INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Research Article

ESTIMATION OF DONEPEZIL HYDROCHLORIDE BY ION COMPLEX EXTRACTIVE SPECTROMETRY

Ravi Kumar V*, Chaitanya S, Sambasiva Rao A, Sreekiran M

Department of Pharmaceutical Analysis, Sri Indu Institute of Pharmacy, Ibrahimpatnam Hyderabad, Andhra Pradesh, India

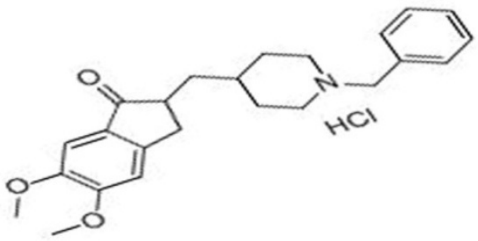
*Corresponding Author: ravikumar.vejandla@gmail.com

ABSTRACT

Donepezil HCl is a drug to relive from Alzheimer's disease which is a progressive, degenerative disease of the brain, causes thinking and memory to become seriously impaired. It is the most common form of dementia and not official in Indian pharmacopoeia. Literature survey has been revealed that there is no relevant visible spectrophotometric method has been reported for the estimation of Donepezil HCL in bulk and in dosage forms. Hence an attempt has been made to develop and validate a simple, economic, rapid and accurate method. The developed method involves formation of extractable ion pair complex of drug with azo-dye in acidic medium. De-ionized water is used as extracting solvent for Eriochrome Black T dye. Extractable complex shows reddish colored complex within a span of 05 minutes. The λmax was 510 nm. The method was used to determine the concentrations in between the range of 0.2- 25 µg ml^{-1}. The calibration curve was plotted. The regression equation is Y= 0.080x+ 0.045. The correlation coefficient obtained was 0.995. The complex was stable for 30 minutes. The proposed method was simple, sensitive and economical for the quantitative determination of Donepezil HCl and was successfully employed for the estimation of bulk drug and in formulation.

Keywords: Donepezil HCl, Eriochrome Black T, UV-Vis. Spectrophotometer, Colorimeter.

INTRODUCTION



Donepezil hydrochloride (DH) is chemically, -2-[(1-Benzyl-4-piperidyl)methyl]-5,6-dimethoxy-1-indanone hydrochloride It is designated as E 2020. Molecular formula is $C_{24}H_{29}NO_3$ and molecular mass is 379.492 g/mol. Solubility of Donepezil is freely soluble in chloroform, soluble in water (2.931 mg/L), partly soluble in 95% ethanol, methanol and practically insoluble in ethyl acetate and n-hexane. According to the literature, the lambda max of Donepezil hydrochloride was found to be 230nm. I.R. broad peaks at 1720, 1680, 1560 cm^{-1} Donepezil hydrochloride is having a major ring of cyclopentanone. The bond angle in cyclopentanone is 120°, due to Baeyer strain theory the carbonyl group is acting as chormophores in the molecule. Ion Complex Extractive Spectrometry (ICES) is a type of charge transfer complex. The complex formed with the drug is due to secondary valence forces, but this force is weak, hence the complex is stable for short time only. Azo dyes are having a azo group which is pH

dependent in action, when an azo dye comes in contact with a drug it forms IPC or charge transfer complex at suitable conditions, it play an important role in estimating the drug content at visible region with the help of Colorimeter. Various azo dyes include: Methyl orange, Methyl red, Congo red, Eriochrome Black T, Disperse Red, Butter Yellow etc. among these **Eriochrome Black T** was selected for the work, its chemical formula can be written as $HOC_{10}H_6N=NC_{10}H_4(OH)(NO_2)SO_3Na$ molecular weight is 461.38[1-4]. A through literature survey has revealed the following reported methods for the estimation of Donepezil in bulk, formulation and biological fluids using different analytical techniques [4-16]. ICES method has been applied for estimation of Donepezil hydrochloride in the present work.

MATERIALS AND METHODS

Materials

All chemical, reagents & solvents are AR grade supplied by Quality traders, Hyderabad. The pure drug Donepezil HCl (DH) was obtained as gift sample from Dr. Reddy's Laboratories, Hyderabad, India and sample tablets two brands M_1 & M_2 are purchased from local medical shop.

Instrumentation

Systronics 2202 UV/VIS double beam spectrophotometer, colorimeter EI-313 was used for the study.

Standard solutions

Stock solution

Donepezil stock solution was prepared accurately by weighing 10 mg of the drug and dissolving in 100 ml of de-ionized water thus making the concentration of 100µg/ml.

