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**SIMULTANEOUS DETERMINATION OF  
ATENOLOL AND NITRENDIPINE  
IN PHARMACEUTICAL DOSAGE FORMS  
BY HPTLC**

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**ABSTRACT**

A new simple, precise, accurate, and rapid high performance thin layer chromatography (HPTLC) method has been developed for the simultaneous determination of atenolol and nitrendipine in pharmaceutical dosage forms. The stationary phase was silica gel 60F HPTLC plates and the mobile phase was chloroform-methanol-toluene-25% ammonia (2:2.5:5.5:0.1). Detection and quantification were done densitometrically at 233 nm. The linearity ranges were 4-10  $\mu\text{g}$  and 1.6-4.0  $\mu\text{g}$  per spot and the percentage recoveries were 101.10 % and 98.43 % for atenolol and nitrendipine, respectively.

**INTRODUCTION**

Atenolol (ATN), 4-(2-hydroxy-3-isopropylaminopropoxy) phenylacetamide, is a cardioselective beta blocker with moderate selectivity for beta 1 receptor.<sup>1</sup>

It is used as an adjunct in the early management of acute myocardial infarction and alcohol withdrawal hyperthyroidism. It is official in the IP,<sup>2</sup> BP,<sup>3</sup> and USP.<sup>4</sup> Various methods such as spectrophotometry,<sup>5,6</sup> gas chromatography<sup>7</sup>(GC), high performance liquid chromatography<sup>8,9</sup> (HPLC), and capillary electrophoresis<sup>10</sup> are reported for its determination.

Nitrendipine (NIT), ethyl methyl 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl) pyridine-3, 5-dicarboxylate, is a calcium channel blocking agent.<sup>16</sup> It is used in the treatment of mild to moderate hypertension, both alone and in combination with diuretics or beta-blockers. It is official in the EP<sup>11</sup> supplement 1998. Various methods such as GC,<sup>12</sup> HPLC,<sup>13</sup> and HPTLC<sup>14</sup> are reported for its determination.

Fixed dose combinations containing ATN and NIT are widely available commercially, and an HPLC method for their simultaneous determination has already been reported.<sup>15</sup> However, there is no reported HPTLC method for the simultaneous determination of these two drugs.

In this paper, we report a new HPTLC method for the simultaneous determination of ATN and NIT from pharmaceutical dosage forms which is simple, precise, accurate, and rapid.

## EXPERIMENTAL

### Instrumentation and Layers

A Camag HPTLC system equipped with LINOMAT-IV automatic sample applicator, twin trough chamber, TLC scanner II, and 3.17 V Cats software was used. Merck 60F silica gel HPTLC plates (20 x 10 cm, 0.2 mm thickness) were used as the stationary phase.

### Reagents and Chemicals

Standard ATN was procured from Ariane Orgachem, India. Purity was checked as per BP 1993 and found to be 99.96 %. Standard NIT was procured from USV Limited, India and its purity was checked by EP supplement 1998 and found to be 99.15 %.

Analytical Reagent grade toluene, methanol, ammonia, and chloroform were used, which were supplied by S. D. Fine Chemicals Ltd, India. Tablets containing ATN and NIT were purchased from the market.

**Mobile Phase**

Chloroform-methanol-toluene-25% ammonia (2:2.5:5.5:0.1) was used as mobile phase.

**Standard Solution**

Stock solutions of ATN and NIT were first prepared by dissolving 0.50 gm of ATN in 100.0 mL of methanol (A) and 0.20 gm of NIT in 100.0 mL of methanol (B). A mixture of 6.0 mL each of solution (A) and (B) was diluted to 25.0 mL with methanol and used as the working standard solution for assay of the drugs.

