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Development of Difference Spectroscopic Method for the Estimation of Tapentadol Hydrochloride in Bulk and in Formulation

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Abstract: A simple, precise and accurate difference spectroscopic method has been developed for the estimation of Tapentadol Hydrochloride in bulk and in pharmaceutical dosage form. The proposed method is based on the principle that Tapentadol Hydrochloride can exhibit two different chemical forms in basic and acidic medium that differ in the absorption spectra in basic and acidic medium. Since the drug was freely soluble in distilled water, a stock solution (1 mg/ml) was prepared with distilled water. Further dilution was made by using 0.1 M sodium hydroxide and 0.1 M hydrochloric acid separately. The maxima and minima in the difference spectra of Tapentadol Hydrochloride were at 290 nm and 269.5 nm, respectively. Difference in absorbance between these maxima and minima was calculated to find out the amplitude. This amplitude was plotted against concentration. Beer's law is valid in the concentration range of 3-18 µg/ ml. The results of analysis have been validated statistically and by recovery studies.
Keywords: Tapentadol Hydrochloride, Difference Spectroscopy, 0.1M Sodium hydroxide,0.1M Hydrochloric acid, ICH guidelines.

Introduction

Tapentadol Hydrochloride (TAP) a new drug, which is chemically (E3-[(1R, 2R)-3-dimethylamino)-1-ethyl-2-methylpropyl] phenol monohydrochloride[1]. TAP is a centrally acting narcotic (opioid) analgesic with a dual mechanism of action. Like classic narcotics such as morphine and hydrocodone, tapentadol activates µ-opioid receptors. In addition, similar to tricyclic antidepressants, tapentadol blocks the neuronal reuptake of norepinephrine, which, in turn, increases synaptic concentrations of this neurotransmitter[2]. Extensive literature survey revealed that the determination of Tapentadol Hydrochloride in pure and its dosage form by RP-HPLC[3] , UV[4] methodurine and oral fluids by using UPLC – Tandem Mass[5] , LC – Tandem Mass spectrometry[6] were reported. However, there is no evidence for the estimation of Tapentadol Hydrochloride in pure and in their dosage forms by spectroscopic method.

Hence the present work aims to develop a simple, precise, accurate and validated difference spectroscopic method for the estimation of TAP in bulk and in tablet dosage form.

Experimental

Shimadzu UV-1700 UV-Visible Spectrophotometer with 1 cm matched quartz cells was used for spectral and absorbance measurements. The spectrophotometric study was done by using Shimadzu - 1700 Double Beam UV - Visible spectrophotometer, (Shimadzu Corporation, Kyoto, Japan) and ELICO SL - 210 Double Beam UV - Visible spectrophotometer, (Elico India Pvt. Ltd., Hyderabad, India) with 1cm

matched quartz cells was used for absorbance measurements.

Tapentadol Hydrochloride was obtained as a gift sample from MSN Laboratories Limited, Hyderabad, India and tablets were procured from the local market (Tapol – 100, containing 100 mg Tapentadol Hydrochloride, marketed by MSN Laboratories Limited, Hyderabad). Hydrochloric acid and sodium hydroxide are AR grade chemicals obtained from the Qualingens India Pvt. Ltd., Mumbai, India. Double distilled water was obtained from the distillation unit.

Preparation of standard stock solution

30 mg of TAP was weighed accurately dissolved in distilled water and made up the volume to 100 ml in a volumetric flask. The solution was further diluted with 0.1 M hydrochloric acid and 0.1 M sodium hydroxide separately to get the concentration of 300 µg/ ml (working standards). Different aliquots were taken from their working standards and diluted with 0.1 M hydrochloric acid and 0.1 M sodium hydroxide separately to prepare a series of concentrations from 3 - 18 µg/ml as reference and test solutions, respectively. Difference spectrum was recorded by placing TAP in 0.1 M hydrochloric acid in reference cell and 0.1 M sodium hydroxide in sample cell. Difference in absorbance between 269.5 nm and 290 nm was calculated to find out the amplitude. The calibration curve was prepared by plotting amplitude versus concentration.

Application of the proposed procedure for the determination of dosage form

Marketed tablet formulation was used for analysis. Twenty tablets were weighed and their average net weight was calculated. The tablets were emptied and the powder was made to a fine powder. The powder equivalent to 30 mg of TAP was weighed and transferred in to 100 ml volumetric flask. Dissolved in distilled water and made up to the volume with the same. The solution was filtered through Whatman filter paper No.41. From the stock solution, 12 µg/ml solutions were prepared separately by using 0.1M hydrochloric acid and 0.1 M sodium hydroxide. The amplitude was calculated by measuring the absorbance of the equimolar concentrations at maxima and minima in the difference spectrum. The amount of TAP was calculated. The procedure was repeated for six times to perform precision.

