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METHOD DEVELOPMENT AND VALIDATION FOR DISSOLUTION METHOD OF TOLVAPTAN IN BULK AND TABLET DOSAGE FORM BY UV SPECTROPHOTOMETRY

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ABSTRACT

A simple, sensitive, accurate, precise and rapid UV spectrophotometric method was developed for the estimation of Tolvaptan in pure form and its formulation. For the estimation of Tolvaptan, solvent system employed was Methanol and Dissolution medium (0.01N Hydrochloric acid + 1% Sodium Lauryl Sulphate) and wavelength of detection was 269nm .The developed method was used to estimate the total drug content in commercially available oral formulation of Tolvaptan and recovery studies were carried out. Sample recovery in the formulation using the above method was in good agreement with their labeled claim, thus suggesting the validity of the method noninterference of formulation excipients in the estimation.

Keywords: Spectrophotometric determination, Tolvaptan, Validation.

INTRODUCTION

Tolvaptan is an orally administered non peptide vasopressin (VP) V2 receptor antagonist that inhibits water re-absorption in the kidney by competitively blocking VP binding, resulting in water diuresis without significantly changing total electrolyte excretion [1-2]. Chemically (±)-4'-[(7-chloro-2, 3, 4, 5-tetrahydro-5-hydroxy-1H-1-benzazepin-1-yl) carbonyl]-*o* tolu *m*-toluidide [3]. Chemical structure of Tolvaptan is shown in Figure 1. It is not official in any pharmacopoeia, few liquid chromatography procedures have been reported for the determination of Tolvaptan [4-5].

MATERIALS AND METHODS

Instrumentation

The instrument used in the present study was double beam UV/Visible spectrophotometer (Model Spectro2060 Analytical tool) with spectral band width of 1 nm. All weighing was done on electronic balance (Model Shimadzu AUX -220).

Reagents and Materials

All chemicals were of AR grade and Triple distilled water was used to prepare solutions.

VALIDATION OF DISSOLUTION METHOD

Preparation of Dissolution Medium

0.85ml of Hydrochloric acid is diluted to 1000ml with distilled water. Mix well. Add 10g of Sodium Lauryl Sulphate, dissolve and mix well.

Preparation of Standard solution

Stock solution of Tolvaptan (660µg/ml) is freshly prepared by transferring accurately weighed 33mg of Tolvaptan into 50ml volumetric flask and dissolved in Methanol and then made up to the mark. The working standard solution (33µg/ml) is prepared by transferring 5ml of the stock solution into a 100ml standard flask and made up to the mark with dissolution medium.

Preparation of Sample

Weigh six tablets individually and run the dissolution test on six tablets by applying the parameter given below.

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Apparatus	USP Apparatus II (Paddle)
RPM	50 RPM
Dissolution medium	0.01N HCL + 1% SLS
Media Volume	900 ml
Time	10, 20, 30, 45, 60 minutes and infinity
Sample collection volume	10 ml
Temperature	37.0 ± 0.5°C

The sample solution portion of about 10ml in each dissolution vessel withdrawn at the specified time points and it is replace by the same amount of blank dissolution medium. These solution are Filtered through a Whatmann filter paper no 41 filter by discarding the first 4ml of the filtrate.

Selection of Wavelength

For the selection of analytical wavelength, working standard solution of Tolvaptan (33 µg/ml) was scanned in the spectrum mode from 200 nm to 400 nm. The absorbance maximum(λmax) was found to be 269 nm. The UV spectrum for Tolvaptan is depicted in Figure 2.

Linearity and range

Different concentrations of Tolvaptan solutions were prepared .The range of the solutions varies from 20% to 140% of standard concentration (µg/ml) of 30 mg. The absorbance of these solutions is noted. The absorbance of the lower level linearity solution (20%) and the higher level linearity solution (140%) in 6 replicates were recorded. The graph of concentration vs absorbance of linearity solutions was plotted.

System precision

The system precision of the method was checked by repeated measurement of the absorbance values of standard solutions (n = 5). The repeatability was expressed in terms of relative standard deviation (RSD). The RSD value for Tolvaptan is shown in Table 2. Relative standard deviation was less than 2 %, which indicates that the proposed method was repeatable.

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In method precision, the % release is not less than 80% (Q) release in 60 minutes. In this developed method, the % release of Tolvaptan 30mg was found to be 98.7% release in 60 minutes.

Recovery

Recovery at each level should be between 95% to 105%. In this method, the recovery at 80%, 100% and 120% level was found to be 101.45 to 103.06, 102.31 to 104.62 and 100.79 to 102.19.

