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Green Spectroscopy of Entacapone in Bulk and Tablets by Hydrotrophy

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Abstract

Background Solubilization of poorly water-soluble drugs has been a very important issue in screening studies of new chemical entities as well as formulation research. Hydrotropy is one of the solubility enhancement methods. **Objective** The primary objective of the present investigation was to employ these hydrotropic solutions to improve solubility of poorly soluble drug, without use of costlier organic solvents. **Methods** Entacapone is a poorly water-soluble drug which shows good aqueous solubility in 20 % Sodium acetate solution and its quantitative estimation in bulk and tablet dosage form was done by UV spectroscopic at 378 nm. **Results** The drug shows linearity in the concentration range of 0.5-5.0 µg/ml and good regression value 0.999 at λ_{max} 378 nm. Statistical data proved accuracy, reproducibility and the precision of the proposed method. The presence of hydrotropic agent Sodium acetate did not interfere in the analysis. **Conclusion** The proposed method is a simple, cost effective, accurate and precise. The estimation of Entacapone using hydrotropy and spectroscopy can be successfully adopted for routine analysis in bulk and tablet dosage form precluding the use of organic solvents.

Keywords
Hydrotrophy, Entacapone, UV Spectroscopy, Sodium acetate

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1.0 INTRODUCTION

Hydrotropy is a molecular phenomenon whereby adding a second solute (the hydrotrope) results in an increase in the aqueous solubility of poorly soluble solutes [1-3]. 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 solubilization, detergent formulation, health care, household applications and also as an extracting 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. A number of poorly water-soluble drugs have been solubilized by use of various concentrations. Aqueous hydrotropic solutions such as sodium benzoate, sodium acetate, sodium salicylate, niacin amide, sodium hydroxide, sodium citrate and urea[4-5]

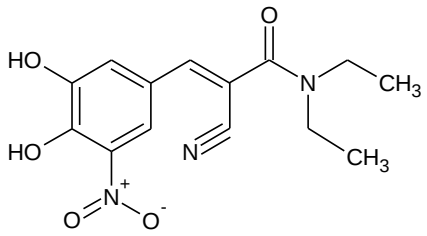

Figure 1: Structure on Entacapone (ETC).

Entacapone (ETC) is chemically known as (2*E*)-2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)-*N*, *N*-diethylprop-2-enamide (Figure 1) and belongs to the class of antiparkinsonian agents[5]. Entacapone is not official in any pharmacopoeia. It is a selective and reversible inhibitor of catechol- o-methyltransferase (COMT), with mainly peripheral actions**.** It is used in combination with levodopa and carbidopa to treat the end-of-dose 'wearing-off' symptoms of Parkinson's disease[6-7]. Hydrotropy is one of the solubility enhancement method for aqueous solubility of poorly water-soluble compounds. Entacapone is poorly water-soluble drug which shows good aqueous solubility in 40 ml of 20% sodium acetate solution.

As per author's best knowledge, some researches on Entacapone is done before which was performed by using different solvents and the different results by using HPLC[8-12], UPLC[13] and Spectroscopy[14-20]. Spectroscopy is the technique of choice even today because of its inherent simplicity, sensitivity, selectivity, accuracy, precision and cost-effectiveness. The recent development of new analytical method with good characteristics such as selectivity and sensitivity are not only sufficient but also fulfills the green analytical approaches[21-22]. Hence, the main objective of the present study was to develop and validate new spectroscopic method precluding the use of organic solvent.

2.0 MATERIALS AND METHOD

2.1 Apparatus

A Shimadzu 1800 double beam UV-VIS spectrophotometer provided with 1 cm matched quartz cell was used for absorbance measurements.

2.2 Reagents and Chemicals

Entacapone drug sample was gifted from Wockhardt Pvt. Ltd., Aurangabad. Tablets of Entacapone were procured from the local market. All other used chemicals and solvents were of analytical grade.

2.3 Method Development

2.3.1 Preliminary solubility studies of the drug

Solubility of Entacapone was determined by saturated aqueous solution of 40% Sodium acetate and distilled water. An excess amount of Entacapone was added to the 100 ml beakers containing mixture of 40ml of 20% Sodium acetate and 60 ml distilled water. The beaker was shaken at 28 ±1ºC. The solution was analyzed by spectroscopy against corresponding solvent as a blank.

