Forced Degradation Studies on Empagliflozin Tablets and Empagliflozin (Raw Material)

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Abstract: **The purpose of this research is to perform forced degradation of Empagliflozin. A forced degradation study of Empagliflozin (raw material and tablet-10 mg & 25mg) were carried out simultaneously. The drugs were subjected to various degradation conditions like acid degradation, base degradation, Oxidative degradation, thermal degradation, and photolytic degradation for 1,3,5 days. Force degradation studies was performed as per *ICH Guidelines, Q1A (R2), Stability testing of New Drugs Substances and products.* Percentage degradation was calculated by performing assay (amount of the drug) in each condition. A simple, accurate, validated, precise and sensitive analytical RP-HPLC method was selected for analysis of drug content. Both raw material and tablet were stable in the degradation study. But Degradation of raw material was slightly higher in comparison to dosage form. For raw material basic stress degraded highest amount of the drug. But 10mg Empagliflozin tablets degraded highest in photolytic stress & 25mg degraded highest amount of the drug in thermal condition. No sample degraded more than 15%. Hence from this study it can be concluded that both raw material and dosage form of Empagliflozin are physically and chemically stable for their shelf life.**

***Keywords*: Forced Degradation Studies, ICH Guidelines, Empagliflozin, Stress conditions.**

1. INTRODUCTION

There were more than 537 million people suffering from Diabetes mellitus in 2022, among which around 90% of cases is of type II Diabetes mellitus. [1] FDA guidelines and ICH guidelines emphasize need for stability testing data to comprehend the impact of environmental factors on the quality of Drug Substance **(DS)** and product over time. Understanding the stability of a molecule is crucial for making informed decisions regarding formulation, packaging, storage conditions, and shelf life. This knowledge is vital for regulatory documentation purposes. ICH along with WHO provide a set of guidelines **(ICH Q1A-E, Q3A-B, Q5C, Q6A-B)** to maintain the standards of the formulations and facilitate the mutual acceptance of stability data for all regulatory authorities across the globe. In general all the guidelines for stability study, the API and Drug Product **(DP)** are tested in different storage condition For example: - Temperature (thermal stability) and Relative Humidity (sensitivity to moisture). For long-term (real time) stability testing, it is recommended to conduct tests for a minimum of 12 months at 30°C ± 2°C with 75% RH ± 5% RH. While accelerated testing should be carried out for a minimum of 6 months at 40°C ± 2°C with 75% RH ± 5% RH. The stability testing requirements set by the ICH for industrially formulated medicines are comprehensive and demanding.[2] They involve a lengthy duration to gather preclinical stability data, making the process rigorous and time-consuming. Accelerated Predictive Stability (APS) studies involve conducting tests over a duration of 3-4 weeks, incorporating extreme temperature and relative humidity (RH) conditions ranging from 40 to 90°C and 10 to 90% RH. These studies aim to provide predictive insights into the long-term stability of pharmaceutical products within a relatively short timeframe. The aim of these stability study is to forecast the degradation kinetics and, consequently, determine the shelf life of the product. Force degradation studies are conducted to identify the majority of degradation products and their degradation reactions associated with an active pharmaceutical ingredient (API). The principal degradation mechanisms encountered in pharmaceuticals are oxidation, hydrolysis, thermal degradation, isomerization, and photolysis.[3] According to a draft guidance, it is recommended to include the results of one-time Force degradation studies in Phase 3 Investigational New Drug (IND) submissions. The registration process for a New Drug Application (NDA) necessitates the inclusion of Force degradation study data, which comprises information on Force degradation products, degradation reaction kinetics, structural elucidation, mass balance, and drug peak purity, among other factors. A Force degradation study offers valuable insights into the degradation pathways of the active pharmaceutical ingredient (API), both in isolation and within the DP. It can help identify potential polymorphic or enantiomeric substances that may arise during degradation. Additionally, the study aids in distinguishing between degradation of the drug itself and any interferences caused by excipients present in the formulation.[4]

