Research Article

"Solid as solvent"- Novel spectrophotometric analysis of naproxen tablets using melted phenol as solvent (Concept of mixed solvency)

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ABSTRACT

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. Maheshwari has given a nice concept, known as mixed-solvency concept. By application of this concept, innumerable solvent systems can be developed. Maheshwari is of the opinion that each substance possesses solubilizing power. He has given several eco-friendly methods in the area of drug estimations and formulations precluding the use of toxic organic solvents. The present investigation is an attempt to show that solids can also be wisely used to act as solvent precluding the use of organic solvents. Present study describes the application of solvent character of melted phenol (at 50-60°C) for spectrophotometric estimation of naproxen tablets. Solubility of naproxen in distilled water was found to be 0.09 mg/ml at room temperature. More than 140 mg of naproxen dissolved in one gram of melted phenol (at 50-60°C). In the present investigation, melted phenol (at 50-60°C) was utilized to extract out (dissolve) the drug from powder of naproxen tablets. Distilled water was used for dilution purpose. Absorbances of standard solutions containing 50,100, 150 and 200 µg/ml were noted at 331 nm against reagent blanks to obtain calibration curve. Proposed method is novel, economic, eco-friendly, rapid, free from toxicity of organic solvent, accurate and reproducible. Recovery studies and statistical data proved the accuracy, reproducibility and precision of the proposed method.

Keywords: Mixed-solvency Concept, Naproxen, Phenol, Spectrophotometric Analysis

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1. INTRODUCTION

A large number of organic solvents like ethanol, methanol, ethylacetate, toluene, chloroform,dimethylformamide, acetonitrile, benzene, dichloromethane, carbon tetrachloride, acetone, hexane etc. have been employed for spectrophotometric estimation of poorly water-soluble drugs. Drawbacks of organic solvents include higher cost, toxicity and pollution. Organic solvents have innumerous 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 alternativesources. The present investigation is an attempt to show that solids can also be wisely used to act as solvent precluding the use of organic solvents.

Maheshwari has proposed the mixed-solvency concept [1-5]. The mixed solvency concept states that all substances whether liquid, gas or solid possess solubilizing power. In order to improve aqueous solubility of a poorly water-soluble drug, the concentrated aqueous solution containing various dissolved excipients (liquids and solids both) can give successful results [6-12]. In some of the studies by Maheshwari [1-3] it was found that additive and synergistic solvent action on the solubility of drug could be obtained by using aqueous

solutions containing different excipients (liquids and solids both). Mixed-solvency concept shall be helpful to formulate various dosage forms of insoluble drugs utilizing safe concentrations of excipients for solubilization.

In the present investigation, melted phenol (at 50-60°C) has been used to solubilize a highly water insoluble drug, naproxen, from its tablet powder for spectrophotometric analysis at 331 nm precluding the use of organic solvent (**Fig. 1**). Melted phenol (at 50-60°C) possesses very good solvent property for naproxen (solubility >140 mg/gm of phenol). Tablet excipients and phenol did not interfere in the spectrophotometric analysis at 331 nm. Phenol does not interfere in spectrophotometric analysis above 300 nm.

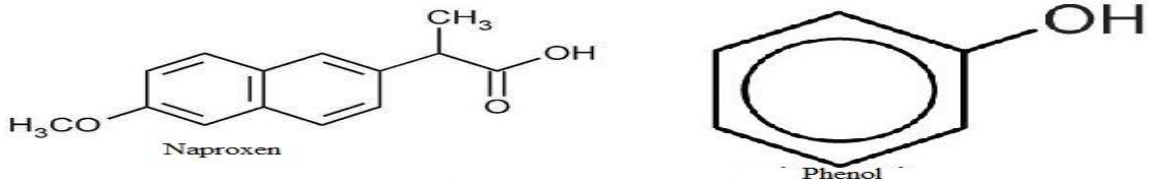

Figure 1 Structure of phenol and naproxen

2. MATERIALS AND METHODS

Naproxen bulk drug sample was a generous gift by M/S Elder Pharmaceuticals Limited, Mumbai (India). All other chemicals used were of analytical grade. Commercial tablets of naproxen were procured from local market.

A Shimadzu-1700 UV visible spectrophotometer with 1 cm matched silica cells was used for spectrophotometric analysis.

2.1 Calibration curve

In order to prepare a calibration curve of naproxen, 100 mg of naproxen standard drug was placed in a 500 ml volumetric flask. Then, 10 gram 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 (200 µg/ml), standard solutions containing 50, 100 and 150 µg/ml were prepared by suitable dilution with distilled water. The absorbances of these solutions (50, 100, 150 and 200 µg/ml) were noted at 331 nm against respective reagent blank.

