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RESEARCH PAPER

# "SOLID AS SOLVENT"- NOVEL SPECTROPHOTOMETRIC ANALYSIS OF FRUSEMIDE TABLETS USING PHENOL AS SOLVENT

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**The pollution and toxicity caused by most of the organic solvents is a big challenge. Using mixed-solvency concept, innumerable solvent systems can be developed based on an assumption that each substance possesses solubilizing power which can be further explored to develop eco-friendly methods in the area of drug estimations and formulations precluding the use of toxic organic solvents. The present research work provides an eco-friendly method to estimate spectrophotometrically, the poorly water soluble drug frusemide in tablet formulation. For this purpose, melted phenol (50-60°C) was utilized to extract out (dissolve) the drug from powder of frusemide tablets. Absorbances of standard solutions containing 20, 40, 60, 80 and 100 μg/ml were noted at 330 nm against reagent blanks to obtain calibration curve. Recovery studies and statistical data proved the accuracy, reproducibility and precision of the proposed method. The presence of tablet excipients and phenol did not interfere in the spectrophotometric estimation of frusemide at 330 nm. Proposed method was found to be novel, economic, eco-friendly, rapid, free from toxicity of organic solvent, accurate and reproducible.**

**Key words:** Mixed-solvency concept, Frusemide, Phenol, Spectrophotometric analysis.

## INTRODUCTION

Majority of drugs show the problem of poor solubility, whether in the case of their analytical estimations or in the field of liquid dosage forms in the form of solutions. Commonly used organic solvents for spectrophotometric analysis of water insoluble drugs include methanol, ethanol, chloroform, benzene, dichloromethane, dimethyl formamide, acetonitrile, ethyl acetate, toluene, carbon tetrachloride, acetone, hexane etc. The main drawbacks of organic solvents include high cost, toxicity and pollution. Organic solvents possess different adverse effects caused by single exposure like dermatitis, headache, drowsiness, nausea, eye irritation and long term exposure causes serious effects such as neurological disorders, chronic renal failure, liver damage, necrosis, mutagenesis disorder. They should be replaced by other eco-friendly alternative sources. The pollution and toxicity caused by most of the organic solvents is a big challenge. The researchers are doing much work to give eco-friendly solutions for this challenge. By application of mixed-solvency concept, innumerable solvent systems can be developed (Maheshwari, 2009a; 2009b; 2010a).

The present research work also provides an eco-friendly method to estimate spectrophotometrically, the frusemide drug in tablet formulations without the help of organic solvent. There are only few safe liquids such as propylene glycol, glycerin, tweens, ethanol, liquid polyethylene glycols (like PEG 200, 300 etc) which are employed by pharmaceutical industries in various dosage forms for making

solution type dosage forms of poorly soluble drugs. Mixed solvency concept provides a means to develop innumerable solvent systems employing combination of the pharmaceutical excipients in small concentrations.

By combining the excipients, additive solvent actions and synergistic solvent actions can be obtained. The problem of toxicity issue due to high concentration of a solvent can be solved in this manner (Maheshwari, 2010b; Maheshwari and Shilpkar, 2012; Maheshwari *et al* 2011a; 2011b; 2012; 2013; Maheshwari and Rajagopalan, 2011; 2012; Bhawsar *et al* 2011; Maheshwari and Karawande, 2013; Agrawal and Maheshwari, 2011; Sree Giri Prasad *et al* 2012; Chandan and Maheshwari, 2013; Vijayaranga Vittal *et al* 2012; Pawar *et al* 2013; Soni *et al* 2014).

The present study supports that solids can also be wisely used to act as solvent precluding the use of organic solvents and describes the application of solvent character of melted phenol (at 50-60°C) for spectrophotometric estimation of frusemide tablets.

## MATERIALS AND METHODS

Frusemide was a generous gift by M/S IPCA Laboratories Limited, Ratlam (India). All other chemicals used were of analytical grade. Commercial tablets of frusemide were procured from local market. A Shimadzu-1700 UV visible spectrophotometer with 1 cm matched silica cells was used for spectrophotometric analysis.

### Preparation of calibration curve

In order to prepare a calibration curve of frusemide, 50 mg of frusemide standard drug was placed in a 500 ml volumetric flask. Then, 10 g of phenol crystals were added and the flask was heated on a water bath (at 50-60°C) to melt the phenol. Then, the flask was shaken to dissolve the drug in the melted phenol. About 400 ml of distilled water (at 50-60°C) was poured in the volumetric flask and the contents were shaken for about 5 min to give a clear solution.

The flask was allowed to cool to room temperature and sufficient distilled water was added to make up the volume (500 ml). From this stock solution (100 $\mu$g/ml), standard solutions containing 20, 40, 60, 80 and 100 $\mu$g/ml were prepared by suitable dilution with distilled water. The absorbances of these solutions were noted at 330 nm against respective reagent blank.

