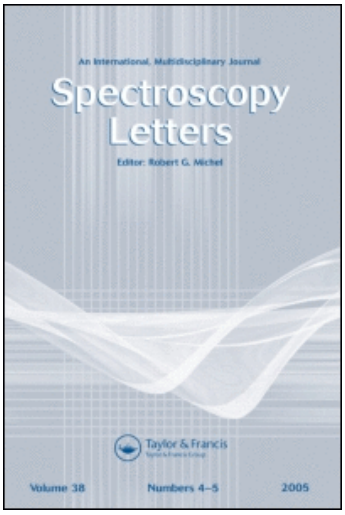

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Spectrofluorimetric Determination of Carazolol and Its Pharmaceutical Formulation

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SPECTROFLUORIMETRIC DETERMINATION OF CARAZOLOL AND ITS PHARMACEUTICAL FORMULATION

Key Words: Spectrofluorimetry, Carazolol Spectrofluorimetric analysis.

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Abstract:

A new spectrofluorimetric method is developed for the assay of carazolol and its pharmaceutical formulation at room temperature. The method is simple, rapid, accurate and sensitive enough for the quantitative determination of carazolol in nanomolar concentrations. Furthermore the proposed method helps in the identification of the drug. The procedure involves establishment of the calibration curve and comparison of the fluorescence intensity of standard alcoholic solution of carazolol to that of the unknown sample under identical conditions and with reference to the linear part of the curve. The maximum wavelengths employed for excitation and emission were 285 nm and 344 nm respectively.

A critical examination of the U.V-Spectrum of carazolol indicates that the fluorescence inner filter effect is negligible below 3.0×10^{-6} M concentrations. The results of spectrofluorimetric determination for carazolol tablets (Conductor(R)) show percentage of recovery 98.8 ± 1.1.

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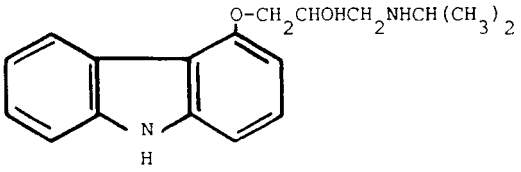
Introduction:

Carazolol, 1-(carbazol-4-yloxy)3-(isopropyl-amino)-2-propanol, is a new adrenergic β-blocker which has the following structural formula:



The analysis of the drug has not been reported in recent literatures. However, the manufacturer's method of assay for carazolol (1) is performed by high-pressure liquid-chromatography (HPLC) technique which has also been employed to determine the drug in its dosage form.

The spectrofluorimetric method proposed in this study is specific, sensitive, quick, simple and accurate for the assay of carazolol and in its dosage forms.

Experimental:

The fluorescence spectrophotometer used in this study was model MPF-44B manufactured by Perkin-Elmer, Norwalk, Connecticut, U.S.A. A Perkin-Elmer X-Y recorder Model 056 was attached to the instrument. Minimum gain control setting was adopted to nullify the effect of noise.

Materials and Methods:

Materials:

Authentic carazolol sample (Batch No. 02-770-508076) and cara-

zolol tablets (Conducton(R)) were kindly donated by KLINGE PHARMA GmbH & CO. (WEST GERMANY). Ethanol (96% v/v) used as a solvent was the product of Riedel-De Haen AG, Seelze, Hannover, West Germany.

Procedure:

(i) Establishment of the Calibration Curve:

Dissolve about 30 mg of pure carazolol accurately weighed in about 25 ml ethanol; transfer quantitatively into 100 ml volumetric flask and complete up to the mark. From this stock solution prepare by serial dilution a series of standard solutions ranging between 1×10^{-8} M to 1.5×10^{-7} M. Set the fluorescence spectrophotometer to zero using ethanol as solvent blank and record the fluorescence intensity of each solution as peaks on a chart paper using wavelength 285 nm for excitation and 344 nm for emission. Plot the fluorescence intensity as peak heights in millimeters versus concentration and ascertain the linear part of the calibration curve.

(ii) For Carazolol Tablets (Conducton(R)):

Weigh accurately twenty tablets and calculate the average weight of tablet. Pulverize the tablets and weigh accurately an aliquot portion of powder containing about 5 mg of carazolol. Transfer quantitatively to 100 ml volumetric flask, add 80 ml ethanol and shake for about 15 min. Adjust to volume using ethanol, centrifuge for few minutes at 3000 r.p.m. Pippette an aliquot portion from the clear solution to produce (by serial dilution) an alcoholic solution of carazolol of

about 1.0×10^{-7} M concentration. The percentage of carazolol in tablet may be determined as follows:

Percentage of carazolol in tablet

$$= \frac{F_t}{F_s} \times 100$$, where F_t and F_s are the fluorescence intensity readings for the alcohlic extract of carazolol powdered tablets and the authentic drug respectively both measured under identical conditions and the fluorescence intensity readings are kept within the linear part of the calibration curve.

