ScienceDirect

Hematology, Transfusion and Cell Therapy

Volume 48, Supplement 1, March 2026, 106295

23

DEVELOPMENT OF A BIFUNCTIONAL CHELATOR FOR GALLIUM AIMING FOR THERANOSTIC APPLICATION IN NUCLEAR MEDICINE

Joaldo Garcia Arruda [a], Fabio Luiz Navarro Marques [a], Célia M.C. Fernandez [b], António R. Paulo [b], Victor Marcelo Deflon [a]

Show more

https://doi.org/10.1016/j.htct.2026.106295

Introduction/Justification

The development of radiopharmaceuticals has advanced considerably in recent decades, focusing on molecules capable of transporting radionuclides that emit ionizing radiation, such as alpha (a) and beta (ß) particles or Auger electrons. An important strategy is theranostics, which integrates diagnosis and therapy in a single agent through radionuclides that also emit gamma () or positron (ß+) radiation, enabling real-time, non-invasive monitoring. In this context, imines, amines, semicarbazones, and thiosemicarbazones have attracted interest due to their biological properties and versatile metal coordination behavior.

Objectives

This work aims to develop a hexadentate bis(imine)-based chelator (H4L) for gallium(III) coordination and to prepare its ^{67}Ga-labeled analogue, followed by characterization and in vitro evaluation for radiopharmaceutical applications.

Materials and Methods

The ligand H4L was synthesized in three steps affording a red solid in 85% yield. The complex [Ga(HL)] was prepared by reacting H4L with [Ga(acac)3] in methanol under reflux for 6h, yielding a yellow solid in ca. 80% yield. Radiolabeling of H4L with 67GaCl3 was achieved within 15 min at room temperature, with radiochemical purity as confirmed by HPLC and iTLC. To evaluate in vitro stability prior to biological assays, the radiocomplex was incubated in PBS at 37°C and analyzed by HPLC after 1h, 2h, and 24h. The ligands and complexes [Ga(HL)] were characterized by FT-IR, NMR spectroscopy, and ESI-MS.

Results

Comparison of the FT-IR spectra of the free ligand H4L and the complex [Ga(HL)] shows a shift in the ν(C=N) stretching region, indicating coordination to the metal center. The proposed structure was further confirmed by ^{1}H NMR data, with signal integration consistent with the expected number of protons. ESI-MS analysis in negative ion mode confirming the formation of both species. Radiolabeling of [67Ga(HL)] evaluated by HPLC showed rapid and efficient complex formation, matching the non-radioactive analogue [Ga(HL)]. iTLC analysis showed a single species and no evidence of hydrolyzed gallium species. Radiochemical purity exceeded 95%. In vitro stability studies revealed an increase in one isomer after 1 h of incubation; however, no release of 67GaCl3 was observed up to 24h, indicating high stability and absence of transchelation.

Conclusion

The chelator H4L was successfully synthesized and coordinated to gallium, yielding [Ga(HL)] and its radioactive analogue [^{67}Ga(HL)] with high radiochemical yield and purity. Structural validation via FT-IR, ^{1}H NMR, and ES-MS confirmed the metal coordination and integrity of the ligand. Furthermore, in vitro stability studies in PBS at 37°C demonstrated that the radiocomplex remained intact for up to 24 hours without metal dissociation, indicating its suitability for future in vivo assessments. These promising results pave the way for structural optimization through spacer units and subsequent bioconjugation studies for the development of new radiopharmaceuticals.

Previous Next

Keywords

Gallium; Radioisotopes; Theranostics; Hexadentate Chelators; Imine group

Conflicts of interest: Not declared.

Acknowledgments/Funding: CNPQ, FAPESP-CEPID #2021-10265-8.

Recommended articles

Cited by (0)