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Research Article

A HIGH PERFORMANCE LIQUID CHROMATOGRAPHIC ASSAY FOR NICORANDIL IN BULK DRUG AND ITS PHARMACEUTICAL DOSAGE FORMS

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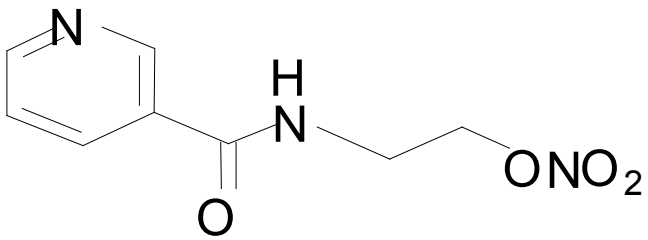
ABSTRACT
A simple, rapid and reproducible high performance reverse phase liquid chromatographic method has been developed for quantitative estimation of Nicorandil in rotacap using a, C18 column and UV detection at 254nm. The isocratic elution was used to quantify the analyte. The samples were chromatographed on C-18 column and the mobile phase was 0.1% formic acid: Acetonitrile (50:50 v/v) was pumped at 1 mL/min. The method was linear between 60- 360 µg/mL, statistically validated for its linearity, precision and accuracy. The intra-and - inter day variation was found to be less than 1% showing high precision of the assay method. It was found that the excipients in the commercial tablet did not interfere with the method.
KEY WORDS: Nicorandil, High performance liquid chromatography (HPLC), Acetonitrile

INTRODUCTION

Nicorandil[1-2] in the treatment of various types of angina pectoris, possesses little hemodynamic effect on heart rate, blood pressure, or cardiac contractility with clinical doses yielding antianginal effects. .

Nicorandil



Structurally, N-[2-(Nitroxy)ethyl]-3-pyridine carboxamide.
Molecular Formula : $C_8H_9N_3O_4$

The aim of this study Nicorandil is latest angina pectoris drug. It is available in tablets dosage form. It is non-official in any pharmacopoeia. The literature survey reveals that few spectrophotometric[3,4,5], and Sensitive HPTLC[6] analytical methods have been reported for determination of Nicorandil in tablets. In present investigation we have developed a simple isocratic RP-HPLC method for quantitative estimation of Nicorandil in bulk drug and pharmaceutical formulations with high accuracy and precision.

MATERIALS AND METHODS

Chemicals and reagents

Nicorandil reference substance obtained from sun pharma, 0.1% Formic acid, Acetonitrile, & Water (HPLC grade) were purchased from Merk Ltd. (Mumbai, India). The commercially Nicorandil available tablet were obtained from local market. Each Nicorandil contains 100mg of active drug.

Selection of chromatographic parameters

- Column - Oyster,BDS, C-18, 250 x 4.6mm. 5µ.
- Flow rate - 1.0ml/min
- Temperature - 30°C
- Detection wavelength - 260nm
- Injection volume - 20µl
- Run time - 17 min
- Mobile phase - 0.1% Formic acid & Acetonitrile (50:50 v/v)

Selection of mobile phase

The solution of Nicorandil was injected into the HPLC system and run in different solvent systems. Different

mobile phases containing methanol, water and acetic acid in different proportions were tried and finally 0.1% formic acid : Acetonitrile (50:50 v/v), was selected as an appropriate mobile phase which gave good resolution and acceptable peak parameters for Nicorandil.

Preparation of mobile phase

0.1% formic acid : acetonitrile (50:50 v/v) was prepared and filter through 0.45 µm membrane filter and sonicated.

Preparation of standard solution

About 100mg of the drug was accurately weighed dissolved in methanol so as to give 1 mg/mL. Subsequent dilutions of this solution were made with methanol to get concentration of 60 to 360 µg/mL of Nicorandil. The standard solutions prepared as above were injected 6 times into a column at a flow rate of 1.0 mL/min. The peak areas of drug concentration were calculated. The regression of the drug concentration over the peak areas was obtained. This regression equation was used to estimate the amount of Nicorandil in tablet dosage form. Nicorandil solution containing 60 µg/ml to 360µg/ml were subjected to the proposed HPLC analysis for finding out intra and interday variations. The recovery studies were carried out by adding known amount of Nicorandil to pre-analyzed and subjecting to proposed RP-HPLC method.

