“Solid as Solvent”- Novel spectrophotometric analysis of metronidazole tablets using solids (Eutectic Liquid of Phenol and Metformin Hydrochloride) As Solubilizing Agents (Mixed Solvency Concept)

RK Maheshwari, Priyanka Vaswani, Rohit Adhav, Toshika Jain

Abstract

The present experiment is a research to show that solid can also be used as solvents in various spectrophotometric methods. In present study we are using eutectic mixture of Phenol and Metformin hydrochloride (PMHCl 41) which is obtained by trituration of crystals of phenol and metformin hydrochloride employed to dissolve Metronidazole from fine tablet triturate powder. Distilled water is used for dilution to carry out spectrophotometric analysis at 320 nm without using any toxic and carcinogenic organic solvents. The solubility of Metronidazole in distilled water at room temperature was found to be 7.28 mg/ml while the solubility of Metronidazole in PMHCl 41 was more than 130 mg/ml. This new miraculous approach can be used in day to day spectrophotometric analysis of compounds. The corresponding approach is accurate and reproducible. The method provides safe and ecofriendly way for the estimation of the compound. The accuracy, reproducibility and precision of the method were confirmed by recovery studies and statistical data. The presence of excipients, eutectic mixture (PMHCl 41) did not interfere in spectrophotometric analysis estimation at 320 nm. PMHCl 41 does not interfere above 300 nm. Proposed method was found to be novel, economic, eco-friendly, rapid, free from toxicity of organic solvent, accurate and reproducible.

Keywords: Mixed Solvency Concept, Metronidazole, Phenol, Metformin hydrochloride, Spectrophotometric Analysis, Eutectic Liquid.

Introduction

Majority of the drugs show the problem of poor solubility, whether in the case of their analytical estimations or in the field of liquid dosage form in the form of solutions. All substances present on the earth possess solubilizing properties. Each substance shall show solubilizing power for some solutes and non-solubilizing power for other. By combining the excipients, additive solvent actions and synergistic solvent actions can be obtained. For water insoluble drugs, commonly used organic solvents for spectrophotometric analysis includes Methanol, Ethanol, Chloroform, Benzene, Dichloromethane, Dimethyl formamide, Acetonitrile, Ethyl acetate, Toluene, Carbon tetrachloride, Acetone, Hexane, etc. The main problems 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 eco-friendly and alternative sources. The use of “solids as solvents” shall prove a boon in pharmaceutical field.

The solvents action of solids can be demonstrated nicely by mixed solvency concept. By application of this concept innumerable solvent systems can be developed. The advantage of mixed solvency concept is employing combination of pharmaceutical excipients in small concentration as a result of which toxicity is reduced.

The present research is an attempt to prove that solid can also be wisely used to act as solvents, precluding the use of organic solvents. The main objective of present study is to demonstrate solvent action of solids. Solid excipients can be nicely employed as solubilizers in the development of pharmaceutical dosage dosage forms in solution form of poorly soluble drugs.
Materials and Methods
Metronidazole bulk drug sample was generous gift by M/S Alkem Laboratories Limited, Mumbai (India). Metformin hydrochloride was generous gift from M/S IPCA Laboratories Ltd., Ratlam (India).
Commercial tablets of Metronidazole were procured from local market. Other chemicals used for research were of analytical grade.
A Shimadzu-1700 UV Visible spectrophotometer with 1 cm matched silica cell was used for spectrophotometric analysis.

Preparation of Eutectic Liquid
Phenol and Metformin hydrochloride were triturated in (4:1) ratio of their respective weight quantity and eutectic liquid (PMHCl 41) was prepared.

Calibration Curve
Accurately weighed 50mg of Metronidazole standard drug was transferred to a 500ml volumetric flask and 10ml of PMHCL 41 was added to it. The flask was shaken to solubilize the drug. Then, about 400 ml distilled water was added and the flask was shaken for 5min to solubilize the contents. The volume was made up to the mark with sufficient distilled water. Filtration was carried out through Whatmann filter paper #41 to remove the tablet excipients. Ten ml of the filtrate was diluted to 50 ml with distilled water. Then, the absorbance of the filtrate was noted at 320 nm against respective reagent blank. Using the calibration curve, the drug content was calculated. Same procedure was repeated for tablet formulation II. The results of analysis were reported as in table 1.

Recovery Studies
The recovery studies were performed in which standard Metronidazole drug was added (15 mg and 30 mg, respectively) to the pre-analyzed tablet powder equivalent to 50 mg Metronidazole and drug content was determined by the proposed method. Results of analysis were reported as in table 2 with statistical evaluation.

Results and Discussion
The Solubility of Metronidazole in distilled water at the room temperature was found to be 7.28 mg/ml. The solubility of Metronidazole in PMHCl 41 was more than 130 mg/ml. It is evident from table 1 that the percent drug estimation in tablet formulation I and II were 98.67 ± 1.228 and 100.28 ± 1.972, respectively. The values are very close to 100, indicating the accuracy and precision of the proposed analytical method. In addition to this, the table 2 emphasizes on the percent recoveries studies which varies from 98.84 ± 1.777 to 100.76 ± 0.924 which are again very close to 100.00, indicating the accuracy and precision of the proposed method. Proposed analytical technique is further supported remarkably by small values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error as indicated in table 2.

Conclusion
The evidence that supports the solvency of Metronidazole in Eutectic liquid of phenol and Metformin Hydrochloride in 4:1 ratio on weight basis was suitably demonstrated by the above research. This supports that the extraction (dissolution) of Metronidazole from fine powder of tablets can be carried out by use of “solid as solvent concept”. The presence of PMHCl 41 does not interfere in spectrophotometric estimation at 320nm. Phenol and metformin hydrochloride do not interfere above 300 nm. The proposed research opens the new dimensions of eco-friendly and safe methods of estimations in pharmaceutical field. The research evokes and builds potential for use of such novel methods for use of “solid as solvents”.

References