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ORIGINAL ARTICLE

Spectrofluorimetric determination of doxepin hydrochloride in commercial dosage forms via ion pair complexation with alizarin red S

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Abstract A simple and sensitive spectrofluorimetric method has been developed for the determination of doxepin hydrochloride in pharmaceutical preparations. It is based on the formation of ion-pair complex between doxepin and alizarin red S at pH 3.09. The ion pair complex was extracted in dichloromethane and the fluorescence intensity was measured at 560 nm after excitation at 490 nm. The optimum conditions for determination were also investigated. The linear range and detection limit were found to be 2–14 and 0.55 μg/ml, respectively. The method has been successfully applied for the analysis of drug in commercial dosage forms. No interference was observed from common pharmaceutical adjuvant. Statistical comparison of the results obtained by the proposed method with that of the reference method shows excellent agreement and indicates no significant difference in accuracy and precision.

1. Introduction

Doxepin hydrochloride is a dibenzoxepin class of antidepressants. It is chemically known as 1-propanamine,3-dibenz[*b*,*e*]oxepin-11(6*H*)-ylidine-*N*, *N*-dimethyl-hydrochloride with a molecular weight of 315.8. It is a white crystalline solid readily soluble in water. The inert ingredients used in the formulations are magnesium stearate, sodium lauryl sulfate and starch. It has been widely used as an effective tricyclic antidepressant in the treatment of psychiatric disorders over the past decades (Chlobowska et al., 2003; Uddin et al., 2008). The starting daily dose of 75 mg is recommended for patients with mild to moderate severity. The dosage may be increased or decreased depending upon the patient's response. The usual optimum dosage range is 75–150 mg/day. However, overdoses of doxepin hydrochloride may lead to some disorders like cardiac arrhythmias, severe hypotension and hypothermia among other disorders (Gossel and Bricker, 1994; Lara et al., 2005). In view of above considerations, an analytical procedure is needed for quality assurance in pharmaceutical preparations.

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United States Pharmacopoeia (The United States, 2008) described a liquid chromatographic method for the assay of doxepin hydrochloride in bulk and formulations. Literature survey reveals that the reported methods mainly focus on chromatographic techniques for the determination of doxepin hydrochloride such as TLC-densitometry (Maslanka and Krzek, 2005), reversed-phase liquid chromatography coupled with UV detector (Ruiz-Angel et al., 2003), ESIMS detector (Gritti and Guiochan 2005), HPLC (Samanidou et al., 2007; Titier et al., 2007; Ma et al., 2009), micellar electrokinetic chromatography (Oteen and Zeinab, 2005; Devasish et al., 2005), GC (Tatarulu, 2006) and capillary zone electrophoresis (Kou et al., 2004). In addition to these, several other methods are also available for the determination of doxepin hydrochloride which includes electrogenerated chemiluminescence (Greenway and Dolman, 1999), resonance light scattering (Wu et al., 2007), polarography (Chodkowski et al., 1992) and electrochemical sensor (Huang et al., 2010). However, procedures involving HPLC and capillary zone electrophoresis are highly expensive while TLC methods are not sensitive and also tedious to adopt for routine analysis. GC methods suffer from thermal instability and tedious sample preparation steps. The applications of polarography in a routine analysis of doxepin may be restricted due to the toxicity of dropping mercury electrode and its sluggish response.

Procedures involving spectrophotometry and spectrofluorimetry have attracted because of their sensitivity, speed and simplicity. One of the advantages is that most of the additives or excipients found in formulations are non-fluorescent in nature and hence, spectrofluorimetry is a good choice for quantitative analysis of drugs in commercial dosage forms. Literature survey revealed that few spectrofluorimetric methods have been reported for the determination of doxepin. A semi automatic extraction-fluorimetric method (Acedo-Valenzuela et al., 2005) for the determination of doxepin based on the ion-pair formation with 9,10-dimethoxyanthracene-2-sulfonate has been reported. In addition, extractive fluorimetric methods based on the fluorescent ion pair complex formation of the drug with eosin Y (Rahman et al., 2009) and tetraiodofluorescein (Devriendt et al., 1973) have also been reported for their assay in pharmaceutical preparations and biological fluids. Spectrophotometric methods have also been developed for quantitation of doxepin hydrochloride involving the reagents such as titanium(IV) thiocyanate and iron(III) thiocyanate (Misiuk, 2005), Reinecke salt (Kurzawa et al., 1999), 3-methyl benzothiazolin-2-one hydrazone (Revanasiddappa and Manju, 1999) and bromophenol blue (Shingbal and Rao, 1985).

