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METHOD DEVELOPMENT AND VALIDATION OF TAPENTADOL HYDROCHLORIDE BY RP-HPLC IN PURE AND TABLET DOSAGE FORM

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ABSTRACT

Tapentadol Hydrochloride is a most recent generation, central-acting pain killer that was approved by the EMA (European Medicines Agency) in 2010 for the treatment of severe chronic pain. Tapentadol Hydrochloride is immediate-release film-coated tablets for oral administration. Tapentadol Hydrochloride is chemically designated as 3-[(1R, 2R)-3-(dimethyl amino)-1-ethyl-2-methylpropyl] phenol mono hydro chloride. The present study is to validate reverse phase high performance chromatography (RP-HPLC) method for the estimation of Tapentadol Hydrochloride. The liquid chromatographic system consisted of following components: Waters E 2695 HPLC model containing, variable wavelength programmable UV / VIS detector 2998 (VP series), Hamilton syringe (705 NR50 µL) and a Rheodyne injector with a 20 µl loop. Chromatographic analysis was performed using Empower 2 software on a Thermo hypersil C18 column with 250 mm x 4.6 mm i.d. and 5 µm particle size by using acetonitrile: pH 7 buffer (50:50%V/V) as mobile phase at an wavelength 217nm. The flow rate was 1.0 ml/min with injection volume of 20 µl. Chromatogram showed peak of Tapentadol Hydrochloride at retention time of 3.582 ± 0.004 min. The method was validated for linearity, sensitivity, precision, accuracy, ruggedness and robustness. The limit of detection and limit of quantitation for estimation of Tapentadol Hydrochloride was found to be 0.057µg/ml and 0.19µg/ml, respectively. Recovery of Tapentadol Hydrochloride was found to be in the range of 98.4 -101.3%. Proposed method can be successfully applied for the quantitative determination of Tapentadol Hydrochloride in pharmaceutical dosage forms.

KEY WORDS: Tapentadol Hydrochloride, RP-HPLC.

1.INTRODUCTION

Tapentadol Hydrochloride is immediate-release film-coated tablets for oral administration. Tapentadol Hydrochloride is a centrally-acting synthetic analgesic. It is mainly used for the treatment of chronic severe disabling pain not responding to non-narcotic analgesics. The synergy between its two mechanisms of action - µ-opioid agonism and noradrenalin uptake inhibition allows approaching pain from two different physiological aspects. Tapentadol Hydrochloride is rapidly absorbed following oral administration, and excreted almost exclusively by the kidneys. The analgesia resulting from Tapentadol administration derives from its primary molecule's action, with no active metabolites involved. Its molecular formula is $C_{14}H_{23}NO \cdot HCl$. It has a molecular weight is 257.80 g / mol. It is a White amorphous powder and is soluble in methanol, sparingly soluble in water and slightly soluble in ethanol. The aim of the Present study was to develop a valid, reliable and convenient HPLC-based method for the determination of Tapentadol Hydrochloride.

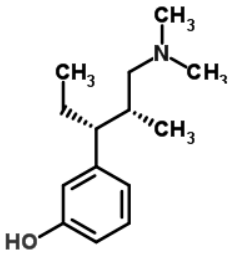

Figure no 1. Molecular Structure of Tapentadol

2.EXPERIMENTAL

2.1. Chemicals and reagents: An analytically pure sample of Tapentadol Hydrochloride was procured as gift sample from Dr.Reddy's Laboratories Ltd. (Hyderabad, India). HPLC grade Methanol and HPLC grade Water was purchased from E. Merck (Ahmadabad). Potassium dihydrogen orthophosphate (AR grade, purity 99.5 %) was purchased from Qualigens. Tablet formulation TYDOL (Brand I) manufactured by Ranbaxy Laboratories Ltd., New Delhi, was purchased from a local pharmacy with labeled amount 50 mg per tablet.

2.2. Chromatographic equipment and conditions: The liquid chromatographic system consisted of following components: Waters e2695 HPLC, variable wavelength programmable UV / VIS detector 2998 (VP series), Hamilton syringe (705 NR50 µL) and a Rheodyne injector with a 20µl loop. Chromatographic analysis was performed using Empower2 software on a Thermo hypersil C18 column with 250 mm x 4.6 mm internal diameter and 5 µm particle sizes. A RP C-18 column equilibrated with mobile phase Acetonitrile: Potassium dihydrogen orthophosphate (50: 50%v/v, pH 7) was used. Mobile phase flow rate was maintained at 1.0 ml/min. Detection wavelength 217 nm was selected by scanning standard drug over a wide range of wavelength 200 nm to 400 nm in spectrophotometer. The sample was injected using a 20 µL fixed loop, and the total run time was 5 min.

2.3. Preparation of mobile phase: Potassium dihydrogen orthophosphate was weighed (136.09 g) and dissolved in 1000 ml of HPLC grade water. 100ml of the above solution was taken and mixed with 100ml of acetonitrile and mixed well. Finally pH was adjusted to 7.0 using triethanolamine. The solution was sonicated for 10 min and filtered using Whatmann filter paper (No. 41).

2.4. Standard preparation: A stock solution of Tapentadol Hydrochloride was prepared by accurately weighing 50 mg of drug, transferring to 50 ml volumetric flask, add 20ml of mobile phase and sonicate up to 15 minutes; make up the volume with the mobile phase. Appropriate aliquot of this solution was further diluted to 100 ml with mobile phase to obtain final standard solution of 50µg/ml of Tapentadol Hydrochloride. Resultant solution was filtered through Whatman filter paper number 41. The standard solution of 20µl was injected.

