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APPENDIX

TABLE 1 : Physical Characteristics [melting points]

Compound	Melting Point (°C)
P-Acetaminophenol	170
O-Monoacetyl-p-acetaminophenol	151
N,O-Diacetyl-p-acetaminophenol	79.5-80

TABLE 2 : R_f Values for Paracetamol and Its Derivatives

Compound	R _f - Value	Colour of the Spot
P-Acetaminophenol	0.18) Purple
O-Monoacetyl-p-acetaminophenol (MAAP)	0.29) under short) wavelength) UV-light
N,O-Diacetyl-p-acetaminophenol (DAAP)	0.62	white spot under long wavelength UV-light

**TABLE 3 : Effect of Temperature on Acetylation**

Temperature (°c) Refluxed for 5 hours	Area Ratio* DAAP/ Benzophenone	Area Ratio* MAAP/ Benzophenone
5	0.0347 ± 0.0023	1.5591 ± 0.1179
29 [room temp.]	0.0398 ± 0.0046	1.4318 ± 0.1369
60	0.0607 ± 0.0032	1.2427 ± 0.0741
90	0.3917 ± 0.0465	0.9915 ± 0.1469
120	1.0534 ± 0.0810	0.4851 ± 0.0559
160	1.4833 ± 0.1000	0.2483 ± 0.0242
200	1.5753 ± 0.0833	0.1657 ± 0.0063
235	1.5944 ± 0.0634	0.1640 ± 0.0121
260	1.5949 ± 0.0790	0.1456 ± 0.0184

* mean ± SD of four separate experiments

TABLE 4 : Effect of Incubating Time on Acetylation at 220°C

Refluxed Time (in minutes)	Area Ratio* DAAP/Benzophenone	Area Ratio* MAAP/Benzophenone
0	0.0135 ± 0.0877	1.2722 ± 0.0427
30	0.4614 ± 0.0712	0.9997 ± 0.0839
60	0.8260 ± 0.0396	0.7284 ± 0.0741
90	1.2314 ± 0.1843	0.4292 ± 0.0663
120	1.4127 ± 0.0907	0.3180 ± 0.0285
150	1.5201 ± 0.0766	0.2321 ± 0.0383
180	1.5574 ± 0.0651	0.1958 ± 0.1112
210	1.5563 ± 0.0241	0.1725 ± 0.1029
270	1.5570 ± 0.1279	0.1352 ± 0.1234
300	1.5457 ± 0.1663	0.1354 ± 0.1298

* mean ± SD of four separate experiments

TABLE 5: Effect of Amount and Composition of Acetylating Reagents [pyridine and acetic anhydride].

Pyridine (in ml)	Acetic Anhydride (in ml)	Area Ratio* DAAP/ Benzophenone
4	4	1.7082 ± 0.0410
4	8	1.7208 ± 0.0822
4	12	1.7180 ± 0.0498
4	16	1.7877 ± 0.0235
2	4	1.7489 ± 0.0358
4	4	1.7082 ± 0.0410
8	4	1.2687 ± 0.0904
12	4	1.0146 ± 0.0952
16	4	0.8206 ± 0.0324
4	4	1.7082 ± 0.0410
8	8	1.7461 ± 0.0568
12	12	1.7000 ± 0.0799
16	16	1.7044 ± 0.0943

* mean ± SD of three separate experiments

TABLE 6: Effect of Varying Concentrations of Paracetamol

Amount (in mg) of Paracetamol BP	Area Ratio* DAAP/ Benzophenone
20	0.1078 ± 0.0018
40	0.2230 ± 0.0021
60	0.3313 ± 0.0024
80	0.4532 ± 0.0053
100	0.5639 ± 0.0082
200	1.1041 ± 0.0285
300	1.6572 ± 0.0235
400	2.1918 ± 0.0302
500	2.7509 ± 0.0311
600	3.2931 ± 0.0130
800	4.3364 ± 0.0513
1000	5.3722 ± 0.0941
1500	7.0295 ± 0.0636

* mean ± SD of six separate experiments

Correlation coefficient(r) between paracetamol BP & area ratio

= 0.9954

TABLE 7 : Standard Curve of Paracetamol in Determination of Paracetamol in Syrup Preparations

Amonut of Paracetamol BP(in mg)	Area Ratio* DAAP/ Benzophenone	%CV
20	0.1078 ± 0.0018	1.66
40	0.2230 ± 0.0021	0.95
60	0.3313 ± 0.0024	0.73
80	0.4532 ± 0.0053	1.17
100	0.5639 ± 0.0082	1.46

* mean ± SD of six separate experiments

Correlation Coefficient (r) between paracetamol BP & area ratio
= 0.9998



TABLE 8 : Quantitative Determination of Paracetamol in Syrup Preparations Using Acetylation-GLC Method

Compound	Density (g/ml)	Weight of syrup taken (g)	Area Ratio* DAAP/Benz.	%Labelled Amount
Syrup. No. 1	1.1783	2.3565	0.2660	99.53
		2.3560	0.2632	98.53
		2.3567	0.2689	100.58
		2.3562	0.2648	99.11
		2.3569	0.2700	100.97
		2.3564	0.2632	98.51
				\bar{X} - 99.54
		SD-1.0385		
		%CV-1.0433		
Syrup No. 2	1.2107	2.4213	0.2721	101.76
		2.4210	0.2696	100.86
		2.4216	0.2722	101.78
		2.4208	0.2690	99.41
		2.4211	0.2711	101.40
		2.4205	0.2684	100.44
				\bar{X} -100.94
		SD-0.9151		
		%CV-0.9065		
Syrup No. 3	1.2470	2.4940	0.2715	101.53
		2.4935	0.2695	100.82
		2.4933	0.2689	100.61
		2.4945	0.2700	100.97
		2.4943	0.2728	101.99
		2.4938	0.2707	101.25
				\bar{X} -101.19
		SD-0.5061		
		%CV-0.5001		

TABLE 8 : Continued-

Compound	Density (g/ml)	Weight of syrup taken (g)	Area Ratio* DAAP/Benz.	%Labelled Amount
Syrup No. 4	1.1183	2.2367	0.2801	104.67
		2.2365	0.2795	104.46
		2.2370	0.2807	104.87
		2.2364	0.2780	103.91
		2.2360	0.2769	103.53
		2.2373	0.2821	105.37
				\bar{X} -104.47
		SD-0.6644		
		%CV-0.6360		
Syrup No. 5	1.2314	2.4623	0.2773	103.67
		2.4620	0.2766	103.43
		2.4618	0.2759	103.18
		2.4615	0.2727	102.02
		2.4625	0.2795	104.46
		2.4628	0.2800	103.57
				\bar{X} -103.57
		SD-0.9487		
		%CV-0.9160		

* mean of six separate determinations

**TABLE 9 : Percent recovery of Paracetamol in Syrup
Preparation No.2 Using Acetylation-GLC Method**

Wt.of Syrup. eqv.to48 mg Paracet. (g).	Weight of. ParacetamolBP added (g)	Area Ratio* DAAP/Benz.	% Recovery
2.4213 2.4216	0.01122 0.01192	0.3358 0.3400	99.39 98.58 $\bar{X} = 98.98$
2.4208 2.4216	0.02254 0.02198	0.4002 0.3955	101.90 98.21 $\bar{X} = 100.06$
2.4205 2.4211	0.03202 0.03151	0.4528 0.4493	100.82 99.01 $\bar{X} = 99.92$

* mean of six separate determinations

TABLE 10 : Quantitative Determination of Paracetamol in Syrup Preparations Using USP XXII Method

Standard's. Absorbance	Compound	Sample's Absorbance	%Labelled Amount
0.690	Syrup No. 1	0.659	100.07
0.683		0.660	100.22
0.685		0.650	98.70
0.682		0.650	98.70
0.690		0.650	98.70
0.683		0.645	97.94
\bar{X} -0.686		\bar{X} -0.652	\bar{X} - 99.06
SD=0.004	SD=0.006	SD=0.8954	
%CV=0.528	%CV=0.903	%CV=0.9039	
	Syrup No. 2	0.661	100.37
		0.665	100.98
		0.660	100.22
		0.654	99.31
		0.650	98.70
		0.655	99.46
		\bar{X} -0.658	\bar{X} -99.84
	SD=0.005	SD=0.8306	
	%CV=0.832	%CV=0.8320	



**TABLE 11 : Percent recovery of Paracetamol in Syrup
Preparation No.2 Using USP XXII Method**

Wt.of Paracet.BP added (g)	Absorbance of mixture	% Recovery
0.01202	0.691	100.05
0.01204	0.691	97.89
		$\bar{X} = 99.97$
0.02208	0.718	99.03
0.02205	0.721	104.12
		$\bar{X} = 101.58$
0.03204	0.748	102.37
0.03197	0.745	99.17
		$\bar{X} = 100.77$

Note: Mean absorbance of standard solution conc. 8 $\mu\text{g/ml}$ was 0.686 ± 0.0036 (based on six separate experiments)
Mean absorbance of paracetamol in syrup No.2 equivalent to 300 mg was 0.658 ± 0.0055 (based on six separate experiments).

TABLE 12 : Standard Curve of Paracetamol for Determination of Paracetamol in Tablet and Injection Preparations

Amount of Paracetamol BP.(mg)	Area Ratio* of DAAP/ Benzophenone	%CV
100	0.5639 ± 0.0082	1.46
200	1.1041 ± 0.0285	2.58
300	1.6572 ± 0.0235	1.42
400	2.2105 ± 0.0232	1.05
500	2.7509 ± 0.0311	1.34

* mean ± SD of six separate experiments

Correlation Coefficient (r) between Paracetamol & area ratio
= 1.0000

**TABLE 13 : Quantitative Determination of Paracetamol in
Tablet Preparations Using Acetylation-GLC
Method**

Compound	Weight/ tablet (g)	Wt of powder taken (g)	Area Ratio* DAAP/Benz.	%Labelled Amount
Tablet No. 1	0.6490	0.3894	1.6917	102.10
		0.3899	1.6898	101.85
		0.3890	1.6860	101.86
		0.3895	1.6924	102.11
		0.3892	1.6908	102.10
		0.3896	1.6900	101.94
Tablet No. 2	0.6063	0.3638	1.6698	100.76
		0.3640	1.6544	99.77
		0.3635	1.6820	101.59
		0.3630	1.6443	99.42
		0.3633	1.6467	99.49
		0.3636	1.6629	100.40
Tablet No. 3	0.5527	0.5527	1.6850	101.69
		0.5525	1.6766	101.22
		0.5522	1.6552	99.97
		0.5530	1.6864	101.72
		0.5524	1.6691	100.78
		0.5524	1.6849	101.74

TABLE 13 : Continued -

Compound	Weight/ tablet (g)	Wt of powder taken (g)	Area Ratio* DAAP/Benz.	%Labelled Amount
Tablet No. 4	0.3979	0.3673	1.7502	105.65
		0.3670	1.7444	105.39
		0.3671	1.7324	104.63
		0.3668	1.7256	104.30
		0.3665	1.7288	104.58
		0.3671	1.7401	105.10
				\bar{X} -104.94
				SD-0.5230
				%CV-0.4983
Tablet No. 5	0.5035	0.5035	1.7268	104.23
		0.5030	1.7112	103.39
		0.5033	1.7024	102.79
		0.5038	1.7088	103.08
		0.5031	1.6956	102.42
		0.5036	1.6998	102.57
				\bar{X} -103.08
				SD-0.6631
				%CV-0.6433