Ensuring chemical stability is crucial for maintaining the desired safety and efficacy of pharmaceutical molecules. FDA and ICH guidelines emphasize the need for stability testing data to comprehend the impact of environmental factors on the quality of DS and product over time. Understanding the stability of a molecule is crucial for making informed decisions regarding formulation, packaging, storage conditions, and shelf life. This knowledge is vital for regulatory documentation purposes. Force degradation involves subjecting the novel DS and DP to conditions that are more intense and severe compared to accelerated conditions, leading to their degradation. It is essential for demonstration of specificity in stability indicating methods. It not only helps establish the method's ability to accurately measure the drug's stability but also provides valuable information regarding the pathways through which degradation occurs and the resulting degradation products. Furthermore, it aids in the identification and characterization of the degradation product structures. According to the ICH guideline, stress testing aims to identify potential degradation products, assess intrinsic stability, establish degradation pathways, and validate stability indicating procedures. [5] Although Force

degradation studies are both a regulatory requirement and a scientific necessity in the process of drug development, the current regulatory guidance offers valuable definitions and overall insights into degradation studies. However, when it comes to specific details regarding the scope, timing, and best practices for conducting degradation studies, the guidance tends to be quite general. Numerous guidance documents address various issues related to stress testing, but these may not always specifically focus on stress testing itself. The FDA and International Conference on Harmonization (ICH) guidance offer limited information regarding strategies and principles for conducting Force degradation studies, particularly when it comes to addressing challenges associated with poorly soluble drugs and exceptionally stable compounds. Specifically, the issue of determining the appropriate level of stress required for conducting stress testing is not explicitly addressed in the available guidance documents. Indeed, applying excessive stress during stress testing can result in degradation profiles that do not accurately represent real storage conditions and may not be relevant to method development. It is crucial to ensure that stress-testing conditions are realistic and not overly severe. In this context, the emphasis should be on the level of stress rather than the extent of degradation. It is worth noting that certain compounds may exhibit minimal degradation even after prolonged exposure to stress conditions.[6] The FDA and International Conference on Harmonization (ICH) guidance offer limited information regarding strategies and principles for conducting Force degradation studies, particularly when it comes to addressing challenges associated with poorly soluble drugs and exceptionally stable compounds. Specifically, the issue of determining the appropriate level of stress required for conducting stress testing is not explicitly addressed in the available guidance documents. Indeed, applying excessive stress during stress testing can result in degradation profiles that do not accurately represent real storage conditions and may not be relevant to method development. [7] It is crucial to ensure that stress-testing conditions are realistic and not overly severe. In this context, the emphasis should be on the level of stress rather than the extent of degradation. It is worth noting that certain compounds may exhibit minimal degradation even after prolonged exposure to stress conditions.[8]

1.1 OBJECTIVE

The purposes of conducting Force degradation studies encompass the following objectives.

- serves as a predictive tool to enable a comprehensive understanding of degradation pathways and stability-related concerns.
- Helps to predict the stability of the active pharmaceutical ingredient (API) in advance, even before real-time stability data becomes available.
- contributes to the development and validation of stability-indicating methodologies.
- Regulatory requirements.
- assists in distinguishing between degradation products that are associated with **DS**s and those that are linked to non-**DS**s, such as excipients, in formulations.
- facilitate the elucidation of the structures of degradation products formed during the degradation process.
- plays a vital role in determining the intrinsic stability of **DS**s.
- identifies the reactions that contribute to the degradation of pharmaceutical products.
- to generate a degradation profile that closely mimics what would be observed in a formal stability study conducted under International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) conditions.
- Generates stable formulation.
- Identifies impurities associated with both **DS**s and excipients.
- Provides valuable insights into the molecular chemistry of a drug.
- Contributes to the selection of appropriate storage conditions and packaging for pharmaceutical products.

1.2 REGULATORY OVERVIEW

The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) has released multiple guidelines that have been extensively deliberated, agreed upon, and adopted by regulatory authorities in the ICH regions, including the United States, Europe, and Japan. These guidelines serve as important reference documents for harmonizing regulatory requirements and facilitating global drug development and registration processes. When addressing the topic of "forced degradation," the majority of ICH guidelines emphasize the significance of conducting Force degradation studies. [10]

- **ICH Q1A – Stability Testing of New DSs and Products**
- **ICH Q1B – Photostability Testing of New DSs and Products**
- **ICH Q2B – Validation of Analytical Procedures: Methodology**
- **ICH Q3A – Impurities in New DSs**
- **ICH Q3B – Impurities in New Products**
- **M4Q(R1) – The common Technical Document (CTD): Quality**

1.3 TEST CONDITIONS OF STRESSES FOR FORCE DEGRADATION STUDIES

As per the current requirement of regulatory authorities Force degradation studies involve subjecting a pharmaceutical product and raw materials to a series of chemical and physical stress tests which are as follows:

