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Original Research Paper

Engineering

SOLID AS SOLVENT - MELTED DIMETHYL UREA AS SOLVENT TO ANALYSE INDOMETHACIN CAPSULES SPECTROPHOTOMETRICALLY AT 265 NM (MIXED SOLVENCY CONCEPT)

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ABSTRACT In the current attempt of research, novel method for spectrophotometric estimation of indomethacin in capsules using melted dimethyl urea as solvent was developed. The main objective behind research is to show "SOLIDS ALSO POSSESS SOLUBILIZING POWER". The current study deals with novel spectrophotometric analytical technique for quantitative estimation of indomethacin in capsules using melted dimethyl urea as solvent. According to the theory proposed byMaheshwari, each& every substance possessessolubilising power, susbstance may be a gas, solid or liquid. Dimethyl ureaimbibes large solubilizing power to indomethacin and having approximate solubility more than 800 mg per gm of melted dimethyl urea whereas aqueous solubility of indomethacin is 0.36 mg/ml at room temperature. Calibration curve of indomethacin was plotted by recording the absorbances of standard solutions of drug. The absorbances were observed at 265 nm against respective reagent blanks.The percent label claims were found very close to 100 (99.33 ± 1.112 and 98.07 ± 1.843) indicating accuracy of the proposed method.Percent recoveries estimated by the proposed method are close to 100 with significant low values of percentage deviation and standard error.Thus, it may be concluded that proposed method is simple, safe and precise and excludes use of toxic organic solvents.

KEYWORDS : Mixed Solvency, Solubilizing Power, Spectrophotometric Analysis, Niacinamide, Nalidixic Acid.

INTRODUCTION-

The mixed solvency concept can serve as a milestone for solubility enhancement and therefore deserves an urgent attention of the scientific community to assess its efficiency and applicability. According to Maheshwari, each and every substance present on earth possesses solubilizing power be it a solid, liquid or gas. Some substances are good solvent for some and at the same time bad solvent for others.

OBJECTIVE-

The main objective of present research is to show that solids also possess solubilizing power. In the present research, melted dimethyl urea (at 135 C) was employed for dissolution of indomethacin without using any organic solvents (therefore eco-friendly method).

MATERIALS AND METHOD-

Indomethacin API was generous gift from M/S Alkem Laboratories Ltd.,Mumbai. Indomethacin tablets were procured from the local market. All other chemicals were of analytical grade.The instrument used was Shimadzu UV-Visible spectrophotometer (model UV-160A) with 1 cm matched silica cells.

EXPERIMENTAL METHODS-

SOLUBILITY STUDIES-

The solubility of indomethacin at roomtemperature was found to be 0.36 mg/ml. Using approximate method of solubility determination, it was found that more than 800 mg indomethacin was dissolved by one gram of melted dimethyl urea(at 104 °C).

CALIBRATION CURVE-

10gm dimethyl urea was taken in a 500ml volumetric flask and it was heated carefully on heating mantle. As soon as dimethyl urea was melted, 50 mg of standard sample of indomethacin was added and the flask was shaken to dissolve the drug. Intermittent heating and shaking was done for complete dissolution of drug. Then, 400 ml of hot distilled water (90 C) was transferred carefully (little at a time) to the volumetric flask and the contents are shaken for about 5 minutes. Then, the flask was allowed to cool to attain the room temperature. Then, the volume was made up 500ml with distilled water. This was the stock solution of drug (100μg/ml),by appropriate dilution of this stock solution with distilled water, standard solutions of the drug (5,10,15,20,25μg/ml) were prepared and their absorbance were noted at 265 nm against the respective reagent blanks and using these values, the calibration curve was obtained.

PROPOSED METHOD-

20 tablets of nalidixic acid, formulation I were weighed and crushed to get a fine powder. 10gms of dimethyl urea was kept in a 500ml volumetric flask and the flask was carefully heated on heating mantle to melt the dimethyl urea. After complete melting of dimethyl urea, tablet powderequivalent to 50mg of drug was transferred to the flask and the flask was shaken for 10 minutes with intermittent heating and shaking. Then, 400ml of hot (90 C) distilled water was carefully (little at a time) added to the flask and the flask was shaken for about 5 minutes. Then, the flask was allowed to cool to attain room temperature and the volume was made up to mark with distilled water. After filtration through Whatmanfilter paper no.41, 5ml filtrate was diluted to 50ml with distilled water and the absorbance was noted at 265 nm against reagent blank. Using calibration curve the drug content was computed. Similar treatment was done for formulation II. All analyses were performed thrice.

