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Novel Application of Hydrotropic Solubilization in the Spectrophotometric Analysis of Paracetamol Tablet

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Concentrated aqueous solutions of various hydrotropic agents like sodium salicylate, sodium benzoate, sodium citrate, sodium acetate, urea and nicotinamide have been observed to enhance aqueous solubilities of a large number of poorly water-soluble drugs. In the present investigation, paracetamol has been selected as a poorly water-soluble drug. There was more than 7-fold enhancement in aqueous solubility of paracetramol by 10.0 M urea solution (as compared to its aqueous solubility). This hydrotropic agent was employed to solubilize the drug from the fine powder of tablet formulations. The selected λ_{max} for spectrophotometric estimation was 245 nm. The hydrotropic agent and additives used in the manufacture of tablets did not interfere in the analysis. Proposed method is new, rapid, simple, accurate and reproducible. Statistical data proved the accuracy, reproducibility and the precision of the proposed method.

Key Words: Hydrotropy, Paracetamol, Urea, Spectrophotometry.

INTRODUCTION

Hydrotropy is a solubilization phenomenon whereby addition of large amount of second solute results in an increase in the aqueous solubility of another solute. Concentrated aqueous solution of a large number of hydrotropic agents have been employed to enhance the aqueous solubility of many poorly water-soluble drugs[1–18]. Maheshwari[1–4] has developed new analytical methods based on hydrotropic solubilization phenomenon for poorly water-soluble drugs cefixime[1], frusemide[2], ketoprofen[3,5], salicylic acid[3] and tinidazole[4]. Various analytical techniques based on hydrotropic solubilization phenomenon for poorly water-soluble drugs ofloxacin[6], metronidazole[7], norfloxacin[7], nalidixic acid[7], tinidazole[7], aceclofenac[8] and hydrochlorthiazide[9] have also been reported in the literature.

There was considerable increase in the solubility of paracetamol (an antipyretic drug) in 10.0 M urea solution (a hydrotropic solution). Therefore, it was thought worthwhile to solubilize the drug present in its tablet powder with 10.0 M urea solution to carry out its spectrophotometric analysis.

EXPERIMENTAL

Paracetamol (4-hydroxy acetanilide) was a generous gift by Shri Pharmaceuticals, Indore, India. All chemicals used were of analytical grade. A Shimadzu UV-Visible recording spectrophotometer (Model-UV 160 A) with 1 cm matched silica cells was used for spectrophotometric analysis. Commerical tablets of paracetamol (Formulation-I, *Crocin* of GSK Asia Pvt. Ltd. and formulation-II, Calpol of Wellcome India Ltd.) were procured from local market.

Calibration curve

The standard solution (500 μg/mL) of paracetamol was prepared in distilled water. The standard solution was diluted with distilled water to obtain various dilutions (5, 10, 15, 20, 25, 30 and 35 μg/mL). A linear relationship was observed over the range of 5 to 35 μg/mL for paracetamol (λ_{max} 245 nm).

Preliminary solubility studies of drug

Solubility of paracetamol was determined in distilled water and 10.0 M urea solution at 27 ± 1°C. Enhancement of solubility of paracetamol in 10.0 M urea solution was found to be more than 7 fold (as compared to its solubility in distilled water).

Analysis of tablet formulations of paracetamol by proposed method using 10.0 M urea solution

Twenty tablets of paracetamol (formulation-I) were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 500 mg of paracetamol was transferred to a 100 mL volumetric flask containing 40 mL of 10.0 M urea solution. The flask was then shaken for 10 min to solubilize the drug and the volume was made up to the mark with distilled water. The solution was filtered through Whatmann filter paper No. 41. The filtrate was divided into two parts A and B. Part A was kept at room temperature for 48 h to check it chemical stability and precipitation, if any. Part B was diluted sufficiently with distilled water and was analyzed on UV-spectrophotometer against-reagent blank. Drug content of tablet formulation-I was then calculated (Table-1). After 48 h, part A solution was analyzed in the same way as part B. Same procedure was followed for formulation-II.

Recovery studies

For recovery studies 50 and 100 mg of paracetamol, pure drug was added to the preanalyzed tablet powder equivalent to 500 mg paracetamol. The procedure of analysis was the same using 10.0 M urea solution. The per cent recoveries for spiked amounts were calculated.

