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Research Article

NOVEL SPECTROPHOTOMETRIC QUANTITATIVE ESTIMATION OF HYDROCHLOROTHIAZIDE IN BULK DRUG AND THEIR DOSAGE FORMS BY USING HYDROTROPIC AGENT

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ABSTRACT

A novel, safe, accurate and sensitive spectrophotometric method was developed using 2 M sodium acetate and 8 M Urea solution as hydrotropic solubilizing agent for the quantitative determination of poorly water-soluble hydrochlorothiazide in tablet dosage form. There were more than 55 and 70 fold enhancements in the solubility of hydrochlorothiazide increases in 2 M sodium acetate and 8 M Urea solution as compared to solubilities in distilled water. Hydrochlorothiazide shows maximum absorbance at 272 nm. Sodium acetate and urea did not show any absorbance above 240 nm, and thus no interference in the estimation was seen. Hydrochlorothiazide is obeyed Beer,s law in the concentration range of 10 t0 50µg/ml (r^2= 0.999) in sodium acetate and 5 to 25 µg/ml (r^2= 0.999) in urea with mean recovery 98.74 and 99.99% in sodium acetate and urea respectively. Proposed method is new, simple, economic, safe, rapid, accurate and reproducible. The developed methods were validated according to ICH guidelines and values of accuracy, precision and other statistical analysis were found to be in good accordance with the prescribed values

Keywords: Hydrochlorothiazide, hydrotropic, sodium acetate, urea, spectrophotometry

INTRODUCTION

Hydrochlorothiazide[1,2], chemically 6-chloro-3, 4-dihydro-2*H*-1, 2, 4-benzothiadi- azine-7-sulphonamide-1, 1-dioxide, is a diuretic and antihypertensive drug, which inhibits the reabsorption of sodium and calcium at the beginning of distal convoluted tubules. HCT is official in IP[3], BP[4,] and USP[5]. Various techniques have been employed to enhance the aqueous solubility. The term "hydrotropy" has been used to designate the increase in aqueous solubility of various poorly water-soluble compounds due to the presence of a large amount of additives. 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. Maheshwari has analyzed various poorly water-soluble drugs using hydrotropic solubilization phenomenon[6-19]. Various organic solvents such as methanol, chloroform and dimethyl formamide, acetonitrile, have been employed for solubilization of poorly water-soluble drugs to carry out spectrophotometric analysis. Drawbacks of organic solvents include their higher cost, toxicity and pollution. Hydrotropic solution may be a proper choice to preclude the use of organic solvents. Several HPLC, HPTLC and spectroscopic methods have been reported for the estimation of HCT by in bulk drug and in combination with other drugs[20-31]. In the preliminary solubility studies there were more than 55 and 70 fold enhancements in the solubility of HCT in 2 M sodium acetate and 8 M urea solution respectively. Therefore, it was thought worthwhile to employ this hydrotropic solution to extract out the drug from fine powder of tablets to carry out spectrophotometric estimation.

MATERIALS AND METHODS

Apparatus

The proposed work was carried out on a shimadzu uv-visible spectrophotometer (model uv-1700 series), which possesses a double beam double detector configuration with matched quarts cells. Reference standard of HCT was a generous gift from matrix laboratories, Mumbai, sodium acetate and urea obtained from Merck Chemical Division, Mumbai. Commercial tablets of HCT, Aquazide (Sun Pharma) and Klorzide (Zydus Ltd) were procured from the local drug market.

Preliminary Solubility Studies

Solubility of HCT was 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, 8 M urea and 2 M sodium acetate solution. There was more than 55 and 70 fold solubility enhanced in sodium acetate as compare with distilled water. This enhancement of solubility is due to the hydrotropic solubilization phenomenon.

Preparation of calibration curve

Accurately weighed 100 mg of the HCT drug sample were transferred in to 100 ml volumetric flask containing 10 ml of 2 M sodium acetate solution and diluted up to 100 ml with distilled water. The standard solution (1000 µg/ml) was further diluted with distilled water to obtain 10, 20, 30, 40 and 50 µg /ml. likewise the dilution ranging from 5-25 were prepared in urea. Detection wavelength was selected for HCT was 272nm. Absorbance was noted against distilled water as blank. Calibration curve was plotted between concentration verses wavelength. Spectra of HCT were shown in Fig-1and Fig-2.