2.3.2 Preparation of standard stock solution:

The standard stock solution (Stock A) was prepared by dissolving 100 mg of Entacapone in 100 ml volumetric flask with 40ml of 20% Sodium acetate (1000 µg/ml). The sub stock solution (Stock B) was obtained by diluting 10 ml of Stock A solution up to 100 ml with distilled water (100 µg/ml). The Stock-B solution was scanned in the UV- range at 400-200nm for the determination of λ max of Entacapone by using blank solution. The λ max of Entacapone was found to be 378 nm as shown in Figure 2.

2.4 Method Validation

2.4.1 Linearity

Pipette out 10 ml standard sub Stock B solution (100µg/ml) in 100 ml volumetric flask and make up the volume up to the mark with distilled water to get concentration of 10µg/ml (Stock C). Different aliquots of Stock C solution of ETC were taken in a series of 10 ml volumetric flasks and volume made up with distilled water to get concentration 0.5-5µg/ml and measure the absorbance at 378 nm. Five replicates of analytes were measured and record the absorbance *versus* concentration as shown in Table 1. Plot a graph concentration *versus* absorbance; a linear correlation was found which obeys Beer Lambert's Law in the concentration range of 0.5-5 µg/ml (Figure 3). 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^2).

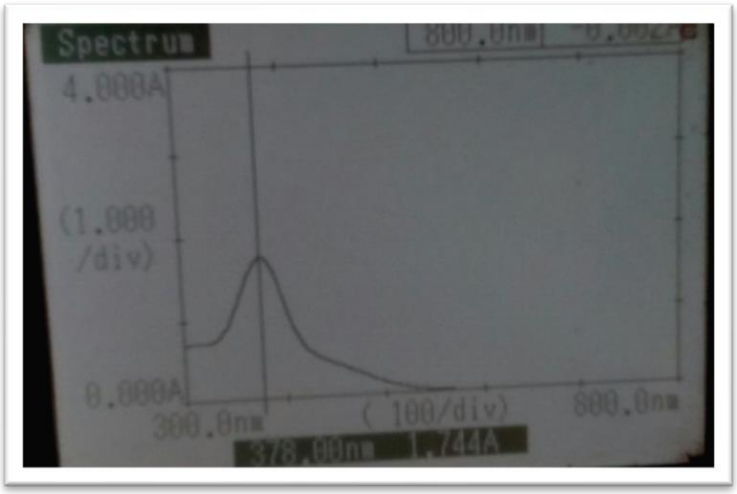

Figure 2: Absorbance spectrum of ETC.

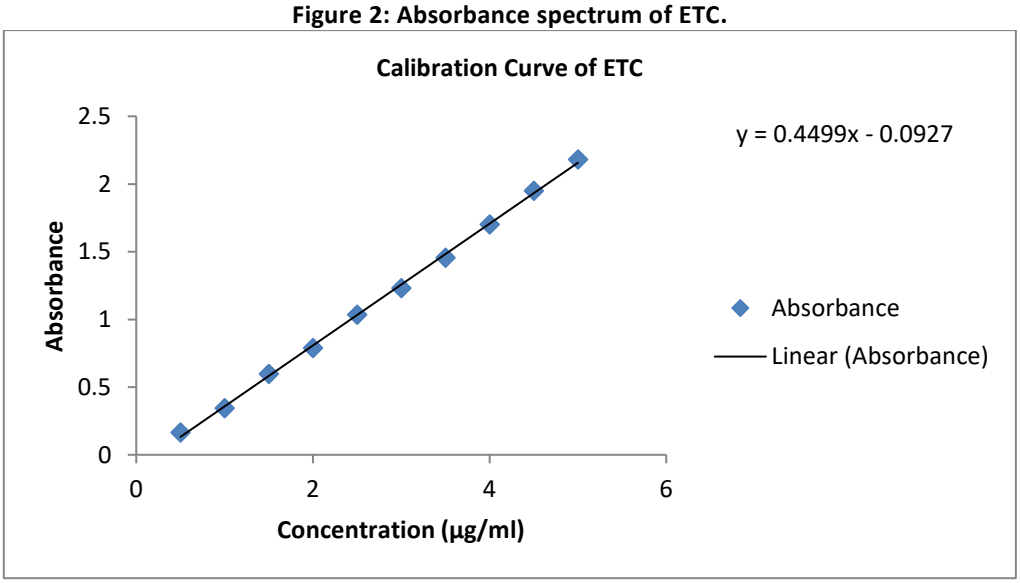

Figure 3: Calibration curve of ETC.

