New quantitative estimation of benzoic acid bulk sample using calcium disodium edetate as hydrotropic solubilizing agent

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In the present investigation, hydrotropic solubilization technique has been employed to solubilize the slightly water soluble topical antifungal drug, benzoic acid (by 1.0 M calcium disodium edetate solution), for its titrimetric analysis. There was more than 15 fold enhancement in aqueous solubility of benzoic acid in 1.0 M calcium disodium edetate solution as compared to the solubility in distilled water. The hydrotropic agent did not interfere in the analysis. The proposed method is new, simple, accurate and reproducible. Statistical data proved the accuracy, reproducibility and precision of the proposed method.

Keywords: Hydrotropy, Benzoic acid, Calcium disodium edetate, Titrimetry

INTRODUCTION
Increasing the aqueous solubility of insoluble and slightly soluble drug is of major importance. 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 ‘hydrotropes’. Sodium benzoate, sodium salicylate, sodium acetate, sodium ascorbate, niacinamide, sodium citrate, urea are the most popular examples of hydrotropic agents which have been used to solubilize a large number of poorly water-soluble compounds [1-19]. Hydrotropic solution of calcium disodium edetate was employed as solubilizing agent to analyze slightly water soluble drug, benzoic acid by titrimetric estimation.

There was tremendous increase in solubility of benzoic acid (a widely used topical antifungal drug) in 1.0 M calcium disodium edetate solution. Therefore, it was thought worthwhile to solubilize the drug with the help of calcium disodium edetate solution to carry out the estimation.

MATERIALS AND METHODS

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

Preliminary solubility studies of drug

Solubility of benzoic acid was determined in distilled water and 1.0 M calcium disodium edetate solution at 27±1°C. Solubility was found to be increased by more than 15 fold in 1.0 M calcium disodium edetate solution as compared to the solubility in distilled water.


Accurately weighed (1.0 gm) benzoic acid bulk sample was dissolved in 15 ml of warm ethanol (95%) previously neutralized to phenolphthalein solution, 20 ml of distilled water was added to it and it was titrated with 0.5 M sodium hydroxide solution using phenolphthalein solution as indicator. Necessary blank determination was adjusted to get drug content (Table 1).
Table 1. Analysis data of benzoic acid bulk sample with statistical evaluation (n=3)

<table>
<thead>
<tr>
<th>Amount of bulk drug taken (mg)</th>
<th>Method of analysis</th>
<th>Percent drug estimated (mean ± SD)</th>
<th>Coefficient of variation (%)</th>
<th>Standard error</th>
</tr>
</thead>
<tbody>
<tr>
<td>1000.0</td>
<td>I.P.M.</td>
<td>101.32±1.082</td>
<td>1.067</td>
<td>0.625</td>
</tr>
<tr>
<td>200.0</td>
<td>P.T.M.</td>
<td>100.89±0.747</td>
<td>0.740</td>
<td>0.431</td>
</tr>
</tbody>
</table>

Where, I.P.M. - Indian Pharmacopoeial Method, P.T.M. - Proposed Titrimetric Method

Analysis of benzoic acid bulk sample by proposed titrimetric method

In the proposed method accurately weighed (200 mg) benzoic acid bulk sample was solubilized in 20 ml of 1.0 M calcium disodium edetate solution by shaking for about 5 minutes and it was titrated with 0.5 M sodium hydroxide solution using phenolphthalein solution as indicator. Necessary blank determination was adjusted to get drug content (Table 1).

RESULTS AND DISCUSSION

Results of solubility studies of benzoic acid revealed that enhancement in solubility in 1.0 M calcium disodium edetate solution was more than 15 fold as compared to its solubility in distilled water.

It is evident from Table 1 the values of mean percent of benzoic acid, estimated in the drug sample were 101.32 and 100.89 by the Indian Pharmacopoeial and proposed titrimetric methods respectively. The amounts of drug estimated by Indian pharmacopoeial and proposed titrimetric methods (Table 1) are very close to each other and very near to 100.0, indicating the accuracy of the proposed method of analysis. This indicates the accuracy of the proposed method. Low values of standard deviation, percent coefficient of variation and standard error (Table 1), further validated the proposed titrimetric method.

CONCLUSION

It was, thus, concluded that the proposed method is new, simple, cost effective, accurate, safe and precise. It can be successfully employed in the routine analysis of benzoic acid in bulk drug sample. No organic solvent were employed. There is good scope for other poorly water-soluble drugs which may be tried to get solubilized in 1.0 M calcium disodium edetate solution (as hydrotropic agent) to carry out their titrimetric and/or spectrophotometric analysis excluding the use of costlier and unsafe organic solvents. The proposed method is worth adopting in the respective pharmacopoeia.

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REFERENCES

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