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Development and Validation of Dissolution Method for Udenafil Tabletse

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ABSTRACT:

The aim of this work was to develop and validate a dissolution test for Udenafil tablet using spectrophotometric method. The dissolution established conditions were: 900 mL of 0.1 N HCl as dissolution medium, using a paddle apparatus at a stirring rate of 50 rpm. The drug release was evaluated by UV spectrophotometric method at 292 nm for Udenafil. In this study % drug release of Udenafil was found to be greater than 90% in 45 minutes. The method was validated to meet requirements for a global regulatory filing which includes linearity, precision, accuracy.

KEYWORDS: Udenafil, Dissolution, UV spectrophotometric method, validation.

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INTRODUCTION:

Udenafil is Chemically 3-{1-methyl-7-oxo-3-propyl-1H,4H,7H-pyrazolo[4,3-d]pyrimidin-5-yl}-N-[2-(1-methylpyrrolidin-2-yl)ethyl]-4-propoxybenzene-1-sulfonamide. Udenafil is Phosphodiesterase 5 (PDE5) inhibitor. [1]Phosphodiesterase 5 (PDE5) inhibitors are the first line therapy for ED. [2-5] Udenafil is the fifth amongst the PDE5 inhibitors class and fulfils this need for a molecule having advantages of the existing agents with a better tolerability profile. Udenafil has been found efficacious in the treatment of various causes and severity of ED with no muscle pain/back pain, which is common side effect of other drugs from this class. [6-13] From Literature survey, only one method UV [1] was reported for the analysis of Udenafil. Hence, the purpose of the present work was to develop and validate dissolution method for Udenafil tablets.

MATERIAL AND METHODS

Instruments

Dissolution apparatus: Type 2 –Paddle (Veego)

Specification**:** USP Standards tablet dissolution test apparatus multi-bath (n=6) Dissolution test was performed in accordance to USP Pharmacopoeia [14] general method. The medium was vacuum degassed under in house vacuum and was maintained at 37.0 ± 0.5°C by using a thermostatic bath. Spectrophotometric measurements were performed on Shimadzu UV –visible double beam spectrophotometer (Model- 1800). All weighing were done on electronic analytical balance (Wensar Dab220).

Dissolution apparatus condition:

- Type: Paddle type (USP type II)
- Speed: 50 rpm
- Temperature: 37±0.5°C
- Media volume: 900 ml

Chemicals and Reagents

The bulk drug, Udenafil was obtained from MSN Labs, Hyderabad. Tablet (Udzire) Udenafil 100 mg was purchased from local market for analysis. All reagents and solvents used were analytical grade. 0.1 N HCl was prepared according to USP Pharmacopoeia.

Selection of a Solvent

0.1 N HCl was selected as dissolution medium for studying % Drug release of drug.

Preparation of Standard Stock Solution

Accurately weighed quantity of Udenafil 100 mg was transferred into 100 ml volumetric flask and final volume of solution was made 100 ml with 0.1 N HCl to get stock solution containing 1 mg/ml of Udenafil in 100 ml volumetric flask. From this solution of 100 µg/ml Udenafil solution was prepared by diluting 10 ml of stock solution with 0.1 N HCl in 100 ml volumetric flask up to the mark.

Preparation of Working Standard Solution of Udenafil

From above solution of Udenafil pipette out 0.8, 1.2, 1.6, 2.0, 2.4, 2.8 ml of the stock solution and were further diluted to 10 ml volumetric flasks with 0.1 N HCl to get concentrations 8, 12, 16, 20, 24, 28µg/ml.

Selection of Analytical Wavelength

From the stock solutions, a working standard was prepared. The absorption spectrum for drug was recorded between 200-400 nm using the concentration of 20µg/ml and it was found to show absorption maxima at 292.

