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REVIEW

DRUG LEVEL MONITORING: CHROMATOGRAPHY OF SOME MINOR GROUPS OF DRUGS

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INTRODUCTION

It is obvious at first sight that the previous chapters of this volume are far from being complete with regard to different types of drugs that are accessible to monitoring by chromatographic methods or to pharmacokinetic studies. In the present chapter we have tried to accumulate additional information about some minor groups of drugs that were not worth a separate chapter although their analysis appears quite important from the pharmacological point of view. Even with this chapter included we are aware of the fact that readers may not find the drug of their interest within this volume because of the vastness of the field which is difficult to fit into a single volume. Another reason is the speed with which this area is expanding and also that we have had to cut the available literature information as we had to keep a reasonable limit on the contributions. The present survey covers the period from January 1978 to June 1984. As a basis for this survey we have used the bibliography section of the Journal of Chromatography and occasionally we have completed the references found herein by additional ones from our own experience. These are the references which from the viewpoint of the Journal of Chromatography bibliography section seemed less important and were purposely deleted at this stage.

We have attempted to summarize the facts that in our opinion are the important ones about a particular drug and which can help the reader in a rapid search for information and possibly for a choice for future experiments of his own. The table form presentation of the data appeared to us the only way how to handle the large amount of available information. In the tables it is possible to find the chromatographic techniques used together with the specification of the stationary and mobile phases, the detection procedures used and the more important parameters of the instrumental techniques. Particular attention is paid to injector, column and detector temperatures, carrier gas and mobile phase flow-rates and gradient set-up. In all cases the source of material for analysis is also specified. Where data were available, the sensitivity limit is also given. It seems to us that the information available from the tables is sufficient for planning and managing new experiments. There are, however, some entries that are incomplete. These are mainly those in which the original papers were not available to us and which we were made aware of through Chemical Abstracts.

The drugs are categorized according to The Merck Index (10th ed., Merck, Rahway, NJ, 1983) and M. Negwer (Organisch-chemische Arzneimitteln und ihre Synonyma, 5th ed., Akademie Verlag, Berlin, 1978) and listed alphabetically. Individual drugs in their vast majority are listed according to their generic names (if available). In those situations where there are commonly used synonyms, these are introduced as a cross-reference or listed in parentheses after the generic name. It should be pointed out, however, that not

all synonyms were considered in this respect. In any case we have avoided chemical names wherever possible.

In those instances where a particular drug can be categorized in two or more different ways, we have attempted to list it under the most common group. In some instances drugs are mentioned that have already occurred in individual chapters of this volume, clearly because of the possibility of multiple therapeutic applications. For complete information the reader is directed to the Index of Compounds Chromatographed.

Also, even at an early stage of compiling the data it became evident that not all metabolites could be specified within the survey as in many instances their chemical structure remains obscure or is only partly solved. In those cases where mixtures of drugs are subjected to chromatography, it was technically not feasible to list all of them in the form of cross-references. Readers are therefore advised to check the whole table relevant to a particular category of drugs for completeness.

TABLE 1

ANTHELMINTICS

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Albendazole + metabolites	TLC	Silica gel	Chloroform—methanol (9:1)	UV or autoradiography		Urine		1
	TLC	Silica gel	Chloroform—diethyl ether—acetic acid (6:1:1)	UV or autoradiography		Urine		1
	TLC	Silica gel	Chloroform—methanol—conc. ammonia (90:10:1)	UV or autoradiography		Urine		1
Dichlorvos, trichlorfon	GC—MS					Blood, tissues		2
	GC—MS					Plasma, erythrocytes	Rearrangement products of metrifonate also separated	3
Diethylcarbamazine (Banocide, Hetrazan)	GC	2% Carbowax 20 M, 5% KOH on Chromosorb G AW DMCS, 100—120 mesh	Nitrogen, 40 ml/min	Nitrogen-sensitive detection	Below 1 ng/ml	Plasma, urine	Column 160° C, injector 180° C, detector 240° C	4
Levamisole	GC	3% OV-17 on Supelcoport, 80—100 mesh, silylated column	Nitrogen, 55 ml/min	FID (rubidium sulphate)	4 ng	Plasma	Injector 255° C, oven 250° C, detector 260° C	5
Mebendazole	HPLC	μBondapak C_{18}	KH_2PO_4—NaOH buffer pH 6.0—acetonitrile (73:27), 2.5 ml/min	UV 313 nm	10 ng/ml	Plasma		6
	HPLC	LiChrosorb Si 60 (5 μm)	Chloroform (500 ml) in 10 l water, mixed, aqueous phase discarded	UV 307 nm	Below 20 ng/ml	Plasma		7
	HPLC	LiChrosorb Si 60	Acetonitrile—chloroform saturated with water—25% ammonia (75:92.5:0.1) pH 6—7, 0.8 ml/min	UV 307 nm	Below 20 ng/ml	Plasma		7
Mebendazole + metabolites	HPLC	LiChrosorb RP-8 (10 μm); pre-column Corasil C_{18}	Methanol—water (55:45) (pump A), methanol—0.05 *M* aq. ammonium phosphate pH 5.5 (55:45) (pump B), 1.7 ml/min	UV 254 nm	20 ng/ml with isocratic elution, 10 ng/ml with gradient elution	Plasma	Isocratic elution: pump A 67% of the mobile phase, pump B the balance; gradient elution: pump A supplies 100% of the mobile phase; at 7 min a current gradient begins which brings pump B up to 45% at 13.2 min	8

Oltipraz	GC	3% OV-17 on Chromosorb Q, 100—120 mesh	Nitrogen, 100 kN/m²	FID	1.0—2.0 μg/ml	Serum, plasma	Oven 235°C, injector 250°C	9
Oxfendazole	HPLC	μBondapak C_{18}	24.5% Acetonitrile in water, 2 ml/min	UV 254 nm	0.005 μg/g	Cow's milk		10
Phenothiazine + metabolite (phenothiazine sulphoxide)	TLC	Silica gel	Chloform—acetone (9:2)	Radioactivity (after elution), or UV at 254/400 nm, relative absorption difference		Urine, blood	Phenothiazine sulphoxide: UV difference measured at 271/400 nm	11
	TLC	Silica gel	Tetrachloromethane—acetone (4:1)	Radioactivity (after elution), or UV at 254/400 nm, relative absorption difference		Urine, blood	Phenothiazine sulphoxide: UV difference measured at 271/400 nm	11
	TLC	Silica gel	Hexane—acetone (3:2)	Radioactivity (after elution), or UV at 254/400 nm, relative absorption difference		Urine, blood	Phenothiazine sulphoxide: UV difference measured at 271/400 nm	11
	TLC	Silica gel	Ethyl acetate—methanol—aq. ammonia (0.88 sp. gr.) (17:2:1)	Radioactivity (after elution), or UV at 254/400 nm, relative absorption difference		Urine, blood	Phenothiazine sulphoxide: UV difference measured at 271/400 nm	11
Piperazine, mononitroso and N,N'-dinitroso derivatives	GC	15% SE-52 on Chromosorb W HP	Helium, 38 ml/min	Thermal energy analyzer	0.2—2.0 ng/ml	Urine, gastric juice, blood	Column 190°C, injector 240°C, furnace 475°C	12
Praziquantel	GC	1.5% OV-3 on Volaspher, 100—120 mesh	Helium, 30 ml/min	NPD	0.01 μg/ml	Serum, urine, faeces	Column 270°C, injector 290°C, detector 300°C	13
	HPLC	RP-18 (5 μm) Spheri-3 (identical pre-column)	38% Aq. acetonitrile, 1.5 ml/min	UV 210 nm	2.5 ng/ml	Serum		14
Thiabendazole, 5-hydroxythiabendazole	HPLC	μBondapak C_{18} (10 μm); pre-column Bondapak C_{18}/ Corasil (37—50 μm)	0.01 *M* Phosphate buffer pH 7.0—methanol (50:50)	Fluorescence at 305/370 nm or 470 cut-off filter	0.1 μg/ml thiabendazole; 0.4 μg/ml 5-hydroxythiabendazole	Serum		15
	HPLC	μBondapak C_{18} (10 μm); pre-column Bondapak C_{18}/ Corasil (37—50 μm)	0.01 *M* Phosphate buffer pH 7.0—methanol (55:45)	Fluorescence at 305/370 nm or 470 cut-off filter	0.1 μg/ml thiabendazole; 0.4 μg/ml 5-hydroxythiabendazole	Serum	Specifically for 5-hydroxythiabendazole	15

Trichlorfon (metrifonate), see Dichlorvos

TABLE 2

ANTIARTERIOSCLEROTICS (HYPOLIPAEMICS)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Bezafibrate	GC	8% OV-101 on Gas-Chrom Q, 80—100 mesh	Nitrogen, 60 ml/min	FID	0.2 μg/ml	Serum, urine	Methyl derivatives; injector, detector 200°C, oven 290°C	16
Ciprofibrate	HPLC	C_2-Phenyl (10 μm), fatty acid analysis column	Tetrahydrofuran—0.1 *M* K_2HPO_4 buffer pH 4—acetonitrile (10:104:96), 2 ml/min	UV 232 nm	0.016 μg/ml	Plasma	Guard column phenyl Corasil 37—50 μm	17
Clofibrate	GC	5% SE-30 on Supelcoport, 80—100 mesh	Nitrogen, 20 ml/min	FID		Plasma	Clean-up procedure; pentafluorobenzoyl derivatives; column programmed 150—245°C, 8°C/min	18
	GC	3% OV-17 on Supelcoport, 80—100 mesh	Nitrogen, 18 ml/min	FID		Plasma	Pentafluorobenzoyl derivatives; column isothermal 180°C	18
Clofibrate, etofibrate, clofibric acid, clofibric acid monoglycolate, nicotinic acid, nicotinic acid monoglycolate	HPLC	μBondapak alkylphenyl	Acetonitrile—0.1 *M* acetate buffer pH 3.75 (50:50), 1.5 ml/min	UV 225 nm		Plasma, urine		19
	HPLC	RCM 100 C_{18}	Acetonitrile—0.05 *M* acetate buffer pH 3.5 (50:50), 6 ml/min	UV 225 nm		Plasma, urine		19
	HPLC	μBondapak alkylphenyl	Acetonitrile—0.1 *M* acetate buffer pH 3.75 (45:55), 1.5 ml/min	UV 225 nm		Plasma,		19
	HPLC	μBondapak alkylphenyl	Methanol—0.1 *M* acetate buffer pH 3.75 (35:65), 1.5 ml/min	UV 225 nm		Plasma, urine		19
	HPLC	RCM 100 C_{18}	Methanol—0.05 *M* acetate buffer pH 3.5 (50:50), 3 ml/min	UV 225 nm		Plasma, urine		19
	HPLC	RCM 100 C_{18}	Acetonitrile—0.05 *M* acetate buffer pH 3.5 (50:50), 3 ml/min	UV 225 nm		Plasma, urine		19
	HPLC	RCM 100 C_{18}	Acetonitrile—0.05 *M* acetate buffer pH 3.5 (30:70), 3 ml/min	UV 225 nm		Plasma, urine		19

Clofibric acid (see also Clofibrate)	GC	3% OV-17 on Chromosorb W HP, 80—100 mesh	Nitrogen, 30 ml/min	FID and UV (compounds in the effluent trapped in 2-propanol)		Serum		20
	GC	Coiled Ni column packed with 10% EGA on Chromosorb W HP, 80—100 mesh	Nitrogen, 30 ml/min	FID and UV (compounds in the effluent trapped in 2-propanol)		Serum		20
	HPLC	μBondapak C_{18}	0.01 *M* Citrate buffer pH 2.5—acetonitrile (65:35)	^{14}C Scintillation		Plasma	^{14}C-Labelled clofibric acid	21
	HPLC	Varian MicroPak CH-10 RP	Acetonitrile—0.5% acetic acid (42:58), 70 ml/h	UV 235 nm	0.5 μg/ml	Plasma, urine, saliva		22
Clofibric acid, probenecid	HPLC	μBondapak C_{18} (10 μm)	Acetonitrile—acetic acid—water (450:5:545), 2 ml/min	UV 235 nm	10 μg/ml (clofibric acid), 15 μg/ml (probenecid)	Plasma, urine		23
Clofibric acid + clofibrate metabolites	TLC	Silica gel	Benzene—acetone—glacial acetic acid (2:2:1)	UV or chemical detection		Urine	Qualitative separation only	24
	TLC	Silica gel	Benzene—ethanol—glacial acetic acid (80:12:1)	UV or chemical detection		Urine	Qualitative separation only	24
	TLC	Silica gel	Chloroform—methanol—glacial acetic acid (24:8:1)	UV or chemical detection		Urine	Qualitative separation only	24
Gemfibrozil + metabolites	GC	3% OV-22 on 80—100 mesh Supelco GCQ (plasma), 10% Poly I-110 on 80—100 mesh Supelco GCQ (urine)	Nitrogen, 50 ml/min	FID	0.5 μg/ml (plasma); 5 μg/ml (urine)	Plasma, urine	Column 180°C, injector 230°C, detector 250°C	25
[1-O-(*p*-Myristyloxy)-α-methylcinnamoyl]-glycerol (LK-903)	TLC	Silica gel	Light petroleum—ethanol (87.5:12.5:1)	Fluorescence at 290/350 nm		Plasma	After first fluorimetry redevelopment in light petroleum—acetone—acetic acid (90:10:15:1) and second fluorimetry	26
Parmidine	TLC	Silica gel	Chloroform—methanol (10:1)	UV 260 nm		Serum, urine		27
Probucol	HPLC	μBondapak C_{18} (10 μm)	Acetonitrile—water (85:15), 2 ml/min	UV 254 nm	0.25 μg/ml	Plasma		28

TABLE 3

ANTIBACTERIALS (INCLUDING ANTISEPTICS, DISINFECTANTS, CHEMOTHERAPEUTICS)

Cross-references between individual mixtures of sulpha drugs are not supplied. Check the whole table for completeness.

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
p-Aminosalicylic acid	HPLC	LiChrosorb C_{18} RP (10 μm)	Methanol—water (20:80) cont. 0.005 *M* tetrabutylammonium hydroxide and 0.01 *M* disodium acid phosphate pH 5.5, 1.0 ml/min	Fluorescence at 270/385 nm	500 pg	Plasma		29
Chlorhexidine (Hibitane)	HPLC	ODS Waters Assoc. RP (10 μm)	1000 μg/ml Toluene-4-sulphonic acid in methanol—water (65:35) 1.5 ml/min	UV 238 nm	0.2 μg/ml	Blood, urine		30
	HPLC	μBondapak C_{18} (10 μm)	Methanol—20 m*M* sodium acetate buffer pH 5 (60:40) + 100 μg/ml pentadecafluoro-octanoic acid, 1.5 ml/min	UV 260 nm	0.1 μg/ml	Urine	Extraction from urine using Sep-Pak	31
Clinoxacin + metabolites	HPLC			UV 254 nm	0.5 ng/ml	Urine		32
Clofazimine (Lamprene)	HPLC	RP-Ultrasphere-octyl (5 μm), 40°C	0.0425 *M* Phosphoric acid in 81% methanol pH 2.4, 1.5 ml/min	UV 285 nm	10 ng/ml	Plasma	Combination with MS	33
	HPTLC	Silica gel	Predevelopment with chloro-form—methanol (1:1), then sampling and development with toluene—acetic acid—water (50:50:4)	Densitometry at 545 nm	5 ng/g	Plasma		34
Clofazimine + metabolites	TLC	Silica gel	Butanol—benzene—water—methanol (2:1:1:1.25), then elution from the plate and purification with HPLC	UV		Urine	Combination with HPLC	35
	HPLC	Altex Ultrasphere ODS RP	60% Methanol—water (first metabolite); 55% methanol—water (second metabolite)			Urine	Combination with HPLC	35

Cotrimoxazole, see Trimethoprim

Cyclindole + metabolites	GC	10% OV-1 on Gas-Chrom Q, 100—120 mesh	Nitrogen, 45 ml/min	FID	Below 10 ng/ml	Blood, urine	^{14}C; column 230° C, flash heater and detector 250° C; trimethylsilylimidazole derivatives	36
Dapsone (DDS, 4,4'-diaminodiphenyl-sulphone) + mono-acetyl derivative	HPLC	μBondapak C_{18} (10 μm)	Acetonitrile—1.5% acetic acid (26:74), 2 ml/min	UV 280 nm	Below 0.2 ng/ml	Serum		37
Dapsone, clofazimine, rifampicin	HPLC	μBondapak C_{18}	(A) Acetonitrile—water (20:80), 2 ml/min; (B) Tetrahydrofuran—0.5% acetic acid (40:60), 1.5 ml/min; (C) Tetrahydrofuran—water (50:50), cont. 0.025 *M* 1-pentanesulphonic acid in glacial acetic acid, 1.5 ml/min	UV 261, 296 nm for dapsone; 287 nm for clofamizine; 242, 256, 337 nm for rifampicin		Serum	Switching of the mobile phase is performed	38
2,4-Diamino-5-[3,5-dimethoxy4-(methyl-thio)benzyl]pyrimidine (Ro-12-6995)	HPLC	LiChrosorb Si 60 (5 μm)	5 ml Methanol and 0.3 ml 33% aq. ammonia diluted to 100 ml with ethyl acetate	Fluorescence at 290/340 nm	0.02 μg/ml	Plasma		39
Ethambutol	GC—MS	2% OV-17 on Gas-Chrom Q, 80—100 mesh	Helium, 40 ml/min	SIM	Below 0.1 μg/ml	Plasma	Column 150° C, injector 180°C, separator 225° C	40
	GC—MS	3% OV-17 on Gas-Chrom Q, 100—120 mesh	Helium, 20 ml/min	MS		Plasma	Column 160° C, injector 190° C, jet separator 200° C, ion-source 250° C	41
	GC	3% SE-30 on Gas-Chrom Q, 100—120 mesh	Nitrogen, 30 ml/min	^{63}Ni ECD	36 ng/ml	Plasma	Column 170° C, injector 190°C, detector 250° C	41
	GC	OV-101 on Gas-Chrom Q, 100—120 mesh	Nitrogen, 20 ml/min	^{63}Ni ECD		Plasma, urine	Column 155° C, injector 210° C, detector 240° C; derivatization with trifluoroacetic anhydride	42
Ethionamide, prothionamide	HPLC	μPorasil (10 μm)	Diethyl ether—methanol (96:4), 1.3 ml/min	UV 295 nm	0.01 μg/ml	Plasma, serum urine		43

