

Figure 1

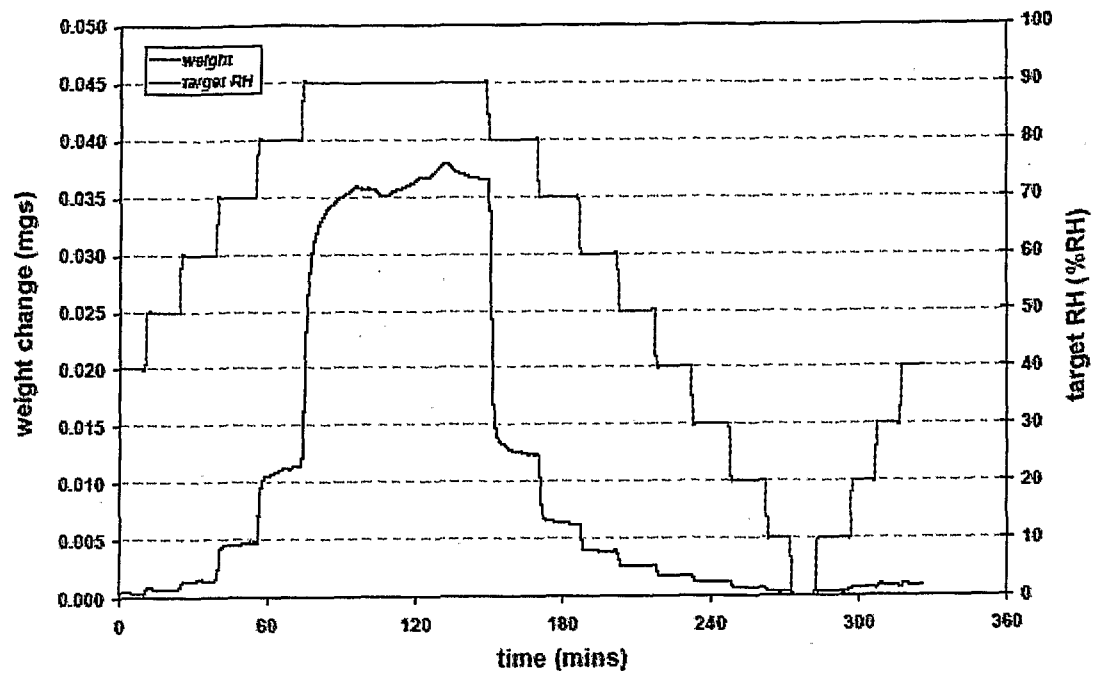


Figure 2

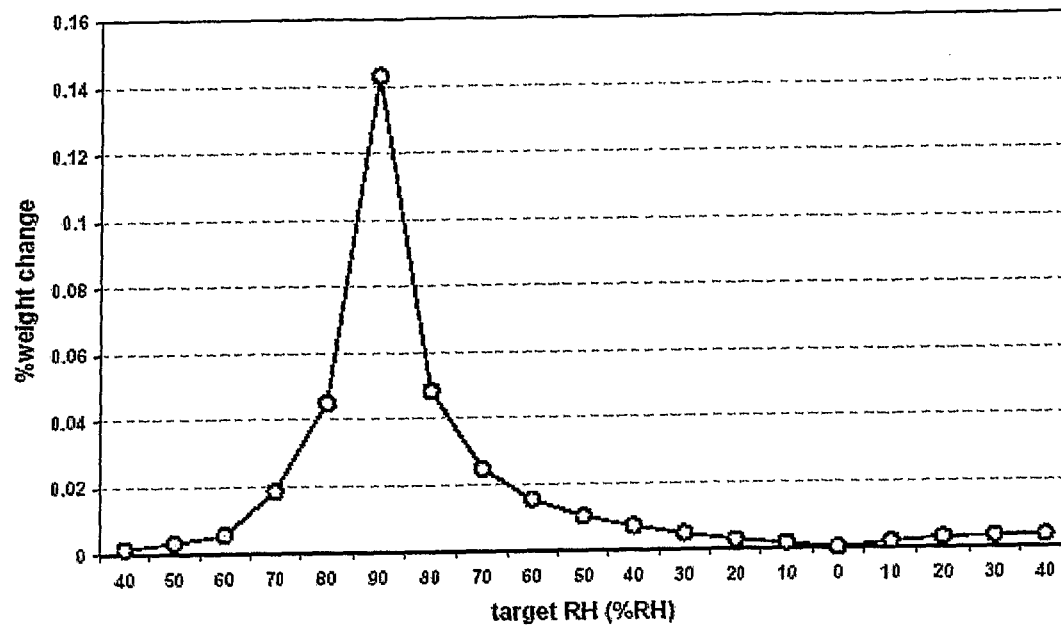


Figure 3

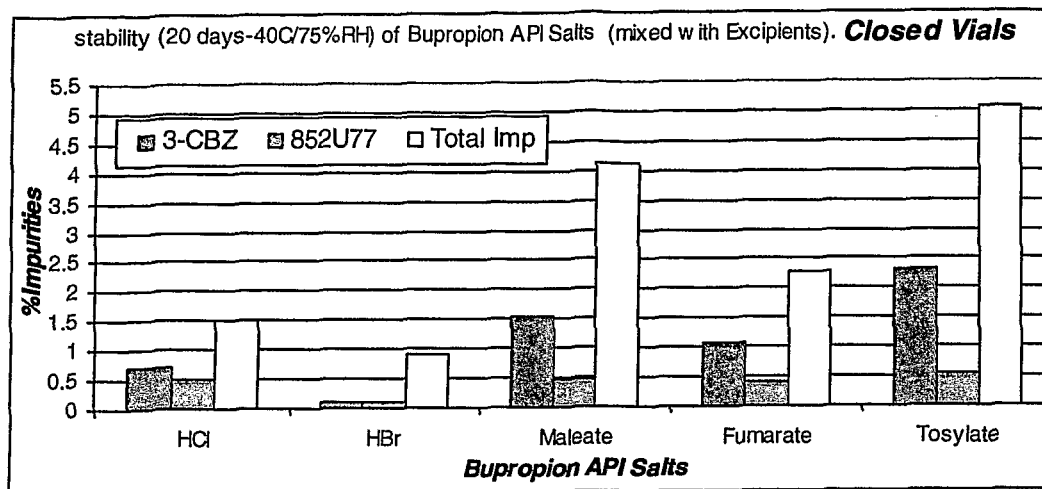


Figure 4

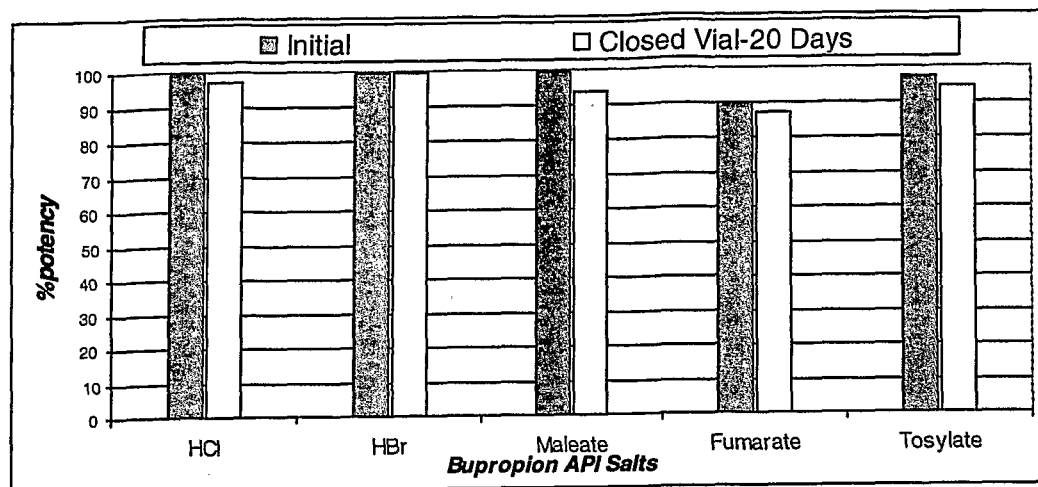


Figure 5

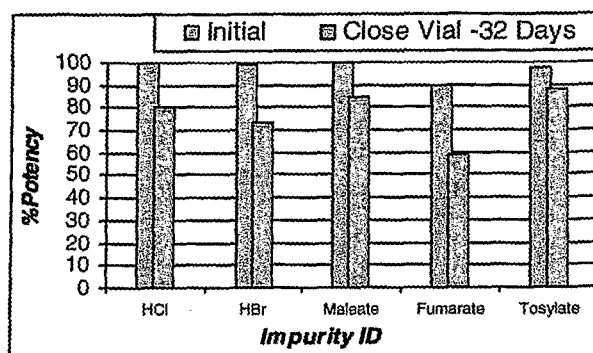


Figure 6

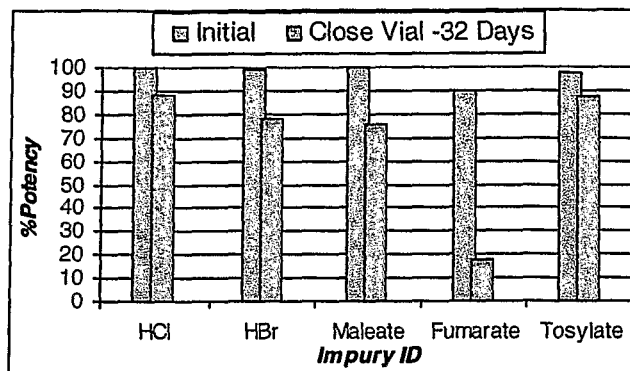


Figure 7

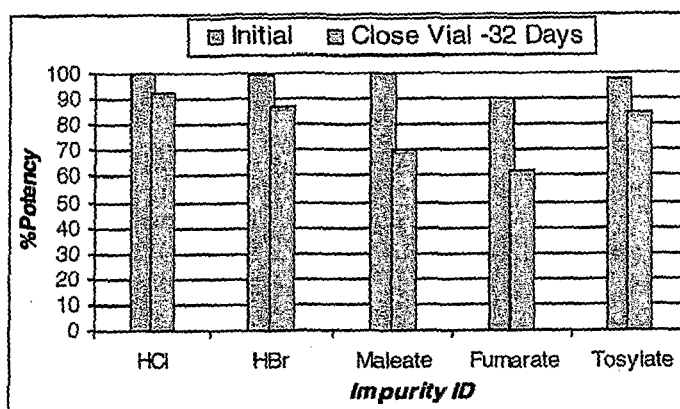
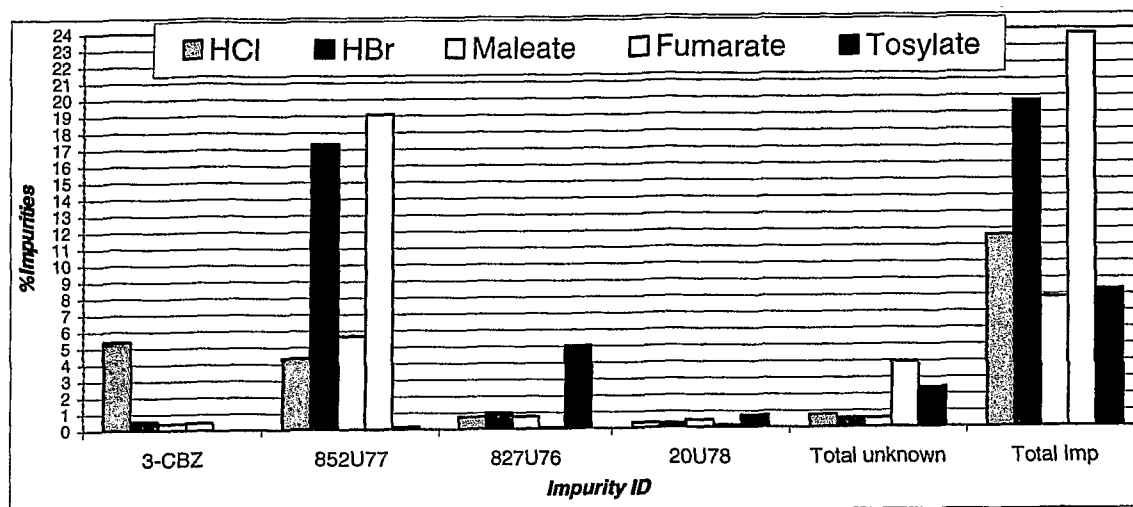
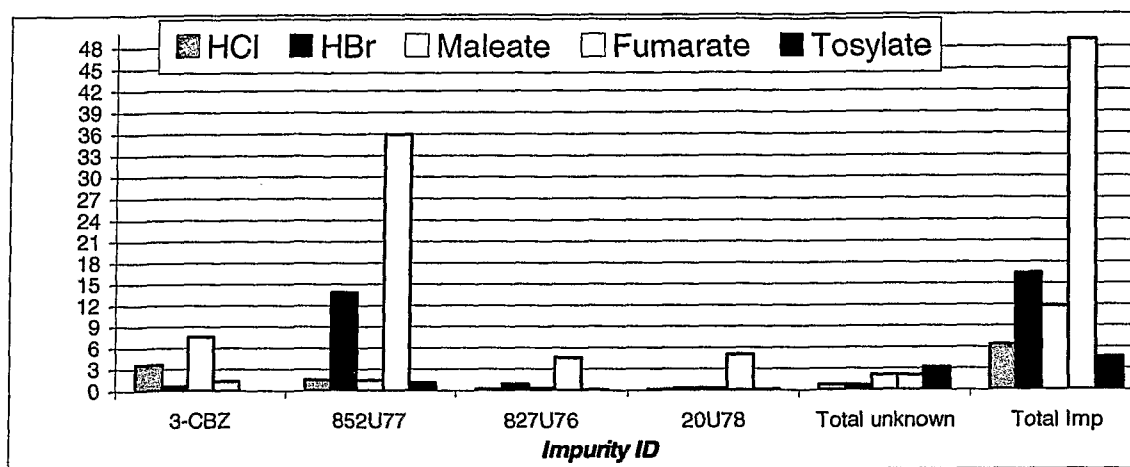


Figure 8



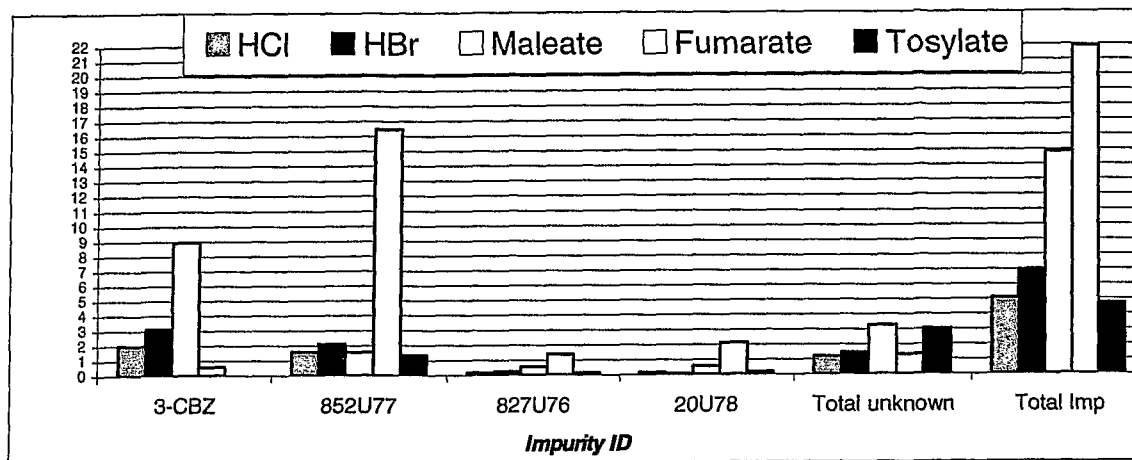
3-CBZ in Tosylate co elutes with p-Tsa peak. Total Imp. Does not include 3-CBZ

Figure 9



3-CBZ in Tosylate co elutes with p-Tsa peak. Total Imp. Does not include 3-CBZ

Figure 10



3-CBZ in Tosylate co elutes with p-Tsa peak. Total Imp. Does not include 3-CBZ

Figure 11

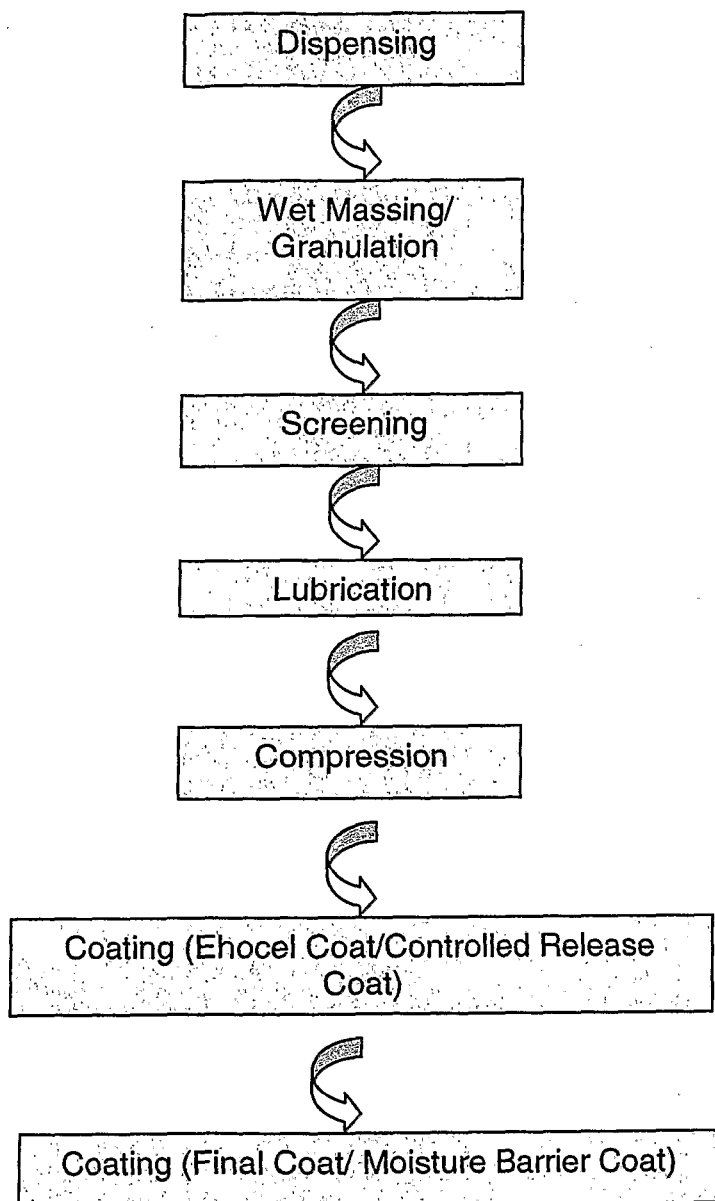


Figure 12

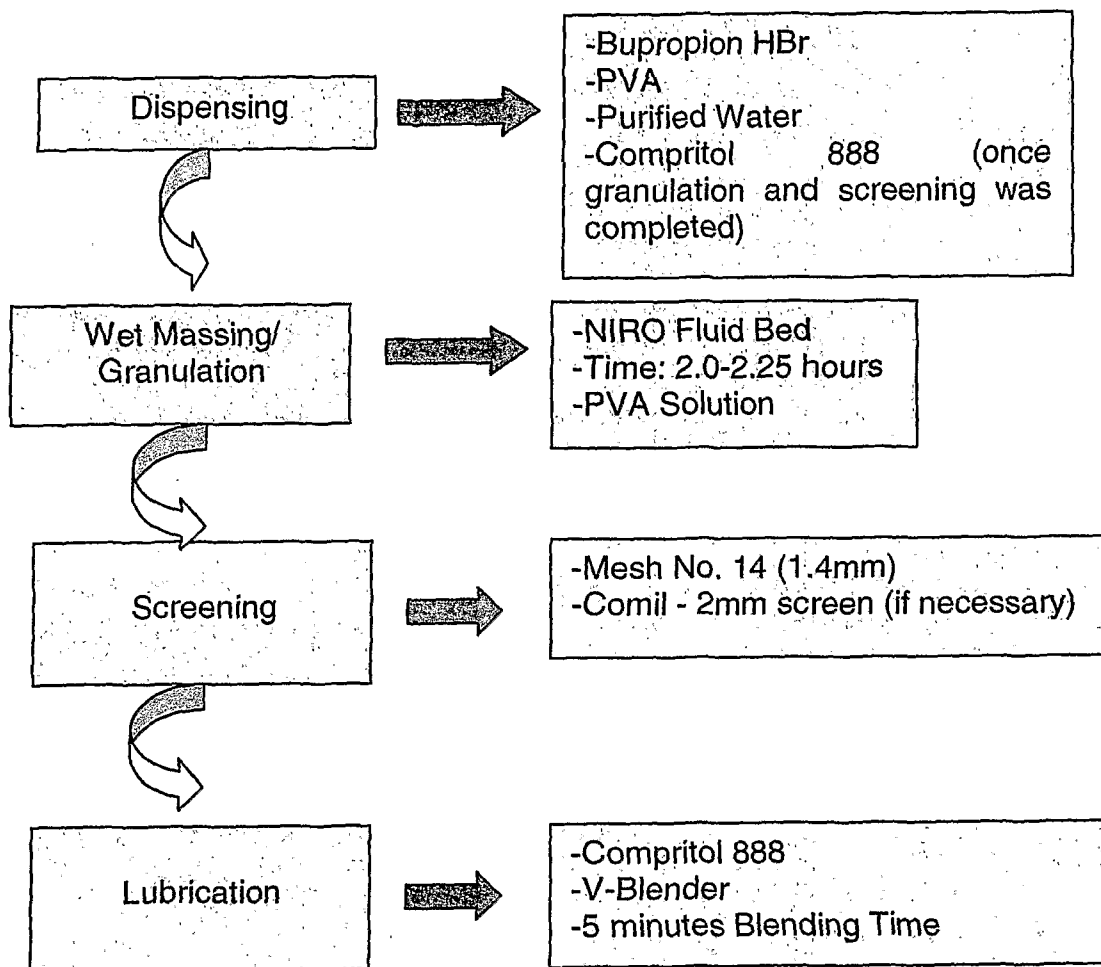


Figure 13

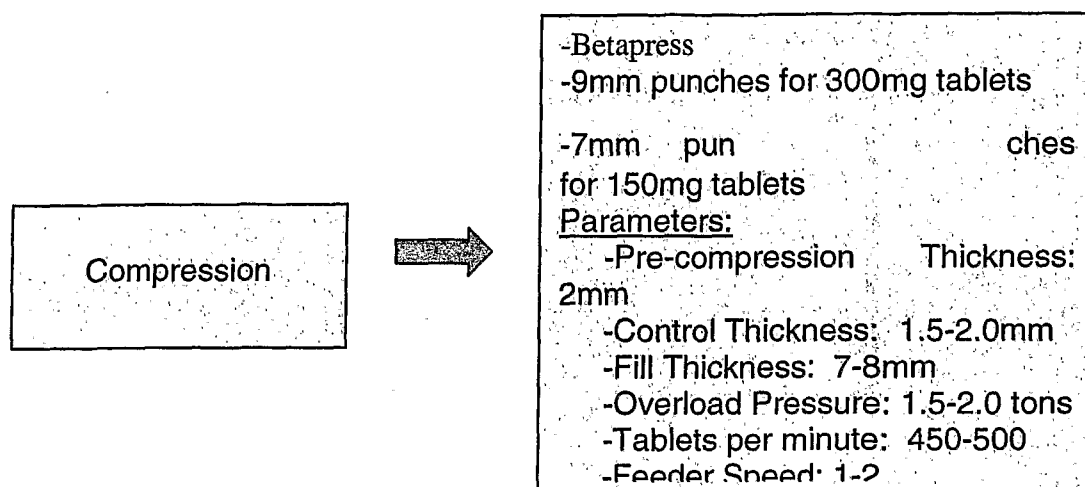


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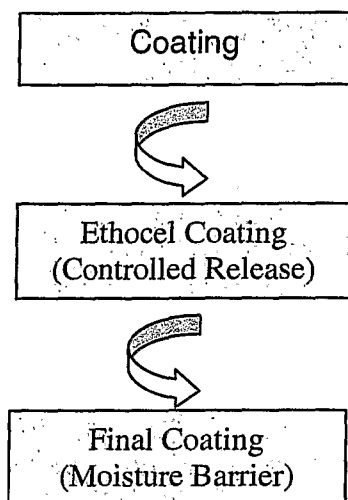


