WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 7, Issue 3, 1247-1252. Research Article ISSN 2277– 7105

UV SPECTROSCOPY ANALYSIS AND DEGRADATION STUDY OF CLOPIDOGREL BISULFATE

Indrajeet S. Patil*, Omkar A. Patil, Sampda V. Kadam, Manoj M. Nitalikar, Shriniwas K. Mohite

Rajarambapu College of Pharmacy, Kasegaon, Kasegaon, Walwa, Sangali, Maharashtra, India.

Article Received on
14 Dec 2017,

Revised on 03 Jan. 2017,
Accepted on 24 Jan. 2018

DOI: 10.20959/wjpr20183-10947

***Corresponding Author**
Indrajeet S. Patil
Rajarambapu College of Pharmacy, Kasegaon, Kasegaon, Walwa, Sangali, Maharashtra, India.

ABSTRACTS

Clopidogrel bisulfate is antiplatelet drug which undergo hepatic first pass metabolism and low oral bioavailability. According to ICH guidelines, the major factors that contribute in degradation of a drug product comprise of temperature, time, photo degradation, pH variation (high and low), acid/base stress testing and/or with humidity. An attempt was made to examine and calculate the quantity of drug in the presence of degradation products by UV-Vi spectroscopy method. According to the WHO, the official assay limit of the content should not less than 97% and not more than 101.05% of labelled amount of Clopidogrel bisulfate. The results of experiment revealed that Clopidogrel bisulfate degrade much especially on exposure to UV light and heat but do not degrades in basic medium whereas slight degradation occurs in acidic medium.

KEYWORDS: Clopidogrel bisulfate, Degradation, UV.

I. INTRODUCTION

Clopidogrel bisulfate, methyl (+)-(S)-(2-chlorophenyl)-6,7dihydrothie no[3,2-c] dihydrothieno[3,2] pyridine5(4H)- acetate sulfate (1:1), is a potent oral antiplatelet agent often used in the treatment of coronary artery disease, peripheral vascular disease and cerebrovascular disease.[1] Clopidogrel bisulfate is an antiplatelet drug, undergoes hepatic first pass metabolism and low oral bioavailability (50%).[2] It selectively and irreversibly inhibit the binding of adenosine diphosphate (ADP) to its platelet receptors thus prevents ADP induced platelet aggregation through an active metabolite.[3] Clopidogrel's platelet inhibiting activity makes it an effective drug for reducing the incidence ischemic strokes,

heart attacks or claudication due to vascular diseases such as atherosclerosis.[4] By the blockade of this receptor inhibits platelet aggregation by blocking activation of the glycoprotein IIb/IIIa pathway. The IIb/IIIa complex function as a receptor, mainly for fibrinogen and vitronectin but also for fibronectin and willebrand factor.[5] It functions via unique mechanisms enhancing the coronary blood flow by shifting energy substrate utilization to glucose through inhibition of fatty acid metabolism.[6] Unlike conventional anti anginal drugs including calcium channel blockers and β-blockers, trimetazidine offers aging individuals a complementary and potentially more effective way to ward off heart attack by enhancing the heart's energy producing function rather than weakening the heart.[7]

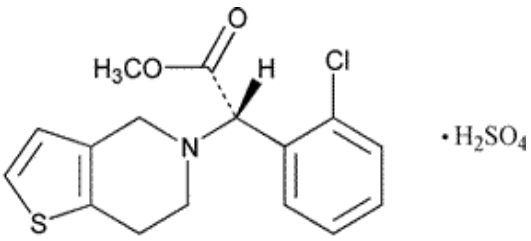

Figure1: Chemical Structure of Clopidogrel bisulfate.

Spectrophotometry is the most preferred technique for degradation studies over other methods because of less equipment cost and economical maintenance advantage. Spectrophotometry technique is based on measuring the absorption of a monochromatic light in the near ultraviolet region (200- 380 nm) by colorless complex. UV spectrophotometry can also be used for stress degradation. According to International Conference of Harmonization (ICH) guideline active pharmaceutical ingredient is focused to various forced degradation conditions which are acidic, basic and light conditions.[8,9] Degradation studies are necessary in the development of new drug product. Many factors are responsible for degradation of drug or product like temperature humidity, and light. In this research work the effect of various factor like acid, base, UV light and heat on Clopidogrel bisulfate was studied.

Parameters Involved in Forced Degradation

Distinctive forced degradation studies on drug substance involves acid/base stress testing, photo degradation, temperature, time, pH variation (low and high).

Acid/Base Stress Testing

Acid/base stress testing is used for the evaluation of forced degradation of a drug substance. This test involves degradation of a drug substance by exposure to basic or acidic medium

over time to its primary degradation products. In carbonyl functional group like alcohol, imines, imides, amides, esters (lactones) aryl amines, carbomets acid and base degradation take place by hydrolysis.

