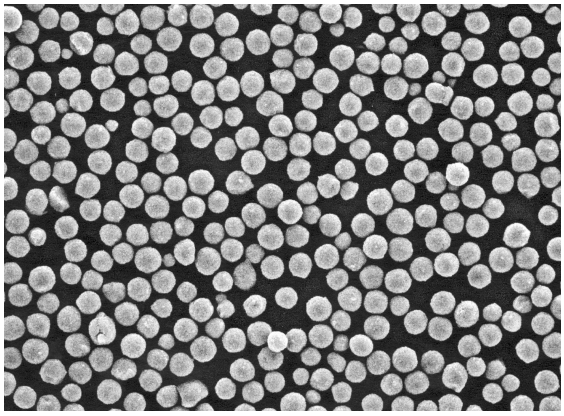
SACHTLEBEN

Polymer Coated Titanium Dioxide as a Reverse Phase Sorbent in Liquid Chromatography



Presented at the PREP 2004 Conference May 23-26 in Baltimore/USA

J. Winkler [a*], B. Hirthe [a], G. Benkner [a], J. Blome [b], C. Spitzwieser [a], R. Wittenberg [a]

[a]Sachtleben Chemie GmbH, Duisburg, Germany
[b]HPLC-Analytik Johannes Blome, Erolzheim
*to whom correspondence should be adressed

SACHTLEBEN

Contents

SACHTLEBEN

Introduction

Porous titanium dioxide is different from other inorganic sorbents used in high pressure liquid chromatography in the sense that it has a high resistance towards the attack of acids as well as bases. Titanium dioxide in the anatase or rutile crystal modification is furthermore completely inert against moisture uptake. For that reason polymer modified titanium dioxide is useful as a sorbent for HPLC under extreme conditions. RP titanium dioxide from Sachtleben carries the name Sachtopore RP .

Physical Properties of Sachtopore

Sachtopore Pore Diameter	100 Å 100	200 Å 200	330 Å 300	2000 Å 2000
Specific surface area [m²/g] (typical values)	55	30	15	<5
Specific pore volume [ml/g] (typical values)	0,21	0,17	0,12	n.d.
Mechanical stability Applicable packing pressure [bar] (typical values)	750	750	750	600

Particle Sizes

Sachtopore is available in particle sizes of 3 µm, 5 µm, 10 µm, 20 µm, 40 µm and 80 µm.

Samples and Elution Technique

The samples were chosen under the aspect of a high or low pKa value, respectively, and the lack of acidic next to basic groups in the molecule wich would lead to ionic structures due to intramolecular acid-base reactions. To supress dissociation basic samples were run under alkaline conditions, whereas acidic samples were run at low mobile phase pH values. All separations were carried out in an isocratic mode.

pH-range

Mobile phases with pH values between 10 and 1,5 were used. Borate buffers were tested because of their high pH values and their low UV cut-off wavelength of 210 nm, making them interesting when UV detectors are used.

Results

From the chromatogramms the plate numbers per mm and peak asymmetrics for each substance were determined. The quotient of plate number to asymmetry was taken as a measure for column performance:

SACHTLEBEN

	pH	Particle size [µm]	Average Plate Number [mm-1]	Average asymmetry	Performance plate number / asymmetry
Fig. 1	10	3	43,1	1,15	37,5
Fig. 2	10	3	44,1	1,27	34,7
Fig. 3	10	5	28,7	1,54	18,6
Fig. 4	10	5	28,3	1,27	22,3
Fig. 5	9,5	5	21,0	1,06	19,8
Fig. 6	9,5	5	22,8	1,31	17,4
Fig. 7	9,5	5	19,8	1,14	17,7
Fig. 8	9	5	35,3	1,38	25,6
Fig. 9	9	3	42,6	1,27	33,5
Fig. 10	2,3	3	47,1	1,13	41,7
Fig. 11	2,3	3	45,2	1,31	34,5
Fig. 12	2,2	5	31,8	1,16	27,4
Fig. 14	1,5	3	45,2	1,30	34,8
Fig. 15	1,5	5	29,7	1,24	23,9
Fig. 16	1,5	5	27,9	1,27	22,0

Preparative LC simulation

To simulate preparative chromatography conditions, Pentifylline was extracted from a tablet of Cosaldon™. Using 10 mM $Na_2B_4O_7$ + 1 mM H_3BO_3 / 20% Acetonitrile (pH 9 in aqueous component) as mobile phase the chromatogramm shown in Fig. 13 was obtained under overload conditions. Impurities were separated at retention time of 1.55, 2.07 and 4.22 minutes. The Pentifylline peak appeared with an almost rectangular shape.

