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Research Article

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New application of hydrotropic solubilization phenomenon in spectroscopic estimation of simvastatin in tablet dosage form

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ABSTRACT

Hydrotropic agents have been employed to increase the aqueous solubility of poorly water soluble drug. This procedure eliminates the limitation of organic solvent such as methanol, ethanol, alcohol, dimethyl formamide, acetonitrile, hexane, acetone used in spectroscopic determination. The problems included are their high cost, toxicity and error (due to volatility). Use of hydrotropic solution for solubilization is a new simple, economic, rapid, accurate and reproducible spectrophotometric estimation method developed using 8M urea for solubilization and determination of simvastatin. Simvastatin was found to be poorly water soluble drug and there was more than 5 times increase in the solubility using 8.0 M urea solution. Urea did not interfere in the spectroscopic determination of simvastatin (λ_{max}-223). Recovery studies and statistical data proved the accuracy, reproducibility and the precision of the proposed method.

Keywords: Hydrotropy, Simvastatin, Spectrophotometry.

INTRODUCTION

Hydrotropy is a solubilization process where addition of large amount of a second solute results in the increase in the aqueous solubility of another solute. Concentrated solutions of these agents like urea (8-10M), Sodium acetate (4M), Sodium citrate (1.25M), Sodium benzoate (2M) were found to increase the aqueous solubility of many poorly water soluble drugs[1-18]. Drugs like ceftixime[1], Frusemide[2], Salicylic acid [3], Ketoprofen [3,4], Tinidazole, Norfloxacine, Hydrochlorthiazide, Metronidazole, atorvastatin [16], etc. has been estimated by using hydrotropic solubilization phenomenon, in their solid dosage form. Simvastatin is found to be poorly water soluble and used in the treatment of hypertension. Not a single UV spectroscopic method was reported for determination and thus selected as a model for evaluation.

EXPERIMENTAL SECTION

The instrument used was Shimadzu uv-visible recording spectrophotometer (model 1700 A) with 1 cm matched silica cells. All chemicals were of analytical grade. The commercially available tablets were procured from local market as *Simcard 5, Simcard 10* manufactured by Merck Pharmaceuticals Ltd. containing 5, 10 mg simvastatin respectively.

Standard stock solution of simvastatin was prepared in distilled water. Standard solution was diluted with distilled water to obtain various dilutions (5, 10, 15, 20, 25, 30, 35, 40, 45, 50 µg/ml) to plot calibration curve. A linear relationship was observed over the range of 5-50 µg/ml.

Solubility of simvastatin was determined in distilled water and 8M urea solution at room temperature (20^oC). Simvastatin was found to be more than 5 fold soluble in urea solution than in distilled water. Urea did not interfere

in the spectrophotometric estimation. It has zero absorbance above 215 nm (λ_{max}-207nm). The pH of 8M urea solution was 9.45, therefore solubility was also determined in the buffer solution of pH 9.45 at 20ºC to observe effect of pH on solubility of simvastatin. There was no noticeable difference found in the solubility. This indicates that the solubility is due to hydrotropic solubilization and not due to pH change.

Twenty tablets of simvastatin were weighed and triturated in pestle mortar to obtain a fine powder. An accurately weighed powder sample of 10 mg of each drug was transferred to 100 ml volumetric flask. 30 ml of 8M urea solution was added and the flask was shaken for about 10 minute to dissolve the drug and a volume was made up to 100 ml. The solution was filtered through whatman 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 its chemical stability and precipitation if any. Part B was diluted appropriately with distilled water and was analyzed on UV-visible spectrophotometer at 223 nm against reagent blank. Drug content of formulation was thus calculated, Table 1. There was no precipitation in part A solution within 48 hour. Also part A solution was analyzed after 48 h. Drug content of part B (fresh solution) and part A (after 48 h) were nearly same. This study indicates that solution can be analyzed within 48 h without any bad effect on stability of drug in presence of urea.

