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DEVELOPMENT ANDVALIDATION OF DONEPEZIL HYDROCHLORIDE IN BULK ANDPHARMACEUTICAL DOSAGE FORM BY UV SPECTROSCOPIC METHOD

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ABSTRACT

Objective: Donepezil hydrochloride is Anti Alzheimer agent drug that is available as tablets on the market for oral administration. The main object of this work is to develop and validate the easiest UV spectroscopic method for the determination of Donepezil hydrochloride for tablet formulation (marketed formulation) Method: A simple, reproducible and efficient method for the determination of Donepezil hydrochloride in bulk and tablet formulations have been developed. The developed method is based on the estimation by UV-Visible spectroscopy. In this method, water was selected as the solvent. A wavelength selected for estimation of Donepezil hydrochloride was 271.5nm. Result: Linearity was found in the concentration range 10 to 80µg/ml (r^2=0.9991). A recovery study was found to be 98.01-99.84 % for Donepezil hydrochloride. The method was found to be precise as % RSD was low in repeatability, intermediate precision, and reproducibility. LOD and LOQ were found to be 1.70 µg/ml and 5.15 µg/ml respectively. Conclusion: The method was found to be very simple, and precise. It also had a good recovery. The Developed method can be used for further routine analysis and stability study of a Donepezil hydrochloride.

INTRODUCTION

Donepezil hydrochloride (centrally acting reversible acetyl cholinesterase inhibitor) is used in the treatment of Alzheimer's disease [1-10]. The molecular formula of Donepezil is $C_{24}H_{29}NO_3$,HCL and molecular weight is 410.0g/mol. A review of the literature revealed that several studies involving method development and estimation of Donepezil hydrochloride have been carried out of RP-HPLC, LC-MS and UV spectrophotometers [11-23]. So, it was thought of interest to develop a simple, precise, accurate and cost-effective method for estimation of Donepezil hydrochloride in bulk and tablet Formulations.

MATERIALS AND METHODS

Material:

Donepezil hydrochloride was obtained as a gift sample from Vega Biotech Private Limited, Vadodara, Gujarat (India). All solvent and other chemicals used were A.R. grade. Double distilled water (fresh) was used during the work.

Preparation and Standard Solution

Standard stock solution of Donepezil hydrochloride

Accurately weighed 100mg quantity of Donepezil hydrochloride was transferred into 100ml volumetric flasks, dissolved and dilute up to mark with distilled water to get 1000µg/ml solution for Donepezil hydrochloride. This 1000µg/ml stock solution further diluted to obtained 100µg/ml solution for Donepezil hydrochloride.

Selection of Wavelength

The standard solution of Donepezil hydrochloride was scanned between 200-400 nm and λ_{max} for Donepezil hydrochloride was selected to 271.5nm.

Preparation of the Calibration Curve

Appropriate aliquots were pipette out from the standard stock solution into a series of 10ml volumetric flasks. The volume was made up to the mark with distilled water to get a set of solution having the concentration ranging from 10,20,30,40,50,60,70,80 µg/ml of Donepezil hydrochloride. Absorbance of above solutions was measured at 271.5 nm and calibration curve of absorbance against concentration was plotted.

Preparation of sample solution (For accuracy or recovery) for tablet formulation

The tablets of Donepezil hydrochloride were powdered and from the triturate, tablet powder equivalent to 100mg of Donepezil hydrochloride was weighed and transferred into a 100ml of volumetric flask, dissolved and diluted up to mark with distilled water. The solution was filtered. Transferred 1ml aliquot of above solution into a 10ml volumetric flask and diluted up to mark with distilled water. From above solution, prepare solution containing 10µg/ml of Donepezil hydrochloride by proper dilution with distilled water.

METHODVALIDATION

Linearity

The linear response of Donepezil hydrochloride was determined by analyzing independent levels of calibration curve in the range of 10-80µg/ml. Accurately measured standard working solutions of Donepezil hydrochloride were transferred to a series of 10ml volumetric flask and diluted up to the mark with distilled water. Absorbance was measured at a wavelength 271.5nm. The drugs follow the Beer's & Lambert's law in the concentration range 10-80µg/ml.

Accuracy

The recovery experiments were carried out in triplicate by spiking previously analyzed samples of the Donepezil hydrochloride (10µg/ml) solution with three different concentrations of standards at 80%, 100% and 120% and the absorbance of all solutions were taken at 271.5nm and percentage recovery of Donepezil hydrochloride was calculated.

Precision

Repeatability

Repeatability measurement was carried out by analyzing solutions containing 10µg/ml of Donepezil hydrochloride six times. Pipette out 1ml aliquot from the stock solution and transfer it to 10ml volumetric flask. Dilute up to mark with distilled water. The absorbance of six aliquots of same concentration was measured and % RSD was calculated.

