SYSTEMATIC IDENTIFICATION OF PSYCHOTROPIC DRUGS BY THIN-LAYER CHROMATOGRAPHY. PART I

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During the course of studies on patients who were given various psychotropic drugs, the thin-layer chromatographic technique was investigated as a possible means of resolving mixtures of drugs and their metabolic products occuring in extracts from biological materials[1].

The heterogeneity of the substances under investigation prompted the need to evaluate various categories of chromatographic systems and detecting reagents as to their possible application for subsequent identification of each compound.

It was the object of the present study to develop a quick and reliable method for the detection of the psychotropic drugs, based on their chromatographic and chromogenic behavior.

The group investigated includes commonly used psychotropic agents with different chemical structure and pharmacological activity: tranquilizers, phenothiazine and nonphenothiazine derivatives, and stimulants of the central nervous system.

EXPERIMENTAL

Equipment

Standard Desaga thin-layer chromatographic equipment and Merck Silica Gel G.

Reagents

Analytical grade chemicals were used to prepare all reagents.

Standard solutions

Standard solutions (1 mg/1 ml) of the drugs were prepared by dissolving the pure substances, obtained from the various manufacturers, in 95 % ethanol.

Detecting reagents

(*A*) *Folin–Ciocalteau reagent* (Fisher Scientific Co., Cat. No. SO-P-24).

Prior to use it was diluted with an equal part of distilled water.

(*B*) *FPN reagent*[2]

5 ml of aqueous 5 % ferric chloride solution are mixed with 45 ml of 70 % perchloric acid–water (1:5) and 50 ml of concentrated nitric acid–water (1:1).

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(*C*) *Mandelin reagent*[3]

1 g of ammonium vanadate is dissolved in 100 ml of concentrated sulfuric acid.

(*D*) *Cinnamaldehyde reagent*

5 ml of cinnamic aldehyde is dissolved in 95 ml of ethanol to which is added 5 ml of concentrated hydrochloric acid.

(*E*) *E-P reagent*[4]

0.25 g of *p*-dimethylaminobenzaldehyde is dissolved in a mixture of 50 g glacial acetic acid, 5 g of 85 % orthophosphoric acid and 20 ml of water*.

(*F*) *Furfural reagent*

Solution A: 1 ml of furfural is dissolved in 99 ml of acetone.

Solution B: 4 ml of concentrated sulfuric acid is added to 96 ml of acetone.

Procedure: spray solution A, then solution B.

Chromatographic systems

System I: methanol–12 *N* ammonium hydroxide (100:1.5)

System II: cyclohexane–diethylamine–benzene (75:20:15)

System III: acetone

System IV: chloroform–methanol (90:10)

System V: benzene–ethanol–12 *N* ammonium hydroxide (95:15:5)

Systems I and V were used with Silica Gel G plates prepared with distilled water. Systems II, III and IV were used with Silica Gel G plates prepared with 0.1 *N* sodium hydroxide.

Procedure

Five 20 × 20 cm plates were coated with a mixture of 25 g of Silica Gel G and 50 ml of diluent, dried for 15 min at room temperature and then conditioned at 100° for 1 h. They were used within 2 h after activation. The thickness of the absorbent layer, when spread, was 250 μ. A series of parallel strips, 1.5 cm wide was marked out on each plate using a scriber. 2–4 μg of each sample were spotted 3 cm from the base of the plate. The spotted samples were air dried and the plate placed in a developing tank, saturated previously with solvent by lining its inside walls with filter paper and by adding 110 ml of the developing solvent 1 h before development.

After the solvent had risen 12 cm from the points of application, the plate was removed from the tank and allowed to dry at room temperature. Then it was observed in ultraviolet light and treated with suitable color reagents. The colors and the fluorescences obtained at room temperature and after heating the plate at 100° for 10 min were noted. The room temperature during the experiments varied between 23° and 27°.

RESULTS

Tables I to VII show the results obtained during the experiments. The R_F values of the drugs in the five chromatographic systems used are the average of ten independent determinations. Daily R_F variation was ± 0.02 in Systems I and III, and ± 0.035 in Systems II, IV and V.

