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DIRECT DETERMINATION OF ANTAZOLINE AND NAPHAZOLINE IN MIXTURES

S. O. Othman
Research and Development Department
Dar Al-Dawa Development and Investment Co.,
Na'ur - Jordan.

ABSTRACT

The simultaneous determination of antazoline sulphate and naphazoline nitrate in nasal and ophthalmic mixtures was achieved using a direct and simple spectrophotomtric method. The absorbance of a suitable dilution of the mixture was read at two wavelengths, viz. 271 and 281 nm and the concentration of each in the mixture was calculated by solving for two simultaneous equations. The choice of wavelengths was such that antazoline shows weak absorption while naphazoline exhibits maximal absorption. The method proved to be simple and rapid with a good degree of reproducibility.

INTRODUCTION

Antazoline and naphazoline are commonly used in nasal and ophthalmic solutions in concentrations of 0.50% (w/v) and 0.025% (w/v) respectively, for the local relief of nasal and occular allergies.

Both antazoline and naphazoline are basic substances having pKa values of 10.0 and 10.4 respectively, and are therefore, officially analysed by non-aqueous titrimetric methods[1,2]. They have also been determined spectrophotometrically by charge transfer complex formation with iodine[3-5]. Furthermore, other methods of analysis have been employed for their determination. Antazoline was determined by a colour development reaction in biological fluids[6], and naphazoline was quantitatively assayed in pharmaceutical mixtures by an anticircular TLC method[7].

In combination, antazoline and naphazoline can be determined colourimetrically, since they exhibit colour reactions with nitric acid and formaldehyde/sulphuric acid, respectively[8]. However, these methods are both tedious and time consuming. Quantitative HPLC determination of combinations of antihistamines and decongestant drugs including antazoline and naphazoline was carried out by Koziol et al.[9] in solid and liquid dosage forms using ion-pair chromatography.

In this study, a direct and simple spectrophotometric method for the simultaneous determination of both antazoline

and naphazoline was used eventhough both substances have overlapping UV absorption spectra. The method is based on measurement of absorbance at two wavelengths and the subsequent calculation of the concentrations of the two components in the mixture by solving for two simultaneous equations.

EXPERIMENTAL

Materials:

Antazoline sulphate and naphazoline nitrate were obtained from Chemische Fabrik Schweizerhall, Basel. The water used was double distilled in glass apparatus.

Standard Solutions:

Antazoline Sulphate: An accurately weighed amount of around 50 mg was dissolved and made up to 50 ml with distilled water and 20 ml of this solution was further diluted to 100 ml with distilled water.

Naphazoline Nitrate: Around 50 mg were accurately weighed into a 100 ml volumetric flask and made up to mark with distilled water. 2 ml were then diluted to 100 ml with water.

Sample Preparation:

The procedure involved no prior preparation or separation and only a twenty five-time dilution of the drops was made with distilled water.

Absorbance Measurements:

These were obtained using a UV-Visible Beckman DU7 spectrophotometer (Beckman Instruments Inc.,Irvine, Calif. 92713). The appropriate dilutions were measured in a 1-cm cell at 271 and 281 nm against a water blank.

Calculations:

The concentrations of antazoline sulphate and naphazoline nitrate in the unknown mixture were calculated using the equations:

$$A^{271} = E_A^{271} C_A d + E_N^{271} C_N d \quad \text{.....(1)}$$

$$A^{281} = E_A^{281} C_A d + E_A^{281} C_N d \quad \text{.....(2)}$$

where, A^{271} and A^{281}: Absorbance of the mixture at 271 and 281 nm, respectively.

E_A^{271} and E_A^{281}: Extinction coefficient of antazoline sulphate at 271 and 281 nm, respectively.

E_N^{271} and E_N^{281}: Extinction coefficient of naphazoline nitrate at 271 and 281 nm, respectively.

C_A and C_N: Concentrations of antazoline sulphate and naphazoline nitrate in the unknown mixture.

Substituting for C_N in equation 1 and C_A in equation 2, and rearranging:

$$C_A = \frac{E_N^{271} A^{281} - E_N^{281} A^{271}}{E_N^{271} E_A^{281} - E_N^{281} E_A^{271}} \quad \text{-------} \quad (3)$$

$$C_N = \frac{E_A^{271} A^{281} - E_A^{281} A^{271}}{E_A^{271} E_N^{281} - E_A^{281} E_N^{271}} \qquad \text{-------} \quad (4)$$

RESULTS AND DISCUSSION

The values of the extinction coefficients (E 1%, 1cm) for both antazoline sulphate and naphazoline nitrate were obtained at 271 and 281 nm using standard solution having concentrations comparable to those of the diluted sample solution (Table 1). The extinction coefficient values obtained for naphazoline nitrate were close to those quoted in the literature [10] (E^{271} = 215; E^{281} = 250), however, antazoline sulphate does not exhibit maxima at these wavelengths but shows absorption peaks at 241 and 291 nm (Figures 1 and 2)

TABLE 1

The Extinction Coefficients (E 1%, 1 cm) of Antazoline Sulphate and Naphazoline Nitrate.

