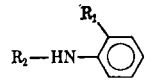
Table I—Optical Anisotropy Factors of *N*-Phenylanthranilates and Their Related Compounds Bound to β-Cyclodextrin



Compound		UV Maximum		CD Maximum		
R_1	R_2	Wavelength, nm	ε, × 10^{-4}	Wavelength, nm	$\Delta\epsilon^a$	g^b, × 10^4
COOH	H	240	0.74			
		310	0.30		(Not observed)	
H	C_6H_5	283	1.40	273	1.21	1.03
COOH	C_6H_5	291	1.26	285	2.36	1.90
		332	0.53	332	0.61	1.15
$COOCH_3$	C_6H_5	287	1.40	293	2.06	1.62
		343	0.64	335	0.78	1.28
COOH	2-COOH—C_6H_4	—	—	233	1.00	0.81
		—	—	242	−0.58	−0.73
		289	1.17	292	−1.45	−1.27
		338	0.73	345	−0.23	−0.32
COOH	3-CF_3—C_6H_4 (Flufenamic acid)	292	1.46	287	1.30	0.93
		320	0.86	328	1.09	1.36
COOH	2,3-Xylyl (Mefenamic acid)	283	0.70	280	−0.33	−0.29
				315	0.61	1.13
		336	0.46	335	0.73	1.16
COOH	2,6-Dichloro-*m*-tolyl (Meclofenamic acid)	285	0.48	275	0.43	0.91
		320	0.43	320	0.03	0.07

[a] Molar ellipticity (deg cm^2 $dmole^{-1}$). [b] Optical anisotropy factor (see text).

clodextrin and fanamates. Stability constants ($K_{1:1}$) determined by the CD method for β-cyclodextrin with flufenamic, mefenamic, and meclofenamic acids were 1300, 630, and 450 M^{-1}, respectively. In contrast to β-cyclodextrin, α-cyclodextrin (cyclohexaamylose) showed no appreciable complex formation. This suggests that the cavity size of α-cyclodextrin is not large enough to include the bulky guest molecules of drugs.

In the series of flufenamic, mefenamic, and meclofenamic acids, the magnitude of the *g* value at the CD bands of the longest wavelength (320–340 nm) agreed with the order of stability constants of the complexes. The stereospecific nature of the *ortho*-substituents in two aromatic rings apparently is responsible for the magnitude and/or sign of the induced CD bands. Meclofenamic acid, in particular, was much less influenced by the asymmetric environment than were other compounds, which could be due to the bulky chlorine and methyl substituents. An NMR study (7, 14) may provide further information on the mode of inclusion of these drug molecules within the β-cyclodextrin cavity. Carbon 13 NMR experiments on these problems are now being conducted in our laboratory.

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Received January 29, 1974.
Accepted for publication April 10, 1974.

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Preliminary Observations on Cardiac Activities of *Cannabis sativa* L. Root Extracts

Keyphrases □ *Cannabis sativa* L. root extracts—cardiac activity of hexane, chloroform, ethanol, water, and hydrochloric acid extracts □ Marijuana—cardiac activities of *Cannabis sativa* L. root extracts □ Cardiac activity—hexane, chloroform, ethanol, water, and hydrochloric acid extracts of *Cannabis sativa* L. roots

To the Editor:

Rodger (1) reported that whiskey extracts (about 45% alcohol) of *Cannabis* roots have been used by American Indians and others to treat "dropsy." Additionally, the extracts were reported to have a digi-

talis-like effect on the heart. Subsequently, Ten Ham *et al.* (2) reported that the cardiac action of an ethanol–water extract (50% alcohol) of *Cannabis* roots was due solely to the potassium content of an infused extract (140 mmoles). This action was exemplified by the following changes in the guinea pig ECG: bradycardia, T wave and QRS complex inversion, and recovery of the heart when infusion was discontinued. We wish to report our preliminary findings indicating the presence of substances other than potassium in *Cannabis* roots of Mexican origin[1] that display cardiac activities.

