

1st Order Derivative Spectrophotometry Determination of Sertraline in Pharmaceutical Tablets by P-Chloranilic Acid

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Abstract

Rapid, accurate and sensitive method has been developed and validated for the determination of Sertraline in pharmaceutical tablets; the present method is based on First Order derivative spectrophotometry of the colored product which was formed by charge transfer complexation of sertraline (n-donor) with π -acceptor chloranilic acid. First derivative spectrophotometry has been evaluated by measuring of the derivative signal at 475.72 nm – 588.40 nm (peak to peak amplitude). Calibration graph was established for 5-100 $\mu\text{g}\cdot\text{mL}^{-1}$ of sertraline with main percentage recoveries. The proposed method was applied successfully to the determination of sertraline in pharmaceutical tablet with good accuracy and precision.

Keywords: Sertraline; Derivative spectrophotometry; P-chloranilic acid; Antidepressant.

Introduction

Sertraline; (1-S,cis)-4-(3,4-dichloroph-enyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthalene amine (Figure 1), is a new antidepressant of the selective serotonin reuptake inhibitor (SSRI). Sertraline has become one of the most widely used medications for the treatment of depression, generalized anxiety disorder, social anxiety disorder, panic disorder, obsessive compulsive disorder and posttraumatic stress disorder^[1].

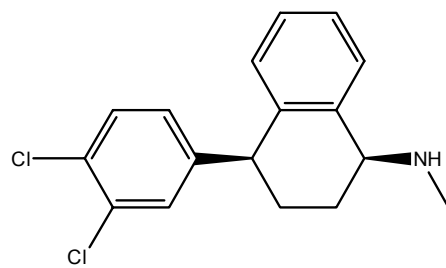


Figure 1: sertraline chemical structure

Several methods have been reported for the determination of sertraline in biological fluids and pharmaceutical forms including gas chromatography–mass spectrometry (GC–MS)^[2-4] or HPLC with UV detection^[5-6]. Furthermore, SRT has been analyzed as a single analyte by GC–MS^[1] or together with other antidepressants

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using HPLC-DAD [7-8] or HPLC coupled to spectrofluorimetric detection after derivatisation [9-10]. The pre-treatment of biological samples is usually carried out by means of liquid-liquid extraction (LLE) [5-9]. Also, sertraline has been determined by liquid chromatography and tandem mass spectrometry (LC-MS/MS) and GC-MS/MS [11-15].

Derivative spectrophotometry is a useful technique for qualitative and quantitative information extracted from spectra composed of unresolved bands [15] and for eliminating the effect of baseline shifts and baseline tilts [15,16]. In addition it helps in reducing the effects of spectral background interferences [17]. The main disadvantage of derivative spectroscopy is that the differentiation degrades to signal to noise ratio so that some form of smoothing after good selection is required in conjunction with differentiation [18].

Charge-transfer complexes result from a donor-acceptor mechanism of Lewis acid-base reaction between two or more different chemical constituents. The formation of electron donor-acceptor complex can be rapidly assessed for its validity as a simple quantitative analytical method for many drug substances, which can act as electron donors [19].

This study presents a new, sensitive and selective method to the determination of sertraline in dosage forms by combination between selectivity of the reagents and derivative spectrophotometry technique to eliminate any interference by starch and excipients .

Experimental

Apparatus

A perkin Elmer lambda 35 double beam UV-Vis spectrophotometer, with 10 mm quartz cuvettes, a fixed slit width (2nm) connected to an dell-PC , computer loaded with (UV WIN LAB) software version 2.85.04 was equipped with HP desk jet printer used for all the absorbance measurements and treatment of data .

Materials and methods

Solvents, materials and reagents used were of analytical reagent grade, suppliers were as follows :

Chloroform (VWR International Ltd) England purity (99.0-99.4%). Acetone (Panreac quimic SA) Barcelona Purity 99.5 %. Ethanol (Panreac quimic SA) Barcelona Purity 99.5 %.

p-chloranilic acid (CAA) (BDH chemicals Ltd Poole England) minimum assay 98 %. Sertraline HCl (SRT.HCl) potency = 98.3 % (Saudi Pharmaceutical Industries & Medical Appliances Corporation (SPIMACO)).

