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A validated non-aqueous potentiometric titration method for the quantitative determination of Azelnidipine from pharmaceutical preparation

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ABSTRACT

A simple precise, rapid accurate and sensitive non-aqueous potentiometric titration method was developed for quantitative determination of azelnidipine from pharmaceutical dosage form. The titration was carried out using standardized 0.1 N perchloric acid. The proposed method was found to be precise with % RSD <1 (n = 6). The method showed strict linearity (r^2 > 0.99) between 20 % to 100 % of 100 mg of drug substance weight. The percentage recovery of azelnidipine in the optimized method was between 100.03 % to 101.85 %. The method is also found to be rugged when checked by different analysts and using different lots of reagents and different makes of titrators.

Keywords: Azelnidipine, perchloric acid, potassium hydrogen phthalate, glacial acetic acid.

INTRODUCTION

Azelnidipine is a lipophilic calcium channel antagonists. Its chemical name is 2-amino-1.4-dihydro-6-methyl-4-(3-nitril phenyl)-3,5-pyridine dicarboxylic acid-3-[1-(dibenzyl)-3-nitrogen heterocyclic ring butyl]-5-isopropyl ester. Azelnidipine can restrain Ca^+ ions outside the cardiac muscle and vascular smooth muscle. They enter the cells through cell membrane and it expands blood vessel, lower peripheral vascular resistance and arterial pressure. In clinic, it is used for treatment of essential hypertension and angina pectoris.

This drug is not official in any pharmacopoeia. In literature survey only HPLC[1, 2]method has been reported for its estimation. A simple precise, rapid accurate and sensitive non-aqueous potentiometric titration method was developed for quantitative determination of azelnidipine from

bulk drug and pharmaceutical formulation. The developed method will useful for pharmaceutical industries and research organizations.

EXPERIMENTAL SECTION

An potentiometric titrator was used (VEEGO-MATIC) for assay method development and validation. A Sartorius analytical balance with 0.01 mg was used.

Reagents and chemical

Reference standard of azelnidipine was obtained from reputed firm with certificate of analysis. Potassium hydrogen phthalate, perchloric acid and glacial acetic acid of A. R. grade were used.

General procedure

Standardization of 0.1 mole perchloric acid

About 0.35 mg of potassium hydrogen phthalate (previously powdered lightly, dried at 120^{o}C for 2 hours) was weighed accurately into clean and dry titration jar. It was dissolved in 50 ml of glacial acetic acid. About 0.1 ml of crystal violet solution (0.5 % w/v in anhydrous glacial acetic acid) was added. It was titrated with 0.1 N perchloric acid until violet colour changes to emerald green. Blank determination was performed out for necessary correction.

The titration was performed in duplicate.

One ml of 0.1 N $HClO_4$ is equivalent to 0.02042 g of potassium hydrogen phthalate ($C_8H_5KO_4$)

$$\text{Normality of perchloric acid} = \frac{W}{\text{B.R.} \times 0.02042}$$

Where W is weight of potassium hydrogen phthalate in g and B.R. is burette reading in ml.

Quantitative determination of azelnidipine

About 0.1 g. of azelnidipine test sample was weighted accurately into a clean and dried titration jar. It was dissolved in 35 ml. of anhydrous glacial acetic acid. It was titrated with 0.1 N perchloric acid potentiometrically. Blank determination was also carried out for necessary correction.

One ml of 0.1 N perchloric acid is equivalent to 0.02913 g. of azelnidipine ($C_{26}H_{26}N$)

% Azelnidipine on the dried basis was calculated as below

$$\% \text{ assay} = \frac{\text{B.R.} \times N \times 0.02913 \times 100}{0.1 \times W}$$

Where B.R. is burette reading in ml at the potentiometric end point. N is actual normality of 0.1 N perchloric acid. W is weight of the sample taken in g.

RESULTS AND DISCUSSION

Determination of azelnidipine

The objective of this work was to determine accurately the content of azelnidipine. The assay of azelnidipine (on the dried basis) of various batches of azelnidipine test sample was analyzed using the above method. It was in the range of 100.03 % to 101.85 %.

