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New spectrophotometric determination of Hydrochlorothiazide in tablets using Mixed Hydrotropic Solubilization Technique

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Abstract

The present investigation illustrates the application of mixed hydrotropy. A novel, safe and sensitive method of spectrophotometric estimation in the ultraviolet region has been developed using a mixed hydrotropic solution containing eight percent each of niacinamide, sodium acetate, sodium benzoate, sodium citrate and urea (total 40% hydrotropic agents), for the quantitative determination of hydrochlorothiazide, a very slightly water soluble diuretic drug in tablet dosage form. Beer's law was obeyed in the concentration range of 20–120 µg/ml. There was more than 25-fold enhancement in aqueous solubility of hydrochlorothiazide in mixed hydrotropic solution as compared with the solubility in distilled water precluding the use of organic solvents. Hydrotropic agents and commonly used tablet excipients did not interfere in spectrophotometric estimation. Results of the analysis were validated statistically and by recovery studies. Statistical data proved accuracy, reproducibility and the precision of the proposed method.

Key words: Hydrochlorothiazide, Mixed hydrotropy, Solubility enhancement, U.V.-Visible Spectrophotometry.

Introduction

Hydrotropes are a class of chemical compounds that cause a several fold increase in the solubility for sparingly soluble solute under normal conditions. This phenomenon termed hydrotropy is considered as a unique and unprecedented solubilization technique because of the easy recovery of dissolved solute and possible re-use of hydrotropic solutions. This technique also facilitates the separation of close boiling isomeric components from their binary mixtures forming simple eutectics [1] and non-isomers in mixtures besides increasing the rate of heterogeneous reactions [2]. Neuberg (1916) identified this pioneering technique for very large solubility enhancements for a variety of sparingly soluble organic solutes. Hydrotropes in

general are water-soluble and surface-active compounds that enhance the solubility of organic solutes like acids, esters, alcohols, aldehydes, ketones, hydrocarbons, and fats [3, 4]. Hydrotropes have been widely used in detergent formulation, health care, household applications [5, 6] and also as an extraction agent for fragrances [7]. Each hydrotrope has a selective ability towards a particular component in the mixture to facilitate easy recovery of the hydrotrope solution by controlled dilution with distilled water [8]. The solubility enhancement of organic solute is due to the formation of molecular structures in the form of complexes [9, 10]. The previous experimental findings concluded that hydrotropy is a process which goes beyond conventional solubilization methods, such as miscibility, co-solvency [11] and the salting-in effect, since the solubilization affected by hydrotropy is higher and more selective compared to other solubilization methods [12].

Maheshwari *et al*. have applied the use of hydrotropy in titrimetric and spectrophotometric estimation of a large number of poorly water-soluble drugs, discouraging the use of organic solvents [13-28]. Sodium benzoate, sodium salicylate, sodium ascorbate, sodium glycinate, niacinamide, sodium citrate and urea are the most popular examples of hydrotropic agents that have been used to solubilize a large number of poorly water-soluble compounds [13-33]. Various organic solvents like methanol, chloroform, alcohol, dimethyl formamide, and benzene have been employed for the solubilization of poorly water soluble drugs for their analysis. Drawbacks of organic solvents include higher cost, toxicity, pollution, and error, in analysis due to volatility. The present study aims to apply the concept of mixed hydrotropic solution of niacinamide, sodium acetate, sodium benzoate, sodium citrate and urea as a solubilizing agent to analyze a very slightly water-soluble drug, hydrochlorothiazide in tablet, by spectrophotometric estimation. Earlier studies showed the application of mixed hydrotropy in spectrophotometric analysis of aceclofenac [34] and titrimetric analysis of ibuprofen [35]. There was more than 25-fold increase in solubility of hydrochlorothiazide (a widely used diuretic drug) in the mixed hydrotropic solution. Therefore, it was thought worthwhile to solubilize the drug with the help of mixed hydrotropy to carry out the estimation. Chemically, hydrochlorothiazide is 6-chloro-3, 4-dihydro-2 *H* -1, 2, 4- benzothiadiazine-7-sulphonamide 1, 1-dioxide.

Materials and Methods

All chemicals and solvents used were of analytical grade. A spectrophotometer (Model UV-160A) (Shimadzu, Kyoto, Japan) with 1 cm matched silica cells was used for spectrophotometric analysis. Hydrochlorothiazide was obtained as a gift sample from M/s Ranbaxy Laboratories Ltd., Dewas; and hydrochlorothiazide tablets were purchased from the local market.