Analysis of tablet formulation

Two marketed formulation Aquazide (Sun Pharma) and Klorzide (Zydus Ltd) were selected for tablet analysis. Twenty tablets of each formulation were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 25 mg of HCT was transferred to two different 100 ml of volumetric flask containing 10 ml of 2 M sodium acetate and 8 m urea solution. The flask was sonicate for about 10 min to solubilize the drug and the volume was made up to mark with distilled water. The solution was filtered through Whatmann filter paper No 41. The filtrate was diluted appropriately with distilled water and was analyzed on UV spectrophotometer against distilled water as blank. Drug content of tablet formulation were calculated using calibration curve and value are reported in Table-1 and Table-2.

Recovery studies

To evaluate the recovery studies, to pre-analyzed tablet solution, a definite amount of drug was added and then its recovery was studied. These studies were performed in by adding fixed amount of pure drug solution to the final dilution while varying the concentration of tablet sample solution in the final dilution and result of recovery studies are presented in Table-3. **Precision studies**

To evaluate precision at different parameter like repeatability, intermediate precision, five dilutions in three replicates were analyzed in same day, in two different days and by two analysts for day to day and analyst to analyst variation and results were shown in Table-4.

RESULTS AND DISCUSSION

Based on the solubility and stability and spectral characteristics of the drug, 2 M sodium acetate and 8 M urea were selected as hydrotropic agent. HCT after solubilized in the selected hydrotropic agent was scanned in spectrum mode and 272nm was selected as wavelength for estimation considering the reproducibility and variability of the obtained result. The developed method was found to be linear in the range of 10-50µg/ml with correlation coefficient (r^2) of 0.999 in sodium acetate and 5-25µg/ml with correlation coefficient (r^2) of 0.999 in urea.

The mean Percent label claims of tablets of HCT in formulation-I and formulation-II estimated by the proposed method were found to be 97.62±0.15, 98.38±0.83 in sodium acetate and 98.06±0.80, 100.11±0.06 in urea respectively. These values are close to 100, indicating the accuracy of the proposed analytical method. Low values of standard deviation, percent coefficient of variation and standard error further validated the proposed method Table-1 and Table-2. The values of mean percent recoveries were also found to be 98.74 ±0.13 and 99.99±0.10% in sodium acetate and urea respectively. All these values were very close to 100. Also the values of standard deviation, percent coefficient of variation and standard error were satisfactorily low Table-3. Result of precision at different level were found be within acceptable limits (RSD ‹ 2) Table-4. Presence of hydrotropic agent do not shows any significant interference in the spectrophotometric assay thus further confirming the applicability and reproducibility of the developed method.

Table 1: Result of tablet analysis

Amount of drug claimed (mg)	Tablet analysis using sodium acetate as hydrotropic agent							
	Amount of drug found (mg)				Percentage estimated in formulation			
	Aquazide		Klorzide		Aquazide		Klorzide	
	R-I	R-II	R-I	R-II	R-I	R-II	R-I	R-II
25	24.42	24.46	23.2	24.96	97.68	97.84	92.8	99.84
25	24.59	24.09	23.99	23.74	98.36	96.36	95.96	94.96
25	23.98	24.09	23.98	23.99	95.92	96.36	95.92	95.96
	Tablet analysis using urea as hydrotropic agent							
Amount of drug claimed (mg)	**Amount of drug found (mg)**				**Percentage estimated in formulation**			
	Aquazide		**Klorzide**		**Aquazide**		**Klorzide**	
	R-I	**R-II**	**R-I**	**R-II**	**R-I**	**R-II**	**R-I**	**R-II**
25	24.12	24.06	25.2	24.96	96.48	96.24	100.8	99.84
25	23.99	24.09	24.99	24.74	95.96	96.36	99.96	98.96
25	23.98	24.09	24.98	24.99	95.92	96.36	99.92	99.96

Table 2: Statistical evaluation of analysis of tablet

Parameter	Sodium acetate		Urea	
	Aquazide	Klorzide	Aquazide	Klorzide
Mean % estimated	97.09	95.91	96.22	99.91
Standard deviation	0.84	0.43	0.12	0.43
% Coefficient of variation	0.87	0.45	0.13	0.43
*Standard error	0.34	0.176	0.05	0.18