Figure 15

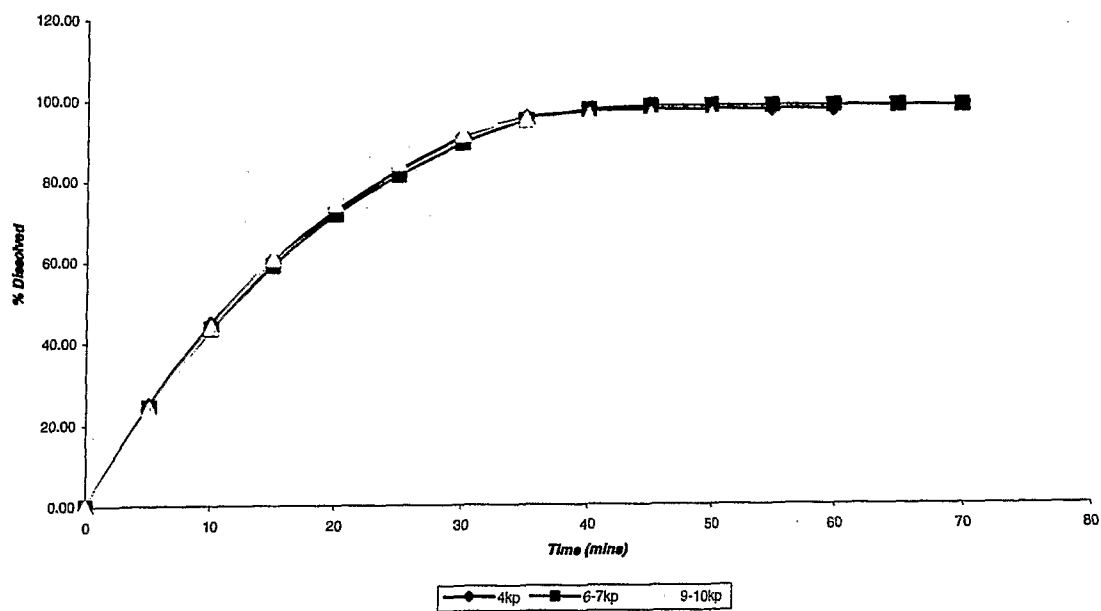


Figure 16

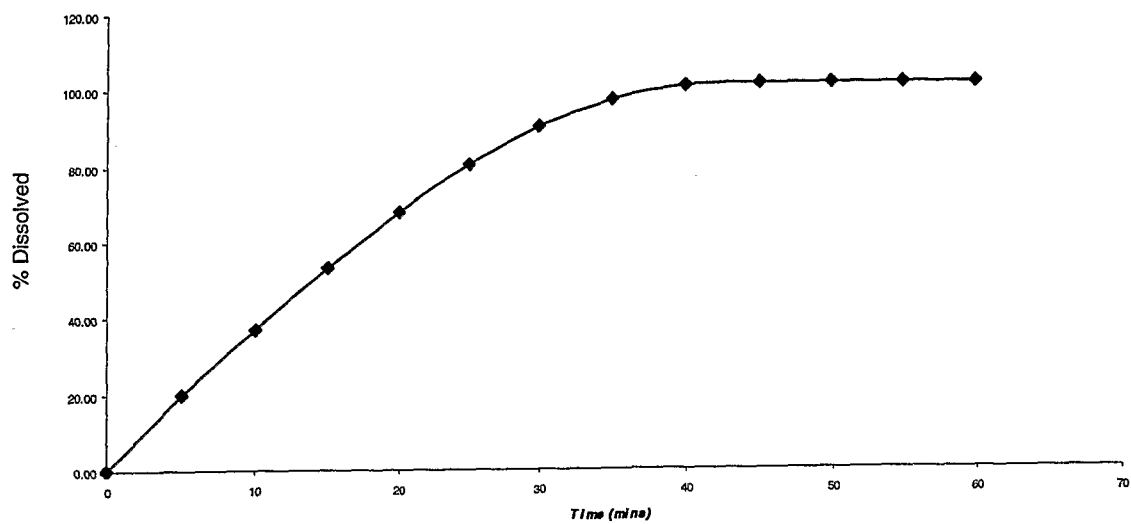


Figure 17

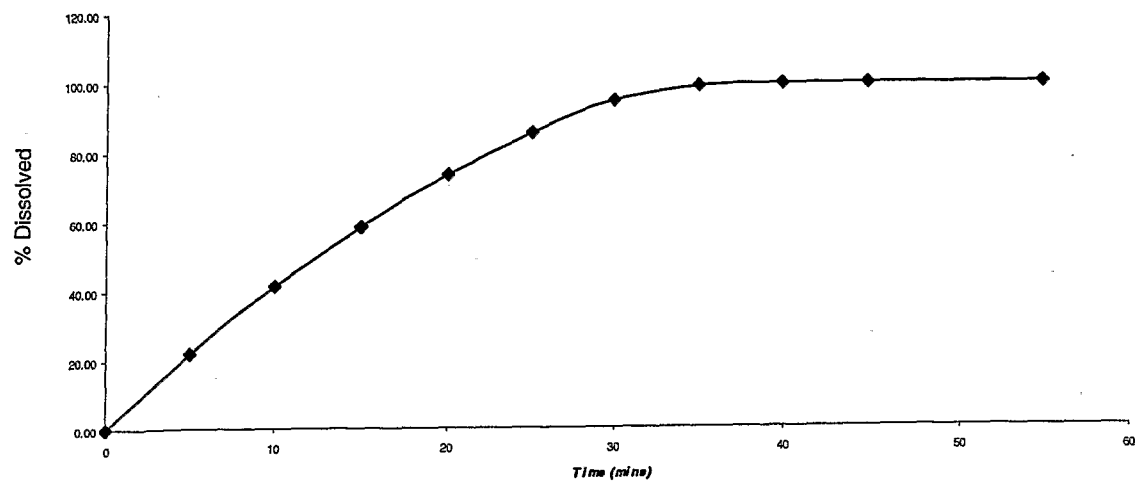


Figure 18

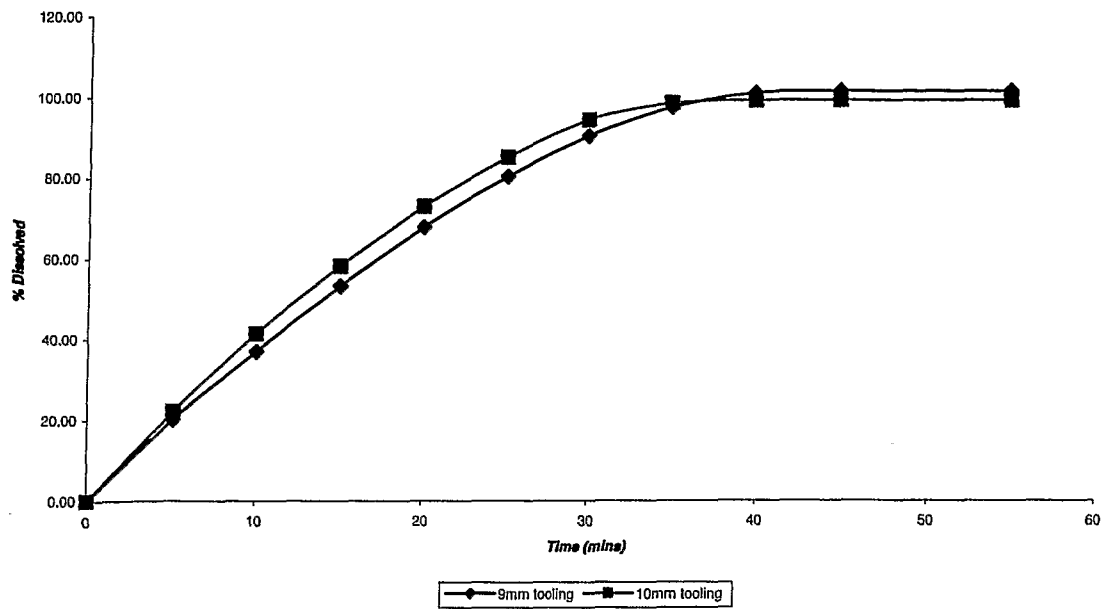


Figure 19

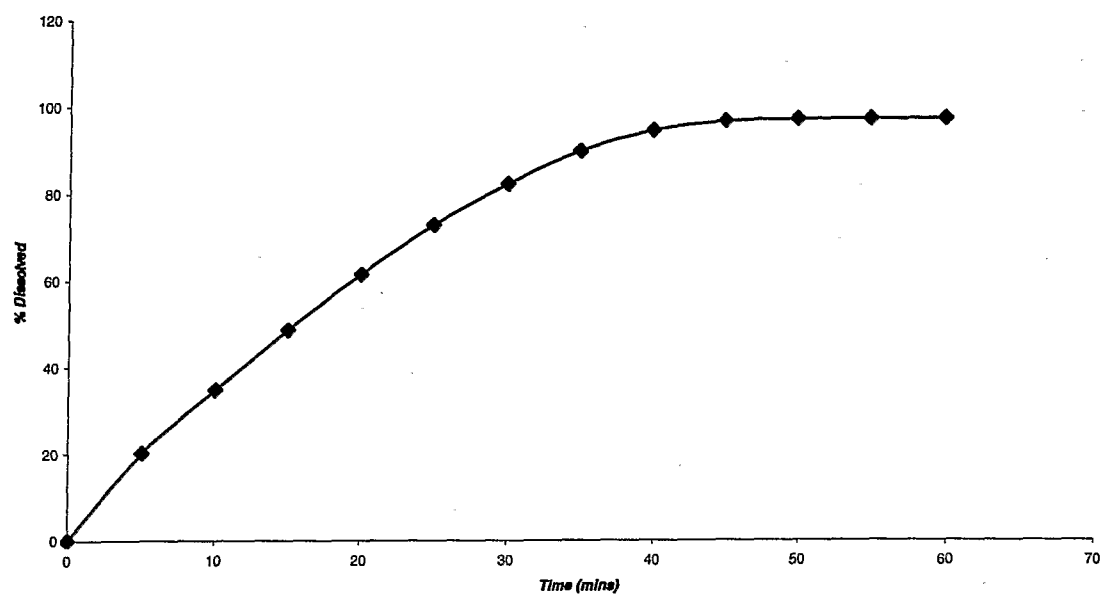


Figure 20

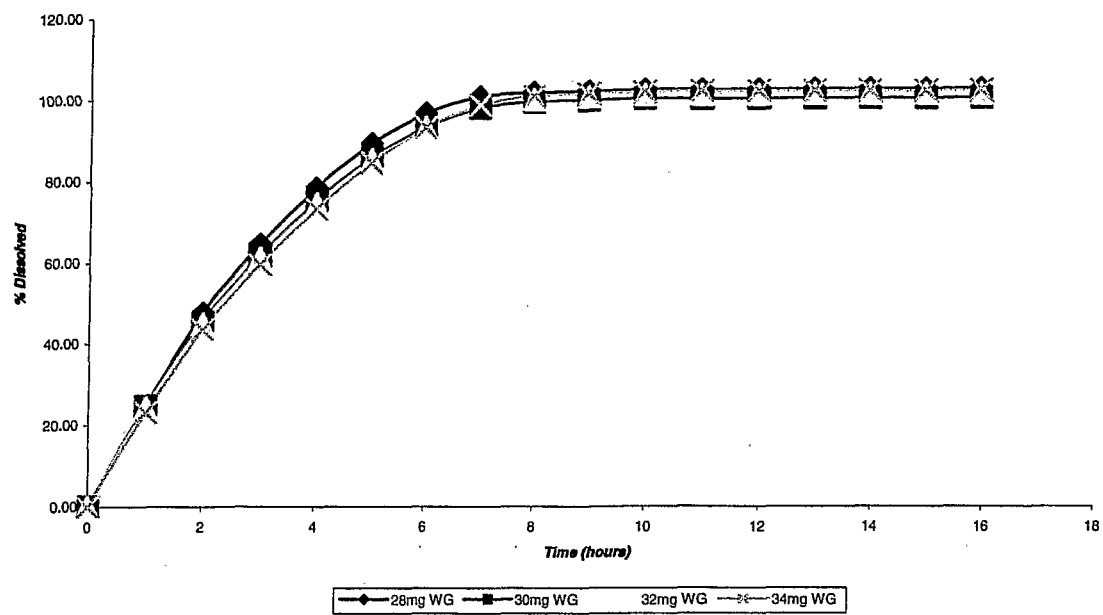


Figure 21

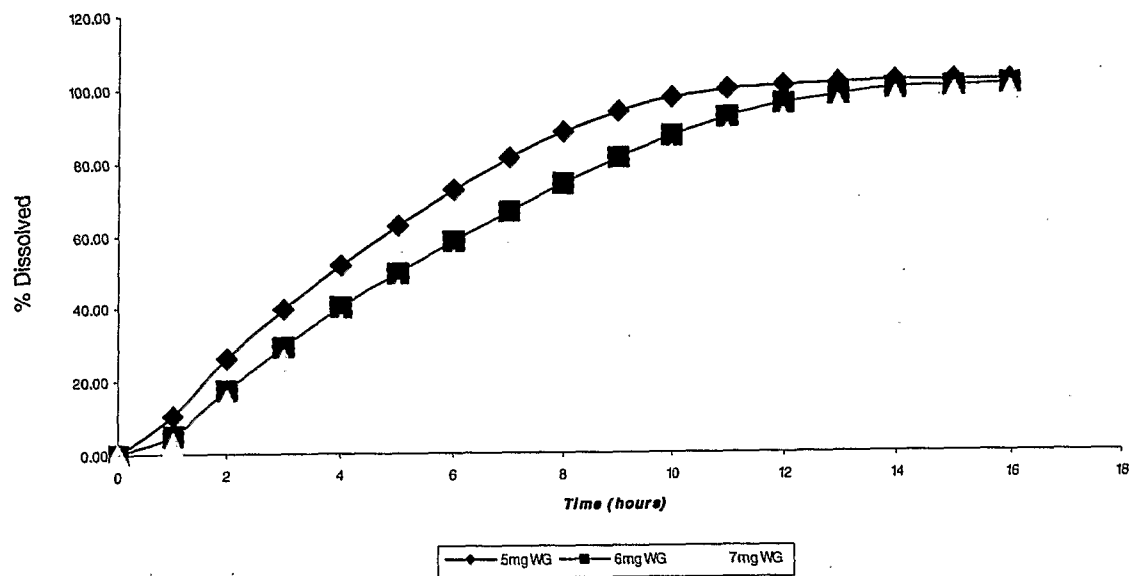


Figure 22

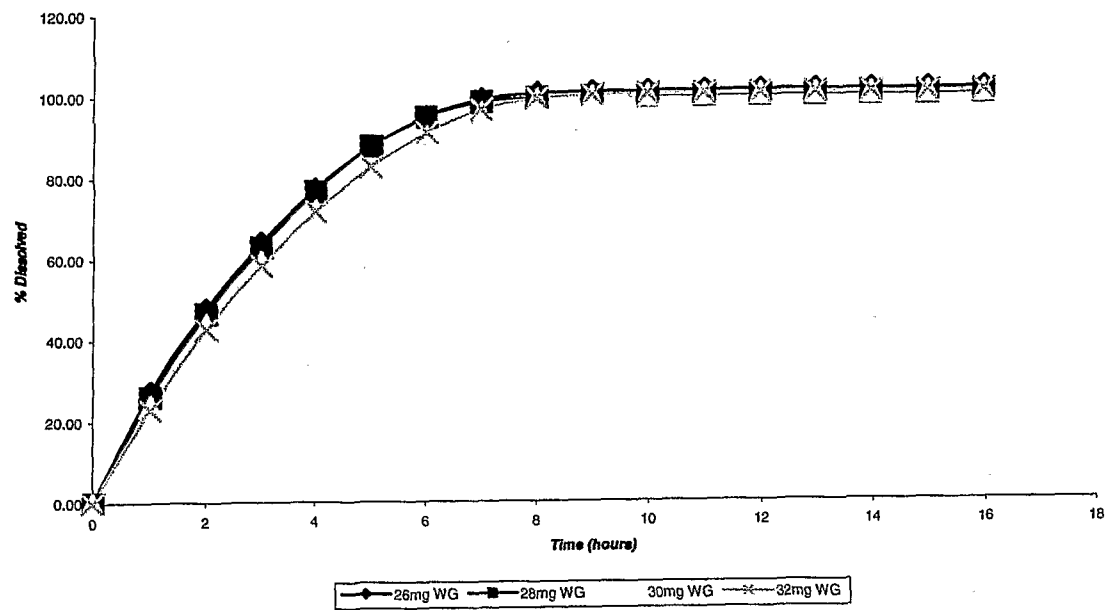


Figure 23

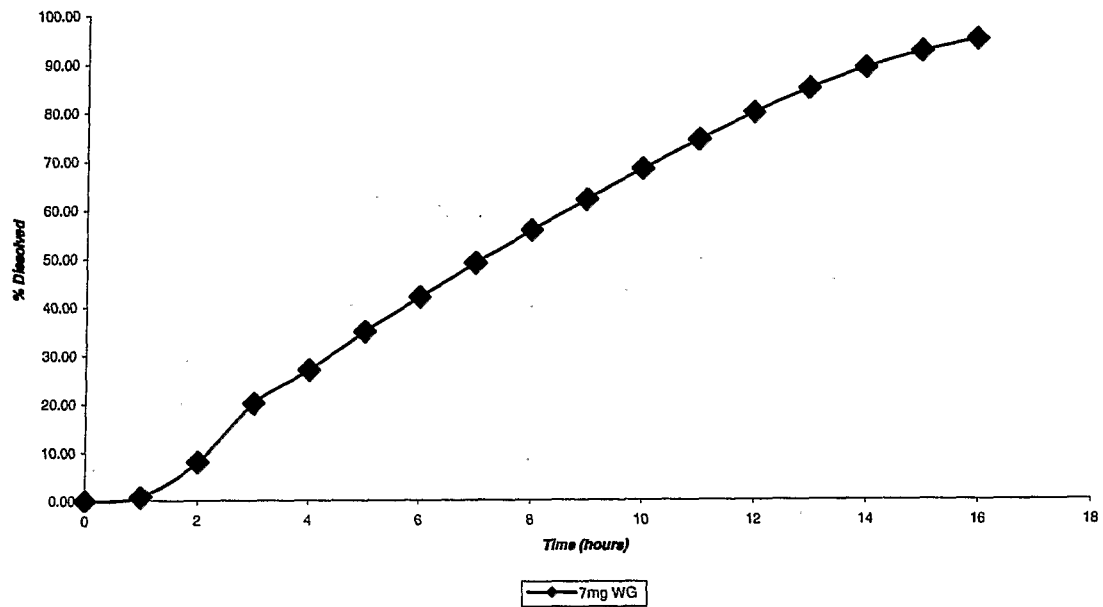


Figure 24

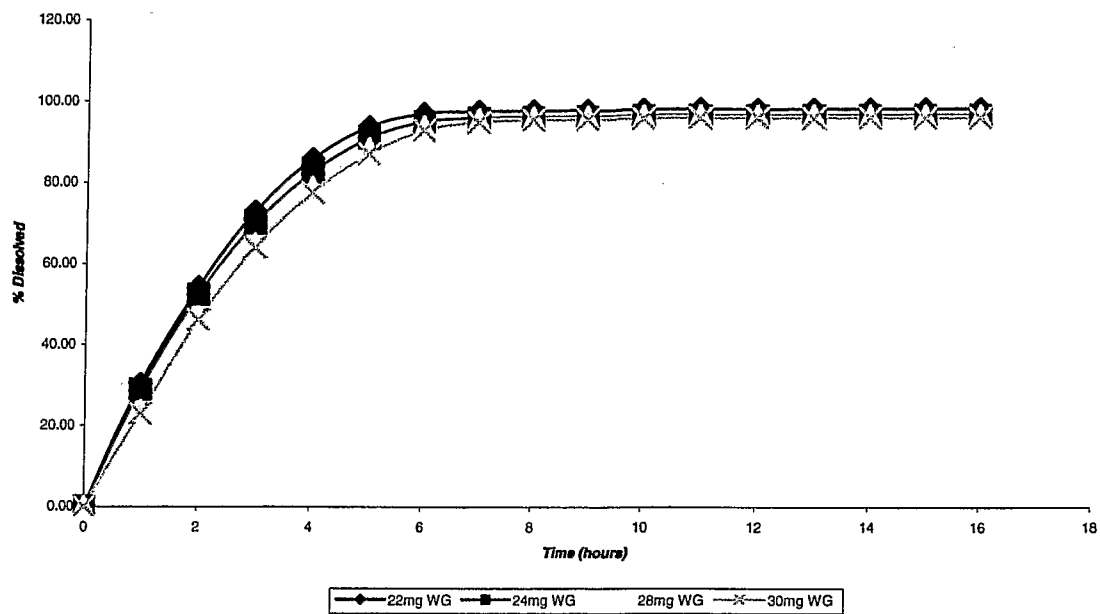


Figure 25

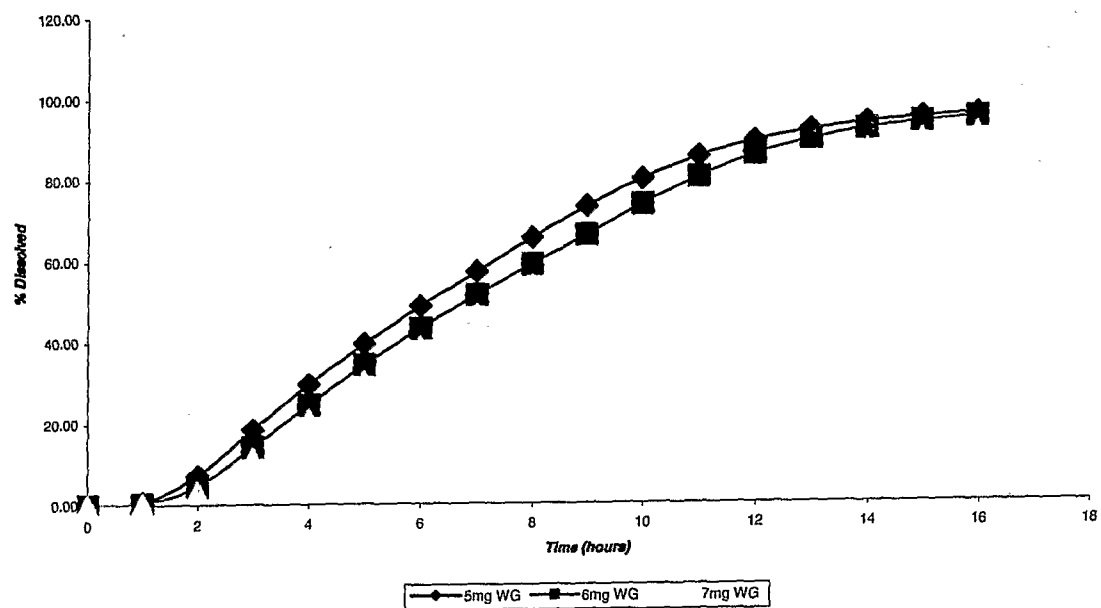


Figure 26

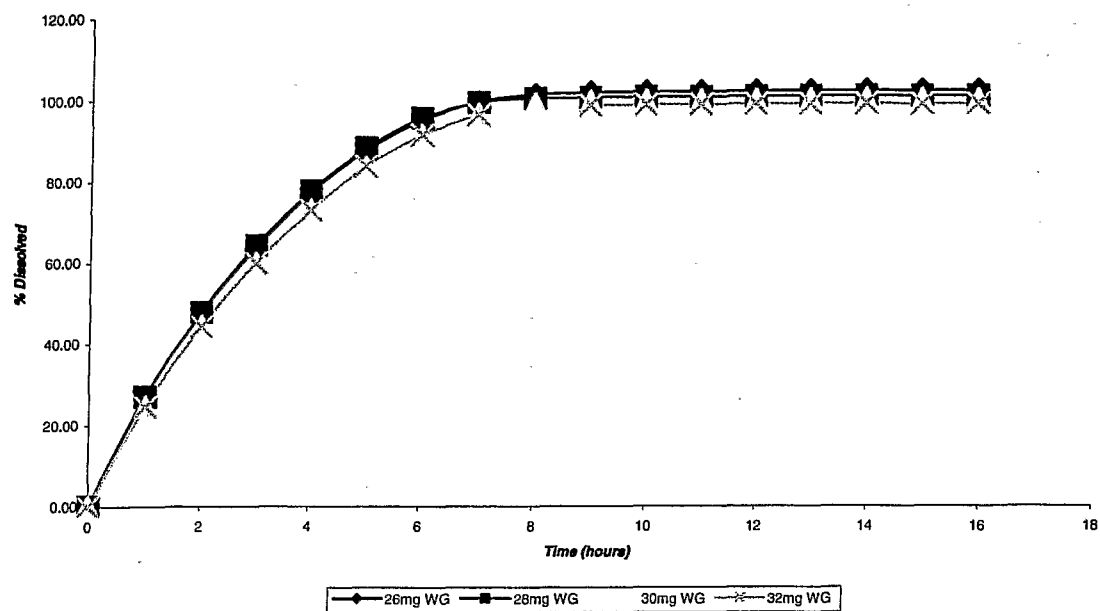


Figure 27

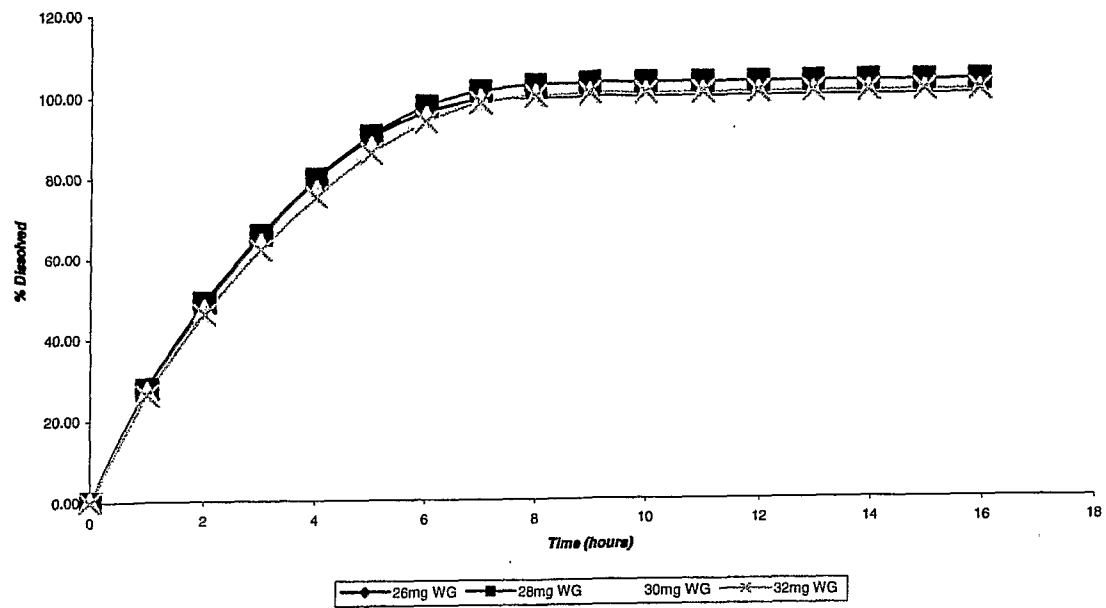


Figure 28

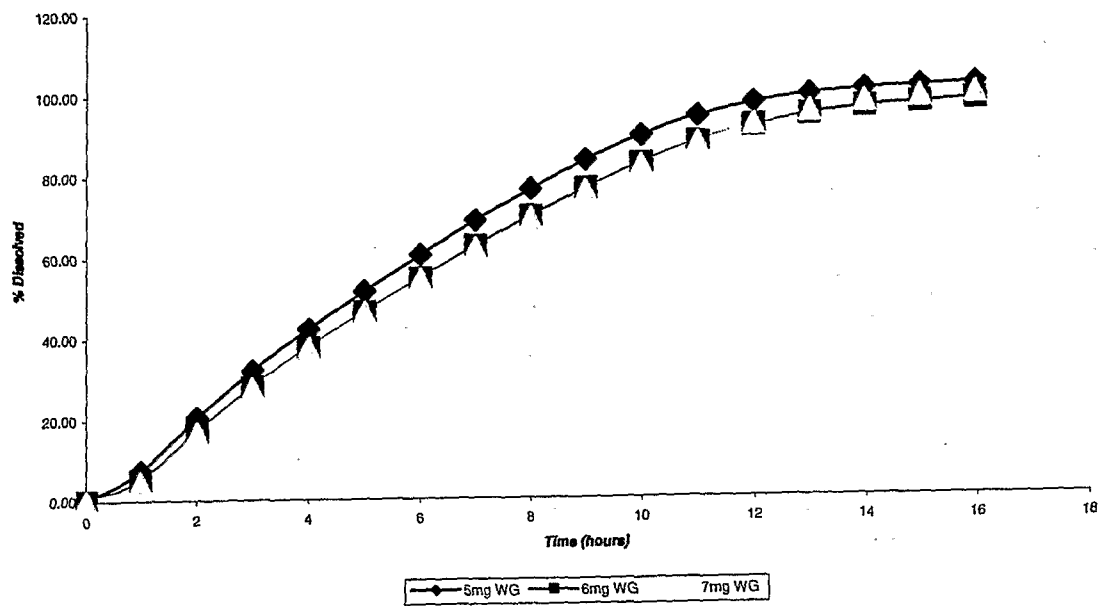


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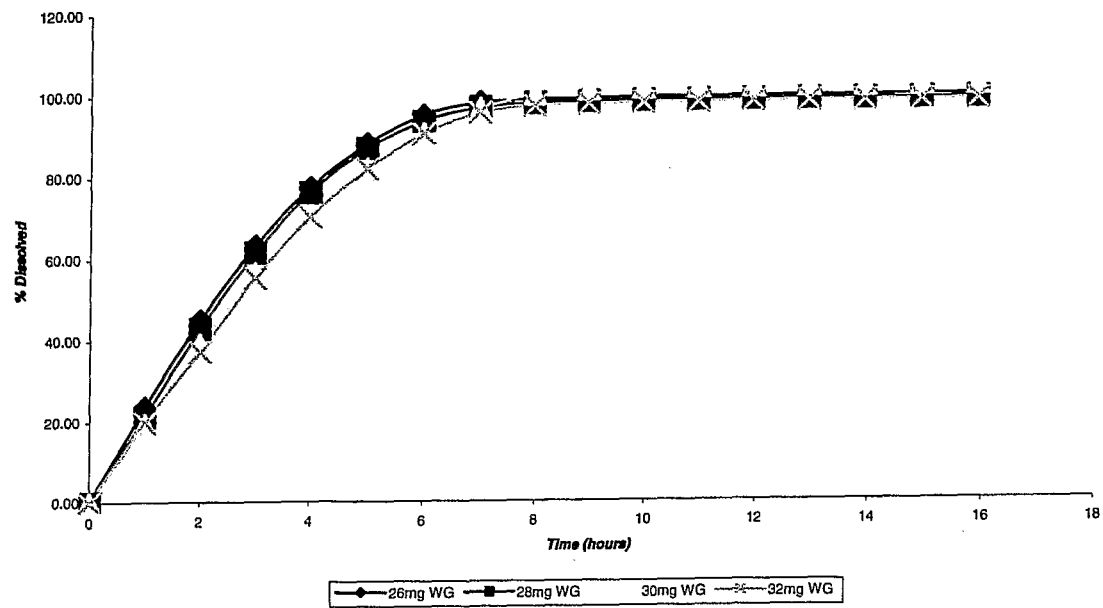


