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Spectrophotometric determination of fluoxetine and sertraline using chloranil, 2, 3 dichloro-5, 6 dicyano benzoquinone and iodine

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Abstract

Spectrophotometric procedures are presented for the determination of two commonly used antidepressant drugs, fluoxetine (I) and sertraline hydrochloride (II). The methods are based mainly on charge transfer complexation reaction of these drugs with either π acceptors chloranil and 2, 3 dichloro-5, 6-dicyanoquinone (DDQ) or σ acceptor iodine. The colored products are quantified spectrophotometrically at 550, 450 and 263 nm for fluoxetine and at 450, 455 and 290 nm for sertraline in chloranil, DDQ and iodine methods, respectively. The molar combining ratio and the optimum assay conditions were studied. The methods determine the cited drugs in concentration ranges of 80–640, 16–112 and 7.5–60 μg/ml with mean percentage recoveries of 99.83, 99.76 and 100.00% and R.S.D. of 1.24, 0.95 and 1.13% in fluoxetine and ranges of 16–160, 15–105 and 6–48 μg/ml with mean percentage recoveries of 100.39, 99.78 and 99.69% and R.S.D. of 1.02, 0.81 and 0.57% in sertraline for chloranil, DDQ and iodine methods, respectively. A more detailed investigation of the complex formed was made with respect to its composition, association constant K_c^{AD}, molar absorptivity ξ_A^{AD} and free energy change ΔG. The proposed methods were applied successfully to the determination of the cited drugs either in pure or dosage forms with good accuracy and precision. The results were compared statistically with those given by the reported methods.

Keywords: Spectrophotometric determination; Fluoxetine; Sertraline; Chloranil; 2, 3 Dichloro-5, 6 dicyano benzoquinone; Iodine

1. Introduction

Fluoxetine and sertraline are selective serotonin reuptake inhibitors which are clinically effective for the treatment of depression. The drugs are chemically known as (±)-*N*-methyl-3-phenyl-3-[α,α,α,-trifluoro-*p*-tolyl) oxy] propylamine hydrochloride [1] and (1*S*,4*S*)-4 [3, 4 dichlorophenyl]-1, 2, 3, 4 tetrahydro-*N*-methyl-1-naphthylamine hydrochloride [2].

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Several methods have been reported for the determination of fluoxetine (I) in biological fluids and pharmaceutical formulations including HPLC [3–10], GC [10–14], fluorescence polarization immunoassay [15] and NMR [16].

Sertraline hydrochloride (II) has been determined in biological fluids and dosage forms by GC mass [17–20], GC [21] and HPLC [22–25].

A favorable characteristic of the proposed procedure is the speed, selectivity and ease of performing the assay. Searching the published methods for the determination of the cited drugs shows that the colorimetric techniques have not been previously applied; consequently the present work describes new colorimetric methods which are cheaper than the published NMR [16] and chromatographic methods for fluoxetine [3–10] and for sertraline [17–25]. Hence the proposed methods are more suitable for routine control analysis in developing countries.

This paper describes the application of the reaction with π and σ acceptors chloranil, DDQ and iodine to the spectrophotometric determination of (I) and (II) in pure and dosage forms.

2. Experimental

2.1. Instrument

A Shimadzu-160 UV/VIS spectrophotometer was used.

2.2. Samples

2.2.1. Fluoxetine hydrochloride

This working standard was kindly supplied by El-Lilly company. Its purity was found to be $99.29 \pm 0.90\%$ according to the reported method [26].

2.2.2. Sertraline hydrochloride

This working standard was kindly supplied by Pfizer Cairo, Egypt. Its purity was found to be $100.12 \pm 0.42\%$ according to the reported method (HPLC manufacturer procedure supplied by Pfizer, pers. commun.).

2.3. Market samples

2.3.1. Prozac capsules (El-Lilly), batch No. 8196A

Each capsule was claimed to contain 20.00 mg fluoxetine hydrochloride, 205.64 mg starch flowable powder and 2.00 mg dimethicone.

