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SHORT COMMUNICATION

Routine detection and identification in urine of stimulants, analgesics, antihistamines, local anaesthetics and other drugs, some of which may be used to modify performance in sport

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MANY sporting authorities throughout the world proscribe, in addition to the stimulants, other classes of drugs, e.g. the narcotics and phenothiazine tranquillizers. Present gas-liquid chromatographic procedures for the routine detection in urine of all these classes of drugs suffer from the disadvantage of using a variety of operating conditions (see for example Kazyak & Knoblock, 1963, who listed retention time data for 59 compounds using a single SE-30 column and temperatures from 115–250°, and also Street, 1967).

The work of Beckett, Tucker & Moffat (1967) on stimulants is therefore now extended, using two isothermal GLC systems, to obtain retention data for 74 additional compounds. This allows the analysis of 116 compounds to be made using only three isothermal GLC systems. Drugs, other than those which may be used to modify performance in sport, are included since sportsmen may use them for medical reasons, e.g. phenacetin in analgesic preparations or a local anaesthetic for injury, and these may interfere with the dope control test.

METHOD

The method previously reported is used with the following modifications.

Extraction procedure A is carried out twice, on the same 5 ml of urine, using (*a*) diethyl ether and (*b*) methylene dichloride. The extracts are concentrated on water baths at 40° and 55° respectively.

1 μl of the ethereal concentrate is injected into System C at 210° and, as before, 5 μl into System B at 140°. 1 μl of the dichloromethane concentrate is also injected into System C at 210°.

Table 1 lists the retention times of the compounds screened using System C at 210° (and also at 120° for comparison) along with System B at 140° for some compounds. A composite chromatogram is represented in Fig. 1, each peak represents approximately 1 μg free base injected in 1 μl solvent.

DISCUSSION

The detection of the metabolite(s) of a drug in urine affords additional proof of the ingestion of the parent compound. Some drug metabolites

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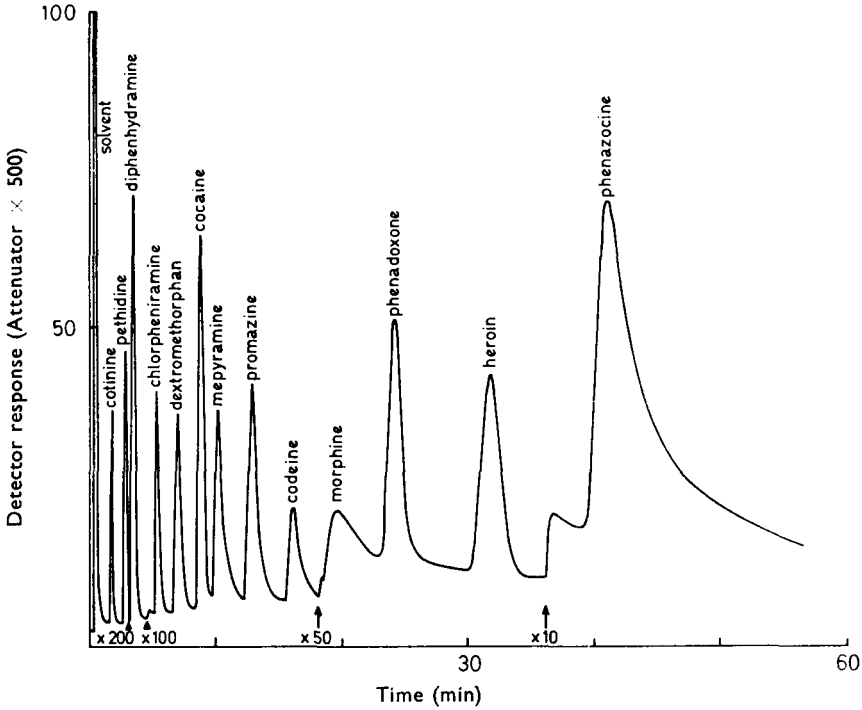

FIG. 1. Composite chromatogram of some pharmaceutical compounds on Column "C" at 210°.

have therefore been included in Table 1, e.g. the cyclic metabolite of methadone (1,5-dimethyl-3,3-diphenyl-2-ethyl-1,2-dehydropyrrolidine). However, there are some classes of metabolites that this method will not detect, e.g. ring hydroxylated compounds, and in these cases modification of the extraction technique is necessary. Glucuronides, and other conjugates of the parent drug, can be hydrolysed to the drug and extracted as usual. Of the compounds examined 34 were shown to be excreted as parent drug after oral administration.

