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Spectrophotometric determination of an Antidiabetic drug Remogliflozin Etabonate by $KMnO_4$ method

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Abstract

For the determination of an antidiabetic drug Remogliflozin Etabonate a simple, rapid ,economic and sensitive spectrophotometric method is developed. The method is indirect, after allowing the reaction between $KMnO_4$ and drug the excess amount of $KMnO_4$ is determined spectrophotometrically. The excess unreacted $KMnO_4$ was made to react it with a fixed amount of Methyl Orange dye and the absorbance is measured at 510nm. For this method Beer's law is obeyed in the concentration range of 2.5- 25 µg/ml . Molar absorptivity and Sandell's sensitivity are found to be 0.58577 x 10^5 L $mol^{-1}cm^{-1}$ and 0.0089 µg/cm^2 respectively. The different parameters affecting the stability and development of colour was thoroughly studies and optimized.The proposed methods are appropriate for determination of Remogliflozin in pharmaceutical formulations.

KEYWORDS: Remogliflozin Etabonate, , Spectrophotometry, Potassium Permanganate , Methyl orange.

INTRODUCTION

For the control of Diabetes Mellitus Type 2, Sodium-glucose cotransporter-2 inhibitors (SGLT-2) are approved, [1,2] alone or in combination with other antidiabetic drugs. Remogliflozin Etabonate(REMO) (Figure 1) is a recent addition to the SGLT-2 class of antidiabetics [3,4] having better glycemic control. Remogliflozin etabonate is a pro-drug of remogliflozin. Remogliflozin inhibits the sodium-glucose transport proteins (SGLT), which are responsible for glucose reabsorption in the kidney. Blocking this transporter causes blood glucose to be eliminated through the urine.[5]

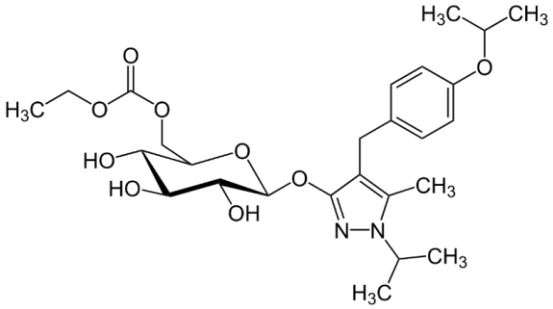

Figure 1: Structure of Remogliflozin Etabonate

Literature survey reveals that two analytical methods [6,7] have been reported for the estimation of remogliflozin alone. A zero-order UV-spectroscopic technique for the estimation of REMO in pharmaceutical preparations, and LC/MS method for estimation of REMO from blood samples. UPLC [8], HPLC and UV second derivative spectroscopic methods [9] have been reported for the concurrent determination of metformin and remogliflozin. However, no simple, rapid spectrophotometric method for the analysis of REMO in pharmaceutical formulations is reported yet. The aim of the present work is to develop simple accurate, precise and validated method for determination of REMO in tablets, which therefore serves as a tool for the quality control of pharmaceutical dosage forms.

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PRINCIPLE OF DEVELOPED METHOD

The proposed spectrophotometric method is indirect after allowing the reaction between $KMnO_4$ and drug the excess amount of $KMnO_4$ is determined spectrophotometrically.[15,16] The excess of $KMnO_4$ was made to react it with a fixed amount of Methyl Orange dye. $KMnO_4$ bleaches the dye by causing oxidative destruction of the dye. Drug when added in increasing concentrations to a fixed concentration of $KMnO_4$, consumes the $KMnO_4$ proportionally and there occurs a fall in the concentration of $KMnO_4$. When a fixed concentration of dye is added to decreasing concentrations of $KMnO_4$ there is increase in the concentration of dye. Thus, a proportional increase in the absorbance at the respective λ max is observed with increasing concentration of drug.

MATERIALS AND METHODS

Instrumentation

All measurements of absorption spectra were made on model LABMAN UV-VIS Spectrophotometer using quartz cells of 1cm path length and wavelength range 320-1000nm was used for absorbance measurement. All chemicals employed in the present study were of analytical grade and purchased from Loba Chemie. Double distilled water was used for preparation of standard solution as well as for all experimental work.

Preparation of standard drug solution

About 16 mg of Remogliflozin Etabonate is exactly weighed and is dissolved in 50 ml of ethyl alcohol. The final dilution is made with ethyl alcohol to 100ml in standard flask. This is 50 ppm drug solution.