This work describes a new spectrofluorimetric method for the determination of doxepin hydrochloride in bulk and pharmaceutical preparations. The proposed method is based on the formation of an ion-pair complex between doxepin and alizarin red S at pH 3.09. The ion-pair complex was completely extracted into dichloromethane which showed fluorescence intensity at 560 nm after excitation at 490 nm. The proposed method offers the advantage of simplicity with respect to reagent, good sensitivity and stability. The reaction conditions were optimized and validated as per guidelines of International Conference on Harmonization (ICH, 1995).

2. Experimental

2.1. Apparatus

All fluorescence spectra were recorded on a Hitachi fluorescence spectrophotometer F-2500 (Tokyo, Japan) equipped with a xenon lamp. All measurements took place in quartz cells with path length 1.0×1.0 cm. Eutech (Cyber scan pH 2100) pH meter was used to measure the pH. All measurements were performed at 25 ± 1°C. The infra red spectra were recorded on a Perkin–Elmer FTIR 1650 spectrophotometer using KBr pellet technique.

2.2. Reagents

Doxepin hydrochloride was obtained from Sigma Chemical Company (St. Louis, MO, USA) and used as received. Spectra-10 capsules (Rexin Pharmaceuticals Private Limited, Himachal Pradesh, India), labeled to contain 10 mg doxepin hydrochloride per capsule, were purchased from local drug stores. Buffer solutions ranging from pH 0.91–5.20 were prepared by mixing 50 ml of 1 N sodium acetate and an appropriate volume of 1 N HCl and diluted to 250 ml with distilled water (Britton, 1932) and 2.74×10^{-3} M alizarin red S (Fluka Chemie AG, Switzerland, M.W. 342.26) solution was freshly prepared in distilled water.

2.3. Preparation of standard solution

An accurately weighed amount (50 mg) of doxepin hydrochloride was transferred into a 50 ml standard flask, dissolved in 20 ml distilled water and then completed to the mark with the same solvent to obtain a stock solution of 1 mg/ml. This stock solution was further diluted with water to obtain a standard working solution of 0.1 mg/ml.

2.4. Procedure for determination of doxepin hydrochloride

Accurately measured aliquots of the working standard solution of doxepin hydrochloride (0.1 mg/ml) equivalent to 20–140 μg were transferred into a series of 50 ml separating funnels. To each funnel, 1.5 ml of buffer solution (pH 3.09) was added followed by 3.0 ml of 0.1% alizarin red S. The contents of separating funnel were shaken well with 2×5 ml dichloromethane for 1.5 min and then allowed to separate the two layers. The fluorescence intensity of the organic layer was measured at 560 nm after excitation at 490 nm. The fluorescence intensity was plotted against the concentration of the drug to get the calibration graph and the corresponding regression equation was also developed.

2.5. Analysis of commercial tablets

The powder contents of five capsules of 10 mg strength of doxepin hydrochloride were treated with 50 ml distilled water and left for 10 min for a complete extraction of the drug. The aqueous extract was filtered through Whatmann No. 42 filter paper (particle retention: 2.5 μm; Whatmann International Limited, Kent, UK) in a 100 ml volumetric flask. The residue was washed with distilled water and then completed

to the volume with distilled water. The prepared solution was diluted quantitatively with distilled water to obtain a suitable concentration for analysis by the proposed method.

2.6. Determination of stoichiometry

Job's method of continuous variations (Skoog et al., 2004) was applied for ascertaining the stoichiometry of the ion-pair complex. This was achieved by combining different volumes, i.e. 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8 and 0.9 ml of doxepin hydrochloride (2.74×10^{-3} M) with 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2 and 0.1 ml, of alizarin red S (2.74×10^{-3} M), respectively, into a 50 ml separating funnel. The contents of the funnel were shaken vigorously with 2×5 ml dichloromethane and then allowed to stand for clear separation of the organic phase. The fluorescence intensity was measured at 560 nm after excitation at 490 nm and plotted against the mole fraction of the drug.