### Preliminary solubility studies

Preliminary solubility studies for frusemide were carried out to observe its solubility behavior. To determine the solubility of the drug in distilled water at room temperature, sufficient excess amount of the drug was added to a 25 ml capacity vial containing distilled water. After putting the vial cap and applying the aluminium seal, the vial was shaken mechanically for 12 h at room temperature (27±1°C) in an orbital flask shaker (Khera Instrument Pvt. Limited, India). The solution was allowed to equilibrate undisturbed for 24 h and then, filtration was done through Whatman filter paper # 41. The filtrate was appropriately diluted with distilled water to measure the absorbance at 330 nm.

In order to determine the approximate solubility of drug in melted phenol, 1 g phenol was transferred to a 10 ml volumetric flask. The weight of the stoppered volumetric flask (initial weight) was noted. Then, the flask was heated on the water bath to melt the phenol (at 50-60°C). About 5 mg of drug was added and the flask was shaken to solubilize the drug. As soon as a clear solution was obtained, again about 5 mg of drug was added and the flask was shaken to solubilize the drug to get a clear solution. Same process was repeated till the melted phenol (at 50-60°C) was saturated with drug. Again the weight of volumetric flask was noted (final weight). Difference in these two weights (initial and final) gave the approximate amount of drug which saturates (nearly) one gram of melted phenol (at 50-60°C).

### Proposed method of analysis

The weight of 20 tablets of frusemide (tablet formulation I) was determined. Then, the tablets were crushed and converted to a fine powder. Tablet powder equivalent to 50 mg frusemide was transferred to a 500 ml volumetric flask and 10 g phenol was added. The flask was heated on a water bath (at 50-60°C) to melt the phenol. Then the flask was shaken vigorously for 10 min by hand shaking to extract (solubilize) the drug from the tablet powder. Then, 400 ml distilled water (at 50-60°C) was added and the flask was again shaken for 5 min by hand to solubilize phenol and drug in water. The flask was allowed to cool to room temperature and sufficient distilled water was added to make up the volume (500 ml). Filtration was carried out through Whatman filter paper #41 to remove the tablet excipients. Ten ml filtrate was diluted to 50 ml with distilled water and the absorbance was

noted at 330 nm against the reagent blank. The drug content was calculated using the calibration curve. Same procedure was repeated for tablet formulation II. Results of analysis of frusemide tablets with statistical evaluation are tabulated in **Table 1**.

**Table 1.** Analysis data of frusemide tablet formulations with statistical evaluation (n=3)

| Tablet formulation | Label claim (mg/tablet) | Percent drug estimated (mean±SD) | Percent coefficient of variation | Standard error |
|---|---|---|---|---|
| I | 40 | 99.81±1.717 | 1.720 | 0.991 |
| II | 40 | 98.12±0.886 | 0.903 | 0.512 |

**Recovery studies**

In order to validate the proposed analytical method, recovery studies were performed for which standard frusemide drug sample was added (15 mg and 30 mg , separately) to the pre-analyzed tablet powder equivalent to 50 mg frusemide and the drug content was determined by the proposed method. The results of analysis with statistical evaluation are reported in the **Table 2**.

**Table 2.** Results of recovery studies with statistical evaluation (n=3)

| Tablet formulation | Drug in pre-analyzed tablet powder (mg) | Amount of standard drug added (mg) | % Recovery estimated (mean ± SD) | Percent coefficient of variation | Standard error |
|---|---|---|---|---|---|
| I | 50 | 15 | 100.88±1.626 | 1.612 | 0.939 |
| I | 50 | 30 | 100.07±1.898 | 1.897 | 1.096 |
| II | 50 | 15 | 99.11 ± 1.111 | 1.121 | 0.641 |
| II | 50 | 30 | 98.88 ± 1.552 | 1.570 | 0.896 |

## RESULTS AND DISCUSSION

The solubility of frusemide in distilled water at room temperature was found to be 0.64 mg/ml. The solubility of frusemide in melted phenol (at 50-60°C) was more than 14 mg/g of phenol. It is evident from **Table 1** that the percent drug estimated in tablet formulation I and II were 99.81±1.717 and 98.12±0.886, respectively. The values are very close to 100.0 indicating the accuracy of the proposed analytical method. Small values of statistical parameters *viz* standard deviation, percent coefficient of variation and standard error further validated the method.

Further, **Table 2** showed that the range of percent recoveries varied from 98.88±1.552 to 100.88±1.626 which are again very close to 100.0, indicating the accuracy of the proposed method. The accuracy of the proposed analytical method is further supported by significantly small values of statistical parameters *viz* standard deviation, percent coefficient of variation and standard error.

## CONCLUSION

The proposed method is new, simple, environment friendly, accurate and reproducible. The proposed method can be successfully employed in the routine analysis of frusemide tablets.

Melted phenol can also be tried with other water insoluble drugs which are estimated above 300 nm. Phenol does not interfere above 300 nm. Obtained accuracy of the proposed analytical method is also indicative of the proof that the solids possess solvent character.

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