2.3.2. Lustral tablets (Pfizer), batch No. 272A23

Each tablet was claimed to contain 100.00 mg sertraline hydrochloride, 48 mg calcium hydrogen phosphate, 89.85 mg microcrystalline cellulose, 9.00 mg hydroxy propyl cellulose, 37.50 mg sodium starch glycolate and 3.75 mg magnesium stearate.

2.4. Reagents and chemicals

All reagents and chemicals used were of analytical grade and the solvents were spectroscopic grade.

1. Chloranil (Aldrich), 0.2% w/v solution in acetone;
2. DDQ (Aldrich), 0.2% w/v solution in acetone;
3. Iodine (El Nasr Pharmaceutical Chemical Co.), 0.0125% and 0.025% w/v solution in dichloroethane for fluoxetine and sertraline, respectively.

2.5. Standard solutions

2.5.1. Stock standard solutions for chloranil and DDQ methods

The standard solutions are stable for at least 1 week when stored in a refrigerator.

Solutions of fluoxetine (I) and sertraline (II) base (0.2% w/v) were prepared as follows: Dissolve an accurately weighed amount of (I) or (II) equivalent to 200 mg of fluoxetine or sertraline base in 20 ml distilled water. Transfer each solution quantitatively into a 125-ml separating funnel, render alkaline with ammonia solution and extract with 4×20 ml chloroform. Wash the extract with 20 ml water, filter through anhydrous sodium sulphate into a 100-ml volumetric flask and make up to volume using chloroform (2 mg/ml).

2.5.2. Working standard solutions

1. For chloranil method: Evaporate 25 ml or 5 ml of the stock solution of fluoxetine or sertraline respectively, and dissolve in 10 ml acetone. Transfer quantitatively into a 25-ml volumetric flask and make up to volume with the same solvent (2 mg/ml of fluoxetine and 0.4 mg/ml of sertraline).
2. For DDQ method: Evaporate 10 ml of stock solution of each drug, dissolve in 25 ml acetone, transfer quantitatively into a 50-ml volumetric flask and make up to volume with the same solvent (0.4 mg/ml for both drugs).

2.5.3. Standard solutions for iodine method

The standard solutions are stable for at least 1 week when stored in a refrigerator.

Solutions (0.03 and 0.06% w/v) of (I) and (II) base in dichloroethane were prepared as follows: Dissolve an accurately weighed amount of (I) and (II) equivalent to 30 or 60 mg of fluoxetine and sertraline base, respectively, in 20 ml water, transfer quantitatively into a 125-ml separating funnel and proceed as under Section 2.5.1 (starting at "render alkaline…") (0.3, 0.6 mg/ml for fluoxetine and sertraline base, respectively).

2.6. Test solutions

2.6.1. For chloranil and DDQ method

An accurately weighed amount of the finely powdered tablets or capsules equivalent to 100 mg of the drug base (I) or (II) was transferred into a 125-ml separating funnel containing 30 ml water and rendered alkaline with ammonia. Extract the drug base as under Section 2.5.1. Prepare working test solution of the same concentration as that mentioned under working standard solutions.

2.6.2. For iodine method

Proceed as mentioned under Section 2.5.3 using aliquots of finely powdered tablets or capsules equivalent to 30 or 60 mg of (I) or (II) base, respectively.

2.7. Procedures

2.7.1. Construction of calibration curves

Calibration curves were constructed according to the optimum conditions mentioned in Table 1 as follows: Into separate 10-ml volumetric flasks, transfer different aliquots of working standard solutions; to each flask, add the specified amount of reagent and in the case of the chloranil and DDQ method leave to stand at the chosen temperature for the optimum time.

Make up to volume using the mentioned solvent and measure the absorbances against the reagent blank at the corresponding λ_{max}.

2.7.2. For dosage forms

Proceed as described under Section 2.7.1 using different aliquots of the test solutions of fluoxetine and sertraline previously mentioned under Section 2.6.

