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Spectrofluorimetric determination of fendiline in tablets

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A simple, sensitive and accurate spectrofluorimetric method was developed for the assay of fendiline in tablets. Validation of the method provided good results concerning linearity, precision and accuracy. The linearity range was found to be 0.1–0.8 mg/l. The fluorescence intensity was measured at 288 nm for fendiline tablet solutions. It was also found that the excipients in the commercial tablets did not interfere with the method.

Fendiline (*N*-[1-phenylethyl]-3,3-diphenylpropylamine hydrochloride, trade name: Sensit®) is a calcium-channel blocker proposed as anti-arrhythmic and anti-anginal agent (Bayer and Mannhold 1987). Fendiline has previously been analyzed using various methods including GC (Lohmann and Diekmann 1991), HPLC (Hermansson and Grahn 1995), capillary zone electrophoresis (Lin et al. 1998), and capillary isotachophoresis (Buzinkaiova et al. 2001). The enantiomeric HPLC separation using a chiral α_1-acid glycoprotein stationary phase with UV detection has been reported (Hermansson and Grahn 1995). Fendiline is not yet included in internationally recognized pharmacopoeias, though various dosage forms containing fendiline are available on the market.

In this paper, a micellar-enhanced spectrofluorimetric method for the determination of fendiline was developed. The method was applied to the determination of fendiline in a pharmaceutical preparation. Fendiline is a compound with a significant native fluorescence although its emission properties are not clearly described. Thus in aqueous or acidic solution, it exhibits a fluorescence emission with wavelength of maximum emission intensity at 288 nm (excitation at 210 nm). The addition of sodium hydroxide or sodium chloride to an aqueous solution of fendiline shifts the fluorescent excitation to 222 nm together with a decrease in the fluorescence emission intensity at 288 nm.

In order to obtain better analytical characteristics for the

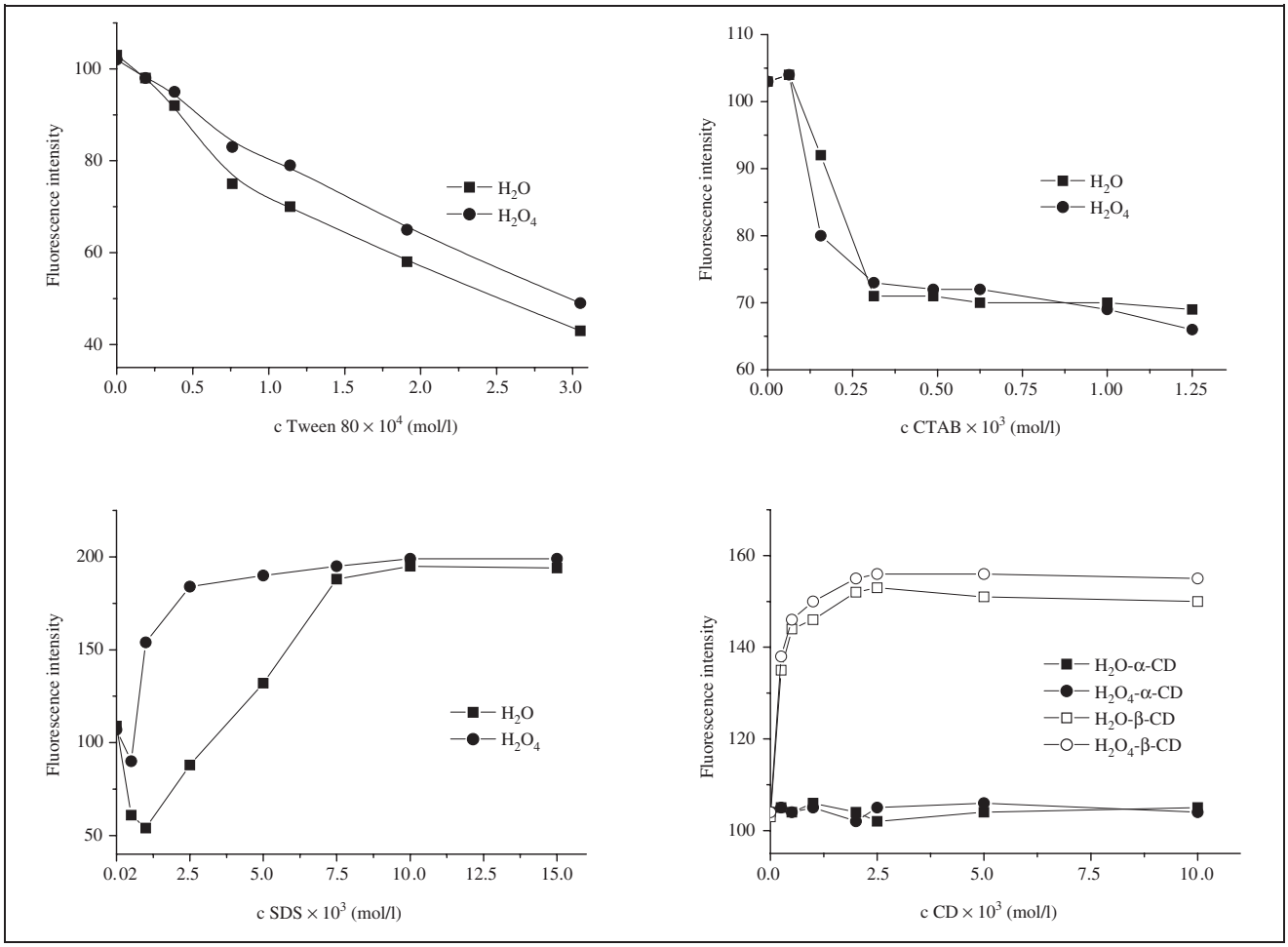

Fig.: Influence of Tween 80, hexadecyltrimethylammonium bromide (CTAB), sodium dodecylsulfate (SDS), α-cyclodextrin (α-CD) and β-cyclodextrin (β-CD) concentration on the fluorescence intensity of fendiline in water and sulfuric acid solutions. Fendiline 0.2 mg/l

