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Evaluation of Donepezil Hydrochloride Using Various Physical Parameters

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ABSTRACT
Donepezil Hydrochloride was evaluated for its physical properties including interference study, acid /base degradation and oxidation degradation. On comparison basis these parameters were studied using different (5mg and 10mg) drug dose. Reverse Phased HPLC technique was used to evaluate the various physical parameters.

Keywords: Donepezil HCl, Degradation, Alzheimer, Oxidative Degradation.

INTRODUCTION

Donepezil HCl is chemically known as (±)-2, 3-dihydro-5, 6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl] methyl]-1*H*-inden-1-one hydrochloride (Fig. 1). It is marketed under the trade name Aricept by its developer Eisai and partner Pfizer. It is a centrally acting reversible acetyl cholinesterase inhibitor. [1]

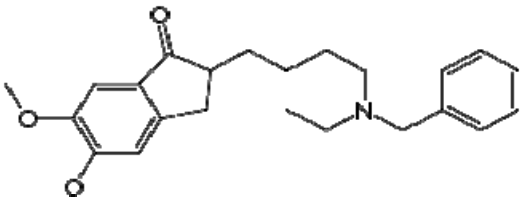

Fig. 1: Chemical structure of Donepezil

Its main therapeutic use is in the palliative treatment of mild to moderate Alzheimer's disease. [2] Donepezil has been tested in other cognitive disorders including Lewy body dementia [3] and vascular dementia. [4] Donepezil has also been found to improve sleep apnea in Alzheimer's patients. [5] It has an oral bioavailability of 100% and easily crosses the blood-brain barrier. Because of the long half-life of about 70 hours, it can be taken once a day. So there is an immense need to develop RP-HPLC method for its estimation in formulation. Accordingly a simple, rapid, precise and accurate method was developed for quality control of drugs formulation. [6-16]

In this research paper, Donepezil Hydrochloride was evaluated for its physical properties including interference study, acid degradation, base degradation and oxidation degradation. On comparison basis these parameters were studied using different (5mg and 10mg) drug dose.

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MATERIAL AND METHODS

Chemical and Reagents

HPLC grade methanol was purchased from SD fine chemical (Ahmedabad, India). Nylon 0.45µm (Gelman laboratory, Mumbai, India). Potassium dihydrogen orthophosphate, orthophosphoric acid and triethylamine were procured from SD fine chemical (Ahmedabad, India).

Interference Study Solutions

Mobile phase preparation

Dissolve 6.8 g of potassium dihydrogen orthophosphate in 100 ml of water and mix. Add 5 ml triethylamine and adjust pH of this solution to 2.2 ± 0.1 with orthophosphoric acid. Mix and filter the solution through 0.45µm nylon filter. Prepare a mixture of buffer pH 2.2 and methanol (60:40 V/V) mix.

Standard solution preparation

Transfer and accurately weighed quantity of about 25 mg of Donepezil Hydrochloride standard in a 25 ml volumetric flask. Add about 35 ml diluent and sonicate to dissolve. Equilibrate to room temperature and make up to volume with diluent. Dilute 5 ml of this solution to 25 ml with diluent and mix.

Sample solution preparation

Weigh 20 tablets and determine the average weight and transfer intact tablets equivalent to about 50 mg of Donepezil hydrochloride to 500 ml volumetric flask. Add about 400 ml of diluent and sonicate for about 30 min. Allow equilibration to room temperature. Dilute to volume with diluent and mix. Filter through 0.45µm nylon filter, discarding first few ml of the filtrate and use the subsequent filtrate.

Placebo solution

Weigh the placebo equivalent to 50 mg of Donepezil hydrochloride and transfer into a 500 ml volumetric flask. Add about 400 ml of diluent and sonicate for about 30 min. Allow equilibration to room temperature and dilute to volume with diluent. Filter through 0.45µm nylon filter, discarding first few ml of the filtrate.

Debenzyl impurity solution

Weigh accurately about 2.5 mg of Debenzyl impurity and transfer into a 25 ml volumetric flask, add about 10 ml of diluent and sonicate for about 5 minutes to dissolve. Dilute to volume with diluent and mix. Dilute further 1.0 ml of this solution to 200 ml with diluent and mix.

Benzylidine impurity solution

Weigh accurately about 2.5 mg of Benzylidine impurity and transfer into a 25 ml volumetric flask. Add about 10 ml of Acetonitrile and sonicate for about 5 minutes to dissolve. Dilute to volume with diluent and mix. Dilute further to 1.0 ml of this solution to 200.0 ml with diluent and mix.

