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Pharmaceutical Sciences	Research Article……!!!

DEVELOPMENT OF A UV-SPECTROPHOTOMETRIC METHOD FOR THE SIMULTANEOUS DETERMINATION OF NIFEDIPINE AND ATENOLOL IN COMBINED DOSAGE FORM

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ABSTRACT

Simultaneous estimation of Nifedipine and Atenolol in combined dosage form as well as in laboratory mixture is studied under this paper. Nifedipine and Atenolol are used in combined dosage form for Cardiovascular System Diseases. Hence it is need to develop method to analyse the drugs simultaneously by UV spectrophotometric method. It is studied by simultaneous equation method in marketed dosage form as well as laboratory mixture. The developed method is validated as per ICH guidelines. The stability study of combined dosage form was carried out by using the IR Spectrum of both the drug.

INTRODUCTION

Nifedipine and Atenolol are available in tablet in combined dosage form in ratio 1: 5 ratio. Nifedipine is 1, 4-dihydropyridine derivative used as Ca^{++} channel blocker, antianginal, and coronary vasodilator. Atenolol is β-adrenoceptor antagonist used as hypertensive. Both the drugs are acting on cardiovascular system. Both the drug simultaneously analysed by multicomponent analysis method using simultaneous equation method.

Both the drugs show the absorbance in UV region in the range 200-400 nm. Nifedipine and Atenolol have λmax 341.2 nm and 273.8 nm respectively. Some of the paper shows that Nifedipine & Atenolol can be analysed UV-spectrophotometer. While some of the literature shows that both the drugs are stable in dosage form & studied by HPLC method.

Analytical Chemistry involves separation, identification and determination of the relative amount of the component in a sample matter. Quality is always associated with accuracy and reproducibility; other criteria can be cost, speed and information. Analytical monitoring of pharmaceutical product or of specific ingredients within the product, is necessary to ensure the safety and efficacy throughout the shelf life, including storage, distribution and use.

If a sample contains two absorbing drugs (X and Y) each of which absorb at different λ_{max} of the other, it may be possible to determine both drugs by the technique of simultaneous equations (Vierodt's method)

MATERIALS AND METHOD
A. Drug
Nifedipine and Atenolol suplid bey Cipla & Lupin Pharmaceuticals Pvt. Ltd. Mumbai.
B. Marketed preparation

The brand name of marketed preparation is Nilol, Presolar, Betatrop manufactured by Cipla Pharmaceuticals Pvt. Ltd. Baddi, & Sun pharma Pvt. Ltd. containing Nifidipine 20mg and 50 mg Atenolol.

C. Reagents and chemicals

All reagents and chemicals purchased from Loba chemicals.

1.   Methanol (AR grade)
2.   Water (distilled)

3. Instruments

 A. Spectrophotometer   -   Double beam UV –visible spectrophotometer with 10 mm

 Matched quartz cell

➢ **Model** - UV 1800 PC (Japan)

➢ **Make** - Shimadzu

 B. Analytical balance   -   Shimadzu aw 220

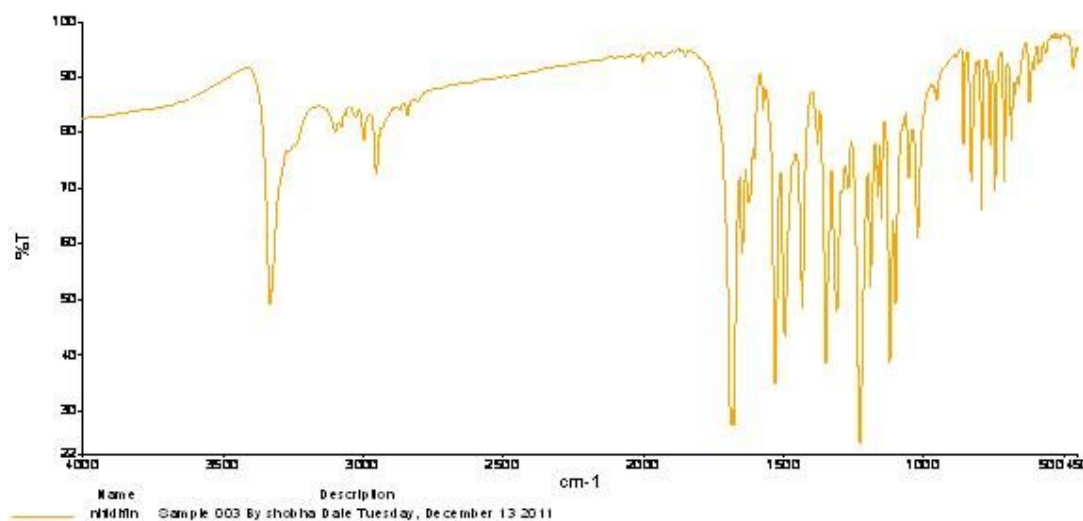 **C. IR** -   PerkinElmer Spectrum 65 FT-IR spectrometer

