Administered Viloxazine Interferes in Liquid-Chromatographic Assay of Normetanephrines, Claude J. Bieuva, Irène H. Ladmirant, Isabelle Scheirs, and Jean Pierre M. Dardenne (Free Univ. of Brussels, Dept. of Chromatography, New Larem lab., 1 ave. L. Gribaumont, 1150 Brussels, Belgium)

Assay of metanephrines (normetanephrine and metanephrine, NM and M, respectively) in urine for diagnosis and characterization of pheochromocytoma or other neural crest tumors is well established (1). These determinations may also be valuable in patients with depressive disorders (2) or essential hypertension (3), in which cases metanephrines are evaluated in conjunction with data on other catecholamine metabolites.

A 57-year-old man with a history of essential hypertension was referred to the laboratory. Results of the laboratory tests were within normal limits except for a major increase of urinary NM as measured by "high-performance" liquid-chromatographic (HPLC) methods involving a WISP 712 sample processor, Model 480 multi-wavelength detector, Model 6000 pump, and Model 840 data chromatography control station (all from Waters Associates, Milford, MA).

The procedure we used included sample clean-up with a commercially available 657-616 column developed for determining urinary M and NM (Bio-Rad Labs., Richmond, CA). For chromatographic separation, we used a Nova-Pak C18 column, 5-μm (diameter) particle size, and a flow rate of 1 mL/min. The detection wavelength was 200 nm.

The mobile phase consisted of 890 mL of distilled water, 110 mL of acetonitrile, and one vial of a counter-paired ion"PIC" B8 (Waters). For the internal standard we used 3-methoxy-4-hydroxybenzylamine hydrochloride. Figure 1 illustrates a typical chromatogram obtained for NM, M, and internal standard. The pattern for the patient's sample was similar, but with a higher concentration of NM.

Because these infrequently noted increases can cause considerable confusion, particularly when they involve patients who have had or are suspected of having hypertension, we evaluated the possibility of interference from drugs.

We therefore repeated the analysis, supplementing, at therapeutic concentrations, normal urine with bromazepam (Lexotan®), sulpiride (Dogmatyl®), viloxazine (Vivalan®), and guanfacine (Estulic®). All these drugs were being taken by the patient when he was referred to us. The resulting peak heights for NM, M, and the internal standard (IS) in the presence of these drugs were as follows:

![Fig. 1. Chromatogram of a mixture of normetanephrine (a), metanephrine (b), and 3-methoxy-4-hydroxybenzylamine hydrochloride (c), the internal standard](image)

We thank Eastman Kodak for providing the necessary slides for these studies.

References
These data indicate that the procedure is reproducible but also that viloxazine clearly interferes with quantification of NM. In our use of the procedure outlined above, this was our first encounter with interferences from tricyclic antidepressants. Instead of modifying the procedure, we had the administration of viloxazine stopped for 24 h, to allow accurate determination of NM concentration.

References

**Phenylpropanolamine and (d)-Norpseudoephedrine Are Indistinguishable by Toxilab**

_Lichtenstein (Div. of Clin. Pharmacol., Univ. of Colorado Sch. of Med., Denver, CO 80262)_

Phenylpropanolamine (d,l-norephedrine) is widely available in the United States in cold-, allergy-, and appetite-suppressant products. Its diastereomer, d-norpseudoephedrine, is not an approved drug in the United States, but it is widely used around the world as an anorexic agent. The two drugs differ significantly in their pharmacological effects (1). Recently, U.S. authorities have become aware of the increasing use in the U.S. of a Mexican appetite-suppressant preparation containing several drugs, including d-norpseudoephedrine (2). Addiction, psychosis, hypertension, and death among users of this preparation have been reported (2). Apparently, the drug is obtained mainly by individuals travelling to Mexican border towns (2).

The "Toxilab" thin-layer chromatographic drug-screening system is used extensively to detect drugs in biological fluids. Toxilab readily identifies phenylpropanolamine in urine. In view of the above-described abuse of d-norpseudoephedrine, we examined the ability of the Toxilab system to distinguish phenylpropanolamine from its congenor d-norpseudoephedrine. Phenylpropanolamine hydrochloride was purchased from Kodak Laboratory and Research Products (Rochester, NY); d-norpseudoephedrine was obtained by isolation via acid--base partitioning from 30 drages of "Adiposetten N," an anorexic preparation containing 10 mg of d-norpseudoephedrine hydrochloride per dragee (Reiss Chemische Werke GmbH and Co. KG, Berlin, F.R.G.). The yield of d-norpseudoephedrine base [uncorr. mp 75–76.5 °C; lit. (3) corr. mp 77–78 °C] was 224 mg (92.7%). Phenylpropanolamine and d-norpseudoephedrine were analyzed separately by the Toxilab procedure (4). The migration and color characteristics of phenylpropanolamine were within the specifications of the Toxilab system, but were indistinguishable from those of d-norpseudoephedrine. The sympathomimetic-amine differentiation procedure also failed to distinguish between the two drugs. Phenylpropanolamine (5) and d-norpseudoephedrine (6) are excreted in human urine unchanged. Thus, the Toxilab system cannot distinguish between these two drugs. Abuse of and overdose with d-norpseudoephedrine may therefore be erroneously attributed to phenylpropanolamine when Toxilab is the drug-detection system being used.

References