Spectrophotometric Determination of Nefidipine in Pharmaceutical Preparations by Coupling Reactions

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Abstract:
A sensitive spectrophotometric procedure was described for the determination of Nifedipine. The procedure is based on reduction of the nitro group, yielding free primary aromatic amine which could be diazotised and coupled to give red azo-dye with λ max at 510 nm and a violet with λ max at 555 nm with Bratton marschal and B- naphthol, respectively.
The procedure was applied for determination of Nifedipine and Coracetene capsules with mean accuracies 100.9, 100.39 and 99.95, 100.5 respectively.
The accuracy and precision of the suggested procedure were compared with the official method (B.P 1993) and the results obtained showed no significant difference between the two methods. Moreover the suggested method was more accurate, sensitive and precise compared to the official titrimetric procedure.
Keywords: Nefidipine, Bratton Marschal, B-naphthol, Diazocoupling.

Introduction:
Different methods were reported for determination of Nefidipine. Direct current and altering current polarographic methods were developed to determine content uniformity and photostability.[1] Visible and UV spectrophotometric methods were also reported; Nifedipine is quantitatively determined in methanolic solution at 350 nm.[2] The nitrozo pyridine of Nifedipine was determined in acid and alkali.[3] Nifedipine and acebutolol HCl in combined tablets were determined using the first derivative at 400 and 352 nm.[4] A fluorimetric assay of Nifedipine based on the reduction of the nitro by $TiCl_3$ and oxidation of the dihydropyridine ring were coupled with o-phthaldialdehyde.[5]
Chromatography was used for evaluation of the decomposition process.[6] Gas chromatographic method with FID allows the analysis of nifedipine in µg concentration range.[7] Nifedipine and its nitropyridine derivative in plasma were analyzed through GLC.[8,9] A HPLC method was developed for the assay of nifedpine in plasma and its main metabolite.[10,11]
Determination of nifedipine by HPLC with electrochemical detection was reported.[12] GC-Mass spectrophotometry has been applied to examine the stability of nifedipine.[13]

Experimental:
Apparatus:
Pv 8625, Uv/visible spectrophotometer.

Chemical and reagents:
Sodium nitrite, 1g % aqueous solution
Hydrochloric acid, 1N aqueous solution.
Sodium hydroxide, 1N.
Sulphuric acid, 0.5 g % aqueous solution.
B-naphthol, 0.5 g % in ethanol.
Bratton Marschal reagent, N-1-naphthylethylene diamine dihydrochloride, 0.1 g % in ethanol.
Nifedipine stock solution, 200mg % ethanol.
Nifedipine capsules labeled to contain 20 mg Nifedipine, from Epico, Egypt.
Coracetine capsules, from smith klein, Beecham, labeled to contain 20 mg Nifedipine.

Procedure:
A- pure drugs:
An accurately weighed amount of the drug (25-100 mg) was transferred to a beaker and about 0.1g zinc metal was added and followed by 10 ml HCl, heated for 30 minutes on a water bath and transferred to 25 ml calibrated flask. The process was completed by adding ethanol.
An aliquot 0.5 ml of the above solution was transferred to 10 ml volumetric flask, 1 ml $NaNO_2$ was added and followed by 1 ml HCl, cooled in ice bath for 15 minutes followed by 1ml sulphuric acid.
This solution was treated with either 1 ml B-naphthol and 1.5 ml NaOH (method I) or 2.5 ml of Brattan Marschal (method II). To the flask was added a volume of H_2O and measured at 555 and 510 nm for method I and II respectively.