Degradation by UV light

Many formulation or products made of synthetic or natural polymer are UV unstable. They degrade or disintegrate expose to continuous sunlight. The degree of disintegration is depends up on degree of exsposer.

Thermal (Heat) and / or humidity stress testing

Many drugs are thermal (heat) and humidity sensitive. Thermal (Heat) and humidity is degrade substance up to its main components. This test is performed by exposing the drug or formulation to thermal / humidity condition.

II. EXPERIMENTAL

Material and Reagents: Pure Clopidogrel bisulfate was procured as a purchase from Yarrow chem. products and all other chemicals used were of AR grade. UV-visible spectrophotometer (JASCO V-630) with quartiz cuvett was used for the studies.

0.1 N hydrochloric acid was prepared by taking 8.3 ml hydrochloric acid (HCl) in 100 ml volumetric flask having purity 37% and the final volume upto the mark of the flask was made with distilled water. Same procedure was followed for the preparation of 0.1N sodium hydroxide solution. 200 ppm Clopidogrel bisulfate solution was prepared by accurately weighing 0.020gm pure Clopidogrel bisulfate and was transferred it into 100ml volumetric flask. Small amount of water was added in volumetric flask to dissolve Clopidogrel bisulfate and final volume was adjusted with distilled water. Absorbance of solution of Clopidogrel bisulfate was measured by UV spectrophotometer at maximum wavelength 220 nm.

Degradation studies

For acid

To study degradation in acid medium or to determine effect of acid on Clopidogrel bisulfate, 5ml of 200ppm Clopidogrel bisulfate solution was mixed with 5ml of 0.1 N hydrochloric acid (HCL) solution and was kept aside for 30 minutes. After 30 minutes absorbance of solution was measured by UV spectrophotometer at maximum wavelength 220nm.

For base

To study degradation in basic medium or to determine effect of base on Clopidogrel bisulfate, 5ml of 200ppm Clopidogrel bisulfate solution was mixed 5ml of 0.1 N sodium hydroxide solution (NaOH) was kept aside for 30 minutes. After 30 minutes absorbance of solution was measured by UV spectrophotometer at maximum wavelength 220nm.

For UV light

To study degradation in UV light medium or to determine effect of UV light on Clopidogrel bisulfate, 5ml of 200ppm Clopidogrel bisulfate solution in test tube and 5ml distilled water was added and kept aside for 30 minutes in UV light of 320nm. After 30 minutes absorbance of solution was measured by UV spectrophotometer at 220 nm.

For thermal (Heat)

To study degradation in thermal medium or to determine effect of heat on Clopidogrel bisulfate, 5 ml of 200 ppm Clopidogrel bisulfate solution was taken and 5ml of distilled water was added and was kept aside for 30 minutes in water bath at 50^0 c. After 30 minutes absorbance of solution was measured by UV spectrophotometer at maximum wavelength 220 nm.

III. RESULTS AND DISCUSSION

Clopidogrel bisulfate was exposed to various physical conditions and degradation effect occurred was studied by UV. Results obtained are mentioned. Absorbance after exposure to different conditions was measured and results are shown in table 1 and shown graphically in fig. 1. Percentage degradation was calculated and is shown in table 2 and graphically in fig. 2.

When Clopidogrel bisulfate was exposed to 0.1N HCl, Clopidogrel bisulfate did not show any significant change in terms of availability (98.65%). But, when Clopidogrel bisulfate was exposed to 0.1 N NaOH, Clopidogrel bisulfate showed highly significant change in term of availability (119.22%). When Clopidogrel bisulfate exposed to heat for 30 minutes, highly decreased availability observed (77.17%) and when exposed to U.V light, Clopidogrel bisulfate also showed decreased availability (92.45%).

It can be concluded that Clopidogrel bisulfate does not get degraded on exposure to acidic medium 0.1N HCl. (98.65 %) but have major degradation effect on exposure to basic

medium 0.1N NaOH (119.22%). When Clopidogrel bisulfate was exposed to UV light and heat for 30 minutes high degradation was observed 92.45% and 77.17% respectively.

Table 1: Absorbance of Clopidogrel bisulfate.

