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Analytical Method Development And Validation of Amisulpride and its Force Degradation

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ABSTRACT

The degradation of novel drug substances and drug products under forced settings is more severe than the degradation under accelerated conditions. It is vital to demonstrate the specificity of stability indicating methods, and it also provides information on the degradation routes and end products of the medicinal ingredient. It also contributes to the illumination of the structure of the degradation products. Forced degradation studies disclose the chemical behavior of the molecule, which contributes in formulation and packaging design.The present study involves the stress induced stability studies such as alkali and acid hydrolytic degradation, oxidative degradation, thermal and photolytic degradation.

Keywords- Force degradation, hydrolytic ,Oxidation, Photolytic, Thermal

1. INTRODUCTION

Studies on forced degradation offer information to enable the identification of potential degradants , degradation pathways, the drug's inherent stability, and the validation of stability-indicating analytic procedures. Understanding a molecule's stability aids in choosing the best formulation, container, and shelf life, all of which are necessary for regulatory documentation. An artificial process called stress testing is used to forcefully degrade a medicine. This process is also referred to as forced degradation. It is a helpful tool for predicting the stability of any formulation product or Active Pharmaceutical Ingredient (API). Alothman ZA, Understanding the contaminants that form when medication items are stored in varied environmental conditions is beneficial. In areas like formulation creation, manufacturing, and packaging where data on substance conduct can be used to enhance a pharmaceutical item, forced degradation investigations may aid in promoting drug advancement. Therefore, it's crucial to understand how a medicine substance behaves under distinct natural circumstances. The drug and dosage form must be considered while studying forced degradation. Processes for dose forms that are solid, liquid, and injectable for various stress investigations vary. We therefore provided a complete overview of forced degradation research in the present review study by applying several regulatory criteria to the selection of the system to perform stress tests on as well as its methodology for isolating and diagnosing deterioration. [1]

Chemical stability of pharmaceutical compounds is a significant issue since it affects the efficacy and safety of the drug. The FDA and ICH recommendations highlight the need for stability testing data to understand how the quality of a drug substance and drug product varies over time as a result of various environmental circumstances. Understanding a molecule's stability facilitates the choice of an appropriate formulation and packaging as well as the provision of appropriate storage conditions and shelf life, all of which are necessary for regulatory paperwork. Drug products and drug compounds are broken down by a process known as forced degradation, which takes place in harsher conditions than accelerated conditions. Bajaj S This process creates degradation products that may be examined to find out how stable a molecule, Studies on forced degradation can be used to determine the intrinsic stability of medicinal molecules. Forced degradation studies can also be used to assess potential polymorphism or enantiomeric compounds, variations in drug-related degradation, and excipient interferences. The forced degradation experiments under a variety of conditions, such as pH, light, oxidation, dry heat, acidic, basic, hydrolysis, etc., are required by ICH recommendations. Additionally, it offers the ability to separate drugs from products of degradation. The FDA and ICH guidelines necessitate forced deterioration in order to understand how a drug substance's and drug product's quality changes over time and in response to various environmental variables. [2][3]

Forced degradation studies offer the following information

a. Determination of likely degradant
b. Determination of degradation pathways,
c. Determining the drug molecule's essential stability
d. Finding analytical techniques for validating stability. [2]

- **Objective for forced degradation**

a. To develop paths for drug substance and drug product degradation.
b. To determine the chemical characteristics of drug compounds.
c. To address stability concerns, define the structure of degradation products.
d. To determine a pharmacological substance's inherent stability in the formulation.
e. To indicate the degradation of the drug material and drug product.
f. To separate degradation products produced by drug products in a formulation from those produced by non-drug products.
g. To produce stability revealing a method's nature that has been developed.
h. To create formulations that are more stable . It also helps determine the expiration date of a particular composition.
i. To produce a deterioration profile resembling what would be seen in an official stability study carried out under ICH guidelines. [3]

Regulatory Perspective in Stability Studies:

The pharmaceutical companies in Europe, the United States, and Japan have all made efforts to establish unified regulations for testing and analysis throughout the development of new pharmaceuticals. The International Conference on Harmonisation (ICH), which has been adopted as law in the US, Japan, and the EU, is the name given to these harmonised regulations. In addition to this, other nations are also using them as a de facto regulatory force. [4]

The ICH guideline Q1A serves as an example of the fundamental stability requirements. Validated SIM must conduct testing of the properties that are vulnerable to change during storage and that are likely to affect the quality, safety, and efficacy. [5]

According to the ICH Q1B, photostability testing ought to be a crucial component of stress research. For most medicinal substances and goods, an ICH dose of 1.2 x 106 and 2.4 x 106 lxh of fluorescent light and 200 wh/m2 UV light is advised to estimate photostability considerations. [6]

The provision of documentation to support the validity and applicability of analytical procedures for the detection and quantification of degradation products is strongly emphasised in ICH guideline Q3B.The guideline provides a comprehensive understanding of the reporting, identification, and quantification thresholds for degradation products in pharmacological compounds. [7]