Table: Linearity, precision and recovery of the analytical procedure for fendiline

Parameter/Medium	Water	0.1 mol/l H_2SO_4	0.015 mol/l SDS	0.015 mol/l SDS − 0.1 mol/l H_2SO_4
Linearity (mg/l)	0.1–0.8	0.1–0.8	0.1–0.8	0.1–0.8
Intercept, $a \pm SD_a$*	-4 ± 5	1 ± 5	3 ± 5	3 ± 4
Slope, $b \pm SD_b$**	537 ± 11	528 ± 11	855 ± 11	859 ± 11
Coefficient of determination, r^2	0.9988	0.9990	0.9995	0.9999
Precision, RSD (%)	0.3	0.2	0.3	0.2
Recovery, mean ± RSD (%)	100.0 ± 0.6	100.0 ± 0.5	99.5 ± 0.8	99.9 ± 0.3

* SD_a – standard deviation of intercept, ** SD_b – standard deviation of slope

determination of fendiline, the fluorescence behavior of fendiline in aqueous and acidic micellar systems of non-ionic surfactant (Tween 80) and ionic surfactants (CTAB and SDS) were investigated. In addition, the fluorescence properties of fendiline were obtained in aqueous and acidic solutions with and without α- and β-cyclodextrins (Fig.). There were an enhancement in the fluorescence intensity of the investigated analyte with SDS and β-cyclodextrin as compared with the results obtained in aqueous/acidic medium under identical instrument adjustments. CTAB additions shift the fluorescent excitation to 218 nm together with a decrease in the emission intensity at 288 nm. Addition of Tween 80 caused only a decrease in emission intensity at 288 nm.

Since the fluorescence emission from the analyte was found greatly enhanced by SDS, this medium was selected. The calibration graphs for fendiline in aqueous and acidic solutions in the absence and in the presence of SDS were obtained by plotting the relative fluorescence intensities versus the analyte concentration (seven calibration solutions used, each of calibration solution was measured in triplicate). The calibration plot was found to be linear in the range 0.1–0.8 mg/l (Table). Precision was determined by assaying six individual samples of Sensit® tablets (50 mg of fendiline per tablet) and it has been expressed as the relative standard deviation (RSD). The accuracy has been determined by the standard addition technique by analyzing six samples of Sensit® (50 mg of fendiline per tablet) spiked with a known amount of analyte (50 mg) and six replicates of original non-spiked samples. The mean recovery of the added analyte was calculated. The spectrofluorimetric method provided satisfactory precision and accuracy for the analysis of fendiline (Table). The RSDs were found to be 0.2% in aqueous and 0.3% in aqueous sulfuric acid media. The recovery was found to be between 99.5 and 100.0%. It was also found that the excipients in the commercial tablets did not interfere with the method. The use of SDS micellar system provides a simple means to enhance the fluorescence from fendiline. Its applicability was evaluated by the analysis of fendiline in pharmaceutical preparation. The statistical calculations for the assay results show good precision of the method with no significant difference between the declared coutent and experimental data.

Experimental

1. Apparatus

All fluorescence measurements were done on a Perkin-Elmer LS 50 Luminescence spectrometer equipped with a xenon discharge lamp (equivalent to 20 kW for 8 μs duration) and 1 × 1 cm quartz cell. The LS 50 spectrometer was interfaced with an Epson PC AX2 microcomputer supplied with FL Data Manager Software (Perkin-Elmer) for spectral acquisition and subsequent manipulation of spectra. The fluorescence emission spectra were obtained at an excitation wavelength of 210 nm (218 nm for CTAB). The fluorescence excitation spectra were obtained at an emission wavelength of 288 nm. The slits of the monochromators were both set at 5.0 nm.

2. Chemicals

Fendiline hydrochloride (Thiemann Arzneimittel, Germany) standard was prepared in water at a concentration of 100 mg/l and stored at 4 °C.
α-Cyclodextrin (α-CD) (Merck), β-cyclodextrin (β-CD) (Merck), Tween 80 (Merck), sodium dodecylsulfate (SDS) (Fluka), hexadecyltrimethylammonium bromide (CTAB) (Fluka). These chemicals were dissolved in water or aqueous solution of sulfuric acid.

3. Sample preparation

Sensit® tablets containing 50, 75, 100 mg of fendiline per tablet were analyzed. In all cases it was assumed that the actual content of the tablet corresponds to that reported by the manufacturing laboratories.
Ten tablets were weighed, pulverized, and an amount of the powder, equivalent to 50 mg of fendiline, was transferred into a beaker. The analyte was extracted by treating the sample with water and stirring the mixture for 30 min. Thereafter the suspension was transferred into a 250.0 ml volumetric flask and made up with water to 250.0 ml volume. The suspension was filtered through a membrane filter, an aliquot (20 μl) of the filtrate was mixed with 5.0 ml of medium (water, 0.1 mol/l sulfuric acid, 0.015 mol/l SDS in water, 0.015 mol/l SDS in 0.1 mol/l sulfuric acid) and the fluorescence spectra were recorded.

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