Pharmaceutical formulation

The sertraline commercial dosage form which was subjected to the analytical procedure was (Lustral tablet) manufacture Pfizer incorporated labeled to contain 50 mg SRT.Base per tablet.

Stock standard solution

Stock standard solution of SRT base $1000 \mu\text{g.mL}^{-1}$ was prepared by taking an accurate weight equivalent to 100 mg SRT base, and dissolving in 20 ml de-ionized water. The solution was rendered alkaline with ammonia solution. The mixture was transferred quantitatively into a 100 ml separating funnel and extracted with 4×20 ml chloroform. The extract was washed, filtered through anhydrous sodium sulphate into a 100 ml volumetric flask and the volume was made up to 100 ml using chloroform .

Working standard solution of SRT.base ($300 \mu\text{g.mL}^{-1}$)

Evaporate 15 ml of the stock standard solution in 50 ml volumetric flask and dissolve in 25 ml absolute ethanol, make up to the mark with same solvent.

Sample preparation solution

Ten tablets of LUSTRAL were accurately weighed and the average weight of tablet was calculated. The tablets were crushed well to a fine powder. A portion of the powder equivalent to 100 mg SRT base was dissolved in 20 ml water. Render alkaline and Extract the drug base as under stock standard solution and working standard solution.

Reagent solutions

0.05 M CAA was prepared by dissolving accurately 522.3 mg of p-chloranilic acid in 50 ml absolute ethanol.

Procedures

construction of calibration curves

Calibration curves were constructed between (dA/d λ) and SRT concentration according to the optimum conditions as follows: into separate 10 ml volumetric flasks, transfer different aliquots of working standard solution: to each flask , add the specified amount of reagent leave to stand at $(25 \pm 5 \text{ }^\circ\text{C})$ for the optimum time.

Make up to volume using the solvent. Record the absorbance against the blank for the range of wavelengths 350-750 nm. Generate the 1st order derivative spectra of the CT complex for the same range 350-750 nm with $\Delta\lambda = 4$ nm.

2.4.4.2. For dosage form:

Proceed as described above using different aliquots of the sertraline test solution previously mentioned under sample preparation solution.

Discussion

Spectrophotometric properties of the colored CT complexes as well as the different parameters affecting the color development between SRT and CAA reagent were extensively studied to determine the optimal conditions for the assay procedure. The parameters including volume of reagent, nature of solvent, temperature, time and stoichiometry.

Absorption spectra

CAA reacts with the amino group of SRT drug and give a bluish intense CT complex at 530 nm, The absorption spectra was measured at 350–750 nm against a blank reagent as shown in figure 2.

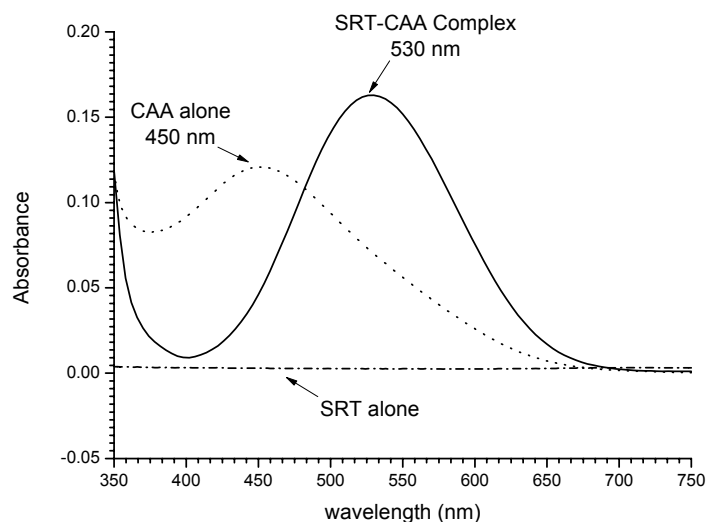


Figure 2: Absorption spectra of CAA-SRT (530 nm), CAA alone and SRT ($50 \mu\text{g.mL}^{-1}$) alone

Optimization of conditions

Effect of reagent concentration

The effect of CAA concentrations on the reaction with SRT was studied. It was found that, when various concentrations of CAA solution added to a certain concentration of SRT (1 mg.mL^{-1}), the absorbance was found to increase rapidly and then remains constant or decreases. A concentration of $3.2 \times 10^{-4} \text{ M}$ of CAA was found to be sufficient for quantitative determination of SRT. It also means that, maximum and reproducible color intensities are obtained. Higher concentrations of reagents did not affect the color intensity as shown in figure 3.

