Research Article

Spectroscopic Determination of Lovastatin By Hydrotropic Solubilization Technique

Deepak N. Patil

Sanjivani Institute of Pharmaceutical Education and Research, Kopargaon, Distt. Ahmednagar, Maharashtra, India.

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 4M sodium acetate for solubilization and determination of lovastatin.

Lovastatin was found to be poorly water soluble drug and there was more than 6 times increase in the solubility using 4M sodium acetate solution. Sodium acetate did not interfere in the spectroscopic determination of lovastatin (λ_{max}-250). Recovery studies and statistical data proved the accuracy, reproducibility and the precision of the proposed method.

Keywords: Hydrotropy, Lovastatin, 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[5], Hydrochlorthiazide[6], Atorvastatin[16], Simvastatin[17] etc. has been estimated by using hydrotropic solubilization phenomenon, in their solid dosage form.

Lovastatin 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

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 *Mevacor 40* manufactured by Lupin Pharmaceuticals Ltd. containing 40 mg lovastatin.

Standard stock solution of lovastatin 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 lovastatin was determined in distilled water and 4M sodium acetate solution at room temperature (20°C). Lovastatin was found to be more than 6 fold soluble in sodium acetate solution than in distilled water. Sodium acetate did not interfere in the spectrophotometric estimation. It has zero absorbance above 240 nm (λ_{max}-233nm). The pH of 4M sodium acetate solution was 4.7, therefore solubility was also determined in the buffer solution of pH 4.7 at 20ºC to observe effect of pH on solubility of lovastatin. 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 lovastatin 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 4M sodium acetate 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 250 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 sodium acetate.

To evaluate validity and reproducibility of the method, recovery studies were performed. Tablet powder 10 mg lovastatin was taken into 100 ml flask and 3 mg of lovastatin (spiked) added in the flask. 30 ml of 4M sodium acetate 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 lovastatin 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 sodium acetate 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.

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 sodium acetate solution provided the aqueous solubility of the drug is increased by sodium acetate solution. Sodium acetate solution is economic and error due to volatility of organic solvent may be minimized.

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Table 1: Recovery study for lovastatin

Tablet formulation	Label claim per Tablet (mg)	% Label claim estimated (Mean*±S.D.)	Amt. of Lovastatin in preanalysed tablet powder (mg)	Lovastatin drug added (mg)	% Recovery Estimated (Mean* ± SD)
Mevacor 40	40	99.13 ± 0.32	28	4	100.12 ± 0.63
	40	99.22 ± 0.45	28	12	99.62 ± 0.84
	40	99.13 ± 0.83	28	20	100.44 ± 0.34

* Mean of three observations

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