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Extractive Spectrophotometric determination of Ranitidine by ion pair complex formation with Indigocarmine

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Abstract : This study describes a simple, sensitive, selective and reproducible extraction-spectrophotometric method for the determination of trace amounts of Ranitidine. In this work, determination of trace amounts of Ranitidine was investigated by the formation of ion-pair whit anionic dye (Indigocarmine) followed by extraction with dichloroethane as an organic solvent, and its absorbanc is measured at 500 nm in room temperature.The effect of different variables such as pH, Indigocarmine concentration and volume of extracting solvent is investigated and an optimum condition for quantitive extraction of Ranitidine is obtained. Calibration graph is linear in the concentration range of between (5-125) mg L^{-1}. The relative standard deviation (RSD) of 7 mg L^{-1} of Ranitidine is 1.85 % and detection limit (LOD) of 7 mg L^{-1} has obtained. Finally, the method is used for quantity determination of Ranitidine in actual sample examined by mean of extraction-spectrophometric and good result is obtained.
Key words: Ranitidine, Indigocarmine, Ion-pair, spectrophotometric method.

1. Introduction

Ranitidine, sold under the trade name Zantac among others, is a medication that decreases stomach acid production [1]. It is commonly used in treatment of peptic ulcer disease, gastroesophageal reflux disease, and Zollinger–Ellison syndrome [1]. There is also tentative evidence of benefit for hives [2]. It can be taken by mouth, by injection into a muscle, or into a vein [1].Common side effects include headaches and pain or burning if given by injection. Serious side effects may include liver problems, a slow heart rate, pneumonia, and the potential of masking stomach cancer. It is also linked to an increased risk of Clostridium difficile colitis [3]. It is generally safe in pregnancy. Ranitidine is an H2 histamine receptor antagonist that works by blocking histamine and thus decreasing the amount of acid released by cells of the stomach [1]. Ranitidine was discovered in 1976 at Glaxo Pharmaceuticals, now a part of GlaxoSmithKline [4, 5]. It is on the World Health Organization's List of Essential Medicines, the most important medications needed in a basic health system [6]. It is available as a generic medication. The wholesale price is about 0.01 to 0.05 USD per pill [7]. In the United States it is about 0.05 USD per dose[1].Several methods have been reported in the literature for the analysis of cefixime trihydrate such as HPLC [8], spectrofluorometry [9],capillary electrophoresis [10], voltammetry [11], flow injection technique [12], mass spectroscopy [13], and so on. Spectrophotometric methods are generally based on the formation of complex between drug and reagent which can be estimated using visible spectrophotometer. The complex between drug and reagent is either an ion-pair type or charge-transfer type. In ion-pair complex formation, ions of opposite electric charge held together in solution by Coulomb attraction to form a distinct chemical entity [13-26]. It behaves as a single unit. Ion-pair formation, initially investigated by

the physical chemists, has been found extremely interesting for the chemical analysis, including pharmaceutical analysis. However, most of these methods suffer from narrow dynamic absorbance–concentration linearity; some of them involve complicated sample treatment and extraction procedures [27-32].The proposed method is based on formation of ion-pair complex of Ranitidine with indigo carmine. Indigo carmine has been used for the first time with significantly low detection limit, high sensitivity, and wider dynamic range. An important feature of this method is that no extraction is required and it is feasible at room temperature. This method could be applied to the analysis of pharmaceutical formulations.

2. Experimental

2.1. Materials and reagents

All chemicals and reagents used were of analytical grade. Ranitidine was obtained from different laboratories. Standard stock solutions of the drug (1000 mgL^{-1}) were prepared in deionized water. Further, their working solutions in the calibration concentration range were prepared by suitable dilution of the stock solution with water. Indigocarmine and dichloroethane were made from Merck. All the chemicals were used as received without further purification.