3. EXPERIMENTAL [3,4]

3.1 Identification of drugs

A. Nifedipine

➢ Melting point –172^{0}C

➢ **IR SPECTRA**

Fig No .1 :- IR Spectra for NIF

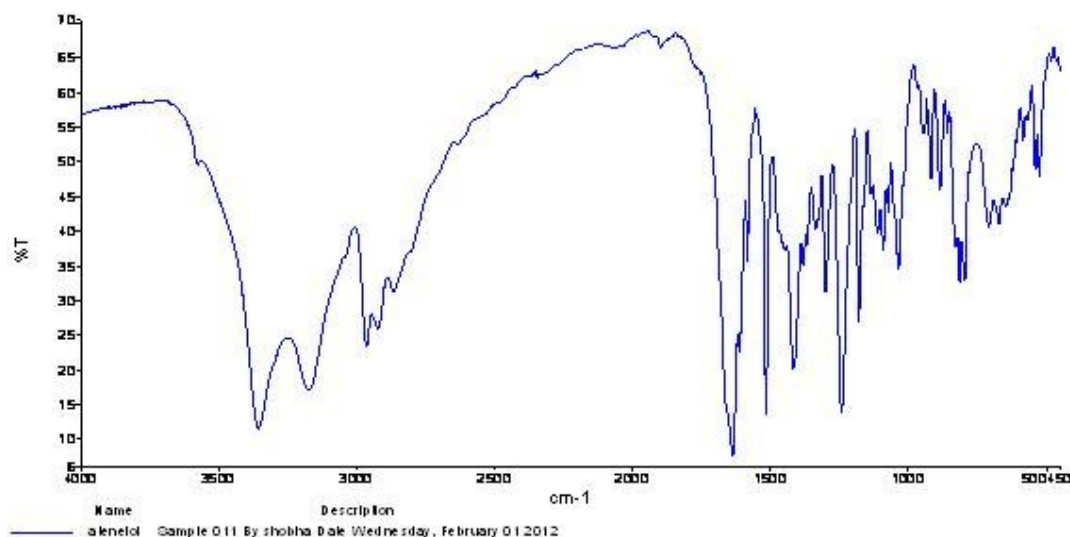### B. Atenolol

➢ Melting point -147 ^{0}C

> ➤ IR SPECTRA

Fig no .2 :- IR Spectra for ATE

4. ESTIMATION OF NIFEDIPINE AND ATENOLOL BY UV-VISIBLE SPECTROSCOPY[5-8]

4.1 Standard solutions:

a) Nifedipine & Atenolol stock solution

An accurately weighed quantity of NIF-ATN equivalent to 100 mg was dissolved separately in 100 ml methanol in 100 ml volumetric flask and volume was made up to 1000 μg/ml.

