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A Novel Application of Hydrotropic Solubilization in the Analysis of Bulk Samples of Ketoprofen and Salicylic Acid

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In the present investigation, hydrotropic solubilization technique has been employed to solubilize the poorly water soluble anti-inflammatory drug, ketoprofen (by 2.0 M sodium benzoate, 2.0 M sodium salicylate and 2.0 M sodium acetate solutions) and the poorly water soluble keratolytic drug, salicylic acid (by 2.0 M sodium benzoate, 8.0 M urea and 1.25 M sodium citrate solutions) for their titrimetric analyses The proposed method is new, simple, accurate and reproducible. Statistical data prove the accuracy reproducibility and precision of the proposed method.

Key Words: Hydrotropy, Ketoprofen, Salicylic acid, Sodium Benzoate, Sodium salicylate, Sodium acetate, Sodium citrate, Urea.

INTRODUCTION

Hydrotropy is a solubilization phenomenon whereby addition of large amount of a second solute results in an increase in the aqueous solubility of another solute. Concentrated aqueous solutions of a large number of hydrotropic agents have been employed to enhance the aqueous solubility of many poorly water soluble drugs[1-11]. Sodium benzoate, sodium salicylate, sodium acetate, sodium ascorbate, niacinamide, sodium citrate, urea are the most popular examples of hydrotropic agents. There was tremendous increase in the solubility of ketoprofen (a widely used non-steroidal antiinflammatory agent) [2-(3-benzoyl-phenyl)propionic acid] in 2.0 M sodium benzoate, 2.0 M sodium salicylate and 2.0 M sodium acetate solutions. Similarly, there was considerable enhancement in the solubility of salicylic acid (a keratolytic drug) in 2.0 M sodium benzoate, 8.0 M urea and 1.25 M sodium citrate solutions. Therefore, it was thought worthwhile to solubilize these drugs in hydrotropic solutions to carry out the titrations.

EXPERIMENTAL

All chemicals and solvents used were of analytical grade. Ketoprofen and salicylic acid were obtained as gift samples from Alkem Lab. Ltd., Mumbai.

Preliminary solubility studies of drugs

Solubilities of ketoprofen and salicylic acid were determined in distilled water and different concentrated solutions of hydrotropic agents at 27 ± 1°C. Enhancement in the solubilities of ketoprofen in 2.0 M sodium benzoate, 2.0 M sodium salicylate and 2.0 M sodium acetate solutions was more than 250-fold, 90-fold and 80-fold, respectively (as compared to its solubility in distilled water). Similarly, enhancement in the solubility of salicylic acid in 8.0 M urea, 2.0 M sodium benzoate and 1.25 M sodium citrate solutions was more than 8-fold, 12-fold and 85-fold, respectively (as compared to their solubilities in distilled water).

Analysis of ketoprofen bulk sample by Indian Pharmacopoeial method[12]

Ketoprofen bulk sample was analyzed by dissolving accurately weighed drug (0.5 g) in 25 mL ethanol (95%) previously neutralized to phenolphthalein solution and titrating it with sodium hydroxide solution (0.1 M) and the drug content was calculated (Table-1).

TABLE-1
ANALYSIS DATA OF KETOPROFEN AND SALICYLIC ACID BULK SAMPLES WITH STATISTICAL EVALUATION

Drug	Amount of drug (mg)	Method of analysis	Amount estimated[a] (mean ± S.D.)	% Coeff. of variation	Standard error
Ketoprofen	500	I.P.[b]	497.2 ± 1.420	1.428	0.635
	500	P.M.S.B.[c]	496.5 ± 1.472	1.482	0.658
	500	P.M.S.S.[d]	498 2 ± 1.076	1.080	0.481
	500	P.M.S.A.[e]	497.5 ± 0.808	0.812	0.361
Salicylic acid	300	I.P.[b]	298.0 ± 1.002	0.995	0.448
	300	P.M.S.B.[c]	297.2 ± 0.982	0.973	0.439
	300	P.M.S.S.[f]	298.8 ± 0.839	0.836	0.375
	300	P.M.S.A.[g]	297.8 ± 1.048	1.040	0.469

[a]Average of five determinations [b]Indian Pharmacopoeia (1996)
[c]Proposed method using 2.0 M sodium benzoate solution
[d]Proposed method using 2.0 M sodium salicylate solution
[e]Proposed metho dusing 2.0 M sodium acetate solution
[f]Proposed method using 8.0 M urea solution
[g]Proposed method using 1.25 M sodium citrate solution.