2.2. Instruments

A Shimadzu 2100 UV–visible spectrophotometer (Shimadzu, Japan), A Jenway model 3510 pH meter was used for pH measurements. An electronic analytical balance (220LA, ADAM) was used for weighting the solid materials.

2.3. Extraction procedure

0.1mL of Ranitidine 1000 mg L^{-1} was transferred into 10 mL volumetric flasks. To it, 0.1 mL of 10% indigocarmine was added and volume was made up to 10 mL with dichloroethane solvent. Adjusting the pH to 4 with 0.1 mol L^{-1} HCl and 0.1 mol L^{-1} NaOH. After 10 minutes of complex formation, the absorbance of solution was measured at 500 nm against the appropriate reagent blank in a cell of path length 10 mm.

3.1. Optimization of extraction conditions

3.1. Effect of pH

The effect of pH on the formation of ion-pairs was examined by varying the pH from 2.0 to 8.0 using 0.1 M HCl. The results obtained above pH 4.0 were not reproducible. The maximum absorbance of the complexes was found at pH 4.0. The results are shown in Figure 1.

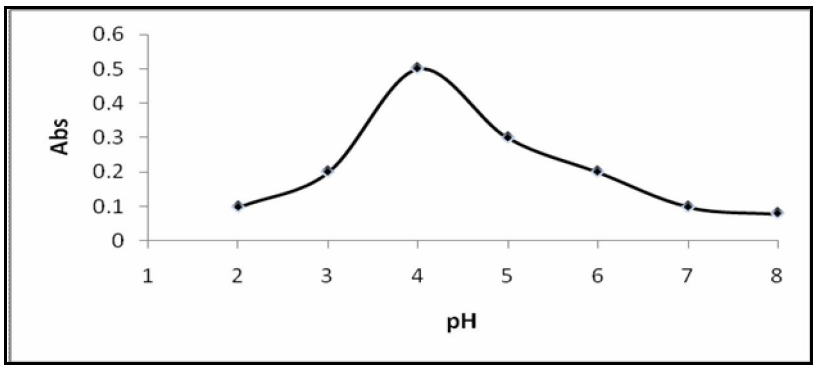

Fig.1. Effect of pH on adsorption of Ranitidine by purposed method

3.2. Effect of concentration and volume indigocarmine

The effect of indigocarmine volume with concentration 10% on the color intensity of the complexes was tested by varying the volumes from 0.08 to 0.13 mL at the selected wavelength. Best results were obtained

with 0.1 mL of 0.10% indigocarmine for all the complexes. However, an excess dye (>0.10 mL) did not affect the color intensity of the complex as well the absorbance (Fig.2).

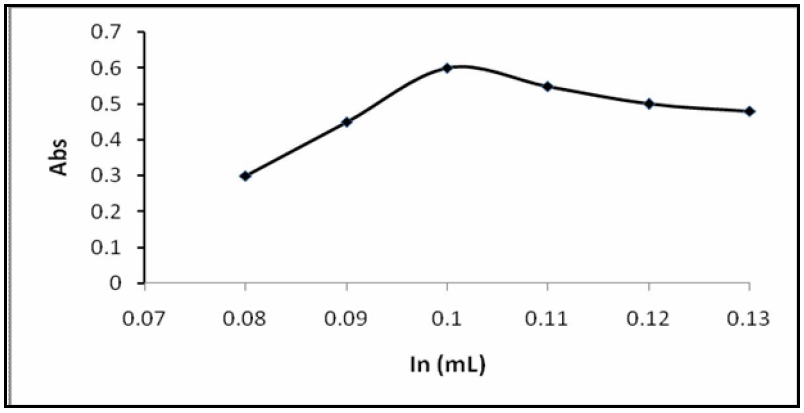

Fig.2. Effect of volume indigocarmine 10% of ion-pair complex of Ranitidine

3.3. Selection of extraction solvent

To study the effect of extracting solvent on ion-pair complexes, the following solvents were investigated ethyl acetate, chloroform, carbon tetrachloride, and dichloroethane. It was found that dichloroethane offered enhanced efficiency for color intensity as well provided selective extraction in comparison to the other solvents and hence it was selected in the present work. Moreover, to achieve quantitative recovery for all the complexes one extraction was adequate. Volumes from 2 to 5 mL of solvent selected for extraction and the best results were obtained with 4 mL of solvent. The result is shown in Figure 3.