4.2   Study of spectra and selection of wavelength:

The aliquot portions of stock solutions of NIF and ATN were diluted appropriately with water to obtain concentration 10 μg/mL of each drug. The solutions were scanned in the range of 400-200 nm in 1 cm cell against blank. The overlain UV absorbance spectrum of NIF and ATN is shown in Fig. No.3. From the overlain spectrum the wavelengths selected for estimation of drugs were   341.2 nm as λ_{max} of Nifedipine and 273.8 nm as λ_{max} of Atenolol.
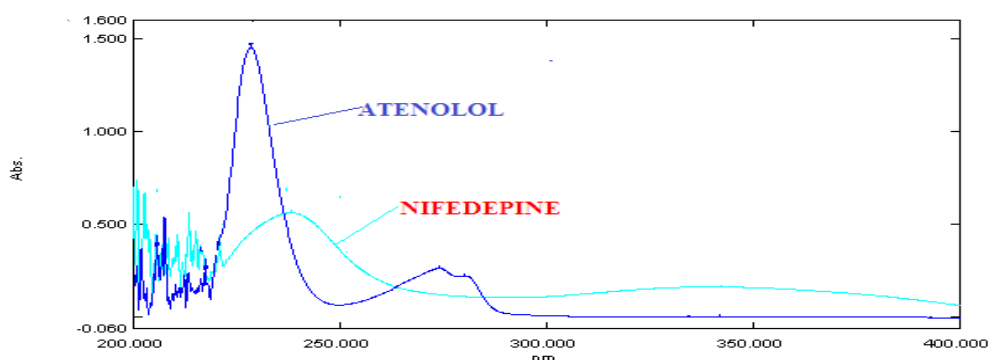

Fig. No.3: Overlain spectra of NIFEDEPINE and ATENOLOL

4.3   Study of Beer-Lamberts law[8]

An aliquot portion of stock solutions of NIF and ATN were diluted appropriately with water to get a series of concentration between 2-10µg/ml for NIF and 5-25µg/ml for ATN. Similarly aliquot portions of stock solutions were mixed (Std. laboratory mixture) and diluted with water to get series of concentration between 2-10 µg/ml and 5-25µg/ml.

The absorbance of each solution was measured at 341.2nm and 273.8nm in 1 cm cell against solvent blank. It was found that it obeys Beer's-Lambert's Law

4.4 Analysis of laboratory mixture by proposed method [7]

In order to see the feasibility of proposed method for simultaneous estimation NIF and ATN in pharmaceutical formulations, the method was first tried for the estimation of the drugs in standard laboratory mixture.

Accurately weighed quantities of NIF 25 mg and ATN 25 mg were taken in 25 ml volumetric flask and dissolved in methanol by vigorous shaking. The volume was made up to the mark with water to get final concentration of about 20 µg/ml NIF and 50 µg/ml ATN. The absorbance of the resulting solutions were measured at 341.2 nm and 273.8 nm in 1 cm cell against blank. Amount of each drug was determined using simultaneous equation as followings

$$Cx = \frac{A2\ ay1 - A1\ ay2}{ax2\ ay1 - ax1\ ay2} \ \text{-------------} \ (1)$$

$$Cx = \frac{A1\ ax1 - A2\ ax2}{ax2\ ay1 - ax1\ ay2} \text{---------------} \ (2)$$

Where,

C_x = Concentration of ATN in µg/mL

C_y = Concentration of NIF in. µg/mL

ax_1 = Absorptivity value of ATE at 273.8 nm.

ax_2 = Absorptivity value of NIF at 341.2 nm.

ay_1 = Absorptivity value of ATN at 273.8 nm.

ay_2 = Absorptivity value of NIF at 341.2 nm.

A_1 = Absorbance of laboratory mixture at 273.8 nm.

A_2 = Absorbance of laboratory mixture at 341.2 nm.

$$\% \text{ Estimation} = \left[\frac{(c \times d)}{w}\right] 100 \text{----------------------- (3)}$$

Where,

C = Cx or Cy = Conc. of ATE or NIF in. µg/mL

D = Dilution factor.

W = Weight of drug either NIF or ATN in laboratory mixture.

Results of estimation of drugs in laboratory mixture are shown in Table No 8.

Table No 1: Result of estimation of NIF and ATN in laboratory mixture

Sr. No	Wt. of pure drug (g)/25ml		Absorbance at		% Estimation*	
	NIF	ATN	34.2 nm	273.8nm	341.2 nm	273.8 nm
1	0.0253	0.0260	0.152	0.133	98.90	100.6
2	0.0258	0.0255	0.158	0.136	100.72	99.00
3	0.0260	0.0253	0.155	0.128	99.2	99.41
				Mean	99.60	99.58
				± S.D.	0.9758	0.9539
				C.V.	0.9797	0.9989