Preparation of calibration curve of hydrochlorothiazide: Accurately weighed 50 mg of hydrochlorothiazide was solubilized by 40 ml of mixed hydrotropic solution of niacinamide, sodium acetate, sodium benzoate, sodium citrate and urea (eight percent each) in a 100 ml volumetric flask, and distilled water was added to make up the volume. This stock solution was further diluted with distilled water to get various dilutions containing 20, 40, 60, 80, 100 and 120, µg/ml of drug. Absorbances were noted at 317 nm against corresponding reagent blanks.

Preliminary solubility studies of hydrochlorothiazide: Solubility of hydrochlorothiazide was determined in distilled water and mixed hydrotropic solution of niacinamide, sodium acetate,

sodium benzoate, sodium citrate and urea (eight percent each) at 28°C ± 1°C. There was more than 25-fold enhancement in the solubility of drug in the mixed hydrotropic solution, as compared with the solubility in distilled water.

Analysis of hydrochlorothiazide tablets by the proposed method: Twenty tablets of hydrochlorothiazide (formulation-I and -II) were weighed and finely powdered. Powder equivalent to 50 mg of hydrochlorothiazide was taken in a 100 ml volumetric flask. Forty milliliters of mixed hydrotropic solution of niacinamide, sodium acetate, sodium benzoate, sodium citrate and urea (eight percent each) was added and the flask was shaken properly for 10 min. to solubilize the drug; and the volume was made up to the mark with distilled water. After filtration through a Whatmann filter paper no. 41, the filtrate was appropriately diluted with distilled water for spectrophotometric estimation against reagent blank to calculate the drug content. [Table-1]

Recovery studies: To evaluate the validity and reproducibility of the proposed method, recovery experiments were carried out. For recovery studies, in pre-analyzed tablet powder equivalent to 50 mg hydrochlorothiazide, bulk drug samples 15 and 30 mg were added as spiked concentrations and drug contents were determined by the proposed analytical method. The results of analysis of recovery studies are presented in Table-2.

Results and Discussion

Results of solubility studies of hydrochlorothiazide revealed that enhancement in solubility in a mixed hydrotropic solution of niacinamide, sodium acetate, sodium benzoate, sodium citrate and urea (eight percent each) was more than 25-fold as compared with its solubility in distilled water. It is evident from Table-1 that the value of mean percent drug (hydrochlorothiazide) estimated by proposed spectrophotometric method for formulation I and II are 98.19 and 99.66, respectively. The amount of drug estimated, by the proposed method for both formulations are very close to 100.0, indicating the accuracy of the proposed method of analysis. Low values of standard deviation, percent coefficient of variation and standard error [Table-1] further validated the proposed method.

Table-1: Analysis data of hydrochlorothiazide tablet formulations with statistical evaluation. (n=3)

Tablet formulation	Label claim (mg/tablet)	Percent drug estimated (Mean ± SD)	Percent coefficient of variation	Standard error
I	12.5	98.19 ± 0.883	0.899	0.510
II	25.0	99.66 ± 0.941	0.944	0.543

The percent recoveries estimated ranged from 98.54 to 100.41. The values are close to 100 indicating the accuracy of the proposed method. The values of standard deviation, percent coefficient of variation and standard error are statistically low and thus validate the proposed method [Table-2].

Table-2: Recovery studies using the proposed analytical method with statistical evaluation. (n=3)

Tablet formulation	Drug present in pre-analyzed tablet powder (mg)	Spiked drug added (mg)	Percent recovery estimated (Mean ± SD)	% Coefficient of variation	Standard error
I	50	15	100.33 ± 1.323	1.319	0.764
I	50	30	98.54 ± 1.660	1.685	0.958
II	50	15	98.81 ± 0.722	0.731	0.422
II	50	30	100.41 ± 1.227	1.222	0.708

Conclusion

It is, thus, concluded that the proposed method is new, simple, environment friendly, accurate and reproducible. The proposed method can be successfully employed in the routine analysis of hydrochlorothiazide in tablets. Like this method, other hydrotropes can also be tried by combining them to improve the solubility of poorly water soluble drugs to be applied in different fields of analysis. Mixed hydrotropy may find wide use in development of aqueous formulations of poorly water soluble drugs in future.

