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Development and Validation of Stabilityindicating RP-HPLC Method for Estimation of Capmatinibinapiform

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ABSTRACT
A simple, rapid, precise, economical & accurate stability indicating RP-HPLC method for the estimationof Capmatinib in API form. .High performance in liquid chromatographic. The separation was achieved byC18 (250 x 4.6mm, 5µ) column and buffer (PH 6.5) : MeoH (60:40) as mobilephase, flow rateof 1.0 ml / minute. Detection is carried out at 231 nanometer. The drug was subjected toforceddegradationconditionofaciddegradation,basedegradation,oxidationdegradation,photodegradation and thermal degradation. It can be applied in routine analysis and pharmaceutical dosageforms.Itcanbeappliedincommercialpharmaceuticaldosageforms.TheICHguidelinesapplicableforforceddegradationstudiesareICHQ1A,Q1B,Q2B.

KEYWORDS: Capmatinib,Stability, RP-HPLC, validation

I. INTRODUCTION

There are 2 main classifications of lung cancer: small cell lung cancer and non-small lung cancer (NSCLC). These 2 types are treated differently. NSCLC begins when healthy cells in the lung change and grow out of control, forming a mass called a tumour, a lesion, or a nodule. This can begin anywhere in the lung and the tumour can be cancerous or benign. When a cancerous lung tumour grows, it may shed cancer cells.

Types of non-small-cell lung cancer (NSCLC)
The different types of NSCLC are:
Adenocarcinoma
Squamous cell carcinoma
Large cell carcinoma

Capmatinib is used to treat a **certain type of non-small cell lung cancer** (NSCLC) that has spread to other parts of the body. Capmatinib is in a class of medications called kinase inhibitors. It works by blocking the action of an abnormal protein that signals cancer cells to multiply.Capmatinib is in a class of medications called **kinase inhibitors**.

It works by blocking the action of an abnormal protein that signals cancer cells to multiply. This helps slow or stop the spread of cancer cells.The mechanism of action of capmatinib is as a Mesenchymal Epithelial Transition Inhibitor, and Cytochrome P450 1A2 Inhibitor, and P-Glycoprotein Inhibitor, and Breast Cancer Resistance Protein Inhibitor, and Multidrug and Toxin Extrusion Transporter 1 Inhibitor, and Multidrug and Toxin Extrusion Transporter 2 K Inhibitor.

Sing Symptoms

Fatigue, Cough, Shortness of breath, Chest pain, if a tumor spreads to the lining of the lung or other parts of the body near the lungs, Loss of appetite, Coughing up phlegm or mucus, Coughing up blood, Unintentional weight loss, Horseness

Treatment

- There are 5 main ways to treat NSCLC:
- Surgery
- Radiation therapy
- Chemotherapy
- Targeted therapy and Immunotherapy

Theforceddegradationof anydrugsubstanceinclude:

1. Acid degradation
2. Base degradation
3. Oxidation degradation
4. Photo degradation
5. Thermal degradation

II. MATERIAL AND METHODS

1. Aciddegradation:

Aciddecomposition studies were performed by transferring one ml of stock solution in to 10 ml ofvolumetricflask.Twomlof0.1 NHClsolutionswasaddedandmixedwellandputfor2 hratRoom temperature. After time period two ml of 0.1m N NaOH Added to neutralize the solution and make up thevolumewithdiluenttoget20µg/mlforCapmatinib.

2. Basedegradation:

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Basedecomposition studies were performed by transferring one ml of stock solution in to10 ml ofvolumetricflask.Twoml of0.1 N NaOHsolutionswasaddedandmixedwell andputfor 2 hr at Room temperature . After time period two ml of 0.1 N HCl Added to neutralize the solution andmake up thevolumewithdiluenttoget20µg/mlforCapmatinibO xidationdegradation:
Oxidationdecompositionstudies wereperformedbytransferringonemlofstocksolutioni nto10mlof volumetric flask. Two ml of 3% H_2O_2 solutions was added and mixed well and put for 2 hr at room temperature.Aftertimeperiodmakeupthevolumewith diluenttoget20µg/mlforCapmatinib.