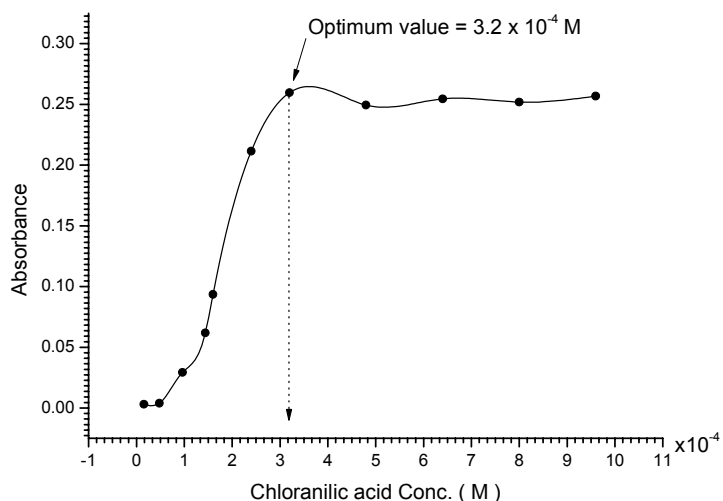


Figure 3: Effect of CAA concentration on the reaction with SRT ($50 \mu\text{g.mL}^{-1}$) at ($25 \pm 5 \text{ }^\circ\text{C}$)

Effect of reaction time

The optimum reaction time was investigated by monitoring the color development at room temperature ($25 \pm 5 \text{ }^\circ\text{C}$) in the range (0.5 - 65 min). Complete color development was achieved after 5 min. The colors remained stable at room temperature for at least 1 day, as shown in figure 4.

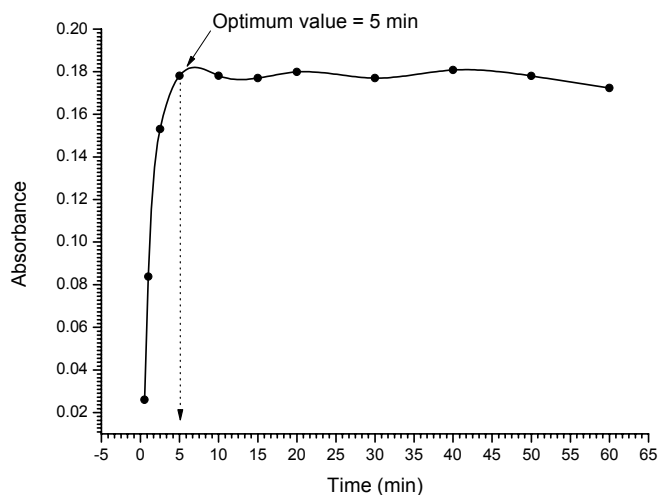


Figure 4: Effect of time on the reaction using SRT ($50 \mu\text{g.mL}^{-1}$) CAA ($3.2 \times 10^{-4} \text{ M}$) at ($25 \pm 5 \text{ }^\circ\text{C}$)

Effect of temperature

The effect of temperature was studied by monitoring the color development in the range ($15\text{-}65 \text{ }^\circ\text{C}$) as shown in figure 5. The absorbance increases with temperature and a maximum measurement was recorded at $25 \text{ }^\circ\text{C}$ and then remains constant.

