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KEYWORDS

Clemastine hydrogen fumarate; Desloratadine; Losartan potassium; Moxepril HCl; Eosin; Binary complex **Abstract** A simple and sensitive spectrophotometric method has been established for the determination of clemastine hydrogen fumarate (I), desloratadine (II), losartan potassium(III) and moxepril HCl(IV) based on binary complex formation with eosin. The method does not involve solvent extraction through the use of a non-ionic surfactant (methylcellulose). The color of the produced complex was measured at 552, 549 nm for (I), (II) while was measured at 540 nm for (III) and (IV). Appropriate conditions were established for the color reaction between eosin and the studied drugs to obtain maximum sensitivity. Under the proposed conditions, the method is applicable over concentration range of 1.25–11.25, 0.31–2.81, 2.5–20 and 1.25–15 μ g/ml for (I), (II), (III) and (IV), respectively. The molar absorptivity (ϵ), sandell sensitivity, detection (LOD) and quantitation limits (LOQ) are calculated. Unlike other reported ion-pair techniques, the suggested methods have the advantage of being applicable for the determination of the four drugs in their pharmaceutical dosage forms without prior extraction with excellent recoveries.

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1. Introduction

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nitis, allergic skin conditions, and pruritus. It causes drowsiness; few procedures are described for its determination including spectrophotometry (Clementina, 2008; Hassan et al., 2008; El Ragehy et al., 1995), HPLC (Jinlong and Jianguo, 2007; Viola et al., 2005). Desloratadine (II) an orally active major metabolite of the nonsedating antihistamine loratadine is a selective, potent, peripheral H₁ receptor antagonist. Very few visible spectrophotometric methods have been described for its determination (Patel et al., 2004; Nahed et al., 2007). Also, liquid chromatography (El-Sherbiny et al., 2007; Jun et al., 2009) technique has been described.

Clemastine (I) used as the hydrogen fumarate in hay fever, rhi-

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Losartan potassium(III) is a highly selective, orally active, non-peptide angiotensin II receptor antagonist indicated for the treatment of hypertension. Determination of Losartan has been carried out by HPLC (Choi et al., 2008; Obando et al., 2008; Budi et al., 2009). However, few spectrophotometric methods have been reported for its analysis (Ibrahim, 2005; Thomas et al., 2007). Moexipril HCl (IV) is a new potent orally active non-sulfhydryl angiotensin-converting enzyme (ACE) inhibitor which is used for the treatment of hypertension and congestive heart failure. Few analytical methods have been developed for the determination of moexipril, including derivative spectrophotometric (Erturk et al., 2003) and spectrophotometric methods (El-Shanwani et al., 2008a). RP-HPLC has been developed for the simultaneous determination of moexipril (El-Shanwani et al., 2008b).

Suitable organic dyes such as eosin were used for determination of many pharmaceutical compounds either spectrophotometry through the formation of binary or ternary complexes (Rahman and Rahman, 2011; Gouda et al., 2008; Walash et al., 2007) or spectrofluorimetry (Ibrahim et al., 2011; Rahman et al., 2009; Rahman and Haque, 2008) or by using both spectrophotometry and spectrofluorimetry (Omar, 2010; Abdellatef, 2007).

Here, for the first time, eosin was applied to react with clemastine hydrogen fumarate (I), desloratadine (II), losartan potassium (III) and moxepril HCl (IV) presenting a rapid and sensitive assay procedure for the studied drugs in pure and in pharmaceutical formulations. The proposed method can be used in laboratories where modern and expensive apparatus, such as that required for GLC or HPLC is not available in most quality control laboratories.

Digital analyzer pH meter (USA) was set to check pH values of acetate buffer solutions.

2.2. Materials and reagents

Clemastine hydrogen fumarate was kindly supplied by Novartis pharmaceutical company (Cairo, Egypt). Its pharmaceutical preparations Tavegyl® tablets (labeled to contain 1 mg clemastine per tablet) and Tavegyl® ampoules (labeled to contain 2 mg clemastine per 2 mL) were obtained from the local drugstore.