ASSAY OF NICORANDIL TABLET

Ten tablets containing 100 mg were weighed and powdered. An accurately weighed portion of the powder equivalent to 100 mg of Nicorandil was transferred to a 100ml volumetric flask containing 50ml of methanol. The contents of the flask were sonicated for 15 minutes. Dissolve Nicorandil and made upto volume with mobile phase and the resulting mixture was filtered through a 0.45µm filter. Subsequent dilution of this solution was made with methanol to get concentration of 20 µg/mL. This solution was injected 6 times into the column. The mean values of peak areas of 6 such determinations were calculated and the drug content in the tablet was quantified by using the regression equation obtained above. The same procedure was followed for the estimation of Nicorandil in other commercially available tablet dosage forms.

RESULTS AND DISCUSSION

The present study was carried out to develop a sensitive, precise and accurate RP-HPLC method for the analysis of Nicorandil in bulk sample or pharmaceutical dosage forms. The column pressure varied from 138-141 kg/cm^2 the retention time for Nicorandil was 6.43 minutes for a run period of 15 minutes. Each sample was injected six times and the same retention times were observed in all cases. The peak area of different concentration set up as above were calculated and average value for 6 such determinations are shown in table 3. The peak area for drug solution was reproducible as indicated by low coefficient of variation (0.762%). A good linear relationship (r= 0.9999) was observed between the concentration of Nicorandil and the respective peak areas. The calibration graph was found to be Y=219.4C-345.7, where Y is the peak area and C is the concentration of Nicorandil in the range of 30 to 360 µg/mL when the Nicorandil solution containing 60 to 360 µg/mL were analyzed by the proposed RP-HPLC method for the finding out the intra and inter day variation, a low co-efficient of variation was observed Table-2.

This shows that the present HPLC method was highly precise. The amount of drug was shown in Table-6, about 99.76% Nicorandil could be recovered from the pre-analyzed sample indicating the high accuracy of the proposed RP-HPLC method. The drug content in the tablet was quantified using the proposed analytical method. The mean content of Nicorandil in two different brands of tablet dosage forms is shown in Table - 6.

The absence of additional peaks indicates no interference of the excipents used in the tablet. The tablets were found to contain 99.89 to 100.08 % of the labeled amount, the less than 1 % C.V. indicates the reproducibility of the assay of Nicorandil in the tablets dosage form. The proposed reversed phase HPLC method was found to be simple, precise, highly accurate, specific and less time consuming.

CONCLUSION

The proposed reverse phase HPLC method was found to be simple, precise, highly accurate, specific and less time consuming for determination of Nicorandil in pure drug and tablets Method validation yields good results and presented good precision and accuracy. It was also found that the excipients in the commercial tablet dosage form did not interfere with the assay. Therefore, the proposed HPLC method is precise and accurate, and can be used for quantitative estimation in of Nicorandil tablets.

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Table 1: Linearity of Nicorandil

On X-axis-µg	On Y-axis-Area
60	12563
150	32241.67
180	39271
240	51944
300	66339.67
360	78352.33

Table 2: Calibration of the RP-HPLC method for the estimation of Nicorandil

Concentration of Nicorandil (µg/mL)	Peak area
30	6281.50
60	12563
90	18844.50
120	25126
150	32241.67
180	39271
210	45451
240	51944
270	59705.70
300	66339.67
330	71822.95
360	78352.33
Regression equation (Y*)	Y* = bC + a
Slope (b)	219.4
Intercept (a)	- 345.7
Correlation coefficient (r)	0.9999

Y* is the peak area and C is the concentration of Nicorandil in the range of 30 to 360 µg/mL.

Table 3 : Precision of Nicorandil & R.S.D. of Nicorandil

S. No.	µg/mL	Area	Retention Time
1	60	12283	6.584
2	60	12117	6.566
3	60	12207	6.573
4	60	12387	6.584
5	60	12206	6.578
6	60	12298	6.596

S.D = 93.418 S.D = 0.0104
Mean = 12249.66 Mean = 8.5802
RSD = 0.762 RSD = 0.120

Table 4 : Inter and intra-day precision for Nicorandil assay in pharmaceutical dosage forms by the proposed RP-HPLC method.

