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RESEARCH ARTICLE

SIMPLE ECOFRIENDLY SPECTROPHOTOMETRIC ESTIMATION OF TINIDAZOLE TABLETS BY APPLICATION OF MIXED-SOLVENCY TECHNIQUES

Rajesh Kumar Maheshwari*, Saurabh Gupta, Abhishek Gharia, Sonu Kumar Garg and Rajendra Shilpkar

Department of Pharmacy, Shri G. S. Institute of Technology and Science, Indore- 452 003, Madhya Pradesh, India.

**E-mails*: rkrkmaheshwari@yahoo.co.in, saurabhpharma04@gmail.com
Tel.: +91-9406621907, +91-8103106780.

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All substances whether liquid, gas or solid possess solubilizing power and hence the concentrated aqueous solution containing various dissolved substances can also improve the solubility of poorly water-soluble drugs. In the present investigation, blends of solubilizers (sodium benzoate, niacinamide as hydrotropic agents, PEG 300, glycerin, propylene glycol as cosolvents and PEG 6000 as a water soluble solid) have been tried for solubilizing tinidazole according to mixed-solvency concept. More than 3 fold enhancement was observed in the solubility of tinidazole in blend-1 (sodium benzoate-8%, niacinamide-2%, PEG 300-3%, glycerin-7%, propylene glycol-3% and PEG 6000-4%) and blend-2 (sodium benzoate-7%, niacinamide-3%, PEG 300-8%, glycerin-4%, propylene glycol-4% and PEG 6000-4%) solutions as compared to solubility in distilled water. Proposed method is new, simple, economic, eco-friendly, safe, rapid, accurate and reproducible. Recovery studies and statistical data proved the accuracy, reproducibility and precision of the proposed method. The presence of hydrotropic agents did not interfere in the analysis.

Key words: Mixed-solvency, Tinidazole, Niacinamide, PEG 300, Glycerin, Propylene glycol.

INTRODUCTION

The mixed-solvency concept states that all substances whether liquid, gas or solid possess solubilizing power and hence the concentrated aqueous solution containing various dissolved substances can also improve the solubility of poorly water-soluble drugs. Various mixed solvency blends and hydrotropic solution have been reported in literature to enhance the aqueous solubility of large number of poorly water soluble drugs *viz*. cefixime, aceclofenac, salicylic acid, tinidazole, amoxicillin, ibuprofen, hydrochlorthiazide, ofloxacin, cephalexin and metronidazole (Maheshwari, 2005; 2006a; 2006b; 2006c; 2006d; 2009a; 2009b; 2010; Maheashwari *et al* 2005a; 2005b; 2006a; 2006b) have been reported in literature to be analyzed by the use of hydrotropic solubilization technique. In present study, mixed-solvency approach has been applied for the enhancement of aqueous solubility of tinidazole (selected as a model poorly water-soluble drug), by making various aqueous solutions containing the blends (keeping total concentrations 30% *w/v* constant) of randomly selected water-soluble substances from among hydrotropes (sodium benzoate, niacinamide, sodium citrate, sodium salicylate); cosolvents (Kristiansen *et al* 1970), (Paruta, 1969), (PEG 300, glycerin, propylene glycol) and water soluble solids (PEG 4000, PEG 6000). Eight solubilizers were used in different concentrations (randomly selected); keeping total dissolved solubilizers 30% *w/v* in solutions. Out of several such blends, two blends having sufficient enhancement in solubilities of tinidazole were selected. Blend-1 (sodium benzoate-8%, niacinamide-2%, PEG 300-3%,

glycerine-7%, propylene glycol-3% and PEG 6000-4%) and Blend-2 (sodium benzoate-7%, niacinamide-3%, PEG 300-8%, glycerin-4%, propylene glycol-4% and PEG 6000-4%) both gave more than 3 fold enhancements in the solubility of tinidazole as compared to solubility in distilled water.

These blend solutions of solubilizing agents have been used to solubilize poorly water-soluble tinidazole from fine powder of tablet formulation for its spectrophotometric determination. Tinidazole (1-[2-(ethylsulphonyl) ethyl]-2-methyl-5-nitroimidazole) is an anti-protozoal drug. The solubilizers (used in estimation of tinidazole) and additives (used in the manufacture of tablets) did not interfere in analysis.

