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Research Article

# Optimization and Validation of Quantitative Spectrophotometric Methods for Determination of Nicorandil Bulk Drug and Its Pharmaceutical Dosage Forms

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**ABSTRACT**

Two simple, sensitive, selective, accurate, precise and economical methods (method A and B) have been developed for the estimation of Nicorandil in bulk drug and its pharmaceutical formulations. Method A is based on 2, 2'- Bipyridyl forms orange coloured complex with $Fe^{2+}$ resulted from oxidation of drug (Nicorandil) with $Fe^{3+}$. The orange coloured chromogen exhibited absorption maximum at 522 nm and obeyed Beer's law in the concentration range of 50-300 µg/ml. Method B is based on 1, 10 phenonthroline forms red coloured complex with $Fe^{2+}$ resulted from oxidation of drug (Nicorandil) with $Fe^{3+}$. The red coloured chromogen has exhibited absorption maximum at 509 nm and obeyed Beer's law in the concentration range of 50-250µg/ml. The results of analysis for both the methods have been validated statistically and by recovery studies. The proposed methods are economical and sensitive for estimation of Nicorandil in bulk drug and its tablet dosage form.

**Keywords:** Nicorandil, 2, 2'- Bipyridyl, 1, 10 phenanthroline, Ferric chloride.

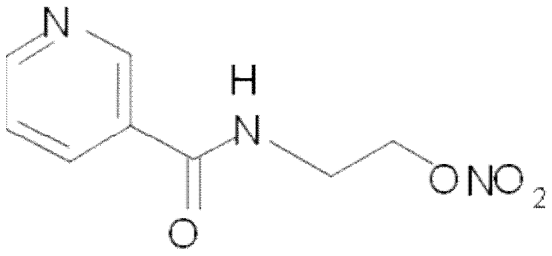
## 1. INTRODUCTION

Nicorandil [1-2] is Anti-anginals & Coronary Vasodilators. angina pectoris, possesses little hemodynamic effect on heart rate, blood pressure, or cardiac contractility with clinical doses yielding antianginal effect N-[2-(Nitroxy)ethyl]-3-pyridine carboxamide

## 2. OBJECTIVE

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 few HPTLC Chromatographic in human plasma[6] have been reported for determination of Nicorandil in tablets.

Hence in the present work spectrophotometric methods has been developed for the estimation of Nicorandil using 2, 2'- Bipyridyl in presence of in method A and 1, 10 phenanthroline in presence of $FeCl_3$ in method B. The above methods are simple, sensitive, accurate and precise and can be used for the routine quality control of this drug in bulk as well as in pharmaceutical formulation.




**Nicorandil**

## 3. MATERIALS AND METHODS

### 3.1 Instruments and reagents

A Shimadzu model 1600 double beam UV/Visible spectrophotometer with spectral

width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cells was used to measure absorbance of the resulting solution.

A Sartorius CP224S analytical balance, an ultra-sonic cleaner (Frontline FS4), Nicorandil pure powder (torrent limited India ), 2,2'- Bipyridyl (0.5 M in ethyl alcohol), Ferric Chloride (0.05 M) solution in double distilled water, 1,10- Phenonthroline (0.05 M in ethyl alcohol) (0.05 M) Ferric Chloride in double distilled water were used. All the chemicals and reagents used were of analytical reagent grade.

The marketed formulation in tablets forms (torrent limited India)

### 3.2 Preparation of standard drug solutions

About 100mg of Nicorandil was accurately weighed and dissolved in 20ml of distilled water in a 100ml volumetric flask. Diluted upto the mark with distilled Water and the final concentration of Nicorandil solution was brought to 1000 µg/ml.

### 3.3 Preparation of calibration curves

**Method A**

**2, 2' – Bipyridyl Method**

Aliquots of Nicorandil ranging from 0.5 – 3.0ml (1ml = 1000µg/ml) were transferred into a series of 10ml volumetric flasks. To each flask aqueous solution of 0.2 ml of Fecl3 (0.05M) and 0.2ml of 2,2'- Bipyridyl (0.5 M) were added. The flasks were heated at 60°C for 20 minutes on water bath. The solution was cooled and the volume was brought upto the mark with distilled water. The absorbance of orange coloured chromogen was measured at 522 nm against reagent blank. The amount of Nicorandil was computed from calibration curve. The coloured chromogen was stable for more than 2 hours.

**Method B**

**1, 10 phenanthroline**

Aliquots of Nicorandil ranging from 0.5 – 2.5ml (1ml = 1000□g/ml) were transferred into a series of 10ml volumetric flasks. To each flask aqueous solution of 0.3ml of FeCl3 (0.05M) and 2.0ml of 1, 10-Phenonthroline (0.05 M) were added. The flasks were heated at 60°C for 20 minutes on water bath. The solution was cooled and the volume was brought upto the mark with distilled water. The absorbance of red coloured chromogen was measured at 509 nm against reagent blank. The amount of Nicorandil was computed from calibration curve. The coloured chromogen was stable for more than 2 hours.

