A Simple Spectrophotometric Method for the Estimation of Prucalopride in Tablet Form

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Abstract:

A sensitive spectrophotometric method is described for the determination of prucalopride in bulk drugs and in pharmaceutical preparations. The method is based on the oxidation of the studied drugs by a known excess of cerium (IV) in acid medium followed by determination of unreacted oxidant by adding a fixed amount of ferrous sulphate followed by addition of ammonium thiocyanate and the decreasing in absorbance through spectrophotometry is measured at 470 nm. In this method the amount of cerium (IV) reacted corresponds to drugs concentration. The experimental conditions were optimized.

Key words: Spectrophotometry, prucalopride and Pharmaceutical.

Materials and Method:

Instrument:

All measurement were done on Lab India 3000 plus double beam UV Visible Spectrophotometer by using 10 mm matched quartz cuvettes.

Reagents :

Preparation of reagents and solutions:

Ceric Ammonium Sulphate (640µg/ml): Ceric Ammonium Sulphate is prepared by dissolving 64 mg of Ceric Ammonium Sulphate (Merck) in 100 ml of distilled water.

Ferrous Ammonium Sulfate solution (400 µg/ml): 40 mg Ferrous Ammonium Sulfate (Fischer scientific) is dissolved in 100 ml of 0.1N Sulfuric acid.

Sulfuric acid (5.0N): 49.04 g of Sulfuric acid (Merck) is dissolved in 100ml distilled water.

Sulfuric acid (0.1N): 4.9 g of Sulfuric acid (Merck) is dissolved in 1000 ml distilled water.

3M Ammonium thiocyanate : 22.836 gm of Ammonium thiocyanate is dissolved in 100ml of distilled water.

Introduction:

Prucalopride is 4-amino-5-chloro-N-[1-(3-methoxypropyl)piperidin-4-yl]-2,3-dihydro-1-benzofuran-7-carboxamide, Prucalopride is a serotonin type 4 (5-HT4) receptor agonist that has potent prokinetic activity and is used as therapy for chronic idiopathic constipation. Prucalopride has been associated with a minimal rate of transient serum enzyme elevations during therapy and has not been implicated in cases of clinically apparent liver injury with jaundice.

Several analytical methods have been reported for assay of prucalopride which includes UV Spectrophotometric method [1], RP-HPLC method[2], UHPLC method[3], Pharmacokinetic method[4], LC QTOF MS method [5].

Assay of prucalopride:

The method is based on the oxidation of the drug by a known excess amount of cerium(IV) sulphate in acid medium, and the determination of the unreacted oxidant by spectrophotometry after treatment with iron(II) sulphate and complexing the iron(III)sulphate

produced with thiocyanate. The resultant blood red colour solution is measuring absorbance at 470 nm against distilled water blank.

The present investigation was undertaking with the aim of developing new, simple, rapid and accurate methods, free from many of the drawbacks usually encountered in other methods, for the analysis of prucalopride in bulk drug form and in various formulations.

(a) Absorbance of prucalopride:

The maximum absorbance of the prucalopride drug treated with cerium(IV) sulphate is ascertained by the following procedure.

1.0 ml of prucalopride solution (50µg/mL) is transferred into a standard flak and followed by the addition of 1 ml of 1 N hydrochloric acid and 1 ml cerium(IV) sulphate, and the overall volume are adjusted to 5 ml by adding a requisite volume of water. The flasks are let stand for 15 min with occasional shaking. Subsequently, 1ml of ammonium ferrous sulphate are added to each flask and the contents are mixed well. After 1 min, 3 ml of 3 M ammonium thiocyanate are added and the volume was made up to the mark, and The resultant solution gives blood red colour .The absorbance of the blood red colour solution is measured in the wavelength of 470 nm, against the reagent blank.

(b) Parameter fixation:

(i) Effect of concentration of hydrochloric acid on the absorbance of complex by cerimetric method:

In each series of 10ml of standard flasks were placed 1ml of prucalopride drug solution followed by the addition of varying amount of 0.5-2.0 ml 1N HC1 and 1ml of cerium(IV) sulphate. The flasks are let stand for 15 min with occasional shaking. Subsequently 1ml of ammonium ferrous sulphate was added to each flask and the contents are mixed well. After l

min 3 ml of 3 M ammonium thiocyanate is added and overall volume is adjusted to 10 ml by adding requisite amount of distilled water. The resultant solution gives blood red colour and the maximum absorbance for the solution is recorded at 470 nm against reagent blank and data are presented in the table 1.

Table. 1:

Effect of concentration of hydrochloric acid solution

Volume of Hydrochloric acid solution(ml)	Absorbance at 470 nm.
0.5	0.416
1.0	0.545
1.5	0.542
2.0	0.544

The data in table 1 indicates that 1.0 ml of 1N HC1 is required for attaining maximum absorbance. Hence it is maintained throughout the experimental studies.