(iii) Calculations:

The calculations are based on the fundamental fluorescence equation (2,3)

$$F = I_o \ (1-10^{-Ecb}) \ \phi$$, where

F = Total fluorescence intensity

I_o = Intensity of exciting light

c = Concentration of fluorescent compound

b = Optical path length

E = Molecular extinction coefficent of the fluorescent compound.

ϕ = Quantum efficiency of solution.

From the relation

$$10^{-Ebc} = e^{-2.303\ Ebc}$$

$$= \frac{1-(2.303\ Ebc)}{1!} + \frac{(2.303\ Ebc)^2}{2!} + \ldots\ldots + , \text{ and}$$

substituting in the first two terms, and neglecting higher terms when c is extremely small, the fluorescence equation becomes

$$F = I_{\cdot} (2.303\ Ebc)_{\cdot} \phi.$$

Thus under certain experimental conditions there will be linear relationship between fluorescence intensity and concentration provided that the inner filter effect (or Ebc) does not exceed 0.05.

Results and Discussion:

The structural formula of carazolol being that of carbazole ring system suggests the possibility of fluorescence activity. Fluorescence may result from $\Pi^* \rightarrow \Pi$ and / or $\Pi^* \rightarrow n$ transitions since both of these electronic transions exist in the chromophoric groups of carazolol structure. Examination of the UV-spectrum (Fig. 1) of carazolol in ethanol indicates wavelength maxima at 220 nm, 240 nm, 285 nm and 330 nm.

Since the excitation spectrum is similar to that of absorption, any of the wavelengths of maximum absorption may be used as a wavelength of excitation for the study of fluorescence intensity. However, irradiation of matter by light of short wavelength is likely to destroy the molecule. It was therefore decided to use radiation of either 285 nm or 330 nm wavelenght. Both wavelengths were tried but the results at 285 nm were more consistent. The uncorrected emission spectrum of carazolol at the excitation wavelength 285 nm is shown in Fig. 2.

