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(RESEARCH ARTICLE)

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Sensitivity of prucalopride succinate in different solvents by UV method

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Abstract

Prucalopride succinate is a selective serotinin 5-HT4 receptor agonist. Two simple UV spectrophotometric methods have been developed for the estimation of Prucalopride succinate in bulk and pharmaceutical formulations. The absorption maxima (λmax) of prucalopride succinate was found to be 226 nm in 0.1N HCL and Phosphate buffer (PH-2.0) respectively and Beer-Lambert's law was obeyed over the concentration range 2- 16µg/ml. LOD and LOQ values of prucalopride succinate was found to be 0.0105 µg/ml, 0.03465 µg/ml and 0.0143 µg/ml, 0.04719 µg/ml in 0.1N HCL and Phosphate buffer respectively. The validation parameters were treated statistically with 't' test and significant differences were observed. The study clearly revealed that the solvents influence the determination of Prucalopride succinate. The methods developed were rapid and easy can be applied for the estimation of Prucalopride succinate in bulk and pharmaceutical formulations.

Keywords: Prucalopride succinate; Hydrochloric acid; Phosphate buffer; UV spectrophotometry

1. Introduction

Prucalopride succinate is a class of dihydro-benzofuran-carboxamide. It causes stimulation of colonic mass movements which provide propulsion force for defecation. Prucalopride succinate, chemically 4-amino-5-chloro-N-[1-(3-methoxy propyl) piperidin-4yl]-2,3-dihydro-1-benzofuran-7-carboxamide,butanedioic acid. The molecular formula of Prucalopride succinate is $C_{22}H_{32}ClN_3O_7$ and its molecular weight is 485.96 g/mol. Choice of solvent can shift peaks to shorter or longer λ depends on their nature of the interaction of the particular solvent with the environment of the chromophore in the excited state of the molecule. Solvents can affect the fine structure of absorption curves as well as the intensities and wavelengths of maxima. There are various methods are available for the estimation of Prucalopride succinate. Among these methods High performance liquid chromatography (HPLC), spectrophotometric methods and LC/MS reported for the quantification of Prucalopride succinate. The influence of solvents for the determination of Prucalopride succinate has not been reported. In the present study two UV spectrophotometric methods were developed for estimation of Prucalopride succinate in bulk and pharmaceutical formulations among these the sensitive one can be confirmed by calculating limit of detection (LOD) and limit of quantification (LOQ) as per ICH guidelines.

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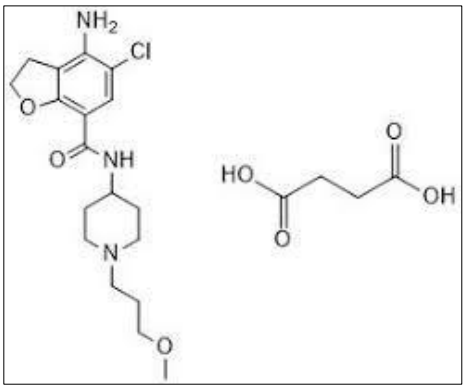

Figure 1 Chemical structure of Prucalopride succinate

2. Materials and methods

Absorbance measurements were made on double beam UV-Visible spectrophotometer with spectral band width of 0.5nm andwavelength accuracy of **±** 0.3nm with 10 mm matched quartz cuvettes (ELICO SL 244) were employed. Prucalopride succinate reference standard was gifted by SUN Pharma Ltd, Guwahati. Hydrochloric acid, Sodium acetate and Acetic acid used was of analytical grade purchased from National scientific Laboratories Vijayawada. Methanol – Govt supply.

2.1. Preparation of standard stock solutions of prucalopride succinate

25mg of Prucalopride succinate pharmaceutical grade was accurately weighed two times separately and transferred into two different 25ml volumetric flasks and dissolved in Methanol, volume was made up to the mark with the same solvent the stock solution obtained was 1000ppm(1mg/ml).

2.2. Determination of λmax

The two different stock solutions were suitably diluted with 0.1N HCL and Phosphate buffer to get a concentration of 10 ppm(10µg/ml) and scanned in the UV region ranges from 200nm-400nm. The wave length at which maximum absorbance observed was noted. The absorbance of the standard solutions containing the 0.1N HCL and Phosphate buffer were observed at 226nm.

2.3. Beer's lambert law

The two different stock solutions were suitably diluted to get concentration range from 2-16µg/ml and their absorbance were measured at λmax 226 nm. Calibration curve constructed for Prucalopride succinate in two different solvents by taking concentration (µg/ml) on x-axis and their absorbances on y-axis.

