Sodium Phase Zirconium Phosphate Nanoplatelets as a Vehicle for Targeted Alpha Therapy

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Introduction

Targeted alpha therapy (TAT) is a type of cancer treatment that has the capability to be highly effective, because alpha particles have a high linear energy transfer (LET) of 50-230 keV/μm and short path length of 50-100 μm (1-5 cell lengths).[1] These inherent properties of alpha particles allow them to distribute a large amount of energy in a small area, thus maximizing dose to targeted cancer cells and minimizing dose to surrounding tissue. ^{225}Ac and ^{230}U are of particular interest for TAT, because they decay to several other short-lived alpha emitters, which increases the dose 3-4 times that of a single alpha particle **(Figure 1)**. However, traditional targeting agents are sensitive to radiolysis, especially when used with radionuclides that undergo successive alpha decays. The daughters of these radionuclides have the potential to break away from the targeting agent where they are more likely to distribute throughout the body and damage healthy tissues, while reducing the dose to cancer cells.

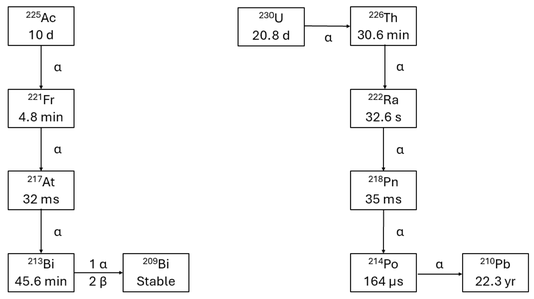


Figure 1. ^{225}Ac decay scheme (left) and ^{230}U decay scheme (right).[2]

One alternative to traditional targeting agents is the use of nanomaterials to entrap the daughter radionuclides. This work is utilizing sodium phase zirconium phosphate (Na-ZrP) nanoplatelets as a potential vehicle for TAT.

Methodology

Alpha zirconium phosphate (α-ZrP) was synthesized by dissolving ~5 grams of $ZrOCl_2 \bullet 8H_2O$ in 20 mL of water, then 30 mL of 4 M H_3PO_4 was added dropwise under constant stirring. The resulting mixture was transferred to a hydrothermal reaction vessel and heated in an oven at 200°C. After the solution was washed and dried, the α-ZrP was ready to be characterized. To convert the α-ZrP into Na-ZrP, 1 M NaOH and 1 M NaCl was added intermittently until a constant pH of ~10 is achieved.[3] The conversion from α-ZrP to Na-ZrP is a necessary step to increase the interlayer distance of the nanoplatelets to increase loading kinetics.

Uranium in the form of uranyl nitrate was added to ~50 mg of Na-ZrP. This solution was heated at 85 °C and aliquots were taken over several hours for ICP-OES analysis. Finally, ^{225}Ac and ^{230}U will be radiolabeled to the Na-ZrP and aliquots will be taken daily to be counted on a gamma counter to determine chemical stability and daughter retention.

Results

α-ZrP and Na-ZrP have been characterized with TEM to determine particle size **(Figure 2)**. XRD, TGA, FTIR, and XPS have also been used to confirm the successful conversion from α-ZrP to Na-ZrP **(Figure 3)**.

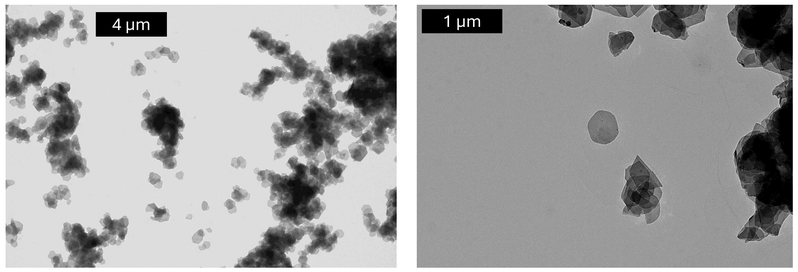
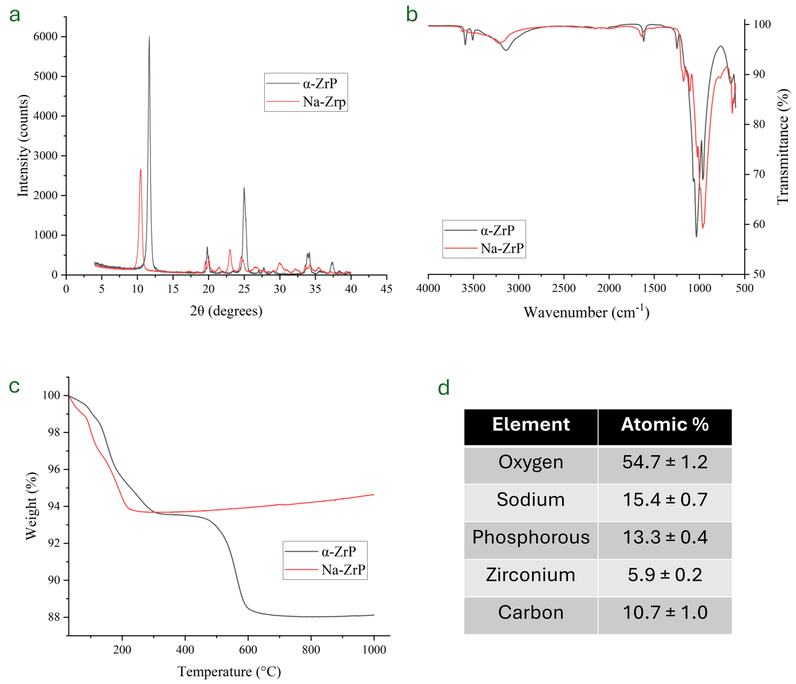


