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GAS CHROMATOGRAPHIC DATA FOR 187 NITROGEN- OR PHOSPHORUS-CONTAINING DRUGS AND METABOLITES OF TOXICOLOGICAL INTEREST ANALYSED ON METHYL SILICONE CAPILLARY COLUMNS

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SUMMARY

Retention data, retention indices and retention times relative to diazepam, associated with 187 nitrogen- or phosphorus-containing drugs and metabolites likely to be found in toxicological analysis, are presented. The work was carried out with cross-linked methyl silicone, siloxane-deactivated fused-silica capillary columns in different gas chromatographs equipped with nitrogen—phosphorus flame ionization detectors and a gas chromatograph—mass spectrometer. Results show the high reproducibility offered by the capillary system, which permits the reduction of identification problems and analysis time.

INTRODUCTION

Capillary gas chromatography has proved to be a powerful tool in the area of underivatized drug analysis [1, 2], especially in the field of routine toxicological screening of biological material. The use of fused-silica columns [3] and recent advances in column preparation, such as non-extractable coatings [4, 5] and siloxane deactivation, ensure high efficiency and reproducibility of the results. The use of phosphorus—nitrogen flame ionization detection (NP-FID) [6, 7] is the most convenient method in toxicological analysis due to its outstanding sensitivity for the detection of traces of drugs and negligible interference from non-nitrogenous compounds, both endogenous and exogenous.

Data banks (retention indices) are available for several stationary phases in packed columns [8—14]. When published data are compared, the most reproducible values are found when methyl silicone phases are used [15]. Owing to the existence in such banks of several overcrowded zones, which

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include substances of considerable toxicological interest, it would be advisable to search for more efficient methods of separation. Hence, cross-linked methyl silicone, siloxane-deactivated capillary columns with their highly increased separation efficiency, reproducibility, stability and flexibility, appear most promising.

At first sight, the retention indices reported on SE-30 or OV-1 packed columns seem to approach those measured on OV-1 capillary columns. However, it has been suggested that it would be worthwhile to set up a separate capillary column data base [16].

So far, retention data for methyl silicone capillary columns have been published only for 33 [17] and 80 [18] drugs.

This paper presents the retention data (retention indices and relative retention times) for 187 nitrogen- or phosphorus-containing drugs and metabolites, on cross-linked methyl silicone, siloxane-deactivated fused-silica capillary columns, likely to be used for screening purposes. Data have been extracted from clinical and forensic specimens after two years of daily routine analysis. Drugs and metabolites were confirmed whenever possible by gas chromatography—mass spectrometry (GC—MS) and, in some cases, structures were tentatively assessed for metabolites.

The authors chose to work with isothermal temperature so as to reduce the analysis time, as it has been shown that retention indices obtained in isothermal runs coincide closely with those determined under temperature-programmed conditions [19]. Injection reproducibility was given special attention and since the work was carried out with four different columns, column-to-column reproducibility was also carefully tested.

EXPERIMENTAL

Instruments

The work was carried out on the following instruments:

A 5890 A Hewlett-Packard gas chromatograph (Avondale, PA, U.S.A.) with a split/splitless capillary injection port and a dual FID and NP-FID system.

Two different units of a 5790 A Hewlett-Packard gas chromatograph with a split/splitless capillary injection port and a dual FID and NP-FID system.

A 5995 Hewlett-Packard gas chromatograph—mass spectrometer, microprocessor controlled, quadropole GC—MS instrument equipped with a split/splitless capillary injection port. The interface to the mass spectrometer is a fused-silica flow restrictor (open split). The data system is a Hewlett-Packard 9825B computer. Mass spectra libraries are subsets of the National Bureau of Standards library, purchased from Hewlett-Packard (HP, Part Nos. 5990-90150, 5990-90151, 5990-90152, 5990-90153).