3. Results and discussion

3.1. Chloranil method

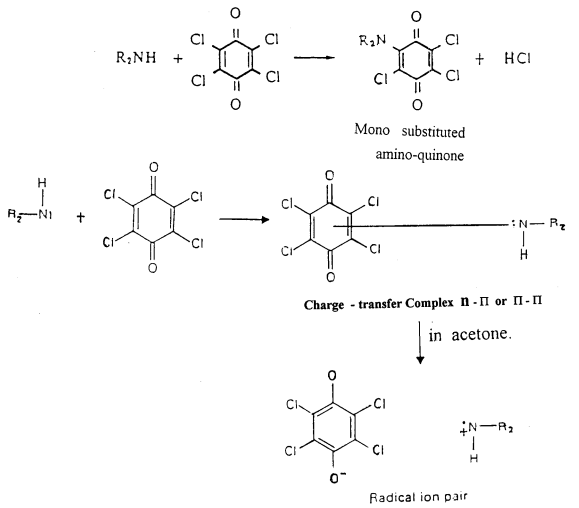
σ and π acceptors react with the basic nitrogenous compounds as n-donors to form charge transfer complexes or radical anions according to the polarity of the solvent used. Hence chloranil, DDQ and iodine used in the proposed methods are selective reagents for the determination of the cited drugs.

Some hydrochloride salts of amines do not react with π or σ acceptors. In the case of chloranil, adding hydrochloric acid to the purple solutions will turn them light yellow (the colour of unreacted p-chloranil). The procedure of neutralizing an amine–HCl with sodium hydroxide or sodium carbonate should not be used because sodium hydroxide itself reacts with p-chloranil to form a blue compound [27]. To determine amine–HCl, it is necessary to first neutralize the hydrochloride and then extract the amine into a non-aqueous solvent. Ibrahim et al. [28] suggested extracting the neutralized amine into chloroform and then evaporating chloroform.

Table 1
Optimum conditions used in the proposed methods

Parameter	Proposed methods					
	Fluoxetine			Sertraline		
	Chloranil	DDQ	Iodine	Chloranil	DDQ	Iodine
Amount of standard taken (mg)	0.8–6.4	0.16–1.12	0.075–0.6	0.16–1.6	0.15–1.05	0.06–0.48
Amount of reagent (ml)	4	3	5	3	1	4
Solvent used	Acetone	Acetone	Dichloroethane	Acetone	Acetone	Dichloroethane
Heating temperature	Heat at 70°C for 30 min	Ambient temperature for 10 min	Ambient temperature	Heat at 70°C for 50 min	Ambient temperature for 10 min	Ambient temperature
λ_{max} (nm)	550	455	263	450	455	290
Stability of the colored product (min)	120	60	20	120	60	20

p sp = 0.5 > 20



Scheme 1.

Chloranil has two types of reactions either by the formation of mono substituted amino-quinones [29] or by the formation of radical ion pairs [30] as shown in Scheme 1.

On studying the absorption curves for the reaction product of fluoxetine with chloranil it was found that the UV–visible spectra are very similar to the UV–visible spectra of mono substituted amino-quinones [31] (absorbance at 550 and 350 nm) (Fig. 1), while in the case of sertraline the absorption spectra of the reaction product is similar to the radical ion pair [32]. The chloranil

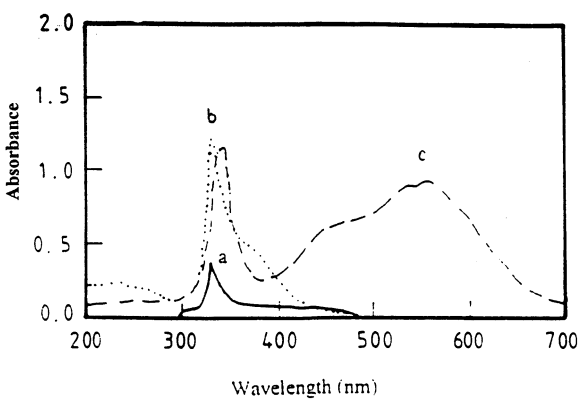


Fig. 1. Absorption spectra of (a) fluoxetine (30 μg/ml) in acetone; (b) chloranil (0.2% w/v) in acetone; (c) fluoxetine (458.5 μg/ml)–chloranil complex in acetone.

