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Research Article

Degradation Study of Dapagliflozin in API by Spectroscopic Method

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Abstract

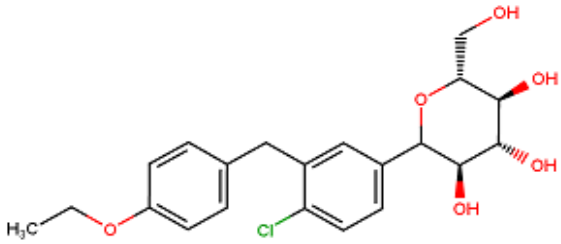
A simple, sensitive, precise, accurate, economic and rapid visible spectroscopic method has been developed for estimation of dapagliflozin in API.Dapagliflozin was subjected to different stress conditions as per ICH guideline Q1A (R2). A stability- indicating UV Spectroscopic method has been developed for analysis of the drug in the presence of the degradation products. Degradation of Dapagliflozin was studied in acid, alkaline, hydrogen peroxide, photolytic, thermal and neutral conditions. The amount of degraded drug was calculated by taking absorbance at 272 nm.The drug was found to be more liable to decompositions in acidic,alkaline,oxidative , neutral medium than in photolytic and thermal conditions.

Key words: Dapagliflozin, UV- Spectroscopy, API, International Conference on 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.[1,2,3] suppressing the SLGT2,dapagliflozin plasma glucose concentration intern by elevating the renal glucose excretion by the kidney. It is chemically known as (1s)-1,5-anhydro-1-C-[4-chloro-3-[(4-ethoxy-phenyl) methyl] phenyl]-D-glucitol(fig.1).It has a molecular formula $C_{24}H_{33}CLO_8$ with molecular weight 408.98. Dapagliflozin is a white crystalline powder which is soluble in water, ethanol, methanol and dimethyl formamide.

The aim of present work was to develop the degradation of DAPA in its API by UV-spectroscopic method.



Material and Methods:

Materials & Reagents:

- Pharmaceutical grade Dapagliflozin standard was obtained as generous gift from Indogo Remedies, Mumbai, Maharashtra, India. All the chemicals and solvents used were of analytical grade.
- The solution of 0.1 N NaOH , 0.1 N HCL, 5% hydrogen peroxide was prepared in double distilled water as per IP 1996 procedure.
- Methanol and other chemicals used which were of analytical grade and were procured from local market.

Instruments:

- Shimadzu UV-1800, double beam spectrophotometer with matching pair of 1cm quartz cuvettes with a fixed slit width 2 nm was used for all spectral measurements.

- Analytical balance (Acculab ALC-2014, Huntigdon Valley, PA)

Results :

Sample	Conc'n used (µg/ml)	Conc'n after Degradation (µg/ml)	% Recovery
Acid hydrolysis	10	7.14	78
Alkaline hydrolysis	10	7.8	71.4
Oxidation	10	7.38	73.8
Photolytic	10	9.52	95.2
Thermal	10	4.28	42.8
Neutral	10	6.42	64.2

Preparation of Standard Stock Solution:

The standard stock solution was prepared by dissolving 10.0 mg of Dapagliflozin in 10.0 ml of methanol to acquire a concentration of 1000µg/mL. The working standard solution of 10 µg/mLwas prepared by appropriate dilution of the stock solution with distilled water.[4,5]

Preparation of Working Standard Stock Solution:

10 ml of standard stock solution was pipette out and made up to 100 ml to get a concentration 100 µg/ml and was treated as the working standard.(fig:1)

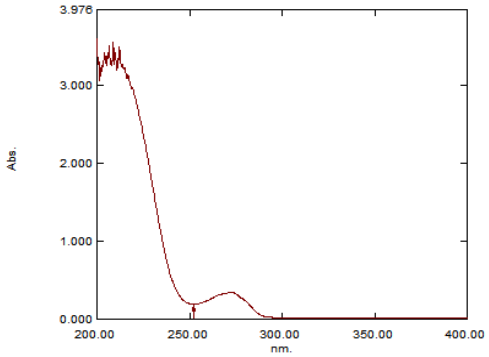


Fig 1 : UV spectrum of standard Dapagliflozin

Forced Degradation Studies

To assess the stability indicating property of the developed HPLC method stress studies were carried out under ICH recommended conditions.Forced degradation of Dapagliflozin was carried out by exposing the bulk sample of acidic, alkaline, oxidative, photolytic, neutral conditions. The aim was to study the ability of the proposed method to, measure the analyte response in presence of its degradation products.[6,7,8,9]

Acidic Degradation

10 mg of drug sample was transferred to 10 mL volumetric flask. To this sufficient quantity of methanol (2 mL) was added to dissolve the drug. To this 2 mL of 0.1 N HCL was added and was kept at room temperature, and further diluted with water to get concentration of 10 µg/mL.(fig:2)

Alkali Degradation

10 mg of drug sample was transferred to 10 mL volumetric flask. To this sufficient quantity of methanol (2mL) was added to dissolve the drug. To this 2 mL of 0.1 N NAOH was added and kept at room temperature, and further diluted with water to get concentration of 10 µg/mL.(fig:3)

Oxidative Degradation

10 mg of drug sample was transferred to 10 mL volumetric flask. To this sufficient quantity of methanol (2 mL) was added to dissolve the drug. To this 2 mL of 5 % H_2O_2 was added and was kept at room temperature for 2 hr, and further diluted with water to get a concentration of 10 µg/mL.(fig:4)

Photolytic Degradation

10 mg of drug sample was placed in closed petri dish and was exposed to sunlight for 4 hrs.and further the solution was dissolved in water to get a concentration of 10 µg/mL. (fig:5)