1.3.1 Thermal stress test/ Thermal degradation
1.3.2 Photolytic degradation
1.3.3 Acid degradation
1.3.4 Base degradation
1.3.5 Oxidative degradation

1.3.1 Thermal Stress Test/Thermal Degradation

As per the guidelines outlined in ICH Q1A, it is advised to conduct stress degradation studies using conditions that are more rigorous than those employed and suggested for accelerated experimental testing conditions. Typically, thermal degradation studies are conducted within the temperature range of 40°C to 80°C. The temperature of 70°C, along with low and high humidity. However, temperatures higher than 80°C may not provide accurate predictions of the degradation pathway. To evaluate the extent of degradation, the drug solution can be subjected to wet heat for several hours. It is recommended to study the impact of temperature in increments of 10°C above the standard accelerated testing range, along with humidity levels of 75% relative humidity or higher..[17]

1.3.2 Photolytic degradation

Photostability testing is considered an important component of stress testing, particularly for drugs or **DP**s that are susceptible to light-induced degradation. It is essential to ensure that exposure to light does not cause any unacceptable changes in the **DS** or product. The ICH guidelines, specifically the ICH Q1B guideline, provide recommendations for conducting photolytic degradation testing. These guidelines suggest exposing samples to visible light under the following conditions:

- The total cumulative illumination should be at least 1.2 million lux hours.
- The integrated near ultraviolet energy should be a minimum of 200-watt hours per square meter, with a spectral distribution ranging from 320 to 400 nanometers. This range enables direct comparisons between the **DS** and **DP** to be made.[18]

1.3.3 Acid degradation

Hydrolytic stress testing involves subjecting the analyte to chemical degradation reactions with water. In addition to water, hydrolysis reactions are typically carried out across a broad pH range by exposing the sample to acidic conditions that facilitate catalysis. The choice of acid for stress testing depends on the stability of the sample, with the concentration being determined by the analyte's stability profile. Hydrochloric acid within the range of 0.1 to 1 M is the most commonly used and recommended reagent for acid hydrolysis. [19]

1.3.4 Base degradation

Basic degradation reactions can be performed across a wide range of pH by subjecting the sample to stress conditions catalyzed by bases. The choice of base for stress testing depends on the stability of the sample. Sodium hydroxide or potassium hydroxide within the concentration range of 0.1 to 1 M are the most commonly used and recommended reagents for base hydrolysis. These bases are considered suitable for inducing hydrolysis reactions during stress testing.[20]

1.3.5 Oxidative degradation

Oxidative stress testing is widely conducted to assess drug degradation. In oxidation testing, it is commonly recommended to use hydrogen peroxide within the concentration range of 3% to 30%. However, other oxidizing agents such as metal ions, oxygen, and radical initiators can also be utilized.

The choice of oxidizing agent and the concentration used in oxidative stress testing should be determined based on the specific characteristics and stability profile of the drug being studied.[21]

Table 1: Some commonly used conditions used for Force degradation studies are shown in the table below [22]

Degradation type	Experimental conditions	Storage conditions	Sampling time (days)
Thermal	Heat Chamber	60-80°C/75% RH	1,3,5
	Heat control	Room temp.	1,3,5
Photolytic	Direct Sunlight	N/A	1,3,5
	Room	N/A	1,3,5
Acid	0.1 M HCl	40-60°C	1,3,5
	Acid Control (no HCl)	40-60°C	1,3,5
Base	0.1 M NaOH	40-60°C	1,3,5
	Base Control (no NaOH)	40-60°C	1,3,5
Oxidative	3% H_2O_2	40-60°C	1,3,5
	No H_2O_2	40-60°C	1,3,5

2. DRUG PROFILE

- Common Name: Empagliflozin
- Synonym: Jardiance, BI-10773 [23]
- Chemical Name: (2S,3R,4R,5S,6R)-2-[4-Chloro-3-[[4-[(3S)-oxolan-3-yl]oxyphenyl] methyl]phenyl]-6-(hydroxymethyl)oxane-3,4,5-triol [23]
- Drug Category: sodium-glucose cotransporter-2 (SGLT2) (Gliflozin class) [23]
- Molecular formula: $C_{23}H_{27}ClO_7$ [24]
- Molecular weight: 450.91 g/mol [24]
- Description: White to off white powder [23]
- Solubility: very slightly soluble in water, slightly soluble in acetonitrile and ethanol, sparingly soluble in methanol and practically insoluble in toluene. [24]
- Melting point: 151-153°C [24]

3. MATERIAL AND METHODOLOGY

3.1 OJECTIVE

The Objective of this study is to conduct a degradation study on dosage form (10mg &25mg tablets) and raw material of Empagliflozin. Test substance are evaluated in different stress conditions for Percentage assay.