The whole study was carried out with four different units (one per instrument) of cross-linked methyl silicone, siloxane-deactivated fused-silica capillary columns (Hewlett-Packard Ultraseries, 25 m × 0.2 mm I.D.). The number of theoretical plates per metre, as reported from the manufacturer and tested by ourselves, was an average of 5000.

Operating conditions

The operating conditions for the chromatographs were: flow-rates of helium,

hydrogen and air, 1, 3 and 50 ml/min, respectively; oven temperature, 250°C; detector and injection port temperatures, 300°C; split ratio, 1:30.

The operating conditions for the GC—MS system were: injection port, oven temperature, flow and split ratio, as described above; ionization energy, 70 eV; ion source temperature, 200°C; analyser temperature, 180°C; transferline temperature, 320°C; scan speed, 1100 a.m.u./s. All spectra are automatically background-substracted and decafluorotriphenylphosphine (DFTPP) normalized by the data system.

Procedure

The following technique was used to determine the relative retention times: everyday samples suitably extracted from clinical and forensic cases were injected directly and then with added diazepam in one of the chromatographs. Suspected drugs in the sample were confirmed in two steps: (a) injection of the chloroformic solution of the commercially available drug plus diazepam; (b) injection of the sample in the GC—MS system. When the drug was not commercially available (e.g. metabolites), the mass spectra library was used and some structures were tentatively assessed.

The following technique was used for the determination of the retention indices: NP-FID was substituted by FID. A chloroform solution of a mixture of the even-numbered hydrocarbons from n-C_{14} to n-C_{34}, along with diazepam, was injected into the chromatograph. With the retention times obtained, a curve of relative retention times plotted against known retention indices was constructed, to be used as a reference to group each of our 187 substances between the nearest pair of consecutive even-numbered hydrocarbons. Then, a chloroform mixture composed of each group of drugs together with the two consecutive even-numbered hydrocarbons selected according to the reference curve was injected into the chromatograph. The retention indices were calculated by the following equation [20]:

$$\mathrm{RI(d)} = 100\,(n) + 200\,\frac{\log t_R(\mathrm{d}) - \log t_R(n)}{\log t_R(n+2) - \log t_R(n)}$$

where RI(d) is the retention index of the drug, n is the carbon number of the hydrocarbon eluting just prior to the drug, $t_R(\mathrm{d})$ is the retention time of the drug, $t_R(n)$ is the retention time of the previous hydrocarbon and $t_R(n+2)$ is the retention time of the hydrocarbon eluting just after the drug.

Retention indices for metabolites which were not available were calculated by interpolation between the two nearest drugs.

RESULTS AND DISCUSSION

Data tables

Table I gives the retention data for 187 nitrogen- or phosphorus-containing drugs, in ascending order of retention index, obtained under the conditions already described. The names of the drugs used in this compilation were taken from Merck Index [21]. The contents of each column are: t_{RR}, mean retention time relative to diazepam; RI, mean retention index; ΔRI, difference between our retention index and the retention index for the same drug in

TABLE I

RELATIVE RETENTION TIMES AND RETENTION INDICES OF 187 NITROGEN- OR PHOSPHORUS-CONTAINING DRUGS AND METABOLITES, USING CROSS-LINKED METHYL SILICONE, SILOXANE-DEACTIVATED CAPILLARY COLUMNS, IN ASCENDING ORDER OF RETENTION DATA

Abbreviations: t_{RR} = mean retention time relative to diazepam; RI = mean retention index; $(RI)_L$ = mean retention index from literature (Ardrey and Moffat compilations, ref. 10); $\Delta RI = RI - (RI)_L$.

