

FORCED DEGRADATION STUDY OF DIFFERENT BRANDS OF METFORMIN AVAILABLE IN INDIA

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Abstract— There are several brands of Metformin. As it is most prescribed oral antihyperglycemic agent that is used for Type II Diabetes Mellitus. The objective of this study is to develop the degradation studies of different brands of Metformin HCl 500mg. Metformin brands were subjected to different stress conditions according to ICH guidelines. The amount of degradation product can be calculated by using UV Spectrophotometer. Deionized water was used as solvent. According to specification of IP, the content official limit of not less than (95%) and not more than (105%) of the label amount with the absorbance at 232nm. result is shown in the form of graphical structure. When the brands i.e Glycomet, Glyciphage and Mefomin were treated with different degradation parameters such as acid, heat and UV light it was found that the drug degradation observed in all three brands of Metformin while no degradation is observed when these three brands were treated with 0.1N NaOH.

Index Terms— Metformin, Drug Degradation, Different brands, UV Spectrophotometer.

I. INTRODUCTION

The chemical stability of a pharmaceutical molecule is a matter of great concern as it affects the safety and efficacy of the drug product. The FDA and ICH guidelines state that there are requirements of stability testing data to understand how the quality of drug substance and drug product changes with time under the influence of various environmental factors. Forced degradation is a process that involves degradation of drug products and drug substances at conditions more severe than the accelerated conditions and thus generates the degradation products that can be studied to determine the stability of the molecule.

The ICH guideline states that stress testing is intended to identify the likely degradation products which further helps in determination of the intrinsic stability indicating procedures used. But these guidelines are very general in conduct of forced degradation and do not provide details about approach towards stress testing. The samples generated from the forced degradation can be used to develop the stability indicating method which can be applied later for analysis of samples generated from accelerated and long term stability studies.

Forced degradation studies are also called as stress testing studies.

Forced degradation studies are carried out to archive following purposes:-

-To establish the degradation pathway of different drug substances and drug products. To determine the intrinsic stability of drug substances in formulation.

-To reveal the degradation mechanism such as hydrolysis, oxidation, thermolysis of the drug substance and drug product.

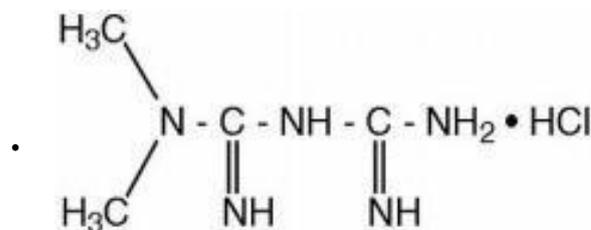
-To produce degradation profile.

-To solve stability related problems.

-To understand chemical properties of drug molecules.

II. DRUG PROFILE

Metformin hydrochloride tablet is an oral antihyperglycemic drug used in the treatment of type II Diabetes. The structural formula of Metformin is as follows:



Metformin HCl is a white to off-white crystalline compound with a

- Molecular formula C₄H₁₁N₅·HCl.
- Molecular weight 165.63.
- Metformin bioavailability of 50 to 60%.
- The pKa of Metformin is 12.4.

If you have Diabetes, your pancreas does not make insulin. This leads to a rise in the level of glucose in the blood. Metformin HCl helps to lower the blood glucose level to as normal a level as possible.

III. EXPERIMENTAL

A. Drug products:

The Metformin brands used are :-

[1] Glycomet 500mg

Each uncoated tablet contains Metformin HCl IP 500mg
excipients.....q.s

Batch No.28014068

Manufacturing Industry:-USV Pvt.Ltd.

Expiry date:- 6/2020

[2] Glyciphage 500mg

Each uncoated tablet contains Metformin HCl IP 0.5 gm
excipientsq.s

Batch No.GA17066

Manufacturing Industry:- FRANCO-INDIAN
PHARMACEUTICALS Pvt.Ltd

Expiry date:- 11/2020

[3] Metformin 500mg

Each uncoated sustain release tablet contain Metformin HCl IP
0.5gm

Batch No.KMJ602A

Manufacturing Industry:- MACLEODS
PHARMACEUTICALS Ltd

Expiry date:-11/2018

B. Materials and Reagents:

All the reagents used were of analytical grade including Hydrochloric acid, Sodium hydroxide, Deionised water .And the materials used for the study are the different brands of Metformin tablet such as Glycomet 500mg , Glyciphage 500mg , Mefomin 500mg.

C. Glasswares:

Volumetric flask, Test tubes, Beakers, Measuring cylinders, Pipette.



All these glasswares are washed properly (Rinsed with deionized water which was freshly prepared in laboratory).

D. Instruments used:

Digital weighing balance, electric water bath,UV Visible Spectrophotometer: (UV-1601).



E. Methods of preparing working solutions:

1) Preparation of NaOH Solution:

In 100ml volumetric flask, 40gm NaOH was taken and Deionized water added in the volumetric flask to dissolve the NaOH.

2) Preparation of HCL:

Total 9ml Hydrochloric acid was taken in the 100ml volumetric flask to make up the volume upto 100ml by adding deionized water.

3) Preparation of Metformin solution:

The tablets of each brand were weighed individually. Each brand was triturated in mortar and pestle individually. Powder was equal to 20mg Metformin. Glycomet (11.4mg), Glyciphage (11mg), Mefomin (15mg) were accurately weighed. In 100ml volumetric flask, all of three brand powders transferred individually. these powder samples were dissolved in deionized water and finally more water was added to make up the volume upto 100ml respectively for each sample. A total of 20mg/100ml concentration solution was preferably obtained . By using spectrophotometer at 232nm wavelength individually all brands absorbance were determined. Take these solutions as stock solution of the different brands.