RECOVERY STUDIES-

Recovery studies taking 15 mg and 30 mg of pure drug as spiked drug together with pre-analysed tablet powder (equivalent to 50 mg) were performed using the same proposed method.

RESULTS AND DISCUSSION-

The aqueous solubility of indomethacin at room temperature was 0.36 mg/ml whereas the solubility of indomethacin in melted dimethyl urea was found to be 83.33mg per gram of melted dimethyl urea at 104 °C. It is evident from Table I that the percent drug estimated in formulation I and II were 99.33 ± 1.112 and 98.07 ± 1.843, respectively. The values are very close to 100, indicating accuracy and precision of the proposed method. Further, Table II shows that the range of percent recoveries varied from 98.96 ± 0.854 to 100.95 ± 1.557which are again very close to 100, indicating the accuracy of the proposed method. Proposed analytical technique is supported significantly by small values of

statistical parameters viz. Standard deviation, percent coefficient of variation and standard error (Table II).

Table 1: Analysis of Commercial Tablets of Nalidixic acid with Statistical Evaluation (n=3)

Tablet Formulation	Label claim per tablet (mg)	% label claim estimated (mean±sd)	% coefficient of variation	Standard error
I	25	99.33±1.112	1.119	0.642
II	25	98.07 ± 1.843	1.879	1.065

Tablet 2:Results of Recovery Studies with Statistical Evaluation (n=3)

Tablet formulation	Drug present in preanalyzed table powder taken (mg)	Pure drug added (spiked)(mg)	% recovery estimated (mean ± sd)	% coefficient of variation	Standard error
I	50	15	100.78± 0.775	0.769	0.448
I	50	30	98.96± 0.854	0.863	0.493
II	50	15	99.44± 1.086	1.092	0.627
II	50	30	100.95± 1.557	1.542	0.899

CONCLUSION-

The mixed solvency concept can be successfully employed in analytical estimation of various drugs. A large number of poorly water-soluble drugs having absorption maxima above 250 nm can be tried for estimation by this method. Such solvents (dimethyl urea) can be tried in place of costlier and toxic organic solvents.

