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Electrochemical study of nisoldipine: analytical application in pharmaceutical forms and photodegradation

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Abstract

The anodic and cathodic behavior of nisoldipine, 3-isobutyl-5-methyl-1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)pyridine-3,5-dicarboxylate, are reported. This drug belongs to the nitroaryl-1,4-dihydropyridine family, known as calcium channel antagonist and employed in therapeuticalls as peripheral and cerebral vasodilators, in the treatment of the arterial hypertension. The cathodic response corresponds to the reduction of the nitroaromatic group to generate the hydroxylamine derivative. The study by dc and d.p.p. reveals the appearance of four signals depending on pH: Signal I (pH 1–11.5) $R-NO_2 + 4H^+ + 4e^- \rightarrow R-NHOH + H_2O$; Signal II (pH 1–5) $R-N^+H_2OH + 2H^+ + 2e^- \rightarrow RN^+H_3 + H_2O$; Signal III (pH > 11.5) $R-NO_2 + e^- \rightleftharpoons R-NO_2^{\bullet -}$; Signal IV (pH > 11.5) $R-NO_2^{\bullet -} + 3e^- + 4H^+ \rightarrow R-NHOH$. In contrast, the anodic response corresponds to the oxidation of the 1,4-dihydropyridine ring to generate the corresponding pyridine derivative. Both, cathodic (d.p.p.) and anodic signals (d.p.v.) were employed to develop analytical methodology for the determination of the drug. The repeatability of the measurements for both methods was adequate with R.S.D. of 1.4% ($n = 10$) and 2.1% ($n = 10$) for d.p.p. and d.p.v., respectively. Also recovery studies, 103.8% (R.S.D. 2.65%) by d.p.p. and 98.7% (R.S.D. 2.1%) by d.p.v. show that the accuracy and precision of the developed methods were adequate. The analytical methods were successfully applied to the determination of nisoldipine in both tablets and capsules. In addition, a preliminary study of the photostability of nisoldipine (using both UV and artificial day light) was completed. The identity of the main electroactive photodegradation products by GC with spectrometry detection is provided. © 1998 Elsevier Science B.V.

Keywords: Voltammetry; Nisoldipine; Tablet assay; Photodegradation

1. Introduction

From some years, our group has studied systematically the redox behaviour of the nitro-aryl-1,4-dihydropyridine family (1,4-DHP) based on both its reduction and oxidation properties. [1–7] Work related with the cyclic voltammetry of some members of this family, [8] the electrochemistry of nicardipine [9,10] and also nifedipine [11] have previously been published. This family is known as calcium channel antagonists and is therapeutically used as peripheral and cerebral vasodilators in the treatment of the arterial hypertension. [12,13]

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Nisoldipine, 3-isobutyl-5-methyl-1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)pyridine-3,5-dicarboxylate (Fig. 1), is a widely used drug belonging to the above described therapeutic group. This drug, in common with other calcium entry blocking drugs, inhibits the inward current of calcium ions through slow channels in the cardiac tissue and vasculature, resulting in peripheral and coronary vasodilation. These actions have made nisoldipine of potential benefit in the treatment of angina pectoris, hypertension and other cardiovascular disorders. [14]

Nisoldipine is well absorbed after oral dosing with peak plasma concentrations reached in about 1.5 hours. Both plasma concentration and area under the plasma concentration–time curve are dose dependent. Nisoldipine has a low systemic bioavailability (3.7 to 8.4%) due to extensive presystemic metabolism. The drug is rapidly and extensively removed by hepatic first-pass metabolism and at least 5 and up to 18 metabolites have been demonstrated, including the reduction of the aromatic nitro group as a minor biotransformation reaction. However, the total number of metabolites identified in plasma and their contribution to the pharmacological activity of nisoldipine are unknown. [14–17]

The drug and its main metabolites have been quantitatively assayed by different methods, including gas chromatography (GC) with electron capture detector, GC–MS, mass spectrometry, GC/radio–GC, HPLC and two dimensional TLC. [17–20] In spite of the electrochemistry of the closely related drug, nifedipine, has been previously studied [2,8,11,21,22] to the best of our knowledge, no electrochemical study has been devoted to nisoldipine. Therefore in this paper we report the anodic and cathodic behaviour of nisoldipine in protic media. Furthermore, the electrochemical characteristics of this drug were applied to develop new methods of analysis for pharmaceutical dosage forms and a preliminary study of its photodegradation. The photodegradation of the closely related drug, nifedipine, has been extensively studied [23–26] however the photodecomposition of nisoldipine is an unexplored matter to date. From the nifedipine photodegradations studies can be concluded that the more important photoproducts are the nitro and the nitroso pyridine derivative.