3. Photodegradation:

Photo decomposition studies were performed by transferring one ml of stock solution in to 10 ml ofvolumetric flask. Volumetric flask was kept in UV Chamber for 4 hrs. After time period make up thevolumewithdiluenttoget20µg/mlforCapmatinib.

4. Thermaldegradation:

20 mg of Capmatinib was taken in 100ml Volumetric flask and put in oven for 2 hrs at 80^0C temperature, Then after Volumetric flask was removed and cools at room temperature, volume was madeup with mobile phase, 1ml of this solution was transferred in 10ml volumetric and volume was madeupwithDiluentstoget20µg/mlforCapmatinib.

III. EXPERIMENTAL WORK

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

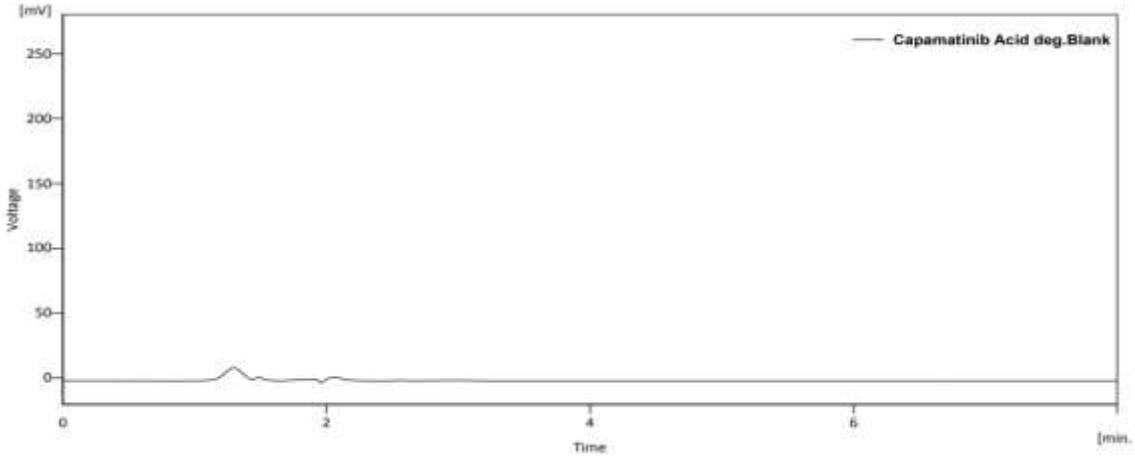

Figure 1: Capmatinib acid degradation of blank

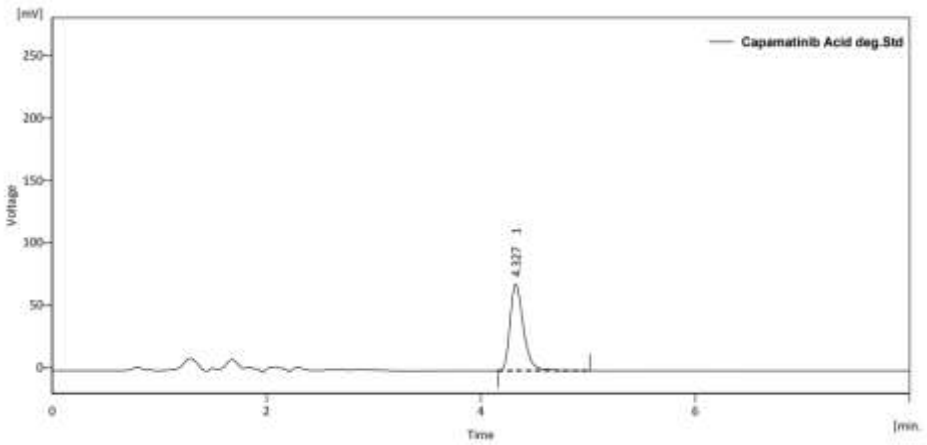

Figure 2: Capmatinib acid degradation of Standard

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ColumnperformanceTable(From 50%-Capmatinib Acid deg.std)

No.	Reten.Time [Min.]	Asymmetry[-]	Efficiency[th.pl]	Resolution [-]
1.	4.327	1.533	6173	-