* mean of six separate determinations

**TABLE 14 : Percent Recovery of Paracetamol in Tablet
Preparation No.1 Using Acetylation-GLC Method**

Wt.of powder eqv.to300mg Paracet.(g)	Weight of paracetamolBP added (g)	Area Ratio* DAAP/Benz.	% Recovery
0.3899	0.03110	1.8607	100.28
0.3890	0.03232	1.8632	100.05
			\bar{X} -100.17
0.3896	0.06064	2.0166	98.28
0.3894	0.06108	2.0202	98.14
			\bar{X} - 98.21
0.3892	0.08956	2.1878	100.27
0.3896	0.09093	2.1020	100.92
			\bar{X} -101.10

* mean of six separate determinations



TABLE 15 : Quantitative Determination of Paracetamol in Tablet Preparations Using USP XXII Method

Standard's Absorbance	Compound	Sample's Absorbance	%Labelled Amount
0.685	Tablet No. 1	0.689	100.58
0.682		0.716	104.68
0.670		0.691	101.02
0.700		0.712	104.09
0.690		0.699	102.19
0.678		0.707	103.36
\bar{X} - 0.684		\bar{X} -0.702	\bar{X} -102.65
SD- 0.010	SD-0.011	SD-1.6640	
%CV-1.503	%CV-1.585	%CV-1.6210	
	Tablet No. 2	0.695	101.61
		0.682	99.71
		0.675	98.68
		0.688	100.58
		0.700	102.34
		0.694	101.46
		\bar{X} - 0.697	\bar{X} -100.73
	SD- 0.014	SD-1.3540	
	%CV-2.003	%CV-1.3440	

TABLE 16 : Percent recovery of Paracetamol in Tablet Preparation No.1 Using USP XXII Method

Wt.of Paracet.BP added (g)	Absorbance of mixture	% Recovery
0.03112	0.786	98.66
0.03023	0.780	97.20
		\bar{X} - 97.93
0.06092	0.864	97.19
0.06194	0.870	100.43
		\bar{X} - 98.81
0.08957	0.948	100.38
0.08943	0.942	98.09
		\bar{X} - 99.24

Note: Mean absorbance of standard solution conc. $8\mu\text{g/ml}$ was 0.684 ± 0.0103 (based on six separate experiments)
 Mean absorbance of paracetamol in tablet No.1 equivalent to 300 mg was 0.702 ± 0.0111 (based on six separate experiments).

TABLE 17 : Quantitative Determination of Paracetamol in Injection Preparations Using Acetylation-GC Method

Compound	Density (g/ml)	Wt of Sol ^Δ taken(g)	Area Ratio* DAAP/Benz.	%Labelled Amount
Injection No. 1	1.0709	1.0652	0.8395	101.06
		1.0630	0.8226	99.20
		1.0627	0.8300	100.19
		1.0638	0.8280	99.79
		1.0622	0.8324	100.48
		1.0619	0.8320	100.45
			\bar{X} =100.20	
			SD=0.6401	
			%CV=0.6388	
Injection No. 2	1.0780	1.0780	0.6943	80.67
		1.0775	0.7021	81.66
		1.0770	0.7011	81.57
		1.0784	0.6952	80.75
		1.0782	0.6947	80.70
		1.0778	0.6945	80.71
			\bar{X} = 81.01	
			SD=0.4702	
			%CV=0.5804	

* mean of six separate determinations



**TABLE 18 : Percent Recovery of Paracetamol in Injection
Preparation No.1 Using Acetylation-GLC Method**

Wt.of inject ⁿ equiv.to150mg Paracet.(g)	Weight. of ParacetamolBP added (g)	Area Ratio* DAAP/Benz.	% Recovery
1.0652	0.03022	0.9996	96.68
1.0621	0.02951	0.9889	98.26
			$\bar{X} = 97.47$
1.0622	0.06048	1.1612	99.21
1.0630	0.06103	1.1548	99.33
			$\bar{X} = 99.27$
1.0619	0.09014	1.3206	98.91
1.0622	0.09127	1.3274	99.97
			$\bar{X} = 99.44$

* mean of six separate determinations

TABLE 19 : Standard Curve of Paracetamol in Human Serum

Concentration of Paracetamol($\mu\text{g}/10\text{ml}$)	Area Ratio* DAAP/ Benzophenone	%CV
4	0.1701 ± 0.0111	6.53
8	0.3272 ± 0.0095	2.90
12	0.4728 ± 0.0084	1.78
16	0.6352 ± 0.0126	1.98
20	0.7651 ± 0.0099	1.29

* mean \pm SD of Three Separate Experiments

Correlation Coefficient (r) between Paracetamol & Area Ratio

- 0.9994

TABLE 20 : Quantitative Determination of Paracetamol in Human Serum Using Acetylation-GLC Method

Peak Area Ratio* DAAP/Benzophenone	Amount of Paracetamol/ ml of Serum(μ g)
0.3288 \pm 0.0019	40.60

* mean \pm SD of six separate determinations

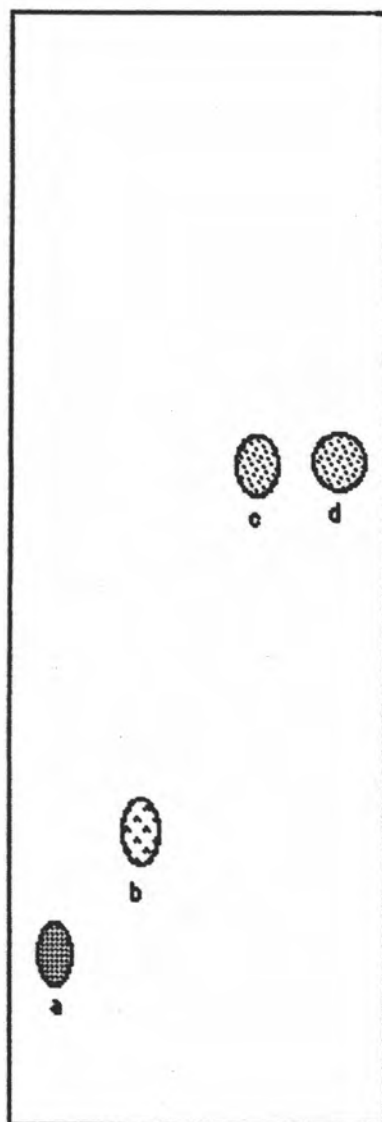


Figure 1. Thin Layer Chromatogram of Paracetamol and Its Derivatives
a - Paracetamol, b - MAAP, c and d - DAAP

