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A NOVEL ESTIMATION OF NICORANDIL IN BULK AND ORAL SOLID DOSAGE FORM BY SPECTROPHOTOMETRY

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ABSTRACT
Two simple, validated and sensitive spectrophotometric methods have been developed for the estimation of nicorandil in bulk and in pharmaceutical formulation (Method A & Method B). The method A involves the determination of nicorandil by standard absorbance method at 262 nm which obeys Beer's law in concentration range of 20-120 ì g/mL. Method B is based on the formation of intensely yellow ammonium salts by the interaction of nicorandil with phenol-2,4-disulphonic acid which obeys Beer's law in concentration range of 10-60 ìg/ml exhibiting maximum absorption at 405 nm under the optimized experimental conditions. The results obtained by the proposed method are acceptable. The methods were extended to tablet formulation and there was no interference from excipients and diluents. These methods have been statistically validated and are found to be precise and accurate.

Keywords: *Nicorandil (NIC), Phenol-2,4-disulphonic acid, yellow ammonium salt, Beer's law.*

INTRODUCTION

Nicorandil is N-[2-(nitroxy)ethyl]-3-pyridinecarboxamide (NIC), activates potassium channel. Nicorandil acts as a balanced coronary and peripheral vasodilator and reduces both preload and after load due to the presence of nitrate group. The potassium channel activation may also exert direct cytoprotective effects by augmenting normal physiological processes protecting the heart against ischemic events[1, 2]. Nicorandil causes vasodilation of coronary and systematic arteries and has been investigated in the treatment of angina pectoris. The potential cardioprotective effect of the drug has received increasing attention. Nicorandil undergoes biotransformation in the liver predominantly by denitration of nicorandil to the pharmacologically inactive metabolite, N-(2-hydroxyethyl)-nicotinamide, followed by side chain degradation to nicotinamide and related metabolites, including nicotinic acid and N-methyl-nicotinamide.

The drug is official in Martindale: The Extra Pharmacopoeia.[3] A search was made in the present investigations; literature survey revealed that the assay of the drug in pure and dosage forms is not official in any pharmacopoeia. Many efforts have been made to determine nicorandil concentration in biological fluids and drug formulations by several analytical methods include high-performance thin layer chromatography (HPTLC),[4] high-performance liquid chromatography (HPLC),[5-11] and gas chromatography coupled with mass spectrometry.[12] A review of literatures revealed no UV-visible spectrophotometric method for the assay of nicorandil in pharmaceutical formulations. The present work describes two simple, sensitive, selective, economical and validated visible spectrophotometric methods for the assay of nicorandil in drug formulations. The first method is based on high molecular absorptivity chromophore of nicorandil. The second method is based on exploiting the oxidizing property of the drug by its nitrate moiety in the chemical structure which yields a yellow colored ammonium salt with phenol-2,4-disulphonic acid and strong ammonia solution.

EXPERIMENTAL

Reagents

Nicorandil, phenol-2,4-disulphonic acid, glacial acetic acid and strong ammonia solution. All the reagents used were of analytical grade.

ASSAY PROCEDURE

METHOD A: Ultraviolet Spectroscopy

Nicorandil could be estimated directly with negligible interference from the additives in oral solid dosage forms. The pure nicorandil was dissolved appropriately in water to produce the required concentration. The solution was scanned between 200-400 nm using

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Systronics UV-Visible Spectrophotometer model 119. Absorption maxima, Beer's-Lambert's concentration range, linearity and estimation of nicorandil in solid oral dosage form were also performed.

Preparation of Standard Stock Solution

The standard stock solution of nicorandil was prepared by dissolving 100 mg of NIC in 25 ml of distilled water in 100 ml volumetric flask and then volume was made up to mark with distilled water.

Absorption Maxima

The standard stock solution was suitably diluted with distilled water to yield a concentration of 60 µg/mL solution. This solution was then scanned in the UV region of 200-400 nm using distilled water as blank. The absorbance spectrum is shown in Figure 1.

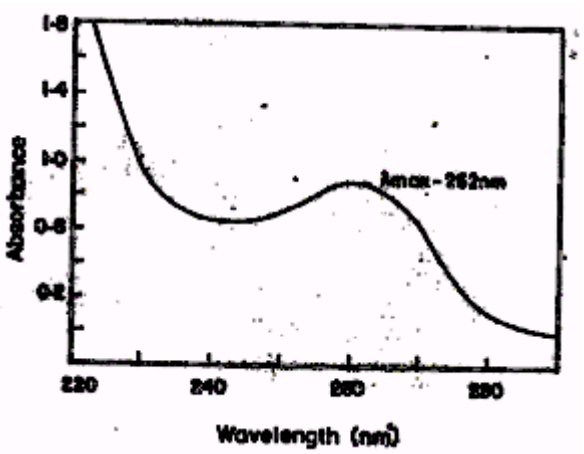


Fig.1: *Absorption maxima of nicorandil by UV spectrophotometry*

Beer's-Lambert's Law Concentration to Confirm Linearity and Range

The standard stock solution of nicorandil was suitably diluted to yield concentrations of 20, 40, 60, 80, 100, 120 and 140ìg/mL. The absorbance were measured at 262 nm and plotted against the concentration of drug as showed in Figure 2.