2.2 Preliminary solubility studies

Preliminary solubility studies for naproxen 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 hours at room temperature in an orbital flask shaker (Khera Instrument Pvt. Ltd., India). The solution was allowed to equilibrate for 24 hours undisturbed and then, filtration was done through Whatmann filter paper # 41.The filtrate was appropriately diluted with distilled water to measure the absorbance at 331 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 stopered 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).

2.3 Proposed method of analysis

The weight of 20 tablets of naproxen (tablet formulation I) was determined. Then, the tablets were crushed and converted to a fine powder. Tablet powder equivalent to 50 mg naproxen 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. The absorbance of the filtrate was noted at 331 nm against the reagent blank. The drug content was calculated using the calibration curve. Same procedure was repeated for tablet formulation II. (**Table 1**) shows the results of analysis of naproxen tablets with statistical evaluation.

2.4 Recovery studies

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

Table 1: Analysis data of naproxen 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	250	99.09 ± 1.229	1.240	0.710
II	750	101.02 ± 0.729	0.722	0.421

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	98.32±1.617	1.645	0.934
I	50	30	98.86±1.921	1.943	1.109
II	50	15	99.49 ± 1.107	1.113	0.639
II	50	30	100.12±0.929	0.928	0.536

3. RESULTS AND DISCUSSION

The solubility of naproxen in distilled water at room temperature was found to be 0.09 mg/ml. The solubility of naproxen in melted phenol (at 50-60°C) was more than 140 mg/gm of phenol.

The values of per cent drug estimated by the proposed method (table 1) were found to be 99.09±1.229 and 101.02±0.729 for formulation I and II, respectively. These values are very close to 100.0 indicating the accuracy of the proposed analytical method. Very low values of standard deviations (1.229 and 0.729 for formulation I and II, respectively), per cent coefficient of variation (1.240 and 0.722 for formulation I and II, respectively) and standard error (0.710 and 0.421 for formulation I and II, respectively) support the accuracy of the proposed analytical method. Further, table 2 shows that the range of percent recoveries varied from 98.32±1.617 to 100.12±0.929 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 (table 2).

4. CONCLUSION

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

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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REFERENCES

1. Maheshwari RK. Solubilization of ibuprofen by mixed solvency approach. The Indian Pharmacist. 2009a; 8: 81-84.
2. Maheshwari RK. Mixed- solvency – A novel concept for solubilization of poorly water-soluble drugs. Delving J Tech Eng Sci. 2009b; 1: 39-43.
3. Maheshwari RK. Potentiation of solvent character by mixed solvency concept: A novel concept of solubilization. Journal of Pharmacy Research. 2010a; 3: 411-413.
4. Maheshwari RK. Mixed-solvency approach"-Boon for solubilization of poorly soluble drugs. Asian J Pharm. 2010b; 4: 60-63.
5. Maheshwari RK. Solid as solvent-Novel spectrophotometric analysis of satranidazole tablets using phenol as solvent. The Indian Pharmacist. 2014a; 12: 37-40.
6. Maheshwari RK. Gupta S, Gharia A. et al. Simple eco-friendly spectrophotometric estimation of tinidazole tablets by application of mixed-solvency technique. Bulletin of Pharmaceutical Research. 2011; 1: 22-25.
7. Maheshwari RK, Rajagopalan R. Formulation and evaluation of paracetamol syrup made by mixed-solvency concept. Der Pharmacia Lettre. 2012a; 4: 170-174.
8. Maheshwari RK, Shilpkar R. Formulation development and evaluation of injection of poorly soluble drug using mixed solvency concept. International Journal of Pharma and Biosciences. 2012b; 3: 179-189.
9. Maheshwari RK. Solid as solvent-Novel spectrophotometric analysis of frusemide tablets using phenol as solvent. Bulletin of Pharmaceutical Research. 2014b; 4: 104-107.
10. Maheshwari RK, Fouzdar A. Solid as solvent-Novel approach for spectrophotometric estimation of solid dosage form of nalidixic acid using solids (eutectic liquid of phenol and niacinamide) as solubilizing agents (mixed solvency concept). European Journal of Biomedical and Pharmaceutical Sciences. 2014c; 1: 424-430.
11. Maheshwari RK. Solid as solvent-Novel spectrophotometric analysis of tinidazole tablets using melted phenol as solvent. Asian Journal of Pharmaceutical Research. 2015; 5: 21-24.
12. Soni LK, Solanki SS, Maheshwari RK. Solubilization of poorly water soluble drug using mixed solvency approach for aqueous injection. British Journal of Pharmaceutical Research. 2014d; 4: 549-568.