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Research Paper

Solid as Solvent" - Novel Spectrophotometric Analysis of Piroxicam Tablets Using Solids (Eutectic Liquid of Phenol and Metformin Hydrochloride) As Solubilizing Agents (Mixed Solvency Concept)

R K Maheshwari, Sunil Goyal*, Rohit Adhav, Priyanka Vaswani

Department of Pharmacy, Shri G S Institute of Technology and Science, Indore 452003, Madhya Pradesh, India

Solubility enhancement of the drugs having poor solubility is a difficult task in several cases in pharmacy field. 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. In the present study, a eutectic liquid (PMHCl 41) obtained by triturating phenol crystals and metformin hydrochloride in 4:1 ratio on weight basis was employed to extract (dissolve) the piroxicam drug from fine powder of tablets. Distilled water was used for dilution purpose to carry out spectrophotometric estimation at 358 nm without utilizing any organic solvent. The solubility of piroxicam in distilled water at room temperature was found to be 0.4 mg/ml while the solubility in PMHCl 41 liquid was more than 125 mg per ml (of PMHCl 41). Proposed method is novel, free from organic solvent, accurate and reproducible. The accuracy, reproducibility and precision of the proposed method were confirmed by recovery studies and statistical data. The presence of tablet excipients, phenol and metformin hydrochloride did not interfere in the spectrophotometric estimation at 358 nm. Phenol and metformin hydrochloride do not interfere above 300 nm.

Keywords – Piroxicam, mixed-solvency concept, phenol, metformin hydrochloride, spectrophotometric analysis, eutectic liquid.

INTRODUCTION

Cosolvency, hydrotropy, micellar solubilization, complexation, pH modification and salt formation are the most frequently employed common techniques of solubility enhancement. A novel technique of solubility enhancement by use of mixed solvency concept has been proposed by Maheshwari[1-6]. All the substances (whether liquids, gases or solids) have solubilizing power. Innumerable solvent systems may be developed using mixed solvency concept. By application of mixed solvency concept[7-17], the drug loading in various pharmaceutical formulations, including NDDS, may be improved and by combining the excipients in appropriate amounts, synergistic solvent actions and additive solvent actions can be obtained and also the problem of toxicity issue due to high concentration of a solvent for desired solubility of the drug can be solved. Maheshwari[6] utilized mixed solvency concept to potentiate the solvent character of a weaker solvent. In this research work it has been shown that a weaker solvent can be made a strong solvent by

incorporation of a solid solubilizer. The solubility of frusemide in ethanol was enhanced about three fold in the presence of 15% w/v niacinamide (a solid solubilizer). Frusemide is sparingly soluble in ethanol and pharmacopoeial method requires dimethyl formamide (a class II organic solvent) for titrimetric analysis of frusemide bulk drug. In this research work, 15% w/v solution of niacinamide in ethanol was successfully employed to carry out titrimetric analysis of frusemide bulk drug, giving an ecofriendly method of analysis because ethanol is a class III organic solvent (relatively safe in comparison to dimethyl formamide). Mixed solvency concept has been nicely employed for the improvement of the solubilities of a large number of poorly soluble drugs[1-29].

Several organic solvents are employed for spectrophotometric analysis of dosage forms of poorly water soluble drugs. Methanol, ethanol, chloroform, acetonitrile, toluene, carbon tetrachloride, dichloromethane, dimethyl formamide, ethyl acetate, acetone and hexane are the most common examples of such solvents. High cost, toxicity and pollution are serious drawbacks of organic solvents. The present investigation is an attempt to show that solids can also be wisely employed for spectrophotometric estimation of poorly soluble drugs without using the organic solvents.

Present study describes the application of solvent character of eutectic liquid (PMHCl 41) of two solid solubilizers, namely, phenol and metformin hydrochloride for spectrophotometric estimation of piroxicam tablets. Piroxicam has got poor solubility in distilled water while very high solubility in a eutectic liquid of two solids, namely phenol and metformin hydrochloride. Phenol and metformin hydrochloride were employed in 4:1 ratio to give eutectic liquid, PMHCl 41. This liquid was used to act as solvent to extract out the drug, piroxicam, from the fine powder of its tablets for spectrophotometric estimation at 358 nm. Distilled water was used for dilution purpose. The solubility of the drug in distilled water is 0.4 mg/ml at room temperature while the approximate solubility in PMHCl 41 is more than 125 mg/ml. Proposed method is novel, accurate, rapid and free from toxicity of organic solvents and reproducible. Recovery studies and statistical data proved the accuracy, reproducibility and precision of the proposed method. There was no interference of tablet excipients, phenol and metformin hydrochloride at 358 nm.

