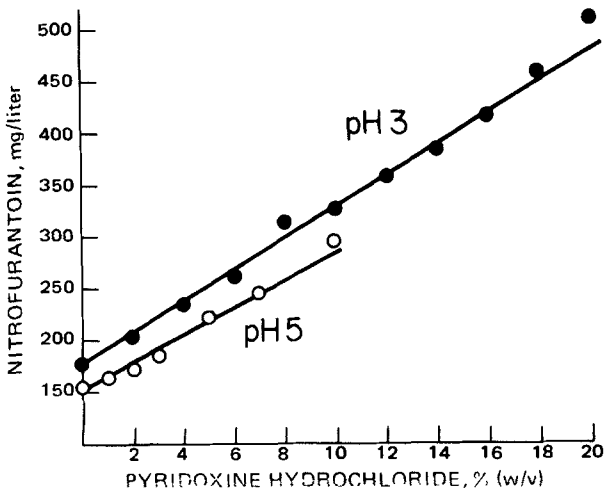

Figure 1—*Nitrofurantoin solubility in aqueous pyridoxine hydrochloride solutions at pH 3 and 5 at 37°.*

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.

Table I—*In Vitro* Inhibition of Rat Lens Aldose Reductase by Various Substances

Inhibitor	Inhibition[a], %			
	10^{-4} *M*	10^{-5} *M*	10^{-6} *M*	10^{-7} *M*
Total crude flavonoid fraction	74	37	0	0
Flavocannabiside	40	10	0	0
Flavosativaside	35	0	0	0
Orientin	90	82	45	0
Quercitrin	100	95	88	55

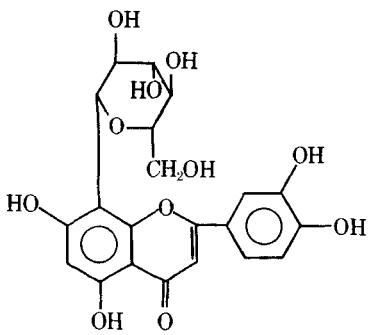
[a] Percentage of inhibition of the aldose reductase activity when compared with controls containing no inhibitors.

three isolated marijuana flavone C-glycosides as potential lens aldose reductase inhibitors.

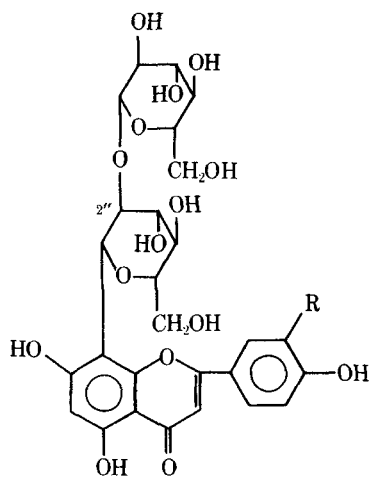
In the present study, I–III as well as the total crude flavonoid fraction from which they were isolated were each tested for inhibitory activity against a partially purified rat lens aldose reductase enzyme according to previously reported methods (3). Each substance was tested four to six times; the results shown in Table I represent mean values. The standard deviation of the results was less than 5%.

The C-diglycosylflavones II and III were relatively weak inhibitors. The C-monoglycosylflavone I proved to be 45% inhibitory at 10^{-6} *M* and compared favorably with the flavonol glycoside IV, which caused a 55% inhibition at 10^{-7} *M*.

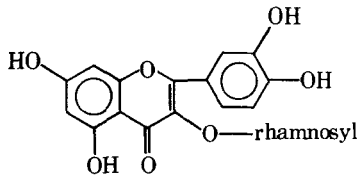
Work is underway to determine the inhibitory effect of I on aldose reductase in a rat lens organ culture assay (4),



I



II: R = OH
III: R = H



IV

and studies using additionally isolated marijuana flavonoids are anticipated[3].

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[x] To whom inquiries should be directed.

[3] *Added in proof:* The following recent reports describe further work dealing with diabetic cataracts and flavonoids: S. D. Varma and J. H. Kinoshita, *Biochem. Pharmacol.*, **25**, 2505 (1976); S. D. Varma, A. Mizuno, and J. H. Kinoshita, *Science*, **195**, 205 (1977).

Use of *In Vitro* Dissolution Data to Predict Plasma Drug Profiles

Keyphrases □ Plasma time profiles—predicted from *in vitro* dissolution data, validity evaluated □ Dissolution rates, *in vitro*—used to predict plasma time profiles, validity evaluated

To the Editor:

Recently, Vaughan and Leach (1) discussed a simple method for predicting plasma time profiles from *in vitro* dissolution data. Basically, their method is to relate the