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Development and Stability Indicating Rp-Hplc Method for Estimation of Lactitol in Api Form

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ABSTRACT
A simple, rapid, precise, economical & accurate stability indicating RP-HPLC method for the estimation of lactitol in APL form. .High performance in liquid chromatographic. The separation was achieved by C_{18} (250 x 4.6mm, 5µ) column and buffer (PH 8.5) : Try – acetate buffer 8.5 – ACN (40:60) as mobile phase, flow rate of 1.0 ml / minute. Detection is carried out 343 nano meter. The drug was subjected to forced degradation condition of acid degradation, base degradation, oxidation degradation, photo degradation and thermal degradation. It can be applied in routine analysis and pharmaceutical dosage forms . It can be applied in commercial pharmaceutical dosage forms. The ICH guidelines applicable for forced degradation studies are ICH Q1A, Q1B, Q2B.
KEYWORDS: Lactitol, Stability indicating RP-HPLC method and validation

I. INTRODUCTION

A condition where stool becomes hard, dry, and difficult to pass and bowel movements don't happen frequently.. Other symptoms may include painful bowel movements, and feeling bloated, uncomfortable, and sluggish.There are main two types of constipation Type 1 Primary constipation Type 2 Secondary constipation
Primary constipation occurs without any clear cause. Secondary constipation occurs as a result of lifestyle factors or an underlying illness.

Normal transit constipation

Normal transit constipation is a condition, in which a person discern to be constipated, but the consistency of these stools is normal, and the stools move through the digestive tract at a regular pace. People with normal transit constipation experience symptoms such as abdominal bloating and pain.

Slow transit constipation

People with slow transit constipation do not experience the normal stimulation of the bowels, called peristalsis. .Therefore, food moves through the digestive tract more slowly than usual, and stools take longer to pass through the colon.
As stool sits in the intestines for longer, the person have less frequent bowel movements.

Outlet constipation

Outlet constipation occurs with a damage to the pelvic floor muscles. These muscles support the bowel and bladder, as well as the uterus in females. This damage can occur for various reasons, including pregnancy and childbirth.

Common Signs and Symptoms of Constipation are as follows:

- Less than three bowel movements in a week
- Dry, hard, or lumpy stools

Treatment

- Take a fiber supplement
- Eat a serving of high-fiber food

The aim of the stabilization studies is the pathway of improvements to a substance over period of time under various storage conditions. The factors and parameters that result the stability are production timeframe, batch factors along with process parameters, excipients efficiency, and environmental conditions like temperature and humidity

The appropriate deteriorated samples for method production assistance is a major challenge when designing a stability indicator method (SIM). Such deteriorated samples in an environment must be real-time stability samples containing all applicable degradant as well as those degradant develop during ordinary storage conditions.. Many experiments have explored the potential of forced deterioration studies to predict real-time degradation

The precision of the stability methods reveal potential impurities of the drug material and of drug components by forced degradation (FD).

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Stress experiments is to generate impurities in a much shorter period.

GMP includes a structured written monitoring program for stability, in which the results can be used to specify the storage requirements, the expiry dates and the use of accurate, meaningful and precise test procedures. If an effort is made to essay drug product stability, the use of such approaches is acceptable. The data are used to assess, expiration date for the drug substance

The rationale of the stability studies research provide data as to how the consistency of the substance varies over a period of time under the control of array of environmental variables, such as humidity, temperature and light, allows the anticipated storage conditions, and shelf life

The types of forced degradation substance include:
1. Acid degradation
2. Base degradation
3. Oxidation degradation
4. Photo degradation
5. Thermal degradation

II. MATERIAL AND METHODS

1. Acid degradation:

Acid decomposition studies were performed by transferring one ml of stock solution in to 10 ml of volumetric flask. Two ml of 1m HCl solutions was added and mixed well and put for 90 minute at 60 degree. After time period two ml of 0.1m NaOH Added to neutralize the solution and make up the volume with diluent to get 20µg/ml for Lactitol.