Materials and methods

Piroxicam bulk drug sample was a generous gift by M/S Shree Pharmaceuticals, Indore (India). Metformin hydrochloride was generous gift from M/S IPCA Laboratories Limited, Ratlam (India).

Commercial tablets of piroxicam (Nesprex-DT of Nestor Pharmaceuticals Limited, Goa and Piroxits DT of Intas Pharmaceuticals Limited, Ahmedabad) were procured from the local market. All other chemicals used were of analytical grade

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

Preparation of eutectic liquid - Phenol and metformin hydrochloride were triturated in 4:1 ratio on weight basis to obtain a eutectic liquid (PMHCl 41).

Calibration curve- Accurately weighed 50 mg of piroxicam standard drug sample was transferred to a 500 ml volumetric flask. Eutectic liquid, PMHCl 41 (10 ml) was transferred to this volumetric flask and the volumetric flask was shaken for few minutes to obtain a clear solution. Now 400 ml of distilled water was added and the flask was shaken for about 5 minutes to get a clear solution. Sufficient of distilled water was added to make up the volume to 500 ml. In this way a stock solution of drug (100 µg/ml) was obtained. After suitable dilutions with distilled water, the standard solutions containing 5, 10, 15, 20 and 25 µg/ml of drug were prepared. Calibration curve was obtained by using the absorbances of these standard solutions, measured against their respective reagent blanks at 358 nm.

Preliminary solubility studies

The equilibrium solubility of piroxicam drug in distilled water was determined. For this, excess amount of drug sample was added to a 25 ml capacity vial containing distilled water. After putting the vial cap and applying the aluminium seal properly, the vial was shaken mechanically for 12 hours at room temperature in an orbital flask shaker (Khera Instrument Pvt. Ltd., India). The vial was kept undisturbed for 24 hours. Then, the filtration was carried out using Whatmann filter paper # 41. The filtrate was appropriately diluted with distilled water and the absorbance was noted at 358 nm. The result of solubility was computed using the calibration curve.

Then, the approximate solubility of drug was determined in the eutectic liquid. For this, 1 ml of PMHCl 41 was taken in a 10 ml volumetric flask and the weight of this flask was noted. About 5 mg of drug was added in the volumetric flask and the flask was shaken to solubilize the drug. As soon as a clear solution was obtained, again about 5 mg of drug was transferred to the flask and the flask was shaken to solubilize the drug. Same procedure was repeated till the eutectic liquid was nearly saturated with the drug (at this stage, slight turbidity was observed). Then, the final weight of the flask was noted. Difference in

these two weights provided the approximate amount of drug solubilized by 1 ml of PMHCl 41. In this way, the approximate solubility of drug in PMHCl 41was determined.

Proposed method of analysis

In order to determine the drug content, twenty tablets of tablet formulation I were weighed accurately. With the help of pestle and mortar, the tablets were crushed to get a fine powder. The powder of tablets equivalent to 50 mg piroxicam was transferred to a 500 ml volumetric flask. Ten ml of PMHCl 41 liquid was added in the flask and the flask was shaken continuously for 10 minutes manually. This step ensured the complete dissolution of piroxicam drug (present in the tablet powder taken) in the 10 ml of PMHCl 41 liquid. Then, about 400 ml of distilled water was added in the flask and the flask was shaken for 5 minutes. This step helps to retain the drug (piroxicam), phenol and metformin hydrochloride in the solution form. Then, the volume was made up to 500 ml with distilled water. After filtration through Whatmann filter paper # 41 (discarding the first few ml of the filtrate), 10 ml of the filtrate was diluted with distilled water up to 50 ml and the absorbance was noted at 358 nm against the reagent blank.

