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NOVEL METHOD FOR SPECTROPHOTOMETRIC ANALYSIS OF SIMULTANEOUS ESTIMATION OF BISOPROLOL FUMARATE TABLET FORMULATIONS USING HYDROTROPY SOLUBILIZATION AGENTS

SMITA SHARMA*, MUKESH CHANDRA SHARMA[a]
Department of Chemistry Chodhary Dilip Singh Kanya Mahavidyalya Bhind (M.P) – 477001, India
[a]*School of Pharmacy, Devi Ahilya Vishwavidyalaya, Indore (M.P) 452001, India*

Quantitative estimation of poorly water-soluble drugs involves use of organic solvents. Major drawbacks of organic solvents include high cost, volatility and toxicity. In the present investigation, hydrotropic solubilization is employed to enhance the aqueous solubilities of poorly water-soluble drugs Bisoprolol Fumarate in one-component tablet formulation for simultaneous spectrophotometric determination. Four simple, accurate and economical procedures employed are simultaneous equation method, absorbance ratio method, calibration method and dual wavelength method. All methods utilize 5.0 M-urea and Sodium citrate solution as, hydrotropic solubilizing agent. In the urea solution, Bisoprolol Fumarate show maximum absorbance at a wavelength of about 271nm respectively and isobestic point is observed at 282 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.

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1. Introduction

Bisoprolol Fumarate is a synthetic ß$_1$-selective (cardioselective) adrenergic receptor blocking agent. Chemically Bisoprolol Fumarate is (±)-1-[4-[[2-(1- Methylethoxy) ethoxy] methyl] phenoxyl-3-[(1-methylethyl) amino]-2-propanol (*E*)-2-utenedloate (2:1) (salt)[1]. It is clinically useful in the treatment of hypertension. It is not official in any of the pharmacopoeias. It is listed in The Merck Index1 and Martindale, The Complete Drug Reference2. Literature survey reveals that only few RP-HPLC methods[3-9] are reported for the determination of Bisoprolol Fumarate in biological fluids using fluorescence detector. 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[10].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.

*Corresponding author: drsmita.sharma@rediffmail.com

2. 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 5 mg strength were procured from local pharmacy of two commercial brands i.e. Concor (MERCK) and Corbis (UNISEARCH). Methanol was of HPLC grade and purchased from Spectrochem, Mumbai and other buffer salts were of analytical grade.

Preliminary solubility studies of drugs:

Solubility of Bisoprolol Fumarate 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 5.0 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 1620 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.

3. Results and discussion

Results of solubility studies indicated that enhancement in aqueous solubilities of Bisoprolol Fumarate in 5.0M urea solution were more than 21 and 25 folds, respectively as compared to their solubilities in distilled water. Therefore, this solution was employed to extract Bisoprolol Fumarate from the fine powder of tablet formulation. The hydrotropic agent (urea and sodium citrate) and excipients used in the manufacture of tablet did not interfere in the analysis because urea does not interfere that drugs which has λmax above 224 nm. Drug content in the extract of 5.0 M urea solution was same within 27 hr and also there was no precipitation of drug. This indicates that the extract can be analyzed within 27hr at least with sufficient accuracy. The first method simultaneous equation was carried out using 281 nm λ max and % drug found was 99.96 ± 0.22 For Bisoprolol Fumarate respectively. The second method Dual wavelength was carried out using 268 and 297.5nm λmax and % drug found was 99.98± 0.14 for Bisoprolol Fumarate respectively.The validation parameters were studied at all wavelengths for the four of methods. Accuracy was determined by calculating the % recovery for the first method it is found 99.96 ± 0.22, second method it is found 99.98± 0.14 for Bisoprolol Fumarate respectively. Precision was calculated as repeatability (standard deviation and % relative standard deviation. Intraday was determined by calculating the % RSD for the first method it is found 0.12-0.15 for the second method it is found 0.65-0.68 for Bisoprolol Fumarate. Interday was determined by calculating the %RSD for the first method it is found 0.29-0.32 for second method it is found 0.45-0.49 for Bisoprolol Fumarate. The optical characteristics of developed methods which are Sandell's sensitivity and molar extinction coefficient was calculated for the first method it is found 0.03741 and 3.392×10^3 second method it is found 0.02940 and 2.3219×10^4 for Bisoprolol Fumarate.

Analysis of Bisoprolol Fumarate tablet by the proposed method

Tablet powder equivalent to 100 mg drug was shaken with 20 ml of 5.0 M urea by continuous shaking for about 15 min and volume made up to 100 ml with distilled water. The resulting solution was filtered through the Whatman filter paper no. 41, and appropriate aliquots

were prepared by diluting with distilled water. Absorbances of different prepared aliquots were observed at 272 nm against reagent blanks.

4. Conclusions

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 6 M urea as solubilizing agent for the UV analysis of other poorly water-soluble drugs simultaneous estimation of Bisoprolol Fumarate in component tablet formulation.

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