2. Base degradation:

Base decomposition studies were performed by transferring one ml of stock solution in to 10 ml of volumetric flask. Two ml of 1n NaOH solutions was added and mixed well and put for 120 minute at 60 degree. After time period two ml of 0.1 N HCl Added to neutralize the solution and make up the volume with diluent to get 20µg/ml for Lactitol.

3. Oxidation degradation:

Oxidation decomposition studies were performed by transferring one ml of stock solution in to 10 ml of volumetric flask. Two ml of 6% H_2O_2 solutions was added and mixed well and put for 50^0C at 60 minutes. After time period make up the volume with diluent to get 20µg/ml for Lactitol.

4. Photo degradation:

Photo decomposition studies were performed by transferring one ml of stock solution in to 10 ml of volumetric flask. Volumetric flask was kept in UV Chamber for 2hrs. After time period make up the volume with diluent to get 20µg/ml for Lactitol.

5. Thermal degradation:

20 mg of Lactitol was taken in 100ml Volumetric flask and put in oven for 2 hrs at 80^0C at 120 minutes. Then after Volumetric flask was removed and cools at room temperature, volume was made up with mobile phase, 1ml of this solution was transferred in 10ml volumetric and volume was made up with Diluents to get 20µg/ml for Lactitol.

III. EXPERIMENTAL WORK

1. Acid Degradation: Lactitol of Acid Degradation Blank is shown in **Figure 1**& Lactitol of Acid Degradation Std. shown in **Figure 2.**

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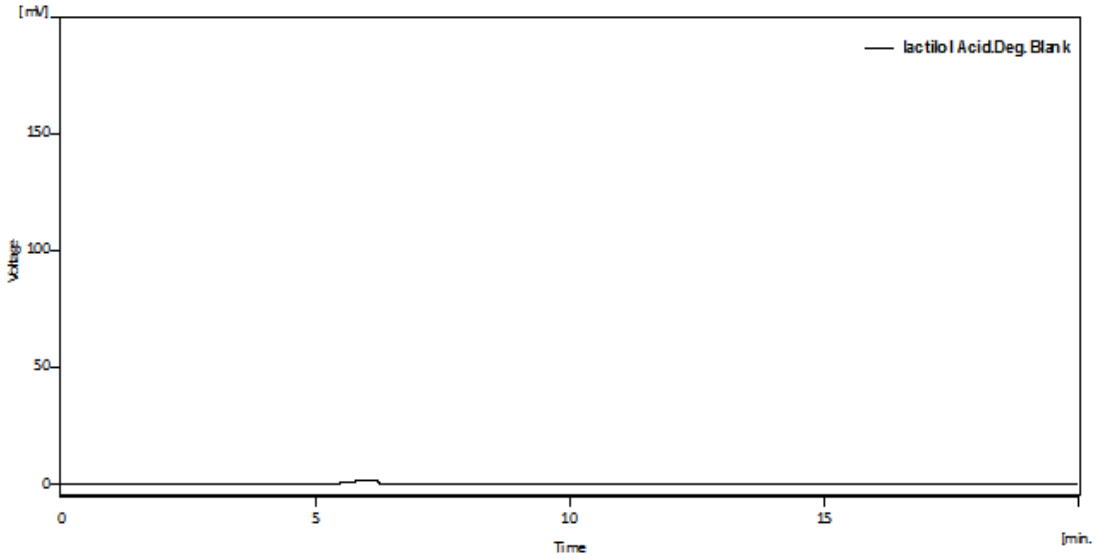