Figure 2. TEM images of α-ZrP with an average diameter of 500 ± 110 nm (left) and Na-ZrP with an average diameter of 550 ± 120 (right).



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Element	Atomic %
Oxygen	54.7 ± 1.2
Sodium	15.4 ± 0.7
Phosphorous	13.3 ± 0.4
Zirconium	5.9 ± 0.2
Carbon	10.7 ± 1.0

Figure 3. Characterization of α-ZrP and Na-ZrP nanoplatelets. XRD spectra (a), FTIR spectra (b), TGA weight percent (c), and XPS atomic composition (d).

The loading of uranium into Na-ZrP nanoplatelets was observed at room temperature and 85 °C in nitric acid at pH 1, 2, and 3 by utilizing ICP-OES **(Figure 4)**. However, under heating at pH 2 and 3 uranium began to hydrolyze from the exchange of sodium which is evidenced by the loading exceeding 100%. At room temperature the uranium did not appear to hydrolyze, but the uranium loading was about 3 times lower than the loading at pH 1 under heating.

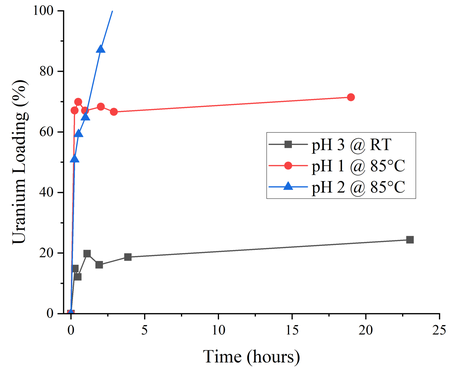

Figure 4. Uranium loading in Na-ZrP by ICP-OES..

Conclusions and Future Work

α-ZrP was successfully synthesized and converted to Na-ZrP, which was confirmed by several characterization methods. Additionally, preliminary loading experiments utilizing natural uranium were also completed. Future work to take place at the University of Utah include chemical stability and daughter retention studies with ^{225}Ac and ^{230}U. These studies will provide further insight into the feasibility of utilizing these radionuclides for TAT with Na-ZrP nanoplatelets. According to a SRIM simulation, ^{221}Fr, the first daughter of ^{225}Ac, is expected to travel about 34.6 nm in the ZrP nanoplatelets, while ^{226}Th travels approximately 34.5 nm due to the recoil effect of alpha particles.[4] Due to the size of the ZrP nanoplatelets, most of the daughters should stay intercalated within this nanomaterial, thus making it a promising vehicle for TAT.

Acknowledgements

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References

(1) Parker, C.; et al. Targeted alpha therapy, an emerging class of cancer agents: a review. *JAMA oncology* **2018**, *4* (12), 1765-1772.
(2) Sonzogni, A. NNDC chart of nuclides. In *International Conference on Nuclear Data for Science and Technology*, **2007**.
(3) Einkauf, J. D.; et al. Ion-Exchange Kinetics of Alpha-Zirconium Phosphate Nanoplatelets for Application in Targeted Alpha Therapy. *Solvent Extraction and Ion Exchange* **2020**, 38 (6), 612-628.
(4) Ziegler, J. F.; et al. SRIM–The stopping and range of ions in matter (2010). *Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms* **2010**, *268* (11-12), 1818-1823.