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APPENDICES

Appendix I

Table 24 Absorbance of isoniazid standard solution in 0.1 N HCl at 266.8 nm.

Concentration (μg/ml)	Absorbance
0	0
5.0	0.200
5.5	0.220
7.5	0.301
10.0	0.398
15.0	0.600
20.0	0.791

Correlation coefficient : 0.9999

Y = 0.03962X + 0.00199

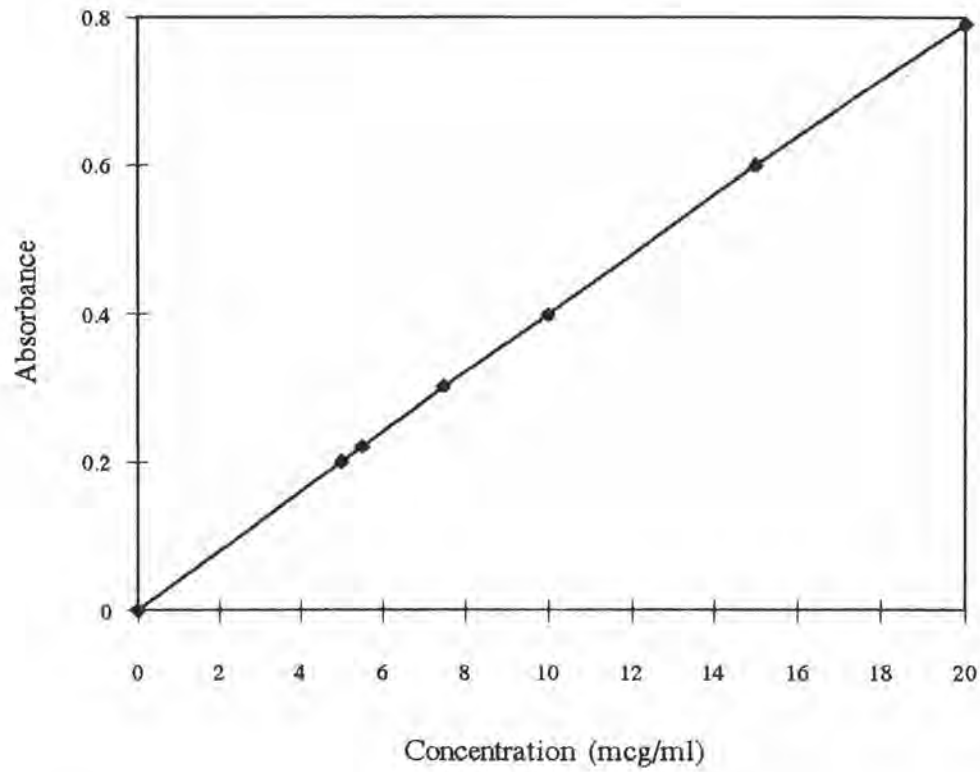


Figure 58 Standard curve of isoniazid in 0.1 N HCl at 266.8 nm.

Table 25 Absorbance of hydrochlorothiazide standard solution in 0.1 N HCl at 273.8 nm.

Concentration (µg/ml)	Absorbance
0	0
3.0	0.210
3.5	0.246
5.0	0.353
7.5	0.531
10.0	0.709

Correlation coefficient : 0.9999

Y = 0.07098X - 0.00161

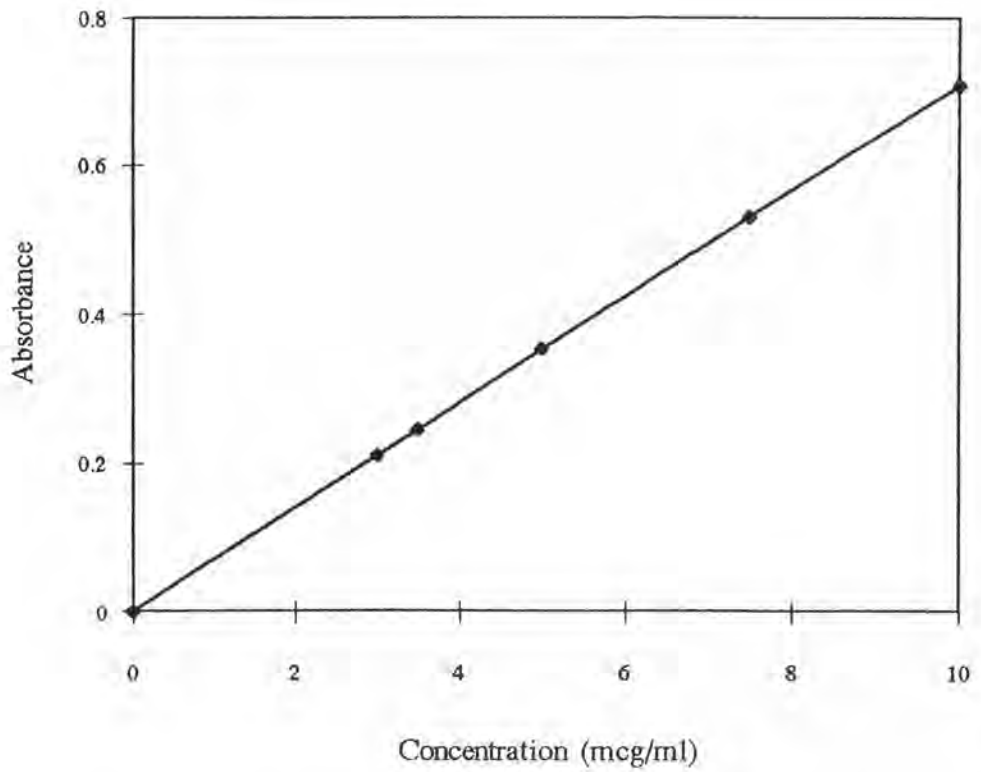


Figure 59 Standard curve of hydrochlorothiazide in 0.1 N HCl at 273.8 nm

Table 26 Absorbance of hydrochlorothiazide standard solution in 0.1 N NaOH at 276.0 nm.

Concentration (µg/ml)	Absorbance
0	0
3.5	0.186
5.0	0.264
7.5	0.391
10.0	0.524
15.0	0.784
17.0	0.889

Correlation coefficient : 0.9999

Y = 0.05217X + 0.00176

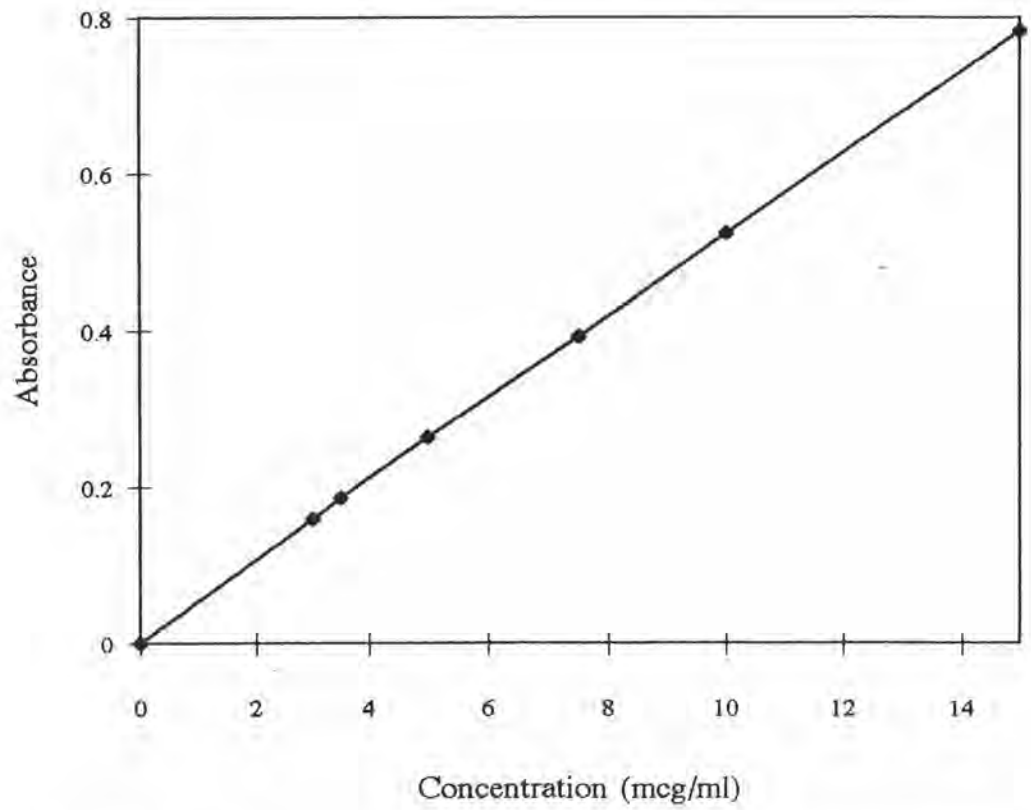


Figure 60 Standard curve of hydrochlorothiazide in 0.1 N NaOH at 276.0 nm

Table 27 Absorbance of potassium dihydrogen phosphate standard solution at 753.9 nm.