The dual extraction used is necessary because heroin, morphine, cotinine, phenacetin, caffeine, cinchonine, and cinchonidine are relatively insoluble in ether.

All the compounds studied gave single peaks which were nearly symmetrical (Fig. 1) with the exceptions of tetrahydroziline, xylometazoline. morphine and cinchonine (System C) and meprobamate (System B), which gave broad diffuse peaks and propoxyphene which gave two peaks (System C). The use of System C is sufficient to detect and identify any of the 74 compounds in Table 1. Further chromatography on System B (at 140°, or at a higher temperature), combined with derivative formation and chromatography, is sufficient to establish unequivocally the identity of the compound.

TABLE 1. GLC DATA FOR SOME PHARMACEUTICAL COMPOUNDS

	Retention time (min) for compounds using systems						
	C	C	B	C		C	
	120°	210°	140°		210°		210°
Benzocaine	18·5	1·2	62·1	*Chlorpheniramine	5·2	Trimeprazine	12·0
Amylocaine	20·9	1·4	4·7	Cyclic Metabolite of Methadone	5·3	*Promazine	12·7
*Phenacetin	36·6	1·6	—			*Antazoline	13·6
Cotinine	33·7	1·7	50·6	Normethadone	6·2	Dexoxadrol	14·2
*Meprobamate	—	2·2	6·3†	Dextromethorphan	7·0	Dihydrocodeine	15·4
				Isomethadone	7·2	*Codeine	16·1
Fenmetramide	—	2·3	—	Xylometazoline	7·3†	Pyrrobutamine	17·3
Norpethidine	—	2·3	25·8	Brompheniramine	7·3	*Morphine**	19·6†
Tryptamine	—	2·4	—	Methaqualone	7·4	Ethylisobutrazine	20·1
Pethidine	—	2·6	13·6	Pipradrol**	7·5	Dipipanone	21·0
*Glutethimide	—	2·7	—	Phenindamine	7·8	Methdilazine	21·1
Prilocaine	—	2·8	46·3	*Propoxyphene	8·4a	*Chlorpromazine	21·9
*Caffeine**	—	2·9	—	*Methadone	8·4	Desmethylchlorpromazine	21·9
Ethoheptazine	—	2·9	—	Amitriptyline	8·7		
*Pheniramine	—	3·0	22·1	Cocaine**	8·8	Didesmethylchlorpromazine	21·9
Etryptamine	—	3·0	—	Primidone	9·3		
Tymazoline	—	3·3	—	*Chlorcyclizine	9·6	Phenadoxone	24·1
*Diphenhydramine	—	3·4	26·8	Triflupromazine	9·7	Methotrimeprazine	24·8
*Lignocaine	—	3·5	43·1	Imipramine	9·9	Pyrathiazine	25·4
*Amidopyrine	—	3·7	—	Desmethylimipramine	10·2	*Heroin	31·6
Orphenadrine	—	3·8	32·3	Mepyramine	10·2	*Chloroquine	31·9
Tetrahydroziline	—	4·2†	—	Triprolidine	10·6	*Cinchonidine	37·6
*Tripelennamine	—	4·3	54·0	Isothipendyl	10·7	*Cinchonine	39·0†
*Methapyrilene	—	4·3	—	Promethazine	11·2	Trifluoroperazine	40·5
*Procaine	—	4·8	—	Pentazocine	11·3	Phenazocine	41·3
Cyclizine	—	5·2	—	Bupivacaine	11·3	Acepromazine	42·9

* Drugs examined by Kazyak & Knoblock (1963).
** Drugs most likely to be used as doping agents
† Broad diffused peak
— No peak observed in 60 min.
Major peak

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