Concentration of Nicorandil (µg/mL)	Observed concentration of Nicorandil			
	Inter day		Intra day	
	Measured conc. SD	%C.V.	Measured conc. SD	%C.V.
300	76.468	0.11439	93.112	0.1394
360	91.761	0.1372	111.734	0.1672

Table 5 : Experimental values obtained in recovery test for Nicorandil tablets by proposed HPLC method

Amount of drug added (µg) to drug solution /powder tablet formulation	Recovery from drug solution		Recovery from powdered tablet formulation	
	Mean Amount(µg) found(n=6)	Mean %Recovery(n=6)	Mean Amount(µg) found(n=6)	Mean %recovery(n=6)
240	239	98.07 ± 0.23	239.7	98.78 ± 0.13
300	295	99.04 ± 0.11	299.39	99.40 ± 0.02
360	358	99.15 ± 0.12	359.8	99.63 ± 0.12

Table 6. Mean (±SD) amount of Nicorandil in tablet dosage forms by the proposed HPLC method.

Brand of tablet	Labelled amount of drug(mg)	Mean(±SD) amount found (mg) by the proposed method(n=6)	Mean(±SD)% Labelled amount(n=6)
T_1	10	9.99 ± 0.02	99.89 ± 0.03
T_2	10	10.009 ± 0.01	100.08 ± 0.02

T1 and T2 are tablets from different manufacturer (Torrent, Zydus)

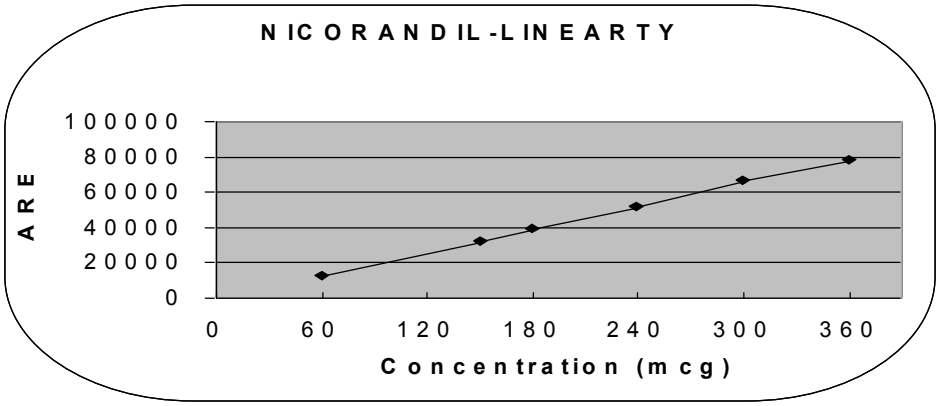

Figure 1: Calibration curve of Nicorandil

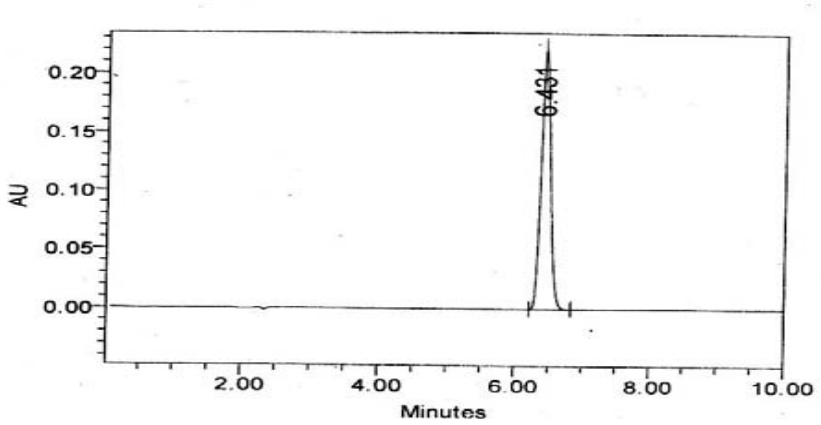

Fig 2: A typical chromatogram For Nicorandil

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