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Leuco crystal violet method for the determination of nicorandil in bulk dosage

Kanchan Upadhyay [a,*], Anupama Asthana [b], Raunak Kumar Tamrakar [c]

[a] *Department of Chemistry, Shri Shankaracharya Vidyalaya, Hudco, Bhilai, C.G., India*
[b] *Department of Chemistry, Govt. V.Y.T.PG Autonomous College, Durg, C.G., 491001, India*
[c] *Department of Applied Physics, Bhilai Institute of Technology (Seth Bankrishan Memorial), Near Bhilai House, Durg, C.G., 491001, India*

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Abstract

Two simple, sensitive and validated spectrophotometric methods have been described for the assay of nicorandil in drug formulations. Method A is based on the determination of nicorandil by using leuco crystal violet (LCV). Nicorandil liberates nitrite on reaction with Zn and NH_4Cl, which reacts with acidified KI to liberate iodine, which reacts with LCV to form crystal violet (CV). The calibration graphs were linear over the concentration ranges 0.1 μgmL^{-1}–2.0 μgmL^{-1}& 0.2 μgmL^{-1}–4.0 μgmL^{-1} respectively. The absorbance of which is measured at 592 nm. Another method is based on diazotization of p-amino acetanilide by liberated nitrite followed by coupling with orcinol, which shows maximum absorbance at 458 nm. The optimum conditions and other analytical parameters were evaluated. The proposed methods have been applied successfully to the analysis of nicorandil in pure form and its dosage forms and no interference was observed from common excipients present in pharmaceutical formulations.

Keywords: Nicorandil; LCV; CV; Orcinol; Spectrophotometric method

1. Introduction

Nicorandil is a cardiovascular drug which posses properties like nitrate and ATP- sensitive potassium channel activating property. It is chemically known as N-[2-(nitroxy) ethyl] 3-pyridine carboxamide. It is selective for vascular potassium channels. It has no significant action on cardiac contractility and conduction. Thus is a novel drug for treatment of angina pectoris [1].

Further many studies have suggested that the drug possess similar safety and efficacy as the other drugs used for angina but efficacy increase after a year on continued treatment [2,3]. The drug has also now been evaluated in combination with other drugs like Lamotrigine [4]. Primary oxidation metabolites of nicorandil are nicorandil-N-oxide and hydroxyl nicorandil. On denitration nicorandil gives N-[2-hydroxy ethyl] nicotinamide, which further is transformed to nicotinamide, nicotine and N-methyl nicotinamide. The denitration occurs primarily in the liver.

Nicorandil is officially listed in Martindale: The Extra Pharmcopeia [5]. The literature revealed many

* Corresponding author.
E-mail address: kanchan.chemistry@gmail.com (K. Upadhyay).
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efforts made to determine nicorandil concentration in biological fluids and drug formulations. The methods include high performance liquid chromatography [6–14], high performance thin layer chromatography [15], gas chromatography coupled with mass spectrometry [16] and polarography [17].

HPLC, GC, and HPTLC methods widely used for pharmaceutical analysis are accurate and precise with good reproducibility but the cost of analysis is quite high owing to expensive instrumentation, reagent and expertise. Hence it is worthwhile to develop simpler and cost effective method for simultaneous estimation of drug for routine analysis of formulation. Spectrophotometric method fulfils such requirements [18–23].

The literature reveals that only few spectrophotometric methods have been developed for determination of nicorandil in drug formulations and biological fluids [24–28].

The main purpose of the present study is to develop spectrometric analysis method for analytical method for analysis of nicrodil. In the proposed methods method A is based on the oxidizing nature of nicorandil for oxidation of potassium iodide to liberate iodine which on reaction with leuco crystal violet (LCV) produces crystal violet (CV) and method B is based on denitration of nicorandil, diazotization of p-amino acetanilide by liberated nitrite and its coupling with orcinol.

2. Materials and methods

2.1. Apparatus

All the absorbance measurements were made by a Systronics spectrophotometer (Model 166) and a Systronics digital pH meter (Model-335) was used for the pH measurements.

2.2. Reagents and solutions

All the reagents used were of analytical reagent grade and double distilled water was used throughout the experiment.

Nicorandil Stock Solution: Reference standard sample of nicorandil was purchased from Zydus medica, Ahmadabad, India and was used as received. The commercial dosage forms of nicorandil such as Nikoran (Torrent Pharmaceutical, Ahmadabad, India), Korandil (Sun Pharm. Industries Ltd. Mumbai, India) and Zynicor (Zydus Medica, Ahmadabad, India) were purchased from the local market. The preparation of the standard stock solution of nicorandil containing 1000 $\mu gmL^{-1}$was done by dissolving 100 mg of nicorandil in 100 mL double distilled water.

Leuco Crystal Violet(LCV)[Eastman Kodak co.]: 250 mg of LCV was dissolved in 200 mL distilled water containing 3 mL 85% phosphoric acid (Merck, India) and the volume was made up to 1 L with distilled water and was stored in amber colored bottle away from sunlight.

***Potassium iodide (Merck, India)*:** 6×10^{-2} M Aqueous solution was prepared in distilled water.

Ammonium chloride (Merck, India): 0.2 M aqueous solution was prepared in distilled water.

***p -Amino acetanilide*:** 0.1% (w/v) aqueous solution was prepared in distilled water.

Orcinol: 1% (w/v) Aqueous solution was prepared in distilled water.

2.3. Procedure

2.3.1. Preparation of calibration graph

2.3.1.1. Method A. Different aliquot containing 0.1 to 2.0 $\mu gmL^{-1}$of nicorandil were accurately measured and transferred into a series of 25 mL standard flask and the volume was adjusted to 5 mL by adding double distilled water. To each flask 4.0 mL of 2×10^{-2} M NH_4Cl and 0.2 gm zinc powder was added and left for 3 min and the content was filtered. To the flask 1 mL of 1 M HCl, 1 mL of LCV and 1 mL of potassium iodide was added. The content was mixed well and the flasks were let to stand for 10 min with occasional shaking then pH of each mixture was adjusted with sodium hydroxide solution. The volume was diluted to the mark with water, mixed well and absorbance was measured at 592 nm against reagent blank.

2.3.1.2. Method B. Varying aliquots of standard nicorandil solution containing 0.2–4.0 μgmL^{-1} nicorandil were accurately measured and transferred into a series of 25 mL calibrated flasks and the total volume was adjusted to 5.0 mL with double distilled water. To each flask 4.0 mL of 2×10^{-2} M NH_4Cl and 0.2 gm zinc powder were added and left for 3 min and filtered. To the flask 1 mL of p-amino-acetanilide and 1.5 mL of 0.05 M HCl is added successively and allowed to stand for 5 min in an ice bath with occasional shaking then 0.5 mL of orcinol solution was added and the volume was adjusted up to the mark with distilled water. The absorbance was measured at 458 nm against the reagent blank.

2.4. Quatitation of nicorandil in pharmaceutical formulations

Twenty tablets were weighed and grounded, and then the powder equivalent to 100 mg nicorandil was