2.4.2 Limit of Detection (LOD) and Limit of Quantification (LOQ)

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample that can be detected but not necessarily quantitated as an exact value. The quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample that can be quantitatively determined with suitable precision and accuracy. The quantitation limit is a parameter of quantitative assays for low levels of compounds in sample matrices and is used particularly for the determination of impurities and/or degradation products. The valve of LOD and LOQ are determined by using standard deviation of the response and slope approach as defined in International Conference on Harmonization (ICH) guidelines[23]. The limit of detection and limit of quantitation of proposed method was found to be 0.35 µg/ml and 0.91 µg/ml respectively.

2.4.3 Precision

To determine precision, 7 days measurement (intra-days and interday) were computed with relative standard deviation (RSD%) for replicate samples (n = 5) using concentration 10, 15 and 20µg/ml Both the intra-day and interday samples were calibrated with standard curve concurrently prepared in the same day of analysis.

2.4.3.1 Intraday Precision

Intraday precision of test method is demonstrated by three samples of the same batch (same concentration) at initial, 24 and 48 hours (Table 1).

Table 1: Intraday-Interday Precision Data of ETC.

ETC taken (µg/ml)	Intraday precision			Interday precision		
	ETC found (µg/ml)	RE %	RSD %	ETC found (µg/ml)	RE %	RSD %
10	10.035	0.2045	0.4992	9.981	0.2197	0.5391
15	15.011	0.3239	0.5259	14.968	0.4437	0.7262
20	20.015	0.4667	0.5711	19.985	0.5863	0.7100

2.4.3.2 Interday Precision

Interday precision of test method is demonstrated by three samples of the same batch (same concentration) on three successive days (Table 1).

2.4.4 Accuracy

To determine the accuracy of the proposed method, recovery study was carried out by adding different amount (80%, 100%. 120%) of bulk sample of Entacapone within the linearity range and results obtained are compiled in Table 2 and show good accuracy for the method.

Table 2: Accuracy data of ETC by Spectroscopy

Level	Amount of ETC added (µg)	Amount of ETC found (µg)	% Recovery	% RSD
80%	8	8.171	100.95	1.43
100%	10	9.907	99.07	1.32
120%	12	11.96	99.66	1.75

2.4.5 Assay

Assay of tablet dosage form was carried by same procedure as mentioned in methodology to equivalent weight of Entacapone (200 mg) by proposed spectroscopic method. The percent purity was found out using regression analysis (Table 3).

Table 3: Assay Results of Marketed ETC Tablet.

Formulation	Equivalent weight of Entacapone (mg)	Amount Found (mg)	% of Drug Found	Assay result %
Marketed Tablet	**200 mg**	**197.80** **199.65** **203.10**	**98.90** **99.82** **101.55**	**100.09**

3.0 RESULT AND DISCUSSION

Using hydrotropy, herewith we solubilize poorly water-soluble drug, Entacapone (Figure 1) with 40ml of 20% sodium acetate precluding the use of organic solvents. The Entacapone hydrotrope was estimated at 378 nm without interference of sodium acetate as shown in Figure 2.

The validation parameters such as linearity (Figure 3), precision (Table 1), accuracy (Table 2) and sensitivity (limit of quantitation and detection) were evaluated as per ICH guidelines. The assay procedure for estimation of the Entacapone in bulk and tablet was optimized without interference of sodium acetate was publicized in Table 3. Thus, the new spectroscopic method was developed and validated according to ICH guidelines. The optical characteristic data and validation parameters of Entacapone were summarized in Table 4.