3.2 SCOPE

This degradation study generates a documented evidence that the tested substances has fulfilled all the degradation criteria s per ICH guidelines.

3.3 METHOD OF ANALYSIS OF EMPAGLIFLOZIN (raw material and product)

Analytical method of quantification of assay for empagliflozin is developed and validated as per ICH guidelines. Validation parameters encompass various aspects, including linearity, accuracy, precision, robustness, ruggedness, detection limit, quantification limit, and stability studies. These parameters are crucial in assessing the reliability and performance of analytical methods. A relative standard deviation (RSD) of less than 2% is considered acceptable, indicating good precision and reproducibility of the analytical method.[26]

Chromatography: HPLC (High Performance Liquid Chromatography)
Column: C18
Column dimension: Length-150*4.6 mm,
Particle size: 5µm
Flow rate: 1.5 ml/minute
Injection volume: 20 µl
Column Temperature: 30°C
Detector type: UV
Wavelength: 227nm
Mobile Phase: Methanol: Buffer (50:50) {Buffer= 0.01M Potassium Dihydrogen Phosphate buffer, pH4.0}
Solvent Mixture: Equal volume of water and methanol [27,28,29,30,31]

3.3.1 Preparation of Buffer (0.01 M Potassium Dihydrogen Phosphate buffer)

1.361 gm of Potassium Dihydrogen Phosphate was weighed accurately and transferred to 1000 ml volumetric flask and sufficient HPLC grade water was added to 1000 ml.

3.3.2 Preparation of Mobile Phase

In a 1000 ml volumetric flask, 500 ml of 0.01 M Potassium Dihydrogen Phosphate buffer (prepared in step number 5.4.2) was added. Then volume make up was done with Methanol to 1000ml.

3.3.3 Preparation of Solvent Mixture

In a 1000 ml volumetric flask 500 ml of Methanol was added and diluted to 1000ml with HPLC grade water.

3.4 Table: List of Samples its exposure days in stress conditions and its codes

S.No.	Stress Conditions	Sample	No. of Days	Codes of Sample
1.	N/A	Empagliflozin Working Stanadard	0	Std.
2.	N/A	API	0	API-D0
3.	N/A	Empagliflozin 10mg tablets	0	E10-D0
4.	N/A	Empagliflozin 25mg tablets	0	E25-D0
5.	Acidic	API	1	A-D1-API
6.			3	A-D3-API
7.			5	A-D5- API
8.		Empagliflozin 10mg tablets	1	A-D1-E10
9.			3	A-D3-E10
10.			5	A-D5- E10
11.		Empagliflozin 25mg tablets	1	A-D1-E25
12.			3	A-D3-E25
13.			5	A-D5-E25
14.	Basic	API	1	B-D1-API
15.			3	B-D3-API
16.			5	B-D5- API
17.		Empagliflozin 10mg tablets	1	B-D1-E10
18.			3	B-D3-E10
19.			5	B-D5- E10
20.		Empagliflozin 25mg tablets	1	B-D1-E25
21.			3	B-D3-E25
22.			5	B-D5-E25
23.	Oxidative	API	1	O-D1-API
24.			3	O-D3-API

25.			5	O-D5- API
26.		Empagliflozin 10mg tablets	1	O-D1-E10
27.			3	O-D3-E10
28.			5	O-D5- E10
29.		Empagliflozin 25mg tablets	1	O-D1-E25
30.			3	O-D3-E25
31.			5	O-D5-E25
32.	Thermal	API	1	T-D1-API
33.			3	T-D3-API
34.			5	T-D5- API
35.		Empagliflozin 10mg tablets	1	T-D1-E10
36.			3	T-D3-E10
37.			5	T-D5- E10
38.		Empagliflozin 25mg tablets	1	T-D1-E25
39.			3	T-D3-E25
40.			5	T-D5-E25
41.	Photolytic	API	1	P-D1-API
42.			3	P-D3-API
43.			5	P-D5- API
44.		Empagliflozin 10mg tablets	1	P-D1-E10
45.			3	P-D3-E10
46.			5	P-D5- E10
47.		Empagliflozin 25mg tablets	1	P-D1-E25
48.			3	P-D3-E25
49.			5	P-D5-E25