Substance	$E^{271} \pm$ S.D.	$E^{281} \pm$ S.D.
Antazoline Sulphate	54.8 ± 0.03	51.1 ± 0.04
Naphazoline Nitrate	214 ± 1.10	247 ± 0.90

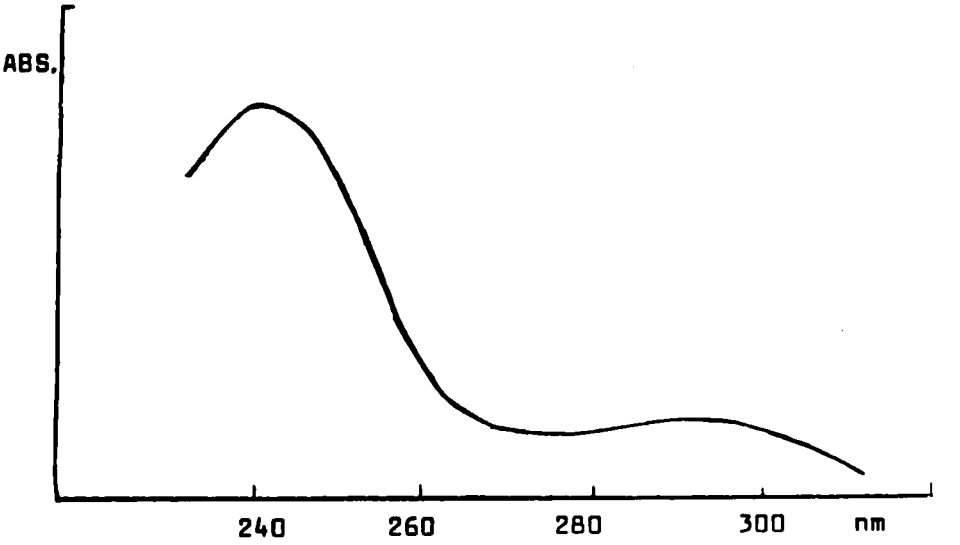

FIGURE 1

UV Absorption Spectrum of Antazoline Sulphate.

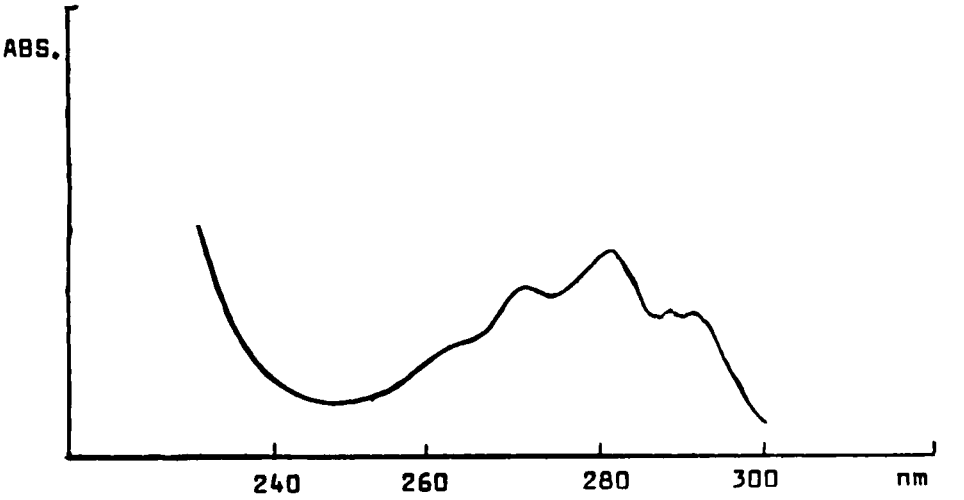

FIGURE 2

UV Absorption Spectrum of Naphazoline Nitrate

Since both substances contribute to the total absorption of the mixture at both wavelengths selected, therefore, measurements of absorbance at the two wavelengths will result in two equations that can be solved simultaneously to calculate the unknown concentrations in the mixture. However, in order for this method to be applied, the absorption of both substances has to be additive at both wavelengths. This was confirmed by taking the absorbance measurements of a mixed standard solution of the two substances. The mixed standard was prepared by diluting 20 ml and 2 ml of the concentrated stock solutions of antazoline and naphazoline, respectively, to 100 ml with distilled water.

The reproducibility of the results in the analysis of both antazoline and naphazoline is depicted in Table 2. Both determinations showed good reproducibility, however, the calculated concentrations of naphazoline were consistently lower than the theoretical value.

The absorption spectra of both substances in water depicted in Figures 1 and 2 show two maxima for antazoline sulphate at 241 and 291 nm and four maxima at 271, 281, 288 and 291 nm for naphazoline nitrate. The greatest absorptivity exhibited by naphazoline was observed at 271 and 281 nm. Since antazoline is generally present in much higher concentrations than naphazoline in pharmaceutical mixtures (0.50% and 0.025%, respectively), therefore, the choice of wavelengths used in this method was

TABLE 2

The Reproducibility of the Calculated Concentrations of Antazoline Sulphate and Naphazoline Nitrate.

Sample	Conc. of Antazoline (% w/v)	Conc. of Naphazoline (% w/v)
1	0.509	0.0241
2	0.513	0.0230
3	0.490	0.0239
4	0.486	0.0245
5	0.521	0.0236
6	0.489	0.0238
7	0.516	0.0243
8	0.487	0.0251
9	0.492	0.0238
Mean =	0.500	Mean = 0.0240
S. D. =	$\pm$ 0.20 x 10^{-3}	S.D.= 0.035 x 10^{-5}

such that antazoline shows weak absorption while naphazoline exhibits maximal absorption.

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