Figure 30

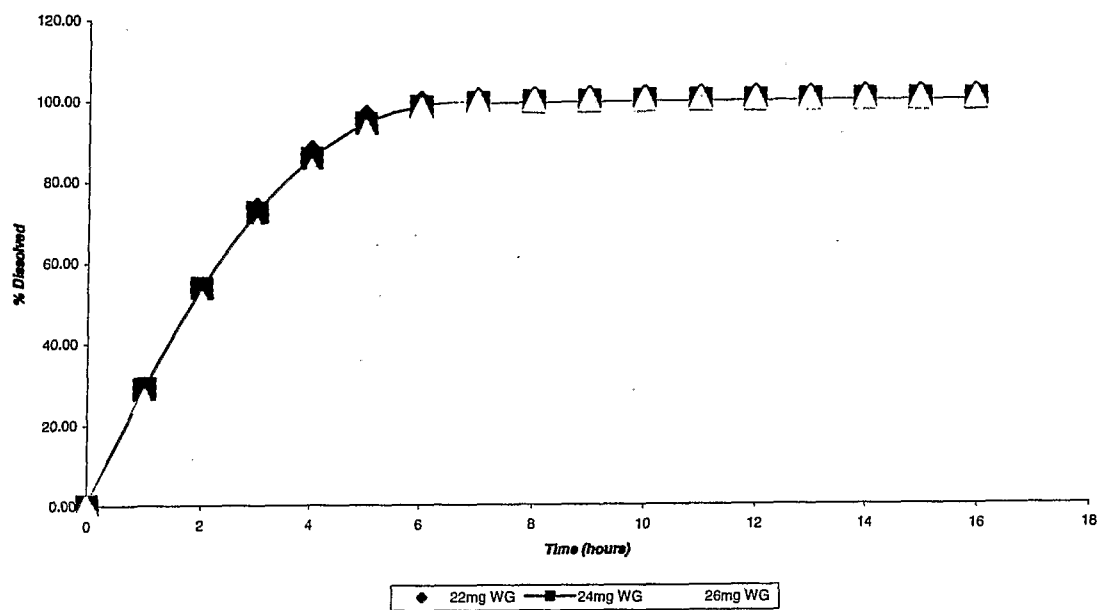


Figure 31

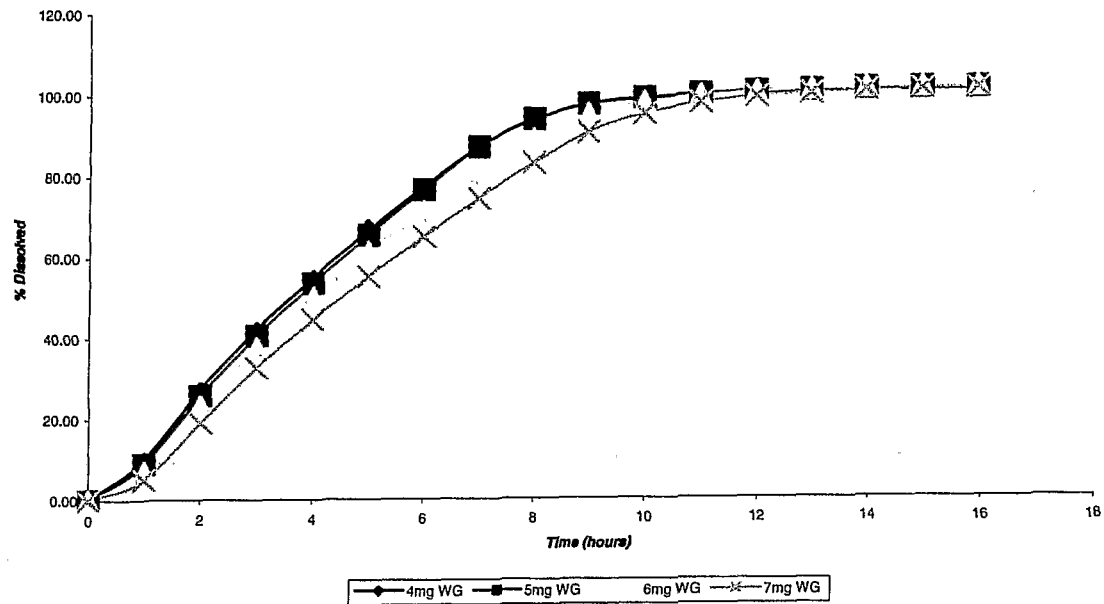


Figure 32

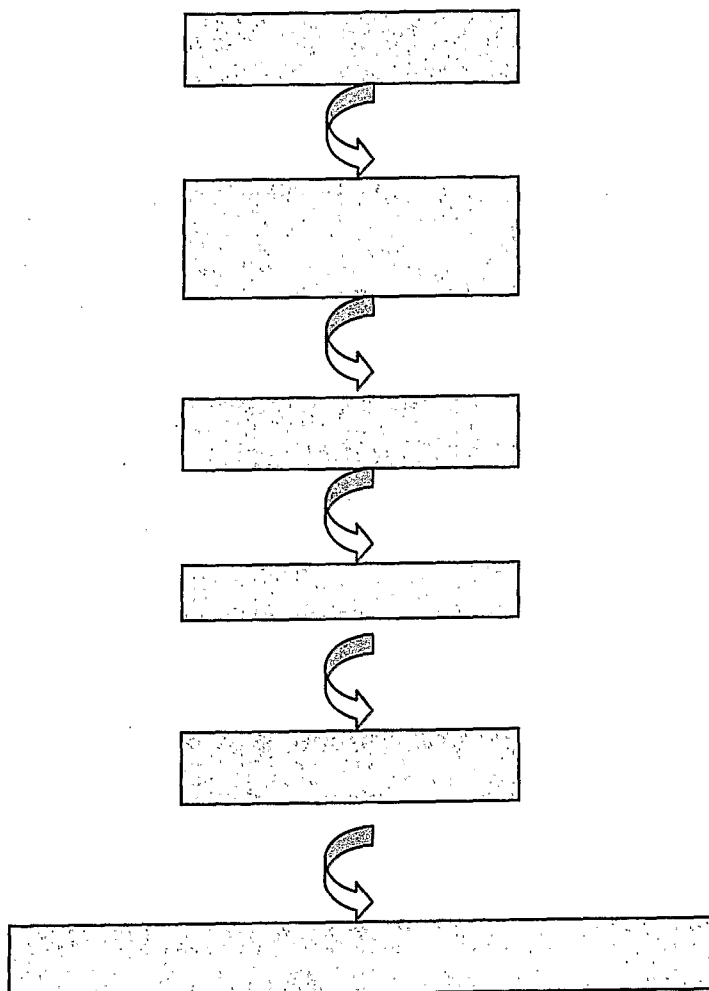


Figure 33

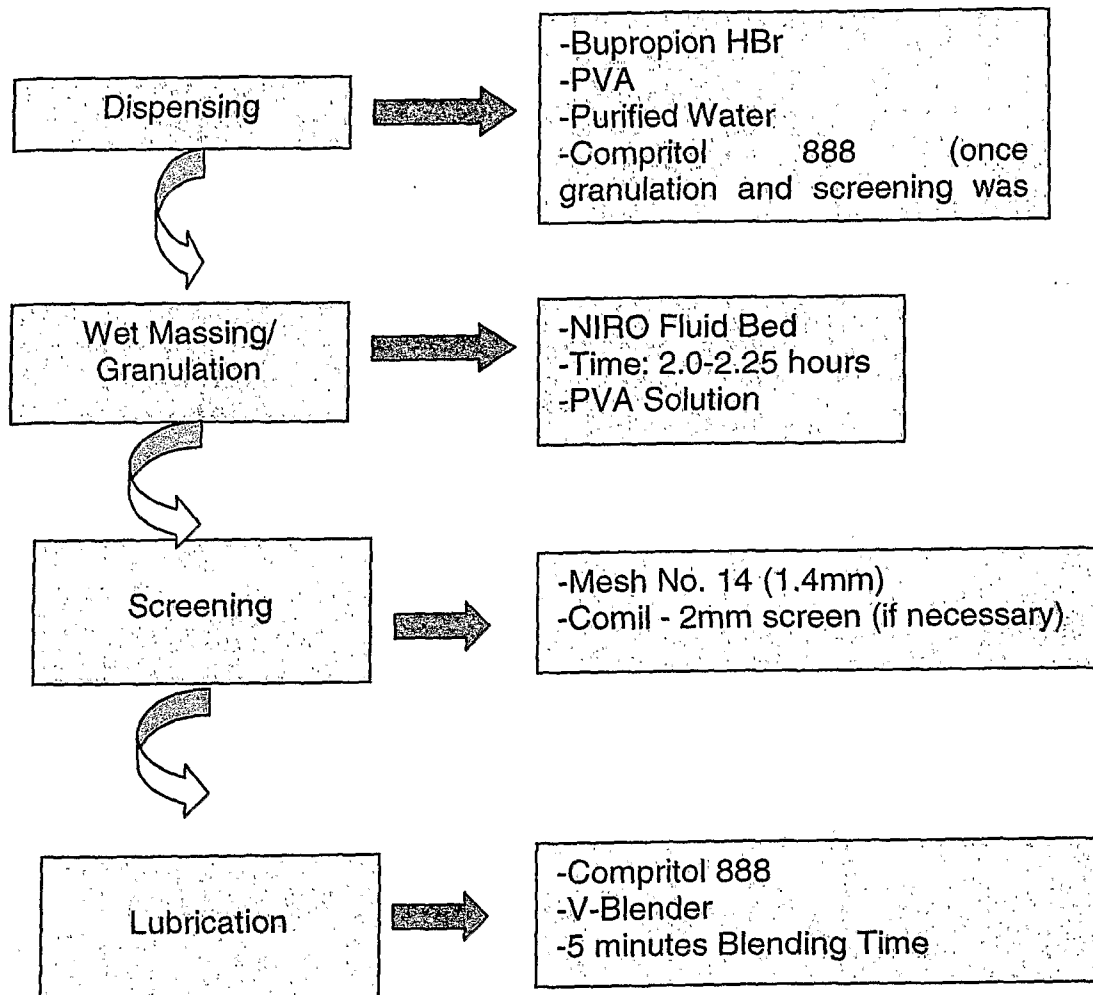


Figure 34

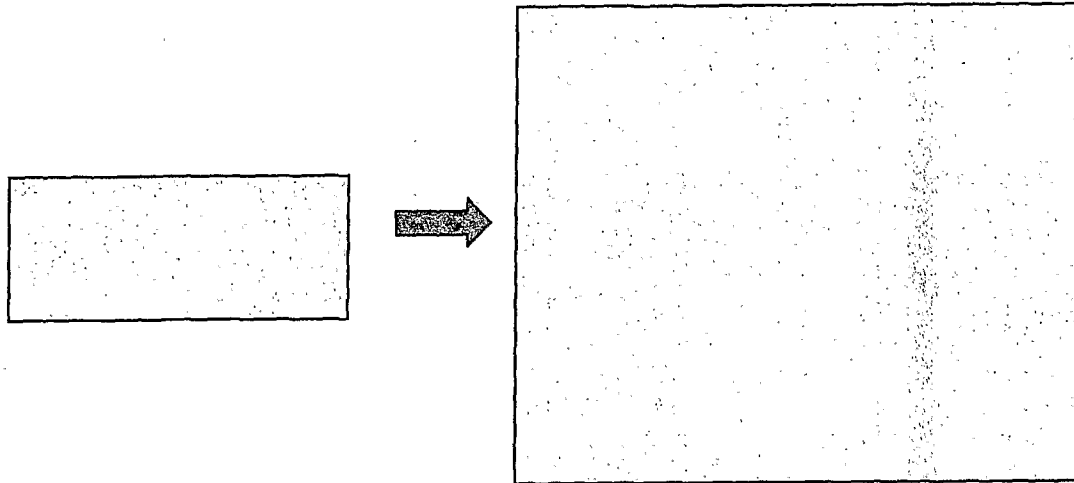


Figure 35

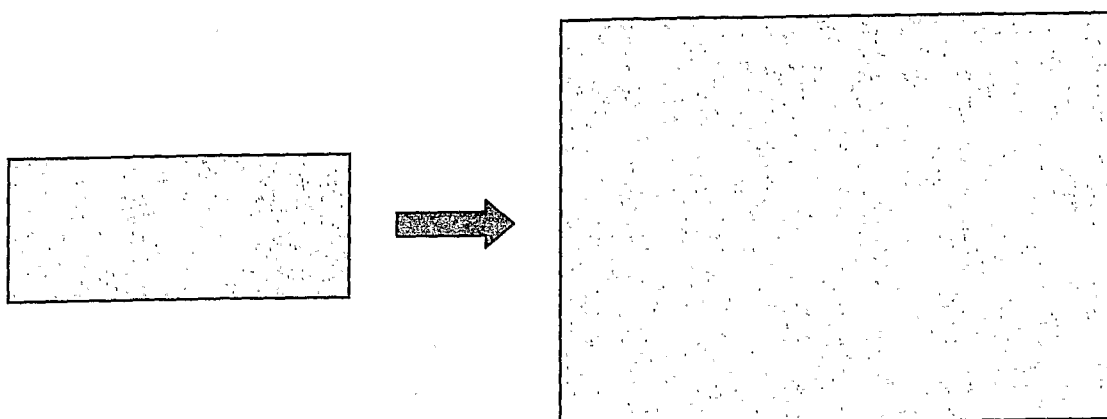


Figure 36

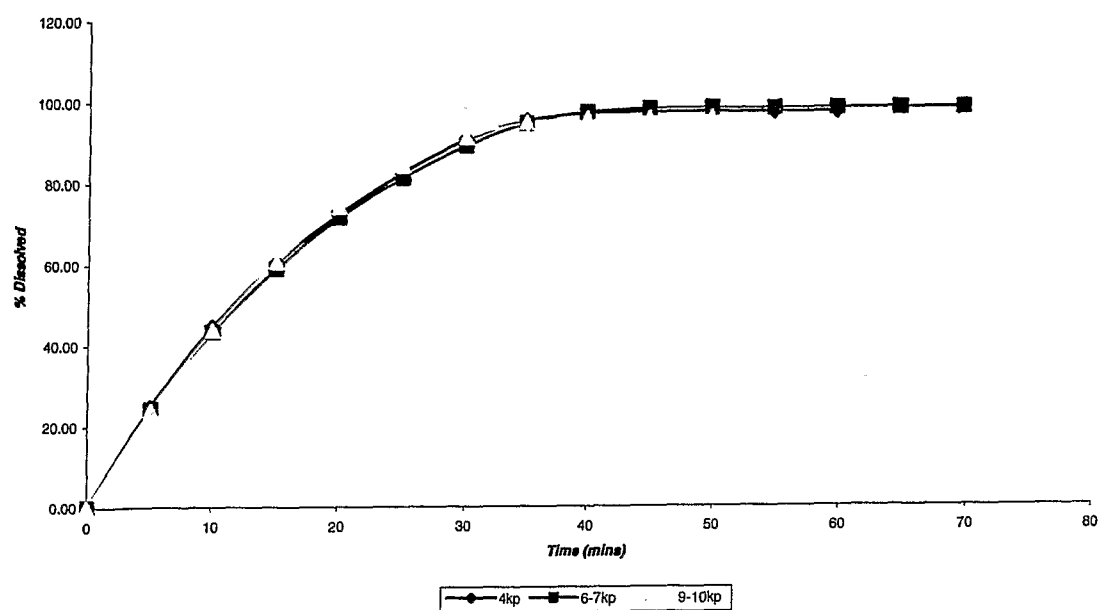


Figure 37

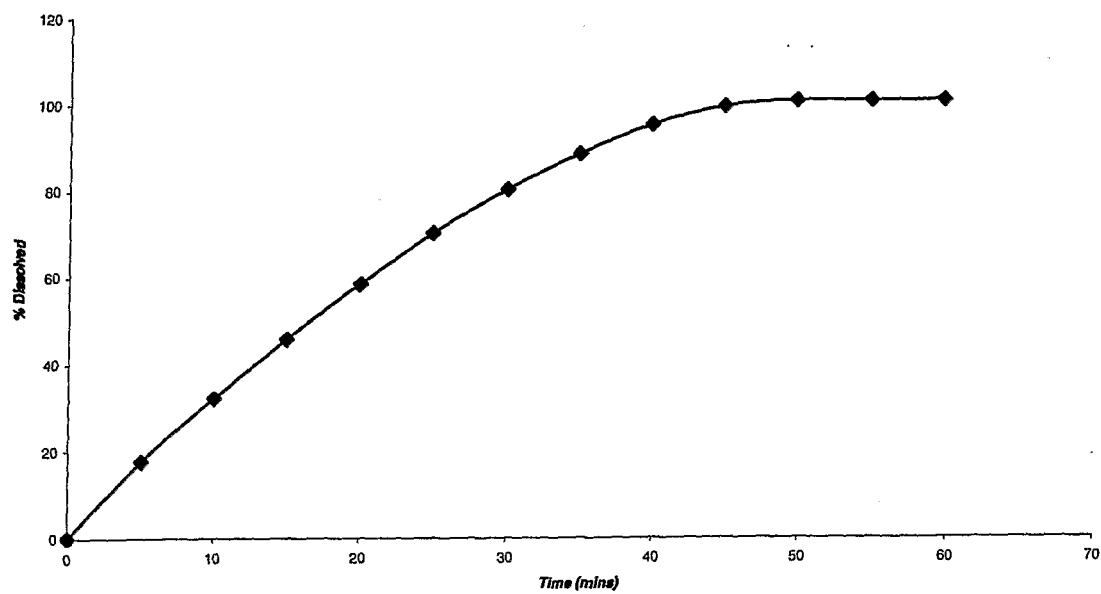


Figure 38

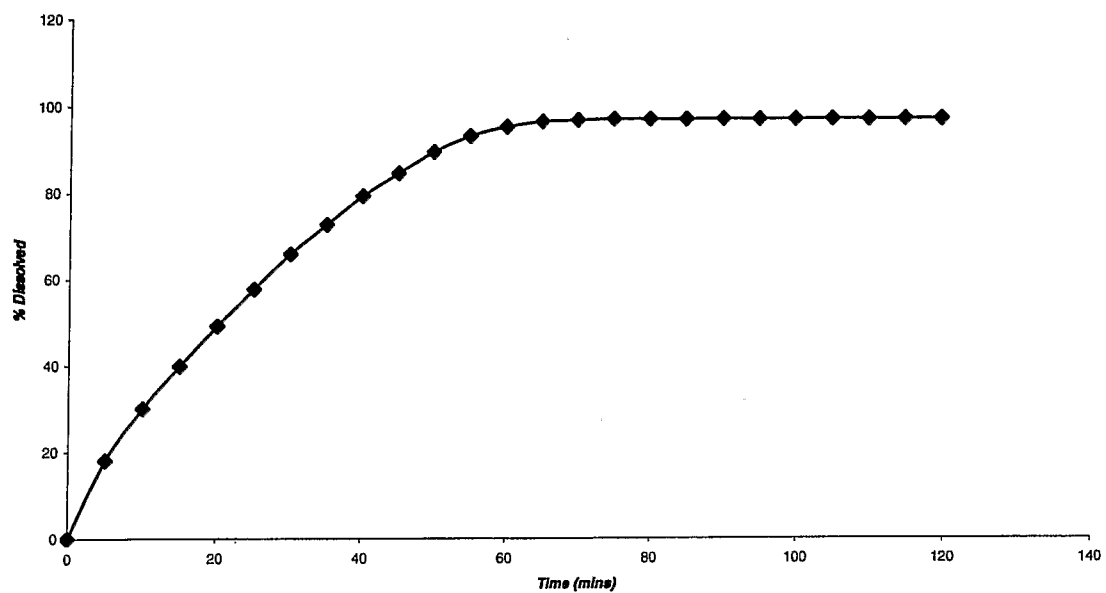


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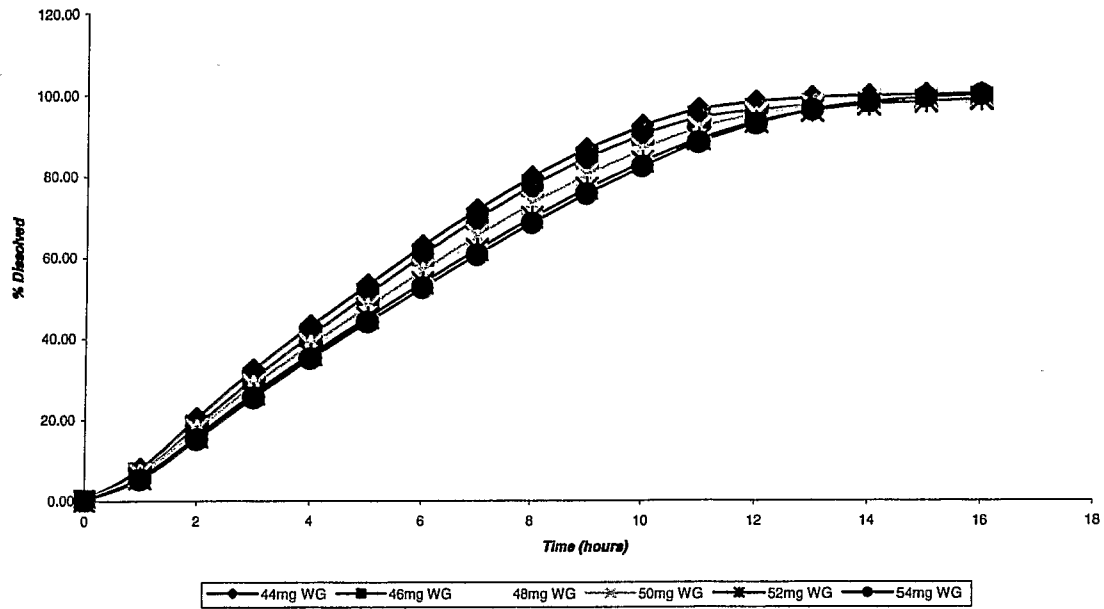


Figure 40

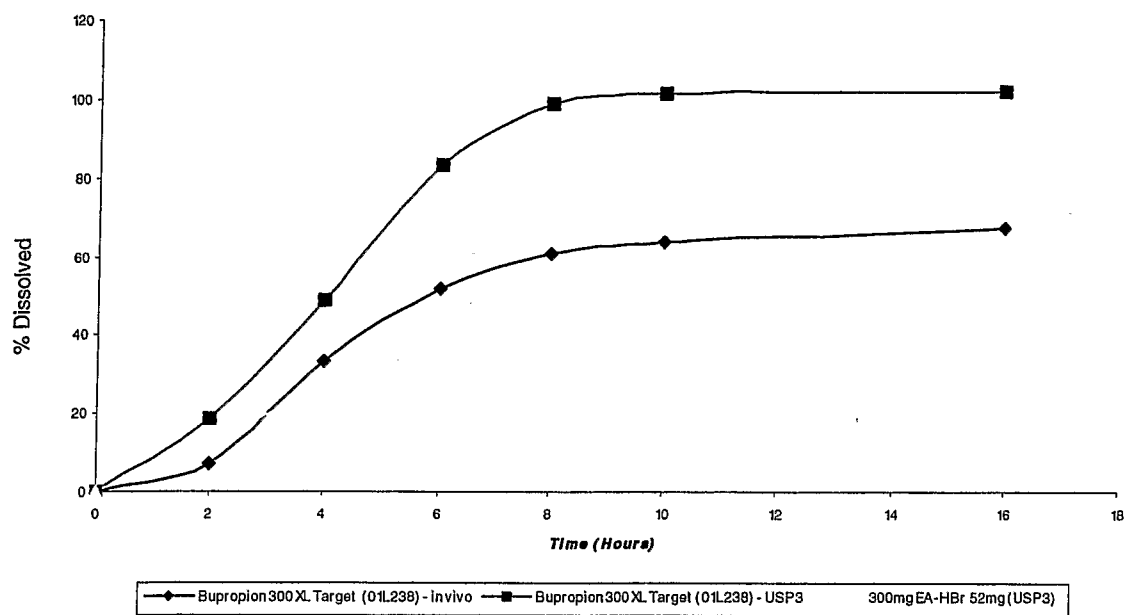


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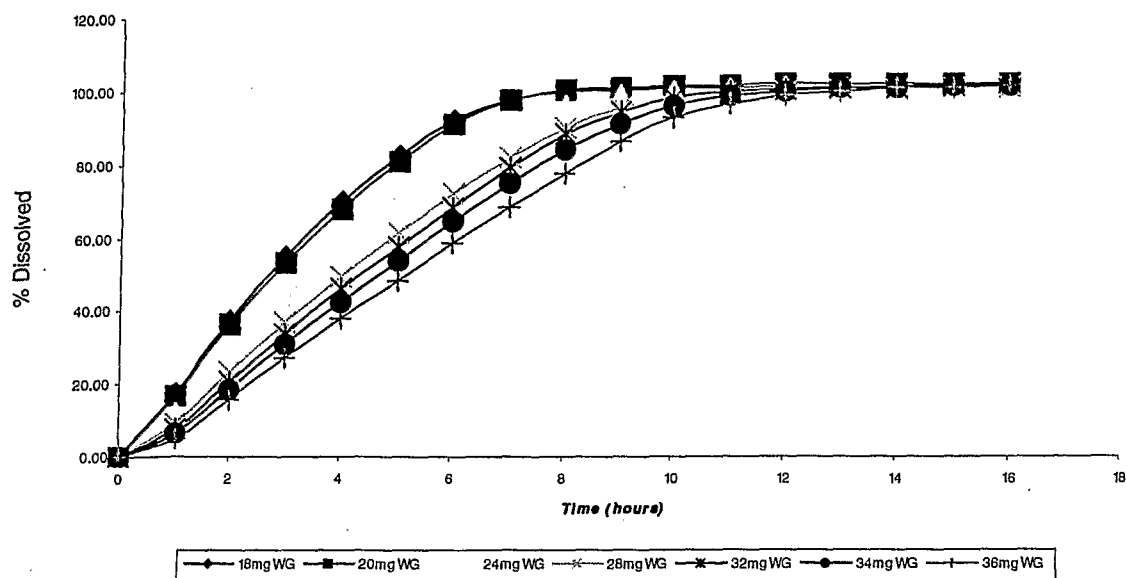


Figure 42

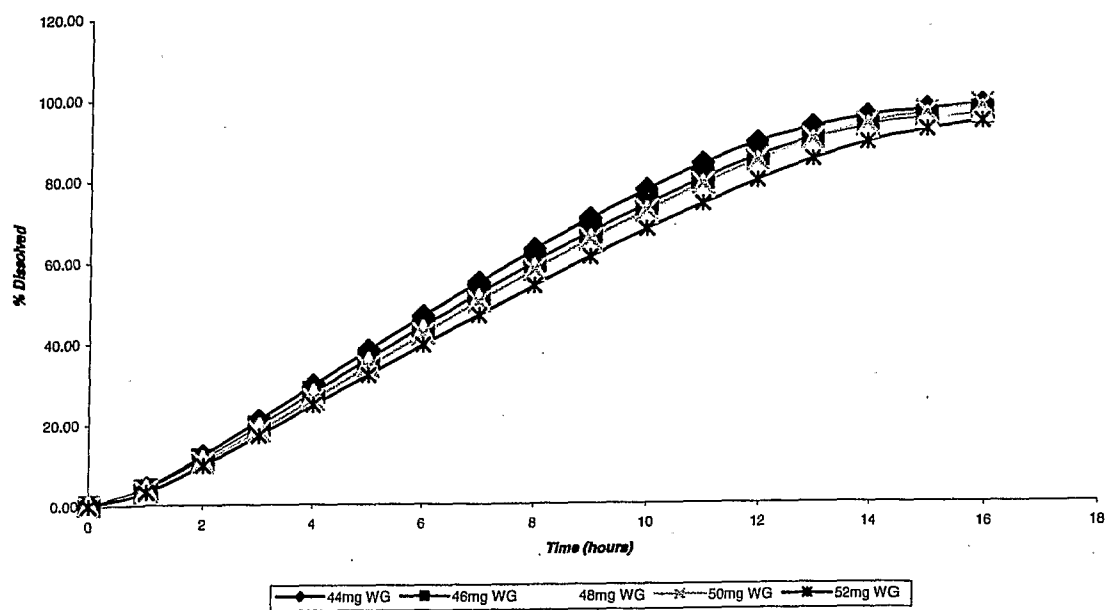


Figure 43

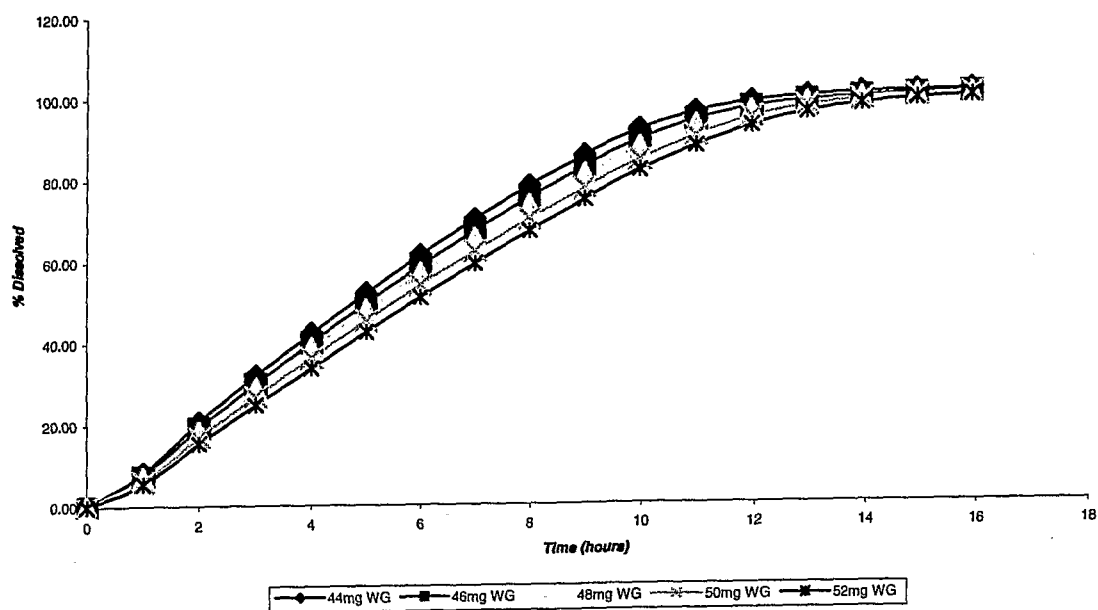


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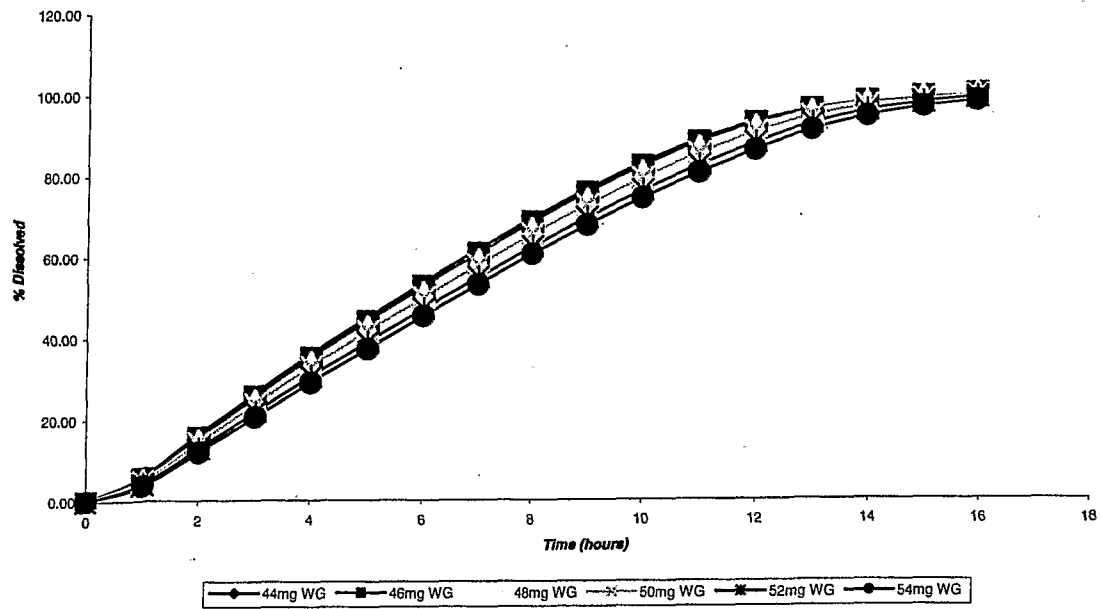