* The sprayed plate, after heating at 100° for 10 min, is placed in a tank saturated with ammonia vapor.

DISCUSSION

Evaluation of the R_F values

In order to identify each drug according to its chromatographic behavior, the R_F values obtained in System I (Table I) were arranged in ascending order (Table II). For a drug to be evaluated, a group was formed including all those drugs having, in

TABLE I

R_F VALUES (× 100) OF THE DRUGS IN FIVE CHROMATOGRAPHIC SYSTEMS*

	System No.				
	I	*II*	*III*	*IV*	*V*
Acepromazine	50	47	18	45	61
Acetophenazine	60	9	8	36	22
Amitriptyline	55	71	26	46	76
Azacyclonol	11	7	0	0	7
Benactizine	68	57	64	72	77
Buclizine	76	22	84	89	9
Carphenazine	64	12	11	43	28
Chlordiazepoxide	66	7	61	49	11
Chlorpromazine	56	65	30	50	73
Chlorprothixene	61	66	37	60	75
Clopenthixol	62	15	16	51	36
Deanol	22	0	0	0	0
Desipramine	23	42	3	12	34
Diazepam	72	34	76	74	68
Ethopropazine	71	64	74	69	89
Etryptamine	41	12	33	7	18
Fluphenazine	67	18	16	44	30
Hydroxyzine	68	22	33	59	40
Imipramine	49	65	19	38	65
Iproniazid	70	5	45	40	21
Isocarboxazid	73	27	79	83	68
Mepazine	59	62	29	57	71
Meprobamate	71	3	76	42	8
Mesoridazine	37	12	1	13	28
Methotrimeprazine	66	64	62	68	82
Methoxypromazine	48	53	18	45	68
Methylphenidate	62	52	40	50	62
Nialamide	58	0	15	17	7
Nortriptyline	31	50	6	19	51
Oxanamide	72	15	75	74	45
Oxazepam	57	3	55	39	8
Perphenazine	65	18	15	43	29
Phenaglycodol	74	27	81	66	40
Phenelzine	74	44	65	73	50
Pipradol	53	66	70	61	84
Prochlorperazine	54	52	10	52	54
Promazine	46	59	17	38	64
Propiomazine	65	54	47	71	72
Rescinnamine	75	5	81	87	72
Thiopropazate	74	50	63	82	75
Thioridazine	54	62	23	53	73
Tranylcypromine	58	52	66	54	51
Trifluoperazine	57	54	12	52	56
Triflupromazine	60	66	38	54	74
Tybamate	74	15	86	72	34

* For details of solvent systems, see text.

TABLE II

R_F VALUES (× 100) IN ASCENDING ORDER WITH RESPECT TO SYSTEM I*

	System No.				
	I	*II*	*III*	*IV*	*V*
Azacyclonol	11	7	0	0	7
Deanol	22	0	0	0	0
Desipramine	23	42	3	12	34
Nortriptyline	31	50	6	19	51
Mesoridazine	37	12	1	13	28
Etryptamine	41	12	33	7	18
Promazine	46	59	17	38	64
Methoxypromazine	48	53	18	45	68
Imipramine	49	65	19	38	65
Acepromazine	50	47	18	45	61
Pipradol	53	66	70	61	84
Prochlorperazine	54	52	10	52	54
Thioridazine	54	62	23	53	73
Amitriptyline	55	71	26	46	76
Chlorpromazine	56	65	30	50	73
Oxazepam	57	3	55	39	8
Trifluoperazine	57	54	12	52	56
Tranylcypromine	58	52	66	54	51
Nialamide	58	0	15	17	7
Mepazine	59	62	29	57	71
Triflupromazine	60	66	38	54	74
Acetophenazine	60	9	8	36	22
Chlorprothixene	61	66	37	60	75
Methylphenidate	62	52	40	50	62
Clopenthixol	62	15	16	51	36
Carphenazine	64	12	11	43	28
Perphenazine	65	18	15	43	29
Propiomazine	65	54	47	71	72
Methotrimeprazine	66	64	62	68	82
Chlordiazepoxide	66	7	61	49	11
Fluphenazine	67	18	16	44	30
Hydroxyzine	68	22	33	59	40
Benactizine	68	57	64	72	77
Iproniazid	70	5	45	40	21
Meprobamate	71	3	76	42	8
Ethopropazine	71	64	74	69	89
Diazepam	72	34	76	74	68
Oxanamide	72	15	75	74	45
Isocarboxazid	73	27	79	83	68
Thiopropazate	74	50	63	82	75
Tybamate	74	15	86	72	34
Phenelzine	74	44	65	73	50
Phenaglycodol	74	27	81	66	40
Rescinnamine	75	5	81	87	72
Buclizine	76	22	84	89	9

