



Research Article

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Development and Validation of Simple UV-Spectrophotometric Method of Quantization of Ondansetron Hydrochloride in Solid Dosage Formulations Using Hydrotropic Solubilization Technique

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ABSTRACT

Commonly used organic solvents for spectrophotometric analysis of water insoluble drugs are methanol, ethanol, chloroform, benzene, toluene etc. The main drawbacks of organic solvents include high cost, toxicity, and pollution. Organic solvents have numerous adverse effects caused by single exposure like dermatitis, headache, drowsiness, nausea, eye irritation and long term exposure causes serious effects such as neurological disorder, chronic renal failure, and liver damage. They should be replaced by other ecofriendly alternative sources. The present study is an attempt to show that solid can also be used to act as solvent precluding the use of organic solvents. A simple, safe and sensitive method of spectrophotometric determination of Ondansetron hydrochloride obeyed beers law in the concentration range of 10-50 μ g/ml at 310 nm. The results of analyses have been validated statistically for linearity, accuracy, precision, LOD and LOQ. The results of validation parameters also indicated that proposed method was found to be accurate, precise, reproducible, sensitive, and suitable for routine quality control analysis for estimation of Ondansetron Hydrochloride in solid dosage formulation.

Keywords: Ondansetron hydrochloride, UV-Spectrophotometry, solid dosage formulation, hydrotropic solubilization technique.

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INTRODUCTION

Increasing the aqueous solubility of insoluble and slightly soluble drugs has been done by various methods to avoid the usage of organic solvents. Because of toxicity, volatility, and also high cost of organic solvents, alternative methods have been developed. Hydrotropic solubilization is the phenomenon by which aqueous solubility of poorly water soluble drugs and insoluble drugs increase. Various techniques have been employed to enhance the aqueous solubility and hydrotrophy is one of them. Sodium salicylate, sodium benzoate, urea, nicotinamide, sodium citrate and sodium acetate are the most common examples of hydrotropic agents utilized to increase the water solubility of drug. [1-20] Maheshwari *et al.*, has analyzed various poorly water-soluble drugs using hydrotropic solubilization phenomenon viz. ketoprofen, salicylic acid [1], frusemide [2], cefixime [3], tinidazole [4], amoxicillin. [5] Maheshwari *et al.*, have developed various analytical techniques employing hydrotropic solubilization phenomenon to analyze poorly water-soluble Drugs like hydrochlorothiazide [6], aceclofenac [7], ofloxacin [8], and nifedipine. [9] Various organic solvents such as methanol, chloroform, and dimethyl formamide and acetonitrile have been employed for solubilization of poorly water-soluble drugs to carry out spectrophotometric analysis.

Ondansetron hydrochloride is chemically 1, 2, 3, and 9-tetrahydro-9-methyl-3-((2-methyl-1H-imidazole-1-yl)methyl)-4H-carbazol-4-one hydrochloride. It is a 5HT₃ receptor antagonist. [10] A survey of literature revealed spectrophotometric methods [11-14] and HPLC method for the estimation of drug. [15] It is a white to off white crystalline powder sparingly soluble in water and alcohol, soluble in methanol. It is used alone or with others to prevent nausea and vomiting caused by cancer drug treatment and radiation therapy.

In the present investigation, 30% solution of niacinamide was employed as solubilizing agent to extract out the drug to estimate tablets spectrophotometrically at 310 nm. Niacinamide does not interfere in spectrophotometric analysis above 300 nm. Proposed method is novel, economic, ecofriendly, rapid, free from toxicity of organic solvent, accurate, and reproducible, Recovery studies and statistical data proved the accuracy, reproducibility, and precision of the proposed method. The presence of tablet excipients did not interfere in the estimation at 310 nm.

MATERIALS AND METHODS

Chemicals and Reagents

Pharmaceutical grade Ondansetron hydrochloride was a gift from Modern Laboratories Pvt. Ltd. and its dosage formulation Vomnil-MD and Emvon-MD were purchased from local market. All other chemicals were of analytical grade and obtained from BDH labs.

Instrumentation

UV Visible spectrophotometer (Model 1800, Shimadzu, Japan) with 10 mm path length connected to a computer was used for spectrophotometric analysis.