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TABLE 3 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
1-Ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-1,8-naphthyridine-3-carboxylic acid (AT-2266)	HPLC	μBondapak C_{18} (10 μm)	Methanol—0.1 *M* citric acid—acetonitrile (9:5:1 or 6:5:1), methanol—5% acetic acid—acetonitrile (6:10:1)	UV 340 nm	0.01 μg/ml (plasma); 0.1 μg/ml urine	Plasma, urine		44
4-Ethylsulphonyl-naphthalene-1-sulphonamine + metabolites	HPLC	Vydac RP (10 μm); μBondapak C_{18} (10 μm); Zorbax ODS (5—7 μm)	43% Methanol in 0.02 *M* ammonium acetate, 0.5 ml/min; isopropanol in 0.02 *M* ammonium acetate, gradient from 1% to 10% over 30 min, 0.5 ml/min	(1) UV 254 or 280 nm; (2) fluorescence 310/390 nm		Urine		45
	HPLC	RP				Urine, liver		46
Fenclofenac	GC	3% SE-30 on Chromosorb	Argon—methane (95:5), 50 ml/min	^{63}Ni ECD	0.3 μl/ml	Plasma	Derivatization with diazomethane	47
Furazolidone	HPLC	Pre-column Perisorb RP-8 (30—40 μm); analytical column Hypersil SAS	Water—acetonitrile (75:25), 1.75 ml/min	UV 360 nm	0.05 mg/kg	Liver, kidney		48
	HPLC	Partisil PXS 10/25 ODS	Methanol—water (30:70), buffered to pH 4.0 with dibasic sodium phosphate (16.5 m*M*) and sodium citrate (13.1 m*M*), 1.1 ml/min	UV, electrochemical detection	1 ng/ml	Plasma, serum		49
Iodochlorhydroxyquin (clioquinol, Chinoform, Vioform)	GC	3% OV-101 on Chromosorb W HP, 80—100 mesh	Argon—methane (9:1), 60 ml/min	ECD	50 ng/ml	Plasma	Column 195°C, injector 250°C, detector 300°C	50
	GC—MS	1% OV-17 on Chromosorb W AW DMCS, 80—100 mesh	Helium, 37 ml/min	Multiple-ion detection	1 ng	Plasma	Separation after acetylation; column, injector 215°C, separator 210°C, ion-source 200°C	51
	RP-HPLC	ODS-HC-SIL-X-I (10 μm); guard column Rheodyne RP-18-MPLC	Methanol—0.05 *M* phosphoric acid (70:30), 1 ml/min	UV 256 nm	0.2 μg	Urine, faeces, liver		52
	HPLC	ODS-HC-SIL-X-1; guard column RP-18-MPLC	Methanol—0.05 *M* phosphoric acid (80:20)	UV 256 nm	Below 1 μg/ml	Plasma		53

Iodochlorhydroxyquin + its conjugate	TLC	Silica gel	*n*-Butanol—acetone—diethylamine—water (30:20:4:30)	UV 267 nm	0.04 μg/ml	Plasma		54
Isoniazid + metabolites (acetylhydrazine, diacetylhydrazine and acetylisoniazid)	GC—MS	1% OV-17	Helium, 30 ml/min	MS	0.01—2 μg/ml for metabolites acetylhydrazine and diacetylhydrazine	Plasma	Trimethylsilyl derivatives of acetylisoniazid and diacetylhydrazine; benzaldehyde hydrazones of isoniazid and acetylhydrazine; column 90—270° C, programmed heating (10° C/min)	55
	GC—MS	1.5% OV-17 on Shimalite W, 80—100 mesh	Helium, 30 ml/min	MS		Rat hepatocytes	Separator 250° C; trimethylsilyl derivatives and benzaldehyde hydrazones	56
	GC—MS			MS		Urine	Trimethylsilyl derivatives	57
	HPLC	RP Ultrasphere-octyl (5 μm), 40° C	0.0425 *M* Phosphoric acid in 81% methanol pH 2.4, 1.5 ml/min	UV 285 nm	10 ng/ml	Serum	Stoichiometric transformation to acetylhydrazine	58
Isoniazid + metabolite (acetylisoniazid), rifampicin + metabolite (desacetylrifampicin)	HPLC	μBondapak C_{18} (10 μm)	Methanol—water (5:95) cont. 5 m*M* *n*-heptanesulphonic acid, 2 ml/min	UV 280 nm	95 ng/ml isoniazid; 85 ng/ml acetylisoniazid	Serum, polymorphonucleocytes, alveolar macrophages		59
	HPLC	Zorbax CN RP (6 μm)	Methanol—water—acetic acid (400:590:10) cont. 3 m*M* $CH_3COONa \cdot 3H_2O$	UV 330 nm	17 ng/ml isoniazid; 50 ng/ml acetylisoniazid	Plasma, serum		60
	HPLC	Silica (5—7 μm)	Chloroform—methanol—water—ammonium hydroxide (84.22:15:0.58:0.2), 0.5 ml/min	UV 254 nm		Plasma		61
	HPLC	Spherisorb nitrile (5 μm)	0.01 *M* Phosphoric acid in acetonitrile—water (20:80), 2 ml/min	UV 266 nm	0.02 μg/ml	Plasma		62
Isoniazid (A), rifampicin (B), acetylisoniazid (C)	HPLC	RP-18	Methanol—1% triethanolamine (85:15, pH 4.0 for A and B; 25:75, pH 4.0 for A and C)	UV 260 nm	0.5 μg A; 1.0 μg B and C	Serum		63
Mandelic acid	GC	(A) 3% OV-1; (B) 3% OV-17; or (C) 3% SP-1000 on Chromosorb W HP, 100—120 mesh	Nitrogen, 20 ml/min	FID	1 μg/ml	Plasma	Determination of butyl esters; column: (A) 120° C, (B) 140° C, (C) 170° C, injector and detector temperatures 30° C higher	64

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TABLE 3 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Methenamine	*GC*	*OV-17 capillary column*	*Nitrogen, 1.0—1.2 ml/min*	*Nitrogen-sensitive detection*		*Plasma, urine*	*Injector 240° C, oven 150° C, detector 250° C*	65
Nalidixic acid	GC	10% OV-17 on Chromosorb W HP, 80—100 mesh	Nitrogen, 20 ml/min	FID	0.1—0.3 μg/ml	Plasma	Column 270° C, injector 290° C, detector 290° C; flufenamic acid was added to deactivate the column	66
	GC	(A) 3% OV-1; (B) 3% OV-17; or (C) 3% SP-1000 on Chromosorb W HP, 100—120 mesh	Nitrogen, 20 ml/min	FID	1 μg/ml	Plasma	Determination of butyl ester; column: (A) 230° C, (B) 250° C, (C) 270° C, injector and detector temperatures 30° C higher	64
	HPLC	Partisil PXS 10/25 PAC	Methanol—0.1 *M* citrate buffer pH 3 (95:15), 1.6 ml/min	UV 254 nm	0.08 μg/ml (plasma); 0.42 μg/ml (urine)	Plasma, urine	Determination of main metabolite, 1-ethyl-1,4-dihydro-4-oxo-1,8-naphthyridine-3,7-dicarboxylic acid	67
	HPLC	(A) μBondapak C_{18}; (B) LiChrosorb 10 RP-18 C_{18} (10 μm)	63% Methanol in water for A; 70% methanol in water for B, 1.5 ml/min	UV 313 nm	10 ng per injection	Plasma		68
Nalidixic acid + metabolites (7-hydroxynalidixic acid and 7-carboxynalidixic acid)	HPLC	RP-8 Hewlett-Packard (10 μm)	Methanol—phosphate buffer pH 8.2 (55:45) cont. 2 g/l N,N,N-trimethylacetyl-ammonium bromide	UV 254 nm	0.5 μg/ml	Plasma, urine		69
Nalidixic acid + metabolite (hydroxy-nalidixic acid)	HPLC	μBondapak C_{18} (10 μm)	Water—methanol (1:1) cont. phosphate buffer pH 7.4; final concentration is 0.016 mol/kg phosphate and 0.12% (w/w) cetrimide, 1.5 ml/min	UV 313 nm	1 μg/ml			70
	TLC	Silica gel	Dioxane—5 × diluted conc. ammonia (3:1)	Fluorescence at 375/430 nm	0.16 μg/ml		Hydroxynalidixic acid may interfere	71
Nitrofurantoin, Urfadyn (hydroxy-methyl furantoin)	HPLC	LiChrosorb 5 RP-8 (5 μm)	Water with 5% ethanol, 1.6 ml/min	UV 370 nm	0.02 μg/ml	Plasma, urine		72
Nitrofurantoin	HPLC	LiChrosorb C_{18} RP	Methanol—0.01 *M* acetic acid (2.5:97.5), 2 ml/min	UV 280, 365 nm		Plasma, urine		73
	HPLC	μBondapak C_{18}	Water—methanol (100:10), gradient to 70:30 in 20 min, 4 ml/min	UV 280 nm		Liver, kidney, lung, small intestine walls, ileum, colon contents	Metabolite M-4 UV 365 nm	74

	HPLC	μBondapak C_{18} RP	Methanol—0.01 *M* sodium acetate buffer pH 5.0 (20:80)	UV 365 nm	Below 0.02 μg/ml	Plasma, urine		75
	HPLC	LiChrosorb	Methanol—water (50:50), 1 ml/min	UV 368—371 nm	0.2 μg/ml (HPLC); 0.4 μg/ml (polarography)	Serum	Combination of HPLC and differential pulse polarography	76
	HPLC	Knaur Fertigsäule RP-2 35°C	Acetonitrile—water—85% phosphoric acid (20:80:0.5), 2.2 ml/min	UV 380 nm	Below 10 μg/ml	Serum, urine		77
Nitrofurantoin, Urfadyn (hydroxymethylfurantoin)	HPLC	μBondapak C_{18}	30% or 40% methanol cont. 0.5% glacial acetic acid	UV 365 nm		Urine		78
Pefloxacin + metabolites (pefloxacin N-oxide, desmethylpefloxacin, norfloxacin)	HPLC	LiChrosorb RP-18 (10 μm)	(A) Dist. water; (B) acetonitrile—water (2:3). For pefloxacin 52% and 48% B; for metabolites gradient starting from 0—20% B and rising at a rate 2.5% per 10 min, 2 ml/min	UV 270 nm	0.05 μg/ml (plasma); 0.5 μg/ml (urine)	Urine, plasma	Mixture of acetonitrile and water contains 0.4% $Na_2HPO_4 \cdot 12H_2O$ and 0.2% tetrabutylammonium iodide pH 9.4	79
Pipemidic acid	HPLC	μBondapak C_{18} RP (10 μm); guard column Co:Pell ODS C_{18} (30 μm)	Serum: 46.8 g $NaH_2PO_4 \cdot 2H_2O$ in 75 ml methanol, 75 ml acetonitrile and 850 ml water; urine: 46.8 g $NaH_2PO_4 \cdot 2H_2O$ in 275 ml methanol and 725 ml water	UV 280 nm	0.1 μg/ml (serum); 5 μg/ml (urine)	Serum, urine		80
Protionamide, see Ethionamide								
Pyrazinamide + metabolites (5-hydroxypyrazine-2-carboxylic acid, pyrazinoic acid)	GC—MS	3% OV-17 on Chromosorb W HP, 80—100 mesh	Isobutane	MS	20 ng/ml	Serum, urine	Silyl derivatives; column programmed 120—180°C (15°C/min), then 250°C; no separator between GC and MS; connecting tube 240°C, inlet 250°C	81

(Continued on p. 414)

TABLE 3 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Resoxacin + N-oxide metabolite	HPLC	Partisil-PXS 10/25 PAC; pre-column Corasil	Acetonitrile—0.2 *M* phosphoric acid (98:2), 2 ml/min	UV 280 nm	0.13 μg/ml resoxacin in plasma; 0.64 μg/ml resoxacin in urine, 0.21 μg/ml metabolite in plasma; 0.60 μg/ml metabolite in urine	Plasma, urine		82
Rifampicin, see Dapsone, Isoniazid and chapter on Antibiotics								
Saddamine	TLC	Silica gel	Benzene—acetic acid (90:30)	UV 254 nm or ^{14}C liquid scintillation counting		Urine		83
Salicylic acid	GC	10 μm Methyl-silicone-coated fused-silica capillary column	Helium, 1.2 ml/min	FID		Urine	Silyl derivatives; injector and splitter 250° C, oven programmed 60—200° C (8° C/min), detector 250° C	84
Salicylic acid, salicyluric acid	HPLC	μBondapak C_{18} (10 μm)	Methanol—water—glacial acetic acid (50:60:1), 2 ml/min	Fluorescence at 240/350 nm	150 ng/ml salicylic acid; 300 ng/ml salicyluric acid	Plasma, urine		85
SC-38538, i.e. sodium 4-[2-(1-methyl-5-nitroimidazolylthio)-ethoxy]benzoate	LC	ODS Hypersil (5 μm)	50% Methanol—0.01 *M* KH_2PO_4, pH 3.5, 2 ml/min	UV 254 nm	0.05 μg/ml	Plasma, urine		86
Sulphadiazine + sulphathiazole, sulphamerazine, sulphapyridine	HPLC	LiChrosorb RP-8 (5 μm) for plasma; LiChrosorb RP-8 (10 μm) for urine; pre-column Whatman Co: Pell ODS	Plasma: pH 5 buffer—acetonitrile (80:16), 40° C, 2 ml/min urine: pH 4 buffer—acetonitrile (92:8), 40° C, 2.5 ml/min	UV 254 nm	250 ng/ml (plasma); 2.5 μg/ml (urine)	Plasma, urine		87

Sulphadiazine, sulphamethazine, sulphamerazine	HPLC	LiChrosorb RP-C_2 (10 μm)	400 ml Methanol + 600 ml water + 1.6 g lithium perchlorate	Electrochemical detection, amperometric determination	10 ng/g	Liver, kidney, muscle tissues		88
	HPLC	LiChrosorb RP-C_2 (10 μm)	Methanol—water (25:75 or 40:60) with 0.01 *M* lithium perchlorate	Electrochemical detection	10 ng/ml	Milk		89
Sulphadiazine, sulphadimethoxine, sulphamethazine, sulphisoxazole	LC—MS	Whatman PXS 10/25 ODS	Linear gradient acetonitrile—water (10:90 to 90:10) over 10 min	UV 254 nm, detector connected with Hewlett-Packard DLI LC—MS system	Low nanogram range	Plasma, urine		90
Sulphadiazine, sulphamerazine, sulphamethoxazole, N-acetylsulphamethoxazole	HPLC	μBondapak/C_{18} RP ODC		UV 254 nm		Plasma	GPC on Sephadex G-25 column connected with HPLC	91
Sulphadiazine, sulphamethoxazole	TLC	Silica gel	Toluene—isopropanol (8:2); chloroform—ethanol (8:1 or 8:2)	Densitometry 575 nm	2.5 μg/ml (plasma); 10 μg/ml (urine)	Urine, plasma		92
Sulphadiazine, sulphadimethoxine, sulphisomidine	TLC				0.5 μg per spot	Plasma		93
Sulphadiazine, sulphamethazine	GC	5% OV-61 on Gas-Chrom Q, 80—100 mesh	5% Methane in argon, 30 ml/min	^{63}Ni ECD	50 pg/ml	Urine	Column 260° C, injector 270° C, detector 350° C	94
	GC, TLC					Fat, kidney, liver, porcine muscle		95
	HPLC	LiChrosorb 10 RP 18	Acetonitrile—10 m*M* acetate buffer pH 4.0 (1:9), 2.0 ml/min	UV 254 nm		Plasma		96

(Continued on p. 416)

TABLE 3 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Sulphamethazine + polar metabolite	HPLC	μBondapak C_{18}	(A) Methanol—water (5:95); (B) acetonitrile—isopropanol—water (5:0.5:94.5); (C) methanol—water (30:70), 2 ml/min	UV 250 nm		Porcine liver	Connected with MS	97
	TLC	Silica gel	Benzene—methyl ethyl ketone—ethanol—water (30:30:30:30)	^{14}C Liquid scintillation		Porcine liver	Metabolite eluted and purified with HPLC (see above)	97
Sulphamethazine + metabolite	TLC	Silica gel	Benzene—methyl ethyl ketone—ethanol—water (30:30:30:30)	^{14}C Liquid scintillation		Liver, kidney, muscle, fat		98
Sulphamethoxazole + N-acetyl metabolite	HPLC	(A) LiChrosorb Si 100 C_{18} RP (10 μm); (B) LiChrosorb C_8 RP (7 μm)	(A) Methanol—water (3:7); (B) acetonitrile—water (1:3)	UV 254 nm	2 μg/ml	Urine		99
	LC	LiChrosorb RP-8 (10 μm) 55° C	Acetonitrile—5 m*M* aq. acetic acid (1:3), 1.0 ml/min	UV 273 nm		Serum		100
Sulphamethoxydiazine + metabolites (aniline, 2-amino-5-methoxypyrimidine, acetanilide, 2-amino-pyrimidine, 2-amino-4-methylpyrimidine, 2-aminothiazole	GC—MS, pyrolysis	8% Carbowax 20 M and 2% KOH on Chromosorb W AW DMCS, 100—120 mesh	*Helium or nitrogen, 50 ml/min*	FID	50 ng	*Urine*	*Pyrolyser connected to GC dual columns; pyrolysis 770° C 5 sec, injector 275° C, detector 350° C, column programmed from 100° C to 245° C (5° C/min)*	101
Sulphamethoxy-pyridazine	HPTLC	Silica gel	Chloroform—acetic acid—methanol (18.2:1.0:0.8)	Fluorescence at 366 nm		Plasma		102
Sulphapyridine	HPLC	RP-18 (5 μm)	0.05 *M* Na_2HPO_4, 0.01 *M* 1-hexanesulphonate, sodium salt, 0.0072 *M* triethylamine and 15% methanol, 1.0 ml/min	Fluorescence at 395/470 nm	5 ng/ml	Saliva	On-line derivatization with fluorescamine	103
Sulphapyridine + N-acetyl derivative	*HPLC*	μBondapak CN	Aq. 0.4% sodium acetate and 4% acetic acid, 2.0—2.3 ml/min	UV 254 nm	0.25 μg/ml	*Plasma, saliva*	Metabolites of propoxyphene may interfere	104
	LC	Silica	Chloroform—acetonitrile—methanol—35% ammonia (65.5:30:4:0.5), 1 ml/min					105
	GC, HPLC				5 ng	Plasma, saliva, urine		106

Sulphapyridine, sulphaguanidine, sulphamerazine, sulphamethazine, sulphanilamide, sulphathiazole, sulphisoxazole, acetylsulphisoxazole	HPLC		Water—methanol (60:40) adjusted to pH 4.0 with acetate buffer	UV 254 nm	10 ng/ml	Plasma		107
Sulphapyridine, sulphamethazine, sulphamethoxazole	HPLC	μBondapak RP C_{18}	0.07 *M* KH_2PO_4—0.07 *M* Na_2HPO_4—ethanol—methanol (780:200:100:100)	UV 254 nm	1 μg/ml	Serum		108
Sulphaquinoxaline	HPLC	Spherisorb S10 W (10 μm)	*n*-Hexane—*n*-hexane saturated with water—chloroform—acetonitrile—methanol—25% ammonia (36:30:15:14.5:4.5:0.05 or 37:30:15:14.5:3.5:0.05)	UV 254 nm	Below 10 ppb	Liver, muscle		109
Sulphisoxazole + N-acetyl metabolite	HPLC	Pre-column Corasil	Water—methanol (60:40) adjusted to pH 4.0 with acetate buffer	UV 254 nm	10 ng/ml	Plasma, urine		110
	HPLC	LiChrosorb RP-18 Hibar II RP	Methanol—0.01 *M* sodium acetate (see Note) pH 4.7 (32:68), 1.2 ml/min	UV 254 nm	Below 0.05 μg/ml	Plasma, urine	0.01 *M* sodium acetate: 680 ml water, 320 ml methanol, 0.6 ml acetic acid and pH adjusted to 4.7 with 4 *M* sodium hydroxide	111, 112
Sulphasalazine (salazosulphapyridine) + metabolite (sulphapyridine)	HPLC	Nucleosil RP-18 (10 μm)	50% Methanol cont. 1 g/l N,N,N-trimethylcetylammonium bromide, 1.3 ml/min	Fluorescence at 310/430 nm	0.25 μg/ml	Plasma		113, 114
	HPLC	Hypersil-SAS (5 μm)	22.5% Methanol and 0.05 *M* phosphate buffer cont. 0.1% tetrabutylammonium hydrogen sulphate, 1 ml/min	UV 290 nm, coupled with fluorescence at 320/389 nm		Plasma		115
	HPLC	LiChrosorb RP-18 (5 μm); guard-column Chrompack	Water adjusted to pH 3.3 with 0.01 *M* citric acid and 20% methanol, 1.4 ml/min	Fluorescence at 305 nm, cut-off filter 396 nm	0.1 μmol/l	Serum, urine, faeces		116
Sulphasalazine + metabolites (5-aminosalicylic acid, N-acetyl-5-aminosalicylic acid, sulphapyridine, N-acetylsulphapyridine	HPLC	Hypersil-SAS (5 μm)	Methanol—0.05 *M* phosphate buffer pH 7.4 (15:85), 1 ml/min	Fluorescence at 310/410 nm, UV 260 nm	0.05 mg/l *p*-aminosalicylic acid; 0.06 mg/l N-acetyl derivative (fluorescence detection)	Plasma		117