*n=3 in 2 replicates

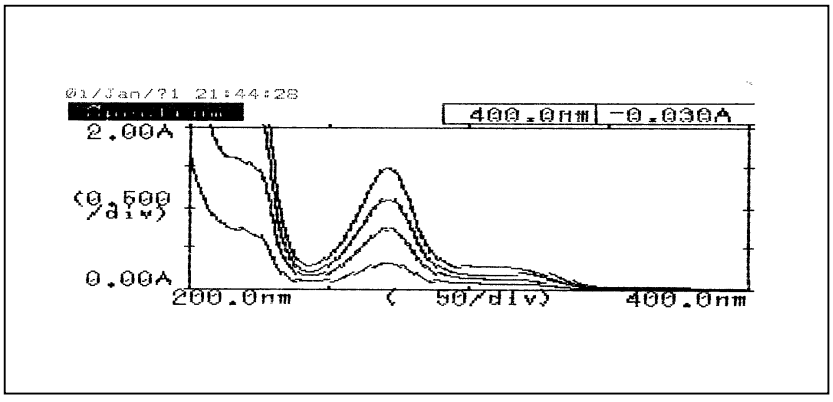

Fig. 1: Spectra of HCT in Sodium acetate as hydrotropic agent

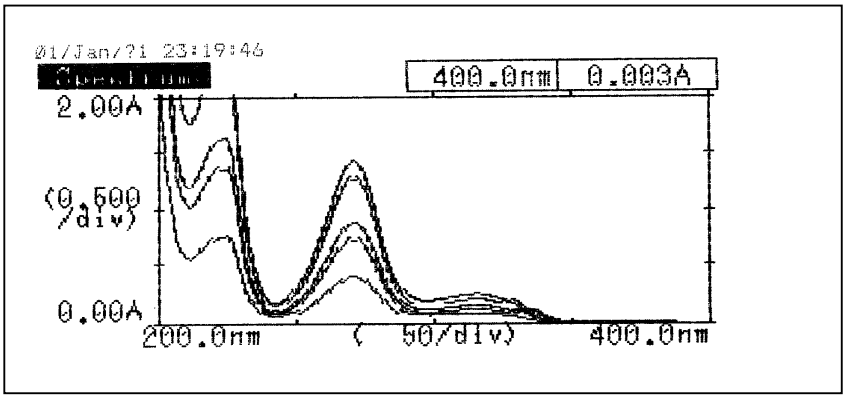

Fig. 2: Spectra of HCT in urea as hydrotropic agent

Table 3: Result of recovery studies of tablet formulation with statically evaluation

Recovery method	Theoretical conc. (µg/ml)	Amount added (µg/ml)	Percentage recovery Mean ± S.D. (n=6)	Percentage coefficient of variation	*Standard error
With sod. acetate	10	20	99.01±1.02	1.03	0.42
	20	20	99.25±0.63	0.64	0.26
	30	20	98.87±1.14	1.15	0.46
	40	20	98.26±1.72	1.75	0.70
	50	20	98.25±0.94	0.96	0.38
With urea	5	20	100.16±0.03	0.03	0.01
	10	20	99.80±0.42	0.42	0.17
	15	20	100.00±0.12	0.12	0.05
	20	20	100.00±0.16	0.16	0.06
	25	20	100.10±0.06	0.06	0.02

* Mean of thirty determinations (6 replicates at 5 concentration level)

Table 4: Result of precision of HCT

	Validation parameter	Percentage mean ± S.D. (n=6)	Percentage RSD
With sod. acetate	Repeatability	99.91±1.06	1.06
	Intermediate precision		
	Day to Day	99.85±1.08	0.64
	Analyst to Analyst	99.03±.97	0.82
With Urea	Repeatability	100.07±1.32	1.32
	Intermediate precision		
	Day to Day	99.96±1.13	1.13
	Analyst to Analyst	100.04±0.86	0.86

CONCLUSION

It was, thus, concluded that the proposed method is new, simple, cost effective, accurately, precise and safe free from pollution and can be successfully employed in the routine analysis of HCT in bulk drug and tablet dosage forms.

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