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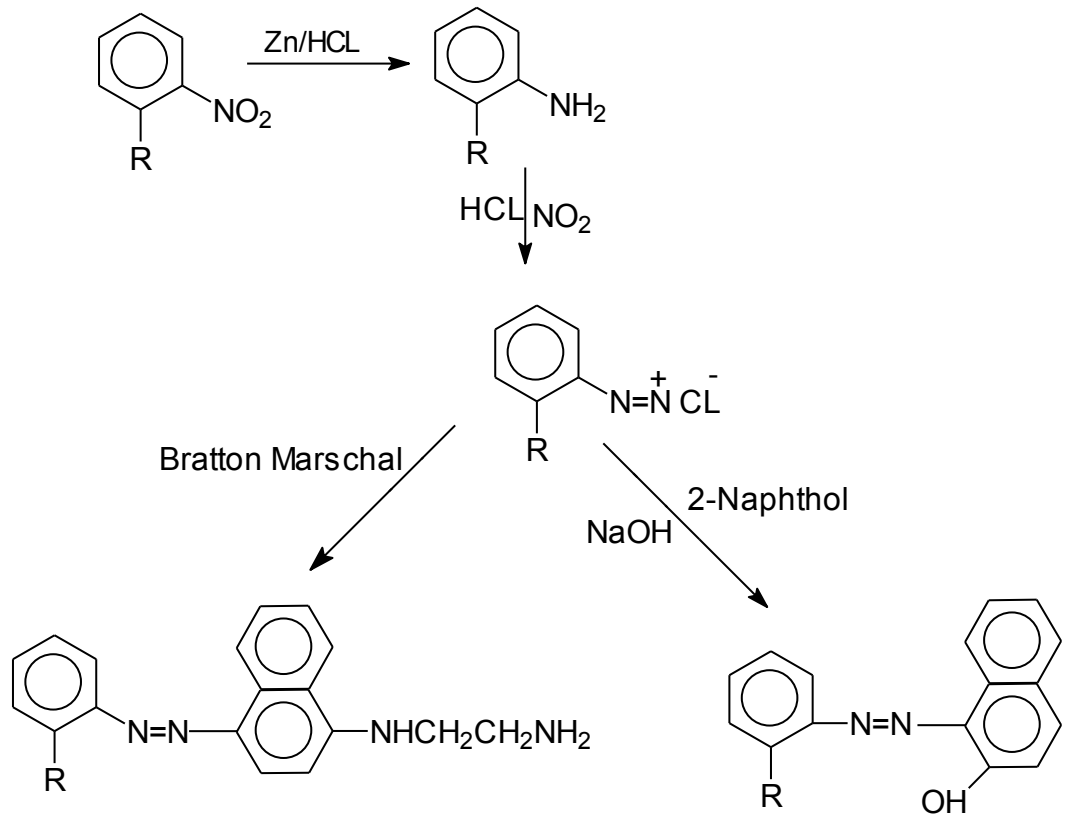
B- Application to capsules:
The contents of 20 capsules were weighed and amount of the powder equivalent to 100 mg of Nifedipine was transferred into a beaker and the assay was completed as above.

Results and discussion:
As Niedipine contain aromatic nitro compound, attempts were made to reduce this group to primary amine, then diasotized and coupled with either B-naphthol or Brattan Marschal reagent to give azodye measured spectrophotometry and the absorption spectra as shown in Fig (1) and scheme (I).
The effect of the reduction time on the absorption spectra is shown in Fig (2). The effect of sodium nitrate volume was explained in Fig (3). The optimum time of diasotization in ice bath as shown in Fig (4).
The effect of the volume of B-naphthol and Brattan Marschal are studied as shown in Fig (5).
The stoichiometry of the reaction as shown in Fig (6) are 1:1 for Nifedipine and each of B-naphthol and Bratton Marschal reagent.
The Linear relationship obtained for the absorbance of the reaction products versus concentration of the parent drug was in the range of (0.03-0.3) mg % in case of B-naphthol and (0.1-0.5) mg % in case of Brattan marschal.
The graphs were described by the regression equation obtained by the least squares method (14) as presented in table I.
The proposed procedures were applied for the determination of Nifedipine and Coracetin capsules, which were also analyzed by the official method (15), and the results obtained as shown in table II.
Statistical analysis of the results using student T test and variance ratio (F) showed that both values did not exceed the theoretical values, thus demonstrating that there is no significant difference between the two methods table III, IV in accuracy and precision.
The proposed methods have advantage of being more sensitive than the official titrimetric method.



