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A NOVEL METHOD FOR QUANTITATIVE DETERMINATION OF ACECLOFENAC IN BULK DRUG AND TABLETS USING SODIUM SALICYLATE AS A HYDROTROPIC SOLUBILIZING AGENT

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Abstract

In titrimetric analysis costlier organic solvents are more often employed to solubilize the poorly water-soluble drugs. Volatility and pollution are drawbacks of such solvents. Various techniques are employed to enhance the aqueous solubility of poorly water-soluble drugs. Hydrotropic solubilization phenomenon has been widely used to enhance the aqueous solubility of large number of poorly water-soluble drugs. Aqueous solubility of aceclofenac bulk drug [a poorly water-soluble NSAID] was enhanced to a great extent i.e., 400 folds with 2.5 M sodium salicylate. The primary objective of the present investigation was to employ this hydrotropic solution to extract the drug from its dosage forms, precluding the use of costlier organic solvents. The proposed method of analysis is new, simple, accurate, environmentally friendly and reproducible. Statistical data proved the accuracy, reproducibility and the precision of the proposed method. The results of titrimetric analysis by use of hydrotropy compared very well with the results of Pharmacopoeial method.

Key Words: Hydrotropy, Solubilization, Aceclofenac, Sodium salicylate, Titrimetry.

Introduction

Hydrotropy refers to the ability of a concentrated solution of a chemical compound to increase the aqueous solubility of another compound [usually a sparingly soluble organic compound]. Compounds that have this property are called 'hydrotopes'. Sodium benzoate, sodium salicylate, sodium acetate, sodium ascorbate, niacinamide and sodium citrate are the most popular examples of hydrotropic agents which have been used to solubilize a large number of poorly water-

soluble compounds [1-14]. Hydrotropic solution, sodium salicylate was employed as solubilizing agent to carryout the analysis of aceclofenac [a poorly water-soluble NSAID] by titrimetric estimation. Chemically, aceclofenac is 2 – [[2, 6- dichlorophenyl] amino] benzeneacetic acid carboxymethyl ester. There was tremendous increase in solubility of aceclofenac in 2.5 M sodium salicylate solution. Therefore, it was thought worthwhile to solubilize this drug in hydrotropic solution to carry out the titrations precluding the use of an organic solvent.

Experimental

Materials and Reagents

The bulk drug sample of aceclofenac was generously supplied by Aristo Pharmaceuticals Limited, Mandideep, (M.P.) Commercial tablets of aceclofenac were procured from local market. Other chemicals used were of analytical grade.

Methods

Preliminary solubility studies of aceclofenac

Solubility of aceclofenac was determined in distilled water and 2.5 M sodium salicylate solution at 27±1ºC. Enhancement in solubility in hydrotropic solution was more than 400 fold [as compared to solubility in distilled water].

Analysis of aceclofenac bulk drug sample by British Pharmacopoeial method

Accurately weighed [0.3 g] aceclofenac bulk drug sample was solubilized in 40 ml alcohol in a conical flask by shaking and titrated with 0.1 M sodium hydroxide solution determining the end point potentiometrically and the amount of aceclofenac was computed [Table-1].

Table 1: Analysis data of bulk drug sample with statistical evaluation

Amount of bulk drug taken [mg]	Method of analysis	Percent drug Estimated * [mean ± Standard deviation]	Percent coefficient of variation	Standard error
300	B .P .M	101.77±1.832	1.800	1.058
300	Proposed Method	100.54±0.822	0.818	0.475

B.P.M-British Pharmacopoeial method

* Mean of three determinations.

Analysis of aceclofenac bulk drug sample by the proposed analytical method

Accurately weighed [0.3 g] aceclofenac bulk drug sample was solubilized in 40 ml of 2.5 M sodium salicylate solution in a conical flask by shaking for about 5 minutes and titrated with 0.1 M sodium hydroxide solution using phenolphthalein solution as indicator. Blank determination was

conducted to make the required corrections and the amount of aceclofenac was computed [Table-1].

Analysis of aceclofenac tablets by the proposed method

Twenty tablets of aceclofenac were weighed and powdered finely. The powder, equivalent to 300 mg aceclofenac was accurately weighed and transferred to a conical flask. After adding, 40 ml of 2.5 M sodium salicylate solution, the flask was shaken for 10 minutes for solubilization of drug from the fine powder of tablets. The drug was titrated with 0.1 M sodium hydroxide solution using phenolphthalein solution as indicator. Blank determination was conducted to make the required corrections and the amount of aceclofenac was computed [Table-2].

Recovery Studies

For recovery studies, pre analyzed tablet powder was spiked with aceclofenac bulk drug sample at two levels. For this, 200 and 300 mg of aceclofenac bulk drug was added to tablet powder equivalent to 500 mg aceclofenac and analyzed by same proposed method. Percentage recoveries were calculated and reported in [Table-3].

Results and Discussion

Solubility studies at preliminary stage showed that the enhancement in solubility of aceclofenac in 2.5 M sodium salicylate solution was more than 400 fold as compared to aqueous solubility. As evident from Table-1 the amount of aceclofenac estimated in bulk drug sample by B.P. method and the proposed method are 101.77±1.832 and 100.54±0.822, respectively. Both values are very close to each other and close to 100 and hence confirm the accuracy of the proposed method. Validation of the proposed method is further confirmed statistically by low values of standard deviation, % coefficient of variation and standard error [Table-1]

Table 2: Analysis data of tablet formulations with statistical evaluation

Tablet formulation	Label claim [mg/tablet]	Percent label claim estimated* [mean ± Standard deviation]	Percent coefficient of variation	Standard error
I	100	99.03±1.277	1.129	0.737
II	100	100.75±0.933	0.926	0.539

* Mean of three determinations.

Table 2 indicates that the percent label claims of aceclofenac estimated in the tablets using the proposed method of analysis [99.03±1.277 and 100.75±0.933] are very close to 100 indicating the accuracy of proposed method. Validation of the proposed method is further confirmed by satisfactory low values of standard deviation, % coefficient of variation and standard error [Table-2].

Table 3: Results of recovery studies of tablet formulations with statistical evaluation

Tablet formulation	Drug in preanalyzed tablet pwder [mg]	Amount of drug added [spiked] [mg]	Percent recovery estimated * [mean± Standard deviation]	Percent coefficient of variation	Standard error
I	500	200	99.33±0.543	0.547	0.313
I	500	300	100.57±0.730	0.726	0.422
II	500	200	99.47±0.808	0.812	0.466
II	500	300	100.94±1.135	1.130	0.759

* Mean of three determinations.

Accuracy, reproducibility and precision of the proposed method were further confirmed by % recovery values which were close to 100 [ranged from 99.33±0.543 to 100.94±1.135] with satisfactory low values of statistical parameters viz standard deviation, % coefficient of variation and standard error [Table-3].

Conclusion

It is, thus, concluded that the proposed method is simple, cost-effective, accurate, safe, precise, and can be successfully employed in routine analysis of aceclofenac bulk drug as well as aceclofenac tablets. There is good scope for other poorly water-soluble drugs which may be solubilized by hydrotropic agents to carry out titrimetric analysis, precluding the use of costlier and unsafe organic solvents.

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