2. Materials and methods

2.1. Reagents and solutions

1. Nisoldipine: 99.8% assay, 100% chromatographically pure (Sanitas Laboratories).
2. Stock solutions: Nisoldipine solutions at a constant concentration of 1×10^{-3} M in ethanol were prepared. All the solutions were adequately protected from light.
3. Routine solutions: 2.5 ml nisoldipine stock solution was taken and diluted to 25 ml with 0.04 M Britton–Robinson or Universal buffer to obtain a final concentration of 1×10^{-4} M in 20% ethanol.
4. Buffer solutions: (1) Universal buffer for pH 2–12-containing 21.01 g citric acid, 13.61 g potassium phosphate, 6.18 g boric acid, 12.1 g Tris and 7.46 g potassium chloride per liter. (2) 0.04 M Britton–Robinson buffer for pH 2–12-containing 0.04 M boric acid, 0.04 M phosphoric acid and 0.04 M acetic acid.
5. Strong alkaline media (H-function): 1 ml of the stock solution was taken and diluted to 25 ml volume with 0.15 M, 0.73 M and 3.67 M NaOH solutions (pH 12.9, 13.7 and 14.54, respectively).
6. Synthetic samples. Excipients to the drug for recovery studies according to manufacturer's

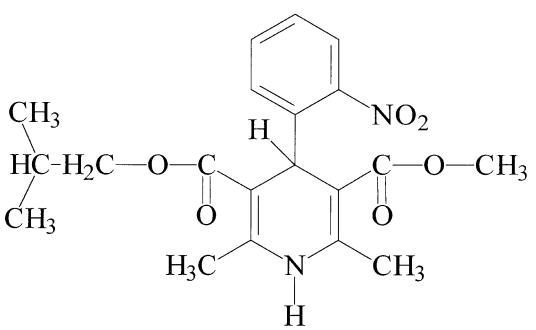


Fig. 1. Chemical structure of nisoldipine.

batch formulas for nisoldipine contained in capsules or tablets were added. The tested exicipients were lactose, starch, sodium glycolate, magnesium stearate and microcrystalline cellulose.

7. Individual tablet assay: Each tablet or capsule (not less than 10) was dispersed in ethanol and sonicated for 10 min, to ensure dissolution of the drug and then an aliquot of 5 ml was taken and diluted to 25 ml volume with 0.04 M Britton–Robinson buffer solution at pH 7.4, transfered to a voltammetric cell and both the differential pulse polarogram and voltammogram were recorded.
8. Preliminary study of photodecomposition (a) powder: independent samples of 10 mg of nisoldipine (pure powder), were let stored in ambient laboratory conditions of light and temperature. Each 24 hours the concentration of nisoldipine in each sample was determined. Each sample was dissolved in 5 ml of ethanol, and 0.1 ml of this solution was diluted to 25 ml volume with ethanol/Britton–Robinson buffer mixture 20/80, pH 7.4. The solution thus obtained was transferred to a voltammetric cell, and differential pulse polarogram measured. (b) solution: independent samples of 1×10^{-3} M nisoldipine ethanol solutions were irradiated with both UV or artificial day light at a constant temperature of 25°C in a black box. Samples were taken every hour and analyzed by both polarography (0 to -1200 mV, Universal buffer/ethanol: 70/30, pH 7.4), and GC–Mass detection (GC–MD).

All reagents used were analytical grade.

3. Apparatus

Polarograph: A Tacussel® assembly operated in dc and d.p.p. mode, consisting of an EPL-3 recorder equipped with a TI-PULS module, similar to one previously described. [27] Operating conditions: pulse amplitude, 60 mV; potential scan rate, 5 mV s^{-1}; drop time, 1 s; voltage range, 0–2000 mV; current range, 1.25 to 5 μA; temperature, 25°C.

Cyclic and differential pulse voltammetry: These techniques were carried out with a totally automated Inelecsa® assembly similar to one previously described. [3]

Voltammetric cell: Tacussel® CPRA measuring cell with dropping mercury electrode, glassy carbon, platinum, carbon paste or hanging mercury electrode as a working electrode, a platinum wire counterelectrode, and a saturated calomel reference electrode (SCE) were used.