FIGURE 1 : LACTITOL ACID DEGRADATION OF BLANK

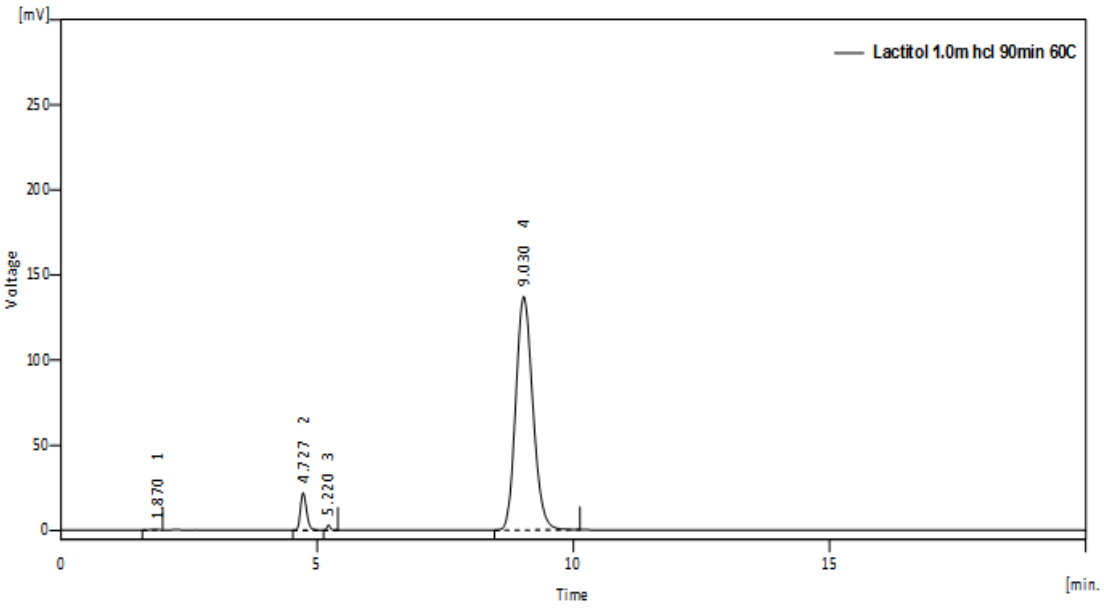

FIGURE 2: CHROMOTOGRAPHY OF ACID DEGRADATION

Column performance Table (from 50% - lactitol 1.0 m hcl 90 minute 60C)

No.	Reten.Time [Min.]	Asymmetry[-]	Efficiency[th.pl]	Resolution [-]
1.	1.870	0.356	2073	-
2.	4.727	1.323	6962	14.617
3.	5.220	1.235	30807	2.855
4.	9.030	1.258	3486	10.428

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2. Base Degradation: Lactitol of Base Degradation Blank is shown in **Figure 3** & Lactitol of Base Degradation Std. shown in **Figure 4**

