

CHAPTER III

Results

Evaluation of drug powder

1. Determination of powder characteristics

The appearance of DS was fine white amorphous powder with electrostatic charge. The photomicrographs of DS was shown in Figure 21. The shape of DS particle was irregular with different mean size. The surface of particle was rough. The appearance of DE was off white translucent crystals. The photomicrographs of DE was shown in Figure 22. The shape was rod in various lengths. The surface of particle was smooth. DE particle was larger than DS particle. DS and DE particle were ranging from 3 to 50 and 50 to 400 μm , respectively.

2. IR spectra

The IR spectra of DS and DE were illustrated in Figures 23 and 24. Spectrum of DE were higher and boarder than spectrum of DS at wavelenght about $2830-3000\text{ cm}^{-1}$ and $3300-3500\text{ cm}^{-1}$, whereas others peak of DE and DS were closely similar.

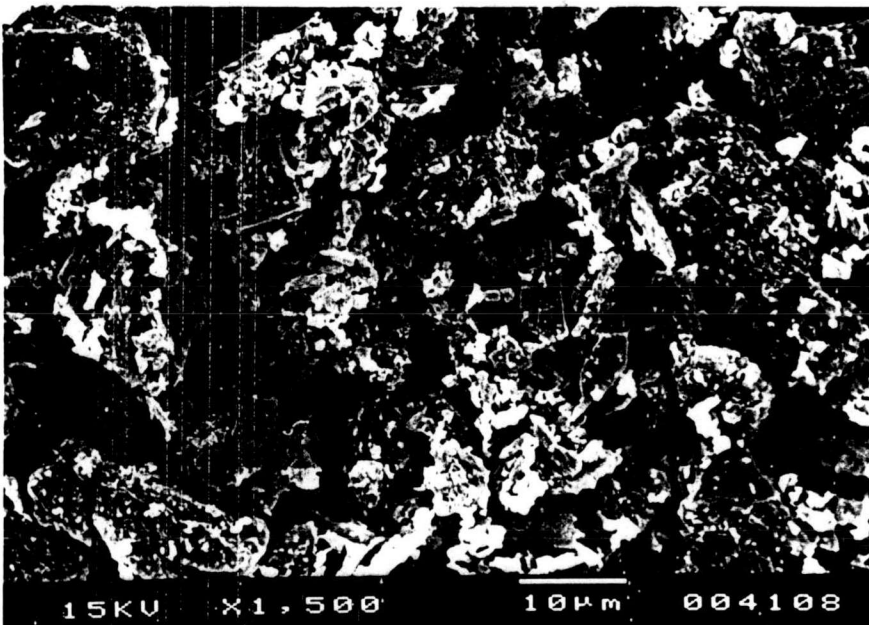
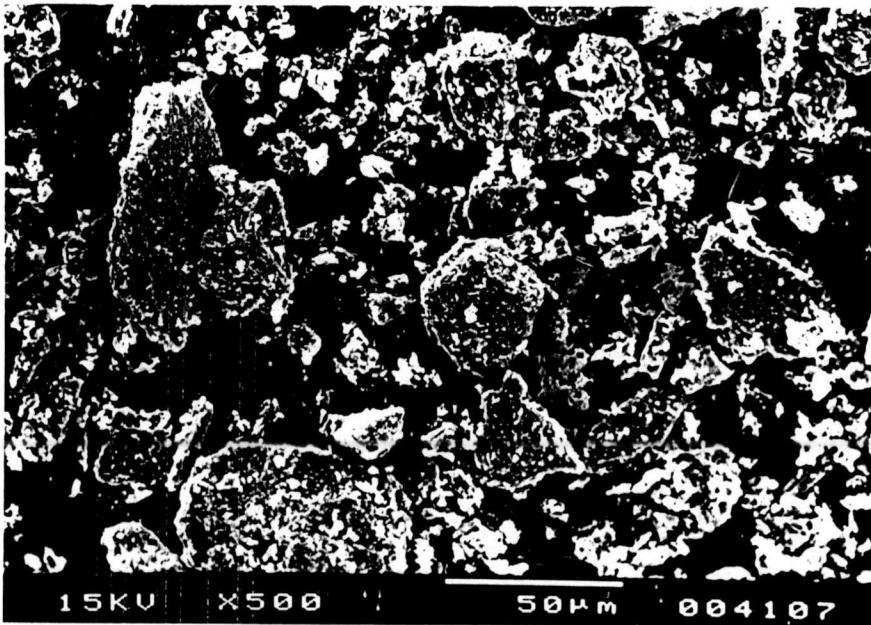


Figure 21 Photomicrograph under scanning electron microscope of DS

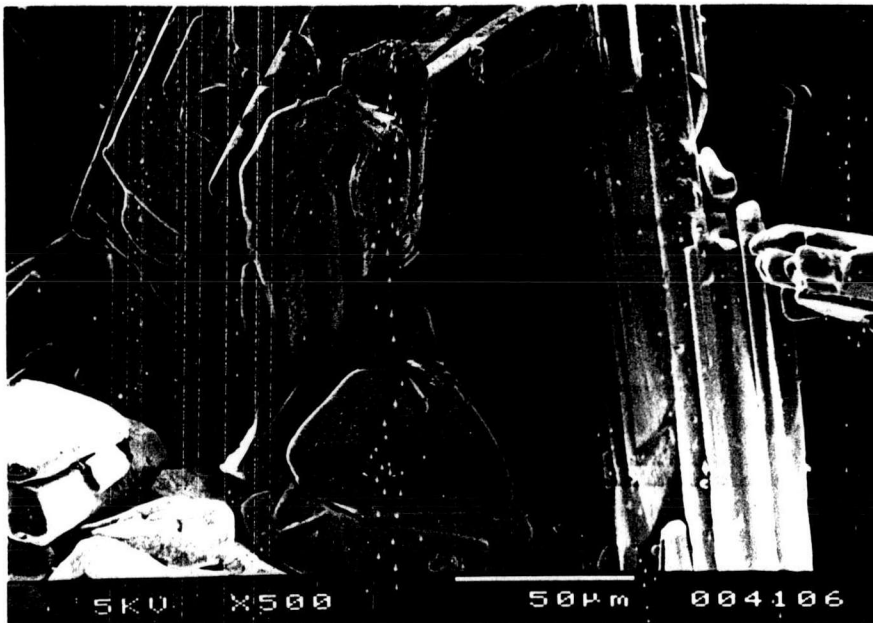


Figure 22 Photomicrograph under scanning electron microscope of DE

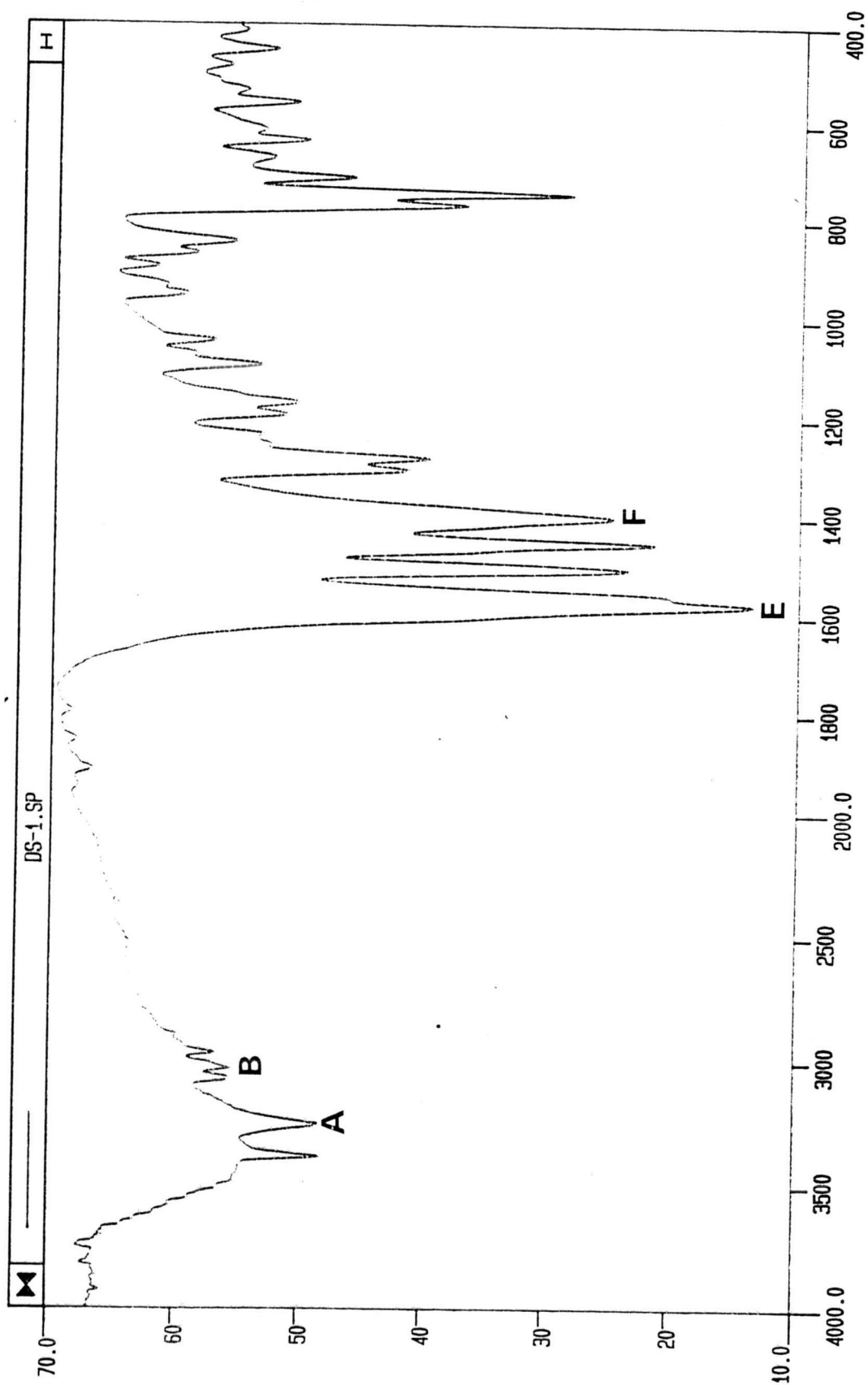


Figure 23 Infrared spectrum of DS

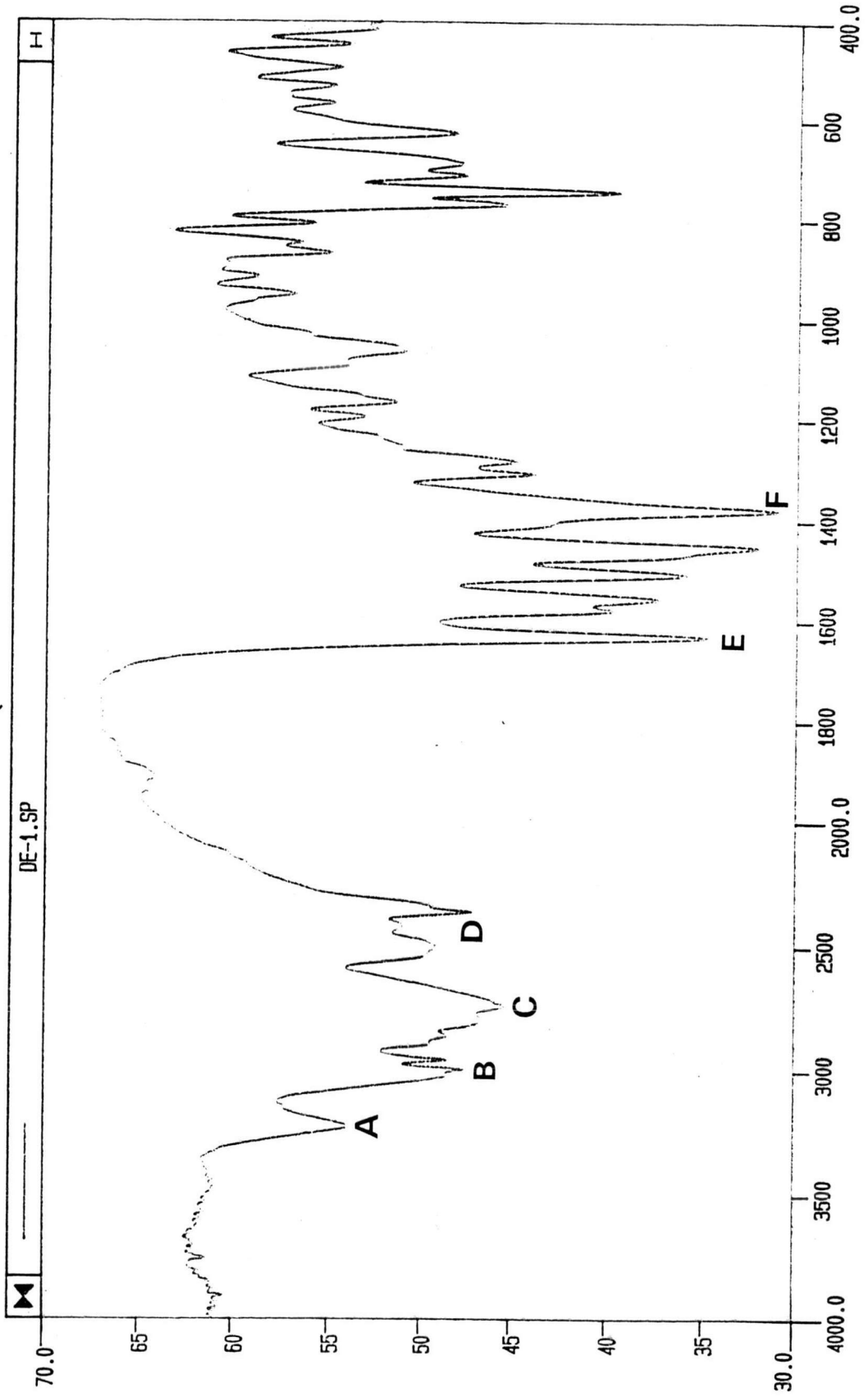


Figure 24 Infrared spectrum of DE

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3. Determination of diclofenac solubility

The solubilities of diclofenac in several solvents at 35 °C were listed in Table 14. The general rank order of solubility of drug in aqueous system was : buffer pH 9 > buffer pH 8 > buffer pH 7 > buffer pH 6 > buffer pH 5. DS is more soluble in aqueous system than DE at the same pH. The general rank order of the solubility of diclofenac in solvent was : methanol > propylene glycol > ethanol > glycerin > isopropyl alcohol > sorbitol solution. Both DS and DE were more soluble in methanol, ethanol, propylene glycol and glycerin than aqueous system. The solubilities of DS and DE were more than 1 g. per 100 mL of medium in buffer pH 8, buffer pH 9, methanol, propylene glycol and glycerin. More than 10 g. of both DS and DE were soluble in 100 mL of methanol and propylene glycol, while less than 10 mg. were soluble in 100 mL of buffer pH 5. DE also can soluble more than 10 g. in 100 mL of ethanol.

