Simultaneous UV-Spectrophotometric Methods for the Estimation of Atenolol and Nifedipine in solid dosage forms

A. V. KASTURE AND MADHURI RAMTEKE*

Department of Pharmaceutical Sciences, Mahatma Jyotiba Fuley Shaikshanik Parisar, Amravati Road, Nagpur-440 033

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Simple, accurate and precise spectrophotometric methods were developed for simultaneous estimation of atenolol and nifedipine in tablets and capsules using absorption correction method and first order derivative zero-crossing method. In the first method atenolol and nifedipine in methanol had λ max at 276.5 nm and 328.5 nm, showing linearity in the concentration range of 0-30 μg/ml and 0-25 μg/ml, respectively. The absorbance of the mixed standard solutions was measured at 328.5 nm and nifedipine was determined using E (1%,1cm) value. The absorbances of the final dilutions was measured at 276.5 nm and the absorbance by atenolol was corrected at 276.5 nm. The content of atenolol was then calculated using E (1%,1cm) value. In the second method the first derivative spectrum was determined. Atenolol showed zero crossing point at 226.5 nm while nifedipine showed zero crossing point at 235 nm. The dA/dλ was measured at 235 nm for atenolol and 226.5 nm for nifedipine and calibration curves were plotted as dA/dλ versus concentration respectively. Quantitative determination of atenolol and nifedipine in tablets and capsules was carried out using standard calibration curve of atenolol and nifedipine by interpolation method. Results of analysis for both the methods were validated statistically and by recovery studies.

Atenolol[1] is an antihypertensive, antianginal and antiarrhythmic drug and chemically is 4-(2-hydroxy-3-isopropylaminopropoxy)phenylacetamide. Nifedipine[2] is antianginal and antihypertensive and chemically is dimethyl-1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl) pyridine-3, 5-dicarboxylate. The Indian Pharmacopoeia describes non-aqueous titration method for the assay of atenolol and nifedipine. Various methods like gas liquid chromatography[3], reversed phase HPLC[4], UV-spectrophotometry[5-8], HPLC[9] are few methods reported in literature for individual drugs. However, very few methods are reported for simultaneous estimation of these drugs in combination and hence the present work was undertaken.

Spectral and absorbance measurements were made on a Shimadzu UV-1601 (Japan) UV/Vis spectrophotometer with 10 mm matched quartz cuvettes. Gift samples of atenolol and nifedipine were obtained from M/s Torrent Pharmaceuticals Ltd., Indrad. Methanol of analytical grade was used. Two different brands of capsules (Beta-Nicardia, Tinofed) and tablets (Nilol, Nifetolol) each containing 50 mg of atenolol and 20 mg of nifedipine were procured from the local pharmacy.

Standard stock solution of atenolol and nifedipine were prepared separately by dissolving 100 mg of each drug in 100 ml methanol (1 mg/ml). Mixed standard solution was prepared by dissolving 50 mg of atenolol and 20 mg of nifedipine in 100 ml methanol. Further dilutions were made from these stock solutions with methanol.

In the first method, 10 μg/ml solution of each drug was successively scanned from 200 nm to 400 nm range and spectra recorded (fig. 1). The wavelength 276.5 nm (λ max for atenolol) and 328.5 nm (λ max for nifedipine) were selected as analytical wavelengths. Calibration curve for both the drugs was obtained using concentration from 05, 10, 15, 20, 25, 30 μg/ml which was linear and obeyed Beer's law in concentration range of 0-30 μg/ml for atenolol and 0-25 μg/ml for nifedipine. The E (1%,1cm) for both the drugs was calculated at analytical wavelengths. The average absorptivities for both the drugs as 276.5 nm and 328.5 nm

*For correspondence

E-mail: madhuriramteke@rediff.com

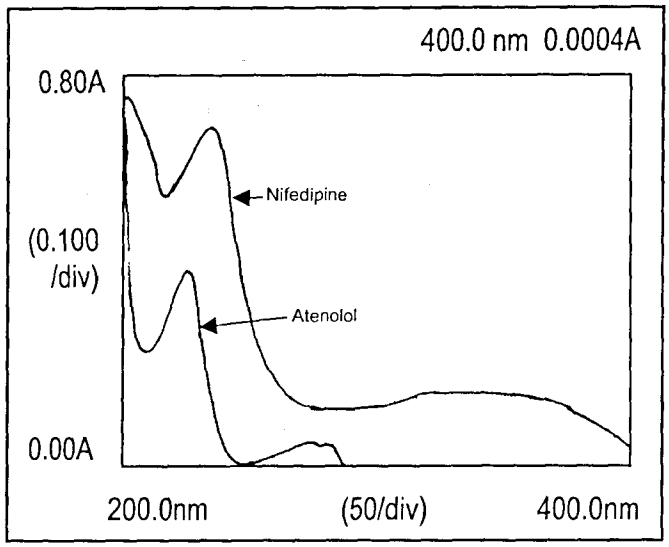

Fig. 1: Overlain spectra of atenolol and nifedipine

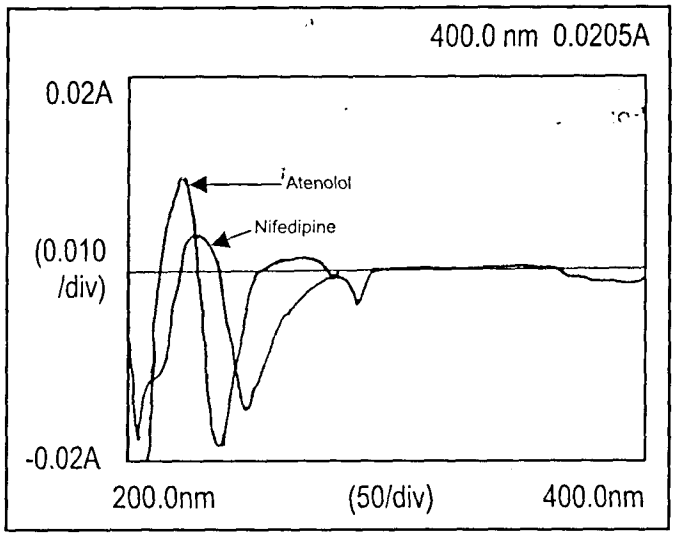

Fig. 2: Overlain spectra of First order derivative – zero crossing of atenolol and nifedipine