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

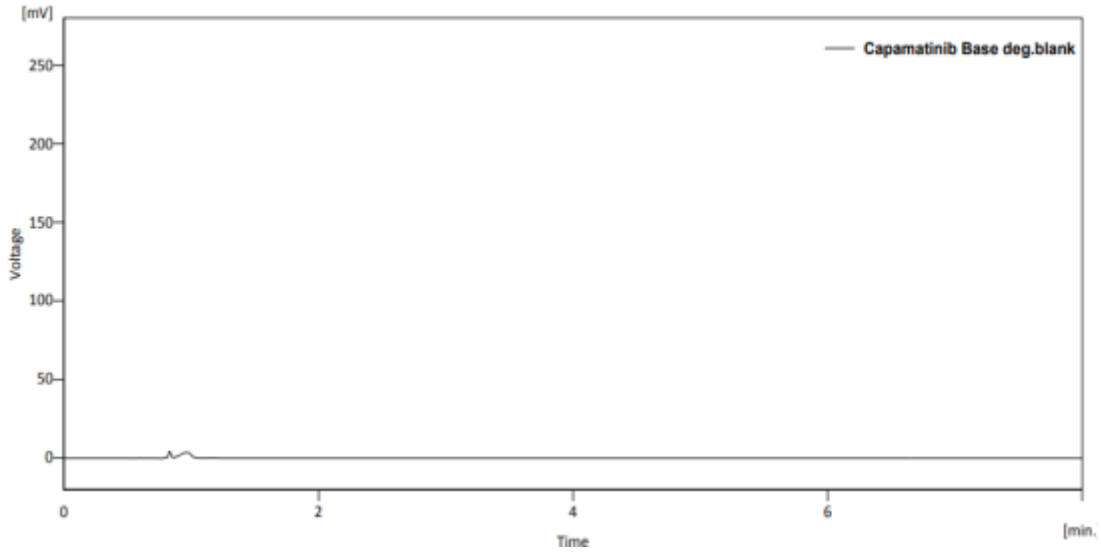

Figure 1:Capmatinib Of Base Deg. Blank

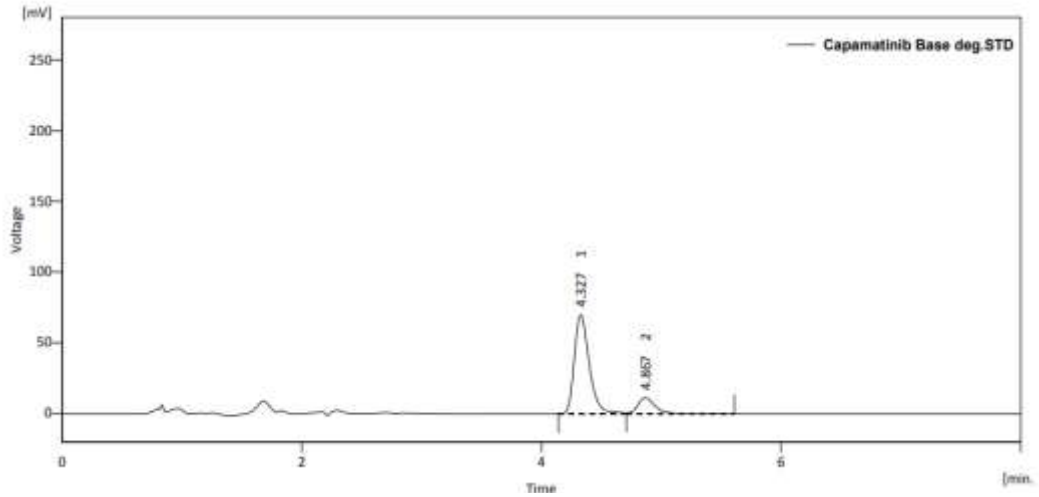

Figure 2: Capmatinib base degradation Standard

Column Performance Table (From 50%-Capmatinib Base deg.std)

	Retension Time (min)	Asymmentry (-)	Efficiency (th.pl)	Resolution (-)
1	4.327	1.533	5834	-
2	4.867	1.486	5832	2.243