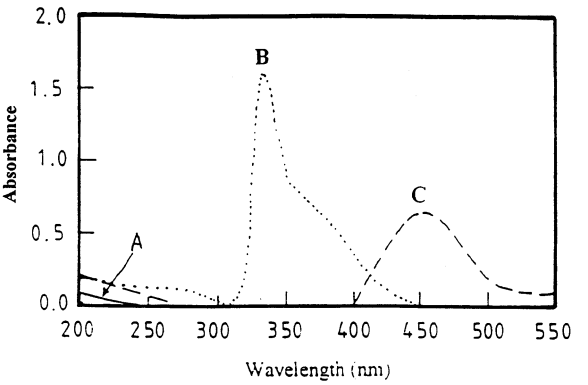


Fig. 2. Absorption spectra of (A) sertraline (1.0 mg/ml) in acetone; (B) chloranil (0.2% w/v) in acetone; (C) sertraline (77.4 μg/ml)–chloranil complex in acetone.

radical ion shows maximum absorption in the region of 440–450 nm (Fig. 2).

Application of Job's method of continuous variation [33] indicated a 1:1 complexation ratio with (I) and (II).

This finding was anticipated because of the formation of a mono substituted amino-quinone product and also the presence of one strong basic or electron-donating center in the structure of the cited drugs. The absorbances of (I) and (II) were used to calculate the association constant using the Benesi–Hildebrand equation [32] which depends on the experimental condition that one of the two component species should be present in large excess, so that its concentration is virtually unaltered on formation of the complex.

where $[A_o]$ and $[D_o]$ are the total concentrations of the interacting species, A_λ^{AD} and ξ_λ^{AD} are the absorbance and molar absorptivity of the complex at the specified λ_{max} and K_c^{AD} is the association constant of the complex. A line was obtained when plotting the values of $[A_o]/A_\lambda^{AD}$ vs $1/[D_o]$ according to the following equations:

$$[A_o]/A_\lambda^{AD} = 7.5 \times 10^{-3} + 1/[D_o]\ (5.42 \times 10^{-6})$$

for fluoxetine. (1)

$$[A_o]/A_\lambda^{AD} = 2 \times 10^{-3} + 1/[D_o]\ (2.67 \times 10^{-6})$$ for sertraline. (2)

Table 2
Association constant K_c^{AD}, molar absorptivity values ξ_λ^{AD} from Benesi–Hildebrandt plots for the complex and the calculated free energy ΔG

Parameter	Fluoxetine	Sertraline
K_c^{AD}	1383.10	749.10
ξ_λ^{AD}	133.33	500
ΔG	−4.26	−3.899

From Eqs. (1) and (2), the association constants K, the molar absorptivities ξ_λ^{AD} and free energy ΔG for the cited drugs were calculated and are shown in Table 2.

However, it should be noted that the value of ξ_λ^{AD} which is the molar absorptivity of the complex itself should not be confused with any stoichiometric values calculated with reference to the amount of any analyte being determined. The latter is best described as Beer's ε value while the former is Benesi–Hildebrandt's ξ_λ^{AD} value.