Assay of Pharmaceutical dosage form

The dissolution experiment was conducted in a six-station bath dissolution apparatus by subjecting six Udzire tablets to 900 mL of dissolution medium, in a paddle dissolution apparatus, and stirring speed of 50 rpm. The temperature was stabilized at 37± 0.5 ° C**.** Aliquots of 1 mL were withdrawn manually at 5, 10, 15, 20, 25, 30, 35, 40, 45 min. The same volume of medium at 37± 0.5 ° C was replaced for constant volume. The sample was filtered through Whatman filter paper and analyzed spectrophotometrically at 292 nm.

Method Validation

Method validation was performed following ICH guidelines. The proposed method has been extensively validated in terms of linearity, accuracy and precision, limit of detection and limit of quantification.

Linearity (Calibration curve)

The calibration curves were plotted over a concentration range of 8-28µg/ml for Udenafil. Accurately measured standard solutions of (0.8, 1.2, 1.6, 2, 2.4, 2.8 ml) Udenafil was transferred to a series of 10 ml of volumetric flasks and diluted to the mark with 0.1 N HCl. The absorbances of the solutions were measured at 292 nm against 0.1 N HCl as blank. The calibration curves were constructed by plotting absorbance versus concentration and the regression equations were calculated. Straight line equations were obtained from these calibration curves. The linear regression equation of Udenafil was $y = 0.0223 x + 0.028$ ($R^2 = 0.9983$).

Accuracy

The recovery study was performed using a well-characterized lot of drug product with tight content uniformity. Udenafil reference substance was added to the dissolution vessels in known amounts at the 80%, 100%, and 120% levels. Accordingly, 80, 100, and 120 mg of reference drug were added along with each 100-mg tablet. The dissolution test was performed on Udzire tablets for 45 min using 900 mL of 0.1 N HCl as medium in a paddle apparatus at 50 rpm. Aliquots of 1 ml were filtered through Whatman filter paper and diluted up to the 10 ml with 0.1 N HCl, analyzed by UV spectrophotometric method at the spiked concentration levels of 80%, 100%, and 120%, respectively. Each concentration was analyzed in triplicate.

Precision

The precision of an analytical procedure expresses the closeness of agreement between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. The precision of the method was verified as repeatability, intra-day, inter-day and reproducibility.

Repeatability (intra assay) was determined by analyzing six samples of Udzire tablets with the optimized dissolution test. Aliquots were collected and evaluated by the UV method at 292 nm. Thus, repeatability was evaluated with the relative

standard deviation (RSD) of the data at the 100% level. The intraday precision and interday precision were determined on same day at three consecutive hours and on different days respectively. The dissolution test was performed using same dissolution conditions described above.

Limit of Detection and Limit of Quantification

ICH guideline describes several approaches to determine the detection and quantification limits. These include visual evaluation, signal-to-noise ratio and the use of standard deviation of the response and the slope of the calibration curve. In the present study, the LOD and LOQ were based on the third approach and were calculated according to the 3.3 × (SD/Slope) and 10 × (SD/Slope) criteria, respectively; where SD is the standard deviation of y-intercept of regression line and S is the slop of the calibration curve.

RESULT AND DISCUSSION

Simple, accurate, rapid and precise Dissolution method by UV-Spectroscopy was developed and validated for estimation of Udenafil marketed formulation. The method was developed using 900mL of 0.1 N HCl at 37.0 ± 0.5 ºC, paddle apparatus, 50 rpm stirring speed and filtration with Whatman filters. In Dissolution study % drug release of Udenafil was found to be greater than 90% in 45 minutes. The linearity was shown in the range of 8-28µg/ml. Correlation coefficient was found to be 0.9983. The average percentage recovery was found to be 98.28%. The average percentage assay result was found to be 97.75%. Precision (% RSD) of Udenafil was found to be 0.9332 – 1.3959%. The LOD and LOQ were 0.46µg/ml and 1.41 µg/ml of Udenafil. The proposed method was precise, accurate and reproducible and acceptable recovery of the analytes, which can be applied for the analysis of Udenafil in Pharmaceutical dosage form.