λ max 510 λ max 555

Scheme I

Table 1: Regression Analysis

	Regression equetion	Correlation Coefficient (r)
Method 1	Y = 2.5277x + 0.0181	1.00035
Method 2	Y = 1.1652x + 0.00456	1.0003

Where:

Y = Absorbance
X = Conc mg %

Table 2: Determination of Nifedipine in Nifedipine and Coracetine Capsule using Method 1 & 2

	Nifedipine		Coracetine	
Conc mg %	Conc found	Recovery %	Conc found	Recovery %
0.15	1 0.149 2 0.151	99.33 100.67	0.148 0.152	99.33 101.30
0.312	1 0.309 2 0.318	99.04 101.92	0.310 0.317	99.35 101.60
0.44	1 0.445 2 0.434	101.14 98.64	0.445 0.436	101.14 98.86
Mean	1 $\bar{X}$ 100.90 SD 1.73 RSD 1.71 2 $\bar{X}$ 100.39 SD 1.66 RSD 1.65		$\bar{X}$ 99.95 SD 1.039 RSD 1.04 $\bar{X}$ 100.5 SD 1.51 RSD 1.5	

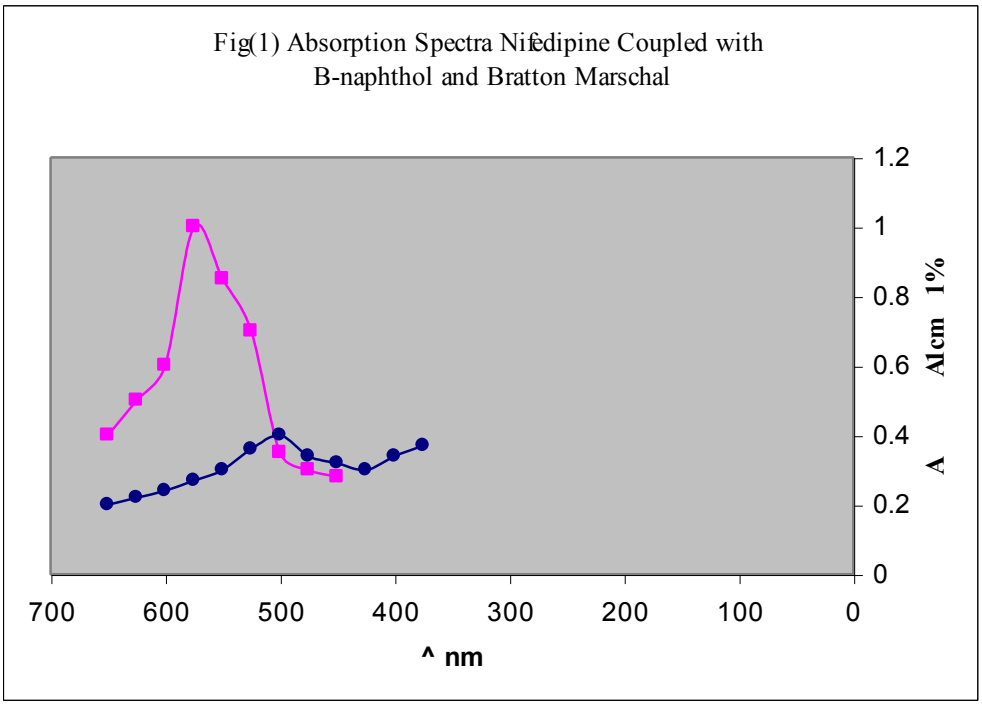
Table 3: Comparison between the proposed method 1 and the Pharmacopoeial method for determination of Nifedipine and Coracetine Capsule

	Nifedipine		Coracetine	
	Proposed 1	Pharm. method	Proposed 1	Pharm. method
N	3	3	3	3
Mean	100.9	99.88	99.95	98.8
SD	1.73	0.937	01.039	1.09
T	0.899	(4.604)	2.4	(4.604)
F ratio	3.41	(49.8)	1.1	(49.8)