Acid Degradation

Weigh accurately tablets powder equivalent to 50 mg of Donepezil and transfer into a 500 ml volumetric flask. Add about 15 ml diluent, sonicate for about 30 minutes to dissolve with intermittent shaking. Add 5.0 ml of 5N HCL solution and expose at 80°C for 5 hours on water bath for neutralization and make up to the volume with diluent and mix. Filter this solution through 0.45µm nylon filter and discard first few ml of filtrate**.** Use subsequent filtrate**.**

Base degradation

Weigh accurately tablet powder equivalent to 50 mg of Donepezil and transfer into a 500 ml volumetric flask. Add about 15 ml diluent, sonicate for about 30 minutes to dissolve with intermittent shaking. Add 5.0 ml of 5 N sodium hydroxide solution and expose for 1 hour at 80°C on water bath for neutralization and make up to the volume with diluent and mix. Filter this solution through 0.45µm nylon filter and discard first few ml of filtrate. Use the subsequent filtrate.

Oxidation degradation

Weigh accurately tablet powder equivalent to 50 mg of Donepezil and transfer into a 500 ml volumetric flask. Add about 15 ml diluent, sonicate for about 30 minutes to dissolve with intermittent shaking. Add 5.0 ml of 3% hydrogen peroxide solution and expose for 5 hours at 80°C on water bath. Allow to cool at room temperature and make up to the volume with diluent and mix. Filter this solution through 0.45µm nylon filter and discard first few ml of filtrate.

RESULTS AND DISCUSSION

Interference Study

The blank solution, placebo solution, impurity solution, standard solution, and sample solution, were prepared and injected. The obtained results are presented in the following Table 1.

Table 1: Results of Interference study of Donepezil Hydrochloride

Name of solution	RT (min)
Blank	No peak is observed
Placebo	No peak is observed
Benzylidine impurity	10.75 minutes
Debenzyl impurity	4.10 minutes
Donepezil hydrochloride in standard	11.44 minutes
Donepezil hydrochloride in sample (5 mg)	11.45 minutes
Donepezil hydrochloride in sample (10 mg)	11.46 minutes

Acid degradation

No significant degradation was observed in the sample treated with 5.0 ml of 5 M Hydrochloric acid solution and kept at 80˚C for 5 hours on water bath. Percentage degradation of 10mg tablet is bit higher as compare 5mg tablet (Table 2).

Table 2: Results of Acid degradation of Donepezil Hydrochloride

Condition	Mean area		% Assay		% degradation		Peak purity index
	5mg	10mg	5mg	10mg	5mg	10mg	
Initial	2872996	2887945	99.8	100.3	_	_	1.000
Treated with 5M HCl solution and kept at 80˚C for 5 hours on water bath	2862705	2850452	99.3	98.9	0.5	1.4	1.000

Table 3: Results of Base degradation of Donepezil Hydrochloride

Condition	Mean area		% Assay		% degradation		Peak purity index
	5mg	10mg	5mg	10mg	5mg	10mg	
Initial	2872996	2887945	99.8	100.3	_	_	1.000
Treated with 5 M NaOH solution and kept at 80˚C for 1 hour on water bath	2635316	2647638	90.5	90.8	9.3	9.5	1.000

Table 4: Results of Oxidative degradation of Donepezil Hydrochloride

Condition	Mean area		% Assay		% degradation		Peak purity index
	5mg	10mg	5mg	10mg	5mg	10mg	
Initial	2872996	2887945	99.8	100.3	_	_	1.000
Treatment with 5.0 ml of 3 % H_2O_2 solution and kept at 80˚C for 5 hours	832816	2841111	98.2	98.6	1.6	1.7	1.000

Base degradation

Degradation of 9.3 % was observed in Donepezil hydrochloride in the sample treated with 5 M sodium hydroxide solution and kept at 80˚C for 1 hour on water bath. Percentage degradation of 10mg tablet is almost same as compare 5mg tablet (Table 3).

Oxidative degradation

No significant degradation was observed in the sample treated with 5.0 ml of 3 % H_2O_2 solution and kept at 80˚C for 5 hours. There is no significant difference in percentage degradation of 10mg tablet in comparisation to 5mg tablet (Table 4).

CONCLUSION

Based on the obtained result it is concluded that there is no interference observed due to blank, impurities and placebo at the retention time of Donepezil hydrochloride in standard solution and sample solution chromatograms. Moreover, the peak purity index of Donepezil was found to be spectrally pure in all the degradation condition with main peak. Based on the above results it is concluded that the method for determination of assay of Donepezil hydrochloride in Donepezil hydrochloride tablets 5mg and 10 mg is specific and stability indicating.

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