INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

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Review Paper

Development of New Radiopharmaceuticals for Targeted Radionuclide Therapy of Brain Cancer

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ARTICLE INFO

Published: 04 Apr. 2025
Keywords:
Radiopharmaceuticals, Radionuclide, Brain Cancer
DOI:
10.5281/zenodo.15140832

ABSTRACT

Recent advances in molecular biology have significantly impacted biomedical applications, offering new hope for both imaging and therapeutics. Research has intensified around the development of radionuclides and their use in radiopharmaceuticals (RPs), which are poised to play a crucial role in shaping future treatment strategies, particularly in cancer care.A key focus of this research is the creation of drug delivery systems that use radionuclides to directly target specific cells. By labeling drugs with radionuclides, these systems ensure that therapeutic particles reach their intended destination, minimizing harm to surrounding healthy tissue. This targeted approach is particularly promising for personalized cancer treatments, as it allows for the selection of radio ligands that can bind to specific molecular receptors or intracellular components in each patient.Advances in nanotechnology have also opened up new possibilities for drug delivery. Nanoparticles can now be designed to carry targeted molecules, such as antibodies, peptides, or ligands, to the tumor site. These nanoparticles can serve both therapeutic and imaging purposes, offering a more precise and effective way to treat and monitor cancer while reducing side effects.Understanding the biology of tumors and the specific receptors they express is critical in developing effective therapies. By engineering radiopharmaceuticals to target these receptors, researchers are creating more efficient, targeted treatments that are better suited to individual patients.In summary, the integration of molecular biology, nanotechnology, and radiopharmaceuticals is paving the way for more personalized, effective cancer treatments, offering exciting potential for improving patient outcomes in the future.

INTRODUCTION

1.Targeted Radionuclide Therapy for Brain Cancer:

- Targeted radionuclide therapy (TRT) is a type of radiation therapy that can be used to treat brain tumors.

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

- A radioactive chemical, called a radionuclide, is attached to a molecule that binds to specific targets on cancer cells. The therapy then delivers a cytotoxic dose of radiation to the cancer cells while minimizing damage to healthy tissue.

2. Brief Overview of Brain Cancer and Current Treatment Challenges

- Brain cancer can be a life-threatening disease that affects the brain's vital structures.
- Brain cancer can be primary, which starts in the brain, or secondary, which starts in another part of the body and spreads to the brain**.**

- **Current Treatment Challenges**
  - Surgery
  - Chemo therapy
  - Radiation therapy
  - Targeted therapies
  - Immuno therapy

3. Importance of Targeted Radionuclide Therapy:

- **Highly specific treatment:** Targets cancer cells while sparing healthy tissue
- **Effective against hard-to-reach tumors:** Can reach tumors deep in the brain or with limited surgical assess.
- **Minimizes side effects:** Reduce harm to surrounding healthy tissue and organs
- **Improves quality of life:** Relieves symptoms, reduces pain, and enhances daily functioning
- **Potential for improved survival rates:** Increases chances of long-term survival and cure
- **Combination therapy:** Can be used in conjunction with surgery, chemotherapy, and immunotherapy for enhanced treatment
- **Personalized medicine:** Allows for tailored treatment plans based on individual patient needs and tumor characteristics
- **Advancements in technology:** Enables precise delivery and monitoring of radiation dose
- **Growing research and development:** Expanding options for various types of brain cancer and other diseases.

BACKGROUND:

1. Overview of Radiopharmaceuticals and Applications:

- Radiopharmaceuticals are medications containing small amounts of radioactive materials, used for diagnostic, therapeutic, and research purposes.
- They offer targeted therapy, non-invasive procedures, and personalized medicine, but also pose risks of radiation exposure, regulatory challenges, and limited availability.
- Common types include Technetium-99m, Iodine-131, Lutetium-177, Fluorine-18, and Strontium-89, used for various applications such as cancer treatment, pain management, and diagnostic imaging.

2. Principle of Targeted Radionuclide Therapy:

- Targeted radionuclide therapy follows 10 key principles to effectively treat diseases like cancer while minimizing harm to healthy tissues.
- These principles include target specificity, radiation type selection, radiopharmaceutical design, optimized biodistribution, precise

dosimetry, personalized medicine, combination therapy, minimizing side effects, monitoring and evaluation, and continuous research and development.