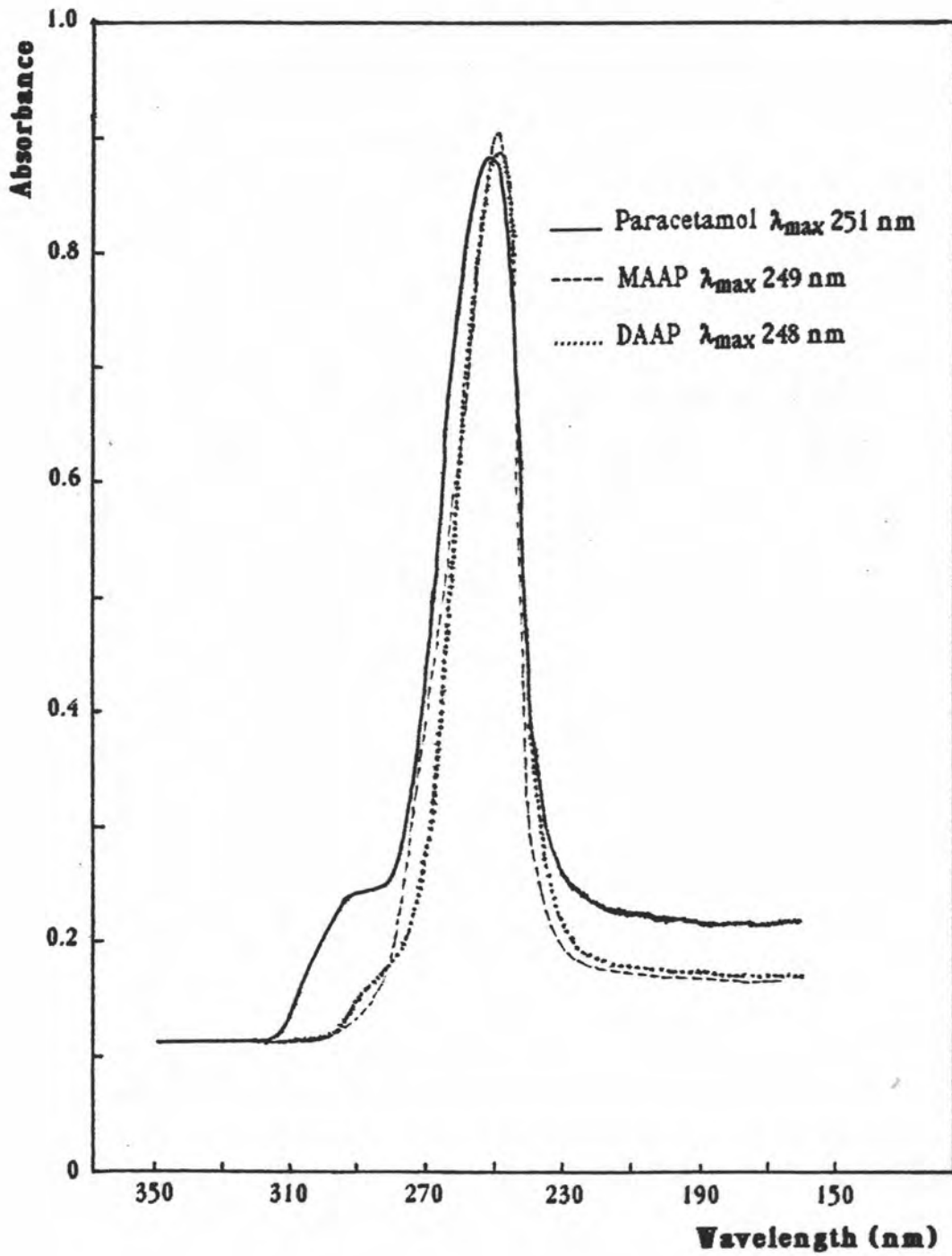


Figure 2. Ultraviolet Spectrum of Paracetamol and Its Derivatives in Chloroform

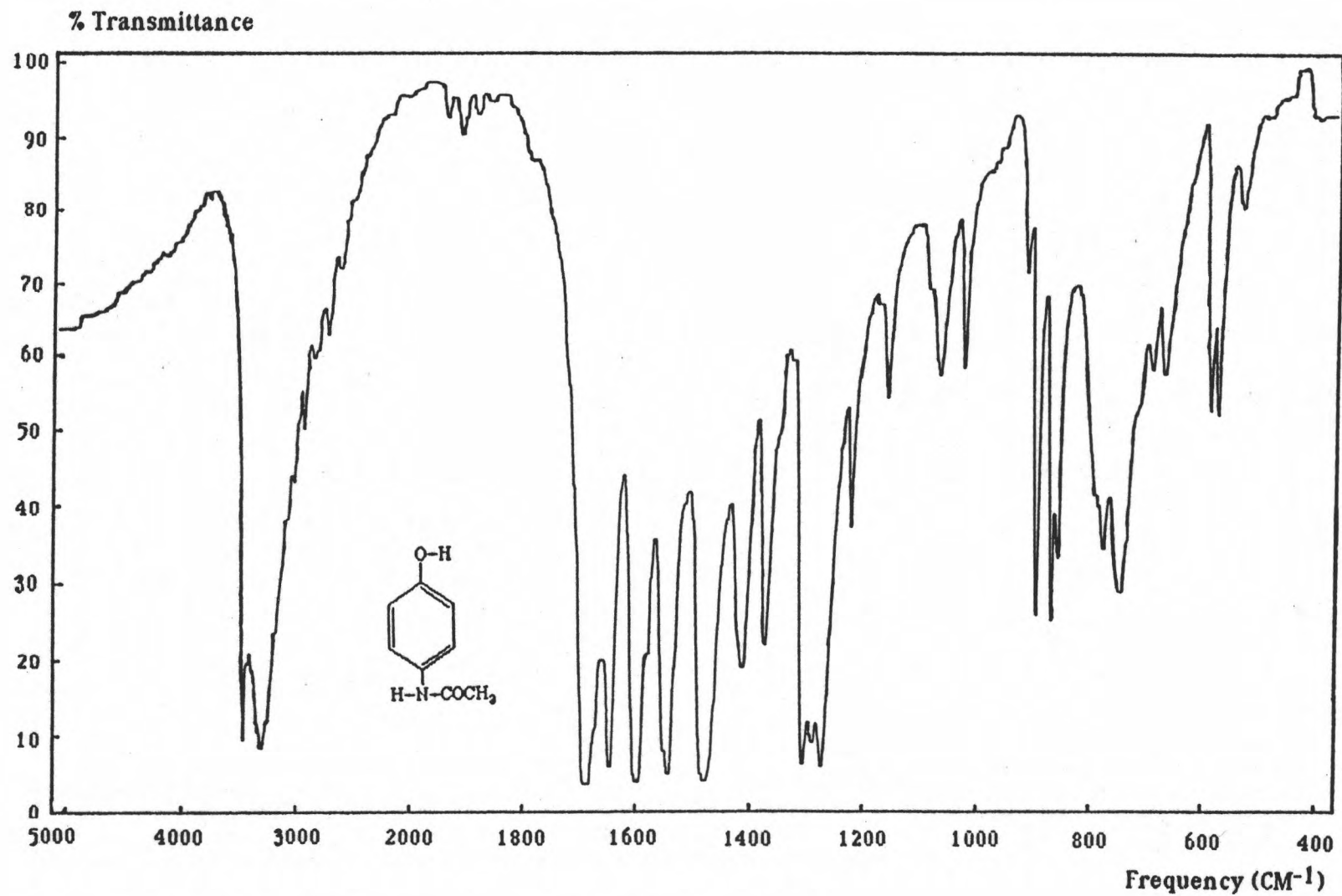


Figure 3. Infrared Spectrum of Paracetamol in KBr Disc

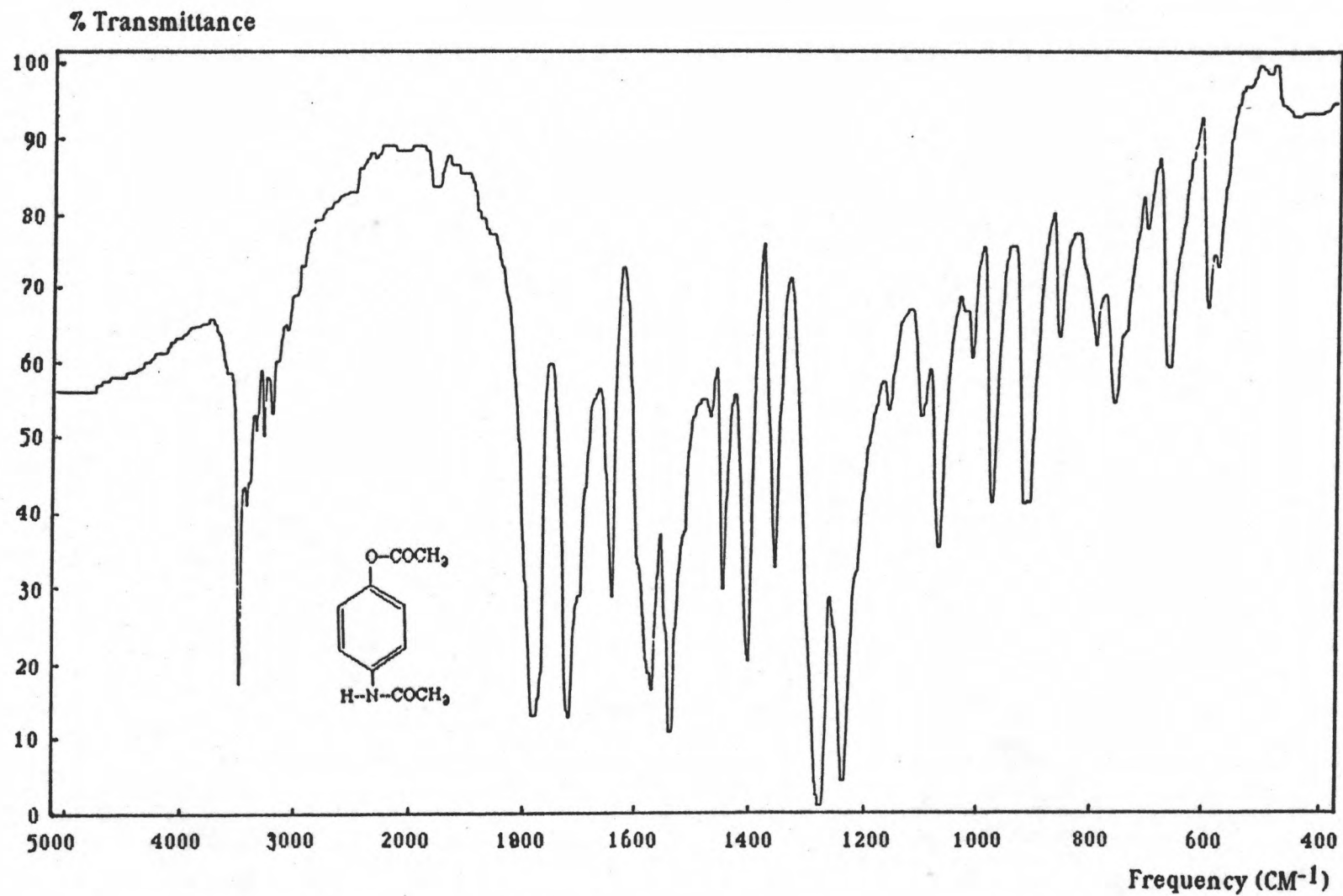


Figure 4. Infrared Spectrum of MAAP in KBr Disc