Figure 45

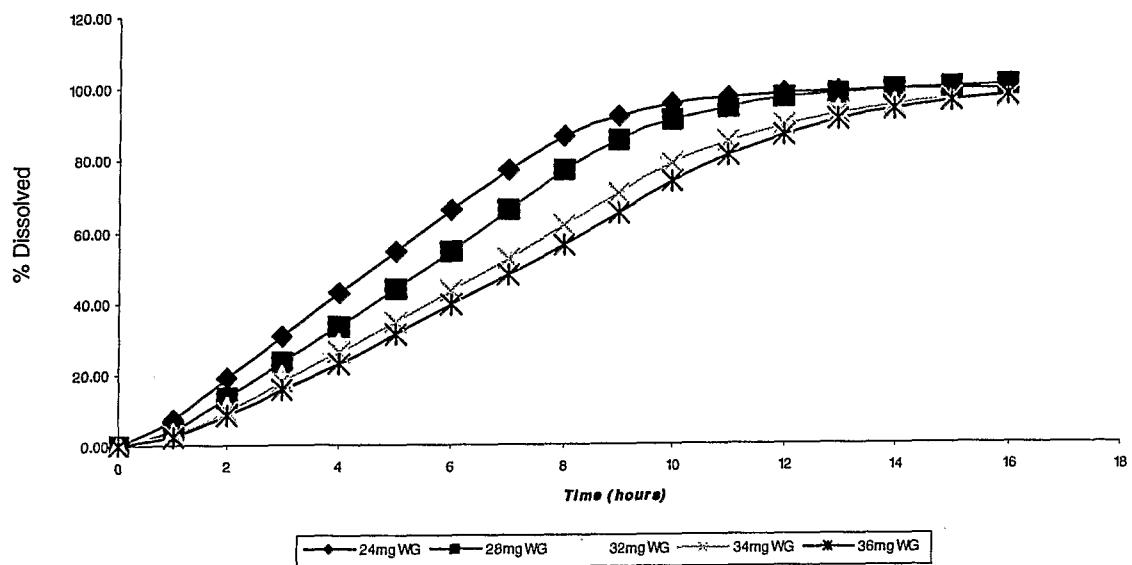


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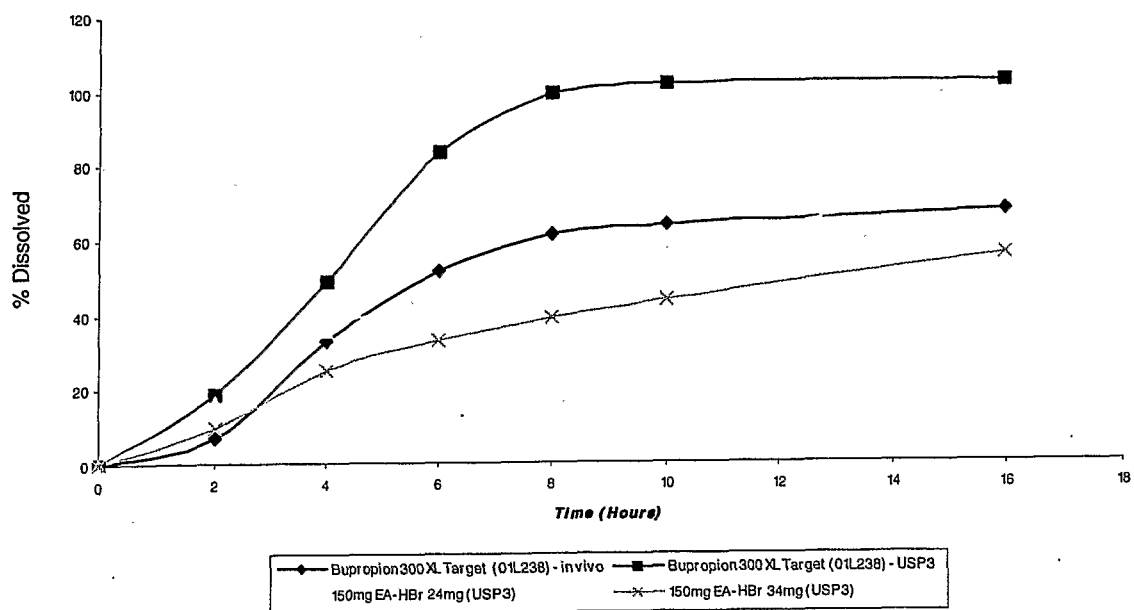


Figure 47

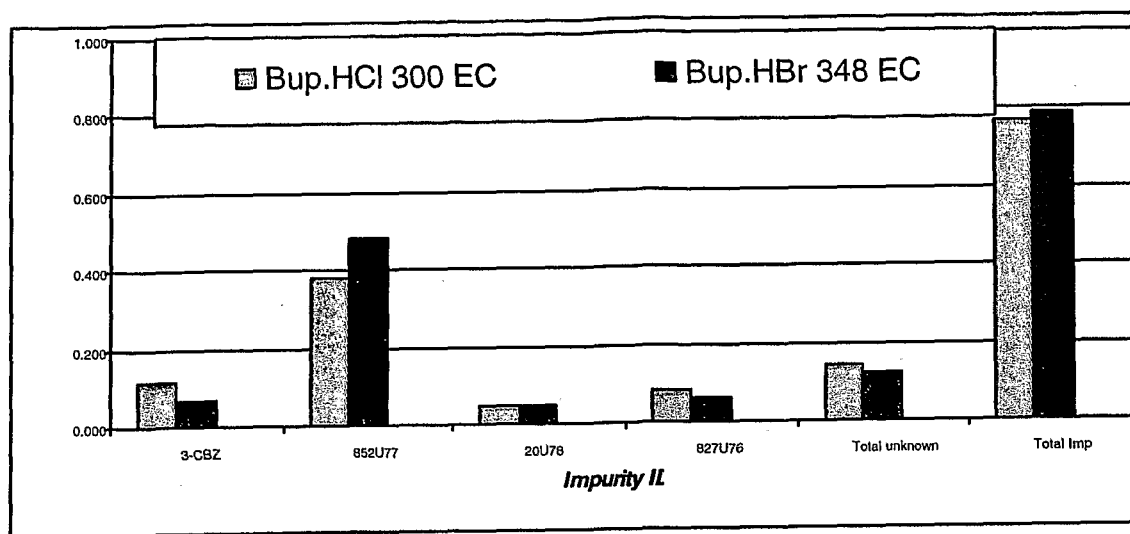


Figure 48

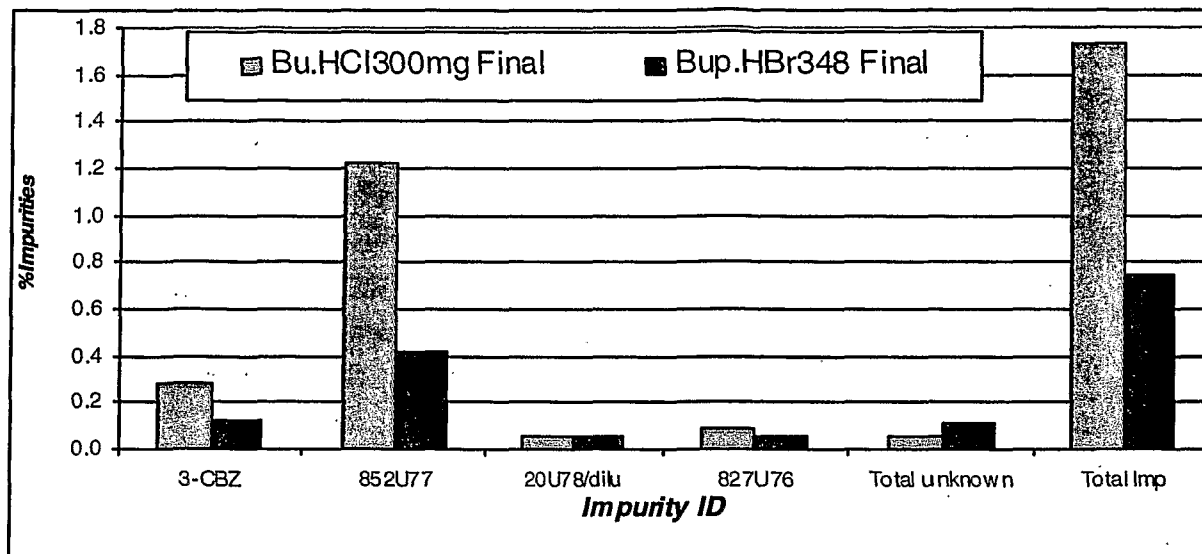


Figure 49

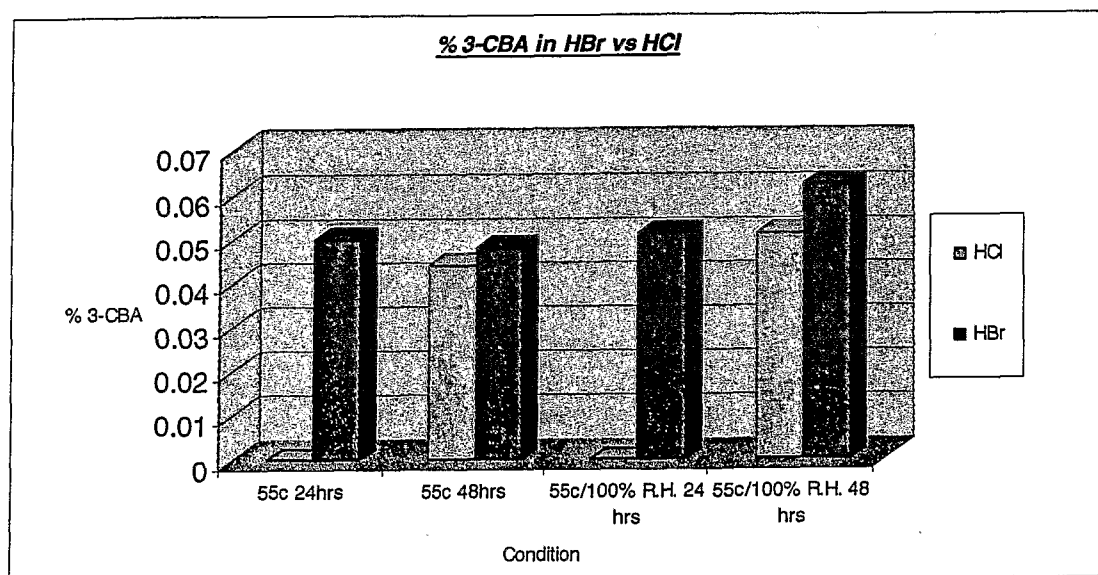
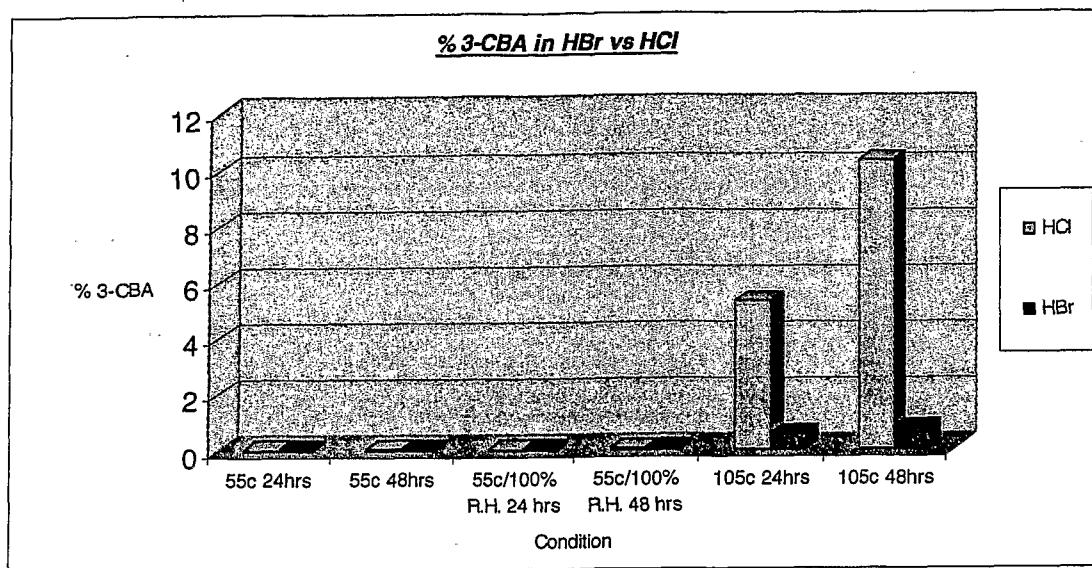


Figure 50

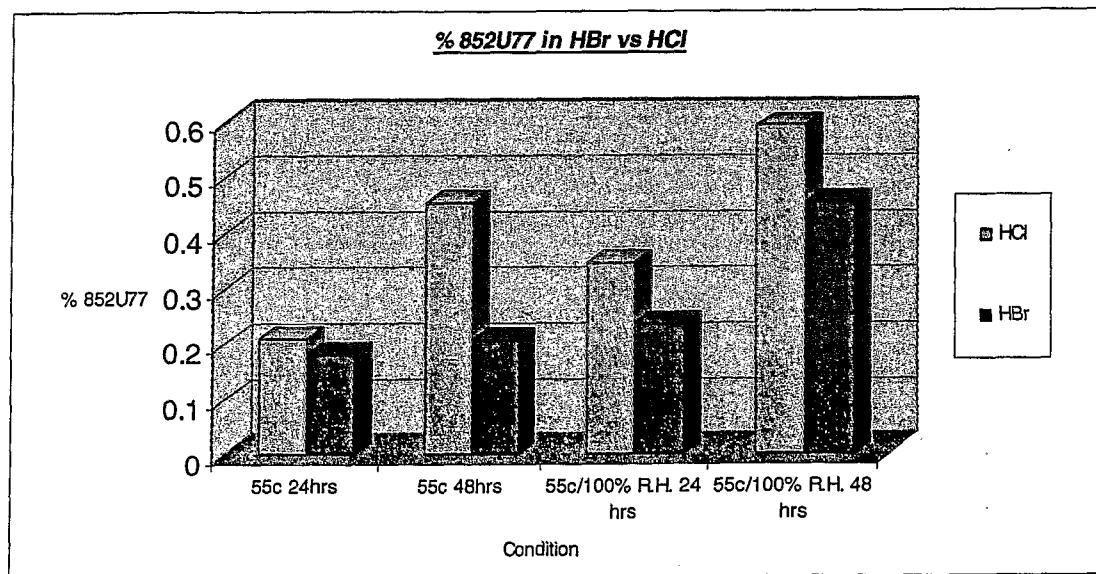
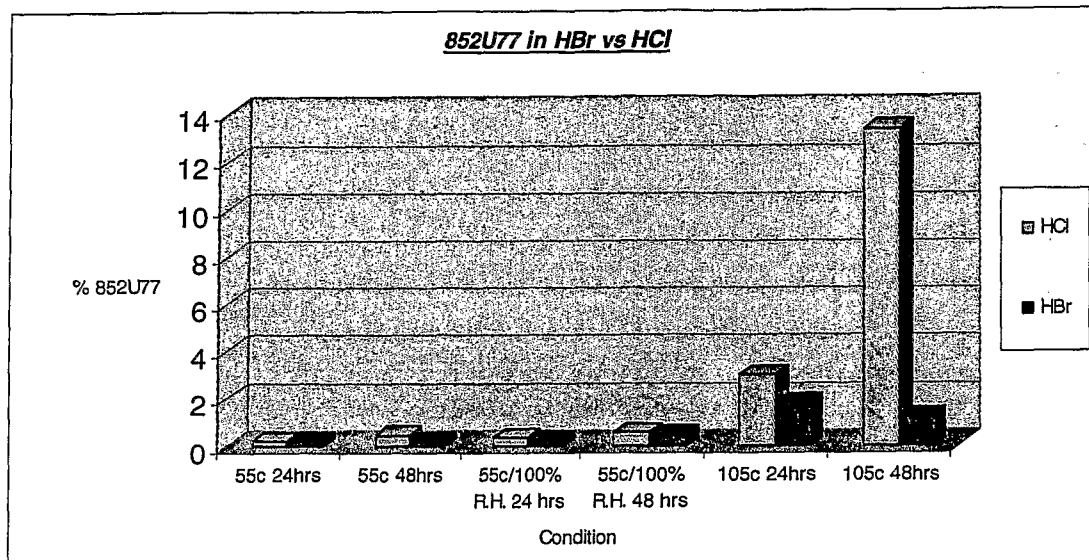


Figure 51

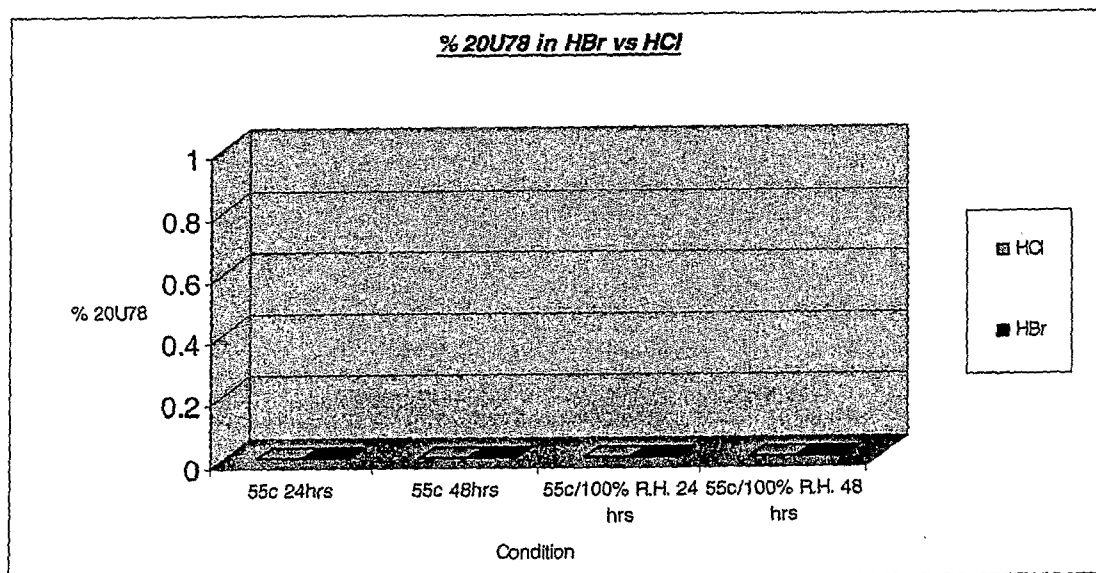
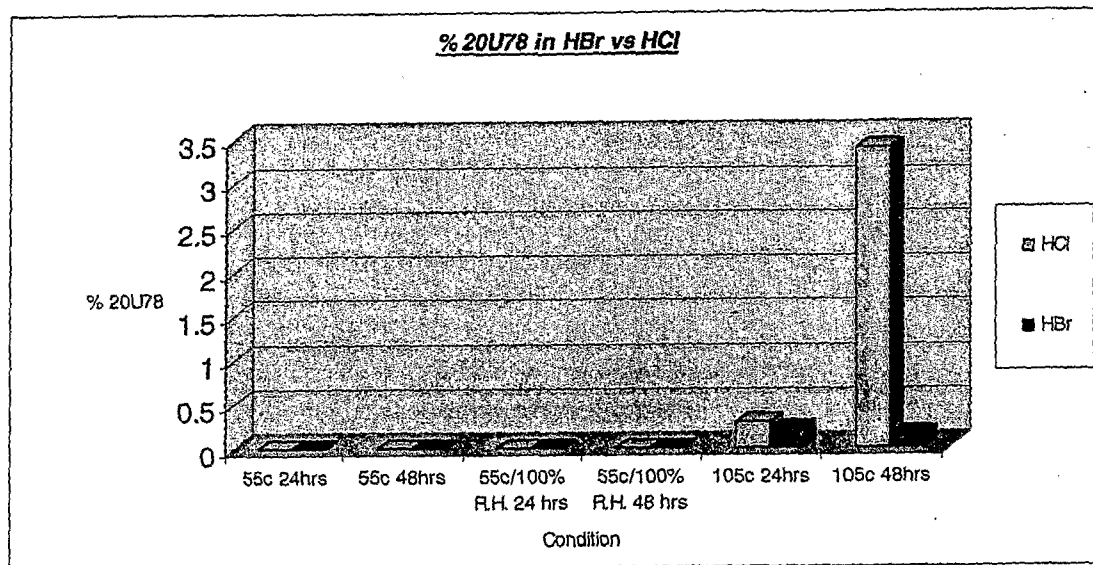