(Continued on p. 418)

TABLE 3 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Sulphasalazine (A) + metabolite [sulphapyridine (B)]	HPLC	(A) LiChrosorb Si 60 (5 μm); (B) μBondapak/Corasil	For A: chloroform—methanol—35% ammonia (96.5:4:0.5); for B: 0.01 *M* phosphate buffer pH 7.7 with 17% acetonitrile, 1 ml/min	UV 365 nm	700 pg/ml A; 5 ng/ml B	Plasma		118
Taurolin + metabolite (1,1-dioxyperhydro-1,2,4-thiadiazine, DPT)	HPLC	Hypersil (5 μm)	Chloroform—heptane (40:60) for DPT; methanol—chloroform (2:98) for DNS taurine amide, 1 ml/min	UV 254 nm or fluorescence	Below 5 μg/ml DPT	Serum	Dns derivatives	119
Tetroxoprim (TXP), sulphadiazine	HPLC	LiChrosorb RP 8 (10 μm) for urine μBondapak C_{18} (10 μm) for serum	Acetonitrile—water pH 7.8 (alkalized with ammonium carbonate), concentration of acetonitrile programmed from 5% to 95% (12 min), 3 ml/min Methanol—water (50:50) adjusted to pH 4.6 with acetic acid for tetroxoprim; acetonitrile—1% acetic acid (16:84) for sulphadiazine	UV 254 nm	50 ng/ml tetroxoprim; 150 ng/ml sulphadiazine	Urine, serum		120
Tetroxoprim (TXP), sulphadiazine (SDZ), methioprim (MTP)	HPLC	ODS Hypersil (5 μm)	TXP and SDZ: 800 ml 0.1 *M* KH_2PO_4 cont. 1% acetic acid, 1% ethyl acetate and 200 ml acetonitrile, 1.3 ml/min; MTP and SDZ: the same mobile phase, 1.3 ml/min for 3 min, then 2.3 ml/min	UV 254 nm	50 ng/ml TXP and 100 ng/ml SDZ; or 40 ng/ml MTP and 100 ng/ml SDZ	Serum, prostatic secret		121
	TLC	Silica gel	Chloroform—methanol—methyl ethyl ketone—ammonia (60:22:10:4); chloroform—*n*-propanol—formic acid (4:4:2); *n*-butanol—water—acetic acid (4:3:1)	^{14}C Autoradiography		Urine, plasma		122
Tetroxoprim, trimethoprim	TLC	Silica gel silanized	0.3 *M* sodium chloride—acetone—10 *M* acetic acid (100:50:0.5)	Fluorescence densitometry	50 ng/ml	Plasma		123

Thiacetazone	HPLC	μBondapak RP (10 μm); pre-column Co:Pell ODS	Acetonitrile—water (3:7), 1.5 ml/min	UV 328 nm	3 ng/ml	Plasma, urine		124
Triclocarban (3,4,4′-trichlorocarbanilide)	HPLC	μBondapak C_{18} RP	Water—acetonitrile (66:34), gradient to 30:70, 2.0 ml/min	UV 258 nm		Urine, plasma		125
	HPLC	μBondapak C_{18} RP	Water—acetonitrile (66:34), gradient to 30:70, 2.0 ml/min	UV 258 nm		Bile		126
Trimethoprim	GC	10% Poly S-179 on Chromosorb W HP, 80—100 mesh	Helium, 45 ml/min	NPD	0.1 μg/ml	Plasma, urine	Column 330° C, injector and manifold 350° C	127
	HPLC	Porasil (10 μm)	Chloroform and a mixture methanol—water—ammonia (150:9:1) (500:25), 1.5 ml/min	UV 258 nm	0.01—0.02 μg/ml	Plasma, blood, urine		128
	HPLC	Nucleosil C_{18} (5 μm)	0.07 *M* KH_2PO_4 pH 4.75—methanol (3:1), 1.5 ml/min	UV 280 nm or electrochemical detection	0.1 ppm (UV) or 0.01 ppm (electrochemical detection)	Plasma, urine		129
Trimethoprim + metabolites	HPLC	LiChrosorb RP-18 (5 μm)	0.1 *M* KH_2PO_4 buffer pH 7.5—acetonitrile cont. $0.7 \cdot 10^{-3}$ *M* tetrabutylammonium hydrogen sulphate (85:15), 1.0 ml/min	UV 254 nm, connected with electrochemical detector	0.1 ppm	Urine	Hydrolysis of conjugates with β-glucuronidase	130
	HPLC	RP-8 (10 μm)	Methanol—0.015 *M* sodium borate pH 9 (35:65), 1.0 ml/min	Fluorescence at 279/370 nm	0.1 μg/ml	Plasma, urine		131
Trimethoprim, sulphadiazine, N-acetylsulphadiazine	HPLC	LiChrosorb Si 60 (10 μm); pre-column LiChrosorb Si 60 (25—40 μm)	Dichloromethane—methanol—25% ammonia (80:19:1), 1.5 ml/min	UV 289 nm	0.03 μg/ml	Serum, urine		132

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TABLE 3 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Trimethoprim, sulphamethazine, sulphadiazine, sulphamerazine, sulphathiazole	TLC				0.1 μg/ml	Serum, plasma, blood		133
Trimethoprim, sulphamethoxazole (co-trimoxazole)	HPLC	RP Spherisorb ODS (10 μm)	Acetonitrile—aq. 0.1 *M* KH_2PO_4 cont. 1% acetic acid and 1% ethyl acetate pH 2.5 (30:70), 1 ml/min; for trimethoprim: methanol—water—acetic acid (40:60:1) pH 3.2, 2 ml/min	UV 254 nm	0.1–0.2 μg/ml	Plasma		134
Trimethoprim, sulphamethoxazole, N-acetylsulphamethoxazole	HPLC	μBondapak C_{18} (10 μm); 30°C for serum, room temperature for urine	Methanol—1% acetic acid (200:800)	UV 230 nm	0.1 μg/ml trimethoprim and 1.0 μg/ml for both sulphonamides	Serum, urine	Small peak of caffeine may interfere in serum	135
	HPLC	LiChrosorb Si-60 (5 μm); pre-column LiChroprep Si-60 (25—40 μm)	Chloroform—methanol—water—ammonia (94.5:5:0.25:0.19) (solvent A), 3 min; then solvent B, dtto (79:20:1:0.15), 8 min; programming 0—3 min solvent A, 3.5 min A+B (1:1), 4—12 min solvent B, 12.5 min A+B (1:1), 13—16 min solvent A, 2 ml/min	UV 280 nm	15 ng/ml trimethoprim; 20 ng/ml sulphamethoxazole; 10 ng/ml acetylsulphamethoxazole	Plasma, urine		136
	HPLC	μBondapak C_{18} RP	Methanol—0.067 *M* phosphate buffer pH 3.5 (35:65), 1 ml/min	UV 225 and 254 nm	0.05 μg/ml trimethoprim; 0.2 μg/ml sulphamethoxazole; 0.5 μg/ml acetyl derivative	Serum		137
	HPLC					Serum, urine		138

Trimethoprim, sulphamethoxazole	HPLC	Waters-RP C_{18} (10 μm)	11.867 g $Na_2HPO_4 \cdot 2H_2O$ dissolved in 1 l water (A); 9.073 g KH_2PO_4 in 1 l water pH 5.0 (B); 9.5 ml A is made to 1 l with B, phosphate buffer pH 5.0; phosphate buffer—ethanol (80:20), 1 ml/min	UV 230 and 280 nm	0.5 μg/ml	Plasma	139
Trimethoprim, sulphamethoxazole + metabolite (N-acetyl-sulphamethoxazole)	RP-LC		45% Methanol—water cont. 10 m*M* phosphoric acid, 2 ml/min	UV 270 nm		Plasma, serum, urine	140
	HPLC					Serum	141
Urfadyn, see Nitrofurantoin							

TABLE 4

ANTICHOLINERGICS AND CHOLINERGICS

See also Antiparkinsonics (Table 12).

Drugs separated	*Method*	*Stationary phase*	*Mobile phase or carrier gas*	Detection	Sensitivity	Source	Note	Ref.
Afloqualone	TLC	Silica gel	Benzene—tetrahydrofuran (3:7 or 1:1); tetrahydrofuran—chloroform—acetone—conc. ammonia (15:10:10:1); *n*-butanol—acetic acid—water (4:1:1)	^{14}C Autoradiography		Urine, plasma, bile	Combination with GC—MS	142, 143
Aprophen	HPLC	Partisil 5	Methanol—acetonitrile (30:70) with 0.01% triethanolamine, 1 ml/min	UV 254 nm		Serum		144
Benzilonium bromide	GC—MS	3% OV-225, column directly interfaced with the ion source	Methane, 20 ml/min	MS	Below 5 ng/ml	Plasma	Oven 175°C, injector 200°C, source 250°C; separation after oxidation to benzophenone	145
Biperiden, see Antiparkinsonics								
(−)-1-Cyclopropylmethyl-4-(3-trifluoromethylthio-5H-dibenzo[*a,d*]cycloheptен-5-ylidene) piperidine	GC	3% OV-17 on Gas-Chrom Q, 80–100 mesh	Helium, 30 ml/min	Nitrogen-sensitive detection	6 ng/ml	Plasma, urine	*Column 250°C, detector 275°C,* injector 300°C	146
Edrophonium, see Pyridostigmine								
Galanthamine hydrobromide	HPLC	Polygosil 60-C_{18} RP (5 μm)	Dichloromethane—*n*-hexane—ethanolamine (500:500:0.5), 1 ml/min	UV 235 nm	5 ng/ml	Serum, urine, bile		147
	HPLC	CP™ Micro-Spher Si (3 μm) Chrompack	Dichloromethane—*n*-hexane—ethanolamine (500:500:0.5), 1 ml/min	UV 235 nm	5 ng/ml	Serum, urine, bile		147
Neostigmine, see Pyridostigmine								
Prifinium bromide	HPLC	LiChrosorb Si 60 (5 μm)	10% 1 *M* Ammonium acetate pH 10 in methanol, 1 ml/min	UV 254 nm	Below 0.5 ng/ml	Serum, urine		148

Proglumide (xylamide)	HPLC	Zorbax SIL	Chloroform—methanol (24:1), 1.5 ml/min	UV 240 nm	0.05 μg/ml	Plasma		149
Propantheline	HPLC	μBondapak C_{18} (10 μm)	Acetonitrile—0.1 *M* KH_2PO_4 pH 3.0 (4:6), 1.5 ml/min	UV 210 nm	Below 5 ng/ml	Serum		150
Pyridostigmine	HPLC	μBondapak C_{18} (10 μm)	37.5% Acetonitrile in water cont. 0.001 *M* sodium dodecyl sulphate and 1% acetic acid, final pH 4.0, 1 ml/min	UV 269 nm	Below 20 ng/ml	Plasma		151
Pyridostigmine, neostigmine, edrophonium + metabolites	HPLC	LiChrosorb RP-18 (10 μm)	0.01 *M* $C_7H_{15}SO_3^-Na^+$ and 0.01 *M* NaH_2PO_4 in acetonitrile—water (15:85), pH 3.0, 2 ml/min	UV 214 nm	Below 5 ng/ml	Serum		152
	HPLC	Ultrasphere-octyl	0.01 *M* $C_7H_{15}SO_3^-Na^+$, 0.01 *M* NaH_2PO_4 and 0.025 *M* trimethylamine chloride in acetonitrile—water (20:80), pH 3.0, 2 ml/min	UV 214 nm	Below 5 ng/ml	Serum		152
	HPLC	Ultrasphere-octyl	Acetonitrile—water (17:83)	UV 214 nm	Below 5 ng/ml	Serum		152
Tacrine (tetrahydroaminoacridin)	HPLC	μBondapak C_{18} (5 μm),	0.1 *M* Phosphoric acid pH 2.8—acetonitrile (16:2), 1.5 ml/min	UV 254 nm or fluorescence at 385/425 nm	100 ng/ml	Plasma	Sep-Pak C_{18} used for extraction	153
Tetrazepam + metabolites	HPLC	RP C_{18} column	Acetonitrile—water (40:60) cont. 5 m*M* perchloric acid and 10 m*M* sodium perchlorate	UV 254 nm		Urine		154
	TLC	Silica gel	Toluene—acetone (9:1)			Urine	Separation of metabolites, combination with IR	154

TABLE 5

ANTICOAGULANTS

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Acenocoumarol (Sintrom)	HPLC	LiChrosorb RP-2 (10 μm)	0.75 g Ammonium acetate in 100 ml acetonitrile—water—acetic acid (37:62:1), 40 ml/h	UV 305 nm	Nanogram range	Plasma		155
	HPLC	LiChrosorb RP-8 (5 μm)	0.1% Acetic acid—acetonitrile—ethyl acetate pH 4.9 (100:90:1), 1.5 ml/min	UV 303 nm	20 ng/ml	Plasma		156
	HPLC	μBondapak C_{18} (10 μm)	Ethanol—water (1:1) cont. 1% of 98% acetic acid, 1.4 ml/min	UV 313 nm	10 ng/ml	Plasma		157
Acenocoumarol + reduced derivative (Aminosintrom)	TLC	Silica gel	Ethyl acetate—methanol—triethanolamine (70:30:3)	UV 366 nm	0.01 μg/ml	Plasma	Layer immersed into fluorescamine solution; reduction of Sintrom by $SnCl_2$ to Aminosintrom	158
	TLC	Silica gel	(A) Light petroleum—acetone (140:60); (B) benzene—ethyl acetate (140:60)	UV 254 nm; then elution and liquid scintillation		Plasma, urine	^{14}C	159
Biscoumacetate	HPLC	μBondapak C_{18}	Methanol—water—acetic acid (56:40:4), 1 ml/min	UV 254 and 280 nm	Below 0.1 μg/ml	Plasma		160
Brodifacoum, see Warfarin								
Difenacoum, see Warfarin								
Diphenadione (diphacinone)	TLC	Silica gel	(A) Toluene—methanol—diethylamine (70:20:10); (B) chloroform—methanol—water (80:20:4); (C) toluene—acetone—acetic acid (75:20:5); (D) toluene—dioxane—acetic acid (76:21:3)	UV and autoradiography		Urine, faeces, liver	^{14}C	161
Ethyl biscoumacetate, see Warfarin								
Nafazatrom	HPLC	LiChrosorb Si 60 (10 μm)	Dichloromethane—methanol (90:10) cont. 0.25% water, 1.0 ml/min	UV and fluorescence at 232/362 nm	5 ng/ml	Plasma		162

Phenindione (Pindione)	GC	10% SE-30 on Chromosorb W NAW HMDS, 60—80 mesh	Nitrogen, 35 ml/min	FID	10 μg/ml	Plasma	Column 270 °C, injector 280°C, detector 300°C	163
Phenprocoumon, (see also Warfarin)	HPLC	LiChrosorb RP-18 (10 μm); pre-column Bondapak C_{18} Corasil (35—50 μm)	Plasma: acetonitrile—water—acetic acid (600:400:5), 2.0 ml/min; urine: gradient elution acetonitrile—water—acetic acid (400:600:5) (A); acetonitrile—acetic acid (1000:5) (B); linear gradient from 0 to 100% B in 30 min, 2.0 ml/min		0.1 μg/ml (plasma); 0.02 μg/ml (urine)	Plasma, urine		164
	TLC	Silica gel	Methanol—triethylamine (80:20) for cleaning the plate; then chloroform—methanol—triethylamine (95:15:5)	UV 254 nm	5 ng/ml	Plasma	Lover edge of the plate is impregnated with pentane—triethylamine (100:10) to stabilize phenprocoumon	165
Previscan (Fluorindion)	GC	10% SE-30 on Chromosorb W NAW HMDS, 60—80 mesh	Nitrogen, 35 ml/min	FID	10 μg/ml	Plasma	Column 270°C, injector 280°C, detector 300°C	163
Warfarin, phenprocoumon	GC	(A) 3% OV-1; (B) 3% OV-17; (C) 3% SP-1000; all on Chromosorb W HP, 100—120 mesh	Nitrogen, 20 ml/min	FID	1 μg/ml	Plasma	Column for warfarin: (A and B) 250°C, (C) 270°C; for phenprocoumon: (A) 230°C, (B) 250°C, (C) 270°C; detector and injector 30°C higher	64
	GC	3.8% Vinyl methyl silicone on Gas-Chrom W HP, 80—100 mesh	Helium, 60 ml/min	FID	0.3 μg/ml	Plasma		166
	GC—MS			SIM		Plasma		167
Warfarin, warfarin alcohol	GC—MS			MS		Plasma		168
Warfarin, phenprocoumon	HPLC	μBondapak C_{18} (10 μm)	Water cont. 0.1% of 99.8% acetic acid—ethanol (1:1), 1.5 ml/min	UV 254 nm		Plasma, urine		169
Warfarin	HPLC	Partisil (5 μm)	*n*-Hexane—ethanol (93.5:6.5), 1.5 ml/min	UV 280 nm	Below 0.05 μg/ml	Serum, plasma		170

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TABLE 5 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Warfarin, difenacoum, brodifacoum (*cis*-, *trans*-isomers)	HPLC	Magnusil 8H C_{22} RP (5 μm)	Methanol, 1 ml/min; cyclohexane—dichloromethane—acetic acid (75:25:0.6), 1 ml/min; or RP chromatography: methanol—water—acetic acid (80:20:0.8), 1 ml/min	Fluorescence at 315/410 nm, UV 260 nm	0.05—0.1 μg/g warfarin; 0.02 μg/g other compounds	Liver, stomach, serum, urine	If analysis of warfarin is not required, sensitivity can be about 1 pg/g	171
Warfarin	HPLC	μBondapak C_{18}	Methanol—acetic acid—water (75:0.5:25), 1 ml/min	UV 313 nm	Below 0.3 μg/ml	Plasma		172
Warfarin + metabolites (diastereomeric warfarin alcohols, 4′-, 6-, 7-, 8-hydroxywarfarin)	HPLC	Partisil-10 PAC (10 μm)	75% *n*-Heptane—25% solution cont. 79.3% 1,2-dichloroethane, 20% ethanol and 0.7% acetic acid, 2 ml/min	Fluorescence at 318/393 nm (295 nm shoulder)	0.18 ng	Urine, plasma	Post-column reagent solution: 10% triethylamine and 90% solution cont. 75% *n*-heptane, 20% 1,2-dichloroethane and 5% ethanol	173
Warfarin, acenocoumarol, ethylbiscoumacetate	HPLC	Silanized LiChrosorb Si 60	0.2 *M* Na_2HPO_4—acetonitrile (75:25) cont. 0.01 *M* tetrabutylammonium bromide			Plasma		174
	HPLC	Bondapak C_{18}			0.06—9.0 μg/ml	Plasma		175
	HPLC	Spherisorb Si (5 μm)	Ethyl acetate—*n*-hexane—methanol—acetic acid (25:74.75:0.25:0.4), 1 ml/min	UV 313 nm	0.16 μg *S*(—); 0.096 μg *R*(+)	Plasma	Separation of isomers *R*(+) and *S*(—); esterification with carbobenzyloxy-L-proline	176
	HPLC	RP	Methanol—water pH 4.3 (63:37)	UV 254 nm	0.5 μg/ml	Plasma		177