(ii)Effect of concentration of cerium(IV) sulphate on the absorbance of complex:

In each series of 10ml standard flasks were placed 1ml of prucalopride drug solution followed by the addition of 1.0 ml of 1N HC1 and varying amount of 0.5-2.0 ml cerium sulphate solution. The flasks are let stand for 15 min with occasional shaking. Subsequently l ml of ammonium ferrous sulphate was added in each flask and the contents are mixed well. After l min 3 ml of 3 M ammonium thiocyanate is added and overall volume is adjusted to 10 ml by adding requisite amount of distilled water. The resultant solution gives blood red colour

and the maximum absorbance for the solution is recorded at 470 nm against reagent blank and data are presented in the table 2.

Table . 2:

Effect of concentration of cerium(IV) sulphate on the absorbance of complex

Volume of cerium(IV) sulphate solution(ml)	Absorbance at 470 nm.
0.5	0.445
1.0	0.555
1.5	0.553
2.0	0.552

The data in table 2 indicates that 1.0 ml of cerium(IV) sulphate is required for attaining maximum absorbance. Hence it is maintained throughout the experimental studies.

(iii) Effect of concentration of Ammonium ferrous sulphate solution on the absorbance of complex:

In each series of 10 ml standard flasks were placed 1ml of prucalopride drug solution followed by the addition of 1.0 ml of 1N HC1 and 1.0 ml of cerium sulphate solution. The flasks are let stand for 15min with occasional shaking. Subsequently varying amount of 0.5-2.0 ml ammonium ferrous sulphate was added in each flask and the contents are mixed well. After l min 3ml of 3 M ammonium thiocyanate is added and overall volume is adjusted to 10 ml by adding requisite amount of distilled water. The resultant solution gives blood red colour and the maximum absorbance for the solution is recorded at 470 nm against water as blank and data are presented in the table 3.

Table .3:

Effect of concentration of ammonium ferrous sulphate solution on the absorbance of complex

Volume of Ammonium ferrous sulphate solution (ml)	Absorbance at 470 nm.
0.5	0.485
1.0	0.565
1.5	0.564
2.0	0.565

The data in table.3 indicates that 1.0 ml of ammonium ferrous sulphate is required for attaining maximum absorbance. Hence it is maintained throughout the experimental studies.

(iv) Effect of concentration of 3 M ammonium thiocyanate solution on the absorbance of complex:

In each series of 10 ml standard flasks were placed 1ml of prucalopride drug solution followed by the addition of 1.0 ml of 1N HC1 and 1.0 ml of cerium sulphate solution. The flasks are let stand for 15 min with occasional shaking. Subsequently 1 ml of Ammonium ferrous sulphate was added in each flask and the contents are mixed well. After 1 min varying amount of 2.0-4.0 ml 3M ammonium thiocyanate is added and overall volume is adjusted to 10 ml by adding requisite amount of distilled water. The resultant solution gives blood red colour and the maximum absorbance for the solution is recorded at 470 nm against reagent blank and data are presented in the table.4

Table.4:

Effect of concentration of 3M ammonium thiocyanate solution on the absorbance of complex

Volume of Ammonium thiocyanate solution (ml)	Absorbance at 470 nm.
2.0	0.494
2.5	0.505
3.0	0.595
3.5	0.594
4.0	0.593

The data in table.4 indicate that 3 ml of ammonium thiocyanate is required for attaining maximum absorbance. Hence it is maintained throughout the experimental studies.

(c) Assay procedure:

In each of a series of 10 ml standard flasks were placed 0.5,1.0,1.5,2.0,2.5& 3.0 ml of prucalopride followed by the addition of 1 ml of 1 M hydrochloric acid and 1 ml cerium(IV) sulphate, and the overall volume are adjusted to 5 ml by adding a requisite volume of water. The flasks are let stand for 15 min with occasional shaking. Subsequently, 1 ml of ammonium ferrous sulphate are added to each flask and the contents are mixed well. After 1 min, 3 ml of 3 M ammonium thiocyanate are added and the volume was made up to the mark, and the absorbance was recorded at 470 nm against water blank. The concentration of the drug in an unknown solution was read from the calibration graph in fig. 1.

(d) Pharmaceutical Formulations:

Twenty tablets are weighed and ground into a fine powder. A portion of the powder equivalent to 100 mg of prucalopride is accurately weighed into a 100 ml calibrated flask, 60 ml of water is added and the contents are shaken thoroughly for about 20 min to extract the drug. The contents are diluted to the mark, mixed well and filtered using a watmann filter paper to remove insoluble residue. An appropriate aliquot is subjected to analysis by spectrophotometry using the procedure described above. The results are given in Table. 6.