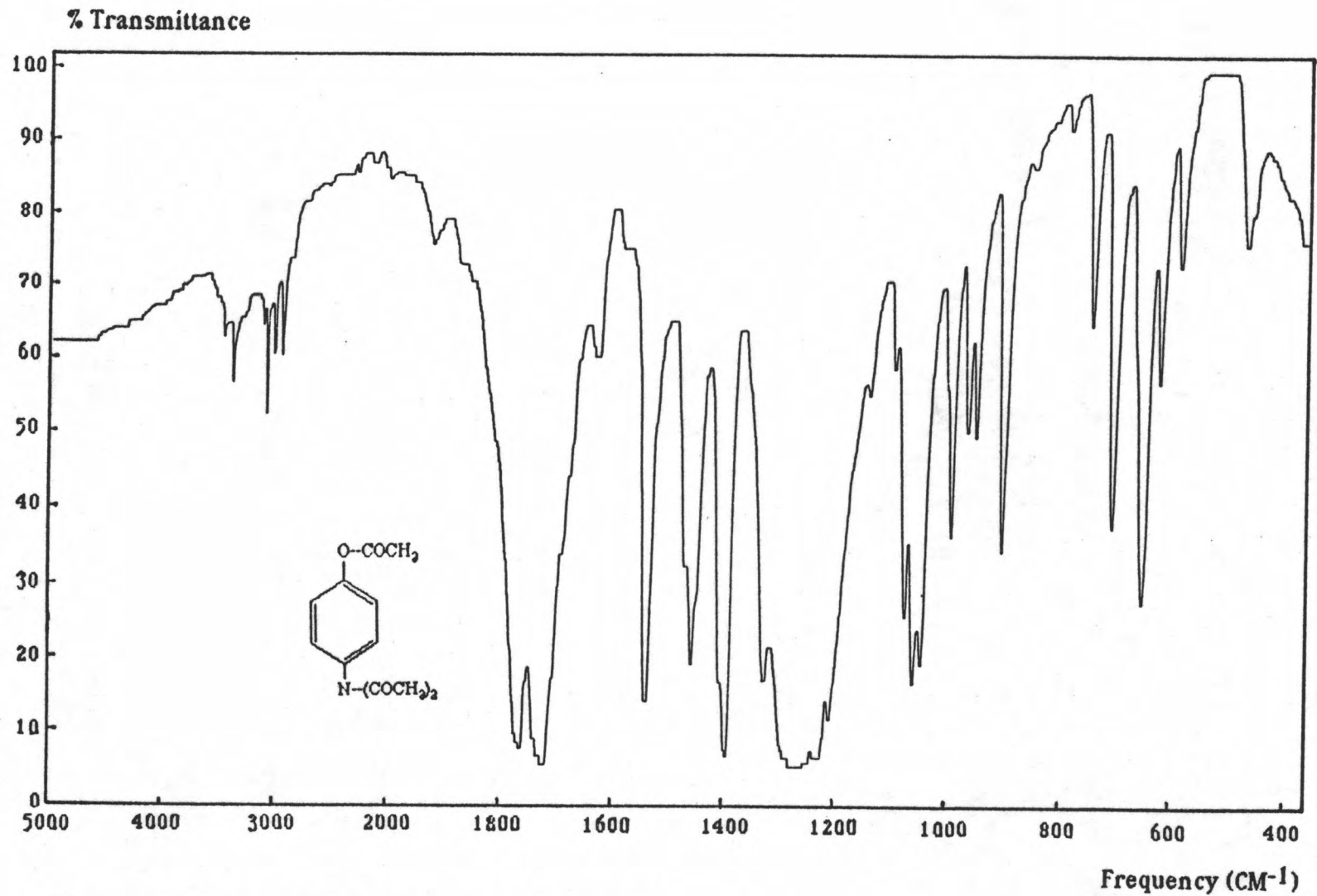


Figure 5. Infrared Spectrum of DAAP in KBr Disc



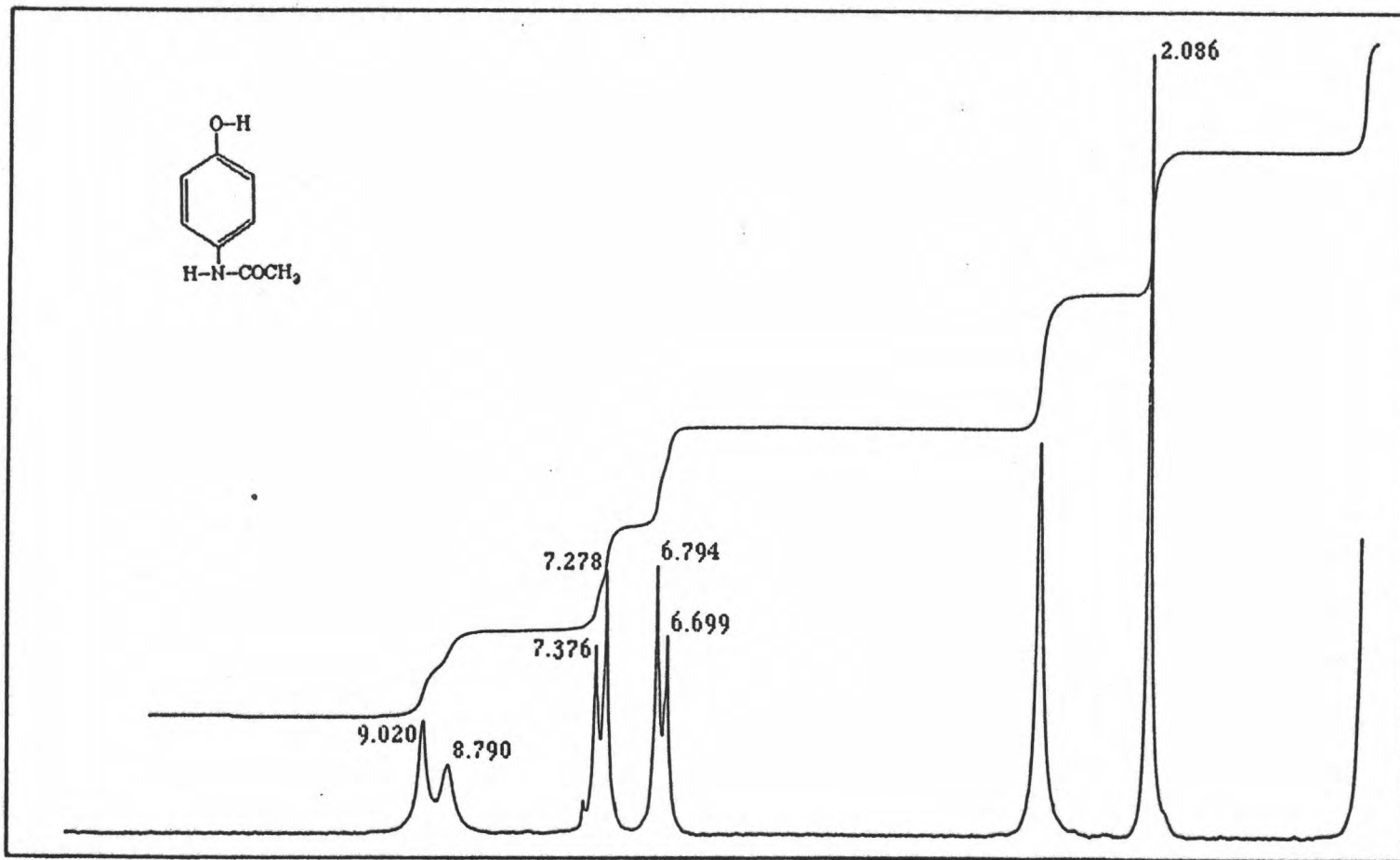


Figure 6. Proton Nuclear Magnetic Resonance Spectrum of Paracetamol in DMSO-d₆

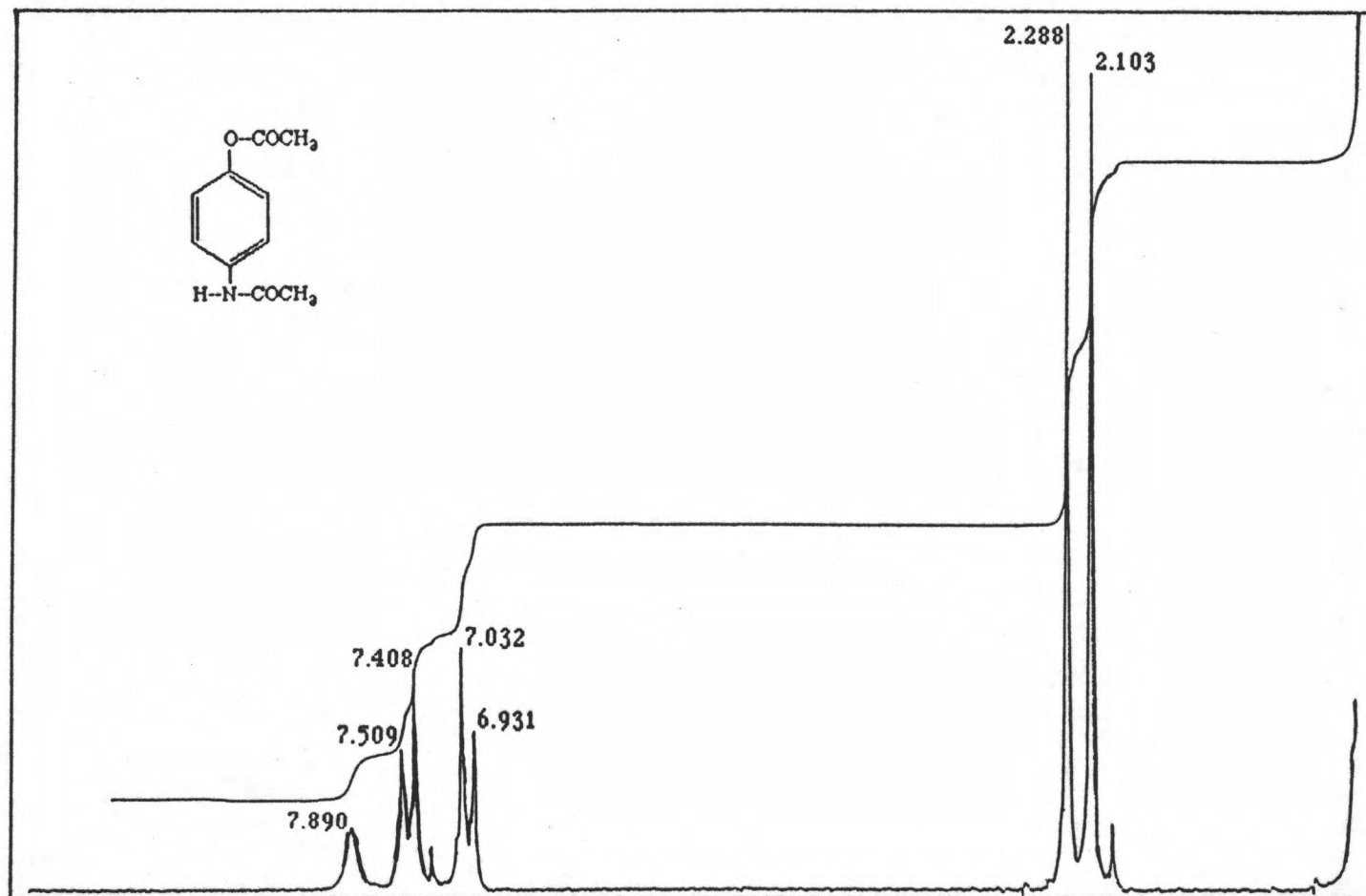


Figure 7. Proton Nuclear Magnetic Resonance Spectrum of MAAP in $\text{CHCl}_3\text{-d}$