TABLE 6

ANTIDIABETICS

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Acetohexamide, hydroxyhexamide (see also Tolbutamide)	LC	LiChrosorb	0.2% Acetic acid—acetonitrile (1:1)			Plasma		178
Carbutamide (see also Tolbutamide)	HPLC	Styrene—divinylbenzene copolymer, ammonium-substituted (Hitachi 3011-N)	0.1 *M* Sodium hydroxide—0.1 *M* sodium chloride in 65% methanol, 1.1 ml/min	UV 254 nm		Serum		179
Chlorpropamide, see Glipizide, Tolbutamide								
Ciglitazone + monohydroxy metabolites	HPLC	Supelcosil LC-18 (5 μm); pre-column Spheri-5 RP 18	Acetonitrile—7 m*M* phosphoric acid pH 2.5 (4:6 or 7:3)	UV 229 nm	0.05 μg/ml	Serum		180
Glibenclamide, see Glyburide								
Glibornuride (see also Glyburide, Tolbutamide)	HPLC	LiChrosorb C_8 RP (10 μm) 50°C	Methanol—water (7:3)	UV 230 nm	0.5 μg/ml	Serum		181
Gliclazide	GC	3% XE 60 on Chromosorb W AW DMCS, 80—100 mesh	Nitrogen, 30 ml/min	^{63}Ni ECD	0.02 μg per sample	Plasma	Derivatization with diazomethane and heptafluorobutyric anhydride; column 220°C, injector and detector 280°C	182
		Silanized glass column; 2% OV-101 on Chromosorb, W AW DMCS, 100—200 mesh	Helium, 30 ml/min	NPD			Column 220°C, injector 280°C, detector 300°C	
	GC			ECD	0.2 μg/ml	Plasma		183
	HPLC	Jasco RP SC-OL	Methanol—0.2% acetic acid (3:2)	UV 227 nm	0.3 μg/ml	Plasma		183
	HPLC	Diaion CDR-10 (7 μm)	Acetonitrile—methanol—1.2 *M* ammonium perchlorate (4:3:7), 0.4 ml/min	UV 227 nm	0.2 μg/ml	Serum, plasma		183, 184
	HPLC	Sc-01 and CDR-10			0.2—0.3 μg/ml	Serum		185
	TLC	Silica gel	Chloroform—acetone—acetic acid (13:6:1); ethyl acetate—chloroform—acetic acid (3:2:1)	Autoradiography		Plasma	^{3}H	186

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TABLE 6 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Glipizide (Glibenese), tolbutamide, chlorpropamide, glyburide (see also Tolbutamide)	HPLC	μBondapak C_{18} (10 μm)	Methanol—0.01 *M* phosphate buffer pH 3.5 (60:40)	UV 225 nm (glipizide)	10 ng/ml glipizide; other drugs approx. several μg/ml	Serum	Only benzene is suitable for extraction; 3-*cis*-hydroxycyclohexyl and 4-*trans*-hydroxycyclohexyl metabolites interfere	187
Glipizide + metabolites and splitting products	TLC	Silica gel	Cyclohexane—ethyl acetate—acetic acid (60:40:2); chloroform—methanol—acetic acid (100:3:1); cyclohexane—ethyl acetate (70:30)	Fluorescence at 366/510 nm	Below 10 ng per spot	Serum	Dns derivatives	188
Glyburide (glibenclamide, glyburone, Maninil), tolbutamide	GC	5% OV-17 on Gas-Chrom G AW DMCS, 80—100 mesh	Argon—methane (95:5), 100 ml/min	^{63}Ni ECD	Below 5 ng/ml	Plasma		189
	HPLC	LiChrosorb RP-18 (5 μm)	Acetonitrile—12 m*M* perchloric acid (47:53), 2.0 ml/min (A); acetonitrile—5 m*M* phosphoric acid, 2 ml/min (B); acetonitrile—phosphate buffer pH 6, 2 ml/min (B); acetonitrile—perchloric acid, 2 ml/min (B)	UV 230 nm	10 ng/ml	Plasma	(A) Separation of contaminants from serum; after 9 min programming to 100% acrylonitrile during 2 min; (B) determination of the drugs	190
	HPLC	LiChrosorb Si-60 (10 μm)	99% Ethanol—*n*-heptane—diisopropyl ether (30:600:400), 2 ml/min	Fluorescence at 468/522 nm	5 ng/ml	Serum	Pre-column derivatization with NBD-chloride (7-chloro-4-nitrobenzofurazane)	191
Glyburide, tolbutamide, glibornuride	HPLC			UV	Below 50 ng/ml	Serum		192
	HPLC	LiChrosorb RP-18	Acetonitrile—0.05% phosphoric acid (45:55), 1.1 ml/min	UV 230 nm	10 ng/ml	Serum		193, 194
	HPLC	Spherisorb ODS (5 μm)	Acetonitrile—1/15 *M* phosphate buffer pH 7 (2:5), 2 ml/min	UV 228 nm	5 ng/ml	Serum		195
	HPLC	LiChrosorb RP-8 (5 μm)	0.05 *M* $NH_4H_2PO_4$—acetonitrile (1:1), 1.2 ml/min	UV 228 nm	20 ng/ml	Serum		196
	HPLC	LiChrosorb RP-8 (10 μm)	0.05 *M* $NH_4H_2PO_4$—acetonitrile (52:48), 1.4 ml/min	Fluorescence at 308/360 nm	10 ng/ml	Serum		197
	HPTLC	Silica gel	Chloroform—methanol—conc. ammonia (15:3:0.2)	Reflectance mode scanning at 300 nm	5 ng/ml	Serum		195
	HPLC	Magnusphere C_{18} RP (5 μm)	0.05 *M* Ammonium phosphate—methanol (38:62), 0.8 ml/min	UV 225 nm	2 ng/ml	Plasma		198
Glycodiazine, see Tolbutamide								

Metformin	GC	3% OV-17 on silanized Chromosorb W, 80—100 mesh	Nitrogen, 40 ml/min	Nitrogen-sensitive detection (KCl salt)	25 ng/ml	Plasma	Oven 250° C; derivatization with *p*-nitrobenzoyl chloride	199
Phenformin (Dipar)	HPLC	μBondapak C_{18}	Methanol—water (1:1) cont. 0.02% acetic acid and $5 \cdot 10^{-3}$ *M* 1-heptanesulphonic acid, 1 ml/min	UV 235 nm	10 ng/ml (plasma); 250 ng/ml (urine)	Plasma, urine		200
Tolazamide, see Tolbutamide								
Tolbutamide, chlorpropamide, glipizide, glibenclamide, glibornuride, tolazamide	GC	3% OV-17 on Gas-Chrom Q, 100—120 mesh	Nitrogen, 40 ml/min	FID, ECD	20 ng/ml	Plasma	Methyl derivatives; injector and detector 330° C, oven 300° C for glipizide derivatives, 220° C for tolbutamide derivatives	201
Tolbutamide, chlorpropamide, carbutamide, tolazamide, glycodiazine	GC	(A) 3% SE-30; (B) 5% SE-30; (C) 2% OV-17; all on Chromosorb W AW DMCS, 80—100 mesh	Helium, 40 ml/min	^{63}Ni ECD	250 ng/ml tolbutamide and chlorpropamide; 3000 ng/ml carbutamide; 500 ng/ml tolazamide; 1500 ng/ml glycodiazine	Blood	Derivatization with diazomethane and trifluoroacetic anhydride; column temperatures: (A) 1 min at 195° C, 10° C/min to 250° C, 5 min at 250° C; (B) 1 min at 220° C, 10° C/min to 280° C, 5 min at 280° C; (C) 1 min at 210° C, 10° C/min to 250° C, 5 min at 250° C	202
Tolbutamide, chlorpropamide	HPLC	μBondapak C_{18} RP	Acetic acid—acetonitrile (72:28), 2.2 ml/min	UV 254 nm	6 μg/ml tolbutamide; 7 μg/ml chlorpropamide	Serum		203
Tolbutamide + metabolite (carboxytolbutamide)	HPLC	μBondapak C_{18} 28° C	Acetonitrile—phosphate buffer pH 3.9 (35:65)	UV 254 nm	2 μg/ml tolbutamide; 0.1 μg/ml carboxytolbutamide	Plasma		204
	HPLC	μBondapak C_{18}	Methanol—0.2% acetic acid (3:2), 1.2 ml/min	UV 228 nm	200 ng/ml	Plasma		200
Tolbutamide + metabolites (carboxytolbutamide, hydroxymethyl derivative)	HPLC	ODS-Sil-X-1	Water—acetonitrile (78:22)			Plasma		205
	Micro-HPLC	μBondapak	Acetonitrile—0.05% phosphoric acid (45:55), 1.5 ml/min	UV 200 nm	0.5 μg/ml	Plasma	100-μl Aliquots	206
	HPTLC	Silica gel	Chloroform—acetic acid—methanol (18.2:1.0:0.8)	Fluorescence at 366 nm		Plasma		102
Tolbutamide, see also Glipizide, Glyburide								

TABLE 7

ANTIEMETICS

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Alizapride	HPLC	μBondapak C_{18}	Methanol—pH 8.1 buffer (80:20), 2 ml/min	Fluorescence at 323/380 nm	5 ng/ml	Plasma, urine		207
Bromide (Viaben) + metabolites	TLC	Silica gel	Chloroform—methanol—ammonia (35:20:5 or 35:25:5)			Urine	Isolation of metabolites for GC and MS	208
Butaperazine, triflupromazine	LC	Micropak CN (10 μm)	90% Acetonitrile or methanol and 10% aq. ammonium acetate; its concentration varied from 0.005 *M* to 0.2 *M*, 2.0—2.5 ml/min	UV and electrochemical detection	10 ng/ml	Blood, plasma		209
Clebopride, see Metoclopramine								
Cyclizine, norcyclizine	GC	5% OV-17 on Chromosorb W HP, 100—120 mesh	Helium, 50 ml/min	NPD	20 pg Cyclizine and 2 ng norcyclizine injected on-column	Plasma, urine	Manifold 321° C, oven 246° C, injector 310° C	210
Domperidone + metabolites	HPLC	LiChrosorb RP 8 (5 μm) or LiChrosorb NH_2 (5 μm)	Linear gradient 100% 0.1 *M* ammonium acetate to 100% mixture of 1 *M* ammonium acetate—methanol—acetonitrile (10:45:45) (A) over 30 min, 1 ml/min; or linear gradient 99% diisopropyl ether and 1% A to 40% of this solvent and 60% A, 2.0 ml/min	UV 240 or 290 nm or ^{14}C liquid scintillation counting		Plasma, urine, bile		211
Hopantenic acid (homopantothenic acid)	GC—MS	3% OV-17 on Chromosorb W AW, 80—100 mesh	Helium, 30 ml/min	Ion source	5 ng/ml	Plasma	Column 220° C, injector 250° C, ion source 230° C; when the drug and internal standard had been detected, the temperature of the column raised to 280° C	212
	GC	3% OV-17 on Chromosorb W AW, 80—100 mesh	Nitrogen, 60 ml/min	FID	5 ng/ml		Column 170° C, 6° C/min to 290° C, injector and detector 280° C	

Meclizine	**GC—MS**				Below 5 ng/ml	Plasma		213
Metoclopramine	GC	3% OV-101 on acid-washed DMCS-treated Gas-Chrom Q, 80—100 mesh	Nitrogen, 37 ml/min	Scandium tritide ECD	5 ng/ml	Plasma	Derivatization with heptafluorobutyrylimidazole; column 200° C, injector and foil 275° C	214
	GC	Fused-silica capillary column, 5% phenylmethylsilicone Ultra No. 2, siloxane-deactivated	Hydrogen, 1.0 ml/min	ECD	Below 4 ng/ml	Plasma	Column 235° C, injector 220° C, detector 350° C	215
	GC	3% OV-17 on Chromosorb W, 80—100 mesh	Argon—methane (95:5), 40 ml/min	^{63}Ni ECD	1 pg per injection	Plasma, blood, urine	Derivatization with heptafluorobutyric anhydride; oven and injector 250° C, detector 350° C	216
	GC—MS	3% OV-17 on Chromosorb W, 80—100 mesh	Helium, 40 ml/min	MS			Oven and injector 250° C, separator 200° C, analyzer 50° C	
	GC	3% OV-225 on Chromosorb W, 80—100 mesh	Argon—methane (95:5), 40 ml/min	^{63}Ni ECD	7 ng/ml	Plasma, urine	Oven 245° C (plasma), 230° C (urine), injector 250° C, detector 350° C	217
	HPLC	Nucleosil C_{18} (5 μm) 50° C	32% Acetic acid (1% solution)—68% acetonitrile—methanol (3:7:1)	UV 273 nm	8 ng/ml	Plasma		218
	HPLC	RP-18	40% *n*-Propanol, 50 m*M* ammonium nitrate pH 7.6, 1.2 ml/min	UV 308 nm	Below 10 ng/ml	Serum		219
	HPLC	Spherisorb	Dichloromethane—methanol—ammonia (90:10:0.5), 1.7 ml/min	UV 308 nm	5 ng/ml	Plasma,		220
	HPLC	Silica gel M131	Methanol—chloroform—conc. ammonia (30:70:0.5), 2 ml/min	UV 280 nm	10 ng/ml (plasma or blood)	Plasma, blood, urine		221
	TLC	Silica gel	2 *M* ammonia—ethanol—ethyl acetate (3:3:8); ethyl acetate—acetic acid—water—ethanol (25:12:8:5); chloroform—methanol—conc. ammonia (70:30:1, 70:30:2 or 90:10:1); 1-butanol—ethyl acetate—acetic acid—water (1:1:1:1)	^{14}C				221

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TABLE 7 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Metoclopramide, clebopride + metabolites	TLC	Silica gel	Methanol—chloroform (1:4); 1,2-dichloroethane—ethanol—ammonia (sp. gr. 0.88) (70:15:2); *n*-butanol—acetic acid—water (4:1:1); 2-propanol—ammonia (sp. gr. 0.88)—water (80:40:5)	Photodensitometry after diazotation and coupling with N-(1-naphthyl)-ethylene diammonium dichloride	20 ng/ml	Liver and other biological material		222
	HPTLC	Silica gel	Chloroform; development in NH_3 atmosphere	Spectrophotometry at 308 nm	36 ng/ml	Serum		223
	HPTLC	Silica gel	Chloroform—acetic acid—methanol (18.2:1.0:0.8)	Fluorescence at 366 nm		Plasma		102
Sulpiride + N-methyl-, N-propyl derivatives, six metabolites	LC—MS			Direct-probe chemical ionization	Nanogram level	Hypophysis		224
	HPLC	C_{18}	(A) Water—acetic acid (99:1); (B) acetonitrile—acetic acid—water (50:1:49); linear gradient from 12 to 60% B in 10 min, 1.2—1.6 ml/min	Fluorescence at 299/342 nm	10 ng/ml	Serum, urine, CSF		225
Sulpiride + metabolites	TLC	Silica gel	Chloroform—methanol—25% ammonium hydroxide (60:40:2); 2-propanol—toluene—25% ammonium hydroxide (60:30:10); benzene—methanol—acetic acid (60:35:5); methanol; *n*-butanol—methanol—water—acetic acid (60:25:25:5)	^{14}C Radioscanning		Faeces		226
	PC	*S+S 2043B* paper	*n*-Butanol—water—25% ammonium hydroxide (80:10:10)					226
Triflupromazine, see Butaperazine								
Trimethobenzamide	GC—MS	3% SE on Supelcoport, 100—120 mesh	Helium, 30 ml/min		0.1 µl/ml	Saliva	Column and ion source 250°C, injector 260°C, separator 270°C	227

TABLE 8

ANTIMYCOTICS (OTHER THAN ANTIBIOTICS)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Benzoic acid	GC	3% OV-1 (A); 3% OV-17 (B); 3% SP-1000 (C); all on Chromosorb W HP, 100—120 mesh	Nitrogen, 20 ml/min	FID	1 μg/ml	Plasma	Preparation of butyl esters; column temperatures: (A) 120°C, (B) 140°C, (C) 150°C, injector and detector 30°C higher	64
Econazole	HPLC	Partisil 10 ODS RP	Methanol—aq. 0.01 *M* KH_2PO_4 pH 4.5 (70:30), 2 ml/min	UV 220 nm	0.04 μg/ml	Plasma		228
Flucytosine (5-fluorocytosine)	HPLC	μBondapak C_{18}	10 mmol KH_2PO_4 buffer pH 7.0, 1.5 ml/min	UV 276 nm	Below 5 μg/ml	Plasma, CSF	5-Fluorouracil interferes	229
	HPLC	LiChrosorb RP (18.5 μm); guard column Bondapak C_{18} Corasil (37—50 μm)	15 m*M* Octane sulphonate in acetic acid—acetonitrile—water (5:7:88), 1.1 ml/min	UV 280 nm	Below 5 μg/ml	Serum		230
Ketoconazole	HPLC	μBondapak CN RP	0.05 *M* KH_2PO_4—sodium hydroxide buffer pH 6.0—acetonitrile (65:35), 2.0 ml/min	UV 205 nm	0.1 μg/ml	Plasma		231
	HPLC	μBondapak C_{18} RP (10 μm)	Acetonitrile—Sorensen's phosphate buffer pH 6.6 (60:40), 1.5 ml/min	Fluorescence at 206/370 nm		Plasma		232
	HPLC	Ultrasphere ODS (5 μm); pre-column Ultrasphere ODS (20 μm)	Water—methanol—diethyl amine (25:75:0.1), 1 ml/min	UV 240 nm	ca. 0.1 μmol/l	Plasma, serum		233
	HPLC	Altex Ultrasphere octadecylsilane; pre-column Whatman C_{18} (30—38 μm)	Methanol—0.02 *M* monobasic sodium phosphate (75:25), 1.0 ml/min	UV 231 nm	0.2 μg/ml	Serum		234
Miconazole	HPLC	μBondapak C_{18} RP 50′	Methanol—tetrahydrofuran—2.5 mmol/l aq. acetate buffer pH 5 (0.25:5:32.5), 2.0 ml/min	UV 254 nm or 280 nm		Plasma	Mobile phase contained 6 mmol/l sulphonate	235
	HPLC	Radial-Pak C_8; pre-column Bondapak C_{18} Corasil	77% Methanol in 0.01 *M* EDTA with 0.005 *M* *n*-nonylamine, 1.5 ml/min	UV 230 nm	0.5 μg/ml	Saliva		236