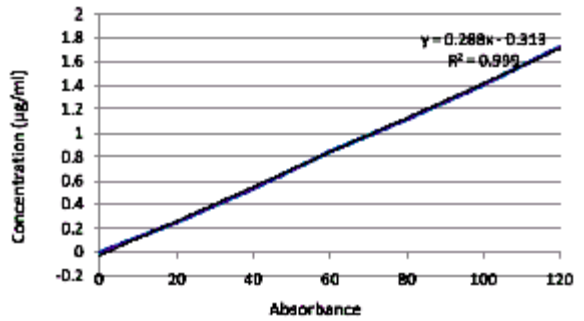


Fig.2: *Standard calibration plot of nicorandil by UV spectrophotometry*

Estimation of Nicorandil in Solid Oral Dosage Form

Twenty tablets were weighed accurately and then powdered. A quantity of powder equivalent to 25 mg of nicorandil was accurately weighed and transferred to a 25 ml standard flask and shaken with little quantity of glacial acetic acid. It was then made up to mark with distilled water. The solution was filtered and the first few ml of the filtrate were discarded; this solution was diluted to concentrations within the Beer's-Lambert's range and the absorbance was measured at 262 nm using distilled water as blank[13]. The results are depicted in Table 1.

Table 1: *Optical characteristics of Nicorandil*

Parameters	Method A	Method B
λmax (nm)	262	405
Beer's law limits(µg/ml)	20-120	10-60
Molar absorptivity (Lmol^{-1} cm^{-1})	126.5	117
Sandell's Sensitivity(µg cm^{-2}/0.001 abs unit)	1.66956	1.3051
Slope (m)	0.288	0.116
Intercept (c)	0.313	0.115
Correlation coefficient (r)	0.999	1
Standard deviation	0.0004	0.003
Relative standard deviation*	0.004	0.003
Limit of detection (LOD)	0.09166	0.85345
Limit of quantification (LOQ)	0.277	2.5862

**each value is the mean of three readings*

METHOD B: Colorimetry

Nicorandil could be determined colorimetrically by interaction with phenol-2,4-disulphonic acid, reduction and subsequent neutralization with strong ammonia. The assay depends on the formation of colored nitro-compounds by the interaction of nicorandil with phenol-2,4-disulphonic acid and strong ammonia to form an intensely yellow ammonium salts. This colored solution was scanned in the range of 350 to 750 nm using Systronics UV-Visible Spectrophotometer Model 119. Various parameters like absorption maxima, Beer's-Lambert's concentration range, linearity and estimation of nicorandil in solid oral dosage form by this new method were performed. The Scheme of reaction is presented below:

Preparation of Standard Stock Solution

The standard stock solution of nicorandil was prepared by dissolving 100 mg of pure NIC in glacial acetic acid in a 25 ml volumetric flask and diluted suitably with distilled water.

Absorption Maxima

To 1 ml of the standard stock solution, 2 ml of phenol-2,4-disulphonic acid was added and allowed to stand for fifteen minutes. Then 50 ml of distilled water was added and made alkaline with strong ammonia solution. The solutions was cooled and diluted to 100ml to yield a concentrations of 40 ìg/mL. This solution was then scanned in the visible region of 350-750 nm using 1 ml glacial acetic acid treated in a similar manner as blank. The absorbance spectrum is shown in Figure 3.

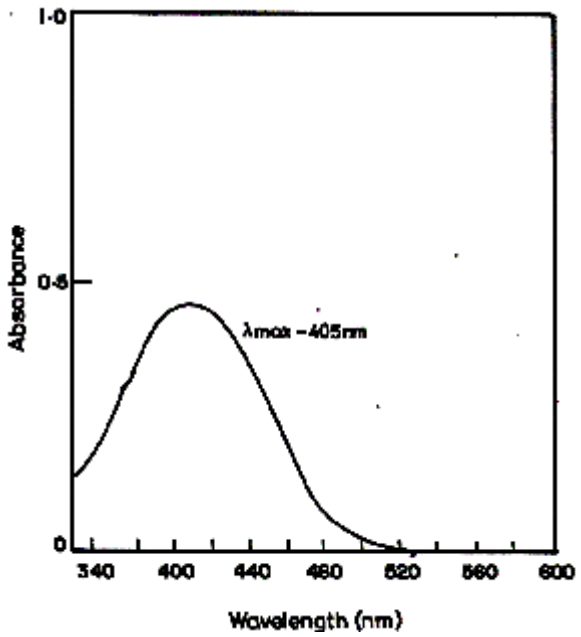
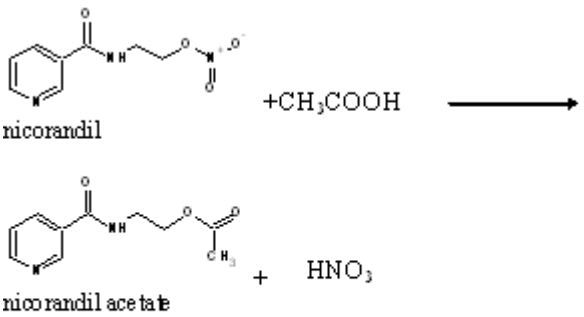