* For details of solvent systems, see text.

System I, R_F values within ± 0.05 of the R_F of the drug under evaluation. Then the components of the group were checked against their corresponding R_F values in System II. Those drugs whose R_F values were over the limits fixed were eliminated. Using this same procedure, the remaining drugs were evaluated in System III and successively in Systems IV and V.

Identification can be achieved in this manner for all the drugs, except two pairs formed by two phenothiazine derivatives and their respective trifluoromethyl analogues: Prochlorperazine–Trifluoperazine and Perphenazine–Fluphenazine. In order to separate and identify the two drugs, a mixture of the phenothiazine derivative and its trifluoromethyl analogue was chromatographed in the five chromatographic systems used. The mixture was resolved into two distinguishable spots in each system, the phenothiazine derivatives having, in each case, lower R_F values than their trifluoromethyl analogues. Identification of the similar pair, Chlorpromazine–Triflupromazine, was achieved in System III.

Chromogenic behavior of the drugs

Colors in daylight and in ultraviolet light obtained with the detecting reagents used are tabulated in Table III.

The different chromogenic comportment of these drugs with respect to the Folin-Ciocalteau reagent leads, to a certain extent, to a differentiation according to their chemical composition. Phenothiazine derivatives are clearly differentiated from nonphenothiazine compounds by the colors they form at room temperature after reaction with the Folin-Ciocalteau reagent. These colors are all in the range of the red, varying from cameo, reddish-pink, brick-red, fuchsia to violet. The only exception is the green-blue color formed by Thioridazine.

It was observed that the different color reactions depend on the absence or presence of a substituent in position 2 in the phenothiazine nucleus, and on the nature of this substituent[5]. Fuchsia colors are produced by 2-chloro substituted phenothiazines, violet by 2-methoxy substituted, cameo by trifluoromethyl derivatives, reddish-pink by compounds containing a keto group in position 2, green-blue by 2-methylmercapto substituted, while phenothiazine derivatives non-substituted in the 2-position form brick-red colors. In the group of phenothiazines studied, compounds with the same substituent in position 2 show a common color reaction independent of the subgroup (propyl dimethylamino, alkyl piperidyl or propyl piperazine) forming the side chain in position 10.

The green-blue color formed by Thioridazine associates this methylmercapto substituted phenothiazine with two dibenz-azepine derivatives, Imipramine and Desipramine, pharmacologically dissimilar, although chemically related to the phenothiazines.

The non-phenothiazine compounds present in this group react with the Folin reagent forming only blue or blue-violet colors at room temperature and after heating. The development of the color depends often on the time and temperature necessary for the reaction to take place. Hydrazine compounds develop color immediately, while thiaxantene and indole derivatives show slower color reactions with development of color after 5 min at room temperature. Blue colored spots are formed by dibenzocycloheptadiene, cyclopropylamine and diphenylmethane derivatives only after heating the plate at 100° for 10 min. Benzodiazepine and glycol derivatives did not form any characteristic color.

