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Breakthroughs and Views

Correspondence regarding October 31, 2003, Breakthroughs and Views by K. Brown and P.L. Carmichael☆

Minoti Sharma*,[1]

Department of Molecular and Cellular Biophysics, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA

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In innumerable literature reports, authentic modified nucleosides have served to identify the same lesions in DNA exposed to the same modifying agents. The formation of detectable tamoxifen–DNA adducts in human endometrial explants exposed in culture to tamoxifen was identified using authentic α-(deoxyguanosyl-N^2) tamoxifen standards [1]. Also, in the same report, three authentic tamoxifen metabolites namely, α-hydroxytamoxifen, 4-hydroxytamoxifen, and *N*-desmethyltamoxifen were used to identify the major metabolites detected in the culture media.

Fig. 1 shows HPLC resolution of mixtures of the above authentic standards used to identify the detectable tamoxifen–DNA adducts and metabolites in the explant culture model [1]. The HPLC conditions in Fig. 1 are identical to those reported for adduct analysis [1].

The authors appreciate the suggestion offered by Brown and Carmichael (October 31, 2003, Breakthroughs and Views) that under the HPLC conditions employed for adduct analysis, the co-elution of any tamoxifen metabolites could be mistaken for DNA adducts [2]. Fig. 1 rules out such a possibility by demonstrating that under the HPLC conditions reported for adduct analysis [1], the metabolites not only resolve from the DNA-adducts, but also from one another. The elution order observed in the HPLC profile, shown in Fig. 1, was based on the polarity of the compounds as expected for reversed-phase HPLC.

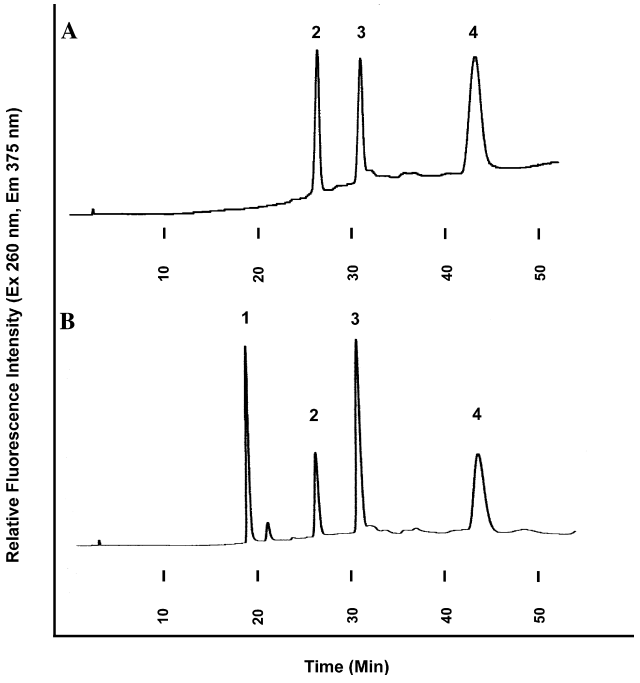

Fig. 1. Reversed-phase HPLC resolution of a mixture of tamoxifen metabolites: (A) α-hydroxytamoxifen (2), 4-hydroxytamoxifen (3), and *N*-desmethyltamoxifen (4); (B) α-(deoxyguanosyl-N^2) tamoxifen adducts [1] plus tamoxifen metabolites shown in (A) using postcolumn, online photochemical activation, and fluorescence detection. HPLC system and elution conditions used are identical to those reported for adduct analysis [1].

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* Fax: 1-716-845-1349.
E-mail address: minoti.sharma@roswellpark.org.
[1] Minoti Sharma on behalf of the coauthors.

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