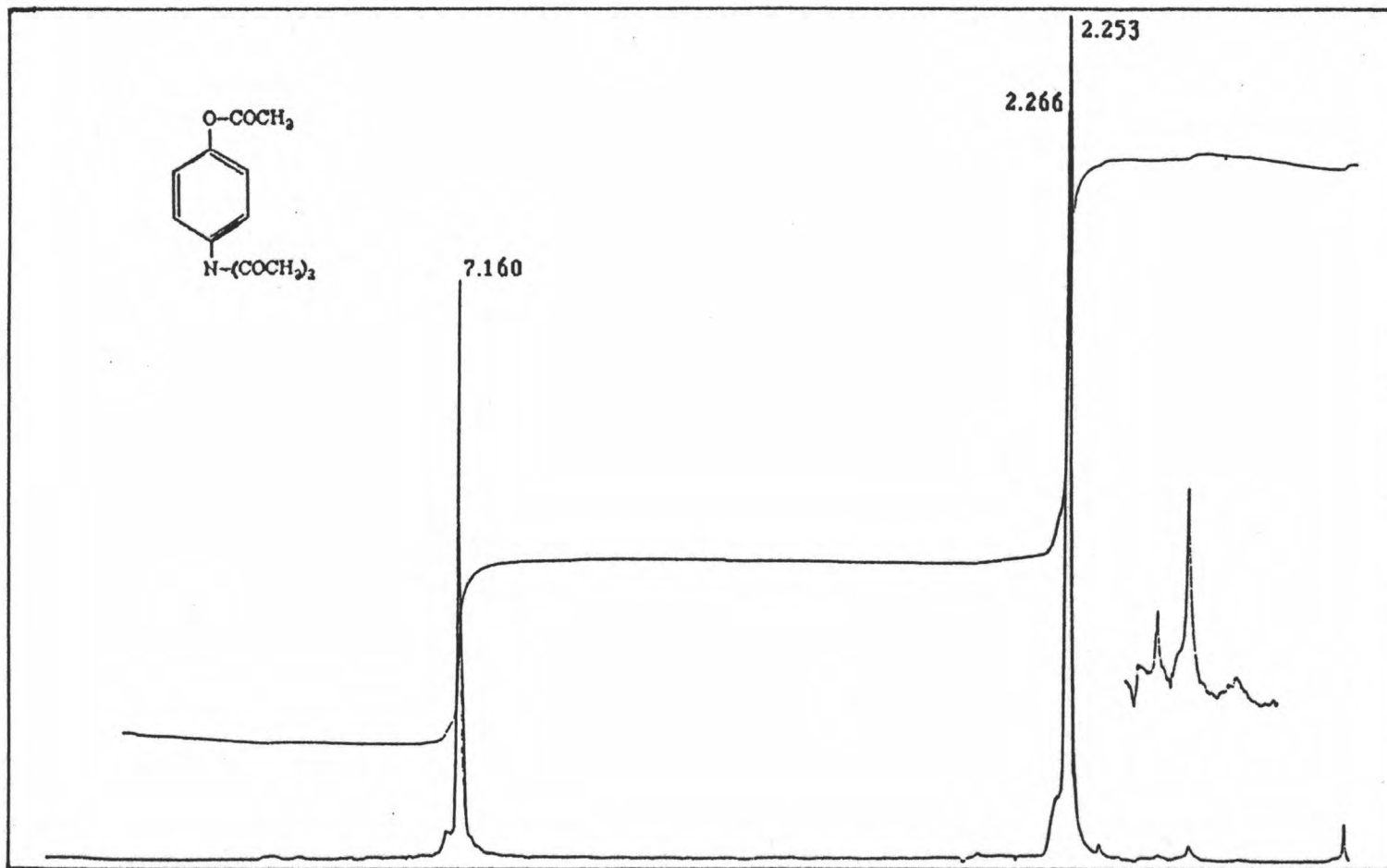


Figure 8. Proton Nuclear Magnetic Resonance Spectrum of DAAP in CHCl_3 -d



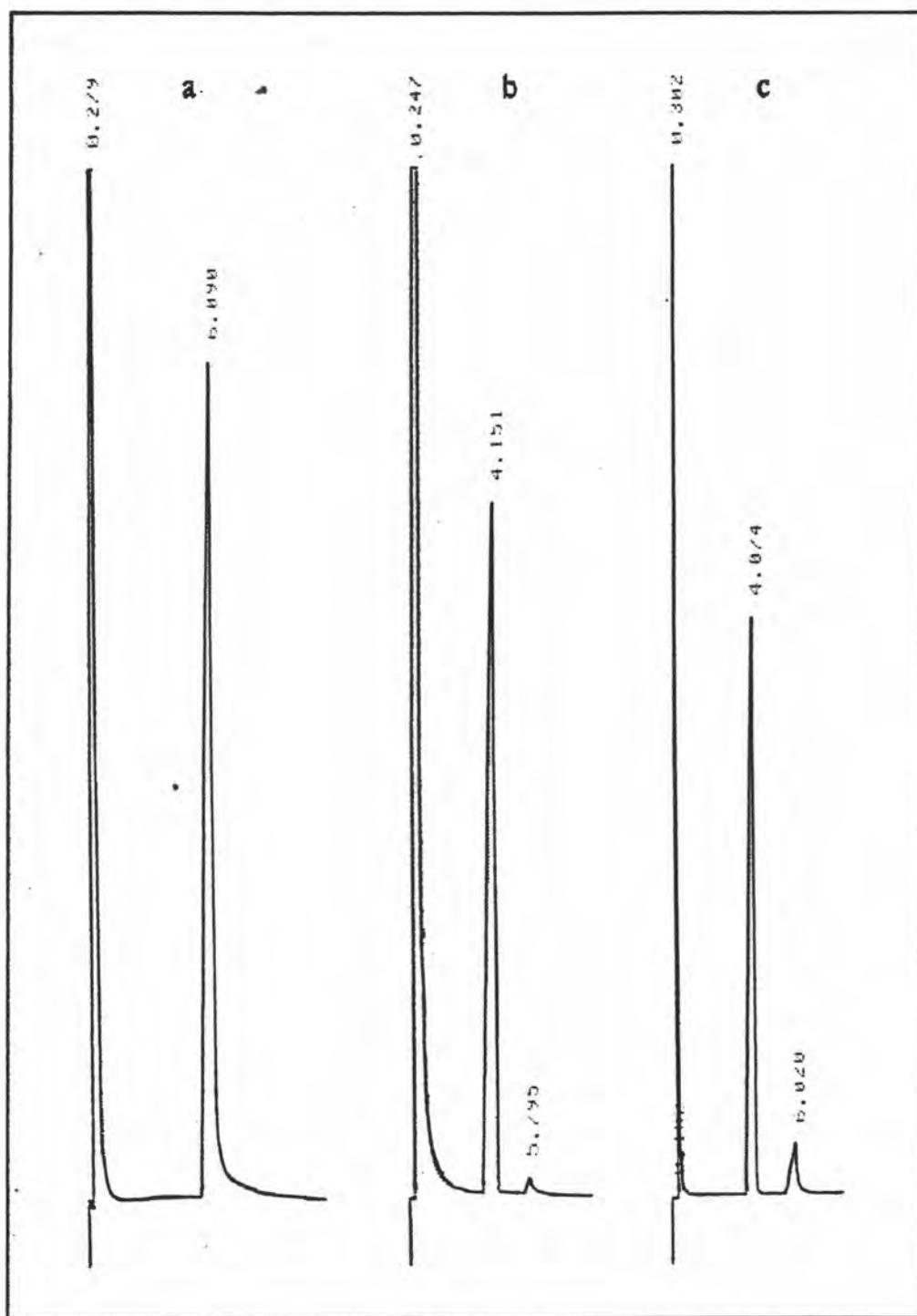


Figure 9. Gas-Liquid Chromatogram of Paracetamol Derivatives
from Sample and Standards

