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New extractant-impregnated iTLC-SG paper facilitates improved TLC analysis for Cu radiolabelled peptides

Johan Svedjehed[1], Marine Bas[2], Steffen Happel[2], Katherine Gagnon[1]

[1]*GE Healthcare, GEMS PET Systems AB, Uppsala, Sweden*
[2]*Triskem, Bruz, France*

katherine.gagnon@ge.com

Objective

One challenge with the analysis of radiochemical purity for Cu-labelled peptides (vs. e.g. ^{68}Ga) is that non-labelled ^{6x}Cu may form artefacts (assumed here by authors to be Cu-acetate complexes) that interfere with the analysis by creating or distorting peaks when using silica gel based solid phase support. Whereas other solid supports may be used (e.g. Whatman paper), development can be extremely slow with generally broad peaks. To eliminate such interferants, while maintaining the faster development of iTLC paper, we investigated the use of iTLC-SG paper impregnated with a Cu-selective extractant to better retain the unlabelled ^{6x}Cu at the origin of the TLC strip.

Methods

Instant thin layer chromatography paper impregnated with silica gel (iTLC-SG, Agilent) was impregnated with the same oxime-based, Cu-selective extractant employed in the "CU Resin [Triskem]". ^{61}Cu was produced via the ^{nat}Ni(d,x)^{61}Cu reaction using a GE PETtrace solid target system and purified as [^{61}Cu]$CuCl_2$ as described previously [1]. Aliquots of [^{61}Cu]$CuCl_2$ were incubated (90°C; 30 min; pH 4.4 [0.3 M acetate buffer]) with varying low concentrations of NOTA-Octreotide trifluoroacetate or NODAGA-RGD trifluoroacetate (ABX). Ligand concentration was not added in excess to ensure incomplete labelling. TLC strips were spotted with the ^{61}Cu-labelled peptide (5 µL) and immediately developed in 1:1 MeOH/1 M ammonium acetate. For comparison, TLC strips of iTLC-SG and Whatman paper (both without the Cu-selective extractant) were also spotted. Strips were 10 cm in length, with origin at ~1 cm, and the solvent front allowed to develop to a minimum of ~7 cm (corresponding to <10 min for the iTLCs, or ~25-30 min for the Whatman paper).

