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Aditya Narayan Jhariya, Ashish Kumar Parashar, Mahendra Patel, Rajesh Kumar Nema
Rishiraj Collage of Pharmacy, Indore-453 331, MP, India

Dilip Kumar
Department of Natural Products, NIPER, Mohali-160 062, Punjab, India

Correspondence

Aditya Narayan Jhariya
Rishiraj college of Pharmacy
Indore (M.P.) 453331, India.

Email:adityanarayanj121@gmail.com

New Analytical Methods for Titrimetric and Spectrophotometric Analysis of Salicylic Acid Bulk Drug Sample

Aditya Narayan Jhariya, Dilip Kumar, Ashish Kumar Parashar, Mahendra Patel, Rajesh Kumar Nema

ABSTRACT

Titrimetric analysis of salicylic acid by Indian Pharmacopoeial method employ the use of ethanol. Organic solvents such as ethanol, chloroform, benzene etc. are costly and possess toxicity and environmental hazard. In order to overcome above drawbacks the concept of mixed solvency could be employed. The aim of present study was to avoid the use of organic solvents and enhance the solubility of salicylic acid in aqueous medium contains solubilizers such as sodium citrate (5% w/v), glycerin (5% w/v), PEG 400 (5% w/v), urea (5% w/v), PEG 300 (10% w/v) and PEG 4000 (10% w/v) correspondingly. A blend of these solubilizing agents used to improve the solubility of salicylic acid by many folds. From the statistical data it was proved that the proposed methods are accurate, precise and reproducible. The concept thus can be a boon in pharmaceutical field as well as a way towards the green chemistry.

Keywords: Mixed solvency, salicylic acid, spectrophotometric analysis, titrimetric analysis.

1. INTRODUCTION

From the literature review it is confirmed that most of the drugs whether discovered or developed are lipophilic. Poor solubility is one of the major problem such drug molecules. The aqueous solubility of poorly soluble drugs is required to be improved for formulation development and analysis. The concept of mixed solvency was proposed with the opinion that almost all substances whether solid, liquid or gas; have the solubilizing power and can increase the aqueous solubility of less soluble drug entities [1-3].

Almost upto 40% of new chemical entities (NCE's) discovered are having poor solubility that leads to the complication of delivery of these molecules as well as several others. In relation to highly soluble compounds, the compounds with relatively lower solubility index manifest *in vivo* consequences such as decreased bioavailability, increased chances of food effects, incomplete release from dosage form or higher inter-patient variability in drug effects. There are certain limitations with the formulation of these compounds for *in vitro* release studies such as limited choice of delivery technology, complex dissolution testing and poor absorption *in vitro*. The concept mixed solvency was proposed to overcome such insolubility effects with drug or their formulations. The concept basically means to increase solubility using blends of solubilizing agents that are thought to work synergistically or having additive solubilizing effect. This method when used for formulation of dosage form can also reduce the concentration of individual solubilizers so that the chances of side effects with higher concentration of solubilizers would be minimized [4-8]. Weaker solvents can be made stronger using proper solubilizers. Hydrotropy is another concept of cosolvency in which it has been used to dissolve diclofenac sodium by using PEG 400, PEG 6000 and PEG 8000 melted at about 60ºC. Melted Ibuprofen and niacinmide also dissolve diclofenac sodium. In supercritical fluid extraction technique liquefied CO_2 is used to dissolve several insoluble compounds which show the solvency power to such substances [9].

Hydrotropic agents are such agents that are used to increase the solubility of poorly water soluble compounds. Hydrotropy and mixed solvency are widely useful solubility enhancing phenomenon and has been found to improve the aqueous solubility of several drugs [10-15].

2. MATERIALS AND METHODS

Salicylic acid was obtained as a gift sample from Alkem Laboratory Ltd. (Mumbai, India). All other chemicals and solvents used for analysis were of AR grade. A UV-Visible spectrophotometer (Shimadzu, Model-UV 160 A) with 1cm matched silica cells were used for spectrophotometric determination.

2.1 Analysis of salicylic acid bulk sample by I.P. method

As per method of I.P., 0.3 g salicylic acid (accurately weighed) sample was dissolved in 50 ml ethanol (organic solvent). The same was then titrated against sodium hydroxide (0.1 M) after adding 20 ml water using phenol-red as indicator.

2.2 Analysis of salicylic acid bulk sample by proposed methods

2.2.1 Titrimetric analysis

A blend of sodium citrate, glycerin, urea, PEG 400, PEG 300 and PEG 4000 was prepared in a conical flask and 0.3 g salicylic acid (accurately weighed) sample was dissolved by shaking for approximately 5 minutes. It was then titrated against 0.1 M sodium hydroxide using phenol-red as indicator.

2.2.2 Preparation of calibration curve of salicylic acid

100 mg salicylic acid was accurately weighed and solubilized in blend (20 ml) of solubilizing agents in a volumetric flask (100 ml). Volume was made up with distilled water. This stock solution was divided into different dilutions of 10, 20, 30, 40 and 50 µg/ml sample and absorbances were recorded at 296 nm against blank.

2.2.3 Spectrophotometric method

For estimation of salicylic acid bulk sample by spectrophotometric method, 100 mg salicylic acid sample was dissolved in blend of solubilizing agents (10 ml) in 100 ml volumetric flask. Volume was made up with distilled water.

3. RESULTS AND DISCUSSION

The results obtained from the proposed method were compared with that obtained from I.P. method and results with improved solubility were obtained (Table 1). The amount of salicylic acid in sample as estimated by I.P. method using organic solvent (ethanol) was found to be 101.54±0.626. On the other hand the amount of salicylic acid estimated using the blend of sodium citrate, glycerin, urea, PEG 400, PEG 300 and PEG 4000 by titrimetric analysis was 101.93±1.828 while that estimated through spectrophotometric analysis was 100.99±0.999.

Table 1: Analysis of salicylic acid and bulk sample with statistical evaluation

Methods of analysis	Bulk drug analyzed (mg)	% Drug estimated (Mean ± S.D.)	% Coefficient of variation	Std. error
I.P. method	300	100.54±0.626	0.623	0.361
Titrimetric method	300	101.93±1.828	1.793	1.055
Spectrophotometric method	300	100.99±0.999	0.989	0.577

4. CONCLUSION

The method prescribed in I.P. is useful but have definite limitations such as use of organic solvents for titrimetric analysis. Organic solvents on the other hand possess limitations such as poor solubility and toxicity. In order to avoid the use of organic solvents for titrimetric analysis the concept of mixed solvency using the blends of solubilizing agents can be more useful and safer. The results obtained from proposed methods clearly indicate improved solubility of salicylic acid. The usefulness of method could be found in the results and data obtained. The method proposed and employed in present experiment is accurate, precise and reproducible and at the same time simple and cost effective. It can be easily employed for routine analysis of bulk samples of drugs in pharmaceutical field. Such methods provide good scope for poorly soluble drugs and their titrimetric a well spectrophotometric analysis.

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