Concentration (µg/ml)	Absorbance
0	0
0.15	0.210
0.18	0.254
0.20	0.281
0.26	0.366
0.30	0.422
0.40	0.562
0.50	0.710

Correlation coefficient : 0.9999

Y = 1.41644X - 0.00171

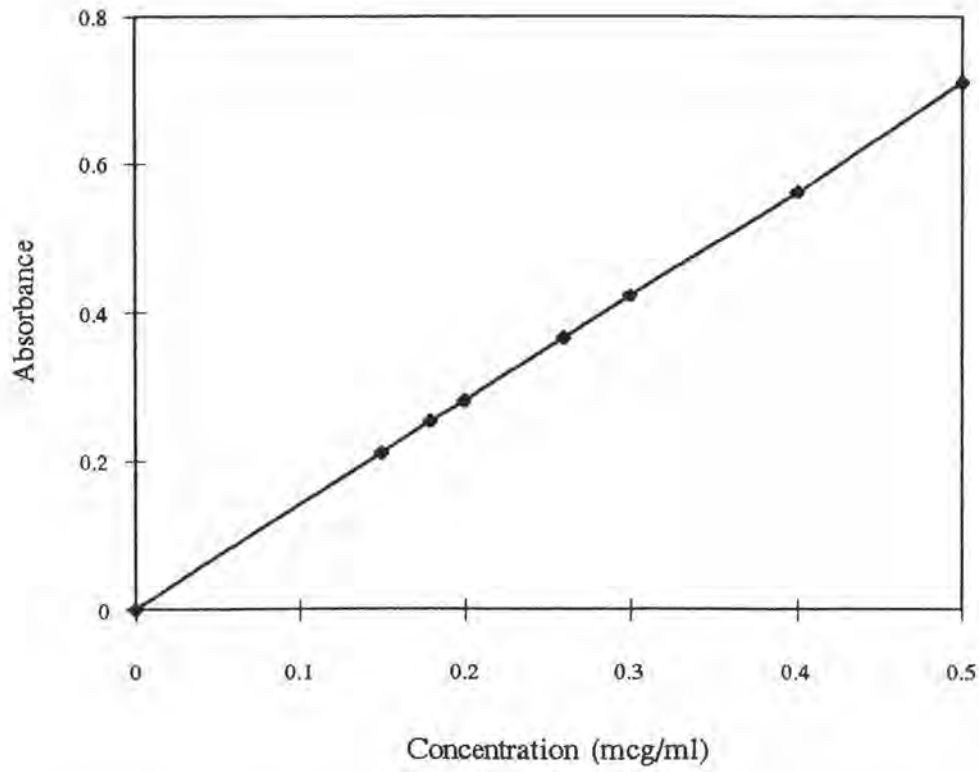


Figure 61 Standard curve of potassium dihydrogen phosphate at 753.9 nm

Appendix II

Table 28 Particle size distribution of various diluents and MDRS

Process Variables	% Weight Retained on Sieve Size					
	base	45	75	90	106	125
MDRS	11.92	19.75	9.47	8.74	13.54	36.58
Era	1.75	32	17	15.5	15.75	17.75
Starch1500	23.5	24.75	16.5	8.5	12.25	15.25
Avicel PH102	18.75	16	10	7.25	11	37.5
Emcompress	0.25	1.25	1.5	1.75	13.75	80.75

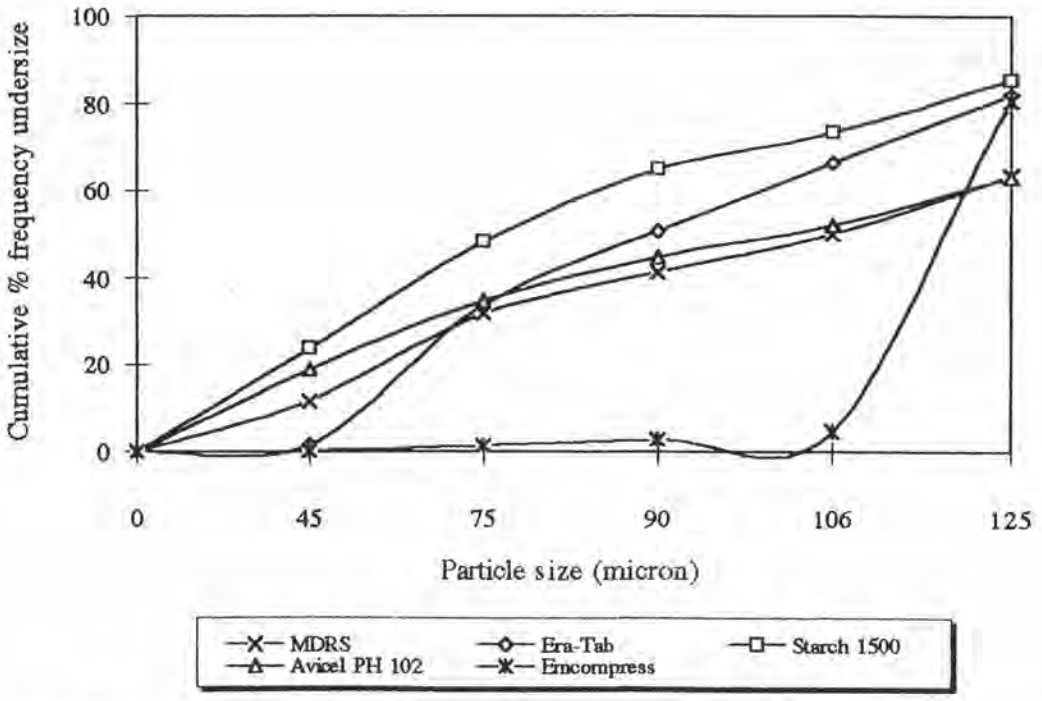


Figure 62 Cumulative % frequency undersize of various diluents and MDRS

Table 29 Cumulative % frequency undersize and Z - value of various diluents and MDRS

Size Range (micron)	Era-Tab		MDRS	
	CUM%	Z value	CUM%	Z value
0-45	1.75	-1.179	11.92	-2.1081
45-75	33.75	-0.4769	31.67	-0.4192
75-90	50.75	-0.2238	41.14	0.0187
90-106	66.25	-0.003	49.88	0.4192
106-125	82	0.3429	63.42	0.9152
>=125	100		100	

CUM% = Cumulative % frequencyundersize

Table 29 (Cont.) Cumulative % frequency undersize and Z - value of various diluents and MDRS

Size Range (micron)	Starch 1500		Avicel PH 102		Emcompress	
	CUM%	Z value	CUM%	Z value	CUM%	Z value
0-45	23.5	-0.7226	18.75	-0.887	0.25	-2.81
45-75	48.25	-0.0438	34.75	-0.3921	1.5	-2.17
75-90	64.75	0.3786	44.75	-0.232	3	-1.88
90-106	73.25	0.6203	52	0.0502	4.75	-1.675
106-125	85.5	1.0582	63	0.3318	18.5	-0.8965
>=125	100		100		100	

