International Journal for Pharmaceutical Research Scholars (IJPRS)

V-3, I-1, 2014 ISSN No: 2277 - 7873

RESEARCH ARTICLE

Development and Validation of a Rapid RP-HPLC Method for Estimation of Nicergoline in Tablet Dosage Forms

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Manuscript No: IJPRS/V3/I1/00088, Received On: 19/02/2014, Accepted On: 22/02/2014

ABSTRACT

A high performance liquid chromatographic method was developed, validated and applied for determination of Nicergoline in pharmaceutical formulations. A LiChrosorb® RP-18 (10 µm, 250x 4 mm) column was used with a mobile phase consisting of acetonitrile: methanol: phosphate buffer (40: 35: 25 % v/v, pH 7.0), a quantitative evaluation was performed at 288 nm with flow rate of 1.5 mL/min, and column cooler temperature was maintained at 25 ºC. The retention time was about 8 min. Suitability of this method for the quantitative determination of the drug was proved by validation in accordance with the requirements laid down by the International Conference of Harmonization (ICH) guidelines. The method is selective, accurate, precise, and can be used for analysis of pharmaceutical preparations in quality control.

KEYWORDS

Nicergoline, RP-HPLC Method, Validation, Quality Control

INTRODUCTION

Nicergoline ([(6a*R*, 9*R*, 10 a*S*) - 10a – Methoxy - 4, 7 – dimethyl - 4, 6, 6a, 7, 8, 9, 10, 10 a – octahydroindolo [4,3-fg]quinolin-9-yl]methyl 5 - bromopyridine-3-carboxylate) (Figure 1) is a non-selective alpha-sympatolytic, antagonist on alpha-adrenergic receptors. It is used for better blood circulation in the central nervous system and legs. Due to its improving effect on the metabolism in the central nervous system, it has been used as a drug for stimulation of mental functions (nootropic) in geriatry[1] to treat symptoms of mental deterioration associated with cerebrovascular insufficiency. It has also been used in peripheral vascular disease, and in acute myocardial infraction with diastolic hypertension.[2-4]

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The common dosage forms of Nicergoline are thus mostly tablets, intramuscular injection and slow intravenous infusion. Literature survey reveals that a few HPLC methods[5-6], Spectrofluorimetry[7], HPTLC method[8] and spectrophotometric methods[9-10] have been reported for the estimation of Nicergoline in bulk and pharmaceutical formulations. In the present study a new RP-HPLC method has been reported for the estimation of Nicergoline from marketed formulations.

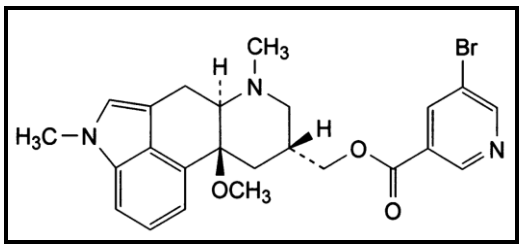

Figure 1: Structure of Nicergoline

As the analytical methods must be validated before being used in the pharmaceutical

industry, the proposed HPLC-UV detection method was validated in accordance with the International Conference on Harmonization (ICH) guidelines[11-12], by assessing its specificity, linearity, accuracy, precision, limit of detection and limit of quantification.

MATERIALS AND METHOD

Reagents and Materials

The working standard of Nicergoline RS (Purity >99%) was provided by (Sigma-Aldrich). The pharmaceutical preparation of Nicergoline (10 mg) was obtained commercially. HPLC grade methanol, acetonitrile, triethylamine and potassium dihydrogen phosphate (Analytical grade) were obtained from Merck (Germany).

Instrumentation

The HPLC system consists of a Shimadzu DGU-20A_5 vaccum degasser, a Shimadzu LC-20AD pump, a Shimadzu SPD-20A UV/VIS detector. The RP-HPLC system was equipped with LC solution software for data processing.

Chromatographic Conditions

The chromatographic separation was achieved on a LiChrosorb® RP-18 column packed with octadecylsilyl silica gel 10 µm, 250x 4 mm, under reversed phase partition conditions. The mobile phase was a 40: 35: 25 % v/v mixture of Acetonitrile: Methanol: Phosphate buffer (Dissolved 6.8 g of potassium dihydrogen phosphate in about 900 mL of water in a 1000-mL volumetric flask, pH 7.0 ± 0.1, adjusted with triethylamine). The flow rate was 1.5 mL/min and the run time was 8 min. Before analysis the mobile phase was degassed by using a sonicator and filtered through a 0.25 µm filter. The column cooler temperature was maintained at (25±2)ºC. The injection volume was 20 µL and the wavelength of detector at 288 nm.

Preparation of Stock Solution of Nicergoline

About 20 mg of Nicergoline was accurately weighed and transferred into 100 mL volumetric flask and dissolved in mobile phase. Calibration standards of Nicergoline were prepared by making serial dilutions of the stock solution at concentrations of 0.05, 0.10, 0.20, 0.30, 0.40 mg/mL.