Degradation conditions

- Hydrolytic conditions

Ionizable functional groups included in the molecule are catalysed during a hydrolytic research in acidic and basic conditions. Acid or base stress testing entails exposing a pharmacological material to acidic or basic conditions in order to force degradation that produces primary degradants in a desired range. The type and concentration of acid or base to use depends on how stable the drug ingredient is. As acceptable reagents for hydrolysis, sodium hydroxide or potassium hydroxide (0.1-1 M) are proposed for base hydrolysis and hydrochloric acid or sulfuric acids (0.1-1 M) for acid hydrolysisThe drug substance structure is used to determine which co-solvent to use. Normal stress testing trials begin at room temperature, and if no degradation occurs, higher temperature (50–70 °C) is next applied. Stress testing should be permitted for a maximum of seven days. To stop further degradation, the deteriorated sample is then neutralised with the appropriate acid, base, or buffer.[9][10]

- Oxidation conditions

In forced degradation investigations, hydrogen peroxide is frequently employed to oxidise the pharmacological compounds, but other oxidising agents can also be utilised, including metal ions, oxygen, and radical initiators such azobisisobutyronitrile (AIBN). The drug substance determines the type of

oxidising agent to use, as well as its concentration and environmental factors. According to reports, exposing the solutions to 0.1-3% hydrogen peroxide for seven days at neutral pH and room temperature, or up to a maximum 20% degradation, may produce relevant degradation products. An electron transfer mechanism is used during the oxidative breakdown of drug material to create reactive anions and cations. Electron transfer oxidation can transform amines, sulphides, and phenols into N-oxides, hydroxylamine, sulfones, and sulfoxide. Functional groups having labile hydrogen, such as those with benzylic, allylic, tertiary, or - positions with regard to hydrogen atoms, are prone to oxidation, which can result in the formation of hydroperoxides, hydroxide, or ketone. [9]

- Photolytic conditions

To show that a light exposure does not cause an unacceptable alteration, the photo stability testing of pharmacological compounds must be assessed. When a pharmaceutical material is exposed to UV or fluorescent light, photo stability studies reveal the main degradants that are created. In ICH guidelines, a few suggested circumstances for photostability testing are listed. Drug material and solid/liquid drug product samples need to be subjected to 200 W h/m2 and 1.2 million lx/h of light, respectively. The most widely accepted wavelength of light to produce photolytic deterioration is between 300 and 800 nm. The 6 million lx h recommended maximum lighting By using a free radical pathway, light stress conditions can cause photo oxidation. Drug photosensitivity is likely to be introduced by functional groups including carbonyls, nitro aromatics, N-oxide, alkenes, aryl chlorides, weak C H and O H bonds, sulphides, and polyenes. [12]

Thermal conditions

Thermal deterioration should be tested under more demanding settings than those suggested by ICH Q1A accelerated testing (for example, dry heat and wet heat). While liquid drug products should be exposed to dry heat, samples of solid-state drug substances and drug products should be heated both dry and wet. Studies might be carried out faster and at higher temperatures. [10]

Amisulpride is a dopamine D2 receptor antagonist used to treat individuals who have surgical nausea and vomiting as well as acute and chronic schizophrenia.

Dopamine receptor antagonist amisulpride is a benzamide derivative that only inhibits dopamine D2 and D3 receptors. Aside from treating both the positive and negative aspects of schizophrenia, amisulpride also has antidepressant effects on those with psychiatric disorders, dysthymia, and serious depression. When compared to other atypical antipsychotic drugs, amisulpride has a significantly lower incidence of extrapyramidal side effects because it primarily affects the limbic system. Acute and chronic schizophrenia illnesses, as well as secondary adverse symptoms in mental health diseases such affective disorders, sad mood, and mental retardation, are all treated in European nations using oral pills of amisulpride. [13]

METHOD

INTRADAY STUDY

HYDROLYTIC DEGRADATION USING 0.1M NaOH [11][12][13]

Standard Preparation

100mg To achieve a concentration of 1 mg/ml, amisulpride was transferred to a volumetric flask and dissolved in 100 ml of distilled water. The remedy was left out in the open. To achieve a final concentration of 10 g/ml, distilled water was added to an aliquot of the solution. The greatest absorbance of the solution was measured at 270 nm after it was scanned in the UV area.

Bulk preparation (Stress)

Amisulpride was weighed and then put into a volumetric flask where it was dissolved in 0.1M NaOH to yield 1mg/ml. The remedy was left out in the open. An aliquot of the solution was diluted with distilled water to achieve a final concentration of 10 g/ml after 30 minutes. The greatest absorbance of the solution was measured at 270 nm after it was scanned in the UV area.The same process was carried out again after a 60- and 90-minute break.

Blank preparation

A 100ml volumetric flask containing 100ml of 0.1M NaOH solution was filled, the solution was allowed to sit at room temperature for 30 minutes, and then an aliquot of the solution was diluted with distilled water to obtain the final concentration. This serves as a placeholder. After the allotted period, the process was carried out three more times. The solution's highest absorbance was detected at 270 nm when compared to a reagent blank that had also had the same treatment. The assay value was estimated after three such determination

HYDROLYTIC DEGRADATION USING 0.1 M HCl

Bulk preparation (stress)

Weighing out 100 mg of amisulpride, we moved it to a volumetric flask and dissolved it in 0.1 M HCl to a concentration of 1 mg/ml. The solution was made available to everyone. An aliquot of the solution was mixed with distilled water and allowed to sit for 30 minutes to get the final concentration of 10 g/ml. The solution's maximum absorbance at 270 nm was discovered when the UV spectrum was inspected. At intervals of 60 and 90 minutes, the same procedure was repeated.