CUM% = Cumulative % frequency undersize

Appendix III

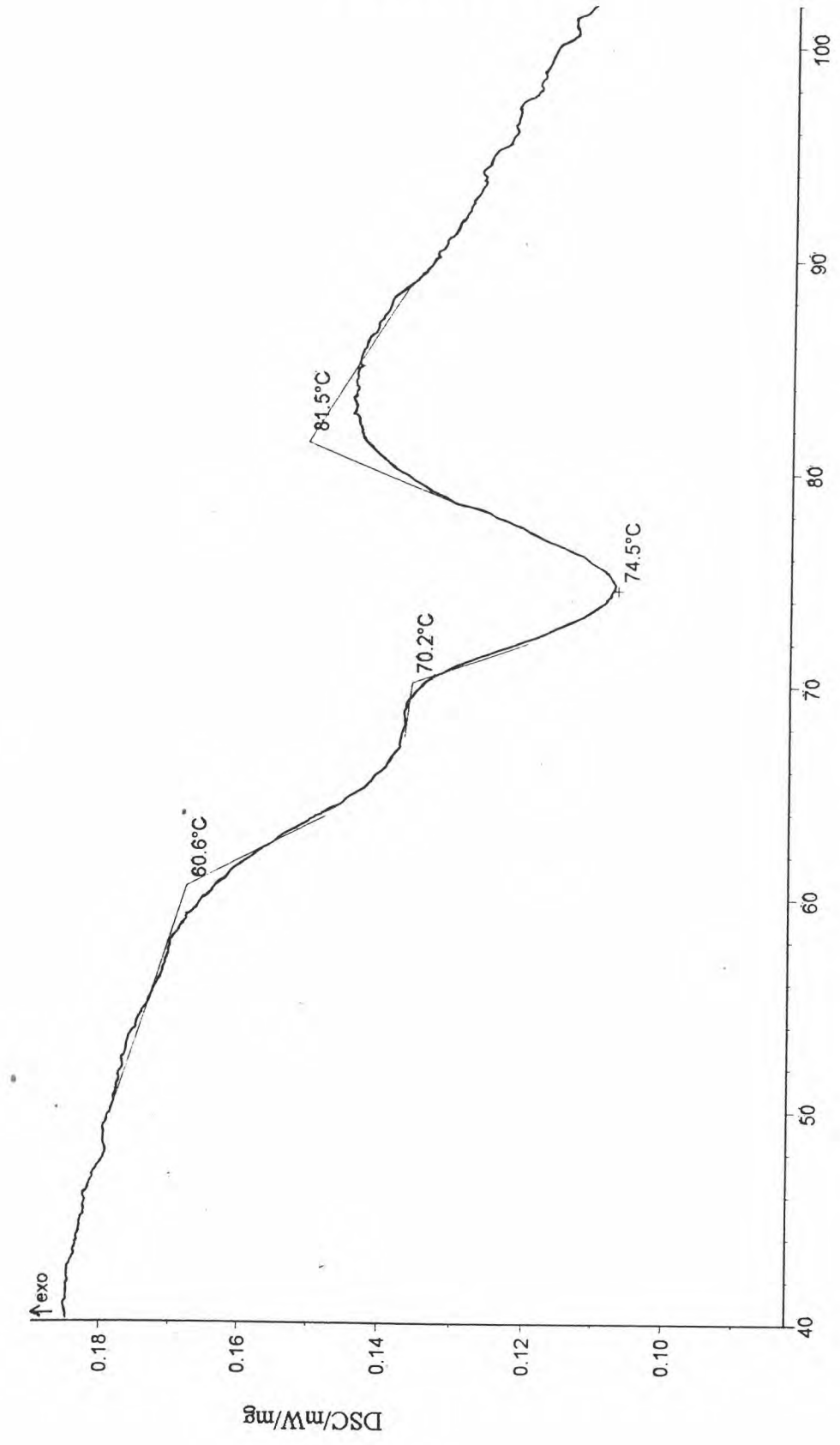


Figure 63 DSC thermogram of native rice starch

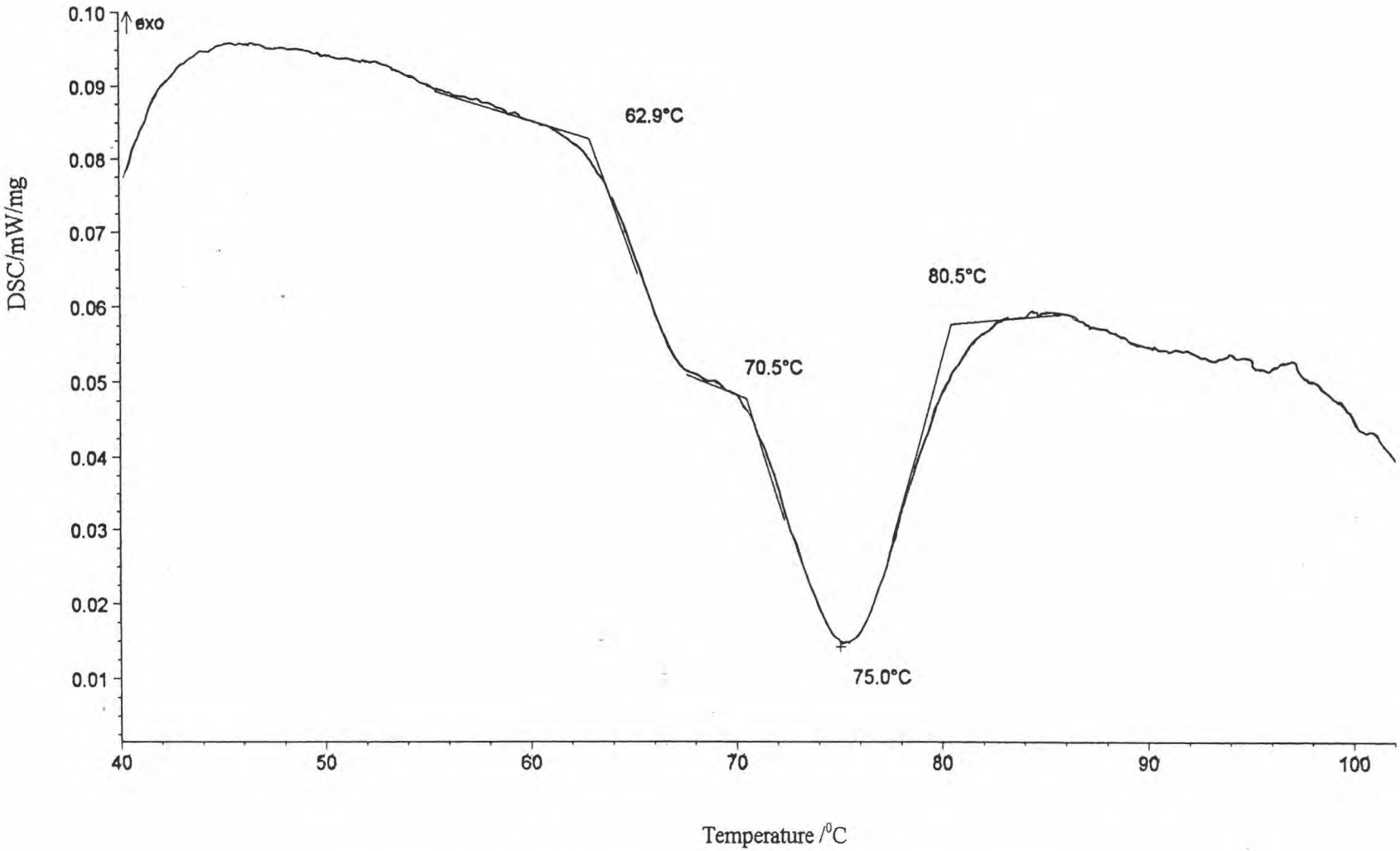


Figure 64 DSC thermogram of deproteinized rice starch