Figure 52

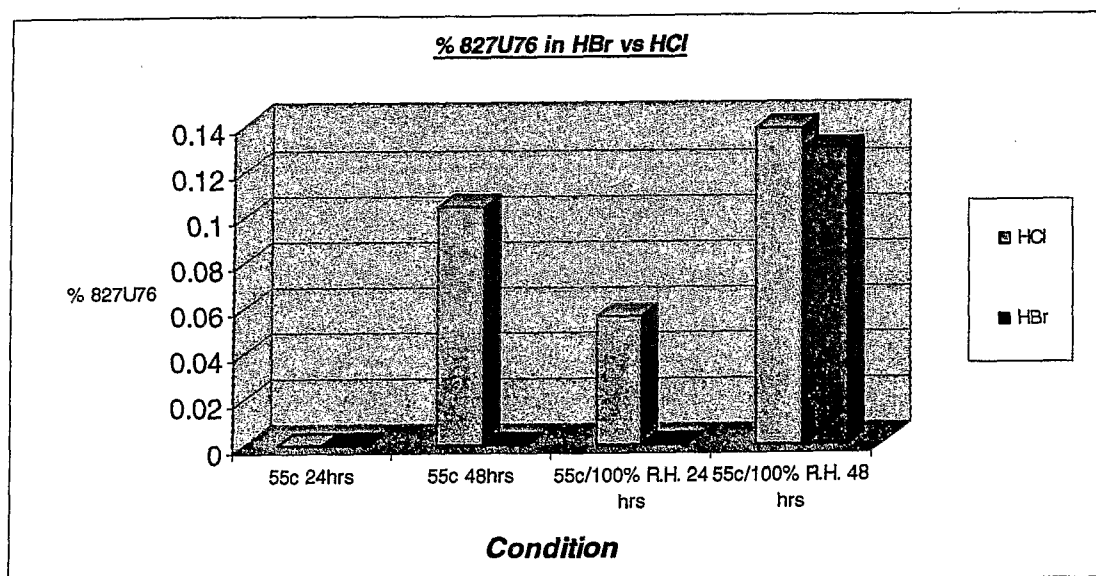
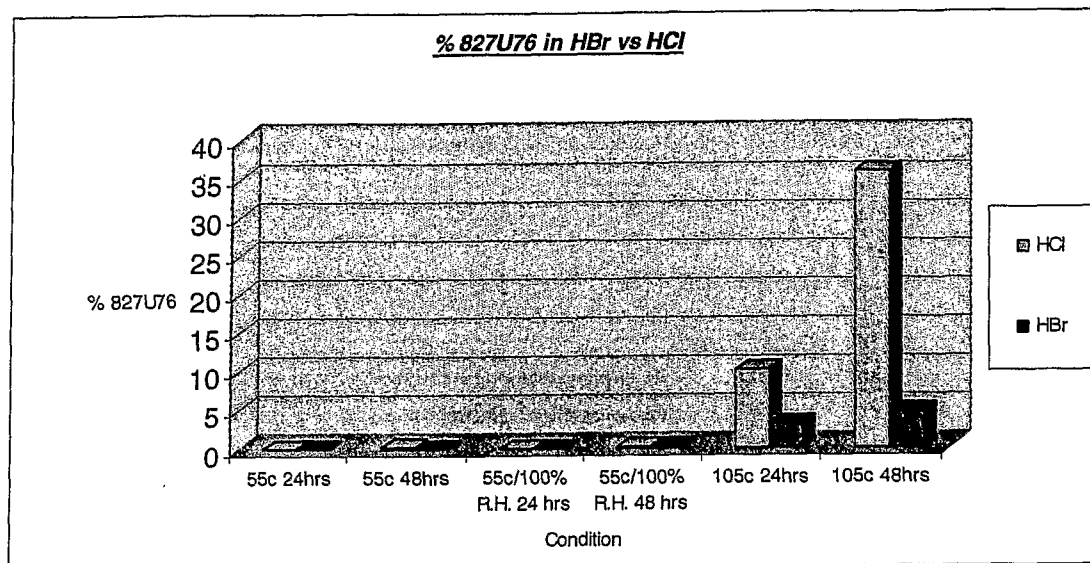
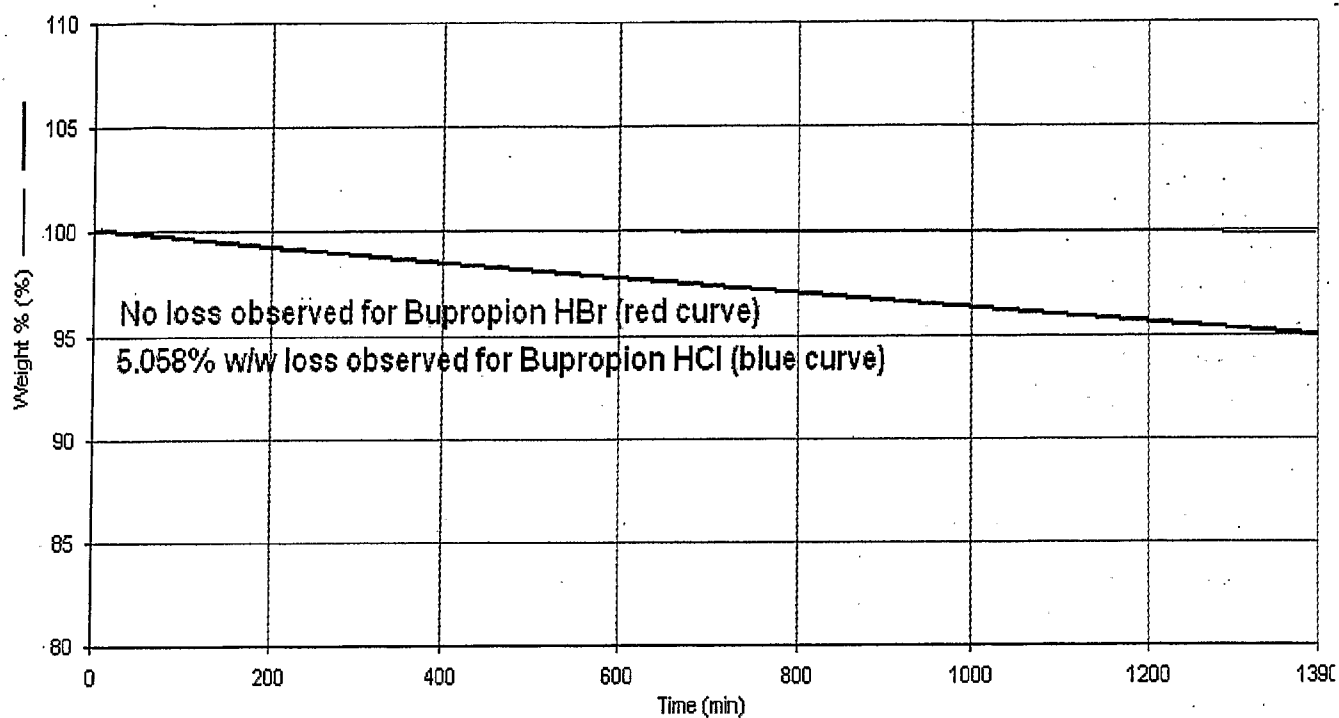


