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A Novel, Simple Method Development and Validation: Force Degradation Studies of Dapagliflozin By UV Spectroscopy

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ABSTRACT

A simple, sensitive, precise, accurate, economic and rapid visible spectroscopic method has been developed for estimation of dapagliflozin in API.Dapagliflozin was subjected to different stress conditions as per ICH guideline Q1A (R2). A stability- indicating UV Spectroscopic method has been developed for analysis of the drug in the presence of the degradation products. Water and Methanol (70:30) is used as a solvent for force degradation study. Degradation of Da-pagliflozin was studied in acid, alkaline, hydrogen peroxide, photolytic, thermal. The amount of Degraded drug was calculated by taking absorbance at 284 nm. The linearity for dapagliflozin was found to be in the range of 10 -60 ug/ml with the regression coefficient of 0.999. The drug was found to be more liable to decompositions in acidic,alkaline,oxidative , than in photolytic and thermal conditions. Photolytic degradation at 254nm. About 5-20% of degradation is observed in thermal degradation. If no degradation is achieved then molecule is stable. This method can be used for determination of Dapagliflozin in quality control of formulations without interferences of the excipients.

Keywords – Dapagliflozin , U V spectroscopy, API , Internationally Conference for harmonization.

INTRODUCTION:

Dapagliflozin belongs to a new class of oral anti Diabetic drugs, called Sodium Glucose Co-transporter 2 (SLGT2) inhibitors. These sodium Glucose co-transporters are responsible for glucose Reabsorption in the kidney. Hence inhibiting the SLGT2 have been proposed as a new strategy in the treatment of diabetes.

It Is defined in chemical terms as (1S)-1, 5-anhydro-1-C-[4-chloro-3-[(4-ethoxy phenyl) methyl]-D-glucite. Structure Of Dapagliflozin shown in Figure 1. This is ethanol, methanol, Dimethyl-sulfoxide, and dimethyl-formamide soluble white Crystalline powder. Dapagliflozin is category III in the Biopharmaceutical Classification System (BCS) according To the European Medicines Agency (EMA), which is more soluble, anud almost impermeable.

Dapagliflozin is effective and decreases both Weights of the body and blood pressure. This drug is efficient In type 2 diabetes mellitus (DM) patients, both as a single Agent, as well as, in combination with other antidiabetic Agents. In addition, recent studies have shown relatively Fast action of dapagliflozin, with decreases in fasting Plasma glucose levels within one week of treatment.[1][2][3]

EXPERIMENTAL :

Preparation of solvent solution :

The solvent solution was prepared by mixture of water & methanol in the proportion of 70:30.

Preparation of standard stock solution :

The standard stock solution was prepared by disolving 10 mg Dapagliflozin in 100 ml of solvent of water & Methanol (70:30).

METHOD :

Instruments - UV spectroscopy

Type - Double beam

Drug - Dapagliflozin

Solvent Water + Methanol - (70:30)

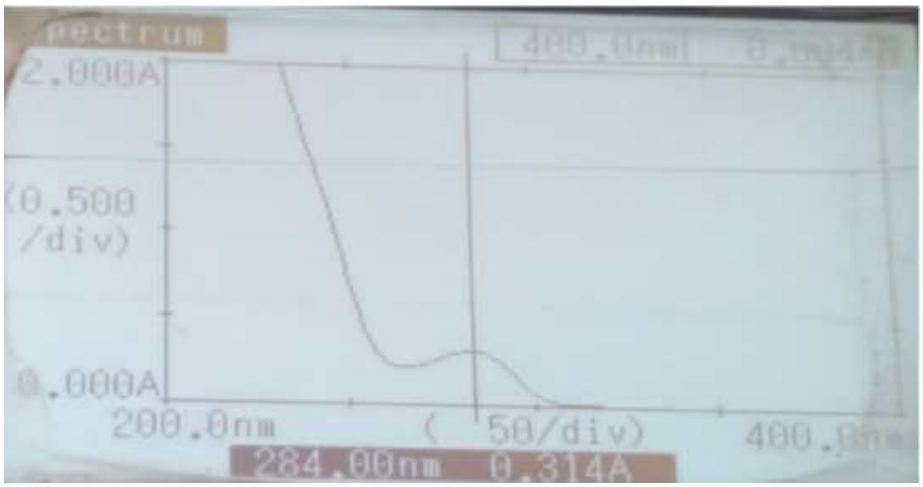
Wavelength - 284 nm

METHOD VALIDATION [6,7,8]

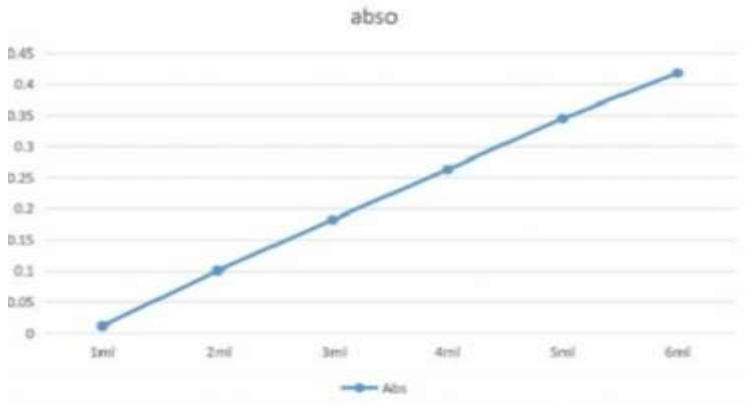
A novel method and development validation :force degradation studies of Dapagliflozin by UV spectroscopy as per ICH guidelines :force degradation studies of Da-Pagliflozin by uv spectroscopic. Method validation is defined as the process that Confirms the analytical procedure employed for a Particular test is suitable for its intended use. Validation assures that a measurement process Produces valid measurements. Results from method Validation are used to judge the quality, reliability of Analytical results. It is an integral part of any good Analytical practice. The proposed method was validated For the parameters like linearity, Accuracy ,Precision , Ruggedness and Robustness as per ICH guideline.