Blank preparation

Weighing out 100 mg of amisulpride, we moved it to a volumetric flask and dissolved it in 0.1 M HCl to a concentration of 1 mg/ml. The solution was made available to everyone. An aliquot of the solution was mixed with distilled water and allowed to sit for 30 minutes to get the final concentration of 10 g/ml. The solution's maximum absorbance at 270 nm was discovered when the UV spectrum was inspected. At intervals of 60 and 90 minutes, the same procedure was repeated.

OXIDATIVE DEGRADATION USING 5%H_2O_2

Bulk preparation (stress)

Amisulpride in the amount of 100 mg was measured, moved into a volumetric flask, and then dissolved in 5% H2O2 to create a concentration of 1 mg/ml. The cure was made available to the public. After 30 minutes, distilled water was used to dilute an aliquot of the solution to a final concentration of 10 g/ml. The solution's UV spectrum was scanned, and the peak absorbance at 270 nm was noted. After intervals of 60 and 90 minutes, this procedure was repeated.

Blank preparation

100ml of a 5% H2O2 solution were added to a 100ml volumetric flask. The solution was made available to everyone. After 30 minutes, a sample of the solution was diluted with distilled water to reach the appropriate concentration. This acts as a stand-in. The procedure was repeated three more times after the allocated time had passed. Comparing the solution to a reagent blank that had likewise had the same treatment, the solution's greatest absorbance was found at 270 nm. Three of these determinations later, the assay value was estimated.

INTER DAY STUDY

HYDROLYTIC DEGRADATION USING 0.1 M NaOH

Bulk Preparation (stress)

Weighing out 100 mg of amisulpride, we moved it to a volumetric flask and dissolved it in 0.1 M NaOH to a concentration of 1 mg/ml.The solution was made available to everyone. The solution was then diluted with distilled water the following day (the first day) to a final concentration of 10 g/ ml. After the solution was scanned in the UV region, its maximum absorbance was determined at 270 nm.Three and five days apart, the identical procedure was carried out. The reference spectra and the obtained spectrum are contrasted.

Blank preparation

A 100ml volumetric flask **n** was filled with 100ml of 0.1M NaOH solutions. The remedy was left out in the open. To obtain the final concentration, distilled water was added to an aliquot of solution the following day. This process is repeated on days three and five.

Three times the process was carried out.after the set period. In comparison to a reagent blank handled in the same manner, the absorbance of the resultant solution showed a maximum of 270 nm. The assay value was estimated after three such determinations.

HYDROLYTIC DEGRADATION USING 0.1M HCl

Bulk Preparation (stress)

Amisulpride 100 mg was weighed and transported to a volumetric flask, where it was dissolved in 0.1 M hydrochloric acid to a concentration of 1 mg/ml.The remedy was left out in the open. Then, on the following day (the first day), distilled water was used to dilute an aliquot of the solution to a final concentration of 10 g/ml. When the solution was scanned in the UV spectrum, the greatest absorbance at 270 nm was noted.For the interim between the third and fifth days, the identical process was performed. The acquired spectrum is evaluated against the reference spectrum.

Blank preparation

A 100ml volumetric flask was filled with 100ml of 0.1M HCl solutions.The following day, the solution was stored at room temperature, and an aliquot was diluted with distilled water to obtain the desired concentration. This process is repeated on days three and five.

Three times the process was carried out.after the set period. In comparison to a reagent blank handled in the same manner, the absorbance of the resultant solution showed a maximum of 270 nm. The assay value was estimated after three such determinations.

OXIDATIVE DEGRADATION USING 5% H_2O_2

Bulk preparation (stress)

Amisulpride 100 mg in bulk was measured, transported to a volumetric flask, and dissolved in 5% hydrogen peroxide to a concentration of 1 mg/ml.The remedy was left out in the open. A portion of the solution was diluted with distilled water the following day (first day) to reach a final concentration of 10 g/ml. The solution was scanned in the UV area, and the operation was repeated after three and five days to record the solution's maximal absorbance at 270 nm.

Blank preparation

A 100ml volumetric flask was filled with 100ml of 5% H2O2 solution, which was stored at room temperature. To achieve the desired concentration, distilled water was diluted an aliquot of solution the following day. After the allotted period, the process was carried out three more times. In comparison to a reagent blank handled in the same manner, the absorbance of the resultant solution showed a maximum of 270 nm. The assay value was estimated after three such determinations.

THERMAL DEGRADATION

Bulk Preparation (stress)

Amisulpride mass weighing 1 gm was measured and put into a Petri plate. A hot air oven set to 50oC was used to bake this Petri dish.The following day, a Petri dish containing 100mg of amisulpride was weighed and transferred to a 100ml volumetric flask. It was dissolved in water till there was 100ml total.To achieve a final concentration of 10 g/ ml, distilled water was used to dilute an aliquot of the solution. The third and fifth days involved repeating the same process.

Blank Preparation

Distilled water was used a blank

PHOTOLYTIC DEGRADATION USING SUNLIGHT

Bulk preparation (stress)

Amisulpride mass weighing 1 gm was measured and put into a Petri plate. The Petri dish was exposed to light. The following day, 100 mg of amisulpride was transferred from a Petri plate to a 100 ml volumetric flask and weighed. It made up 100ml after being dissolved in distilled water.To achieve a final concentration of 10 g/ml, distilled water was used to dilute an aliquot of solution. The third and fifth days involved repeating the same process.

Blank Preparation

Distilled water was used a blank

RESULT AND DISCUSSION

1. HYDROLYTIC DEGRADATION STUDY USING 0.1M SODIUM HYDROXIDE

The hydrolytic degradation research was carried out in accordance with the technique outlined in the experimental work.UV Spectrophotometry was used to calculate the assay value of active substances.