CONCLUSION

A simple dissolution test developed and validated for Udenafil tablets are considered satisfactory. The conditions that allowed the dissolution determinations are 900mL of 0.1 N HCl at 37.0 ± 0.5 ºC, paddle apparatus, 50 rpm stirring speed and filtration with Whatman filters. In these conditions, the Udenafil stability is good. The % drug delivery is higher than 90% in 45 minutes in evaluated product. Therefore, the proposed method is successfully applied and suggested for the quality control studies of Udenafil in pharmaceutical dosage forms contributing to assure the therapeutic efficacy of the drug.

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TABLES AND FIGURES

Table 1: Regression analysis data and summary of validation parameters for the proposed method

Parameter	Dissolution method by UV Spectrophotometry
	Udenafil
Concentration range (µg/ml)	8-28
Regression equation	y = 0.0223 x + 0.028
Slope	0.0223
Intercept	0.028
Correlation Coefficient (r^2)	0.9983
Accuracy (% recovery, n=3)	98.2804
Repeatability (%RSD, n = 6)	0.9919
Intraday (%RSD, n=3)	0.9332 – 1.3959
Interday (%RSD, n=3)	1.0348 – 1.5567
LOD (µg/ml)	0.46
LOQ (µg/ml)	1.41

Table 2: Recovery data of proposed method

Level (%)	Test amount (µg/ml)	Spiked STD amount (µg/ml)	Total amount (µg/ml)	STD amount recovered (µg/ml)	% Mean recovery ± SD. (n=3)
80	11.11	8.88	19.99	8.6906	97.8679 ± 0.6974
100	11.11	11.11	22.22	10.8667	97.8102 ± 0.7299
120	11.11	13.33	24.44	13.2184	99.1632 ± 1.0967

Table 3: Analysis of Udenafil by proposed method

Sr. no	Time	% drug release (n=6) ± S.D
1	5	29.3318 ± 0.5785
2	10	45.8672 ± 0.8850
3	15	53.7250 ± 0.7680
4	20	64.5753 ± 0.7297
5	25	72.5640 ± 0.4295
6	30	74.8900 ± 0.8356
7	35	86.8260 ± 0.8862
8	40	91.6110 ± 0.5794
9	45	97.7527 ± 0.9696