Assay of Tablet Formulation

The contents of twenty commercial tablets were weighed and their mean mass was determined. After grinding the tablets into a fine powder in a glass mortar, an accurately weighed quantity of the tablet powder equivalent to 20 mg of Nicergoline was quantitatively transferred into a 100 mL volumetric flask with about 50 mL mobile phase. The contents were sonicated for 5 minutes. The mixture was then made up to 100 mL with the same mixture. The solution was then filtered through a membrane syringe filter (pore size 0.45 µm). The sample solution was injected and the peak area was measured for determination of Nicergoline in a tablet formulation.

RESULTS AND DISCUSSION

Linearity

Linearity of the method was confirmed by preparing Nicergoline standard curve for the analytical range of 50 – 400 µg/mL. The solutions were chromatographed six times, in accordance with the International Conference on Harmonization. Statistical analysis using the least square regression indicated excellent linearity for Nicergoline in the mentioned range. A good correlation between Nicergoline peak areas and drug concentration was observed with $r^2 \geq 0.999$ (Table 1).

The label claim, present in tablet formulation, was found to be 10.02 mg. A typical chromatogram of Nicergoline is shown in Figure 2. Precision of the method was confirmed by the analysis of formulation repeated six times (Table 2).

Accuracy

To check the accuracy of the developed methods and to study the interference of formulation excipients, analytical recovery experiments were carried out as per ICH guidelines. The results of the recovery studies and their statistical validation data given in Table 3 indicate high accuracy of the proposed

Table 1: Results from study of linearity

Methods	λ, nm	Range (µg/mL)	LR	R	LOD (µg/mL)	LOQ (µg/mL)
RP-HPLC	288	50 - 400	Y=14534924X-14719	0.999	0.5	1.25

Table 2: Results from assay of tablet formulation

Sample	Assay, mg/tablet
	Nicergoline
1	10.13
2	9.98
3	9.83
4	10.12
5	9.96
6	10.08
Average	10.02
RSD %	1.155

Table 3: Accuracy of Nicergoline

Parameters	% Taken	Mass taken (mg/1 tabl.)	Mass found (mg/1 tabl.)	% Found	% Recovery
			4.96	49.60	99.20
	50.00	5.0	4.89	48.90	97.80
			5.06	50.60	101.2
			10.13	101.3	101.3
	100.0	10.00	9.98	99.80	99.80
			9.83	98.30	98.30
			14.95	149.5	99.67
	150.0	15.0	14.87	148.7	99.13
			15.10	150.2	100.1
X					99.61
SD					±1.175
% RSD					1.180

method. The percentage recovery was found to be in the range of 98.00-102.0%.

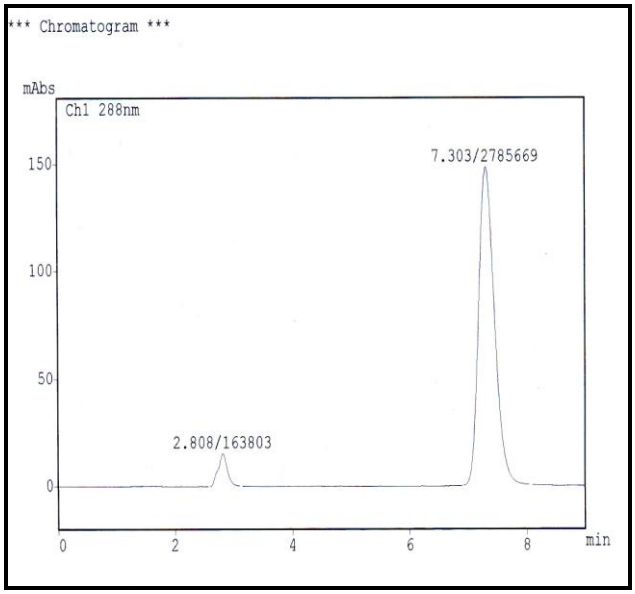

Figure 2: Typical chromatogram of Nicergoline

Robustness

As defined by the ICH, the robustness of an analytical procedure describes its capability to remain unaffected by small and deliberate variations in method parameters. Robustness was performed by small variation in the chromatographic conditions and found to be unaffected by small variations like ± 2% variation in volume of mobile phase composition, ± 0.1 mL/min in flow rate of mobile phase, ±0.1 variation in pH.

Specificity

The specificity of the HPLC method was ascertained by analyzing standard drug and sample solutions. The retention time of Nicergoline was confirmed by comparing the retention time with that of the standard.

CONCLUSION

A simple isocratic RP-HPLC method with UV detection has been developed for determination of Nicergoline. The method was validated for accuracy, precision, specificity, robustness and linearity. The run time is relatively short (8 min), which enables rapid quantification of many samples in routine and quality control analysis of tablets.

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