Intra Day Results of Hydrolytic Degradation Using 0.1M NaOH

Sr. No.	Drug	Absorbance	Standard	Time
1	Bulk	0.6152	0.6210	30mins
		0.6145		
		0.6112		
3	Bulk	0.6106	0.6210	60mins
		0.6106		
		0.6100		
5	Bulk	0.6095	0.6210	90mins
		0.6097		
		0.6095		

Results Obtained From Hydrolytic Degradation 0.1M NaOH

Stress Condition (Alkali Hydrolysis)	Time	ssay Percentage Content (%)
0.1 M SodiumHydroxide	30mins	98.76
	60mins	98.29
	90mins	98.15

Inter Day Result of Hydrolytic Degradation Using 0.1M NaOH

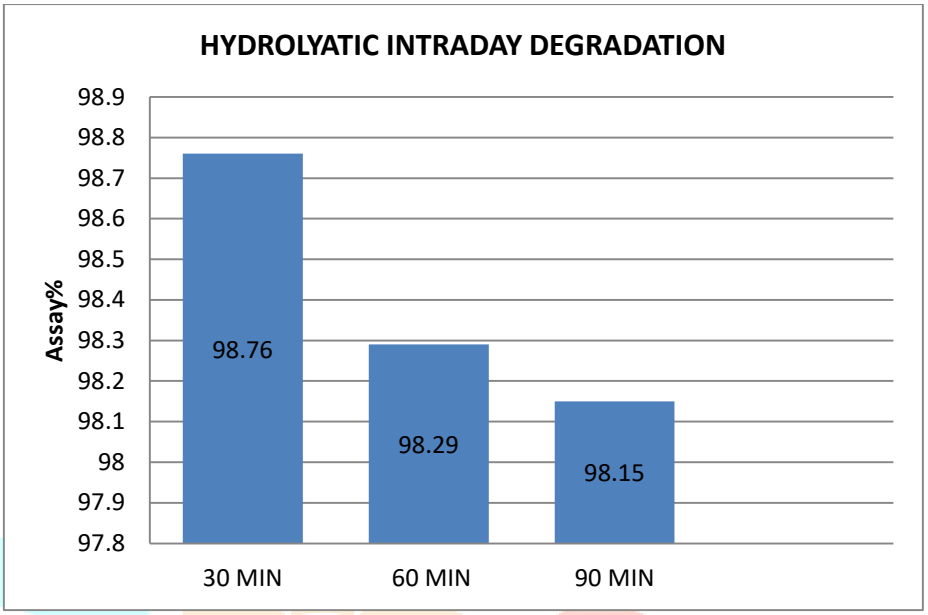
Sr. No.	Drug	Absorbance	Standard	Time
1	Bulk	0.6095	0.6210	1st day
		0.6095		
		0.6093		
2	Bulk	0.6085	0.6210	3 rd day
		0.6083		
		0.6080		
3	Bulk	0.6069	0.6210	5 th day
		0.6068		
		0.6071		

Results Obtained From Hydrolytic Degradation 0.1 M NaOH

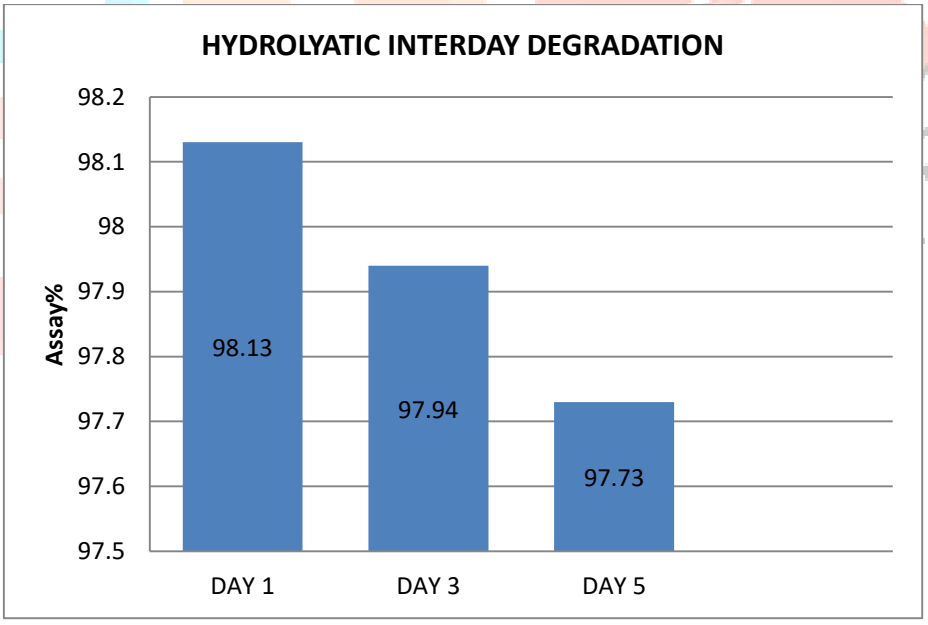
Stress Condition (Alkali Hydrolysis)	Time	ılk PercentageContent (%)
0.1M SodiumHydroxide	1st Day	98.13
	3rd day	97.94
	5th day	97.73

GRAPHICAL REPRESENTATION OF INTRA DAY AND INTERDAY STUDY (0.1M NaOH)