2.4. The proposed methods are validated for the following parameters

2.4.1. Linearity

Linearity range of the proposed UV methods were find out. In order to find out the linearity range of proposed UV methods a curve was constructed by plotting absorbance obtained for the analyte against its concentrations in 0.1N HCL and Phosphate buffer. A series of 2(µg/ml), 4(µg/ml), 6(µg/ml), 8(µg/ml), 10(µg/ml), 12(µg/ml) ,14(µg/ml) and 16(µg/ml) were prepared for standard calibration curve and absorbance were observed. The results were subjected to regression analysis by the least squares method to calculate slope(m), intercept(c) and regression coefficient (R^2).

2.5. Precision

Precision of method was determined in terms of repeatability (with in run precision), intermediate precision and reproducibility (between run precision).

2.6. Repeatability

Repeatability of the method was determined by analyzing three samples of 4(µg/ml), 8(µg/ml), 12(µg/ml) concentration in two different solvents and the %RSD and SE were calculated.

2.7. Intermediate precision

2.7.1. Intraday precision

It was calculated by analyzing six test samples of Prucalopride succinate on the same day, and the intraday precision of the method was determined by evaluating the samples of Prucalopride succinate on different days or and on two different spectrophotometers in the same laboratory.

2.8. Reproducibility

The sample solutions were prepared and analyzed in different labs.

2.9. Sensitivity

The sensitivity of the proposed UV method was measured in terms of limit of detection (LOD) and limit of quantification (LOQ).The LOD and LOQ were calculated using formula:

$$LOD=3.3\ \sigma/s\ \&\ LOQ=10\ \sigma/s$$

Where

σ= standard deviation of Y-intercepts of regression lines.

S= slope of the calibration curve.

2.10. Sandell's sensitivity and molar absorption coefficient

It is calculated by using the following formula

$$S = \epsilon.\ p$$

Where

S = sandell's sensitivity
ϵ = specific extinction coefficient
P = concentration of substance in mg/liter.

2.11. Robustness

To determine the robustness of the method, the experimental conditions were altered and assay was evaluated. Sample solutions were prepared and absorbances were observed at ± 5nm from absorption maxima.

2.12. Accuracy

Accuracy of the methods were confirmed by studying recovery at three different concentrations for 80, 100, 120% of these expected, in accordance with ICH guidelines by replicate analysis. Standard drug solutions were added to a pre analyzed sample solution and %drug content was measured.

2.13. Analysis of tablet formulations

Twenty tablets from each brand (Suminat-25 and Suminat-50) were weighed and grained into a fine powder using a Pestle and Mortar. An amount of tablet powder equivalent to 25 mg of PCS was extracted with methanol and dilutions were made with respective solvents,filtered using Whatmann No.42 filter. Analyze these solutions by using proposed UV methods.

2.14. Recovery study

To further ascertain the accuracy and reliability of the proposed methods, recovery experiments were performed via standard-addition procedure. Pre-analyzed tablet powder was spiked with pure PCS at three different levels and the total was found by the proposed methods. Each determination was repeated three times. The percent recovery of pure PCS added was within the permissible limits indicating the absence of inactive ingredients in the assay. These results are depicted in Table.No.6

3. Results and discussion

The wavelength maxima obtained for Prucalopride succinate in two different solvents were 226nm in 0.1N HCL and Phosphate buffer respectively (Fig.Nos.4&5). The developed UV spectrophotometric methods followed beer's law in the range of 2-16µg/ml(Fig.Nos.2&3).The relative standard deviation values were observed less than '1' indicates precision of the method, the lower standard error value indicates the accuracy of the method. The molar extinction coefficient, sandell's sensitivity, and LOD & LOQ values were calculated as per ICH guide lines, the values are depicted in table no.5. Based on LOD and LOQ values, the solvents were ranked 0.1N HCL > Phosphate buffer. The study clearly revealed the sensitivity of the method improved in thepresence of 0.1N HCL than in Phosphate buffer. 0.1N HCL was found to be more sensitive as it offered lowest LOD and LOQ values. LOD and LOQ values are subjected to statistically and data shown in Table.No:3&4. Significant differences were observed between the solvents used for the determination of drug. Lowest LOD and LOQ values were observed with the solvent i.e 0.1N HCL. The LOD and LOQ values of Prucalopride succinate in 0.1N HCL and Phosphate buffer were subjected to **t**-test. The calculated 't value compared with t- table value, the observed value was greater than the table value indicated that the significant differences between the LOD and LOQ values of Prucalopride succinate in two different solvents.

