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DEVELOPMENT AND VALIDATION OF UV SPECTROSCOPIC METHOD FOR THE ESTIMATION OF REMOGLIFLOZIN ETABONATE IN BULK AND TABLETS

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ABSTRACT

Development and implementation of a simple, precise and accurate area under curve spectroscopic method for the estimation of Remogliflozin etabonate in bulk and pharmaceutical dosage form. The drug indicates that the maximum absorption (λ_{max}) at 275nm in n-hexane solution and AUC in absorption spectrum is measured in the wavelength range from 270 to 280nm at a concentration range of 2-10µg/ml according to Beer's law. Linearity analysis showed anR^2 of 0.9998. The % recovery was found to be 98.5-100.7%. The LOD and LOQ were found to be 0.0130 and 0.039µg/ml. The %RSD was found less than 2. The method has been validated for according for linearity, precision, accuracy, robustness, ruggedness, LOD and LOQ according to ICH guidelines.

KEYWORDS

Remogliflozin etabonate, Area under curve spectroscopy, Validation and Pharmaceutical formulations.

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INTRODUCTION

Remogliflozin etabonate is a drug of the gliflozin class drug used in the treatment of non-alcoholic steatohepatitis and type 2 diabetes. Remogliflozin was discovered by a Japanese company and is commercially launched first in India by Glenmark in May 2019.

Oral formulation of Remogliflozin etabonate is available as a prodrug of a benzyl pyrazole glucoside-based inhibitor of renal sodium-glucose co-transporter subtype 2 (SGLT2) with anti-hyperglycaemic Properties. Upon administration and absorption, the inactive prodrug is converted to its active form, Remogliflozin

etabonate and acts selectively on the sodium-glucose co-transporter subtype 2 (SGLT2).

Clinical Studies

Remogliflozin etabonate has been shown toimprove urinary glucose excretion in rats and humans. Early studies in diabetics patients improved plasma glucose levels[1-2]. Remogliflozin etabonate has been studied at doses up to 1000mg[3].

Literature survey revealed that there were few analytical methods have been reported for the determination of Remogliflozin etabonatein pure drug and pharmaceutical dosage forms by using UV spectrophotometric[4-8], HPLC[9-16] and HPTLC[17-20] so far.

The aim of present work is to develop and validate a novel, rapid, simple, precise and specific Area under curve (AUC) Spectrophotometric method for estimation of Remogliflozin etabonatein bulk and tablet dosage form.

MATERIAL AND METHODS

Instrument

UV-Visible double beam spectrophotometer, SHIMADZU (model UV-1700) with UV probe software. All weights were taken in analytical balance.

Chemicals

Remogliflozin etabonate pure drug was obtained as a gift sample from Shree Icon Laboratories Ltd, Vijayawada and its pharmaceutical dosage form Remogliflozin etabonate 20 tablet labelled claim 100mg from local pharmacy manufactured by Glenmark Pharmaceuticals Ltd.

Solvent

N-Hexane was used as a solvent.

Selection of analytical wavelength

Appropriate dilutions of Remogliflozin etabonate were prepared from standard stock solution and using spectrophotometer solution was scanned in the wavelength range 200-400nm. Area under Curve [AUC] in absorption spectra were measured between the wavelength range 270 to 280nm as the detection wavelength (Figure No.2).

Preparation of standard stock solution

100mg of Remogliflozin etabonate was weighed accurately and transferred in to 100ml volumetric flask and diluted inn-Hexane up to mark. From this, 10ml of the solution was further diluted into 100µg/ml and pipetted 0.2, 0.4, 0.6, 0.8 and 1.0ml into 10ml individual volumetric flask and diluted in n-Hexane up to mark, this gives 2, 4, 6, 8 and 10µg/ml concentration.

Preparation of sample solution:

20 tablets of Remogliflozin etabonate marketed formulations was weighed and powdered. A required quantity of tablet powder equivalent to 100mg of Remogliflozin etabonate was transferred into a 100ml of volumetric flask then it was diluted with n-Hexaneand made up to the mark.

Method and validation

The method was validated according to ICH guidelines[21-23].