The study results indicated that Amisulpride was unstable in alkali condition. Shows the results of intraday degradation and the assay values of standard and sample



Graph For Hydrolytic Intraday Degradation



Graph For Hydrolytic Interday Degradation

2. HYDROLYTIC DEGRADATION USING 0.1M HYDROCHLORIC ACID

Intra Day Results of Hydrolytic Degradation Using 0.1M HCL

Sr. No.	Drug	Absorbance	Standard	Time
1	Bulk	0.5985	0.6210	30mins
		0.5985		
		0.5983		
3	Bulk	0.5980	0.6210	60mins
		0.5972		
		0.5972		
5	Bulk	0.5885	0.6210	90mins
		0.5880		
		0.5883		

Each value is the mean of three determinations

Results Obtained From Hydrolytic Degradation 0.1M HCl

Stress Condition (Acid Hydrolysis)	Time	Assay PercentageContent (%)
0.1 M HydrochloricAcid	30mins	96.36
	60mins	96.21
	90mins	94.72

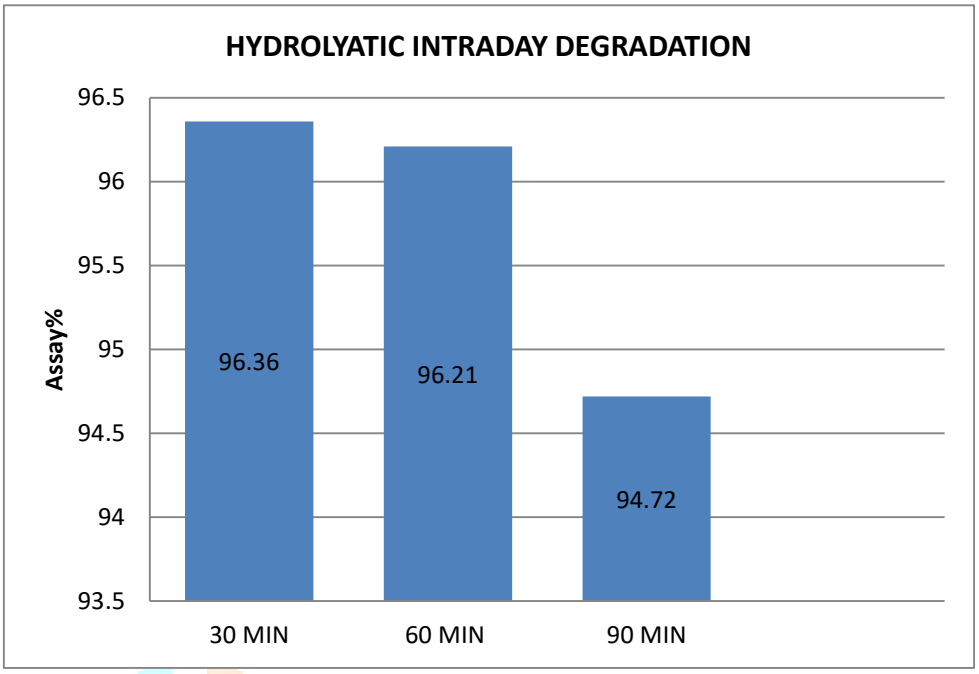
Inter Day Result Of Hydrolytic Degradation Using 0.1 M HCl

Sr. No.	Drug	Absorbance	Standard	Time
1	Bulk	0.5880	0.6210	1st day
		0.5877		
		0.5877		
2	Bulk	0.5870	0.6210	3 rd day
		0.5869		
		0.5870		
3	Bulk	0.5858	0.6210	5 th day
		0.5855		
		0.5554		

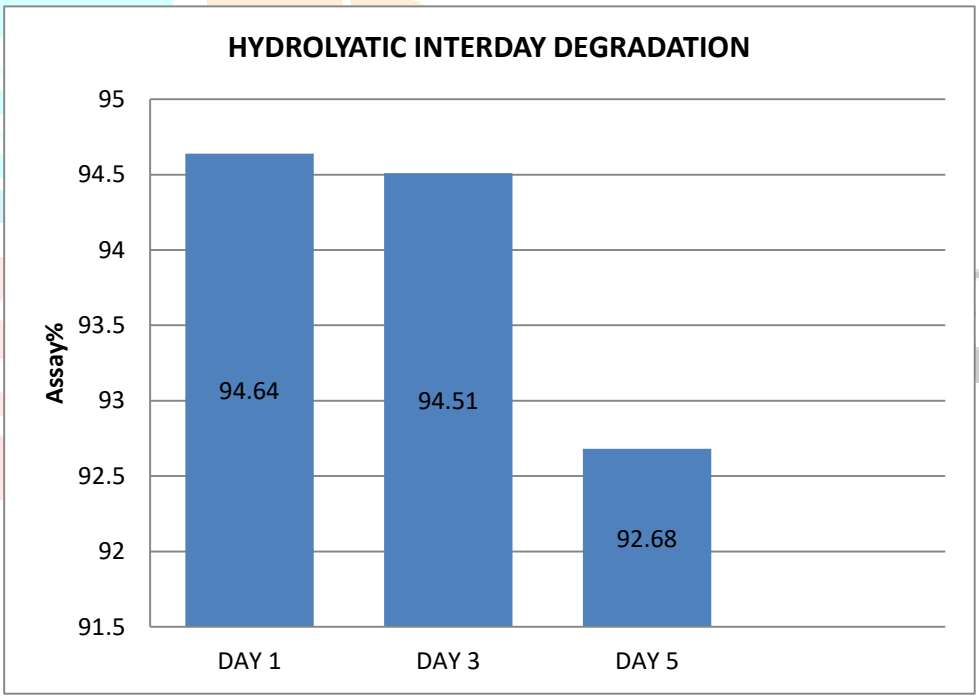
Results Obtained From Hydrolytic Degradation 0.1M HCl