Desloratadine was kindly supplied by Minapharm pharmaceutical company (Cairo, Egypt). Its pharmaceutical preparation Desa® tablets (labeled to contain 5 mg desloratadine per tablet) were obtained from the local drugstore.

Losartan potassium was kindly supplied by Amoun pharmaceutical company (Obor, Egypt). Its pharmaceutical preparation Losar® tablets (labeled to contain 50 mg losartan potassium per tablet) were obtained from the local drugstore.

Moexipril hydrochloride was kindly supplied by Minapharm pharmaceutical company (Cairo, Egypt). Its pharmaceutical preparation Primox® tablets (labeled to contain 15 mg moexipril hydrochloride (IV) per tablet) were obtained from the local drugstore.

Eosin (El-Nasr chemical company, Egypt) was prepared as 0.1%, 0.2% solution in distilled water.

Acetate buffer pH 2.8, 3.7 (British Pharmacopoeia, 2007). Methylcellulose, 0.3%, 0.5% w/v.

All other chemicals and reagents used were of analytical grade and all solutions were prepared with double distilled water.

2. Experimental

2.1. Apparatus

Spectrophotometric measurements were carried out using a Shimadzu recording spectrophotometer UV 1800 equipped with 10 mm matched quartz cells.

2.3.1. Preparation of iosartan potassium and moxepril HCl standard solutions

2.3. Standard solutions

Stock working solutions were prepared to contain 0.5 mg/ml, dissolved in distilled water then the volumes were completed to 50 ml with distilled water in 50 ml volumetric flasks.

Table 1 Characteristic parameters for the reaction of studied drugs with Eosin.^a

Parameter	Clemastine hydrogen fumarate	Desloratadine	Losartan potassium	Moexipril HCl
λ_{\max} (nm)	552	549	540	540
Beers law limits (µg/ml)	1.25–11.25	0.31-2.81	2.5-20	1.25–15
Vol and conc of methyl cellulose	0.5 ml-0.5%	0.5 ml-0.3%	0.5 ml-0.5%	0.5 ml-0.5%
Vol and conc of eosin	1 ml-0.2%	2 ml-0.1%	1 ml-0.1%	1 ml-0.1%
Buffer PH	3.7	2.8	2.8	2.8
Buffer vol	1.5	1	0.2	0.5
Temp. (°C)	25 ± 5	50	60	25 ± 5
Time (min)	5	10	5	10
Regression equation ^b				
Slope (b)	0.0706	0.228	0.035	0.0447
Intercept (a)	0.1574	0.1138	0.1323	0.1105
Correlation coefficient (r^2)	0.9998	0.9999	0.9998	0.9998
LOD (µg/ml)	0.72	0.9	0.82	0.75
LOQ (µg/ml)	2.39	3	2.73	2.51
Sandell sensitivity ($\mu g \ cm^{-2}$)	0.01	0.003	0.02	0.014
ε (×10 ⁵) (L mol ⁻¹ cm ⁻¹)	0.53	0.96	0.25	0.36

^a Average of three experiments.

^b A = a + bc



Figure 1 Absorption curves of 11.25 μ g/ml clemastine hydrogen fumarate, 2.81 μ g/ml desloratadine, 20 μ g/ml losartan potassium, 15 μ g/ml moxepril HCl with eosin.

2.3.2. Preparation of clemastine hydrogen fumarate and desloratadine standard solutions

Stock working solutions were prepared to contain 0.5 mg/ml, dissolved in least amount of methanol (3 ml) and then the volumes were completed to 50 ml with distilled water in 50 ml volumetric flasks.

Working solutions of lower concentrations were prepared by appropriate dilutions of the standard solutions.



Figure 2 Effect of buffer volume on the ion pair complex formation between eosin and $11.25 \,\mu$ g/ml clemastine hydrogen fumarate, 2.81 μ g/ml desloratadine, 20 μ g/ml losartan potassium, 15 μ g/ml moxepril HCl.