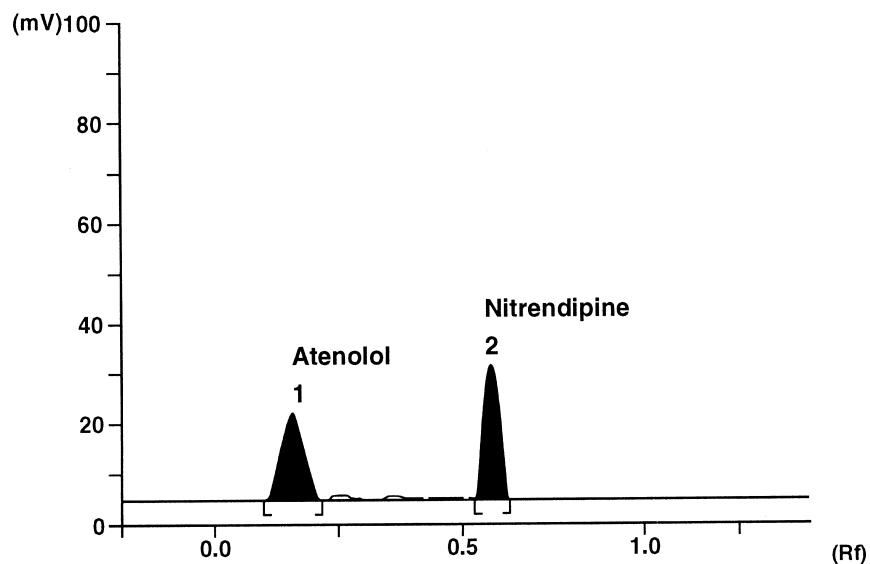
**Procedure for Calibration**

Varying volumes of standard stock solutions of ATN solution (A) and NIT solution (B) were taken in different 25 mL volumetric flasks and diluted to the mark with methanol. Five  $\mu\text{L}$  of each of these solutions was applied on HPTLC plates in 6.0 mm bands with the CAMAG (Muttens, Switzerland) Linomat IV sample applicator. The plates were developed for 50 mm in a CAMAG twin-trough chamber containing the mobile phase. The plates were dried with a hot air blower.

Densitometric evaluation was performed at 233 nm using a deuterium lamp and the scanner described above. Peak areas were recorded for all the tracks. Calibration curves were constructed by plotting peak areas (Y-axis) against the amount of the drug in  $\mu\text{g}$  (X-axis), and the linear relationship was evaluated by calculation of the regression line by the method of least squares.

**Procedure for Assay**

Twenty tablets were weighed and pulverized, and an amount of the powder equivalent to 60.0 mg of ATN and 24.0 mg of NIT was taken in a 25 mL volumetric flask, sonicated for 10 min, and diluted to the mark with methanol. The solution was filtered through Whatman No. 42 filter paper. Five mL of filtrate was further diluted to 10.0 mL with methanol. Five  $\mu\text{L}$  of this filtrate was applied to the HPTLC plate and developed, dried, and scanned. The peak areas were recorded as described in the calibration procedure. The amounts of ATN and NIT were computed by external standard quantification using the relationship:



**Figure 1.** Typical chromatogram of atenolol and nitrendipine.

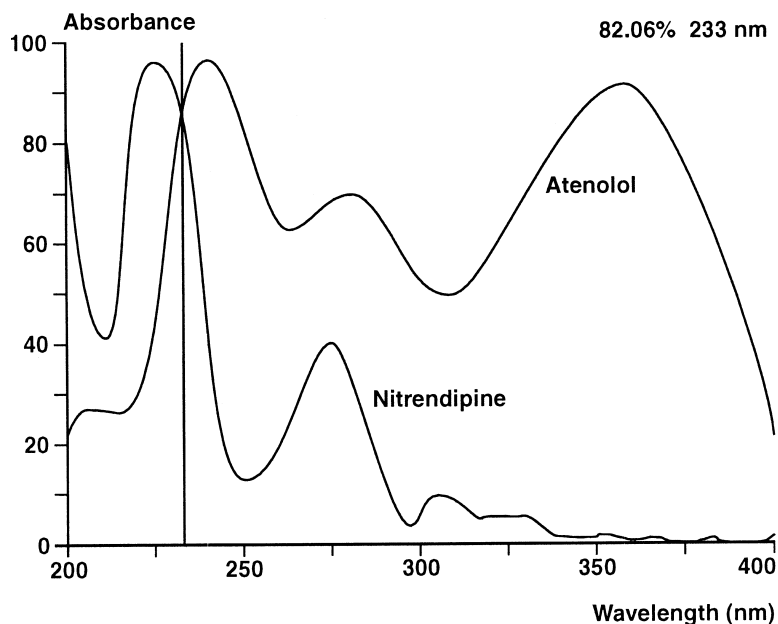
$$W = \frac{A_T \cdot C \cdot D}{A_s \cdot W_a}$$

where  $W$  = amount of the drug (ATN / NIT) per tablet,  
 $W_a$  = amount of the tablet powder taken for analysis,  
 $A_T$  = area of the test sample,  
 $A_s$  = area of the standard,  
 $C$  = concentration of the standard,  
 $D$  = dilution factor.