Test solution

For analysis of drug in tablet dosage form, twenty tablets were weighed accurately and triturated in the mortar to get fine powder. The amount of tablet powder equivalent to 10 mg of DH was weighed and transferred to 100 ml volumetric flask and dissolved in de-ionized water. The solution was kept in ultrasonicator for 10 min and filtered through Whatman's filter paper No. 41.

Dye solution

1 gram of the dye was accurately weighed and dissolved in 100 ml of de ionized water, to make 1% solution.

Buffer solution

Acid phthalate buffer was prepared at pH 2.2 by taking 50 ml of 0.2M potassium hydrogen phthalate in 200ml volumetric flask, add 49.5ml of 0.2M HCl and add water to make up the required volume.

METHOD DEVELOPMENT

Preparation of Calibration curve

The standard stock solution 100µg/ml was taken and further diluted to get different dilutions in the range of 0.5 – 25µg/ml, the prepared solutions were taken in 125 ml separating funnels, was add 1ml of buffer and 1 ml of dye solution in each of them, the contents were shaken for 10 minutes. The colored complex was extracted using chloroform in the proportions of 5:3:2 ml and are washed completely to separate the colored complex. The reddish colored complex was measured at 510 nm. Calibration curve was plotted and regression line was calculated. The ICES method was validated for achieving the best results.

Assay for marketed products

Twenty tablets were weighed and powdered. Equivalent to 10 mg of DH was weighed and transferred to 100 ml volumetric flask and dissolved up to 100ml with de-ionized water. The resulting solution was sonicated and filtered through Whatmann No 41. The resulting solution was diluted for the required amount and its absorbance was calculated. The percentage strength of drug in tablet was found.

RESULTS AND DISCUSSION

ICES method was validated, by comparing the UV & Visible results of time domain precision curve in fig.: 3 by which the stability of complex was checked. It states the change in absorption with respect to time, as the complex formed with drug cannot be stable for long time. So to estimate the time until the method was repeated, for this 10µg/ml dilution was considered and the absorbance was measured for every 10 minutes interval until the drastic change in the absorption. The

graph was plotted with time (min) on X-axis and Absorbance on Y-axis. From the above carried method, it is found that ICES is a very simple rapid method for analyzing Donepezil in tablet form. It was observed that the complex formed between drug and dye is stable for 30minutes. In the Table 7 optical characteristics were observed. The only limitation of this method is that, long term studies are not possible since the complex formed begins to degrade after 30 minutes. It is seen in time domain precision curve Fig 3.
Calibration curve Values by using UV-Spectroscopy & colorimeter are clearly mentioned, in the Table 1. The values for Std. drug concentration verses absorbance are taken and plotted a linear graph as calibration curve which is shown in Fig 1 In the same way for Std. drug complex with dye, absorbance values are taken by using colorimeter at different concentrations are illustrated in Table 2 for the same calibration curve had been plotted observed in Fig 2.

Tablet Assay

By using the formulae it was determined and report mentioned in table 3.
y= mx+c
m = Slope of the calibration curve
y = Absorbance of the sample
c = X-intercept Calculating for x we get, the formula as X = y-c/m

Percent Label claim = Concentration of sample / Concentration of sample theoretically x 100

METHOD VALIDATION[17-18]

Linearity

The linearity range is the detect-ability that obeys Beer's law is dependent on the compound analysis. The working sample concentration and sample tested for accuracy should be in the linear range. The behavior of UV response vs concentration may have linear or non-linear relationship. To establish the range of linearity between drug concentration (5, 10, 15, 20 & 25 µg/ml) and absorbance were mentioned in Table 1 & Table 2 and calibration curve was in Fig 1 & Fig 2 respectively for UV-spectroscopy & colorimeter.

LOD & LOQ

The limit of detection (LOD) is defined as the lowest concentration of an analyte that can be readily detected but not necessarily quantified. The limit of quantitation (LOQ) is defined as the lowest concentration of an analyte that can be quantified with acceptable precision and accuracy. LOD and LOQ were 0.2µg/ ml and 0.33 µg/ml for UV method and LOD is 0.4 µg/ml & LOQ is 0.56 µg/ml respectively which were mentioned in Table 4.

Ruggedness

ICH defines robustness as measure of the method's capability to remain unaffected by small, but delebrate variations in method parameters. It can be partlyrealistic, system suitability specifications. Thus it is important to set tight, but realistic, system suitability specifications.data obtained from studies for robustnessare in Table 5.

Time Domain Precision which is compared for both the methods UV-spectroscopy & colorimeter where the values were mentioned in Table 6 and also the graphical representation was observed in Fig 3.