Evaluation of Diclofenac Stability

1. Stability of DS

The percentage of content of diclofenac sodium in pH 5, 6, 7, 8 and 9 buffer solution after 5 months of storage at 35, 45, 55 and 65 °C were shown in Table 15. A plot of DS concentration remained in pH 5, 6, 7, 8 and 9 at various temperatures versus time of storage were

Table 14 Solubility of DS and DE at 35 C (mg/100 mL)

Solvent	DS	DE
Buffer pH 5	7.03 [0.03]	5.79 [0.25]
Buffer pH 6	81.22 [0.08]	26.29 [0.22]
Buffer pH 7	1143.20 [4.81]	783.78 [10.60]
Buffer pH 8	1596.09 [8.54]	1402.50 [4.50]
Buffer pH 9	2160.08 [18.39]	1472.72 [24.29]
Methanol	36552.44 [66.13]	30961.68 [8.16]
Ethanol	6440.20 [1.49]	10939.98 [32.50]
Isopropyl Alcohol	700.50 [0.65]	2662.72 [7.91]
Propylene Glycol	13414.24 [62.43]	16764.33 [173.38]
Glycerin	3311.48 [0.00]	6948.33 [53.31]
Sorbitol Solution	160.67 [0.14]	455.51 [33.34]

n = 2

Table 15 The percent of DS remained in pH 5,6,7,8 and 9 solution after 5 months of storage at 35, 45, 55 and 65 C

pH	Temp. (C)	Percent DS remained at months							r ²
		0	0.5	1	2	3	4	5	
5	35	94.18	87.21	76.67	73.74	64.22	61.76	53.17	0.9467
	45	94.18	83.33	58.77	48.01	35.07	27.46	15.98	0.9282
	55	94.18	62.66	8.70	5.52	1.66	4.74	4.44	0.5427
	65	94.18	56.59	8.94	5.35	1.15	3.77	4.13	0.5397
6	35	100.86	97.06	95.27	97.02	97.75	95.72	94.83	0.3941
	45	100.86	97.26	93.25	93.56	93.06	89.42	88.21	0.8492
	55	100.86	93.97	83.94	77.58	69.67	65.75	61.02	0.9405
	65	100.86	94.21	82.74	78.32	69.99	63.73	58.77	0.9511
7	35	107.43	104.47	101.68	104.25	104.25	99.23	102.54	0.3889
	45	107.43	104.76	100.12	101.73	99.49	92.23	95.87	0.7828
	55	107.43	102.34	90.01	84.61	77.01	72.82	69.40	0.9230
	65	107.43	100.99	89.66	83.88	76.17	68.22	66.18	0.9438
8	35	103.40	100.65	97.49	99.03	97.88	95.25	97.83	0.5461
	45	103.40	100.17	95.68	97.29	95.74	90.70	92.83	0.7630
	55	103.40	97.67	88.01	83.20	78.02	73.06	70.17	0.9281
	65	103.40	97.35	87.23	83.01	75.53	69.85	67.79	0.9351
9	35	101.81	98.21	95.92	96.99	96.03	94.86	95.66	0.5626
	45	101.81	98.86	95.23	96.74	94.13	89.59	92.37	0.7705
	55	101.81	97.39	89.07	82.80	78.73	72.89	73.66	0.9075
	65	101.81	93.85	87.35	81.62	74.63	67.51	70.79	0.8964

illustrated in Figures 25, 26, 27, 28 and 29, respectively. A plot of DS concentration in several pH solution at 35, 45, 55 and 65 °C versus time of storage were shown in Figures 30, 31, 32 and 33, respectively.

DS in pH 5 solution degraded more than 10 percent label amount after 2 weeks of storage at any temperature. DS in pH 6, 7, 8 and 9 solution remained more than 90 percent of content after 5 months of storage at 35 °C. DS in pH 7, 8 and 9 solution remained more than 90 percent label amount after 5 months of storage at 45 °C whereas DS in pH 6 solution degraded more than 10 percent label amount after 4 months of storage at the same temperature. But DS in pH 6, 8 and 9 solution remained less than 90 percent label amount after 2 weeks of storage at 55 and 65°C. While DS in pH 7 solution degraded more than 10 percent label amount after 2 months of storage at 55 and 65 °C.

After 5 months of storage at 35, 45, 55 and 65 °C the content of DS in pH 5 solution was reduced to 53.17, 15.98, 4.44 and 4.13 percent label amount. The content in pH 6 solution was 94.83, 88.21, 61.02 and 58.77 percent label amount, respectively. The content in pH 7 solution was 102.54, 95.87, 69.40 and 66.18 percent label amount, respectively. The content in pH 8 solution was 97.83, 92.83, 70.17 and 67.79 percent label amount, respectively. While the content in pH 9 solution was 95.66, 92.37, 73.66 and 70.79 percent label amount, respectively.

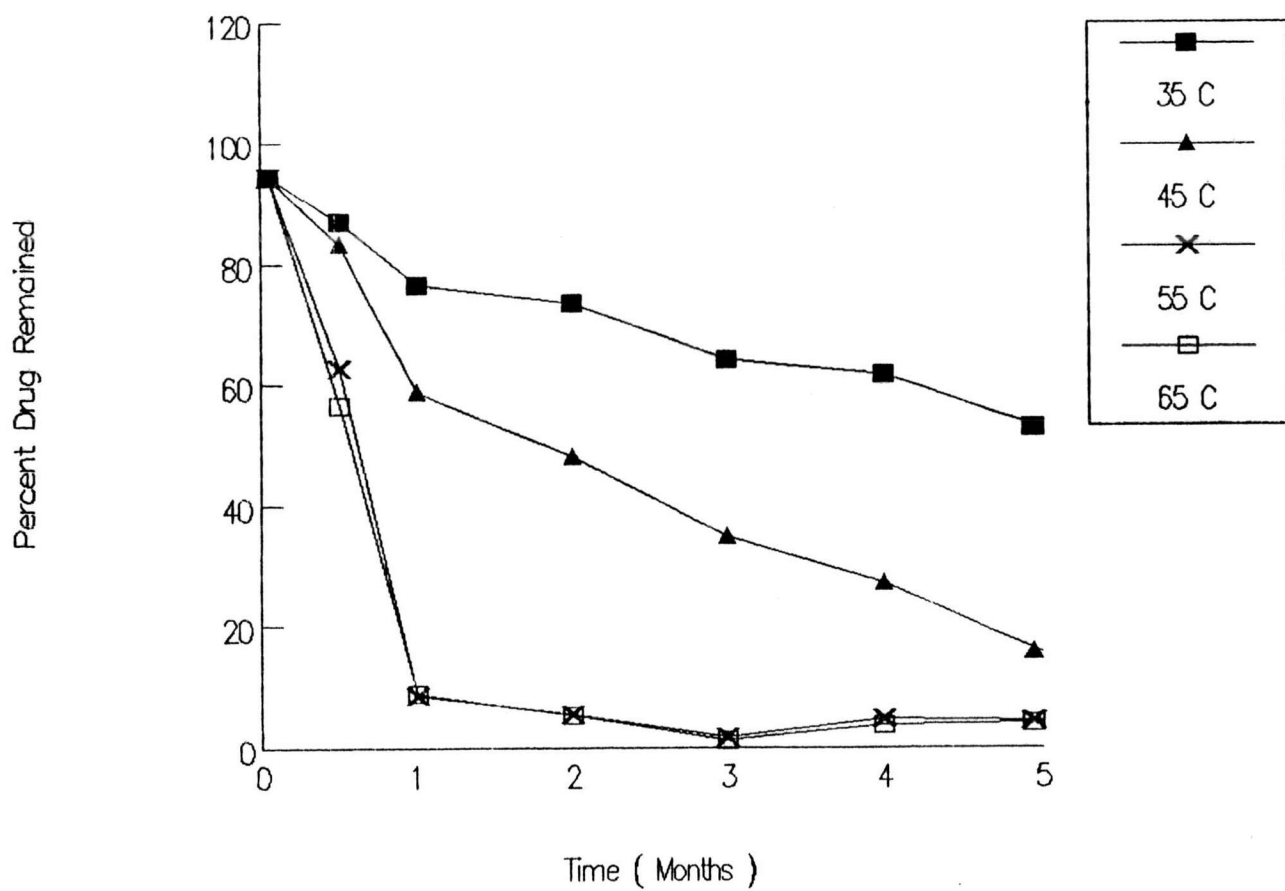


Figure 25 Plots of Percent label amount of DS in pH 5 buffer solution versus time of storage at 35, 45, 55 and 65 °C

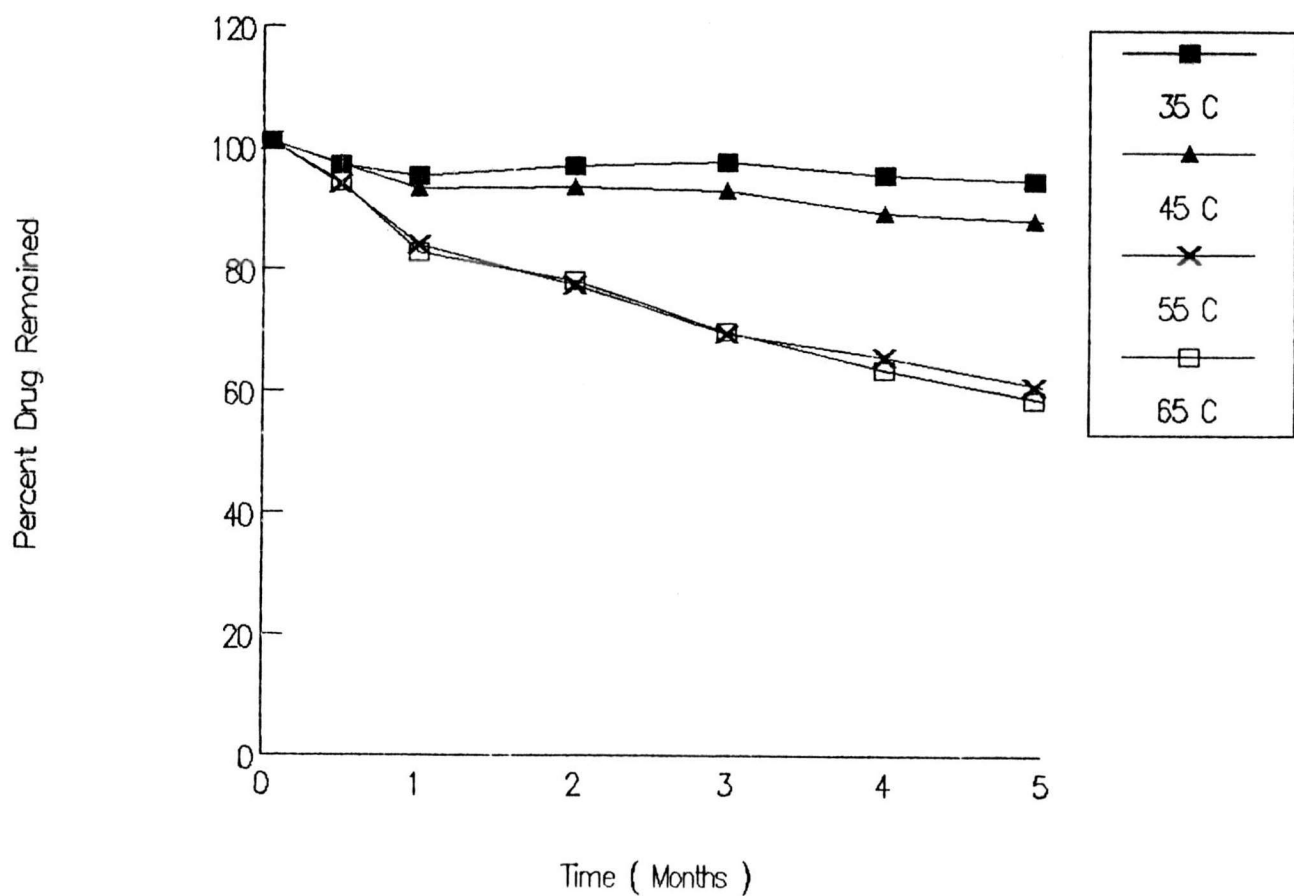


Figure 26 Plots of Percent label amount of DS in pH 6 buffer solution versus time of storage at 35, 45, 55 and 65 °C