2.7. Procedure for reference method (Revanasiddappa and Manju, 1999)

Portions of standard doxepin hydrochloride solution (0.1 mg/ml) corresponding to 0.5–3.0 μg/ml were pipetted into a series of 10 ml volumetric flask. To each flask 1 ml of 0.4% 3-methylbenzthiazolinone-2-hydrazone solution and 3 ml of 1% iron(III) chloride solution prepared in 1 M hydrochloric acid were added and diluted to the mark with distilled water. The contents of the solution were mixed thoroughly and the absorbance of the solution was measured after 50 min at 620 nm against the reagent blank prepared simultaneously except the drug .The amount of the drug in a given sample can be estimated either from the calibration graph or the corresponding linear regression equation.

3. Results and discussion

Doxepin hydrochloride is non-fluorescent in nature and hence, its derivatization with a fluorogenic reagent is necessary for its determination by spectrofluorimetry. The fluorogenic reagents such as 9,10-dimethoxyanthracene-2-sulfonate (Acedo-Valenzuela et al., 2005), tetraiodofluorescein (Devriendt et al., 1973) and eosin Y (Rahman et al., 2009) have been found to form the fluorescent ion-pair complex with doxepin in acidic medium. The resulting ion-pair complexes were quantitatively extracted into dichloromethane and determined spectrofluorimetrically. The reaction of doxepin with alizarin red S has not been investigated yet. Therefore, the present study was devoted to investigate the reaction of doxepin with alizarin red S and employment of the reaction in the development of a sensitive and simple spectrofluorimetric method for its determination in pharmaceutical preparations. In the present study aqueous solution of doxepin hydrochloride was found to react with alizarin red S at pH 3.09 resulting in the formation of the fluorescent ion-pair complex which was quantitatively extracted into dichloromethane. The excitation and emission spectra are shown in Fig. 1.

3.1. Stoichiometry and reaction mechanism

The stoichiometry of the reaction between doxepin and alizarin red S was investigated by Job's method. Job's plot

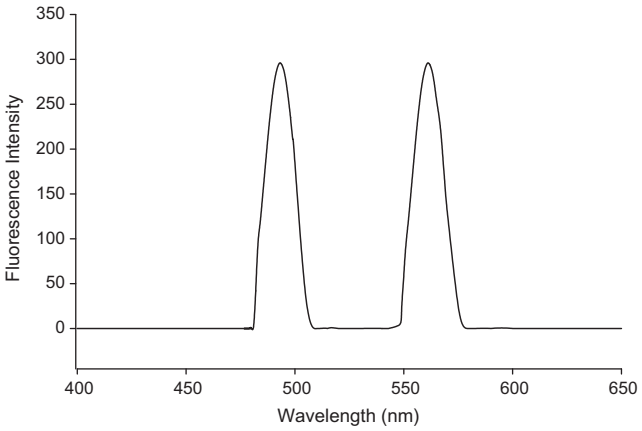


Figure 1 Excitation and emission spectra of fluorescent ion-pair complex.

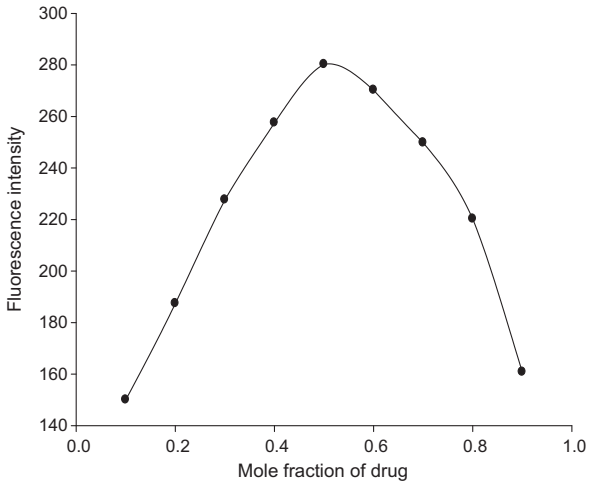


Figure 2 Job's plot to establish the stoichiometry of the reaction.

(Fig. 2) has revealed that the molar combining ratio between doxepin and alizarin red S is 1:1. The apparent formation constant and Gibb's free energy (ΔG) were calculated and found to be 1.56×10^6 and -35.31 kJ/mol, respectively.

Doxepin is a derivative of dibenzoxepine and its basic characteristics are due to the presence of tertiary amino group in the aliphatic chain. In acidic medium doxepin is protonated while alizarin red S (3,4-dihyroxy-9,10-dioxo-2-anthracene sulfonic acid sodium salt) ionizes in aqueous solution providing a negative charge on it. Thus one mole of doxepin reacted with one mole of alizarin red S resulting in the formation of fluorescent ion-pair complex which is easily extractable in dichloromethane.

