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Recent Trends in Therapeutic Radiopharmaceuticals

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ABSTRACT

Radiopharmaceuticals have been majorly used in ages for the diagnostic agent and therapeutic agents .Recent years enormous efforts have been made to formulate holistic formulation for the therapeutic effect of Radiopharmaceuticals .Due to its versatile applications in cancer , Theraspheres -which are glass beads microparticals containing yttrium 90 isotope as a therapeutic agents for Osteosarcoma and its liposomes containing yttrium 90 for the treatment of throat and neck cancer have been formulated .These new formulations have added a new dimension in the field of Research and Development .This review explains need of Radiopharmaceuticals ,their advantages over conventional drug delivery systems and there different application in pharmaceutical fields .

Keywords: Radiopharmaceuticals, Osteosarcoma, Therasphere, Yttrium 90, Hydroxyapatite

1. INTRODUCTION

Radiopharmaceutical used as therapeutic agents (frequently known as RPTs) are designed to deliver high doses of radiation to selected malignant sites in target organs or tissues, while minimizing the radiation doses to surrounding healthy cells. Over the past several years, several types of RPTs with special properties, including compounds for labelling monoclonal antibodies, have been used in animal and human clinical trials with promising results. Many radiolabeled particles, microspheres and liposomes are appropriate for therapy, once the encapsulated diagnostic radioisotope has been exchanged for therapeutic one from the α- or β- emitter group. The modern trend in radiopharmaceutical research for oncology is development of RPTs that may be said to be tumour – seeking and tumour specific. In therapeutic radiopharmaceuticals application – unlike the case of external radiation therapy where the radiation from an external sealed radioactive sources is focused on the site to be irradiated- the product is administered to patient orally or intravenously and is selectively taken up or localized in the site to be irradiated. External beam radiation requires about ten treatments over a period of 30 days to deliver a dose of 2000 to 2500 radicals (rads). In contrast, therapeutic radiopharmaceuticals safely delivers an average dose of 15000 rads in single treatment with minimal damage to healthy surrounding tissues. Currently this novel approach is finding success in fighting different cancers viz. liver, head and neck cancer, spleen cancer etc.

2. ADVANTAGES OF THERAPEUTIC RADIO-PHARMACEUTICALS

After administration these radiopharmaceuticals get entrapped in the web of small blood vessels feeding a tumour and thus deliver the required concentration of radioactivity at the target site. The radioactivity is never released from the carrier and acts from within. The effective treatment range is up to 90µm for alpha emitters, for beta emitters the range is not more than 12mm and for gamma emitters the range is up to several centimetres. Withdrawal problems are not there in case of biodegradable carrier system.

3. CRITERIA FOR SELECTION OF SUITABLE RADIONUCLIDES

For therapeutic purposes, the selection of a suitable radionuclide for specific application takes into account a number of factors. These include the physical characteristics of radionuclide itself, mainly the type and energy of the radiation emitted and the radionuclide's half-life, exact location of the target area to be treated and Absorption, Distribution, Metabolism and Excretion of Radiopharmaceuticals can be followed by scintigraphy. The rationale or strategy in RPT is to deposit the greatest amount of energy in the shortest time to the malignant target cells, while sparing the healthy one from unwanted radiation. The deposition of energy is measured by what is known as Linear Energy Transfer (LET), which is different for alpha, beta, or gamma radiation.

4. TYPES AND PROPERTIES OF RADIATIONS

4.1 Alpha Emitters

Among alpha-particles emitters, only two radionuclides have been considered and studied as potential therapeutic agents: astatine-211 and bismuth-212. Largely because of the extremely high radio toxicity and short half-lives of alpha emitting RPTs, a good deal of laboratory research still is needed to develop them for medical therapy uses.