Calibration curve

Standard stock solution of Ondansetron hydrochloride was prepared by weighing 50 mg of Ondansetron hydrochloride and transferred to a 100 ml volumetric flask and dissolved in 20 ml aqueous solution of 30% niacinamide then finally volume was made up to 100ml with distilled water to get a concentration of 500µg/ml. Appropriate volumes of this solution were further diluted with distilled water to obtain final concentrations in the range of 10-50µg/ml. The absorptions of these standard solutions were noted at 310 nm against respective reagent blanks.

Table 1: Data of Calibration curve

S. No.	Concentration (µg/ml)	Stock Solution in (ml)	Final volume with distilled water (ml)	Absorbance at 310 nm
1	10	2	100	0.47
2	20	4	100	0.897
3	30	6	100	1.299
4	40	8	100	1.718
5	50	10	100	2.071

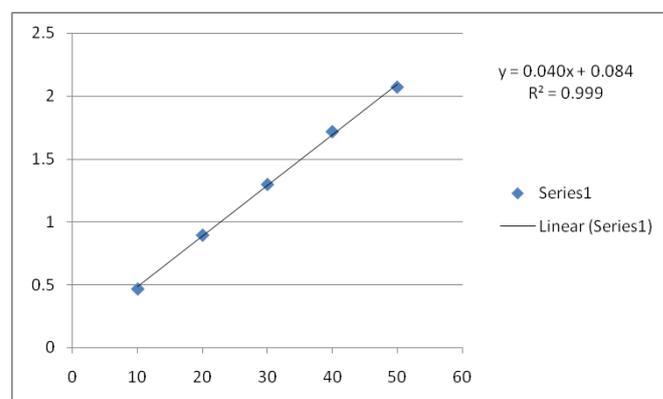


Fig. 1: Calibration curve of Ondansetron hydrochloride

Preliminary solubility studies

To determine the solubility of the drug in distilled water and aqueous solution containing 30% of niacinamide at room temperature sufficient excess amount of the drug was added to a 25 ml capacity vial containing distilled water and the aqueous solution. After putting the vial caps and applying the aluminum seals, the vials were shaken mechanically for 12 hours at room temperature (27°C) in an orbital flask shaker. The solution was allowed to equilibrate for 24 hours undisturbed and then filtration was done through Whatmann filter paper#41. The filtrate was appropriately diluted with distilled water to measure the absorbance at 310 nm against reagent blanks.

Proposed method of analysis

20 tablets of Formulation I was accurately weighed and finely powdered. Amount of powder equivalent to 50 mg of drug was transferred into 100 ml volumetric flask with 20 ml of aqueous solution of 30% Niacinamide and sonicated for 20 minutes. The flask was filled to mark with distilled water and the resulting

solution was filtered. Four ml of the above filtrate was diluted to 100 ml with distilled water. The absorbance was noted at 310 nm against the reagent blank. The drug was calculated using the calibration curve. Same procedure was repeated for the tablet formulation II. The result of analysis is reported in Table 2.

Recovery studies

Table 2: Analysis data of Ondansetron HCl tablet formulations with statistical evaluation (n=3)

Drug	Formulation	Label claim mg/tab	% Labeled claim estimated (mean \pm SD)	Percent coefficient of variation	Standard Error
Ondansetron hydrochloride	I	4	101.30 \pm 0.360	0.355	0.207
Ondansetron hydrochloride	II	4	101.06 \pm 0.418	0.412	0.241

Table 3: Results of recovery studies with statistical evaluation. n=3

Tablet Formulation	Drug in pre-analyzed tablet powder (mg)	Amount of standard drug added(mg)	%Recovery estimate (mean \pm SD)	Percent coefficient of variation	Standard error
I	50	40	100.79 \pm 1.257	1.247	0.725
I	50	50	100.02 \pm 0.993	0.992	0.573
I	50	60	100.30 \pm 0.894	0.891	0.516
II	50	40	100.53 \pm 0.874	0.870	0.504
II	50	50	100.01 \pm 0.985	0.984	0.568
II	50	60	100.14 \pm 1.058	1.056	0.610

Table 4: Developed UV method specification

Instrument and specification	UV-Spectrophotometer Shimadzu 1800
Scanning Range	200 nm to 400 nm
Solvent Used	Hydrotropic Solvent
Strength of Solvent	30%
Composition of Solvent	Niacinamide Solution
Wavelength Maxima of Ondansetron hydrochloride	310 nm