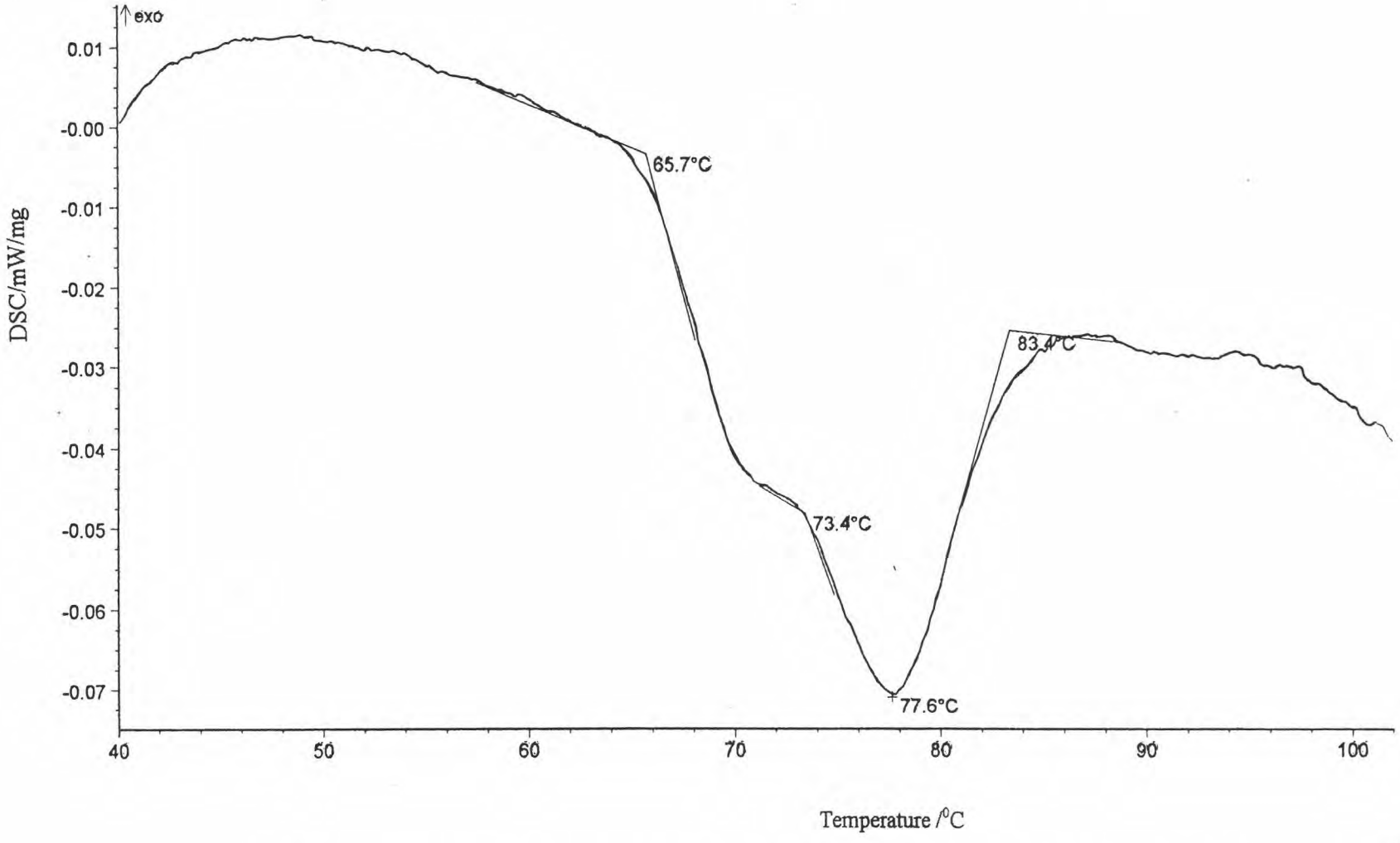


Figure 65 DSC thermogram of crosslinked of deproteinized rice starch

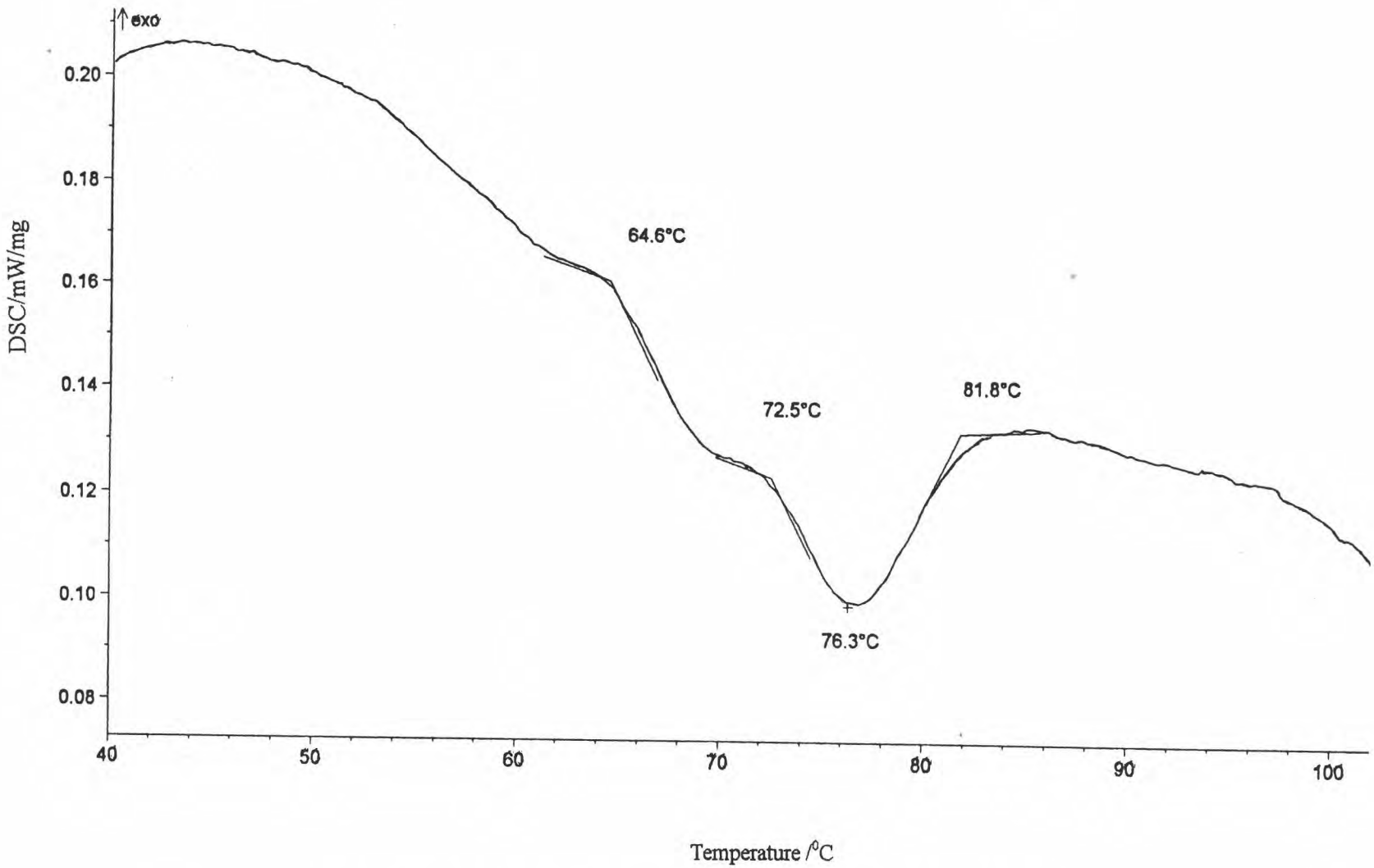


Figure 66 DSC thermogram of modified rice starch

Appendix IV