The infra red spectra of doxepin hydrochloride, alizarin red S and the doxepin-alizarin red S ion pair complex were recorded in the region 4000–400 cm^{-1}. The results are presented in Fig. 3. Some characteristic frequencies are listed in Table 1. The IR spectrum of the complex shows bandcharacteristics for functional groups of doxepin and alizarin red S, such as:

(i) Presence of $\gtrless N^+$–H at 2693 cm^{-1}, $(-CH_2-)_2$ at 764 cm^{-1}, (–C–O–C–) at 1005 cm^{-1} confirms the presence of doxepin in the complex.

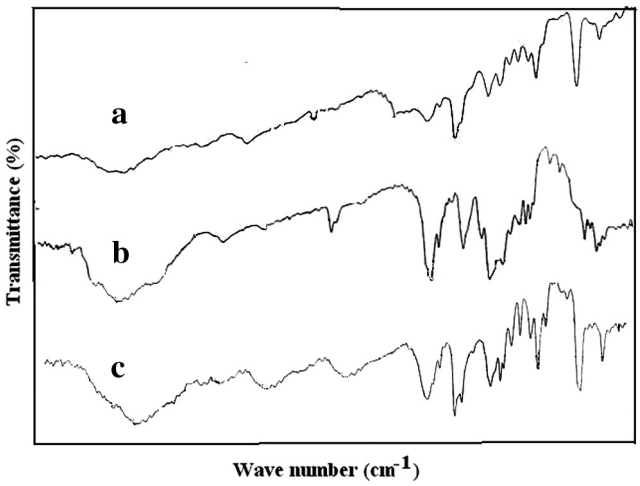


Figure 3 IR Spectra of a – doxepin hydrochloride; b – Alizarin red- S; c – doxepin-alizarin red-S ion-pair complex.

(ii) Presence of C–S at 633 cm^{-1}, $–SO_3$ at 1275, 1219 and 1053 cm^{-1} authenticates the involvement of alizarin red S in the complex formation.

Based on the combining ratio and literature background, the reaction pathway between doxepin and alizarin red S was postulated to proceed as shown in Scheme 1.

3.2. Optimization of experimental conditions

To optimize the assay variables, the effects of concentration of alizarin red S, reaction time, pH, extracting solvent and shaking time for extraction on the fluorescence intensity of the ion-pair complex formed were carefully studied.

3.2.1. Effect of volume of reagent

The effect of volume of 2.74×10^{-3} M alizarin red S on the fluorescence intensity was studied in the range of 0.5–3.4 ml; keeping the amount of the drug (10 μg/ml) constant. The results are shown in Fig. 4. The maximum fluorescence intensity was obtained with 2.7 ml of the reagent. At higher volumes of 2.74×10^{-3} M alizarin red S up to 3.4 ml, the fluorescence intensity was not affected. Thus, a volume of 3.0 ml of 2.74×10^{-3} M alizarin red S was chosen as an optimum volume for all measurements.

3.2.2. Effect of reaction time

The effect of reaction time on the formation of ion-pair complex was studied at 25 ± 1 °C. It was observed that the complex got stabilized immediately after mixing the drug and reagent and remained stable for about 1 h.

3.2.3. Effect of pH

The effect of pH on the formation of ion-pair complex was studied by carrying out the reaction in sodium acetate–HCl buffer solution of pH 0.91–5.20. It was evident from Fig. 5 that maximum fluorescence intensity was obtained at pH 3.09. In order to keep the high sensitivity for the determination of doxepin hydrochloride, the subsequent experiments were carried out at pH 3.09.

3.2.4. Effect of volume of pH 3.09 buffer solution

The effect of volume of pH 3.09 buffer solution on the fluorescence intensity was investigated in the range of 0.5–2.0 ml (Fig. 6). The highest fluorescence intensity was obtained with 1.5 ml of buffer (pH 3.09) solution, beyond this, a further increase in the volume of buffer solution resulted in no change in the fluorescence intensity of the complex. Therefore, 1.5 ml of pH 3.09 buffer solution was adopted as an optimum volume for fluorescence measurements.

3.2.5. Solvent effect

In order to select the most appropriate solvent for extracting the ion-pair complex, different solvents were tested such as chloroform, carbon tertrachloride, dichloromethane, dichloroethane and ethyl acetate. The maximum fluorescence intensity was obtained when extraction was carried out with dichloromethane. Therefore, dichloromethane was chosen as the most appropriate solvent for the extraction of ion pair complex.