a) MAAP, b) DAAP, c) Reaction Mixture of MAAP and DAAP

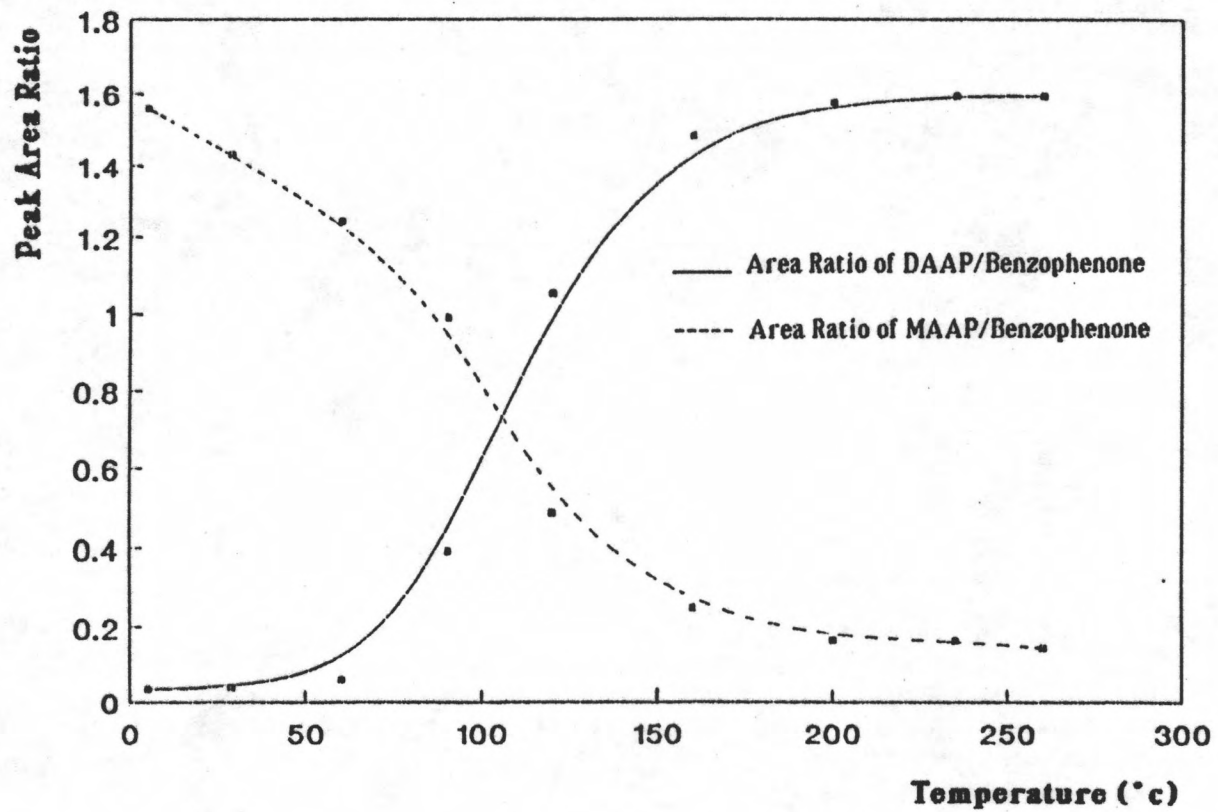


Figure 10. Effect of Temperature on Acetylation

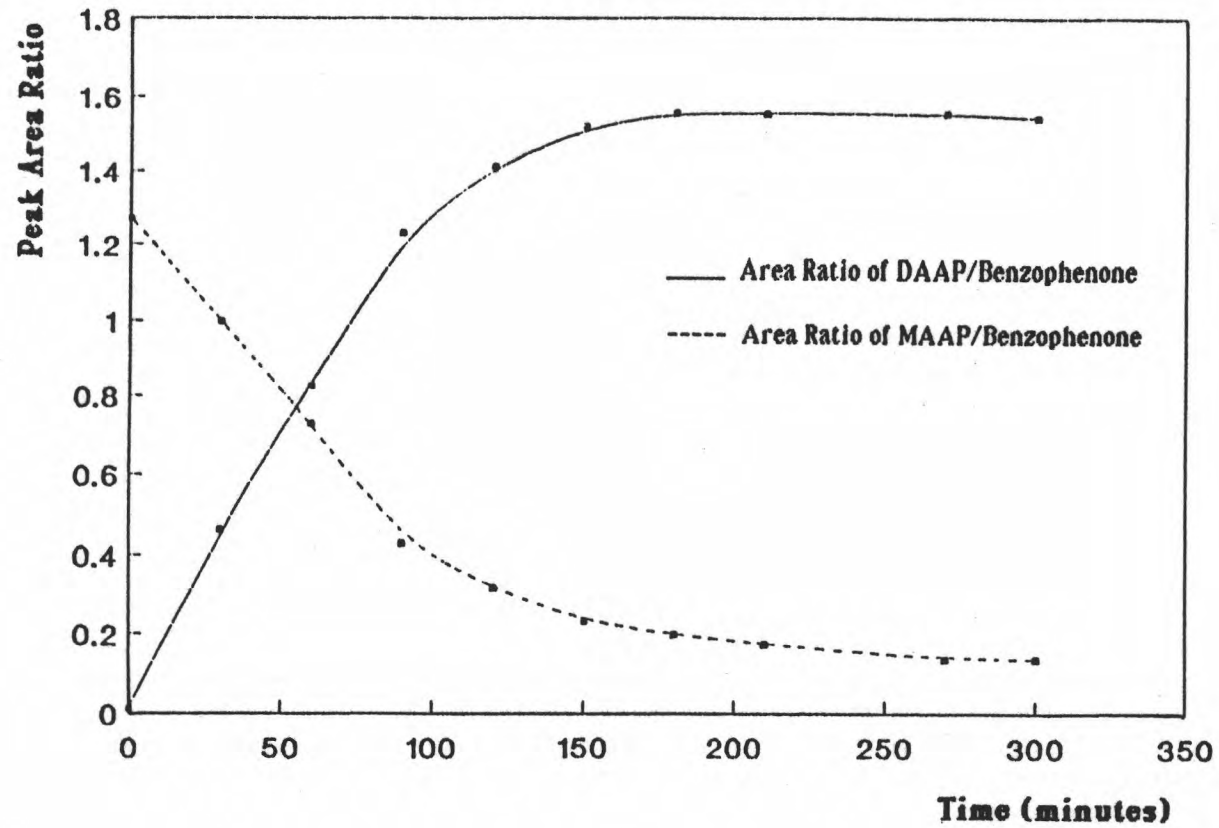


Figure 11. Effect of Incubation Time on Acetylation at 220°C

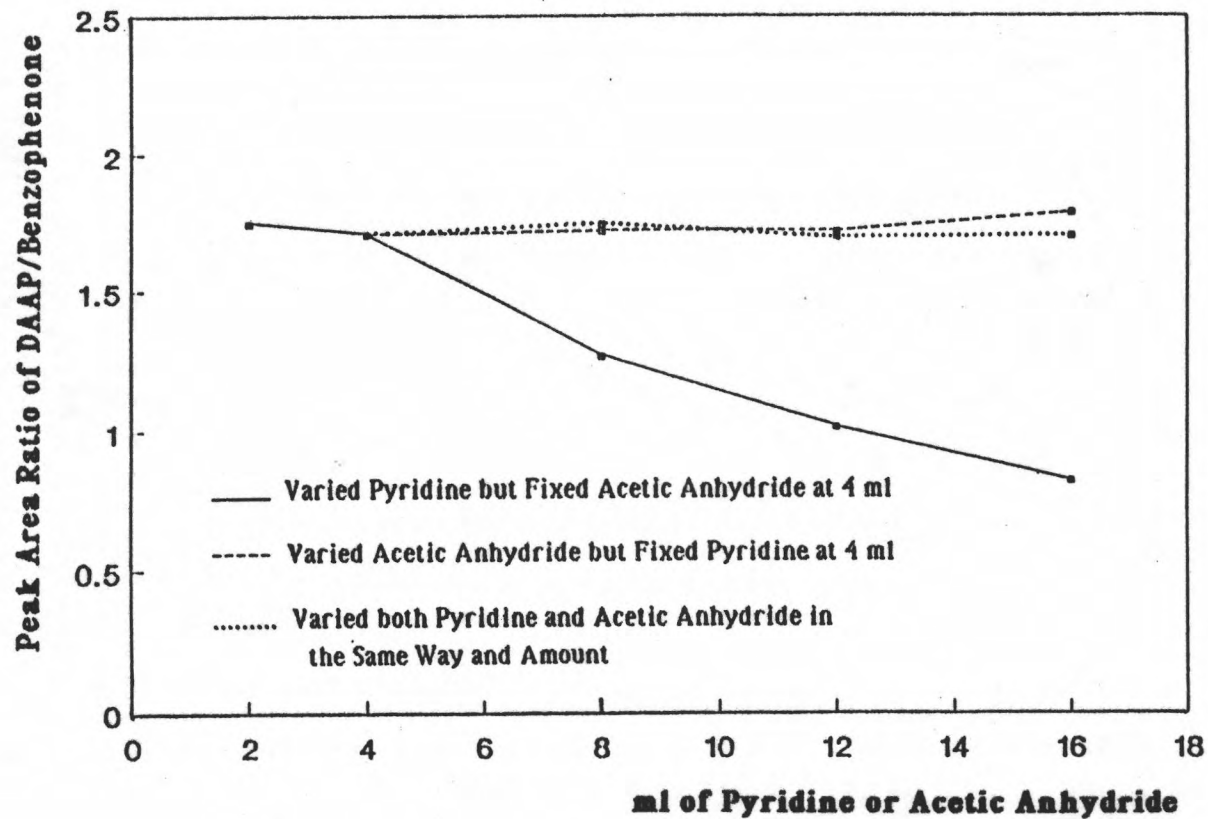


Figure 12. Effect of Amount and Composition of Acetylation Reagents (pyridine and acetic anhydride)

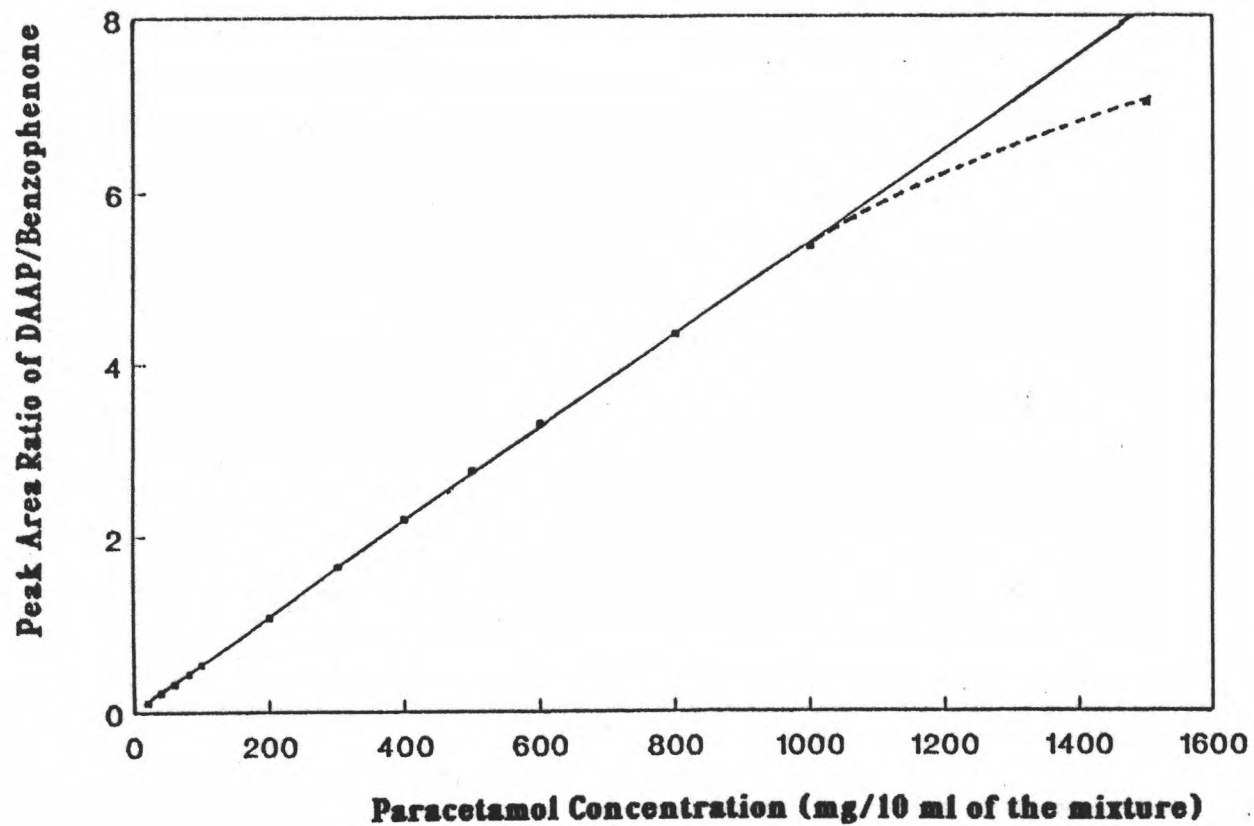


Figure 13. Effect of Varying Concentrations of Paracetamol

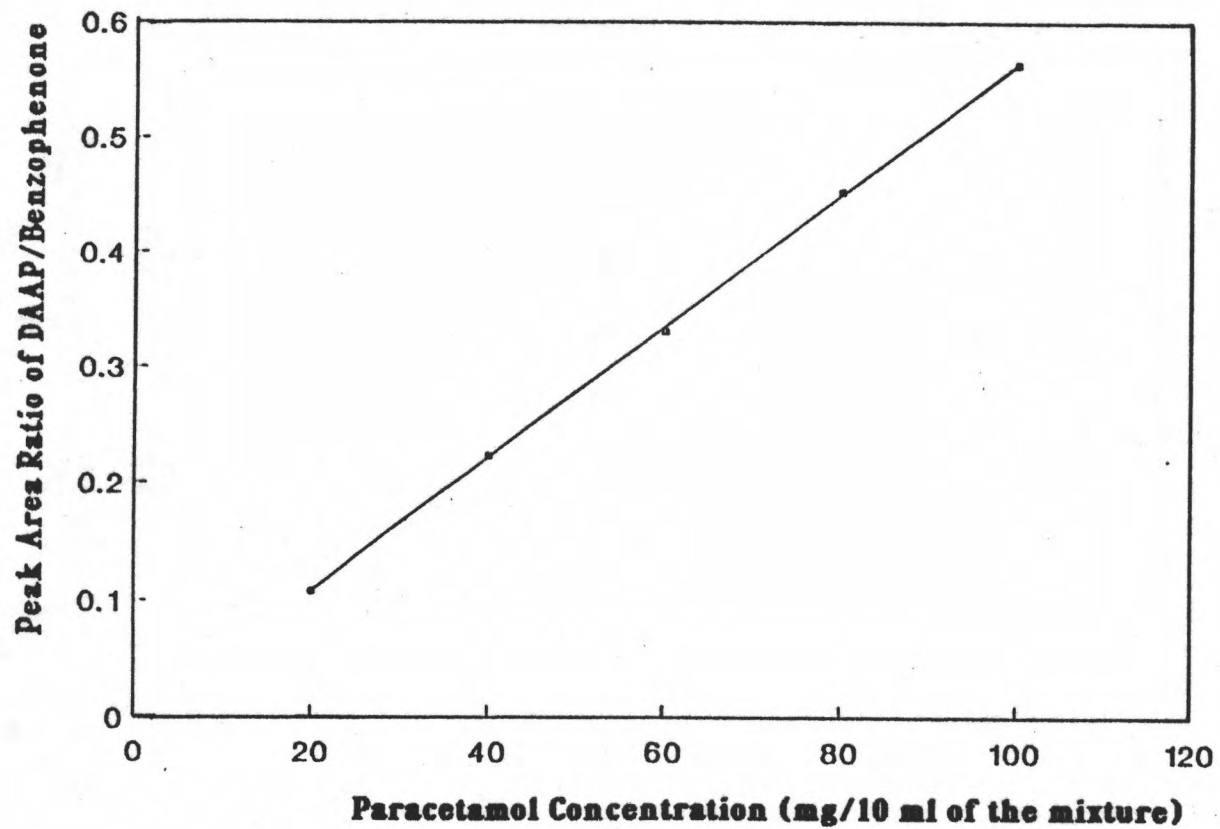


Figure 14. Standard Curve of Paracetamol for Determination of Paracetamol in Syrup Preparations

