CHAPTER 7

STABILITY STUDIES

7.0 STABILITY STUDIES

Stability of a drug has been defined as the ability of a particular formulation, in a special container, to remain within its physical, chemical, therapeutic and toxicological specifications. The period of stability of a pharmaceutical preparation may be defined as the time from the date of manufacture of the formulation until its chemical or biological activity is lost below 90 % of labeled potency and its physical characteristic have not changed appreciably or deleteriously

The stability studies were carried out in accordance with the ICH guidelines for stability. The samples were subjected to stability in HDPE bottles with induction seal. The samples were subjected to stability at 40°C/75%RH (accelerated stability) for 1, 2, 3, 6months and at 25°C/60%RH (controlled room temperature) at 3, 6, 9, 12months as mentioned in table 1-7. The parameters studied are the drug content (Assay), average weight, dissolution studies, description and water by KF.

Condition	1Month	2Month	3Month	6Month	9Month	12Month
40°C/75%RH	√	√	√	√	--	--
25°C/60%RH	--	--	√	√	√	√

Table 1 - 7 List of stability Stations

7.1 Materials and Methods

Accelerated and long term stability studies were carried out on the optimized formulations. To access the stability, optimized formulations were stored at 40 ± 2°C /75 ± 5% RH for 1, 2, 3, 6months and at 25 ± 2°C /60 ± 5% RH for 3, 6, 9, 12months and were observed for physical change (appearance), drug content, dissolution, average weight and water by KF. The method of stability studies was in conformity with the recommendations in WHO document pertaining to stability testing of products intended for global market (Mathews, 1999) and ICH guidelines. The samples were withdrawn periodically and evaluated for physical change (appearance), drug content, dissolution, average weight and water by KF. (Mathews, 1999; Verma et al., 2003)

7.2 Pack Style

The selected formulations were packed in 60cc HDPE bottle with induction seal. The packed formulations were stored upto 6 months in ICH certified stability chambers (40 °C / 75 % RH) and upto 12months (25 °C / 60 % RH).

7.3 Evaluation of the Samples

The samples were withdrawn at specified intervals and evaluated for the appearance, drug content, average weight, dissolution and water by KF. Drug content, Dissolution was determined by specific methods such as UV/HPLC methods given in chapter 3(for butorphanol) and chapter5 (for lornoxicam) for the respective drug.

7.4 In-house Specifications and Limits

For determining the physical changes, drug content, water by KF, average weight and dissolution in-house specifications were generated as mentioned below in table 2-7 and 3-7.

Description	(%) Assay	Avereage weight (mg)	% drug dissolved					Water Content
			2 Hr	4 Hr	8 Hr	14 Hr	24 Hr	
White colored, circular, biconvex, film coated tablet, plain on both side	95.00 to 105.00 %	245 ± 3%	NMT 15%	10-30%	30-55%	50-80%	NLT 80%	NMT 5%
Complies	101.62	242.60	9.1	20.3	36.2	58.8	91.3	2.9

Table 2 - 7 Initial results Butorphanol Tartrate

Description	(%) Assay	Avereage weight (mg)	% Drug Dissolved				Water Content
			2 Hr	4 Hr	8 Hr	12 Hr	
Yellow colored, circular, biconvex, film coated tablet, plain on both side	95.00 to 105 %	180 ± 3%	NMT 40%	40 - 60%	70-80%	NLT 85%	NMT 5%

Complies	100.2	181.83mg	29.7	49.70	77.20	95.40	2.4

Table 3 - 7 Initial results of Lornoxicam

7.5 Results

STABILITY DATA OF BUTORPHANOL TARTARATE EXTENDED RELEASE TABLETS 40°C/75%RH:

Stability condition	**Specifications**	**Description**	**(%) Assay**	**Avereage weight**	**% drug dissolved**					**Water Content**	**F2 (With Respect to initial)**
					2 Hr	**4 Hr**	**8 Hr**	**14 Hr**	**24 Hr**		
	Pack Style		95.00 to 105.00%	245 ± 3%	NMT 15%	10-30%	30 to 55	50 to 80	NLT 80	NMT 5%	
Initial	HDPE Bottle	White colored, circular, biconvex, film coated tablet, plain on both side	101.62	242.60mg	9.1	20.3	36.2	58.8	91.3	2.9	Not Applicable
1M 40°C/75%RH	HDPE Bottle	Complies	100.92	246.70mg	8.1	24.5	34.9	59.6	95.1	2.8	80
2M 40°C/75%RH	HDPE Bottle	Complies	100.56	241.32mg	12.3	21.2	38.8	56.7	92.4	3.2	81
3M 40°C/75%RH	HDPE Bottle	Complies	99.98	240.61	10.2	20.1	37.7	59.1	90.3	3.4	90
6M 40°C/75%RH	HDPE Bottle	Complies	101.2	243.91	11.4	24.5	34.2	56.2	89.2	3.1	77

