of caproic, caprylic and capric methyl esters was chromatographed with a DEGS column at 175°, both with a flow rate of 70 ml/min. Each of the peak compounds from six runs of chromatograph was accumulatively collected in one trap. The recoveries for the five compounds were 95, 100, 94, 90 and 100 % respectively. Each of the peak compounds thus collected was rechromatographed. Their chromatograms indicated that they were as pure as when they were collected with individual traps directly connected to the sample exhaust tube of the gas chromatograph.

The collector does not create measurable back pressure to the chromatographic column even when the flow rate is as high as 150 ml/min. When the flow rate is 60 ml/min, the time lag for the carrier gas to reach the trap farthest from the detector is $^1/_3$ sec. For compounds of a higher boiling point which have a tendency to form "fog", the temperature of the coolant in bath (J) for the cold traps should not be lower than necessary for condensing the compound.

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The effect of ultraviolet irradiation on chlorpromazine*

I. Aerobic condition

Introduction

The picture of the metabolic end-products of chlorpromazine in psychotic patients has become clearer in recent years following a number of reports on the isolation and identification of the metabolites. Glucuronidation was found to be the major mechanism of the metabolism of this drug. A number of studies[1–4] concerning the excretion of non-polar metabolites, namely, unchanged chlorpromazine (CP) and its sulfoxides (CPO), have been reported. Chlorpromazine sulfoxide was found to be 1–18 % and unchanged drug was reported to be less than 1 % of the administered dose[2]. The ratio of the unchanged drug to its sulfoxide was approximately 1:16. The CPO was identified to be a mixture of chlorpromazine sulfoxide and two demethylated products, namely Nor_1-CPO and Nor_2-CPO in which Nor_2-CPO predominates. The same findings have been reported by FISHMAN AND GOLDENBERG[5]. In the report[6] on a quantitative analysis of four groups of urinary metabolites in psychotic patients, chlorpromazine glucuronides (CPGL) were found to be the major metabolites. An average of 44.6 % of CPGL was found in urine followed by CPO (7.7 %), $CPOH_1$**

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** $CPOH_1$ = Hydroxyl chlorpromazine (urinary metabolite, R_F 0.57, reacted blue with 50 % H_2SO_4, purple with 5 % $FeCl_3$, I.R.: 2.70–2.85 μ)[6].

(4.8 %) and CP (1 %). The chlorpromazine glucuronides were further fractionated into 9 fractions and their physical properties were described[7].

In the quantitative analysis of urinary chlorpromazine metabolites it was observed that when samples were exposed to room light over a period of 72 h, a new compound (R_F 0.89) appeared on the chromatogram. It is speculated that a small amount of ultraviolet (U.V.) emission produced by the fluorescent lamps resulted in the oxidation of some of the metabolites.

A nitrite and dinitrophenylhydrazine derivative of a substance from the U.V.-irradiated CP solution were reported[8,9]. However, it appears that the compounds produced by the U.V.-oxidation are mixtures and not a single compound. Photosensitization[10,11] and photo-allergy were reported after the administration of chlorpromazine. It is speculated that the photo-oxidation products might be responsible for these conditions. Therefore, it will be of interest to pursue the photo-oxidation study of chlorpromazine.

Experimental

An aqueous solution of chlorpromazine·HCl was placed in a porcelain evaporating dish and irradiated with U.V.-light (Mineralight R-51, 70 W) for a period of 24, 48 and 72 h. After the irradiation, changes in the color as well as pH (from 5.9 to 1.72) of the solution were noted. The solution was applied in a 1 cm band on 30 × 35 cm Whatman 3MM paper. The chromatogram was developed in ascending manner in a neutral solvent system, *n*-butanol–ethanol–water (5:2:2), overnight. The dried chromatogram was sprayed with 50 % sulfuric acid. Twelve compounds with R_F values ranging from 0.10 to 0.92, and color reactions ranging from pink–blue–purple were observed (Table I). Several compounds reacted blue to purple with 10% ferric chloride solution. Differences in the intensity of fluorescence among the chromatograms of these compounds were observed.