a) Linearity :

Various stock solutions were pr,epared form the 100ug/ml in the concentration range 10- 60ug/ml and scanned by UV visible spectrophotometer and linearity range found to be in 10-60 ug/ml.



b) Accuracy:-



The accuracy of the proposecovery studies at three different levels I. e 50%, 100%, 150% . The recovery studies were carried out by adding known amount of standard solution of the drug to pre-analysed tablet solutions .The resulting solutions were then re-analysed by proposed methods.

c) Precision :

Precision of the methods was studied as intra-day, inter-day and repeatability. Intra-day study was performed by analyzing, the three different concentration of drug for three times in the same day. Inter-day precision was performed by analyzing three different concentration of the drug for three days in a week. Repeatability was performed by analyzing same concentration of drugs for six times.

d) Robustness:

Robustness was carried out by two different wavelengths (+/-2 nm) i.e 282 nm and 286 nm . The respective absorbance is noted and result was noted in %RSD.

e) Ruggedness:-

Ruggedness of the proposed method is determined by analysis of aliquots from homogenous slot by different analysts using similar operational and environmental conditions.

FORCE DEGRADATION STUDIES:

The International Conference on Harmonization (ICH) guideline entitled stability testing of new drug substances and products requires that stress testing be carried out to elucidate the inherent stability characteristics of the active substance. The aim of this work was to perform the stress degradation studies on the Dapagliflozin using the method developed

1)Acidic Degradation

2)alkaline Degradation

3)Thermal Degradation

4)Photolytic Degradation

5)Oxidative Degradation

1)Acidic Degradation :-

2 ml of stock solution was transferred to 10 mL volumetric flask. To this sufficient quantity of methanol and water (30:70) was added to dissolve the drug. To this 1 mL of 0.5 N HCL was added and was kept at room temperature, and further diluted with methanol and water (30:70) to get concentration of 10 µg/mL.

2)Alkali Degradation :-

2 ml of stock solution was transferred to 10 mL volumetric flask. To this sufficient quantity of methanol and water (30:70) was added to dissolve the drug. To this 1 mL of 0.5 N NAOH was added and kept at room temperature, and further diluted with methanol and water (30:70) to get concentration of 10 µg/mL.

3) Thermal Degradation :-

Dapagliflozin sample was taken in a petriplate and exposed to a temperature of 60°c for 48 ours in an oven. After 48 hours, 10 mg of the sample was diluted with methanol and water (30:70) in order to make the volume up to 10 ml. From this solution, dilutions were carried out to achieve the appropriate concentration (20µg/ml) and the solution was taken in cuvette for the UV-VIS Analysis.

4) Photolytic Degradation:-

Sample of Dapagliflozin was exposed to near ultraviolet lamp in photostablity chamber providing illumination of not less than 1.2 million lux hours. Ten milligrams sample was dissolved in methanol & water (30:70) and volume made up to 10 ml. From this solution appropriate dilution (20µg/ml) was made using methanol & water(30:70)and taken in cuvette for the U.V analysis.

5) Oxidative Degradation:-

To 2 ml of the stock solution of Dapagliflozin (1000µg/ml), 1 ml of 3% w/v of hydrogen peroxide added in 10 ml of volumetric flask and the volume was made up to the mark with methanol & water (30:70). The volumetric flask was then kept at room temperature for 15 min. For the blank, 1 ml of the 30 % w/v of hydrogen peroxide was kept at normal condition for overnight in 10 ml of volumetric flask. Both solutions were heated on boiling water bath to remove the excess of hydrogen peroxide. Finally, after 15 minutes dilutions were made from the stock solution to achieve the required concentration (30µg/ml). The solution was then taken in a cuvette and analysed in UV. [4][5][6][7][8]

RESULT :

Method Validation

Parameters	**UV Visible Spectroscopy**
Wavelength	284nm
Linearity range	10-60
Correlation Coefficient	0.999
Precision (%RSD)	

Intraday (n=6)	0.196
Interday (n=6)	0.188
Ruggedness (%RSD)	
Analyst 1	0.968
Analysts 2	0.689
Robustness(%RSD)	
Wavelength 1 (282)	1.256
Wavelength 2 (286)	1.306

Force Degradation Studies

Condition	**Time**	**%Degradation**
Acidic degradation	60 Minutes	83%
Alkaline degradation	60Minutes	89.69%
Photolytic degradation	2 hrs	88.5%
Thermal degradation	2 hrs	79%
Oxidative degradation ($3\%H_2O_2$)	60 Minutes	98%

CONCLUSION:

The method was successfully applied for the force degradation studies of Dapagliflozin in API and pharmaceutical Dosage form. Study the quality of the marketed Drug with this method. Study the applicability of The method for formulation containing Dapagliflozin in multicomponent dosage form.

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