PREPARATION AND PRELIMINARY BIOLOGICAL EVALUATION OF $^{175}$Yb LABELED HYDROXYAPATITE FOR POSSIBLE USE IN RADIATION SYNOVECTOMY OF SMALL JOINTS

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Introduction

Radiation synovectomy, which involves local intraarticular injection of suitable $\beta$ emitting radionuclides in the form of radiocolloids or radiolabeled particulates into the affected synovial joints, has been successfully employed in the treatment of rheumatoid arthritis and other types of inflammatory arthropathies [1,2]. Owing to its suitable nuclear decay properties [$E_{\beta_{\text{max}}} = 480$ keV, $E_1 = 113$ keV (1.9%), 282 keV (3.1%), 396 keV (6.5%)] and feasibility of production in adequate specific activity by thermal neutron irradiation in a nuclear reactor, $^{175}$Yb could be considered as a promising radionuclide for developing potential agents for radiosynoviorthesis of small-size joints. Hydroxyapatite (HA) [Ca$_{10}$(PO$_4$)$_6$(OH)$_2$] is one of the preferred particulates for effective management of synovial inflammation, owing to its excellent biocompatibility [2,3]. The present paper describes the preparation and preliminary biological studies of $^{175}$Yb labeled hydroxyapatite (HA) particles, for use as a potential agent, for radiosynoviorthesis of small-size joints.

Experimental

Production and radiochemical processing of $^{175}$Yb

$^{175}$Yb was produced, by thermal neutron bombardment on enriched (98.6% $^{174}$Yb) Yb$_2$O$_3$ target in the CIRUS reactor, at a flux of $-3 \times 10^{17}$ n/cm$^2$/s for 7 days. The irradiated target was dissolved in 0.1 M HCl by gentle warming. Radionuclidic purity as well as the yield of $^{175}$Yb activity produced was ascertained by recording the $\gamma$ ray spectra using a HPGe detector coupled to a 4 K Multi Channel Analyzer (MCA) system.
**Synthesis of HA**

Hydroxyapatite particles (particle size range 1-20 µ particle) was synthesized and characterized by following the procedure already reported earlier [2].

**Preparation of \(^{175}\text{Yb}-\text{HA}\)**

Preparation of \(^{175}\text{Yb}\)-labeled HA was carried out, by adding 50 µL of \(^{175}\text{YbCl}_3\) solution (−10 MBq \(^{175}\text{Yb}\)) containing 250 mg of Yb carrier to a suspension of 10 mg HA in 850 µL of normal saline after the addition of 100 mL of 0.5 M NaHCO₃ buffer (pH ~9). The reaction mixture was vortexed thoroughly and was kept mixing at room temperature for 30 min, in a rotary shaker after adjusting the pH to ~7.

**Biological studies**

The biological efficacy of \(^{175}\text{Yb}\)-labeled HA particles thus prepared, was studied, by injecting the preparation (−7.4 MBq) in one of the knee joints in normal Wistar rats and recording scintigraphic images at 30 min, 3 h, 24h, 48 h, 72 h and 7 days time intervals, using a single head digital SPECT gamma camera. Blood samples were drawn at the same time intervals from tail vein.

**Results and Discussion**

**Production of \(^{175}\text{Yb}\)**

About 5.5 GBq/mg (150 mCi/mg) of \(^{175}\text{Yb}\) activity was obtained at 24 h post EOB, after 7 d irradiation at a flux of 3 x 10¹³ n/cm²/s, using enriched (98.6% \(^{174}\text{Yb}\)) \(\text{Yb}_2\text{O}_3\) target. The radionuclidic purity of \(^{175}\text{Yb}\) produced was ~100% as obtained from the analysis of the gamma ray spectrum.

**Optimization studies**

In order to obtain the optimum protocol for maximum radiolabeling yield, several experiments were carried out, by varying reaction parameters such as, HA concentration (1-40 µg/mL), pH (2-11), carrier Yb concentration (20-500 µg/mL) and incubation time (5 - 60 min). A maximum complexation yield of ~99% was obtained, when 10 mg/mL of HA was used and the reaction was carried out for 30 min at room temperature at pH ~7. The \(^{175}\text{Yb}\)-HA complex, prepared under optimized reaction conditions, showed excellent stability even after 14 days at room temperature.

**Biological studies**

The scintigraphic images of Wistar rats (Fig. 1), recorded after injecting \(^{175}\text{Yb}\)-HA in knee joints, indicate near-complete retention of the activity in the synovium even...
after 7 d post-injection. No detectable activity was observable in any other organs. This is further confirmed by measuring the blood activity which did not show any radioactivity.

Conclusion

The radiolabeling of HA particles with $^{175}$Yb was carried out in high yield and the labeled particles showed excellent stability. The scintigraphic images of $^{175}$Yb-HA revealed no leaching of the activity from the synovial joints of the knee in Wistar rats, thereby indicating its potential as a therapeutic agent in the management of arthritis.

References


About the Authors

Dr Sudipta Chakraborty is a gold medalist of Jadavpur University, Kolkata and obtained M.Sc. (Chemistry) degree in 1997. He joined the Radiopharmaceuticals Division, BARC, after graduating from BARC Training School in 1999 (42nd Batch, Chemistry discipline). Since then he has been actively involved in research and development work on therapeutic radiopharmaceuticals. He obtained Ph.D. degree in Chemistry from Mumbai University in 2006. Dr Chakraborty has to his credit about 20 publications in international journals and 35 papers in various national and international symposia/conferences.

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Dr (Mrs.) Sharmila Banerjee joined the Radiopharmaceuticals Division, BARC in 1996. Prior to that, she obtained her M.Sc. degree in Organic Chemistry from the University of Calcutta and Ph.D. degree from Indian Institute of Technology, Mumbai in 1992. She is currently heading the Radiopharmaceutical Chemistry Section of the Radiopharmaceuticals Division. Her current areas of interest include research in the field of radiopharmaceuticals chemistry aiming at the development of new diagnostic and therapeutic radiopharmaceuticals. She is a recognized guide for M.Sc. and Ph.D. under the University of Mumbai. She has about 100 publications in international journals including review articles.

Dr (Mrs.) Meera Venkatesh joined the Training School of Bhabha Atomic Research Centre in the year 1976 after completing Bachelors Degree in Chemistry from Bombay University. She joined the Radiopharmaceuticals Division in 1977 and has been engaged in research and development of Radiopharmaceuticals and radiometric assays since then. Dr. Meera obtained her doctorate degree from Bombay University in 1986 for her work in the field of Radioimmunoassays. She did her post-doctoral fellowship at the University of Missouri, USA during 1992-94 in the field of therapeutic radiopharmaceuticals and later in 1999 served as a visiting professor at the same university. Currently, Dr. Meera is heading the Radiopharmaceuticals Division, BARC and concurrently serves in the capacity of General Manager of Quality Control at the Board of Radiation and Isotope Technology. She has published over 150 papers in international journals, international and national symposia/conferences and has authored a few invited articles. She has served as an expert in the field of Radiopharmaceuticals and Radiometric assays for the International Atomic Energy Agency.

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