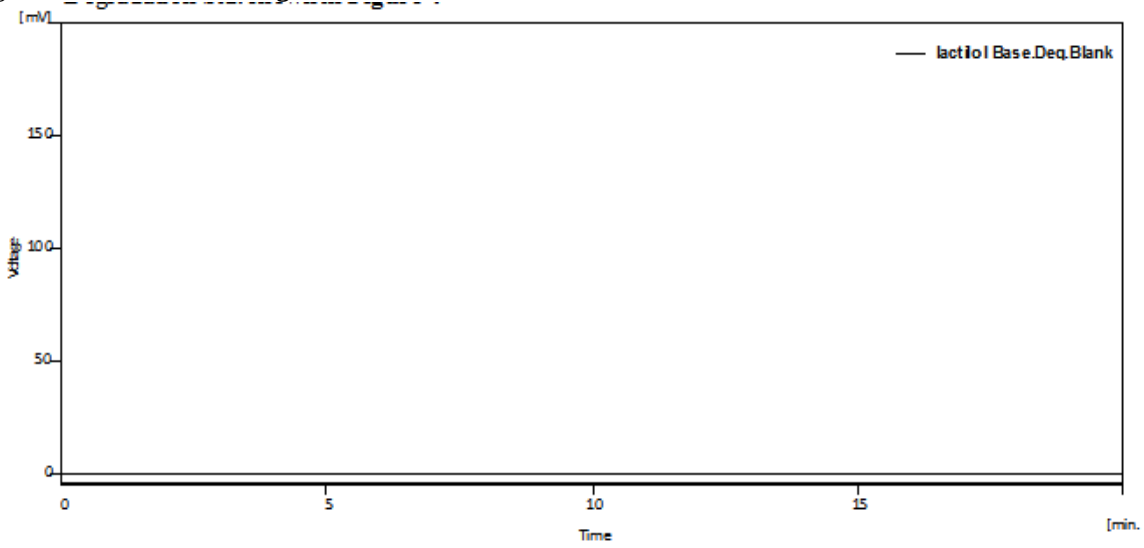

FIGURE 3: LACTITOL OF BASE DEG. BLANK

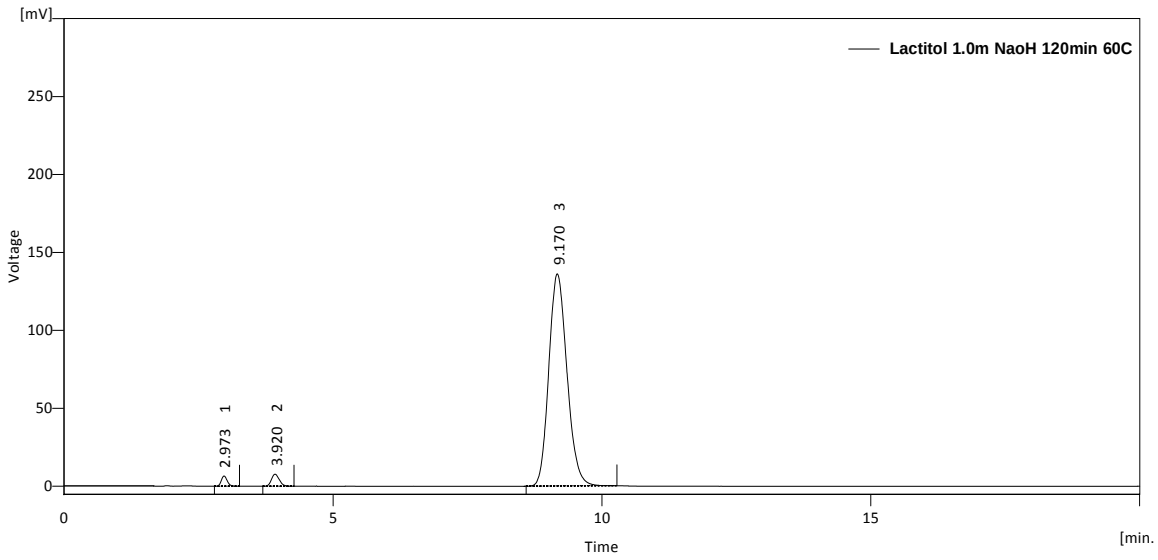

FIGURE 4: CHROMOTOGRAPHY OF BASE DEG.

Column performance Table (from 50% - lactitol 1.0 m NaoH 120 minute 60C)

No.	Reten.Time [Min.]	Asymmetry[-]	Efficiency[th.pl]	Resolution [-]
1.	2.973	1.233	3401	-
2.	3.920	1.256	3468	4.027
3.	9.170	1.253	3465	11.806

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3. Oxidation degradation: Lactitol of Oxidation Degradation Blank is shown in **Figure 5** & Lactitol of Oxidation Degradation Std. shown in **Figure 6**