On the basis of this different chromogenic comportment of the drugs in respect to the Folin reagent, it was possible to achieve the separation and identification of each compound in one chromatographic system. Table IV shows the chromatographic data for the identification of the drugs in System V. The evaluation of the R_F values

TABLE III

CHROMOGENIC BEHAVIOR OF THE DRUGS

	Fluorescence on untreated plates	*Reagent*	
		A	
		Room temp.	*100°*
Acepromazine	Pink	Reddish pink	Red
Acetophenazine	Pink	Reddish pink	Red
Amitriptyline	—	White	Bluish
Azacyclonol	—	White	Bluish
Benactizine	—	White	White
Buclizine	—	White	White
Carphenazine	Pink	Reddish pink	Pink
Chlordiazepoxide	Violet	White	White
Chlorpromazine	—	Fuchsia	Fuchsia
Chlorprothixene	Violet	Bluish in 5 min	Violet
Clopenthixol	—	Bluish in 5 min	Violet
Deanol	—	White	White
Desipramine	—	Green-blue	Green-blue
Diazepam	—	White	White
Ethopropazine	—	Reddish pink	Violet
Etryptamine	—	Bluish in 5 min	Blue-violet
Fluphenazine	—	Cameo	Cameo
Hydroxyzine	Green-yellow	White	Bluish
Imipramine	—	Green-blue	Green-blue
Iproniazid	—	Bluish	Blue
Isocarboxazid	—	Bluish	Blue
Mepazine	—	Brick-red	Violet
Meprobamate	—	White	White
Mesoridazine	Blue-green	Red-violet	Deep violet
Methotrimeprazine	—	Deep violet	Deep blue
Methoxypromazine	—	Deep violet	Deep blue
Methylphenidate	—	White	White
Nialamide	—	Bluish	Blue
Nortriptyline	—	White	Bluish
Oxanamide	—	White	Bluish
Oxazepam	—	White	White
Perphenazine	—	Fuchsia	Fuchsia
Phenaglycodol	—	White	Bluish
Phenelzine	—	Bluish	Blue
Pipradol	—	White	Bluish
Prochlorperazine	—	Fuchsia	Fuchsia
Promazine	—	Brick-red	Violet
Propiomazine	Yellow	Reddish pink	Deep violet
Rescinnamine	Blue	Bluish in 5 min	Olive green
Thiopropazate	—	Fuchsia	Fuchsia
Thioridazine	—	Green-blue	Green
Tranylcypromine	—	White	Bluish
Trifluoperazine	—	Cameo	Cameo
Triflupromazine	Violet	Cameo	Rose-grey
Tybamate	—	White	White

[a] Pink spotted blue.
[b] The color in parentheses denotes the inside color of the spot.
[c] Olive green on cooling.
[d] Br = brilliant.
[e] Chr = chrome.

B			*C*			
Room temp.	*100°*	*Fluorescence*	*Room temp.*	*Fluorescence*	*100°*	*Fluorescence*
Reddish pink	—	—	Flesh	—	Flesh	—
Reddish pink	—	—	Flesh	—	Flesh	—
—	Yellow	—	Pink blue[a]	Violet (yellow)[b]	Violet[c]	Rust
—	Yellow	—	Lilac	Violet (green)	Flesh	Green
—	Yellow	Orange	Pink	—	Red-violet	Red
—	Yellow	Orange	—	—	Orange	Gold
Reddish pink	—	—	Flesh	—	Flesh	—
—	Yellow	—	—	Green-violet	Yellow	Green
Reddish pink	—	—	Fuchsia	—	Violet	—
—	—	—	Reddish pink	Br. orange[d]	Orange	Green (orange)
Reddish pink	—	Pink	Reddish pink	Br. orange[d]	Orange	Green (orange)
—	Lemon chr.[e]	—	—	—	Lilac	Violet
Green-blue	Deep blue[c]	—	Deep blue	—	Deep blue[c]	Green
—	—	—	—	Green-violet	Lilac	Green
Reddish pink	—	—	Reddish pink	—	Reddish pink	—
—	Lemon chr.	—	Orange	Yellow	Brown	Violet
Pink	—	—	Flesh	—	Flesh	—
—	Yellow	Br. gold	—	—	Flesh	Violet
Green-blue	Deep blue[c]	—	Deep blue	—	Deep blue[c]	Green
—	Lemon chr.	Violet	Lilac	—	Lilac	Violet
—	—	Blue	—	—	Lilac	Violet
Orange	—	—	Brown	—	Brick-red	—
—	Yellow	—	Brown	—	Gold	—
Reddish pink	Violet	—	Brick-red	—	Deep blue	—
Violet	—	—	Violet	—	Violet	—
Violet	—	—	Violet	—	Violet	—
—	—	—	—	—	Lilac	Violet
—	—	—	Lilac	Violet	Bluish	Green
—	Yellow	—	Pink-blue[a]	Violet (yellow)	Violet[c]	Rust
—	—	—	Lilac	—	Lilac	Violet
—	Yellow	Br. green	—	Green-violet	Deep yellow	Green
Reddish pink	—	—	Fuchsia	—	Fuchsia	—
—	—	Br. green	Bluish	—	Violet	Violet
—	—	—	Pink	—	Flesh	Pink
—	Orange	—	—	—	Violet	Pink
Reddish pink	—	—	Fuchsia	—	Fuchsia	—
Orange	—	—	Brown	—	Brick-red	—
Reddish pink	—	—	Flesh	—	Flesh	—
—	Yellow	—	Reddish pink	—	Brown	Violet
Reddish pink	—	—	Fuchsia	—	Fuchsia	—
Green-blue	Violet	—	Green-blue	—	Deep blue	—
—	—	—	Lilac	—	Lilac	Violet
Pink	—	—	Flesh	—	Flesh	—
Pink	—	—	Flesh	—	Flesh	—
—	—	—	—	—	Lilac	Pink