Gas chromatography (GC): A 8000 Fisons GC with MD 800 mass detector (electron impact detector) was used. Operating conditions: injector temperature 150°C, programm temperature 20°C min^{-1} (7.5 min) and final temperature 300°C.

Irradation sources: For artificial day light a 100 W Philips bulb was used. For UV irradiation a UV Blak–Ray long wave ultraviolet lamp, UVP model B 100 AP (50 Hz, 2.0 A) with a 100 W Par 38 Mercury lamp equipped with a 366 nm filter was used.

4. Results and discussion

4.1. Anodic behavior

Nisoldipine in a hydroalcoholic solution can be oxidized on platinum, glassy carbon and carbon paste electrodes in a broad pH range, producing only one anodic peak (Fig. 2).

The peak potential versus pH plot (Fig. 3) shows three linear segments. In the acidic range ($pH < 5$), the process is pH-independent. In this zone, the transfer of the first electron would play a major role, becoming to be the rate-determining step of the oxidation process, probably generating a highly reactive radical cation [28].

On the other hand, the voltammetric response shows a pH-dependent behaviour above pH 5, with slopes of 35 mV pH^{-1} between pH 5 and 8 and 62 mV pH^{-1} between pH 8 and 12. This behaviour implies a change in the mechanism, due to the protonation step occurring at a lower rate probably as a consequence of a change in ionization state of the participating molecules. There is no reported pK_a for the dihydropyridines but perhaps the oxidated product pyridines has an

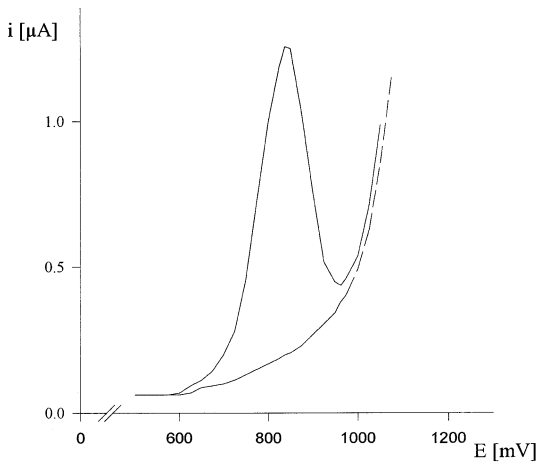


Fig. 2. Full line: Differential pulse voltammogram of a 0.1 mM nisoldipine solution at pH 7.4 in 0.04 M Britton–Robinson buffer/ethanol 70/30 mixture, dashed line: only buffer solution. (Glassy carbon working electrode).

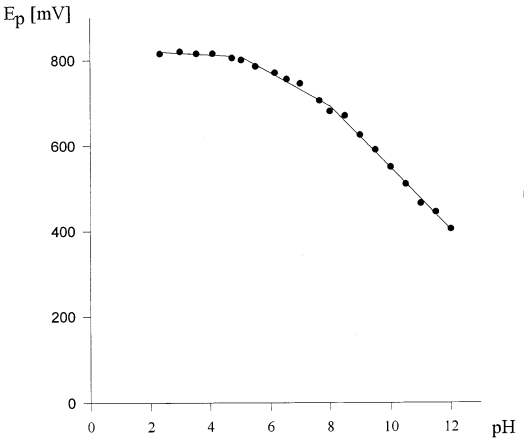


Fig. 3. Peak potential dependence of 0.1 mM nisoldipine solution with pH (d.p.v., glassy carbon electrode).

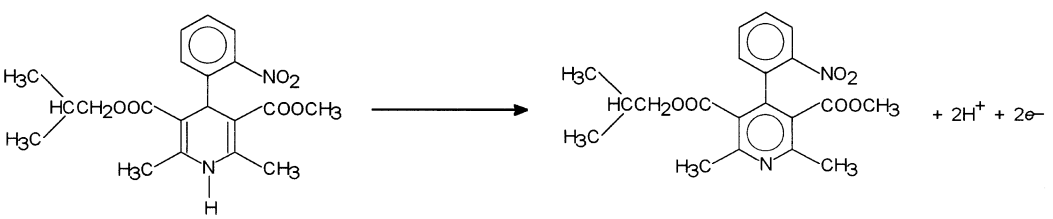
ionization around this region. The limiting current is not significantly affected by the pH, indicating that it is controlled by the diffusion of the electroactive species on the electrode surface. Nevertheless, the peak potential is influenced by the drug concentration, indicating that an adsorption phenomenon is affecting the diffusion control.

