^{177}Lu-Labeled sodium pyrophosphate

^{177}Lu-PYP

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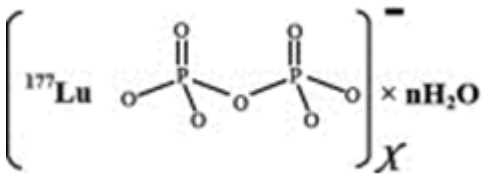
Chemical name:	^{177}Lu-Labeled sodium pyrophosphate
Abbreviated name:	^{177}Lu-PYP
Synonym:	
Agent Category:	Compounds
Target:	Bone
Target Category:	Others
Method of detection:	Single-photon emission computed tomography (SPECT); gamma planar imaging
Source of signal / contrast:	^{177}Lu
Activation:	No
Studies:	• Rodents



Structure of sodium pyrophosphate (1).

Background

[PubMed]

^{177}Lu-Labeled sodium pyrophosphate, abbreviated as ^{177}Lu-PYP, was synthesized by Abbasi for use in imaging bone metastatic tumors and controlling metastasis-induced bone pain (1).

Malignant tumors, especially advanced carcinomas of prostate, breast, and lung, often metastasize to the bone and cause severe pain (2). Management of bone pain is challenging, and localized radiation therapy is one of the effective methods for this

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purpose (3-5). However, bone pain recurs at the treated sites, and patients often suffer from multiple tumor metastases. In such cases, systemic therapy and imaging with radiolabeled bone-seeking agents is one therapeutic option because of the efficacy, low cost, and low toxicity of this type of treatment. Radionuclides suitable for systemic radiotherapy of bone pain include ^{32}P, ^{89}Sr, ^{186}Re, ^{188}Re, ^{153}Sm, and ^{177}Lu, while bisphosphonates are often the carriers that are used to deliver the radionuclides to bone tissue because of their exceptional affinity for hydroxyapatite (1, 6). The phosphonate group in these compounds serves both as a ligand for radiometals and a functional group for hydroxyapatite binding. Radiometals have also been attached through a chelator conjugated to bisphosphonates (3).

Pyrophosphate and its analogs have long been used as bone-seeking compounds for pain relief (2). These agents differ in the efficacy and duration of pain palliation, as well as anti-tumor effect, toxicity, and cost. Abbasi labeled the pyrophosphate with ^{177}Lu for both imaging and pain management purposes (1). ^{177}Lu has a long half-life ($t_{½}$ = 6.71 days) and decays to stable ^{177}Hf. ^{177}Lu has both beta particle emissions (E_{max} = 497 keV (78.6%), 384 keV (9.1%), and 176 keV (12.2%)) for radiotherapy and gamma emissions (E_{max} = 113 keV (6.4%) and 208 keV (11%)) for imaging. Furthermore, ^{177}Lu can be generated at a large scale with excellent radionuclide purity and high specific activity. Abbasi performed single-photon emission computed tomography (SPECT) imaging with ^{177}Lu-PYP and demonstrated its high uptake in the skeletal tissue of a normal rabbit, suggesting that it may be useful as a bone-pain palliation agent (1).

Related Resource Links:

Imaging agents related to bisphosphonates in MICAD

Bisphosphonate-related clinical trials in ClinicalTrials.gov

Bisphosphonate compounds in PubChem

Synthesis

[PubMed]

Abbasi produced ^{177}Lu by irradiating natural lutetium foil target at a flux of ~1.0 × 10^{14} n/cm^2 per s for 12 h (1). The total activity was calculated to be 15,257.69 MBq (412.37 mCi), and the specific activity was ~1,388.24 MBq/mg (37.52 mCi/mg) at the end of bombardment (EOB). The measured total activity was 12,099 MBq (327 mCi) at 54 h after EOB. Analysis of the gamma ray spectrum of the irradiated target revealed major γ-peaks at 72, 113, 208, 250, and 321 keV. The radionuclide purity of ^{177}Lu was >99%.

Tetrasodium pyrophosphate (purity, 95.0%; molecular weight, 265.9) was commercially available. Radiolabeling was achieved by incubation of pyrophosphate with $^{177}LuCl_3$ solution for several minutes at room temperature (as labeling occurs instantly). The molar ratios of sodium pyrophosphate/Lu were 552.45, 534.76, 266.66, 159.45, 60.24, 27.25, 20.83, and 10.25, respectively, and the radiochemical yields of these formulations were

determined to be 99.94 ± 0.08, 99.96 ± 0.03, 99.93 ± 0.03, 99.88 ± 0.09, 99.24 ± 0.24, 45.21 ± 0.58, 39.17 ± 0.97, and 16.33 ± 0.34%, respectively. Radiochemical purity was >99%. The specific activity was ~0.49 GBq/mg (13.16 mCi/mg). There was no significant difference for the radiochemical yield at various temperatures (20, 40, 60 and 80 °C) and at different time intervals (1, 6, 18, and 24 h) after the initiation of reaction.

The charge of ^{177}Lu-PYP was determined with radio-electrophoresis (0.025 M phosphate buffer, pH 6.9) (1). $^{177}LuCl_3$ did not show any movement from the point of spotting, while ^{177}Lu-PYP migrated 7.0 ± 0.2 cm towards the anode within 1 h under 300 V and 45 mA, indicating a negative charge of ^{177}Lu-PYP.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

No data are available.

Animal Studies

Rodents

[PubMed]

SPECT images were obtained at 24 h after injection of ^{177}Lu-PYP (~10 MBq, ~0.27 mCi) into the ear vein of a rabbit, showing significant radioactivity in the skeleton and very high uptake in the liver (1). No detailed data were provided. No indication of whether Lu salt or LuPYP localized in the bone from the imaging experiments.

Other Non-Primate Mammals

[PubMed]

No references are currently available.

Non-Human Primates

[PubMed]

No references are currently available.

Human Studies

[PubMed]

No references are currently available.

References

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