Table 4 - 7 STABILITY DATA OF BUTORPHANOL TARTARATE EXTENDED RELEASE TABLETS 40°C/75%RH

Storage Condition	Specifications	Description	(%) Assay	Avereage weight	% drug dissolved					Water Content	F2 (With Respect to initial)
					2 Hr	4 hr	8 Hr	14 Hr	24 Hr		
	Pack Style		95.00 to 105.00%	245 ± 3%	NMT 15%	NMT 5%	30 to 55	50 to 80	NLT 80	NMT 5%	
3M 25°C/60%RH	HDPE Bottle	Complies	99.92	247.82	7.1	22.4	37.3	58.2	93.2	3.2	87
6M 25°C/60%RH	HDPE Bottle	Complies	100.22	241.6	10.2	23.7	40.4	59.1	90.5	2.8	76
9M 25°C/60%RH	HDPE Bottle	Complies	99.1	243.47	8.2	22.8	39.5	59.7	87.8	3.0	79
12M 25°C/60%RH	HDPE Bottle	Complies	99.62	244.58	9.4	22.3	37.4	56.2	90.5	3 1	87

Table 5 - 7 STABILITY DATA OF BUTORPHANOL TARTARATE EXTENDED RELEASE TABLETS 25°C/60%RH

Table 4-7 and 5-7 respectively shows stability data for BT up to 6M 40°C/75%RH and 12M 25°C/60%RH. Figure 1-7 and 2-7 respectively shows stability data up to 12M 25°C/60%RH and 6M 40°C/75%RH.