RESULTS AND DISCUSSION

Results of solubility studies indicated that enhancement in aqueous solubility of paracetamol in 10.0 M urea solution was more than 7-fold as compared to solubility in distilled water. Therefore, this solution was employed to extract out

paracetamol from fine powder of tablet formulation. It is evident from Table-1 that per cent label claim obtained was 98.854 ± 1.055 in formulation-I and 98.133 ± 0.283 in formulation-II. Per cent label claims are very close to 100 with low values of standard deviation, per cent coefficient of variation and standard error, showing the accuracy of the proposed method. Recovery studies were further performed to confirm the accuracy, precision and reproducibility of the proposed method. As evident from Table-2, per cent recovery values ranged from 99.08 ± 0.782 to 100.04 ± 1.707. The proposed method was further validated for its accuracy, precision and reproducibility with per cent recovery values close to 100 and very low values of standard deviation, per cent coefficient of variation and standard error. Urea (the hydrotropic agent) and additives used in the manufacture of tablets did not interfere in the analysis.

TABLE-1
RESULTS OF ANALYSIS OF COMMERCIAL TABLET FORMULATIONS WITH STATISTICAL EVALUATION

Tablet formulation	Label claim (mg)	Per cent label claim estimated* (mean ± S.D.)	Per cent coefficient of variation	Standard error
I	500	98.854 ± 1.055	1.067	0.609
II	500	98.133 ± 0.283	0.288	0.163

*Average of three determinations.

TABLE-2
RECOVERY STUDY FOR SPIKED CONCENTRATION OF PARACETAMOL ADDED TO THE PREANALYZED DOSAGE FORM

Table formulation	Amount of drug (mg)	Pure paracetamol added (mg) (spiked)	Per cent recovery estimated* (mean ± S.D.)	Per cent coefficient of variation	Standard error
I	500	50	100.04 ± 1.707	1.706	0.991
	500	100	99.08 ± 0.782	0.789	0.451
II	500	50	99.68 ± 1.209	1.213	0.701
	500	100	99.62 ± 1.293	1.300	0.746

*Average of three determinations.

Drug content in extract of 10.0 M urea solution was same within 48 h and also there was no precipitation in 48 h. This indicates that the extract can be analyzed within 48 h at least, with sufficient accuracy.

Conclusions

Ethanol, methanol, acetonitrile, hexane, cyclohexane, diethyl ether, chloroform, carbon tetrachloride, toluene and acetone have been employed for solubilization of poorly water-soluble drugs for their spectrophotometric analysis. Most of the organic solvents are toxic, costlier and are responsible for pollution. Inaccuracy due to volatility is another drawback of organic solvents. Using

sparingly water-soluble drug paracetamol, as a model drug, the the authors want to emphasize on the use of hydrotropic solutions as solubilizing agents. Urea does not interfere in the spectrophotometric estimation of drugs having λ_{max} above 250 nm. Thus other poorly water-soluble drugs can be checked for their solubilities in hydrotropic solutions. If they have good solubilities, they can easily be estimated by the use of such hydrotropic agents, excluding the use of organic solvents, provided their λ_{max} is more than 250 nm. It is concluded that the proposed method is new, simple, accurate, safe, precise, cost-effective, free from pollution and can be successfully employed in the routine analysis of paracetamol tablets.

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REFERENCES

1. R.K. Maheshwari, *Indian Pharmacist*, **4**, 63 (2005).
2. ————, *Indian Pharmacist*, **4**, 55 (2005).
3. ————, *Asian J. Chem.*, **18**, 393 (2006).
4. ————, *Asian J. Chem.*, **18**, 660 (2006).
5. ————, *Pharma Review*, **3**, 123 (2005).
6. R.K. Maheshwari, S.C. Chaturvedi and N.K. Jain, *Indian Drugs* (in press).
7. ————, *Indian J. Pharm. Sci.* (in press).
8. ————, *Indian Drugs* (in press).
9. ————, *Indian Drugs*, **42**, 541 (2005).
10. N.K. Jain, R.K. Agrawal and A.K. Singhai, *Pharmazie*, **45**, 221 (1990).
11. G.D. Poochikian and J.C. Cradock, *J. Pharm. Sci.*, **68**, 728 (1979).
12. S. Ueda, *Chem. Pharm. Bull.*, **14**, 2 (1996).
13. A.A. Rasool, A.A. Hussain and L.W. Dittert, *J. Pharm. Sci.*, 80, 387 (1991).
14. I.A. Darwish, A.T. Florence and A.M. Saleh, *J. Pharm. Sci.*, **78**, 577 (1989).
15. P. Simamora, J.M. Alvarez and S.H. Yalkowsky, *Int. J. Pharm.*, **213**, 25 (2001).
16. R.E. Coffman and D.O. Kildsig, *J. Pharm. Sci.*, **85**, 951 (1996).
17. A.M. Saleh, A.R. Ebian and M.A. Etman, *J. Pharm. Sci.*, **75**, 644 (1986).
18. M. Miyahara and T. Takahasi, *Chem. Pharm. Bull.*, **30**, 288 (1982).

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