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Polarographic Determination of Fluvoxamine Maleate in Tablets

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The differential pulse polarographic (DPP) method was developed for the determination of fluvoxamine maleate (I). At pH = 3. 7, (I) give a peak at - 0. 73 V in aqueous solution. The developed method was applied to the assay of the drug substance in commercial tablet formulations. The results were statistically compared with those obtained by reference methods (HPLC and direct current polarographic method) using t- and F- tests at 95 % confidence level.

Key Words: Fluvoxamine maleate, differential pulse polarography, determination, tablets.

1. Introduction

Fluvoxamine (Fig. 1) is a selective serotonin reuptake inhibitor used in the treatment of a variety of depressed states[1]. For the determination of fluvoxamine and fluvoxamine maleate in dosage forms, various analytical techniques including HPLC[2−5], fluorimetry[6] UV- Visible spectrophotometry[4] and DC[7] are used. Fluvoxamine with its oxime ether group has a structural feature that could be used for electrochemical reduction[8]. This study describes a new differential pulse (DP) polarographic method for quantitative analysis of (I) in tablets.

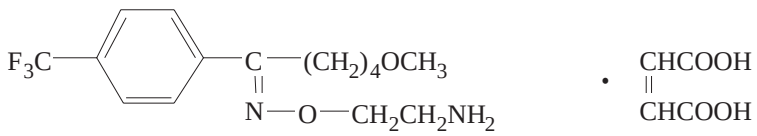

Figure 1. Fluvoxamine Maleate

2. Experimental

2.1. Materials

Pharmaceutica-grade fluvoxamine maleate (Bilsan) was used as received. HPLC-grade Acetonitrile and other analytical grade chemicals were purchased from E. Merck. Milli Q water was used.

2.2. Apparatus

Metrohm Herisau Polarograph E 506 polarecord VA 526 in conjunction with the following three electrodes system. Working electrode: static mercury dropping electrode (SMDE), reference electrode: Ag/AgCl (3 M KCl), auxiliary electrode: glassy carbon rod. The HPLC system consisted of the component a C_{18} 10 μm Bondapak column (300 x 3.9 mm i.d) a model 510 solvent delivery system and a model 481 model variable wavelength spectrophotometer was from Waters.

2.3. Solutions

A stock solution of (I) (1 mg ml^{-1}) was prepared with Britton - Robinson (BR) buffer solution (pH = 7.4). Standard solutions were obtained by diluting the stock solution with 0.1 M acetate buffer solution (pH = 3.7).

2.4. Procedure

A stock solution of fluvoxamine maleate (1 mg ml^{-1}) in Britton - Robinson buffer solution pH = 7.4 was prepared. An aliquout of this solution (0.5 2.5 ml) was diluted to 25 ml with buffer solution of selected pH (mostly an 0.1 M acetate buffer solution pH = 3.7 was used as the supporting electrolyte). DP polarograms were recorded after deaeration with N_2 for ten minutes.

2.5. Sample Preparation

Twenty tablets were weighed and powdered. An accurately weighed portion of the powder equivalent to approximately 250 mg of (I) was transferred into a 50 ml volumetric flask using 20-25 ml BP buffer solution (pH = 7.4). The mixture was shaken for 30 min and diluted to the volume with BR buffer solution. After filtration, 1.5 ml of the filtrate was transferred into a 25 ml volumetric flask and diluted to the volume with 0.1 M acetate buffer solution (pH = 3.7). The quantity of I in the tablets was calculated using the regression equation of the calibration curve.

2.6. Results and Discussion

For the recording of the best polarogram, the type of extraction solvent, buffer solution and polarographic conditions were investigated. The polarographic reduction of fluvoxamine base was carried out in 0.1 N HCl, acetate buffer solution and Britton Robinson buffer solutions as supporting electrolytes in the pH range between 1.0 and 9.0. At each pH in the range between 1.1 and 6.0 a well-defined peak appeared; at higher pH it was difficult to measure the peak as the polarograms were undefined. In a previous paper (7) it was reported that surprisingly fluvoxamine maleate, which consist s of a polarographic cation and anion, exhibited in acidic medium only one well defined polarogram. At pH = 1. 0 the substance was not

stable in solution, due to hydrolysis of fluvoxamine. The isolation of the precipitate formed yielded a white, crystalline powder melting between 42.5 and 44 °C. At pH = 3.7 reproducible were obtained in 10 h, so that the oxime ether group of fluvoxamine is stable enough under these conditions for electrochemical reduction. The method involves the extraction of (I) from tablets with BR buffer solution, approriate dilution with acetate buffer solution and recording of DP polarograms between - 0.4 and 1.4 volts. E_{peak} was observed at 0.73 V v.s Ag / AgCl (3 M KCl) (Fig. 2)