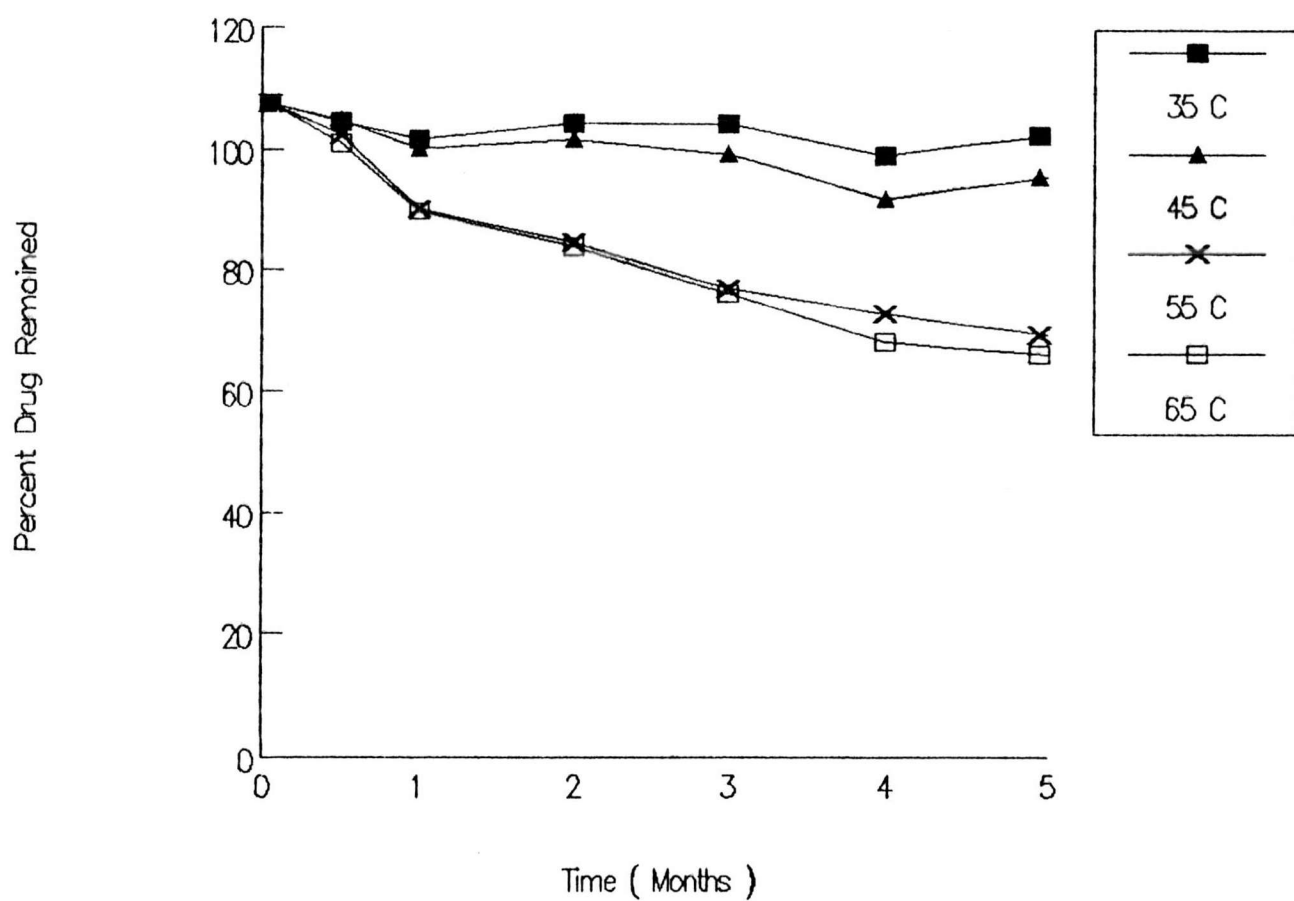


Figure 27 Plots of Percent label amount of DS in pH 7 buffer solution versus time of storage at 35, 45, 55 and 65 °C

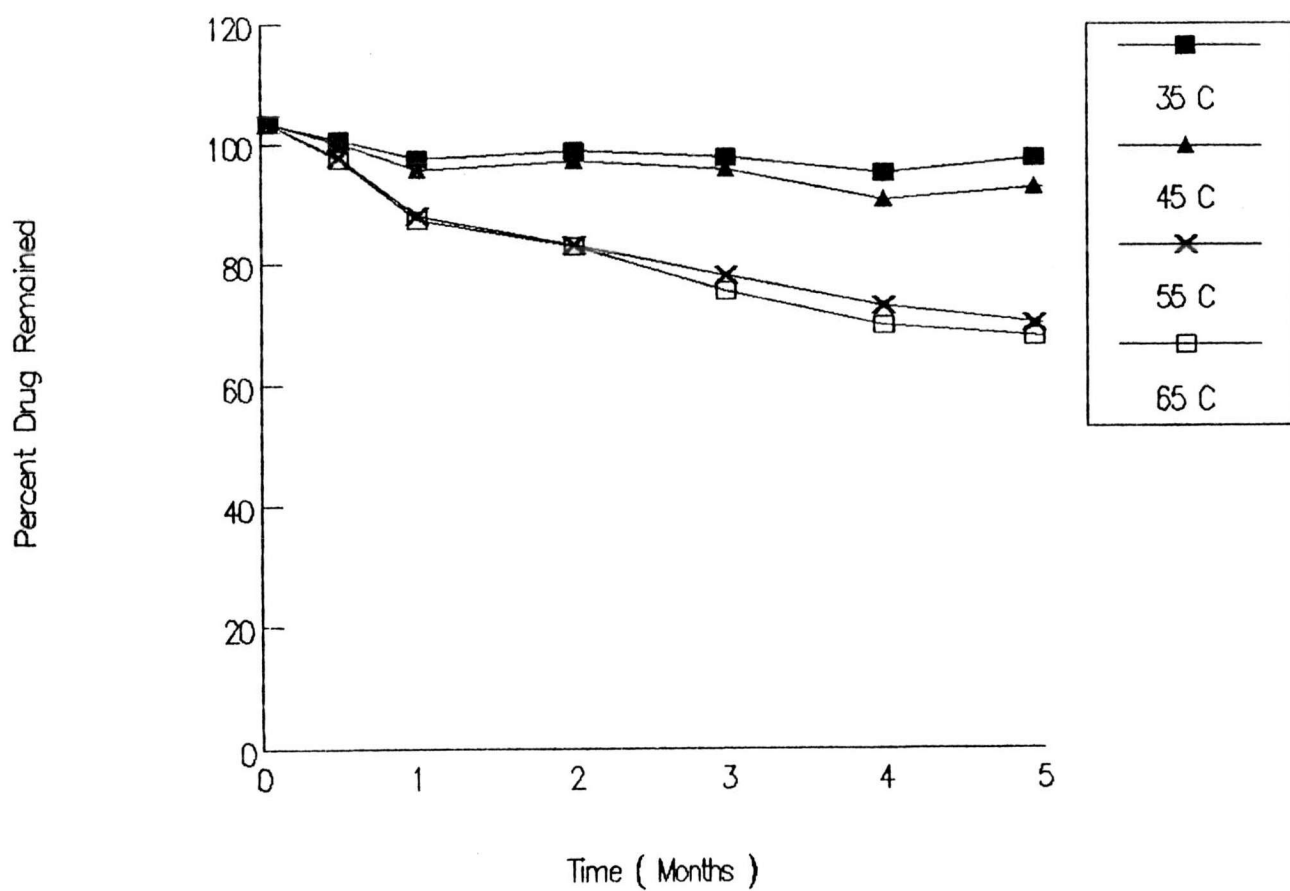


Figure 28 Plots of Percent label amount of DS in pH 8 buffer solution versus time of storage at 35, 45, 55 and 65 °C

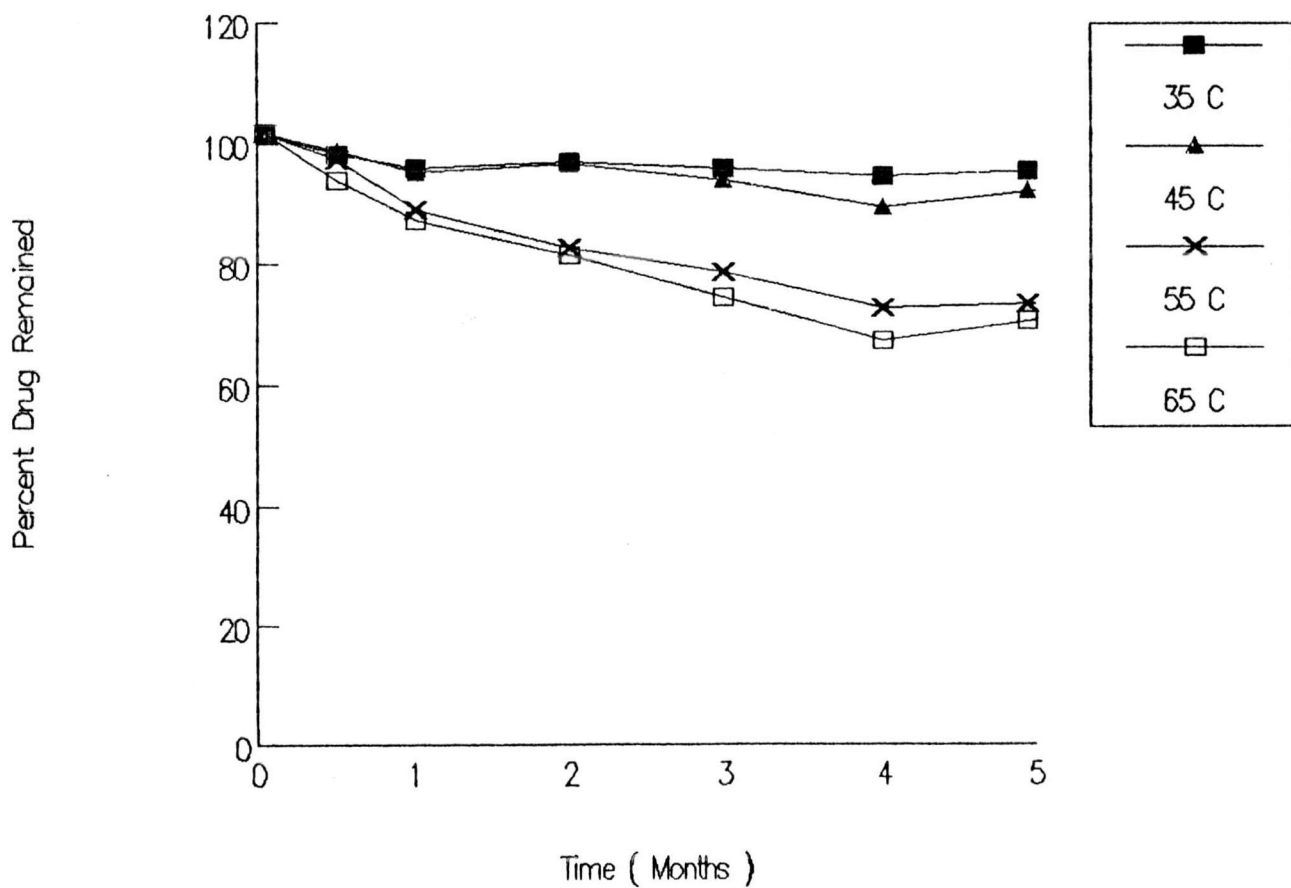


Figure 29 Plots of Percent label amount of DS in pH 9 buffer solution versus time of storage at 35, 45, 55 and 65 °C