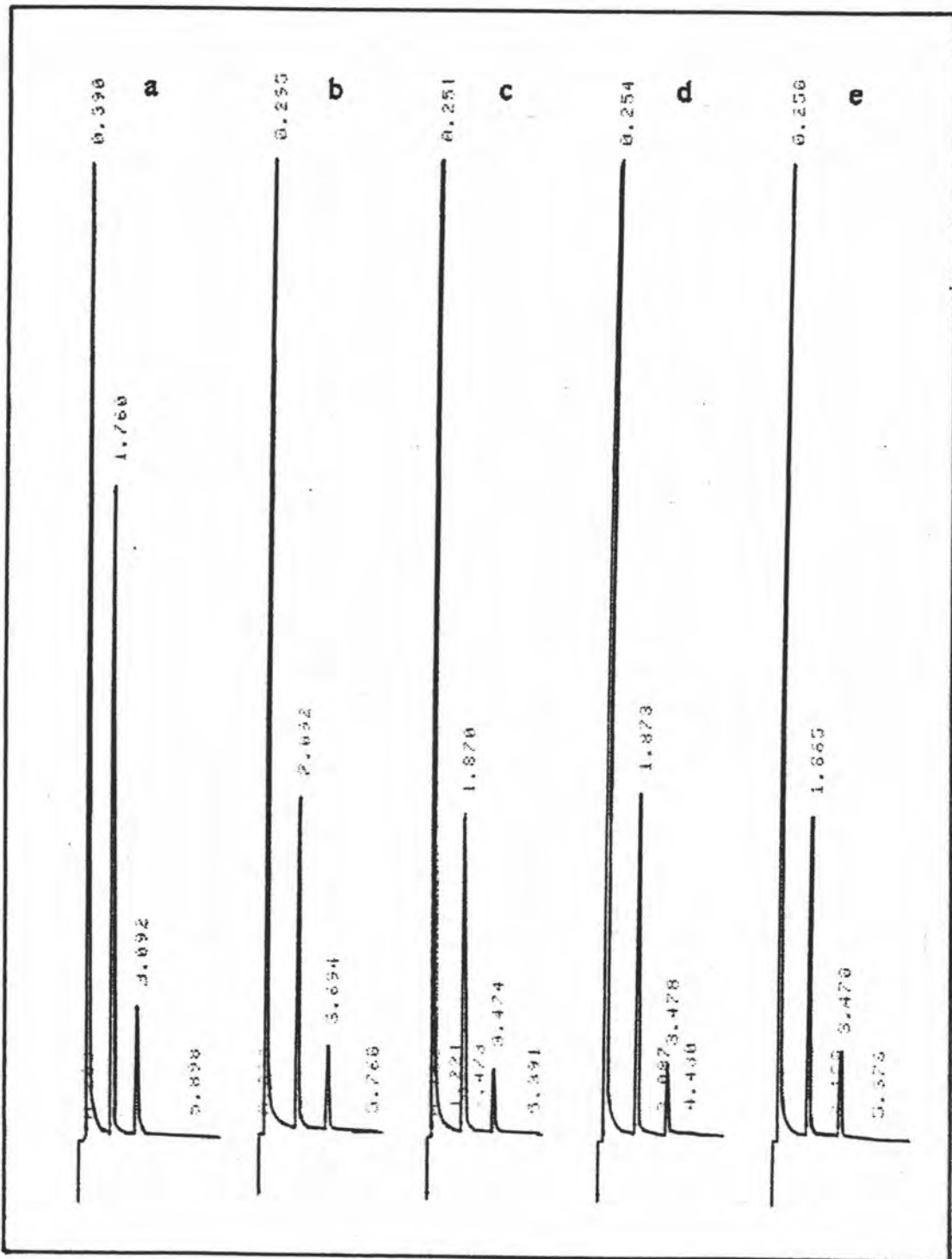


Figure 15. Chromatogram of Paracetamol in Syrup Preparations

a) Syrup No.1, b) Syrup No.2, c) Syrup No.3

d) Syrup No.4, e) Syrup No.5

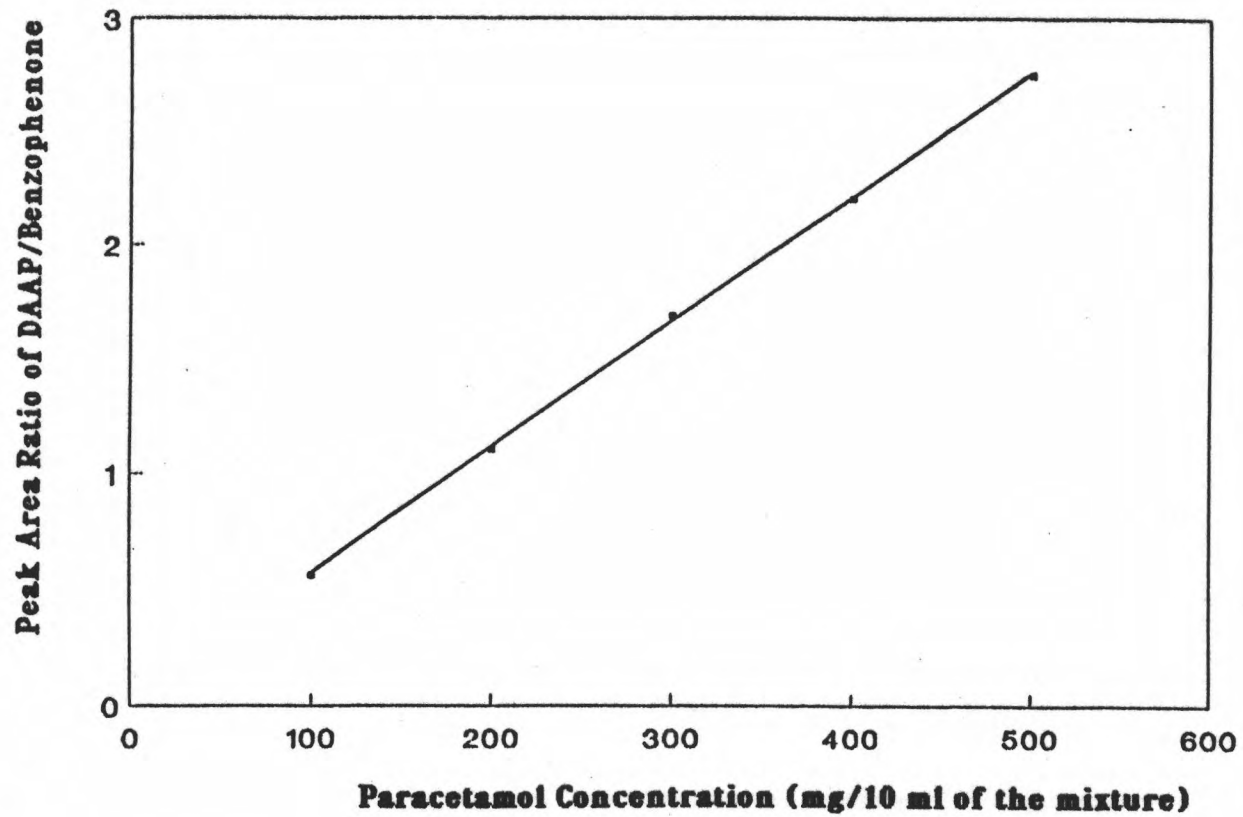


Figure 16. Standard Curve of Paracetamol for Determination of Paracetamol in Tablet and Injection Preparations