REFERENCES

1. R. K. Maheshwari, S. C. Chaturvedi & N.K. Jain, "Application of Hydrotropic Solubilization Phenomenon in Spectrophotometric Analysis of Hydrochlorothiazide Tablets," Indian Drugs, 42(8), August 2005, P. 541-544.
2. R. K Maheshwari, Solid as Solvent"- "Novel Approach for Spectrophotometric Estimation of Nalidixic Acid Tablets Using Solids (Eutectic Liquid of Phenol and Niacinamide) As Solubilizing Agents (Mixed Solvency Concept), The Pharma Review 2015;113-117
3. R. K. Maheshwari, "Solid as Solvent"- Novel Spectrophotometric Analysis of Tinidazole Tablets Using Melted Phenol as Solvent, Asian Journal of Pharmaceutical Research 2015;5(1):21-24.
4. Stuart F, Gibaldi M. Effect of urea on solubility, Role of water structure. Int. J. Pharm; 1967. 56, 370-375.
5. Jain NK, Agrawal RK, Singhai AK. Formulation of aqueous injection of carbamazepine. Pharmazie, 1990; 45, 221-222.
6. Jain NK, Singhai AK, Jain S. Hydrotropic solubilization of ketoprofen. Pharmazie, 1996; 51, 236-239.
7. Jain NK, Singhai AK, Jain S. Enhanced solubilization and formulation of an aqueous injection of piroxicam. Pharmazie, 1997; 52, 942-946.
8. Suzuki H, Sunada H. Mechanistic studies on hydrotropic solubilization of nifidipine in nicotinamide solution. Chem. Pharm. Bull, 1998; 46, 126-130.
9. Silva et al, Hydrotropic Solubilizaton, Thermochemica Acta, 1999; 328, 161-167.
10. Simamora P, Alvarez JM, Yalkowsky S. Solubilization of rapamycin. Int. J. Pharm., 2001; 212, 25-29.
11. Rawat S, Jain NK. Hydrotropic solubilization of some cox-2 inhibitors. Indian Drugs, 2006; 43, 565-574
12. Maheshwari RK. Novel application of hydrotropic solubilization in the spectrophotometric analysis of piroxicam in solid dosage form. Indian drugs, 2006; 43, 683-685.
13. Jain N.K, Nahar M. Formulation and evaluation of saquinavir injection .Ind. J. Pharm. Sc, 2006; 68, 608-614.
14. Maheshwari RK. Mixed hydrotropy in spectrophotometric analysis of aceclofenac. The Indian Pharmacist, 2007; 6, 67-69.
15. Sanghvi R, Evans D, Yalkowsky SH . Stacking complexation by nicotinamide: A useful way of enhancing drug solubility. Int. J. Pharm, 2007; 336, 35
16. Gupta S, Maheshwari RK. Novel application of mixed solvency concept in the development of fast release formulation of poorly water soluble drug using liquisolid technique and its evaluation. S.G.S.I.T.S, Indore, 2011.
17. Jain R, Maheshwari RK, George P. Formulation development and evaluation of controlled release tablets of lamotrigine using mixed solvency concept. Bulletin of Pharmaceutical Research 2015; 5(1):14-9.
18. Maheshwari R, Shilpkar R. Formulation development and evaluation of injection of poorly soluble drug using mixed solvency concept. International Journal of Pharma and Biosciences ,2012; 3, 179-189.
19. Chandan 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 (AJP) 2014; 7 (2).
20. Maheshwari RK, Karawande V U. 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; 15, 167-195.
21. Rajagopalan R. Formulation and evaluation of Paracetamol syrup made by mixed solvency concept. Scholars Research Library 2012; 4 (1), 170-174.
22. Gupta P, Maheshwari R K. formulation development of dry syrup and dry injection for reconstitution of a poorly water soluble drug (ornidazole) using mixed solvency concept and their evaluation, 2016; 59- 91.
23. Mehtani D, Maheshwari R K. Formulation development and optimization of niosomes using mixed solvency approach for transdermal delivery of poorly soluble drug and its evaluation S.G.S.I.T.S, Indore, 2011.
24. Yadav N, Maheshwari RK. Formulation development of microspheres using mixed solvency concept: Design development and optimization of controlled release microsphere of furosemide by mixed solvency concept, S.G.S.I.T.S, Indore, 2012.
25. Agrawal A, Maheshwari R. Formulation development and evaluation of in situ nasal gel of poorly water soluble drug using mixed solvency concept. Asian Journal of Pharmaceutics (AJP) 2011; 5 (3); 131-140.
26. Gour V, Garg A, Shukla A, Yadav A K. Development and Evaluation of Metronidazole Injection by Mixed Solvency Approach. Asian Journal of Biomaterial Research 2016; 2 (1), 38-45.
27. Maheshwari R K, Agarwal S. Formulationdevelopment and evaluationof in situ nasal gel of poorly water soluble drug using mixed solvency concept. Asian Journal of Pharmaceutics; 5(3), 131-140.
28. George P, Maheshwari RK. Formulation development of dry dosage forms of a poorly water soluble drug (cefixime Tihydrate) using mixed solvency concept and their evaluation. Dept of pharmacy, S.G.S.I.T.S, Indore,2015.
29. Sirole M, Maheshwari RK. Formulation development of non-aqueous ear drop of gatifloxacine and ofloxacine using mixed solvency concept. S.G.S.I.T.S.,Indore,2012.
30. Soni I, Maheshwari RK. Formulation development of fast release solid dispersions of poorly water soluble drugs, gatifloxacin and naproxen, employing novel npplication of mixed solvency concept and their evaluations. Dept of pharmacy, S.G.S.I.T.S, Indore, 2015.
31. Jatwa D, Maheshwari R K. Formulation development of solid-SEEDS based capsule dosage form of diazepam using novel application of mixed solvemcy concept and its evaluation. S.G.S.I.T.S, Indore, 2012.
32. Maheshwari RK, Chaklan N. Novel pharmaceutical application of mixed solvency for solubility enhancement of piroxicam, development of its solid dispersions and fast dissolving oral film. S.G.S.I.T.S, Indore, 2009.
33. Maheshwari RK, Putliwala M, Padiyar A. Novel Approach for Spectrophotometric Estimation of Naproxen Tablet Dosage Form using Solids (Eutectic liquid of Phenol and Niacinamide) as Solubilizing agents (Mixed Solvency Concept).Asian Journal of Pharmaceutical Research, 2015; Vol 5, Issue 1, 25-28.
34. Abdelbary GA, Amin MM, Abdelmoteleb M. Novel Mixed Hydrotropic Solubilization of Zaleplon: Formulation of Oral Tablets and In-vivo Neuropharmacological Characterization by Monitoring Plasma GABA Level. Journal of Drug Delivery Science and Technology 2016; doi: 10.1016/j.jddst.2016.03.014.
35. Maheshwari RK, Shah AP, Pandey L, Tiwari SP. "Solid as Solvent": Novel spectrophotometric analytical technique for quantitative analysis of tinidazole tablets using solids (eutectic liquid of phenol and metformin hydrochloride) as solubilizing agents (mixed solvency concept).The Pharma Innovation Journal 2016;5(3):01-02.
36. Soni LK, Solanki SS, Maheshwari RK. Studies on Mixed Solvency concept in formulation development of oral solution (syrup) of poorly water soluble drugs. Journal of Harmonized Research in Pharmacy 2015; (4), 305-315.
37. Singh A, Maheshwari RK. "Solid as Solvent"-Novel Spectrophotometric analytical Technique for Quantitative Estimation of Piroxicam in tablets using Solids (Eutectic liquid of Phenol and Lignocaine Hydrochloride) as Solubilizing Agents (mixed solvency concept). World Journal of Pharmaceutical Research, Volume 5, Issue 2, 1560-1567.
38. Maheshwari RK, Vamoriya P, Joshi S, Kori S. "Solid as Solvent"-Novel Spectrophotometric analysis of Metronidazole tablets using Phenol as Solvent .European Journal of Biomedical and Pharmaceutical Sciences, http://www.ejbps.com 2015; Volume: 2, Issue: 4, 1240-1247.
39. Maheshwari RK, Jain R, George P. Formulation Development and Evaluation of Controlled Release Tablets of Lamotrigine using Mixed Solvency Concept. An Official Publication of Association of Pharmacy Professionals, Bulletin of pharmaceutical Research 2015; 5(1): 14-19.
40. Jain DK, Patel V, Banjare L, Jain N, Maheshwari RK. "Solid as Solvent"- Novel Technique for Spectrophotometric Analysis of Ornidazole Tablets using Melted Phenol as Solvent. Asian Journal of Biomedical and Pharmaceutical Sciences.
41. Jain S, Maheshwari RK, Nema RK, Singhvi I. Development and Validation of Simple Spectrophotometric Method of Quantization of Ondansetron Hydrochloride in Solid Dosage Formulations using Hydrotropic Solubilization Technique. International Journal of Pharmaceutical Sciences and Drug Research, 2017; 9(5)210-213.
42. Maheshwari RK, Solanki SS, Soni LK. "Solid as Solvent"- Novel Spectrophotometric Analytical Technique for Furesemide Tablets using Solids(Eutectic Liquid of Phenol and Niacinamide) as Solubilizing Agents(Mixed Solveny Concept). International Journal of Advances In Pharmaceutical Research .
43. Padiyar A, Maheshwari RK, Jain S. Formulation and Development of High Concentration Diclofenac Sodium Injection using Mixed Solvency Concept