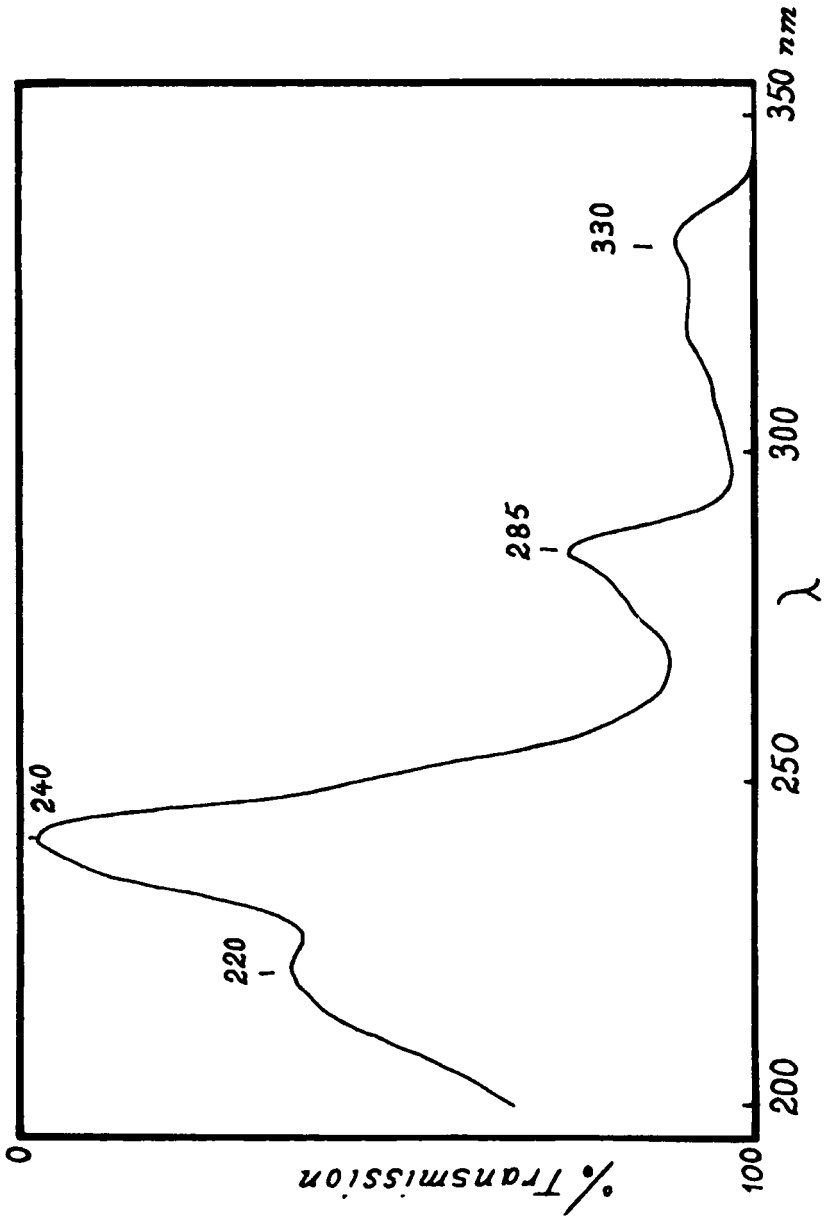


Fig. 1 U.V. Spectrum of Carazolol in ethanol.

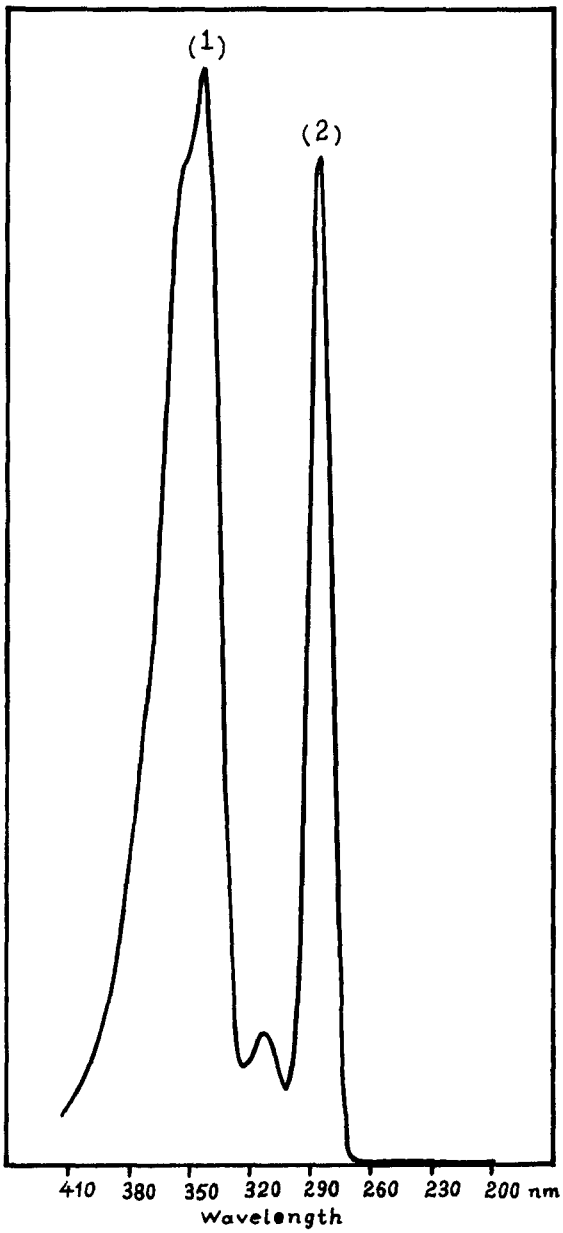


Fig. (2) Uncorrected Emission Spectrum of carazolol in ethanol.
(1) Emission peak (2) Scattered Light peak.

In this study care was taken to control the factors that affect the fluorescence of the compound, such as, solvent temperature, concentration and existence of quenching agents. Preliminary studies using n-hexane, ethanol and 0.1 N - HCl as solvents revealed maximum emission at 340 nm, 344 nm and 354 nm respectively. This is consistent with the observed fact in spectrofluorimetric studies that the bathochromic shift increases as the polarity of the solvent increases. To check against interferences of excipients in tablets, the UV-spectrum and the emission spectrum were run for the alcoholic extract of the powdered tablets. These spectra were found identical to those of authentic carazolol.

The plot of peak heights in millimeters versus concentration of carazolol in shown in Fig. 3. It can be seen that the linear relationship between fluorescence intensity and concentration holds in the range of 1.0×10^{-8} M to 1.5×10^{-7} M.

The percent recoveries when the proposed method is adopted for the assay of authentic carazolol and its tablets (Conducton$^{(R)}$) are shown in Table 1. These results, in addition to those of spiking experiments, demonstrated good precision and accuracy.