Drug/metabolite	t_{RR}	RI	$(RI)_L$	ΔRI
Amphetamine	0.040			
Methamphetamine	0.045			
Acetanilide	0.050			
Bemegride	0.052			
Nicotine	0.053			
Nicotinamide	0.055			
Barbital	0.060			
4-Aminopyridine	0.070			
Methyldemeton	0.073			
Piracetam	0.075			
Pyrithyldione	0.076			
Salicylamide	0.078			
Isoniazid	0.080			
Allobarbital	0.098	1609	1606	3
Pentylenetetrazole	0.100	1615		
Acetaminophen	0.110	1650	1687	37
Butalbital	0.124	1694	1668	24
Phenacetin	0.126	1699	1675	24
Atrazine	0.130	1711	1655	56
Cotinine	0.132	1716	1678	38
Simazine	0.134	1722	1690	32
Amobarbital	0.136	1727	1718	9
Dimethoate	0.138	1733	1725	6
Malaoxon	0.140	1738		
Pentobarbital	0.150	1763	1740	23
Meperidine	0.155	1775	1751	24
Secobarbital	0.160	1786	1763	23
Hydrocotarnine	0.165	1798		
Sparteine	0.180	1830	1801	29
Caffeine	0.185	1840	1810	30
Carisoprodol	0.190	1850	1830	20
Glutethimide	0.205	1879	1836	43
Diphenhydramine	0.210	1888	1873	15
Antipyrine	0.215	1847	1848	1
Methylparathion	0.220	1905	1851	54
Thiopental	0.224	1912	1859	53
Lidocaine	0.225	1914	1870	44
Amidopyrine	0.226	1917	1903	14
Pirimiphos, methyl	0.228	1919		
Fenitrothion	0.230	1922		
Malathion	0.235	1930	1917	13
Mephobarbital	0.240	1938		
Doxylamine	0.250	1953	1906	47
Ampyrone	0.253	1957	1950	7

TABLE I (continued)

Drug/metabolite	t_{RR}	RI	$(RI)_L$	ΔRI
Theophylline	0.256	1962	1999	37
Phencyclidin	0.260	1968	1904	64
Propyphenazone	0.262	1971	1925	46
Cyclobarbital	0.264	1973	1963	10
Chlorpyrifos	0.270	1982		
Parathion	0.275	1989	1943	46
Phenobarbital	0.280	1995	1957	38
Dipyrone	0.290	2005	1983	22
Iminoestilbene (carbamazepine metabolite)	0.300	2021		
Phentoate	0.310	2033		
Chlorpheniramine	0.320	2044	2002	22
Procaine	0.324	2049	2018	31
Chlorfenvinphos	0.328	2053		
Propyphenazone metabolite 1	0.330	2056		
2-Amino-5-chlorobenzophenone (oxazepam benzophenone)	0.340	2067	2039	28
Folpet	0.350	2077	2015	62
Methadone metabolite (1,5-dimethyl-3,3-diphenyl-2-ethylidene pyrrolidine)	0.360	2087		
Niflumic acid	0.365	2093		
Heptabarbital	0.370	2098	2058	40
Norephedrine	0.380	2107		
Carbinoxamine	0.382	2109	2080	29
Tetrachlorvinphos	0.384	2112		
Clonidine	0.386	2113		
2-Methylamino-5-chlorobenzophenone (diazepam benzophenone)	0.388	2115	2107	8
Cycrimine	0.400	2126	2114	12
Dicyclomine	0.430	2144	2097	47
Propyphenazone metabolite 2 (methylamino)	0.450	2169		
Propyphenazone metabolite 3 (formylamino)	0.470	2185		
Nomifensine	0.472	2187	2122	65
Dextromethorphan	0.475	2189	2140	49
2-Amino-5,2-dichlorobenzophenone (lorazepam benzophenone)	0.478	2191	2120	71
Methadone	0.480	2194	2148	46
Methaqualone	0.485	2197	2125	
Lupimine	0.500	2208		
Dextropropoxifene	0.534	2229	2188	41
Cocaine	0.536	2233	2187	46
Amitriptyline	0.540	2236	2196	40
Dyphylline	0.541	2237		
2-(2-Amino-5-bromobenzoyl)pyridine (bromazepam derivative)	0.546	2240	2243	3
Ethosuximide	0.548	2241		
Primidone	0.550	2243	2247	4
Dipyrone metabolite 1	0.555	2246		
Trimipramine	0.560	2249	2201	48
Propyphenazone metabolite 4	0.565	2253		
Nortriptyline	0.570	2256	2210	46
Dipyrone metabolite 2	0.575	2259		
Imipramine	0.580	2262	2223	39
Ethion	0.584	2265	2020	45