Figure 1. Chemical structure of Tolvaptan

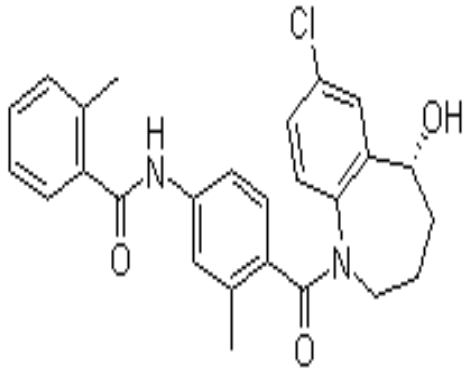

Figure 2. UV Spectra of Tolvaptan

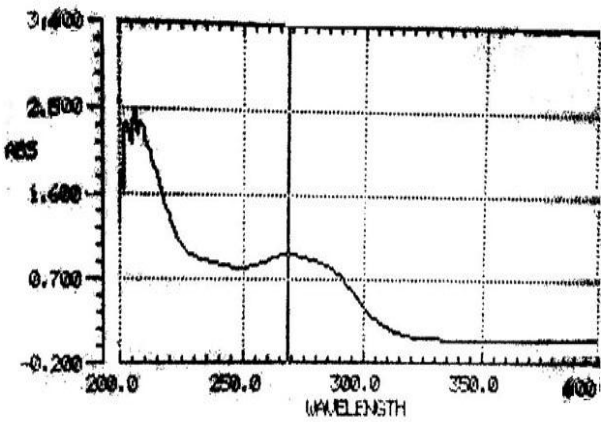

Table 1. The graph of concentration vs absorbance of linearity solutions

S.No	% Level	Concentration in µg/ml	Mean Absorbance
1	20	6.6	0.232
2	40	13.2	0.454
3	60	19.8	0.682
4	80	26.4	0.917
5	100	33.0	1.124
6	120	39.6	1.372
7	140	46.2	1.591

Figure 3. The graph of concentration vs absorbance of linearity solutions

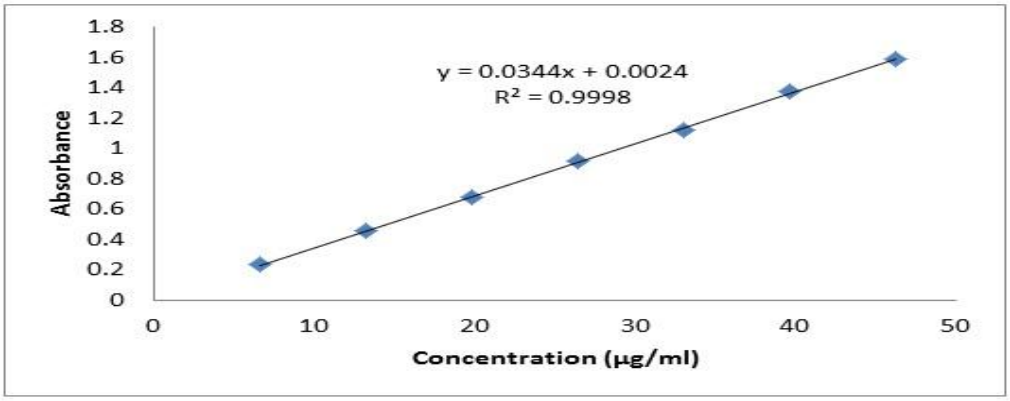

Table 2. System precision for Tolvaptan 33 µg/ml

S.No	Absorbance (33 µg/ml)
1	1.126
2	1.130
3	1.121
4	1.123
5	1.124
Mean	1.125
% RSD	0.179

Table 3. Method precision for Tolvaptan 30 mg

S.No	Absorbance (30mg)
1	1.129
2	1.123
3	1.121
4	1.120
5	1.119
Mean	1.122
% RSD	0.130

RESULTS AND DISCUSSION

To develop accurate, precise and sensitive UV spectrophotometric method for Tolvaptan various solvent systems such as water, methanol etc. were tried alone and in combinations or in the presence of surfactants in different propotions. The final decision of using 0.01N HCL + 1% SLS in water was based on sensitivity, minimal interference, suitability for drug content estimation and cost. The linearity range in the concentration range of 6.6-46.2µg/ml. The optical characteristics such as correlation co-efficient, slope and intercept was found to be 0.999, 0.034 and 0.002.

CONCLUSION

The proposed analytical method are rapid, accurate, precise and reproducible and hence can be used for the routine analysis of Tolvaptan in bulk, tablet dosage forms. The sample recoveries from the formulation were in good agreement with their respective label claims, which suggested non-interference of excipients in the estimation.

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