## A colour reaction for psychotropic drugs on thin layer chromatograms

Evolving from a selective test for organosulphur compounds[1] a procedure has been described for the colorimetric estimation of the anthelmintic phenothiazine which depends on treatment with bromine in the presence of aniline[2]. It was shown that the obviously mixed reddish colour resulting from treatment with bromine alone[3] was due to a series of coloured products whose formation was controlled primarily by the amount of phenothiazine present. The function of the aniline was to direct the course of reaction to the appearance of one main product.

The present note describes a logical extension of the test to the detection on chromatograms of psychotropic drugs whose structure is based on the phenothiazine nucleus. In accordance with the results previously described use is made of differences in colour depending on whether the material is treated with bromine directly or in the presence of aniline.

The opportunity has been taken to modify the method of aniline treatment. Previously incorporation of this on to chromatograms was achieved by dipping in solutions in light petroleum. In the present work this has been done conveniently by exposing to aniline vapour.

*Experimental*

*Materials.* Commercial samples of pharmaceutical quality were used without further treatment.

*Procedure.* Thin layer chromatography was carried out with plates of silica gel G (0.25 mm thickness) using a mixture of ethanol–water–acetic acid (20:20:1) as developing solvent. Materials (50 $\mu$g) were loaded on to the chromatogram either from a chloroform or an alcohol solution (in the case of prochlorperazine and thioproperazine).

Spots were visualized by exposure to bromine vapour directly or after previous exposure to aniline vapour for periods up to 30 min.

*Results*

Results are presented in Table I.

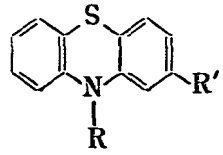
*Discussion*

Results show that the materials may be divided into two groups—those which in the direct test give a predominantly brown colour changing to green (promethazine and ethopropazine) compared to the red colours given by the second group. In the latter a repeatable variety of shades is given and the descriptions crimson, rose pink, and orange pink are very meaningful.

This division into two groups is sustained in the aniline test. Here the predominant colour given by the first group is green, particularly after standing, while the remaining materials give a mauve colour.

Structural influence on the sensitivity of the test appears with the perazines, characterized by the N-methylpiperazine substitution in the main side chain. The colours in both the direct and aniline tests, while easily recognizable, are much weaker. With uniform loading of the chromatograms this difference in sensitivity itself may

TABLE I

CHROMATOGRAPHY OF PSYCHOTROPIC DRUGS OF THE TYPE: 

| *Spot No.* | *Material** | *Structure* | | *Colour* | | $R_F$** |
|---|---|---|---|---|---|---|
| | | *R* | *R'* | *With bromine* | *With bromine after aniline* | |
| 1 | Promethazine | —$CH_2$—CH(Me)—$N(Me)_2$ | H | Green-brown changing to green | Green | 0.41 |
| 2 | Ethopropazine | —$CH_2$·CH(Me)·$N(Et)_2$ | H | Brown changing to green | Green, intensifying with time | 0.36 |
| 3 | Chlorpromazine sample 1 | —$CH_2$·$CH_2$·$CH_2$·$N(Me)_2$ | Cl | Crimson | Mauve-purple | 0.39 |
| 4 | Chlorpromazine sample 2 | —$CH_2$·$CH_2$·$CH_2$·$N(Me)_2$ | Cl | Crimson | Mauve-purple | 0.39 |
| 5 | Trimeprazine (tartrate) | —$CH_2$·CH(Me)·$CH_2$·$N(Me)_2$ | H | Rose-pink | Mauve-purple | 0.41 |
| 6 | Prochlorperazine (maleate) | —$CH_2$·$CH_2$·$CH_2$·N(piperazine)·Me | Cl | Crimson | Mauve-purple | 0.25 |
| 7 | Trifluoperazine | —$CH_2$·$CH_2$·$CH_2$·N(piperazine)·Me | —$CF_3$ | Orange-pink | Mauve-purple | 0.28 |
| 8 | Thioperazine (methanesulphonate) | —$CH_2$·$CH_2$·$CH_2$·N(piperazine)·Me | —$SO_2N(Me)_2$ | Pink | Pale mauve | 0.25 |
| 9 | Methotrimepazine | —$CH_2$·CH(Me)·$CH_2$·$N(Me)_2$ | —OMe | Blue | Deep mauve changing to blue | 0.42 |

* As hydrochloride unless otherwise stated.
** The $R_F$ value is subject to change with temperature.

be used to assist identification being so markedly associated with the structure of the drug.

It should be noted that the strong test given by other members of the series permits reduction (to 20 $\mu$g) in the amount used.

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1 R. F. BAYFIELD, V. CLARKE AND E. R. COLE, *J. Chromatog.*, 19 (1965) 370.
2 R. F. BAYFIELD AND E. R. COLE, *Anal. Chim. Acta*, 34 (1966) 193.
3 H. L. CUPPLES, *Ind. Eng. Chem., Anal. Ed.*, 14 (1942) 53.

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## Thin-layer chromatography of some phenothiazine derivatives

Thin-layer chromatography (TLC) is increasingly being used to identify pharmaceutical mixtures[1] and also to determine quantitatively their composition. This technique has been used successfully in the separation of many phenothiazine derivatives. The separation of hydroxy derivatives, chlorophenothiazine and bromopromazine has, nevertheless, remained a problem. Their separation with the aid of TLC is reported below.

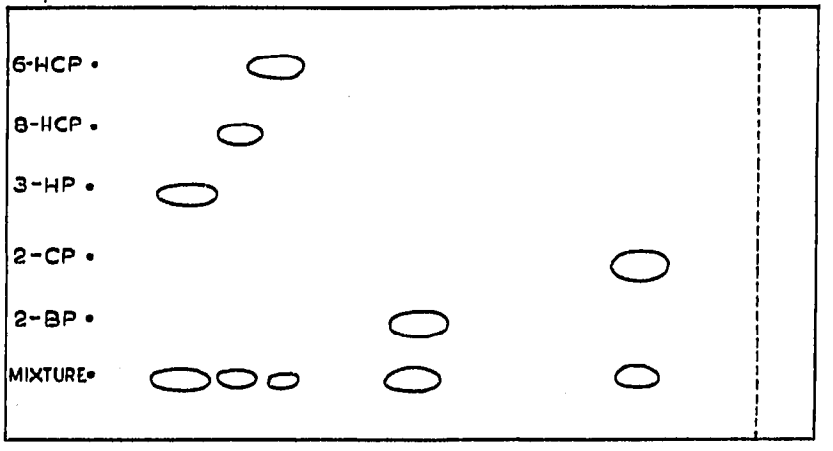


Fig. 1. Separation of 6-hydroxychloropromazine (6-HCP), 8-hydroxychloropromazine (8-HCP), 3-hydroxypromazine (3-HP), 2-chlorophenothiazine (2-CP) and 2-bromopromazine (2-BP).

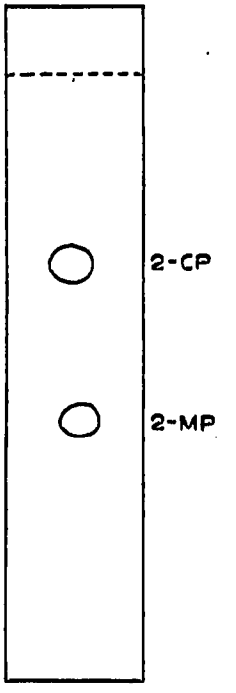


Fig. 2. Separation of 2-chlorophenothiazine (2-CP) and 2-methoxyphenothiazine (2-MP).