MATERIALS AND METHODS

Materials

Tinidazole was a generous gift by Alkem Lab. Ltd., Mumbai (India). All chemicals used were of analytical grade. A Shimadzu UV-Visible recording spectrophotometer (Model-UV 160 A) with 1 cm matched silica cells was used for spectrophotometric analysis. Commercial tablets of tinidazole were procured from the market.

Methods

Calibration curve for blend-1

Accurately weighed 50 mg of tinidazole bulk drug was transferred to 25 ml volumetric flask containing 20 ml of blend-1 solution and shaken to solubilize it. Volume was made up to the mark with distilled water. The stock solution was further diluted with distilled water to obtain various standard solutions of concentrations 5, 10, 15, 20, and 25 μg/ml. The absorbances of these solutions were noted at 318 nm against reagent blank to get calibration curve.

Calibration curve for blend-2

Same procedure, as adopted for blend-1, was followed for blend-2 and calibration curve in blend 2 was prepared.

Preliminary solubility studies

The aqueous solution containing various solubilizers improved the solubility of tinidazole. Blend-1 and Blend-2 gave solubility enhancement more than 3 fold and hence selected for spectrophotometric analysis.

Analysis of tablet formulation of tinidazole (Indian Pharmacopoeia 2007)

Twenty tablets (formulation-I) were weighed and powdered. Tablet powder equivalent to 150 mg tinidazole was transferred to 100 ml volumetric flask containing 20 ml of methanol and shaken well. Volume was made up to the mark with methanol. The contents were shaken well again and filtered through Whatman filter paper no. 41. Filtered extract was appropriately diluted with methanol and absorbance was noted at 310 nm against reagent blank and drug content was calculated. Same method was followed for tablet formulation-II. The results of analysis are reported.

Analysis of tablet formulation of tinidazole by the proposed method using blend-1

Tablet powder (formulation-1 and formulation-2) equivalent to 50 mg tinidazole was transferred to 25 ml volumetric flask containing 20 ml of blend-1 and shaken well for 10 min. Volume was made up to the mark with distilled water. The content were shaken well again and filtered through Whatman filter paper no. 41. Filtered extract was appropriately diluted with distilled water and absorbance was noted at 318 nm against reagent blank and drug content was calculated.

Analysis of tablet formulation of tinidazole by the proposed method using blend-2

The method of analysis using blend-2 was exactly same as used employing blend-1. Blend-2 was used in place of blend-1. The result of analysis are reported.

Recovery studies

To perform recovery studies, tinidazole pure drug was added (15 mg and 30 mg separately) to tablet powder equivalent to 50 mg tinidazole and drug content was determined by the proposed methods. The results of analysis are reported.

RESULT

The percent label claims were 100.39±1.082 and 101.08±1.873 using blend-1 for formulation I and II respectively and 100.67±0.880 and 99.63±0.479 using blend-2 for formulation I and II respectively. The percent label claims using IP 2007 method were 100.15±1.351 to 100.19±0.990 for formulation I and II respectively. Percent label claims were close to 100 with low values of standard deviation, percent coefficient of variation and standard

error (**Table 1**). Therefore, these indicate the accuracy of the proposed methods. Also the results of analysis obtained using proposed methods are very comparable with the results of analysis using IP 2007 method which confirms the accuracy of the proposed methods. Accuracy, reproducibility and precision of the proposed methods were further confirmed by percent recovery values. The percent recovery values ranged from 98.87±1.444 to 100.88±1.399 in cases of proposed methods employing blend-1 and blend-2. Percent recovery values were close to 100 with low values of standard deviation, percent coefficient of variation and standard error (**Table 2**) which indicates the accuracy of the proposed methods and validate the methods.

CONCLUSION

Ethanol, methanol, acetonitrile, chloroform, hexane, cyclohexane, diethyl ether, toluene and acetone have been employed for solubilization of poorly water-soluble drugs for their spectrophotometric analysis. Most of the organic solvents are toxic, costlier and responsible for pollution. Inaccuracy due to volatility is another drawback of organic solvents. IP 2007 method of analysis of tinidazole tablets employs methanol. It is thus concluded that the proposed method of analysis is new, simple, cost-effective, environment friendly, safe, accurate and reproducible. The method can be successfully employed in the routine analysis of tinidazole in tablet formulation.

