

The Atomic Absorption Spectrophotometric Method for Indirect Determination of Nimodipine in Tablets

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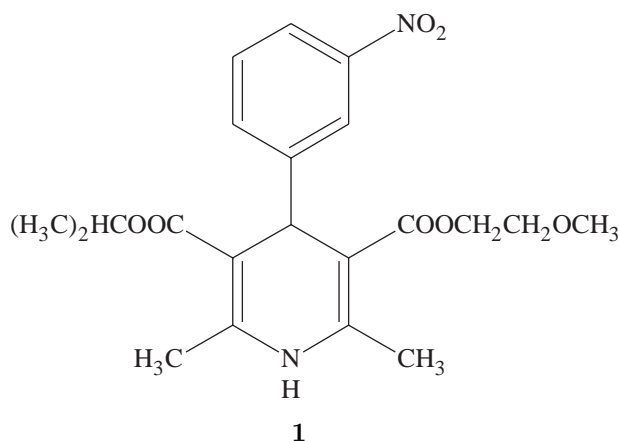
A simple indirect atomic absorption spectrophotometric (AAS) method is described for the analysis of nimodipine in tablet formulations. The method is based on the reduction of the antihypertensive drug substances including an aromatic nitro group by boiling them with cadmium metal in 0.05 N HCl medium under CO₂ atmosphere for 1 h under reflux. The amounts of the drugs were calculated by determining the atomic absorbances of the released Cd⁺². The calibration graphs were plotted between the absorbance Cd⁺² concentrations in the range of 0.242 to 1.209 µg.cm⁻³ for nimodipine. As a reference method, the spectrophotometric procedure was developed. The 2 methods developed were applied to the assay of nimodipine in commercial tablet formulations, and a statistical comparison of the results with those obtained from the reference method showed good agreement. The method has the advantage of being simple, inexpensive, and easy to perform.

Key Words: Aromatic nitro compounds, Cadmium ion, Pharmaceutical analysis, Indirect determination.

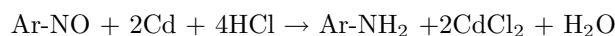
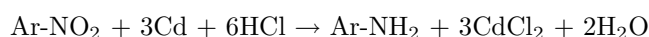
Introduction

Nimodipine is a cardioselective drug used in the treatment of hypertension. Its formula is presented in **1**. For the assay of nimodipine liquid chromatographic methods have been reported¹ as official methods. For the determination of this drug in dosage forms, various analytical techniques including spectrophotometry²⁻¹², spectrofluorometry¹³, gas chromatography¹⁴, thin layer chromatography¹⁵, high performance liquid chromatography¹⁶⁻²² and polarography²³ have been reported.

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There is no atomic absorption spectrophotometric (AAS) method in the literature for the analysis of this drug. In the present study 2 analytical methods, a spectrophotometric method and an indirect AAS method, were developed for nimodipine^{24,25}. The reductions of the nitro and nitroso groups with the cadmium metal were determined as follows²⁶⁻²⁸:



Experimental

Materials

A pharmaceutical grade sample of nimodipine (Bayer, Turkey) was used as received and other analytical grade chemicals were purchased from Merck, namely, Hydrochloric acid (HCl), acetone, ethanol (EtOH), methanol (MeOH), cadmium granules, cadmium sulphate, α -naphthylamine, ammonium sulphamate, glacial acetic acid and sodium nitrate. Bidistilled water was used.

Instrumentations

A Varian SpectrAA-20 spectrophotometer was used for atomic absorbance measurements. A cadmium hollow-cathode lamp was used under the following operation conditions: wavelength 228.8 nm, slit-width 0.5 nm, lamp current 4 mA, laminar flow burner, air flow 3.5 L/min, and acetylene flow 1.5 L/min. A Philips PU 8700 UV-Visible spectrophotometer and 10 mm quartz cells were used for spectrophotometric measurements.

Calibration procedure

0.2282 g of cadmium sulphate was weighed for the stock solution of Cd^{+2} . Standard solutions for the preparation of the calibration curve were obtained by diluting the stock solutions appropriately. Standard solutions for nimodipine were obtained by following the AAS method. Standard solutions were prepared in the range 0.3 to 1.5 $\mu\text{g}\cdot\text{cm}^{-3}$.

AAS method

A total of 15 mg of nimodipine was weighed accurately and diluted to volume with MeOH in a 10 cm³ calibrated flask as stock solution. A solution equivalent to approximately 3 mg of nimodipine was prepared by adding 2 mL of the stock solution, 10 mL of 0.05 N HCl and a Cd granule. The mixture was boiled for 60 min under CO₂ atmosphere. The mixture was transferred into a 50 cm³ calibrated flask and the volume was completed with H₂O. The solution was prepared by diluting this solution to the desired concentration. The atomic absorbance of the Cd²⁺ in this solution was measured at 228.8 nm against a blank prepared under identical conditions.