Table 4: Optical characteristic data and validation parameter of ETC

Parameter	Analytical data
λ max (nm)	378
Molar extinction coefficient	$3.1077x10^3$
Sandell's sensitivity	0.1824
Correlation co-efficient (r)	0.999
Limit of detection (LOD, µg/ml)	0.35
Limit of quantification (LOQ, µg/ml)	0.91
Linearity Range (µg/ml)	0.5-5

Precision	0.49-0.72
Accuracy (Recovery data)	99.07-100.95
Assay of marketed tablets (%)	98.90-101.55

In comparison with the existing spectroscopic methods for the quantification of Entacapone, the present modified method can be considered new as it practices sodium acetate as solubilizing agent rather than urea at the same wavelength 378 nm with less time as exposed in Table 5. In addition, the proposed method can be considered green as it demonstrates that spectroscopy can be utilized without the usage of organic solvents and reagents with better sensitivity compared with other methods. Overall the proposed new and eco-friendly spectroscopic method is economical and suitable for quality control of Entacapone in bulk.

Table 5: Spectrophotometric Comparison among Proposed and Published methods I-VII[14-20].

Parameter / Method	Solvent	Reagents	Sonication / Heating Time (Min.)	Absorption maxima at λmax (nm)
Proposed Method	Distilled water	Sodium Acetate (40 ml)	5 min for sonication	378
I	Distilled water	8 m Urea (80 ml)	10 min for sonication	378
II	Distilled water	0.01 M NaOH		375
III	Distilled water	0.1 M NaOH		421
IV	10% acetonitrile			384.4
V	Methanol			308
	Ethanol	Ferric chloride (0.4% w/v)		309
VI	Distilled water	Ferric chloride (0.4% w/v)		391
	Aqueous solution of 0.1 N HCl and 0.1 N NaOH	Ferric chloride (0.4% w/v)		305 and 425 respectively
VII (Method A)	Distilled water	Bathophenanthroline, Ferric chloride solution, Othophosphoric acid	20 minutes for heating	535
VII (Method B)	Distilled water	P-nitroaniline (0.5%w/v), Sodium nitrite (3%w/v), HCl solution (10%v/v), NaOH solution		470

4.0 CONCLUSION

From the result and discussion, it can be concluded that spectroscopic method has been found to be new, accurate, precise and economical with better sensitivity for the estimation of Entacapone in bulk drugs and dosage forms as comparison with published methods (Table 5).

Due to low detection limit and quantitation limit of proposed method (0.35 µg/ml and 0.91 µg/ml respectively), it may be used for analyzing Entacapone particularly where sophisticated instruments like HPLC is not available. Thus, in addition, the proposed method employs an inexpensive instrument. Overall the present method can be considered green and economical as it demonstrates that spectroscopy can be utilized without the usage of organic solvent. And suitable for quality control of Entacapone in bulk drugs and pharmaceutical dosage forms.

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6.0 REFERENCES

1. Maheshwari RK. Application of hydrotropic solubilization phenomenon in spectrophotometric estimation of norfloxacin in tablets. Indian J. Pharm. Edu. Res 2006; 40: 237-240.
2. Maheshwari RK, Maheshwari RB, Bhatt P. Simultaneous spectrophotometric estimation of norfloxacin and tinidazole in two component tablet formulations. Asian J. Chem 2007; 18: 1481-1486.
3. Maheshwari RK, Chaturvedi SC, Jain NK. Novel application of Hydrotropic solubilising additives in