Table I: Method of precision

Weight of Azelnidipine in g.	Burette reading in ml	Normality of perchloric acid	%Assay
0.1	3.5	0.09991	101.85
0.1	3.45	0.09991	100.39
0.1	3.5	0.09991	101.85
0.1	3.45	0.09991	100.39
0.1	3.45	0.09991	100.39
0.1	3.5	0.09991	101.85
			Mean 101.12 %
			Standard deviation 0.7996
			% RSD 0.7908

Table II: Linearity

Level	Weight of Azelnidipine in g.	Burette reading ml	Normality of perchloric acid	% Assay
1.	0.020	0.7	0.09989	101.85
2	0.040	1.4	0.09989	101.85
3	0.060	2.05	0.09989	99.425
4	0.080	2.75	0.09989	100.03
5	0.100	3.45	0.09989	100.39
				Mean 100.710 %
				Standard deviation 1.0987
				% RSD 0.01090

Analytical method validation

The method precision was checked after analyzing six different preparations of homogeneous test sample of azelnidipine. The % RSD of results obtained was found to be 0.7908. It confirms good precision of the method. The results are presented in table I.

Table III: Regression values

Correlation coefficient	0.9998
Slope (m)	34.25
Intercept (c)	0.015
Regression equation	y = 34.25x + 0.015

Table IV: Accuracy and recovery

Level	Weight of azelinidipine added (g.)	Weight of Azelinidipine found (g.)	% Assay	Mean % assay
1	0.020	0.0203	101.853	101.85
	0.020	0.0203	101.853	
	0.020	0.0203	101.853	
2	0.040	0.0407	101.85	101.85
	0.040	0.0407	101.85	
	0.040	0.0407	101.85	
3	0.060	0.05991	99.425	100.23
	0.060	0.06111	101.85	
	0.060	0.05991	99.425	
4	0.080	0.0800	100.03	99.42
	0.080	0.0785	98.20	
	0.080	0.0800	100.03	
5	0.100	0.1004	100.39	100.87
	0.100	0.1004	100.39	
	0.100	0.1018	101.85.	

Linearity

For the establishment of method linearity ,five different weights of azelnidipine test samples corresponding to 20 % ,40 %, 60 % , 80 % and 100 % of the about weight (0.1 g.) were taken and analyzed for percentage of azelnidipine content. The results are in table II. The potentiometric

titration was conducted once at each level. Calibration curve was drawn by plotting test sample weight in gram on x axis and titre values on y axis.

The values of correlation coefficient, slope and intercept are given in table III.

Accuracy and recovery

Accuracy was determined at five different levels i.e., 20 %, 40 %, 60 %, 80 % and 100 % of the nominal concentration. (0.1 g.) The titration was conducted in triplicate at each level and the titre value was recorded. The tire value obtained in linearity study was considered as true value during the calculation of percentage (%) recovery. The percentage recovery is calculated using following equation.

$$\text{Percentage recovery} = \frac{\text{Titre value} \times 100}{\text{True titre value}}$$

The percentage range recovery of azelnidipine was in 99.42 to 101.85 %. It confirms the accuracy of the proposed method. (Table IV).

Ruggedness

The ruggedness of the method is defined as degree of reproducibility of results obtained by analysis of azelnidipine sample under variety of normal test conditions such as different laboratories, different analysts and different lots of reagents. Quantitative determination of azelnidipine was conducted potentiometrically on one laboratory. It was again tested in another laboratory using different instrument by different analyst. The assays obtained in two different laboratories were well in agreement. It proved ruggedness of the proposed method.

CONCLUSION

The proposed method of non-aqueous potentiometric titration was found to be precise, accurate and rugged. It requires simple apparatus as compared to methods reported in literature. The values of percentage recovery and standard deviation showed sensitivity. The method was completely validated. It showed satisfactory data for all the parameters of validation. Hence it can be applied for routine quality control application. Hence method is strongly recommended for quality control of method of azelnidipine.

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