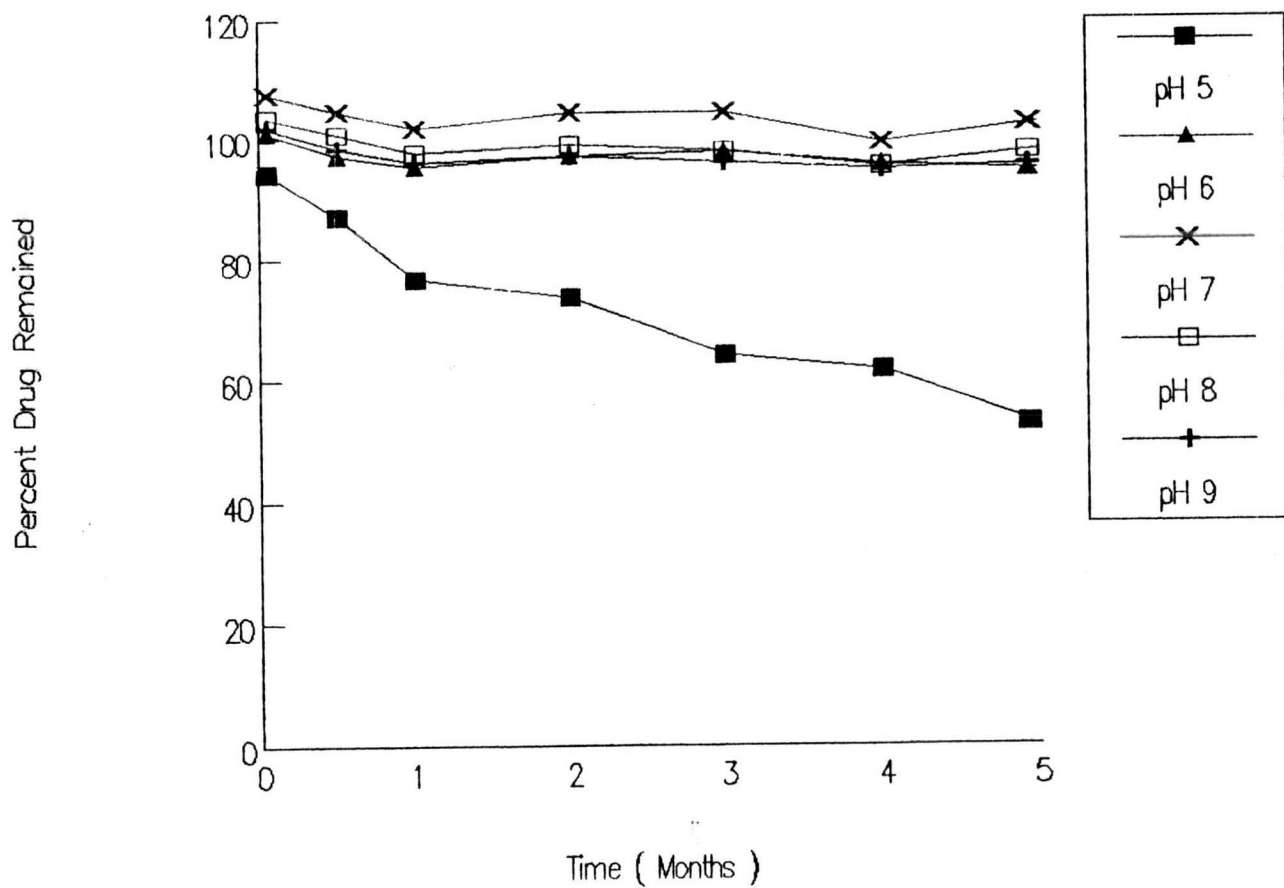


Figure 30 Plots of Percent label amount of DS in pH 5, 6, 7, 8 and 9 buffer solution versus time of storage at 35 °C

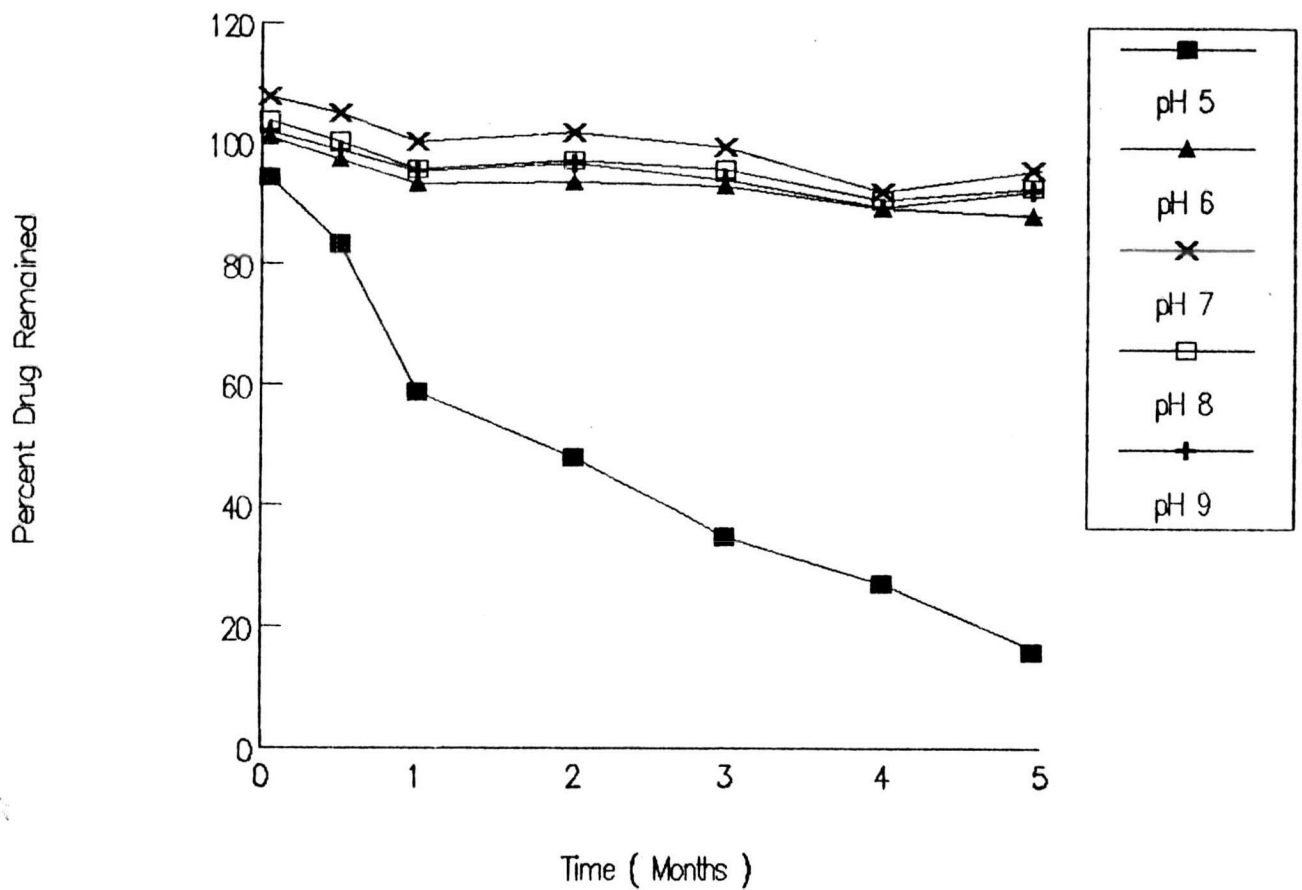


Figure 31 Plots of Percent label amount of DS in pH 5, 6, 7, 8 and 9 buffer solution versus time of storage at 45 °C

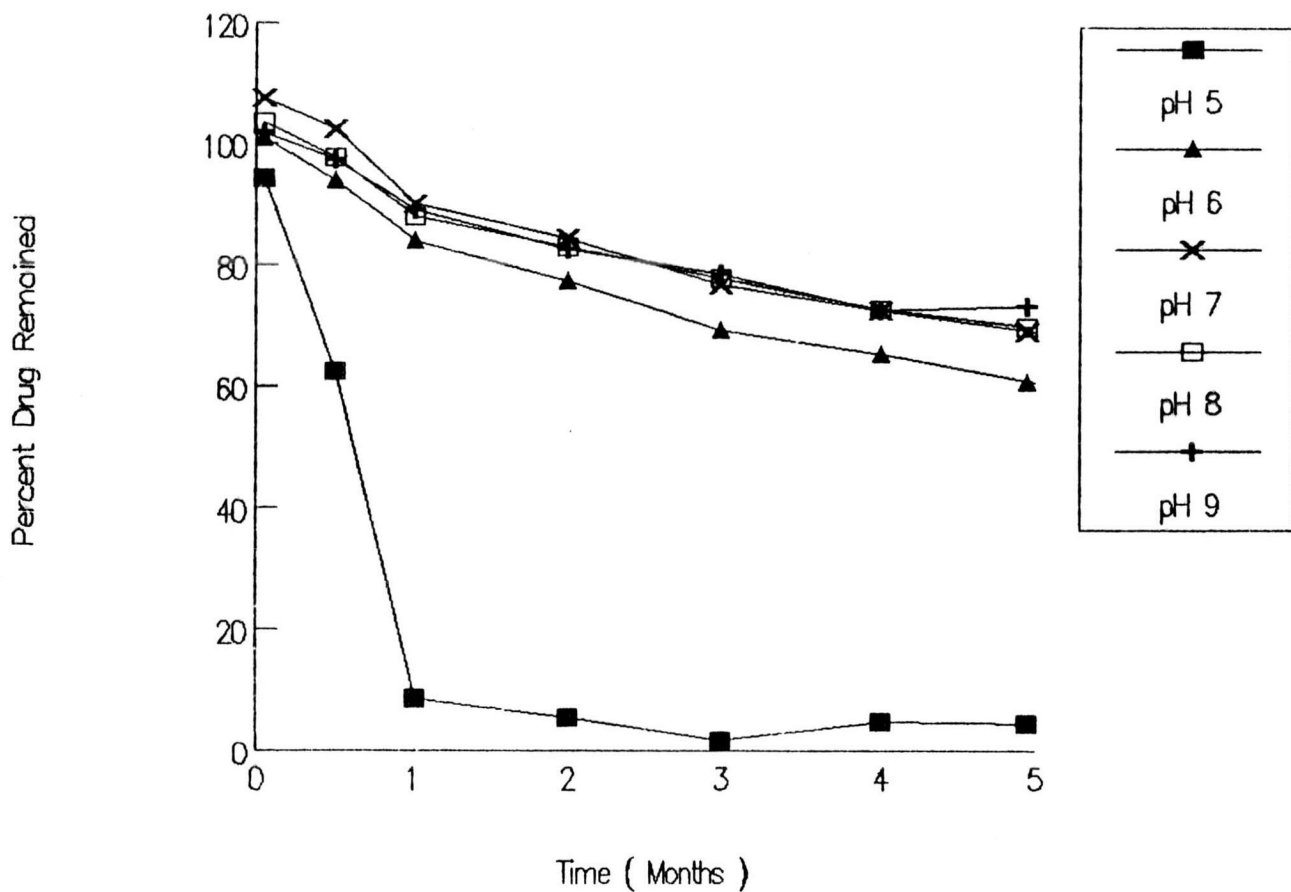


Figure 32 Plots of Percent label amount of DS in pH 5, 6, 7, 8 and 9 buffer solution versus time of storage at 55 °C

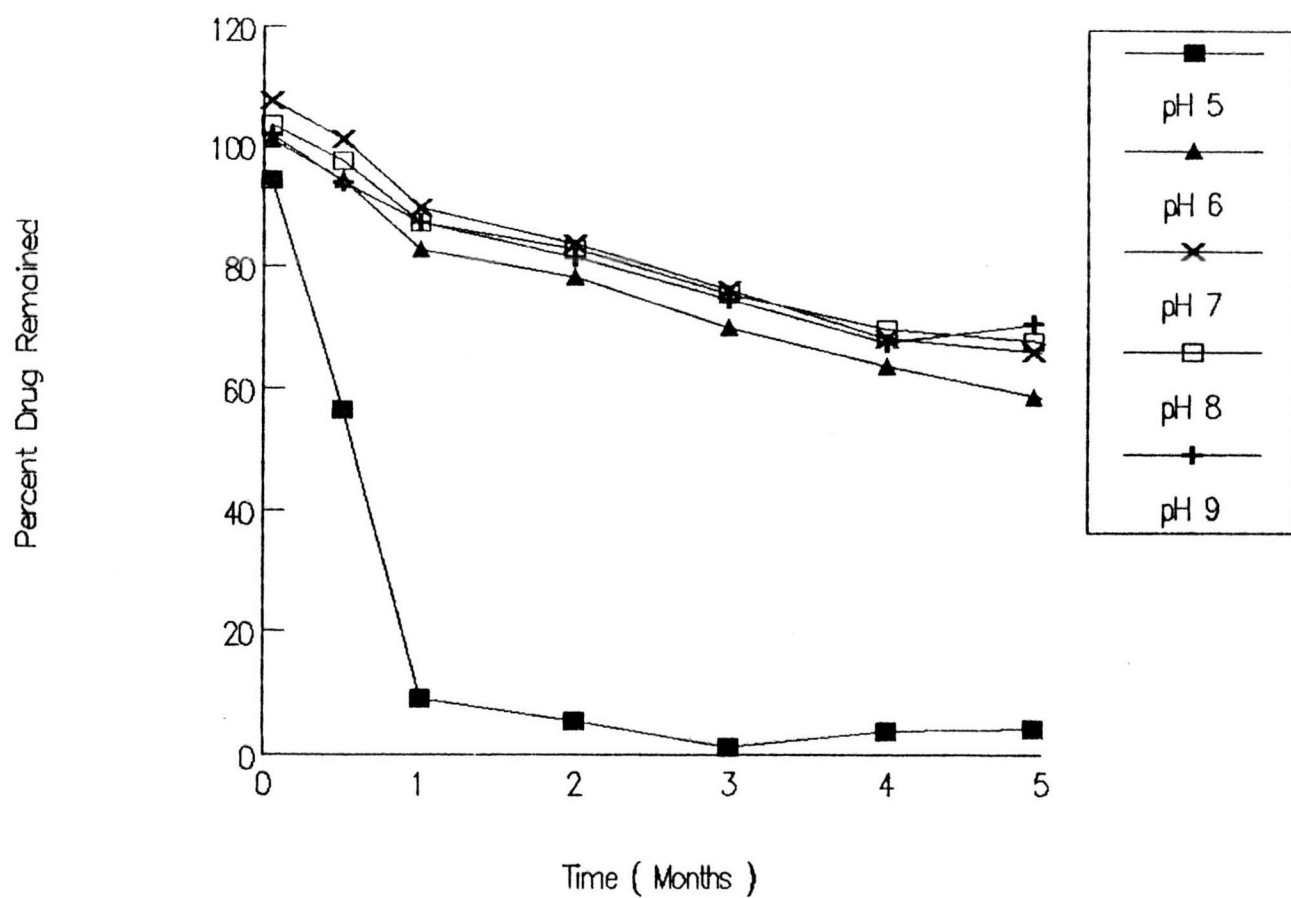


Figure 33 Plots of Percent label amount of DS in pH 5, 6, 7, 8 and 9 buffer solution versus time of storage at 65 °C

2. Stability data of DE

The concentration and percentage of DE in pH 5, 6, 7, 8 and 9 solution remained during 5 months of storage at 35, 45, 55 and 65 °C were shown in Table 16. Plots of DE concentration in pH 5, 6, 7, 8 and 9 solution at several temperatures versus time of storage were shown in Figures 34, 35, 36, 37 and 38, respectively. Plots of DE concentration in various pH at 35, 45, 55 and 65 °C versus time of storage were illustrated in Figures 39, 40, 41 and 42, respectively.