Conclusion

Polymer modified Sachtopore is useful as a reverse phase sorbent in the separation for samples with high aciditics or basicitics and/or under extreme pH values of the mobile phase. The use of reverse phase Sachtopore in preparative chromatography under similary challenging conditions appears promising.

SACHTLEBEN

List of Separations

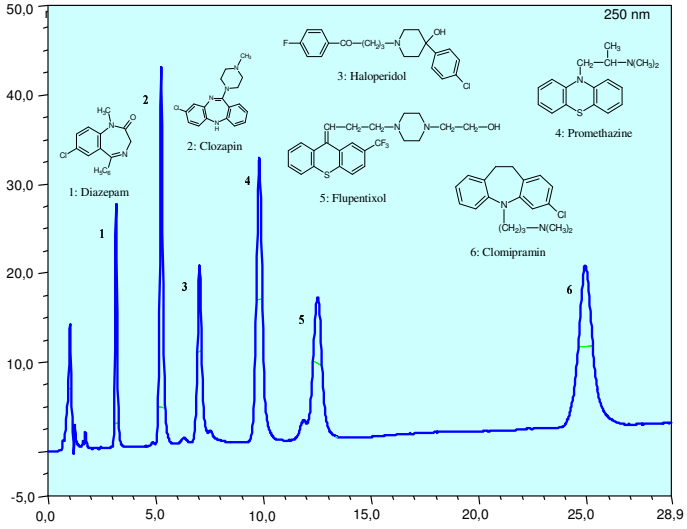
SACHTLEBEN

Alphabetical Listing of Drugs

Drug	in Fig.	Drug	in Fig.
Aminoantipyrine	8	Isosorbide dinitrate	6 / 9
Aminophenazone	8	Olanzapine	2
Amiodarone	4	Oxyphenylbutazone	11/12/14
Antipyrine	8	Paracetamol	8
benzoic acid	15	Pentifylline	9/13
Betahistine	6	Phenazine	12
Carbinoxamine	3	Phenol	15
Chlomipramin	1	Phenylbutazone	11/12/14
Chlorphenamine	3	Phenyltoloxamine	3
Clofibrate	6	p-nitro benzoic acid	15
Clopazine	1	Paracetamole	8
Clozapine	2	Prazosin	6 / 9
Clomipramine	1	maleic acid	3
Diclofenac	10	Medazepame	2
Diflunisal	10/11/12	Metoprolol	4
Dihydroergocristine	7	Naproxen	11/12/14
Dihydroergocornine	7	Nifedipine	4
Dihydroergocryptine	7	Promethazine	1
Dihydroergotamin methylsulfate	6	Propylphenazone	11/12/13
Diphenylpyraline	3	Reserpine	5
Dipyridamole	4	Rofecoxib	12
Doxepin	2	salicylic acid	15
Ergotamine	6	Thymol	16
Etafenone	4	Trapidil	4
ethenzamide	8	Verapamil	4
Flupentixol	1	Vincamin	9
fumaric acid	15	4-hydroxybenzoic acid ethyl ester	16
Haloperidol	1	4-hydroxybenzoic acid methyl ester	16
Ibuprofene	11/14	4-hydroxybenzoic acid propyl ester	16
Indometacine	10/11		

SACHTLEBEN

Fig. 1: **RP Separation of Antipsychotic Drugs** **pH 10**



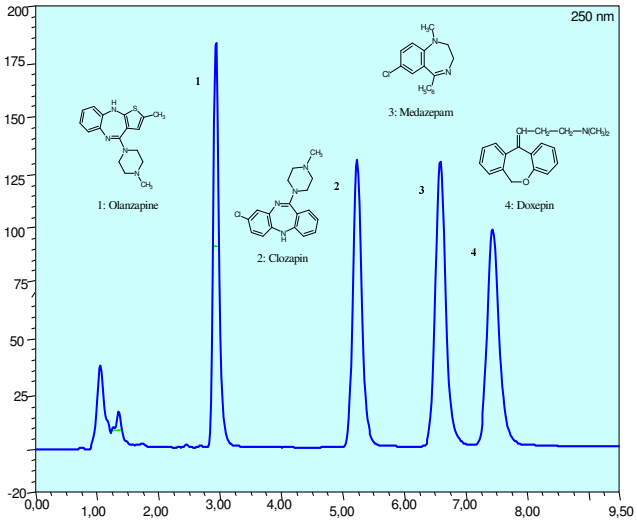
Column
Sachtopore RP (300 Å, 4 µm, 150 x