Table 1 Linearity of Prucalopride succinate in 0.1N HCL

Sr. No.	Concentration(ppm)	Absorbance
1.	2	0.1297
2.	4	0.2565
3.	6	0.4429
4.	8	0.5188
5.	10	0.6468
6.	12	0.7783
7.	14	0.9654
8.	16	1.0356

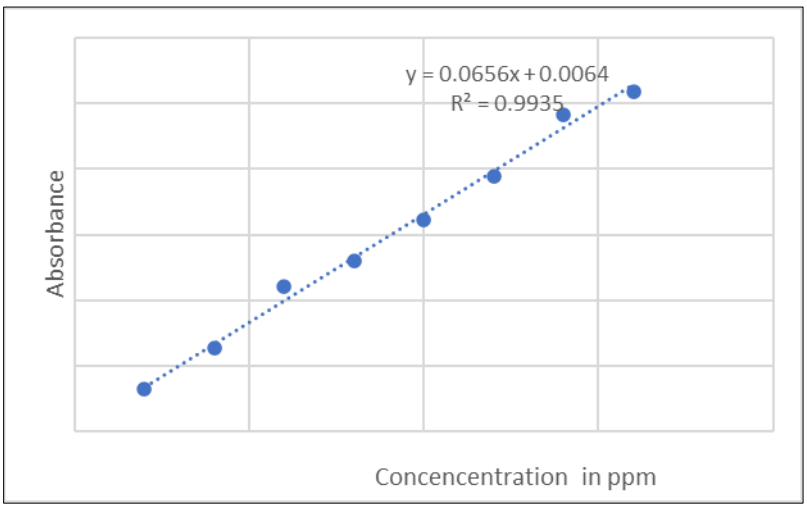

Figure 2 Calibration curve of Prucalopride succinate in 0.1N HCL

Table 2 Linearity of Prucalopride in Phosphate buffer

Sr. No.	Concentration(ppm)	Absorbance
1.	2	0.1299
2.	4	0.2788
3.	6	0.3799
4.	8	0.4694
5.	10	0.6439
6.	12	0.7345
7.	14	0.8341
8.	16	1.032