DE in pH 5 solution remained less than 90 percent label amount after 3 months of storage at 35, 45 and 55 °C. But it reduced to 85.86 percent label amount after 2 months of storage at 65 °C. DE in pH 6, 7, 8 and 9 solution remained more than 90 percent of content after 5 months of storage at 35 and 45 °C. But DE in pH 6, 7, 8 and 9 solution remained less than 90 percent label amount after 2 months of storage at 55 and 65 °C.

After 5 months of storage at 35, 45, 55 and 65 °C the content of DE in pH 5 solution was reduced to 87.60, 89.08, 63.69 and 57.95 percent label amount. The content in pH 6 solution was 97.31, 91.39, 63.32 and 58.95 percent label amount, respectively. The content in pH 7 solution was 97.83, 92.22, 64.96 and 62.11 percent label amount, respectively. The content in pH 8 solution was 99.08, 94.65,

Table 16 The percent of DE remained in pH 5,6,7,8 and 9 solution after 5 months of storage at 35, 45, 55 and 65 C

pH	Temp. (C)	Percent DE remained at months							r ²
		0	0.5	1	2	3	4	5	
5	35	115.64	90.44	109.29	106.31	71.63	91.45	87.60	0.3659
	45	115.64	91.13	110.40	107.51	88.19	88.71	89.08	0.4850
	55	115.64	107.04	101.46	90.27	80.22	70.19	63.69	0.9896
	65	115.64	101.86	100.21	85.86	75.30	64.10	57.95	0.9785
6	35	103.08	103.64	102.72	100.81	100.45	99.95	97.31	0.9248
	45	103.08	102.84	102.97	98.43	98.36	98.58	91.39	0.8325
	55	103.08	99.74	94.95	86.69	80.32	71.79	63.32	0.9986
	65	103.08	99.61	95.03	84.24	72.99	66.33	58.95	0.9931
7	35	105.65	104.95	105.23	97.34	101.31	101.77	97.83	0.5433
	45	105.65	103.71	100.48	97.28	98.28	90.33	92.22	0.8822
	55	105.65	99.69	94.73	87.74	78.52	70.31	64.96	0.9934
	65	105.65	100.47	94.89	82.36	75.89	68.12	62.11	0.9836
8	35	105.83	105.06	102.92	100.63	102.43	105.32	99.08	0.3307
	45	105.83	104.01	102.76	98.06	99.79	100.25	94.65	0.7739
	55	105.83	101.31	96.97	87.63	84.86	75.57	71.40	0.9837
	65	105.83	100.99	94.99	84.90	83.77	72.64	69.44	0.9672
9	35	107.53	104.33	101.82	99.72	102.55	100.36	99.60	0.5899
	45	107.53	104.12	101.15	98.13	100.30	99.06	95.86	0.7449
	55	107.53	101.43	97.85	88.29	86.87	82.80	76.61	0.9522
	65	107.53	101.29	95.35	85.14	82.10	78.77	70.02	0.9539

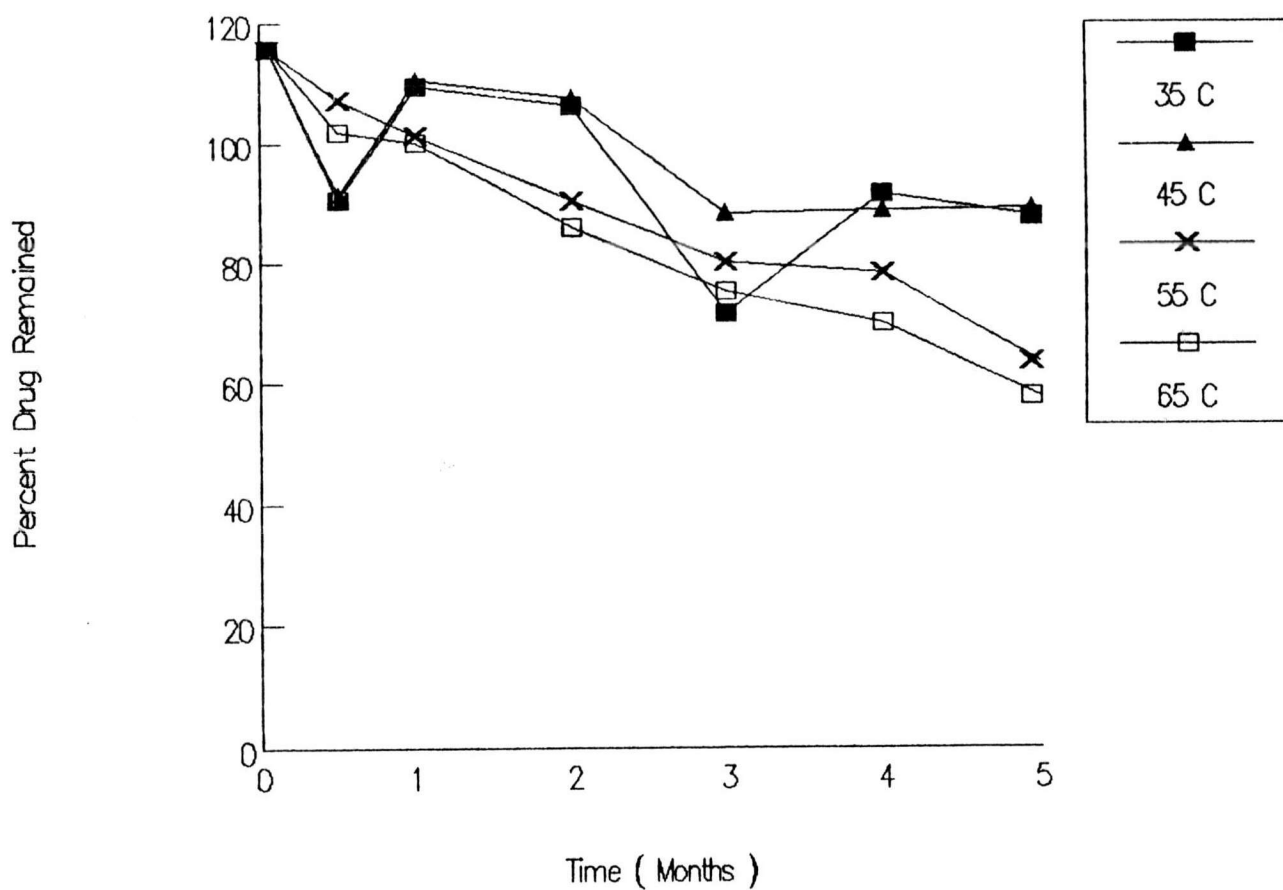


Figure 34 Plots of Percent label amount of DE in pH 5 buffer solution versus time of storage at 35, 45, 55 and 65 °C

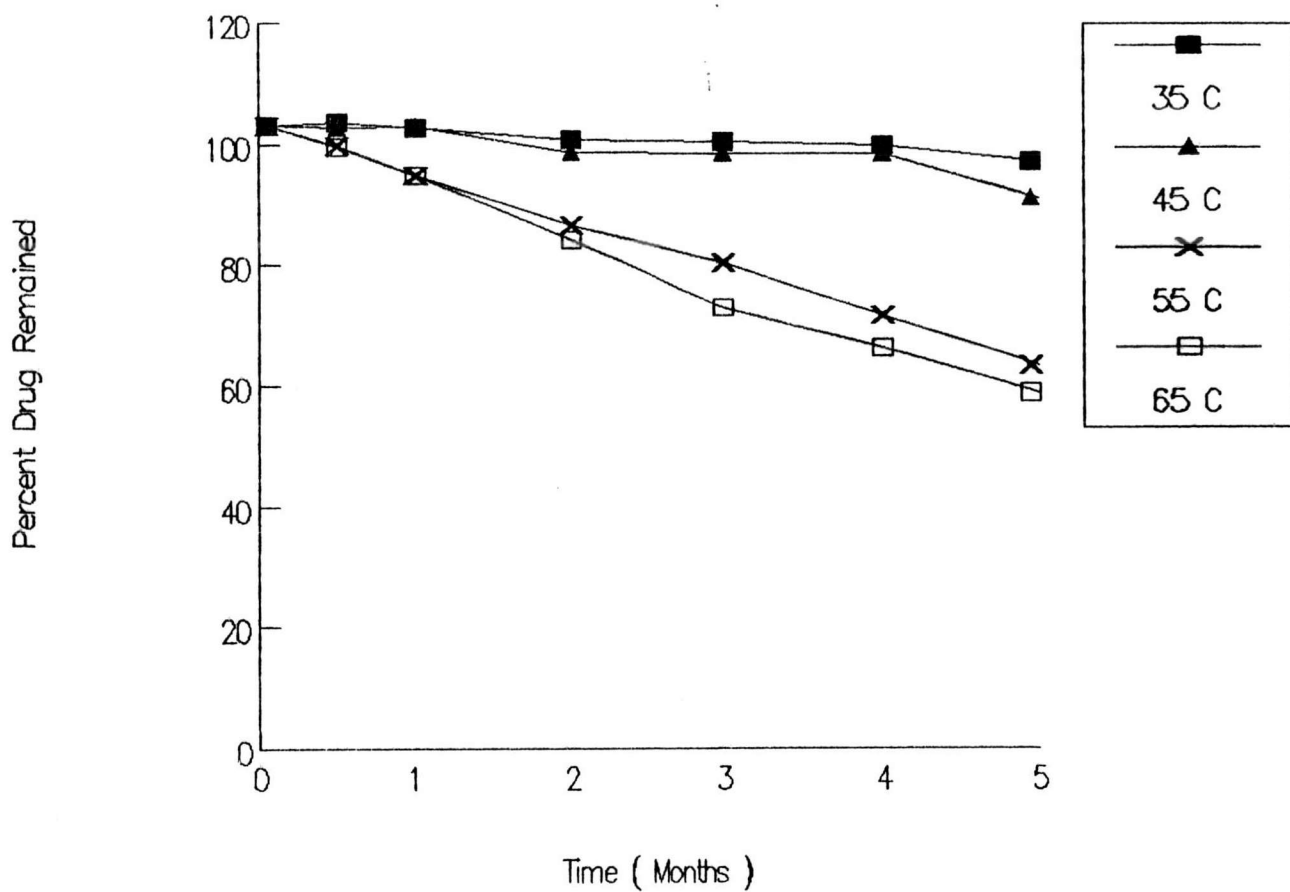


Figure 35 Plots of Percent label amount of DE in pH 6 buffer solution versus time of storage at 35, 45, 55 and 65 °C