3.5 CALCULATION OF ASSAY

Percentage Assay =

$$\frac{\textbf{Area of Test}}{\textbf{Area of WS}} \textbf{X} \frac{\textbf{Wt. of WS}}{\textbf{100}} \textbf{X} \frac{\textbf{100}}{\textbf{Weight of Test}} \textbf{X} \frac{\textbf{Potency of WS}}{\textbf{100}} \textbf{X} \frac{\textbf{100} - \textbf{WC of WS}}{\textbf{100}} \textbf{XAvg. wt. of Tablet}$$

Where,
WS = Working Standard
WC= Water content
Wt. = Weight
Avg. = Average

4. RESULT

As per above dilutions and formula percentage assay of each stage and analysis.

4.1 ANALYSIS ON DAY 0

Standard weight (mg)	Average Area of Standard	Sample	Weight of Test (mg)	Area of test	% Assay	Average % Assay
50.6	13549393	API (D0-API)	51.3	14054609	101.36	100.97
			50.6	13754699	100.57	
		Empagliflozin 10mg tablets (D0-E10)	705.7	13219892	98.89	99.65
			705.9	13426719	100.41	
		Empagliflozin 25mg tablets (D0-E25)	560.5	13489921	100.16	100.47
			561.0	13584918	100.77	

4.2 ANALYSIS ON DAY 1

St. weight (mg)	Average Area of Standard	Stress Condition	Sample	Weight of Test (mg)	Area of test	% Assay	Average % Assay
51.1	13168124	THERMAL	T-D1-API	50.4	13139796	100.23	99.86
				50.7	13122245	99.50	
			T-D1-E10	706.4	12577882	97.67	97.92
				704.9	12613848	98.16	
			T-D1-E25	561.3	12685687	97.73	97.61
				562.4	12678683	97.49	
51.1	13168124	ACIDIC	A-D1-API	51.1	1036842	97.13	97.83
				50.6	1037520	98.53	
			A-D1-E10	705.7	1000293	97.19	97.37
				705.9	1004180	97.54	
			A-D1-E25	560.5	996155	96.07	96.15
				561.0	998701	96.23	
51.1	13168124	BASIC	B-D1-API	51.3	1032699	96.74	97.65
				50.6	1037736	98.55	
			B-D1-E10	705.7	998318	97.00	96.78
				705.9	994135	96.57	
			B-D1-E25	560.5	1000138	96.45	96.12
				561.0	994204	95.79	
50.9	12619487	OXIDATIVE	O-D1-API	51.3	998222	98.54	97.93
				50.4	982113	97.33	
			O-D1-E10	706.9	964726	97.26	98.00
				702.3	972984	98.74	
			O-D1-E25	561.2	981371	98.25	97.62
				565.9	977025	97.00	
51.1	13168124	PHOTOLYTIC	P-D1-API	50.2	12862800	98.50	98.45
				50.1	12823882	98.40	
			P-D1-E10	702.5	12596803	98.36	98.12
				701.3	12514093	97.88	
			P-D1-E25	561.3	12677774	97.67	98.06
				560.7	12764211	98.44	

4.3 ANALYSIS ON DAY 3

St. weight (mg)	Average Area of Standard	Stress Condition	Sample	Weight of Test (mg)	Area of test	% Assay	Average % Assay
50.1	12683410	THERMAL	T-D3-API	51.9	12725946	95.95	95.61
				52.3	12731573	95.26	
			T-D3-E10	706.2	11875745	93.90	94.31
				715.6	12138982	94.12	
			T-D3-E25	578.9	12378278	93.59	93.85
				580.6	12102642	97.68	
50.1	12683410	ACIDIC	A-D3-API	51.3	980775	93.52	93.32
				50.6	963272	93.12	
			A-D3-E10	705.7	963025	95.25	96.03
				705.9	979049	96.80	
			A-D3-E25	560.5	975872	95.80	95.74
				561.0	975503	95.67	
50.1	12683410	BASIC	B-D3-API	51.3	981560	93.59	93.76
				50.6	971707	93.93	
			B-D3-E10	705.7	963381	95.28	95.20
				705.9	961916	95.11	
			B-D3-E25	560.5	978405	96.05	95.79
				561.0	974116	95.54	
50.7	12687890	OXIDATIVE	O-D3-API	50.6	981099	95.94	95.29
				50.4	963875	94.63	
			O-D3-E10	706.9	952402	95.13	95.84
				702.3	960309	96.55	
			O-D1-E25	561.2	959176	95.13	94.56
				565.9	955503	93.98	
51.1	12683410	PHOTOLYTIC	P-D3-API	51.3	12244175	93.40	93.45
				51.7	12352745	93.50	
			P-D3-E10	703.1	12026743	95.51	94.87
				704.8	11893594	94.23	
			P-D3-E25	565.9	12115617	94.24	94.51
				569.0	12251620	94.78	