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

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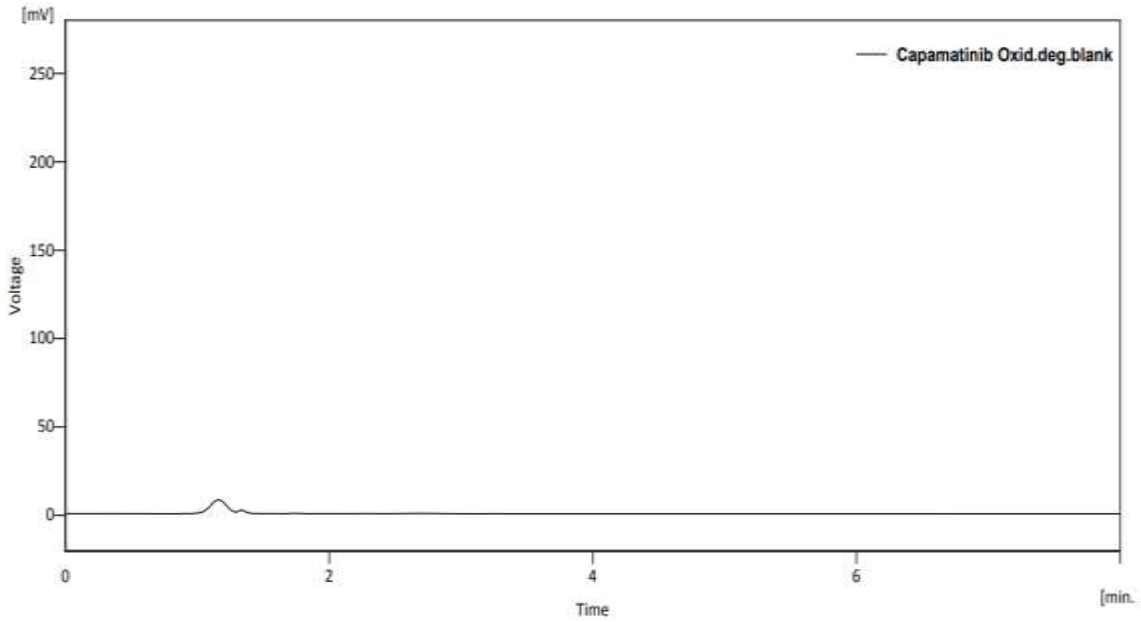

Figure 5:**Oxidation Degradation blank**

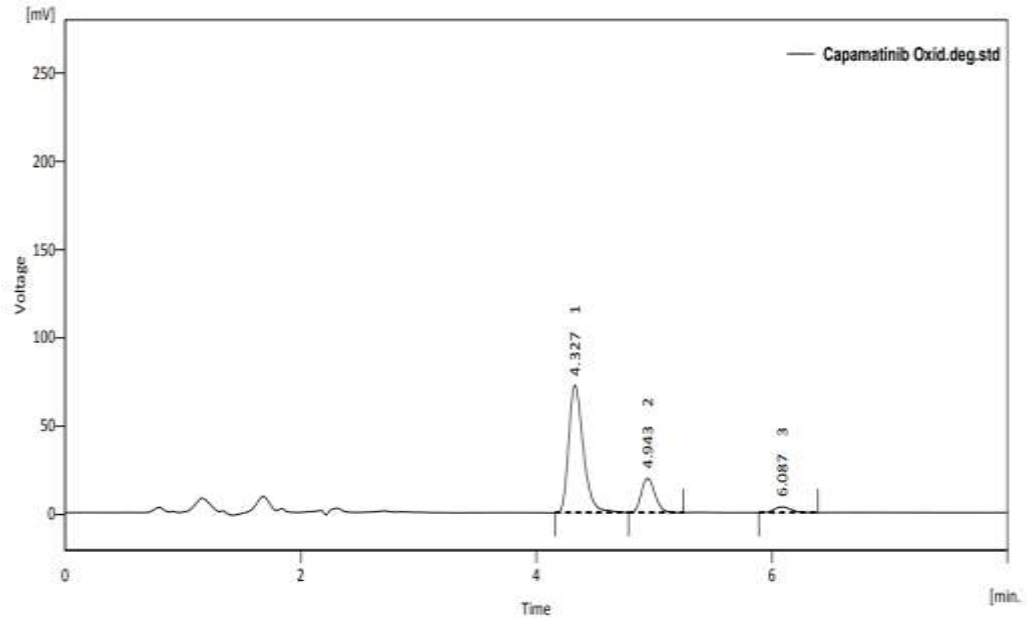

Figure 6 :Chromatogram of Oxidation Degradation Standard

Column Performance Table (From 50%-CapmatinibOxi.deg.std)