was found to be 61.83 and 2.32 for atenolol and 120.20 and 149.64 for nifedipine. The absorbance ratio of nifedipine at 276.5 nm and 328.5 nm was calculated as E (1%,1cm) value for nifedipine at 276.5 nm/E (1%,1cm) value for nifedipine at 328.5 nm and was determined as 0.80.

Various dilutions from the mixed standard solution were prepared and the absorbance of these solutions were measured at 328.5 and nifedipine was determined using E (1%,1cm) value 149.64 at 328.5 nm. The absorbances of the final dilution was measured at 276.5 nm and the absorbance of atenolol was corrected at 276.5 nm by subtracting the product of absorption of mixture at 328.5 nm and absorption factor from the absorbance of mixture at 276.5 nm. The content of atenolol was then calculated using E (1%,1cm).

For analysis of commercial formulations, twenty tablets and capsules of two different brands were weighed. An accurately weighed quantity of powder equivalent to 10 mg of atenolol was transferred to a 100 ml volumetric flask. The contents were dissolved in methanol and the volume was made to 100 ml. The resulting solution was filtered through grade-I filter paper and volume made to 100 ml with methanol. Further dilutions were made and the content of atenolol and nifedipine was determined in the same manner as described earlier. The results of estimation of atenolol and nifedipine in marketed formulation are given in Table 1.

TABLE 1 : RESULTS OF ANALYSIS OF COMMERCIAL FORMULATIONS BY ABSORPTION CORRECTION METHOD

Formulation	Ingredient	Label claim mg/formulation	Amount found mg/formulation	% label claim	±SD	% recovery
Nilol	Atenolol	50	49.86	99.71	0.86	100.07
	Nifedipine	20	19.81	99.03	1.00	99.44
Nifetolol	Atenolol	50	50.17	100.34	0.94	100.13
	Nifedipine	20	19.79	98.83	1.62	99.42
Beta-Nicardia	Atenolol	50	49.98	99.95	0.42	100.19
	Nifedipine	20	19.95	99.77	0.70	99.63
Tinofed	Atenolol	50	50.04	100.07	0.53	100.30
	Nifedipine	20	19.98	99.47	0.55	99.28

TABLE 2 : RESULTS OF ANALYSIS OF COMMERCIAL FORMULATIONS BY FIRST ORDER DERIVATIVE ZERO CROSSING METHOD

Formulation	Ingredient	Label claim mg/formulation	Amount found mg/formulation	% label claim	±SD	% recovery
Nilol	Atenolol	50	49.91	99.82	1.17	99.91
	Nifedipine	20	19.88	99.40	1.50	99.91
Nifetolol	Atenolol	50	50.29	100.59	0.75	100.10
	Nifedipine	20	19.98	99.90	1.56	99.90
Beta-Nicardia	Atenolol	50	50.22	100.47	1.19	100.05
	Nifedipine	20	20.15	100.75	1.05	99.78
Tinofed	Atenolol	50	49.90	99.80	1.18	100.71
	Nifedipine	20	20.02	100.12	1.50	100.62

In the second method atenolol and nifedipine in marketed formulations were estimated by using first order derivative zero crossing method. The standard solutions of atenolol and nifedipine (10 μg/ml) each in methanol were scanned to obtain first derivative spectrum at wavelength interval of 0.1 nm. The overlain spectra was recorded (fig. 2) which showed atenolol had zero crossing point at 226.5 nm while nifedipine showed zero crossing point at 235 nm. At the zero crossing point of atenolol (226.5 nm) nifedipine showed a measurable $dA/d\lambda$ where as at the zero crossing point of nifedipine (235 nm) atenolol showed appreciable $dA/d\lambda$. Hence the wavelengths 226.5 nm and 235 nm were selected as analytical wavelengths for determination of nifedipine and atenolol respectively. Calibration curves for atenolol (0-30 μg/ml) and nifedipine (0-12 μg/ml) were plotted as $dA/d\lambda$ versus concentration. Tablet and capsule solutions were prepared in a way similar to that described in previous method. The derivative absorbances of these solutions were measured at the analytical wavelengths and concentrations of both the drugs was obtained from the standard calibration curves by interpolation method. The results of estimation of atenolol and nifedipine in marketed formulations is shown in Table 2.

To evaluate the validity and reproducibility of the method, known amount of pure drug was added to previously analyzed samples and the samples were reanalyzed by the proposed method. The percentage recovery for method I and II is given in Table 1 and Table 2.

Atenolol and nifedipine in combination is widely used in the treatment of hypertension. Both these drugs have varying solubility in different solvents. However, they are freely soluble in methanol. Using this solvent and adopting spectrophotometer as instrument two methods have been developed. Both methods give reliable and accurate results and hence, can be adopted in routine analysis of this drug combination in marketed formulations.

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