Cyclic voltammetric experiments on glassy carbon electrode show only one anodic peak, totally irreversible, with a current function value ($i_p/v^{1/2}$) independent of sweep rate, confirming the diffusion control of the process.

In the nisoldipine chemical structure, the most easily oxidizable group is the 1,4-DHP ring, as can be observed in analogous molecules, [7] to give the corresponding pyridine derivative in a two electron oxidation process, which can be summarized by the following overall equation:

4.2. Cathodic behaviour

Nisoldipine contains a nitro aromatic group capable of giving a reduction wave at the dropping mercury electrode. The dc polarographic reduction of the drug in hydroalcoholic solution (Universal or Britton–Robinson buffer/ethanol 70/30, $\mu = 0.3$M) produces a main well-defined cathodic wave over the entire pH range (wave I in Fig. 4). This wave strongly depends on pH, shifting cathodically with increasing pH (between pH 2 and 11). The $E_{1/2}$ versus pH graph (Fig. 5) shows three linear portions with breaks at approximately pH 6 and 11. The slope of the first linear portion was -67 mV pH^{-1} unit and the second one was -50.3 mV pH^{-1} (wave I). This behaviour is probably due to a change in the rate-determining step in the electrode surface process, as has been described by Pezattini et al. for nitrobenzene. [29] At strongly basic pH (> 12) the



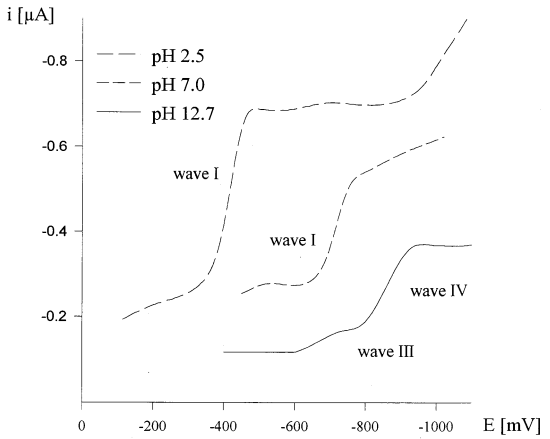


Fig. 4. d.c. polarographic wave evolution of 0.1 mM nisoldipine solution with pH.

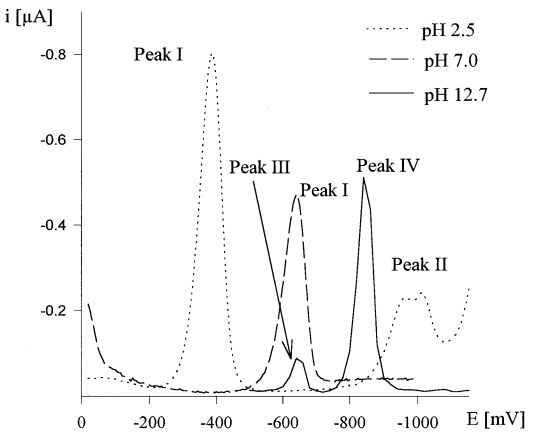


Fig. 6. d.p. polarographic peak evolution of 0.1 mM nisoldipine solution with pH.

main wave I was split in two new waves at -700 and -900 mV, respectively (waves III and IV).

On the other hand, by using d.p.p. mode it is possible to distinguish four signals (Fig. 6). In acidic media (pH < 5) nisoldipine produces two peaks; when the pH exceeded pH 5, there was only one. Both peaks strongly depend on pH, shifting cathodically with increasing pH. The graph of E_p versus pH (Fig. 7) shows two linear portions with breaks at approximately pH 6.5 and 11 for the first peak (peak I) and a simple linear behaviour for the second peak (pH 2–5) (peak II). The slopes of each linear portion were 49.2 mV pH^{-1}, 61.9 mV pH^{-1} and 93.4 mV pH^{-1} for peak I and II respectively. The others two signals which are pH-independent were observed in strong alkaline pH (> 12) (peaks III and IV).