2.5. Sample preparation: Twenty tablets each containing 50 mg of Tapentadol Hydrochloride were accurately weighed and finely powdered. Tablet powder equivalent to 50 mg of Tapentadol Hydrochloride was transferred to a 50 ml of volumetric flask containing mobile phase (approximately 20 ml) and sonicated for few minutes to dissolve the drug and then filtered through Whatman filter paper. The filtrate volume was adjusted up to the mark. Further pipette out 5 ml of the above solution into a 100 ml volumetric flask and dilute up to the mark with the same solvent to get the required concentration of 50 µg/ml. The resulting solution was filtered through Whatman filter paper (No. 41). The sample volume of 20µl was injected. The chromatogram of sample preparation obtained was shown in figure 2.

2.6. Validation of the method: Once the HPLC method development was completed, the method is validated in terms of parameters like linearity, system suitability, specificity, sensitivity, precision, accuracy, ruggedness and robustness.

2.6.1. Linearity: Appropriate aliquots of Tapentadol Hydrochloride stock solutions (1000 µg/ml) were taken in different 10 ml volumetric flasks to obtain the concentrations of 50-150µg/ml. These solutions were injected into chromatographic system. The chromatograms were obtained and peak area was determined for each concentration of drug solution. Calibration curve of Tapentadol Hydrochloride was constructed by plotting peak area vs. applied concentration of Tapentadol Hydrochloride and regression equation was computed which was shown in figure 3. The slope, intercept, and correlation coefficient were also determined and were shown in table 2**.**

2.6.2. System suitability: Retention time (RT), number of theoretical plates (N) and tailing factor (T) were evaluated for six replicate injections of the drug at a concentration of 50 µg/ml. The results which were given in table 1 were within acceptable limits.

2.6.3. Specificity: The peak for Tapentadol Hydrochloride from the tablet formulation was identified by comparing its retention time with those of standard Tapentadol Hydrochloride.

2.6.4. Sensitivity: The sensitivity of measurement of Tapentadol Hydrochloride by use of the proposed method was estimated in terms of the limit of detection (LOD) and the limit of quantification (LOQ). The LOD is calculated as three times the noise level, while ten times the noise value gave the LOQ. In order to estimate the LOD and LOQ values, the blank sample was injected six times and the peak area of this blank was calculated as noise level. LOD and LOQ were found to be 0.057 and 0.19µg/ml, respectively.

2.6.5. Precision: To demonstrate the precision of method (Method Precision), six samples from the same batch of formulation were analyzed individually and the assay content (Tapentadol Hydrochloride) of each sample was estimated. The average for the six determinations was calculated along with the % RSD for the replicate determinations.

2.6.6. Accuracy: Previously analyzed samples of Tapentadol Hydrochloride (10 µg/ml) were spiked with 50, 100, and 150 % extra Tapentadol Hydrochloride standard and the mixtures were analyzed by the proposed

method. The experiment was performed in triplicate and recovery of the pure drug was calculated. Standard deviation of the % recovery and % RSD were calculated. These things were validated as per the ICH guidelines (IFPMIA 1994, 1996).

3. RESULTS

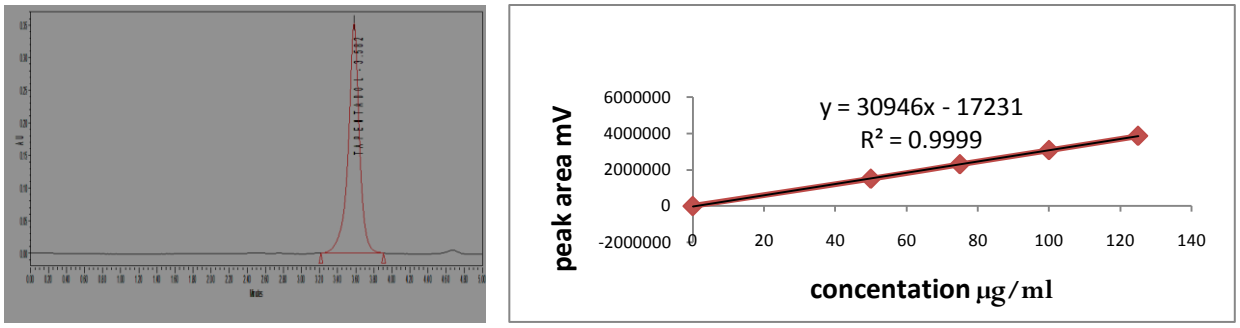

Figure no 2 &3 Chromatogram and Calibration curve of Tapentadol hydrochloride by RP – HPLC

Table no 1 System suitability studies of Tapentadol hydrochloride by RP-HPLC method

Property	Values	Required limits
Retention time (tR)	3.582 ± 0.004 min	RSD ≤ 1%
Theoretical plates (N)	4624.52 ± 163.48	N > 2000
Tailing factor (T)	0.89± 0.117	T ≤ 2

Table no 2Characteristic parameters of Tapentadol hydrochloride for the proposed RP-HPLC method

Parameters	RP-HPLC
Calibration range (µg/ml)	50-150
Detection wavelength (nm)	217 nm
Mobile phase (Acetonitrile : Buffer)	50 : 50 (v / v, pH 7.0)
Accuracy	99.66%
Intraday method precision Interday method precision	0.58 1.19
Retention time (Min) (tR)	3.582 ± 0.004 min
Slope (b)	30946
Intercept (a)	1723.1
Regression equation (y*)	y = 30946x +1723.1
Correlation coefficient(R2)	0.999
Limit of detection (µg/ml)	0.057
Limit of quantitation (µg/ml)	0.19

4. CONCLUSION

A few methods were available to determine the concentration of Tapentadol Hydrochloride, but we present here a validated, reliable and convenient assay for the simultaneous determination of peak area and concentration levels of Tapentadol HCl. The developed procedure was most suitable, the developed method was simple, accurate, precise, specific, and could separate the drug.

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