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The following comments pertain exclusively to a Letter to the Editor by B. K. Tang and W. Kalow (1) that concludes that the "Butler methods" developed by our laboratory (2) for determining CYP1A2 activity are inadequate and that adoption of these methods "in cancer research would lead to results that are not much better than half-truths." Because our method, which measures the urinary molar ratio of (17X + 17U)/137X, and that of Tang and Kalow (3), which uses the urinary ratio of (AAMU + 1X + 1U)/17U, are both being used in a variety of cancer epidemiology and biomarker studies, we again wish to comment on the validity of our original method.

The basis for the conclusions of Tang and Kalow is derived from previous work by these authors (3) in which they reported that caffeine (137X) excretion is urine flow-dependent and that their ratio of (17X + 17U)/137X reflects only a polymorphism in renal clearance of caffeine. We have previously stated (4) that, although caffeine clearance is indeed dependent on urine flow, we could find no evidence that caffeine urinary concentrations are urine flow-dependent under our experimental conditions and methods of analysis. Furthermore, our results agree with those of Birkett and Miners (5), who have also reported that urinary caffeine concentrations are independent of urine flow rate. In a recent study, in which we found comparable trimodal distributions for both the (17X + 17U)/137X ratio and the caffeine breath test, we noted a urinary constituent that often co-migrates with caffeine on a variety of HPLC columns. Moreover, its excretion was highly dependent on urine flow rate. This constituent is typically present in 20–40% of urine samples that we have examined and seems to be of dietary origin. Accordingly, our selection of HPLC columns for use in caffeine urinary metabolite determinations has required the use of computerized photodiode-array detection systems that assure peak purities by comparisons with spectral libraries of authentic standards. Generally, we have found a similar proportion (1:1:1) of columns (even from the same manufac-

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³The abbreviation used is: HPLC, high-performance liquid chromatography.
statistical approaches, by conducting additional family and nutritional epidemiological studies, and by sequencing genes that control CYP1A2 expression or inducibility.

References


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