RESULTS AND DISCUSSION

Method: Area under curve spectroscopy

Linearity

The linearity of an analytical method is its capacity to show the test results that are directly proportional to the concentration of the analyte in the sample within the range. The linearity was established in the range of 2-10µg/ml and Area under Curve [AUC] in absorption spectra were measured between the wavelength of 270 to 280nm as absorbance values are shown in Table No.1 (Figure No.3). The calibration curve was prepared by plotting graph against the concentration and absorbance and therefore the graph shown in (Figure No.4). Statistical parameter like slope, intercept, regression equation, correlation coefficient and Sandell's sensitivity were determined. (Table No.2).

Precision

The precision of an analytical method expresses the closeness of a series of individual analyte measurements obtained from multiple sampling of the equivalent sample. Precision was determined by intra-day and inter-day study. Intra-day precision was determined by analysing the same concentration for six times in a same day. Inter-day precision was determined by analysing the same concentration daily for six days. (Table No.3).

Accuracy

The accuracy of an analytical method says that closeness of test results obtained by that method to the true value. To assess the accuracy of the developed method, recovery studies were carried out at three different levels as 50%, 100% and 150%. In which the formulation concentration kept constant and varied pure drug concentration. (Table No.4).

Ruggedness

The ruggedness is defined as the reproducibility of results when the method is performed under the variation in conditions. This includes different analyst, laboratories, instruments, temperature etc. Ruggedness was determined between different analyst, the value of %RSD was found to be less than 2. (Table No.5).

LOD and LOQ

Thelimit of detection is an individual analytical method is the smallest amount of analyte in a sample which can be reliably detected by the analytical method. The limit of quantitation is an individual analytical procedure is the smallest amount of analyte in a sample which can be quantitatively determined. LOD and LOQ were calculated using formula.

LOD = 3.3(SD)/S and LOQ = 3(LOD)

LOD and LOQ value of were found Remogliflozin etabonate be 0.0130 and 0.039µg/ml.

Table No.1: Calibration curve at 270-280nm by AUC method

S.No	Concentration in µg/ml	Absorbance ±Standard deviation*
1	0	0
2	2	0.187±0.0005
3	4	0.359±0.000745
4	6	0.549±0.001708
5	8	0.737±0.001675
6	10	0.912±0.001118

*Average of six determinations

Table No.2: Regression parameter for Remogliflozin etabonate at 270-280nm by AUC method

S.No	Regression parameter	Results
1	Range (µg/ml)	2-10
2	Λmax (nm)	270-280
3	Regression Equation	Y= 0.0914x+0.0002
4	Slope (b)	0.0914
5	Intercept(a)	0.0002
6	Correlation Coefficient (r^2)	0.9998
7	Sandell's equation	0.0109
8	Limit of detection (µg/ml)	0.0130
9	Limit of quantitation (µg/ml)	0.039

Table No.3: Precision results for Remogliflozin etabonate at 270-280nm by AUC method

S.No	Concentration (µg/ml)	Intra-day Absorbance ±Standard deviation*	%RSD**	Inter-day Absorbance ±Standard deviation*	%RSD**
1	2	0.188±0.000816	0.434	0.187±0.0005	0.263
2	4	0.360±0.00037	0.102	0.360±0.00146	0.405
3	6	0.549±0.00137	0.249	0.550±0.0015	0.272
4	8	0.737±0.00173	0.234	0.738±0.00191	0.258
5	10	0.913±0.00129	0.141	0.913±0.00173	0.189

*Average of six determinations, **% relative standard deviation

Table No.4: Accuracy results for Remogliflozin etabonate at 270-280 by AUC method

S.No	Spiked Levels	Amount of Sample (µg/ml)	Amount of Standard (µg/ml)	Amount Recovered	% Recovery ±Standard deviation*	%RSD**
1	50	6	3	8.93	99.16 ±0.286	0.288
2	100	6	6	11.83	98.5 ±0.180	0.182
3	150	6	9	15.11	100.7 ±0.213	0.211

*Average of six determinations, **% relative standard deviation

Table No.5: Ruggedness results for Remogliflozin etabonate at270-280nm by AUC method

S.No	Analysts	Analyst 1	Analyst 2
1	Mean absorbance	0.549	0.549
2	±Standard deviation*	0.001354	0.001041
3	%RSD	0.245	0.189