- By adhering to these guidelines, treatment can be tailored to individual patient needs, maximizing its potential benefits.

3. Current Radiopharmaceuticals Used in Brain Cancer:

- **Glioblastoma:**

Bq-BC8 (Lutetium-177 labeled peptide) and I-131-TM-601 (Iodine-131 labeled antibody)

- **Malignant glioma**:

Y-90-DOTA (Yttrium-90 labeled peptide) and Lu-177-DOTATATE (Lutetium-177 labeled peptide)

- **Brain metastases:**

Rhenium-186 (Rhenium-186 labeled liposomes) and Samarium-153 (Samarium-153 labeled liposomes)

- **Neuroblastoma:**

I-131-MIBG (Iodine-131 labeled metaiodobenzylguanidine)

- **Medulloblastoma:**

Y-90-DOTA (Yttrium-90 labeled peptide)

New Radiopharmaceuticals and Developement

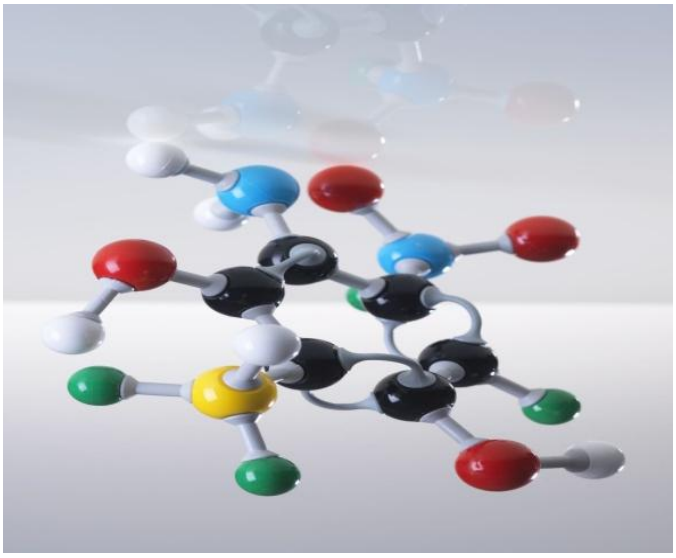

Fig No:1

- GBR-1303 radiolabelled antibody targeting Glioblastoma.
- DOTATOCI radiolabeled peptide targeting somatostasis receptor.
- LU-177- PSMA-617: radiolabeled small molecule targeting PSMA in Brain metastasis.

Pre-Clinical Studies:

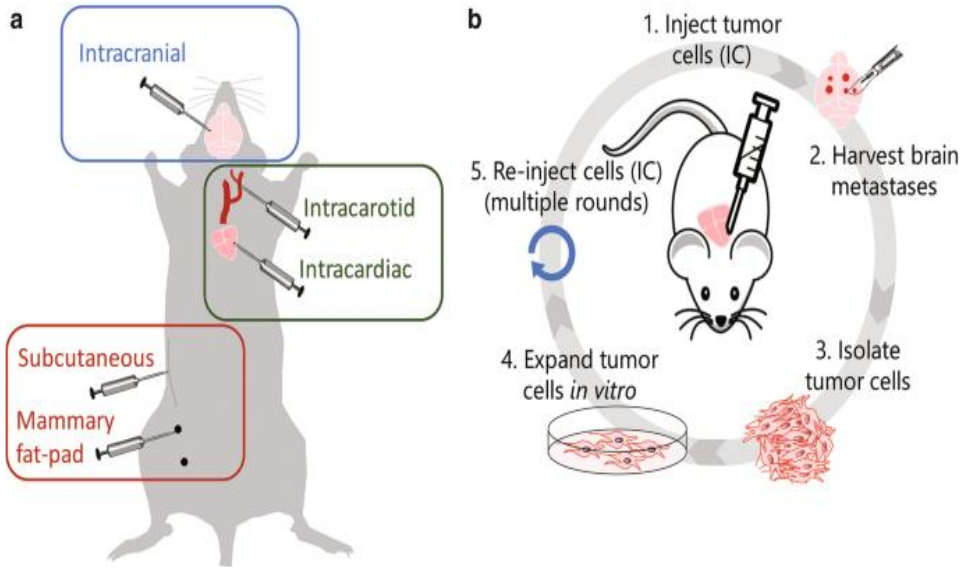

Fig No:02

Preclinical studies in new radiopharmaceuticals for targeted radionuclide therapy of brain cancer involve researching and testing new radiopharmaceuticals (RPs) that selectively target and destroy cancer cells in the brain while minimizing harm to healthy cells.