3.2. DDQ method

DDQ is a π acceptor ready to form charge transfer complex with many n-donors [33]. The cited drugs act as n-donors to form reddish violet chromagen with DDQ exhibiting strong absorption maxima at 455, 540 and 588 nm (Fig. 3). These bands may be attributed to the formation of DDQ radical anions which are formed by complete transfer of n-electrons from donor to acceptor moiety in a polar medium as shown in the following equation:

$$\underset{\text{Donor}}{\ddot{D}} + \underset{\text{Acceptor}}{\text{A}} \rightarrow [D \rightarrow A] \rightarrow \underset{\text{Radical anions}}{\dot{D}^+ + \dot{A}^-}$$

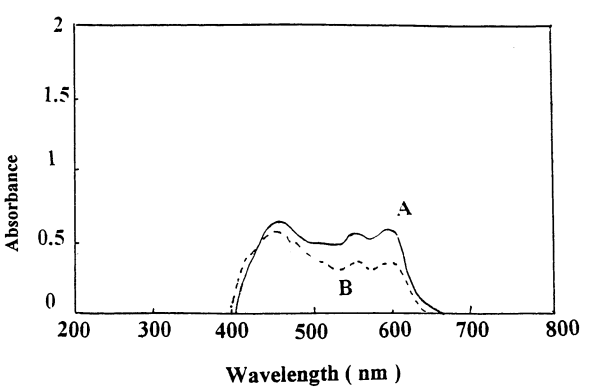


Fig. 3. Absorption spectra of (a) fluoxetine–DDQ complex (67 μg/ml); (b) sertraline–DDQ complex (61 μg/ml).

The stoichiometry of the reactions was studied by Job's method [31]. It was found that the ratio was 1:1 (donor/acceptor) for (I) and (II) with DDQ reagents.

The spectrophotometric properties of the colour species formed with chloranil and DDQ as well as the different parameters affecting the colour development were extensively studied to determine the optical conditions for the assay procedures. The reaction was studied as a function of the volume of the reagent, nature of the solvent, and effect of temperature on the formation of the complex (Table 1). Stability of colours and the molar ratio were also studied.

Thus the relationship between the concentration of (I), (II) and the absorbency of the colour formed using chloranil and DDQ was determined. Using the chloranil procedure, Beer's law is obeyed in the concentration ranges of 80–640 and 16–160 μg/ml with mean percentage recoveries of 99.83 and 100.39% and R.S.D. of 1.24 and 1.02% for (I) and (II) respectively, as shown in Table 3.

On using DDQ, the sensitivity ranges were found to be 16–112 and 15–105 μg/ml with mean percentage recoveries of 99.76 and 99.78% and R.S.D. of 0.95 and 0.81% for (I) and (II), respectively as shown in Table 3.

Also, Table 3 illustrates sensitivity ranges, molar absorptivity, regression equations, correlation coefficients and mean accuracy percentages for both proposed methods.

3.3. Iodine method

Some n-donor drugs react with σ electron acceptor iodine forming charge-transfer complex followed by triiode ion pair [34] formation. Charge-transfer complexes formed have a high absorption band at 300 nm and a lower band formed has a maximum at 365 nm followed by the formation of triiode ion pair which is accompanied by variation in maximum absorption to a wavelength region ranging from 270 to 310 nm [34]. It is suggested that the cited drugs react with

Table 3
Spectral data for the reaction of fluoxetine and sertraline base with chloranil, DDQ and iodine[a]

Parameter	Fluoxetine			Sertraline		
	Chloranil	DDQ	Iodine	Chloranil	DDQ	Iodine
Linearity range (μg/ml)	80–640	16–112	7.5–60	16–160	15–105	6–48
Molar absorptivity	4.85×10^{2}	32.41×10^{2}	78.49×10^{2}	28.31×10^{2}	31.25×10^{2}	85.50×10^{2}
Intercept (a)	−0.02	−0.0016	−0.019	−0.01	−0.002	0
R.S.D. (%) of intercept	7.62×10^{-4}	9.2×10^{-5}	1.4×10^{-3}	6.29×10^{-4}	8.16×10^{-5}	3.97×10^{-5}
Slope (b)	0.0016	0.0094	0.0236	0.0084	0.0092	0.0250
R.S.D. (%) of slope	7.68×10^{-5}	1.19×10^{-4}	7.1×10^{-5}	2.52×10^{-4}	1.20×10^{-4}	8.06×10^{-5}
Correlation coefficient (r)	1.000	1.000	1.000	0.993	0.995	0.998
Mean ± R.S.D. (%)	99.83 ± 1.24	99.76 ± 0.95	100.00 ± 1.13	100.39 ± 1.02	99.78 ± 0.81	99.69 ± 0.57