Eluent
72% Water
(+ 20 mM Na2CO3 + 10 mM NaHC
28% Acetonitrile

Flow
1 ml/min

Detection
UV, 250 nm

Fig. 2: **RP Separation of Antipsychotic Drugs** **pH 10**



Column
Sachtopore RP (300 Å, 3 µm, 150 x 4 mm)

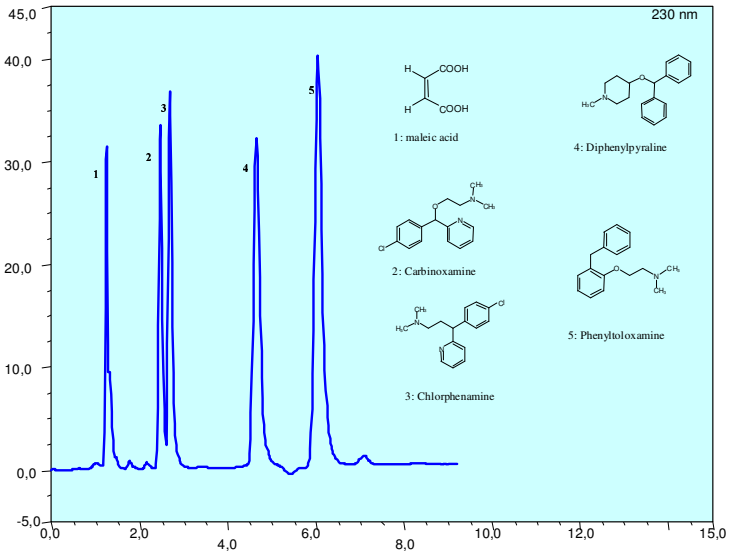
Eluent
72% Water
(+ 20 mM Na2CO3 + 10 mM NaHCO3)
28% Acetonitrile

Flow
1 ml/min

Detection
UV, 250 nm

SACHTLEBEN

Fig. 3: **RP Separation of Antihistimines** **pH 10**



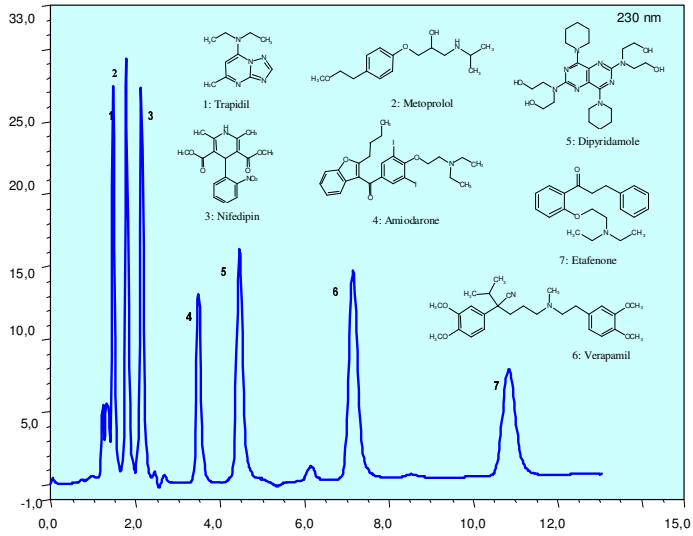
Column
Sachtopore RP (300 Å, 3 µm, 150 x 4 mm)

Eluent
70% Water
(+ 10 mM Borax + 10 mM Soda)
30% Acetonitrile

Flow
1 ml/min

Detection
UV, 230 nm

Fig. 4: **RP Separation of Cardiac Drugs** **pH 10**



Column
Sachtopore RP (300 Å, 3 µm, 150 x 4 mm)