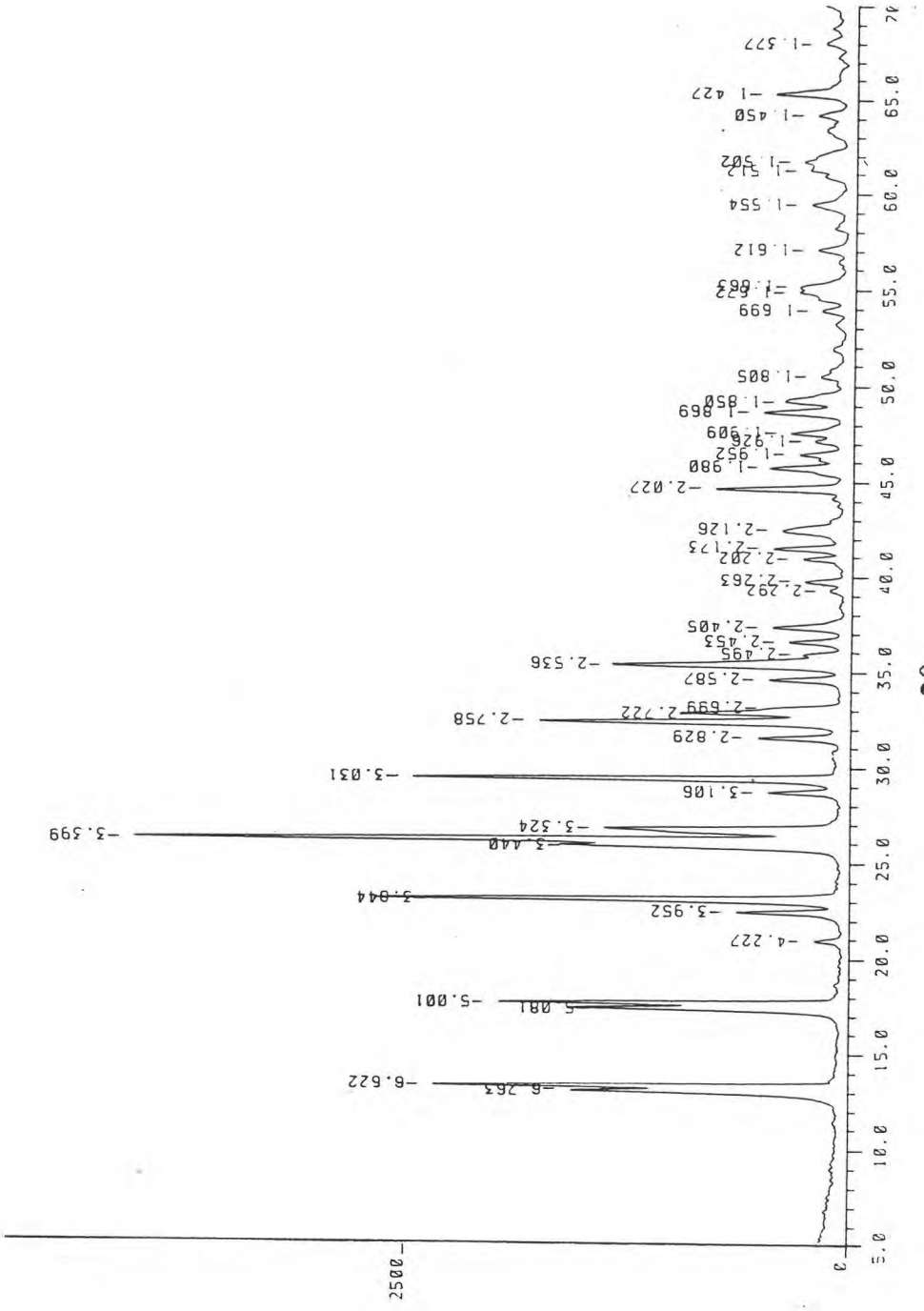


Figure 67 X-ray diffractogram of sodium trimetaphosphate

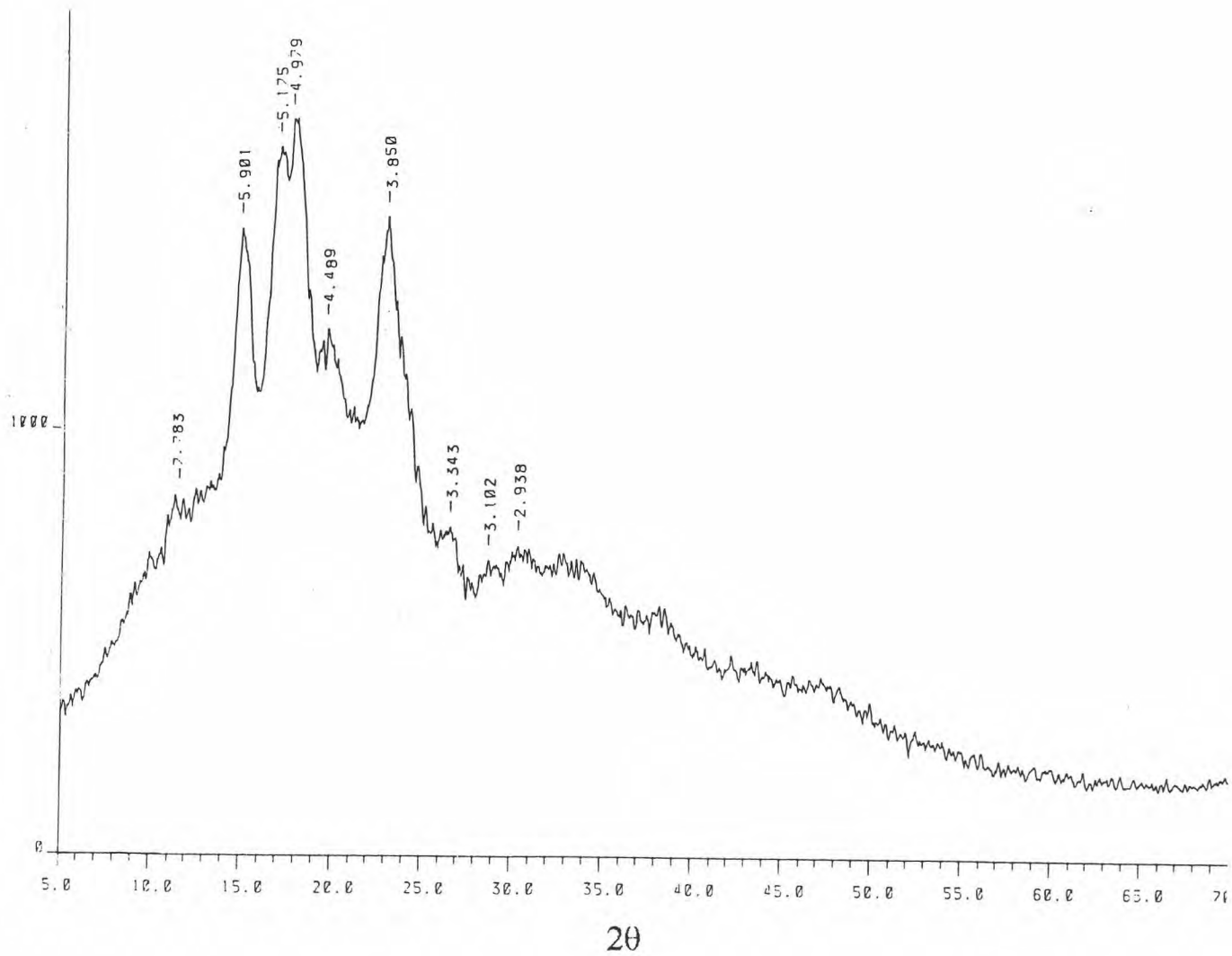


Figure 68 X-ray diffractogram of native rice starch

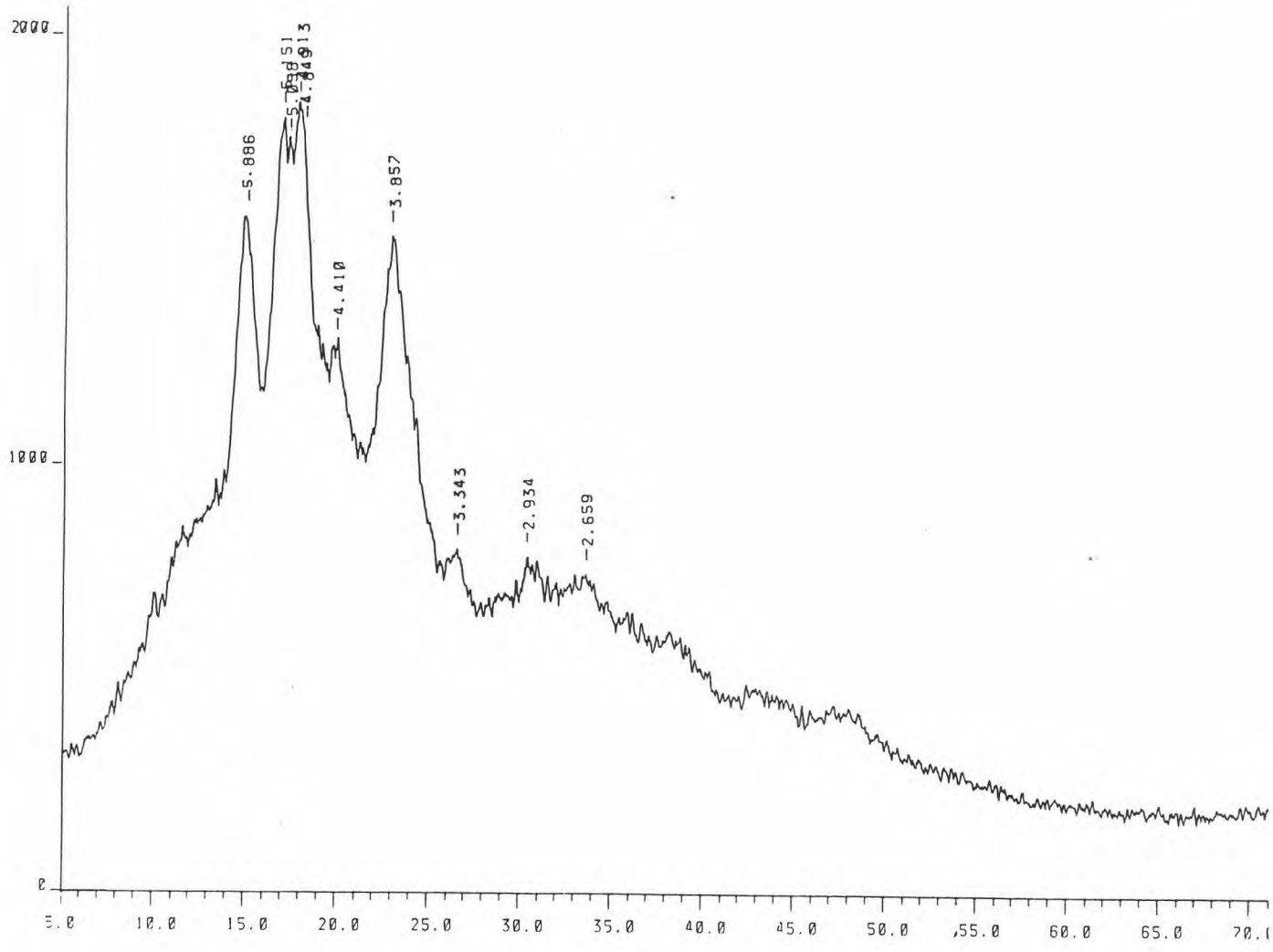