Controlled potential coulometric measurements indicate that the first peak is due to a four-electron reduction and the more cathodic peak involves a two-electron reduction process. The highest peak, which occurs at less negative potential, is due to the reduction of the nitro group to produce the hydroxylamine derivative and is electrochemically irreversible. The overall well-known

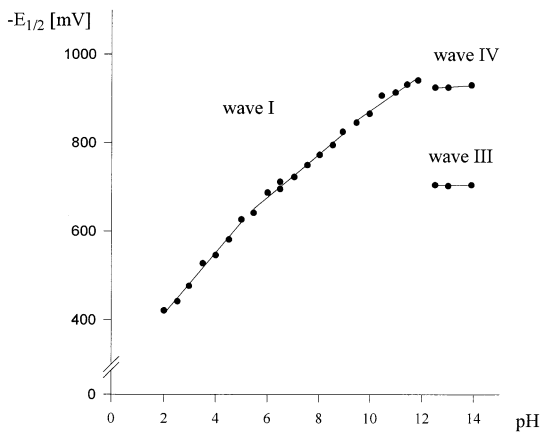


Fig. 5. Half wave potentials dependence of 0.1 mM nisoldipine solution with pH.

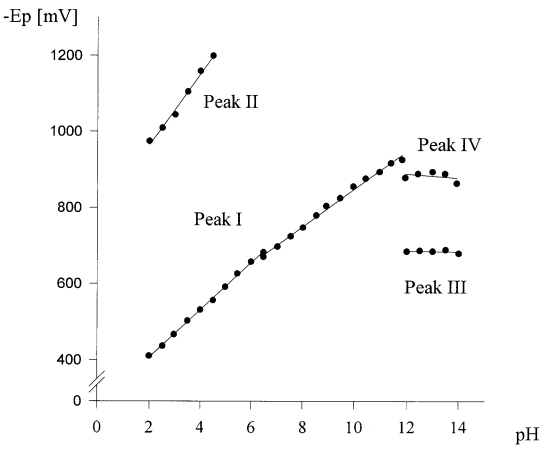


Fig. 7. Peak potential dependence of 0.1 mM nisoldipine solution with pH (d.p.p.).

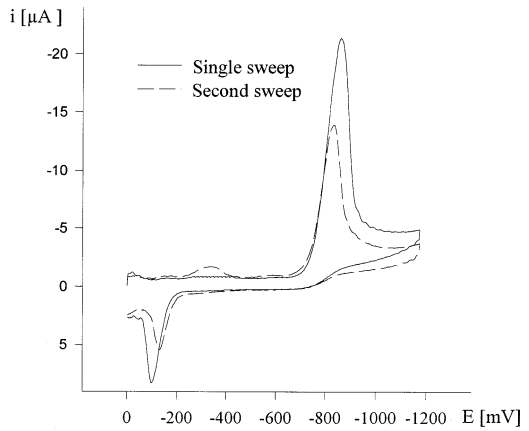


Fig. 8. Cyclic voltammograms of a 1 mM nisoldipine solution at first and second sweep (pH 7.4; 0.04 M Britton–Robinson buffer/ethanol 70/30).

reaction involved in this reduction process is as follows:

$$R{-}NO_2 + 4H^+ + 4e^- \rightarrow R{-}NHOH + H_2O \quad (1)$$

However, this observed single peak is a combination of the following reactions:

$$R{-}NO_2 + 2H^+ + 2e^- \rightleftharpoons R{-}NO + H_2O \quad \text{slow} \quad (2)$$

$$R{-}NO + 2H^+ + 2e^- \rightarrow R{-}NHOH \quad \text{fast} \quad (3)$$

These two reactions, Eq. (2) and Eq. (3), are combined to give a single four-electron polarographic wave, since the nitroso compound is reduced at more positive potentials than nitro compounds; thus the nitroso compound is not isolated but is immediately reduced to the hydroxylamine derivative. This behaviour was confirmed by cyclic voltammetry experiments (Fig. 8). In the first scan we have only one cathodic peak ($E_p = -860$ mV) with strong adsorptive character, due to the four-electron reduction of the nisoldipine nitro group to the hydroxylamine derivative. Also, we have an anodic peak ($E_p = -100$ mV) due to the oxidation of the hydroxylamine derivative formed in the first sweep. Multiple scans show a couple ($E_{pa} = -130$ mV, $E_{pc} = -332$ mV) due to the corresponding nitroso-hydroxylamine redox reaction. Consequently, the above behaviour for nisoldipine follows the general pattern for nitroaromatic compounds. [4,30–32] Furthermore, the electroreduction behaviour of nisoldipine is very related with the nifedipine's behaviour, however we have observed a slight difference in the reduction potential of the nitro group between both drugs. Specifically, when we compare the cyclic voltammograms of solutions from nifedipine and nisoldipine in the same conditions, we have found that the nitro group in nisoldipine is reduced about 50 mV more cathodic than nifedipine. This difference can be explained for the influence of the more bulky substituent in position 3 of the dihydropyridine moiety in the nisoldipine molecule.