Stress Condition (Acid Hydrolysis)	Time	Assay percentagecontent (%)
0.1 M Hydrochloric 0.2 acid	1st Day	94.64
	3rd Day	94.51
	5th Day	92.68

GRAPHCAL REPESENATION OF INTRA DAY & INTERDAY STUDY (0.1M HCl)



Graph For Hydrolytic Intraday Degradation



3. OXIDATIVE DEGRADATION USING 5% HYDROGEN PEROXIDE

Intra Day Results Of Oxidative Degradation Using 5% H_2O_2

Sr. No.	Drug	Absorbance	Standard	Time
1	Bulk	0.5992	0.6210	30 mins
		0.5991		
		0.5991		
3	Bulk	0.5991	0.6210	60mins
		0.5989		
		0.5988		
5	Bulk	0.5983	0.6210	90mins
		0.5983		
		0.5982		

Results Obtained from Oxidative Degradation 5% H_2O_2

Stress Condition (Oxidation)	Time	Assay Percentage content (%)
5% H_2O_2	30mins	96.47
	60mins	96.44
	90mins	96.33

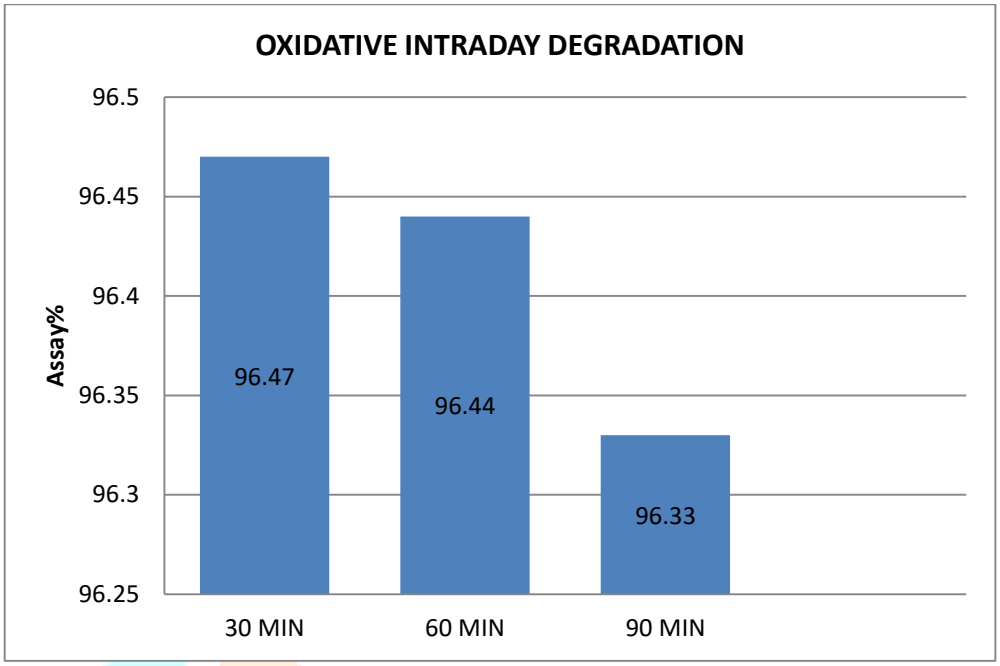
Inter Day Result Of Oxidative Degradation Using 5% H_2O_2

Sr. No.	Drug	Absorbance	Standard	Time
1	Bulk	0.5983	0.6210	1st day
		0.5980		
		0.5983		
2	Bulk	0.5962	0.6210	3 rd day
		0.5960		
		0.5953		
3	Bulk	0.5894	0.6210	5 th day
		0.5892		
		0.5896		

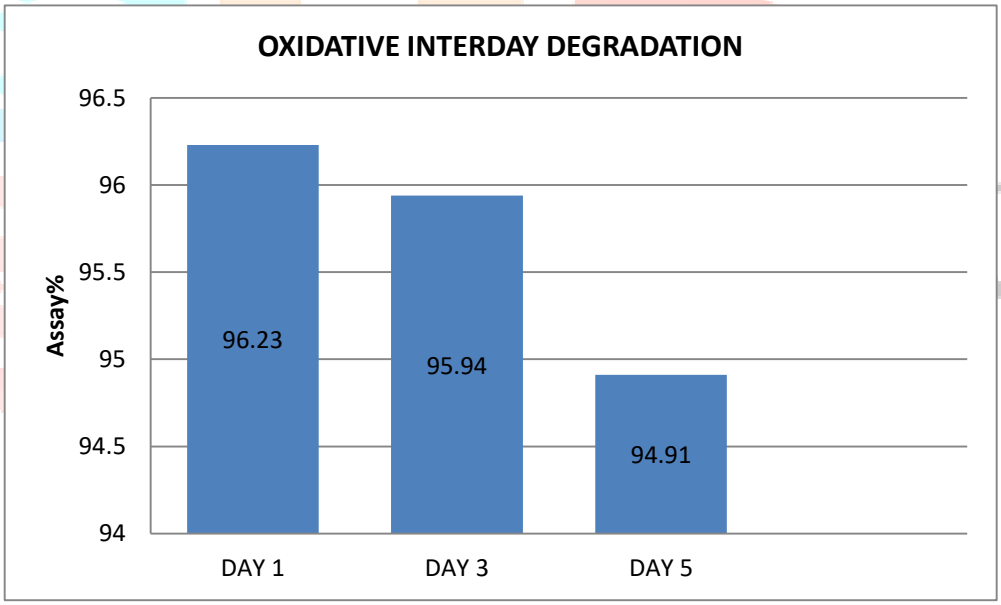
Results Obtained From Oxidative Degradation 5% H_2O_2