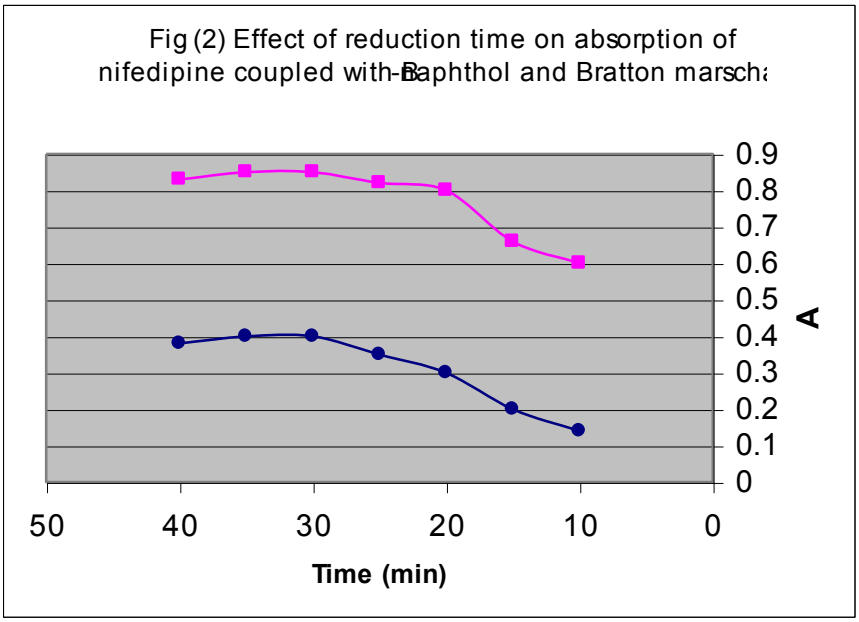
Figures in Parentheses are the theoretical values

Table 4 Comparison between the Proposed method (1) and the Pharmacopoeial method for the determination of Nifedipine and Coracetine Capsule

	Nifedipine		Coracetine	
	Propose 1	Pharm. method	Propose 1	Pharm. method
N	3	3	3	3
Mean	100.39	99.88	100.5	98.8
S.D	1.65	0.937	1.51	1.09
T	0.466	(4.604)	1.58	(4.604)
F ratio	3. 1	(49.8)	1.92	(49.8)



Bratton marschal (●) and B-naphthol (■)



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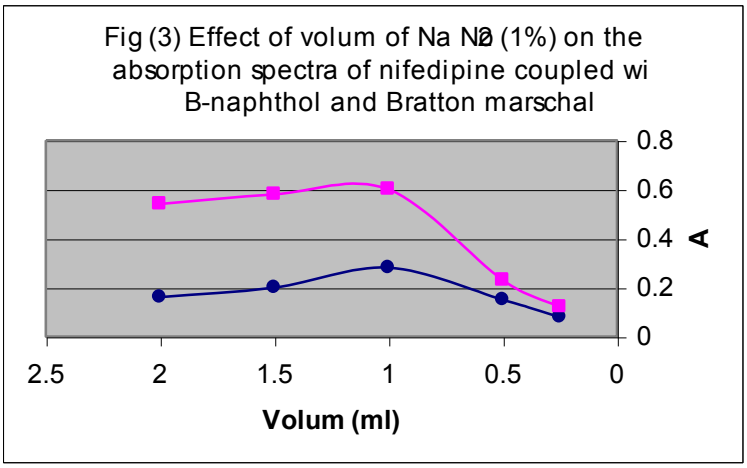