These studies aim to:

- Identify and synthesize new RPs with high affinity and selectivity for brain cancer cells.
- Evaluate their efficacy, toxicity, and pharmacokinetics in animal models.
- Optimize dosing and treatment regimens.

Clinical Trials

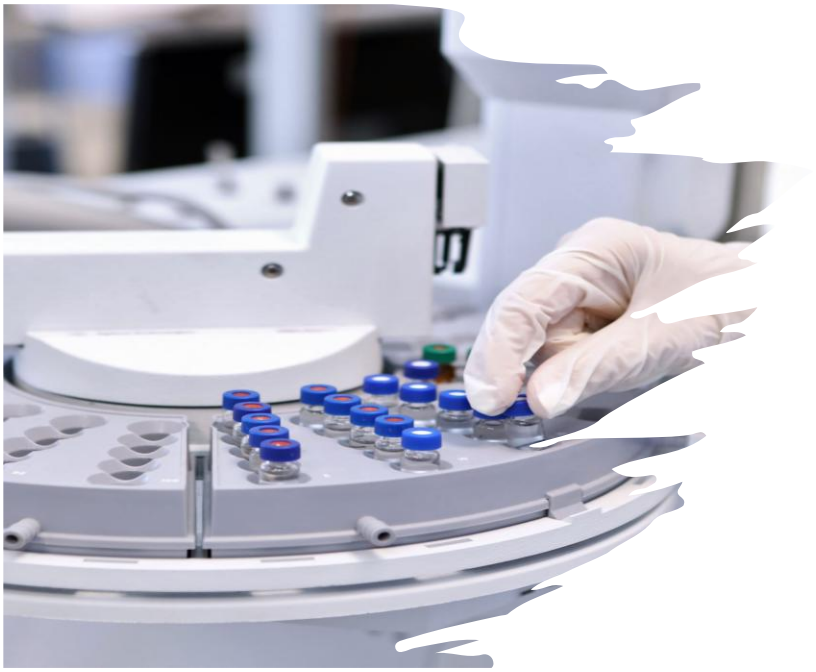

Fig No:03

Clinical trials for radiopharmaceuticals are conducted to establish their safety and efficacy as diagnostic or therapeutic agents.

Comparison

- To prove efficacy, radiopharmaceuticals are compared to existing agents or other relevant medicinal products and procedures.

Phases

- Most radiopharmaceutical trials are in the early stages of development, with over 80% in Phase 1, Phase 1-2, or Phase 2.

Radiopharmaceutical Development Initiative (RDI)

- RDI involves both early and late phases.

Biomarkers

- Biomarkers are important for selecting treatments and evaluating the clinical performance of radiopharmaceuticals

Challenges and Future Directions:

Challenges	Future Directions
Blood-brain barrier penetration	Nanoparticle-based delivery systems
Tumor heterogeneity	Novel radiopharmaceuticals
Radiation resistance	Combination therapies
Normal tissue toxicity	Personalized medicine
Limited tumor specificity	Imaging-guided therapy

CONCLUSION:

- In conclusion, radiopharmaceuticals for targeted radionuclide therapy of brain cancer offer a promising approach to improve treatment outcomes.
- Despite challenges such as blood-brain barrier penetration and tumor heterogeneity, advances in nanoparticle-based delivery systems, novel radiopharmaceuticals, and combination therapies hold great potential.
- Further research and clinical trials are needed to overcome existing limitations and fully realize the benefits of this innovative treatment approach.

With continued advancements, targeted radionuclide therapy may become a game-changer for brain cancer patients, offering improved survival rates, reduced side effects, and enhanced quality of life.

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HOW TO CITE: Supriya P.*, Swarnalatha S., U. Rajashekhar, Development of New Radiopharmaceuticals for Targeted Radionuclide Therapy of Brain Cancer, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 4, 476-480. https://doi.org/10.5281/zenodo.15140832