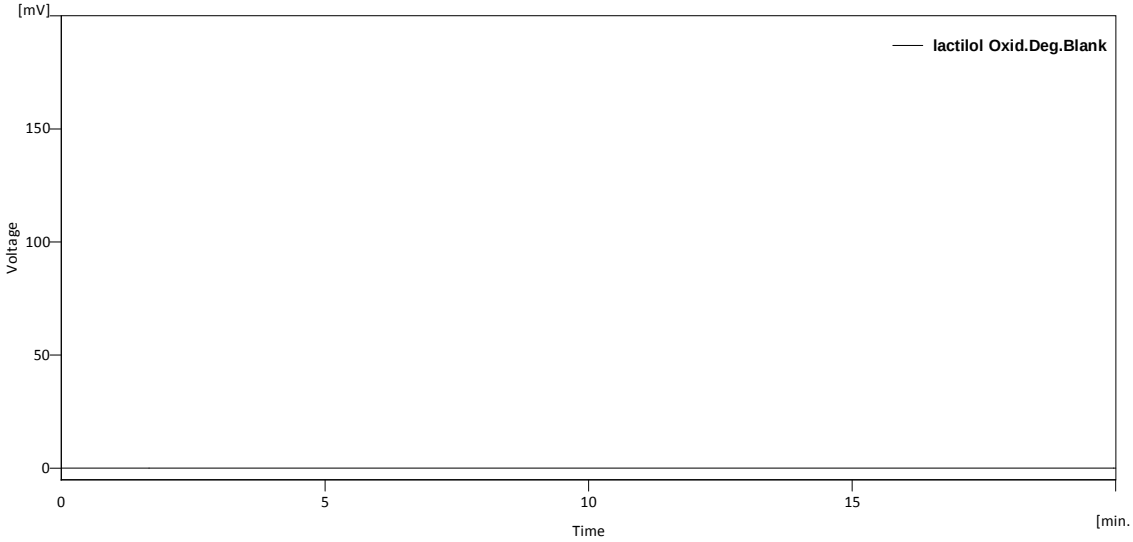

FIGURE 5: LACTITOL OF OXID. DEG.BLANK

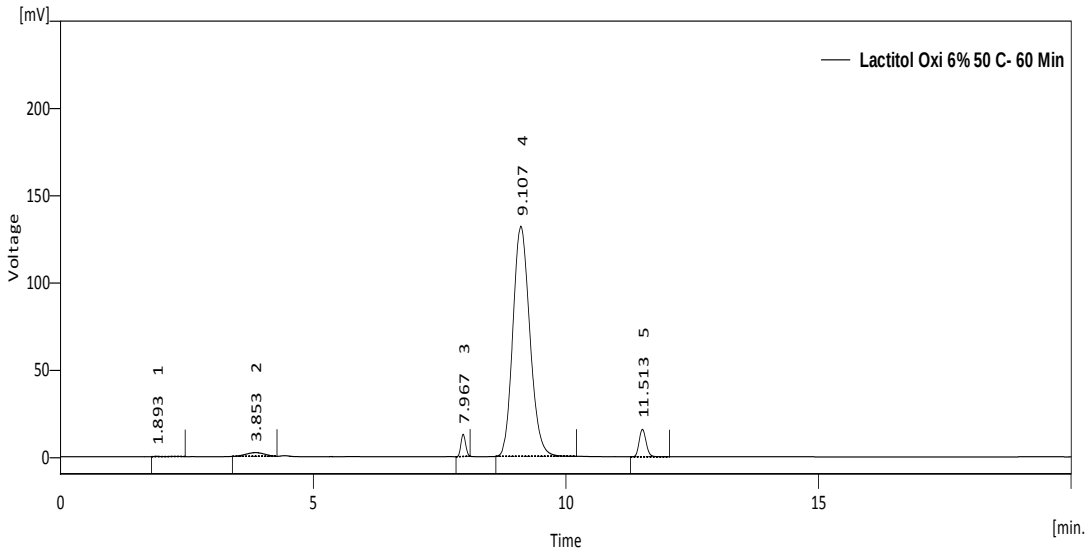

FIGURE 6: CHROMOTOGRAPHY OF OXIDATION DEGRADATION

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Column performance Table (from 50% - lactitol Oxi 6% 50C -60 Min)

No.	Reten.Time [Min.]	Asymmetry[-]	Efficiency[th.pl]	Resolution [-]
1.	1.893	7.714	1986	-
2.	3.853	0.936	466	4.436
3.	7.967	1.154	32929	9.250
4.	9.107	1.256	3480	2.875
5.	11.513	1.243	32638	5.517
6.	28.393	1.209	32624	38.203
7.	45.110	1.231	33130	20.636

4. Photo degradation: Lactitol of Photo Degradation Blank is shown in **Figure 7** & Lactitol of Photo Degradation Std. shown in **Figure 8**