Preparation of Reagents

1. 4 $x10^{-4}$M $KMnO_4$ (Merck, Mumbai, India): Dissolve 6.32 mg of potassium permanganate in 100ml of distilled water and standardized using H.A Brights Procedure[10] .
2. 2.4 $x10^{-3}$M Methyl Orange (Himedia Laboratories Pvt, Limited, Mumbai): Dissolve 80 mg methyl orange in 100ml of distilled water.
3. Concentrated H_2SO_4 (S.D. Fine Chem Limited, Mumbai) diluted appropriately with distilled water to get 2M acid solution.

Experimental procedure

Different portions (0.5- 5.0 mL, 50 µg/mL) of standard Remogliflozin Etabonate solution is delivered into a series of 10 mL calibrated standard flask. Then to each flask, 1ml of 2M H_2SO_4 was added, followed by 1ml of $KMnO_4$ solution (4 $x10^{-4}$M). The contents are mixed and the flasks is kept aside for 15 min under occasional shaking. Finally, 1ml of Methyl Orange solution (2.4 $x10^{-3}$M) is added to each flask, diluted to the mark with water and the absorbance of solution is measured at 510 nm against a reagent blank.

RESULT AND DISCUSSION

The Absorbance Measurement of the Colored Complex of Remogliflozin Etabonate

The absorbance of the colored complex solution is measured against a reagent blank prepared under identical conditions from 360 to 600 nm. Absorption spectra of Remogliflozin Etabonate shows intense peak at 510 nm (Fig-3)

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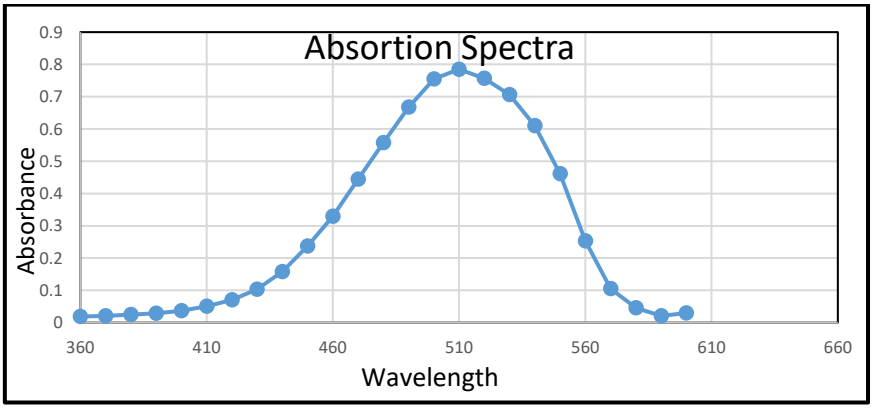

Figure 3: Absorption spectra showing λ max 510nm

Calibration Curve

The calibration curve is found to be linear indicating that Beer's law is obeyed in the concentration range of (2.5-25 µg/mL, 50µg/ml) for the developed method (Fig-4).

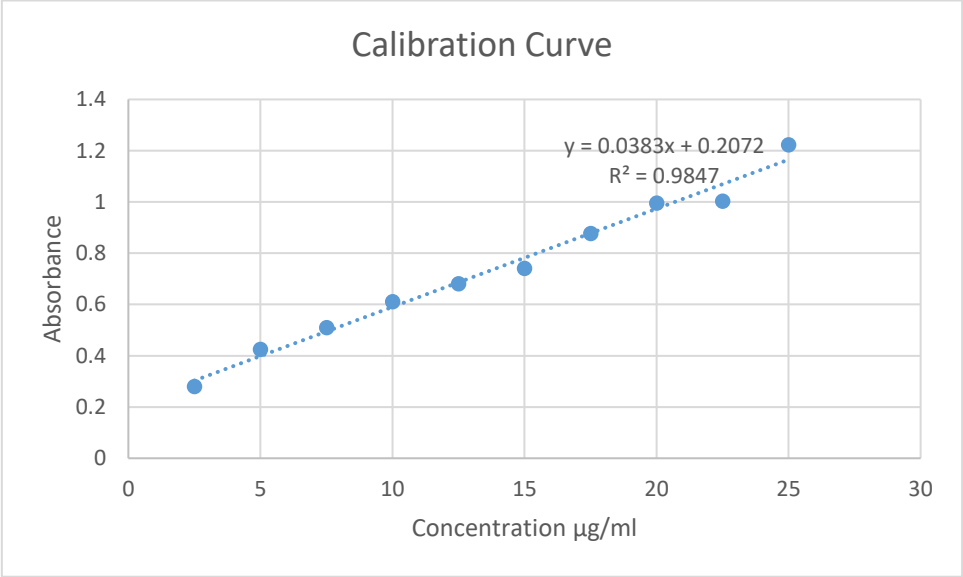

Figure 4: Calibration Curve

Effect of Heating Time On Absorbance of Developed System

The color development for developed method was studied by varying time . (Fig-5). From the variation graph (absorbance against varying time) it has been concluded that 15 minutes are sufficient for full color development hence 15 minutes time is selected for color development for further studies.