Figure 69 X-ray diffractogram of deproteinized rice starch

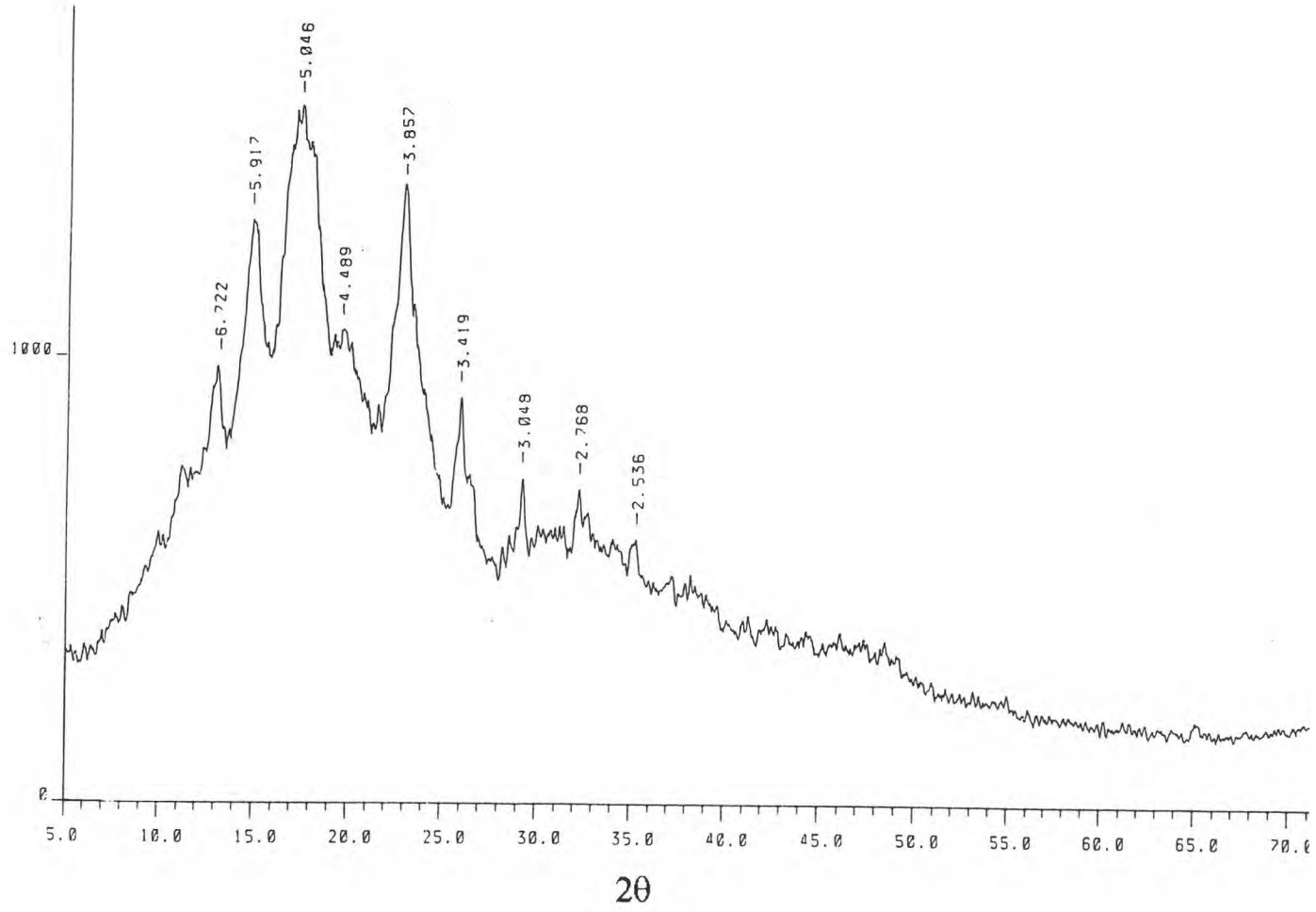


Figure 70 X-ray diffractogram of phisical mixture of deproteinized rice starch and sodium trimetaphosphate