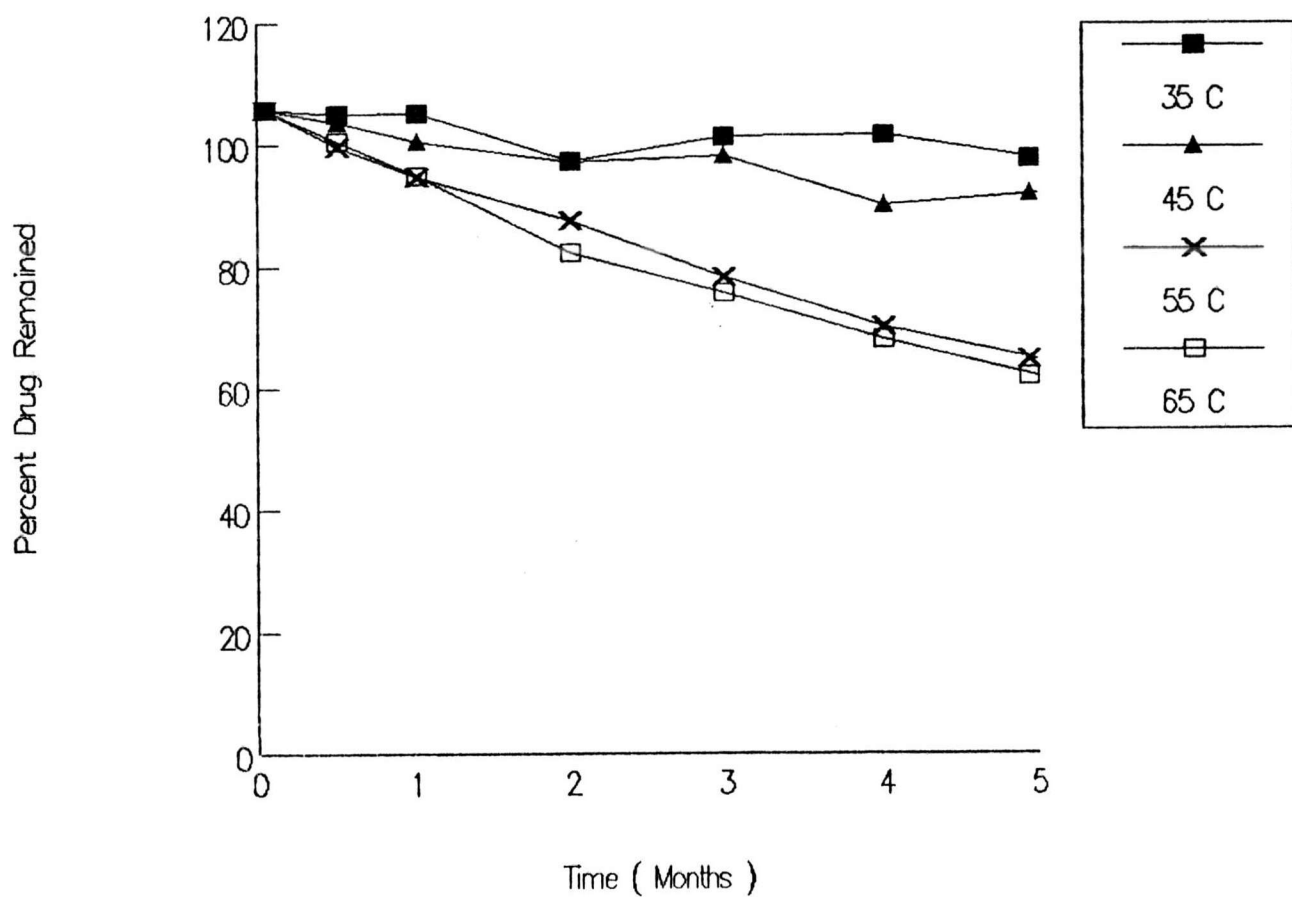


Figure 36 Plots of Percent label amount of DE in pH 7 buffer solution versus time of storage at 35, 45, 55 and 65 °C

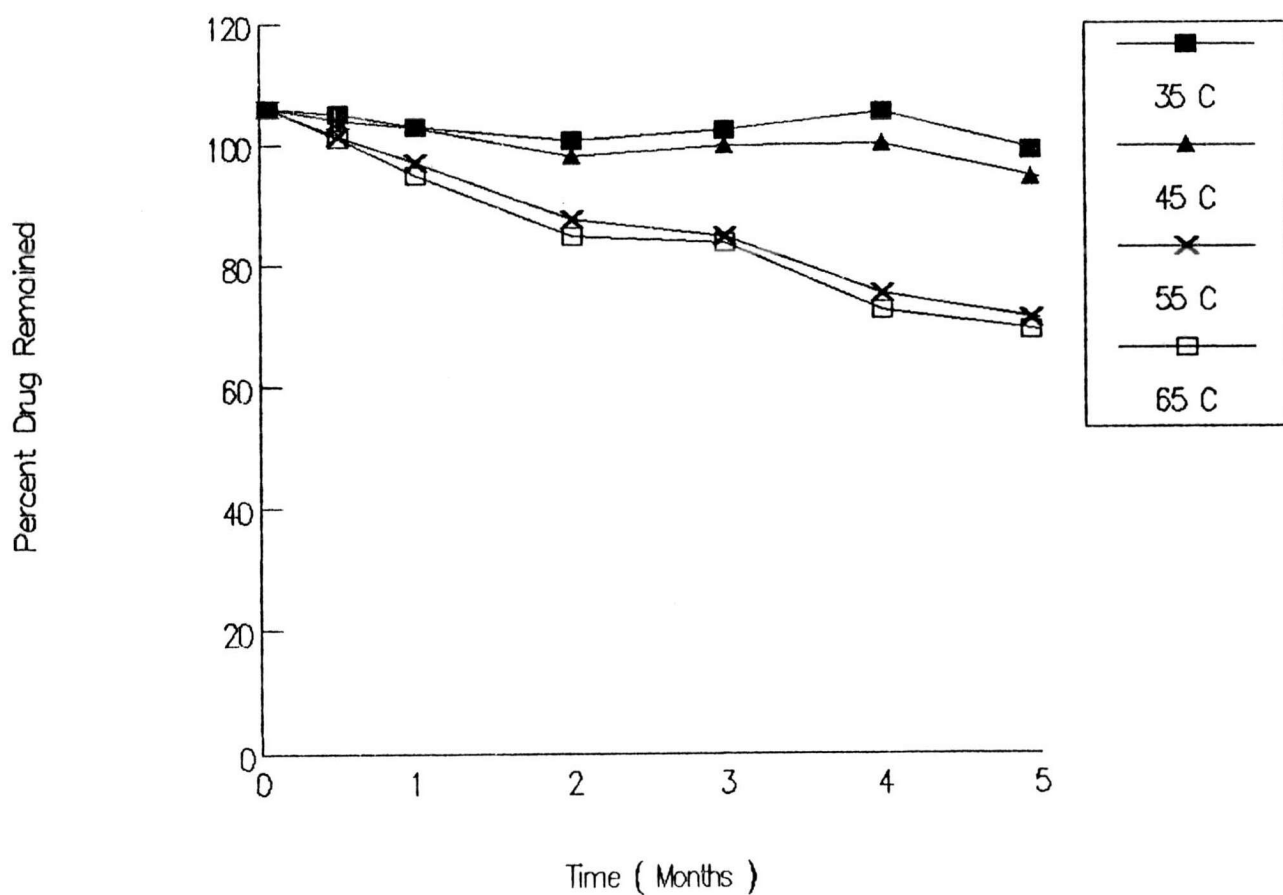


Figure 37 Plots of Percent label amount of DE in pH 8 buffer solution versus time of storage at 35, 45, 55 and 65 °C

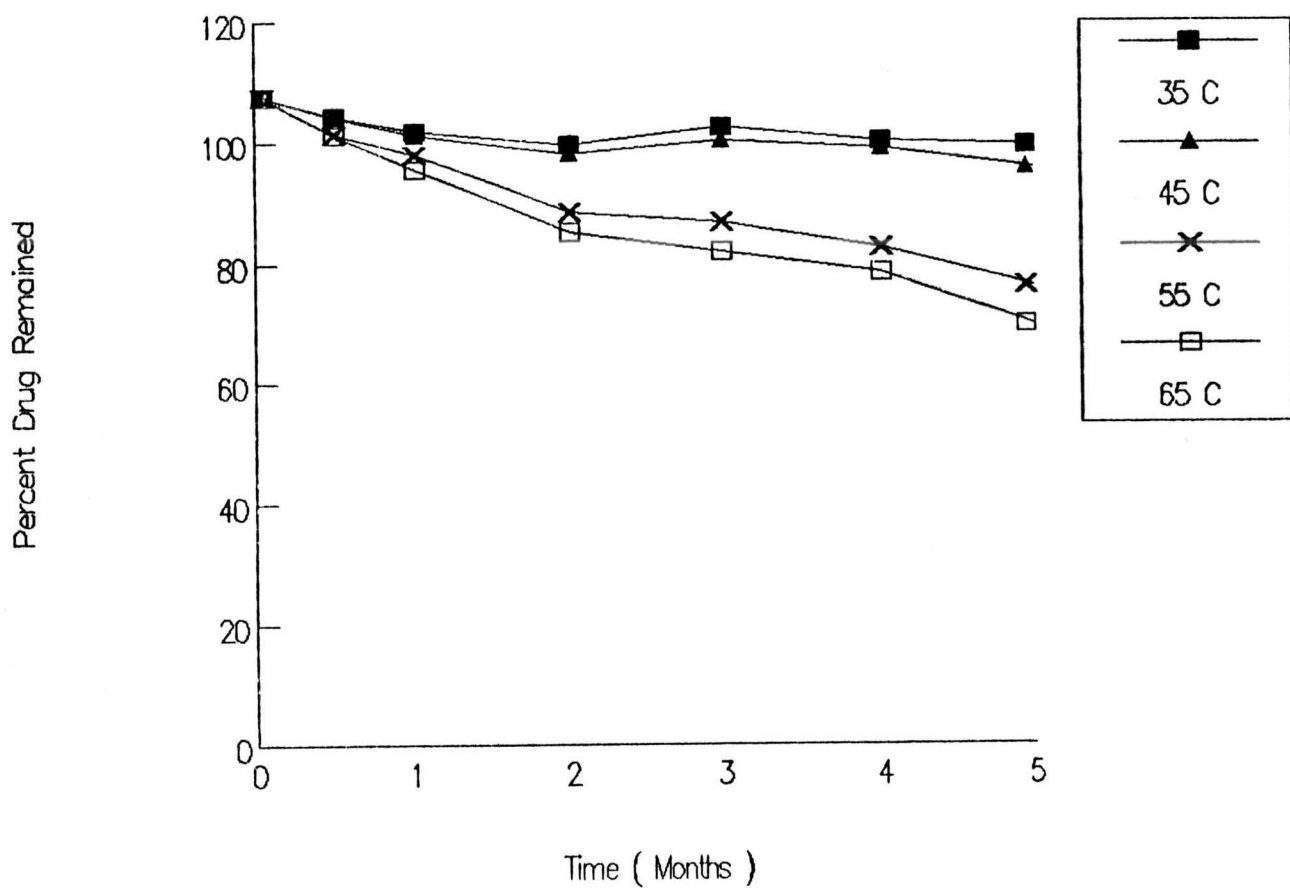


Figure 38 Plots of Percent label amount of DE in pH 9 buffer solution versus time of storage at 35, 45, 55 and 65 °C

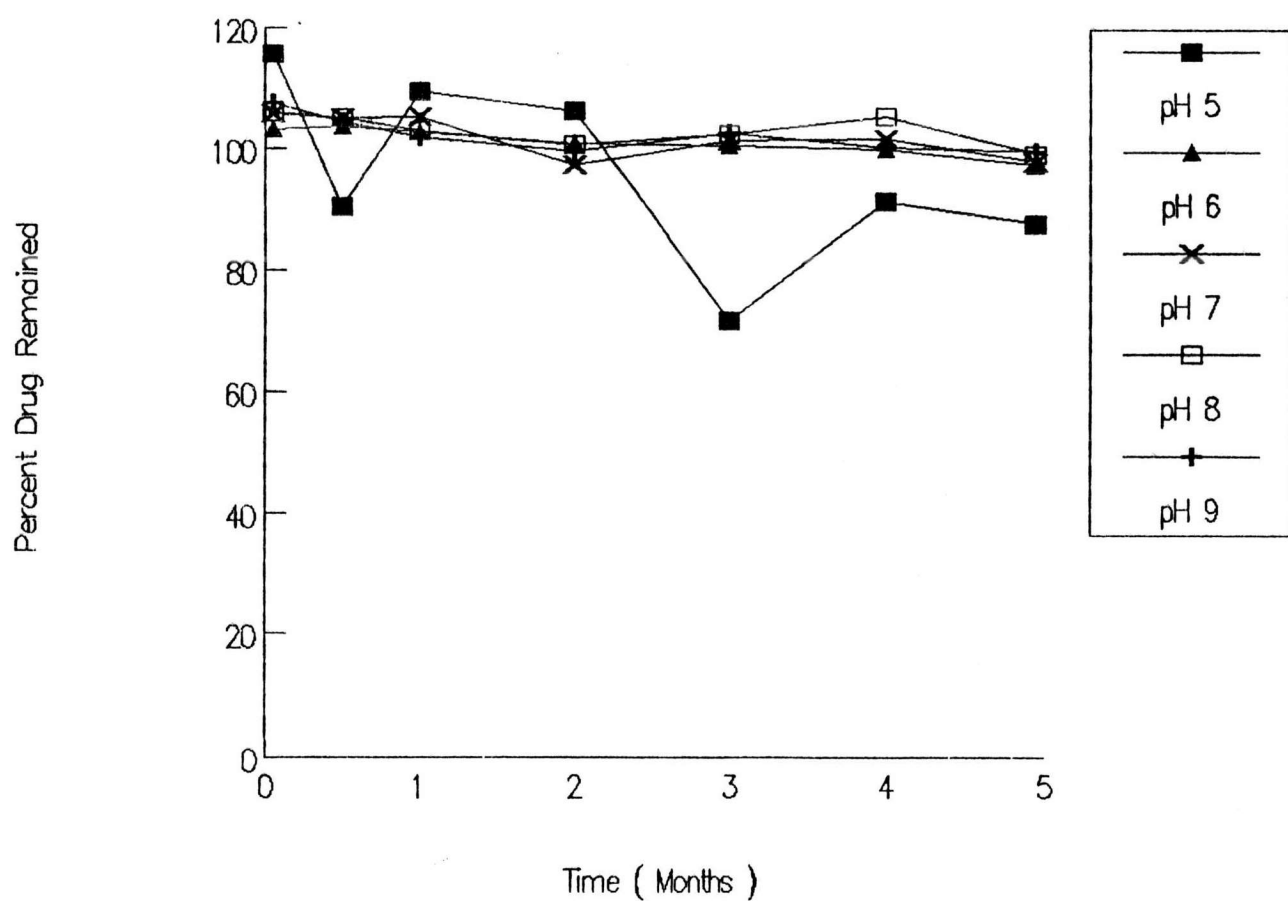


Figure 39 Plots of Percent label amount of DE in pH 5, 6, 7, 8 and 9 buffer solution versus time of storage at 35 °C