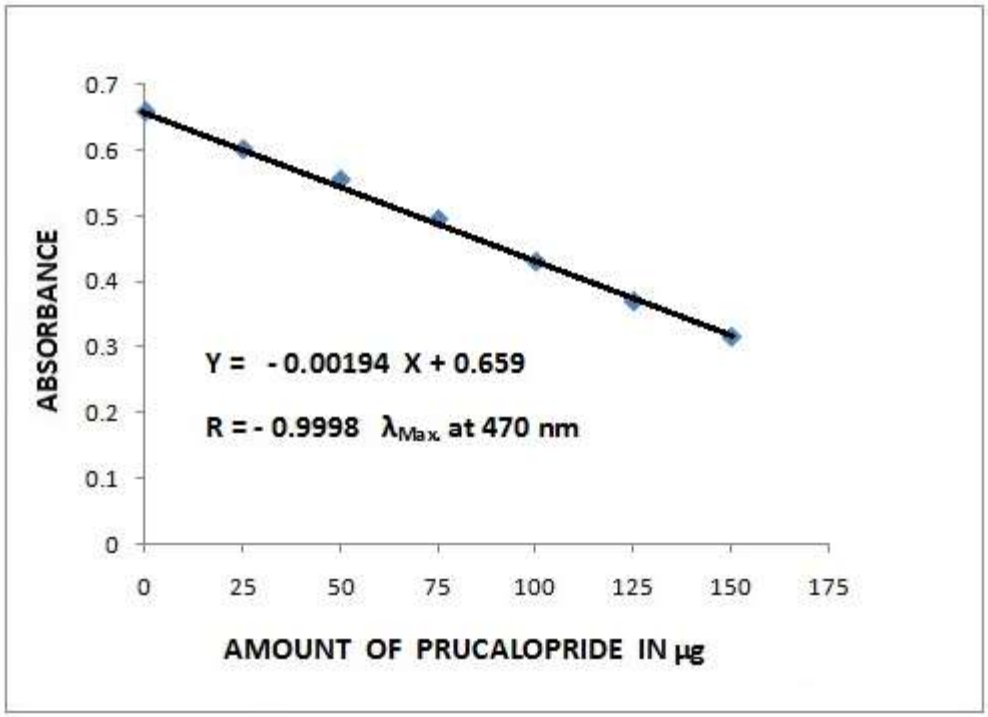

Fig. 1: Calibration curve of prucalopride

Table.5:

Optical characteristics of the proposed methods

parameters	Proposed method
λmax (nm) Beer's law limit (µg/mL)	470 25-125
Molar absorptivity (l mole^{-1} cm-^{1})	7.064X10^{3}
Sandell's sensitivity(µg cm-^{2} / 0.001 absorbance unit)	0.1415
Regression equation (Y = bx+a) Slope (b) Intercept (a) correlation coefficient (r)	Y=-0.00194X+0.659 -0.00194 0.659 -0.9998

*Y = bX+a, where Y is the absorbance and X concentration in µg/ml.

Table.6:
Assay of prucalopride in Pharmaceutical formulations

Sample	Labelled Amount (mg)	*Amount Found (mg)±S.D	% of Label claim	*t_{cal}
1	7.5	7.533±0.0015	100.45	0.419
2	7.5	7.688±0.005	102.51	0.595

***Average of five determinations based on label claim.**

(e)Results and Discussion:

The method is based on the oxidation of prucalopride with a known excess of cerium(IV) sulphate and the determination of the unreacted oxidant by spectrophotometry. This method is based on the oxidation of prucalopride by a measured excess of cerium (IV) sulphate in HCl medium, reduction of the residual oxidant by a fixed amount of iron (II) and subsequent formation of iron (III)-thiocyanate complex, which is measured at 470 nm. When a fixed concentration of cerium (IV) sulphate is reacted with increasing concentrations of prucalopride, there will be a proportional decrease in the concentration of the oxidant. The unreacted oxidant, when treated with a fixed concentration of iron (II) accounts for a proportional decrease in the iron (III) concentration. This is observed as a proportional decrease in the absorbance of iron (III)-thiocyanate complex with the drug concentration, which formed the basis for the assay of drug. The Standard deviation and t_{cal} of the prucalopride is calculated from five measurements of replicate samples. The values of Standard deviation and t_{cal} were shown in Table.5. The values of standard deviation values are low, indicates high accuracy and reproducibility of the method. The data of assay values of commercial formulations is subjected to statistical evaluation for student 't' test to study the proposed method. The calculated 't' values are less than 't' theoretical values with 4 (n-1= 5-1) degrees of freedom at 5% level of significance indicate that there is no significant difference between proposed method and standard method. Commonly encountered excipients such as starch, talc, glucose, alginate and stearate did not interfere in the proposed methods.

The described method is rapid and reliable, and hence can be used for routine analysis.

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