International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 1506-1511 www.ijprajournal.com ISSN: 2456-4494

Overview on Radio-isotopes used in Anti-cancer treatment

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Date of Submission: 15-08-2024 Date of Acceptance: 25-08-2024

ABSTRACT –
Basically, radiopharmaceuticals deal with the use of radioactive nuclides as therapeutic agents in the treatment of various diseases and, in some cases, as sterilizing agents. The therapeutic effect is dependent on the radioactive potential of nuclides, which are used to destroy cancerous cells by either implanting nuclides near the tumor or using immunobiology to deliver nuclides only to the diseased cells.The use of radiopharmaceutical therapy (RPT) is becoming more widespread as a targeted cancer treatment that is both safe and efficient. In RPT, medications that either bind specifically to cancer cells or accumulate through physiological processes are used to administer radiation either locally or systemically. Nearly all radionuclides employed in RPT produce image-emitting photons, making it possible to visualize the therapeutic agent's biodistribution non-invasively. When compared to nearly every other systemic cancer treatment option, radiation therapy has demonstrated effectiveness with little toxicity. The FDA recently approved multiple RPT medicines, highlighting the treatment's extraordinary potential. This Review covers the Co-60 and Cs-137 radio isotopes and literature on Radiopharmaceutical agents used in anti-cancer therapy.

Keywords – Radioactive isotopes, cancer, radiopharmaceutical therapy.

I. INTRODUCTION –

Radioactive isotopes employed as cancer therapies or for diagnosis purposes are known as radiopharmaceuticals. The unstable nucleus of radioactive isotopes decays or releases excess radiation or energy until the nucleus becomes stable. Thus far, scientists have identified radioactive materials capable of targeting multiple cancer types, including thyroid, lymphoma, ovarian, brain, and bone cancer. The exact cause of thyroid cancer is uncertain or poorly understood, however environmental and genetic factors may play a role. Patients with thyroid cancer are treated with medication, surgery, and radiation therapy to eradicate any remaining malignant cells from the surgical incision. radioactive materials given in many forms, including intravenous, interstitial, and orally [as pills].A radiopharmaceutical is a drug made up of radioactive substances i.e. radionuclides. Sometimes it combines with the mAb which attaches to the cancerous cell. Examples of radioactive substances are Cobalt-60, Iodine, Bismuth, Radium, Strontium and Yttrium [Y]. Conventional malignant tumor medication exhibits an absence of specificity, poor solubility and distribution, unfavorable pharmacology and high tissue harm or toxicity. Targeted drug delivery systems like passive and active targeting nanocarriers, with diameters ranging from 10-100 nm are developed to enhance the biodistribution, medicine, therapeutic and toxicity properties of agents used in cancer diagnostics and therapeutics. Radiopharmaceuticals consist of two components, a targeting carrier and a trace amount of radionuclide with a specific radiation [1].

It is significantly less reliant, in contrast to biologic therapy, on knowledge of signaling pathways and the discovery of drugs that block the suspected pathway (or pathways) responsible for the cancer phenotype. Interestingly, 97% of "targeted" cancer therapies—that is, biologics—fail clinical trials. This is partly because the medications chosen for clinical trial research aim at the incorrect pathway. Radiation is delivered by radionuclides with varying emission properties, mainly β-particles or very powerful α-particles. A significant benefit over current therapeutic procedures is that, in almost all circumstances, nuclear medicine imaging techniques can visualize the radio-nuclides to evaluate the agent's targeting. This allows for a precision medicine approach to the delivery of Radiopharmaceutical Therapy (RPT) [2,3].

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Advantages of Radioactive Isotopes In Cancer –

- Identify the abnormalities early in the progression of the diseases.
- Provide precise results if the right metabolic timing and methodology are used.
- For the treatment of cancer, a variety of stable isotopes are available.
- When a patient receives conventional treatment, immune reactions are extremely sensitive and particular.
- Lower doses are less expensive and easier to dispose of.
- Needed is a more dependable, simple administration process and isolation technique.

