Estimation of tramadol hydrochloride and diclofenac sodium

Derivative Spectrophotometric Method for Estimation ofTramadol Hydrochloride and Diclofenac Sodium in Pharmaceutical Dosage Form

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ABSTRACT

Purpose: Tramadol is opioid analgesic and diclofenac is NSAID and are used in severe to moderate pain management. Combination of Tramadol and Diclofenac drugs were approved by FDA to market in India with a dose of 50 mg for TRA and 75 mg DIC respectively. *Method:* The employed method is based on first order derivative spectrophotometry. Wavelengths 278. 7 nm and 281. 7 nm were selected for the estimation of the Tramadol and Diclofenac respectively by taking the first order derivative spectra. The concentrations of both drugs were determined by proposed method. The results of analysis have been validated statistically and by recovery studies as per ICH guidelines. *Result:* Both the drugs obey Beer's law in the concentration range of 5-30 µg mL $^{-1}$ and 5-45 µg mL $^{-1}$ with regression 0. 9997 and 0. 9990, intercept- 0. 0008 and 0. 0062 and slope- 0. 004 and 0. 0316 for TRA and DIC respectively. The accuracy and reproducibility results are close to 100% with 2% RSD. *Conclusion:* A simple, accurate, precise, sensitive and economical procedures for simultaneous estimation of Tramadol and Diclofenac in tablet dosage form have been developed

Key words: Tramadol, Diclofenac, First order derivative spectrophotometry, ICH guidelines, Validation, FDA

Introduction

Tramadol Hydrochloride (TRA) is a synthetic 4-phenylpiperidine analogue of codeine. Chemically it is cis -2-[(dimethylamino) methyl]-1-(3 methoxyphenyl) cyclohexanol hydrochloride (Figure-1), is a centrally acting opioid analgesic, indicated in the treatment of moderate to severe pain. TRA is used to treat postoperative (dental, cancer etc.) pain, treatment of rheumatoid arthritis, restless legs syndrome, motor neuron disease and fibromyalgia and as an adjuvant to NSAID therapy [1-8] .

Chemically Diclofenac Sodium (DIC) is 2-{2-[(2, 6- dichlorophenyl) amino] phenyl} acetic acid (Figure -2), is a nonsteroidal anti-inflammatory (NSAID) drug. DIC gives anti-inflammatory, antipyretic, and analgesic action thought the inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX). DIC is used in acute to chronic treatment of signs and symptoms of osteoarthritis and rheumatoid arthritis [9-19] .

Tramadol (50 mg) and Diclofenac (75 mg) combination, resulting central and peripheral analgesia a “ balanced analgesia” used in wider spectrum of pain management. In the literature survey it was found that various analytical methods involving spectrophotometry [1-4] , HPLC (High-performance liquid chromatography) [5-7] , stability-indicating RP-HPLC (Reverse phase high performance liquid chromatography) [8] , and GC/MS (Gas chromatography-mass spectrophotometry) [7] have been reported for TRA in single form and in combination with other drugs. Several analytical methods have been reported for DIC in single form and in combination with other drugs including

spectrophotometry [9-12] , HPLC [13-16] , RP-HPLC [17, 18] , and LC-MS (Liquid chromatography-mass spectrophotometry) [19] .

Extensive literature survey reveals that derivative spectrophotometric method is yet not reported for simultaneous determination of TRA and DIC in tablet dosage form. In the present work an attempt is being made to develop simple, precise, accurate and reproducible first-order derivative UV-spectrophotometric method for simultaneous estimation of TRA and DIC in combined dosage form.

Materials and Methods

Apparatus and Instruments

The instrument used in the present study was UV- spectrophotometer UV-1800 (Shimadzu, Japan) with spectral bandwidth of 2 nm and 10 mm a matched quartz cell was used. All weighing was done on Digital balance (Anamed).

Chemicals and Reagents

Analytically pure drug sample of TRA and DIC was kindly provided by Supriya Lifescience Ltd. (Mumbai, India) and J. B. Chemicals & Pharmaceuticals Ltd. (Gujarat, India) respectively. The pharmaceutical dosage form used in this study was unavailable in market but has been approved by the FDA to market in India. So this bilayer (Core) tablets manufactured in School of Pharmacy, S. R. T. M. University, Nanded, labeled to contain 50 mg of TRA

and 75 mg of DIC. All chemicals (AR grade) were purchased from RANKEM, Delhi, India.