Thermal Degradation

The bulk sample was exposed to dry heat 80^{0}C. in oven at for 2 hrs. by placing 10 mg of dapagliflozin in closed petri dish. All the stress conditions samples were appropriately diluted to get a final concentration of 10 µg/mL solution and were scanned over a range of 400 to 200 nm by placing respective solvents as blank.(fig:6)

Neutral Degradation

10 mg of drug sample was transferred to 10 mL volumetric flask. To this sufficient quantity of methanol (2 mL) was added to dissolve the drug. To

this 2 mL of water was added and was kept at room temperature for 12 hr, and further diluted with water to get a concentration of 10 µg /ml.(fig:7)

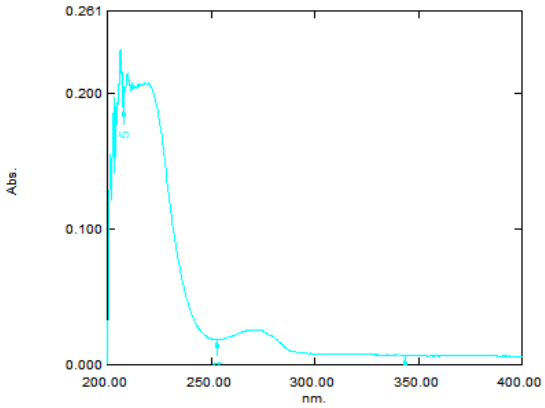


Fig 2 : Degradation in acidic condition

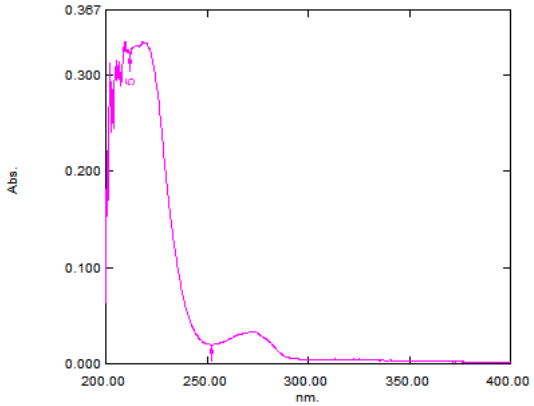


Fig 3 : Degradation in alkaline condition

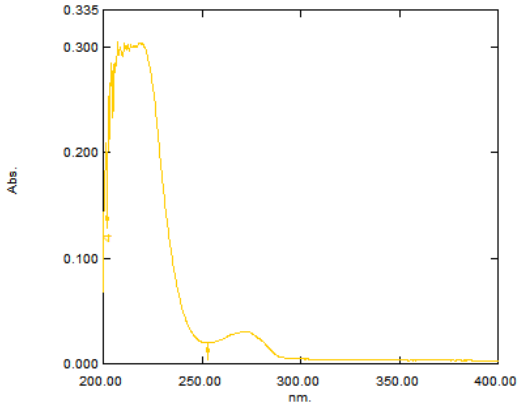


Fig 4: Degradation in Oxidative Condition

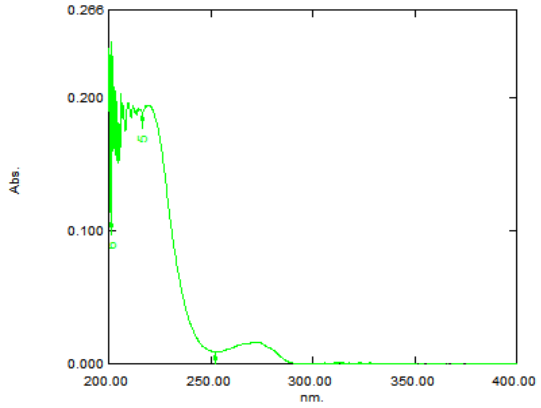


Fig 5: Degradation in photolytic condition

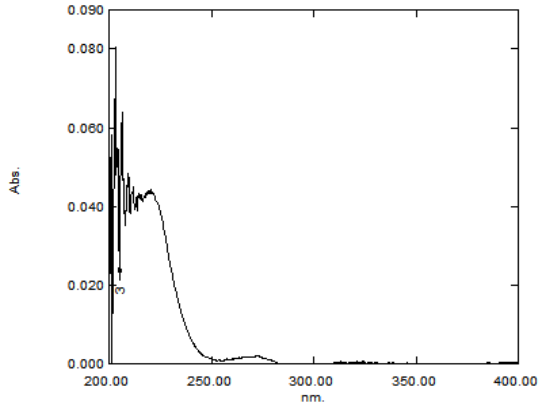


Fig 6: Degradation in Thermal Condition

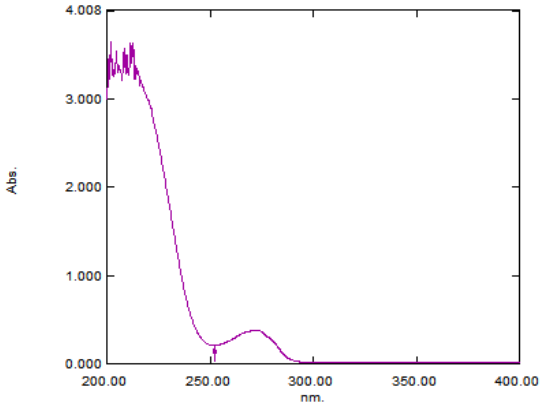


Fig 7: Degradation in Neutral Condition

Conclusion:

The method was successfully applied for the estimation 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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