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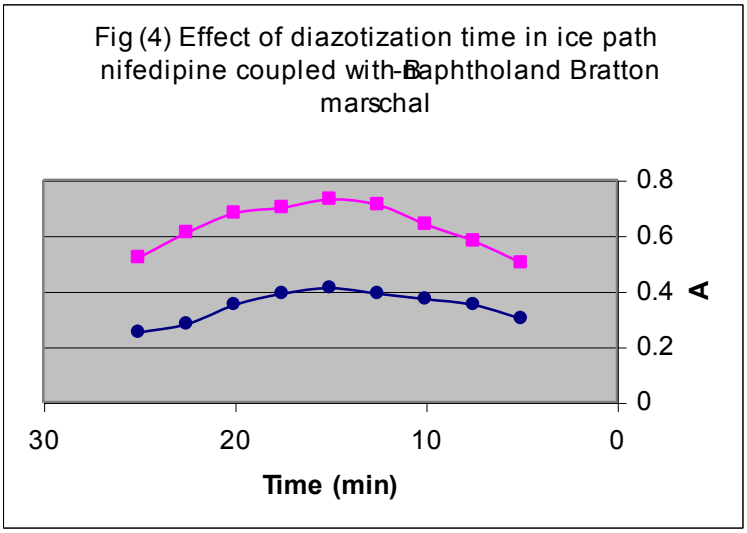

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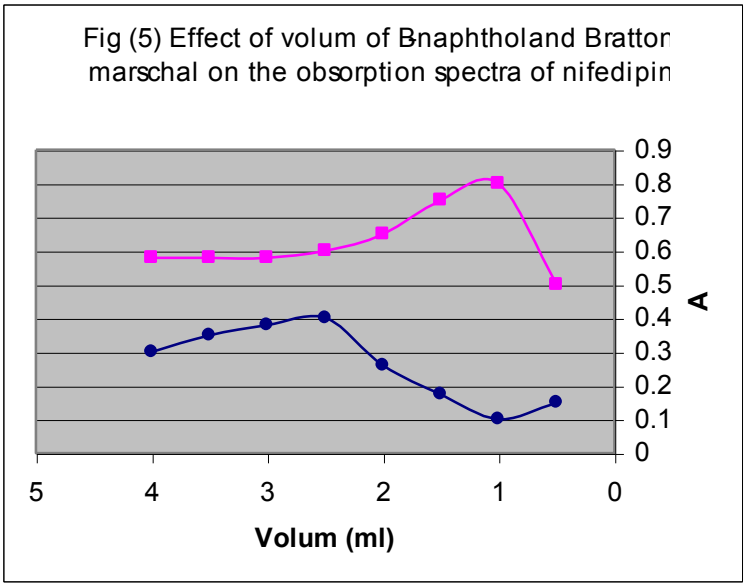
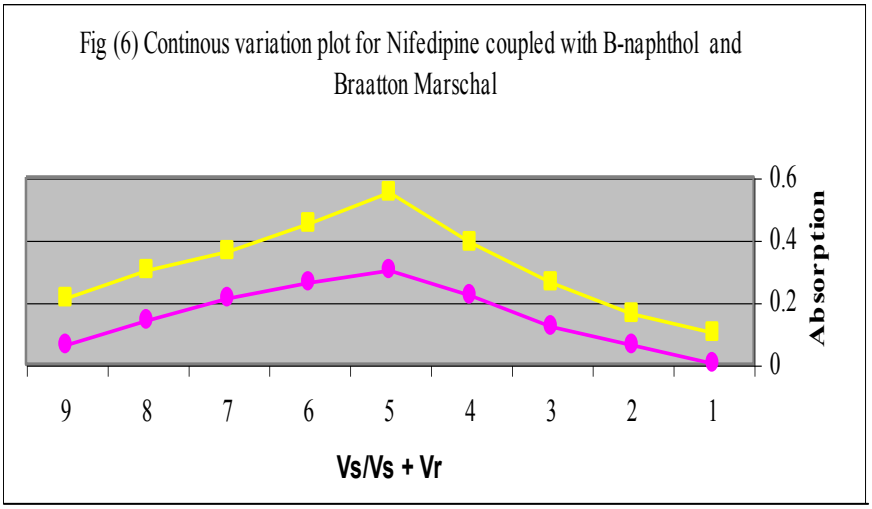


Bratton marschal (●) and B-naphthol (■)



Bratton marschal (●) and B-naphthol (■)

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