Preparation of standard stock solutions

Accurately weighed 10 mg of TRA and DIC transferred to two separate 100 mL volumetric flasks. Added sufficient methanol and sonicated for 5 min. and volume was made upto 100 mL with methanol. 1 mL of the stock solution was further diluted to 10 mL with methanol to get a working standard solution of concentration 10 µg mL^{-1} of both TRA and DIC and scanned in the wavelength range of 200-400 nm.

First-Order Derivative Spectroscopic Method [20, 21]

Working standard solution of concentration 10 µg mL^{-1} of both TRA and DIC were scanned in spectrum mode between 400-200 nm using methanol as a blank. Then zero order spectrums of both the drugs were transformed mathematically into their individual first order derivative spectrum and first derivative overlain of both the drugs were obtained in 400-200 nm which is shown in figure 3, figure 4 and figure 5.

It was observed that wavelengths selected for quantification of both the drugs were 281. 7 nm for TRA and 271. 7 nm for DIC in such a way that at zero crossing of one drug another drug shows substantial absorbance (Zero crossing method). Therefore these two wavelengths were employed for the estimation of TRA and DIC without any interference. The calibration curves were plotted at these two wavelengths.

Preparation of Sample Stock Solution

Contents of twenty tablets were weighed accurately and powdered. Powder equivalent to 50 mg of TRA and 75 mg of DIC was weighed and dissolved in 50 mL of methanol with the aid of ultrasonication for 5 min. The solution was filtered through Whatman filter paper no. 41 to a 100 mL volumetric flask. Filter paper was washed with methanol, adding washings to the volumetric flask and volume was made up to the mark with methanol to get sample stock solution which was further diluted with methanol to get final concentration of solution (TRA 10 µg mL^{-1} and DIC 15 µg mL^{-1}) in the linearity range.

Results and Discussions

Linearity and range

A standard stock solution was prepared for both TRA and DIC; they were serially diluted to yield six for TRA and nine for DIC standard solutions. For UV spectrophotometric method, linearity was obtained in concentration range of 5-30 µg mL^{-1} and 5-45 µg mL^{-1} ; with regression 0. 9997 and 0. 9990, intercept- 0. 0008 and 0. 0062 and slope 0. 004 and 0. 0316 for TRA and DIC respectively. The results are depicted in table1.

Accuracy and precision

To ascertain the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%) as per ICH guidelines. Known amount of pure TRA and DIC were

added in preanalyzed powder of tablet formulation and analysis was carried out by proposed method for recovery at each level and % recovery, SD, % RSD was calculated. Results of recovery studies are shown in Table 2. The accuracy and reproducibility is evident from the data as results are close to 100 % and the value of standard deviation and % R. S. D. were found to be < 2 %; shows the high precision of the method. The proposed method is simple, economical, rapid, precise and accurate. Hence it can be used for routine analysis of TRA and DIC in tablet formulation.

Specificity

The proposed method was found to be specific as there is no interference from other excipients.

Results of analysis of tablet formulation

Analysis of formulated tablet was carried out and the amounts recovered were expressed as percentage amount of tablet claim. The percentage recovery for TRA is 100. 52±1. 486 and DIC is 99. 57±0. 555 respectively. The proposed methods was evaluated by the assay (n = 6) of formulated tablets containing TRA and DIC. The results of assay are presented in Table 3.

LOD and LOQ

LOD was found to be 0. 0686 µg mL $^{-1}$ and 0. 155 µg mL $^{-1}$ for TRA and DIC respectively. LOQ was found to be 0. 2081 µg mL $^{-1}$ and 0. 4719 µg mL $^{-1}$ for TRA and DIC respectively. The results of LOD and LOQ are shown in table 4.

Conclusion

The first-order derivative spectrophotometric method has been developed for simultaneous determination of TRA and DIC in combined dosage form. The developed and validated first order derivative spectrophotometric method is simple, economic, accurate and reproducible. The method was validated as per ICH guidelines in terms of linearity, specificity, accuracy, precision, limits of detection (LOD) and limits of quantification (LOQ). The proposed validated method can be utilized for routine analysis and quality control assay of TRA and DIC in combined dosage form.

Acknowledgments

The authors are very thankful to Supriya Lifescience Ltd., Mumbai and J. B. Chemicals & Pharmaceuticals Ltd., Gujarat, India for providing Tramadol Hydrochloride and Diclofenac sodium respectively as gift samples of pure drugs. Authors are also very thankful to School of Pharmacy, Swami Ramanand Teerth Marathwada University, Nanded, Maharashtra, India for providing all the necessary facilities to complete research work very successfully.

Conflict of interest

The authors report no conflicts of interest.