This procedure was applied thrice (n=3). Exactly the same procedure was used for assay of tablet formulation II. The drug contents were determined using the calibration curve and the results of analysis were recorded in Table 1.

Table I: Analysis data of piroxicam 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	20	101.39 ± 1.419	1.399	0.819
II	20	99.57±1.914	1.922	1.105

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	100.41±0.992	0.988	0.573
I	50	30	101.74±1.290	1.268	0.745
II	50	15	99.81 ±1.082	1.084	0.625
II	50	30	101.31±1.012	0.999	0.584

Results and Discussion

The solubility of piroxicam in distilled water at room temperature was found to be 0.4 mg/ml. The approximate solubility of piroxicam in PMHCl 41 was more than 125 mg per ml (of PMHCl 41).

It is evident from table 1, that the percent drug estimated in tablet formulation I and II were 101.39±1.419 and 99.57±1.914, 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 (table 1) further validated the method. Further, table 2 shows that the range of percent recoveries varied from 99.81±1.082 to 101.74±1.290 which are again very close to 100.0, indicating the accuracy of the proposed method. Proposed analytical technique is further supported by significantly low values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error (table 2).

Conclusion

In the present study, a eutectic liquid obtained by triturating phenol crystals and metformin hydrochloride in 4:1 ratio on weight basis was employed to extract (dissolve) piroxicam drug from fine powder of its tablets. Dilution was made with distilled water to carry out spectrophotometric estimation at 358 nm without the help of organic solvent. Proposed method is novel, 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 phenol, metformin hydrochloride and the tablet excipients did not interfere in the spectrophotometric estimation at 358 nm. Phenol and metformin hydrochloride do not interfere above 300 nm.

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REFERENCES

1. Maheshwari RK. “Mixed-solvency approach”- Boon for solubilization of poorly soluble drugs. Asian Journal of Pharmaceutics 2010; Jan-March: 60-63.
2. Maheshwari RK. Solubilization of ibuprofen by mixed solvency approach. The Indian Pharmacist 2009; 8(87): 81-84.
3. Maheshwari RK. “Mixed- solvency” – A novel concept for solubilization of poorly water-soluble drugs. Delving J. Tech. Eng. Sci. 2009;1(1): 39-43.
4. Rajesh Kumar Maheshwari, “Solid as

solvent", Novel spectrophotometric analysis of satranidazole tablets using phenol as solvent. The Indian Pharmacist 2014, vol. XII, 37-40.

5. Maheshwari RK. "Solid as solvent"-Novel spectrophotometric analysis of tinidazole tablets using melted phenol as solvent. Asian Journal of Pharmaceutical Research 2015;5(1):21-24.

6. Maheshwari RK. Potentiation of solvent character by mixed solvency concept: A novel concept of solubilization. Journal of Pharmacy Research 2010; 3(2): 411-413.

7. Maheshwari RK, Shilpkar R. Formulation development and evaluation of injection of poorly soluble drug using mixed solvency concept. International Journal of Pharma and Biosciences 2012; Vol. 3 / Issue I/ Jan-Mar: 179-189.

8. Maheshwari RK, Rajagopalan R. Formulation and evaluation of paracetamol syrup made by mixed-solvency concept. Der Pharmacia Lettre 2012; 4(1): 170-174.

9. Soni LK, Solanki SS, Maheshwari RK. Solubilization of poorly water soluble drug using mixed solvency approach for aqueous injection. British Journal of Pharmaceutical Research 2014; 4(5): 549-568

10. R. K. Maheshwari, Naveen Chaklan, Sugandha Singh, Novel pharmaceutical application of mixed solvency concept for development of solid dispersions of piroxicam, European Journal of Biomedical and Pharmaceutical Sciences 2015;1(3):578-591.

11. Maheshwari RK, Karawande VU, Application of novel concept of mixed solvency in the design and development of floating microspheres of furosemide. International journal of Pharmacy and Pharmaceutical Sciences 2013, vol.15: 167-195.

12. Agrawal A, Maheshwari RK. Formulation development and evaluation of in situ nasal gel of poorly water soluble drug using mixed solvency concept. Asian Journal of Pharmaceutics 2011; 5(3); 131-140.