The developed unsprayed chromatograms were cut and separated into 12 fractions using a strip of acid-sprayed chromatogram as a guide. The accumulated paper strips of each fraction were extracted with 50 % ethanol. The ethanol extract of each fraction was evaporated in a Buchler flash-evaporator below 50°. The residue of each fraction was rechromatographed twice as described above. Picrates were prepared from the purified fraction by adding an equal quantity of saturated picric acid in ethanol into the sample solution (in ethanol). The precipitate was collected on a filter paper and recrystallized from methanol. The melting point, R_F value, color reactions with 50 % sulfuric acid and 10 % ferric chloride reagent, ultraviolet absorption peaks (in a Bausch & Lomb "Spectronic 505") and infrared spectra (in a Perkin-Elmer Model 237) of each fraction were obtained.

Results and discussion

Table I shows the physical properties of the 12 compounds isolated from the mixture of ultraviolet irradiated solution of chlorpromazine·HCl. The unchanged chlorpromazine was recovered from the top of chromatograms. The fraction 1 was identified to be chlorpromazine-N-oxide (Table I) from its color reactions, mixed melting point of the picrate with an authentic specimen (no depression, 174–177°) and R_F on cochromatograms (0.92). The electrophoretic pattern of this fraction was found to be the same with that of reference chlorpromazine-N-oxide. The fraction 2 showed a purple

TABLE I

ULTRAVIOLET IRRADIATED PRODUCTS OF CHLORPROMAZINE·HCl

Fractions	*Reference material*[a]	*Color on paper*	*Color under U.V.-lamp*	*Color reactions*		*R_F (pure fraction)*	*M. p. (°C)*[b] *(picrate)*	*U.V.-absorption peak (mμ)*
				50% H_2SO_4	*10% $FeCl_3$*			
1		No color	Violet	Pink	Pink	0.92	173–175	258, 308
	CPNO	No color	Violet	Pink	Pink	0.92	175–177	257, 308
2		No color	Yellow	Purple	Brownish-purple	0.84	120–122	266, 340
3		No color	Reddish-purple	Red	NR[c]	0.79	207–210	240, 278, 300, 342
	CPO	No color	Reddish-purple	Red	NR	0.80	208–210	240, 278, 300, 343
4		No color	Grey	Orange	NR	0.76		262, 283, 310, 362
5		Yellow	Light blue	Purple	Brownish-purple	0.71	76–80 (base)	262, 324
6		Grey	Sky blue	Lavender[d]	Bluish-green	0.63	127–132	260, 321
7		Green	Blue	Blue	Yellowish-brown	0.56	153–158	226, 260
8		Red	Pinkish-purple	Bluish-green	NR	0.49	78–80	240, 272, 333
9		Yellow	Light blue	Bluish-purple	Purple	0.42	92–93	260, 310
10		Tan	Yellowish-brown	Purple	Purple	0.33	140–143	258, 310
11		No color	Purple	Purple	NR	0.30	120–122	259
12		Light brown	Orange	Purple	NR	0.08	152–156	258

[a] CPNO = chlorpromazine-N-oxide; CPO = chlorpromazine sulfoxide.

[b] Melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected.

[c] NR = no color reaction.

[d] Color changed to blue in the presence of excess 50% H_2SO_4.

color reaction with ferric chloride reagent, suggesting a ring oxidation in this compound, I.R.: 2.8 μ (hydroxyl). A urinary chlorpromazine metabolite ($CPOH_2$)* from patients was found to have similar physical properties with this compound[6], except ultraviolet absorption peaks. The fraction 3 was identified to be chlorpromazine sulfoxide from its color reaction, R_F value, melting point of the picrate, and ultraviolet and infrared absorption spectra. Mixed melting point of the picrate with an authentic specimen did not show depression (208–212°). The electrophoretic pattern of the fraction 3 was identical with that of reference chlorpromazine sulfoxide. The nature of the other fractions is currently under investigation. About 20–25% of the starting material was recovered from the 24 h irradiated solution. As the duration of irradiation time was increased to 48–72 h, the intensity of chromatograms of the fractions 6, 7, 8, 9 and 10 increased while that of the fractions 3, 4 and 5 decreased. At the end of 72 h, only a trace of the starting material was found on chromatograms. Ninhydrin test and nitroprusside test were negative in all fractions, indicating that no demethylated derivative was formed under these conditions. This experiment was also carried out under anaerobic conditions. The results of this experiment will be reported later.

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* $CPOH_2$ = Hydroxyl chlorpromazine (urinary metabolite, R_F 0.83, reacted purple with 50% H_2SO_4, brownish-purple with 10% $FeCl_3$, I.R.: 2.8 μ).