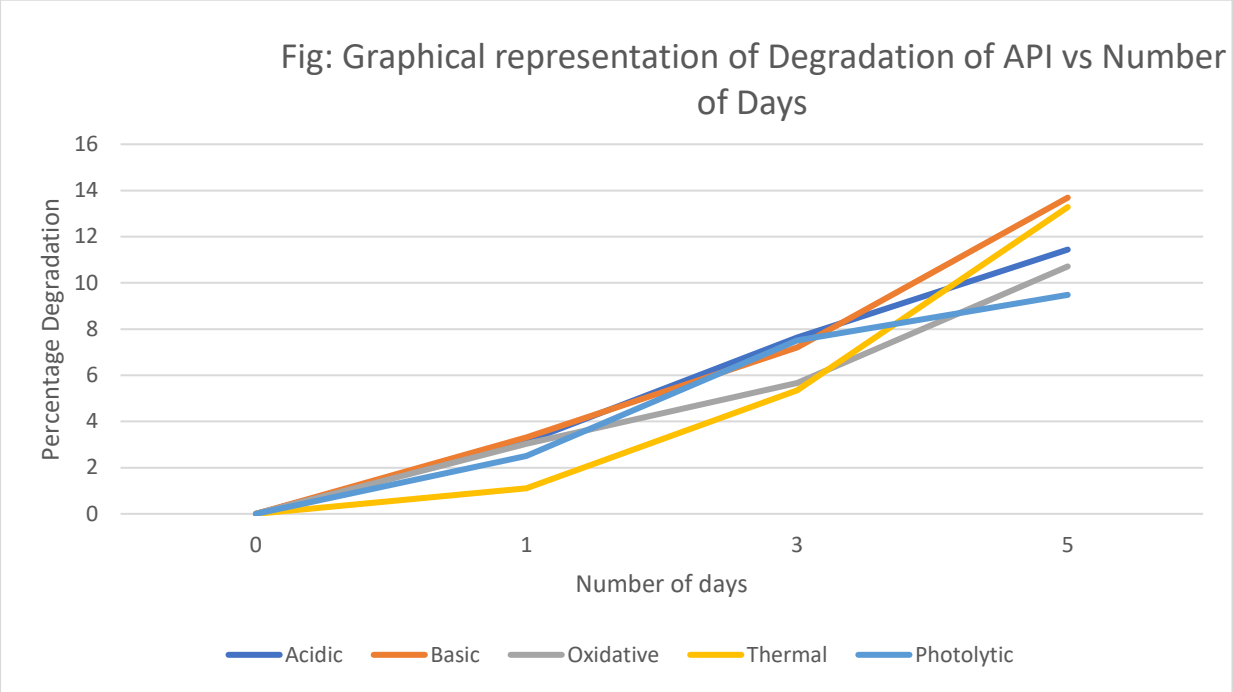
4.4 ANALYSIS ON DAY 5

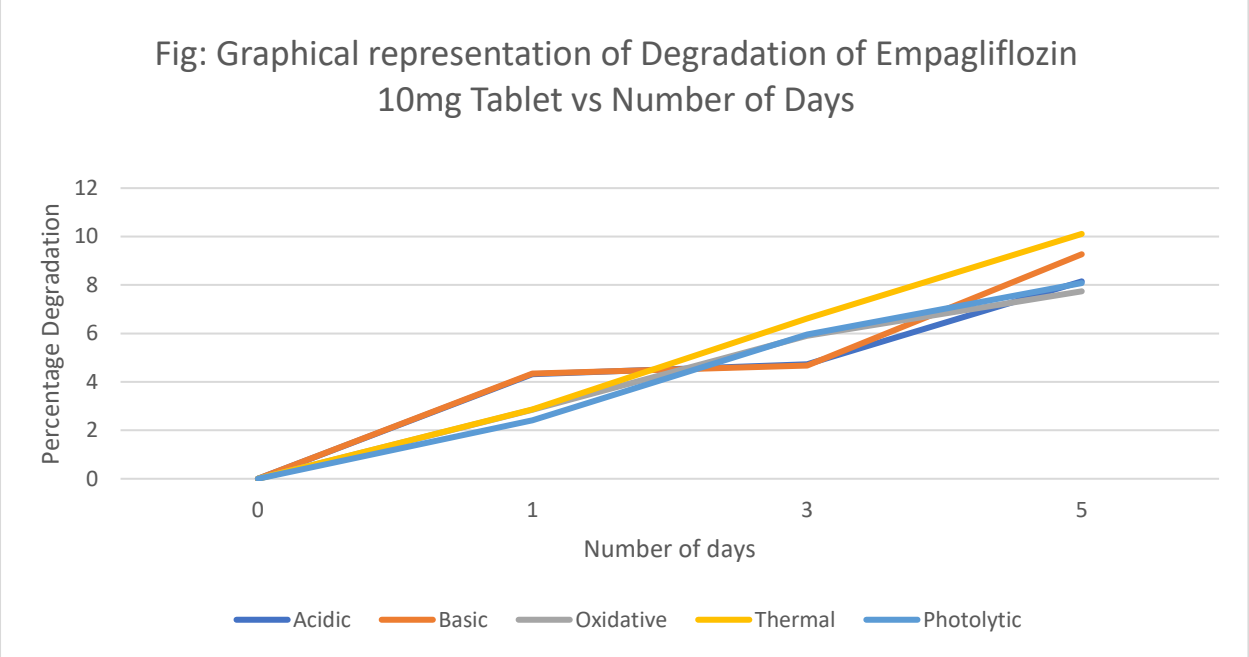
St. weight (mg)	Average Area of Standard	Stress Condition	Sample	Weight of Test (mg)	Area of test	% Assay	Average % Assay
50.3	12687473	THERMAL	T-D5-API	52.6	11797235	88.09	87.68
				52.9	11755186	87.28	
			T-D5-E10	732.8	11960391	91.01	91.24
				748.6	12157373	91.01	
			T-D5-E25	587.2	12018443	90.42	90.36
				590.6	12070865	90.29	
50.3	12687473	ACIDIC	A-D5-API	51.3	924969	88.52	89.52
				50.6	932931	90.52	
			A-D5-E10	705.7	924170	91.74	91.13
				705.9	912217	90.53	
			A-D5-E25	560.5	936607	92.28	92.32
				561.0	938267	92.36	
50.3	12687473	BASIC	B-D5-API	51.3	902710	86.39	87.27
				50.6	908457	88.14	
			B-D5-E10	705.7	929996	92.32	92.24
				705.9	928621	92.10	
			B-D5-E25	560.5	931764	91.80	91.20
				561.0	920060	90.60	
49.9	12620260	OXIDATIVE	O-D5-API	50.6	939431	90.90	90.25
				50.4	922226	89.59	