Spectrophotometric method

The amine group determined by the reduction of the aromatic nitro group by following the AAS method was spectrophotometrically determined by using diazotization-coupling. After the reduction of the aromatic nitro compound, the 2 mL samples taken from the standard solutions in different concentrations were prepared with 1 mL of 2.5 N HCl and 0.5 mL of 1.0% sodium nitrite solution. The mixture was shaken and allowed to settle for 2 min. Then 1 mL of 1% ammonium sulphamate was added and the mixture was allowed to settle for 2 min. Finally, 1 mL of 0.2% α -naphthylamine solution was added. The absorbance in this mixture was measured at 526 nm against a blank prepared under identical conditions after 10 min.

Sample preparation

Twenty tablets were weighed and powdered. MeOH was added to an accurately weighed amount of the powder equivalent to approximately 3 mg of nimodipine in a 10 cm³ calibrated flask. The mixture was shaken, and diluted to volume with MeOH and filtrate. The filtrate was used for AAS and visible spectrophotometric determinations after the appropriate dilutions.

Results and Discussion

To determine the optimal conditions for this method, the solvent dissolving the substances, HCl concentration and the boiling time were investigated and checked. Optimal conditions were chosen as 2 mL of MeOH, 0.05 M HCl and 60 min boiling time, since this gives the highest absorbance value. Under the experimental conditions described a linear relationship was obtained between atomic absorbance (A) and Cd⁺² concentration (C) in the final solution over a 0.3 to 1.5 $\mu\text{g}\cdot\text{cm}^{-3}$ nimodipine (0.242-1.209 $\mu\text{g}\cdot\text{cm}^{-3}$ Cd⁺²) range. A linear relation was also obtained between atomic absorbance value (A) and Cd⁺² concentration (C) at 0.3-1.5 $\mu\text{g}\cdot\text{cm}^{-3}$. The regression equation of the calibration curve was calculated as shown in Table 1. The recovery the ratio of nimodipine was 99.6% at RSD of 1.1% . The solutions were stable at room conditions for 3 months but were unstable under light. There were no significant differences between using H₂O or HCl to dilute. The amount of cadmium dissolved on the surface of the metal in acidic media is not significant^{26,28}. All of the solutions were prepared by completing to volume with H₂O.

Commercially available tablets containing 30 mg of nimodipine were successfully analysed using the proposed method. The drug was also analysed using a visible spectrophotometric method as a method of comparison based on diazotization- coupling of the amine group formed during the reduction of the aromatic nitro group. The assay results obtained from both methods were statistically compared at a 95% confidence

level using t- and F- tests. As shown in Table 2, there was no significant difference between the mean values or precisions of the 2 methods.

Table 1. Calibration equation for AAS.

Nimodipine Concentration ($\mu\text{g}\cdot\text{cm}^{-3}$)	Cd^{2+} Concentration in Nimodipine ($\mu\text{g}\cdot\text{cm}^{-3}$)	Absorbances Nimodipine	Cd^{2+} Concentration ($\mu\text{g}\cdot\text{cm}^{-3}$)	Absorbances Cd^{2+}
0.3	0.242	0.062	0.3	0.085
0.6	0.484	0.125	0.6	0.163
0.9	0.725	0.187	0.9	0.239
1.2	0.967	0.242	1.2	0.312
1.5	1.209	0.310	1.5	0.393
A = 0.254 C + 0.001 r = 0.9996			A = 0.255 C + 0.009 r = 0.9999	

Table 2. Assay result of commercial tablets containing 30 mg of Nimodipine.

n	AAS Method	Visible Spectrophotometric Method
1	29.9	30.2
2	30.1	29.8
3	31.3	30.5
4	29.1	30.1
5	29.9	29.7
6	30.3	30.9
7	29.8	29.1
8	28.9	29.3
9	30.2	29.9
10	31.1	30.2
11	30.4	30.1
12	30.1	29.9
13	29.7	29.4
X_{ort}	30.1	29.9
S	0.67	0.49
$S/ X_{ort}\cdot 100$	2.22	1.64
$X_{ort} \pm t.S/\sqrt{n}$	30.1 ± 0.16	29.9 ± 0.12
t- test	0.87	
F- test	1.87	

^a $\lambda_{max} = 526 \text{ nm}$

^b $t = 2.179, F = 2.690$ for $p = 0.05$ and $n = 13$

The other functional groups and tablet ingredients do not impact used on this method. Therefore, it can be used for analysis of nimodipine in pharmaceutical dosage forms. An important advantage of this reduction reaction is that 4 different methods of determination can be applied to the same solution. These are AAS, polarography, complexometric titration with EDTA and visible spectrophotometry. The other advantages are reagent stability and reaction selectivity. Producing 3 mols of Cd^{+2} per 1 mol of nitro group causes the results to be more precise and accurate.

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