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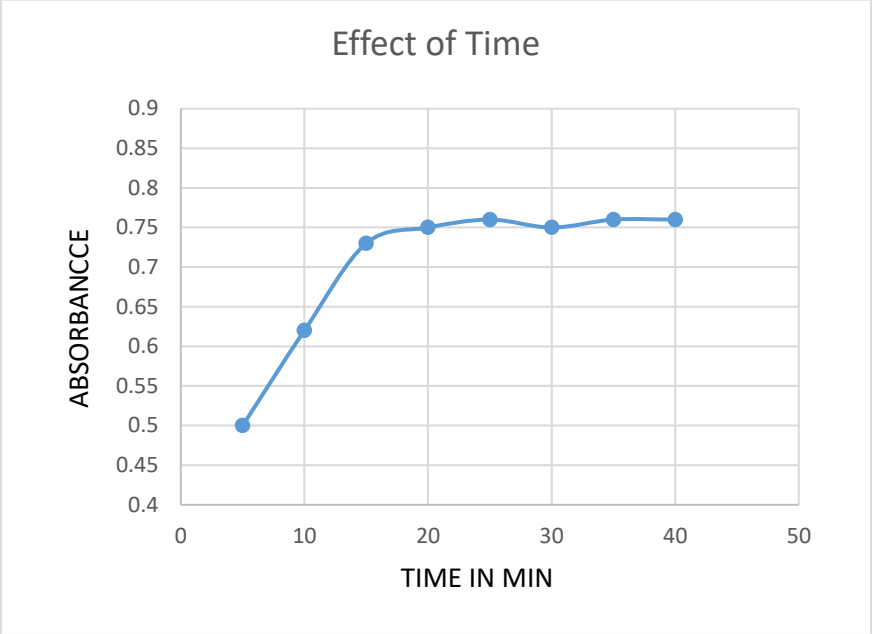

Figure 5: Effect Of Heating Time On Absorbance Of Developed System

Optimization of Parameters

The experiment was repeated several times in order to determine maximum concentration of methyl orange and KMnO4 spectrophotometrically and it is found that KMnO4 concentration of 4 $x10^{-4}$M was found to be sufficient to bleach the color of methyl orange upto concentration of 2.4 $x10^{-3}$M Methyl Orange. Sulphuric acid was found to be best for this method. A contact time of 15min was found to be sufficient for a reaction between drug and KMnO4,

Regression parameters, Optical characteristics Precision and Accuracy of Method A & B are shown in Table -1. Determination of Pharmaceutical Formulations of REMO by our proposed method and reference method is shown in Table-2.

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Parameters	Results
Maximum Wavelength λ_{max}	510 nm
Beer's Law Limits µg/mL	2.5-25
Sandell's Sensitivity (µg/cm^2 /0.0001 Absorbance)	0.0089
Molar Absorptivity Lt/mole/cm	0.58577 x 10^5 L
Slope(b)[a]	0.0383
Intercept(a)[a]	0.2072
Standard Deviation on intercept(S_a)	0.082739
Correlation Coefficient (r)	0.992339
Standard Deviation (S)	0.292288
Variation from mean at 95% level confidence limit	0.085432

Table-1 Regression parameters, Optical characteristics Precision and Accuracy

[a]Regression equation Y=a+bC , Where Y stands for absorbance and C is concentration in µg/mL b is %Relative standard deviation which is calculated for ten determination

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Table-2 Determination of Pharmaceutical Formulations of Remogliflozin Etabonate

Drug	Manufacturing company	Labelled amount(mg)	Amount found by Proposed Method(mg)	Amount found by Standard Method(mg)
Zucator 100	Torrent Pharmaceuticals Ltd	100	99.87	99.96

CONCLUSION

A simple, rapid, economic and sensitive Spectrophotometric methods was developed for the determination of Remogliflozin Etabonate in bulk drug and in tablets. This method can be successfully applied for the analysis of pharmaceutical formulations in any laboratory.

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