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Note

Thin-layer detection of pentazocine, tripelennamine, phencyclidine and propoxyphene alone or in combination with opiates in drug abuse urine screening programs

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A simple, inexpensive and reliable thin-layer chromatographic (TLC) procedure is reported for detection of the widespread abuse of pentazocine* (Talwin), tripelennamine* (Pyribenzamine), propoxyphene (Darvon) and phencyclidine (PCP). The pharmacology, the commonly-used street names of PCP and the life-saving service of urinalysis provided by our laboratory were all previously discussed by Kaistha[1]. Pyribenzazine is an antihistamine commonly used to dilute pentazocine in the street samples. The method is capable of detecting the above drugs alone or in combination with opiates. The concurrent detection of morphine was felt necessary because the initial feasibility study showed the presence of pentazocine and morphine in urines of drug-dependent individuals. In addition to tripelennamine, three commonly used antihistamines such as methapyrilene (Histadyl —an antihistamine used to dilute heroin in street samples), diphenhydramine (Bendadryl) and chlorpheniramine (Chlor-Trimeton) were included in this study.

The technique involves the use of paper impregnated with SA2 cation-exchange resin to absorb these and other drugs of abuse as reported earlier[2–6]. The ion-exchange paper is soaked in 20–50 ml of fresh undiluted urine and shaken for 20–30 min on a reciprocating shaker. The paper is then removed and transferred to a 4-oz. wide-mouthed screw-capped jar. The paper is rinsed with 10 ml of water (the rinsings being discarded) and extracted at pH 10.1 using 3 ml of ammonium chloride–ammonium hydroxide buffer and 15 ml chloroform–isopropanol (5:2) as described earlier[3–6]. The lower organic layer is pipetted into a 15-ml non-graduated conical centrifuge tube containing 5 drops of 0.5% sulfuric acid in methanol and the solvent is evaporated in an oven as described previously[2–6]. The residue along the sides of the tube is washed with 0.5–1 ml of methanol, vortexed and the sides of tube are again washed with a few drops of methanol. The methanol is evaporated to dryness as described above. The residue thus obtained is chromatographed on 20 × 20 cm Gelman pre-coated silica gel glass microfiber sheets (ITLC Type SA). Detection Procedure A (see below) is used if pentazocine, antihistamines (tripelennamine, methapyrilene and diphenhydramine), methadone and/or its major metabolite, propoxyphene and its major metabolite, norpropoxyphene, and phencyclidine are to be detected. Detection Pro-

* A combination of pentazocine and tripelennamine is sold on the street as T's and Blue's.

cedure B (see below) is used if opiates (morphine, codeine, quinine–heroin adulterant and chlorpheniramine) are to be tested in addition to the above drugs.

DETECTION PROCEDURES

Procedure A for the detection of pentazocine, antihistamines, methadone, propoxyphene and PCP

The residue obtained after the evaporation of solvent is dissolved in 30–50 μl of methanol, vortexed, and the entire extract is spotted. Four standards (one at each edge and two interspaced in the center between urine specimens) and 9 samples are spotted on each sheet (Standard 1 is pentazocine, tripelennamine or methapyrilene and chlorpheniramine, each 1 mg/ml in methanol; Standard 2 is morphine, codeine, quinine, methadone and its major metabolite, each 1 mg/ml in methanol; Standard 3 is pentazocine, propoxyphene, norpropoxyphene and PCP, each 1 mg/ml in methanol; Standard 4 is dyphenhydramine, 1 mg/ml in methanol). The spots are air dried and the plate is dried for 5–7 min (7 min if there is high humidity in the air in an oven at 85–90° prior to its development in 100 ml of fresh* Solvent D[2–6] (ethylacetate–cyclohexane–methanol–ammonium hydroxide (56:40:0.8:0.4); 180 ml of this solvent are used if two plates are to be placed in the tank). The solvent is allowed to travel a distance of 15–15.5 cm (travelling time *ca.* 40–45 min), then the plate is air dried and after further drying in the oven for 5 min at 85–90°, it is sprayed with iodoplatinate[2–6].

Antihistamines (tripelennamine, methapyrilene and chlorpheniramine), norpropoxyphene and nicotine appear as varying shades of grey to blue (the blue color of norpropoxyphene changes to pinkish brown within a minute but reappears as blue if the plate is resprayed with iodoplatinate; sometimes this spot appears as a blue streak); the major metabolite of methadone** appears as greyish brown but changes to brown within a few minutes while methadone, PCP, pentazocine (unchanged) and diphenhydramine are seen as varying shades of pink to brown (sometimes PCP may appear as a greyish spot but changes immediately to brown). The plate is then oversprayed with iodine–potassium iodide reagent[2–6] to detect the minute concentration (less than 5–7 μg) of pentazocine which appears as a brown color at the level of the pentazocine standard (less than 5–7 μg pentazocine standard is seen after this spray). At this stage, if a single spot, not accompanied by tripelennamine or methapyrilene, is seen at the level of the pentazocine standard in any of the unknown specimens, it is advisable to overspray the plate with Munier's modified Dragendorff reagent[5] which would change the brown spot due to diphenhydramine** into a greyish blue spot on keeping the plate exposed at room temperature for about 5 min. This step would eliminate any false positives due to diphenhydramine.