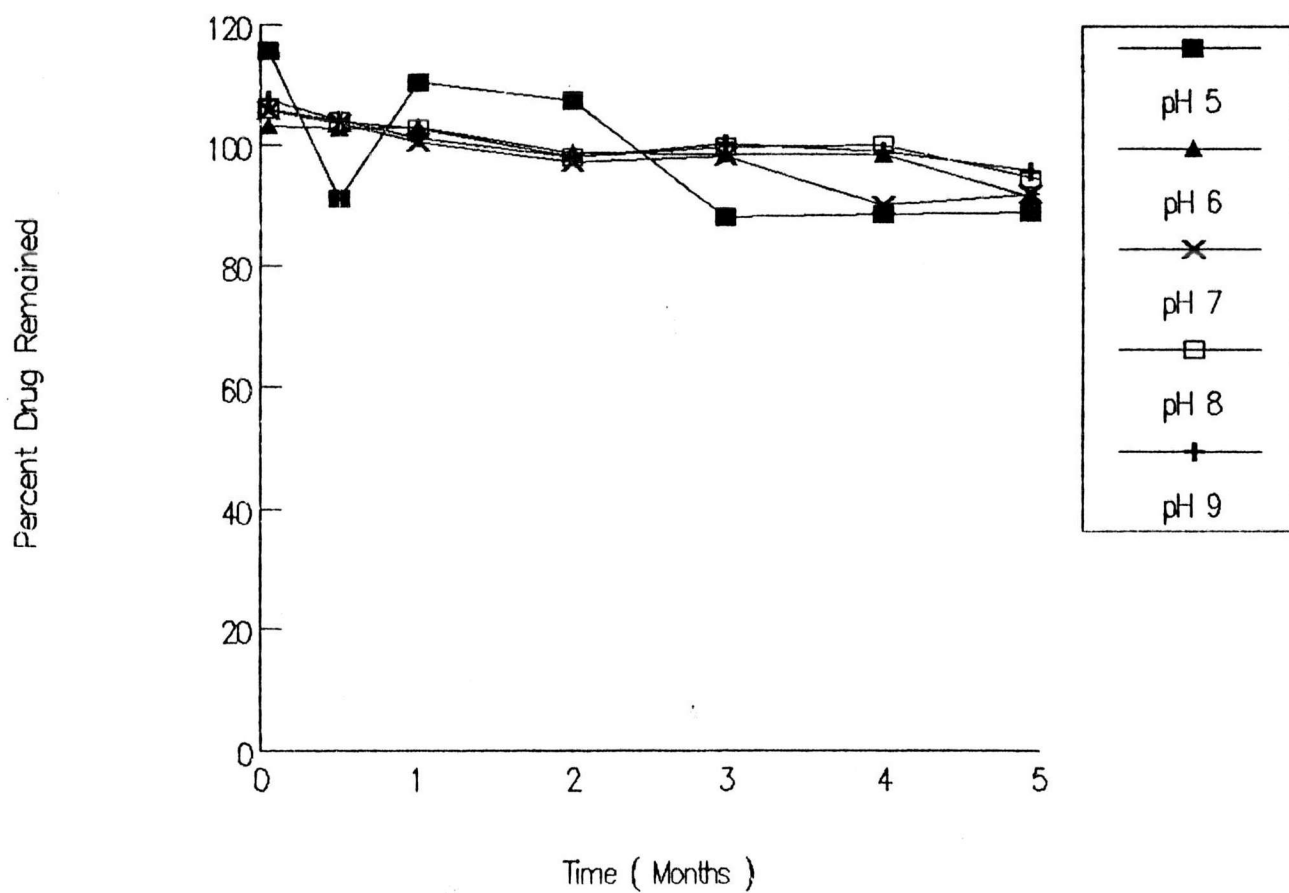


Figure 40 Plots of Percent label amount of DE in pH 5, 6, 7, 8 and 9 buffer solution versus time of storage at 45 °C

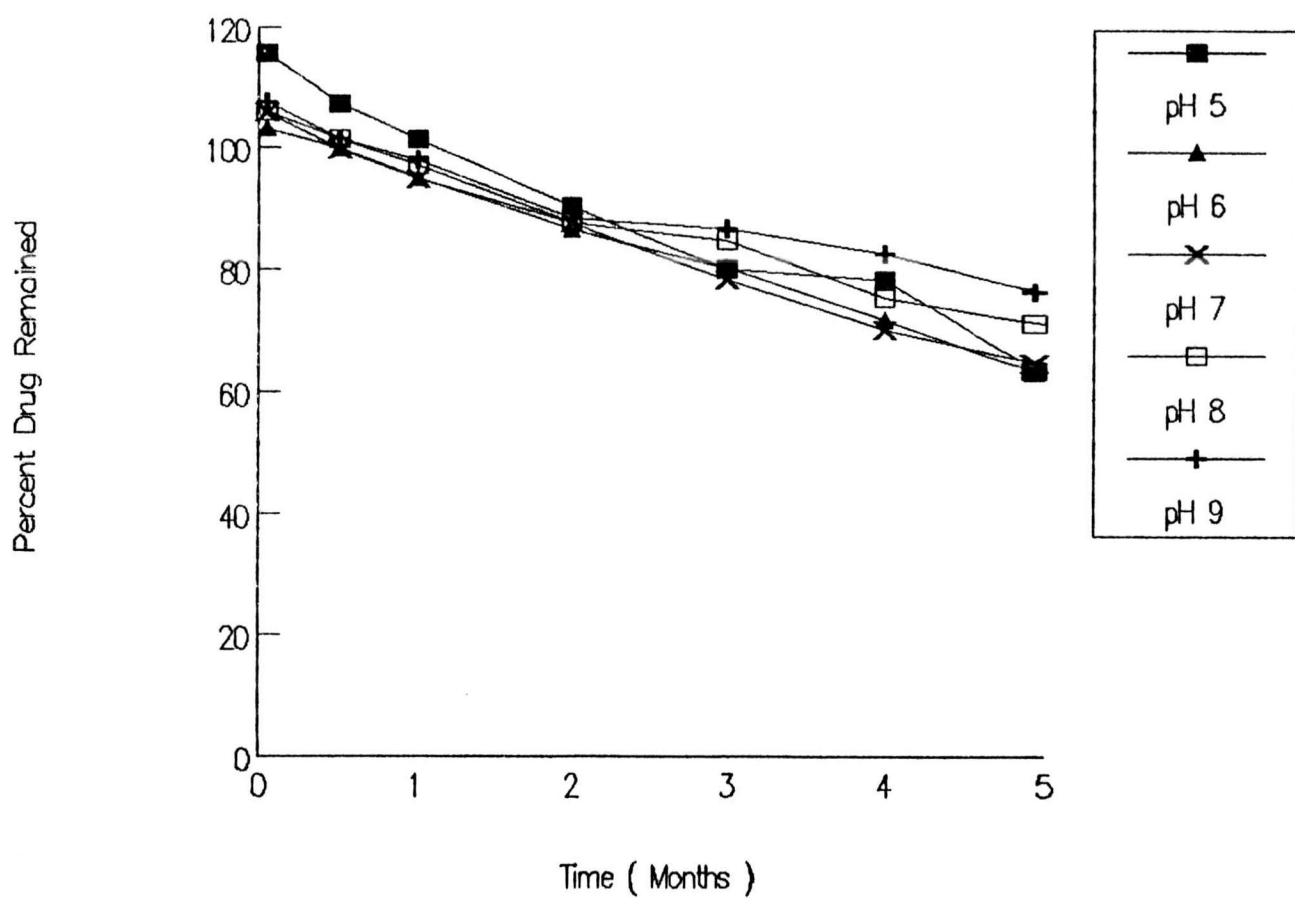


Figure 41 Plots of Percent label amount of DE in pH 5, 6, 7, 8 and 9 buffer solution versus time of storage at 55 °C

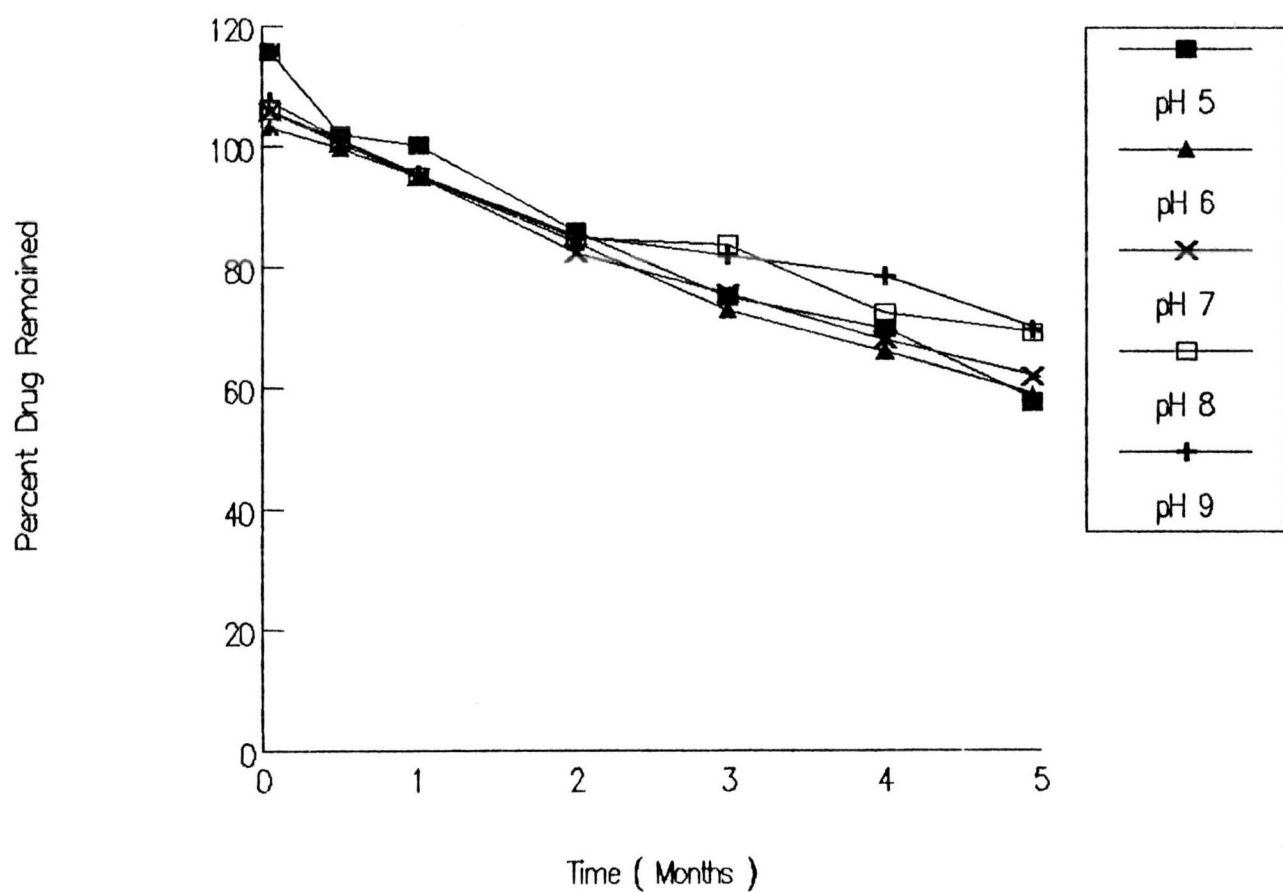


Figure 42 Plots of Percent label amount of DE in pH 5, 6, 7, 8 and 9 buffer solution versus time of storage at 65 °C

71.40 and 69.44 percent label amount, respectively. While the content in pH 9 solution was 99.60, 95.86, 76.61 and 70.02 percent label amount, respectively.

Appearance Evaluation of Preparation

The appearance of all preparations was summerized in Table 17.

1. Creams

In this study all cream preparations were oil in water type. Cream base with or without drug had the same characteristic in appearance study.

Formulations 1-5 and 11-15 which contained Span and Tween as emulsifier were white, viscous cream with coarse texture. These cream preparations evidently segragated after freeze-thaw cycle.

Formulations 6-12 and 16-22 which contained cetomacrogol 1000 as emulsifier were aslo white, viscous, but with smooth and fine texture. Phase separation was not noticed after freeze-thaw cycle.