4.2 Beta Emitters

Radionuclides that emit beta particles, are the only ones that have been used in therapeutic nuclear medicine. This is due to various reasons. Beta particles have penetration ranges in the tissue on the order of millimetres to a few centimetres, appropriate depths for the irradiation of small to medium sized tumours. Secondly, some of the most promising beta- emitting radionuclides have desirable half-lives, varying from several hours to days. Lastly, many of these radionuclides are easily produced in nuclear research reactors, facilitating their availability. Radionuclides emitting beta particles are widely used. They include phosphorus-32, strontium-89, and iodine-131, which might be considered the "first generation" of therapeutic radionuclides. Among the "second generation" of beta emitting RPTs are samarium-153, rhenium-186, copper-67, and holmium-166.

4.3 Gamma Emitters

Gamma radiation exhibits low values of linear energy transfer, as it penetrates relatively deeply, on the order of several centimetres, and does not deposit much energy along its track. Consequently, pure gamma-emitting radionuclides usually are not used for therapeutic purposes.

5. THERAPEUTIC RADIOPHARMACEUTICAL FOR CANCER TREATMENT

Over the past considerable interest has emerged in the use of radiopharmaceuticals to relieve intense bone pain resulting from metastasis from breast, prostate, and lung cancer. Their application has been demonstrated in clinical practice, and a number of governmental and commercial laboratories are actively engaged in the development and clinical evaluation of RPTs for treatment of patients with painful skeletal metastasis. The most appropriate radionuclides for bone therapy are those decaying by emission of medium energy beta particles. Beta particles of energy between 1 to 2 MeV have been shown to be effective since they are able to penetrate only required few millimetres of the malignant tissue without compromising the bone marrow too much, a consideration of paramount importance when designing new RPT for bone therapy. Besides phosphorus-32 and strontium-89, a number of radionuclides are rapidly drawing interest for bone cancer therapy. These include samarium-153, rhenium-186, and to a lesser extent holmium-166 and dysprosium-165.

6. RECENT ADVANCEMENT IN THERAPEUTIC RADIOPHARMACEUTICALS

6.1 Therasphere

Therasphere is a liver cancer therapy that consist of millions of small glass microsphere (20 to 30 micrometres in diameter) containing radioactive Y-90. The product is injected by physician into the artery of the patient's liver through a catheter, which allows the treatment to be delivered directly to the tumour via blood flow. Therasphere is used in the European Union and in Canada for the treatment of hepatic positioned arterial catheters. Common side effects include mild to moderate fatigue, pain and nausea for about a week. Physician describe these symptoms as similar to those of the flu. Some patients experience some loss of appetite and temporary changes in several blood tests.

6.2 Hydroxyapatite Nanoparticles Containing Yttrium-90

Osteosarcoma is the most common primary malignant bone tumours, affecting mostly children, adolescents and young adults. This is an aggressive tumour that results in high mortality rate and poor prognosis. Due to the low sensitivity of osteosarcoma to ionizing radiation, such treatment is not used very often and it can be recommended only to postsurgical therapy. As an alternative therapy, functionalized nanomaterial's allow their accumulation in tumour tissues due to their unique properties, making them good agents to act as stable carriers for radionuclides.

7. FUTURE PROSPECTUS

For therapeutic radiopharmaceuticals more exhaustive search is required for the materials which are more biocompatible and biodegradable after the delivery of radioisotopes. The labelling methods are to be improved so that highly stable radiolabeled therapeutic radiopharmaceutical can be produced in a single short step ,using a simple radiolabeling kit. There is need for the preparation of more uniform radiopharmaceutical that will allow for better and more reliable bio-distribution. Internal radiation therapy is likely to play a substantial role in the control hepatic cancer as well as other in the near future.

8. CONCLUSION

External beam radiation requires about ten treatments over a period of 30 days to deliver a dose of 2000 to 2500 rads. In contrast, therapeutic radiopharmaceuticals safely deliver an average dose of 15000 rads in single treatment with minimal damage to healthy surrounding tissues. Therapeutic radiopharmaceutical are very stable and have a proven efficacy in the field of treatment of diseases especially cancer. These therapeutic radiopharmaceutical serve as one of the future materials in the battle against cancer and tumours.