Figure 3 Effect of eosin volume on absorbance of $10 \ \mu g/ml$ clemastine hydrogen fumarate, 2.81 $\mu g/ml$ desloratadine, 20 $\mu g/ml$ losartan potassium and 15 $\mu g/ml$ moxepril HCl.



Figure 4 Effect of temperature on absorbance of $10 \,\mu\text{g/ml}$ clemastine hydrogen fumarate, 2.81 $\mu\text{g/ml}$ desloratadine, 20 $\mu\text{g/ml}$ losartan potassium and 15 $\mu\text{g/ml}$ moxepril HCl.



Figure 5 Stability of the ion pair complex formed between eosin and 11.25 μ g/ml clemastine hydrogen fumarate, 2.81 μ g/ml desloratadine, 20 μ g/ml losartan potassium and 15 μ g/ml moxepril HCl.

2.3.3. Preparation of methyl cellulose

Methyl cellulose was prepared by dissolving the appropriate amount in w/v hot water (80 °C) with stirring for 10 min then chilling to 5 °C.

2.4. General procedures

To different aliquots of standard solutions [equivalent to (0.0125-0.1125), (0.0031-0.0281), (0.025-0.2), (0.0125-0.15)] mg of (I), (II), (III) and (IV), specific volumes of eosin (0.1%, 0.2% w/v) followed by specified volumes of acetate buffer of certain pHs then 0.5 ml methyl cellulose (0.3%, 0.5% w/v) were added except for moxepril HCl, methyl cellulose added at first followed by acetate buffer PH 2.8. The contents were left for the specified time at certain temperatures as stated in Table 1.

Then the mixtures were diluted with distilled water and the absorbencies were measured at 552, 549 nm for (I), (II) while was measured at 540 nm for (III) and (IV) against a reagent blank prepared in the same manner.

2.5. Procedure for pharmaceutical formulations

2.5.1. For tablets

A accurately weighted quantity of the well mixed powders were dissolved in distilled water except for (I) and (II) which were extracted with methanol (3 ml), then the volumes were completed to the mark with distilled water in 25 ml calibrated flasks, filtered and the assay was completed as under general procedure.

2.5.2. For tavegyl ampoule

Accurate volume of tavegyl vial equivalent to 6.25 mg of clemastine hydrogen fumarate was measured, completed to 50 ml



Figure 6 Continuous variation plot for clemastine hydrogen fumarate, desloratadine $(1.56 \times 10^{-4} \text{ M})$, losartan potassium and moxepril HCl $(3.125 \times 10^{-4} \text{ M})$ with eosin $(1.56 \times 10^{-4} \text{ and } 3.125 \times 10^{-4} \text{ M})$, respectively).

Table 2 Application	of the standard	addition techn	ique to the	spectrophotome	stric determination	of the studied	drugs I–II	with eosin in p	harmaceutical dos	age forms*.	
Tavegyl® tablets				Tavegyl® ampc	oules			Desa® tablets			
Claimed taken (µg/ml)	Authentic added (µg/ml)	Found conc. μg/ml	Recovery (%)	Claimed taken (μg/ml)	Authentic added (µg/ml)	Found conc (µg/ml)	Recovery (%)	Claimed taken (µg/ml)	Authentic added (µg/ml)	Found conc (µg/ml)	Recovery (%)
1.25		1.24	99.26	1.25		1.24	99.26	0.31			
	1.25	1.24	99.26		1.25	1.24	99.26		0.31	0.30 0.31	97.91 99.32
	2.5	2.49	99.49		2.5	2.52	100.62		0.63	0.63	69.66
	3.75	3.79	101.08		3.75	3.72	99.19		0.94	0.96	101.81
	5	4.95	99.04		7.5	7.63	101.72		1.25	1.25	100.07
	6.25	6.24	99.85		8.75	8.75	99.98		1.56	1.55	99.30
	7.5	7.54	100.59		10	9.97	99.66		1.87	1.86	99.49
	8.75	8.75	96.66		11.25	11.13	98.91		2.5	2.51	100.39
Mean			6.66				16.66				100.01
Variance			0.53				0.96				0.79
S.D.			0.73				0.98				0.89
S.E.			0.28				0.37				0.34
* Average of three expe	eriments.										

with double distilled water and the procedure was completed as under general procedure.