(*continued on p. 412*)

TABLE III (*continued*)

CHROMOGENIC BEHAVIOR OF THE DRUGS

	Reagent		
	D		
	Room temp.	*100°*	*Fluorescence*
Acepromazine	Cameo	Violet	—
Acetophenazine	Cameo	—	Violet
Amitriptyline	—	—	—
Azacyclonol	—	—	Violet
Benactizine	—	—	—
Buclizine	—	—	—
Carphenazine	Cameo	—	Violet
Chlordiazepoxide	Green-yellow	—	Blue
Chlorpromazine	Reddish-pink	—	—
Chlorprothixene	—	—	Violet
Clopenthixol	—	—	Violet
Deanol	Green-yellow	—	—
Desipramine	Green-yellow	Green	Green
Diazepam	—	—	Blue-violet
Ethopropazine	Pink	—	—
Etryptamine	Green-yellow	Lemon chrome	Violet
Fluphenazine	Cameo	—	—
Hydroxyzine	—	—	—
Imipramine	Green-yellow	Green	Green
Iproniazid	Yellow	—	—
Isocarboxazid	Yellow	—	—
Mepazine	Pink	—	—
Meprobamate	—	—	Pink
Mesoridazine	Reddish-pink	—	—
Methotrimeprazine	Violet	—	—
Methoxypromazine	Violet	—	—
Methylphenidate	—	—	—
Nialamide	Yellow	—	—
Nortriptyline	—	—	Pink
Oxanamide	—	—	Pink
Oxazepam	—	—	Blue
Perphenazine	Reddish-pink	—	—
Phenaglycodol	—	—	Pink
Phenelzine	Yellow	—	—
Pipradol	—	—	—
Prochlorperazine	Reddish-pink	—	—
Promazine	Pink	—	—
Propiomazine	Cameo	Lilac	—
Rescinnamine	Yellow	Pink	Green
Thiopropazate	Reddish-pink	—	—
Thioridazine	Green	—	—
Tranylcypromine	—	—	Gold
Trifluoperazine	Cameo	—	—
Triflupromazine	Cameo	—	—
Tybamate	—	—	—