Degradation Parameters	Readings after 30 Minutes			
	1	2	3	Average
Before	1.7869	1.7865	1.7870	1.7868
After acid	1.7624	1.7626	1.7630	1.7626
After base	2.1304	2.1306	2.1304	2.1304
After heat	1.3789	1.3792	1.3786	1.3789
After U.V	1.6523	1.6524	1.6527	1.6524

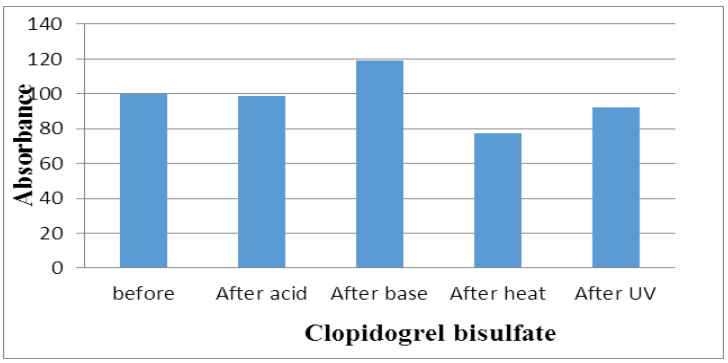

Figure 2: Absorbance of Clopidogrel bisulfate.

Table 2: Degradation Pattern in Percentage of Clopidogrel bisulfate.

Degradation Parameters	Readings after 30 Minutes			
	1	2	3	Average
Before	100	100.04	100.01	100.01
After acid	98.64	98.68	98.65	98.65
After base	119.22	119.24	119.22	119.22
After heat	77.17	77.16	77.20	77.17
After U.V	92.46	92.45	92.46	92.45

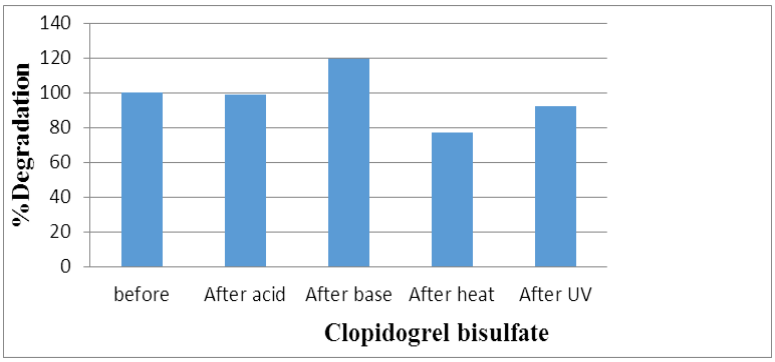

Figure 3: Degradation Pattern of Clopidogrel bisulfate.

IV. CONCLUSION

According to specification given in WHO monographic for Clopidogrel bisulfate, the official assay limit of the content should not less than 97% and not more than 101.05% of the estimated potency. From our result we concluded that Clopidogrel bisulfate degrades to a very larger extend when exposed to basic medium whereas it also degrades in the presence of acidic medium, heat and UV light.

V. REFERANCES

1. Dwarakanadha R P, Swarnalatha D, Sidda R B, Karthik S K P, Sardar U M. Design; Development and Characterization of Clopidogrel Bisulfate Transdermal Drug Delivery System; *Asian J Pharm. Clin. Res.*, 2015; 8(2): 277-280.
2. Gajanan D, Dinesh K J, Vinod K P; Formulation and Evaluation of Transdermal Drug Delivery System of Clopidogrel Bisulfate; *AJPLS*, 2011; 1(3): 269-277.
3. Kalyan L K, Hemant K J; Development and Validation of UV Spectrophotometric Method for Determination of S (-) Metoprolol Succinate and Clopidogrel Bisulphate in Bulk and Tablet Dosage Form; *Int J Pharm Pharm Sci*., 2013; 5(3): 593-598.
4. Dr. U.C.Mashelkar, Sanjay D.R; A LCMS Compatible Stability-Indicating HPLC Assay Method for Clopidogrel bisulphate; *Int J Chemtech Res*., 2010; 2(2): 822-829.
5. A. Mounika, N.Sriram; Method Development and validation of Clopidogrel bisulphate by Reverse Phase HPLC in Bulk and Pharmaceutical Dosage Forms; *IJPAR*, 2012; 1(1): 1-7.
6. Abdulwali A S, Mahmoud M A, Maged A N, Ala`a M. A. Almaktari; Formulation and evaluation of trimetazidine hydrochloride and clopidogrel bisulphate multi-unit solid dosage forms; *JOCPR*, 2014; 6(2): 421-426.
7. A Onay-Besikci; S Guner; E Arioglu; I Ozakca; AT Ozcelikay; VM Altan, Can J Physiol Pharmacol, 2007; 85(5): 527-35.
8. Safila N, Safeena N, Nimra W, Fatima Q; Degradation Study of Lincomycin by UV Spectroscopy; *AJBAS*, 2014; 6(5): 131-134.
9. Octavian C, Adela-Maria S, Ionela B, Adina T F, Johny N; Development and Validation of an HPLC Method for Simultaneous Quantification of Clopidogrel Bisulfate, Its Carboxylic Acid Metabolite and Atorvastatin in Human Plasma: Application to a Pharmacokinetic Study; *JAMC*, 2015; 1-12.