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Spectrophotometric Determination of Desloratadine, Fexofenadine HCL, Etodolac, Moexipril HCL and Thiocolchicoside in Pure and Pharmaceutical Formulations

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ABSTRACT

A simple, sensitive and accurate spectrophotometric method was developed for determination of desloratadine (I), fexofenadine HCl (II), etodolac (III), moexipril HCl (IV) and thiocolchicoside (τ). The method depends on oxidation of each of studied drugs with alkaline potassium permanganate where a green colour peaking at 607 nm is produced. The optimization of various experimental conditions was described. Beer's law was obeyed in the range (2.5-25), (0.25-1.125), (0.1-1), (2.5-25) and (2.5-25) µg/ml for drugs (I), (II), (III), (IV) and (τ) respectively. The molar absorptivity (ε), sandell sensitivity, detection (LOD) and quantitation limits (LOQ) are calculated. The procedure was favorably applied for determination of certain pharmaceutical dosage forms containing the studied drugs. The obtained results were compared with the official and reported methods. There were no significant differences between the proposed and reference methods.

Key words: Desloratadine, Fexofenadine HCl, Etodolac, Moexipril HCl, Thiocolchicoside, potassium permanganate.

INTRODUCTION

Desloratadine (I), an orally active major metabolite of the nonsedating antihistamine loratadine, is a selective, potent, peripheral H_1 receptor antagonist[1]. Very few visible spectrophotometric methods have been described for determination of Desloratadine[2,3]. To analyze this drug in tablets, reversed-phase column liquid chromatography[4-7] and gas chromatography[8] techniques have also been described.

Fexofenadine HCl (II) is a potent long-acting histamine H_1-receptor antagonist[9]. Few analytical methods have been reported for its determination including spectrophotometric methods[10-14] and high performance liquid chromatography (HPLC)[10, 15-20].

Etodolac (III) is a non-steroidal antiinflamatory drug[21]. There are very few reported methods for the determination of etodolac in biological fluids, pharmaceutical formulations and in presence of its enantiomer. Of those studies reported, the techniques used include HPLC [22-25], in addition to spectrofluorimetric[26] and spectrophotometric methods[26-29].

Moexipril hydrochloride (IV) is a new potent orally active non-sulfhydryl angiotensin-converting enzyme inhibitor which is used for the treatment of hypertension and congestive heart failure[30]. A few analytical methods have been developed for the determination of moexipril, including derivative spectrophotometric[31], spectrophotometric methods[32]. RP-HPLC methods have been developed for the simultaneous determination of moexipril[32-34].

Thiocolchicoside (τ) is a potent muscle relaxant[35]. Analytical methods published for the determination of thiocolchicoside to date, are either

non-specific radioimmunoassay techniques[36,37], HPLC [38], TLC [39]. A survey of the literature reveals that there is No spectrophotometric method reported for determination of thiocolchicoside.

This paper represents a simple, accurate and sensitive method for determination of desloratadine (I), fexofenadine HCl (II), etodolac (III), moexipril hydrochloride (IV) and thiocolchicoside (τ) either in pure form or in its pharmaceutical formulations. In addition the proposed method is not susceptible to interference from common excepients.

EXPERIMENTAL

Apparatus

A Shimadzu recording spectrophotometric UV 260 equipment with 10 mm matched quartz cells.

Materials and reagents

Chemicals of analytical grade and double distilled water were used throughout the work. Desloratadine, Desa® tablets labelled to contain 5 mg desloratadine per tablet (Minapharm Company for pharmaceuticals, Egypt).

Fexofenadine HCl, Rapido® capsules labelled to contain 120 mg fexofenodine HCl per capsule (Sedico Company for Pharmaceuticals, Egypt) and fastel® tablets labelled to contain 120 mg fexofenadine HCl per tablet (Aventis Company for pharmaceuticals, Egypt).

Etodolac, Etodolac® tablets labelled to contain 300 mg etodolac per tablet (European Egyptian Pharmaceutical Industry, Egypt).

Moexipril hydrochloride, Primox® tablets labelled to contain 15 mg moexipril HCl per tablet (Minapharm Company for pharmaceuticals, Egypt).

Thiocolchicoside, Relaxine® tablets labelled to contain 4 mg thiocolchicoside per tablet (Memphis Company for pharmaceuticals, Egypt).

Sodium hydroxide, (El-Nasr chemical company, Egypt)

Potassium permanganate, (El-Nasr chemical company, Egypt). 0.0726 % W/V aqueous solution.