### 3.4 Analysis of pharmaceutical preparations

Two brands of commercial Nicorandil tablets were analysed by the proposed method. An accurately weighed quantity (equivalent to about 100mg) of Nicorandil tablets were taken and crushed the tablets in the form of fine powder. Dissolved the powder in 40ml distilled water and shaken for 2 -3 min, filtered through cotton wool into 100ml volumetric flask. The volume was made upto the mark with distilled water (1000 µg/ml).

### 3.5 Recovery studies

To study the accuracy and reproducibility of the proposed method, recovery studies were carried out by adding known amount of the drugs to the preanalyzed formulations and reanalyzing the mixture by proposed method. Results of recovery studies are reported in Table 1

**Table 1: Assay and Recovery of nicorandil in pharmaceutical Dosage Form**

| Tablets* | Labelled Amount | Amount found by proposed methods | | Reference method (UV method) | Recovery of proposed methods (%) | |
|---|---|---|---|---|---|---|
| | | A | B | | A | B |
| $T_1$ | 10 mg | 9.90±0.1 | 9.99±0.02 | 9.98 ±0.1 | 99.48±0.1 | 99.28 |
| $T_2$ | 10 mg | 9.98±0.02 | 9.95±0.05 | 9.97 ± 0.2 | 98.88±0.11 | 98.92 |

*$T_1$ and $T_2$ the tablets from different manufacturer (Torrent, Zydus) were analysed.

**Average of 8 observations (10 mg of Nicorandil was added and recovered).

## RESULT AND DISCUSSION

Method A is based on 2,2'- Bipyridyl forms orange coloured complex with Fe2+ resulted from oxidation of drug (Nicorandil) with Fe3+. The orange coloured chromogen exhibited absorption maximum at 522 nm and obeyed Beer's law in the concentration range of 50-300 µg/ml. The method is found to be simple, sensitive, accurate and precise. Colored chromogen was found to be stable for more than 2 h at room temperature for both the drugs. The linearity was found in the concentration range of 50 to 300 µg/ml (r =0.9999) .

Method B based on oxidation followed by complex formation reaction.Using1,10 phenanthroline formation of red coloured complex when Nicorandil is treated with 1,10 phenanthroline in presence Fe2+ resulted from oxidation of drug with Fe3+. The red coloured chromogen exhibited absorption maximum at 509 nm and obeyed Beer's law in the concentration range of 50-250 mcg /ml The coloured chrmogen was stable for more than 2 hour (r=0.9999). The optical characteristics such as Beers law limit, sandell's sensitivity, molar extinction coefficient, percent relative standard deviation (calculation from eight measurements containing ¾ th of the amount of the upper Beers law limit) were calculated. Regression Characteristics like slope, intercept, correlation coefficient and percentage range of errors (0.05 and 0.01 confidence limits), LOD, LOQ, Error's in bulk sample and standard error of estimation were calculated.

Commercial formulation of Nicorandil was successfully analyzed by proposed spectrophotometric methods and results are calculated. To evaluate validity and reproducibility of the methods, fixed amounts of drug were added to the preanalyzed formulation. These results of percentage recovery are calculated. There is no interference of additive and exicipients in proposed analytical methods. The proposed spectrophotometric methods for the estimation of Nicorandil are simple, sensitive, accurate and precise and can be used for the routine quality control of this drug in bulk as well as in pharmaceutical formulation.

**Table 2: Optical Characteristics and Precision**

| Parameters | Method-A | Method-B |
|---|---|---|
| $\lambda_{max}$ (nm) | 522 | 509 |
| Beer's law limits (µg/ml) (c) | 50-300 | 50– 250 |
| Color | Orange | red |
| Molar absorptivity (lit/mol$^{-1}$ cm$^{-1}$) | 0.5669x 10$^{3}$ | 0.842x 10$^{3}$ |
| Limit of Detection (LOD/ mcgml$^{-1}$) | 0.927 | 0.831 |
| Limit of Quantification (LOQ/ mcgml$^{-1}$) | 2.810 | 2.52 |
| Sandell's sensitivity (µg/ml/0.001 abs units) | 0.0372 | 0.0250 |
| Regression equation (Y*) | | |
| Slope (b) | 0.00269 | 0.00397 |
| Intercept (a) | -0.00385 | 0.003 |
| Standard error of estimation (Se) | 0.0006745 | 0.0002672 |
| Correlation coefficient (r) | 0.9999 | 0.9999 |
| % RSD | 0.11266 | 0.1253 |
| Confidence limits with 0.05 level ± | 0.000675 | 0.001178 |
| Confidence limits with 0.01 level ± | 0.000999 | 0.001564 |
| 0% Error in bulk Samples*** | 0.31 | 0.12 |

*Y=bC+a, where C is the concentration of Nicorandil in µg/ml
and Y is the absorbance at the respective maximum absorbency,
**Average for eight determination, ***Average for three determination

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