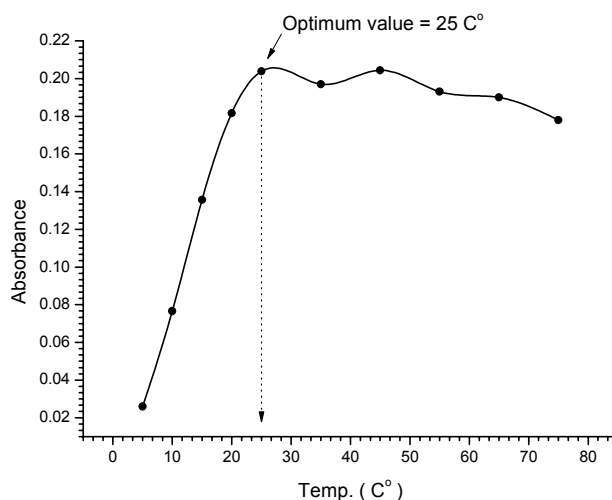


Figure 5: Effect of temperature on CT complexes using SRT ($50 \mu\text{g.mL}^{-1}$) CAA ($3.2 \times 10^{-4} \text{ M}$)

Effect of solvent

In order to select the most appropriate solvent, the reactions were carried out in different solvents. Small shifts in the position of the maximum absorption peak were observed, and the absorption intensities were also influenced. Chloroform, ethanol, methanol, acetonitril all were studied and from the results depicted in table 1 no significant changes were found with these solvents, however, absolute ethanol was chosen for safety considerations.

Table 1: Effect of solvent on CT complexes using SRT ($50 \mu\text{g.mL}^{-1}$) CAA ($3.2 \times 10^{-4} \text{ M}$) for 5 min

Solvent	Absorbance
Acetonitrile	0.1072
Chloroform	0.1025
Ethanol	0.1085
Methanol	0.1090

Effect of surfactants

The presence of any surfactant is a potentially important parameter because of the electro properties. The surfactants may increase or decrease the absorbance of CT complex and in certain cases they have no effect on the absorbance readings. Different surfactants were used in this study . SLS , CTABr and Brij-35 as anionic, cationic and nonionic surfactants, respectively, but no significant effects were observed, as shown in table 2 .

Table 2: Effect of surfactants on CT complexes using PRX ($50 \mu\text{g.mL}^{-1}$) PBQ ($20 \times 10^{-4} \text{ M}$) for 15 min

Surfactant	Absorbance
Brij-35	0.0884
CTABr	0.0893
SLS	0.0943
Without	0.0983

Stoichiometry and suggested Mechanism of reactions

The stoichiometric ratio of the drug to reagent was investigated in order to determine the ratio between SRT and CAA reagent. The results show that 1:1 complex was formed between the drug and the reagent as shown in figure 6 and the mechanism of the reaction could be suggested as shown in figure 7.