Figure 53



CONFIDENTIAL INFORMATION

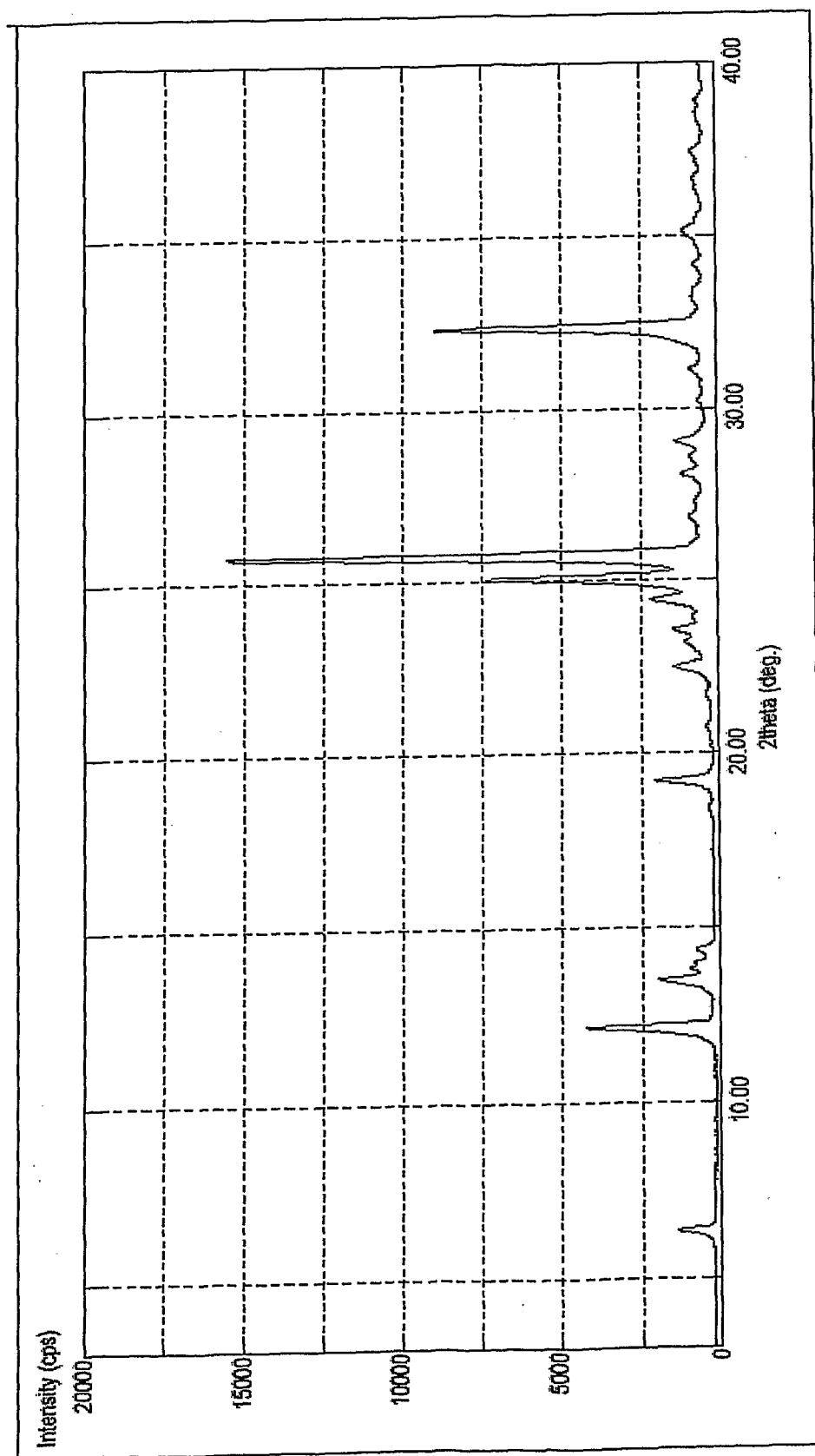


Figure 54

PXRD of Bupropion Hydrobromide Polymorphic Form I

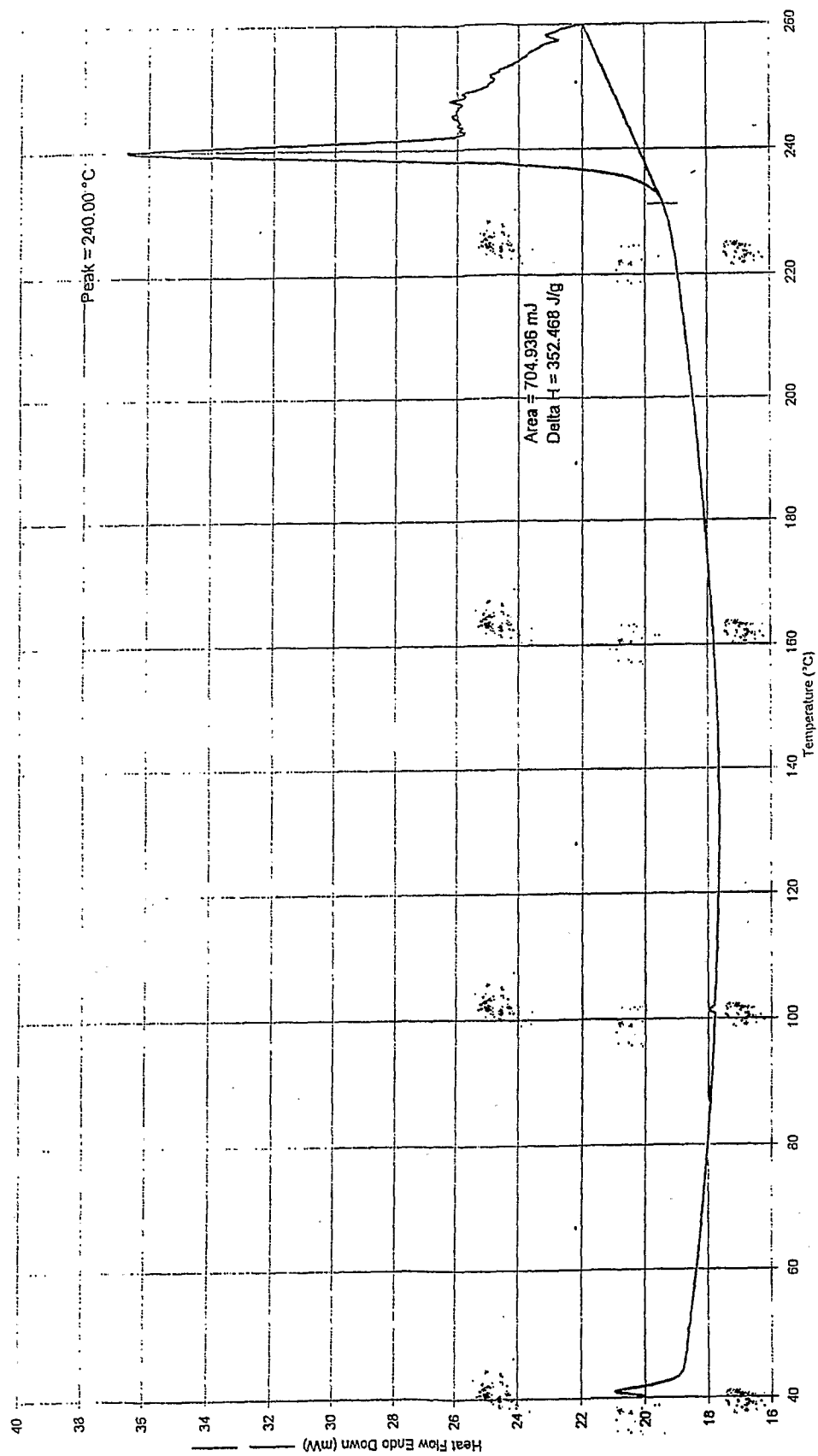


Figure 55
DSC of Bupropion Hydrobromide Polymorphic Form I

CONFIDENTIAL INFORMATION

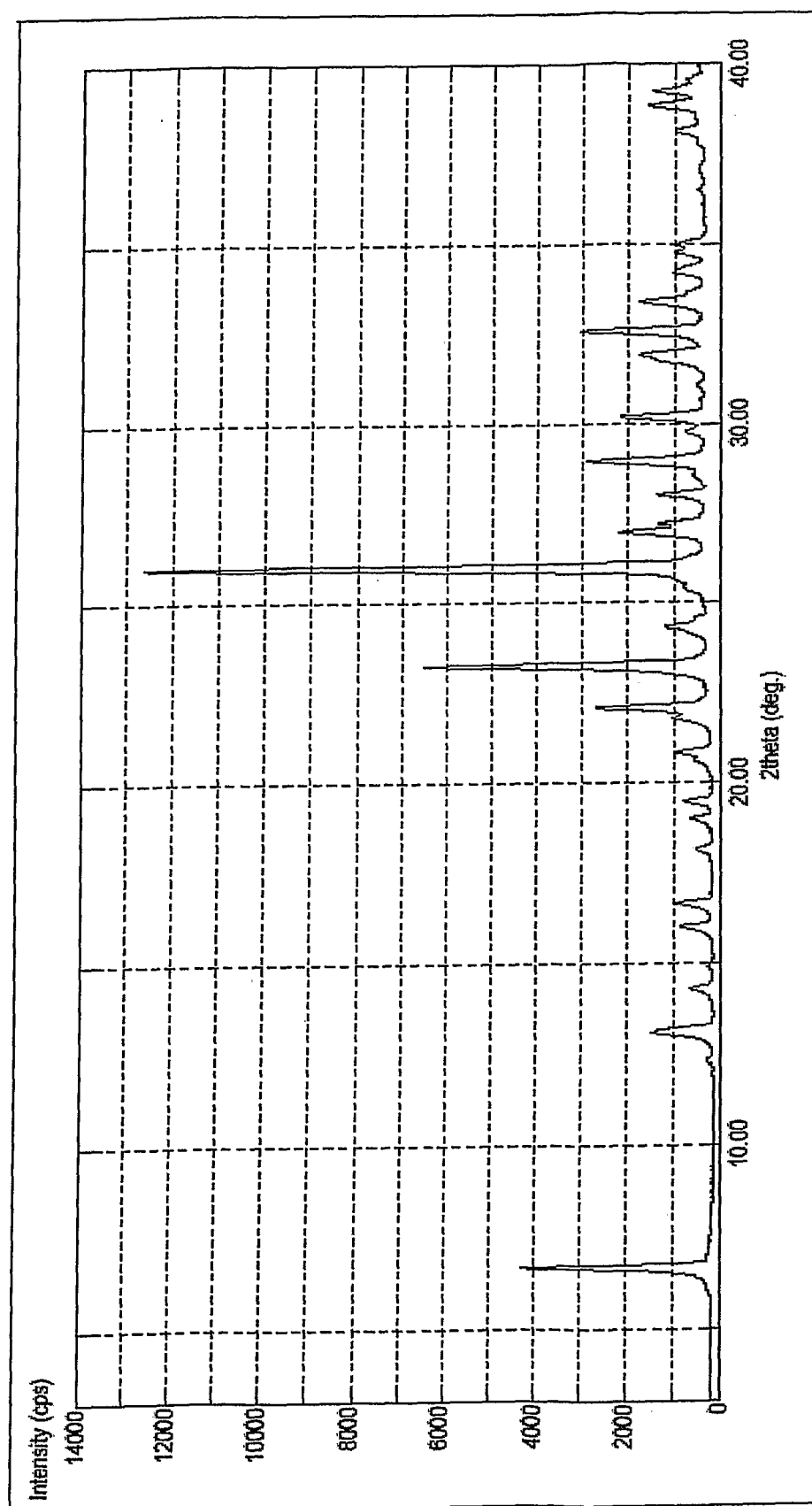


Figure 56
PXRD of Bupropion Hydrobromide Polymorphic Form II

CONFIDENTIAL INFORMATION

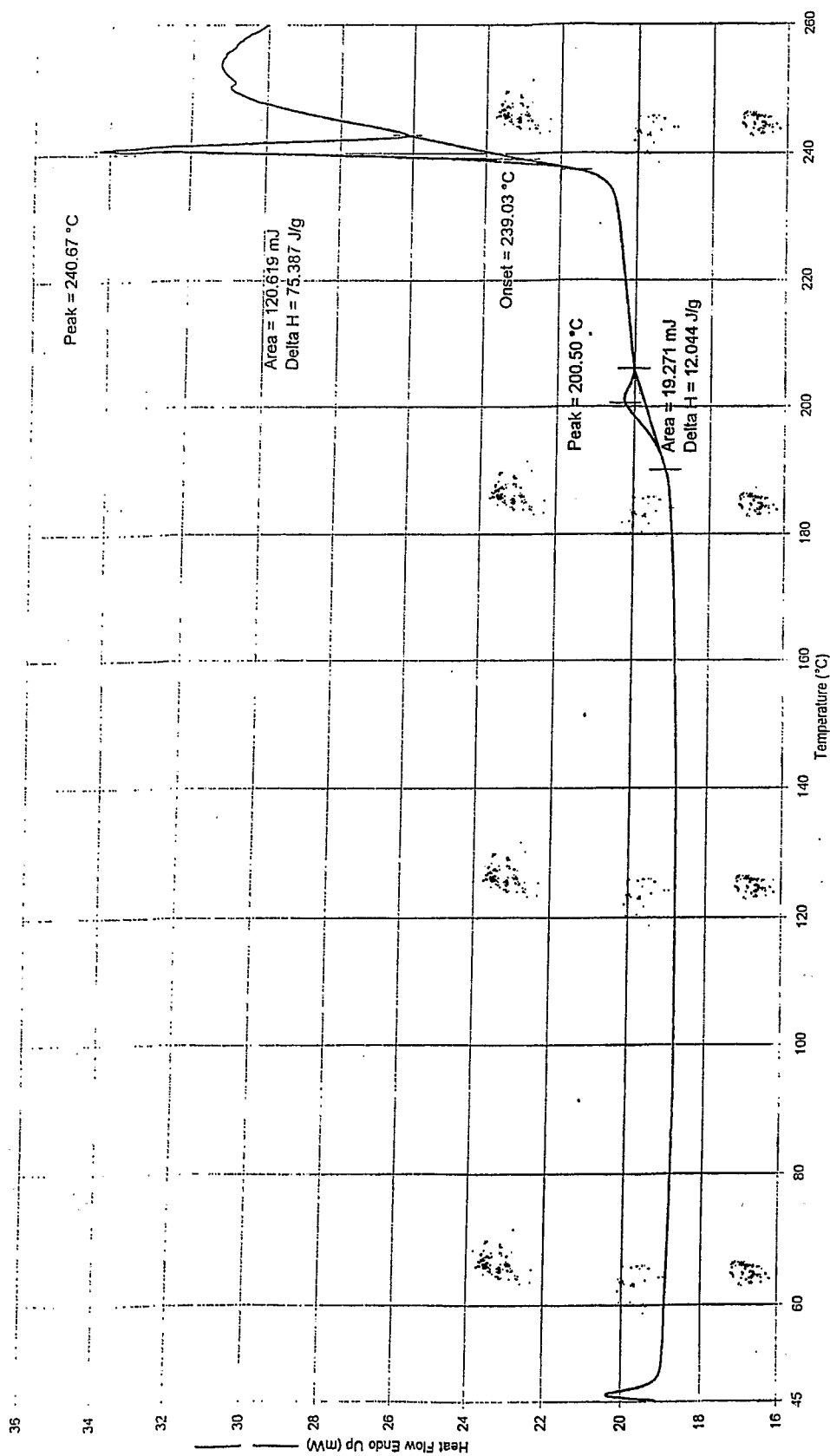


Figure 57
DSC of Bupropion Hydrobromide Polymorphic Form II

CONFIDENTIAL INFORMATION

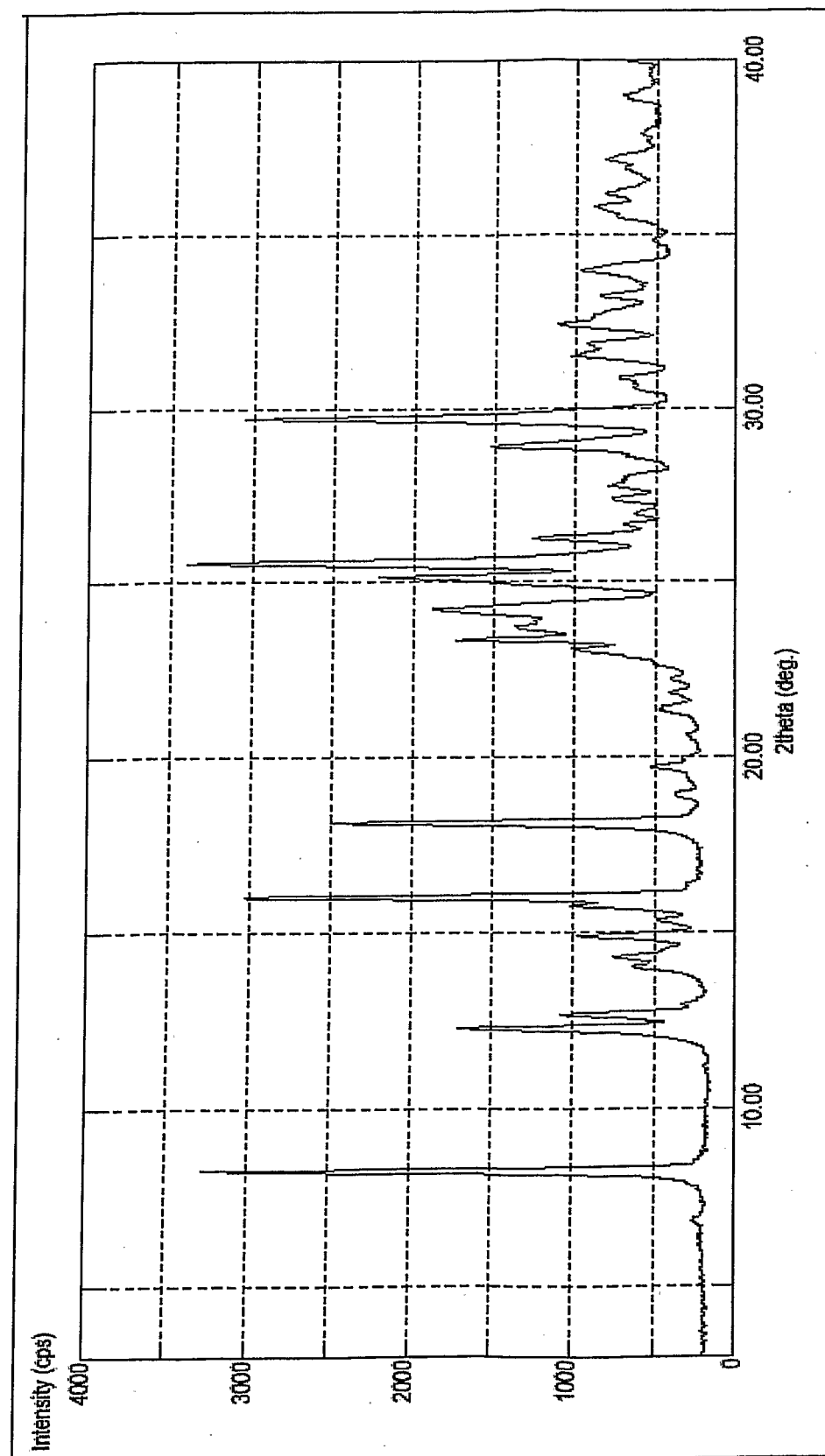


Figure 58
PXRD of Bupropion Hydrobromide Polymorphic Form III

CONFIDENTIAL INFORMATION