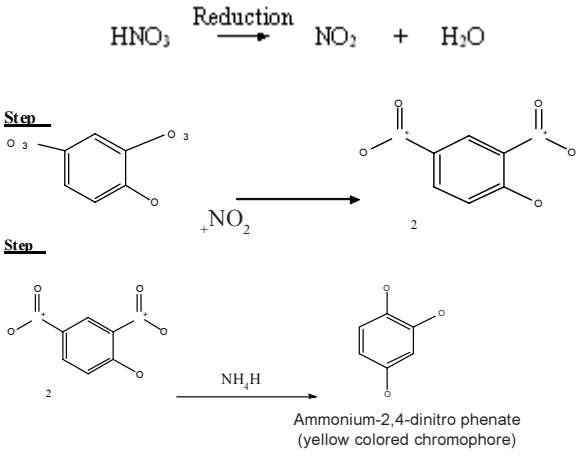
Fig. 3: *Absorption maxima of nicorandil by colorimetry*

Reaction

Step-1



Step-2



Beer's-Lambert's Law Concentration to Confirm Linearity and Range

The aliquots of standard stock solution of nicorandil were taken to get 10, 20, 30, 40, 50 and 60 ìg/mL. To the aliquots, 2 ml of phenol-2,4-disulphonic acid was added and allowed to stand for fifteen minutes. Then 50 ml of distilled water was added and made alkaline with strong ammonia solution. The solutions were cooled and diluted to 100 ml. The absorbance of these solutions was measured at 405 nm using 1 ml of glacial acetic acid treated in a similar manner as blank and plotted against the concentration of drug as showed in Figure 4.

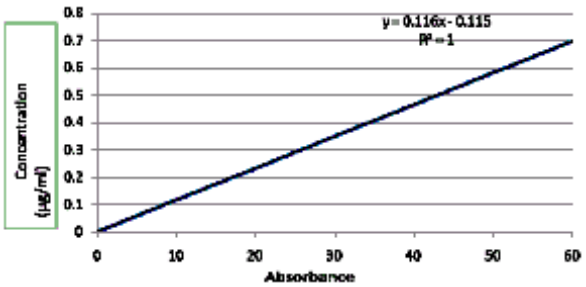


Fig.4: *Standard calibration plot of nicorandil by colorimetry*

Estimation of Nicorandil in Solid Oral Dosage Form

The average weight of twenty tablets were determined and powdered. A quantity of powder equivalent to 25 mg of nicorandil was accurately weighed and transferred to a 25 ml standard flask and shaken with little quantity of glacial acetic acid. It was then made to volume with distilled water. The solution was then filtered and 1 ml of filtrate was transferred to a 100 ml standard flask, 2 ml of phenol-2,4-disulphonic acid was added and allowed to stand for fifteen minutes. Then 50 ml of distilled water was added and made alkaline with strong ammonia solution. The solutions was cooled and diluted to 100ml. The absorbance of this solution was measured at 405 nm using 1 ml of glacial acetic acid treated in a similar manner as blank[14-15]. The results are depicted in Table 2.

Table 2: *Assay of nicorandil in tablet formulation*

Drug	Label claim (mg/tablet)	Amount found (mg/tab)		Percent label claim		Percent deviation	
		Method A	Method B	Method A	Method B	Method A	Method B
Nicorandil	5	5.002 4.972 5.012	5.037 4.993 4.917	100.04 99.44 100.24	100.74 99.86 98.34	(+) 0.04 (-) 0.56 (+) 0.24	(+) 0.74 (-) 0.14 (-) 1.66

**each value is the mean of three readings*

Recovery Study

To study the accuracy, reproducibility and specificity of the method A and B, recovery studies were carried out by addition of standard drug solution to pre-analyzed sample and the contents were reanalyzed by the proposed methods. The percentage recovery is shown in Table 3.

Table 3: *Recovery of nicorandil by proposed methods*

Sample	Amount of drug added (µg/mL)		Amount of drug recovered (µg/mL)		Percent recovery	
	Method A	Method B	Method A	Method B	Method A	Method B
1	10	10	9.879	9.874	98.79	98.74
2	15	15	14.885	14.966	99.23	99.77
3	20	20	19.962	19.973	99.91	99.86

RESULTS AND DISCUSSION

The optical characteristics such as RSD, correlation coefficient, slope and intercept for the two methods were calculated and the results are summarized in Table 1. Interference studies revealed that the excipients and additives did not interfere as shown in Table 2. To evaluate the validity and reproducibility of the methods, recovery studies were carried out by adding a known amount of pure drug to previously analyzed capsules powder sample and re-analyzed. The result obtained is presented in Table 3. These methods are economical, simple, sensitive, accurate and rapid for the routine determination of NIC in bulk and in formulations. The two methods can be easily and conveniently adopted for routine quality analysis.

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