3.2.6. Effect of shaking time for extraction

The effect of the shaking time for the extraction of ion-pair complex in dichloromethane was studied in the range of 0.5–2.5 min. The maximum fluorescence intensity of the complex was obtained at 1.0 min shaking and above this up to 2.5 min, the fluorescence intensity remained constant. Therefore, 1.5 min was used as an optimum shaking time throughout the determination process. The ion-pair complex was quantitatively recovered in two extractions.

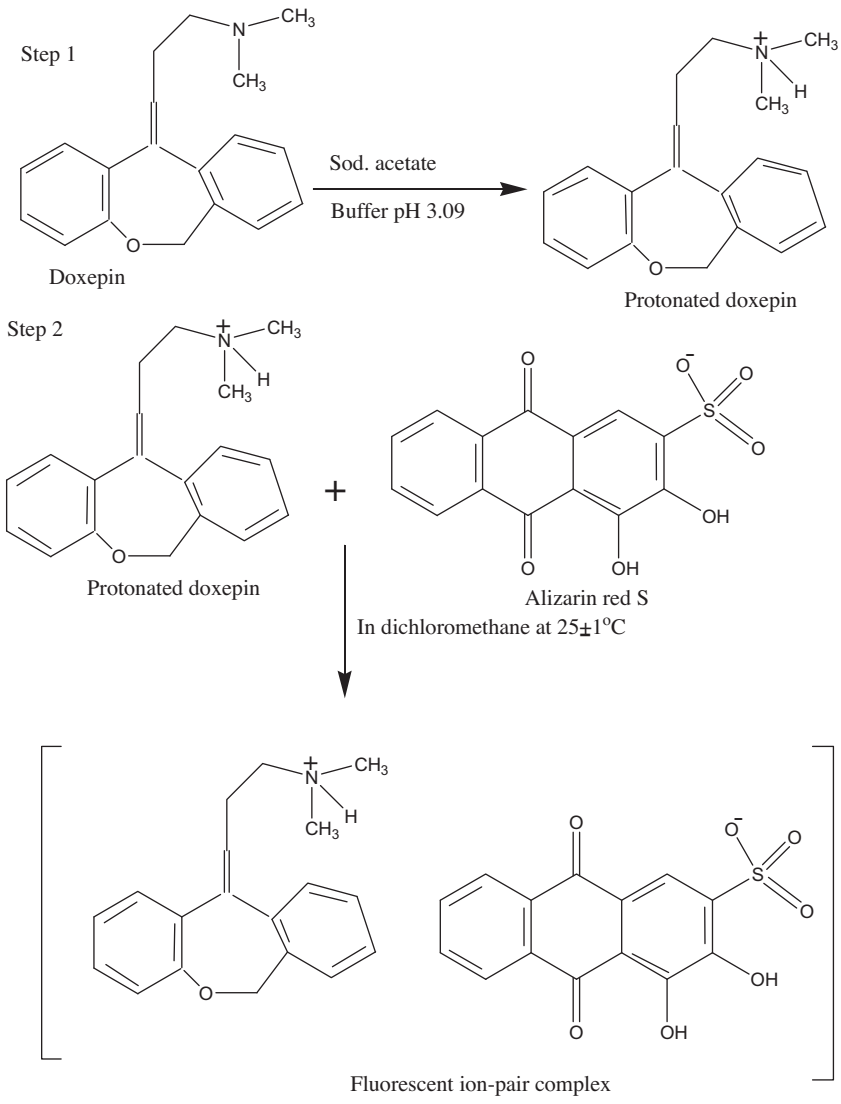
4. Method validation

4.1. Linearity and limits of detection and quantitation

Under the optimized experimental conditions, the calibration curve was constructed by plotting fluorescence intensity as a function of the corresponding doxepin hydrochloride concentration (Fig. 7). The linear relationship was obtained in the

Table 1 Representative infra red frequencies of doxepin hydrochloride, alizarin red S and doxepin-alizarin red S ion-pair complex.