Intraday precision

The intraday precision was determined for standard solution of Donepezil hydrochloride (10µg/ml) for three times on same day. The results were reported in terms of % RSD and it should be less than 2%.

Interday precision

The interday precision was determined for standard solution of Donepezil hydrochloride (10µg/ml) for the three times on different day. Percentage relative standard deviation should be less than 2%.

Reproducibility

Reproducibility was performed by preparing the standard solution of Donepezil hydrochloride (10µg/ml) and analyzed them by different analyst.

The limit of detection (LOD) and Limit of Quantification (LOQ)

The limit of detection and the limit of quantification was measured according to the ICH guideline. It was measured by the following equation.

Assay

Donepezil hydrochloride finely powdered and powdered equivalent to 10mg of Donepezil hydrochloride was dissolved in distilled water then sonicate it for 5 min. Further dilution was carried out to obtain 10µg/ml concentration of Donepezil hydrochloride The % drug content was calculated.

RESULTS

Melting Point

The melting point of Donepezil hydrochloride was found to be 217-223(°C). The melting point of drug sample corresponds to the

reported melting range, indicating the authenticity of drug sample.

Wavelength selection

UV spectra Donepezil hydrochloride was taken in water (Tableno 1)andλ_{max} was observed at 271.5 nm. Henceλ_{max}forDonepezil hydrochloride was found to be 271.5 nm.

Linearityand Range

The Linearity graph of Donepezil hydrochloride is shown in fig. 2. Calibration graph at 271.5 nm show in fig. 3. Linearity range of Donepezil hydrochloride was found to be 10 to 80µg/ml. The linearity equation was found to be y = 0.0142x- 0.0032. Correlation coefficient forDonepezil hydrochloride was 0.9991 which indicate purposed method is linear.

Table1 Trial and Error of Solvents

SELECTIONOFSOLVENT	INFERENCE
n-hexane	Insoluble
Ethyl acetate	Insoluble
Ethanol	Slightly soluble
Acetonitrile	Slightly soluble
Glacial acetic acid	Spectrum was not proper
Chloroform	Spectrum was obtained but not precise
Distilled water	Proper spectra was observed (271.5nm)

Figure 1. Spectra of Donepezil hydrochloride for wavelength estimation

Figure 2. Spectra of Donepezil hydrochloride for linearity

Table 2 Data of Calibration curve for Donepezil hydrochloride

Sr.No.	Concentration µg/ml	MeanABS.±SD
1.	10	0.137±0.0025
2.	20	0.229±0.0091
3.	30	0.340±0.0109
4.	40	0.454±0.0205
5.	50	0.557±0.0260
6.	60	0.676±0.0365
7.	70	0.789±0.0403
8.	80	0.898±0.0567

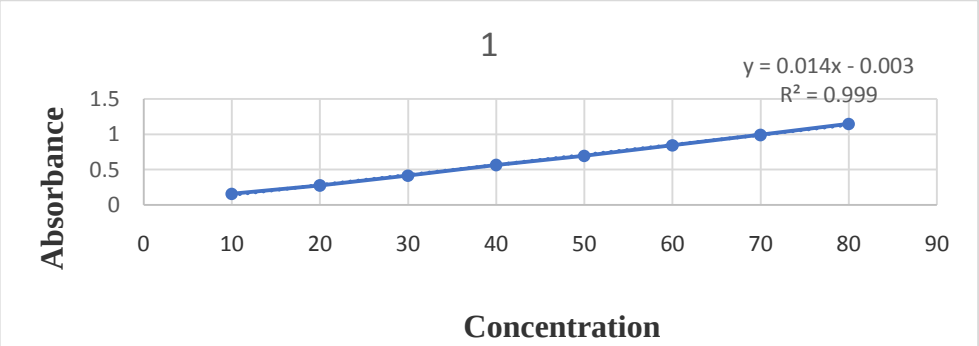

Figure3 Calibration Graph of Donepezil hydrochloride

Precision

Repeatability

Data of Repeatability is given in table no 3.%RSD was found to be 0.605%which indicates the purposed method is precise.

Intermediate precision

Intraday precision

Intraday precision is given in table no 4.%RSD was found to be 0.51%which indicates the purposed method is precise.

Interday precision:

Interday precision is given in table no 5.% RSD was found to be 0.520% which indicates the purposed method is precise.

Reproducibility precision

Reproducibility precision was found to be table no 6.%RSD was found to be 0.523 %which indicates the purposed method is reproducible.

Accuracy

% Recovery data obtained by proposed method are shown in the following table 7. All the data shows the purposed method is accurate.

Assay

No any interference excipient for λ_{max} of Donepezil hydrochloride. Hence the purposed method is applicable for routine estimation of Donepezil hydrochloride in the tablet dosage form. The result is shown in following the table8.The %purity of Donepezil hydrochloride was found to be 95.35%.

LOD &LOQ

LOD and LOQ are calculated based on standard derivation and slop of calibration curve and the data are shown in following table9.

