F is a positron-emitting radioisotope and is used in radiopharmaceutical imaging such as PET scanning. Two compounds, namely fluorodeoxyglucose (^{18}F-FDG) and derivatives of ^{18}F choline, are under intense clinical investigation and/or use.

$$^{18}_{9}\mathbf{F} \rightarrow {}^{18}_{8}\mathbf{O} + \nu_e + \beta^+$$

^{18}F-FDG is a glucose derivative that contains a radiolabel (^{18}F) at the 2′ position replacing the hydroxyl group. ^{18}F-FDG is administered intravenously and is used as an assessment of problems with glucose metabolism, especially in the brain, often associated with epilepsy and in cancer. Areas where an increased absorption of ^{18}F-FDG are visible correlate to areas where an increased glucose metabolism is present. ^{18}F-FDG is distributed around the body like glucose and is cleared renally.



fludeoxyglucose (^{18}F)

^{18}F-FDG is generally used to assess the extent of the tumor in a cancer patient. Cancerous tissue is characterized by increased cell proliferation, which requires energy, and therefore an increased amount of glucose. This leads to an accumulation of ^{18}F-FDG in malignant tumors and allows judging the degree of

metastasis formed. This information is important for any surgical procedure and for the initial assessment of the cancer stage.

Unfortunately, there are limitations to the use of ^{18}F-FDG, as its uptake is not very specific. As a result, other conditions can also cause an accumulation of ^{18}F-FDG and can lead to misdiagnosis. These conditions include inflammation and healing of wounds, which also show increased glucose metabolism.

Therefore, a variety of other ^{18}F-labelled compounds are under intense scrutiny as alternative PET scanning agents. This includes ^{18}F-choline. Choline is a compound incorporated into the cell membrane and therefore cells dividing at a fast rate have an increased need for this substance. Studies for a range of tumors were undertaken, but most studies focused on prostate cancer.

Best of Luck…

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