## RESULTS AND DISCUSSION

### Chromatography

The mobile phase resolved ATN and NIT very efficiently, as shown in Figure 1. The  $R_f$  values were 0.17 and 0.54 for ATN and NIT, respectively. The resolution factor was 6.09 and the tailing factors were 1.0 for both. The wavelength of 233 nm was selected for the densitometric evaluation because there was maximum overlap of the spectra of ATN and NIT shown in Figure 2.



**Figure 2.** Reflectance spectra of atenolol and nitrendipine.

### Linearity, Limit of Detection, and Limit of Quantification

The plot of the peak areas versus the concentrations of ATN and NIT was found to be linear in the range of 4.0 to 10.0  $\mu\text{g}$  and 1.6 to 4.0  $\mu\text{g}$  per spot, respectively.

The calibration curves could be represented by the following linear regression equations:

$$y_{\text{ATN}} = 39.73 x + 134.28 \quad (r = 0.999)$$

$$y_{\text{NIT}} = 73.67 x + 308.72 \quad (r = 0.999)$$

where  $y$  = area,  $x$  = concentration of the drug in  $\mu\text{g}$  / spot. These equations were used for direct evaluation of these drugs.

The limits of detection for ATN and NIT were found to be 0.046  $\mu\text{g}$  ( $S/N = 3$ ) and 0.046  $\mu\text{g}$  ( $S/N = 2.5$ ), respectively. The limits of quantification were 0.140  $\mu\text{g}$  for ATN and 0.140  $\mu\text{g}$  for NIT.

Table 1

## Assay of ATN and NIT in Tablets by HPTLC

Sample	ATN			NIT		
	Label Claim/ Tablet	Amount Found <sup>a</sup> / Tablet	RSD	Label Claim/ Tablet	Amount Found <sup>a</sup> / Tablet	RSD
Tablet Cardif Beta 20 <sup>b</sup>	50 mg	50.03 mg	0.57%	20 mg	20.07 mg	1.13%

<sup>a</sup> Average of seven replicate experiments. <sup>b</sup> Mfg. By Concept Pharma, India; Batch #6003; Mfg. 04/96; Exp. 03/99.

Table 2

## Results of Recovery Analysis

Sample	Drug	Amt. Of	Amt.	%	% RSD	Total
		Std. Drug Added, mg	Recov. mg/tab	Recov. n = 3		
Tablet Cardif Beta 20	ATN	0.00	50.22	---	2.64	101.10
		5.01	55.27	100.80	1.56	
		10.03	60.44	101.90	1.75	
		15.00	65.34	100.50	0.74	
	NIT	0.00	19.86	---	0.96	98.43
		1.50	21.38	99.34	0.92	
		3.02	22.88	99.02	0.57	
		4.43	24.29	96.93	1.40	

## Assay

The content of ATN and NIT found in "Cardif Beta-20" tablets by the proposed method are as shown in Table 1. The label claim was 50 mg of ATN and 20 mg of NIT per tablet. The amounts found by our proposed method were 51.03 mg and 21.07 mg, with RSD 0.57 % and 1.12 %, respectively.

### Accuracy

The accuracy of the proposed method was confirmed by recovery experiments. Three different levels of standards were added to the pre-analysed tablet sample, each level was repeated three times, and the percentage recoveries were calculated. The total mean percentage recoveries of ATN and NIT were 101.10 % and 98.43 %, respectively, as shown in Table 2. These results indicate that the method is accurate and precise and, also, there is no interference due to the excipients present in the brand of tablet.

### CONCLUSION

The proposed HPTLC method is simple, precise, accurate, and rapid for the simultaneous determination of ATN and NIT from tablet dosage forms. Hence, it can be easily and conveniently employed for the routine quality control analysis of these drugs.

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