Stress Condition(Oxidation)	Time	Assay PercentageContent (%)
5% H_2O_2	1^{st} Day	96.23
	3^{rd} Day	95.94
	5^{th} Day	94.91

GRAPHCAL REPESENATION OF INTRA DAY & INTERDAY STUDY



Graph For Oxidative Intraday Degradation



Graph For Oxidative Interday Degradation

4. THERMAL DEGRADATION

Amisulpride standard and sample kept in heating chamber at 50˚C.The standard and samples powders were collected at different time intervals and the assay values were calculated by UV

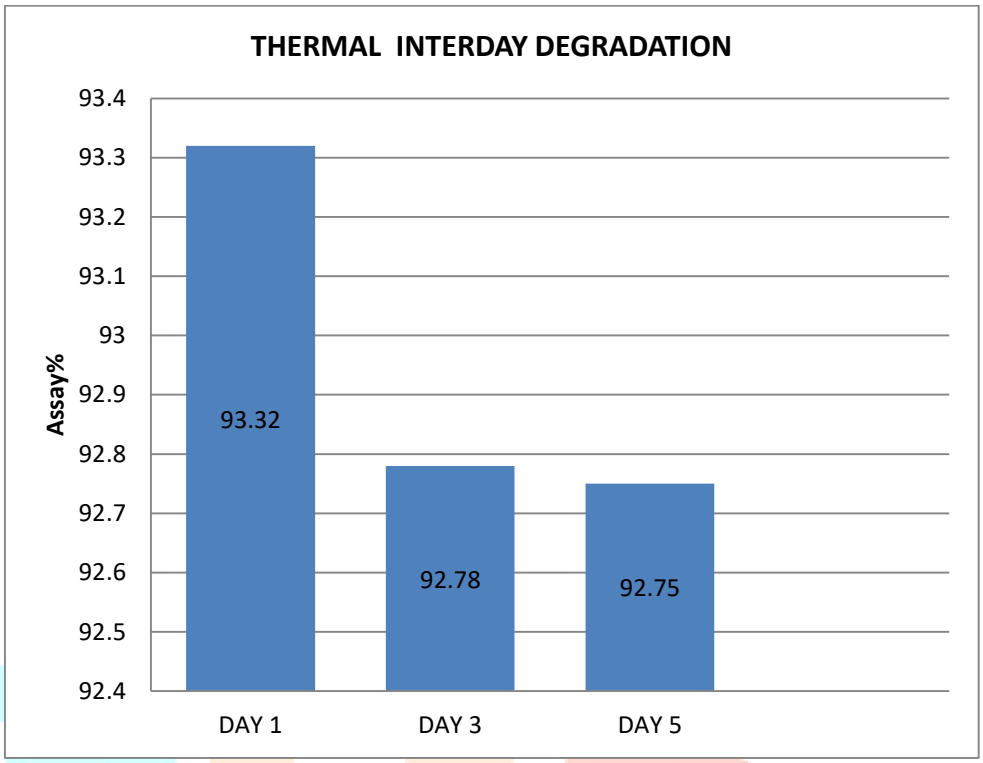
Interday Absorbance values for Thermal Degradation at 50˚C

Sr. No.	Drug	Absorbance	Standard	Time
1	Bulk	0.5796	0.6210	1 st Day
		0.5796		
		0.5794		
3	Bulk	0.5763	0.6210	3 rd Day
		0.5762		
		0.5760		
5	Bulk	0.5760	0.6210	5 th Day
		0.5763		
		0.5758		

Results Obtained from Thermal Degradation at 50˚C

Stress Condition (Oxidation)	Time	Assay Percentage content(%)
50˚C	1st Day	93.32
	3 rd Day	92.78
	5 th Day	92.75

GRAPHICAL REPRESENSATION OF THERMALDEGRADATION STUDY



Graph for Thermal Degradation5. PHOTOLYTIC DEGRADATION USING SUNLIGHT

Amisulpride standard was kept in heating chamber at 50˚C.The standard and sample powders were collected at different time intervals and the assay value were calculated by UV Spectroscopy