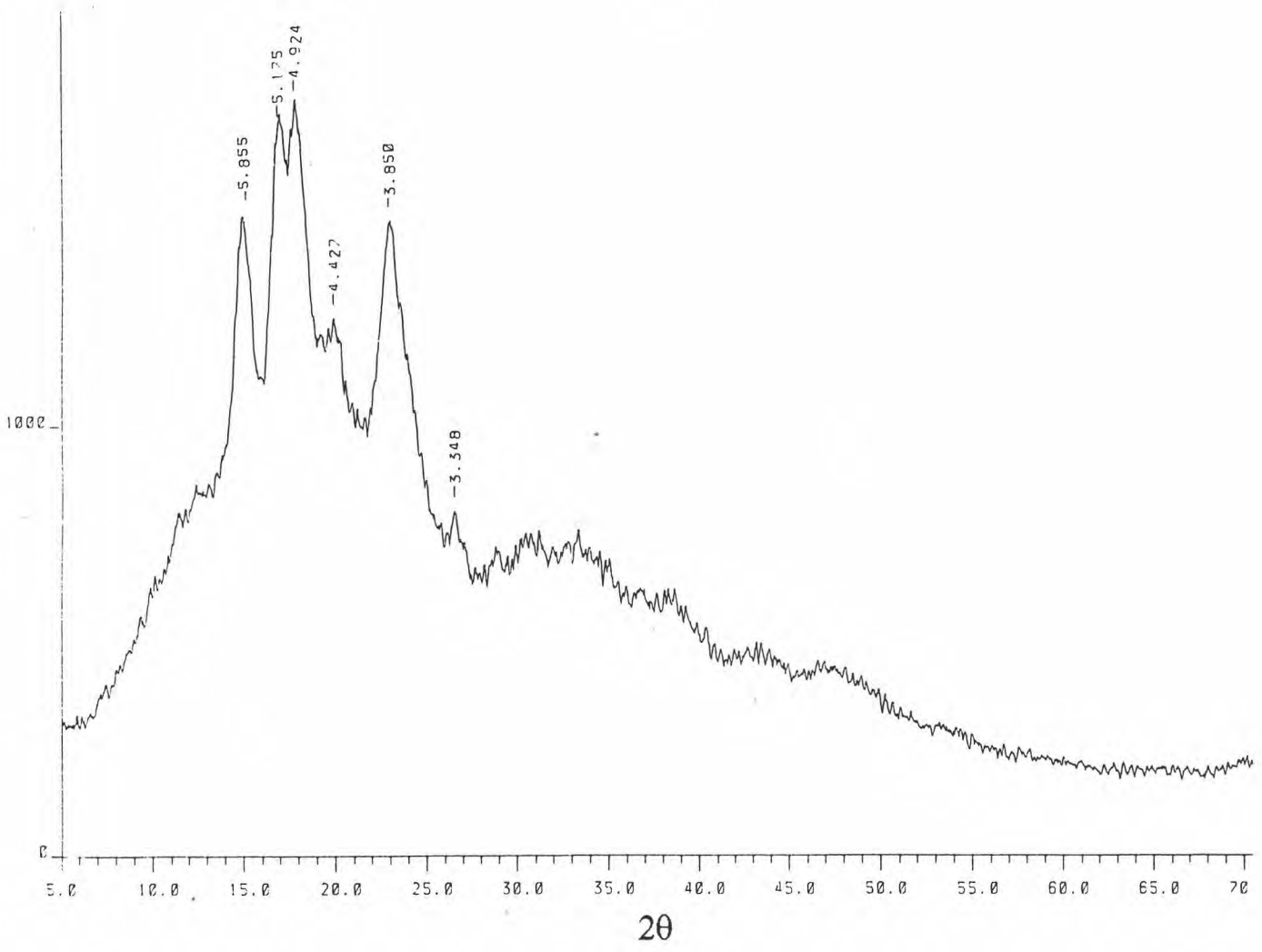


Figure 71 X-ray diffractogram of crosslinked of deproteinized rice starch

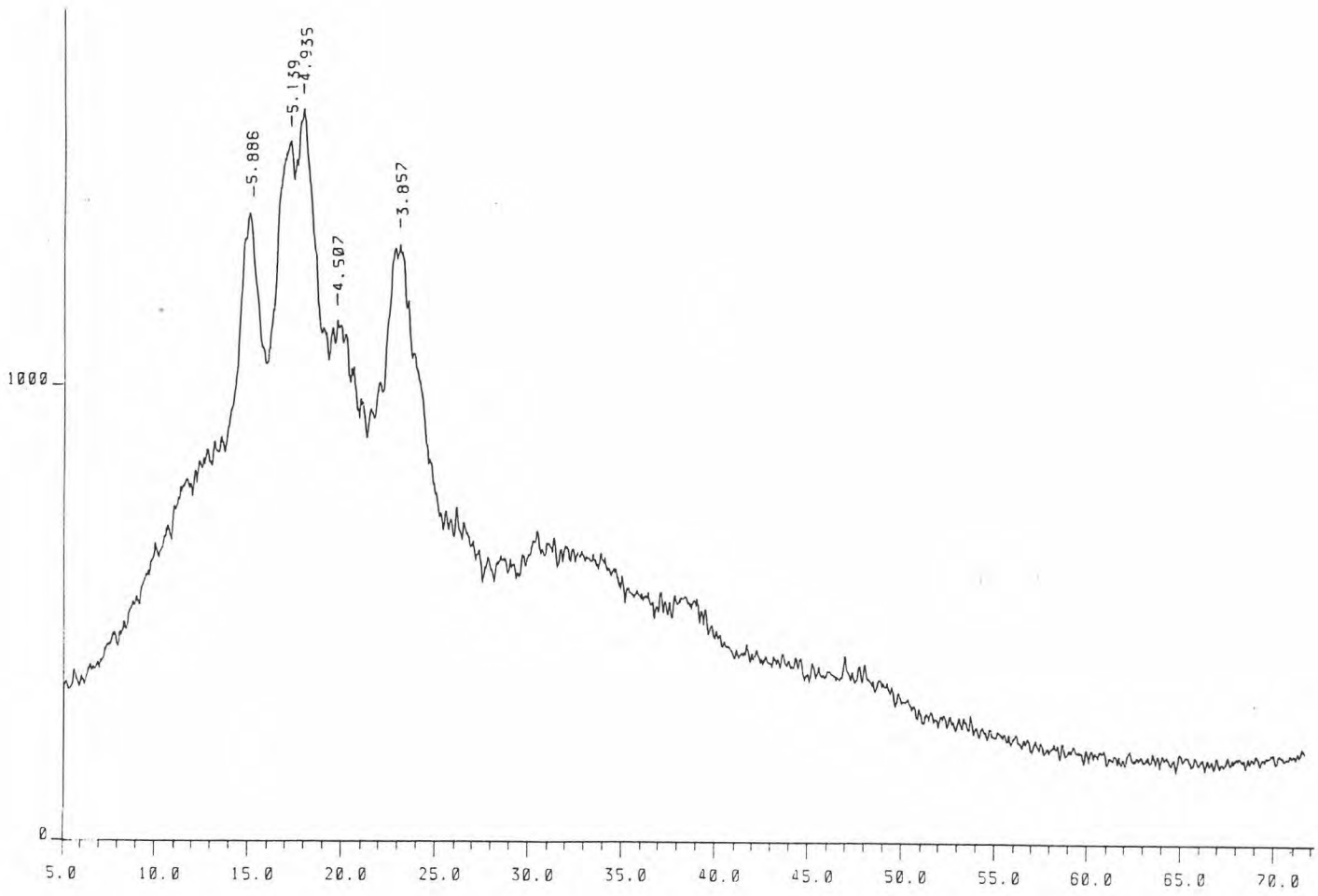


Figure 72 X-ray diffractogram of modified rice starch

Appendix V

Table 30 Analysis of variance for bulk density of various diluents and MDRS

Source of Variation	DF	SS	MS	F-value
Among Group	4	0.5448	0.1362	3516.526
Within Group	10	0.0004	3.87E-0.5	
Total	14	0.5452		

$F_{0.05}(4,10) = 3.48$

Table 31 Dependent comparison (Duncan's new multiple range test) for bulk density of various diluents and MDRS

	MDRS	Era-Tab®	Starch 1500®	AvicelPH102®	Emcompress®
MDRS	-	S	S	S	S
Era-Tab®		-	S	S	S
Starch 1500®			-	S	S
AvicelPH102®				-	S
Emcompress®					-

S = Significant

NS = Non-significant

Table 32 Analysis of variance for tapped density of various diluents and MDRS

Source of Variation	DF	SS	MS	F-value
Among Group	4	0.6718	0.1679	3197.432
Within Group	10	0.0005	5.25E-05	
Total	14	0.6724		

$$F_{0.05}(4,10) = 3.48$$

Table 33 Dependent comparison (Duncan's new multiple range test) for tapped density of various diluents and MDRS

	MDRS	Era-Tab®	Starch 1500®	AvicelPH102®	Emcompress®
MDRS	-	S	S	S	S
Era-Tab®		-	S	S	S
Starch 1500®			-	S	S
AvicelPH102®				-	S
Emcompress®					-

S = Significant

NS = Non-significant

Table 34 Analysis of variance for % compressibility various diluents and MDRS

Source of Variation	DF	SS	MS	F-value
Among Group	4	351.4966	87.8741	86.1173
Within Group	10	10.2040	1.0204	
Total	14	361.7006		

$$F_{0.05}(4,10) = 3.48$$

Table 35 Dependent comparison (Duncan's new multiple range test) for % compressibility of various diluents and MDRS

	MDRS	Era-Tab®	Starch 1500®	AvicelPH102®	Emcompress®
MDRS	-	S	S	S	S
Era-Tab®		-	S	S	S
Starch 1500®			-	S	S
AvicelPH102®				-	S
Emcompress®					-

S = Significant

NS = Non-significant

Table 36 Analysis of variance for angle of repose of various diluents and MDRS

Source of Variation	DF	SS	MS	F-value
Among Group	4	137.1965	34.2991	16.1234
Within Group	10	21.2728	2.1273	
Total	14	158.4694		

$$F_{0.05}(4,10) = 3.48$$

Table 37 Dependent comparison (Duncan's new multiple range test) for angle of repose of various diluents and MDRS

	MDRS	Era-Tab®	Starch 1500®	AvicelPH102®	Emcompress®
MDRS	-	S	S	S	S
Era-Tab®		-	S	S	S
Starch 1500®			-	NS	NS
AvicelPH102®				-	NS
Emcompress®					-

S = Significant

NS = Non-significant

Table 38 Analysis of variance for flow rate of various diluents and MDRS

Source of Variation	DF	SS	MS	F-value
Among Group	4	655.6735	163.9184	187.391
Within Group	10	8.7474	0.8747	
Total	14	664.4209		

$$F_{0.05}(4,10) = 3.48$$

Table 39 Dependent comparison (Duncan's new multiple range test) for flow rate of various diluents and MDRS

	MDRS	Era-Tab®	Starch 1500®	AvicelPH102®	Emcompress®
MDRS	-	S	-	-	S
Era-Tab®		-	-	-	S
Starch 1500®			-	-	-
AvicelPH102®				-	-
Emcompress®					-

S = Significant

NS = Non-significant

Table 40 Analysis of variance for moisture content of various diluents and MDRS

Source of Variation	DF	SS	MS	F-value
Among Group	4	28.8826	7.2206	14.0788
Within Group	10	5.1287	0.5128	
Total	14	34.0111		

$$F_{0.05}(4,10) = 3.48$$

Table 41 Dependent comparison (Duncan's new multiple range test) for moisture content of various diluents and MDRS

	MDRS	Era-Tab®	Starch 1500®	AvicelPH102®	Emcompress®
MDRS	-	S	S	S	S
Era-Tab®		-	S	NS	NS
Starch 1500®			-	NS	S
AvicelPH102®				-	NS
Emcompress®					-

S = Significant

NS = Non-significant

Table 42 Analysis of variance for disintegration time of isoniazid tablets prepared from various diluents and MDRS

Source of Variation	DF	SS	MS	F-value
Among Group	3	587.0569	195.6856	2672.734
Within Group	20	1.4643	0.0732	
Total	23	588.5212		

$$F_{0.05}(3,20) = 3.10$$

Table 43 Dependent comparison (Duncan's new multiple range test) for disintegration time of isoniazid tablets prepared from various diluents and MDRS