[a] $A = a + bc$ (regression equation).

iodine to form a triiode ion pair with a higher band absorption maxima at 265, 290 nm for (I) and (II) respectively, and a lower band at 365 nm for both drugs as shown in Figs. 4 and 5. The reaction is representative in the following equation:

$$R_2 - N: + I_2 \rightarrow R_2 - N - I_2 \rightarrow [R_2 - N - I]I^- \rightarrow \underset{\text{Triiode ion pair}}{[R_2 - N^+ - I]I_3^-}$$

This was postulated on the basis of the molar ratio of cited drugs to iodine (1:1) and consideration of previous reports [35] on similar reactions. Regarding the third step in the above equation, iodine alone does not absorb at the wavelength of maximum absorption, hence the stoichiometry will show only the iodide ion released as a result of 1 mol of iodine being consumed in the second step [34].

The optimum conditions for the reaction between iodine and the cited drugs were carefully studied and the results are represented in Table 1.

Beer's law is obeyed in concentration ranges of 7.5–60 and 6–48 μg/ml with mean percentage accuracy of 100.00 and 99.69% and R.S.D. of 1.13 and 0.57% for (I) and (II) respectively. Spectral data for the reaction products of (I) and (II) are given in Table 3.

The proposed methods were applied to the analysis of marketed products, the validity was assessed by applying the standard addition technique and the results obtained are presented in Table 4. There was no evidence of interference from the excipients.

The results of the proposed methods were statistically compared with those obtained by the reported methods [26] (HPLC manufacturer procedure supplied by Pfizer, pers. commun.). Table 5 shows that the calculated F- and t-values are less than the theoretical ones, confirming accuracy and precision at the 95% confidence level.

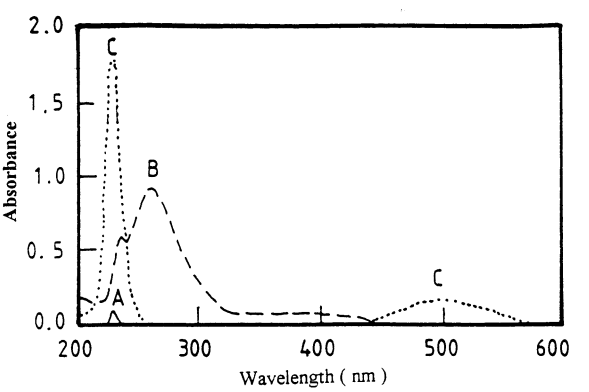


Fig. 4. Absorption spectra of (a) fluoxetine (3 μg/ml) in dichloroethane; (b) iodine (0.0125% w/v) in dichloroethane; (c) fluoxetine (39 μg/ml)–iodine complex in dichloroethane.

Table 5
Statistical comparison between results of analysis of bulk powder of fluoxetine and sertraline applying the proposed and reported methods[a]

	Fluoxetine				Sertraline			
	Chloranil method	DDQ method	Iodine method	Reported method [26]	Chloranil method	DDQ method	Iodine method	Reported method[b]
Mean + R.S.D.	99.83* ± 1.24	99.7* ± 0.95	100.00* ± 1.13	99.29* ± 0.90	100.39* ± 1.021	99.78* ± 0.81	99.69* ± 5.7	100.12* ± 0.42
Variance	1.54	0.90	1.28	0.81	1.04	0.66	0.32	
N	6	6	6	6	6	6	6	5
F-value	1.9 (5.1)	1.11 (5.1)	1.58 (5.1)		5.2 (6.3)	3.3 (6.3)	1.6 (6.3)	
t-value	0.35 (2.228)	0.29 (2.228)	0.63 (2.228)		0.82 (2.262)	0.76 (2.262)	2.22 (2.262)	

[a] The figures between parentheses are the theoretical values of F and t at $P = 0.05$.
[b] HPLC manufacturer procedure supplied by Pfizer; *The average of six determinations; **The average of five determinations.