CONCLUSION

The experiment conducted for determining the analytical behavior in time-domain using UV and ICES methods with ten minutes interval resulted that the determination was found to be repetitive in UV method while under the ICES method the absorbance was found to be drastically varying exhibiting the time dependency of the analysis using ICES method. The behavioral aspect of these two methods in time-domain has been drawn graphically represented in Fig 3 and the various optical characteristics have been mentioned in Table 7 which were compared fo0r both methods. From both the methods, it is evident that UV method is more suitable for analysis rather than ICES visible spectrometry. But the analysis by UV requires sheer practice and expensive. ICES is a suitable method for small scale analysis of Donepezil Hydrochloride using colorimeter, as it is cheap. Donepezil can be estimated with ease and can save time. Hence forth this report gives a perfect simple and rapid technique.

ACKNOWLDGEMENT

We are thankful to our respective Chairman Mr.R.Venkat Rao, for providing us the instruments and also to our Principal Dr.A.Sambasivarao who given permission to carry out the work. We are also thankful to technical assistants who spared their time with us.

REFERENCES

1. Bhupinder M and Manju M. Alkanes and Cycloalkanes. Organic Chemistry. 2009;172.
2. Kalsi PS.Ultraviolet Spectroscopy. Spectroscopy of Organic Compounds. 2008;(5):49-50.
3. Patrick JS. Complexation and Protein Binding. Martin's Physical Pharmacy and Pharmaceutical Sciences. 2008;(5):270-271.
4. Jayanna BK, Nagendrappa G, Arunkumar and Ninge G. Spectrophotometric estimation of Donepezil hydrochloride in tablets. J Phar Biomed Sci.2009;1(1):1-3.
5. Pappa H, Farrú R, Vilanova PO, Palacios M and Pizzorno**.** A new HPLC method to determine Donepezil hydrochloride in tablets. J Pharm Biomed Anal.2002; 27(1-2): 177-182.
6. Krishna Reddy NV, Phani.R.S.Ch and R.Ramesh Raju. RP–HPLC method development for analysis and assay of donepezil in formulation. An International Journal of Advances in Pharmaceutical Sciences.2010;1(1):100-103.
7. Tushar GB and Patel PK.RP-HPLC Method for the Estimation of Donepezil Hydrochloride Dosage Form. E-J Chem. 2009;6(2):594-600.
8. Dharmaraj SS, Kannan S and Lakshmi SD.Development and validation of RP- HPLC method for estimation of Donepezil HCl from bulk and marketed dosage forms. J Chem Pharm.2010;2(6):62-67.
9. Sastry BS, Gananadhamu S, Devadasu C and Balaji K. New RP-HPLC method for estimation of donepezil hydrochloride in pharmaceutical formulations. International Journal of Chemical Sciences.2008;6(4):1976-1983.
10. Lu YH, Wen HM, Li W, Chi YM and Zhang ZX. Determination of donepezil in human plasma by HPLC-MS. Yao Xue Xue Bao.2003;38(3):203-206.
11. Ma Wuxiang and Huang Liping. RP-HPLC determination of donepezil in human plasma by solid-phase extraction. Zhongguo Yiyuan Yaoxue Zazhi.2006;6(2):149-151.
12. Yasui-Furukori, N, Furuya R and Takahatam T. Determination of donepezil, an acetylcholinesterase inhibitor, in human plasma by high-performance liquid chromatography with ultraviolet absorbance detection. J Chromatogr B Analytical Technologies Biomed Life Sci.2002;768:261-265.
13. Nakashima K, Itoh K, Kono M and Nakashima MN. Determination of donepezil hydrochloride in human and rat plasma, blood and brain microdialysates by HPLC with a short C30 column. J Pharm Biomed Anal.2006;41:201-206.
14. Sangshetti JN, Mahaparale PR and Shinde DB. Spectrometric estimation of Donepezil hydrochloride in bulk and tablet formulation. Applied sciences. (3): 109-112.
15. Dharmaraj SS, Kannan S and Lakshmi DS. Development and Validation of RP-HPLC method for the estimation of Donepezil from bulk and marketed dosage forms. J Chem Pharm. 2010; 2(6):62-67.
16. Srinivasan, Renuga D, Balaji. A New Validated Stability Indicating RP-UPLC Method. Int J Cur Research . 2010; (5): 88-95.
17. ICH (1996) Harmonized tripartite guideline: validation of analytical procedures: Methodology.Q2B.
18. ICH (1996) Harmonized tripartite guideline: validation of analytical procedures.Q2A.