(Continued on p. 78)

TABLE I (continued)

Drug/metabolite	t_{RR}	RI	$(RI)_L$	ΔRI
Mianserin	0.588	2267		
Atropine	0.590	2269	2199	70
Doxepine	0.595	2271	2217	54
Medazepam	0.600	2275	2226	49
4-Acetylaminoantipyrine (aminophenazone metabolite)	0.605	2278		
Dipyrone metabolite 3	0.670	2315		
Trihexyphenidyl	0.675	2318		
Pentazocine	0.680	2321	2275	54
Melitracene	0.690	2326	2268	58
Biperiden	0.700	2331	2266	65
Carbamazepine	0.710	2337	2290	47
Trimeprazine	0.720	2343	2309	34
Phenytoin	0.730	2347	2330	17
Alimemazine	0.740	2352		
Chlorothiazide	0.760	2362		
Promazine	0.770	2367	2316	51
Promethazine	0.770	2367	2359	8
Oxazepam (dehydratation product)	0.780	2371	2336	35
Methaqualone metabolite 1	0.790	2376		
Maprotiline	0.800	2381	2356	25
2-Amino-5-nitrobenzophenone (nitrazepam benzophenone)	0.820	2390	2388	2
2-Amino-2'-fluoro-5-nitrobenzophenone (flunitrazepam benzophenone)	0.850	2401	2363	38
Amitriptyline metabolite 1	0.860	2405		
Cyproheptadine	0.870	2409	2366	43
Pizotifen	0.875	2412	2375	37
Benzydamine	0.880	2414	2368	46
Dextropropoxyphene metabolite 1	0.885	2416		
Pyridafenthion	0.890	2418		
Codeine	0.900	2422	2376	46
Amitriptyline metabolite 2	0.910	2426		
Lorazepam	0.920	2430	2402	28
Chlorpheniramine metabolite	0.930	2434		
Dextropropoxyphene metabolite 2	0.950	2442		
Clemastine	0.960	2446	2415	31
Methaqualone metabolite 2	0.970	2450		
Chlorimipramine	0.980	2454	2406	48
Oxyphenbutazone	0.990	2458		
Diazepam	1.000	2461	2425	36
N-1-Desalkylflurazepam (flurazepam metabolite)	1.020	2469		
Dibenzepin	1.040	2476	2443	33
Aprindine	1.050	2480		
2-Amino-2'-chloro-5-nitrobenzophenone (clonazepam benzophenone)	1.090	2494	2516	22
Ethylmorfine	1.120	2504		
Azinphos-methyl	1.130	2507	2430	77
Methaqualone metabolite 3	1.140	2510		
Morphine (BSTFA derivative)	1.150	2513		
Desmethyldiazepam	1.160	2517	2496	21
Chlordiazepoxide	1.170	2520	2453	67
Chlorpromazine	1.190	2526	2486	40
Acetylcodeine	1.200	2530	2510	20

TABLE I (continued)