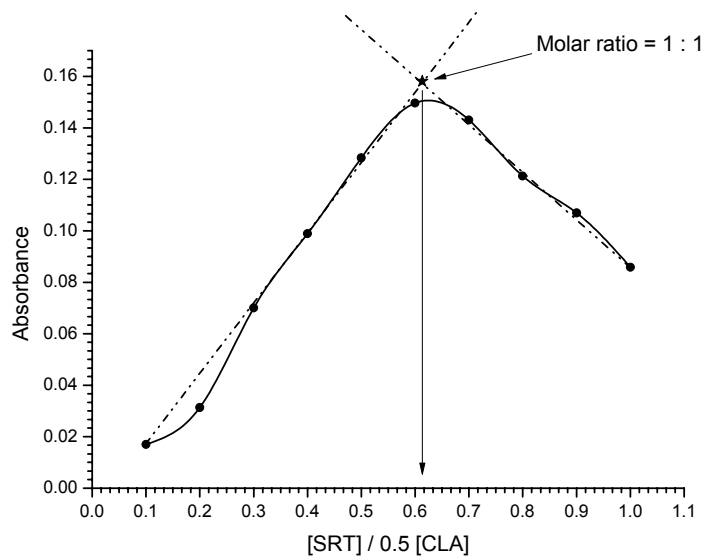


Figure 6: Stoichiometry detection by molar ratio method SRT-CAA complex

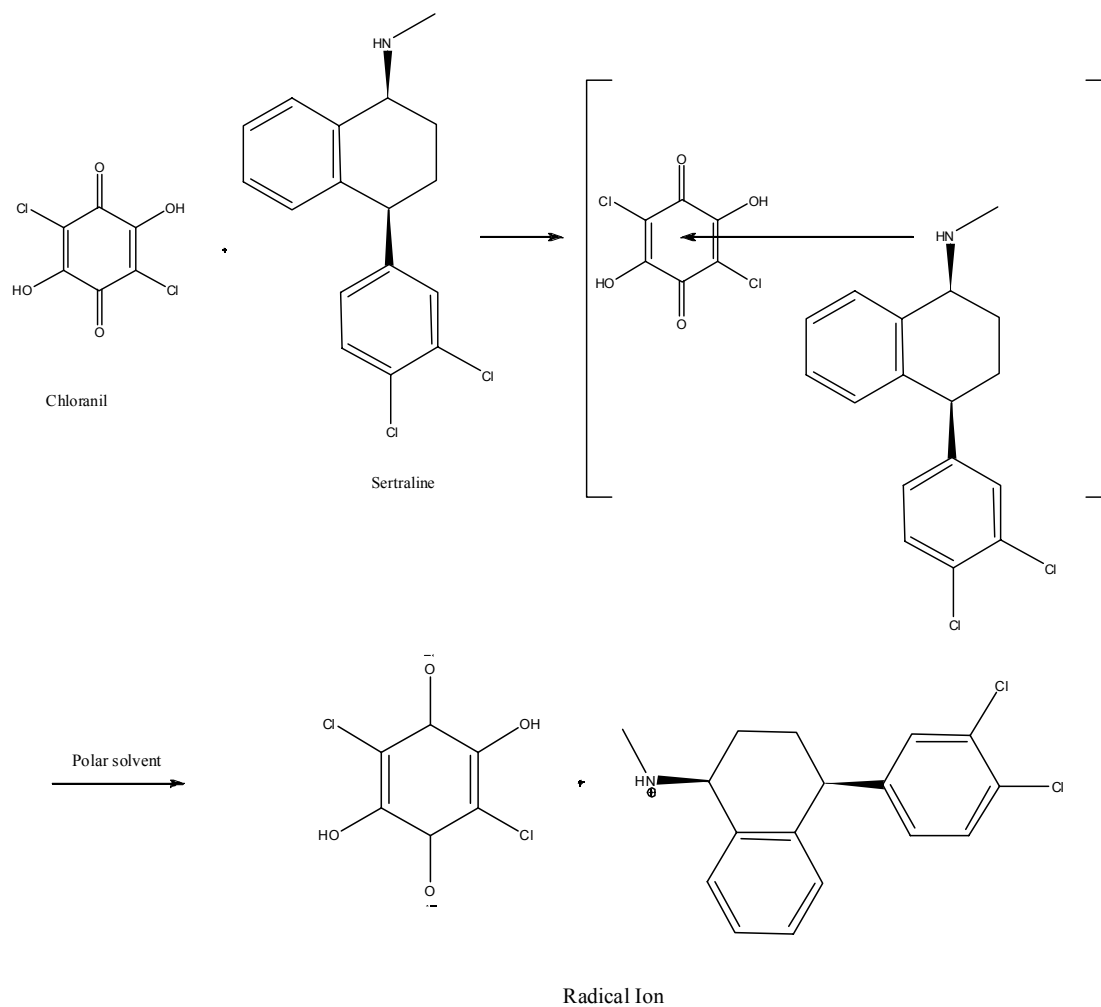


Figure 7: Suggested mechanism of the reaction

Results

Analytical performance

Derivative spectra

The selectivity of the method is significantly enhanced by recording derivative spectra under the specified optimum reaction conditions to eliminate any interference by starch or excipients. The first Order derivative spectrum is inspected by the peak to peak method to select suitable wavelengths for obtaining linear analytical calibration graphs. Derivative spectra of SRT-CAA complex has been estimated by the peak to peak method (between 475.72 nm and 588.40 nm), as shown in figure 8.