Analysis of ketoprofen bulk sample by proposed method

In the proposed method, accurately weighed (0.5 g) ketoprofen bulk sample was solubilized in 25 mL of sodium benzoate solution (2.0 M) in a conical flask by shaking for about 5 min and titrated with sodium hydroxide solution (0.1 M) using phenolphthalein solution as indicator. Blank determination was carried out to make necessary correction and amount of ketoprofen was calculated (Table-1).

Similar procedure was repeated using 50 mL of sodium salicylate solution (2.0 M) and 50 mL of sodium acetate solution (2.0 M) (in place of 25 mL of 2.0

M sodium benzoate solution) for solubilization of ketoprofen and the results of analysis are shown in Table-1.

Analysis of salicylic acid bulk sample by Indian Pharmacopoeial method[13]

Accurately weighed (0.3 g) salicylic acid bulk sample was dissolved in 50 mL of ethanol. After adding 20 mL distilled water, it was titrated with sodium hydroxide solution (0.1 M) using phenol red solution as indicator. Necessary blank determination was adjusted to get drug content (Table-1).

Analysis of salicylic acid bulk sample by proposed method

In the proposed method, accurately weighed (0.3 g) salicylic acid bulk sample was solubilized in 25 mL of sodium citrate solution (1.25 M) in a conical flask by shaking for about 5 min and titrated with sodium hydroxide solution (0.1 M) using phenol red solution as indicator. Necessary correction was done by conducting blank determination and amount of salicylic acid was calculated (Table-1). Similar procedure was followed using 50 mL of sodium benzoate solution (2.0 M) and 50 mL of urea solution (8.0 M) for solubilization of salicylic acid (in place of 25 mL of sodium citrate solution (1.25 M) and salicylic acid content was determined (Table-1).

RESULTS AND DISCUSSION

It is evident from Table-1 that the amount of ketoprofen estimated in pure sample by Indian Pharmacopoeial method is 497.2 ± 1.420. In the proposed method of analysis, the amounts of ketoprofen estimated by use of 2.0 M sodium benzoate, 2.0 M sodium salicylate and 2.0 M sodium acetate solutions were 496.5 ± 1.472, 498.2 ± 1.076 and 497.5 ± 0.808, respectively. The results of analysis by proposed method are very close to the results of analysis by standard method (Indian Pharmacopoeial method). Validation of the proposed method is further confirmed statistically by low values of % coefficient of variation and standard error (Table-1).

The amount of salicylic acid estimated in bulk sample of salicylic acid by Indian Pharmacopoeial method is 298.0 ± 1.002 (Table-1). The amounts estimated by the proposed method were 297.2 ± 0.982, 298.8 ± 0.839 and 297.8 ± 1.048 using 2.0 M sodium benzoate, 8.0 M urea and 1.25 M sodium citrate solutions, respectively (Table-1). Amounts of salicylic acid estimated by the proposed method are highly comparable to the amount estimated by a standard method of analysis (Indian Pharmacopoeial method).

Conclusions

It is thus concluded that the proposed method is new, simple, cost-effective, accurate, safe and precise and can be successfully employed in the routine analysis of ketoprofen and salicylic acid in bulk drug samples. There is a good scope for other poorly water soluble drugs which may be tried to get solubilized by suitable hydrotropic agents to carry out their titrimetric analysis excluding the use of costlier and unsafe organic solvents.

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