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ECOFRIENDLY AND ECONOMIC ESTIMATION OF ATENOLOL AND PARACETAMOL USING SODIUM BENZOATE AS HYDROTROPE

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Abstract

Hydrotropy is the term that has been used to designate the increase in aqueous solubility of poorly water-soluble compounds in hydrotropic solutions. In the present investigation, hydrotropic solubilisation phenomenon was employed to solubilise poorly water-soluble drugs Atenolol and Paracetamol from bulk. The solubility of Atenolol and Paracetamol was enhanced to a greater extent in 2M Sodium benzoate. Atenolol and Paracetamol form a coloured complex with a colouring agent like Methyl orange and Ferroin shows maximum absorbance at about 551 nm and 514 nm respectively. Atenolol shows linearity in the concentration range of 1-3 µg/ml and good regression value 0.9831 at λ max 551nm. Paracetamol shows linearity in the concentration range of 0-3500 µg/ml and good regression value 0.9986 at λmax 514nm. The results of recovery study revealed that any small change in the drug concentration in the solution could be accurately determined by the proposed method. The value of LOD and LOQ was found to be 0.4874µg/ml and 1.4770µg/ml for Atenolol and 162.85 µg/ml and 493.51µg/ml for Paracetamol that indicate good sensitivity of proposed method. The proposed methods are accurate, precise, new, simple, cost effective and ecofriendly. The estimation of Atenolol and Paracetamol using hydrotropy and spectrometry can be successfully adopted for routine analysis in bulk.

Keywords: Hydrotrope, Atenolol, Paracetamol, Spectrometry, Sodium benzoate.

Introduction

Nowadays, in the development of new analytical procedures, care about the toxicity and danger of the reagents used and the wastes produced are as important as any other analytical feature. Hence, there is a urgent necessity to

develop methods which are less harmful to human and to the environment according to 12 principles of Green Chemistry [1,2].

Hydrotropy is a molecular phenomenon whereby adding a second solute (the hydrotrope) results in an increase in the aqueous solubility of poorly soluble solutes [3]. This phenomenon termed hydrotropy is considered as a unique and unprecedented solubilization technique because of the easy recovery of dissolved solute and possible re-use of hydrotrope solutions. This technique also facilitates the separation of close boiling isomers and non-isomers in mixtures besides increasing the rate of heterogeneous reactions. Hydrotropes in general are water-soluble and surface-active compounds that enhance the solubility of organic solutes like acids, esters, alcohols, aldehydes, ketones, hydrocarbons, and fats. Hydrotropes have been widely used in drug solubilisation detergent formulation, health care, household applications and also as an extraction agent for fragrances Each hydrotrope has a selective ability towards a particular component in the mixture to facilitate easy recovery of the hydrotrope solution by controlled dilution with distilled water. The solubility enhancement of organic solute is due to the formation of molecular structures in the form of complexes. A number of poorly water-soluble drugs have been solubilised by use of various concentrations. Aqueous hydrotropic solutions such as sodium benzoate, sodium salicylate, niacin amide, sodium hydroxide, sodium citrate and urea [4]. Hydrotropic solution, 2M Sodium benzoate was employed as solubilizing agent to carry out the analysis of Atenolol (beta blockers) and Paracetamol (analgesic) poorly water-soluble drugs by spectroscopic estimation. Therefore, it was thought worthwhile to solubilize this drug in hydrotropic solution to carry out the quantitative estimation by spectroscopy precluding the use of an organic solvent [5].

Chemically, Atenolol is (RS)-2-{4-[2-hydroxy-3-(propan-2-ylamino) propoxy] phenyl} acetamide (Fig.1). Atenolol (Tenormin) is a selective β1 receptor antagonist, a drug belonging to the group of beta blockers (β-blockers), used primarily in cardiovascular diseases [6-8]. Literature survey reveals that various methods have been reported for estimation of Atenolol such as UV spectrophotometry [9-11] reverse phase HPLC, UPLC, HPTLC [12-14] individually and in combination dosage form with other drugs.

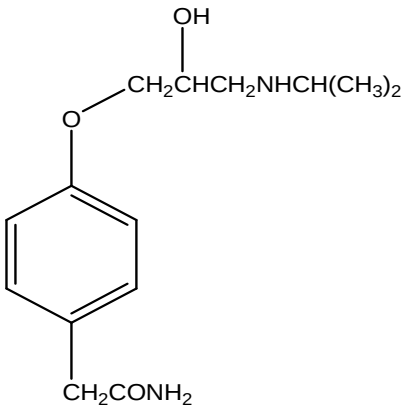

Fig. 1. Structure of Atenolol.