On the other hand, the smallest secondary polarographic peak (peak II), which occurs at more negative potential in acidic media involving two electrons, corresponds to the reduction of protonated hydroxylamine according to the following reaction:

$$R^+NH_2OH + 2H^+ + 2e^- \rightarrow R^+NH_3 + H_2O \quad (4)$$

From the study of the pH-dependence by d.p.p. is possible to assume the existence of two different behaviours, one that exists between pH 2 and 11.5 and other, at upper pHs. At pH > 12 the peak I is split in two signals, corresponding to:

$$\text{Peak III} \quad RNO_2 + e^- \rightleftharpoons RNO_2^{\bullet -} \quad \text{(fast)} \quad (5)$$

Peak IV

$$RNO_2^{\bullet -} + 3e^- + 4H^+ \rightarrow RNHOH + 2H_2O \quad (6)$$

As can be seen, protons are not involved in Eq. (5), consequently peak III is pH-independent. In case of peak IV, its pH-independence can be explained considering that the first step in the overall Eq. (6) would be the slow transfer of the first electron.

For further studies we have selected the main peak at pH 7.4, due to the four-electron reduction of the nitro group to the hydroxylamine derivative.

This peak shows a linear dependence between the limiting current and the square root of the mercury column height (corrected for back pressure). Also, we have obtained a value of 0.21 for

the slope of the straight line between the logarithm of the limiting current versus the logarithm of the drop time. [33] Both of these studies permit us to conclude that the electrode process is diffusion controlled. Furthermore, this diffusion control was confirmed with the results obtained from the study of the limiting current–temperature dependence. We have found a temperature coefficient of 2.54%, confirming that the process is diffusion controlled.

In parallel with the above results we have obtained a linear relation between the peak current and the nisoldipine concentration in a wide range (1×10^{-3}–5×10^{-6} M).

4.3. Analytical methods

4.3.1. Individual pharmaceutical dosage form assays

Based on the above results, it is feasible to employ d.p.p. in the quantitative determination of the drug. For quantization we have selected the calibration curve method for nisoldipine concentrations ranging between 1×10^{-4} and 1×10^{-5} M at pH 7.4. The regression equation for the calibration curve is:

$$i_p(\mu A) = 23648.16C(M) + 0.04411,$$
$$r = 0.9998,\ n = 11$$

The repeatability of the measurement was adequate, with a R.S.D. of 1.4% on ten experiments, with a detection limit of 2.5×10^{-6} M. The recovery study for synthetic samples (Table 1), shows a average recovery of 103.8%, with a R.S.D. of 2.7%, indicating adequate precision and accuracy for the method.

Furthermore, making use of the anodic behaviour of nisoldipine we also have developed an analytical methodology by d.p.v. on the carbon paste electrode.

We have obtained a linear relationship between the peak current (i_p) and the nisoldipine concentration in the range of 4×10^{-6} to 4×10^{-4} M. For the quantitative determination the calibration curve method was employed. This curve is described by the following linear regression equation:

$$i_p(\mu A) = 1571C(M) + 0.739, \quad r = 0.999,\ n = 10$$

The repeatability of the measurement was adequate, with a R.S.D. of 1.4%, and a calculated detection limit of 1.8×10^{-6} M. The recovery study for synthetic samples (Table 1) show a recovery average of 98.7%, with a R.S.D. of 2.1%, indicating adequate precision and accuracy of the method.

Both developed methods (d.p.p., d.p.v.) were applied to the determination of the drug in pharmaceutical dosage forms (Table 2). The procedure and its application to pharmaceutical forms represents a good alternative for the quality control, because the preparation of the sample is easy and the excipients does not interfere with the determination and consequently, separations or extraction procedures are not needed. It is necessary to emphasize that this drug is not included in any Pharmacopeia.

Table 1
Recovery study for nisoldipine, by differential pulse polarography and differential pulse voltammetry[a]

Differential pulse polarography		Differential pulse voltammetry	
Found (mg)	Recovery (%)	Found (mg)	Recovery (%)
10.6	106.4	9.9	99.0
10.6	106.4	10.0	100.0
10.5	104.6	9.8	98.0
10.8	108.3	10.0	100.0
10.2	102.3	10.0	100.0
10.4	103.7	10.2	102.0
10.4	103.7	10.0	100.0
10.2	102.3	9.8	98.0
10.0	100.0	9.8	98.0
10.0	100.0	9.7	97.0
Average			
10.4	103.8	9.9	98.7
S.D.			
0.3	2.7	0.2	2.1
C.V. (%)			
2.7	2.7	2.1	2.1

[a]Each sample was prepared independently, containing 10.0 mg of nisoldipine and exicipients according to the batch formula.