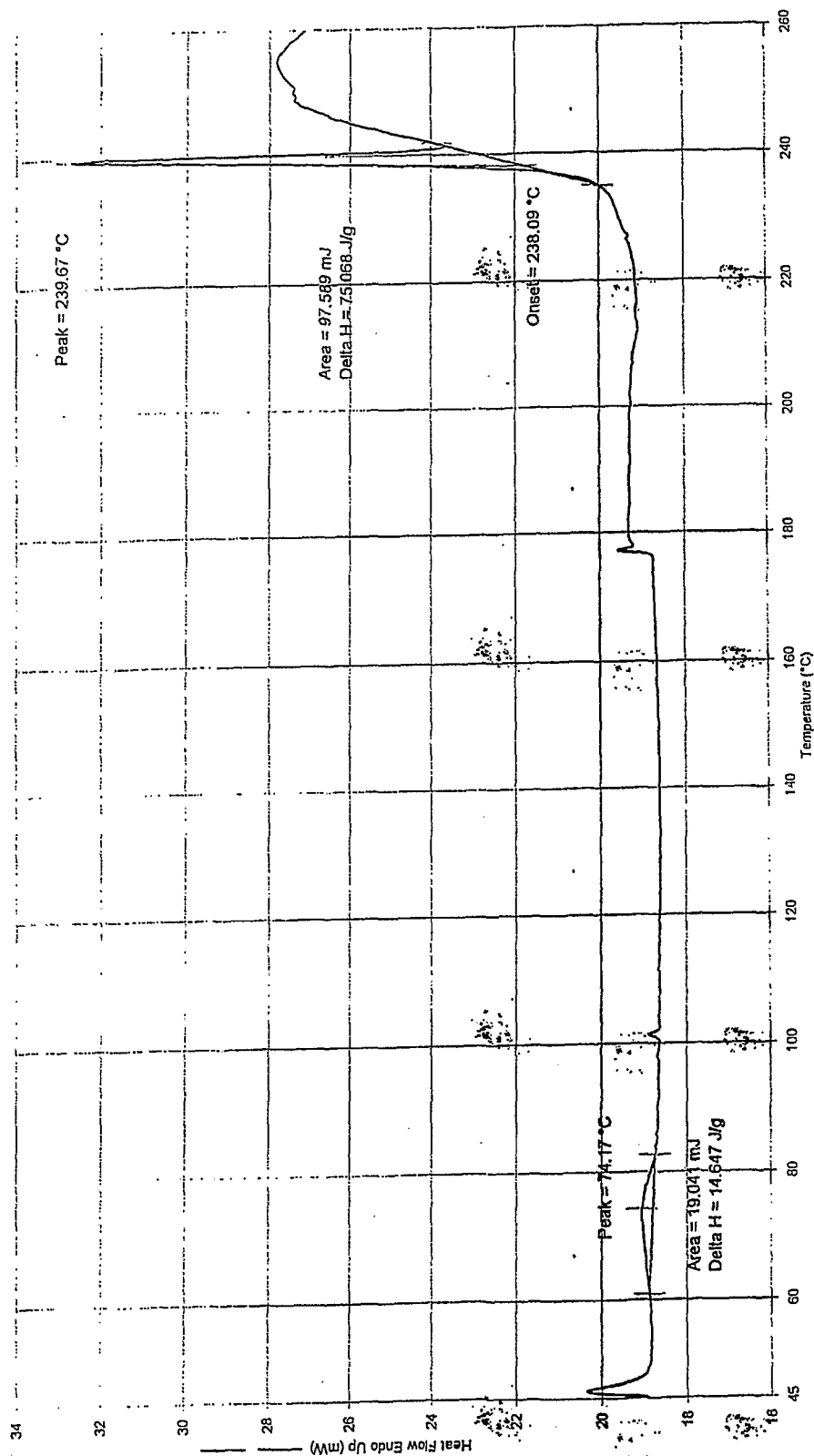


Figure 59
DSC of Bupropion Hydrobromide Polymorphic Form III

CONFIDENTIAL INFORMATION

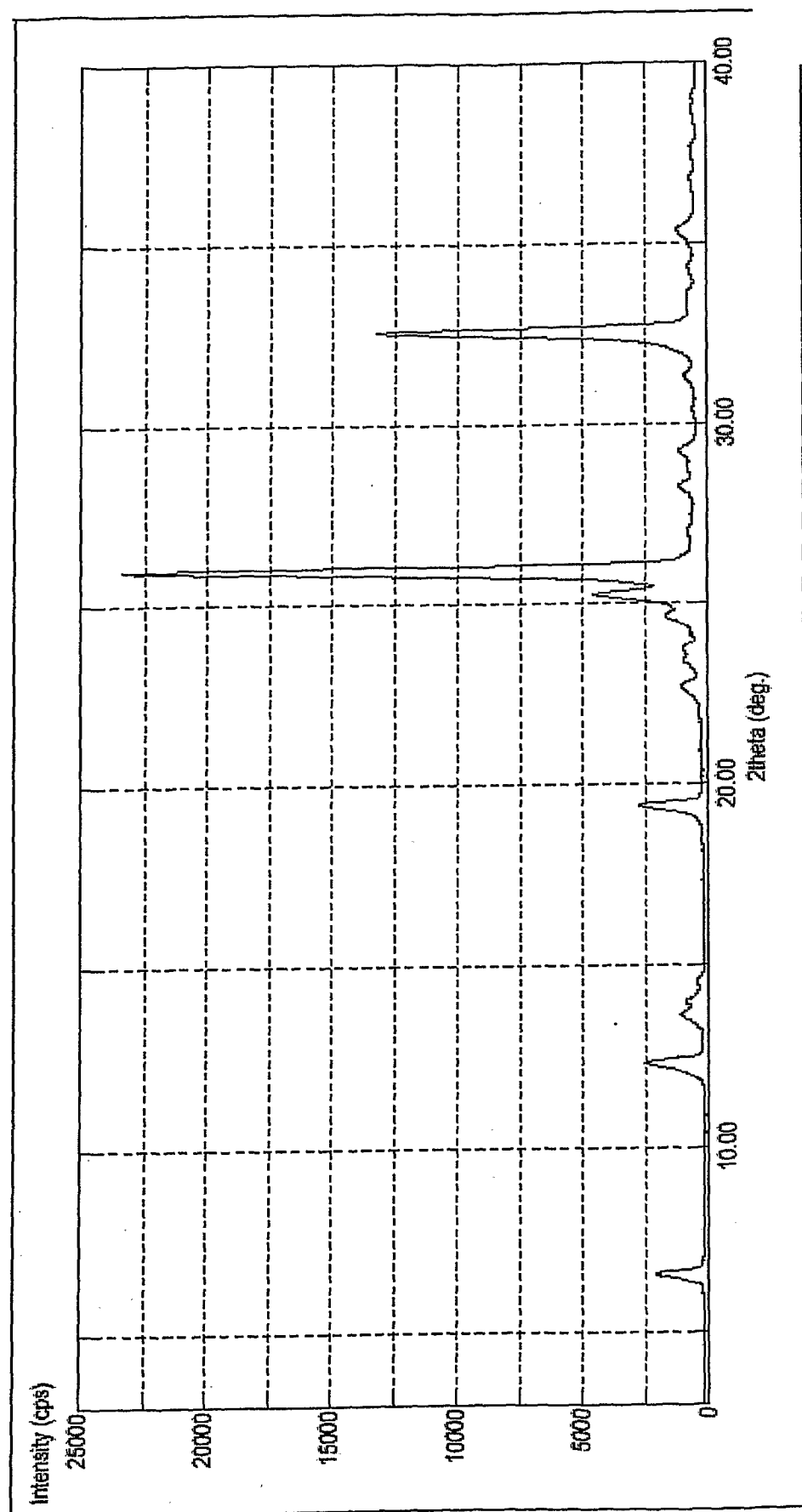


Figure 60
PXRD of Bupropion Hydrobromide Form I after 6 months in ICH Conditions (40°C, 75% R.H.)

CONFIDENTIAL INFORMATION

Chemi SpA

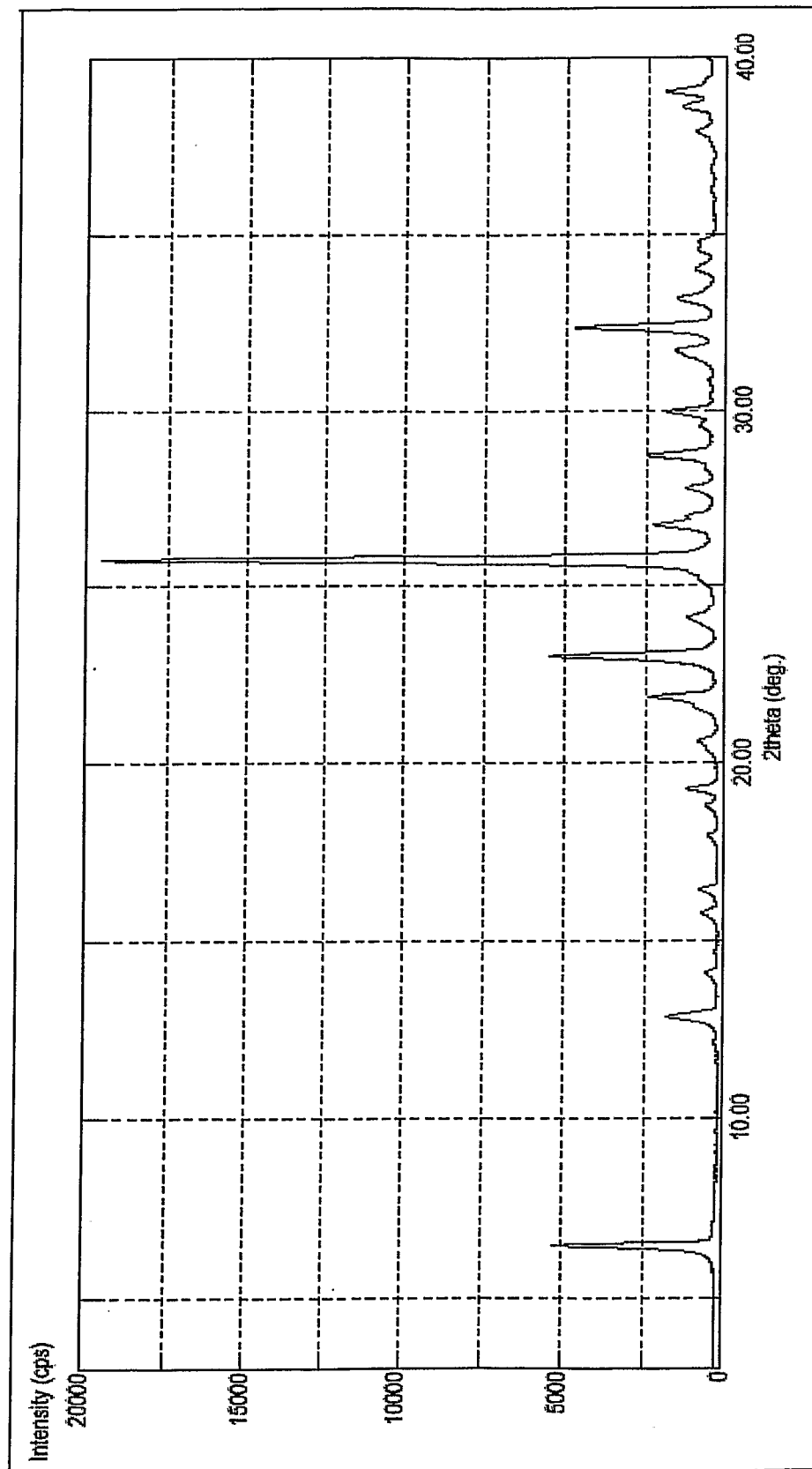


Figure 61
PXRD of Bupropion Hydrobromide Polymorphic Form II after 1 month in ICH Conditions (40°C, 75% R.H.)

CONFIDENTIAL INFORMATION

Chemi SpA

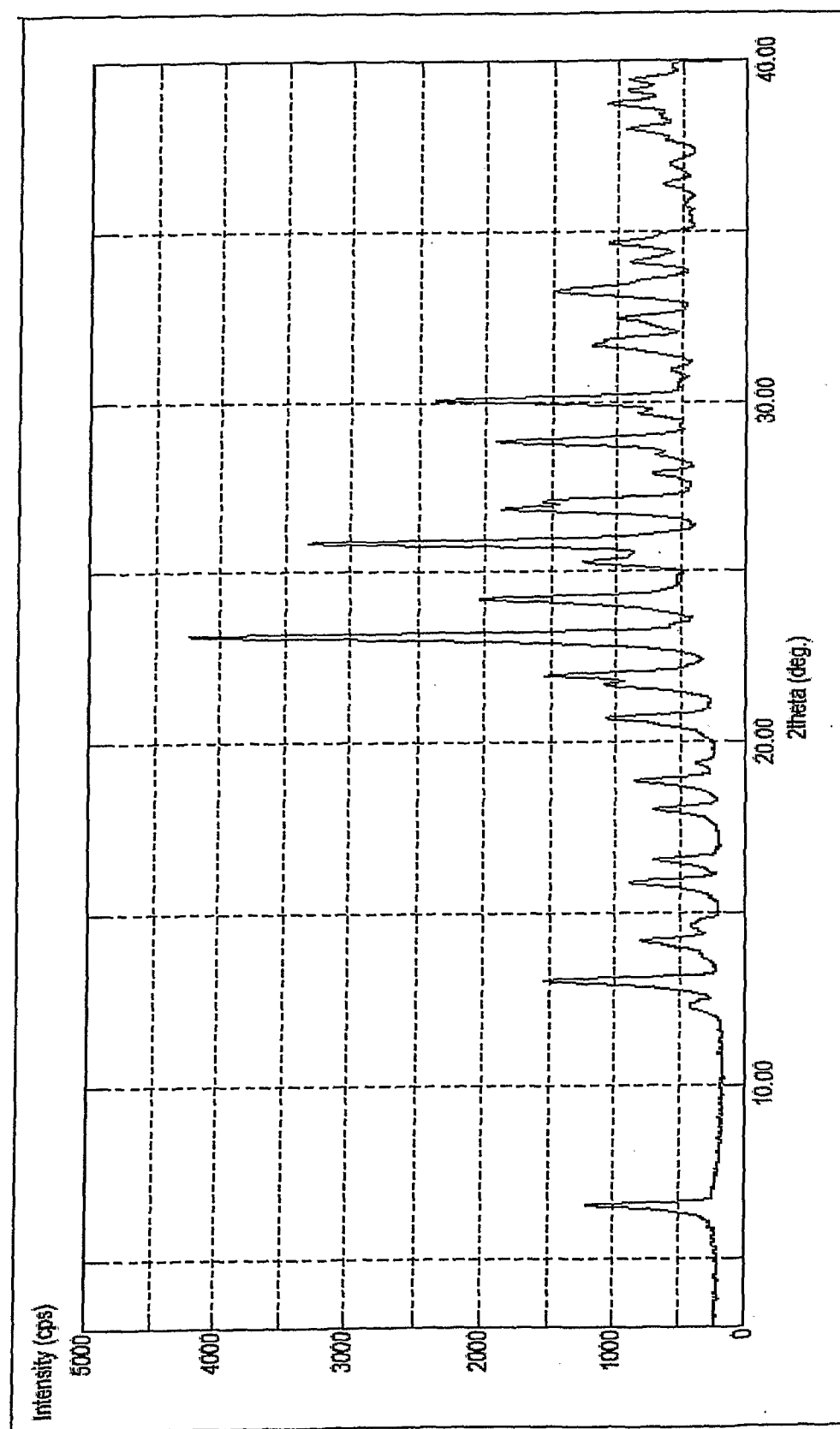


Figure 62
PXRD of Bupropion Hydrobromide Polymorphic Form III after 1 month in ICH Conditions (40°C, 75% R.H.)