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TABLE 8 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Oxiconazole	GC	3% SP-2250 on Supelcoport, 80—100 mesh	Nitrogen, 40 ml/min	^{63}Ni 10 mCi ECD or ^{63}Ni 15 mCi ECD	1 ng/ml	Plasma	Column 270—290° C, injector 300° C, detector 350° C	237
Salicylic acid, see Antibacterials								
Sulconazole	HPLC	μBondapak C_{18} RP; pre-column Co:Pell ODS Whatman	Acetonitrile—0.01 *M* NaH_2PO_4 buffer pH 8.0 (66:34), 2 ml/min	UV 229 nm	Less than 0.5 μg/ml	Plasma		238

TABLE 9

ANTIHISTAMINES

See also Antiulcer drugs (Table 14). Cross-references between individual types of antihistamines are not supplied. Check the whole table for completeness

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Astemizole	HPLC	R Sil C_{18} HL (5 μm)	Acetonitrile—water (50:50), 0.6 ml/min	UV 254 nm	1 ng/ml (plasma); 5 ng/ml (other biological material)	Plasma, tissue		239
Azelastin	GC—MS	Silanized glass column, 3% OV-1 on Shimalite W, 80—100 mesh	Helium, 20 ml/min	Multiple-ion detection	0.5 ng/ml	Plasma	Column 280°C, flash heater 310°C, ion source 330°C	240
Bromodiphenyl-hydramine (bromazine) + metabolites	TLC	Silica gel	Benzene; chloroform—acetone (90:10); acetone—25% ammonia (100:1); chloroform—methanol—ammonia (90:10:1); benzene—methanol (96:4); chloroform—acetone (98:2)	Chemical detection		Urine	Isolation and identification of metabolites	241
Carbinoxamine	GC	Capillary fused-silica open column, coated with SE-30	Helium	Nitrogen-sensitive detection	0.2 ng/ml	Serum	Oven programmed 185°C to 250°C (10°C/min), detector 300°C, injector 260°C	242
Chlorpheniramine	GC	3% OV-17 on Chromosorb Q AW DMCS, 100—120 mesh	Nitrogen, 1.68 kg/cm²	FID	Below 60 ng	Urine	Oven 210°C, injector 250°C; column silanized	243
	GC	2% OV-101 on Chromosorb W HP, 120 mesh	Helium, 30 ml/min	NPD	1 ng/ml	Plasma	Column 215°C, injector 200°C, detector 300°C	244
Chlorpheniramine + metabolites	GC	3% SP-2250 phenyl-methylsilicone oil on Supelcoport, 100—120 mesh; also studied 2% OV-101 on Chromosorb W, 100—120 mesh; 3% OV-17 on Gas-Chrom Q, 80—100	Helium, 20 ml/min	NPD	0.5 ng/ml	Plasma	Column 210°C, injector and detector 300°C	245

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TABLE 9 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
		mesh; 3% Carbowax 20 M (pretreated with 5% KOH), 80—100 mesh						
Chlorpheniramine	GC	3% OV-1 on Gas-Chrom Q, 100—120 mesh	Nitrogen, 35 ml/min	FID, nitrogen-sensitive detection	Below 2.5 μg	Urine	Simultaneous determination with phenylpropanolamine (sympathomimetics); injector 240° C, detector 280° C, column 230° C	246
	HPLC	μBondapak C_{18} (10 μm)	For plasma and saliva: acetonitrile—phosphate buffer 0.075 *M* $NH_4H_2PO_4$ in 0.16% phosphoric acid (20:80); for urine: 0.05 *M* $NH_4H_2PO_4$ in 0.11% phosphoric acid; both 2 ml/min	UV 254 nm	Below 2 ng/ml	Plasma, urine, saliva		247
	HPLC	μBondapak C_{18} RP (< 10 μm)	20% Acetonitrile in phosphate buffer (0.075 *M* monobasic ammonium phosphate in 0.016 *M* phosphoric acid, 1 ml/min	UV 264 nm		Plasma	Influence of docusate sodium on the release of chlorpheniramine	248
	HPLC	μBondapak C_{18} RP (10 μm)	Acetonitrile—0.075 *M* monobasic ammonium phosphate pH 2.6 (1:4), 1.0 ml/min	UV 254 nm	1 ng/ml	Plasma		249
	HPLC	μBondapak C_{18} RP	25% Acetonitrile in 0.075 *M* phosphate buffer, 2 ml/min	UV 254 nm	1 ng/ml	Urine		250
Chlorpheniramine + metabolites	TLC	Silica gel	Ethyl acetate—methanol—conc. ammonia (10:9:1); benzene—diethyl ether—glacial acetic acid—methanol (60:30:9:1); chloroform—acetone (7:1); methanol; ethyl acetate—methanol (1:1); chloroform—acetone (3:1); toluene—acetone (3:2)	UV, fluorescamine, ^{14}C autoradiography		Urine	Methylation of polar metabolites	251
Chlorpromazine, haloperidol	HPLC	MicroPak CN (10 μm)	10% 0.005 *M* Ammonium acetate in methanol	OD 254 nm	1 ng/ml	Plasma		252
Chlorpromazine	HPLC	LiChrosorb C_{18} RP (10 μm); precolumn Co:Pell ODS (30—38 μm)	42% Acetonitrile and 3% *n*-nonylamine in 0.02 *M* phosphate buffer pH 2.5, 2 ml/min	UV 254 nm	1 ng/ml	Plasma		253

Cinnarizine	HPLC	Spherisorb 5 ODS	Methanol—aq. 0.05 *M* ammonium dihydrogen phosphate (850:250), 1 ml/min	UV 285 nm	2 ng/ml	Plasma		254
	HPLC	LiChrosorb RP-8 (5 μm); pre-column LiChrosorb RP-20 (30 μm)	Methanol—sodium acetate buffer pH 5.2 (85:15), 2.0 ml/min	UV 250 nm	2 ng/ml	Plasma		255
Cyproheptadine	GC	3% SP-2250 on Supelcoport, 80—100 mesh	Helium, 30 ml/min	Nitrogen-sensitive detector	Below 3 ng/ml	Plasma, urine	Column 230° C, detector 300° C, injector 275° C	256
	HPLC	μBondapak (10 μm), 40°C	37% Acetonitrile in 0.1% phosphoric acid, 2 ml/min	UV 285 nm		Urine, plasma		257
Dimethindene	GC	10% Apiezon L-2% KOH on Chromosorb W AW, 80—100 mesh	Nitrogen, 30 ml/min	FID	About 4 ng/ml	Serum, urine	Column 240° C, injector 200° C, detector 250° C	258
Diphenhydramine (see also Antiparkinsonics, Orphenadrin)	GC	3% SP-2250 on Supelcoport, 100—120 mesh	Helium, 30 ml/min	Nitrogen-sensitive detector	Below 0.2 μg/ml	Serum	Injector 250° C, detector 300° C, column programmed 130—250° C (8° C/min); drugs were absorbed from 1 ml of serum onto XAD-2 resin	259
Diphenhydramine	GC	3% SP-2250 on Supelcoport, 80—100 mesh	Helium, 30 ml/min	NPD	1 ng/ml	Plasma	Injector 310° C, column 205° C, detector 275° C	260
Doxepin	GC	3% SP-2250 on Supelcoport, 100—120 mesh	Helium, 30 ml/min	Nitrogen-sensitive detector	Below 0.2 μg/ml	Serum	Injector 250° C, detector 300° C, column programmed 130– 260° C (8° C/min)	
Doxylamine	HPLC	μPorasil (10 μm)	8 Parts chloroform, 1 part acetonitrile and 1 part mixture methanol—ammonium hydroxide—ammonium chloride (57:2:1), 1.5 ml/min	UV 254 nm	Below 5 ng/ml	Plasma		261
Meclizine, see Antiemetics								

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TABLE 9 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Methapyrilene (see also Pyrilamine)	GC	2% OV-1 on Chromosorb G HP, 100—120 mesh	Nitrogen (extra dry), 60 ml/min	NPD	Below 2 ng/ml	Plasma,	Oven 230°C, injector 250°C, detector 300°C	262
	GC	3% SP-2250 on Supelcoport, 100—120 mesh	Helium, 30 ml/min	Nitrogen-sensitive detection	Below 0.2 μg/ml	Serum	Injector 250°C, detector 300°C, column programmed 130—260°C (8°C/min)	259
Metiamide	TLC	Silica gel	Ethyl acetate—methanol—ammonia (5:1:1 or 10:1:1); propanol—ammonia (50:1)	UV 254 nm ^{3}H scintillation		Urine		263
2-Methoxy-11-oxo-11H-pyrido[2,1-*b*]-quinazoline-8-carboxylic acid	HPLC	μBondapak C_{18} RP (10 μm)	2 Ampoules PIC reagent A, each cont. 0.005 *M* tetrabutylammonium phosphate in 14 ml phosphate buffer pH 7.5 per 1 l methanol—water (1:1), 2.0 ml/min	UV 265 nm, fluorescence at 360/475 nm or 280/418 nm	100 ng/ml (UV); 5 ng/ml (fluoresence)	Blood, plasma, urine		264
trans-3-[6-(Methylthio)-4-oxo-4H-quinazolin]-3-propanoic acid	HPLC	μBondapak C_{18} (10 μm)	Acetonitrile—methanol—0.001 *M* ascorbic acid pH 3.25 (36:28:36), 1 ml/min	Fluorescence at 245/418 nm	0.125 μg/ml	Plasma		265
Mianserin	GC—MS	1% UXR on Gas-Chrom Q	Helium	MS		Plasma	Column 210°C, injector and detector 270°C	266
	GC	3% SP-2250 on Supelcoport, 80—100 mesh	Nitrogen, 20 ml/min	NPD	1 ng/ml	Plasma	Oven 230°C, injector and detector 260°C	267
Mianserin + metabolites	LC	Partisil-10 ODS-3 (10 μm) or LC-1, Supelco (5 μm)	0.1 *M* Acetate buffer pH 4.2—acetonitrile (67:37) with 0.005 *M* sodium heptane sulphonate, 1.5 ml/min	Electrochemical detector	5 ng/ml	Plasma	Chlorpromazine, its metabolites and hydroxylated metabolites of loxapine interfere	268
Oxaprotiline *R*(−) and *S*(+)	HPLC	LiChrosorb Si 60 (10 μm)	1,2-Dichloroethane—*n*-heptane—ethanol (82:15:3), 4 ml/min	UV 260 nm, ^{14}C liquid scintillation counting	2 ng/ml	Blood, urine	Enantiomers were reacted with optically pure N-trifluoroacetyl-*S*(−)-prolyl chloride	269
Oxmetidine	HPLC	(A) Ultrasphere Si (5 μm); (B) Ultrasphere ODS RP (5 μm) 75°C	(A) Acetonitrile—methanol—water—ammonium hydroxide (*sp. gr.* 0.88) (200:40:10:1.5), 1.8 ml/min; (B) acetonitrile—0.02 *M* camphorsulphonic acid (30:70), 2 ml/min	UV 226 nm	Below 5 ng/ml	Plasma, urine, bile		270

Oxmetidine + sulphoxide metabolite	HPLC	Ultrasphere ODS (5 μm)	Water—methanol—acetonitrile (45:44:11) cont. 0.095 mol/l pentanesulphonic acid, 1.5 ml/min	UV 226 nm	0.5 μg/ml (oxmetidine), below 0.25 μg/ml (metabolite)	Plasma, urine, bile		271
	HPLC	LiChrosorb Si 60 (5 μm)	Acetonitrile—water—ammonium hydroxide (2500:125:1.5)	UV 228 nm	0.01—0.02 μg/ml	Plasma, urine		272
Promethazine	GC—MS	3% Carbowax K 20M + 1% KOH on Chromosorb W AW DMCS, 80—100 mesh	Nitrogen, 12 ml/min	Nitrogen-sensitive detection, MS	5 ng/g (ml)	Liver or kidney homogenate, blood, plasma, urine	Oven 220° C, injector 270° C, detector 300° C	273
	GC	3% OV-17 on acid-washed Chromosorb W, 80—100 mesh	Nitrogen, 40 ml/min	Rubidium bead alkaline FID		Plasma, urine	All-glass silanized; column 260° C, injector and detector 270° C	274
Promethazine + metabolites	HPLC	Hypersil 5 SAS	Methanol containing 30% 0.05 *M* Sorensen's phosphate buffer pH 7.4, 0.7 ml/min	UV 248 nm	0.2 ng/ml	Blood		275
Promethazine, trimeprazine, 21 compounds of phenothiazine-, thioxanthine-, dibenzazepine- and butyrophenone-like structures	LC	MicroPak CN (10 μm)	90% Acetonitrile or methanol and 10% aq. ammonium acetate (conc. varied from 0.005 *M* to 0.2 *M*), 2.0—2.5 ml/min	UV and electrochemical detection	10 ng/ml	Blood, plasma		209
Promethazine, 12 compounds of phenothiazine-, thioxanthine- and butyrophenone-like structures	HPLC	MicroPak CN	10% 0.005—0.1 *M* Ammonium acetate in methanol or acetonitrile	Electrochemical detection		Plasma		276
	LC	MCH-10 RP Varian	Methanol—water (84:16), 2 ml/min	UV 254 nm	1 ng/ml	Serum		277
Promethazine	HPLC	LiChrosorb C_{18} RP (10 μm); precolumn Co: Pell ODS (30—38 μm)	42% Acetonitrile and 3% *n*-nonylamine in 0.02 *M* phosphate buffer pH 2.5, 2 ml/min	UV 254 nm	ca. 1 ng/ml	Plasma		253

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TABLE 9 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Proxicromil + metabolites	HPLC	Hi Chrom 5 SODS HPLC	Stepped gradient; for metabolites: methanol—0.5% ammonium acetate (45:55); for proxicromil: methanol—ammonium acetate (60:40)	UV 260 nm		Urine, faeces		278
	TLC	Silica gel	Chloroform—diethyl ether—formic acid (7:2:1)	^{14}C Autoradiography			Identification of metabolites	
Pyrilamine, triprolidine, methapyrilene	GC	3% SP-2100 DB, 80—100 mesh	Helium, 25 ml/min	Rubidium bead NPD	10 ng/g (waste water)	Feedstuffs, urine, waste water	Injector 220° C, oven 200° C, detector 280° C	279
	HPLC	Altex (5 μm) Si Ultrasphere (for pyrilamine and methapyrilene); Altex (5 μm) Ultrasphere ODS (for triprolidine)	Dichloromethane—2-propanol (99.5:0.5) cont. 0.005 *M* triethylamine, 2 ml/min	Fluorescence at 310/360 nm	10 μg/g (feed); 1 ng/g (urine)			
			Methanol—0.01 M monobasic potassium phosphate buffer (90:10) cont. 0.005 *M* tetramethylammonium hydrogen chloride pH 7.0, 1.0 ml/min	*UV 254 nm*				
Pyrilamine							A review with 253 references including analytical methods	280
SK 8F 93479, i.e. 2-{2-[5-(dimethylaminomethyl)furan-2-ylmethylthio]ethylamino}5-(6-methylpyrid-3-ylmethyl)-4-pyrimidin-4-one	HPLC	Ultrasphere Altex (5 μm)	Acetonitrile—methanol—water—ammonia (sp. gr. 0.88) (200:80:10:1.5), 2 ml/min	UV 220 nm	0.025 μg/ml	Plasma		281
Sodium cromoglycate	Anion-exchange HPLC	Partisil SAX (10 μm)	Phosphate buffer (pH 2.3), 36 ml/min	UV 325 nm	About 0.2 μg/ml	Urine		282
Trimeprazine, see Promethazine								
Tripelenamine, pentazocine	GC	3% OV-17 on Chromosorb W HP, 80—100 mesh	Nitrogen, 30 ml/min	Nitrogen-sensitive detector		Blood	Column 220° C, injector 250° C, detector 275° C; interference of chlorpheniramine and methapyrilene	283
Triprolidine (see also Pyrilamine)	TLC	Silica gel	Methanol—ammonia—chloroform (10:1:89)	Fluorimetry at 300/405 nm	0.8 ng/ml	Plasma		284

TABLE 10

ANTIMALARIALS

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Amodiaquine, see Chloroquine								
Chlorguanide (Proguanil), cycloguanil + metabolite (4-chlorophenylbiguanide)	HPLC	Hypersil ODS (5 μm)	Acetonitrile—water (1:1), cont. 0.17 *M* phosphoric acid and 0.0125 *M* NaH_2PO_4, 1.5 ml/min	UV 247 nm	60 ng/ml	Serum	Lauryl sulphate as pairing ion	285
Chloroquine, pyrimethamine, quinine, sulphadoxine	GC	2% OV-17 on Chromosorb W AW DMCS, 100—120 mesh	Nitrogen, 30 ml/min	NPD (thermoionic)	0.23 ng/ml chloroquine; 0.52 ng/ml quinine; 0.191 ng/ml pyrimethamine; 2.31 ng/ml sulphadoxine	Blood, urine	Column programmed 200—290° C (8° C/min), detector 350° C, injector 250° C	286
	GC	3% OV-1—OV-17 (1:3) on Gas-Chrom Q, 100—120 mesh	Nitrogen, 50 ml/min	Nitrogen-sensitive detection	20 ng/ml	Blood	Column 235° C, injector and detector 300° C	287
Chloroquine + metabolite	GC—MS	3% OV-17 on Gas-Chrom Q, 80—100 mesh	Nitrogen, 40 ml/min	MS	0.2 μmol/l	Plasma, urine	Derivatization with trifluoroacetic anhydride; column (silanized) 250° C, injector and detector 300° C	288
Chloroquine + metabolite	GC	Fused-silica capillary column, siloxane-deactivated and coated with OV-1	Helium, 3—4 ml/min	Nitrogen-sensitive detection	5 ng/ml chloroquine; 15 ng/ml metabolite	Blood	Perfluoroacylation; column programmed 125—230° C (20° C/min) (method A) or 220° C (method B), injector 125° C, detector 290° C	289
	GC—MS	5% OV-101 on Gas-Chrom Q, 100—120 mesh	Helium, 16 ml/min	MS		Blood	Derivatization with bis(pentafluoropropionic) anhydride	
	GC—MS	3% OV-17 on Supelcoport, 80—100 mesh	Nitrogen, 30 ml/min	FID, MS	Below 10 μg/ml	Urine	Column 230° C, injector 240° C detector 265° C; prior to GC TLC on silica in 25% ammonia—methanol (3:200); UV detection	290