*Average of six determinations, **% relative standard deviation

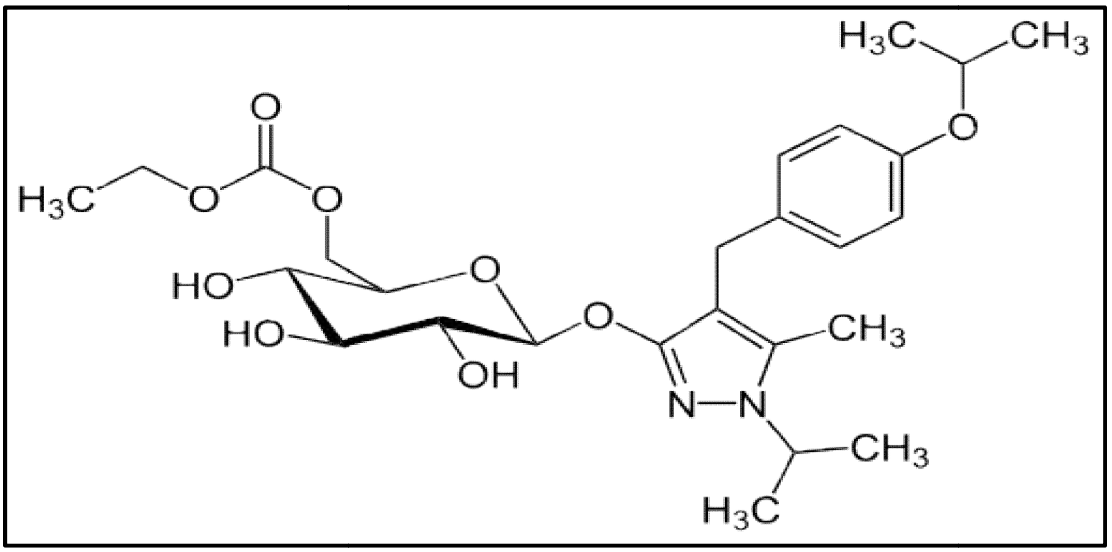

Figure No.1: Chemical structure of Remogliflozin etabonate

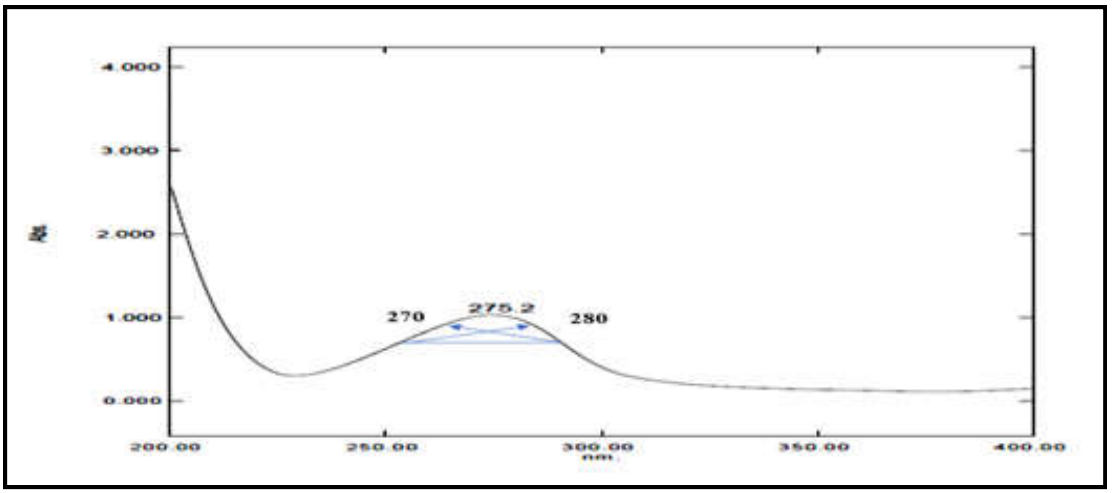

Figure No.2: AUC spectrum of Remogliflozin etabonate at 270-280nm

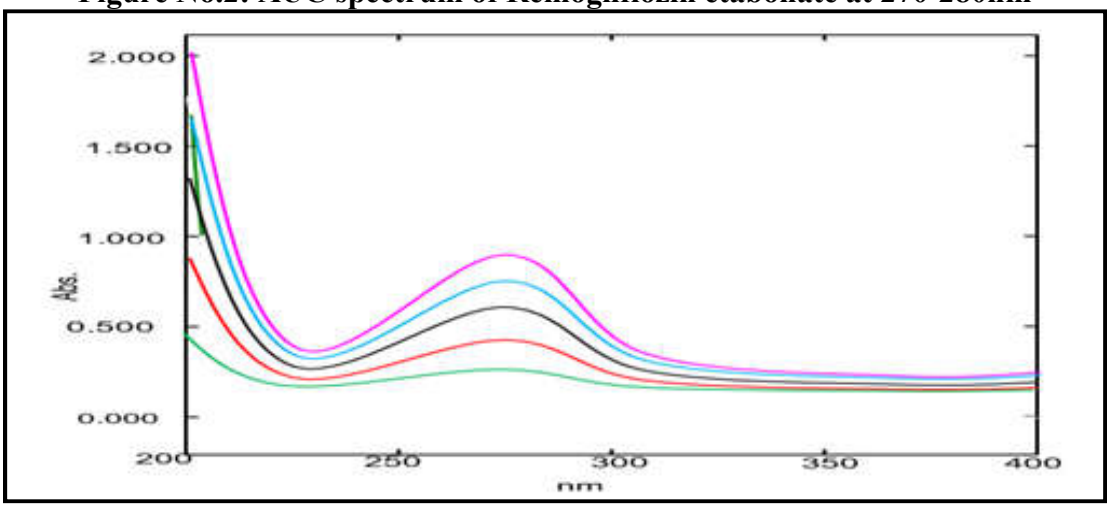

Figure No.3: AUC overlain spectra of Remogliflozin etabonate showing absorbance at270-280nm

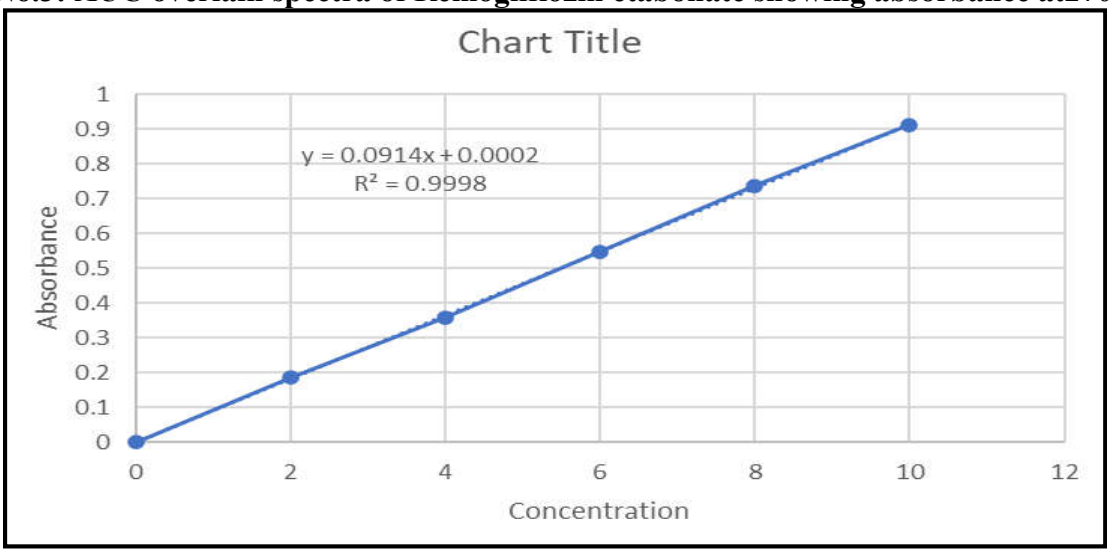

Figure No.4: Calibration curve of Remogliflozin etabonate at 270-280nm by AUC method

CONCLUSION

As per ICH guidelines, the present analytical was carried and met the acceptance criteria. It was concluded that the developed analytical method was simple, specific, accurate, economical and sensitive and can be used for routine analysis of Remogliflozin etabonate in bulk drug and in pharmaceutical dosage forms.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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