Drug/metabolite	t_{RR}	RI	$(RI)_L$	ΔRI
Pinazepam	1.205	2531		
Thioridazine metabolite 1	1.210	2533		
2-Amino-5-chloro-2'-fluorobenzophenone (flurazepam benzophenone)	1.240	2542		
6-Monoacetylmorphine	1.250	2545	2537	8
Methotrimeprazine	1.290	2557	2514	43
Clobazam	1.320	2565	2645	80
Methotrimeprazine metabolite 1	1.330	2568		
Trimethoprim	1.350	2574	2638	64
Monodesethylchloroquine (chloroquine metabolite)	1.355	2575		
Dextropropoxyphene metabolite 3	1.360	2576		
Azinphos-ethyl	1.370	2579		
Benzoylecgonine	1.380	2582	2570	12
Methotrimeprazine metabolite 2	1.450	2600		
Flunitrazepam	1.490	2610	2645	35
Bromazepam	1.500	2613	2663	50
Thioridazine metabolite 2	1.540	2623		
Metoclopramide	1.550	2624	2630	6
N-1-Desalkyl-3-hydroxyflurazepam (flurazepam metabolite)	1.560	2628		
7-Aminoflunitrazepam	1.580	2632		
Chloroquine	1.600	2637	2590	47
Diamorphine	1.610	2639	2614	15
Amoxapine	1.640	2646		
Methotrimeprazine metabolite 3	1.720	2664		
Isopropamide	1.790	2679		
Clothiapine	1.940	2709		
Acepromazine	2.000	2720		
Nitrazepam	2.050	2740	2750	10
Thioridazine metabolite 3	2.200	2756		
Flurazepam	2.400	2788	2785	3
Clonazepam	2.480	2800	2885	85
Mequitazine	2.500	2804		
Quinidine	2.520	2807	2784	23
Quinine	2.580	2815	2803	12
Papaverine	2.600	2818		
Clozapine	2.900	2859		
Hydroxyzine	3.100	2884	2807	77
Methotrimeprazine metabolite 4	3.330	2911		
Methotrimeprazine metabolite 5	3.460	2925		
Pipothiazine	3.500	2930		
Haloperidol	3.530	2932		
Triazolam	4.300	3007		
Meclozine	4.700	3040	3033	7
Cinnarizine	4.900	3055	3065	10
Strychnine	5.000	3063	3119	44
Mequitazine metabolite	6.020	3127		

the literature when possible. We have chosen the Ardrey and Moffat compilation of 1981 [10], as it is the most extensive.

Retention indices for drugs ranging from amphetamine to isoniazid are purposely not given, as they cannot be separated from the solvent at this

TABLE II

RELATIVE RETENTION TIMES AND RETENTION INDICES OF 187 NITROGEN- OR PHOSPHORUS-CONTAINING DRUGS AND METABOLITES, USING CROSS-LINKED METHYL SILICONE, SILOXANE-DEACTIVATED CAPILLARY COLUMNS, ARRANGED IN ALPHABETICAL ORDER

Abbreviations: t_{RR} = mean retention time relative to diazepam; RI = mean retention index.

Drug/metabolite	t_{RR}	RI
Acepromazine	2.000	2720
Acetanilide	0.050	
Acetaminophen	0.110	1650
4-Acetylaminoantipyrine (aminophenazone metabolite)	0.605	2278
Acetylcodeine	1.200	2530
Alimemazine	0.740	2352
Allobarbital	0.098	1609
Amidopyrine	0.226	1917
2-(2-Amino-5-bromobenzoyl)pyridine (bromazepam derivative)	0.546	2240
2-Amino-5-chlorobenzophenone (oxazepam benzophenone)	0.340	2067
2-Amino-5-chloro-2'-fluorobenzophenone (flurazepam benzophenone)	1.240	2542
2-Amino-2'-chloro-5-nitrobenzophenone (clonazepam benzophenone)	1.090	2494
2-Amino-5,2'-dichlorobenzophenone (lorazepam benzophenone)	0.478	2191
7-Aminoflunitrazepam (flunitrazepam metabolite)	1.580	2632
2-Amino-2'-fluoro-5-nitrobenzophenone (flunitrazepam benzophenone)	0.850	2401
2-Amino-5-nitrobenzophenone (nitrazepam benzophenone)	0.820	2390
4-Aminopyridine	0.070	
Amitriptyline	0.540	2236
Amitriptyline metabolite 1	0.860	2405
Amitriptyline metabolite 2	0.910	2426
Amobarbital	0.136	1727
Amoxapine	1.640	2646
Amphetamine	0.040	
Ampyrone	0.253	1957
Antipyrine	0.215	1847
Aprindine	1.050	2480
Atrazine	0.130	1711
Atropine	0.590	2269
Azinphos-ethyl	1.370	2579
Azinphos-methyl	1.130	2507
Barbital	0.060	
Bemegride	0.052	
Benzoylecgonine	1.380	2582
Benzydamine	0.880	2414
Biperiden	0.700	2331
Bromazepam	1.500	2613
Butalbital	0.124	1694
Caffeine	0.185	1840
Carbamazepine	0.710	2337
Carbamazepine metabolite (7-iminoestilbene)	0.300	2021
Carbinoxamine	0.382	2109
Carisoprodol	0.190	1850
Chlordiazepoxide	1.170	2520
Chlorfenvinphos	0.328	2053
Chlorimipramine	0.980	2454
Chloroquine	1.600	2637