Advantages of Modern Teletherapy Units-

The situation has fundamentally changed as a result of atomic reactors producing very significant volumes of cesium-137 and cobalt-60. As previously mentioned, sources that are comparable to hundreds or even thousands of kilos of radium are frequently found. In fact, radioactive material comparable to more than all of the radium in the world may be found in a single multi-kilocurie unit. With such big sources, it is possible to operate at the necessary distance (50 to 100 cm) from the tumor while maintaining a radiation intensity that requires only brief radiation exposures during each treatment session [4].

While it is true that the modern teletherapy unit is a derivative of the radium bomb, it is more common to compare these devices to super voltage X-ray equipment and 250 kV X-ray sets these days. Two benefits of an isotope teletherapy unit over a so-called typical X-ray set running at 200-250 kV are particularly noteworthy. The isotope unit is significantly easier to create mechanically and produces radiation with a higher energy.

Cobalt-60 emits gamma rays that have an average energy of 1.25 MeV (million electron volts), making them essentially mono-energetic. The energy of those from cesium-137 is 0.66 MeV. By contrast, the average energy of X-rays from a 250 kV set is barely a tenth of the energy of cobalt. This is approximately 0.13 MeV.

The primary benefit of the cobalt gamma rays' higher energy is their increased penetrating power, among other benefits. As a result, radiation damages overlaying tissue less when it reaches deep-lying tissue due to reduced absorption. Additionally, this knowledge permits some simplification of the treatment methodology.

It is impossible to overstate a cobalt unit's mechanical simplicity, which is its second key benefit. This is probably a deciding factor in less developed nations. An X-ray set is a very complicated electrical device with a number of moving parts that can and often do malfunction, including the transformer, high-tension wires, and X-ray tube. A cobalt unit, on the other hand, essentially has nothing that could malfunction. Anisotopic teletherapy units shouldn't require much maintenance after installation [5].

Why Co-60 and Cs-137?

There are drawbacks to an isotopic supply as well. Since the radiation from an isotope unit cannot be switched off, unlike an X-ray set or accelerator, the radioactive source must be surrounded by a large container filled with lead or another heavy substance. The operating beam emerges from this container through a variable-sized opening called the collimator, which is closed by a shutter when no radiation is needed. The collimator, shutter, and container are the three main components that determine the design of an isotope teletherapy device.

An additional drawback of an isotopic source is that radioactive decay causes a steady decline in its activity.

An additional drawback of an isotopic source is that radioactive decay causes a steady decline in its activity. Over time, the radiation intensity decreases to the point where a complete replacement of the source is required. It goes without saying that the isotope selected should have the slowest rate of decay feasible so that source replacement is only required occasionally. The "half-life" of cesium-137 is approximately 30 years, but the "half-life" of cobalt-60 is 5.3 years. It is possible to outline the primary prerequisites of an isotope for use in teletherapy as follows:

It needs to meet three requirements: (i) be highly energetic gamma ray emitter; (ii) have a long half-life; and (iii) be widely accessible (iv) It needs to be readily available with a high "specific activity" in order to concentrate radioactive material that emits radiation at a very high intensity into a source with a tiny physical footprint. Practically speaking, the only isotopes that adequately meet these criteria are Cs-137 and Co-60.

Mechanism and biological effects –

The mechanism of action for RPT is radiation-induced killing of cells. The effects of radiation on tissues and tumors were first studied

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not long after radiation and radioactivity were discovered. RPT benefits from the extensive body of knowledge that is radiation.

But radiation and RPT are not the same, and it's critical to comprehend how those differences affect treatment. Where and how long does the agent localize are the key questions for RPT. As mentioned in the "Dosimetry" section, the responses to these queries provide an indication of the tumor versus normal tissue absorbed dose as well as a potential treatment success factor [6].

The rate at which a dose is administered affects the biological consequences of that dose on a tumor. When 30 Gy is administered to a tumor over several weeks at an exponentially decreasing dose rate—which is commonly the case with radiation therapy—the result will differ significantly from when the same amount is administered at the much higher dose rates used in radiotherapy, such as daily 2-Gy fractions spread over 15 days. The tumor's biological healing capacity and radiosensitivity will determine how the biological outcome differs. Normal organs are likewise subject to dose-rate issues.