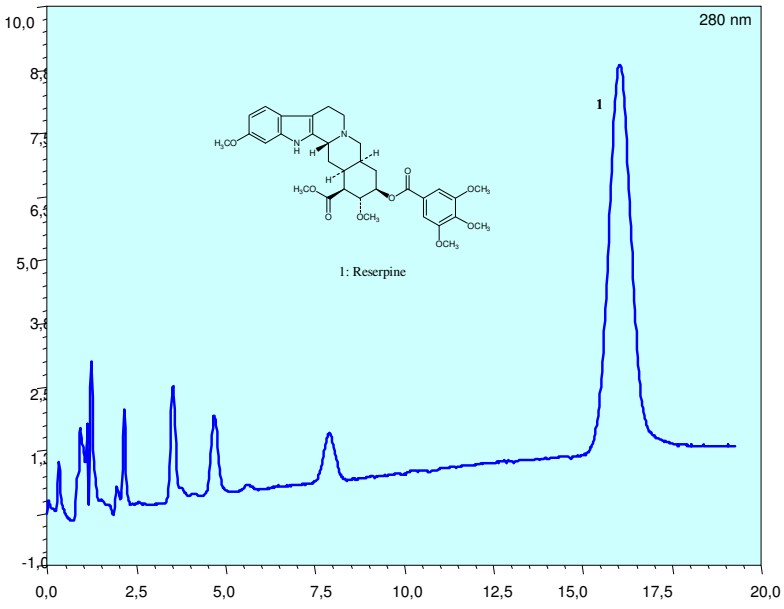
Eluent
70% Water
(+ 10 mM Borax + 10 mM Soda)
30% Acetonitrile

Flow
1 ml/min

Detection
UV, 230 nm

SACHTLEBEN

Fig. 5: **RP Separation of Indole Alkaloids** **pH 9,5**



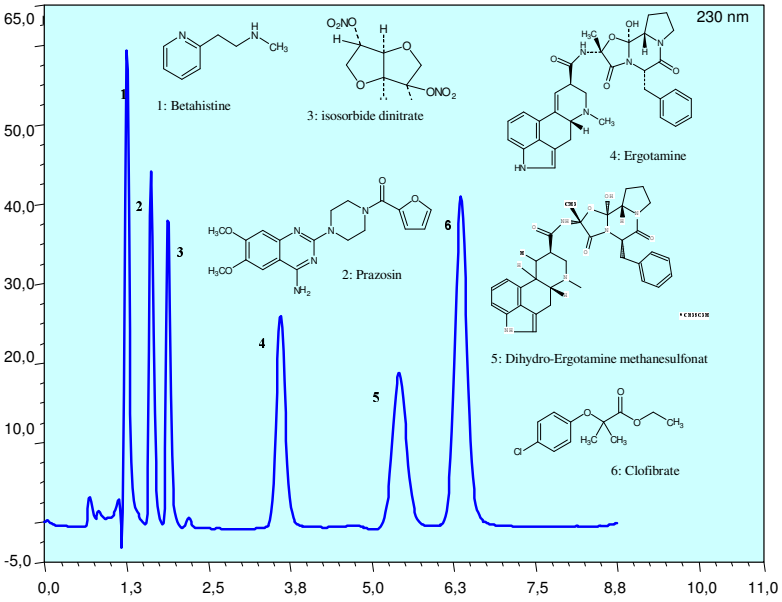
Column
Sachtopore RP (300 Å, 5 µm, 150 x 4 mm)

Eluent
70% Water
(+ 10 mM KH2PO4 30 mM Na2CO3)
30% Acetonitrile

Flow
1 ml/min

Detection
UV, 280 nm

Fig. 6: **RP Separation of Antihypertensives** **pH 9,5**



Column
Sachtopore RP (300 Å, 5 µm, 150 x 4 mm)

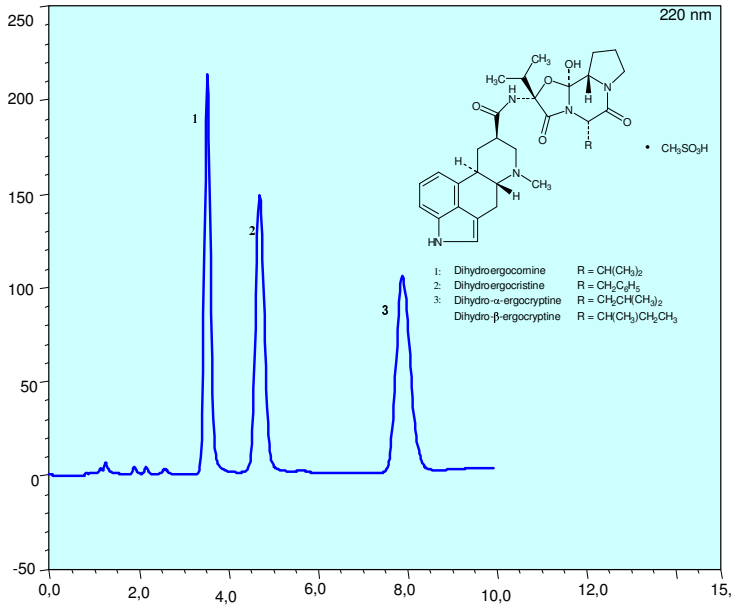
Eluent
70% Water
(+ 40 mM NH3 + 10 mM K2HPO4
+ 10 mM Na2CO3)
30% Acetonitrile