			O-D5-E10	706.9	934469	92.36	92.27
				702.3	926551	92.17	
			O-D5-E25	561.2	944763	92.72	92.73
				565.9	952873	92.74	
50.3	12687473	PHOTOLYTIC	P-D5-API	51.2	11987473	91.53	91.48
				50.3	11708433	91.42	
			P-D5-E10	712.9	11495468	90.37	91.02
				714.6	11689864	91.68	
			P-D5-E25	565.9	11795580	92.68	92.39
				569.0	11770659	92.10	

4.5 PERCENTAGE DEGRADATION SUMMARY

Samples	Assay on Day 0:	Stress Conditions	% Degradation on		
			DAY 1	DAY 3	DAY 5
API	100.96%	Acidic	3.13	7.64	11.44
		Basic	3.31	7.20	13.69
		Oxidative	3.03	5.67	10.71
		Thermal	1.10	5.35	13.28
		Photolytic	2.51	7.51	9.48
Empagliflozin 10mg Tablet	99.65%	Acidic	2.28	6.33	8.52
		Basic	2.87	4.45	7.41
		Oxidative	1.65	4.36	7.38
		Thermal	1.73	4.04	8.41
		Photolytic	1.53	4.78	8.63
Empagliflozin 25mg Tablet	100.47%	Acidic	4.32	4.73	8.15
		Basic	4.35	4.68	9.27
		Oxidative	2.85	5.91	7.74
		Thermal	2.86	6.62	10.11
		Photolytic	2.41	5.96	8.08