The treatment modality's decreased therapeutic potential with reduced target cell quantity is a critical element that is crucial to comprehend. If there are fewer target cells to kill for a given radiation absorbed dose, there is a greater likelihood that all of the cells will be killed in radiotherapy. This is because the probability of killing all of the cells increases as the number of target cells drops. with contrast, with RPT, fewer cells do not necessarily equate to a higher chance of tumor control. This occurs as a result of uneven radiation delivery to each cell. A lesser percentage of the radiation is deposited into the targeted cells when there are fewer cells in the sample, if the radiation is coming from a radionuclide on the surface of tumor cells [7-10].

Table 1: Selected Radiopharmaceutical therapeutic products that are under development or available on market.

Sr.No	RPT agent	Company	Indication	Properties	Development phase	Ref no
1.	Radium-223 chloride	Bayer	Bone metastasis	Calcium analogue	Commercially available	[11,12]
2.	Y-loaded resin microspheres	CDH Genetech/ Sirtex	Hepatic malignancies	Radioembolization of liver microvasculature	Commercially available	[13,14]
3.	Lu-labelled DOTATATE	Novartis/AAA	Neuroendocrine tumours	SSR-mediated binding	Commercially available	[15,16]
4.	I-labelled aCD45	Actinium Pharmaceuticals	Bone marrow transplant preparation	1I-based antibody targeting CD45+ cells for bone marrow ablation before transplantation	Phase III; recruiting	[17,18]
5.	Lu-labelled PSMA-617	Novartis/ Endocyte	Tumour neovasculature, Prostate cancer	PSMA-mediated binding	Phase III; active, not recruiting	[19,20]
6.	Ho microspheres	Terumo	Hepatic malignancies	Radioembolization of liver microvasculature	Phase II; unknown recruitment status	[21,22]
7.	Lu-labelled DOTA-JR11	Ipsen	Neuroendocrine tumours	SSR-mediated binding and internalization	Phase I/II	[23]
8.	Lu-labelled PSMA-R2	Novartis/AAA	Prostate cancer, tumour neovasculature	PSMA-mediated binding and internalization	Phase I/II; recruiting	[24,25]

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9.	Ac-labelled aCD38	Actinium Pharmaceuticals	Multiple myeloma	CD38 antibody α-targeting	Phase I; recruiting	[26,27]
10.	Th-labelled MSLN-TTC	Bayer	Mesothelin+ tumours	Anti-mesothelin–α-emitter immunoconjugate	Phase I; recruiting	[28,29]
11.	Th-labelled aCD22-TTC	Bayer	Lymphoma	Anti-CD22–α-emitter immunoconjugate; CD22+ tumours (lymphoma)	Phase I; active, not recruiting	[30]
12.	Ac-labelled FPX-01	J&J/Fusion Pharma	NSCLC, pan-cancer target	Insulin growth factor 1+ tumours	Phase I; recruiting	[31]
13.	Pb-labelled DOTAMTATE	OranoMed/ Radiomedix	SSR+ tumours	SSR-mediated binding	Phase I; active, not recruiting	[32,33]
14.	Pb-labelled PLE	OranoMed/ Cellectar	Solid tumours	-	Preclinical	-
15.	Pb-labelled aCD37a	OranoMed/ NordicNanovector	Leukaemia/ lymphoma	CD37 antibody α-targeting	Preclinical	-

II. CONCLUSION –

In summary, this article provides Radiopharmaceuticals can also be used to diagnose certain cancers, as oncologists can track radioactivity throughout the body after the drugs are administered to determine if cancer is present. Gamma camera or a similar gamma imaging device are special imaging system that are used for diagnostic purpose.

Conflict of Interest –

There is no conflict of interest.

Acknowledgement –

Authors are grateful to Principal and guide of Dattakala College of Pharmacy, Bhigwan, Pune, India, for providing encouragement and support for critically preparing this manuscript.

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Volume 9, Issue 4 July-Aug 2024, pp: 1506-1511 www.ijprajournal.com ISSN: 2456-4494

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