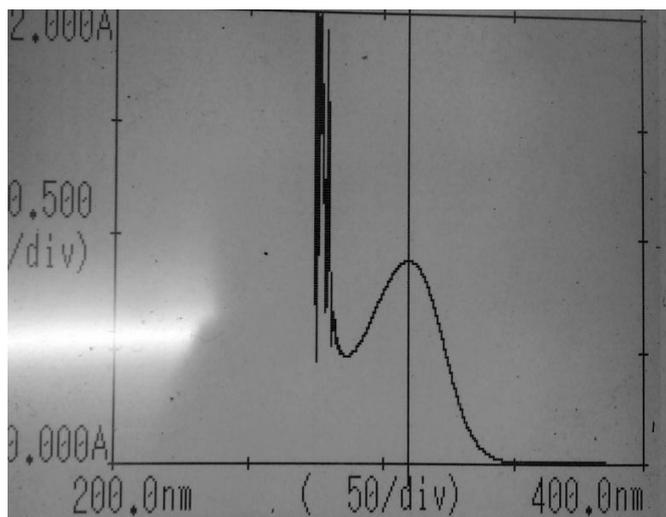


Fig. 2: UV-Spectrum of Ondansetron hydrochloride

RESULTS AND DISCUSSION

The developed UV-spectrophotometric method was validated as per ICH guidelines in terms of linearity, and range, specificity, precision, sensitivity and accuracy.

In order to determine linearity range of developed method a series of solutions were prepared using Ondansetron hydrochloride stock solution at concentration range of 10-50 μ g/ml. The absorbance of the resultant solutions was measured at 310 nm against reagent blank. The calibration curves were constructed

To perform the recovery studies, standard Ondansetron hydrochloride drug was added (40 mg, 50 mg and 60 mg separately) to the pre-analyzed tablet powder equivalent to 50 mg of Ondansetron hydrochloride and the drug content was determined by the proposed method. Results of analysis were reported in Table 3.

by plotting concentration on X axis and absorbance on Y axis. R² value not less than 0.999 was regarded as acceptance criteria (Figure 1).

Specificity was performed to exclude the possibilities of interference of solvent in the region of maximum absorbance peaks of Ondansetron hydrochloride. The specificity of the method was tested under the normal conditions and results of the tests proved that the components other than Ondansetron hydrochloride did not produce the deductible peaks at the maximum absorbance peaks of the drug.

Accuracy of the developed method was determined by recovery studies at three different levels. The pre analyzed samples were spiked with 80, 100 and 120% of mixed standard solution. The mixtures were analyzed and the recoveries were determined. The recovery study was carried out in triplicate. The mean % recovery of the Ondansetron hydrochloride at each level should not be less than 98% and not more than 102% was considered as the acceptance criteria.

Precision was studied to find out intra- day and inter-day variations in the test method of Ondansetron hydrochloride, Intra- day assay precision was found by analysis of standard drug thrice on the same day in different intervals of time. Inter-day assay precision was carried out on three different days and percentage relative standard deviation (%RSD) was calculated. The %RSD should not be more than 2.0%.

Sensitivity of proposed method was estimated in terms of limit of Detection (LOD) and Limit of quantification (LOQ). The LOD and LOQ of Ondansetron hydrochloride by proposed methods were determined using calibration standards. LOD and LOQ were calculated as 3.3s/S and 10s/S respectively. Where S is the slope of calibration curve and s is standard deviation of response.

The solubility of Ondansetron hydrochloride in distilled water was found to be 0.02% at room temperature. The solubility of Ondansetron hydrochloride in aqueous solution of 30% niacinamide was 1.0%. It is evident from Table 2 that the percent drug estimated in tablet formulation of formulation-I and of formulation-II were 101.30 ± 0.360 and 101.06 ± 0.418 respectively. These values are very close to 100, indicating the precision of the proposed analytical method. Further Table 3 shows that the range of percent recoveries varied from 100.01 ± 0.985 to 100.79 ± 1.257 which are again very close to 100, indicating the accuracy of the proposed method. Proposed analytical method is further supported significantly by small values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error (Table 3). The limit of detection was found to be $1.7 \mu\text{g/ml}$ and the limit of quantification was found to be $5.1 \mu\text{g/ml}$.

A rapid, simple, and non toxic UV spectrophotometric method has been developed for the determination and quantification of Ondansetron hydrochloride in the tablet dosage form. The present method also validated as per ICH guidelines for linearity, precision, accuracy. The results of all these parameter show that the present UV spectrophotometric method found to be precise, linear, rapid, and accurate and can be used for routine quality control analysis of Ondansetron hydrochloride in tablet dosage formulation in any laboratory.

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