Pursuit of Purity: Measurement of chelation binding affinities for NOTA, DOTA, and desferal with applications to effective specific activity

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Introduction

The effective specific activity of a radioisotope is an indirect and highly useful way to describe a radioactive sample's purity. A high effective specific activity combines the concept of an isotopically pure product with suitability via selectivity of a particular chelating body. The primary goals of this work are twofold: 1) To determine which metallic impurities have the largest impact on the effective specific activity for a given chelator, and 2) to form a model based on the binding affinities of each metal for to calculate a 'theoretical effective specific activity' from broad band trace metal analysis. If successful, this information can be used to guide the production of high specific activity products through the systematic elimination of high-impact metallic impurities.

Material and Methods

Phosphor plate thin layer chromatography (TLC) was used to measure the effective specific activity of ^{64}Cu by NOTA and DOTA, and ^{89}Zr by desferal (DF). Typical measured effective specific activities are 2–5 Ci/µmol for ^{64}Cu and 1–2 Ci/µmol for ^{89}Zr.

Samples were created containing increasing cod competitive burdens (X) of $CuCl_2$, $ZnCl_2$, $FeCl_2$, $NiCl_2$, $CrCl_3$, $CoCl_2$, $MnCl_2$, and YCl_3. Standard concentrations were measured by microwave plasma atomic emission spectrometry. 50 pmol of NOTA, DOTA, or DF were added following the activity aliquots of ^{64}Cu or ^{89}Zr. Labeling efficiencies (^{64}Cu-NOTA, ^{64}Cu-DOTA, ^{89}Zr-DF) were measured using TLC's, and were fit by linear regression to the form $f(X) = b/(1 - AX)$, where A is the chelation affinity (inverse of dissociation constant) and X is the molar ratio of the metallic impurity to the amount of chelator.

Results and Conclusion

Affinity of Zr for DF was assumed to be unity, while the affinities of Cu for NOTA and DOTA were explicitly measured and were found to be 0.93 ± 0.13 and 5.2 ± 3.2 respectively.

It was found that Cu had the highest affinity for NOTA by a factor of 266, and that Zr had the highest affinity for DF by a factor of 40.

- In order of decreasing affinity to NOTA: Cu, Zn, Fe, Co, Cr, Y, and Ni.
- In order of decreasing affinity to DOTA: Cu, Y, Zn, Co, Ni, Cr, and Fe.
- In order of decreasing affinity to DF: Zr, Y, Cu, Zn, Ni, Fe, Co, Cr.

These results suggest that aside from the carrier element it is most important to remove zinc from ^{64}Cu products prior to chelation with NOTA and yttrium from ^{64}Cu and ^{89}Zr products prior to chelation with DOTA and DF, respectively. Therefore, it is logical to believe that ^{89}Zr effective specific activities could be greatly improved by secondary separations with the goal of removing additional yttrium target material.

Chelation affinities of NOTA, DOTA, and DF for several common metals have successfully been investigated. These values will guide our future attempts to provide high effective specific activity ^{64}Cu and ^{89}Zr. Furthermore, a preliminary model has been formed to calculate effective specific activity from the quantitative broad band analysis of trace metals. Future work will include chelator affinity measurements for other likely contaminants, such as scandium, titanium, zirconium, molybdenum, niobium, gold, gallium, and germanium. Details will be presented.

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Metal	Measured Dissociation Constants NOTA	DOTA	DF
Copper	1.06 ± 0.15	5.22 ± 3.15	125 ± 107
Zinc	266 ± 13	152 ± 31	16076 ± 8132
Iron	715 ± 187	1.42E6 ± 5.84E7	76552 ± 16700
Nickel	24237 ± 4128	2789 ± 967	13477 ± 897
Cobalt	1056 ± 373	476 ± 203	88489 ± 181802
Chromium	1326 ± 189	11660 ± 3475	2.11E12 ± 9.26E19
Yttrium	4257 ± 1031	30 ± 22	40 ± 15

TABLE 1. Measured dissociation constants of common metals for NOTA, DOTA, and DF

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