	$\nu(\rangle N^+–H)$	$\nu(C{=}O)$	$\nu(C–N)$	$\nu(C–S)$	$\nu(–CH_2–)_2$	$\nu(–C–O–C–)$	$\nu(SO_3)$ cm^{-1}
Doxepin HCl	2692	–	1215 1107		766	1004	
Alizarin red S	–	1639	–	642			1070 1262 1200
Doxepin-alizarin red S ion-pair complex	2693	1639	1219 1108	633	764	1005	1053 1275 1219



Scheme 1

concentration range of 2–14 μg/ml. The regression analysis of calibration data gave the regression cited in Table 2 with a correlation coefficient of 0.9995. The limit of detection (LOD) and limit of quantitation (LOQ) were calculated according to the ICH guidelines for validation of analytical procedures (Tatarulu, 2006). The LOD and LOQ values were found to be 0.55 and 1.82 μg/ml, respectively. The parameters for analytical performance of the proposed method are summarized in Table 2.

4.2. Precision and repeatability

To evaluate intra-day and inter-day precisions, analysis of doxepin hydrochloride at three concentration levels (2, 4, 6) μg/ml was carried out by performing five experiments on the same day using the same analyte standard solution and over five consecutive days using different solutions. The results are summarized in Table 3. The intra-day and inter-day RSD values ranged from 0.05% to 0.37% and 0.02% to 0.30%, respectively, reflecting the usefulness of the method in routine use.

4.3. Accuracy and recovery

The accuracy of the proposed method was tested by performing recoveryexperiments through standard addition technique. For this known quantities of pure doxepin hydrochloride were mixed with definite amounts of preanalyzed commercial dosage forms and mixtures were analyzed following the proposed method. The results are reported in Table 4. The percent recoveries obtained were quantitative (99.64–100.6%) indicating the good accuracy of the method.

4.4. Selectivity

The selectivity of the proposed method was evaluated by analyzing the standard solution of doxepin hydrochloride in the presence of tablet excipients such as lactose, sucrose, mannitol, starch and magnesium stearate. It was observed that these excipients did not interfere with the proposed method. The results of the recovery experiment also indicated that neither

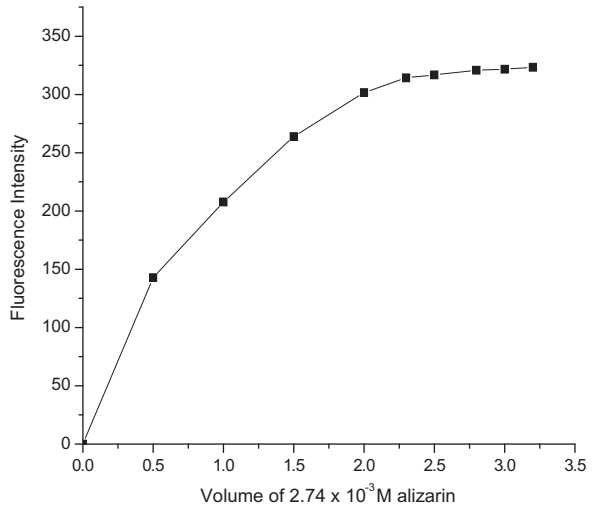


Figure 4 Effect of volume of 2.74×10^{-3} M alizarin red S on the fluorescence intensity of complex (doxepin hydrochloride 10 μg/ml).

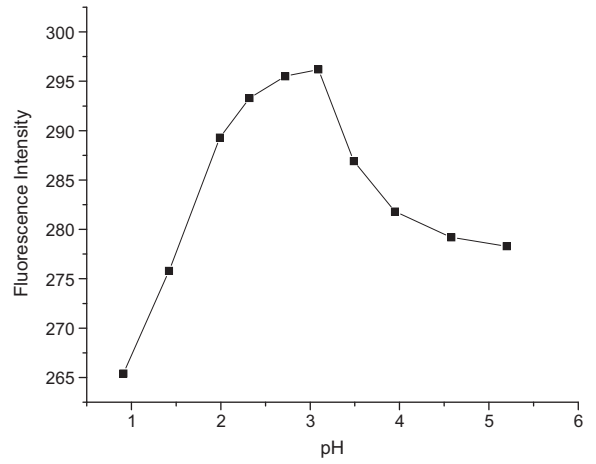


Figure 5 Effect of pH on the fluorescence intensity of the ion-pair complex.