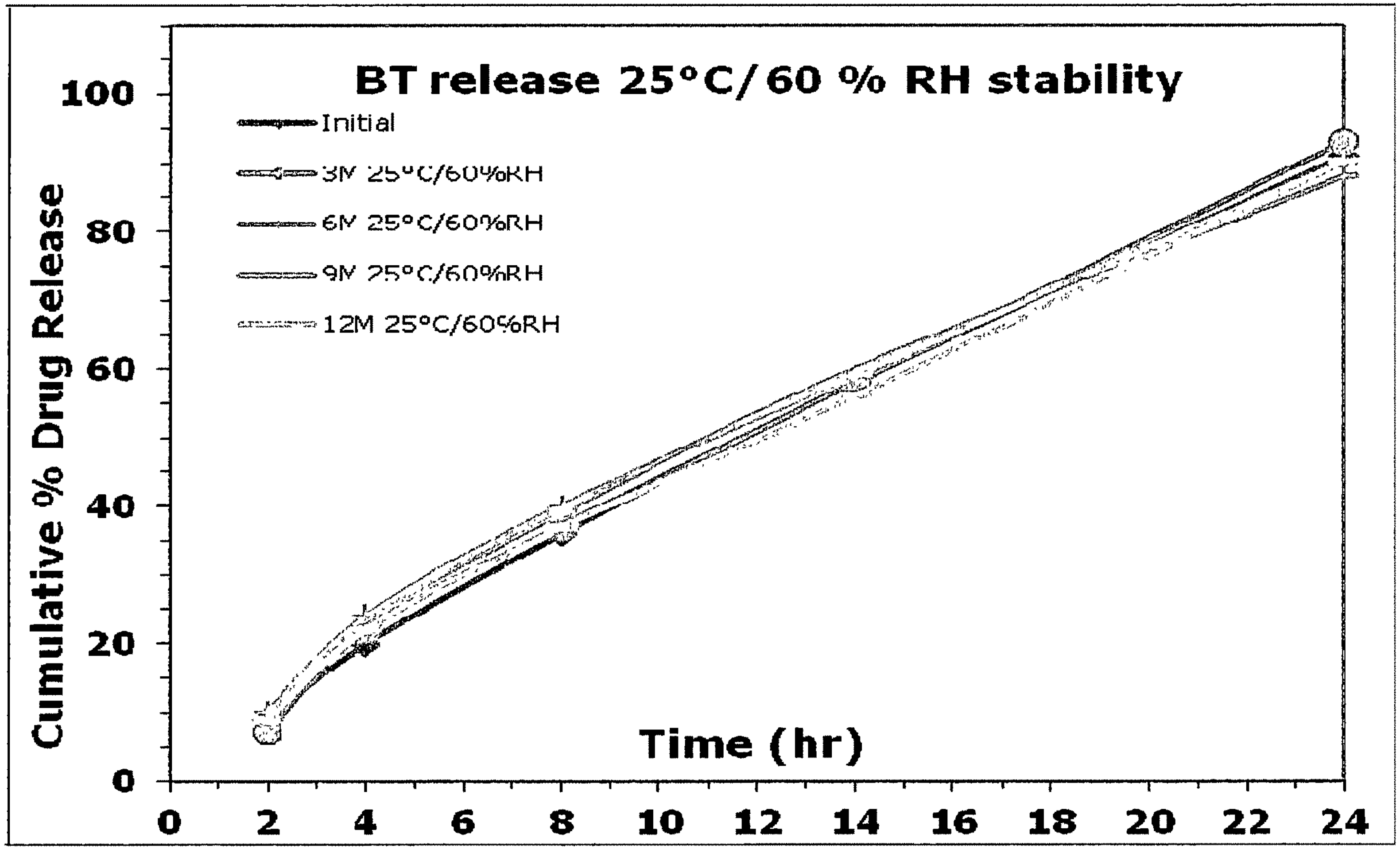

Figure 1 - 7 STABILITY GRAPH OF BUTORPHANOL TARTARATE ER TABLETS 25°C/60%RH

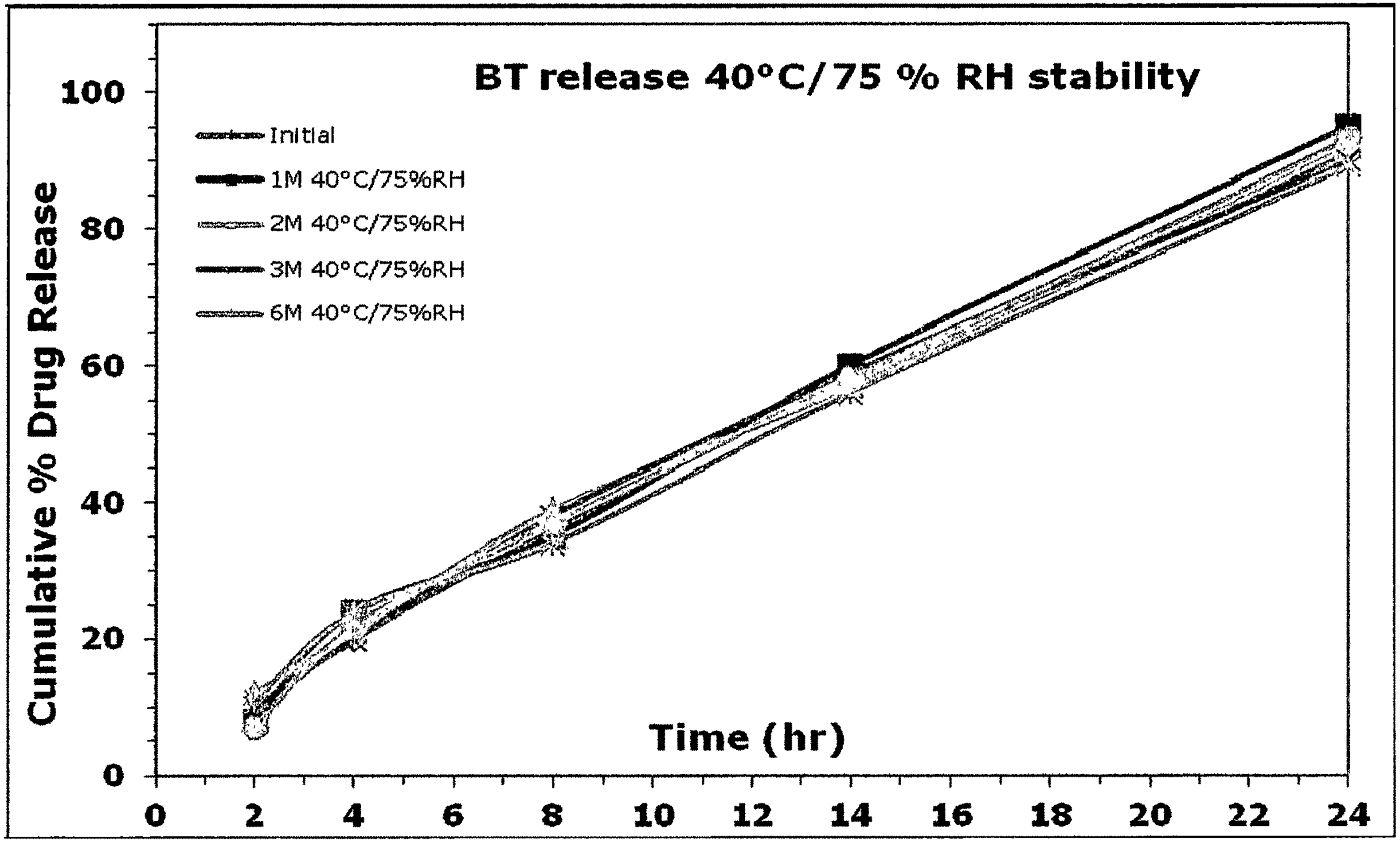

Figure 2 - 7 STABILITY GRAPH OF BUTORPHANOL TARTARATE ER TABLETS 40°C/75%RH

STABILITY DATA OF LORNOXICAM EXTENDED RELEASE TABLETS:

Stability condition	Specifications	Description	(%) Assay	Avereage weight	% Drug Dissolved				Water Content	F2 (With Respect to initial)
					2 Hr	4 Hr	8 Hr	12 Hr		
	Pack Style		95.00 to 105 %	180 ± 3%	NMT 40%	40 to 60%	70-80%	NLT 85	NMT 5%	
Initial	HDPE Bottle	Yellow colored, circular, biconvex, film coated tablet, plain on both side	100.2	181.83mg	29.7	49.70	77.20	95.40	2.4	
1M 40°C/75%RH	HDPE Bottle	Complies	99.8	180.64mg	32.1	53.2	75.3	92.8	2.7	80
2M 40°C/75%RH	HDPE Bottle	Complies	99.4	182.9mg	26.4	50.9	78.1	94.2	2.6	81
3M 40°C/75%RH	HDPE Bottle	Complies	100.9	178.6mh	28.6	54.3	75.2	95.1	2.4	80
