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NOTE

Spectrophotometric Determination of Repaglinide and Ezetamibe

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A simple and sensitive visible spectrophotometric method has been developed for the estimation of repaglinide and ezetamibe in pure as well as pharmaceutical formulations. This method is based on the reduced form of the Folin-Ciocalteu reagent under alkaline conditions which exhibits maximum absorbance at 755 and 750 nm for RPG or EZM respectively. Beer's law is obeyed at the concentration range of 2.5–15 μg/mL for repaglinide and ezetamibe. The method has been statistically evaluated and is found to be precise and accurate.

Key Words: Spectrophotometric estimation, Repaglinide, Ezetamibe.

Repaglinide (RPG) is an anti-diabetic agent. Chemically RPG is 2-ethoxy-4-[2-[[3-methyl-1-[2-(1-piperidinyl)phenyl]butyl]amino]-2-oxoethyl] benzoic acid. Ezetamibe (EZM)[3] is a cholesterol reducing agent. Chemically, EZM is 1-(4-fluorophenyl)-3-[(3s)-3-(4-fluorophenyl)-3-hydroxy propyl]-4-(4-hydroxyphenyl) 2-azetidinone. A few HPLC methods[1, 2] have been reported for RPG. Literature survey reveals that no visible spectrophotometric methods are reported for the estimation of RPG and EZM. The present method describes the reaction of repaglinide or ezetamibe with Folin-Ciocalteu reagent in alkaline medium to develop blue coloured species, which exhibits absorption maximum at 755 nm or 750 nm.

Spectral and absorbance measurements were made on Systronics UV-Visible spectrophotometer-117 with 10 mm matched quartz cells. All the chemicals used were of analytical grade.

Folin-Ciocalteu reagent (1.0 N): 50 mL of FC reagent (2N) was diluted to 100 mL with distilled water.

Preparation of standard and sample solutions: Accurately weighed 100 mg of RPG was dissolved in 5 mL of methanol and made up to 100 mL with distilled water. The stock solution was further diluted with distilled water to get a working standard solution of 50 μg/mL.

Ten tablets of RPG were accurately weighed and finely powdered. The powder equivalent to 100 mg of the drug was dissolved in methanol, made up to 100 mL with distilled water and filtered. This solution was further diluted with water to get 50 μg/mL of working standard solution.

Accurately weighed 100mg of EZM was dissolved in 10 mL of sodium hydroxide (0.1 N) and made up to 100 mL with distilled water. The stock solution was further diluted with distilled water to get working standard solution of 50 μg/mL.

Ten tablets of EZM were accurately weighed and finely powdered. The powder equivalent to 100 mg of the drug was dissolved in 10 mL of sodium hydroxide (0.1 N), made up to 100 mL with distilled water and filtered. The solution was further diluted with water to get 50 μg/mL working standard solution.

Assay procedure: Aliquot volumes of standard RPG or EZM solution ranging from 0.5 to 3.0 mL (50 μg/mL) were transferred to a series of 10 mL volumetric flasks. To each of the flasks, 0.5 mL of FC reagent and 1 mL of 2 M sodium carbonate for RPG or 1.0 mL of FC and 4.0 mL of 1 M sodium carbonate for EZM were added and kept aside for 5 min at room temperature. The solutions were made up to volume with distilled water. The absorbance of the blue coloured species formed was measured at 755 nm or 750 nm respectively against a reagent blank. The amount of the drug present in the sample was computed from the Beer-Lambert plot.

RPG or EZM with sodium carbonate reduces Folin-Ciocalteu reagent to form a blue-coloured species having maximum colour sensitivity, stability and minimum blank colour. The experimental conditions were optimized by studying the effect of Folin-Ciocalteu reagent concentration, alkali concentration and sequence of addition.

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, per cent relative standard deviation regression equation, correlation coefficients, % range of error (0.05 and 0.01 confidence limits) obtained are shown in Table-1.

TABLE-1
OPTICAL CHARACTERSTICS AND PRECISION OF THE PROPOSED METHODS FOR RPG and EZM

Parameter	RPG	EZM
λ_{max} (nm)	755	750
Beer's law limit (μg/mL)	2.5–15	2.5–15
Sandell's sensitivity (μg cm^{-2}/0.001 absorbance unit)	0.022	0.025
Molar absorptivity (L mol^{-1} cm^{-1})	2.03×10^4	1.61×10^4
Regression equation (Y = a + bC)		
Slope (b)	0.048	0.039
Intercept (a)	–0.02	0.0031
Correlation coefficient (r)	0.9992	0.9998
Relative standard deviation (%)*	1.1204	0.8136
%Range of error (Confidence limits)*		
0.05 level	0.9368	0.6803
0.01 level	1.3860	1.0065

*Average of eight determinations

Pharmaceutical formulations of RPG and EZM were successfully analyzed by the proposed method. The results obtained by the proposed method and reported method are presented in Table-2. To evaluate the validity and reproducibility of the method, known amounts of pure drug were added to previously analyzed samples and the mixtures were analyzed by the proposed method; there is no interference of other ingredients present in formulations. These results indicate that the method is simple, rapid with reasonable precision and accuracy and is applicable to various formulations of repaglinide and ezetamibe.

TABLE-2
ASSAY AND RECOVERY OF RPG AND EZM IN DOSAGE FORMS

Name of the dosage form	Labelled amount (mg)	Content of drug found (mg)		Recovery by proposed methods* (%)
		Proposed method	Reported method[R]	
Repaginide				
Tablet I	2	2.00	2.01	100.0
Tablet II	2	2.02	1.99	101.0
Ezetamibe				
Tablet I	10	10.14	10.05	101.4
Tablet II	10	10.04	10.02	100.4

* Recovery amount is the average of five determinations.
R Reference was UV method developed in the laboratory.

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