the estimation of aspirin in bulk sample and tablets. Int J Pharm Excip 2005; 4: 84-88.
4. Theneshkumar S, Gnanaprakash D, Gandhi NN. Enhancement of Solubility and Mass Transfer Coefficient of Salicylic Acid Through Hydrotropy; J Zhejiang Univ Sci A; 2009; 10(5): 739-745.
5. Sunil JK, Ajaygiri KG. Research on Application of Hydrotropy: A Review, Int.J. of Sci, Eng and Tech Res. 2014 ;3(10):2617-2619
6. Singer C, Adverse effects in the treatment of Parkinson's disease, Expert Review of Neurotherapeutics, 2002, 2(1):105–118.
7. Neil M.J.O. (Ed by) The Merck Index – An Encyclopedia of chemicals, Drugs and Biological. Merck and Co. Inc., 13th Edn. 3626; P. 637.
8. Nadejda S, Zarema K, Sanford B, Amanda ME, Patricia W, Samir W, Development of characterization methods for entacapone in a pharmaceutical bulk Journal of Pharmaceutical and Biomedical Analysis, 2011;54(4):860-865.
9. Prasoon B, Deepak V, Shailendra KS, Archana G, HPLC Method for Estimation of Drug Release of Entacapone in Entacapone, Levodopa and Carbidopa Tablets. Int J Pharm Sci Res 2017; 8(4): 1734-43.
10. Buchi NN, S Madhavi, SK AS, U Chandra T. Development and Validation Of RP-HPLC-PDA method for the simultaneous estimation of levodopa, carbidopaand entacapone In Bulk and pharmaceutical dosage forms. Indo-American Journal of Pharmaceutical Research, 2014; 4(11): 5235-5241.
11. V. Rama K, K. Bala MK, Babu BH, Development and validation of liquid chromatographic method for the simultaneous estimation of Levodopa, Carbidopa and Entacapone in the combined dosage form, Journal of Pharmacy Research, 8(3), 2014; 281-288
12. Dasari P, Arava V, Bhoomireddy R, Ch.VSL, Kameswarrao, Bethi M. Development and Validation of a RP-HPLC Method for Determination of Related Substances and Degradants in Entacapone. Journal of Chromatographic Science, 2016; 54(8), 1310–1323.
13. Alagar RM, Ch. Shyamsundar, David B, Rao KNV, Selva KD, Analytical Method Development and Validation for Simultaneous Estimation of Carbidopa, Levadopa and Entacapone in its Bulk and Tablet dosage form by UPLC. Int. Res, J, Pharm, 2013; 4(11):53-56.
14. Ruchi J, Nilesh J, Deepak KJ, Surendra KJ, A novel approach using hydrotropic solubalization Technique for Quantitative estimation of Entacapone in bulk drug and dosage form. Advanced Pharmaceutical Bulletin, 2013; 3; 409-413.
15. Koradia SK, Agola AS, Jivani NP, Manek RA, Pandey S. Development and Validation of Derivative Spectrophotometric Method for Determination of Entacaponein Pharmaceutical Formulation, International Journal of Pharma Research and Development, 2009, 8110):1-7.
16. Koradia SK, Jivani NP, Malaviya SV, Chauhan SP, Vaghani SS. Development and Validation of Spectrophotometric Method for the Estimation of Entacapone in Pharmaceutical Formulations. Int. J. Chem. Sci; 2009, 7(1):349-352.
17. Chalikwar SS, Shirkhedkar AA, Bagul MA, Jain PS. Surana SJ. Development and validation of zero- and first-order derivative area under curve spectrophotometric methods for the determination of entacapone in bulk material and in tablets. Pharmaceutical Methods, 2012;3(1):14-17.
18. Shah J, Banerjee SK, Chhabra GS, Spectrophotometric Method Development and Validation for Entacapone in Bulk and Formulation, Bulletin of Pharmaceutical Research 2011;1(2):7-9.
19. Nashwah GM, and Mohamed SM, Determination of Antiparkinsonism Drug Entacapone, J. Chil. Chem. Soc 2010; 55: 85-89.
20. Neeha T and Devala RG. New spectrophotometric methods for the determination of Entacapone in bulk and pharmaceutical dosage forms, Elixir Appl. Chem. 2011; 38; 4064-4065.
21. Armenta S, Garrigues S, Dela Guardia; Green analytical chemistry. Tr. Ana. Chem. 27; 2008; 497-511.
22. Patil VP; Gaikwad AD; Kulkarni VS; Kawade RV; Kale SH; Green analytical chemistry: an overview; Inventi Rapid: Pharm Ana & Qual. Assurance; 2012; (2). 294.
23. International Conference on Hormonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised Tripartite Guideline, Validation of Analytical Procedures: Text and Methodology Q2 (R 1), Complementary Guideline on Methodology dated 06 November 1996, incorporated in November 2005, London.