Recovery studies

The accuracy of the proposed method was examined by determining the recovery of the drug by standard addition technique. To the preanalysed formulation, a known amount of TAP raw material was added in different concentrations *viz*., 80%, 100%, and 120% in both the reference and sample solutions. The procedure was repeated as per the analysis of formulation. The amplitude was calculated and the amount of TAP recovered was determined. This was repeated for six times.

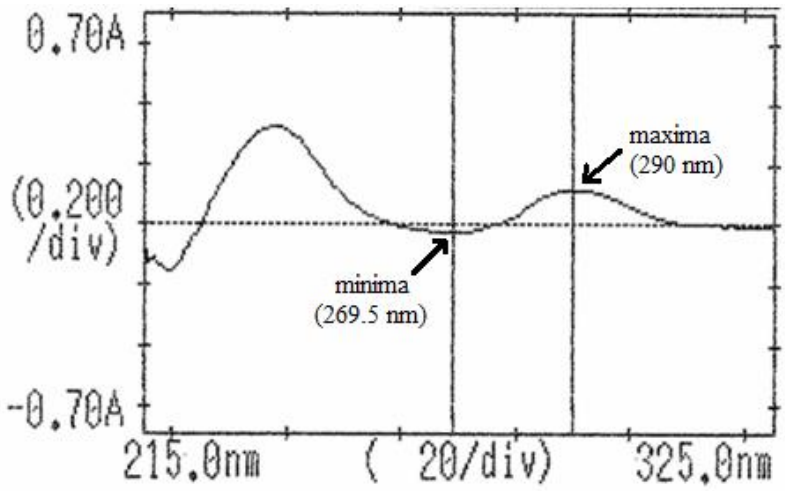

Figure 1. Difference spectrum of TAP (10 µg/ml solution of TAP in 0.1 M HCl was taken as blank and the same concentration of drug in 0.1 M NaOH as sample).

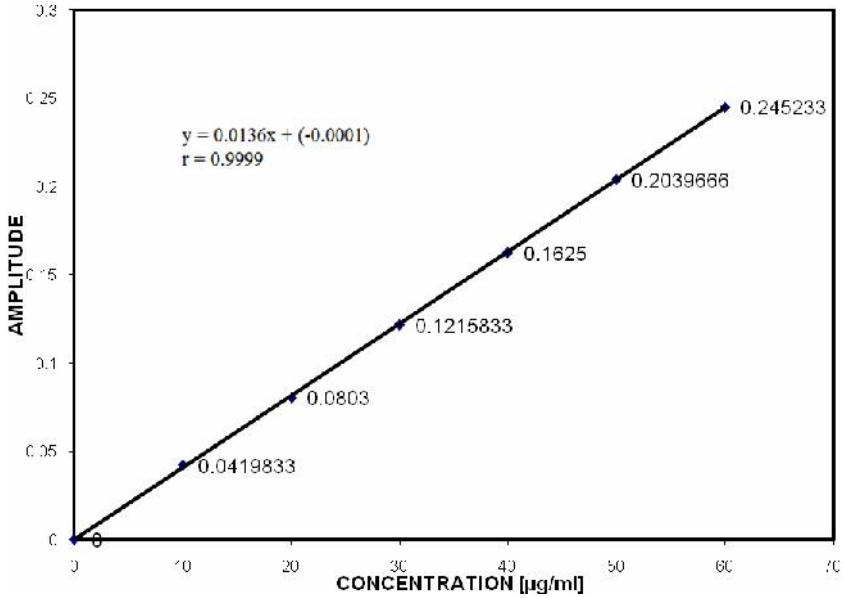

Figure 2 calibration plot for TAP

Table 1. Optical Parameters for the performance of the proposed method

PARAMETERS	VALUES*
Wave length maxima	290 nm
Wave length minima	269.5 nm
Beer's law limit (µg/ ml)	3 - 18
Sandell's sensitivity (µg/cm^2/0.001 A.U)	0.2452
Molar absorptivity (L mol^{-1} cm^{-1})	1.6858×10^3
Correlation coefficient (r)	0.9999
Regression equation(y=mx+c)	Y = 0.0136x + (-0.0001)
Slope(m)	0.0136
Intercept(c)	-0.0001
LOD (µg/ ml)	0.6689
LOQ (µg/ ml)	2.0270
Standard error	0.0002
Residual sum of squares	0.0000045
t-test	0.2325

*Mean of six observations

Table 2. Application of the proposed method for the analysis of dosage form containing TAP

Sample No	Labeled amount (mg/tab)	Percentage Obtained*	Mean (%)±SD	% RSD	%SE	CL	F-value
1	100	101.41					
2	100	99.79					
3	100	101.15	100.60±0.59	0.5837	0.0163	0.0637	0.1057
4	100	100.38					
5	100	100.51					
6	100	100.37					

*Mean of six observations; $F_{tab\ (\alpha=0.05;df1=5,\ df2=30)}$=2.5335;
CL-confidence limit; SE-standard error; RSD-residual sum of squares: SD standard deviation.