No.	Retension Time (min)	Asymmentry (-)	Efficiency (th.pl)	Resolution (-)
1	4.327	1.533	5834	-
2	4.943	1.333	8011	2.765
3	6.087	1.297	8362	4.694

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

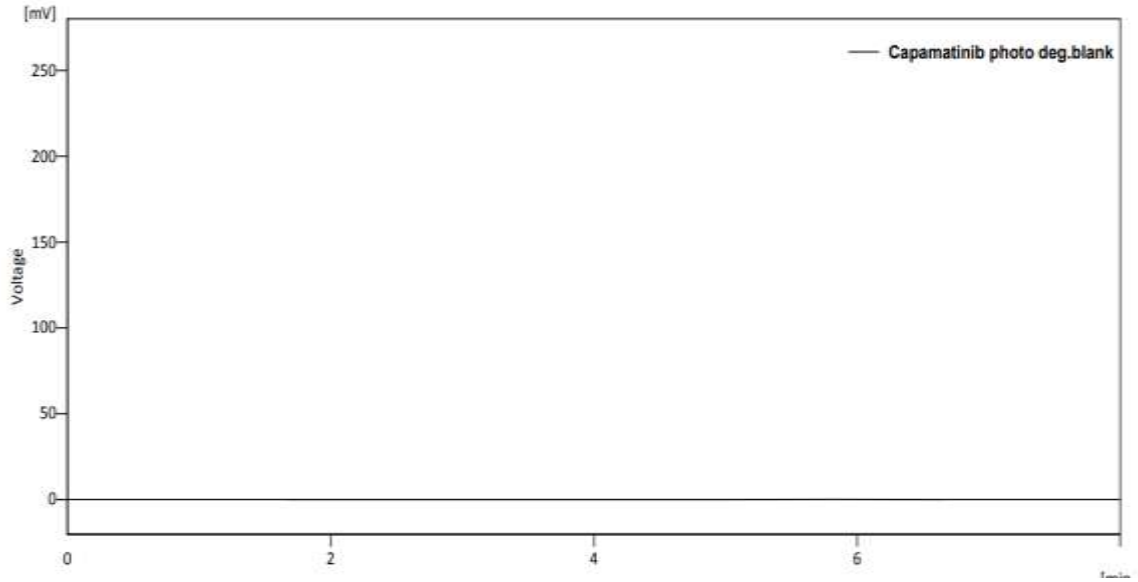

Figure 7: Chromatogram of Photo Degradation Blank

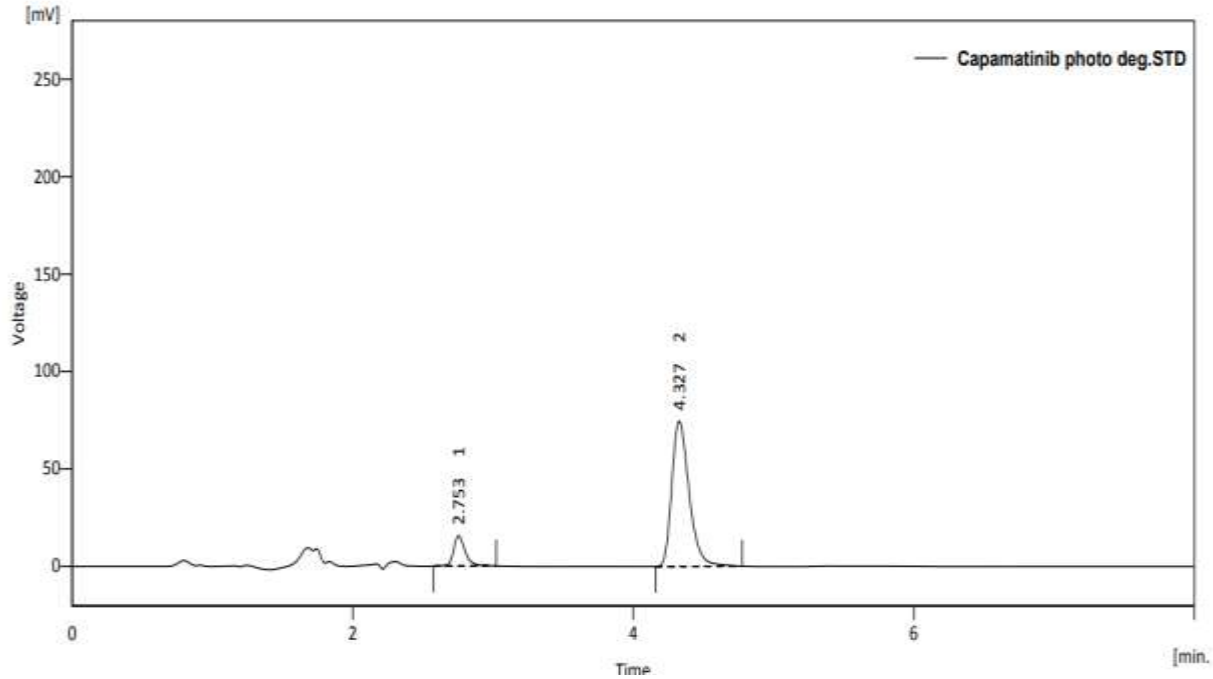

Figure 8: Chromatogram of Photo Degradation Standard

Column Performance Table (From 50%-Capmatinib Photo deg.std)

	Retension Time (min)	Asymmentry (-)	Efficiency (th.pl)	Resolution (-)
1	2.753	1.550	5591	-
2	4.327	1.533	5834	8.416