E				*F*		
Room temp.	*100°*	*Fluorescence*	*NH_3*	*Room temp.*	*100°*	*Fluorescence*
Pink	—	—	—	Cameo	—	—
Pink	—	—	—	Cameo	—	—
—	—	—	—	—	—	—
—	—	—	—	—	—	—
—	—	—	—	—	—	—
—	—	—	—	—	—	—
Pink	—	—	—	Cameo	—	—
Yellow	—	Violet	Br. orange	—	—	—
Pink	—	—	—	Reddish-pink	—	—
—	Br. orange	Br. orange	—	—	Cameo	Br. orange
—	Br. orange	Br. orange	—	—	Cameo	Br. orange
Yellow	—	—	Lemon chromo	—	—	—
Olive green	Olive green	—	Gray	Bluish	Bluish	—
—	—	Blue	—	—	—	Br. green
Pink	—	—	—	Cameo	—	—
—	Violet	Blue	Olive green	Orange	Brown	—
Pink	—	—	—	Cameo	—	—
—	—	—	—	—	—	—
Olive green	Olive green	—	Gray	Bluish	Bluish	—
Yellow	Yellow	—	Deep yellow	—	—	—
Yellow	Lemon chromo	—	Deep yellow	—	—	—
Pink	—	—	—	Pink	—	—
—	Lemon chromo	—	—	Violet	Violet	Red
Pink	—	—	—	Reddish-pink	Green-blue	—
Violet	—	—	Olive green	Violet	—	—
Violet	—	—	Olive green	Violet	—	—
—	—	—	—	—	—	—
Yellow	—	—	Lemon chromo	—	—	—
—	—	—	—	—	—	—
—	—	—	—	—	Green	—
Yellow	Yellow	Blue	Pink	—	—	Green
Pink	—	—	—	Reddish-pink	—	—
—	—	Violet	—	—	Violet	—
Yellow	—	—	Lemon chromo	—	Brown	—
—	—	—	—	—	—	—
Reddish-pink	—	—	—	Reddish-pink	—	—
Pink	—	—	—	Pink	—	—
Pink	—	—	—	Pink	—	—
Yellow	Brown	Green-blue	Olive green	Yellow	Blue	Green
Reddish-pink	—	—	—	Reddish-pink	—	—
Green-blue	Blue	—	—	Green	—	—
—	Yellow	—	Lemon chromo	—	—	Violet
Pink	—	—	—	Cameo	—	—
Pink	—	—	—	Cameo	—	—
—	Yellow	—	—	—	Violet	Violet

TABLE IV

CHROMATOGRAPHIC DATA FOR THE IDENTIFICATION OF THE DRUGS IN SYSTEM V

	R_F values System V	Fluorescence on untreated plates	Reagent								
			A		C				E	F	
			Room temp.	100°	Room temp.	Fluo-rescence	100°	Fluo-rescence	NH_3	100°	Fluo-rescence
Deanol	0		White	White							
Nialamide	7		Bluish	Blue							
Azacyclonol	7		White	Bluish							
Oxazepam	8		White	White			Yellow	Green			
Meprobamate	8		White	White			Gold	—			Red
Buclizine	9		White	White			Orange	Gold			
Chlordiazepoxide	11	Violet	White	White			Yellow	Green	Br. orange		
Etryptamine	18		Bluish in 5 min	Blue-violet							
Iproniazide	21		Bluish	Blue							
Acetophenazine	22	Pink	Reddish-pink								
Carphenazine	28	Pink	Reddish-pink								
Mesoridazine	28	Blue-green	Red-violet								
Perphenazine	29		Fuchsia								
Fluphenazine	30		Cameo								
Desipramine	34		Green-blue								
Tybamate	34		White	White			Lilac	Pink			
Clopentixol	36		Bluish in 5 min	Violet							Br.Orange
Hydroxyzine	40	Green-yell.	White	Bluish							
Phenaglycodol	40		White	Bluish						Violet	
Oxanamide	45		White	Bluish						Green	
Phenelzine	50		Bluish	Blue							

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Nortriptyline	51		White	Bluish	Pink-blue[a]	Violet (yellow[b])			
Tranylcypromine	51		White	Bluish	Lilac	—			
Prochlorperazine	54		Fuchsia						
Trifluoperazine	56		Cameo						
Acepromazine	61	Pink	Reddish-pink						
Methylphenidate	62		White	White			Lilac	Violet	
Promazine	64		Brick-red						
Imipramine	65		Green-blue						
Isocarboxazid	68		Bluish	Blue					
Diazepam	68		White	White			Lilac	Green	
Methoxypromazine	68		Deep violet						
Mepazine	71		Brick-red						
Rescinnamine	72	Blue	Bluish in 5 min	Olive green					
Propiomazine	72	Yellow	Redd.-pink						
Thioridazine	73		Green-blue						
Chlorpromazine	73		Fuchsia						
Triflupromazine	74	Violet	Cameo						
Chlorprothixene	75	Violet	Bluish in 5 min	Violet					Br.Orange[c]
Thiopropazate	75		Fuchsia						
Amitriptyline	76		White	Bluish					
Benactizine	77		White	White			Red-violet	Red	
Methotrimeprazine	82		Deep violet						
Pipradol	84		White	Bluish					
Ethopropazine	89		Reddish-pink						

[a] Pink spotted blue.
[b] Color in parentheses denotes the inside color of the spot.
[c] Br = brilliant.