2.6. Stoichiometric relationship

Job's method of continuous variations (Rose, 1964) was employed using equimolar $(1.56 \times 10^{-4} \text{ M})$ standard solutions of clemastine hydrogen fumarate, desloratadine and $(3.125 \times 10^{-4} \text{ M})$ of losartan potassium, moxepril HCl with eosin $(1.56 \times 10^{-4} \text{ and } 3.125 \times 10^{-4} \text{ M})$, respectively).

A series of solutions were prepared in which the total volume of drugs and eosin was kept at 6.0 mL then diluted to volume in 10-mL calibrated flask with distilled water following the above mentioned procedure.

3. Results and discussion

The four studied drugs reacted with eosin through an ion-pair salt formation, forming a reddish orange chromophore with λ_{max} at 552, 549 nm for (I), (II) while was measured at 540 nm for (III) and (IV) (Fig. 1).

To optimize the assay parameters, the effects of pH, reaction time, effect of temperature, type, concentration and volume of surfactant, eosin concentration and volume, order of addition of reactants were studied.

3.1. Effect of pH on the ion-pair formations

In order to establish the optimum pH value, different volumes of acetate buffer solutions of different pHs (1.08–6) were examined. The highest absorbance values were obtained at pH 2.8 for drugs (II), (III), (IV) or at pH 3.7 for (I). Furthermore, the amount of buffer added varied from 0.1–2 ml and the optimum volume was found to be 1, 0.2, 0.5 ml for (II), (III) and (IV) and 1.5 ml for (I) to give the highest absorbance values (Fig. 2).

3.2. Effect of type and concentration of surfactant

The effect of surfactants on the absorbance of the solution of the binary complex was examined using various dispersing agents, such as sodium lauryl sulfate, methylcellulose, Tween 80, and brij. Among the surfactants studied, best results were obtained in the presence of methylcellulose.

The optimum results were obtained using 0.5 ml methyl cellulose 0.5% for (I), (III) and (IV) and 0.5 ml of 0.3% for (II).

3.3. Effect of eosin concentration, volume

When various concentrations of eosin were added to the studied drugs (0.05–0.5% w/v), it was found that the ion-pair formation was optimized using 1 ml eosin 0.1% w/v for (III), (IV), and 2 ml for (II) while using 1 ml 0.2% w/v for (I) (Fig. 3).

3.4. Effect of time and temperature

The optimum reaction time was determined by following the color development from ambient temperature 25 ± 5 °C to 70 ± 5 °C. It was found that 5, 10 min at room temperature was optimum for clemastine, moxepril HCl, respectively for

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Losar® tablets				Primox® tablets			
Claimed taken μg/ml)	Authentic added (mg/ml)	Found conc. (µg/ml)	Recovery (%)	Claimed taken (μg/ml)	Authentic added (µg/ml)	Found conc. (µg/ml)	Recovery (%)
				2.5			
		5.05	100.98			2.47	98.88
	5	4.99	99.83		1.25	1.24	99.33
	7.5	7.45	99.31		2.5	2.49	99.78
	10	9.96	99.62		5	4.96	99.11
	12.5	12.45	99.58		8.75	8.71	99.58
	15	15.14	100.91		10	10.08	100.78
	17.5	17.36	99.21		11.25	11.11	98.73
	20	20.16	100.82				
Mean			9.99				99.55
Variance			0.48				0.50
S.D.			0.69				0.71
5.E.			0.26				0.29
^a Average of three exp	beriments.						

