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NOVEL APPROACH FOR SPECTROPHOTOMETRIC ESTIMATION OF NAPROXEN IN TABLET DOSAGE FORM USING SOLIDS (EUTECTIC LIQUID OF PHENOL AND NIACINAMIDE) AS SOLUBILIZING AGENT (MIXED SOLVENCY CONCEPT)

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ABSTRACT

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 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 alternative sources. 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. The main objective of the present study is to demonstrate the solvent action of solids. In the present study, a eutectic liquid obtained by triturating phenol crystals and niacinamide in 25:10 ratio on weight basis was employed to extract (dissolve) naproxen drug from fine powder of tablets. Dilution was made with distilled water to carry out spectrophotometric estimation at 331 nm without the help of organic solvent. The solubility of naproxen in distilled water at room temperature was found to be 0.09 mg/ml. The solubility of naproxen in PNM 2510 was more than 90 mg per ml of PNM 2510. 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. The presence of tablet excipients, phenol and niacinamide did not interfere in the spectrophotometric estimation at 331 nm. Phenol and niacinamide do not interfere above 300 nm.

Key words: Mixed-solvency concept, naproxen, phenol, niacinamide, spectrophotometric analysis, eutectic liquid.

INTRODUCTION

There are very few safe liquids e g 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, proposed by Maheshwari[1-3] provides a means to develop innumerable solvent systems employing combination of the pharmaceutical excipients in small concentrations. Each substance present on the earth has got solubilizing power. 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. The solubility of a large number of poorly soluble drugs has been enhanced by mixed solvency concept [1-20].

Commonly used organic solvents for spectrophotometric analysis of water insoluble drugs include methanol, ethanol, chloroform, benzene, dichloromethane, dimethyl formamide, actonitrile, ethyl acetate, toluene, carbon tetrachloride, acetone, hexane etc. The main drawbacks of organic solvents include high 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 alternative sources. The present investigation

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is an attempt to show that solids can also be wisely used to act as solvent precluding the use of organic solvents. In a separate study, author has attempted soxhelation using phenol as solvent. The vapours of boiling phenol got condensed in extraction chamber to effect the extraction of active constituents from powder of crude drugs.

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. The main objective of the present study is to demonstrate the solvent action of solids. In the present study, a eutectic liquid obtained by triturating phenol crystals and niacinamide in 25:10 ratio on weight basis was employed to extract (dissolve) naproxen drug from fine powder of tablets. Dilution was made with distilled water to carry out spectrophotometric estimation at 331 nm without the help of organic solvent. 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. The presence of tablet excipients, phenol and niacinamide did not interfere in the spectrophotometric estimation at 331 nm. Phenol and niacinamide do not interfere above 300 nm.

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.

Preparation of eutectic liquid

Phenol and niacinamide were triturated in 25:10 ratio on weight basis to obtain a eutectic liquid (PNM 2510).

Calibration curve

Accurately weighed 100 mg of naproxen standard drug was transferred to a 10 ml volumetric flask. Five ml of PNM 2510 was added and the flask was shaken to dissolve the drug. Then the volume was made up to 10 ml with PNM 2510 and the flask was shaken to homogenize the contents. One ml of this solution was transferred to a 100 ml volumetric flask and about 80 ml of distilled water was added and the flask was shaken for 5 min to solubilise the contents. Then, the volume was made up to 100 ml with distilled water to get a stock solution 100 µg/ml drug. Similarly, 1.2, 1.4, 1.6 and 1.8 ml of drug solution in PNM 2510 were used to obtain standard solutions containing 120, 140, 160 and 180 µg/ml drug. The absorbances of these standard solutions were noted at 331 nm against respective reagent blanks.

Preliminary solubility studies

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 PNM 2510, 1 ml of PNM 2510 was transferred to a 10 ml volumetric flask. The weight of the stopered volumetric flask (initial weight) was noted. 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 liquid 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 ml of PNM 2510.

Proposed method of analysis

Twenty tablets of tablet formulation I were weighed and crushed to get a fine powder. Tablet powder equivalent to 100 mg naproxen was transferred to a 10 ml volumetric flask. Then, 8 ml of PNM 2510 was transferred to it and the flask was shaken vigorously for 10 min by hand shaking to extract (solubilize) the drug from the tablet powder. Then, volume was made up to 10 ml with PNM 2510 and the flask was shaken for few min to homogenize the contents. After this, 1 ml of the liquid of the flask was transferred to a 100 ml volumetric flask and 80 ml of distilled water, was added and the flask was again shaken for 5 min by hand to solubilize phenol, niacinamide and drug in the distilled water. Then, sufficient distilled water was added to make up the volume up to 100 ml. Filtration was carried out through Whatmann filter paper # 41 to remove the tablet excipients. Then, 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. The results of analysis are reported in table 1.

Recovery studies

To perform the recovery studies, standard naproxen drug was added (25 mg and 50 mg , separately) to the pre-analyzed tablet powder equivalent to 100 mg naproxen and the drug content was determined by the proposed method. Results of analysis are reported in table 2 with statistical evaluation.

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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	750	98.39 ± 1.187	1.206	0.685
II	250	98.01 ± 1.886	1.924	1.089

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	100	25	98.88 ± 0.467	0.472	0.270
I	100	50	99.44 ±1.333	1.340	0.770
II	100	25	101.31 ± 1.744	1.721	1.007
II	100	50	100.29±1.084	1.081	0.626

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 PNM 2510 was more than 90 mg per ml of PNM 2510.

It is evident from table 1 that the percent drug estimated in tablet formulation I and II were 98.39±1.187 and 98.01±1.886, 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 shows that the percent recoveries varied from 98.88±0.467 to 101.31±1.744, which are again very close to 100.0, indicating the accuracy of the proposed method which is further supported by significantly small values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error (Table 2).

CONCLUSION

The proposed method is new, simple, environment friendly, accurate and reproducible. The proposed method can be successfully employed in the routine analysis of naproxen tablets. PNM 2510 can also be tried with other water insoluble drugs which are estimated above 300 nm. Phenol and niacinamide do not interfere above 300 nm.

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