TABLE V

SCHEME FOR SYSTEMATIC SEPARATION OF PHENOTHIAZINE DERIVATIVES

	Fluphenazine	*Trifluoperazine*	*Triflupromazine*	*Acepromazine*	*Acetophenazine*	*Carphenazine*	*Ethopropazine*	*Propiomazine*	*Mepazine*	*Promazine*	*Chlorpromazine*	*Mesoridazine*	*Perphenazine*	*Prochlorperazine*	*Thiopropazate*	*Methotrimepazine*	*Methoxypromazine*	*Thioridazine*
Fluphenazine	—	V	V	V	V	II	III	V	II	II	III	IV	IV	III	III	II	V	II
Trifluoperazine	V	—	V	II	V	V	III	V	III	V	III	V	II	III	III	III	V	III
Triflupromazine	V	V	—	II	V	V	III	III	III	V	III	V	II	III	III	III	V	III
Acepromazine	V	II	II	—	V	V	III	V	II	II	III	IV	V	III	III	III	II	II
Acetophenazine	V	V	V	V	—	IV	V	IV	IV	V	V	IV	V	V	IV	V	V	IV
Carphenazine	II	V	V	V	IV	—	V	IV	IV	V	V	IV	II	V	IV	V	V	IV
Ethopropazine	III	III	III	III	V	V	—	V	III	III	III	III	III	III	II	III	III	III
Propiomazine	V	V	III	V	IV	IV	V	—	IV	V	III	IV	III	III	IV	V	V	IV
Mepazine	II	III	III	II	IV	IV	III	IV	—	IV	II	II	II	II	III	III	IV	III
Promazine	II	V	V	II	V	V	III	V	IV	—	V	II	II	V	III	III	II	IV
Chlorpromazine	III	–III	III	III	V	V	III	III	II	V	—	III	II	III	III	III	III	III
Mesoridazine	IV	V	V	IV	IV	IV	III	IV	II	II	III	—	IV	V	III	III	II	II
Perphenazine	IV	II	II	V	V	II	III	III	II	II	II	IV	—	V	III	III	V	II
Prochlorperazine	III	III	III	III	V	V	III	III	II	V	III	V	V	—	III	III	III	III
Thiopropazate	III	III	III	III	IV	IV	II	IV	III	III	III	III	III	III	—	II	III	III
Methotrimepazine	II	III	III	III	V	V	III	V	III	III	III	III	III	III	II	—	III	III
Methoxipromazine	V	V	V	II	V	V	III	V	IV	II	III	II	V	III	III	III	—	II
Thioridazine	II	III	III	II	IV	IV	III	IV	III	IV	III	II	II	III	III	III	II	—

