In-house synthesis and development of PSMA-617 and PSMA-11, a ligand for nuclear cancer medicine, as an import-substitute

Extensive expression of prostate specific membrane antigen (PSMA) is common in all prostate cancers (PCa) which make it a potential target in cancer diagnosis and therapy. Unlike other tissues like kidney, small intestine, or brain, expression of PSMA in malecious tissues is ~1000-fold higher. In this respect PSMA-617, a peptide based Lu-labeled ligand, for PSMA is being used as a nuclear medicine in the radiotherapy of prostate cancer. However, this ligand is highly expensive and not readily available in India. In order to cater the need of PSMA-ligand based nuclear medicine and treatment of Indian cancer patients, we have now successfully accomplished the synthesis of PSMA-617 (Fig. A), as an import substitutes, from their constituent amino acid components. PSMA is structurally complicated molecule and its synthesis is extremely challenging. By using novel synthetic strategies, the urea part of the ligand is constructed using triphosgene chemistry while the amino acids were assembled using coupling chemistry. Using this method, we have now achieved synthesis of up to 5 mg of material. By employing our synthetic strategy, the cost of the ligand is reduced to approximately ten times as compared to commercially available drug. This ligand has been labeled with Lutetium-177 at BRIT, Vashi, with a radio chemical purity of 99.5%. RPC approval is obtained to use it as therapeutic agent in the treatment of prostate cancer. Currently, PSMA-617, indigenously developed in BOD, is used for therapy of prostate cancer patients in India (Fig. B). Uninterrupted supply of PSMA-617 to BRIT is highly helpful in therapy of large number of prostate cancer patients in India.

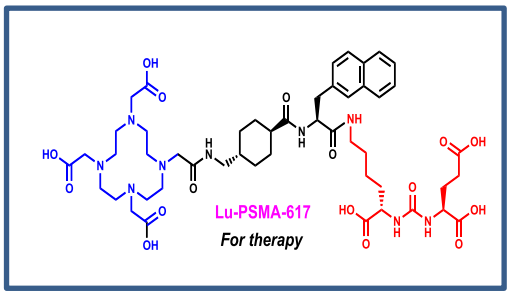

Fig. 1A

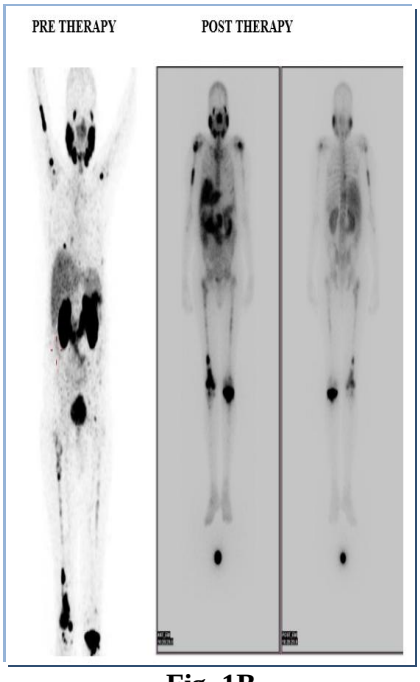

Fig. 1B