## Solvent extraction following oxidation of astatine for the use of a $^{211}Rn-^{211}At$ generator<sup>†</sup>

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Radionuclide therapy, utilizing radioactive substances for targeted treatment of tumors, is increasingly prevalent.<sup>1)</sup> A promising  $\alpha$ -emitter for this therapy is a statine-211  $(^{211}At)$  due to its suitable half-life and high  $\alpha$  emission probability. A <sup>211</sup>Rn-<sup>211</sup>At generator is being developed to enhance <sup>211</sup>At availability, allowing distribution to locations distant from accelerators.<sup>2)</sup> The chemical behavior of At, similar to iodine, makes it valuable for labeled compound synthesis in radionuclide therapy.<sup>3)</sup> The study investigates the back-extraction of  $^{211}$ At into ethanol for potential <sup>211</sup>At labeling of compounds. Oxidants, including N-chlorosuccinimide, N-bromosuccinimide, and Niodidosuccinimide, are employed to optimize solvent extraction of <sup>211</sup>At. The study aims to clarify the extraction mechanism of <sup>211</sup>At species and propose an efficient and safe system suitable for targeted  $\alpha$ -therapy.

The production of <sup>211</sup>At involved two methods: the  $^{209}$ Bi $(\alpha, 2n)$  reaction and milking of  $^{211}$ Rn produced in the  $^{209}$ Bi $(^{7}$ Li, 5n) reaction. The  $^{211}$ At obtained from these processes was back-extracted from dodecane into an aqueous ethanol solution. For comparison with the <sup>211</sup>At data, <sup>131</sup>I tracer solution was added to 6 M HNO<sub>3</sub> and extracted to dodecane. Solventextraction experiments were conducted with <sup>211</sup>At and  $^{131}$ I, varying conditions like time (experiment (a)), oxidizing agents (NBS, NCS, NIS, bromine water, HBr), concentrations (experiment (b), and ethanol content (experiment (c)). Thin-layer chromatography was used to analyze extraction of the At species identified according to Refs. 4) and 5) (experiment (d)), and radioactivity measurements were performed using a liquid scintillation counter and a Ge semiconductor detector.

The results of the solvent extraction experiments of (a) to (d) are as follows: Experiment (a) revealed a substantial increase in the back-extraction rate of <sup>211</sup>At when NBS or bromine water was added. Both NBS and bromine showed an initial high backextraction rate, but their effectiveness decreased over time. Experiment (b) demonstrated that NBS had

the highest impact on increasing the back-extraction rate of <sup>211</sup>At among the oxidizing agents NCS, NBS, and NIS. HBr also increased the back-extraction rate, but to a lesser extent than NBS. Experiment (c) showed that the presence of bromine water significantly increased the back-extraction rate of <sup>211</sup>At, while the back-extraction rate of <sup>131</sup>I remained largely unchanged. This suggested that <sup>211</sup>At changed to a chemical form easily back-extracted with the addition of bromine water. Experiment (d) involved thin-layer chromatography (TLC) to analyze At species. The addition of NBS or bromine water increased the proportion of At species with higher oxidation numbers, indicating oxidation of At. However, the TLC results may not capture all chemical forms present in the solution, and the oxidation might occur on the TLC plate surface. Overall, NBS was identified as the preferred choice due to its solid form, storability, and sustained oxidizing power.

In conclusion, from the similarity of the effects of NBS and bromine, we conclude that bromine produced from NBS increased the <sup>211</sup>At back-extraction rate. Among NCS, NBS, and NIS, NBS had the strongest effect on <sup>211</sup>At back-extraction. Comparing the results for <sup>211</sup>At and <sup>131</sup>I, the addition of bromine water increased the back-extraction rate of only <sup>211</sup>At. This indicates that some <sup>211</sup>At species, which are more easily oxidized than other halogen species, contribute to the increase of the back-extraction rate. TLC revealed that <sup>211</sup>At was oxidized by the addition of NBS and bromine water.

## References

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