Table 2
Uniformity Content of nisoldipine in tablet and capsules by differential pulse polarography and differential pulse voltammetry

Differential pulse voltammetry		Differential pulse polarography
mg/capsule[a]	mg/tablet[b]	mg/tablet[b]
5.10	9.90	10.17
4.70	9.70	9.32
5.30	9.70	10.54
4.90	10.20	9.83
5.10	10.00	9.83
5.00	10.20	10.17
4.90	9.30	9.91
5.00	9.60	9.83
4.90	10.00	10.0
4.90	9.80	9.80
Average		
4.98	9.84	9.94
S.D.		
0.16	0.28	0.32
C.V. (%)		
3.2	2.8	3.20

[a]Corasol, Sanitas Laboratory. Declared composition: 5 mg nisoldipine per capsule.
[b]Syscor, Bayer Laboratory. Declared composition: 10 mg nisoldipine per tablet.

4.3.2. Photodegradation applications

The d.p.p. technique was employed to follow the degradation of the drug. In this case, we have studied the photodecomposition of ethanol solutions of nisoldipine, with two types of irradiation conditions: artificial daylight and UV light. The use of the d.p.p. technique allowed us to obtain some qualitative information about the molecular changes involved in the photodegradation process which were confirmed using GC–MD. The progress of the photodegradation was followed by changes in the d.p. polarograms up to 8 hours exposure. The evolution of the polarograms of both, the artificial daylight and UV light irradiated solutions of nisoldipine are shown in Fig. 9. At zero exposure time, only one cathodic peak was observed (− 700 mV), due to the reduction of the nitro group of the drug. The GC–MD spectra corresponding at zero exposure time (unaltered nisoldipine) shows a retention time of 12.935 min. and the main molecular ions are; m/z: 388 (M); 371 (M–2H–$^{\bullet}CH_3$); 270 (M–2H–$^{\bullet}CH_3$–$^{\bullet}COOCH_2CH(CH_3)_2$; 284 (M–2H–$^{\bullet}COOCH_2CH(CH_3)_2$. When nisoldipine solution samples were exposed to UV light, the d.p. polarogram was alterated as follows: (a) the peak at − 700 mV due to the nitro group in nisoldipine vanished and at more positive potentials, a peak at − 580 mV appeared. The polarographic peak associated with the aromatic nitro group at − 580 mV, can be explained considering that the nitropyridine derivative is one of the degradation products. This assumption was confirmed by GC–MD: r.t. 10.619 min; m/z: 371 (M–$^{\bullet}CH_3$); 284 (M–H–$^{\bullet}COOCH_2CH(CH_3)_2$); 340 (M–$^{\bullet}NO_2$). The gas chromatogram and the mass spectra for the nitropyridine derivative was obtained after 8 hours exposition. Consequently, this derivative is more easily