TABLE II (continued)

Drug/metabolite	t_{RR}	RI
Chloroquine metabolite (monodesethylchloroquine)	1.350	2574
Chlorothiazide	0.760	2362
Chlorpheniramine	0.320	2044
Chlorpheniramine metabolite	0.930	2434
Chlorpromazine	1.190	2526
Chlorpyrifos	0.270	1982
Cinnarizine	4.900	3055
Clemastine	0.960	2446
Clobazam	1.320	2565
Clonazepam	2.480	2800
Clonidine	0.386	2113
Clothiapine	1.940	2709
Clozapine	2.900	2859
Cocaine	0.536	2233
Codeine	0.900	2422
Cotinine	0.132	1716
Cyclobarbital	0.264	1973
Cycrimine	0.400	2126
Cyproheptadine	0.870	2409
Desmethyldiazepam	1.160	2517
Dextromethorphan	0.475	2189
Dextropropoxiphene	0.534	2229
Dextropropoxiphene metabolite 1	0.885	2416
Dextropropoxiphene metabolite 2	0.950	2442
Dextropropoxiphene metabolite 3	1.360	2576
Diamorphine	1.610	2639
Diazepam	1.000	2461
Dibenzepin	1.040	2476
Dicyclomine	0.430	2144
Dimethoate	0.138	1733
Diphenhydramine	0.210	1888
Dipyrone	0.290	2005
Dipyrone metabolite 1	0.555	2246
Dipyrone metabolite 2	0.575	2259
Dipyrone metabolite 3	0.670	2315
Doxepine	0.595	2271
Doxylamine	0.250	1953
Dyphylline	0.541	2237
Ethion	0.584	2265
Ethosuximide	0.548	2241
Ethylmorphine	1.120	2504
Fenitrothion	0.230	1922
Flunitrazepam	1.490	2610
Flurazepam	2.400	2788
Flurazepam metabolite (N-1-desalkylflurazepam)	1.020	2469
Flurazepam metabolite (N-1-desalkyl-3-hydroxyflurazepam)	1.560	2628
Folpet	0.350	2077
Glutethimide	0.205	1879
Heptabarbital	0.370	2098
Hydrocotarnine	0.165	1798
Hydroxyzine	3.100	2884
Haloperidol	3.530	2932
Imipramine	0.580	2262

(Continued on p. 82)

TABLE II (continued)

