International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol. 3, No.1, pp 253-255, Jan-Mar 2011

Spectrophotometric Determination and Application of Hydrotropic Solubilization in the Quantitative Analysis of Ranitidine Hydrochloride in Pharmaceutical Dosage Form

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Abstract: Quantitative estimation of poorly water-soluble drugs involves use of organic solvents. British pharmacopoeial method of analysis for Ranitidine hydrochloride tablet involves the use of a toxic and volatile solvent absolute ethanol. In the present investigation, hydrotropic solubilization is employed to enhance the aqueous solubilities of poorly water-soluble drugs Ranitidine hydrochloride in one-component tablet formulation for simultaneous spectrophotometric determination. All methods utilize 10.0 M-urea solution as, hydrotropic solubilizing agent. In the urea solution, Ranitidine hydrochloride show maximum absorbance at a wavelength of about 299 nm. The hydrotropic agent and additives used in the manufacture of tablets did not interfere in the analysis. The results of analysis have been validated statistically and by recovery studies. The proposed method utilizes solution of a non-toxic, non-volatile material, urea which is a hydrotropic agent. The objective of the present investigation is to explore the application of hydrotropy in spectrophotometric analysis of poorly water-soluble drugs to replace organic solvents which may be costlier, toxic and pollutant.

Key words: Spectrophotometric ,Hydrotropic Solubilization ,Quantitative Analysis ,Ranitidine Hydrochloride .

Introduction

Ranitidine hydrochloride is an H2 blocker which decreases the amount of acid produced in the stomach [1]. For a hygroscopic drug ranitidine, which absorbs moisture from the environment, its physical and chemical instability in the presence of moisture has a major impact on the choice of formulation excipients, the selection of processing method, and the design of the product package [2, 3]. Investigators have described moisture uptake rate of various commercial brands of ranitidine in the rate and extent of moisture absorption [4]. Ranitidine hydrochloride is extensively used as anti-ulcerant, gastroesophageal reflux disease and conditions where the stomach produces too much acid, such as Zollinger-Ellison syndrome. Over the counter ranitidine is used to prevent and treat symptoms of heartburn associated with acid indigestion and sour stomach. Hydrotropic solubilization is one of the methods to enhance the aqueous solubility of poorly water-soluble drugs. The term hydrotropy has been used to designate the increase in solubility in water of various substances due to the presence of large amounts of additives. Concentrated aqueous solutions of a large number of hydrotropic agents have been employed to enhance the aqueous solubility of many poorly water-soluble drugs[5-10].Hence the objective of the work is to develop new spectrophotometric methods for its estimation in bulk and pharmaceutical formulations with good accuracy, simplicity, precision and economy. The term hydrotropy has been used to designate the increase in solubility of various substances in water, due to the presence of large

amounts of additives. A large number of poorly water-soluble drugs have been solubilized using various hydrotropic solutions Sodium benzoate, Niacinamide, Sodium salicylate, Sodium acetate, Sodium citrate, and Urea have been employed to enhance the aqueous solubility of many poorly water-soluble drug. The aim of the present work was to develop a simple, rapid, precise, reproducible and economical method for the simultaneous estimation of the binary drug formulation using simultaneous equation method, absorbance ratio method, dual wavelength method and calibration method.

Experimental

Material and Methods:

UV/Visible spectrophotometer (Shimadzu Model 1601) was employed with spectral bandwidth of 1 nm and wavelength accuracy of 0.3 nm (with automatic wavelength correction with a pair of 1 cm matched quartz cells). Tablets of 300 mg strength were procured from local pharmacy of commercial brands i.e. Histac Ranbaxy Pharmaceutical Industries India. Absolute Ethanol was of HPLC grade and purchased from Spectrochem, Mumbai and other buffer salts were of analytical grade.

Preliminary solubility studies of drugs:

Solubility of Ranitidine hydrochloride were determined at 25±1°c. An excess amount of drug was added to screw capped 30 ml glass vials containing different aqueous systems viz. distilled water, buffer of pH 8, buffer of pH 8.0, 4.5 M sodium citrate solution, 1.5M sodium acetate and 10.0 M urea solution. The vials were shaken mechanically for 18 hr at 25±1° in a mechanical shaker. These solutions were allowed to equilibrate for the next 35 hr, and then centrifuged for 35 min at 2200 rpm. The supernatant of each vial was filtered through Whatmann filter paper No. 41. The filtrates were diluted suitably, and analyzed spectrophotometrically against corresponding solvent blank. From the preliminary solubility studies of drugs the hydrotropic agent selected was Urea.

Calibration curve –

In a 100 ml volumetric flask, about equivalent to 300 mg Ranitidine hydrochloride (accurately weighed) was transferred. To this flask 10 ml of 10 M urea solution was added and drug was dissolved in it. Distilled water was used to make up the volume up to the mark to give a stock solution (2 mg/ml). This stock solution was diluted suitably with distilled water to produce various standard solutions containing 50, 100, 150, 200, 250 and 300 mcg/ml of drug. Absorbances of these solutions were observed at 299 nm against corresponding reagent blank.