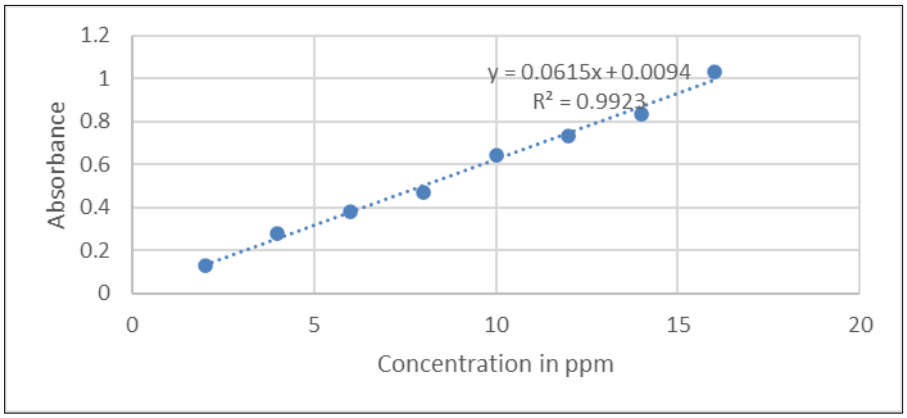

Figure 3 Calibration curve of Prucalopride succinate in Phosphate buffer

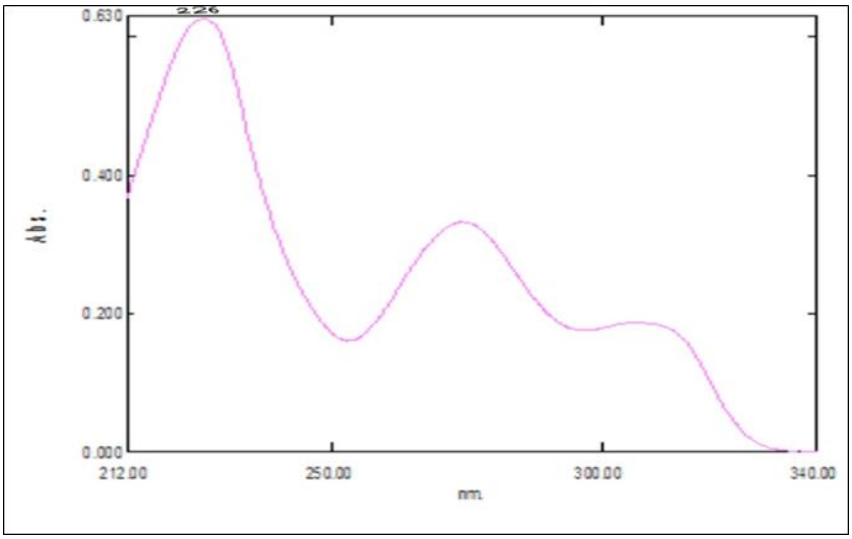

Figure 4 λmax of Prucalopride succinate in 0.1N HCL

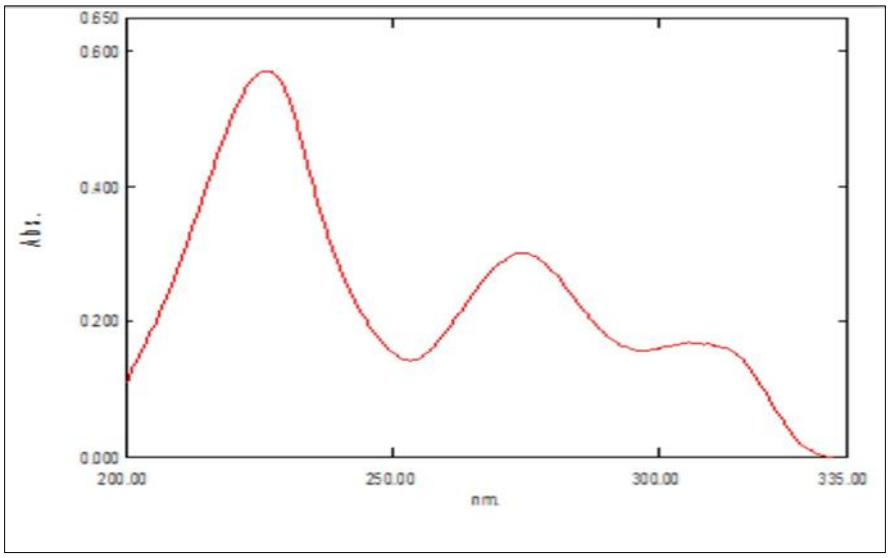

Figure 5 λmax of Prucalopride succinate in Phosphate buffer

Table 3 Limit of Detection (LOD)

S.No	0.1N HCL LOD± S.D(n=6)	Phosphate buffer LOD ± S.D(n=6)	t_{Cal}	t_{Tab}	D.F
1.	0.0105 ± 6 X10^{-4}	0.0143± 9.26 X10^{-4}	4.78	2.228	10

D.F = Degrees of freedom , t_{Cal} - Caluculated t value, t_{Tab} – t table value

Table 4 Limit of Quantification (LOQ)

Sr. No	0.1N HCL, LOQ±S.D(n=6)	Phosphate buffer LOQ±S.D(n=6)	t_{Cal}	t_{Tab}	D.F
1.	0.03465±8.02X10^{-4}	0.04719±7.26X10^{-4}	12.64	2.228	10

D.F = Degrees of freedom , tCal - Caluculated t value, tTab – t table value

Table 5 Validation Parameters of Proposed UV methods

S.no	Parameters	0.1N HCL	Phosphate buffer
1.	λ_{max}	226	226
2.	Range	2-16 µg/ml	2-16 µg/ml
3.	Regression equation	Y=0.0656x+0.0064	Y=0.0615x+0.0094
4.	Slope	0.0656	0.0615
5.	Intercept	0.0064	0.0094
6.	$A^{1\%}{}_{1cm}$	664	628
7.	R^2	0.9935	0.9923
8.	Molar absorption coefficient (litre/mole/cm-1)	3.266 X 10^4	3.052 X 10^4
9.	LOD	0.0105 µg/ml	0.0143 µg/ml
10.	LOQ	0.03465µg/ml	0.04719 µg/ml
11.	Sandell's sensitivity (µg/cm2/0.001absorbance unit)	0.0152	0.0164

Table 6 Results of recovery study by standard addition method

Brand Name of Tablets	0.1N HCL				Phosphate buffer			
	PCS in tablets (µg/ml)	Pure PCS added (µg/ml)	Total found (µg/ml)	Pure PCS recovered percent ±S.D	PCS in tablets (µg/ml)	Pure PCS added (µg/ml)	Total found (µg/ml)	Pure PCS recovered percent ± S.D
Consticalo 2	3	1.5	4.54	102.7 ± 1.53	3	1.5	4.53	102 ±1.63
	3	3	6.03	101±1.24	3	3	5.99	99.67±1.37
	3	4.5	7.54	101 ± 1.36	3	4.5	7.52	100.4±0.82
Prugonist 2	6	1.5	7.48	98.67 ±0.85	6	1.5	7.48	98.67±0.93
	6	3	8.98	99.33± 0.76	6	3	8.97	99 ± 0.79
	6	4.5	10.54	101±1.12	6	4.5	10.48	99.5 ±1.35

Mean value of three determinations, PCS: Prucalopride succinate, S.D : Standard deviation

4. Conclusion

The proposed methods were easy to perform and applicable for estimation of Prucalopride succinate in bulk and pharmaceutical formulations in Quality control laboratories.

Compliance with ethical standards

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Disclosure of Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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