13. Prashant B, Rawat S, Mahajan YY, Galgatte UC, Maheshwari RK. Formulation development and evaluation of aqueous injection of poorly soluble drug made by novel application of mixed solvency concept. International Journal of Drug Delivery 2013; vol: No. 2: 152-166.

14. Maheshwari Y, Mishra DK, Mahajan SC, Maheshwari P, Maheshwari RK, Jain J. Novel pharmaceutical application of mixed solvency in the formulation development of syrups (liquid oral solutions) of poorly water-soluble drugs. International Journal of Pharmacy 2013; 3(4): 753-758.

15. Chandna C, Maheshwari RK. Mixed solvency concept in reducing surfactant concentration of self emulsifying drug delivery systems of candesartan cilexetil using D-optimal mixture design. Asian Journal of Pharmaceutics 2013,

April-June issue: 83-91.

16. Maheshwari RK, Rajagopalan R. Formulation and evaluation of tinidazole syrup made by mixed-solvency concept. Der Pharmacia Lettre 2011; 3(6): 266-271.

17. Love Kumar Soni, Shailendra Singh Solanki, Rajesh Kumar Maheshwari. Studies on mixed solvency concept in formulation development of oral solution (syrup) of poorly water soluble drug, Journal of Harmonized Research in Pharmacy 2015;4(4):305-315.

18. R. K. Maheshwari, A. Fouzdar, "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 2014; 1(3):424-430.

19. Rajesh Kumar Maheshwari, Ravish Jain, Priya George. Formulation development and evaluation of controlled release tablets of lamotrigine using mixed solvency concept, Bulletin of Pharmaceutical Research 2015;5(1):14-19.

20. Maheshwari RK. "Solid as solvent"- Novel spectophotometric analysis of norfloxacin tablets using phenol as solvent". International Journal of Current Pharmaceutical Research 2014;6:76-78.

21. Maheshwari RK, Upadhyay N, Jain J, Patani M, Mathuria KC. New spectrophotometric estimation of naproxen tablet formulation employing mixed solvency concept (at 331 nm). International Journal of Pharmacy and Technology 2011; Vol. 3/ Issue No. 4/ 3618-3623.

22. Maheshwari RK, Gupta S, Gharia A, Garg SK, Shilpkar R. Simple eco-friendly spectrophotometric estimation of tinidazole tablets by application of mixed-solvency technique. Bulletin of Pharmaceutical Research 2011; 1(1): 22-25.

23. Bhawsar N, Maheshwari RK, Ansari A, Saktawat Y. New spectrophotometric estimation of gatifloxacin in the tablets using mixed solvency approach. International Journal of Pharmaceutical Science 2011; Vol. 2/ Issue 2/ Apr-Jun: 270-274.

24. Vijayranga G, Deveswaran R, Bharath S, Basavraj BV, Madhavan V. Development of an analytical method for spectrophotometric estimation of ketoprofen using mixed solvency approach. International Journal of Pharmaceutical Sciences and Research 2012; 4:1053-1056.

25. Maheshwari RK, Upadhyay N, Jain J, Patani M, Pandey R. New spectrophotometric analysis of gatifloxacin tablets utilizing mixed solvency

concept (at 288 nm). Der Pharmacia Lettre 2012; 4(1): 1-4.

26. Maheshwari RK, Putliwala M, Padiyar A. 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). Asian Journal of Pharmaceutical Research, 2015;5(1):25-28.

27. Maheshwari, R. K., Padiyar,A, Putliwala, M., Utilization of mixed solvency technique in spectrophotometric analysis of cefixime trihydrate tablets, International Journal of Pharmaceutical Research and Analysis 2015;5(1):01-03.

28. Rajesh Kumar Maheshwari, Masheer Ahmed Khan, Nupur Maheshwari, Neelesh Maheshwari, "Solid as solvent"-Novel spectrophotometric analytical method for metronidazole tablets using solids (eutectic liquid of phenol and niacinamide) as solubilizing agents (mixed solvency concept). Research Journal of Pharmacy and Technology 2016;9(6):705-708.

29. Maheshwari RK. "Solid as solvent"-Novel spectrophotometric analysis of frusemide tablets using phenol as solvent. Bulletin of Pharmaceutical Research 2014;4(2):104-107.

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