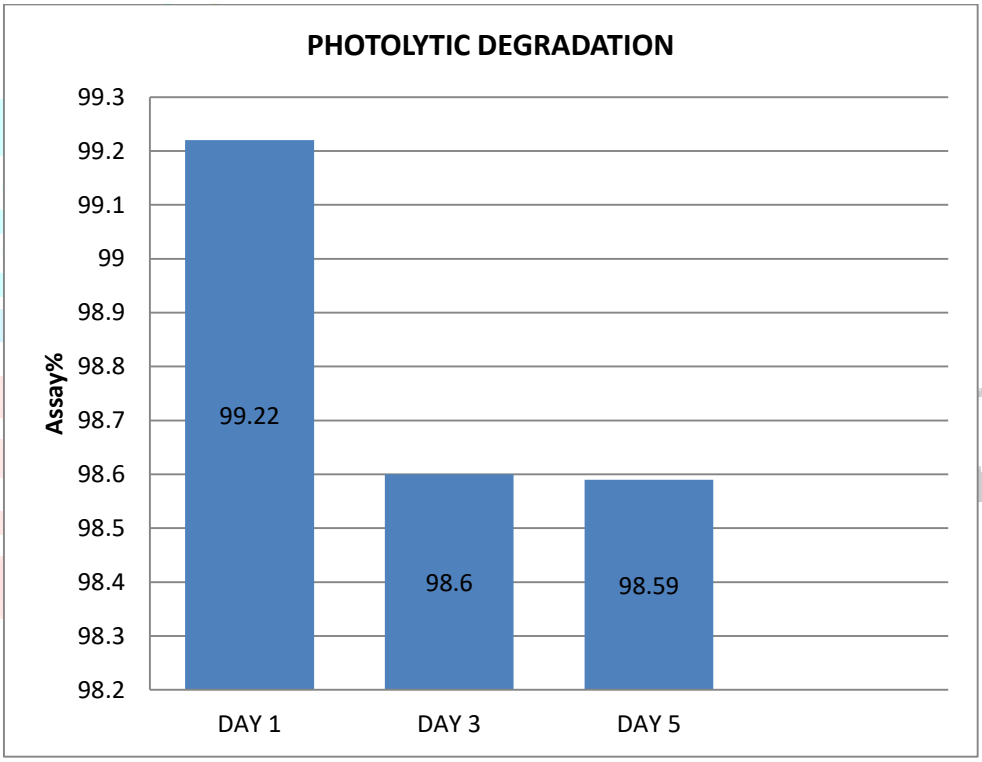
Interday Absorbance Values for Photolytic Degradation

Sr .No.	Drug	Absorbance	Standard	Time
1	Bulk	0.6180	0.6210	1 st Day
		0.6180		
		0.6125		
2	Bulk	0.6125	06210	3 rd Day
		0.6123		
		0.6123		
3	Bulk	0.6122	0.6210	5 th Day
		0.6122		
		0.6125		

Results Obtained from Photolytic Degradation

Stress Condition (Oxidation)	Time	Assay Percentage content (%)
Sunlight	1st Day	99.22
	3 rd Day	98.60
	5 th Day	98.59

GRAPHICAL REPRESENTATION OF PHOTOLYTICDEGRADATION STUDY



Graph for Photolytic Degradation

DISCUSSION AND CONCLUSION

I. The present study involves the stress induced stability studies such as alkali and acid hydrolytic degradation, oxidative degradation, thermal and photolytic degradation.

II. Degraded samples were quantified by UV method and the results of bulk are compared with that of standard.

III. An important feature in this study was that sample undergoes greater hydrolytic degradation (both acid & alkali) than other degradation methods used.

REFERENCES

1. Sharma MK, Murugesan M. Forced degradation study an essential approach to develop stability indicating method. J Chromatogr Sep Tech. 2017;8(1):349.
2. Alothman ZA, Rahman N, Siddiqui MR. Review on pharmaceutical impurities, stability studies and degradation products: an analytical approach. Reviews in Advanced Sciences and Engineering. 2013 Jun 1;2(2):155-66.
3. Bajaj S, Singla D, Sakhuja N. Stability testing of pharmaceutical products. Journal of applied pharmaceutical science. 2012 Mar 30(Issue):129-38.
4. Yasmeen A, Sofi G. A review of regulatory guidelines on stability studies. The Journal of Phytopharmacology. 2019;8:147-51.
5. ICH. Harmonized tripartite guideline. Stability testing of new drug substances and Products Q1A (R2). February 2003.
6. ICH. Harmonized Guideline: Stability Testing: Photo Stability Testing of New Drug Substances and Products Q1B, November 1996.
7. *Impurities in New Drug Substance Q3A(R2)*; International Conference on Harmonization (ICH).
8. ICH. Harmonized Guideline: Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products Q5C, November 1995.
9. ICH. Harmonized Guideline: Stability Testing: Requirements for New Dosage Forms QIC, November 1996.
10. ICH. Harmonized Guideline: Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products Q1D. February 2002.
11. ICH. Harmonized Guideline: Evaluation of Stability Data Q1E, February 2003.
12. Blessy MR, Patel RD, Prajapati PN, Agrawal YK. Development of forced degradation and stability indicating studies of drugs—A review. Journal of pharmaceutical analysis. 2014 Jun 1;4(3):159-65.
13. Iram F, Iram H, Iqbal AZ, Husain A. Forced degradation studies. Journal of Analytical & Pharmaceutical Research. 2016;3(6):73.
14. Venkataraman S, Manasa M. Forced degradation studies: Regulatory guidance, characterization of drugs, and their degradation products-a review. Drug Invention Today. 2018 Feb 1;10(2).
15. Rein W, Coulouvrat C, Dondey-Nouvel L. Safety profile of amisulpride in short-and long-term use. Acta Psychiatrica Scandinavica. 2000 Jan;101(400):23-7.
16. https://go.drugbank.com/drugs/DB06288
17. FDA Approved Drug Products: BARHEMSYS (amisulpride) injection, for intravenous use [Link] https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/209510Orig1s002Lbl.pdf