6M 40°C/75%RH	HDPE Bottle	Complies	99.8	183.62mg	29.7	52.1	76.1	92.2	3.2	84

Table 6 -7 STABILITY DATA OF LORNOXICAM ER TABLETS 40°C/75%RH

Stability condition	Specifications	Description	(%) Assay	Avereage weight	% Drug Dissolved				Water Content	F2 (With Respect to initial)
					2 Hr	4 Hr	8 Hr	12 Hr		
	Pack Style		95.00 to 105 %	180 ± 3%	NMT 40%	40 to 60%	70-80%	NLT 85	NMT 5%	
3M 25°C/60%RH	HDPE Bottle	Complies	100.6	182.87mg	28.1	48.1	74.3	96.2	2.5	82
6M 25°C/60%RH	HDPE Bottle	Complies	99.5	180.94mg	31.7	52.1	77.7	94.5	2.6	86
9M 25°C/60%RH	HDPE Bottle	Complies	98.9	184.35mg	30.3	52.8	76.5	92.3	3.0	81
12M 25°C/60%RH	HDPE Bottle	Complies	99.6	185.82mg	34.1	54.4	76.9	94.4	2.9	76

Table 7 - 7 STABILITY DATA OF LORNOXICAM ER TABLETS 25°C/60%RH

Table 6-7 and 6-7 respectively shows stability data up to for LOR 6M 40°C/75%RH and 12M 25°C/60%RH. Figure 3-7 and 4-7 respectively shows stability data up to 12M 25°C/60%RH and 6M 40°C/75%RH.