INTERIM STABILITY REPORT

"Modified Release Formulations of a Bupropion Salt"
 Inventor: W. Oberegger, et al.
 Figure 63; Sheet 63 of 69
 Docket: 56819.000001; Customer No. 21967

Project: BUP 10121	Product: Bupropion HBr XL Tablets 348mg		Lot No.: Bup-HBr-XL-348-025-5
Active Drug Mfg Site: N/A	Product Mfg Site: N/A	Packg. Date: N/A	Expiry Date: N/A
Active Drug Mfg Date: N/A	Product Mfg Date: N/A	Container: Bottle	Stability Study #: STAB-05/064
Active Drug Lot #: N/A	Product Batch Size: N/A	Closure: N/A	Stability Program: Long term
Active Drug Expiry Date: N/A	Product Description: N/A	Count: 90's	Storage Conditions: 25°C/60%RH
			Schedule: Initial, 3M, 6M, 9M, 12M

TEST & METHODS	SPECIFICATIONS	INITIAL				3 MONTHS		6 MONTHS		9 MONTHS		12 MONTHS	
		Date: May 20/05				Date: Aug 20/05		Date: Nov 20/05		Date: Feb 20/06		Date: May 20/06	
	Lab Sample #	E05-71				H05-35		K05-51		B06-51			
	Report Results	Off-white colour, round tablets				Conforms		Conforms		Conforms			
	Report Results	99.6				99.4		97.4		96.8			
Impurities (%)	3-CBA	0.012				0.046		0.071		0.172			
	852U77	0.028				0.138		0.185		0.207			
	20U78/diluent	0.034				0.051		0.040		0.046			
	827U76	ND				0.011		0.018		0.010			
Major Unknown	Report Results	0.253 (RRT 0.14)				0.186 (RRT 0.13)		0.657 (RRT 0.09)		0.177 (RRT 0.15)			
Total Unknown	Report Results	0.376				0.342		1.055		0.280			
Total Impurities	Report Results	0.45				0.59		1.37		0.72			
KF (%)	Report Results	0.62				0.85		0.42		0.49			
Dissolution*													
2H	NMT 20%	14 - 19 (16)				13 - 17 (15)		12 - 17 (14)		12 - 20 (16)			
4H	20 - 45%	33 - 40 (36)				30 - 35 (32)		29 - 36 (32)		29 - 40 (34)			
8H	65 - 85%	64 - 72 (68)				57 - 64 (61)		54 - 63 (58)		55 - 68 (61)			
16H	NLT 80%	92 - 101 (96)				91 - 98 (94)		89 - 97 (93)		92 - 100 (96)			

*Tentative specification

Reviewed by / Date:

"Modified Release Formulations of a Bupropion Salt"

Inventor: W. Oberegger, et al.

Figure 64(1): Sheet 64 of 69

Docket: 56819.000001; Customer No. 21967

Project: BUP 10121		Product: Bupropion HBr EA Tablets 300mg				Lot No.: Bup-HBr-EA-300-001-3	
Active Drug Mfg Site:	N/A	Product Mfg Site:	N/A	Packg. Site:	N/A	Packg. Date:	N/A
Active Drug Mfg Date:	N/A	Product Mfg Date:	Apr 19/05	Container:	Bottle	Desiccant:	N/A
Active Drug Lot #:	N/A	Product Batch Size:	N/A	Closure:	N/A	Count:	90 counts
Active Drug Expiry Date:	N/A	Product Description: Coated Tablets - 54mg Wt gain					Storage Conditions: 40°C/75%RH
							Schedule: Initial, 1M, 2M, 3M, 6M

TEST & METHODS	SPECIFICATIONS	INITIAL	1 MONTH	2 MONTHS	3 MONTHS	6 MONTHS
		Date: Jun 13/05	Date: Jul 13/05	Date: Aug 13/05	Date: Sep 13/05	Date: Dec 13/05
	Lab Sample #	F05-5	G05-10	H05-24	I05-13	L05-23
Description Assay (%) Impurities (%)	Report Results		Conforms	Conforms	Conforms	Conforms
	Report Results	102.3	99.6	98.0 (*)	101.8	101.0
	NMT 0.7%	0.017	0.052	0.180	0.170	0.318
	NMT 1.0%	0.023	0.221	0.438	0.256	0.221
	NMT 0.3%	0.044	0.036	0.032	0.057	0.059
	NMT 0.4%	0.013	0.043	0.032	0.030	0.037
	Report Results	0.623 (RRT 0.10)	0.315 (RRT 0.10)	0.205 (RRT 0.13)	0.245 (RRT 0.14)	0.651 (RRT 0.10)
	Report Results	1.054	0.675	0.381	0.421	1.125
	Report Results	1.15	1.03	1.06	0.93	1.76
	Report Results	1.02	0.81	1.39	0.79	0.42
Dissolution*						
	2H	13 - 15 (14)	14 - 17 (16)	15 - 17 (16)	14 - 18 (16)	12 - 13 (13)
	4H	32 - 35 (33)	33 - 37 (35)	35 - 38 (36)	33 - 38 (35)	28 - 31 (30)
	8H	64 - 69 (66)	64 - 69 (67)	65 - 71 (68)	62 - 68 (65)	55 - 59 (57)
16H	NLT 80%	96 - 101 (98)	97 - 100 (98)	97 - 102 (99)	95 - 99 (97)	90 - 92 (91)

***Tentative specification**

Comments: Note: Impurity results calculated based on correct values

Reviewed by / Date:

INTERIM STABILITY REPORT

Project: BUP 10121	Product: Bupropion HBr EA Tablets 300mg				Lot No.: Bup-HBr-EA-300-001-5
Active Drug Mfg Site: N/A	Product Mfg Site: N/A	Packg. Site: N/A	Packg. Date: N/A	Expiry Date: N/A	Stability Study #: STAB-05/072
Active Drug Mfg Date: N/A	Product Mfg Date: Apr 19/05	Container: Bottle	Desiccant: N/A		Stability Program: Accelerated
Active Drug Lot #: N/A	Product Batch Size: N/A	Closure: N/A	Count: 90 counts		Storage Conditions: 40°C/75%RH
Active Drug Expiry Date: N/A	Product Description: Coated Tablets - 54mg Wt gain				Schedule: Initial, 1M, 2M, 3M, 6M
				Approved by / Date:	

Bupropion HBr XL 174mg core, Lot# Bup-HBr-XL-004-5 core

Tests	Initial	Open-Closed bottle stability (40C/75% RH)			
		10 Days-Open	10Days -Closed	20 Days-Open	20Days-Closed
%Assay	100.1	98.7	98.2	99.2	97.6
%Impurities					
3-CBZ	0.010	0.179	0.184	0.276	0.465
852U77	0.019	0.209	0.268	0.248	0.416
20U78/dilu	0.054	0.055	0.060	0.058	0.063
827U76	0.026	0.131	0.308	0.102	0.497
Total unknown	0.054	0.043	0.075	0.042	0.038
Total	016	0.62	0.89	0.73	1.48

Bupropion HBr XL 348mg core , Lot# Bup-HBr-XL-009-5 core

Tests	Initial	Open-Closed bottle stability (40C/75% RH)			
		10 Days-Open	10Days -Closed	20 Days-Open	20Days-Closed
%Assay	98.3	97.8	95.6	96.9	98.0
%Impurities					
3-CBZ	0.016	0.106	0.121	0.146	0.166
852U77	0.091	0.391	0.411	0.414	0.483
20U78/dilu	0.054	0.051	0.055	0.056	0.055
827U76	0.020	0.077	0.102	0.059	0.119
Total unknown	0.053	0.126	0.156	0.124	0.142
Total	0.23^	0.74	0.84	0.80	0.97

Bupropion HCl XL 150mg core , Lot# 05E056

Tests	Initial	Open-Closed bottle stability (40C/75% RH)			
		10 Days-Open	10Days -Closed	20 Days-Open	20Days-Closed
%Assay	97.5	98.4	97.5	98.1	97.6
%Impurities					
3-CBZ	0.006	0.079	0.052	0.185	0.238
852U77	0.043	0.406	0.342	0.520	0.685
20U78/dilu	0.044	0.046	0.046	0.059	0.052
827U76	0.028	0.050	0.074	0.069	0.127
Total unknown	0.058	0.051	0.066	0.044	0.040
Total	0.18	0.63	0.58	0.88	1.14

Bupropion HCl XL 300mg core , Lot# 05D380

Tests	Initial	Open-Closed bottle stability (40C/75% RH)			
		10 Days-Open	10Days -Closed	20 Days-Open	20Days-Closed
%Assay	99.2	99.1	98.4	96.8	97.1
%Impurities					
3-CBZ	0.006	0.100	0.016	0.245	0.171
852U77	0.037	0.409	0.274	0.564	0.515
20U78/dilu	0.044	0.045	0.046	0.051	0.050
827U76	0.015	0.058	0.039	0.099	0.105
Total unknown	0.044	0.038	0.045	0.032	0.052
Total	0.15	0.65	0.42	0.99	0.90

Bup-Stab-HBr-XL174 -150- 300-348 core-study-2b

Bupropion HBr XL 348mg tablets (final) - Lot# Bup-HBr-XL-012-5 (USP3)

Medium/Time Points	Vessel-1	Vessel-2	Vessel-3	Vessel-4	Vessel-5	Vessel-6	Mean
SGF pH 1.2 2hrs	9.0	8.3	8.9	11.6	8.8	8.6	9.2
Acetate buffer pH 4.5 2hrs	15.8	15.0	19.3	18.5	17.5	18.2	17.4
Phosphate buffer SIF pH 6.8 2hrs	26.8	25.4	24.9	33.3	27.7	24.2	27.1
2hrs	24.2	15.5	24.8	31.9	37.8	15.3	24.9
2hrs	22.5	19.5	16.6	1.4	2.4	25.8	14.7
6hrs	1.0	11.6	0.8	0.2	0.2	6.1	3.3
Total %Released	99.3	95.3	95.3	96.9	94.4	98.2	96.6

Wellbutrin XL 300mg tablets (final) - Lot# 05A116 (USP3)

Medium/Time Points	Vessel-1	Vessel-2	Vessel-3	Vessel-4	Vessel-5	Vessel-6	Mean
SGF pH 1.2 2hrs	3.1	2.7	2.1	1.8	2.8	2.6	2.5
Acetate buffer pH 4.5 2hrs	53.0	38.8	32.6	10.7	20.1	38.8	32.3
Phosphate buffer SIF pH 6.8 2hrs	30.8	36.4	37.0	47.8	46.1	33.5	38.6
2hrs	5.6	15.2	25.0	22.4	22.8	19.6	18.4
2hrs	2.2	3.1	1.6	13.7	2.8	0.8	4.0
6hrs	0.9	0.3	0.2	0.9	0.2	0.1	0.4
Total %Released	95.7	96.3	98.4	97.3	94.8	95.2	96.3

Bupropion HBr XL 348mg tablets (ECI) - Lot# Bup-HBr-XL-012-5 (EC 32mg wg.) (USP3)

Medium/Time Points	Vessel-1	Vessel-2	Vessel-3	Vessel-4	Vessel-5	Vessel-6	Mean
SGF pH 1.2 2hrs	47.6	45.7	45.0	51.3	42.7	48.0	46.7
Acetate buffer pH 4.5 2hrs	38.0	37.9	37.3	37.9	36.0	38.0	37.5
Phosphate buffer SIF pH 6.8 2hrs	13.0	13.9	16.0	10.3	15.8	12.3	13.5
2hrs	1.9	2.1	3.1	0.9	3.5	1.5	2.2
2hrs	0.4	0.5	0.9	0.2	1.0	0.3	0.6
6hrs	0.2	0.2	0.4	0.1	0.4	0.1	0.2
Total %Released	100.9	100.3	102.7	100.6	99.4	100.2	100.7

Wellbutrin XL 300mg tablets (ECI) - Lot# 05D047 (USP3)

Medium/Time Points	Vessel-1	Vessel-2	Vessel-3	Vessel-4	Vessel-5	Vessel-6	Mean
SGF pH 1.2 2hrs	63.1	61.5	58.9	58.2	57.9	60.8	60.1
Acetate buffer pH 4.5 2hrs	32.9	35.4	36.6	38.2	37.2	35.3	35.9
Phosphate buffer SIF pH 6.8 2hrs	0.6	0.9	1.0	1.0	1.1	0.9	0.9
2hrs	0.0	0.1	0.1	0.1	0.1	0.1	0.1
2hrs	0.0	0.0	0.0	0.0	0.0	0.0	0.0
6hrs	0.0	0.1	0.1	0.0	0.1	0.0	0.0
Total %Released	96.7	97.9	96.6	97.6	96.3	97.1	97.0

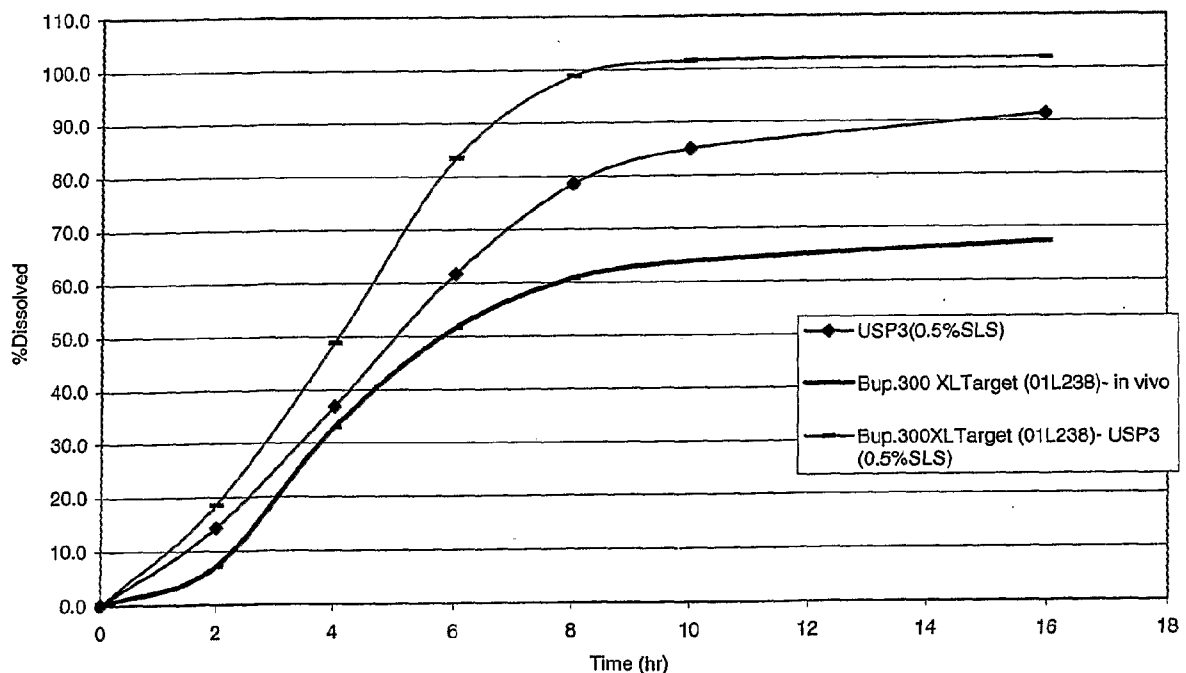
Bup-HBr-348mg-W/XL 300- EC and final coat-USP3

SP-3 Different media (SGF pH 1.2+0.5%SLS, Acetate buffer pH 4.5 & Phosphate buffer pH 6.8)**Bupropion HBr 348mg Lot 05E304**

Medium/Time Points	Vessel-1	Vessel-2	Vessel-3	Vessel-4	Vessel-5	Vessel-6	Mean
SGF pH 1.2 + 0.5%SLS 2hrs	14.5	14.6	12.5	14.9	13.3	16.3	14.3
Acetate buffer pH 4.5 2hrs	23.2	21.7	19.6	23.1	22.2	26.0	22.6
Phosphate buffer SGF pH 6.8 2hrs	26.1	25.1	23.9	24.7	25.3	23.6	24.8
2hrs	16.1	20.7	16.5	14.3	16.7	16.3	16.8
	12.9	15.2	9.4	10.2	10.4	10.6	11.4
	2.5	1.1	2.6	14.4	11.3	6.8	6.4
6hrs							
Total %Released	95.3	98.2	84.5	101.6	99.1	99.5	96.4

Time (hrs)	SP3(0.5%SLS)	Bup.300 XLTarget (01L238) in vivo	Bup.300XLTarget (01L238)- USP3 (0.5%SLS)			
0	0.0	0.0	0.0			
2	14.3	7.1	18.5			
4	36.9	36.0	48.8			
6	61.7	51.5	83.4			
8	78.5	66.8	98.9			
10	84.9	69.8	101.5			
16	91.3	67.2	101.9			

Bupropion HBr 348mg, lot 05E304 (USP3) vs In vivo Bup-HCl XL 300mg (also USP3-0.5%SLS)

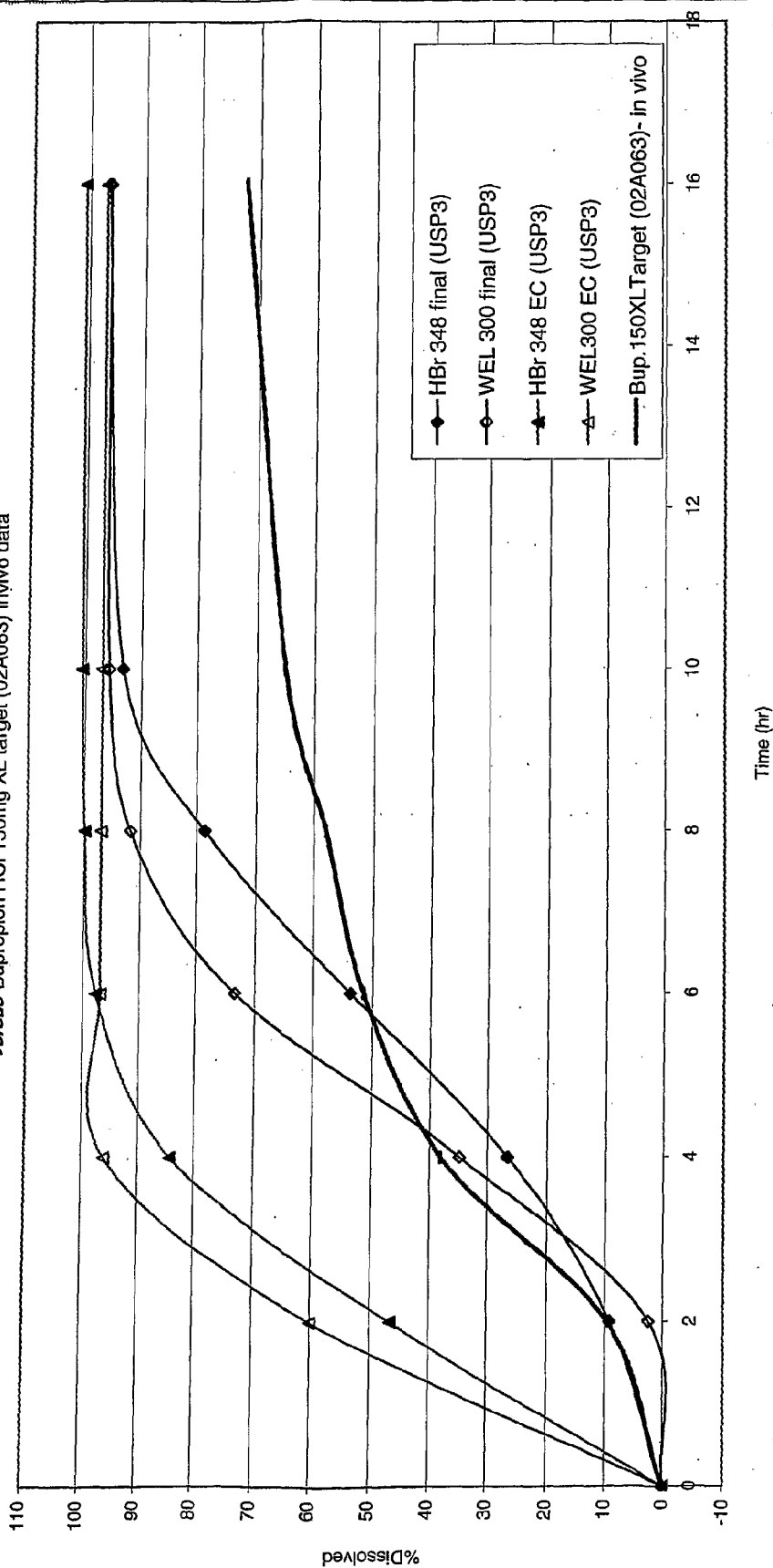


Cumulative data

(USP3- SGF pH1.2, Acbuffer pH4.5,
Phosp. Buffer pH 6.8)

Time (hrs)	HBr 348 final (USP3)	WEL 300 final (USP3)	HBr 348 EC (USP3)	WEL 300 EC (USP3)	Bup.150XL Target (02A063)- in vivo
0	0.0	0.0	0.0	0.0	0.0
2	9.2	2.5	46.7	60.1	9.7
4	26.6	34.8	84.2	96.0	38.1
6	53.7	73.4	97.7	96.9	51.5
8	78.6	91.8	99.9	97.0	58.0
10	93.3	95.8	100.5	97.0	65.0
16	96.6	96.2	100.7	97.0	72.3

Comparative diss profiles of Bupropion HBr XL 348mg & Wellbutrin XL (final & EC) tablets in USP3-different media (SGF, acetate and pH6.8 buffers)-Cumulative data
versus Bupropion HCl 150mg XL target (02A063) in vivo data



BupHBr-348mg-WXL 300- EC and final coat-USP3