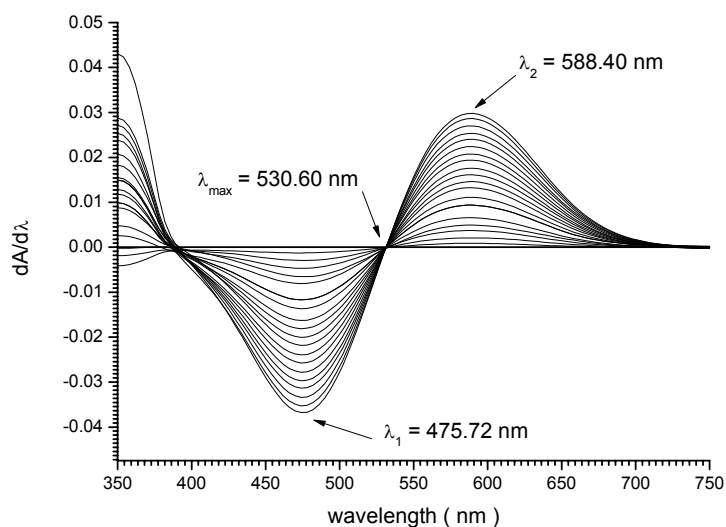


Figure 8: 1st order DS used for determination of SRT (5-100 $\mu\text{g/ml}$) using CAA reagent

Validation of the analytical methods

The calibration curve employed in the present study was constructed as shown in figure 9. The regression equations for the results were derived using the least-squares method. In all cases, Beer's law plots were linear with very small intercepts and excellent correlation coefficients in the general concentration range of 5-100 $\mu\text{g.mL}^{-1}$ (Table 3). The limits of detection (LOD) and limits of quantification (LOQ) were determined ^[20] using the formula: $\text{LOD or LOQ} = \kappa \text{S.D/b}$, where $\kappa = 3$ for LOD and 10 for LOQ, S.D is the standard deviation, and b is the slope. Based on seven replicate measurements, all parameters are shown in table 3.

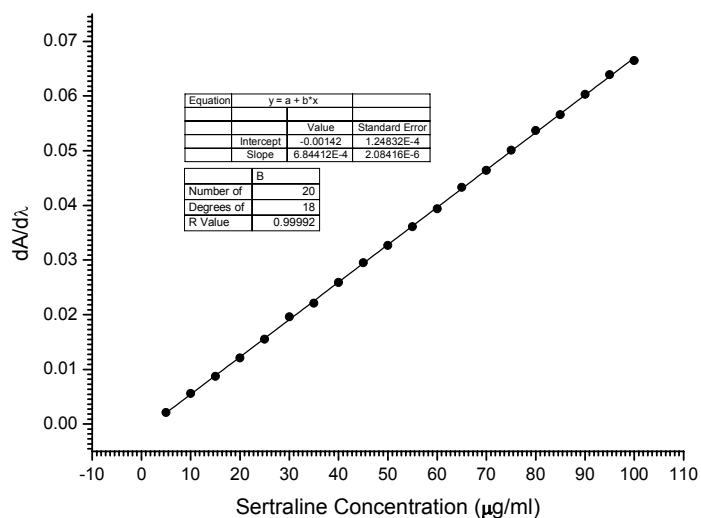


Figure 9: Calibration curve to determination of Sertraline based on 1st Order derivative spectra of CT complex (SRT-CAA)

Table 3: Quantitative parameters for the charge-transfer reaction of Sertraline with CAA acceptor .

Acceptor reagent	Range $\mu\text{g.mL}^{-1}$	Intercept $\times 10^{-3}$	Slop $\times 10^{-3}$	Correlation coefficient	Molar abs. L/mol.cm	LOD $\mu\text{g.mL}^{-1}$	LOQ $\mu\text{g.mL}^{-1}$
CAA	5-100	-1.42	0.68	0.99992	6.0×10^2	1.3	2.4

Application of analysis on tablets

The proposed method was successfully applied to the determination of Sertraline in pharmaceutical tablet (LUSTRAL) by calibration curve technique. The results obtained given in table 4, reveal a good recovery and non-interference from commonly encountered excipients, additives and stabilizers, since the proposed method depends on the combination between selectivity of the reagent and elimination of any interference by derivative spectrophotometry technique.

Table 4: Determination of Sertraline in LUSTRAL using proposed CAA method.

Values	Proposed method	Published method [21]
Mean	100.3	99.69
\pm Sd	0.92	0.57
n	7	6
Variance	0.85	0.33
% Rsd	3.05	----
t (2.45)*	1.15	----
F (4.95)*	2.58	----

*Theoretical values at 95 % confidence limit .