Table 4
Assay results for dosage forms of fluoxetine and sertraline using the proposed and reported methods

Preparation	Chloranil method (recovery ± R.S.D.%)	DDQ method (recovery ± R.S.D.%)	Iodine method (recovery ± R.S.D.%)	Reported method (found ± R.S.D.%)
Fluoxetine				
Prozac capsules; 20 mg/capsule, B.N. 8196A	99.61 ± 0.71*	100.18 ± 0.98*	99.09 ± 0.50*	99.50 ± 1.50*
	$F = 4.5$ (10.2) $t = 0.09$ (2.776)	$F = 1.55$ (10.2) $t = 0.54$ (2.776)	$F = 9.0$ (10.2) $t = 0.37$ (2.776)	
Sertraline				
Lustral tablets, 100 mg/tablet, B.N. 272A23	100.24 ± 0.63*	99.97 ± 0.63*	99.52 ± 0.86*	99.47 ± 1.12**
	$F = 3.13$ (6) $t = 0.95$ (2.447)	$F = 3.13$ (6) $t = 0.59$ (2.447)	$F = 1.69$ (6) $t = 0.06$ (2.447)	

* The average of three experiments.
** The average of five experiments.

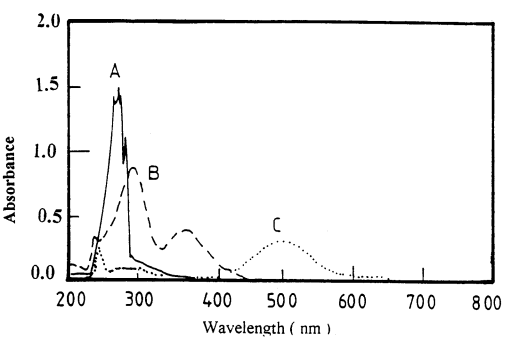


Fig. 5. Absorption spectra of (A) sertraline (5 μg/ml) in dichloroethane; (B) iodine (0.025% w/v) in dichloroethane; (C) sertraline (39 μg/ml)–iodine complex in dichloroethane.

4. Conclusion

The suggested methods have the advantage of being simple, accurate, sensitive and suitable for routine analysis in control laboratories. These methods utilize a single step reaction and single solvents. No substantial differences among the three proposed methods arose from analysis of the experimental results. The iodine acceptor method was more sensitive than the others due to the higher molar absorptivity and it determines up to 6–60 μg/ml of the cited drugs. DDQ and iodine methods are faster than the chloranil method. The color of chloranil and DDQ are more stable than the color of the iodine method. These methods can be used as general methods for the spectrophotometric determination of fluoxetine and sertraline hydrochloride in bulk powder and in pharmaceutical formulations.