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TABLE 10 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Chloroquine + metabolites	GC	J&W DB-5 and SGE BP-5 fused-silica capillary column	Nitrogen, 1 ml/min	Nitrogen-sensitive detector (thermoionic)	3 ng/ml chloroquine; 10 ng/ml metabolite	Blood	Column 255°C, injector and detector 280°C	291
Chloroquine + metabolite	HPLC	Nucleosil C_{18} (5—10 μm) (when drug is injected after extraction from biological material); LiChrosorb RP-8 (10 μm) (when direct injection of biological material is used)	Acetonitrile—phosphate buffer pH 3 (40:60), 0.8—1.0 ml/min	UV 254 or 340 nm; fluorescence at 335 nm (370-nm cut-off filter)	ca. 0.5 nmol/l	Plasma, blood, urine		292
Chloroquine + desethyl metabolite	HPLC	Nucleosil C_{18} (5—10 μm); guard column LiChrosorb RP 8	Acetonitrile—phosphate buffer (40:60), 0.8—1.0 ml/min	Fluorescence	0.5 μmol/l	Serum, plasma, blood cells, urine		293
	Ion-pair RP-HPLC	Partisil-10 ODS-3 RO	Methanol—water—acetic acid (80:19:1) cont. 0.005 *M* sodium heptanesulphonate, 1 ml/min	UV 344 nm	20 ng/ml	Blood, urine		294
Chloroquine + desethyl metabolite	LC	LiChrosorb Si 60 (5 μm)	Acetonitrile—methanol—diethylamine (80:19.5:0.5), 1 ml/min	Fluorescence at 335 nm (370-nm cut-off filter)	1 ng/ml chloroquine; 0.5 ng/ml desethyl metabolite	Plasma, red blood cells, urine		295
Chloroquine + desethyl metabolite	HPLC	μBondapak C_{18} (10 μm)	0.02 *M* PIC B-7 reagent—acetonitrile (66:34), 1.0 ml/min	UV 340 nm		Plasma		296
Chloroquine + metabolite	HPLC	Dupont Zorbax-Zil (5—6 μm)	Hexane—methyl *tert.*-butyl ether—methanol—diethylamine (37.25:37.25:25:0.5), 1.0 ml/min	UV 340 nm, fluorescence at 320/380 nm	5 ng/ml	Blood		297
Chloroquine, amodiaquin, pyrimethamine, quinine	HPLC	Dupont Zorbax Sil (5—6 μm)	Hexane—methyl *tert.*-butyl ether—methanol—diethylamine (46:46:7.5:0.5)	UV 254 nm		Blood		297

Chloroquine + desethyl and bis(diethyl) metabolites	HPLC	LiChrosorb 10 RP 18	Water—acetonitrile (68:32) cont. sodium perchlorate, trimethylammonium chloride and sodium acetate, pH adjusted to 9.25 with borate buffer, 1 ml/min		1 ng/ml	Plasma		298
	TLC	Silica gel, activated	Benzene—methanol—diethylamine (7.5:1.5:1); chloroform—ethyl acetate (1:1)	UV 200—400 nm		Cord blood, neonatal blood, urine		299
Cycloguanil, see Chlorguanide								
DL-3-Di-*n*-butylamino-1-[2,6-bis(trifluoromethylphenyl)-4-pyridyl]propanol	TLC	Silica gel	*n*-Butanol—acetic acid—water (66:17:17); benzene—methanol (3:1)	^{14}C Autoradiography		Urine, faeces, plasma, blood, tissue samples, expired air		300
Diminazene	HPLC	Radial Pak CN (10 μm); CN pre-column	Acetonitrile—water (50:50) cont. 0.2% triethylamine pH 4.2	UV 254 nm	About 0.05 μg	Plasma		301
Mefloquin + DL-*threo*-α-2′-piperidyl-2-(4-trifluoromethylphenyl)-6-trifluoromethyl-4-pyridinemethanol	GC	3% OV-17 on silanized Chromosorb W, 100—200 mesh	Nitrogen, 30 ml/min	FID or ^{63}Ni ECD	1 ng/ml (ECD); 100 ng/ml (FID)	Blood	Derivatization with hexamethyldisilazane and trimethylchlorosilane; column programmed 160—250° C (1° C/min), injector and detector 250° C	302
	HPLC	μBondapak C_{18}	0.005 *M* Low UV PIC B 8 in methanol—water (70:30), 1 ml/min	UV 222 nm	Below 10 ng/ml	Plasma, blood		303
	TLC	Silica gel	Heptane—*n*-butanol—glacial acetic acid (8:1:1) (six serial developments); *n*-butanol—glacial acetic acid—water (66:17:17)	UV 254 nm, ^{14}C autoradiography		Urine, faeces, blood, expired air		304
	TLC	Silica gel	Dichloromethane—methanol—acetic acid (98:8:2); dichloromethane—methanol—conc. ammonium hydroxide (80:19:1); chloroform—methyl ethyl ketone—methanol (20:65:15); benzene—methyl acetate—methanol (40:40:20)	^{14}C Liquid scintillation counting		Blood, bile, urine, faeces		305

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TABLE 10 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Mefloquin + metabolite	TLC	Silica gel	Dichloromethane—methanol—acetic acid (80:10:10)	UV 300 nm, densitometry	100 ng/ml	Blood, plasma		306
Maloprim, see Pyrimethamine								
Primaquine	GC	3% SP-2401 on Supelcoport, 80—100 mesh	Nitrogen, 46 ml/min	^{63}Ni ECD	1—2 ng/ml	Blood	Derivatization with heptafluorobutyric anhydride; column 235°C, injector 200°C, detector 300°C	307
	GC	3% OV-17 on Anachrom ABS, 110—120 mesh	Carrier gas, 30 ml/min	Nitrogen-sensitive detection, FID			Column 265°C	308
	HPLC	Partisil ODS III RP (10 μm)	Water—acetonitrile—methanol (60:30:10) cont. $5 \cdot 10^{-4}$ *M* octanesulphonic acid, 1.5 ml/min	UV	1 ng/ml	Plasma, urine	Mobile phase buffered to pH 3.5	309
Primaquine + metabolite [8-(3-carboxy-1-methylpropylamino)-6-methoxyquinoline]	HPLC	μBondapak C_{18} RP (10 μm); pre-column Whatman C_{18}	6.6 g K_2HPO_4, 8.4 g KH_2PO_4, 2.4 l methanol, 1.6 l water, cont. 4 g N,N-dimethyloctylamine, 1.0 ml/min	UV 254 and 280 nm; liquid scintillation counting	0.05 μg/ml	Plasma, lungs, adrenal glands, liver, faeces		308, 310
	HPLC	μBondapak CN RP (10 μm)	Acetonitrile—0.08 *M* citrate buffer pH 5.0 (77:23), 1 ml/min	ECD	0.2 ng	Plasma, urine		311
Primaquine + metabolites	TLC					Urine		312
Pyrimethamine, metoprine	GC	10% OV-17 on Chromosorb W HP, 100—120 mesh	Nitrogen, 35 ml/min	ECD	Below 5 ng/ml	Plasma	Oven 235°C, injector 300°C, detector 350°C; when internal standard is eluted, the temperature was programmed to 280°C (16°C/min)	313
	GC	3% OV-17 on Chromosorb 750 80—100 mesh	Argon—methane (9:1), 60 ml/min (plasma), 50 ml/min (urine)	^{63}Ni ECD		Plasma, urine	Column 235°C, detector 350°C (plasma), column 220°C (urine)	314
Pyrimethamine, dapsone (maloprim), monoacetyldapsone, metoprine	HPLC	Spherisorb S5W (5 μm)	Diisopropyl ether—methanol—21% ammonia (96:4:0.1), 2 ml/min	UV 254 nm	5 ng per injection	Plasma		315
	LC	μBondapak C_{18} (10 μm)	Methanol—acetonitrile—water (25:15:60) cont. 0.005 *M* pentanesulphonic acid, 1.5 ml/min	UV 254 nm	5 ng/ml	Plasma		316

	HPLC	LiChrosorb Si 60 (5 μm)	Methanol—acetonitrile—25% ammonia—diisopropyl ether (6:25:0.1:71)	Fluorescence at 290/345 nm	10 ng/ml	Plasma		317
Pyrimethamine, sulphadoxine, N^4-acetylsulphadoxine	HPLC	μBondapak C_{18} (10 μm)	Methanol—acetonitrile—water (25:15:60) cont. 0.005 *M* 1-pentanesulphonic acid, 1.5 ml/min	UV 254	5 ng/ml pyrimethamine; 50 ng/ml sulphadoxine; 3 ng/ml N-acetylsulphadoxine	Plasma		318
Pyrimethamine, see also Chloroquine								
Quinine, quinidine, metabolites (see also Chloroquine)	GC, GC—MS	Silanized glass coil column, 1% SE-30 on Gas-Chrom Q, 100—120 mesh		MS		Urine		319
	HPLC	μBondapak C_{18} RP	(A) Water—acetic acid (99:1); (B) water—acetonitrile—acetic acid (40:59:1)	UV 254 nm		Urine	Proportion of B varied from 10 to 85%	
	HPLC	μBondapak C_{18} RP	(A) Water—acetic acid (99:1); (B) water—acetonitrile—acetic acid—tetrahydrofuran (40:59:1:0.1), 1.8 ml/min	UV 254 nm		Urine	Proportion of B varied from 10 to 80% (semipreparative method)	
Sulphadoxine, see Pyrimethamine								
DL-*threo*-α-(2-Piperidyl)-2-trifluoromethyl-6-(4-trifluoromethylphenyl)-4-pyridinomethanol	TLC	Silica gel	*n*-Butanol—acetic acid—water (66:17:17); benzene—methanol (3:1)	^{14}C Autoradiography, UV 254 nm		Plasma, red blood cells, urine, faeces, expired air		320

TABLE 11

ANTIPARASITICS, ANTIPROTOZOAL DRUGS (EXCLUDING ANTIMALARIALS)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Avermectins	HPLC	Zorbax ODS	Acetonitrile—methanol—water (53:35:7), 0.8 ml/min	UV 254 nm	2 ng/ml	Plasma		321
Azanidazole (Triclose)	HPLC	Partisil 10 ODS/2 RP (10 μm)	52% Methanol in aq. KH_2PO_4 (0.1%), 2 ml/min	UV 368 nm	10 ng/ml	Plasma, urine		322
3a,4,5,6,7,7a-Hexahydro-3-(1-methyl-5-nitro-1H-imidazol-2-yl)-1,2-benzisoxazole	GC—MS	SE-30 capillary column	Helium, 1 ml/min			Liver	Derivatization with N,O-bis-(trimethylsilyl)trifluoroacetamide; column 220° C	323
	TLC	Silica gel	Toluene—ethyl acetate (3:1); dichloromethane; dichloromethane—methanol (9:1); trimethylpentane—2-propanol (4:1)	^{14}C Liquid scintillation counting		Liver		323
Iodochlorhydroxyquin, see Antibacterials								
5-Isopropyl-1-methyl-2-nitro-1H-imidazole (DL 347)	GC	3% OV-25 on Chromosorb G HP, 80—100 mesh	Helium, 40 ml/min	FID or ^{14}C counter detection		Urine	Column programmed 100° C to 230° C (3° C/min), inlet and detector 250° C	324
	GC—MS	3% OV-25 on Chromosorb G HP, 80—100 mesh	Helium, 15 ml/min	MS		Urine	Column programmed 120° C to 250° C (4° C/min), inlet 280° C, manifold 240° C, gas inlet 250° C, ion source 200° C	324
	TLC	Silica gel	Benzene—methanol (95:5 or 80:20); chloroform—methanol (99:1, 95:5 or 80:20)	^{14}C Autoradiography		Urine		324
Metronidazole (see also Ornidazole)	GC	3% OV-11 on Supelcoport, 100—120 mesh	Nitrogen, 50 ml/min	^{63}Ni ECD	50 ng/ml	Blood	Derivatization with (trimethylsilyl)trifluoroacetamide; column 180° C, injector 150° C, detector 250° C	325
Metronidazole, misonidazole	HPLC	μBondapak C_{18} RP	8% Acetonitrile in 10^{-3} *M* phosphate buffer pH 4.0, 2 ml/min	UV 324 nm	0.5 μg/ml	Plasma, urine		326

Metronidazole, tinidazole	HPLC	Spherisorb S5 ODS (5 μm)	0.01 *M* Phosphate buffer pH 5.5 mixed with 15% acetonitrile, 1 ml/min	UV 320 nm	25 ng/ml metronidazole	Plasma, faeces		327
Metronidazole, tinidazole	HPLC	μBondapak C_{18}	7% Acetonitrile in 20 m*M* acetate buffer pH 4.0; 1.5 ml/min for metronidazole; 2.0 ml/min for tinidazole	UV 320 nm	0.5 μg/ml metronidazole; 2.0 μg/ml tinidazole	Plasma		328
Metronidazole + metabolites (hydroxymetronidazole-1-acetic acid)	HPLC	μBondapak C_{18} RP (10 μm)	0.005 *M* KH_2PO_4 pH 4.5—methanol—tetrahydrofuran (82.6:16.5:0.9), 1.4 ml/min	UV 234 nm	0.05 μg/ml	Plasma, urine		329
Metronidazole + metabolites	HPLC	μBondapak C_{18} RP	Methanol—acetonitrile—0.005 *M* KH_2PO_4 pH 4.0 (4:3:93)		6.8 μg/ml	Plasma		330
Metronidazole + major metabolites [1-(2-hydroxyethyl)-2-hydroxymethyl-5-nitroimidazole (II); 2-methyl-5-nitroimidazole-1-acetic acid (III)]	HPLC	Spherisorb 5-10 ODS	0.1 *M* $(NH_4)_2HPO_4$—methanol (5:1), 0.5 ml/min	UV 328 nm	20—50 ng/ml (plasma), 1 μg/ml (urine) metronidazole and II, 2.5 μg/ml III (urine)	Plasma, urine		331
	HPLC	LiChrosorb RP 8	Ethanol—water (1:9), 2 ml/min	UV 371 nm	1 μg/ml	Plasma		332
	HPLC						Procainamide interferes	333
	HPLC					Biological fluids		334
Metronidazole, misonidazole + metabolites	HPTLC	RP-18 (Merck)	*n*-Hexane—acetone—ethanol (19:6:1)	UV 320 nm; scanning densitometry	0.5 μg/ml	Serum, urine		335
Misonidazole + desmethyl metabolite	HPLC	μBondapak C_{18} RP (10 μm)	19% Methanol—water, 2 ml/min	UV 313 nm	Below 2 μg/ml	Plasma, urine, tissue homogenates		336
Misonidazole + desmethyl metabolite (see also Metronidazole)	HPLC	LiChrosorb 10 RP-18 (10 μm)	Methanol—water (20:80), 2 ml/min	UV 313 nm	1.4 μg/ml misonidazole; 0.7 μg/ml desmethyl derivative	Plasma		337

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TABLE 11 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Misonidazole + desmethyl metabolite	HPLC	Partisil PXS 5/25 ODS	19% Methanol—water, 2 ml/min			Rat liver	Details see ref. 320	338
Misonidazole + desmethyl metabolite	HPLC	Ultrasphere ODS (5 μm), Altex; Varian MCH-10 (10 μm); Varian MCH-5 (5 μm); Varian MCH-N-cap 5 (5 μm)	1 m*M* Potassium phosphate buffer pH 4.0—acetonitrile (93:7), 1.5 ml/min	UV 323 or 313 nm	0.4 μg/ml misonidazole; 0.2 μg/ml desmethylmisonidazole	Plasma, serum		339
Misonidazole + desmethyl metabolite (1-methyl-2-nitro-5-vinyl imidazole), cyclophosphamide, 5-fluorouracil	TLC	Silica gel	Ethyl acetate—dichloromethane—methanol (5:3:1 or 15:10:1); dichloromethane—methanol (7.5:1); chloroform—ethyl acetate—ethanol (7.5:7.5:1)	Densitometry at 320 nm	1 μg/ml	Plasma	Sep-Pak C_{18} extraction	340
Nitrimidazole	HPLC	μBondapak C_{18} (10 μm)	Methanol—water (30:70) cont. PIC reagent B-7, 2 ml/min	UV 313 nm	5 μg/ml	Blood		341
Ornidazole, metronidazole	GC	3% OV-11 on Supelcoport, 100—120 mesh	Nitrogen, 50 ml/min	^{63}Ni ECD	50 ng/ml	Blood	Derivatization with N,O-bis-(trimethylsilyl)trifluoroacetamide; column 180° C, injector 150° C, detector 250° C	325
Ornidazole + metabolites: 1-(chloromethyl)-2-hydroxymethyl-5-nitroimidazole-1-ethanol; 3-(2-methyl-5-nitroimidazole-1-yl)-1,2-propanediol	HPLC	μBondapak C_{18} RP (10 μm)	Water—ethanol (1:9), 2 ml/min	UV 318 nm	0.2 μg/ml	Plasma	Also possible LiChrosorb RP-2, RP-8 or RP-18	342
Salicylhydroxamic acid	HPLC	Magnusphere C_{22} RP (5 μm)	0.043 *M* $NH_4H_2PO_4$—methanol (70:30) pH 2.0, 1.2 ml/min	UV 300 nm	0.1 μg/ml	Plasma		343
Satranidazole	GC	3% OV-11 on Supelcoport, 100—120 mesh	Nitrogen, 40 ml/min	^{63}Ni ECD	50 ng/ml	Blood	Derivatization with N,O-bis-(trimethylsilyl)trifluoroacetamide; column 280° C, injector 220° C, detector 300° C	325

Secnidazole	GC	3% OV-11 on Supelcoport, 100—120 mesh	Nitrogen, 50 ml/min	^{63}Ni ECD	50 ng/ml	Blood	Derivatization with N,O-bis-(trimethylsilyl)trifluoroacetamide; column 180° C, injector 150° C, detector 250° C	325
Tinidazole (see also Metronidazole)	GC	3% OV-11 on Supelcoport, 100—120 mesh	Nitrogen, 45 ml/min	^{63}Ni ECD	50 ng/ml	Blood	Derivatization with N,O-bis-(trimethylsilyl)trifluoroacetamide; column 260° C, injector 200° C, detector 300° C	325
	GC	3% OV-11 on Gas-Chrom Q, 80—100 mesh	Nitrogen, 20 ml/min	NPD	20 ng/ml	Plasma, tissue	Column 215°C, injector and detector 245° C	344
Tinidazole + two metabolites: ethyl[2-(2-hydroxymethyl-5-nitro-1-imidazolyl)ethyl]sulphone; its O-glucuronide conjugate	HPLC	μBondapak/Phenyl RP	0.05 *M* KH_2PO_4—NaOH buffer pH 7.0—methanol (86:14), 2 ml/min	UV 313 nm	0.1 μg/ml	Plasma		345
	HPLC	ETH Permaphase (25—37 μm)	Hexane—chloroform—ethanol (90:15:0.5), 1 ml/min	UV 315 nm	0.2 μg/ml	Plasma		346
	HPLC	Silica gel	Chloroform—acetic acid—methanol (18.2:1.0:0.8)	Fluorescence at 366 nm		Plasma		102

