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**Interferences by Cephalosporin Antibiotics in Urinary Tests for Metabolic Disorders**, Joseph L. Potter,<sup>1,4</sup> G. Dean Timmons,<sup>2</sup> and William G. Kofron<sup>3</sup> [Depts. of <sup>1</sup> Pathol. and Lab. Med. and <sup>2</sup> Pediatrics (Div. of Neurol.), Children's Hospital Med. Center of Akron, and <sup>3</sup> Dept. of Chem., Univ. of Akron, Akron, OH; <sup>4</sup> author for correspondence: fax 216-358-3307]

Interferences due to dietary intake and administered drugs remain a source of concern in clinical pathology and medicine (1-3). Here, we describe the confounding of multiple laboratory tests engendered by the administration of cefaclor to a pediatric patient. The observations were based on three structural characteristics of the cefaclor molecule (Fig. 1B): its aliphatic amino group, which conferred ninhydrin reactivity; a functional aldehyde-equivalent structure comprising C-6 and positions 1 and 5 of the dihydrothiazine ring, which appears to be responsible for its reducing action; and the conjugated double-bond system involving the dihydrothiazine ring and the carboxyl group, which confer the ultraviolet absorption property of the compound.

Paper chromatography, paper electrophoresis, and ninhydrin staining were carried out as previously described (3, 4). Peroxide oxidation was performed by mixing the sample with one-tenth volume of 30% hydrogen peroxide at room temperature for 30 min. Oxidation of cefaclor was also carried out by adding hydroxy(tosyloxy)iodobenzene (Koser's reagent) to an acidified solution of cefaclor, precipitation from solution with triethylamine, washing with cold alcohol, and air drying. Infrared analyses were carried out with a Bomem MB100 (Bomem, Quebec, PQ) FTIR spectrometer, and <sup>1</sup>H and <sup>13</sup>C nuclear magnetic resonance spectra were determined in deuteriochloroform. Ultraviolet spectra were determined with a Gilford spectrophotometer Model 250 (Ciba Corning Diagnostics, Oberlin, OH). Ion-exchange chromatography of the amino acids was carried out in a Beckman 6300 analyzer (Beckman Instruments, Fullerton, CA). Reducing sugars were measured with the customary five-drop Clinitest (Miles, Elkhart, IN) method. Antibacterial activity was assessed semiquantitatively with 6-mm-diameter Whatman No. 3 MM (Whatman, Clifton, NJ) discs applied to agar plates streaked with *Streptococcus faecalis*. Antibiotics were commercial products purified in the laboratory.

The ninhydrin reactivity of cefaclor led to its detection in three different routine methodologies for the analysis of amino acids: paper chromatography, where it tended to migrate with an *R<sub>f</sub>* of about 0.5; paper electrophoresis, where it migrated somewhat more slowly than glycine at an acid pH; and ion-exchange chromatography, where it comigrated with glycine and alanine. Peroxide oxidation or Koser's reagent converted cefaclor to a compound that retained its ninhydrin reactivity but migrated more slowly in the paper systems. Ultraviolet, infrared, and magnetic resonance spectroscopy indicated that the oxidation conditions resulted in the formation of the sulfoxide derivative of cefaclor without other alterations in its molecular structure. The complete loss of antibacterial activity associated with the sulfoxide derivative of cefaclor indicates the importance of the oxidation state of the sulfur atom in relation to the biological activity of the antibiotic.

The false-positive sugar reaction of the cephalosporins and of the penicillins has been recognized for many years. Ten cephalosporin compounds representing first-, second-,