Flow
1 ml/min

Detection
UV, 230 nm

SACHTLEBEN

Fig. 7: **RP Separation of Ergot Alkaloids** **pH 9,5**



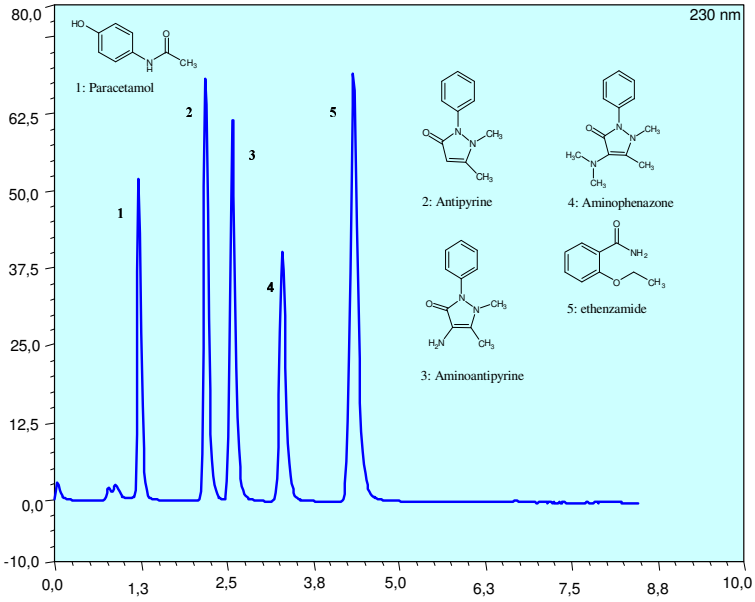
Column
Sachtopore RP (200 Å, 5 µm, 150 x 4 mm)

Eluent
70% Water
(+ 10 mM K2HPO4 + 30 mM Na2CO3)
30% Acetonitrile

Flow
1 ml/min

Detection
UV, 220 nm

Fig. 8: **RP Separation of Antipyretic Drugs** **pH 9**



Column
Sachtopore RP (300 Å, 5 µm, 150 x 4 mm)

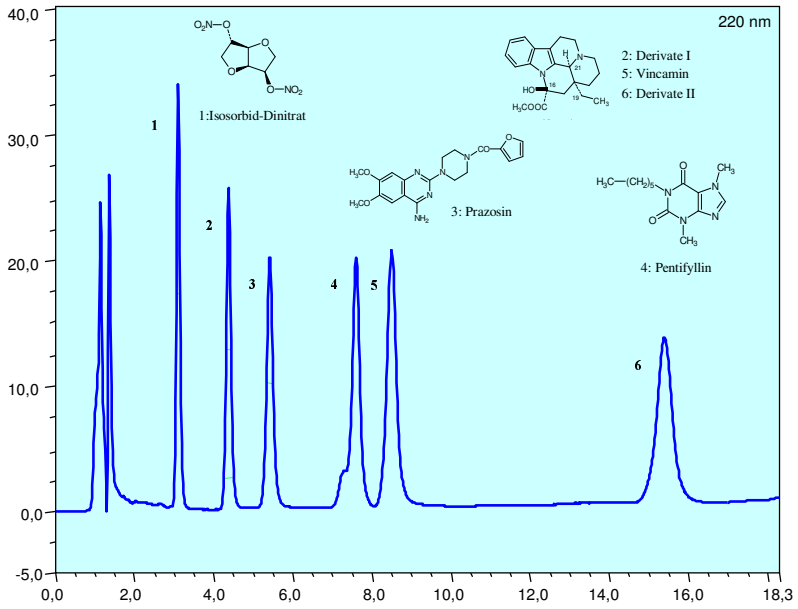
Eluent
91% Water
(+ 5 mM Borax)
9% Acetonitrile