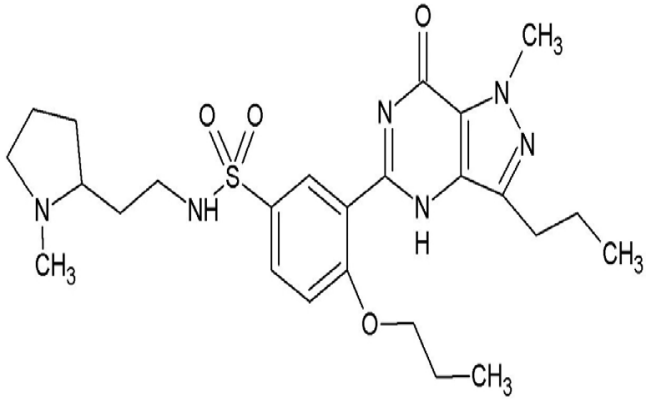

Figure 1: Structure of Udenafil

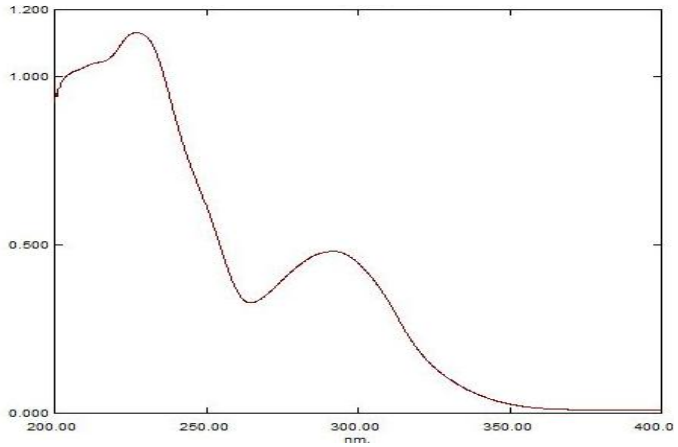

Figure 2: UV Spectrum for Udenafil (20 µg/ml) at 292 nm

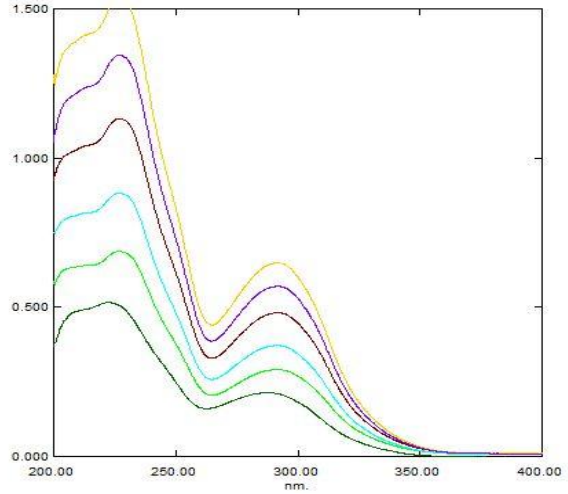

Figure 3: Overlain spectrum of Udenafil (8-28 µg/ml) in 0.1 N HCl.

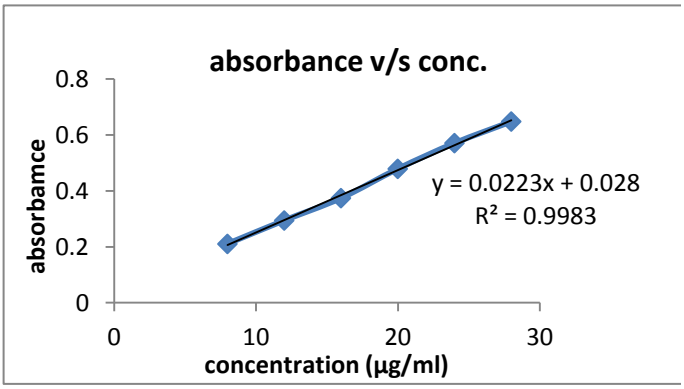

Figure 4: Calibration curve of Udenafil at 292 nm in 0.1 N HCl.

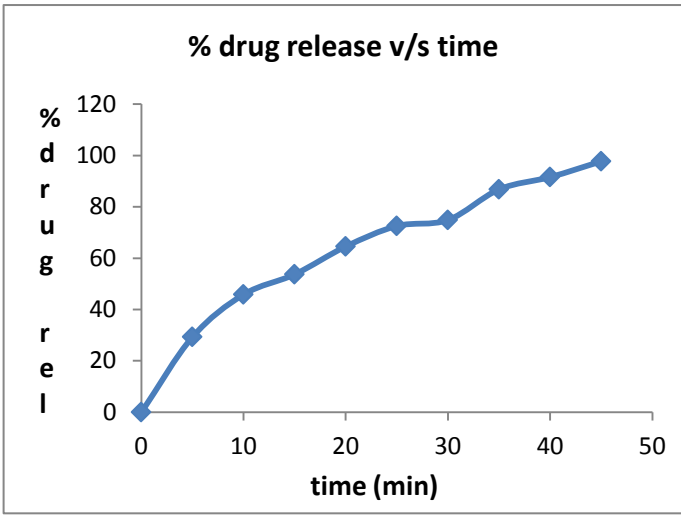

Figure 5: Dissolution profile of Udenafil in 0.1 N HCl

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