To evaluate validity and reproducibility of the method, recovery studies were performed. Tablet powder 10 mg simvastatin was taken into 100 ml flask and 3 mg of simvastatin (spiked) added in the flask. 30 ml of 8M urea solution was added and the whole method of analysis was repeated in the same way as mentioned previously. Recovery studies were repeated using 5 mg of Atrovastatin Calcium drug (spiked).

From table 1 it is evident that there is a good agreement between the amount found and those claimed by the manufacturer. Percent label claim is very close to 100% indicating the proposed method was precise. There was no interference of urea and other additives added in the formulation. The accuracy of the proposed method was further confirmed by the recovery studies. Percent recovery estimated by this proposed method is given in Table 1.

Table1. Recovery study for simvastatin

Tablet formulation	Label claim per Tablet (mg)	% Label claim estimated (Mean*±S.D.)	Amt. of Simvastatin in preanalysed tablet powder (mg)	Simvastatin drug added (mg)	% Recovery Estimated (Mean* ± SD)
I	5	99.56 ± 0.52	5	5	100.56 ± 0.52
	5	99.43 ± 0.33	5	10	100.32 ± 0.54
II	10	100.12 ± 0.53	10	5	100.78 ± 0.67
	10	100.28 ± 0.98	10	10	99.20 ± 0.35

** Mean of five observations*

CONCLUSION

It may conclude that proposed method is simple, safe and precise. A large number of poorly water soluble drugs as well as their salt form can be tried with using urea solution provided the aqueous solubility of the drug is increased by urea solution. Urea solution is economic and error due to volatility of organic solvent may be minimized.

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REFERENCES

[1] Maheshwari R.K.: *The Indian Pharmacist* **2005**, Vol.IV(no.36), 63-68
[2] Maheshwari R.K.: *The Indian Pharmacist* **2005**, Vol.IV(no.34), 55-58
[3] Maheshwari R.K.: A novel application of hydrotropic solubilization in analysis of bulk samples of ketoprofen and salicylic acid. *Asian J. Chem*. (In press)
[4] Jain Nilesh, Ruchi Jain, Arti Jain, Sharad P. Pandey and Deepak Kumar Jain **2010** *Eurasian J. Anal. Chem*. 5(3): 212-217.
[5] Maheshwari R.K.: *Indian Drugs* **2005** 42, 541-544.
[6] Maheshwari R.K., Chaturvedi S.C. and Jain N.K.: *Indian J. Pharm. Sci.* **2006**, 68(2),195-198.
[7] Merukar SS, Mhaskar PS, Bavaskar SR, Burade KB, Dhabale PN, **2010**. *International Journal of Chem. Tech Research*, 2 (1),462-465.
[8] Ueda S.: *Chem. Pharm. Bull*. **1966**, 14, 29-38.
[9] Higuchi T. and Drubulis A.: *J. Pharm. Sci*. **1961**, 50, 905-909.
[10] Saleh A.M. and Daabis N.A.: *Pharmazie* **1974**, 29, 525-527.

[11] Simamora P., Alvarez J.M. and yalkowsky S.H.: *Int. J. Pharm*. **2001**, 213, 25-29
[12] Jain N.K. and Patel V.V.: *The Eastern Pharmacist* **1986**, 29, 51-54.
[13] Etman M.A. and Hada A.H.: *Acta Pharm*. **1999**, 49, 291-298.
[14] Agrawal S.S., Pancholi S.S., Jain N.K. and Agrawal G.P.: *Int. J. Pharm*. **2004**, 274, 149-155.
[15] Jain N., Yang G., Tabibi S.E. and Yalkowsky S.H.: *Int. J. Pharm*. **2001**, 225, 41-47.
[16] Dipak Kale and Deepak Patil,; *J. GMP Industrial Pharm*. **2009**, 4, 16-18.
[17] Jain Nilesh, Ruchi Jain, Sneha Kulkarni, Deepak Kumar Jain and Surendra Jain: **2011** *J. Chem. Pharm. Res*., 3(1):548-552.
[18] Sharma MC, Sharma Smita and Sharma AD: **2010** *J. Chem. Pharm. Res*., 2010, 2(2): 416-420