Drug/metabolite	t_{RR}	RI
Isoniazid	0.080	
Isopropamide	1.790	2679
Lidocaine	0.225	1914
Lorazepam	0.920	2430
Lupinine	0.500	2208
Malaoxon	0.140	1738
Malathion	0.235	1930
Maprotiline	0.800	2381
Meclozine	4.700	3040
Medazepam	0.600	2275
Melitracene	0.690	2326
Meperidine	0.155	1775
Mephobarbital	0.240	1938
Mequitazine	2.500	2804
Mequitazine metabolite	6.020	3127
Methadone	0.480	2194
Methadone metabolite (1,5-dimethyl-3,3-diphenyl-2-ethylidene pyrrolidine)	0.360	2087
Methamphetamine	0.045	
Methaqualone	0.485	2197
Methaqualone metabolite 1	0.790	2376
Methaqualone metabolite 2	0.970	2450
Methaqualone metabolite 3	1.140	2510
Methotrimeprazine	1.290	2557
Methotrimeprazine metabolite 1	1.330	2568
Methotrimeprazine metabolite 2	1.450	2600
Methotrimeprazine metabolite 3	1.720	2664
Methotrimeprazine metabolite 4	3.330	2911
Methotrimeprazine metabolite 5	3.460	2925
2-Methylamino-5-chlorobenzophenone (diazepam benzophenone)	0.388	2115
Methyldemeton	0.073	
Methylparathion	0.220	1905
Metoclopramide	1.550	2624
Mianserin	0.588	2267
6-Monoacetylmorphine	1.250	2545
Morphine (BSTFA derivative)	1.150	2513
Nicotinamide	0.055	
Nicotine	0.050	
Niflumic acid	0.365	2093
Nitrazepam	2.050	2740
Nomifensine	0.472	2187
Norephedrine	0.380	2107
Nortriptyline	0.570	2256
Oxazepam (dehydratation product)	0.780	2371
Oxyphenbutazone	0.990	2458
Papaverine	2.600	2818
Parathion	0.275	1989
Pentazocine	0.680	2321
Pentobarbital	0.150	1763
Pentylenetetrazole	0.100	1615
Phenacetin	0.126	1699
Phencyclidin	0.260	1968
Phenobarbital	0.280	1995

TABLE II (continued)

Drug/metabolite	t_{RR}	RI
Phentoate	0.310	2033
Phenytoin	0.730	2347
Pinazepam	1.205	2531
Pipothiazine	3.500	2930
Piracetam	0.075	
Pirimiphos-methyl	0.228	1919
Pizotifen	0.875	2412
Primidone	0.550	2243
Procaine	0.324	2049
Promazine	0.770	2367
Promethazine	0.770	2367
Propyphenazone	0.262	1971
Propyphenazone metabolite 1	0.330	2056
Propyphenazone metabolite 2 (methylamino)	0.450	2169
Propyphenazone metabolite 3 (formylamino)	0.470	2185
Propyphenazone metabolite 4	0.565	2253
Pyridafenthion	0.890	2418
Pyrithyldione	0.076	
Quinidine	2.520	2807
Quinine	2.580	2815
Salicylamide	0.078	
Secobarbital	0.160	1786
Simazine	0.134	1722
Sparteine	0.180	1830
Strychnine	5.000	3063
Tetrachlorvinphos	0.384	2112
Theophylline	0.256	1962
Thiopental	0.224	1912
Thioridazine metabolite 1	1.210	2533
Thioridazine metabolite 2	1.540	2623
Thioridazine metabolite 3	2.200	2756
Triazolam	4.300	3007
Trihexyphenidyl	0.675	2318
Trimeprazine	0.720	2343
Trimethoprim	1.350	2574
Trimipramine	0.560	2249

temperature when using FID. We present their retention times relative to diazepam in order to emphasize NP-FID, which gives a poor response to the solvent and thus allows these drugs to be visualized separately from the said solvent.

The comparison between our retention indices and those in the literature show a mean of 35.2 units for ΔRI, which is accepted for inter-laboratory measurements [10, 12]. Perhaps it is important to note that only fifteen ΔRI values, from the 103 drugs compared, were found to be negative. Further work in this field will prove whether this tendency of retention index to increase, when using capillary columns, has some special significance.