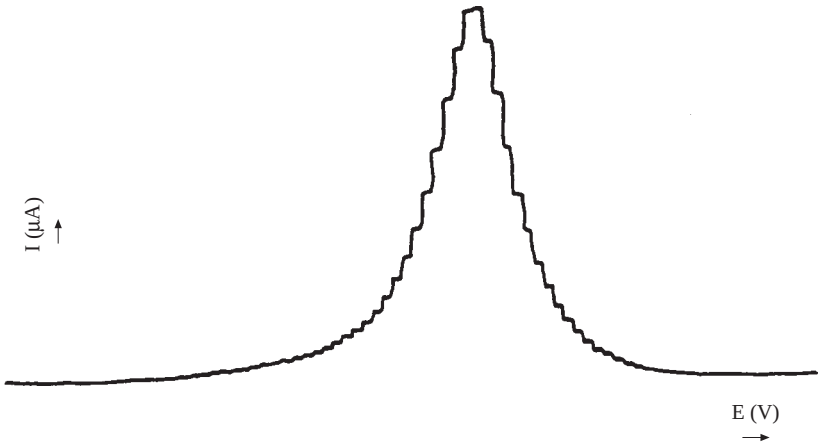

Figure 2. Polarographic peak of fluvoxamine maleate (c = 60 μg ml^{-1}) at pH = 3.7, U_{start}= -0.4V Polarographic conditions are V_{start} = - 0.4 V, ΔU = - 1.0 V, mm / t_{drop}= 2.0, t_{drop} = 1.0 s and pulse amplitude = 50 mV.

Five different DP polarograms were recorded using the stock solution of (I) in BP buffer solution (0.5 2.5 ml) was diluted to 25 ml with 0.1 M acetate buffer solution. A calibration graph was plotted between ipeak and drug concentration (c). A linear relation was obtained between fluvoxamine maleate amounts (c) (20 - 100 μg ml^{-1}). As seen Fig. 3 the regression equation of the calibration curve was calculated as

I_{peak} = 4 x 10^{-3} c + 0.02 (r = 0.9997) (i_{peak}: μA, c: μA, c: μg ml^{-1})

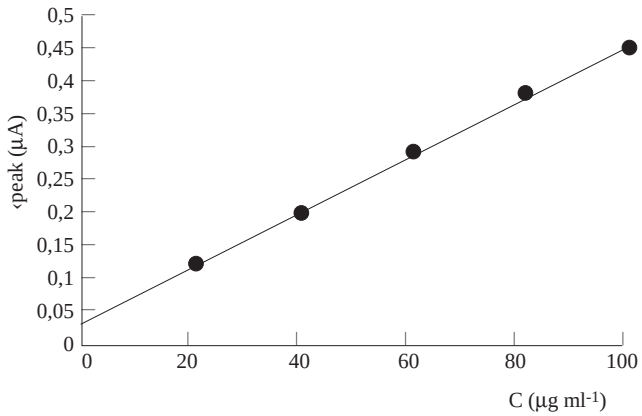

Figure 3. Calibration Curve

Commercially available tablets containing (I) were analysed by the developed DPP method, direct current (DC) polarographic method (7) and reference HPLC method (4) for comparison. The methods were compared statistically with each other and the HPLC method of reference. There was no significant difference between the mean values and precisions of the two methods at the 95 % confidence level (Table 1). Thus none of the excipients commonly employed in the tablet dosage form of fluvoxamine maleate (for instance mannitol, maize starch, talcum and polyvidone) were found to interfere with the assay of the drug (5).

Table 1. Analysis of Fluvoxamine Maleate in Tablets (Labelled to contain 50 mg of fluvoxamine maleate per tablet).

Methods	DPP (a)	DCP (b)	HPLC (c)
Mean $\pm$ t. s / $\sqrt{n}$	99.7 $\pm$ 0.55	99.5 $\pm$ 0.72	100.4 $\pm$ 0.76
t-test of significance*	$T_{a,b} = 0.50$		
	$t_{a,c} = 1.50$		
	$t_{b,c} = 1.75$		
F- test of significance*	$F_{a,b} = 1.73$		
	$F_{a,c}= 1.90$		
	$F_{b,c}= 1.10$		

*t = 2. 23; F = 5.05 for p = 0.05 and $n_1 = n_2 = 6$

In conclusion, the developed methods do not require expensive reagents and present new alternatives for the rapid and precise determination of fluvoxamine maleate. Detection limits were 5 μg ml^1, 20 μg ml^1, 5 μg ml^1 for the DCP, DPP and HPLC methods respectively. The method developed is more sensitive than DCP methods. It is easier to measure I_{peak} values than $I_{diffusion}$ values. It can be applied for quality control testing.

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