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* Solvent D after storage overnight and up to 4 g/h has yielded better separation of the drugs listed in standards 1, 3 and 4.

** Some recent batches of ITLC Type SA plates received from Gelman Instrument Company (Ann Arbor, Mich., U.S.A.) were not able to separate a mixture of diphenhydramine and pentazocine; methadone and its major metabolite were also seen as a single spot. This matter is being investigated by the Company.

Procedure B for the detection of morphine, codeine, quinine in addition to the drugs included under Procedure A

Procedure B is a two-phase development and spraying system. Phase I is exactly the same as Detection Procedure A up to the spraying step. The plate is developed up to 15–15.5 cm in Solvent D and air dried. After further drying for 5 min in the oven at 85–90°, the lower 2.0–2.5 cm portion of the plate is covered and the upper uncovered portion is sprayed with iodoplatinate followed by iodine–potassium iodide and Munier's modified Dragendorff reagents as proposed under Procedure A. The drugs found positive are circled and then the plate is dried in the oven for 5 min at 85–90° and placed in 100 ml of Solvent C[2–6] (ethyl acetate–cyclohexane–ammonium hydroxide–methanol–water (70:15:2:8:0.5); 150 ml of this are used if two plates are to be placed in the tank). The solvent is allowed to travel a distance of 7–8 cm (travelling time 7–10 min). The plate is air dried and after further drying in the oven for 5 min at 85–90° is sprayed with 0.5% (w/v) sulfuric acid (in water) to test for the presence of quinine and its metabolites. The plate is examined under shortwave UV light; quinine and its major metabolite which appear as bright blue fluorescent spots are circled. The plate is then dried for 5 min at 85–90°, and sprayed with iodoplatinate[2–6], morphine appears as navy blue, codeine, quinine and its metabolites as brown spots. Norpropoxyphene, the major metabolite of propoxyphene if not seen earlier due to covering of the lower 2.0 to 2.5 cm portion of the plate as proposed under Procedure A, is seen now as brownish or pinkish blue or blue streak changing to pinkish brown; if this spot was seen earlier under Procedure A, it will again appear at a higher R_F value as brownish or pinkish blue streak and changing to pinkish brown. Chlorpheniramine which hardly moves with Solvent D, is now seen as greyish blue spot at an R_F value of about 0.76–0.84.

When the objective is to detect opiates along with drugs included under Procedure A, the lower portion of the plate about 2.0–2.5 cm should be covered after

TABLE I

R_F VALUES* USING SOLVENT D (PROCEDURE I)

Drugs	*Average range of R_F values*	
	Volume used: 100 ml	*Volume used: 180 ml*
Pentazocine	0.35–0.42	0.39–0.60
Tripelennamine	0.16–0.33	0.23–0.42
Chlorpheniramine	0.06–0.07	0.12–0.13
Methapyriline	0.16–0.33	0.23–0.42
Diphenhydramine	0.40–0.52	0.40–0.52
Methadone	0.43–0.58	0.43–0.67
Major methadone metabolite (2-ethylidine-1,5-dimethyl-3,3-diphenylpyrrolidine)	0.5 –0.71	0.64–0.79
Propoxyphene	0.71–0.80	0.69–0.87
Norpropoxyphene (major metabolite of propoxyhene)	0.03–0.1	0.19–0.20
Phencyclidine	0.82–0.92	0.82–0.94
Nicotine	0.19–0.22	0.26–0.27

* Although R_F values may vary from day to day and even from plate to plate because of factors like humidity, adsorbent activity of layers, uniformity of layer thickness, yet the resolving pattern remains the same.

TABLE II

R_F VALUES USING SOLVENT C (PROCEDURE II)

Volume used: 150 ml.

Drugs	*Average range of R_F values*
Norpropoxyphene (major metabolite of propoxyphene)	0.72–0.76
Chlorpheniramine	0.76–0.84
Nicotine	0.87–0.88
Morphine	0.14–0.28
Codeine	0.31–0.50
Quinine	0.43–0.61
Major quinine metabolite	0.31–0.33

developing with Solvent D and before the application of iodoplatinate spray as outlined under Procedure A. R_F values of the above drugs are given in Tables I and II.

The proposed procedure for the identification of pentazocine is based on the detection of unchanged drug excreted in the urine. The metabolism of pentazocine and propoxyphene was discussed by Kaistha earlier[1]. It has been reported that about 9.5% of the ingested pentazocine is excreted unchanged in 24 h[1]. Kaistha and Jaffe[7] were able to detect unchanged drug up to 70 h using the ion-exchange paper technique after the oral ingestion of a 50-mg tablet; however, the direct extraction of urine (liquid–liquid extraction) could not detect pentazocine after 24 h. The sensitivity of the proposed method for the detection of pentazocine, propoxyphene, tripelennamine or methapyrilene and PCP is 1 μg/ml of urine, the minimum volume of urine needed is 20 ml. Since tripelennamine and methapyrilene have the same R_F values, the results are reported as antihistamines. Both of these antihistamines are used as adulterants for pentazocine and heroin. Quinine[7]is also reported as an opiate because it is widely used to dilute heroin street samples. A technician can analyze 130 urine specimens per day for the drugs included under Procedure A and 110 specimens for drugs included in both procedures. Both of the above procedures are currently being employed to detect the alleged widespread abuse of Talwin and Pyribenzamine.

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