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SIMULTANEOUS SPECTROPHOTOMETRIC ESTIMATION OF ETOPOSIDETABLET FORMULATIONS USING HYDROTROPY SOLUBILIZATION AGENTS

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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 Etoposide 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 8.0M-urea solution as, hydrotropic solubilizing agent. In the urea solution, Etoposide show maximum absorbance at a wavelength of about 320nm respectively and isobestic point is observed at 294nm. 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

Etoposide is a semi synthetic derivative of epipodophyllotoxin and believed to act by the inhibition of topoisomerase enzyme and/or induction of direct DNA breaks [1, 2]. It is preferably used for the treatment of patients with small cell lung cancer, testicular tumors, Kaposi's sarcoma and lymphomas. Several HPLC methods were reported for etoposide with UV [3, 4], fluorescence [5] and electrochemical [6, 7] detectors with complicated extraction procedures. 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[8-11]. 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.

2. Experimental

2.1 Materials 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). Formulations of etoposide used for the study were soft

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gelatin capsules (Etosid, Cipla LTD,India) containing 50 mg etoposide, U.S.P. Etosid capsules contain excipients like ferric oxide red and titanium dioxide. Methanol was of HPLC grade and purchased from Spectrochem, Mumbai and other buffer salts were of analytical grade.

2.2 Preliminary solubility studies of drugs:

Solubility of Etoposide were determined at 28±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 7.8, 0.5 M sodium benzoate solution, 2.0M sodium acetate and 4.0M urea solution. The vials were shaken mechanically for 12 h at 28±1°, in a mechanical shaker. These solutions were allowed to equilibrate for the next 24 hs, and then centrifuged for 5 min at 1200 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 Etoposide in 4.0M urea solution were more than 56 and 59 folds, respectively as compared to their solubilities in distilled water. Therefore, this solution was employed to extract Etoposide from the fine powder of tablet formulation. The hydrotropic agent (urea) 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 256nm. Drug content in the extract of4.0 M urea solution was same within 21 hr and also there was no precipitation of drug. This indicates that the extract can be analyzed within 21hr at least with sufficient accuracy. The first method simultaneous equation was carried out using 322 nm λmax and % drug found was 100.30 ± 0.12 For Etoposide respectively. The second method Q- analysis was carried out using 322nm λmax and %drug found was 101.12± 0.43 and for Etoposide respectively and is absorptive point was 311nm. The third method Dual wavelength was carried out using 320 and 300nm λmax and % drug found was 99.76± 0.21 for Etoposide respectively. The fourth method Calibration method was carried out using 300 nm and 241nm λmax and % drug found was 101.5± 0.31 for Etoposide 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 99.6±0.71, second method it is found 100.4±0.58 for Etoposide respectively. For the third method it is found 99.99±0.21for Etoposide respectively. For the fourth method it is found 102.1±0.81 for Etoposide 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 0.21-0.32 for the second method it is found 0.43-0.12 for the third method it is found 0.32-0.51 fourth method it is found 0.33-0.59 for Etoposide. Interday was determined by calculating the %RSD for the first method it is found 0.34-0.51 for second method it is found 0.25-0.32for the third method it is found 0.27-0.67 for fourth method it is found 0.237-0.57 for Etoposide. The optical characteristics of developed methods which are Sandell's sensitivity and molar extinction coefficient was calculated for the first method it is found 0.022728 and 1.839×10^9 ,second method it is found 0.032190 and 1.4315×10^9 ,third method it is found 0.06372 and 2.4321×10^9, fourth method it is found 0.037281 and 3.7831× 109 for Etoposide.

4. Conclusion

It is thus concluded, that the developed methods are new, simple, cost effective, accurate, safe, free from pollution and precise, and can be successfully employed in the routine simultaneous estimation of Etoposide in component tablet formulation.

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