Flow
1 ml/min

Detection
UV, 230 nm

SACHTLEBEN

Fig. 9: **RP Separation of Antihypertensives** **pH 9**



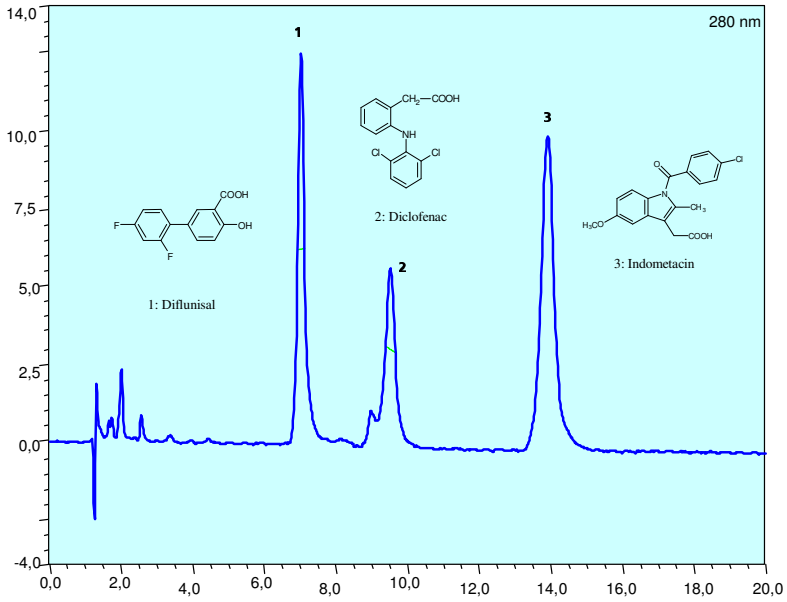
Column
Sachtopore RP (300 Å, 3 µm, 150 x 4 mm)

Eluent
81% Water
(+ 10 mM Na2B4O7 + 1 mM H3BO3)
19% Acetonitrile

Flow
1 ml/min

Detection
UV, 220 nm

Fig. 10: **RP Separation of Antiphlogistic Drugs** **pH 2,3**



Column
Sachtopore RP (300 Å, 3 µm, 150 x 4 mm)

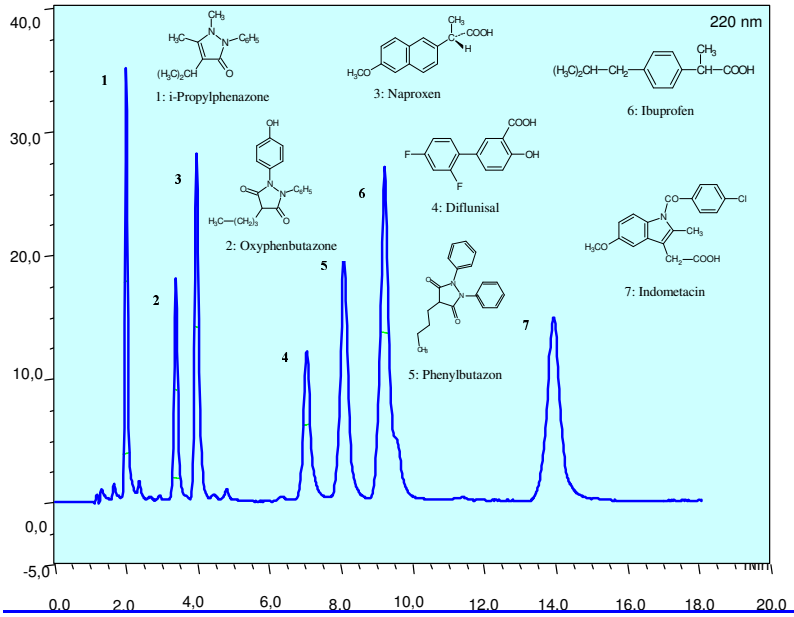
Eluent
74% Water
(+ 50 mM H3PO4 + 25 mM KH2PO4)
26% Acetonitrile

Flow
1 ml/min

Detection
UV, 280 nm

SACHTLEBEN

Fig. 11: **RP Separation of Antiphlogistic Drugs** **pH 2,3**



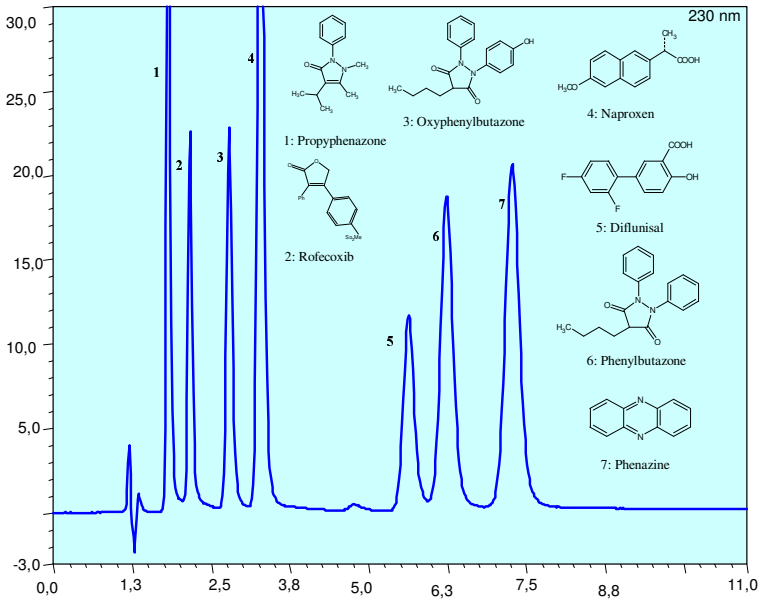
Column
Sachtopore RP (300 Å, 3 µm, 150 x 4 mm)