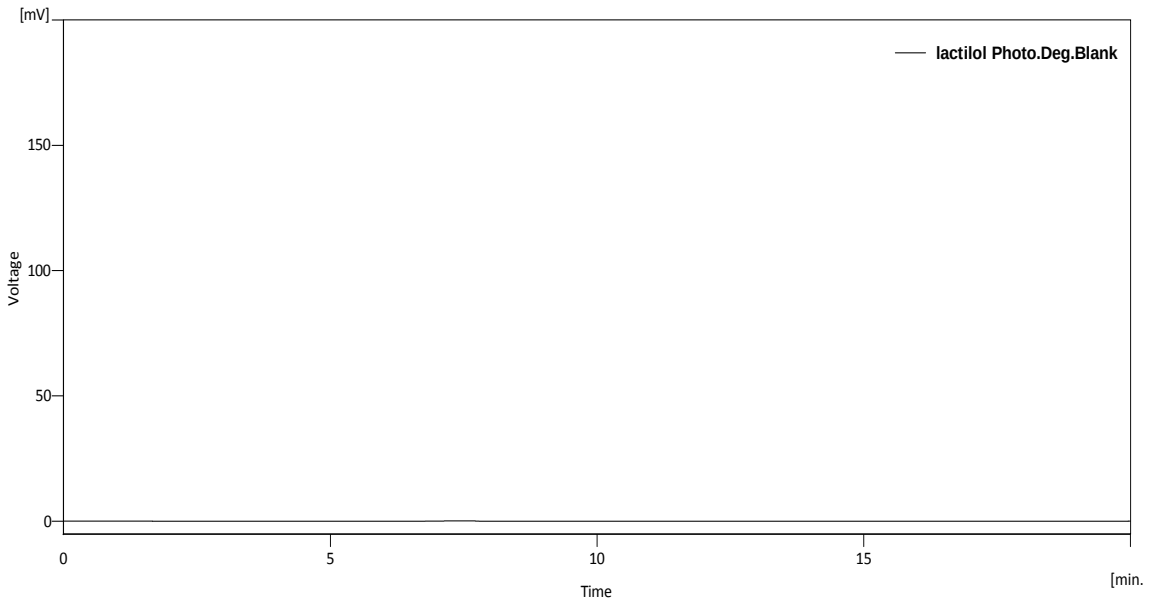

FIGURE 7: LACTITOL OF PHOTO DEG. BLANK

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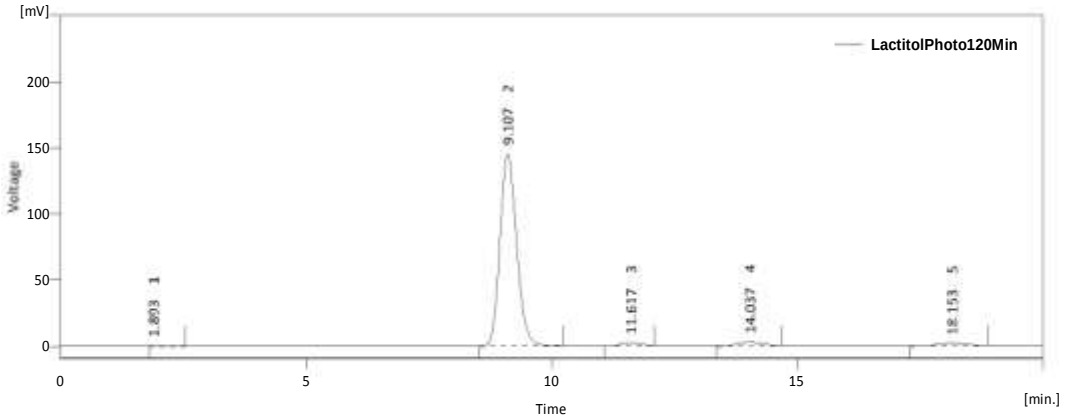

FIGURE 8: CHROMOTOGRAPHY OF PHOTO DEG.