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References

[1] NS Tavaren; VK Jadhav. *Journal of Crystal Growth*, **1999**, 198-99, 1320-25.
[2] M Agarwal; VG Gaikar. *Separations Technology*, **1992**, 2, 79-84.
[3] SE Friberg; J Yang; T Huang. *Industrial and Engineering Chemistry Research*, **1996,** 35, 2856-59.
[4] VG Gaikar; PV Phatak. *Separation Science and Technology*, **1999**, 34, 439-59.
[5] SE Friberg; C Brancewicz. *Langmuir*, **1994**, 10, 2945-9.
[6] IC Rigoli; CC Schmitt; MG Neumann. *Journal of Photochemistry and Photobiology A: Chemistry*, **2007**, 188, 329-33.
[7] DV Dandekar; GK Jayaprakash; BS Patil. *Food Chemistry*, **2008**, 109, 515-20.
[8] EJ Colonia; AB Dixit; NS Tavare. *Journal of Chemical & Engineering Data*, **1998**, 43, 220-5.
[9] CRE Mansur; RV Pires; G Gonzalez; EF Lucas. *Langmuir*, **2005**, 21, 2696-703.
[10] T Ooya; HK Moo; M Saitoh; E Tamiya; K Park. *Science and Technology of Advanced Materials*, **2005**, 6, 452-6.
[11] P Bauduin; A Renoncourt; A Kopf; D Touraud; W Kunz. *Langmuir*, **2005**, 21, 6769-75.
[12] D Balasubramanian; V Srinivas; VG Gaikar; M Sharma. *The Journal of Physical Chemistry*, **1989**, 93, 3865-70.
[13] RK Maheshwari. *Journal of Pharmaceutical and Biomedical Analysis*, **2006**, 40, 237-40.

[14] RK Maheshwari. *The Indian Pharmacist*, **2006**, 5, 87-90.
[15] RK Maheshwari. *Indian Drugs*, **2006**, 43, 683-5.
[16] RK Maheshwari; SC Chaturvedi; NK Jain. *Indian Journal of Pharmaceutical Science*, **2006**, 68, 195-8.
[17] RK Maheshwari; RB Maheshwari; P Bhatt. *Asian J Chem.*, **2007,** 18, 1481-6.
[18] RK Maheshwari; SC Chaturvedi; NK Jain. *Int J Pharmaceu Excipients*, **2005**, 4, 84-8.
[19] RK Maheshwari; V Chavda; K Sahoo; S Varghese. *Asian J Pharmaceutics*, **2006,** 1, 30-2.
[20] RK Maheshwari; SC Chaturvedi; NK Jain. *Indian J Pharmaceut Sci.*, **2007,** 69, 101-5.
[21] RK Maheshwari; N Dubey; N Dubey; M Singh. *Asian J Chem.*, **2008,** 20, 375-9.
[22] RK Maheshwari; S Deswal; D Tiwari; N Ali; B Pothen; S Jain. *Indian J Pharmaceut Sci.*, **2007,** 69, 822-6.
[23] RK Maheshwari; RS Shukla. *Asian J Chem.*, **2008,** 20, 4221-4.
[24] RK Maheshwari; D Arif, P Mittal; P Manchandani, A Indurkhya; S Jawade. *J Appl Chem Resh.*, **2008,** 5, 63-8.
[25] RK Maheshwari; V Patidar; D Maliwal; A Jain. *Res J Pharm and Tech.*, **2008,** 1, 357-61.
[26] RK Maheshwari; MS Rajput; S Sinha. *Int J Current Pharmaceut Res.*, **2009**, 1, 38-41.
[27] RK Maheshwari; MS Rajput; V Nair. *J Pharm Res.*, **2010**, 3, 6-8
[28] RK Maheshwari; N Govil; M Rai; MS Rajput. *Int J Pharma Bio Sci.*, **2010**, 1, 1-3.
[29] GK Poochikian; JC Cradock. *J Pharm Sci.*, **1979,** 68, 728-32.
[30] A Darwish; AT Florence; AM Saleh. *J Pharm Sci*., **1989,** 78, 577-81.
[31] MA Etman; RO Salama; MA Shamsedeen; A El-Kamel. *Indian J Pharm Sci.*, **2001,** 63, 459-67.
[32] AA Rasool; A Hussain; LW Dittert. *J Pharm Sci.*, **1999,** 80, 387-93.
[33] NK Jain; RK Agrawal; AK Singhai. *Pharmazie*, **1990,** 45, 221-5.
[34] RK Maheshwari. *The Indian Pharmacist*, **2007**, 6, 67-9.
[35] RK Maheshwari. *The Indian Pharmacist*, **2009,** 8, 81-4.