Among the cycloalkyl substituents, the cyclopentyl group had a more favorable action than the cyclohexyl group.

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COMMUNICATIONS

Correction to "Ionization Constants of Cephalosporin Zwitterionic Compounds"

Keyphrases □ Ionization constants—cephalosporin zwitterionic compounds, error in equations corrected □ Cephalosporin zwitterionic compounds—ionization constants, error in equations corrected □ Zwitterionic cephalosporin compounds—ionization constants, error in equations corrected

To the Editor:

In reviewing the derivation given in the paper "Ionization Constants of Cephalosporin Zwitterionic Compounds" (1), it was found that a factor was dropped in Eq. 12. This omission introduced an error into succeeding equations, and it is the purpose of this communication to correct this error.

The experimental results and calculations were made using the equations shown below rather than those in the paper and, therefore, do not need to be changed. In addition, the *Results and Discussion* section is correct in the paper.

The correct form of Eq. 12 is:

$$[A] = \left\{ \frac{[B] + [H^+] - [OH^-] - [A]}{K_3K_4 - \{H^+\}^2 \dfrac{Y_{NR^-}}{Y_{+HNRH}}} \right\} \left\{ K_3K_4 + K_3\{H^+\} \frac{Y_{NR^-}}{Y_{NRH}} \right\} + [Z]$$

The correct form of Eq. 13 is:

$$\{H^+\}^2 \frac{Y_{NR^-}}{Y_{+HNRH}} \{[Z] - [A]\} = K_3\{H^+\} \frac{Y_{NR^-}}{Y_{NRH}} \left\{ [B] + \frac{\{H^+\}}{Y_{H^+}} - \frac{K_\omega}{\{H^+\}Y_{OH^-}} - [A] \right\} + K_3K_4 \left\{ [B] + \frac{\{H^+\}}{Y_{H^+}} - \frac{K_\omega}{\{H^+\}Y_{OH^-}} - 2[A] + [Z] \right\}$$

The correct form of Eq. 14 is:

$$\delta = K_3\epsilon + K_3K_4\xi$$

A plot of δ/ξ *versus* ϵ/ξ will be linear with a slope of K_3 and δ/ξ will equal K_3K_4 at $\epsilon/\xi = 0$. Also, the value of ϵ/ξ at $\delta/\xi = 0$ will equal $-K_4$.

Equation 14 (as corrected here) may be solved using simultaneous equations by utilizing titrimetric and spectrophotometric data obtained at each of two pH values. By labeling the two sets of data as 1 and 2, K_3 and K_4 can be calculated according to:

$$K_3 = \frac{\dfrac{\delta_1}{\xi_1} - \dfrac{\delta_2}{\xi_2}}{\dfrac{\epsilon_1}{\xi_1} - \dfrac{\epsilon_2}{\xi_2}}$$

$$K_4 = \frac{\delta_1 - K_3\epsilon_1}{K_3\xi_1}$$

which are the corrected forms of Eqs. 15 and 16, respectively.

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Nitrofurantoin Solubility in Aqueous Pyridoxine Hydrochloride Solutions

Keyphrases □ Nitrofurantoin—aqueous solubility, effect of pyridoxine hydrochloride ■ Solubility—nitrofurantoin in aqueous solutions, effect of pyridoxine hydrochloride □ Pyridoxine hydrochloride—effect on aqueous solubility of nitrofurantoin ■ Antibacterials, urinary—nitrofurantoin, aqueous solubility, effect of pyridoxine hydrochloride □ Vitamins—pyridoxine hydrochloride, effect on aqueous solubility of nitrofurantoin

To the Editor:

Excess nitrofurantoin (approximately 50 mg) was added to 40 ml of an appropriate test solution (0–20.0% pyridoxine hydrochloride in aqueous pH 3 or 5 buffer[1]) in a 45-ml screw-capped bottle. The tightly closed container was wrapped in aluminum foil to keep out light, placed in a constant-temperature water bath at 37 ± 0.1°, and rotated[2] for at least 20 hr. Experiments indicated that equilibrium was established within 10–16 hr. The test so-

[1] Citric acid–dibasic sodium phosphate buffer; ionic strength of 0.7.

[2] Menhold rotating apparatus, Lester, Pa.