4.6 Graphical representation of Degradation





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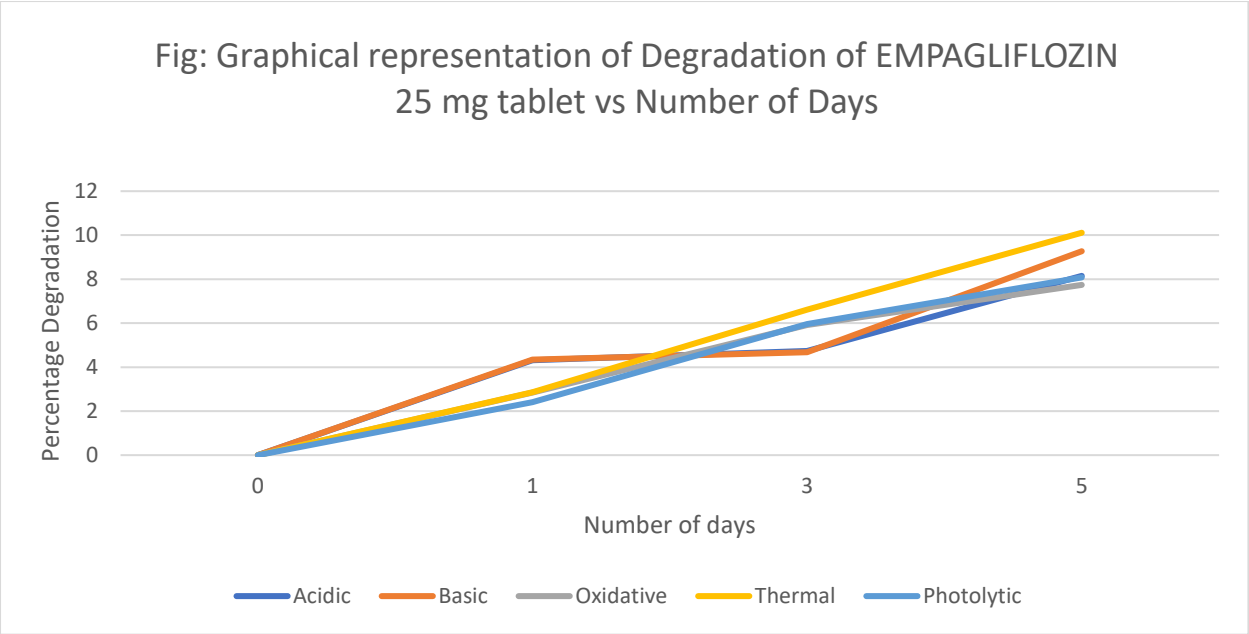

5. DISCUSSION

On first day, API degraded lowest in thermal condition and highest in basic condition. Empagliflozin 10mg tablets degraded lowest in photolytic condition and highest in basic condition. Empagliflozin 25mg tablets degraded lowest in photolytic conditions and highest in basic condition.

On third day, API degraded lowest in thermal condition and highest in acidic condition. Empagliflozin 10mg tablets degraded lowest in thermal condition and highest in acidic condition. Empagliflozin 25mg tablets degraded lowest in basic conditions and highest in thermal condition.

On fifth day, API degraded lowest in photolytic condition and highest in basic condition. Empagliflozin 10mg tablets degraded lowest in oxidative condition and highest in photolytic condition. Empagliflozin 25mg tablets degraded lowest in oxidative conditions and highest in thermal condition.

From above results Empagliflozin API is mostly degrative in acidic or basic environment while Empagliflozin Tablets are more degrative in Thermal or Photolytic conditions.

Degradation of API was higher in all cases in comparison to tablets. Empagliflozin 25mg tablets degraded slightly more than 10 mg tablet, it may be due to percentage of API in dosage form higher.

No samples crossed the degradation limit (>20%). Thus, all samples passed the degradation studies and can be proved pharmaceutically stable in all stress conditions recommended by ICH guidelines.

6. CONCLUSION

A simple, accurate, validated, precise and sensitive analytical RP-HPLC method was selected for analysis of drug content. All samples were stable in applied stress conditions like acidic, basic, oxidative, thermal and photolytic degradations. For raw material was slightly higher in comparison to tablet dosage form. For raw material more degradation was seen in basic condition than any other stress conditions. Tablets degraded highest in basic hydrolysis than in any other conditions. Empagliflozin 10 mg tablet was comparatively stable than 25mg tablet. Overall, the samples passed the degradation study criteria as per the Q1A (R2), guidelines.

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