Metabolites are numbered according to ascending order of retention index. In some samples, e.g. urines, and depending on the drug, metabolites are the only clue for tracing the parent drug.

Table II has been generated from the data in Table I, to help locate the retention data for a known compound; this table contains the same drugs as Table I in alphabetical order. Note that the metabolites of a given drug are listed under the parent drug so as to remind the analyst of the possibility of finding them when analysing a biological sample containing the parent drug.

Reproducibility

The precision of the relative retention time was tested with a mixture of drugs, carefully chosen in order to cover a wide range (from caffeine to strychnine) and to give the best idea of the degree of tailing due to its molecular formula (phenobarbital). The reproducibility of t_{RR} for one column is presented in Table III. The column-to-column variations in t_{RR} for two randomly selected columns are also shown in Table III.

TABLE III

REPRODUCIBILITY OF t_{RR} ON ONE COLUMN AND ON TWO RANDOMLY SELECTED COLUMNS FOR A MIXTURE OF DRUGS COVERING A WIDE RANGE OF t_{RR} VALUES

n = 8; internal standard = diazepam; t_{RR} = retention time relative to diazepam; S.D. = standard deviation; C.V. = coefficient of variation.

Drug	Injection-to-injection variation			Column-to-column variation			
	Mean t_{RR}	S.D.	C.V. (%)	t_{RR}		S.D.	C.V. (%)
				Column 1	Column 2		
Caffeine	0.186	$4.96 \cdot 10^{-3}$	2.66	0.182	0.192	$5 \cdot 10^{-3}$	2.67
Phenobarbital	0.280	$2.39 \cdot 10^{-3}$	0.83	0.288	0.275	$6 \cdot 10^{-3}$	2.30
Methadone	0.488	$1.14 \cdot 10^{-3}$	0.28	0.482	0.490	$3 \cdot 10^{-3}$	0.82
Oxazepam	0.782	$1.98 \cdot 10^{-3}$	0.25	0.772	0.767	$2 \cdot 10^{-3}$	0.32
Diamorphine	1.620	$1.4 \cdot 10^{-2}$	0.89	1.636	1.604	$1.6 \cdot 10^{-2}$	0.98
Clothiapine	1.940	$2.4 \cdot 10^{-2}$	1.23	1.905	1.968	$3.1 \cdot 10^{-2}$	1.60
Clozapine	2.900	$3.2 \cdot 10^{-2}$	1.10	2.864	2.946	$4.1 \cdot 10^{-2}$	1.39
Triazolam	4.300	$1.3 \cdot 10^{-2}$	0.30	4.300	4.340	$1.9 \cdot 10^{-2}$	0.46
Strychnine	5.000	$1.5 \cdot 10^{-1}$	3.00	4.820	5.180	$1.8 \cdot 10^{-1}$	3.60

The results are far superior to the repeatability obtained using packed columns, and they ensure, in most cases, a consistent drug identification. In zones where distance between drugs (t_{RR}) is less than the calculated standard deviation, the possibilities of identification are reduced to only a few drugs. The connection with the GC—MS system working under the same conditions, will provide the correct answer with minimum expense and effort, as the field has already been well delimited.

CONCLUSIONS

It is hoped that these tables will enable analytical toxicologists involved with capillary gas chromatography and NP-FID to identify unknown compounds more easily. We have included drugs of the utmost toxicological interest and have determined the retention data for several metabolites that have not been previously described in the literature.

The high resolution offered by capillary columns makes them the most

suitable system for drug analysis. The advantages of reproducibility of the ultra-performance capillary columns reduce identification problems and analysis time. The possibility of practical use of relative retention times, owing to the small standard deviation for day-to-day and column-to-column variations, should also be emphasized. The application of these data to the GC—MS system, using the same operating conditions, improve the rapid and accurate identification of drugs in unknown samples.

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