Table 1. Results of spectrophotometric analysis of tinidazole tablets with statistical evaluation

Tablet formulation	Label claim (mg)	Method	Percent Label claim estimated* (mean ± SD)	Percent coefficient of variation	Standard error
I	300	IP method	101.15±1.351	1.336	0.780
I	300	Blend-1 method	100.39±1.082	1.078	0.625
I	300	Blend-2 method	100.67±0.880	0.874	0.508
II	300	IP method	100.19±0.990	0.988	0.572
II	300	Blend-1 method	101.08±1.873	1.853	1.081
II	300	Blend-2 method	99.63±0.479	0.481	0.277

*n = 3

Table 2. Results of recovery studies with statistical evaluation using proposed methods

Tablet formulation	Drug present in pre-analyzed tablet powder (mg)	Pure drug added (Spiked) (mg)	Method	% Recovery estimated (mean ± S.D)	Percent coefficient of variation	Standard error
I	50	15	Blend-1 method	99.31±1.222	1.230	0.706
I	50	15	Blend-2 method	100.55±0.993	0.988	0.573
I	50	30	Blend-1 method	100.88±1.399	1.387	0.808
I	50	30	Blend-2 method	99.42±0.773	0.778	0.446
II	50	15	Blend-1 method	98.87±1.444	1.461	0.834
II	50	15	Blend-2 method	99.45±1.876	1.886	1.083
II	50	30	Blend-1 method	100.49±1.207	1.201	0.697
II	50	30	Blend-2 method	99.71±1.768	1.773	1.021

*n = 3

REFERENCES

Indian Pharmacopoeia, Indian Pharmacopoeia Commission, Ghaziabad, 2007;3:1185-6.

Kristiansen H. Nakano M. Nakano NI, Higuchi T. Effects of solvent composition on association between small organic species. *J. Pharm. Sci*. 1970;59(8):1103-6. [DOI: 10.1002/jps.2600590808]

Maheshwari RK. Spectrophotometric determination of cefixime in tablets by hydrotropic solubilization phenomenon. *The Indian Pharmacist* 2005;IV(36): 63-8.

Maheshwari RK. Application of hydrotropic solubilization in the analysis of aceclofenac. *Asian. J. Chem*. 2006a;18(2): 1572-4.

Maheshwari RK. A novel application of hydrotropic solubilization in the analysis of bulk samples of ketoprofen and salicylic acid. *Asian. J. Chem*. 2006b; 18(1):393-6.

Maheshwari RK. Novel application of hydrotropic solubilization in the spectrophotometric analysis of tinidazole in dosage form, *Asian. J. Chem*. 2006c;18(1): 640-4.

Maheshwari RK. Spectrophotometric analysis of amoxicillin in tablets using hydrotropic solubilization technique. *Asian. J. Chem*. 2006d;18(4):3194-6.

Maheshwari RK., "Mixed-Solvency" – A novel concept for solubilization of poorly water-soluble drugs. *Delving J. Tech. Eng. Sci.* 2009a;1(1):39-43.

Maheshwari RK. Solubilization of ibuprofen by mixed-solvency approach. *The Indian Pharmacist* 2009b;8(87): 81-4.

Maheshwari RK. "Mixed-solvency approach" - Boon for solubilization of poorly water-soluble drugs. *Asian. J. Pharm*. 2010;4(1):60-3. [DOI: 10.4103/0973-8398.63981]

Maheshwari RK, Chaturvedi SC, Jain NK. Application of hydrotropic solubilization phenomenon in spectrophotometric analysis of hydrochlorthiazide tablets. *Indian Drugs* 2005a;42(8):541-4.

Maheshwari RK, Chaturvedi SC, Jain NK. Application of hydrotropy in spectrophotometric determination of pharmaceutical dosage forms. *Indian Drugs* 2005b; 42(11):760-3.

Maheshwari RK, Chaturvedi SC, Jain NK. Novel spectrophotometric estimation of some poorly water soluble drugs using hydrotropic solubilizing agents. *Indian J. Pharm. Sci*. 2006a;68(2):195-8. [DOI: 10.4103/0250-474X.25714]

Maheshwari RK, Pandey SP, Lovelekar A, Chavda V, Ajmera A, Gupta HM. Novel application of hydrotropic solubilization in the spectrophotometric analysis of cephalexin in solid dosage form. *Asian. J. Chem*. 2006b; 18(2):1451-4.

Paruta AN. Solubility of parabens in ethanol-water mixtures. *J. Pharm. Sci*. 1969;58(3):364-6. [DOI: 10.1002/jps.2600580319]

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