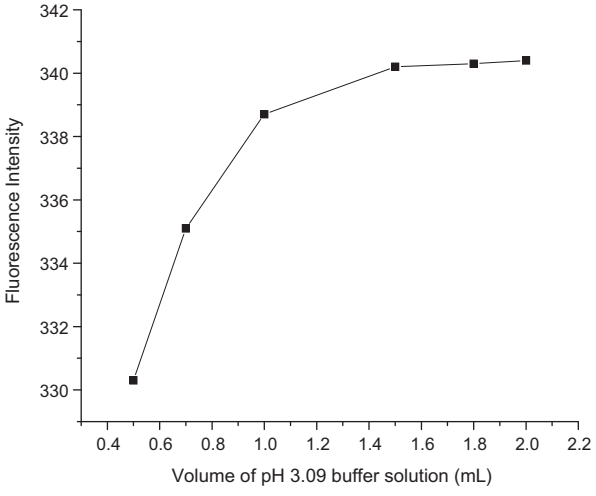


Figure 6 Effect of the volume of pH-3.09 buffer solution on the fluorescence intensity of the ion-pair complex.

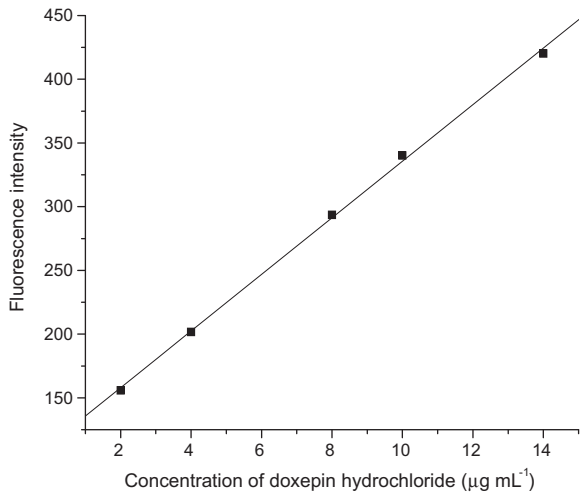


Figure 7 Calibration curve for determination of doxepin hydrochloride.

Table 2 Statistical parameters for the determination of doxepin by the proposed method.

Parameters	Value
λ_{ex} (nm)	490
λ_{em} (nm)	560
Linear range (μg/ml)	2–14
Intercept, *a*	113.6
Slope, *b*	22.203
Correlation coefficient (*r*)	0.9995
LOD (μg/ml)	0.55
LOQ (μg/ml)	1.82

the accuracy nor the precision of the proposed method is affected by the coformulated substances.

4.5. Robustness

The method robustness was tested by varying several parameters and studying the effect on the fluorescence intensity. The effect of varying the volumes of 2.74×10^{-3} M alizarin red S solution from 2.8 to 3.4 ml was examined. It was found that there was no change in the fluorescence intensity of the complex. The study of variation of volume of buffer solution of pH 3.09 from 1.3 to 1.7 ml showed that it did not affect the percentage recovery of the drug. Results of variation in the experimental parameters, as well as carrying out the experiment at room temperature, proved their reliability during the normal use and suggested that the proposed method is robust.

5. Application

The proposed method was applied to the determination of doxepin hydrochloride in commercial formulations. Five replicate determinations were made using the proposed method and the reference method (Revanasiddappa and Manju, 1999). The results are summarized in Table 5. The results were reproducible with low RSD values. The results obtained for the analysis

Table 3 Test of precision of the proposed method.

Proposed method	Concentration (μg/ml)		RSD%	SAE[b]	C.L[c]
	Taken	Found[a] ± SD			
Intraday	2.00	2.006 ± 0.010	0.05	0.005	0.012
	7.00	7.035 ± 0.011	0.16	0.005	0.013
	12.00	12.037 ± 0.448	0.37	0.200	0.556
Interday	2.00	2.001 ± 0.015	0.07	0.007	0.018
	7.00	7.030 ± 0.014	0.02	0.006	0.017
	12.00	12.031 ± 0.036	0.30	0.016	0.044

[a] Mean for five independent determinations.
[b] SAE, standard analytical error.
[c] C.L., confidence limit at 95% confidence level and four degrees of freedom ($t = 2.776$).

Table 4 Recovery of doxepin hydrochloride by standard addition technique.

Concentration (μg/ml)				
Spectra-10 (taken)	Standard added	Found ± SD	R.S.D (%)	Recovery[a] (%)
6	3	8.968 ± 0.050	0.56	99.64
6	5	11.068 ± 0.068	0.61	100.61
6	6	12.041 ± 0.070	0.58	100.34

[a] Mean for five independent analyses.

Table 5 Applicability of the proposed method in pharmaceutical formulations and its comparison with the reference method (Revanasiddappa and Manju, 1999).