Drug	Eosin method		Official or reported methods
Clemastine hydrogen fumarate	Mean \pm R.S.D Variance Student- <i>t</i> -test <i>F</i> -test <i>n</i>	100.24 ± 0.629 0.4 1.23 (1.86) ^a 1.96 (5.14) ^a 7	99.74 ± 0.452 (Rahman and Rahman, 2011) 0.2 - - 3
Desloratadine	Mean ± R.S.D Variance Student- <i>t</i> -test <i>F</i> -test <i>n</i>	$\begin{array}{l} 100.02\pm0.848\\ 0.72\\ 0.536\left(1.77\right)^{a}\\ 1.46\left(3.86\right)^{a}\\ 8\end{array}$	99.76 ± 1.03 (Nahed et al., 2007) 1.06 - 7
Losartan potassium	Mean ± R.S.D Variance Student- <i>t</i> -test <i>F</i> -test <i>n</i>	$\begin{array}{l} 99.89 \pm 0.722 \\ 0.52 \\ 0.524 \left(1.86 \right)^{a} \\ 1.29 \left(5.14 \right)^{a} \\ 7 \end{array}$	99.62 ± 0.823 (Ibrahim, 2005) 0.67 - - 3
Moxepril HCl	Mean ± R.S.D Variance Student- <i>t</i> -test <i>F</i> -test <i>n</i>	$\begin{array}{l} 100.14 \pm 0.751 \\ 0.57 \\ 0.86 (1.74)^{\rm a} \\ 1.28 (3.22)^{\rm a} \\ 9 \end{array}$	99.86 ± 0.66 (Erturk et al., 2003) 0.44 - - 10

 Table 4
 Determination of clemastine hydrogen fumarate, desloratadine, losartan potassium and moxepril HCl by eosin method compared with official or reported methods.

British Pharmacopoeia recommended non aqueous titration for clemastine using 0.1 M perchloric acid with potentiometric determination of the end-point (Rahman and Rahman, 2011).

Spectrophotometric determination of desloratadine, losartan and moxepril through its reaction with NBD-Cl, TCNQ or through derivative spectrophotometry, respectively (Nahed et al., 2007; Ibrahim, 2005; Erturk et al., 2003).

^a The figures in parenthesis are the theoretical values for *t*- and *F*-tests (p < 0.05).

production of maximum absorbance. In case of desloratadine, the maximum increase in absorbance was observed after 10 min at 50 °C then decreased gradually. In the case of losartan potassium, a gradual increase in absorbance was observed till it reached maximum after 5 min at 60 °C as seen in Fig. 4.

3.5. Effect of order of addition of reactants,

The most favorable sequence is drug-eosin-buffer-surfactant for drugs (I), (II) and (III) while drug-eosin-surfactant-buffer for (IV) to attain the highest color intensity and more stability.

There was less than a 1.0% variation in absorbance of all formed complexes during the first 45 min. of measurement and remained stable for at least 1 h for all the studied drugs (Fig. 5).

3.6. Composition of the ion-pair complexes

The composition of the ion-pair was studied by Job's method of continuous variation (Rose, 1964) and was found to be 1:1 for (I), (III) and (IV) while 1:2 for (II) with eosin (Fig. 6).

4. Method validation

Under the described experimental conditions, standard calibration curves for, clemastine hydrogen fumarate, desloratadine, losartan potassium and moxepril HCl with eosin were constructed by plotting absorbance against concentration.

Conformity with Beer's law was evident in the concentration range of the final dilution cited in Table 1. The linear regression equation for each drug was listed in Table 1. The correlation coefficient was 0.9998–0.9999 indicating good linearity.

5. Analytical applications

The proposed method was applied to determine the studied drugs in their pharmaceutical dosage forms. Satisfactory results were obtained. To check the validity of the proposed method, the standard addition technique was applied by adding them to the analyzed pharmaceutical dosage forms.

The recovery of each drug was calculated by comparing the concentration obtained from the spiked mixtures with those of the drug. The results of analysis of the commercial dosage forms and the recovery study are shown in Tables 2 and 3. The results obtained were compared with the official and reported methods (Nahed et al., 2007; Ibrahim, 2005; Erturk et al., 2003; British Pharmacopoeia, 2007). Statistical comparison of the results was performed with regard to accuracy and precision using Student-*t*-test and *F*-ratio at 95% confidence level (Table 4). No significant differences were found between the proposed methods and official or reported methods.

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