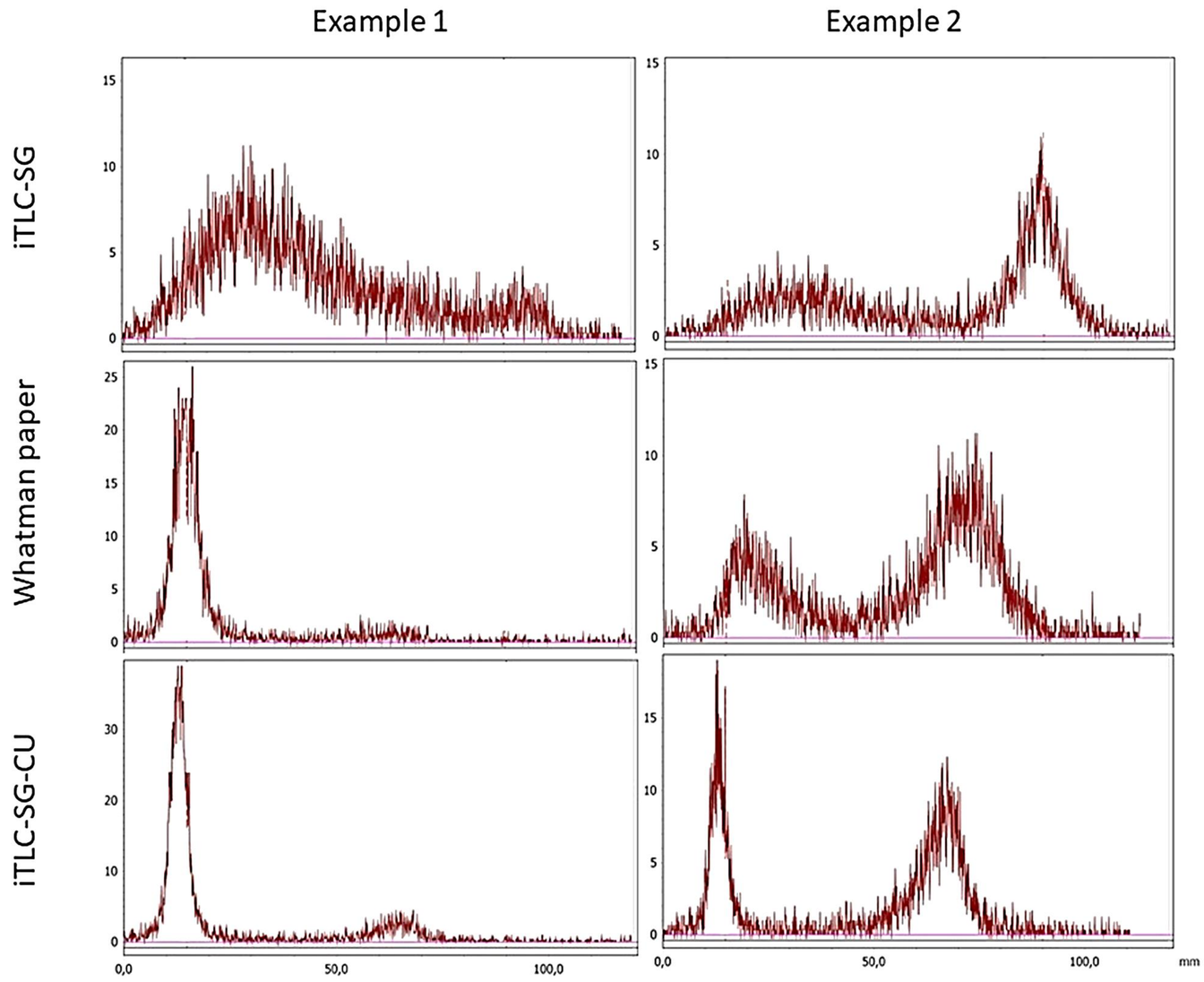

Figure 1. TLC scans of [^{61}Cu]Cu-NOTA-octreotide spotted on: top, iTLC-SG; middle, Whatman paper; bottom extractant-impregnated iTLC-SG. Example 1 notes elevated levels of unlabelled ^{61}Cu, while example 2 notes comparable levels of labelled to unlabelled ^{61}Cu.

Results

TLC scans of [^{61}Cu]Cu-NOTA-octreotide with elevated levels of unlabelled ^{61}Cu are presented in Figure 1 as example 1, while [^{61}Cu]Cu-NOTA-octreotide scans at comparable levels of labelled and unlabelled ^{61}Cu are presented as example 2. Results for [^{61}Cu]Cu-NODAGA-RGD were similar and are thus not presented for the sake of brevity.

By comparing the scans, the benefit of the extractant can clearly be seen. For non-impregnated iTLC-SG and Whatman papers, wide, non-uniform peaks of low resolution can be observed. The extractant-impregnated iTLC-SG on the other hand clearly shows sharper, separated peaks with the added benefit of short development time vs. the Whatman paper. The differences between the TLC strips were even more pronounced when decreasing the amount of peptide.

Conclusion

By impregnating iTLC-SG paper with a Cu-selective extractant, superior resolution compared to standard iTLC-SG and Whatman paper was attained when analyzing [^{61}Cu]Cu-NOTA-octreotide and [^{61}Cu]Cu-NODAGA-RGD using TLC.

References

1. J. Svedjehed, K. Gagnon. A quest for simplicity: Automated cassette-based purification of [^{61}Cu]$CuCl_2$ from solid Ni targets using a single time-list. Nucl Med Biol, 108-109, S1 (2022), P-220, ppS170.

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