Dried, ground root material was percolated consecutively with hexane, chloroform, 95% ethanol, water, and 5% hydrochloric acid. The potassium content of the first four extracts prepared for infusion[2] was determined by atomic absorption spectroscopy and found to be 0.109, 0.181, 16.9, and 36.0 mmoles, respectively[3]. Ten Ham *et al.* (2) reported the potassium content of their infusion-prepared ethanol–water extract by flame photometery to be 140 mmoles/liter. Cardiac activity, although different from that observed by Ten Ham *et al.* (2), was found in the hexane, chloroform, and ethanol extracts; however, no activity of a detrimental nature was observed in the aqueous or 5% hydrochloric acid extracts.

Cardiac screening was done using anesthetized male guinea pigs. The right jugular veins were cannulated with polyethylene tubing to a distance of approximately 1 cm from the heart. Infusion of the dried extracts (emulsified in 2% sorbitan ester[4], 3% polysorbate 60, and 4% ethanol in water)[2] was then carried out at the rate of 0.2 ml/min and was continued until the heart stopped or for 90 min. The ECG was monitored through bipolar leads attached on either side of the thorax at the base of the front limbs[5].

For each extract, the ECG of a vehicle-only control animal was recorded which showed slight bradycardia, an increase in the PR interval, and an increase in the QRS complex amplitude. The hexane extract was fractionated into polar and nonpolar portions[6]. The cardiac activity was mainly associated with the less polar fraction which contained insignificant traces of potassium. Infusion of the hexane extract had a rapid and pronounced effect on the heart. Bradycardia, prolonged PR intervals, and A–V conduction blockade developed quickly. After 18 min, atrial activity had disappeared, with death occurring following 23 min of continuous infusion of the extract. The chloroform extract[2] produced effects similar to those caused by infusion of a 140-mmole solution of potassium chloride, as described previously (2); however, there was no inversion of the T wave. The A–V conduction was severely impaired and the heart irreversibly stopped. The ethanol extract[2], in addition to causing irreversible heart stoppage, produced a more pronounced arrhythmia than any other extract; during later stages of infusion, a prominent conduction blockade was observed within 10 min after the appearance of multiple P waves. The heart then entered a short period of ventricular fibrillation and collapsed. Once definite arrhythmias were observed, termination of infusion did not stop the progressive deterioration of the heart.

The aqueous and 5% hydrochloric acid extract infusions[2] were apparently not toxic and, indeed, when compared with the control animals receiving the suspension vehicle alone, fewer changes in the ECG were observed. Bradycardia was not seen, but three of four subjects showed an increase in heart rate of 25–40%.

These preliminary data strongly suggest that *Cannabis* roots of Mexican origin do contain organic component(s) that produce cardiac activities quite different than those classically observed with potassium ions. It is quite possible that Mexican *Cannabis* roots contain chemicals not found in other "variants." This is the case for the cannabinoids (3, 4). Thus, this could explain the difference in findings by Ten Ham *et al.* (2) and our group. Further fractionations of these extracts are underway in an effort to isolate the principle(s) responsible for the observed cardiac activities.

[1] Mexican roots from plants grown on the University of Mississippi campus in 1972. Voucher specimens are located in the *Cannabis sativa* L. Herbarium, School of Pharmacy, University of Mississippi.

[2] Concentration of extracts was 18.4 mg/ml.

[3] Jarrell Ash dual-atom atomic absorption spectrograph.

[4] Arlacel.

[5] Beckman RN dynograph.

[6] Concentration of fractions prepared for infusion was 9.2 mg/ml each.

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Received February 22, 1974.
Accepted for publication April 9, 1974.
Supported by Contract HSM-42-70-109 from the National Institute on Drug Abuse and by the Research Institute of Pharmaceutical Sciences.

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Lidocaine: A Case of Intraamide Hydrogen Bonding

Keyphrases □ Lidocaine—spectroscopic data supporting intraamide hydrogen bonding, *trans*-planar configuration □ Hydrogen bonding—spectroscopic data supporting lidocaine intraamide hydrogen bonding, *trans*-planar configuration

To the Editor:

In 1969, Neville and Cook (1) described some interesting and unusual spectroscopic data on lidocaine (2-diethylamino-2′,6′-acetoxylidide). These data were interpreted in terms of a *cis*-amide configu-