Table 1: Data for Conc. & abs. for pure drug by using UV-Spectroscopy

Concentration	Absorbance
0	0.00
5	0.282
10	0.613
15	0.99
20	1.276
25	1.59
30	1.89

Fig. 1: calibration curve of pure drug using UV spectroscopy

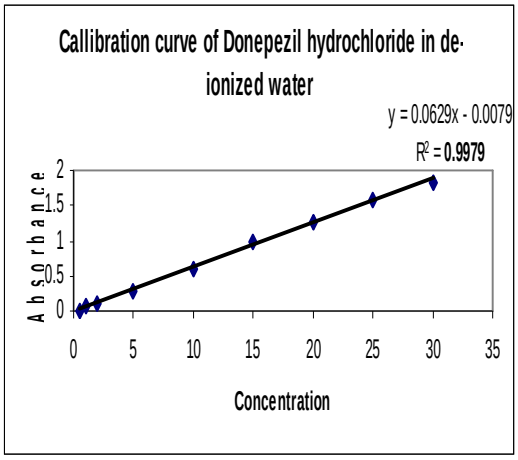


Fig. 2: Calibration curve for pure drug complex with dye

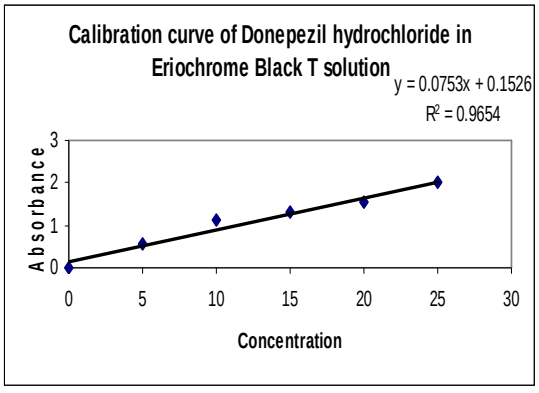


Table 2: Data for Conc. & abs. for pure drug Complex with dye by using Colorimeter

Concentration	Absorbance
0	0
5	0.576
10	1.124
15	1.304
20	1.536
25	1.886

Table 3: Marketed brands of Donepezil tablet assay data.

TABLET SAMPLES	LABEL CLAIM (mg)	OBSERVED CONTENT (mg)	% OF DRUG FOUND
*M-1	5	4.989	99.78
**M-2	5	4.993	99.86

*M-1 is Dopezil (Ranbaxy) **M-2 is Dorent (Torrent)

Table 4: Values of LOD & LOQ for two methods

Method	LOD (µg/ml)	LOQ (µg/ml)
UV	0.2	0.33
ICES	0.4	0.56

Table 5: Ruggedness

Experiment performed	Absorption Maxima	
	UV (nm)	ICES (nm)
LAB-1	230	510
LAB-2	230.6	509.4

Table 6: Data for time Domain Precision.

Time (min.)	Absorbance of 10 µg/ml solution	
	UV method	ICES
10	0.612	1.124
20	0.612	1.123
30	0.612	1.123
40	0.611	1.063
50	0.609	0.643

Fig. 3: Domain curve comparing both methods UV Spectrophotometer & Colorimeter

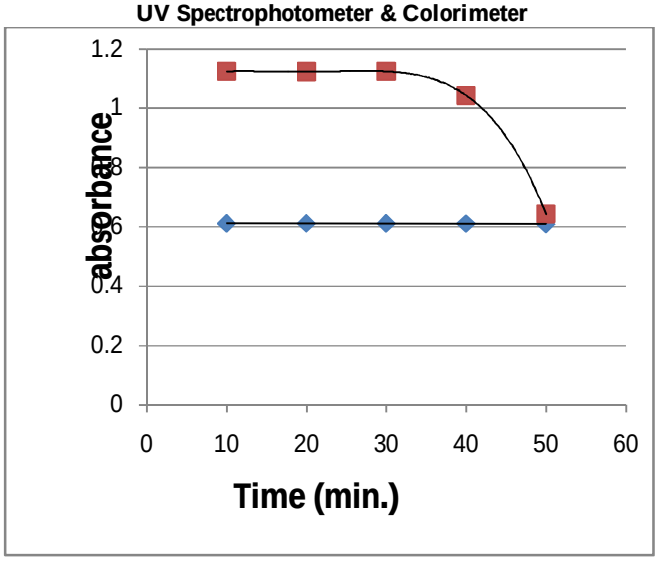


Table 7: Optical characteristic data for UV & ICES methods.

Optical characteristics	UV method	ICES method
λ – maximum	230.8nm	508.0nm
Beer's law limit	5 – 40 µg/ml	5 – 20 µg/ml
Molar absorption	1.38 x 10^5 mol^{-1} cm^{-1}	3.277 x 10^4 mol^{-1} cm^{-1}
Correlation co-efficient	0.9979	0.9654
Significance values	0.0036	0.0023
RQS	0.9978	0.9728