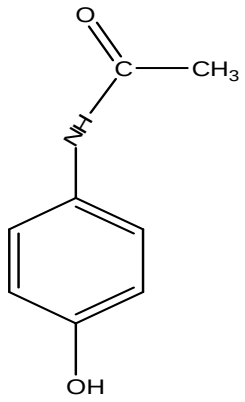

Fig. 2. Structure of Paracetamol.

Paracetamol is chemically N-(4-hydroxy phenyl) acetamide (Fig.2), used as antipyretic and analgesic [15]. A number of methods are available for Paracetamol determination in various types of samples. These include titrimetry [16], HPLC [17], voltammetry [18-20], spectrofluorimetry [21] and UV/visible spectrophotometry [22-23] individually and in combination dosage form with other drugs.

2. Materials and Methods

2.1 Materials and Reagents:

The bulk drug sample of Atenolol and Paracetamol were generously supplied by Wockhradt Pvt.LTD, Aurangabad (Maharashtra). Other chemicals used were of analytical grade.

2.1.1 Preparation of bromate bromide solution:

Dissolve 0.835 g of potassium bromate and 1.16 g of potassium bromide in 500 ml of distilled water. Take 1 ml of the above solution and dilute it upto 100ml distilled water to get a concentration of 10µg/ml.

2.1.2 Preparation of standard stock solution of Atenolol:

The standard stock solution (Stock A) was prepared by dissolving 100 mg of Atenolol in 20ml of 2M Sodium benzoate and make the volume upto 100 ml with distilled water. Take 1 ml of stock solution A and make the volume with 100 ml distilled water to get a concentration of 10 µg/ml (Stock B). Take 3 ml of stock solution B, add 1 ml distilled water, 2 ml of 5M HCl and 1ml of bromate bromide solution and keep it for 10 min. with occasional shaking. Add 1 ml Methyl orange solution as a colouring agent and dilute upto 10 ml with distilled

water and this solution was scanned in the UV-visible range at 800-200nm for the determination of λ max of Atenolol by using blank solution. The λ max of Atenolol was found to be 551nm as shown in Fig. 3.

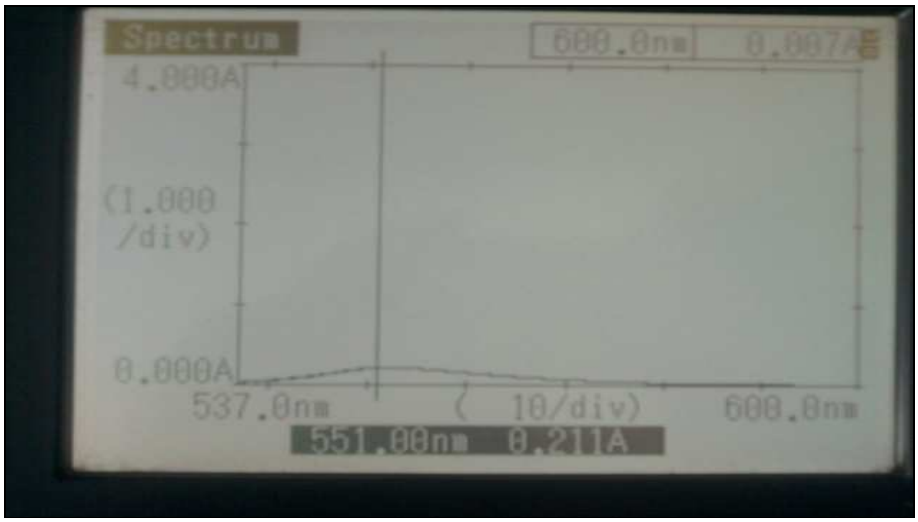

Fig.3: Spectrum of Atenolol.

Take 1, 1.5, 2, 2.5, 3 ml of stock B and add 3, 2.5, 2, 1.5 and 1 ml of distilled water. Add 2 ml of 5M HCl and 1ml of bromate bromide solution in each dilution. Keep these for 10 min. with occasional shaking. Add 1 ml Methyl orange solution as a colouring agent in each dilution and make the volume upto 10 ml with distilled water. The calibration curve for Atenolol was prepared by the drug having concentration in a range1-3 µg/ml. The absorbance of resulting solutions was measured at λ max 551nm and a calibration curve was plotted to get the linearity (Fig.4) and regression values (Table.1)