and its Evaluation. International Journal of Advanced Pharmaceutics, 2016; vol 6, issue 2, 78-84.
44. Jain S, Maheshwari RK, Nema RK, Singhvi I. Development and Validation of Simple UV-Spectrophotometric Method of Quantization of Domperidone in Solid Dosage Formulation using Mixed Solvency Concept, Research and Reviews: A journal of Design and Discovery, Volume 4, Issue 2.
45. Jain S, Maheshwari RK, Nema RK, Singhvi I. Development and Validation of Simple UV- Spectrophotometric Method of Diazepam in Bulk and Solid Dosage Formulation using Mixed Solvency Concept, International Journal of Current Pharmaceutical Research, 2017; Vol 9, Issue 6,.
46. Jain S, Maheshwari RK, Nema RK, Singhvi I. Development and Validation of Simple UV- Spectrophtometric Method of Quantization of Nifedipine in Solid Dosage Formulation using Mixed Solvency Concept, World Journal of Pharmaceutical Research, Volume 6, Issue 13, 1014-1021.
47. Maheshwari RK, Dahima R."Solid as Solvent": Novel Spectrophotometric Analytical Technique for Quantitative Estimation of Tinidazole in tablets using solids (eutectic liquid of phenol and lignocaine hydrochloride) as solubilizing agents (Mixed Solvency Concept). Journal of Drug Delivery and Therapeutics, 2017;7(3):127-130
48. Maheshwari RK, Padiyar A, Putliwala M. Utilization of Mixed Solvency Concept in Spectrophotometric Analysis of Cefixime Trihydrate Tablets. International Journal of Pharmaceutical Research and Analysis, Vol 5, Issue 1, 1-3.
49. Maheshwari RK. "Solid as Solvent"- Novel Spectrophotometric Analysis of Tinidazole Tablets using Phenol as Solvent. Asian Journal of Pharmaceutical Research,2015;Vol5,Issue1,21-24