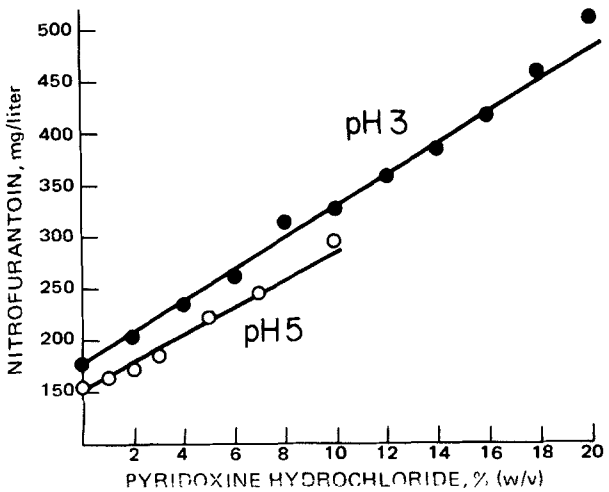

Figure 1—*Nitrofurantoin solubility in aqueous pyridoxine hydrochloride solutions at pH 3 and 5 at 37°.*

lutions were then filtered[3] (0.45-μm pore size), and the filtrate was diluted with deionized distilled water to a proper concentration (40–100 mg/liter) for spectrophotometric assay using the method of Conklin and Hollifield (1). At least three experimental runs were made for each test medium.

Figure 1 shows the effect of pyridoxine hydrochloride on nitrofurantoin solubility at two pH values. The addition of pyridoxine hydrochloride significantly increased nitrofurantoin solubility, and this increase was linearly dependent on the pyridoxine concentration. The higher initial solubility of nitrofurantoin in pH 3 solution than in pH 5 solution (no pyridoxine) agrees with earlier studies (2), and this trend of higher solubility was maintained for the experimental concentration range of pyridoxine hydrochloride.

Mattheus and Heise (3) reported that the nitrofurantoin concentration in urine during simultaneous administration in humans of pyridoxine (up to 100 mg) was increased on an average of 62%. They suggested that pyridoxine might increase nitrofurantoin absorption through the gut and also proposed possible effects on kidney filtration, plasma protein binding, and metabolic processes. Our data indicate that the relatively small amount of pyridoxine hydrochloride (100 mg) might increase slightly nitrofurantoin solubility in the gut if the two drugs are given simultaneously; however, this increased solubility could not account for the higher nitrofurantoin concentrations reported in the urine.

Any interaction between pyridoxine and nitrofurantoin molecules in solution could not be detected by spectral analysis including difference spectroscopy. Surface tension measurements indicated that pyridoxine hydrochloride had negligible surface activity.

Further investigations are being conducted in these laboratories to determine the effect of pyridoxine hydrochloride and pyridoxine derivatives on the solubility of other drugs and to elucidate the mechanism(s) of action of this solubilization phenomenon.

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[3] Millipore.

Cannabis sativa L. (Marijuana) IX: Lens Aldose Reductase Inhibitory Activity of Marijuana Flavone C-Glycosides

Keyphrases □ *Cannabis sativa*—three flavone C-glycosides isolated, effect on rat lens aldose reductase evaluated □ Flavone C-glycosides, various—isolated from *Cannabis sativa*, effect on rat lens aldose reductase □ Marijuana flavonoids—various flavone C-glycosides, effect on rat lens aldose reductase □ Aldose reductase, rat lens—effect of three flavone C-glycosides isolated from *Cannabis sativa*

To the Editor:

Pursuant to ongoing studies (1) dealing with the isolation and characterization of biologically active substances from *Cannabis sativa* L. (marijuana), we recently isolated and elucidated the structures of one known and two new flavone C-glycoside compounds from the aerial parts of a Mexican strain of marijuana[1]. The known compound was orientin (I) and the new compounds, named flavocannabiside (II) and flavosativaside (III), corresponded to orientin-2″-*O*-β-D-glucopyranoside and vitexin-2″-*O*-β-D-glucopyranoside, respectively[2].

A recent report (2) indicated that certain flavonoids were potent inhibitors of lens aldose reductase, an enzyme that has been implicated in the pathogenesis of cataracts in humans suffering from diabetes and galactosemia. In that report, eight flavonoids representing a limited number of flavonoid types were studied: one flavanone (hesperitin), two flavones (quercetin and morin), four flavonol glycosides [quercitrin (IV), myricitrin, rutin, and robinin], and one isoflavone (2-carbethoxy-5,7-dihdroxy-4′-methoxyisoflavone). Quercitrin, quercetin, and myricitrin were found to be more potent than two of the previously known aldose reductase inhibitors, tetramethyleneglutaric acid and 1,2-dioxo-1*H*-benz[*de*]isoquinoline-2(3*H*)-acetic acid. However, since no flavone C-glycosides were included in that study, it was considered worthwhile to evaluate the

[1] The plant material used was the air-dried flowering tops of female plants grown for 14 weeks and harvested at the University of Mississippi during the 1971 season. This material was identified as *Cannabis sativa* L. (Cannabaceae) by Dr. Maynard W. Quimby, Department of Pharmacognosy, University of Mississippi. A voucher specimen representing material (Batch 10-CMF-71-CT-72) collected for this investigation is available for inspection at the Herbarium, Department of Pharmacognosy, University of Mississippi.

[2] To be published.