TABLE 12

ANTIPARKINSONICS

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Amantadine (Symmetrel)	GC	5% Apiezon L on Gas-Chrom Q, 100—120 mesh	Nitrogen, 60 ml/min	FID	Below 0.1 μg/ml (plasma); 4 μg/ml (urine)	Plasma, urine	Silanized glass; column and oven 150°C, injector 250°C, detector 300°C	347
	GC—MS	3% OV-225 on Gas-Chrom Q; 3% OV-17 on Chromosorb W HP; 3% OV-101 on Gas-Chrom Q	Carrier gas, 40 ml/min	MS		Plasma	Derivatization: N-acetyl or isothiocyanate derivatives, columns 170°C, 180°C or 160°C	348
	GC—MS	3% OV-225 on Gas-Chrom Q	Helium, 30 ml/min	MS			Column 190°C, ion source 280°C	
	GC	5% SE-30 on Chromosorb W HP, 80—100 mesh	Argon—methane (90:10), 75 ml/min	ECD	Below 10 ng/ml	Plasma, urine	Silanized glass; derivatization with trichloroacetyl chloride; column 200°C, injector 250°C, detector 300°C	349
	GC	10% Apiezon L and 2% KOH on Chromosorb W AW, 80—100 mesh	Nitrogen, 50 ml/min	FID	0.5 μg/ml	Urine	Column 145°C, detector 170°C, injector 180°C	350
Benserazide	TLC + Elpho	Cellulose; first direction Elpho, second direction TLC	ad (1) Aq. buffer pH 4.4 (1/6 *M* in pyridine, 1/3 *M* in acetic acid), 18 mA, 80 min; ad (2) 2-propanol—water—acetic acid (50:50:5)	^{14}C Autoradiography		Plasma, urine		351
Benztropine	GC—MS	1% OV-17 on Gas-Chrom Q, 100—200 mesh	Helium, 20 ml/min (conditioned)	Electron-impact ionization	5 ng/ml	Urine, plasma	Silanized glass column; column 220°C, flask heater 230°C, separator 240°C, ion source 270°C	352
Benztropine, trihexylphenidyl	LC	Micropak CN (10 μm)	Acetonitrile or methanol—aq. 0.005—0.2 *M* ammonium acetate (90:10), 2.0—2.5 ml/min	UV and electrochemical detection	10 ng/ml	Blood, plasma		209
Biperiden	GC	OV-101 capillary column	Helium, 2 ml/min	Nitrogen-sensitive detection	250 pg/ml	Serum	Column 215°C, injector 250°C, detector 300°C	353

Bromocriptine (Parlodel)	GC	1% OV-17 on Celite JJ CQ, 100—120 *mesh*	Argon—methane (9:1), 50 ml/min	Detection in a pulsed mode (*150 μsec*)	0.5 ng/ml	Plasma	Derivatization with hexamethyldisilazane; column 245° C, injector 250° C, detector 350° C	354
	GC—MS	3% OV-101 on Celite JJ CQ, 100—120 mesh	Helium, 20 ml/min	MS	1.0 ng/ml	Plasma	Column 180° C, injector 200° C, molecule separator 260° C, ion source 290° C	
	HPLC	μBondapak C_{18}	Methanol—water (65:35), cont. 0.01 *M* 1-heptanesulphonic acid, 1.5 ml/min	UV 254 nm	10 ng/ml	Plasma		
Carbidopa, see Levodopa								
Deprenyl (Jumex)	GC	Carbowax 20 M glass capillary column	Nitrogen, 2.5 ml/min	NPD	400 pg/ml	Plasma	Column programmed from 70° C to 105° C (20° C/min), then to 170° C (4° C/min) injector 200° C, detector 280° C	355
Deprenyl + metabolites	TLC	Silica gel	(1) Chloroform—methanol—borate buffer pH 6.5 (7:5:1); (2) *butanol—acetic acid—water* (3:1:1); (3) *tert.*-butanol—ammonia—water—methanol (20:1:4:2); (4) phenol—water (8:2)	UV 254 nm		Urine		356
Levodopa (L-dopa) + metabolites, (dopamine, norepinephrine)	GC—MS	3% OV-1 on Supelcoport, 80—100 mesh	Nitrogen, 30 ml/min	^{63}Ni ECD, MS	0.5 pg (metabolites)	Brain extracts	Silanized glass columns; catecholamines converted to N-2,6-dinitro-4-trifluoromethylphenyl-O-trimethylsilyl derivatives	357
Levodopa, carbidopa, 3,4-dihydroxyphenylacetic acid	HPLC	Spherisorb ODS (*5 μm*)	100 m*M* NaH_2PO_4, 20 m*M* citric acid, 1.25 m*M* sodium 1-octanesulphonic acid, 0.15 m*M* sodium EDTA in 8% methanol, 1 ml/min	Electrochemical detection	15 ng/ml	Blood, plasma		358
	HPLC	Ultrasphere-octyl Altex (5 μm)	Citrate—phosphate buffer pH 3.1 cont. 6.5 m*M* 1-octanesulphonic acid and 14% methanol; disodium salt of EDTA was added to final conc. 2 m*M*, 1.2 ml/min	Amperometric detection	25 ng/ml	Plasma		359

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TABLE 12 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Orphenadrin (Disipal) + metabolite	GC	3% OV-17 on Chromosorb W AW DMCS HP, 80—100 mesh	Nitrogen, 40 ml/min	FID	0.8 μg/ml	Serum	Silanized glass column; column 250°C, injector 260°C, detector 270°C	360
Orphenadrin, diphenhydramin	GC	Capillary fused-silica DB-1 column	Helium, 1.2 bars		2 ng/ml	Serum	Oven 50°C (1 min), then to 180°C (5°C/min) and to 210°C (6°C/min), injector 200°C	361
Procyclidine (Kemadrin)	GC	3% OV-17 on Chromosorb W HP, 60—80 mesh	Nitrogen, 20 ml/min	FID		Plasma	Methyl derivatives; oven 140°C 2 min, then programmed to 230°C, 4°C/min, injector 230°C, detector 280°C	362
	GC	5% OV-17 on Chromosorb W HP, 100—120 mesh	Helium, 50 ml/min	NPD	20 ng/ml	Plasma, urine	Manifold 321°C, oven 246°C, injector 310°C	363
Procyclidine + metabolite [1-(3-hydroxycyclohexyl)-1-phenyl-3-(1-pyrrolidinyl)-1-propanol)]	GC—MS	2% OV-101 and 0.2% Carbowax 20 M on Chromosorb W HP, 100—120 mesh	Helium, 20 ml/min	MS		Urine	Column programmed 130°C to 230°C (8°C/min), injector 150°C	364
	TLC	Silica gel	Chloroform—methanol—conc. ammonium hydroxide (50:50:1); then transfer to second plate, methanol—conc. ammonium hydroxide (100:1.5)				Preparative TLC	
Trihexylphenidyl, see Benztropine								

TABLE 13

ANTITUSSIVES

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Bezitramide (Burgodin) + two metabolites [mainly 1-(4-piperidinyl)-1,3-dihydro-2H-benzimidazol-2-one]	HPLC	LiChrosorb RP-2 (10 μm)	Acetonitrile—methanol—isopropylamine (930:70:5), 6.9 mm/sec	UV 280 nm	Below 1 μg/ml	Urine	Basic metabolite of droperidol can be separated	365
Bromhexine (Adamexine)	GC	4% SE-30 on Gas-Chrom Q, 100—120 mesh	Argon—methane (95:5), 28 ml/min	15 mCi ^{63}Ni ECD	About 1.0 ng/ml 1.0 ng/ml	Plasma	Silanized glass column; derivatization with trifluoroacetic anhydride; oven 255° C, injector 280° C, detector 330° C	366
	HPLC	μBondapak C_{18} (10 μm); pre-column Nucleosil C_{18} (10 μm)	Acetonitrile—methanol—0.01 *M* phosphate buffer pH 7.0 (40:40:20 for plasma and 41:41:18 for urine)	UV 254 nm	5 ng/ml (plasma); 2.5 ng/ml (urine)	Plasma, urine		367
	GC	Capillary column OV-17	Helium, 2 ml/min	NPD	0.5 ng/ml	Plasma	Column programmed from 60° C to 140° C (10° C/min), then to 230° C (5° C/min), injector 240° C, detector 260° C	368
	GC—MS	Capillary column OV-17	Helium, 2 ml/min	SIM			Column programmed from 60° C to 230° C (10° C/min), injector 260° C	
	TLC	Silica gel	Ethyl acetate—acetic acid—water (60:15:15)	Diazotation and coupling, or fluorogenic labelling with fluorescamine and fluorimetry at 510 nm	250 ng/ml	Plasma		369
Codeine	GC	1% OV-17 on Chromosorb W HP, 100—120 mesh	Helium, 30 ml/min	Nitrogen-sensitive detection	5 ng/ml	Plasma	Column 235° C, injector 260° C, detector 300° C	370
Codeine, other opiates + metabolites	GC—MS	3% OV-210, OV 101, OV-17, OV-225 or Silar-5CP on Gas-Chrom Q, 100—120 mesh	Nitrogen, 20 ml/min	FID, MS	0.01 μg/ml	Urine	Trimethylsilyl derivatives; column programmed from 170° C to 260° C (10° C/min) (36-cm column), or 220° C to 260° C (10° C/min) (183-cm column), injector 190° C, detector 275° C	371

(Continued on p. 454)

TABLE 13 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Codeine, other opiates	GC	Glass-capillary column (borosilicate, deactivated with N-cyclohexyl-3-azetidenol); or Carbowax 20 M, OV-1, OV-17, OV-225 Carbowax 20 M fused silica	Helium, 35 ml/min	ECD	5 ng/ml	Plasma, blood	Derivatization with pentafluoropropionic anhydride; column 220° C, injector 250° C, detector 300° C	372
Codeine, other opiates	GC, GC—MS	3% Silar-5CP (A), 3% Silar-10C, 3% OV-225 (B) or 3% OV-17 (C) on Gas-Chrom Q, 100—120 mesh	Nitrogen, 50 ml/min	FID, MS	10 μg/ml	Urine	Trimethylsilyl derivatives; column: codeine underivatized 250° C (A), 240° C (B, C); silylated 250° C (A), 210° C (B), 240° C (C); injector 275° C detector 275° C	373
	HPLC	μPorasil (10 μm); pre-column Vydac 101 SC	Dichloromethane—methanol—33% ammonia (90:10:0.1), 1.5 ml/min	UV 254 nm	50 ng/ml	Plasma		374
	HPLC	C_{18} μBondapak; pre-column Co:Pell ODS	Methanol—water (21:79) cont. 1.5 g phosphoric acid, 2 ml/min	Fluorescence at 213/320 nm	4 ng/ml	Plasma		375
	HPTLC	Silica gel	Chloroform—acetic acid—methanol (18.2:1.0:0.8)	Fluorescence at 366 nm		Plasma		102
2',4'-Dimethyl-6'-methoxy-3-(2-methyl-piperidyl)-propion-aldehyde (or K-242)	HPLC	Spherisorb CN (5 μm)	30% Acetonitrile in 15 m*M* sodium phosphate pH 4.0, 1.5 ml/min	UV 214 nm	2 ng/ml	Plasma		376
Eprazinone (Eftapan, Mucitux) + metabolites	GC—MS	3% OV-17 on Gas-Chrom Q, 100—120 mesh	Helium, 20 ml/min	MS		Urine	Identification of metabolites; oven programmed 100° C to 280° C (15° C/min), ion source 250° C, separator 260° C	377
	TLC	Silica gel	Methanol—ammonium hydroxide (100:1); cyclohexane—diethylamine (9:1); chloroform—acetone (85:15); benzene—ethyl acetate—diethylamine (7:2:1); benzene—ethanol—ammonium hydroxide (80:20:1)	Chemical (Dragendorff)	0.5 μg			

Guaiphenesin + metabolite [β-(2-methoxyphenoxy)-lactic acid]	HPLC	LiChrosorb RP 8 (5 μm), 30°C	Methanol—0.01 *M* citrate buffer pH 6.5 (40:60), 1 ml/min	UV 275 nm	Below 5 μg/ml	Plasma		378
Hydrocodone	GC	3% OV-7 on Supelcoport, 100—120 mesh	Argon—methane (95:5), 40 ml/min	^{63}Ni ECD	1 ng/ml	Serum	Silanized glass column; oven 265°C, injector 280°C, detector 300°C	379
	GC	Capillary column with SE-30	Helium	Nitrogen-sensitive detector	0.2 ng/ml	Serum	Oven programmed 185°C to 250°C (10°C/min), injector 260°C, detector 300°C	380
Noscapine, noscapine acid	LC	LiChrosorb Si 60 (5 μm) Spherisorb S 5 ODS	Hexane—methanol—chloroform—diethylamine (86.5:10.1:3.4:0.034), 1 ml/min 0.005 *M* Pentanesulphonic acid in methanol—water—acetic acid—triethylamine (40:53:6:1), 1 ml/min	UV 310 nm	5 ng/ml (straight phase); 15 ng/ml (RP)	Plasma		381
Racemethorphan (dextromethorphan)	GC	3% OV-25 on Supelcoport, 80—100 mesh	Argon—methane (95:5), 50—55 ml/min	^{63}Ni ECD	Below 1 ng/ml	Serum	Silanized glass column; derivatization with pentafluorobenzyl carbonate; oven 250°C, injector 265°C, detector 300°C	382
	GC	2% OV-101 on Chromosorb W HP, 100—120 mesh		Nitrogen-sensitive detector	1 ng/ml	Plasma		383
Racemethorphan + metabolites (dextrorphan, 3-hydroxy-9α,13α,14α-morphinan, 3-methoxy-9α,13α,14α-morphinan)	HPLC	Spherisorb phenyl RP (5 μm)	10 m*M* Monobasic potassium phosphate—acetonitrile (45:55) pH 4.0, 1.2 ml/min	UV 280 nm	0.017—0.09 μg/ml (base); 0.11—0.21 μg/ml in hydrolyzed or non-hydrolyzed urine	Urine		384
Zipeprol + metabolites	GC	(1) Apiezon L on Chromosorb W AW DMCS, 80—100 mesh; (2) 3% OV-17 on Chromosorb S AW DMCS, 80—100 mesh; (3) 1% OV-1 on Supelcoport, 100—120 mesh; (4) 2% OV-1 + 2% KOH on Chromosorb W 100—120 mesh; (5) 3% SE-30 on Chromosorb W, 100—120 mesh; (6) 3% SP-2250 on Supelcoport, 100—120 mesh	Nitrogen	FID		Urine	Derivatization; trifluoroacetyl- and silyl derivatives; TLC-preparative isolation of individual metabolites	385

TABLE 14

ANTIULCER DRUGS

Check also Antihistamines for completeness.

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Aldioxa	HPLC	Zorbax ODS (5—6 μm)	Acetonitrile—water (27:73); after 3 min of the appearance of the peak the mobile phase was changed to methanol—water (70:30) (18 min), then again changed to aq. acetonitrile, 1.0 ml/min	UV 241 nm	100 ng/ml	Plasma	Hydrolysis of aldioxa to allantoin and its conversion to xanthylallantoin, which is determined (derivatization with xanthydrol). Sep-Pak C_{18} cartridges for extraction	386
Cimetidine	HPLC	Partisil 10 ODS (10 μm)	Acetonitrile—water—ammonium hydroxide (1000:50:1), 2.5 ml/min	UV 228 nm	0.1 μg/ml, using 750 μl of plasma	Plasma		387
	HPLC	Ultrasphere ODS (5 μm); pre-column Perisorb RP-2 (30—40 μm) between pump and injector; LiChrosorb RP-2 (10 μm) before analytical column	10 m*M* Phosphate buffer (pH 8.0)—methanol (80:20), 1.7 ml/min	UV 220 nm	0.1 μg/ml	Plasma, urine		388
	HPLC	Partisil 10 ODS-3	Acetonitrile—10 m*M* potassium phosphate pH 4.8 (7:93), 2.0 ml/min	UV 228 nm	0.1 μl/ml (200 μl of biological fluid was used)	Serum, urine	Interference of procainamide and tolazamide	389
	HPLC	MicroPak CN-10 (10 μm)	Acetonitrile (15 min), 1 ml/min, then acetonitrile—0.01 *M* NaH_2PO_4 (50:50)	UV 228 nm	0.1 μg/ml (0.05 μg/ml)	Plasma		390
	HPLC	Partisil 10 ODS	1/15 *M* Monobasic potassium phosphate—1/15 *M* dibasic sodium phosphate—methanol, (815:100:185), 2.5 ml/min	UV 228 nm	0.1 μg/ml	Urine, plasma	Sep-Pak C_{18} cartridges for extraction	391
	HPLC	LiChrosorb Si-100 (10 μm)	Acetonitrile—methanol—water—25% ammonium hydroxide (250:30:10:0.4), 1 ml/min	UV 228 nm	0.03 μg/ml	Plasma		392
	HPLC	LiChrosorb RP-18 (5 μm)	Methanol—0.01 *M* ammonium carbamate pH 8.9 (40:60), 1.2 ml/min	UV 220 nm	0.08 μmol/l	Plasma		393

Cimetidine + metabolite (cimetidine sulphoxide)	HPLC	LiChrosorb Si 60 (5 μm)	Acetonitrile—methanol—water—ammonium hydroxide (sp. gr. 0.88) (250:20:6:1.5), 1 ml/min	UV 228 nm	0.05 μg/ml cimetidine; 0.2 μg/ml cimetidine sulphoxide	Plasma, urine		394
	HPLC	Zorbax Sil; pre-column Whatman HC Pellosil	Acetonitrile—methanol—water—ammonium hydroxide (1000:50:50:2) pH 10.5, 3 ml/min	UV 228 nm	0.05 μg/ml	Serum, plasma, urine		395
	HPLC	RP Radial-Pak A Waters Assoc.	1% Triethylamine and 5% acetonitrile in water (pH 3.0, phosphoric acid), 3 ml/min	UV 228 nm	25 ng/ml	Plasma, urine		396, 397
	HPLC					Urine, faeces	According to ref. 395	398
	HPLC					Serum, plasma		399
	HPLC	μBondapak C_{18}	Methanol—5 m*M* KH_2PO_4 pH 2.8 (10:90), 20 ml/min	UV 228 nm	Below 0.1 μg/ml	Serum		400
	HPLC	LiChrosorb Si 60 or Partisil 5	Acetonitrile—methanol—water—ammonia (1000:200:20:5)	UV 228 nm		Serum		401
	HPLC	LiChrosorb Si 60 (5 μm)	Acetonitrile—conc. ammonia—water (1000:2.5:20), 1.6 ml/min	UV 228 nm	0.05 μg/ml	Blood		402
	HPLC	RP Ultrasphere-octyl	Methanol—0.075 *M* monobasic ammonium phosphate pH 2.5 (15:85)	UV 220 nm	0.02 μg/ml	Plasma, gastric fluid		403
	TLC	Silica gel	Ethanol—acetic acid—water	Photometry at 626 nm (Folin—Ciocalteau reagent)	2 μg/ml	Blood, urine		402
	TLC	Silica gel	Ethyl aceatate—methanol—ammonium hydroxide (sp. gr. 0.88) (8:1:1); acetone—ethyl acetate—ammonium hydroxide (sp. gr. 0.88) (5:2:2)	UV, ^{14}C autoradiography		Urine, faeces		398
Cimetidine, metiamide + metabolites	TLC	Silica gel	Ethyl acetate—methanol—ammonium hydroxide (sp. gr. 0.88) (5:1:1 or 8:1:1); dichloromethane—methanol saturated with ammonium hydroxide (4:1)	^{14}C, ^{3}H Autoradiography		Plasma, urine		405