Table 17 Physical appearance of DS and DE topical preparations

Formula	Dosage	Color	Clarity	ppt.	Viscosity	Texture	F-T test
1- 5 11-15	Cream	White	Turbid	-	-	Coarse	NP
6-10 16-20	Cream	White	Turbid	-	-	Fine	Pass
21,23,25 27,29,31 33,35,37 39,41	C.Gel	No	Tran.	No	Vicious	Fine	Pass
22,24,26 34,36,43 44,48,49	C.Gel	No	Tran.	White	Liquid	Coarse	-
28,30,32 38,40,42 45,46,47 50,51,52	C.Gel	No	Tran.	No	Liquid	Fine	-
53,54,59 60	S.Gel	No	Tran	No	Viscous	Fine	Pass
55	P.Gel	No	Tran	No	Viscous	Fine	Pass
56,61	P.Gel	No	Tran.	No	Liquid	Fine	-
57,58,62 63	P.Gel	No	Tran.	No	Viscous	Fine	Pass
64-71	Emul.	White	Turbid	-	Viscous	Fine	NP
72,77,79 80,82,87 89,90	O-W	No	Tran.	No	Viscous	Fine	Pass
73,74,75 76,83,84 85,86	O-W	White	Turbid	-	Liquid	Coarse	NP
78,81,88 91	O-W	White	Turbid	-	Viscous	Fine	Pass

Remark : ppt. = Precipitation S.Gel = Sodium CMC gel
Tran. = Transparent P.Gel = Poloxamer gel
NP = Not Pass F-T = Freeze-Thaw
C.Gel = Carbopol gel

2. Carbopol Gels

Formulations with odd number between 21-41 which contained no drug were clear, transparent and viscous gels.

Formulations 22, 24, 26, 34, 36, 43, 44, 48 and 49 which contained diclofenac and 10-20 percent of propylene glycol were clear liquid gels with white precipitate and translucent crystal.

Formulations 28, 30, 32, 38, 40, 42, 45-47 and 50-52 which contained diclofenac and 25 percent of propylene glycol were clear, liquid gels.

3. Sodium Carboxymethylcellulose Gels

Formulations 53, 54, 59 and 60 were transparent, viscous gel without phase separation after freeze-thaw cycle.

4. Poloxamer Gels

Formulation 56 and 61 which contained 20 percent of poloxamer and diclofenac were transparent, liquid gels.

Formulation 55 which contained 20 percent of poloxamer and no diclofenac was transparent, viscous gel.

Formulations 57, 58, 62 and 63 which contained 25-30

percent of poloxamer and diclofenac were transparent, viscous gels at room temperature and no seegrates appeared after freeze-thaw cycles.

5. Emulsions

Oil in water type emulsion, formulations 64-71 which contained Span and Tween as emulsifier were white, viscous, homogenized emulsion but these emulsion segregated after freeze-thaw cycles.

6. Oil-Water Gels

Formulations 72, 77, 79, 80, 82, 87, 89 and 90 which contained 0-5 percent of castor oil as an oil phase were transparent, viscous gels and had no phase separation after freeze-thaw cycles.

Formulations 73, 74, 83 and 84 which contained 5-10 percent silicone oil as an oil phase were turbid, liquid gel with phase separation after freeze-thaw cycles.

Formulations 75, 76, 85 and 86 which contained 5-10 percent mineral oil as an oil phase were turbid, liquid gels with phase separation after freeze-thaw cycles.

Formulations 78, 81, 88 and 91 which contained 8-10 percent castor oil as an oil phase were turbid, viscous gels

and had no phase separation after freeze-thaw cycles.

Content Determination of Drug in Preparations

The selected preparation with good appearance and no phase separation after freeze-thaw cycle was analysed spectrophotometrically and the results were shown in Table 18. The contents of diclofenac in these preparations were varied from 98 to 102 percent.

In-Vitro Release Studies

1. Creams

The percentage of drug released from cream over a period of 60 minutes, were listed in Table 19. It could be seen that formulation of different composition and percent of oil phase exhibited different release of drug while both salts of diclofenac released quite similar from formulations composed of mineral oil, stearyl alcohol and cetyl alcohol as oil phase A but released differently in preparations contained stearic acid, mineral oil, stearyl alcohol, white beeswax and spermaceti as an oil phase B. DS was released 12.49 and 7.58 percent from formulation 7 and 8 which contained 17 and 27 percent of oil phase A, respectively. DS was released 7.64 and 6.38 percent from formulations 9 and 10 which contained 17 and 27 percent of oil phase B, respectively.

Table 18 Percent label amount of diclofenac in
topical preparations

Formula	Dosage form	% label amount
7	cream	98.61 [0.07]
8	cream	98.92 [0.03]
9	cream	99.11 [0.45]
10	cream	98.74 [0.10]
17	cream	98.05 [0.05]
18	cream	98.37 [0.24]
19	cream	98.73 [0.11]
20	cream	98.48 [0.07]
53	hydrophilic gel	99.38 [0.03]
54	hydrophilic gel	98.85 [0.04]
57	hydrophilic gel	99.73 [0.27]
58	hydrophilic gel	100.28 [0.08]
59	hydrophilic gel	98.94 [0.04]
60	hydrophilic gel	98.95 [0.25]
62	hydrophilic gel	100.5 [0.15]
63	hydrophilic gel	100.24 [0.23]
79	Oil-Water gel	101.35 [0.30]
80	Oil-Water gel	100.98 [0.08]
81	Oil-Water gel	100.63 [0.22]
89	Oil-Water gel	100.76 [0.07]
90	Oil-Water gel	100.34 [0.14]
91	Oil-Water gel	100.56 [0.01]
Product A	Oil-Water gel	98.92 [0.10]
Product B	Oil-Water gel	99.16 [0.43]
Product C	hydrophilic gel	98.84 [0.18]

n = 2

Table 19 The percent of diclofenac released from creams

Time (min.)	Formulation							
	7	8	9	10	17	18	19	20
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5	3.18 [0.37]	2.49 [0.40]	1.52 [0.12]	0.99 [0.17]	2.77 [0.29]	1.64 [0.17]	2.26 [0.36]	1.56 [0.10]
10	4.97 [0.17]	3.58 [0.32]	2.48 [0.11]	1.70 [0.18]	4.46 [0.33]	2.79 [0.39]	3.60 [0.32]	2.64 [0.16]
15	5.87 [0.56]	4.56 [0.36]	3.22 [0.14]	2.30 [0.19]	5.61 [0.17]	3.53 [0.37]	4.53 [0.35]	3.39 [0.11]
25	7.38 [0.55]	5.41 [0.13]	4.62 [0.24]	3.36 [0.11]	7.63 [0.13]	4.72 [0.44]	6.16 [0.30]	4.65 [0.14]
40	9.49 [1.05]	6.36 [0.20]	6.12 [0.22]	4.79 [0.13]	9.85 [0.27]	5.72 [0.50]	7.66 [0.25]	5.96 [0.31]
60	12.49 [1.06]	7.58 [0.29]	7.64 [0.20]	6.38 [0.27]	12.15 [0.37]	7.11 [0.79]	9.62 [0.08]	7.42 [0.35]

n = 3

DE was released 12.15 and 7.12 percent from formulations 17 and 18 which contained 17 and 27 percent of oil phase A, respectively. DE was released 9.62 and 7.42 percent from formulations 19 and 20 which contained 17 and 27 percent of oil phase B, respectively.

2. Hydrophilic Gels

The percentages of drug released from hydrophilic gels over a period of 60 minutes were exhibited in Table 20. It was noted that both composition of formulation and salt of drug affected the release of diclofenac. DS was released 57.41, 48.48, 24.17 and 18.02 percent from formulations 53, 54, 57 and 58 which contained 1.5, 2 percent of sodium CMC, 25, 30 percent of poloxamer, respectively.

DE was released 12.15, 7.12, 9.62 and 7.42 percent from formulations 59, 60, 62 and 63 which contained 1.5, 2 percent of sodium CMC, 25, 30 percent of poloxamer, respectively.

3. Oil-Water Gels

The percentages of drug release from oil-water gel over a period of 360 minutes were exhibited in Table 21. DS was released 73.06, 66.40 and 61.21 percent from formulations 79, 80 and 81 which contained 0, 4 and 8 percent of oil after 6 hours of release study, respectively.

Table 20 The percent of DS and DE released from hydrophilic gels

Time (min.)	Formulation							
	53	54	57	58	59	60	62	63
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5	8.39 [0.42]	7.29 [0.40]	3.54 [0.34]	2.92 [0.31]	6.43 [0.02]	5.88 [0.16]	2.70 [0.12]	2.42 [0.37]
10	14.29 [0.90]	12.56 [0.54]	5.38 [0.56]	4.32 [0.39]	10.67 [0.11]	9.97 [0.16]	4.20 [0.17]	3.94 [0.27]
15	20.23 [1.32]	17.22 [0.63]	7.21 [0.51]	5.44 [0.66]	14.63 [0.11]	14.78 [0.55]	5.71 [0.11]	5.07 [0.33]
25	28.68 [2.80]	25.06 [0.73]	10.50 [0.60]	7.59 [0.82]	22.17 [0.49]	20.88 [0.86]	8.60 [0.56]	6.80 [0.46]
40	42.54 [2.24]	35.48 [0.77]	16.41 [0.85]	12.22 [1.46]	31.08 [0.60]	29.86 [1.37]	14.35 [0.90]	11.43 [0.71]
60	57.41 [3.88]	48.49 [0.98]	24.17 [1.09]	18.02 [2.07]	45.74 [0.76]	41.22 [0.88]	22.58 [1.15]	18.04 [1.49]

n = 3

Table 21 The percent of DS and DE released from Oil-Water Gels

Time (min.)	Formulation					
	79	80	81	89	90	91
0	0.00	0.00	0.00	0.00	0.00	0.00
5	3.19 [0.28]	3.31 [0.83]	3.40 [0.64]	3.32 [0.34]	3.24 [0.15]	3.49 [0.21]
10	5.08 [0.47]	4.49 [1.05]	5.08 [0.98]	4.60 [0.56]	5.28 [0.44]	4.53 [0.22]
15	6.58 [0.51]	5.73 [1.17]	7.03 [1.26]	6.07 [0.75]	7.53 [0.32]	5.54 [0.33]
25	9.50 [1.35]	8.31 [1.52]	10.12 [1.52]	9.58 [1.44]	11.34 [0.34]	7.54 [0.72]
40	14.63 [1.56]	12.97 [2.68]	15.07 [1.85]	15.89 [1.48]	18.06 [0.30]	11.88 [1.25]
60	21.35 [2.11]	19.22 [4.25]	21.12 [1.87]	23.95 [1.93]	25.80 [0.71]	17.89 [2.17]
90	29.11 [2.36]	27.25 [5.20]	28.12 [2.02]	33.61 [2.25]	34.00 [1.10]	25.44 [2.35]
120	36.93 [3.10]	34.87 [6.19]	34.35 [1.86]	40.64 [5.00]	40.30 [0.43]	32.12 [2.60]
180	49.11 [2.32]	43.26 [2.59]	43.00 [0.90]	53.13 [4.07]	51.04 [2.00]	41.85 [2.60]
240	58.90 [3.36]	52.80 [2.30]	49.84 [0.20]	63.41 [5.59]	59.44 [2.02]	49.43 [3.10]
300	66.78 [3.29]	60.47 [1.70]	56.91 [0.97]	69.94 [5.82]	65.59 [1.58]	55.37 [3.21]
360	73.06 [4.46]	66.40 [2.02]	61.21 [2.05]	73.45 [4.58]	71.02 [3.20]	61.32 [3.56]

n = 3

DE was released 73.45, 71.02 and 61.31 percent after 6 hours of release study from formulation 89, 90 and 91 which contained 0, 4 and 8 percent of oil , respectively. It could be concluded that amount of oil affected the release of drug.

4. Commercial Products

Three commercial products were used in this release study. The percentages of drug release from commercial products, over a period of 360 minutes, were shown in Table 22. DS was released 93.25 percent from product C after 6 hours of study. DE was release 89.19 and 95.79 percent from products A and B after 6 hours of study, respectively.

Table 22 The percent of drug released from commercial products

Time (min.)	Commercial product		
	A	B	C
0	0.00	0.00	0.00
5	4.18 [0.12]	4.19 [0.34]	5.84 [0.48]
10	6.79 [0.10]	6.87 [0.70]	9.63 [1.06]
15	9.42 [0.15]	9.42 [1.29]	12.72 [1.80]
25	13.88 [0.93]	13.93 [1.57]	17.91 [1.99]
40	21.41 [1.59]	21.12 [2.73]	25.97 [3.32]
60	30.57 [2.10]	30.97 [3.07]	36.25 [3.67]
90	43.33 [3.08]	44.39 [5.43]	49.88 [5.39]
120	53.79 [2.53]	56.05 [7.56]	61.52 [6.65]
180	71.38 [4.21]	74.37 [7.39]	76.08 [5.54]
240	84.55 [2.62]	85.64 [7.15]	83.23 [3.07]
300	85.12 [0.77]	89.03 [4.91]	90.87 [3.08]
360	89.19 [2.26]	95.79 [2.02]	93.25 [2.15]

n = 3