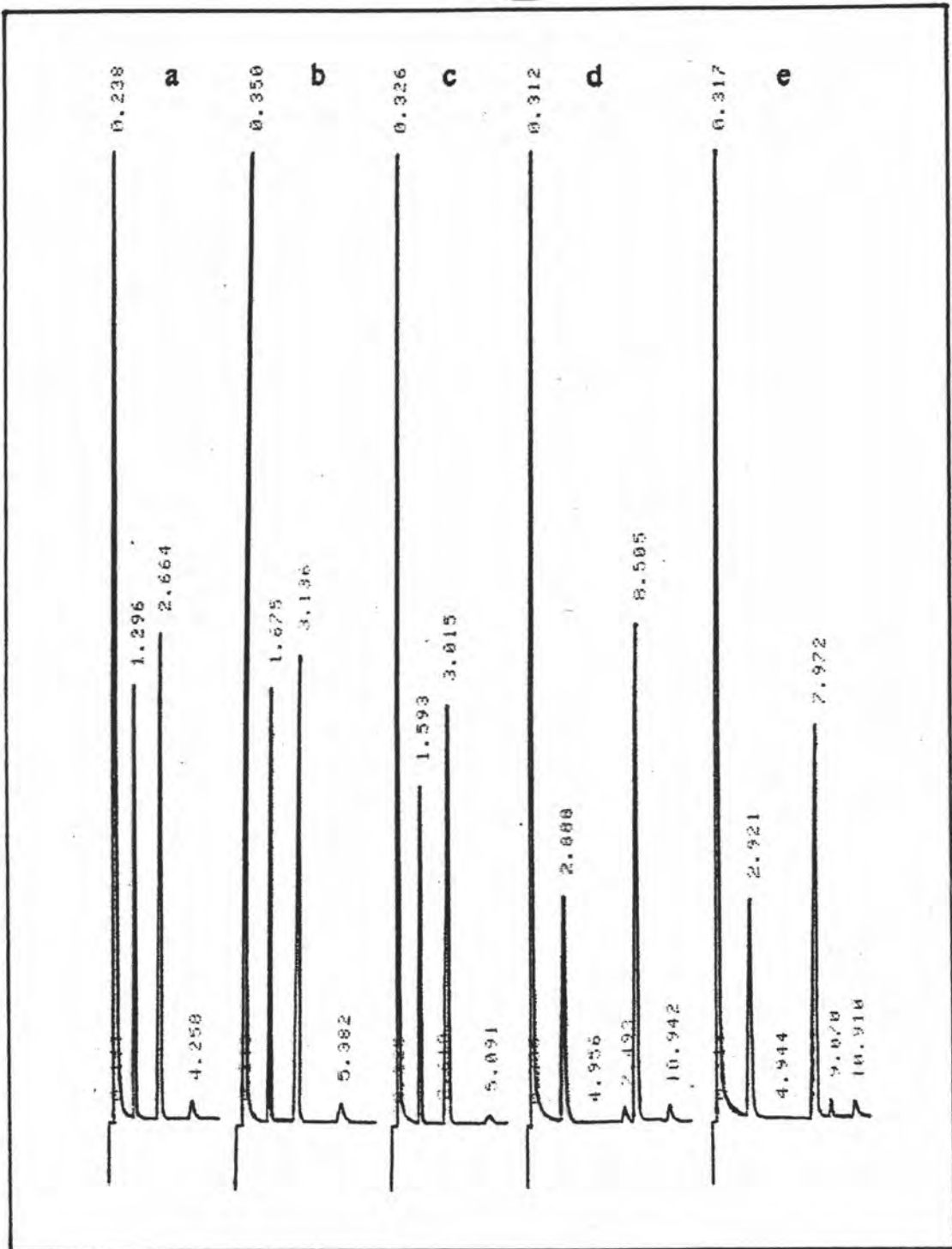


Figure 17. Chromatogram of Paracetamol in Tablet Preparations

a) Tablet No.1, b) Tablet No.2, c) Tablet No.3

d) Tablet No.4, e) Tablet No.5

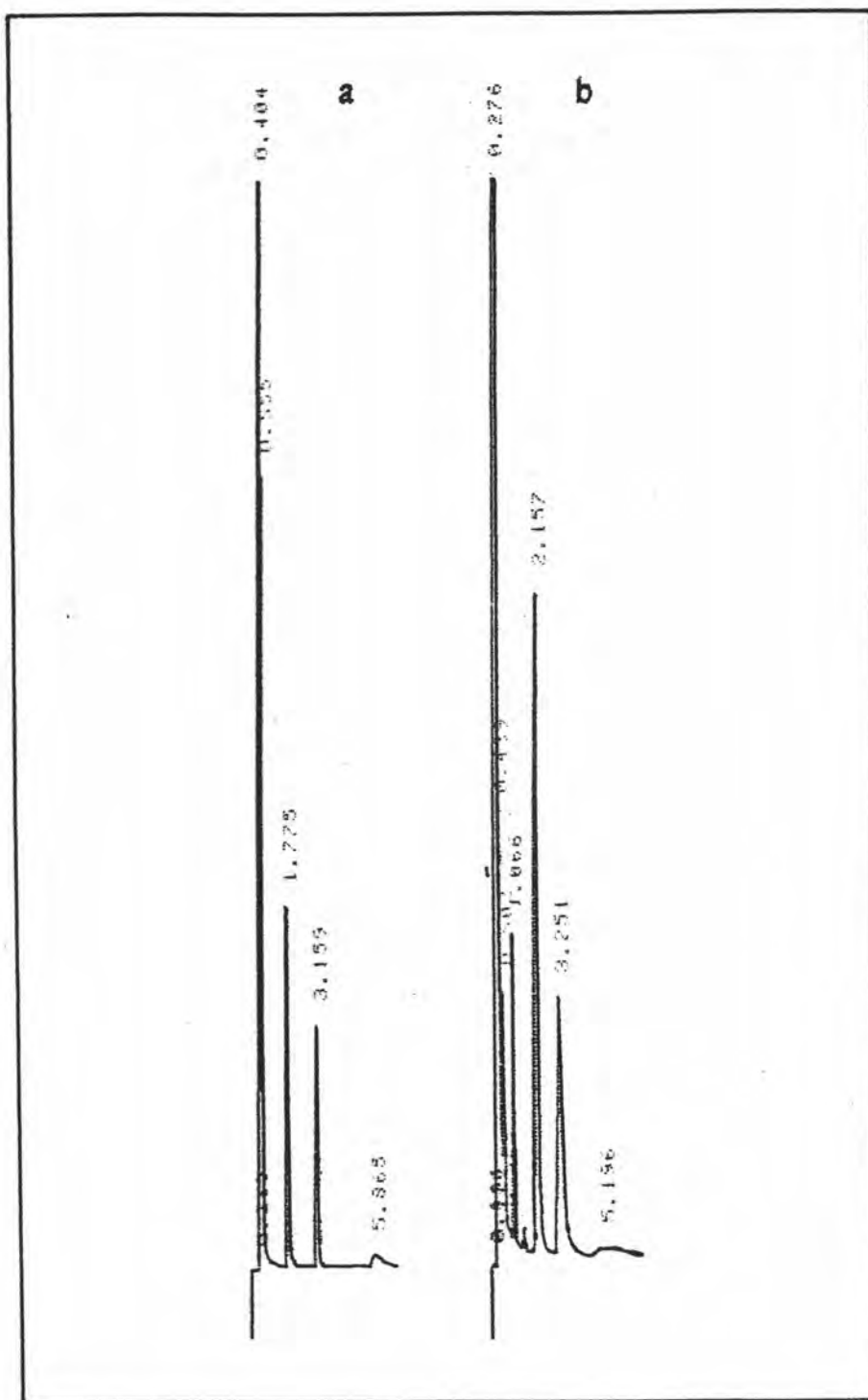


Figure 18. Chromatogram of Paracetamol in Injection Preparations
a) Injection No.1, b) Injection No.2

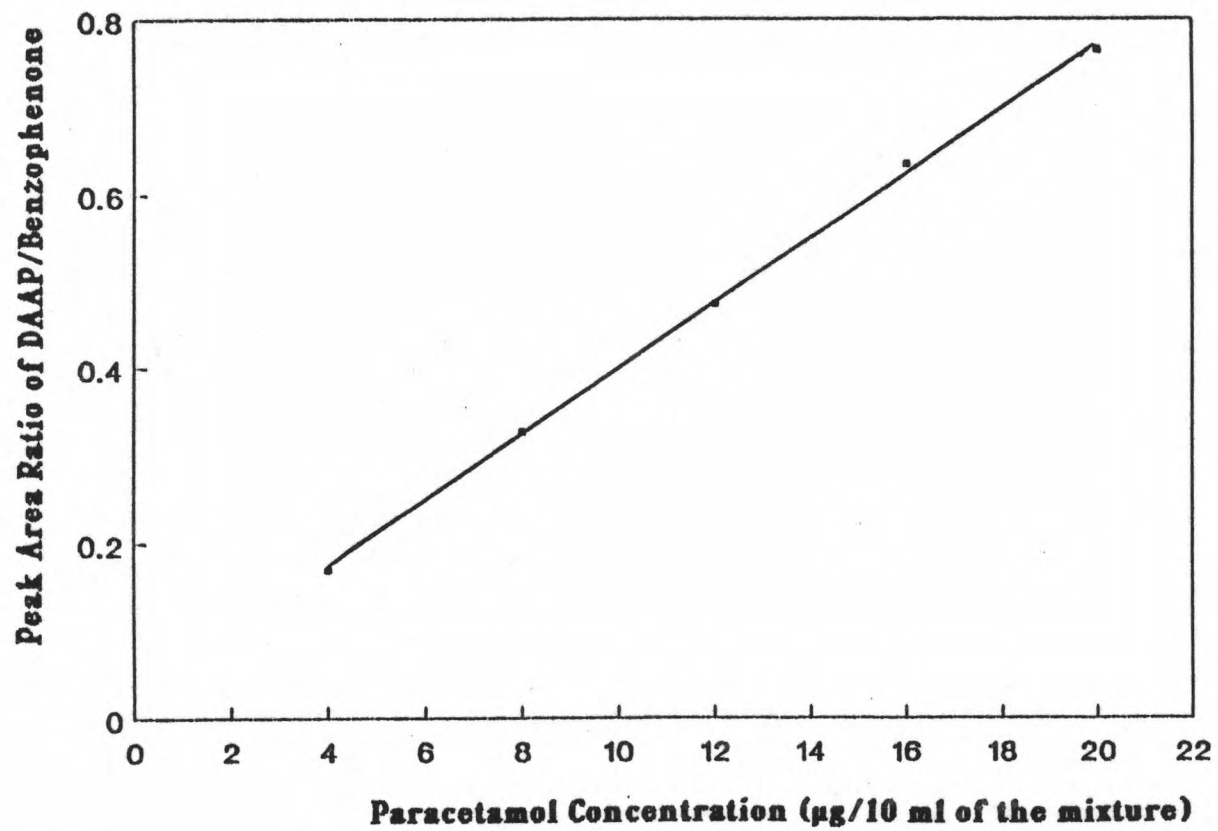


Figure 19. Standard Curve of Paracetamol in Human Serum

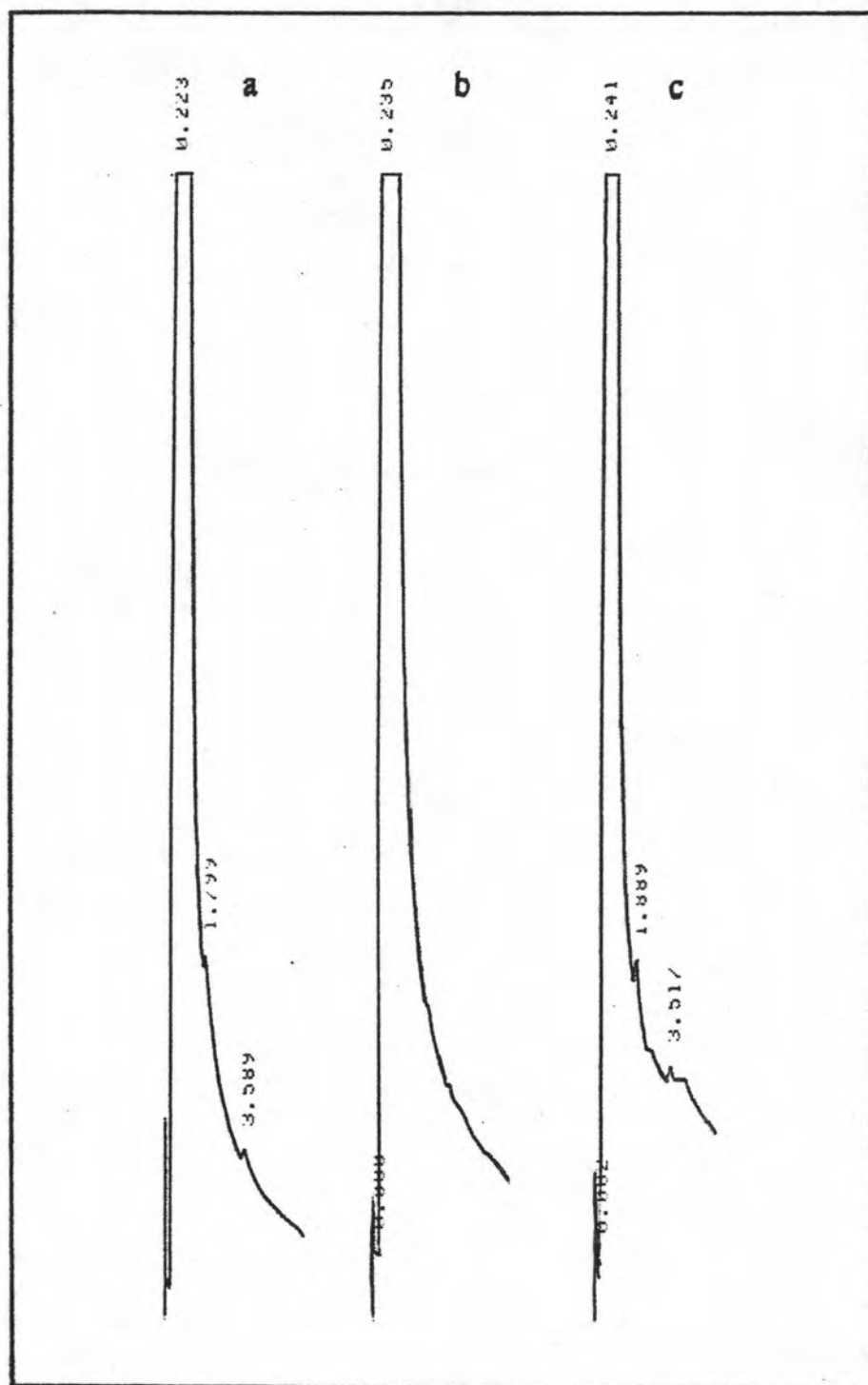


Figure 20. Chromatogram of Paracetamol in Human Serum
a) Standard Solution of Paracetamol BP,
b) Blank Serum, c) Serum with Paracetamol BP

VITA

Miss Sirivipa Amatayakul was born in January 3rd, 1964 in Edinburgh, U.K. Graduated with a Bachelor degree in Pharmacy in 1987 from the Faculty of Pharmacy of Chiang Mai University, Chiang Mai.

