

## Corrected TLC-Data of 16 Hydrolysis-Derivatives of Commonly Used Benzodiazepines in 10 Systems \*)

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### SIKLIKLA KULLANILAN BENZODİAZEPİNLERİN 16 HİDROLİZ TÜREVİNİN 10 SİSTEMDE ELDE EDİLEN DÜZELTİLMİŞ İTK-VERİLERİ

#### Özet

Bu dergide yayınladığımız [*Adli Tıp Derg. (ATD)*, 1, 22-29 (1985)] 61 benzodiazepin ve metabolitlerinin düzeltilmiş ince tabaka kromatografisi,  $R_f$ -değerlerine ek olarak, 16 hidroliz ürünü (*aminobenzofenon*'lar ve *benzoilpiridin*'ler) ile ilgili düzeltilmiş  $R_f$ -verilerini elde ettik. Bu ayrılma ürünleri bazı olgularda metabolit ve/veya biyolojik materyalde artefakt şeklinde ortaya çıkabilir. Küçük fakat önemli olan bu nokta uygulanan inceleme yöntemlerinin ana temelini oluşturur.

#### Summary

In addition to the corrected  $R_f$ -values of 61 benzodiazepines and metabolites which were recently published in this journal [*Adli Tıp Derg. (ATD)*, 1, 22-29 (1985)] we have investigated the corrected  $R_f$ -values of 16 hydrolysis products (*aminobenzophenones* and *benzoylpyridines*) in 10 (!) systems. These cleavage products may occur as metabolites in some cases and/or artefacts in biological materials. They are, in addition to this minor important fact, the basis of largely applied screening methods.

**Keywords :** *Benzodiazepines - Metabolites - Aminobenzophenones - Benzoylpyridines - Hydrolysis products - Corrected  $R_f$ -values*

\*) Part of Thesis of *W.-R. Schneider*.

## INTRODUCTION

Recently we published the corrected  $R_f$ -values of 61 benzodiazepines and metabolites in two running-systems (1). In the meantime «*The International Association of Forensic Toxicologists (TIAFT)*» and the «*Deutsche Forschungsgemeinschaft (DFG)*» prepared under the auspices of the Committee for Systematic Toxicological Analysis (*STA*) of *TIAFT* an extensive and highly valuable collection of thin layer chromatographic  $R_f$ -values of toxicologically relevant substances on standardised systems which is to be published in the nearest future (2).

As this compilation contains only data of the complete benzodiazepines and metabolites prior to cleavage (no hydrolysis products) we decided to collect and publish also these data with regard to the fact that the hydrolysis products (*aminobenzophenones* and *benzoylpyridines*) may occur as metabolites and artifacts in the biological samples\*. That is why they should be incorporated in the useful collection of corrected  $R_f$ -values.

The basic principles of the corrected  $R_f$ -value concept are reported in the literature (1, 2).

We used the 10 systems which are described in the *DFG/TIAFT* publication (2), see Table 1.

The abbreviations are listed in Table 2. For more details see (3).

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\*) In addition to this minor important fact, the hydrolysis products are the basis of largely applied screening procedures see (3).

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Table I. Running systems according to (2).

Solvent*	Adsorbent	Reference compounds**	hR <sub>f</sub>
(1) Chloroform-acetone (80 + 20)	Silica	Paracetamol	15
		Clonazepam	35
		Secobarbital	55
		Methylphenobarbital	70
(2) Ethyl acetate	Silica	Sulfathiazole	20
		Phenacetin	38
		Salicylamide	55
		Secobarbital	68
(3) Chloroform-methanol (90 + 10)	Silica	Hydrochlorothiazide	11
		Sulfafurazole	33
		Phenacetin	52
		Prazepam	72
(4) Ethyl acetate-methanol- conc. ammonia (85 + 10 + 5)	Silica	Morphine	20
		Codeine	35
		Hydroxyzine	53
		Trimipramine	80
(5) Methanol	Silica	Codeine	20
		Trimipramine	36
		Hydroxyzine	56
		Diazepam	82
(6) Methanol-n-butanol (60 + 40); 0.1 mol/l NaBr	Silica	Codeine	22
		Diphenhydramine	48
		Quinine	65
		Diazepam	85
(7) Methanol-conc. ammonia (100 + 1.5)	Silica impregnated with 0.1 mol/l KOH and dried	Atropine	18
		Codeine	33
		Chlorprothixene	56
		Diazepam	75
(8) Cyclohexane-toluene- diethylamine (75 + 15 + 10)	Silica impregnated with 0.1 mol/l KOH and dried	Codeine	6
		Desipramine	20
		Prazepam	36
		Trimipramine	62
(9) Chloroform-methanol (90 + 10)	Silica impregnated with 0.1 mol/l KOH and dried	Desipramine	11
		Physostigmine	36
		Trimipramine	54
		Lidocaine	71
(10) Acetone	Silica impregnated with 0.1 mol/l KOH and dried	Amitriptyline	15
		Procaine	30
		Papaverine	47
		Cinnarizine	66