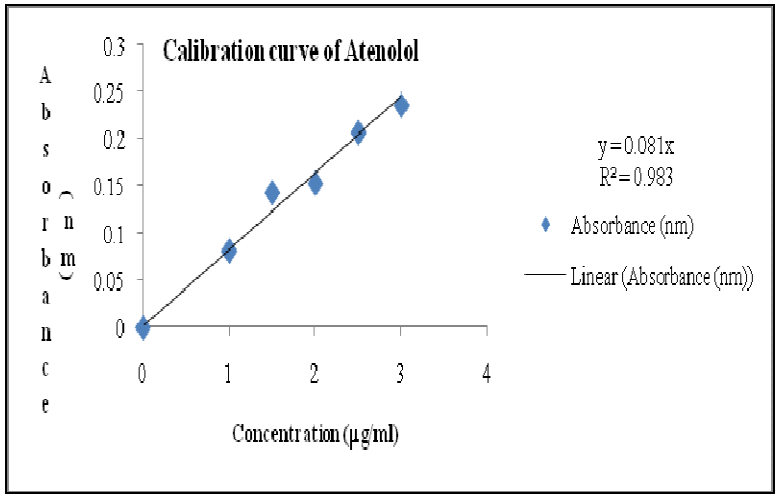

Fig. 4: Calibration curve of Atenolol.

Table 1: Regression parameters and sensitivity values.

Parameters	Analytical data of Atenolol	Analytical data of Paracetamol
Linearity Range (µg/ml)	0-3	0-3000
λ max (nm)	551	514
ε, L/mol/cm	2.1037×10^{2}	3.4114×10^{2}
Sandell sensitivity, µg/cm^2	1.2658	0.443131
Slope (b)	0.0816	0.0002
Intercept (a)	0.0000	0.0000
Standard deviation about regression (Sy)	±0.01253	±0.05708
Standard deviation of Slope (Sb)	$\pm 5.189 \times 10^{-3}$	$\pm 2.1577 \times 10^{-5}$
Standard deviation of intercept (Sa)	±0.01004	±0.03889
Correlation co-efficient (r)	0.9831	0.9982
Limit of detection (LOD,µg/ml)	0.4874	162.85
Limit of quantification (LOQ,µg/ml)	1.4770	493.51

2.1.3 Preparation of standard stock solution of Paracetamol:

The standard stock solution (Stock A) was prepared by dissolving 500 mg of Paracetamol in 100 ml of 2M Sodium benzoate and 2ml of 20% v/v. Ferroin solution as a colouring agent. The Stock-A solution was scanned in the UV-visible range at 800-200nm for the determination of λ max of Paracetamol by using blank solution. The λ max of Paracetamol was found to be 514 nm (Fig.5). The calibration curve for Paracetamol was prepared by the drug having concentration in a range 500, 1000, 1500, 2000, 2500, and 3000 µg/ml. The absorbance of resulting solutions was measured at λ max 514 nm and a calibration curve was plotted to get the linearity (Fig.6) and regression values (Table.1).

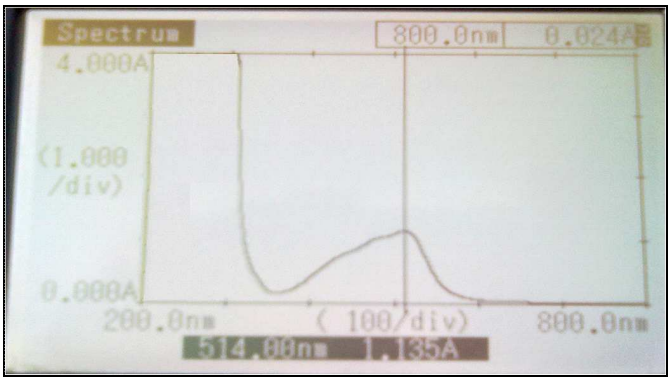

Fig. 5: Spectrum of Paracetamol.

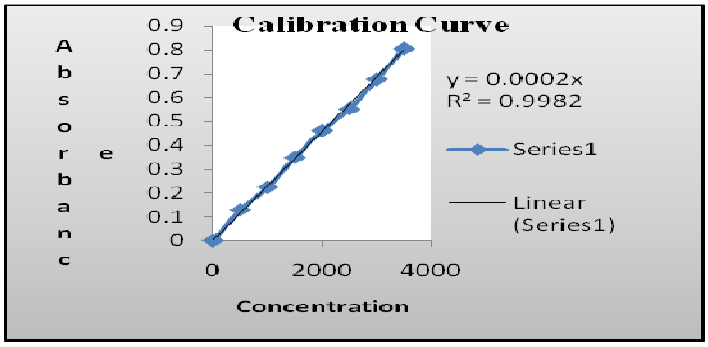

Fig.6: Calibration curve of Paracetamol.

2.2 Instrumentation:

The UV-Visible spectrophotometer **(**Shimadzu 1800) model digital spectrophotometer was used.

