Astatine-211 extraction and fundamental chemistry in nitric acid media

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Instruction

Astatine-211 has a half-life of 7.2 hours, a high linear energy transfer (97 keV·μm^{-1} maximum), a quantitative decay by α-emission (41.80% immediate, 58.20% ec), and no serial decay. As such, it is one of a small number of α-emitting radionuclides whose decay characteristics are ideal for use in Targeted Alpha Therapy (TAT). Moreover, what little is known of astatine chemistry indicates that the element possesses diverse avenues of interaction and bonding, with both metallic and halogenic properties having been observed [1]. Its chemistry, however, is perhaps the most poorly understood of all naturally occurring elements due to its extreme unavailability. Since production parameters limit recovered astatine to ultra-trace amounts, characterization of the element and its behaviors is chiefly limited to separation and mobility experiments measured by gamma or alpha spectrometry. Studies at Texas A&M are ongoing to explore promising solvent systems that preferentially extract ^{211}At out of nitric acid, with an eye also towards understanding astatine speciation and interactions.

2022-2023 progress in research

From August 2022 to April 2023, the Isotope Production team at Texas A&M University produced over 500 mCi of astatine-211 across 7 distinct production runs. Following each successful ^{211}At production the irradiated Bi target is dissolved and extracted with the assistance of an automated dissolution apparatus (hereafter, ADA), and the ^{211}At collected by extraction chemistry or chromatography. Established procedures are used for shipment [2], and these have been further developed this year to increase loading efficiency across multiple columns. This has permitted regular

Table I. Extraction constants, K_{ext}, of ^{211}At with select ketones.

Ketone		***n***	K_{ext}	R^2
4-butoxyacetophenone*		1.07 ± 0.11	120 ± 13	0.934
2,4,6-trimethylacetophenone*		1.01 ± 0.10	68 ± 7	0.984
1,3-dibenzoylpropane‡		1.06 ± 0.10	50.4 ± 3.3	0.958
Acetophenone*		1.11 ± 0.13	8.3 ± 0.7	0.885
dibenzoylmethane‡		1.19 ± 0.08	5.4 ± 0.26	0.977
3-octanone‡		0.91 ± 0.04	5.2 ± 0.11	0.992
2,2,2-trifluoroacetophenone*		0.48 ± 0.05		

*Contributed, †Previously published

shipment of ^{211}At to both MD Anderson UAB. Progress has also been made in advancing fundamental chemistry of astatine through research into new extraction systems. Work on ketone extraction systems has expanded to include functionally tuned ketone interactions with astatine (Table I).

From the systems tested, several extraction constants have been calculated according to equations and derivations given elsewhere [3].

It is apparent that the electron donating groups have the anticipated effect of increasing the D-values of ^{211}At extraction in nitric acid systems, likely due to increased n-pair donation from the ketone moiety. Studies have also been done with *ortho*-, *meta*-, and *para*- substituted benzophenones, which demonstrate the expected trends, albeit with much lower distribution ratios. It is likely that the out-of-plane strain of these benzophenones limit donation of electron density, and the proximity of the aryl groups provides some steric hindrance to the AtO^+ interaction. The 2,2,2-trfluoroacetophenone extracted so poorly that a K_{ext} could not be calculated by the same method, further corroborating the effect of donating and withdrawing substituents on the AtO^+–ketone interaction.

Earlier work demonstrated very high distribution ratios of ^{211}At using methyl anthranilate to extract out of dilute HNO_3 [4]. Several aniline derivatives have been tested (figure 2) to elucidate the mechanism by which the responsible interaction occurs. For these experiments ^{211}At is isolated by 1-octanol impregnated TK400 resin [5], which attends the subsequent liquid-liquid extraction as a surfactant preventing third-phase formation. Of the derivatives tested, 2,6-diethylaniline possessed the highest D-values (>1000), by a factor of 2. It is possible that the occupied *ortho* positions are assisting in directing a *para* position interaction with astatine.

First steps in the qualification and quantification of astatine's redox species in nitric acid media have been taken by the development of the following: (I) a radio-thin-layer chromatography analysis method (radio-TLC) for tracking astatine polarity and speciation in a reaction, (II) the isolation of astatine from bismuth by ion exchange chromatographic resins selected according to our batch studies (Fig.7) [6],[6] and (III) the control of astatine speciation through redox agents. Utilized together, the control of astatine oxidation states may be established, and a subsequent exploration of AtO^+/At^+ equilibrium will be

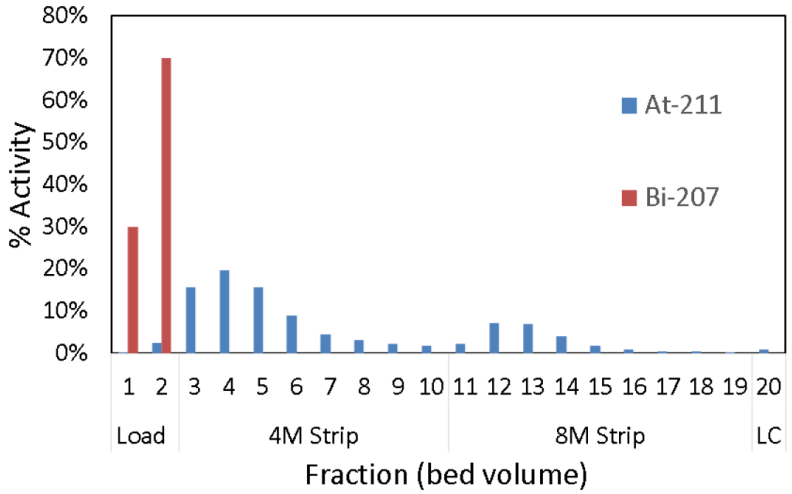

Fig. 1. Separation of 211At and 207Bi on Dowex 50x4 cation exchange resin. Column 4mm ID x 80mm length.

undertaken. Furthermore, of the ion exchange resins tested, Dowex 50x4 seemed most promising for the removal of bismuth from astatine. This resin was tested by column extraction, demonstrating quantitative elution of Bi in the load fractions, immediately followed by At in the 4M HNO_3 strip (Fig. 1). It is believed this separation can be improved with 2 M loading, followed by a water wash/flush, and then a high acidity (>6M) strip.

Experimental studies performed this year have also begun to explore several classes of extractant not yet adequately addressed in literature, including ionic liquids, deep eutectic liquids,[7] phosphines, phosphine-oxides, and crown ethers. Results acquired thus far are both chemically and pragmatically interesting, with the latter two classes expanding further on AtO^+ molecular cation interactions with oxygen functional groups in the extractants used.

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