

## Discussion

# Solid-phase extraction method for the determination of diltiazem and its metabolites by high-performance liquid chromatography: fact or fallacy?

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In a recent paper published in this journal, Rutledge et al. [1] made some comments on liquid–solid extraction methods developed for the determination of diltiazem and its metabolites in plasma samples. In view of our experience with this procedure [2,3], we would like to discuss some important points concerning the interest in solid-phase extraction for the determination of these compounds in plasma.

The only difficulty in the solid-phase extraction procedure was the optimization of the method and particularly the choice of suitable eluents for the conditioning, washing and elution steps. However, when the procedure is optimized, this method is more rapid and reliable than the conventional liquid–liquid extraction method which involves laborious double-step extractions with diethyl ether followed by acidic back-extraction, which is time-consuming.

In contrast to the liquid–liquid procedure, the solid-phase extraction method leads to an im-

provement in the analytical recovery (the average recoveries are greater than 90% for all compounds), which is closely related to an improvement in the detection limit, especially for N-demethyldeacetyldiltiazem ( $M_2$ ) and deacetyldiltiazem ( $M_1$ ) metabolites, which are found at low levels in plasma from patients undergoing diltiazem therapy [3]. The minimum amount detectable was 0.15 ng for  $M_1$  and  $M_2$  and 0.30 ng for N-demethyldiltiazem (MA) and diltiazem with a coefficient of variation of less than 10%. Further, using the solid-phase extraction procedure, there is no risk of degradation of diltiazem and its metabolites owing to stressing conditions such as acidic or basic conditions [3,4].

Further, with regard to the economic aspects evoked by Rutledge et al. [1], the cost of extraction columns must be reconsidered in view of the time saving and the efficiency of the solid-phase extraction procedure, that also has the advantage of being easily automated.

To conclude, solid-phase extraction is a more convenient, rapid, sensitive and efficient method than the liquid–liquid extraction procedure to obtain clean plasma extracts with optimum recoveries.

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