F. Procedure for degradation studies:

1) For Acid:

Forced degradation of drug substance in acidic media was performed by taking 5ml of 20mg/100ml of Glycomet, Glyciphage and Mefomin in 3 separated test tubes then 5ml 0.1NHCl was added in each test tube. The sample was left for 30 min. and then the solutions were transferred to a separate cuvette after the time period completion and UV absorbance of the solution was measured at 232nm wavelength.

2) For Base:

Forced degradation of drug substance in basic media was performed by taking 5ml of 20mg/100ml solution of Glycomet, Glyciphage and Mefomin in 3 separate test tubes, then 5ml of 0.1N NaOH was added in each test tube and the sample was left for 30 min and then UV absorbance of solution was measured at 232nm wavelength.

3) For UV light:

The forced degradation of drug substance in UV light was performed by taking the 5ml of 20mg/100ml solution of Glycomet, Glyciphage and Mefomin in 3 separate test tubes.

Then 5ml of water was added in each test tube and these test tubes were exposed to UV light for 30 minutes and then UV absorbance of solution was measured at 232nm wavelength.

4) For Heat:

The forced degradation of drug substance in thermal (heat) environment was performed by taking 5ml of 20mg/100ml solution of Glycomet, Glyciphage and Mefomin taken in separate test tube then 5ml of water was added in each test tube and these solutions were kept in water bath at 50°C for 30 min and the absorbance of solution was measured at 232nm wavelength by using UV spectrophotometer.

G. Result:

We have conducted the degradation study on forced degradation parameters of three brands of metformin i.e. Glycomet 500mg tablets USV private limited, Glyciphage 500 mg tablets of FRANCO-INDIAN PHARMACEUTICALS PVT.LTD. and Mefomin 500mg tablets MACLEODS PHARMACEUTICALS LTD. Their absorbance for degradation parameters before and after treatment (acid, base, UV and heat) are given in (table 2) and their graphical representation shown in (fig. 3)

Table 2: Absorbance of different brands of Metformin

Treatment	Glycomet	Glyciphage	Mefomin
Before	1.823	1.816	1.823
After acid	1.541	1.530	1.512
After base	1.832	1.824	1.826
After heat	0.998	1.588	1.286
After UV	1.001	1.601	1.616

When different brands of metformin (Glycomet, Glyciphage, Mefomin) were subjected to 0.1N HCL, absorbance decreases. When brands of metformin were subjected to 0.1 N NaOH, drugs shows slightly increase in the absorbance. When Glycomet, Glyciphage, Mefomin were exposed to UV- light there is decrease in absorption. When Glycomet, Glyciphage, Mefomin were subjected to Heat at 50°C for 30 minutes drugs shows great decrease in the absorbance.

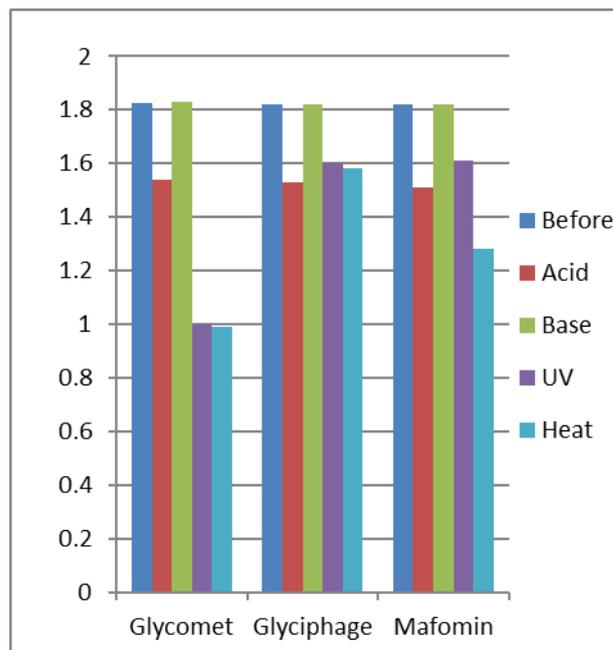


Figure 3: Degradation pattern of different brands of Metformin

Table 3: Percent degradation of different brands of Metformin

PARAMETERS	Glycomet	Glyciphage	Mefomin
Acid	84.53	83.92	82.94
Base	100.4	100.4	100.16
UV	54.90	88.16	88.64
Heat	54.74	87.44	70.54

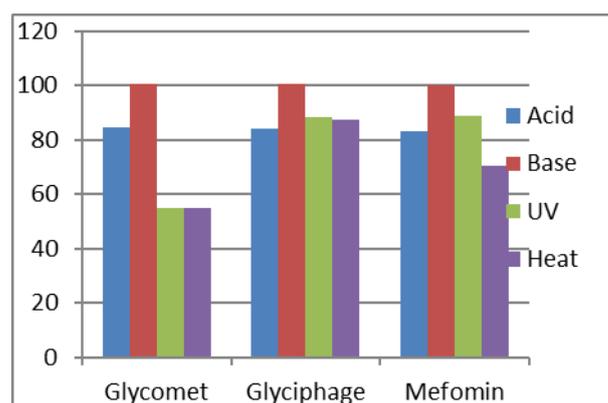


Figure 2: Percent degradation of different brands of metformin

IV. CONCLUSION:

According to specification of Indian pharmacopoeia, the content official limit of not less than (95%) and not more than

(105%) [3,4] of the label amount our hypothesis was that When all different brands of Metformin were exposed to the different degradation parameters .The result of study concludes that , when the different brands of Metformin were treated with the 0.1N HCL degradation was observed in all three brands. When all three brands of Metformin were exposed to UV light and heat degradation is observed in all brands of Metformin while no degradation is observed when the all three brands of Metformin when treated with 0.1N NaOH.

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