Column performance Table (from 50% - lactitol Photo 120 Min Min)

No.	Reten.Time [Min.]	Asymmetry[-]	Efficiency[th.pl]	Resolution [-]
1.	1.893	8.286	1986	-
2.	9.107	1.267	3480	18.322
3.	11.617	1.101	3862	3.677
4.	14.037	1.140	3697	2.896
5.	18.153	1.064	3872	3.939

5. Thermal Degradation: Lactitol of Thermal Degradation Blank is shown in **Figure 9 &** Lactitol of Thermal Degradation Std. shown in **Figure 10.**

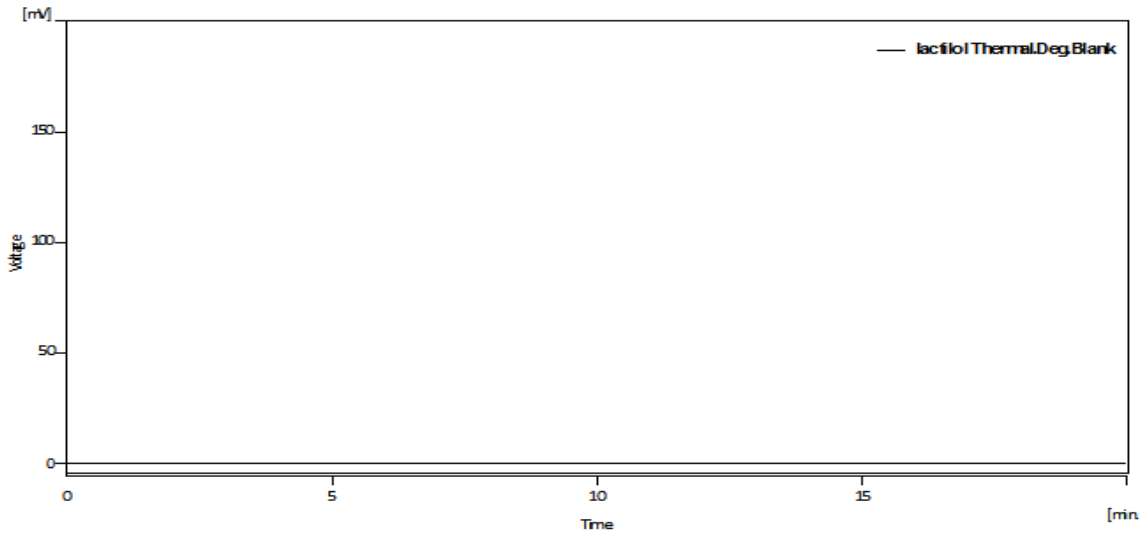

FIGURE 9: LACTITOL THERMAL DEG. BLANK

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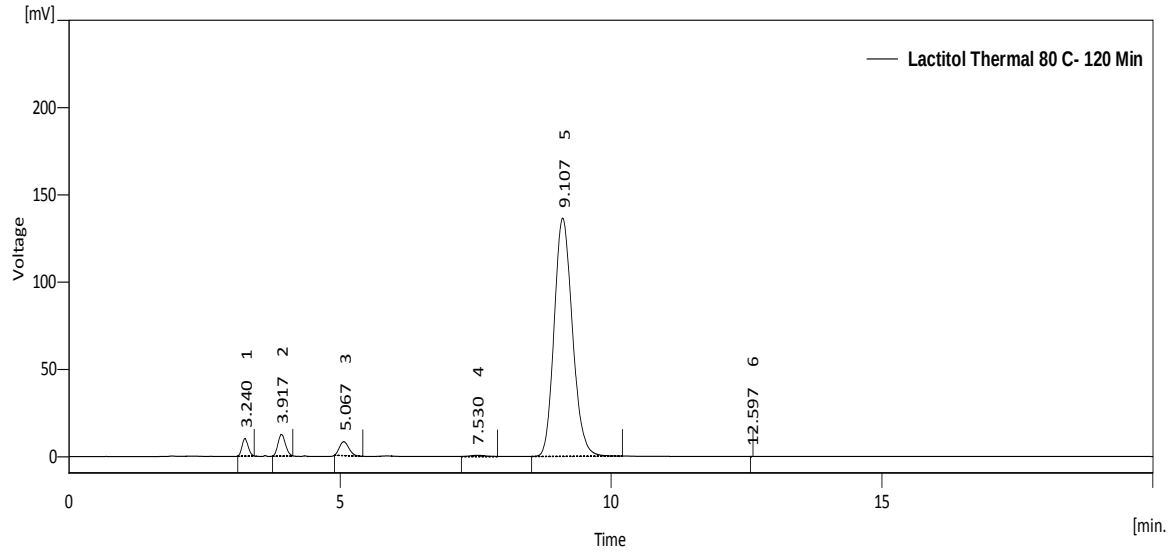

FIGURE 10: CHROMOTOGRAPHY OF THERMAL DEG.