Eluent
74% Water
(+ 50 mM H3PO4 + 25 mM KH2PO4)
26% Acetonitrile

Flow
1 ml/min

Detection
UV, 220 nm

Fig. 12: **RP Separation of Antiphlogistic Drugs** **pH 2,2**



Column
Sachtopore RP (200 Å, 5 µm, 150 x 4 mm)

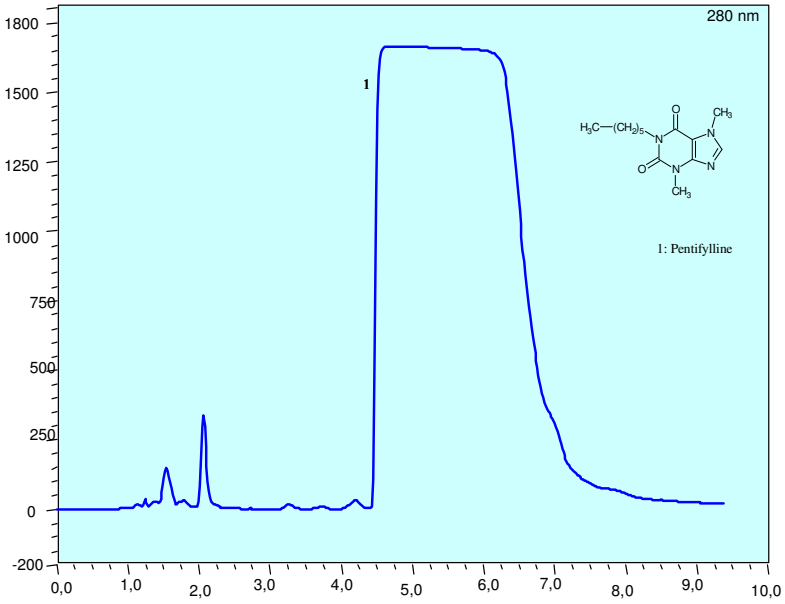
Eluent
73% Water
(+ 40 mM NaH2PO4 + 55 mM H3PO4)
27% Acetonitrile

Flow
1 ml/min

Detection
UV, 230 nm

SACHTLEBEN

Fig.13: **Preperative Separation of Pentifylline** **pH 8,8**



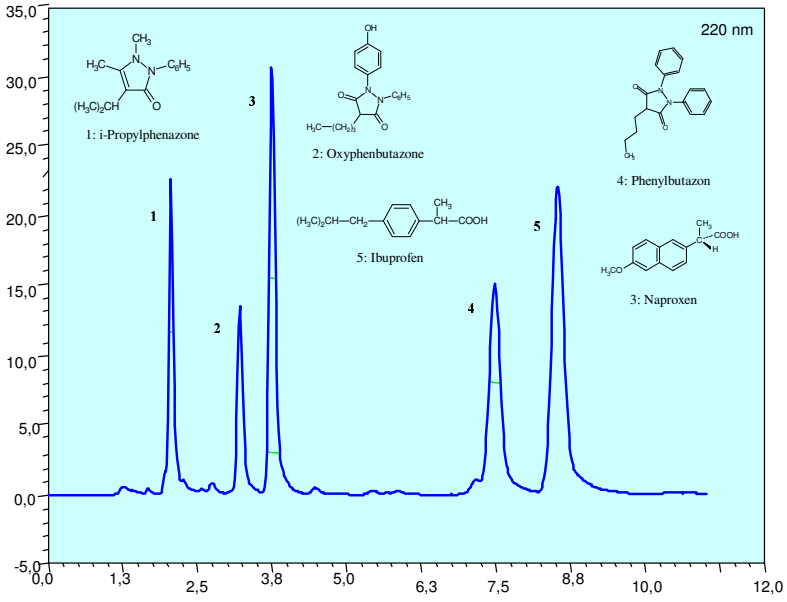
Column
Sachtopore RP (300 Å, 3 µm, 150x4 mm)