Table3 Repeatability data by UV spectrophotometry

Sr. No.	Concentration(µg/ml)	Absorbance	Average	STDEV	%RSD
1.	10	0.192	0.1931	0.0011	**0.605**
2.	10	0.193			
3.	10	0.192			
4.	10	0.194			
5.	10	0.193			
6.	10	0.195			

(n=6)

Table4 Intraday precision data of Donepezil hydrochloride.

Sr. No.	Concentration (µg/ml)	Absorbance	Average	STDEV	%RSD
1.	10	0.194	0.193	0.001	**0.51**
2.	10	0.192			
3.	10	0.193			

(n=3)

Table5 Interday precision data of Donepezil hydrochloride.

Sr.no.	Interday	Concentration (µg/ml)	Absorbance	Average	STDEV	%RSD
1.	Day1	10	0.192	0.192	0.001	**0.520**
2.	Day2	10	0.193			
3.	Day3	10	0.191			

(n=3)

Table6 Reproducibility precision data of Donepezil hydrochloride.

Sr.no.	Reproducibility	Concentration (µg/ml)	Absorbance	Average	STDEV	% RSD
1.	Analyst1	10	0.190	0.191	0.001	**0.523**
2.	Analyst2	10	0.192			
3.	Analyst3	10	0.191			

(n=3)

Table7 %Recovery of Donepezil hydrochloride.

Sr. no.	Level	Conc. of test solution	Conc. of standard solution	ABS.	Conc. (µg/ml)	% recovery	Average	STD.	% RSD
1.	80	10	0.8	0.249	18	98.66	0.249	0.002	**0.833**
2.	80	10	0.8	0.248	18	98.27			
3.	80	10	0.8	0.252	18	99.84			
1.	100	10	1.0	0.277	20	98.66	0.277	0.001	**0.361**
2.	100	10	1.0	0.276	20	98.30			
3.	100	10	1.0	0.278	20	99.01			
1.	120	10	1.2	0.303	22	98.01	0.305	0.002	**0.655**
2.	120	10	1.2	0.305	22	98.65			
3.	120	10	1.2	0.307	22	99.29			

Table 8 Assay Donepezil hydrochloride in table tdosage form by UV.

Formulation	Label claim (mg/tablet)	Amt. Found (mg/tablet)	Drug content (%) ± SD
Donepezil hydrochloride	10mg	9.686mg	96.86±0.0030

Table 9 DataofLOD&LOQ.

Drug	LOD(µg/ml)	LOQ(µg/ml)
Donepezil hydrochloride	1.70	5.15

Table10Summaryofvalidationparameters.

Sr.no.	Parameters	Donepezil hydrochloride
1.	Melting point of the drug**(°C**	217-223
2.	Linearity**(µg/ml)**	10-80
3.	Correction coefficients**(R^2)**	0.9991
4.	Precision 1.Repeatibility**(%RSD)(n=6)** 2.Intraday **(%RSD) (n=3)** 3.Interday**(%RSD)(n=3)** 4.Reproducibility precision **(%RSD) (n=3)**	 0.605 0.518 0.520 0.523
5.	Accuracy**(%Recovery)(n=3)**	98.01-99.8
6.	Assay**(%)**	96.86
7.	LOD**(µg/ml))(n=6)**	1.70
8.	LOQ**(µg/ml))(n=6)**	5.15

DISCUSSION

The main objective of this work was to develop a simple method for the estimation of Donepezil hydrochloridein bulk and tablet dosage forms. First for the identification, a melting point study was performed. The melting point of the drug sample corresponds to the reported melting range, indicating the authenticity of the drug sample. UV spectra Donepezil hydrochloride was taken in water and$\lambda_{max}$was observed at 271.5nm.Hence$\lambda_{max}$for Donepezil hydrochloride was found to be 271.5nm.The linearity range of Donepezil hydrochloride was found to be10to80µg/ml. The linearity equation was found to be y = 0.0142x- 0.0032. The Correlation coefficient for Donepezil hydrochloride was 0.9991 which indicates the purposed method is linear. The data of repeatability, intermediate precision and reproducibility indicated that the optimized method was found to be precise. It also found to be accurate as per result of the recovery. The %purity of Donepezil hydrochloride was found to be 96.86% which is within a limit (table 10).

CONCLUSION

The proposed methods were found to be simple, sensitive, economical, accurate and precise and showed no interference from the common additives and excipients. The developed method was validated in terms of linearity, accuracy, precision in accordance with the ICH guidelines. The standard derivation and %RSD calculated for purposed method are within a limit, indicating high degree of precision. The results of the analysis of tablet dosage forms by the proposed methods are reproducible, reliable and accurate for determination of Donepezil hydrochloride. This spectrophotometric method can be used successfully for the routine analysis of donepezil hydrochloride in tablet dosage form of donepezil.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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