3. Method Validation

3.1 Linearity, Detection and Quantification Limits:

A linear correlation was found between absorbance and concentration of Atenolol and Paracetamol. Regression analysis of Beer's law data using the method of least squares was made to evaluate the slope (b), intercept (a) and the correlation coefficient (r) (Table 1). The graph shows negligible intercept and is described by the regression equation y = a + bx, where y is the absorbance and x is concentration in µg/ml. The limits of detection (LOD) and quantification (LOQ), sensitivity parameters such as molar absorptivity and Sandell sensitivity are also contained in Table 1.

3.2 Precision:

Precision of the method was calculated in terms of intermediate precision (intra-day and inter-day) [24].

Three different concentrations of Atenolol and Paracetamol were analyzed in seven replicates during the same day (intra-day precision) and five consecutive days (inter-day precision). The RSD (%) values of intra-day and inter-day studies showed good precision (Table 2 and Table 3) respectively.

Table-2: Evaluation of intra-day and inter-day accuracy and precision of Atenolol.

Atenolol taken (µg/ml)	**Intraday accuracy and precision**			**Interaday accuracy and precision**		
	Atenolol found (µg/ml)	**RE %**	**RSD %**	**Atenolol found (µg/ml)**	**RE %**	**RSD %**
1.5	1.49	0.34	1.93	1.48	1.57	2.56
2.0	2.03	-2.17	1.82	1.96	2.23	3.82
2.5	2.44	2.50	1.02	2.43	2.84	2.72

RE- Relative error; RSD- Relative standard deviation

Table -3: Evaluation of intra-day and inter-day accuracy and precision of Paracetamol.

Paracetamol taken (µg/ml)	**Intraday accuracy and precision**			**Interaday accuracy and precision**		
	Paracetamol found (µg/ml)	**RE %**	**RSD %**	**Paracetamol found (µg/ml)**	**RE %**	**RSD %**
1000	1002.60	0.681	0.2784	999.5	0.76	0.18
1500	1503.69	0.316	0.118	1501	1.12	0.18
2000	1992.2	0.9474	0.3868	1999.16	1.07	0.13

RE- Relative error; RSD- Relative standard deviation

3.3 Accuracy:

Accuracy of an analytical method is the closeness between the reference value and the found value [24]. Accuracy was evaluated as percentage relative error between the measured concentrations and actual

concentrations for Atenolol and Paracetamol (Bias %). The results obtained are compiled in Table 2 and Table 3 which show good accuracy for the method.

4. Result And Discussion

Spectrophotometric estimation of Atenolol and Paracetamol as carried out using Sodium benzoate hydrotrope and form a coloured complex with a colouring agent like Methyl orange and Ferroin respectively.

The calibration curve for Atenolol is linear over the range of 0-3 μg/ml and is described by the regressionequation A = 0.0816 C with a regression coefficient (r) of 0.9831 (n = 6). The calculated molar absorptivity and Sandell sensitivity values are 2.1037×10^2 L/mol/cm and 1.2658μg/cm^2, respectively. The limits of detection (LOD) and quantification (LOQ) calculated as per ICH guidelines are 0.4874 and 1.4770 μg/ml, respectively.

The calibration curve for Paracetamol is linear over the range of 0-3000 μg/ml and is described by the regression equation A = 0.0002 C with a regression coefficient (r) of 0.9982 (n = 7). The calculated molar absorptivity and Sandell sensitivity values are 3.4114×10^2 L/mol/cm and 0.4431μg/cm^2, respectively. The limits of detection (LOD) and quantification (LOQ) calculated as per ICH guidelines are 162.85 and 493.51 μg/ml, respectively.

For Atenolol, the within-day accuracy expressed as relative error was better than 2.5% with precision (RSD) ranging from 1.02 to 1.93%. The between-day accuracy ranged from 1.5-3.0% with a precision less than 4%.

For Paracetamol, the within-day accuracy expressed as relative error was better than 2.5% with precision (RSD) ranging from 0.11 to 0.38%. The between-day accuracy ranged from 0.76-1.12% with a precision less than 4%.

5. Conclusion

By this Study we can conclude that, Solubility is the most important physical characteristic of a drug for its oral bioavailability, formulation, development of different dosage form of different drugs and for quantitative analysis. Solubility can be enhanced by many techniques among them hydrotropy is one of them. Atenolol and Paracetamol form hydrotrope with 2M Sodium Benzoate. This paper presents a spectrophotometric evaluation of

Atenolol and Paracetamol exposing the advantages as regards to simplicity, lower cost, better sensitivity and precluding the use of organic solvents. In addition, the proposed methods employ an inexpensive instrument. The proposed methods are simple, precise and accurate for the determination of Atenolol and Paracetamol.

6. Acknowledgement

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