References

[1] S. Budavari, Merck Index, 11th edn, Merck, Darmstadt, 1989, p. 4112.
[2] S. Budavari, Merck Index, 12th edn, Merck, Darmstadt, 1996, p. 8613.
[3] J.F. Nash, R.J. Bopp, R.H. Carmichael, K.Z. Farid, L. Lemberger, Clin. Chem. 28 (1982) 2100.
[4] S.H.Y. Wong, S.S. Dellafera, R. Fernandes, H. Kranzler, J. Chromatogr. 499 (1990) 601.
[5] J.G. Flood, P.R. Puopolo, Clin. Chem. 37 (1991) 1304.
[6] P. Thomare, K. Wang, V. van der Meerch-Mougeot, B. Diquet, J. Chromatogr. 121 (1992) 217.
[7] A. El-Yazigi, D.A. Ruines, Ther. Drug Monit. 15 (1993) 305.
[8] J.H. Nichols, J.R. Charlson, G.M. Lawson, Clin. Chem. 40 (1994) 1312.
[9] D.D. Writh, B.A. Olsen, D.K. Hallenbeck, M.G. Lake, S.M. Gregg, F.M. Perry, Chromatographia 46 (1997) 511.
[10] G. Aymard, P. Lidi, Y.T. Pham, B. Diquet, J. Chromatogr. Biomed. Appl. 700 (1997) 183.
[11] V. Dixit, H. Nguyen, V.M. Dixit, J. Chromatogr. Biomed. Appl. 101 (1991) 379.
[12] G.A. Torok-Both, G.B. Baker, R.T. Coutts, K.F. Mckenna, L.J. Aspeslet, J. Chromatogr. Biomed. Appl. 117 (1992) 99.
[13] R.T. Sane, A.B. Jani, J.K. Ghodge, A.J. Vaidya, S.S. Kotwal, Indian Drugs 29 (1992) 237.

[14] S. Raghuveer, A.B. Avadhanulu, A.R.R. Pantulu, Indian Drugs 30 (1993) 83.
[15] M. Adamczyk, J.R. Fishpaugh, C.A. Harrington, D.E. Hortter, Ther. Drug Monit. 16 (1994) 298.
[16] R.A. Komoroski, Anal. Chem. 66 (1994) 1024A.
[17] B. Levine, A.J. Jenkins, J.E. Smialek, J. Anal. Toxicol. 18 (1994) 272.
[18] D. Rogowsky, M. Marr, G. Long, C. Moore, J. Chromatogr. Biomed. Appl. 655 (1994) 138.
[19] B.K. Logan, P.N. Friel, G.A. Case, J. Anal. Toxicol. 18 (1994) 139.
[20] H.G. Fouda, R.A. Ronfeld, D.J. Weidler, J. Chromatogr. Biomed. Appl. 61 (1987) 197.
[21] L.M. Tremaine, E.A. Joerg, J. Chromatogr. Biomed. Appl. 88 (1989) 423.
[22] R.N. Gupta, S.A. Dziurdzy, Clin. Chem. 40 (1994) 498.
[23] H.L. Wiener, H.K. Kramer, M.E.A. Reith, J. Chromatogr. Biomed. Appl. 92 (1990) 467.
[24] J. Patel, E.P. Spencer, R.J. Flangan, Biomed. Chromatogr. 10 (1996) 351.
[25] I.M. McIntyre, C.V. King, V. Staikos, J. Gall, O.H. Drummer, J. Forensic Sci. 42 (1997) 951.
[26] K. Klorey, Analytical Profiles of Drug Substances, vol. 19, Academic Press, New York, 1990, p. 193.
[27] M.A. Slifkin, R.A. Sumner, J.G. Heathcote, Spectrochim. Acta 23A (1967) 751.
[28] E.S.A. Ibrahim, A.S. Issa, A.A. Salem, M.S. Mahrous, Talanta 30 (1983) 531.
[29] D. Buckley, H.B. Hembest, P. Slade, J. Chem. Soc. (1957) 4891.
[30] A. Taha, G. Rucker, Arch. Pharm. 310 (1977) 485.
[31] A.S. Douglas, M.W. Donald, Principles of Instrumental Analysis, Holt, Rinehart and Winston, New York, 1971, p. 104.
[32] R. Foster, I.B.C. Matheson, Spectrochim. Acta 23A (1967) 2037.
[33] R. Foster, Organic Charge Transfer Complexes, Academic Press, London, 1969.
[34] M.A. Magda, B. Saied, M.E. Sobhi, A.A. Afaf, Analyst 109 (1984) 1417.
[35] A.M. Taha, N.A. El-Rabbat, F.A. Abdel Fattah, Analyst 105 (1980) 568.