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TABLE 14 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Cimetidine	HPTLC	Silica gel	Chloroform—acetic acid—methanol (18.2:1.0:0.8)	Fluorescence at 366 nm		Plasma		102
N-2-(Diisopropylaminoethyl)-N-(4,6-dimethyl-2-pyridyl)-N',N'-dimethylurea	GC	1.5% or 3% OV-17 on Gas-Chrom Q, 100—120 mesh	Hydrogen, helium, air, 3.5, 20, 100 ml/min or 60, 46, 550 ml/min	Nitrogen-sensitive detection, FID		Plasma, urine	Derivatization with bis(trimethylsilyl)trifluoroacetamide, trifluoroacetic anhydride; column 210, 225 or 245°C, injector 260°C, interface 275°C	406
	GC—MS	1% OV-17 on Supelcoport, 80—100 mesh	Helium, 30 ml/min	MS			Oven 180—200°C, source 270°C, separator 270°C, injector 230°C	
	TLC	Silica gel	Chloroform saturated with ammonium hydroxide—methanol (19:1); acetone—conc. ammonium hydroxide; chloroform—methanol—acetic acid (47.5:47.5:5); benzene—dioxane—conc. ammonium hydroxide (60:35:5); upper phase: benzene—dioxane—conc. ammonium hydroxide (10:80:10); methanol—conc. ammonium hydroxide (100:1.5)	^{14}C Radioscanning and UV				
Geranylgeranylacetone	GC—MS	3% OV-17 on Gas-Chrom Q, 100—120 mesh	Helium, 30 ml/min	MS	1 ng/ml	Serum	Derivatization with O-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine; column 270°C, injector and separator 300°C, ion source 330°C	407
Oxmetidine, see Antihistamines								
Pirenzepine (Gastrozepine), ranitidine	HPLC	LiChrosorb RP-8 (5 μm) (for Gastrozepine); 23°C, Spherisorb ODS (5 μm) (for ranitidine); 51°C	Methanol—0.05 *M* phosphate buffer pH 7.0	UV—VIS spectrophotometry, ranitidine 320 nm, gastrozepine 283 nm		Blood		408
Ranitidine + metabolites	HPLC	Spherisorb ODS (5 μm), 45°C	Methanol—0.0005 *M* aq. NaH_2PO_4 + 0.005 *M* aq. sodium dodecyl sulphate (60:40), 1 ml/min	UV 320 nm	0.8 μg/ml	Urine, serum		409
	HPLC	Spherisorb S5 CN	Methanol—2-propanol—5 *M* ammonium acetate (50:50:1), 0.5 ml/min	UV 320 nm	1 μg/ml	Urine	Combination with MS-SIM technique	410
Ranitidine (see also Pirenzepine)	HPLC	RP			10 ng/ml	Plasma		411
						Urine, faeces, other biological material	^{14}C	412

TABLE 15

ANTIVIRAL COMPOUNDS

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Acyclovir	HPLC	Zorbax ODS silica (5 μm)	0.005 *M* Sodium acetate and 0.0025 *M* heptanesulphonic acid, sodium salt (pH 6.5)	UV 254 nm	10 μ*M*	Plasma, urine		413
Amantadine, see Antiparkinsonics								
Arildone	GC	3% OV-1 on Gas-Chrom Q, 100—120 mesh	Argon—methane (93:7), 60 ml/min	ECD	1.4 ng/ml (urine); 6.4 ng/ml (plasma); 12.6 ng/g (faeces)	Plasma, urine, faeces	Derivatization with O-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine; column 275°C (285°C for faecal analysis), injector, detector 300°C	414
Arildone + metabolites	HPLC	LiChrosorb RP-8 or LiChrosorb RP-18	Acetonitrile—water—98% formic acid (1000:20:2 or 10:90:0.5); water—formic acid (100:0.1), 2 ml/min	UV 280 nm or radioactivity measuring	Below 0.12 μg/ml	Blood	Gradient for metabolite study: water—acetonitrile- formic acid (100:0:0.1 to 0:100:0.1)	415
	TLC	Silica gel	*n*-Hexane—diethyl ether (1:1); chloroform—methanol (99:1); chloroform—ethanol (80:20)	^{14}C Radioactivity scanning				
Cytarabine (cytosine arabinoside)	GC	3% SE-30, 3% OV-17, 3% OV-25, 3% OV-210, all on Gas-Chrom Q, 100—120 mesh	Nitrogen, 30 ml/min	NPD	500 pg	Plasma	Derivatization: acetyl methyl derivatives, trimethylsilyl dimethyl derivatives, propyl and dimethylsilyl methyl derivatives, trimethylsilyl alkyl alkoxime derivatives, deuterated derivatives; column 200—250°C depending on the t_R, injector 280°C, detector 300°C	416
	GC—MS	3% SE-30 on Chromosorb W, 80—100 mesh; or 3% OV-17 on Gas-Chrom Q, 100—120 mesh	Helium, 30 ml/min	MS	50 pg	Plasma	Column 230°C (SE-30), 265°C (OV-17)	
	GC, GC—MS	3% SE-30 on Chromosorb W, 80—100 mesh; 3% OV-17 on Gas-Chrom Q, 100—120 mesh	Helium, 45 ml/min	NPD, MS	1 ng/ml	Plasma	Column 225°C (SE-30), 275°C (OV-17), injector 290°C, detector 400°C; derivatization: acetylation and methylation	417

(Continued on p. 460)

TABLE 15 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Cytarabine + metabolites	HPLC	Aminex A-27 or A-29 (13.5 or 9.0 μm), 65°C; or RP μBondapak (10 μm); guard column Co:Pell ODS	0.025 *M* Sodium citrate and 0.08 *M* sodium tetraborate buffer, 0.7 ml/min 0.01 *M* Potassium phosphate, 0.6 ml/min	UV 270 nm	2.5 ng	Plasma, urine		418
	HPLC	Spherisorb ODS (5 μm)	0.05 *M* Phosphate buffer pH 7.0, 1.6 ml/min	UV 270 nm	50 ng/ml	Plasma, CSF	1 l of 0.05 *M* disodium phosphate + 704 ml of 0.05 *M* potassium phosphate	419
	HPLC	Partisil PXS 10/25 SCX	0.01 *M* Ammonium formate pH 4.8, 1.0 ml/min	UV 254 nm	20 ng/ml	Plasma		420
	HPLC	Ultrasphere—octyl (5 μm)	Methanol—0.01 *M* potassium phosphate buffer pH 7.0 (1.5:98.5), 1.6 ml/min	UV 281 nm		Plasma		421
Enviroxime	HPLC	Zorbax C_8	Methanol—0.14 *M* sodium acetate (65:35) cont. 3 mg/l disodium edetate, 0.9 ml/min; 28°C	Electrochemical detection	4 ng/ml (plasma); 15 ng/ml (nasal wash); 20 ng/ml (urine)	Plasma, nasal wash, urine		422
Hypoxanthine arabinoside, see Vidarabine								
Inosine pranobex (Inosiplex)	TLC	Silica gel	Multiple development: (1) *n*-butanol—acetic acid—water (4:1:2) (10—15 cm); (2) *n*-butanol—acetic acid—water (4:1:2) (3—4 cm); (3) *n*-butanol—2 *M* ammonium hydroxide (10:2) (to the top)	^{14}C Autoradiography		Urine		423
Moroxydine	GC	2% OV-225 on Chromosorb G	Nitrogen, 30 ml/min	Scandium ^{3}H ECD	21 ng/ml	Plasma, serum	Derivatization with chlorodifluoroacetic anhydride; column 220°C, injector 230°C, detector 280°C	424
Ribavirin (Virazole)	GC—MS	3% OV-17 or 3% SE-30 on Chromosorb W HP, 80—100 mesh	Methane, 133.3 Pa pressure	MS	10 ng/ml (serum); 0.5 μg/ml (urine)	Serum, urine	Derivatization: silylation; column programmed 175°C to 240°C (8°C/min), then 270°C (serum), 230°C (urine isothermally), injector 260°C, connecting tube 240°C	425
	HPLC	μBondapak C_{18} (10 μm)	5 m*M* Ammonium formate	UV 235 nm (220—228 nm)	20 pmol	Urine, plasma		426

Riboxamide	HPLC	(A) ODS Hypersil (5 μm); (B) μBondapak C_{18} (10 μm); (C) μBondapak CN (10 μm); (D) Hypersil (5 μm); anion-exchange columns: (E) Partisil 10 SAX (10 μm); (F) μBondapak C_{18} (10 μm) + HTAB; (G) ODS Hypersil (5 μm) + HTAB; (H) Hypersil (5 μm) + HTAB	0.1% Sulphuric acid (pH 2.1) for A; 10 m*M* phosphate buffer (pH 7.0) for A—E; 10 m*M* phosphate buffer (pH 6.0) for F—H	UV 254 nm	40 ng/ml	Plasma	Automated column switching; 1 m*M* HTAB (hexadecyltrimethylammonium bromide)	427
Vidarabine, hypoxanthine arabinoside	HPLC	LiChrosorb RP-8 (5 μm), 40°C	Acetonitrile—5 m*M* pentanesulphonate buffer pH 7.2, 1.0 ml/min	UV 250 nm	0.5 μg/ml (serum or CSF); 2.5 μg/ml (urine)	Serum, urine, CSF		428

TABLE 16

APPETITE DEPRESSANTS

Cross references between individual types of antidepressants are not supplied. Check the whole table for completeness.

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
6-Chloro-2-(1-perazinyl)pyrazine	GC	3% OV-210 on Gas-Chrom Q, 100—120 mesh	Argon—methane, 50 ml/min	^{63}Ni ECD	10 ng/ml	Plasma, urine	Column 190—205° C, injector and detector by 20—30° C higher than the column	429
	GC—MS	3% OV 210 on Gas-Chrom Q, 100—120 mesh	Helium, 30 ml/min	MS			Source 270° C, separator 250° C, injector 245° C	
Phendimetrazine, phenmetrazine	GC	SP-2250 on Supelcoport, 100—120 mesh	Helium, 30 ml/min		Below 10 ng/ml	Biological fluids	Oven 150° C, injector 250° C, detector 350° C; interference with diethylpropion	430
Phentermine, mephentermine	GC	12.5% Apiezon L and 2% IGEPAL CO-880 on Chromosorb W AW (washed with 5% KOH/methanol)	Helium, 60 ml/min	FID	ca. ng/ml	Blood, urine	Oven 140° C, injector 200° C detector 400° C	431
Amphetamine, ephedrine, mephentermine, methamphetamine phendimetrazine, β-phenethylamine, phenmetrazine, phentermine	GC	10% Apiezon L—10% KOH on Chromosorb W (NAW), 80—100 mesh; or 3% OV-225 on Chromosorb W (AW + DMCS), 80—100 mesh		FID	1.5 μg/ml phenmetrazine	Urine	Column 150° C, GC comparison with EMIT and RIA trifluoroacetamide derivatives	432, 433
Chlorphentermine, clortermine, diethylpropion, fenfluramine, mazindol, phendimetrazine, phenmetrazine, phentermine	TLC	Silica gel	(1) Ethyl acetate—methanol—water—ammonia (85:13.5:1:1); (2) dioxane—benzene—ammonia (35:60:5); (3) ethyl acetate—cyclohexane—ammonia (60:40:0.1); (4) chloroform—ammonia—acetone (95:0.1:5)	Chemical detection	Limits in μg/ml: chlorphentermine 1.0, clortermine 1.0, diethylpropion 0.1, fenfluramine 0.3, mazindol 0.1, phendimetrazine 0.1, phenmetrazine 0.5, phentermine 1.0	Urine	Column reactions; TLC comparison with EMIT; tables of interfering substances	434

(−)-*threo*-Chloro-citric acid	GC—MS	OV-17 on μPartisorb	Methane, 1.5 kg/cm²	MS	0.1—0.6 μg/ml	Plasma	Column 170°C, injector 300°C, interface 250°C, transfer line 250°C	436
Tiflorex + metabolite (nortiflorex)	GC	3% OV-17 on Gas-Chrom Q, 80—100 mesh	Nitrogen, 50 ml/min	^{63}Ni ECD	1 ng/ml (tiflorex); 0.5 ng/ml (metabolite)	Plasma	Derivatization with trichloro-acetyl chloride; column 210°C, injector 250°C, detector 275°C	437

TABLE 17

IMMUNOSUPPRESSIVES

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
Azathioprine + metabolite (6-mercaptopurine)	HPLC	μBondapak C_{18} (10 μm) for azathioprine; LiChrosorb RP-18 (10 μm) for mercaptopurine	11% Acetonitrile in 0.01 *M* sodium acetate buffer (pH 4.0), 2 ml/min 1% Methanol, 0.5% acetonitrile and 60 ng DTE in 0.005 *M* potassium phosphate buffer pH 4.0, 2 ml/min	UV 280 nm UV 325 nm	0.05 μg/ml 5 ng/ml	Plasma		438
	HPLC	μBondapak C_{18} (10 μm)	9% Acetonitrile in 0.01 *M* aq. KH_2PO_4 solution, 1.5 ml/min	UV 280 nm	2 ng/ml	Serum	6-Mercaptopurine is converted to stable derivative with N-ethylmaleinimide prior to chromatography	439
Azathioprine + metabolites (6-mercaptopurine, 8-hydroxyazathioprine, 8-hydroxy-6-mercaptopurine)	HPLC	Determination of 8-hydroxy-6-mercaptopurine: μBondapak C_{18} (10 μm)	4% Methanol and 0.5% acetic acid in 0.005 *M* heptanesulphonic acid pH 3.6, 1.5 ml/min	UV 325 nm		Plasma	Details see ref. 438	440
	HPLC	Bondapak C_{18}	Methanol—water (30:70)		Below 0.6 μg/ml	Blood		441
Bredinin	HPLC	LiChrosorb NH_2 (10 μm)	0.1 *M* Imidazole hydrochloride buffer pH 7.0—acetonitrile (30:70), 1 ml/min	UV 280 nm	0.25 μg/ml	Serum		442
Cyclosporin A (Sandimmune)	HPLC	LiChrosorb RP-8, 72°C	(A) Water—acetonitrile—methanol (5:75:20), 1.5 ml/min; (B) water—acetonitrile—methanol (60:20:20), shape of the gradient is described	UV 210 nm	About 20 ng/ml	Plasma, urine		443
	HPLC	Supelcosil LC-8 (5 μm) 75°C (A); segment containing cyclosporin is automatically diverted to an LC-18 Supelcosil (5 μm), 75°C (B)	(A) 5 l Acetonitrile—water (55:45), 3 ml/min; (B) 3 l acetonitrile—water (75:25), 1 ml/min	UV 202 nm	8 ng/ml (plasma); 20 ng/ml (blood)	Plasma, blood	Semiautomated HPLC	444

	HPLC	Supelco LC-18 (5 μm), 75°C	Acetonitrile—water (68.5:31.5), 1.4 ml/min	UV 202 nm	130 ng/ml (blood); 110 ng/ml (plasma)	Plasma, blood	445
	HPLC	Ultrasphere ODS (5 μm), 70°C; pre-column Vydac C_{18} RP	(A) 1% TFA in water; (B) acetonitrile; linear gradient from A—B (35:65) to (5:95), 15 min	UV 205/215 nm	ca. 100 ng/ml	Serum	446
	HPLC	Ultrasphere-octyl RP (5 μm)	Acetonitrile—methanol—water (47:20:33), 1.5 ml/min	UV 210 nm	31 μg/ml	Plasma	Comparison with RIA	447
Cyclosporin A + metabolites	HPLC	Purity of cyclosporin: LiChrosorb RP-8 (10 μm); or Bondapak-phenyl (10 μm), 50°C; metabolites: LiChrosorb RP-18 (10 μm), 70°C	Acetonitrile—water (6:4)			Plasma		448
	LC	Purification of metabolites: Amberlite XAD-2 (100—200 μm); DEAE-Sephadex A-25; μBondapak-Phenyl, Porasil B (27—75 μm)	Gradient development, methanol—acetonitrile—water, 4 ml/min Water—methanol or water—methanol—0.05 *M* ammonium hydrogen phosphate, stepped elution with pure solvents			Urine, bile, faeces		448
Cyclosporin A, cyclosporin D	HPLC	Perisorb RP-8 (30—40 μm); LiChrosorb RP-18 (5 μm), 70°C; Ultrasphere ODS; guard column Perisorb RP-2 (30—40 μm)	(1) Acetonitrile—methanol—water (35:20:45); (2) acetonitrile—water (55:45); (3) acetonitrile—water (72:28); (4) tetrahydrofuran; (5) acetonitrile—water (90:10); (6) methanol	UV	20 ng/ml	Plasma, blood	Column-switching HPLC	449
	HPLC	μBondapak C_{18} RP, 60°C	Methanol—water (95:5), 1 ml/min	UV 220 nm	About 100 ng/ml	Blood	C_{18} Sample-preparation cartridges	450
	HPLC	RP			100 ng/ml	Plasma		451

(Continued on p. 466)

TABLE 17 (continued)

Drugs separated	Method	Stationary phase	Mobile phase or carrier gas	Detection	Sensitivity	Source	Note	Ref.
erythro-9-(2-Hydroxy-3-nonyl)hypoxanthine	HPLC	Ultrasphere ODS (5 μm), 30° C	(1) Methanol—0.05 *M* phosphoric acid (25:75); (2) methanol—0.05 *M* sodium phosphate pH 7.0 (25:75); (3) methanol—0.05 *M* phosphoric acid (10:90), 1 ml/min	UV 254 nm		Urine	Also GC—MS of trimethylsilyl derivatives on 1% OV-17; column 190° C, ion source 250° C	452
	Preparative HPLC	Spherisorb ODS RT (10 μm)	(4) Methanol—water—acetic acid (26:74:0.22); (5) methanol—water (26:74) (6) Methanol—0.05 *M* phosphoric acid (26:74), 3 ml/min				Also preparative TLC on silica gel in seven solvent systems; liquid scintillation counting; ^{14}C derivatives	
6-Mercaptopurine	GC	3% SP 2250 DA on Supelcoport, 100—120 mesh	Helium, 20 ml/min	FID	20 ng/ml	Serum	Derivatization with trimethylanilinium hydroxide; column 220° C, injector and detector 300° C	453
	HPLC	Altex Ultrasphere ODS (5 μm); precolumn Co:Pell ODS (30—38 μm)	Acetonitrile—acetic acid—water (3.5:0.2:96.3), 1.4 ml/min	UV 322 nm	5 ng/ml	Plasma		454

3. LIST OF ABBREVIATIONS

aq.	= aqueous
conc.	= concentrated
cont.	= containing
CSF	= cerebrospinal fluid
dist.	= distilled
DTE	= dithioerythritol
ECD	= electron-capture detection
EMIT	= enzyme-multiplied immunoassay technique
FID	= flame ionization detection
GC	= gas chromatography
HPLC	= high-performance liquid chromatography
HPTLC	= high-performance thin-layer chromatography
HTAB	= hexadecyltrimethylammonium bromide
IR	= infrared
LC	= liquid chromatography
MS	= mass spectrometry
NPD	= nitrogen—phosphorus detection
PC	= paper chromatography
PIC	= PIC reagent B-7, heptanesulphonic acid containing acetic acid (PIC reagent B-7, Waters Assoc., Milford, MA, U.S.A.)
RIA	= radioimmunoassay
RP	= reversed-phase
SIM	= selected-ion monitoring
TFA	= trifluoroacetic acid
TLC	= thin-layer chromatography
t_R	= retention time
UV	= ultraviolet

4. SUMMARY

Some important facts about the chromatographic separation of a number of selected categories of drugs are summarized. The data refer to the chromatographic method of choice, stationary phase, mobile phase (carrier gas), detection procedure and (where available) method sensitivity. Also, fundamental instrumental parameters, namely injector, column and detector temperature, carrier gas and mobile phase flow-rate and gradient set-up are reported here. In all cases also the source material used for analysis is specified. The data are presented in table form, each table dealing with a particular category of drugs. The following categories of drugs are being dealt with: anthelmintics, antiarteriosclerotics, antibacterials, anticholinergics and cholinergics, anticoagulants, antidiabetics, antiemetics, antimycotics, antihistamines, antimalarials, antiparasitics, antiparkinsonics, antitussives, antiulcer drugs, antiviral compounds, appetite depressants and immunosuppressives.

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