Eluent
81% Water
(+ 10 mM Na2B4O7 + 1 mM H3BO3)
19% Acetonitrile

Flow
1 ml/min

Detection
UV, 280 nm

Fig. 14: **RP Separation of Antiphlogistic Drugs** **pH 1,5**



Column
Sachtopore RP (300 Å, 3 µm, 150 x 4 mm)

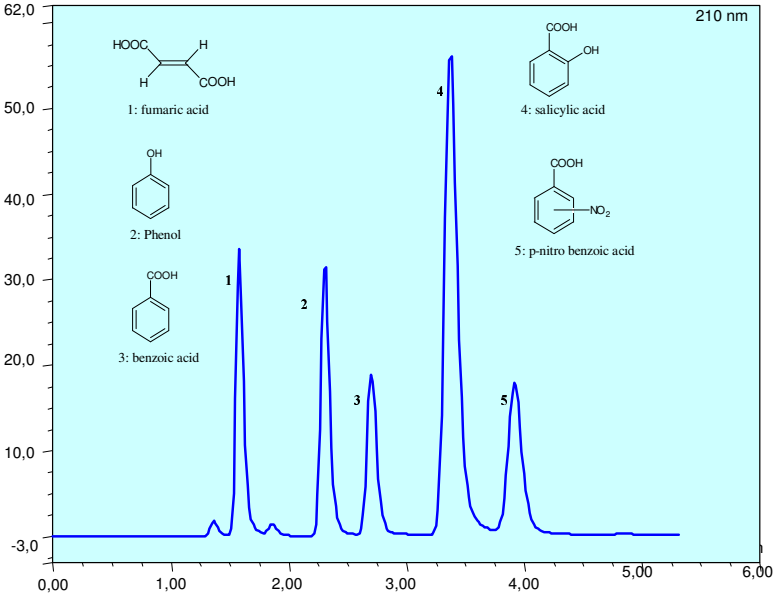
Eluent
74% Water
(+ 50 mM H3PO4 + 5 mM KH2PO4)
26% Acetonitrile

Flow
1 ml/min

Detection
UV, 220 nm

SACHTLEBEN

Fig. 15: **RP Separation of Antiseptics** **pH 1,5**



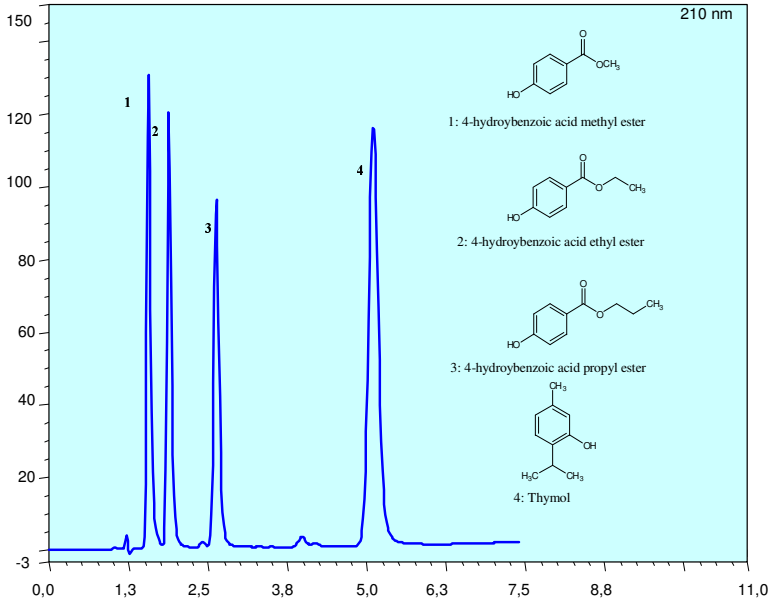
Column
Sachtopore RP (200 Å, 5 µm, 150 x 4 mm)

Eluent
85% Water
(+ 20 mM H3PO4)
15% Acetonitrile

Flow
0,8 ml/min

Detection
UV, 210 nm

Fig. 16: **RP Separation of Antiseptics** **pH 1,5**



Column
Sachtopore RP (200 Å, 5 µm, 150 x 4 mm)

Eluent
75% Water
(+ 20 mM H3PO4)
25% Acetonitrile

Flow
1 ml/min

Detection
UV, 210 nm