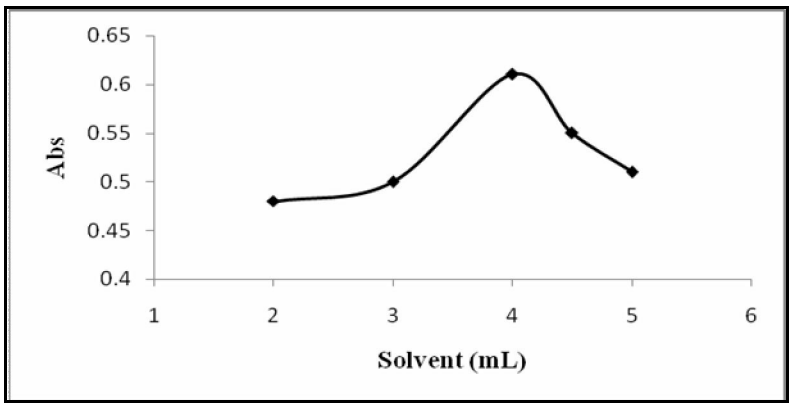

Fig.3. Effect of solvent volume on ion-pair complex of Ranitidine

3.4. Effect of shaking mode and time

The affect of different approaches for extracting the ion-pair complexes was assessed by employing a magnetic stirrer, a vortex mixture, and a separating funnel. Although quantitative results were obtained in all modes of extraction, slightly higher absorbance values were found during vortex mixing. Further, shaking times ranging from 1.0 to 5.0 min was studied and the optimum time for maximum extraction was 2.0 min for all ion-pair complexes.

3.5. Effect of temperature and stability of the ion-pair complexes

Temperature effect on ion-pair complexes was studied at 25, 30, and 35°C. It was found that the complexes were stable up to 30°C with negligible change in the absorbance values. Due to the volatile nature of

the solvent above this temperature, there was a slight increase in the absorbance of the complexes. Nevertheless, best results were found at 25°C and all the complexes were stable for a minimum period of 24 h.

3.6. Analytical characteristics of the method

The linearity of the methods was established by preparing calibration standards at the different concentrations for Ranitidine. A linear relationship was found between the measured absorbance and the concentration range studied for drug, with correlation coefficients (r^2) ≥ 0.9980. The linear range for analyt was 10-125 mg L^{-1}. The LOD (limit of detection) was calculated using the expression, 3s/S, where "s" is the standard deviation of the blank and "S" is the slope of the calibration line. LOD is defined as the lowest concentration of an analyte that can be reliably detected but not necessarily quantified, under the optimized experimental conditions. LOD of the method was found to be 7mg L^{-1}.

3.7. Applications

The proposed method has been successfully applied to the determination of Ranitidine in pharmaceutical formulation such as tablets. Calibration curve method and standard addition method were adopted for quantitative analysis (table 1).

Table 1. Application of presented method to tablet samples.

Ranitidine tablet	Ranitidine		% Recovery
	Added (mg L^{-1})	Found (mg L^{-1})	
Daru Pakhsh Company	0	100	-
	5	106	120
Sobhan Daru Company	0	120	-
	5	125	100
Aboreyhan Company	0	85	-
	5	89	80

4. Conclusion

In the proposed method, an ion-pair complex of selected drug with indigocarmine was studied under the optimized extraction conditions. The developed and validated methods are selective, rapid, and economical and the results obtained showed acceptable recovery of the drug. Additionally, the drug was successfully estimated in their pure forms as well as in their respective formulations without any interference from the commonly used additives and excipients.

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