British pharmacopoeia method -

Twenty tablets (formulation I) were weighed and powdered finely. A portion of this powder containing 50 mg Ranitidine hydrochloride was accurately weighed and transferred to a 250 ml volumetric flask. Absolute ethanol (100 ml) was added and the suspension was heated to 75^{o}C and shaken for 15 min. After cooling, it was diluted to 300 ml with Absolute ethanol and filtered through a sintered glass funnel. The filtrate was diluted suitably with methanol to produce a solution containing 0.01% w/v of Ranitidine hydrochloride. The absorbance of this solution was noted at 299 nm. The drug content was calculated using 64.32 as the value of A [1%, 1 cm].

Analysis of Ranitidine hydrochloride in tablets by the proposed method –

Tablet powder equivalent to 300 mg Ranitidine hydrochloride was transferred to a 100 ml volumetric flask containing 10 ml of 10 M urea solution. Flask was shaken for about 35 minutes to solubilize the drug present in tablet powder and volume was made up to the mark with distilled water. After filtration through sintered glass funnel the filtrate was appropriately diluted with distilled water and absorbance was noted at 299 nm against reagent blank. Using the calibration curve, the drug content was computed. Recovery studies were performed by spiking the preanalyzed tablet powder with Ranitidine hydrochloride bulk drug sample at three levels and determining the drug content by the proposed method. Each type of analysis was performed six times.

Table I: Analysis Data of Tablet Formulations with Statistical Evaluation

Tablet Formulation	Label Claim (mg/Tablet)	%Label Claim Estimated* (Mean±S.D.)	% Coeff. of Variation	Standard Error
I	300	100.12±0.56	0.65	0.21

*** Mean (n = 6)**

Table II: Results of Recovery Studies of Tablet Formulations with Statistical Evaluation

Tablet Formulation	Drug in Preanalyzed Tablet Powder (mg)	Amount of Drug Added (Spiked) (mg)	%Recovery Estimated* (Mean±S.D.)	%Coeff. of Variation	Standard Error
I	300	50	99.11±1.32	0.42	0.14
	300	100	97.27±0.54	0.58	0.21
	300	200	101.11±1.03	1.14	0.65

*** Mean (n = 6)**

Result and Discussion-

For the analysis of tablets, twenty tablets of Ranitidine hydrochloride were weighed and crushed finely. Powder equivalent to 150 mg Ranitidine hydrochloride was accurately weighed and transferred to a conical flask. After adding 100 ml of 10 M Urea solution, the flask was shaken for 25 min for solubilization of the drug. 10.0M Urea was used to titrate the drug using phenolphthalein solution as indicator. Blank determination was carried out by titrating 25 ml of sodium benzoate solution (2.0 M) with sodium hydroxide solution (.01 M) using phenolphthalein solution as indicator. Necessary correction was made to calculate the drug content (Table I). For recovery studies, preanalyzed tablet powder was spiked with Ranitidine hydrochloride bulk drug sample at three levels and analyzed by same proposed method. Percent recoveries were estimated by the difference and listed in Table II. Solubility studies showed that the enhancement in solubility of Ranitidine hydrochloride in 10.0 M Urea solution was more than 1500 fold as compared to its aqueous solubility. Since the pH of 10.0 M Urea solution was 8.2, therefore the solubility of drug was determined in buffer of pH 8.2 to check the effect of alkalinity on the solubility of drug. Enhancement in solubility of drug in buffer of pH 8.2 was more than 500 fold only. Therefore tremendous enhancement in solubility of drug in 10.0 M Urea solution is attributed due to hydrotropic solubilization phenomenon. Hence, it was thought worthwhile to extract out the drug from its fine powder to carryout titrimetric analysis. As evident from Table I, the percent label claims of Ranitidine hydrochloride estimated (100.21±0.11 and 99.94±0.06) are very close to 455 indicating the accuracy of the proposed method. Validation of the proposed method is further confirmed by satisfactory low values of standard deviation, percent coefficient of variation and standard error. Accuracy, reproducibility and precision of the proposed methods were further confirmed by percent recovery values which were close to 250 (ranged in between 94.21±0.12 and 105.18±0.10) with satisfactory low values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error (Table II). There was no involvement of organic solvent for dissolution of drug. Thus, it may be concluded that the proposed method is new, simple, cost-effective, accurate, environmentally friendly and precise and can be successfully employed in the routine analysis of Ranitidine hydrochloride tablets.

Conclusion

It may be concluded that the proposed method of analysis is new, simple, cost-effective, environment-friendly, safe, accurate, and reproducible. Decided advantage is that the organic solvent is precluded, but not at the expense of accuracy. Definitely, there is further scope of 10 M urea as solubilizing agent for the UV analysis of other poorly water-soluble drugs simultaneous estimation of Ranitidine hydrochloride in component tablet formulation.

Acknowledgement

Author are grateful to Head, School of Pharmacy, DAVV, Indore for providing necessary facilities.

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