\*) Eluent composition: volume + volume; Saturated systems are used throughout except for systems 5 and 6 which are used with unsaturated solvent tanks.

\*\*\*) Solutions of the four reference compounds at a concentration of approximately 2 g/l of each drug.

**Table 2.** Abbreviations according to (3).

<i>ACB</i>	: 2-Amino-5-chlorobenzophenone (e.g. from Oxazepam)
<i>MACB</i>	: 5-Chloro-2-(methylamino) benzophenone (e.g. from Diazepam)
<i>ANB</i>	: 2-Amino-5-nitrobenzophenone (e.g. from Nitrazepam)
<i>DAB</i>	: 2, 5-Diaminobenzophenone (e.g. from 7-Amino-Nitrazepam)
<i>ADB</i>	: 2-Amino-2', 5-dichlorobenzophenone (e.g. from Lorazepam)
<i>ANCB</i>	: 2-Amino-2'-chloro-5-nitrobenzophenone (e.g. from Clonazepam)
<i>DCB</i>	: 2,5-Diamino-2'-chloro-benzophenone (e.g. from 7-Amino-Clonazepam)
<i>CCB</i>	: 5-Chloro-2-[(Cyclopropylmethyl) amino] benzophenone (e.g. from Prazepam)
<i>DCFB</i>	: 5-Chloro-2-[2-(diethylamino) ethylamino]-2'-fluorobenzophenone (e.g. from Flurazepam)
<i>ACFB</i>	: 2-Amino-5-chloro-2'-fluorobenzophenone (e.g. from 1-Desalkyl-Flurazepam)
<i>HCFB</i>	: 5-Chloro-2'-fluoro-2- (hydroxyethylamino) benzophenone (e.g. from 1-Hydroxyethyl-Flurazepam)
<i>ABP</i>	: (2-Amino-5-bromophenyl) (pyridin-2-yl) methanone (e.g. from Bromazepam)
<i>MNFB</i>	: 2'-Fluoro-2-(methylamino)-5-nitrobenzophenone (e.g. from Flunitrazepam)
<i>ANFB</i>	: 2-Amino-2'-fluoro-5-nitrobenzophenone (e.g. from 1-Desmethyl-Flunitrazepam)
<i>MDB</i>	: 2', 5-Dichloro-2-(methylamino) benzophenone (e.g. from Lormetazepam)
<i>TCB</i>	: 5-Chloro-2-(2,2,2-trifluoroethylamino) benzophenone (e.g. from Halazepam)

The results are described in the following Table 3.

**Table 3.** Hydrolysis products and corrected  $R_f$ -values in system.

Hydrolysis Product	Corrected $R_f$ -values in system									
	1	2	3	4	5	6	7	8	9	10
<i>ACB</i>	76	69	76	86	90	91	78	12	76	71
<i>MACB</i>	82	72	82	88	89	93	79	53	81	71
<i>ANB</i>	71	65	68	85	90	91	77	5	69	69
<i>DAB</i>	37	41	54	81	80	79	72	5	57	57
<i>ADB</i>	77	70	76	87	89	93	78	11	76	70
<i>ANCB</i>	72	66	70	86	87	93	77	4	69	70
<i>DCB</i>	41	46	55	82	80	80	74	5	59	61
<i>CCB</i>	83	74	82	88	92	95	80	58	82	74
<i>DCFB</i>	9	8	41	83	45	51	67	53	60	51
<i>ACFB</i>	76	68	74	86	89	93	78	11	75	70
<i>HCFB</i>	48	50	57	82	87	91	77	7	60	66
<i>ABP</i>	64	61	66	85	86	88	77	9	68	69
<i>MNFB</i>	79	63	80	86	89	90	77	20	79	71
<i>ANFB</i>	71	66	68	86	87	91	77	4	69	70
<i>MDB</i>	81	69	81	87	82	93	75	49	81	71
<i>TCB</i>	81	74	81	89	94	95	82	49	81	75

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