*n = 3

4.4 Analysis of marketed formulation by proposed method[6]

FIVE tablets were accurately weighed and average weight of tablet was calculated. The tablets were reduced to fine powder and mixed thoroughly. A quantity of tablet powder equivalent to 20 mg of NIF was transferred to 25 ml volumetric flask and dissolved in methanol with vigorous shaking and volume was made up to the mark with water. The solution was filtered through Whatman filter paper no. 42. The aliquot portion of filtrate was further diluted to get final concentration of about 20&10 µg/mL NIF and 50&25 µg/mL ATN. The absorbance of sample solution was measured at 341.2 nm and 273.8 nm in 1 cm cell against blank. The content of NIF and ATN in tablet was calculated using the following formula No. 19.

$$\% \text{ Label Claim} = \left[\frac{Cx \text{ or } Cy \times d \times W}{Wm \times d} \right] 100 \text{ ------------(4)}$$

Where,

Cx or Cy = Conc. of ATE or NIF in μg/ml.

W   = Average weight of tablet

Wm   = Weight of sample taken.

L   = Labeled claim of sample take

Results of estimation of drugs in tablet are shown in Table No 2.

Table No 2: Result of estimation of NIF and ATN in tablet formulation

Sr. No.	Wt. of tablet powder (g/25ml)	Absorbance at		% Label claim*	
		341.2 nm	273.8 nm	NIF	ATN
1	0.226	0.158	0.235	99.20	100.90
2	0.235	0.168	0.239	100.72	99.30
3	0.230	0.160	0.230	99.30	101.08
			Mean	99.74	100.42
			± S.D.	0.8502	0.9997
			C.V.	0.8556	0.9797

   *n = 3

4.5 % Estimation Marketed formulation result

From evoluation of assay we can done % estimation of drug in various marketed formulation Or brands which contain the NIF & ATE drug combination**.**

Results of estimation of drugs in various brands are shown in Table No. 3

Table No.3: Result of estimation of Marketed formulation formulation

Tablet	Drug	Label Claim (mg/capsule)	Estimated Amount (mg/tablet)	% Label Claim	% RSD
1. Nilol	nifedipine	20	20.15	100.75	1.075
	Atenolol	50	49.22	98.44	0.6821
2. Betanicardiya	nifedipine	20	19.18	97.99	0.6981
	Atenolol	50	51.21	102.00	1.234
3.presolor(cap)	nifedipine	20	20.55	102.75	1.675
	Atenolol	50	50.77	101.54	0.987

*n=3

5. RESULTS AND DISCUSSION

An attempt has been made to develop a fast, sensitive, precise, reproducible and economical analytical method for simultaneous estimation of NIFEDIPINE and ATENOLOL in their combined dosage form. NIF & ATE has estimated at 341.2nm& 273.8nm in the solution of methanol. In this method drugs obey Beer's law in the concentration range of 2-10 μg/ml. For NIF&5 -25 μg/ml.

The values of SD or RSD are within the prescribed limit of 2 %, showing high precision of the method, as shown in Table No. 2 & 3 During the linearity study it was observed that absorbance values of NIF and ATE in the marketed formulation were linear in the range of 80 % to 120 % of the test concentration with R2 close to one for this method of analysis.

CONCLUSION

The proposed method is simple for simultaneous analysis of nifedipine and atenolol in combined formulation. Two sampling wavelength 341.2nm and 273.8nm were used for analysis of NIF and ATE. The proposed method of analysis was validated by analyzing the laboratory prepared samples. The results were satisfactory.

The mean recovery was 99.5% for NIF and 101.66% for ATE respectively. The sample recoveries in all formulations were in good agreement with their respective label claims without interference of excipient and the other additives. The results confirm that proposed method is simple, accurate, precise, economical and efficient. It can be directly and easily applied to the analysis of the combined pharmaceutical tablet Formulation of NIF and ATE.

The present method is quick and cost effective as compared to chromatographic techniques. Therefore, it can be concluded that the proposed method provides an alternative procedure for the quality control of NIF and ATE in pharmaceutical formulations.

FUTURE SCOPE

Nifedipine and Atenolol, is a combination recommended as antianganal. This can be estimated by the technique like HPTLC. Nifedipine and Atenolol can be further estimated by HPLC method by changing the mobile phase composition. Comparative estimation of different brands can be conducted. The method can be developed for estimation of the proposed drugs in bio-fluids. Nifedipine and Atenolol can be further estimated by UV method by changing the solvent & different method selection

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