Column performance Table (from 50% - lactitol Thermal 80C-120 Min)

No.	Reten.Time [Min.]	Asymmetry[-]	Efficiency[th.pl]	Resolution [-]
1.	3.240	1.267	3441	-
2.	3.917	1.211	3615	2.811
3.	5.067	1.311	3805	3.904
4.	7.530	1.214	3651	5.957
5.	9.107	1.256	3480	2.826
6.	12.597	0.857	976739	10.442

IV. RESULT:

1. Acid Degradation:

Table 1: (Uncal – lactitol 1.0 m hcl 90 min. 60C)

No.	Reten.Time [Min.]	Area[mV.s]	Area [%]	Height [mV]
1.	1.870	2.706	0.1	0.297
2.	4.727	182.284	5.4	21.998
3.	5.220	12.892	0.4	2.968
4.	9.030	3176.606	94.1	137.154
	Total	**3374.487**	**100**	**162.417**

2. Base Degradation:

Table 2 : (Uncal-lactitol 1.0 m NaoH 120 minute 60C)

No.	Reten.Time [Min.]	Area[mV.s]	Area[%]	Height[mV]
1.	2.973	50.244	1.5	6.595
2.	3.920	77.629	2.3	7.737

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3.	9.170	3202.418	96.2	136.162
	Total	**3330.291**	**100.0**	**150.493**

3. Oxidation Degradation:

Table 3: (Uncal-lactitol Oxi 6% 50C -60 Min)

No.	Reten.Time [Min.]	Area[mV.s]	Area[%]	Height[mV]
1.	1.893	4.402	0.1	0.284
2.	3.853	54.380	1.4	2.122
3.	7.967	81.525	2.1	12.677
4.	9.107	3075.696	79.7	131.895
5.	11.513	150.191	3.9	15.666
6.	28.393	215.563	5.6	9.187
7.	45.110	277.137	7.2	7.428
	Total	**3858.894**	**100**	**179.259**

4. Photo Degradation:

Table 4: (Uncal-lactitol Photo 120 Min)

No.	Reten.Time [Min.]	Area[mV.s]	Area[%]	Height[mV]
1.	1.893	5.692	0.2	0.323
2.	9.107	3398.202	93.1	145.483
3.	11.617	63.416	1.7	2.339
4.	14.037	101.485	2.8	2.988
5.	18.153	82.028	2.2	1.946
	Total	**3650.913**	**100**	**153.078**

5. Thermal Degradation:

Table 5: (Uncal-lactitol Thermal 80C-120 Min)

No.	Reten.Time [Min.]	Area[mV.s]	Area[%]	Height[mV]
1.	3.240	77.582	2.2	9.814
2.	3.917	117.406	3.4	12.243
3.	5.067	96.718	2.8	7.979
4.	7.530	12.001	0.3	0.663
5.	9.107	3187.947	91.3	136.486
6.	12.597	0.002	4.481e-05	0.001
	Total	**3491.654**	**100.0**	**167.186**

V. CONCLUSION:

Forced degradation studies give knowledge on possible degradation pathways and degradation products of the API and help explain the structure of the degradants. Degradation products cause from forced degradation studies are helpful possible degradation products which may or may not be applicable under storage conditions but they help in the developing stability indicating method. It helps in drug development process and the stability of the molecule. This information will further help improve the formulation manufacturing process and access to storage conditions.The aim of strategy used for forced degradation is to create the required amount of degradation i.e., 5–20%. A properly planned and performed forced degradation study is used to generate proper sample for development of stability indicating method.

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