Potential Problem in GLC Determination of Ibuprofen Caused by Solid Support

Keyphrases □ Ibuprofen—GLC analysis in plasma, effect of varying solid support materials □ GLC—analysis, ibuprofen in plasma, effect of varying solid support materials □ Solid supports, GLC—effect on ibuprofen analysis □ Anti-inflammatory agents—ibuprofen, GLC analysis in plasma, effect of varying solid support materials

To the Editor:

A sensitive and specific GLC method for the determination of ibuprofen [(±)-2-(*p*-isobutylphenyl)propionic acid] in plasma was reported previously (1). The assay involves a single extraction followed by methylation of the carboxyl moiety of ibuprofen to form ibuprofen methyl ester. Chromatography is carried out on a column packed with 6% diethylene glycol succinate on 80–100-mesh silanized diatomaceous earth. The purpose of this communication is to report a problem encountered due to differences between apparently equivalent solid support materials obtained from different manufacturers.

Using Diatoport-S[1] as the solid support, Kaiser and VanGiessen (1) obtained chromatograms that showed a return to a consistently clean baseline 10 min after sample injection. Essentially identical results were obtained when Gas Chrom Q[2] was used as the solid support. In a slightly different chromatographic system (using nitrogen rather than helium as the carrier at a flow rate of 50 ml/min and a 1.82-m × 2-mm i.d. coiled glass column), Anakrom-SD[3] (90–100 mesh) coated with 6% diethylene glycol succinate was used as received from the manufacturer. With this support material, a contaminant was eluted with a retention time of 23 min; return to baseline was achieved only 70–90 min after sample injection (Fig. 1). Similar results were obtained when Anakrom-SD was used under the exact chromatographic conditions described by Kaiser and VanGiessen (1).

Sequential elimination of reagents from the methylation scheme revealed that the contaminant was associated with the use of triethylamine, which functions to increase the rate of methylation. Essentially identical results were obtained with triethylamine (reagent grade) from three different sources[4]. Mass spectral analysis of the eluate comprising the contaminant peak indicated that it was triethylamine or a closely related compound.

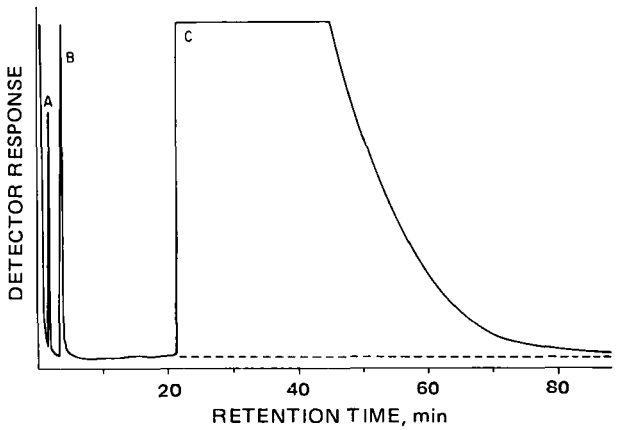

Figure 1—*Gas–liquid chromatogram of ibuprofen recovered from chloroform and methylated (1), using Anakrom-SD as the solid support. Key: A, naphthalene internal standard; B, ibuprofen methyl ester; C, peak obtained when triethylamine is included in the methylation procedure; and - - - -, normal baseline when triethylamine is omitted.*

Triethylamine can be eliminated from the procedure by allowing methanol to react with the imidazole intermediate for 20 min. This step has no effect on the specificity or sensitivity of the assay. However, it may be preferred to retain triethylamine (which reduces the reaction time to less than 5 min) and to use a solid support material that does not produce the chromatographic peak associated with triethylamine.

(1) D. G. Kaiser and G. J. VanGiessen, *J. Pharm. Sci.*, **63**, 219(1974).

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