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

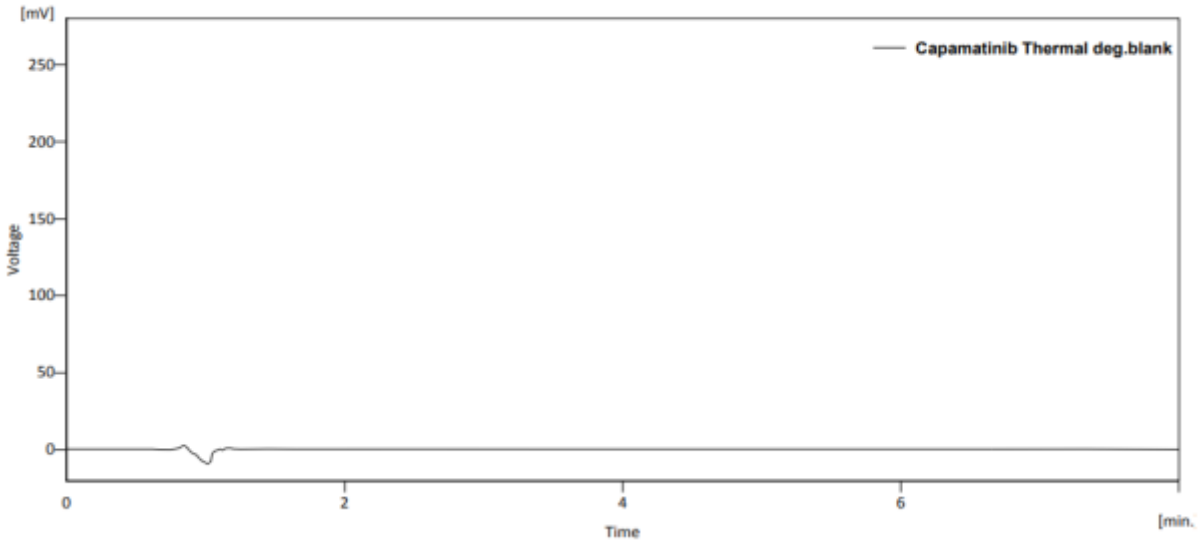

Figure 9: Chromatogram of Thermal Degradation Blank

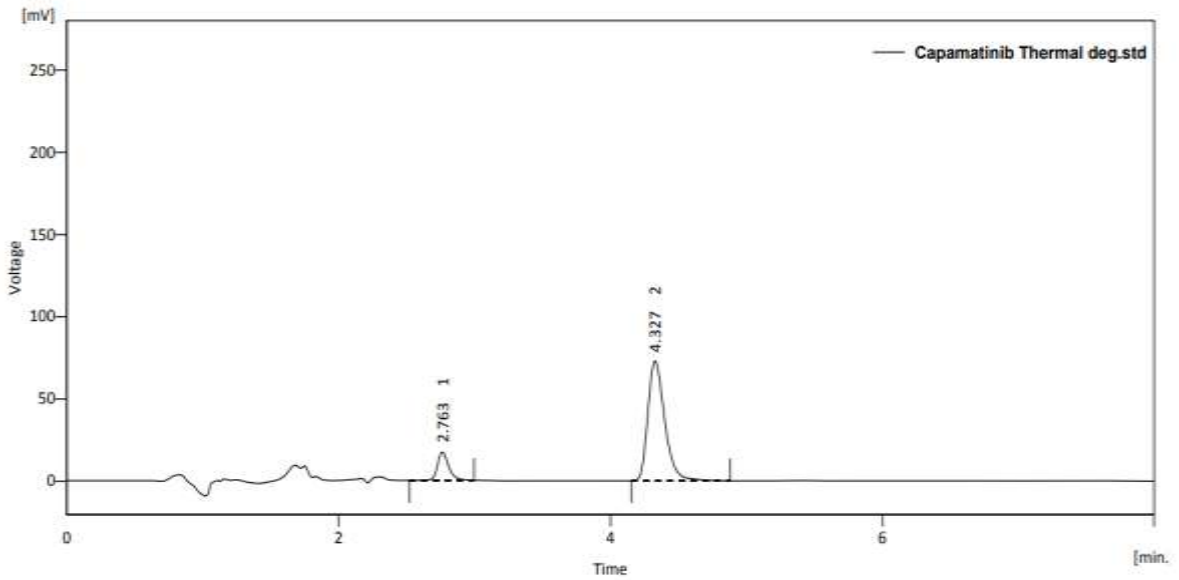

Figure 10: Chromatogram of Thermal Degradation Standard

Column Performance Table (From 50%-Capmatinib Thermal deg.std)

No.	Retension Time (min)	Asymmentry (-)	Efficiency (th.pl)	Resolution (-)
1	2.763	1.476	5632	-
2	4.327	1.533	5834	8.363

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IV. RESULT:

1. Acid Degradation:

Table 1: (Uncal – CapmatinibAcid degradation Std)

No.	Reten.Time [Min.]	Area[mV.s]	Area [%]	Height [mV]
1.	4.327	596.316	100.0	69.155
	Total	**596.316**	**100.0**	**69.155**

2. Base Degradation:

Table2 : (Uncal-CapmatinibBase degradation Std)

No.	Reten.Time [Min.]	Area[mV.s]	Area[%]	Height[mV]
1.	4.327	601.391	84.2	69.843
2.	4.327	112.482	15.8	11.279
	Total	**713.873**	**100.0**	**81.121**

3. Oxidation Degradation:

Table3: (Uncal-CapmatinibOxi.deg.Std)

No.	Reten.Time [Min.]	Area[mV.s]	Area[%]	Height[mV]
1.	4.327	621.441	76.7	72.106
2.	4.943	156.883	19.4	19.386
3.	6.087	32.046	4.0	3.271
	Total	**810.370**	**100.0**	**94.763**

4. Photo Degradation:

Table 4: (Uncal-Capmatinib Photo deg. Std)

No.	Reten.Time [Min.]	Area[mV.s]	Area[%]	Height[mV]
1.	2.753	88.640	12.1	15.539
2.	4.327	640.919	87.9	74.584
	Total	**729.558**	**100.0**	**90.123**

5. Thermal Degradation:

Table 5: (Uncal-Capmatinib Thermal deg.Std))

No.	Reten.Time [Min.]	Area[mV.s]	Area[%]	Height[mV]
1.	2.763	98.836	13.6	17.190
2.	4.327	628.178	86.4	72.867
	Total	**727.014**	**100.0**	**90.057**

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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