Table 3. Intra-day and inter-day precision

Type of precision	% Label Claim ±S.D*	%SE	%RSD	CL
Intraday	99.67±0.32	0.0353	0.3188	0.0294
Interday	99.85±0.27	0.0296	0.2667	0.0251

* Mean of three observations

CL-confidence limit; SE-standard error; RSD-residual sum of squares: SD standard deviation.

Table 4. Robustness and Ruggedness studies of TAP

Validation parameter	Conditions varied	%RSD
Robustness (n= 6)	Small changes in the molarity (±0.01M)	0.9850
Ruggedness (n= 6)	Analyst-I	0.2364
	Analyst-II	0.4066
	Instrument-I	0.7191
	Instrument-II	0.4620

RSD-residual sum of squares.

Table 5. Results from recovery studies

Spike level [%]	Amount present (µg/ml)	Amount* added (µg/ml)	Amount* recovered (µg/ml)	Mean recovery [%]	%RSD	Bias
80 %	6.0506	4.4018	10.3927	98.85±0.38	0.39	1.15
100 %	6.0506	5.9142	11.9079	99.04±0.12	0.13	0.96
120 %	6.0506	7.3007	13.2321	98.37±0.33	0.25	1.63

* Mean of three observations

Results and Discussion

A simple, precise, accurate difference spectrophotometric method has been developed for the estimation of TAP in pure and in formulations. In this method, the measured value is the difference in absorbance (DA) between two equimolar solutions of the analyte in different chemical forms which exhibit different spectral characteristics. The difference spectrum of TAP in 0.1 M NaOH was recorded by taking TAP in 0.1 M HCl solution as blank. The difference spectrum showed that the maxima at 290 nm and minima at 269.5 nm. (Figure 1). In alkaline solution, drug shows more intense peak than acidic peak. Therefore DA is positive. Six point calibration graphs were constructed covering a concentration range 3 - 18 µg/ml. Six independent determinations were performed at each concentration. Linear relationships between amplitude of maxima and minima of difference spectra versus the corresponding drug concentrations were observed (figure 2). The standard deviation of the slope and intercept were low. The correlation coefficient (r2) exceeded 0.9999. The calculated F value equal to 27868.61 is highly significant. A student's *t* - test was performed to determine whether the experimental intercept (c) of the regression equation was not significantly different from the theoretical zero value. It concerns the comparison of $t = c/sc$, where c is the intercept of regression equation and sc is the standard deviation of c, with tabulated data of the *t* distribution. As the calculated *t* - test ($t = 0.2325$) does not exceed to (0.01%) 1.680, the intercept of regression equation is not significantly different from zero. The LOD and LOQ were calculated (Table 1).

The repeatability study (n = 6) was carried out and the amount of TAP was found to be 100.60±0.59 with % RSD value of 0.5837. F-value, CL (confidence limit) and SE (standard error) also tabulated. It showed that the method was precise and the equipment used for the study worked correctly for the developed analytical method and being highly repetitive (Table 2). For the intermediate precision, a study carried out by the same analyst working on three times in the same day and three consecutive days indicated the % RSD of 0.3188 and 0.2667 for inter day and intraday analysis, respectively. Both the percentage RSD values were of below 2%, indicated that the intermediate precision was confirmed (Table 3). Robustness was studied by changing the molarities (±0.01M) of both hydrochloric acid and sodium hydroxide. The calculated %RSD was 0.9850, it indicates that the

robustness for proposed method was acceptable. Ruggedness was studied by inter-analyst and inter-instrument. %RSD for Ruggedness was found to be < 0.9851, it indicating the acceptance of the ruggedness. All the formulations may contain excipients, lubricating agents and binders which are added along with the active drug constituents. These substances may cause some interference during the estimation of the active drug constituents. This was determined by accuracy. The data for accuracy were expressed in terms of percentage recoveries of TAP in the real samples. These results are summarized in Table 4. The mean recovery data of TAP in real sample were within the range of 98.22% and 101.58%, mean % RSD was 1.439, satisfying the acceptance criteria for the study. All the above validation parameters were performed as per ICH guidelines[7].

Conclusion

The proposed method is simple, accurate, precise and selective for the estimation of TAP in bulk and in tablet dosage forms. The method is economical, rapid and do not require any sophisticated instruments contrast to chromatographic method. Hence it can be effectively applied for the routine quality control analysis of TAP in bulk and in tablet dosage forms.

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