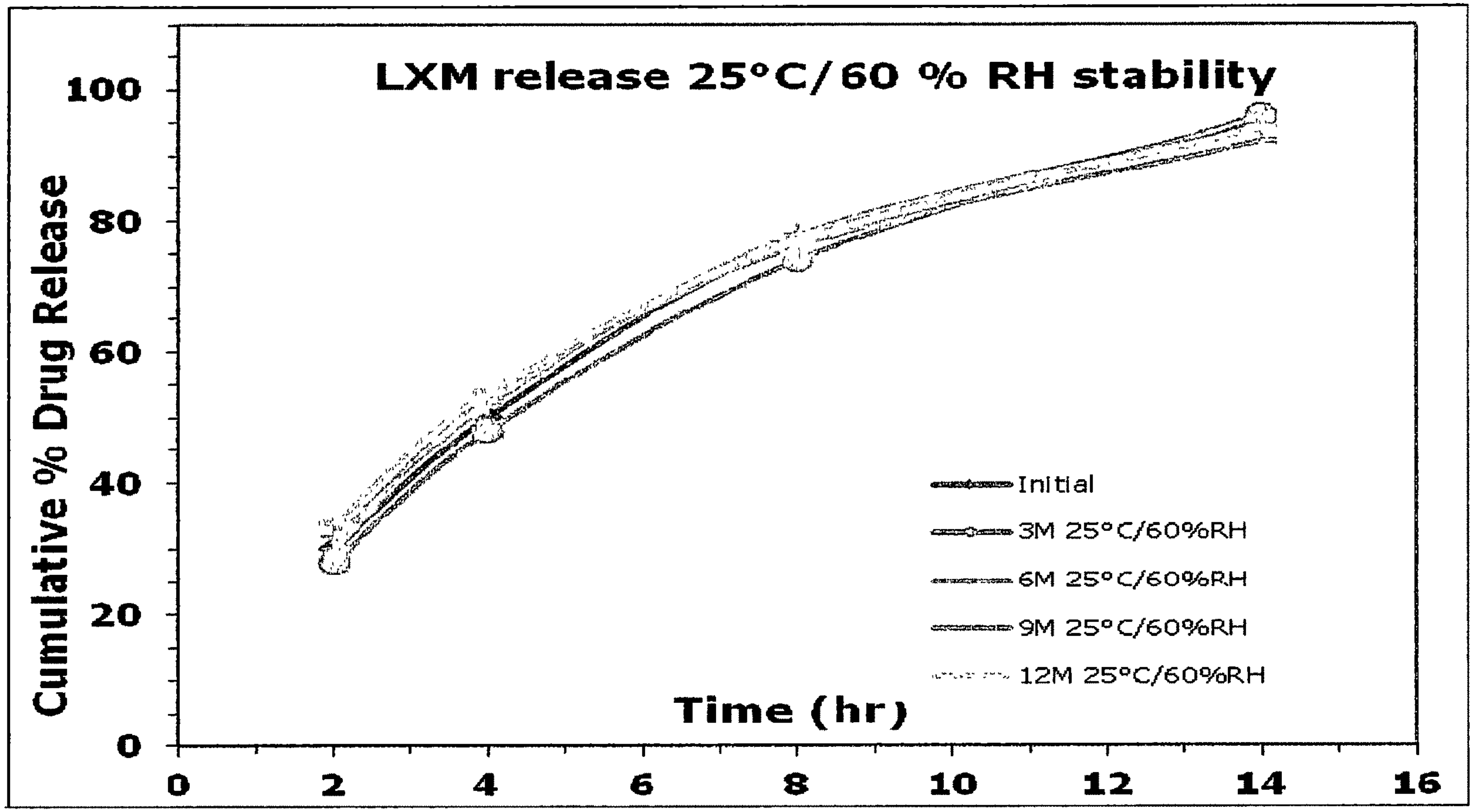

Figure 3 - 7 STABILITY GRAPH OF LORNOXICAM ER TABLETS 25°C/60%RH

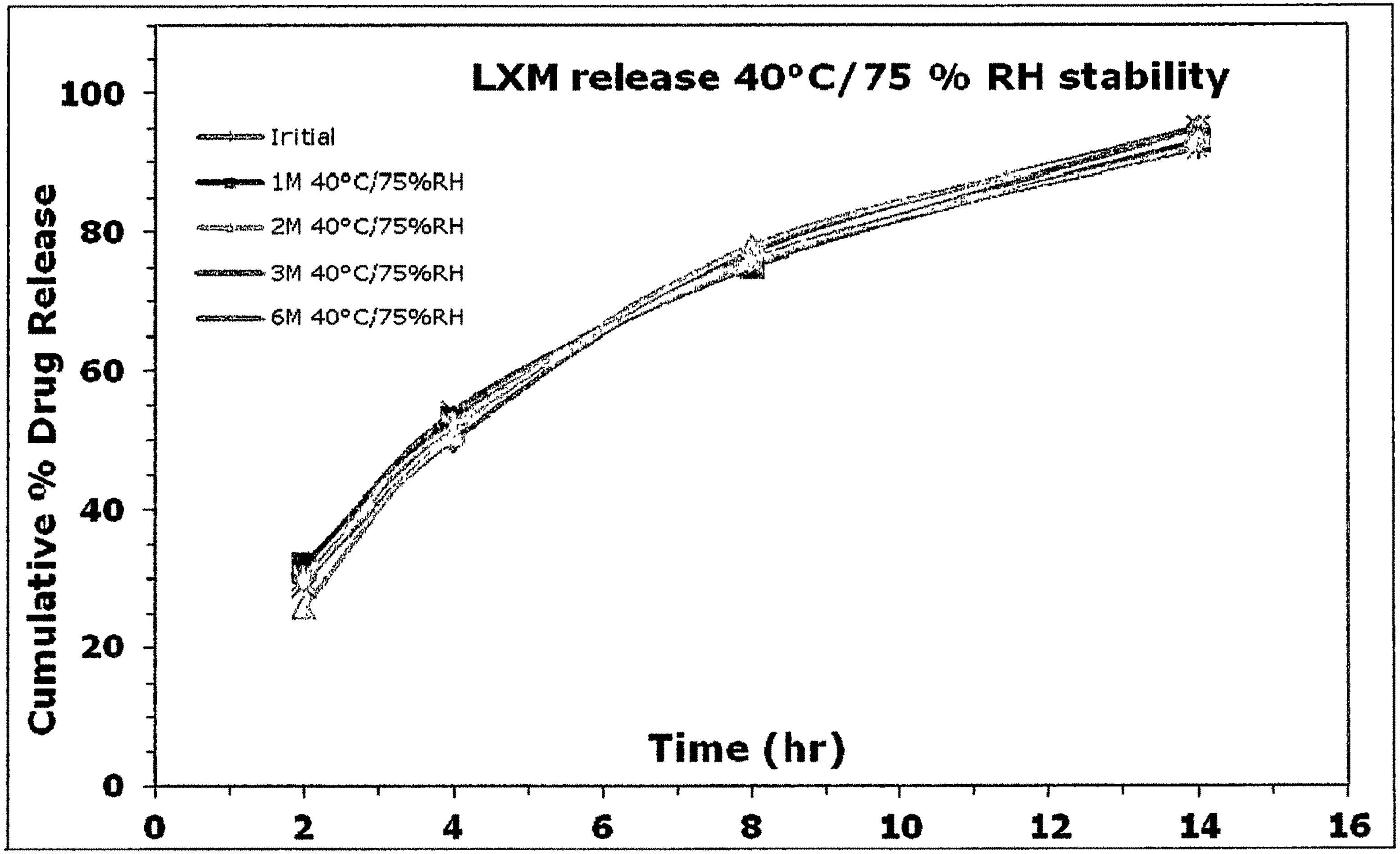

Figure 4 - 7 STABILITY GRAPH OF LORNOXICAM ER TABLETS 40°C/75%RH

7.6 Discussion

During and after the completion of the stability studies, all the studied parameters like description, assay, water by KF, average weight were found to be within the predefined limits. It was also observed that the drug release studies showed no significant change in the dissolution (with respect to the initial dissolution). The graphs of the dissolution studies are depicted in the figure No 1-7,2-7,3-7,4-7. The dissolution studies were compared using the similarity factor (f2). The f2 values > 50 clearly indicate a similar dissolution profile as compared to the initial drug release.

7.7 Conclusion:

It can be concluded from the results of accelerated and long term stability studies that the optimized formulations were found to be stable and consistent in terms of all the studied parameters. Henceforth, the optimized formulations could provide a minimum shelf life of one year

7.8 References:

- "Developing Solid Oral Dosage FormsPharmaceutical : Theory and Practice" Elsevier Publication 2009 Edited by David LeBlond "Statistical Design and Analysis of Long-term Stability Studies for Drug Products"
- ICH Q1C. (1997).Stability Testing for New Dosage Forms, May.
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