TABLE VI

SCHEME FOR SYSTEMATIC SEPARATION OF NONPHENOTHIAZINE TRANQUILIZERS

	Chlorprothixene	*Clopenthixol*	*Rescinnamine*	*Azacyclonol*	*Hydroxyzine*	*Oxanamide*	*Phenaglycodol*	*Benactizine*	*Buclizine*	*Chlordiazepoxide*	*Diazepam*	*Meprobamate*	*Oxazepam*	*Tybamate*
Chlorprothixene	—	II	II	V	III	III	III	II	II	II	II	II	V	II
Clopentixol	II	—	III	V	III	III	III	II	II	II	II	II	V	III
Rescinnamine	II	III	—	V	IV	IV	IV	II	II	II	II	II	V	V
Azacyclonol	V	V	V	—	IV	IV	IV	II	II	II	II	II	V	II
Hydroxyzine	III	III	IV	IV	—	IV	IV	II	II	II	II	II	V	II
Oxanamide	III	III	IV	IV	IV	—	IV	II	II	II	II	II	V	II
Phenaglycodol	III	III	IV	IV	IV	IV	—	II	II	II	II	II	V	II
Benactizine	II	II	V	IV	II	II	II	—	II	II	II	II	IV	II
Buclizine	II	II	V	II	V	II	V	II	—	II	II	II	IV	II
Chlordiazepoxide	II	II	V	IV	II	II	II	II	II	—	II	II	IV	III
Diazepam	II	II	V	IV	II	II	II	II	II	II	—	II	IV	II
Meprobamate	II	II	V	III	IV	II	II	II	II	II	II	—	III	II
Oxazepam	V	V	V	III	IV	IV	IV	IV	IV	IV	IV	III	—	V
Tybamate	II	III	V	II	V	II	II	II	II	III	II	II	V	—

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TABLE VII

SCHEME FOR SYSTEMATIC IDENTIFICATION OF STIMULANTS

	Desipramine	*Imipramine*	*Iproniazide*	*Isocarboxazid*	*Nialamide*	*Phenelzine*	*Etryptamine*	*Amitriptyline*	*Nortriptyline*	*Pipradol*	*Tranylcypromine*	*Deanol*	*Methylphenidate*
Desipramine	—	V	V	V	II	V	II	V	V	V	V	II	III
Imipramine	V	—	II	II	V	II	II	V	IV	V	V	II	III
Iproniazide	V	II	—	V	V	V	II	II	III	II	II	V	II
Isocarboxazid	V	II	V	—	III	V	II	II	IV	II	II	V	II
Nialamide	II	V	V	III	—	V	III	V	V	V	V	IV	V
Phenelzine	V	II	V	V	V	—	III	II	IV	II	II	V	II
Etryptamine	II	II	II	II	III	III	—	V	II	V	V	V	IV
Amitriptyline	V	V	II	II	V	II	V	—	IV	V	V	V	V
Nortriptyline	V	IV	III	IV	V	IV	II	IV	—	IV	IV	II	III
Pipradol	V	V	II	II	V	II	V	V	IV	—	V	V	V
Tranylcypromine	V	V	II	II	V	II	V	V	IV	V	—	V	V
Deanol	II	II	V	V	IV	V	V	V	II	V	V	—	V
Methylphenidate	III	III	II	II	V	II	IV	V	III	V	V	V	—

and the colors obtained by means of the Folin and the Mandelin reagents leads to the identification of each compound. The E-P reagent was used to differentiate Chlordiazepoxide from Oxazepam and the furfural reagent to differentiate Phenaglycodol from Oxanamide. The brilliant fluorescence formed by Meprobamate, Clopentixol and Chlorprotixene with the furfural reagent are also reported, as they are characteristic of these drugs. Depending on the system selected, no identification was achieved for one, or more than one, pair of phenothiazine derivatives. The use of a second chromatographic system was necessary for the resolution of these pairs.

Evaluation of the data obtained

From the data obtained it appeared that a quick identification of the drugs can be achieved by combining their chromogenic behavior with their chromatographic comportment in two selected systems.

Since an initial differentiation between the different classes of the compounds under investigation can be achieved by means of the Folin reagent, all the drugs were classified in groups according to the color produced after reacting with this detecting reagent. It was observed that System I[6] can be used as a common chromatographic system since it gives clear separation of many drugs with similar chromogenic behavior. The selection of the second system was based on the evaluation of the R_F values obtained in System I and on the best resolution achieved for each drug in respect to the others yielding the same color reaction.

Tables V, VI and VII show the second system selected for the resolution and the identification of each pair of drugs forming the three pharmacological classes investigated.

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SUMMARY

Thin-layer chromatographic investigation was conducted on a group of 45 psychotropic drugs with different chemical composition and pharmacological activity in order to expedite their identification. R_F values of the drugs in five chromatographic systems and color reactions with several detecting reagents are reported.

A procedure is presented which leads to the resolution and the identification of each pair of drugs in two selected chromatographic systems. It is based on the different chromogenic behavior of these compounds in respect to the Folin-Ciocalteau reagent.

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