Statistical calculations were made in order to check the confidence and correlation between the suggested spectrophotometric procedure and the published method [21]. From the calculated t- and F-values at the 95% confidence level, it is clear that, the results obtained by the proposed method are in good agreement with those obtained by a reference method. The calculated standard deviation, S.D. = 0.42 and 0.47, and relative standard deviation, R.S.D. = 1.39 and 1.57 for PRX with PBQ and PCL, respectively. The small values of S.D. and R.S.D. indicate the reliability, accuracy and precision of the suggested procedures.

Conclusions

The above quantitative study can show that this methodology of quantitative analysis using derivative spectroscopy has provided to be much better than the earlier reported ones. The LOD and LOQ reported by this method are far better than the ones reported in previous applied methods. The major advantage of this method is it's applicability to a wide range of concentration of the pharmaceutical formulation being analyzed, mild experimental conditions and high sensitivity.

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References

- [1] Kim, K. M.; Jung, B. H.; Choi, M.H.; Woo, J.S.; Paeng, K.-J.; Chung, B.C., *J. Chromatography B*, 2002, 769, 333-339.
- [2] Larry, M. T.; Joerg, E. A., *J. Chromatography B*, 1989, 496, 423-429.
- [3] Hassan G. F.; Ronfeld, R. A., *J. Chromatography B*, 1987, 417, 197-202.
- [4] Rogowsky, D.; Marr, M.; Long, G.; Moore, C., *J. Chromatography B*, 1994, 655, 138-141.
- [5] Wiener, H.L.; Kramer, H.K.; Reith, M.E.A., *J. Chromatography B*, 1990, 527, 467-472.
- [6] Logan, B.K.; Friel, P.N.; Case, G.A., *Anal. J., Toxicol.* , 1994, 18, 139-142.
- [7] Titier, K.; Castaing, N.; Scotto-Gomez, E.; Pehourcq, F.; Moore, N.; Molimard, M., *Therapeutic Drug Monitoring*, 2003 , 25 (5), 581-587.
- [8] Duverneuil, C.; De la Grandmaison G.L.; De Mazancourt P.; Alvarez J.-C. , *Therapeutic Drug Monitoring*, 2003, 25 (5), 565-573.
- [9] Lucca, A.; Gentilini, G.; Lopez-Silva, S.; Soldarini, A., *Therapeutic Drug Monitoring*, 2000, 22 (3), 271-276.
- [10] Patel, J.; Spencer, E.P.; Flanagan, R.J., *Biomedical Chromatography*, 1996, 10 (6), 351-354.
- [11] Moraes, M.E.A.; Lerner, F.E.; Perozin, M.; Moraes, M.O.; Frota Bezerra, F.A.; Sucupira, M.; Corso, G.; De Nucci, G., *Inter. Jour. of Clin. Pharma. And Therap.*, 1998, 36 (12), 661-665.
- [12] Ronfeld, R.A.; Wilner, K.D.; Baris, B.A., *Clinical Pharmacokinetics*, 1997, 32, 50-55.
- [13] Frahnert, C.; Rao, M.L.; Grasmader, K. , *J. of Chromatography B*, 2003, 794 (1), 35-47.
- [14] Vatassery, G.T.; Holden, L.A.; Hazel, D.K.; Dysken, M.W., *Clinical Biochemistry*, 1997, 30 (7), 565-568.
- [15] Koytchev, R.; Ozalp, Y.; Erenmemisoglu, A.; Van Der Meer, M.J.; Alpan, R.S. , *Arzneimittel-Forschung / Drug Research* ,2004 , 54 (9 A) , 629-633.
- [16] Dubrovkin, I. M., *Journal of Applied Spectroscopy*, 1983, 39, 885-899.
- [17] Jun-Sheng, Yu; Zu-Xun, Zhang, *Journal of Electro analytical Chemistry*, 1996, 403, 1-9.
- [18] Ana Petidier; Soledad Rubio; Agustina Gómez-Hens; Miguel Valcárcel, 1986, *pharm. Bio. Anal.* , 157, 212-220.
- [19] Asad, R., *Chem. Pharm. Bull.*, 2006, 54, 432-434.
- [20] The United States Pharmacopeia 24, 2000 , The National Formulary, US Pharmacopeia Convention Inc, Rockville, 19:2151–2152 .
- [21] Bebawy, L.I.; El-Kousy, N.; Suddik, J.K.; Shokry, M., *J. Pharm. Biomed. Anal.* , 1999, 21, 133-142.