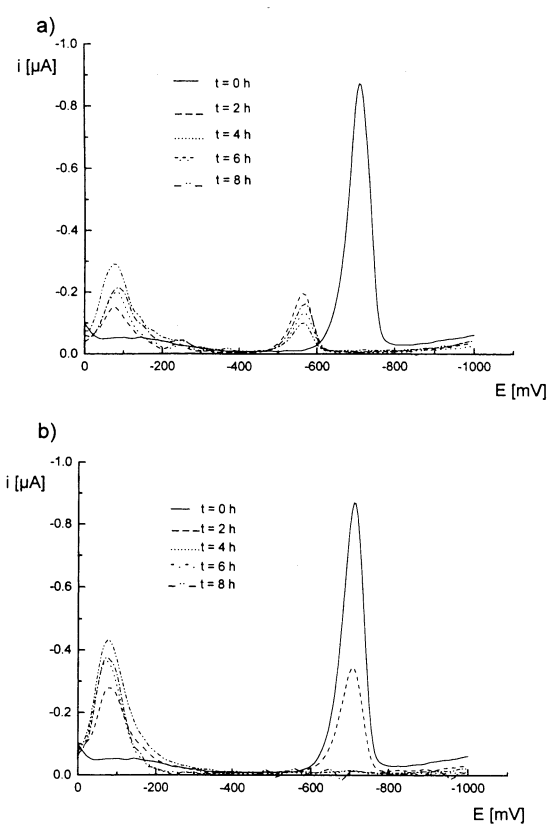


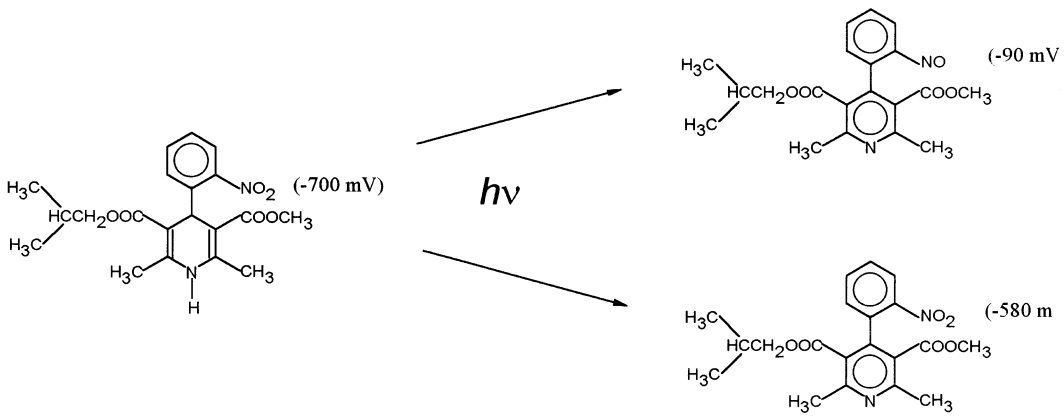
Fig. 9. d.p. polarograms evolution of a nisoldipine solution (pH 7.4; 0.04 M Britton–Robinson buffer/ethanol 70/30) (a) UV irradiation (b) artificial day light irradiation.

reducible than the nitro group on nisoldipine, because the coplanarity between the benzene and pyridine rings, permits an extended conjugation and a higher electron delocalization. (b) a new peak appears at −90 mV. From the value of peak potential of this peak, is possible to conclude that it corresponds to the reduction of a nitroso group (nitroso pyridine derivative) to give the hydroxylamine derivative. The identity of this compound also was confirmed by GC–MD. The following parameters are in accord with a nitroso pyridine derivative: r.t. 9.818 min; *m/z*: 370 (M); 270 (M + H–$^{\bullet}COOCH_2CH(CH_3)_2$; 238 (M + H–$^{\bullet}$COOCH2CH$(CH_3)_2$–$^{\bullet}$NO); 311 (M–$^{\bullet}COOCH_3$). Furthermore, the d.p. polarograms of the artificial daylight nisoldipine solutions exhibit only one new cathodic peak at −90 mV that corresponds to the nitroso derivative. This fact was confirmed by the results of GC–MD: r.t. 9.818 min; *m/z*: 370 (M); 270 (M + H–$^{\bullet}COOCH_2CH(CH_3)_2$; 238 (M + H–$^{\bullet}$COOCH2CH$(CH_3)_2$–$^{\bullet}$NO); 311 (M–$^{\bullet}COOCH_3$).

The polarographic peaks described above and the corresponding GC–MD results are in accord with two main molecular changes induced by UV light exposure. Firstly, the nitro aromatic group is reduced to a nitroso aromatic group, secondly, the dihydropyridine moiety is oxidized to a pyridine ring. These molecular changes induced by light permit us to propose a preliminary overall reaction for the nisoldipine photodegradation. (The peak potential of each reducible group is shown in parenthesis).

This photodegradation pathway is similar with the previously described for nifedipine showing that the different substituent in 3-position of the dihydropyridine moiety should not affect the overall photochemical behaviour. Also, the photodecomposition of nisoldipine powder (solid state) in normal laboratory conditions (daylight and 25°C) was monitored. It was found that the peak current decays with the exposure time, however during the short time scale of the proposed routine analytical procedure nisoldipine powder remains unaltered. Furthermore, from the obtained results summarized in the above scheme is clear that the polarographic technique permits to clearly distinguish between nisoldipine ($E_p = -700$ mV), the nitropyridine-photodegradation product ($E_p = -580$ mV) and the nitrosopyridine-photodegradation product ($E_p = -90$ mV), consequently the potential degradants of nisoldipine do not interfere with the assay.

Thus, as can be concluded of this work, light exposure produces changes in the main redox centres of the molecule (nitro group and dihydropyridine moiety), consequently the electrochemical techniques are a very useful tool for both, to quantitative determine uniformity content of tablets or other dosage forms accurately and precisely and to follow photodecomposition of this drug.



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