REFERENCES

1. Harbert JC. Therapy with intra-arterial radioactive particles. In Harbert JC, EckelmanWC, and Neumann RD(Eds). Nuclear medicine: Diagnosis and therapy. Thieme Medical Publishers, New York, 1996, Page No.-1141-1155
2. Blanchard RJ, Grotenhuis I, LaFave JW, Frye CW, and Perry JN. Treatment of experimental tumours. Arch Surg. 1964; 89: 406-410.
3. Knight CG, Bard DR and Page Thomas DP. Liposomes as carriers of antiarthritic agents. Ann. N.Y. Acad. Sci. 1988; 415-428.
4. Hafeli U, German R, Pauger G, Casillas S, and Dietz D. Production of Rhenium – powder with a jet mill and its incorporation in radioactive microsphere for treatment of liver tumours. In Bryskin BD(Ed). Rhenium and Rhenium Alloys. TMS(Minerals, Metals and Material Society), Warrendale, PA. (1997) Pp 469-477
5. Zalutsky MR, Noska MA, Gallagher PW, Shortkroff S, AND Sledge CB. Use of liposomes as carriers for radiation synovectomy. Nucl. Med. Biol. Int. J. Rad. Appl. Instr. Part B. 1988; 151-156.
6. Papisov MI, Savelyev VY, Sergienko VB, and Torchilin VP. Magnetic drug targeting. In vivo Kinetics of radiolabeled magnetic drug carriers. Int. J. Pharm. 1987; 201-206.
7. Zielinski FW, Kasprzyk. Synthesis and quality control testing of P-32 Labeled ion exchange resin microsphere for radiation therapy of hepatic neoplasms. Int. J. Radiat Isot. 1983; 1343-1350.
8. Robertson WW, Janssen HF, Walker RN. Passive movement of radioactive microsphere from bone and soft tissue in extremity. J. Orthop Res. 1985;405-411.
9. Grady ED. International radiation therapy of hepatic Cancer. Dis Colon Rectum. 1979; 371-376.
10. Wunderlich G, Pinkert J, Andreeff M, Stintz M, Knapp FF Jr, Kropp J, Franke WG. Preparation and biodistribution of rhenium-188 labeled albumin microsphere B20: a promising new agent for radiotherapy. Appl Radiat Isot. 2000; 63-68.
11. Yan, Morris. Hepatic cryotherapy for liver metastases from colorectal carcinoma. ANZ journal of Surgery. SRS 39th Annual Scientific Meeting, (2002).
12. V.R Sinha, V. Goyel, A. Trehan. Radioactive Microsphere in therapeutics. Pharmazie 2004; 59: 419-426.
13. Urs Hafeli. Radioactive Microsphere for Medical Application. Cleveland Clinic Foundatio, Radiation Oncology Department T28. Page No.-3-29.
14. Marcelo F, Cipreste, Edesia M.B. Sousa. Polyvinyi alcohol/collagen/hydroxyapatite Nanoparticles Hybrid System

Containing Yttrium-90 as a potential Agent to treat Osteosarcoma. Journal of Biomaterials and Nanobiotechonology. 2014; 24-30.

15. Delbarre F, Roucayrol JC, Ingrand J, Sanchez A, Menkes CJ, and Aignan M, Une nouvelle. Yttrium-90 in persistent synovitis of knee- a single centre comparision. The retention and extra- articular spread of four yttrium-90 radiocolloids. Brit. J. Radiology. 1975; 377-381.
16. Remington, "The Science and Practice of Pharmacy, 21st Edition, Published By Lippnicott Williams & Wilkins, Volume-I, Page No.-479-492.
17. The United State Pharmacopeia & The National Formulary-2000, Asian Edition. Published By United states Pharmacopeial Convention, INC. Page No.-1988-1990.
18. Bentley's, " Textbook of Pharmaceutics", 8th Edition. Published By Bailliere Tindall London, Page No.-367-429.
19. Ansel's, "Pharmaceutical Dosage Forms and Drug Delivery Systems", 8th Edition, Publishe By Lippnicott Williams & Wilkins, Page No.-570-599.