	MDRS	Era-Tab®	Starch 1500®	AvicelPH102®
MDRS	-	S	S	S
Era-Tab®		-	S	S
Starch 1500®			-	S
AvicelPH102®				-

S = Significant

NS = Non-significant

Table 44 analysis of variance for disintegration time of hydrochlorothiazide tablets prepared from various diluents and MDRS

Source of Variation	DF	SS	MS	F-value
Among Group	3	38.8168	12.9389	229.0654
Within Group	20	1.1297	0.0564	
Total	23	39.9465		

$$F_{0.05}(3,20) = 3.10$$

Table 45 Dependent comparison (Duncan's new multiple range Test) for disintegration time of hydrochlorothiazide tablets prepared from various diluents and MDRS

	MDRS	Era-Tab®	Starch 1500®	AvicelPH102®
MDRS	-	S	S	S
Era-Tab®		-	S	S
Starch 1500®			-	S
AvicelPH102®				-

S = Significant

NS = Non-significant

Table 46 Analysis of variance for $T_{80\%}$ of isoniazid tablets prepared from various diluents and MDRS

Source of Variation	DF	SS	MS	F-value
Among Group	3	7.6300	2.5433	12.1802
Within Group	20	4.1761	0.2088	
Total	23	11.8062		

$$F_{0.05}(3,20) = 3.10$$

Table 47 Dependent comparison (Duncan's new multiple range Test) for $T_{80\%}$ of isoniazid tablets prepared from various diluents and MDRS

	MDRS	Era-Tab®	Starch 1500®	AvicelPH102®
MDRS	-	NS	S	S
Era-Tab®		-	S	S
Starch 1500®			-	NS
AvicelPH102®				-

S = Significant

NS = Non-significant

Table 48 Analysis of variance for $T_{60\%}$ of hydrochlorothiazide tablets prepared from various diluents and MDRS

Source of Variation	DF	SS	MS	F-value
Among Group	3	250.6327	83.5442	140.0987
Within Group	20	11.9264	0.5963	
Total	23	262.5592		

$$F_{0.05}(3,20) = 3.10$$

Table 49 Dependent comparison (Duncan's new multiple range test) for $T_{60\%}$ of hydrochlorothiazide tablets prepared from various diluents and MDRS

	MDRS	Era-Tab®	Starch 1500®	AvicelPH102®
MDRS	-	S	S	S
Era-Tab®		-	S	S
Starch 1500®			-	S
AvicelPH102®				-

S = Significant

NS = Non-significant

Appendix VI

Table 29 Dissolution of isoniazid tablets prepared with commercial diluents and modified rice starch

Diluents	% Drug Dissolved Time (min)									
	2	4	6	8	10	15	20	25	30	45
MDRS	22.03 (2.19)	35.81 (4.22)	50.43 (3.73)	68.35 (2.49)	83.49 (1.59)	94.95 (1.66)	95.90 (1.92)	97.47 (1.17)	98.73 (1.07)	99.92 (1.17)
Era-Tab	23.11 (0.24)	36.91 (1.17)	52.64 (2.55)	69.95 (3.97)	84.82 (1.87)	96.84 (1.87)	97.03 (1.14)	99.11 (2.57)	99.61 (2.54)	100.0 1 (1.9
Starch 1500	13.93 (0.74)	30.14 (1.50)	47.63 (1.94)	63.33 (1.18)	77.73 (2.23)	96.14 (0.97)	97.81 (0.62)	97.77 (1.14)	98.16 (1.08)	98.31 (1.23)
Avicel PH 102	16.43 (0.71)	33.38 (1.07)	51.20 (1.76)	66.86 (1.58)	78.65 (1.91)	94.95 (0.21)	98.60 (0.37)	99.03 (0.94)	99.46 (0.75)	99.93 (0.87)

Table 30 Dissolution of hydrochlorothiazide tablets prepared with commercial diluents and modified rice starch

Diluents	% Drug Dissolved Time (min)									
	2	5	10	15	20	25	30	40	50	60
MDRS	9.01 (1.71)	22.11 (3.22)	46.12 (6.11)	59.63 (5.43)	66.79 (3.80)	70.31 (4.78)	74.33 (0.89)	75.22 (0.66)	78.73 (2.21)	80.75 (0.78)
Era-Tab	24.87 (7.42)	40.62 (1.56)	56.78 (2.50)	63.39 (2.05)	68.59 (2.87)	71.11 (0.93)	74.49 (1.81)	74.75 (3.03)	78.04 (2.38)	80.09 (6.87)
Starch 1500	13.79 (1.96)	33.48 (1.91)	49.02 (7.42)	56.95 (2.72)	63.15 (4.25)	69.31 (3.25	70.69 (3.89)	72.79 (2.39)	76.57 (1.29)	77.88 (1.21)
Avicel PH 102	19.68 (3.87)	39.94 (2.64)	58.69 (2.81)	69.26 (2.55)	75.47 (1.73)	79.21 (1.53)	81.64 (2.60)	83.13 (1.37)	86.51 (1.68)	86.55 (1.37)

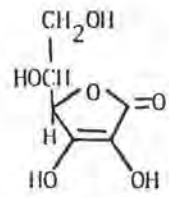
Appendix VII

Ascorbic acid (Meshal and Hassan, 1982)

Chemical name : L-Ascorbic acid

Empirical formula : $C_6H_8O_6$

Structural formula :



Molecular weight : 176.12

Appearance : White or slightly yellow crystals or powder. Odorless or almost odorless; pleasant sharp acidic taste.

Solubilty : soluble in 3.5 parts of water and 25 parts of 95 % alcohol. Insoluble in ether, light petrolatum, benzene and chloroform.

Melting range : 190-192 ^{0}C

pK_a : Ascorbic acid is a moderately strong organic acid, two ionization constant pK_{a1}: = 4.17 and pK_{a2} = 11.57

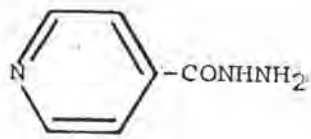
Stability : In aqueous solution, it is easily oxidized. The oxidation rate is dependent on the pH and on oxygen concentration and is catalyzed by metal ions, especially by Cu^{2+} and Fe^{3+}. The stability of ascorbic acid in solid dosage forms is good, moisture content is controlled

Isoniazid (Brewer, 1977)

Chemical name : 4-Pyridinecarboxylic acid hydrazide

Empirical formula : $C_6H_7N_3O$

Structural formula :



Molecular weight : 137.14

Appearance : Colorless or white crystalline powder which is odorless and has at first a slightly sweet and then bitter taste.

Solubility : 150 mg/ml in water, 200 mg/ml in ethanol, insoluble in benzene.

Melting range : 170-174 ^{0}C

pK_a : pK_{a1} = 2.13, pK_{a2} = 3.81 and pK_{a3} = 11.03

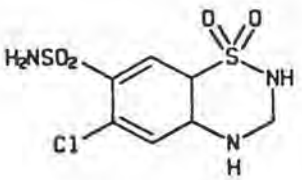
Stability : Cu (II) and Mn (II) ions accelerated the degradation of isoniazid in the presence of hydrogen peroxide. The browning reaction between lactose and isoniazid can occure in solid state.

Hydrochlorothiazide (Connors,1986; Deppler, 1981)

Chemical name : 6-Chloro-3,4-dihydro-7-sulfamoyl-2H-1,2,4-benzo-thiadiazine 1,1-dioxide

Empirical formula : $C_7H_8ClN_3O_4S_2$

Structural formula :



Molecular weight : 297.73

Appearance : White , or practically white , practically odourless, crystalline powder. Slightly bitter taste.

Solubility	:	It is very slightly soluble in water and soluble in dilute alkalis and in methanol, ethanol, or acetone.
Melting range	:	265-270 ^{0}C
pK_a	:	pK_a of hydrochlorothiazide are 8.6 and 9.9 at 60 ^{0}C.
Stability	:	Hydrochlorothiazide stored at room temperature for five years shows no degradation and heat affects it very slowly. In a compatibility study with Aerosil 2000, calcium stearate and talc using diffuse reflectance spectroscopy , no indications of degradation under usual manufacturing and storage conditions were found.

Appendix VIII

Percent phosphate = Percent phosphorus X 3.065

$$\text{Degree of substitution} = \frac{162 \times \text{Percent phosphate}}{9500 - (86 \times \text{Percent phosphate})}$$

$$\text{Degree of crosslinking} = \frac{1}{\text{Degree of substitution}}$$

VITAE

Mr. Wanlop Weecharangsan was born on March 13, 1970. He got his Bachelor degree of Pharmaceutical Science in 1993 from Faculty of Pharmacy, Mahidol University, Bangkok, Thailand.