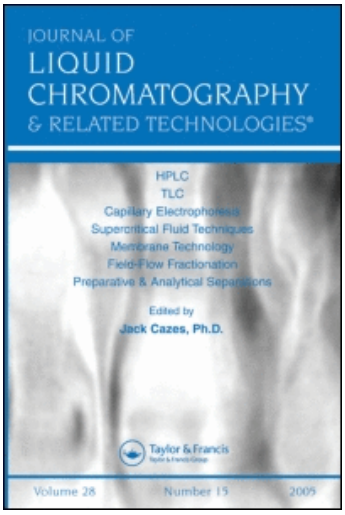

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Letter to the Editor

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LETTER TO THE EDITOR

Correspondence re: T. J. Stolzer et al. Determination of Suramin in plasma and urine by reverse-phase high-performance liquid chromatography. J. Liq. Chromatog. 10:3451-3462 (1987)

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Sir:

Stolzer et al. have recently published a modification (1) of the HPLC method for suramin analysis of Klecker and Collins (2). There are several similarities between the methods of Stolzer and Klecker. Both methods use 0.5 ml of plasma for extraction. Both methods add 50 µl of a naphthalenesulfonic acid compound as an internal standard. Both methods add 100 µl of the tetrabutylammonium cation and 1 ml of organic precipitant. Both methods use three cumulative extractions to optimize extraction efficiency.

There are a few relatively minor differences between the two methods. Stolzer uses congo red in place of trypan blue. Congo red and trypan blue have similar skeleton structures but differ in the

number of naphthalenesulfonic acids they contain. Their internal standard is presumably chemically pure when purchased, whereas other internal standards for suramin determination have required further purification before use. In addition Stolzer states that congo red is not a carcinogen, while trypan blue, another suramin internal standard, is a carcinogen. The method by Stolzer uses an isocratic mobile phase instead of a gradient system. Stolzer uses acetonitrile as his protein precipitant and as the organic modifier in his HPLC mobile phase in place of methanol.

The major difference between the two methods is the use of an isocratic reversed-phase ion-pairing mobile phase in place of a gradient reversed-phase ion-pairing mobile phase. Although an isocratic system is different from the method of Klecker, two other groups have reported suramin analysis methods with similar isocratic reversed-phase ion-pairing mobile phases (3,4). All the methods use the tetrabutylammonium cation for ion-pairing.

Stolzer was not able to reproduce the method of Klecker and felt that the method was limited. The only difficulty which they described for the latter method was a shifting retention time of the internal standard, trypan blue. I do not believe that the problem arises from trypan blue. Schattenkerk et al. have also reported a suramin analysis procedure using trypan blue as their internal standard (5). Since the extraction scheme is so similar, I assume that the reason Stolzer had difficulty with reproducibility of the method by Klecker was due to the inability to reproduce the gradient conditions from sample run to sample run. A small change in the organic composition of the mobile phase from run-to-run might cause the peak shifting described by Stolzer. I chose a methanol gradient

system as a result of the recommendation by Majors, who stated that the optimum system for reversed-phase ion-pairing applications is a water-methanol gradient (6). In fact, his recommendation was influenced by Gloor and Johnson, who used a water-methanol gradient, at pH 6.5, with the tetrabutylammonium cation to separate the structurely similar naphthalenetrisulfonic acid compound FD&C Red #2 (7).

Collins et al. have published a detailed report on the pharmacology of suramin (8). This publication presents a summary of the analysis method by Klecker and has been cited frequently by other authors using the method directly or with modification (9,10,11). All of these reports provide data from suramin measurements in patient urine and/or plasma. The question of reproducibility was never raised among these authors. Suramin is currently being investigated as an anti-cancer agent. The original analysis method reported by Klecker is still performed as described to measure suramin in patient samples.

In conclusion, Stolzer et al. have provided improvements to the method by Klecker. The internal standard, congo red, can be used directly without further purification. In addition, they have provided a potentially useful isocratic mobile phase for the measurement of suramin. However, these contributions, in themselves, lack sufficient improvement or detail to warrant a full publication. Analytical methods are commonly adapted from literature sources to conform to an individual's environment, equipment or purpose. I feel that an unfounded criticism of the method of Klecker was used to increase the publishability of the article by Stolzer. As author of the original suramin method, I feel that its reliability has been inappropriately questioned. Finally, their claim that "little is

known about the pharmacology of suramin" shows their failure to recognize the extensive published literature of suramin. The Journal should be more complete in their mansucript screening process in order to avoid publication of similar methods with little improvement and to prevent inaccurate and unfounded criticism of current methodology.

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