Pharmaceutical formulation Tablet	Proposed method		Reference method		t and F value[b]	θ_L[c]	θ_U[c]
	Recovery[a](%)	RSD (%)	Recovery[a] (%)	RSD (%)			
Spectra-10	100.12	0.41	100.19	0.43	$t = 0.264$, $F = 1.1004$	0.992	1.006

[a] Mean for five independent analyses.
[b] Theoritical t ($v = 8$) and F values at 95% confidence level are 2.306 and 6.39, respectively.
[c] A bias, based on recovery experiments, of ±2% is acceptable.

of doxepin hydrochloride in drug formulation were compared statistically with those obtained by reference method. Student's t-test and F-test values at 95% confidence level did not exceed the theoretical value of 2.306 and 6.39 for t-test and F-test, respectively; indicating no significant difference between the performances of the methods compared regarding accuracy and precision. The interval hypothesis (Hartman et al., 1995) test has also been performed to check the reliability of the proposed method by calculating the lower (θ_L) and upper (θ_U) acceptance limits using the equation:

$$\theta^2\left(\bar{X}_1^2 - S_P^2 t_{tab}^2/n_1\right) - 2\theta\bar{x}_1 * \bar{x}_2 + \theta^2\left(\bar{X}_2^2 - S_P^2 t_{tab}^2/n_2\right) = 0 \quad (1)$$

The values of θ_L and θ_U of the confidence interval were obtained as:

$$\theta_L = -b - (b^2 - 4ac)^{1/2}/2a \quad (2)$$

$$\theta_U = -b + (b^2 - 4ac)^{1/2}/2a \quad (3)$$

where

$$a = \bar{X}_1^2 - S_p^2 t_{tab}^2/n_1 \quad (4)$$

$$b = -2\bar{X}_1\bar{X}_2 \quad (5)$$

$$c = \bar{X}_2^2 - S_p^2 t_{tab}^2/n_2 \quad (6)$$

The values of θ_L and θ_U are reported in Table 5. It is concluded based on θ_L and θ_U values that the proposed method is not biased because the true bias is smaller than ±2.0%; indicating the compliance of regulatory guidelines (Acceptable methods, 1992).

The performance of the proposed method was compared with other existing methods (Table 6). It is evident that the present method has a wider linear range with low values of LOD and RSD as compared to the existing spectrofluorimetric method (Rahman et al., 2009) suitable for the determination of doxepin hydrochloride in pharmaceutical preparations. The proposed method is also simpler than the spectrophotometric methods (Devriendt et al., 1973; Misiuk, 2005; Kurzawa, 1999) requiring less analysis time. The polarographic method is not usually recommended owing to the toxicity of dropping mercury electrode. HPLC is more sensitive but involves expensive instrumental set up which an ordinary laboratory cannot

Table 6 Comparison of performance of the proposed method with other existing methods for determination of doxepin hydrochloride.

Techniques/reagents	Linear range (μg/ml)	LOD (μg/ml)	RSD (%)	References
Spectrofluorimetry				
Eosin Y	0.1–0.8	0.95	0.59	Rahman et al. (2009)
Alizarin red S	2.0–14	0.55	0.41	This work
Spectrophotometry				
3-Methyl benzothiazolin-2-one hydrazone	0.8–10	–	1.1	Revanasiddappa and Manju (1999)
Titanium(IV) thiocyanate	5–50	0.34	0.43	Misiuk (2005)
Iron (III) thiocyanate	3–30	0.26	0.32	Misiuk (2005)
Reinecke salt	30–450	–	1.69	Kurzawa et al. (1999)
Densitometric - TLC	131.3–1050	0.033	1.89	Maslanka and Krzek (2005)
Polarography	10–50	–	0.94	Chodkowski et al. (1992)
Reversed-phase liquid chromatography	30–70	–	<2.0	Ruiz-Angel et al. (2003)
Electrochemical sensor	3.158×10^{-4}–3.158×10^{-4}	3.158×10^{-5}	2.5	Huang et al. (2010)

afford. Thus, the proposed method is most suitable for a routine analysis of doxepin in commercial dosage forms.

6. Conclusions

The proposed method does not require any laborious clean up procedure before measurement. In addition the method shows good accuracy and precision. The method shows no interferences from the common excipients and additives. The statistical parameters and recovery data revealed good accuracy and precision of the proposed method. Therefore, it is concluded that the proposed method is simple, sensitive and rapid for the determination of doxepin hydrochloride in commercial dosage forms.

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