The proposed spectrofluorimetric method compares well with the manufacturer's method with respect to sensitivity, accuracy, specificity and simplicity. The proposed method may be used to estimate the level of carazolol in biological fluids.

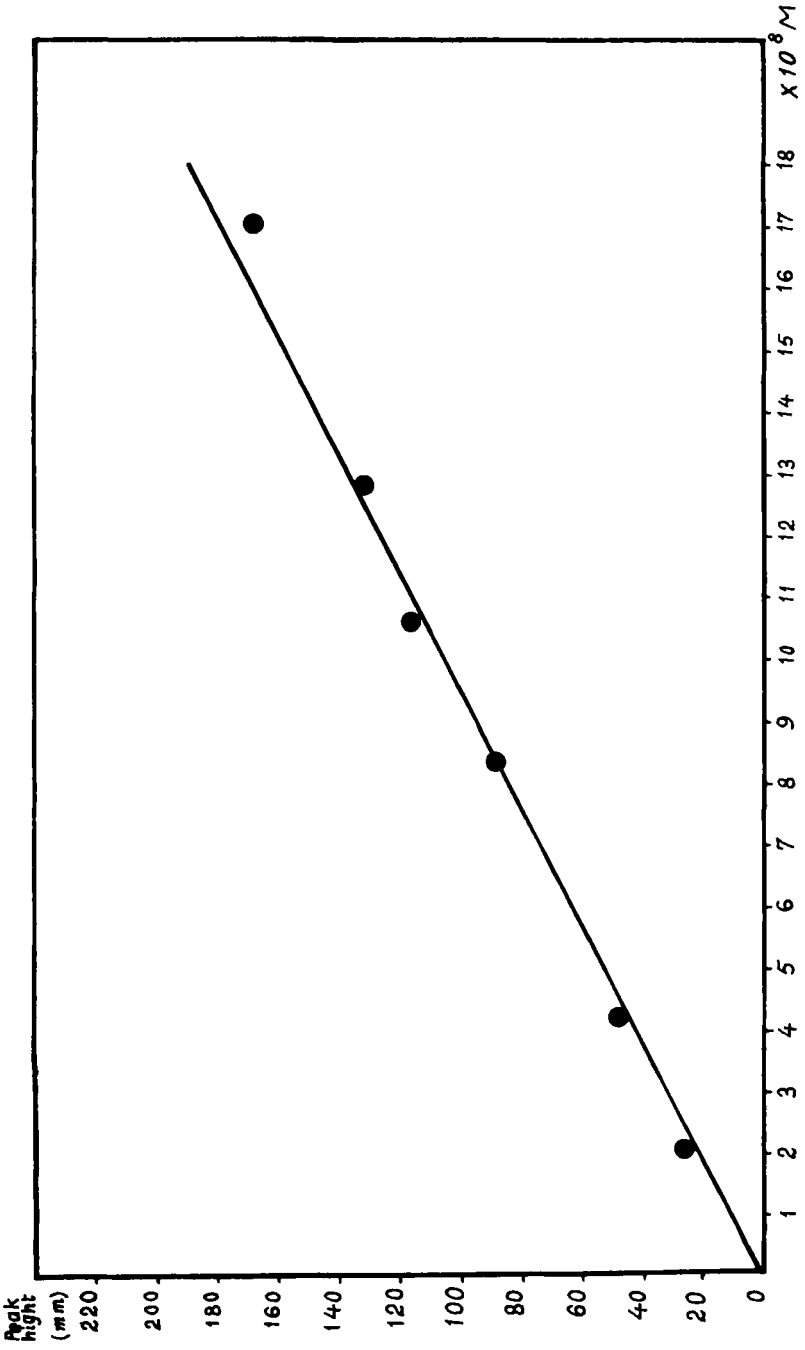


Fig. 3 Flourescence intensity versus concentration of carazolol in ethanol. Minimum gain control setting was adopted.

Table 1. Spectrofluorimetric Determination of Carazolol.

Compound	Amount Taken (mg)	Amount of Authentic Added (mg)	Percentage of Recovery*
Authentic carazolol.	30**	--	99.4 ± 0.8
Carazolol tablets (Conducton(R))	5***	--	98.9 ± 1.1
		5	99.2 ± 0.9

* The figure stands for a mean of six runs and standard deviation.

** Thirty milligrams were initially accurately weighed and standard solutions in the range of 1. x 10^{-8} M to 1.5 x 10^{-7} M concentraions were prepared.

*** Amount of powdered tablets containing 5 mg of carazolol was accurately weighed.

Acknowlegement:

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