Standard solutions

Preparation of moxepril HCl and thiocolchicoside standard solutions,

Stock working solution was prepared to contain 1 mg/ml, dissolved in distilled water and completed to the mark with the same solvent.

Preparation of fexofenadine HCl, etodolac and desloratadine standard solutions,

Stock working solutions was prepared to contain 1 mg/ml, dissolved in least amount of methanol (3 ml) then the volume was completed with double distilled water for fexofenadine HCl, etodolac or dissolved in acetonitrile for desloratadine.

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

General procedures

To different aliquots of standard solutions [equivalent to (0.025-0.25), (0.005-0.01125), (0.0.001-.01), (.025-0.25) and (0.05-0.25) mg of (I), (II), (III), (IV)and (t), specific volumes of NaOH solution of certain molarities were added followed by specified amounts of $KMnO_4$ (0.0726 % W/V) as stated in (Table 1).

The contents were left for specified times. Then the mixtures were diluted with distilled water and the absorbance was measured at 607 nm for all the studied drugs against a reagent blank prepared in the same manner.

Procedure for pharmaceutical formulations, For tablets

A accurately weighted quantity of the well mixed powders were dissolved in the solvents mentioned before except for I, IV and V were extracted with acetonitrile, then the volumes were completed to the mark with the same solvents in 25 ml calibrated flasks, filtered and the assay was completed as under general procedure.

For Rapido capsules

An accurately weighted amount of the mixed contents of 10 capsules equivalent to 12.5 mg distilled water extracted with methanol (3ml), and then completed to 25 ml with distilled water,

filtered and the assay was completed as under general procedure.

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

RESULTS AND DISCUSSION

The reaction between the selected drugs and $KMnO_4$ in alkaline medium yields a green color due to the formation of manganate ion (MnO_4^{2-}) with λ_{max} at 607 nm, Fig. 1.

At this wavelength, all the parameters affecting the development and stability of the reaction product were optimized.

Investigation of assay parameters

Effect of time

The optimum time for analysis of the studied drugs using $KMnO_4$ was 15 min. for (I), (III), (t) and 20 min. for (II) and (IV). The colour was stable for 25 min for (II), (III), 20 min. for (I), (IV) while remained stable for more than one hour and half in case of (t) Fig. 2.

Effect of reagent volume

The optimum volume of 0.0726 % $KMnO_4$ was 4, 3.5 or 2.5 ml in case of (I), (II), (III) and 3 ml for (IV) and (τ) Fig. 3.

Effect of sodium hydroxide concentration

1 ml of 0.3 M sodium hydroxide gave maximum colour intensity in case of (II), (III), 1.5, 2 ml for (V) and (I) while using 2 ml of 0.2 M sodium hydroxide for (IV).

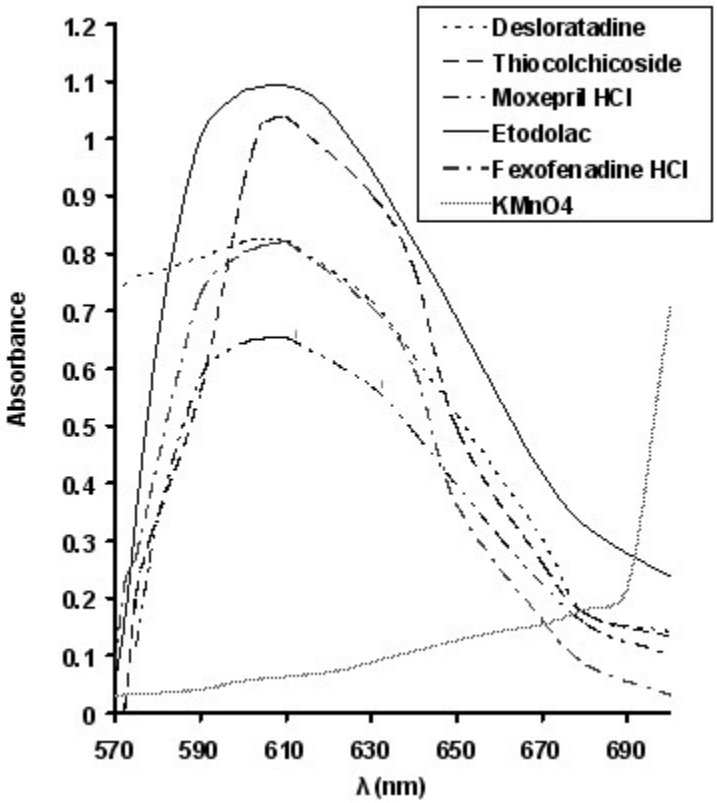

Fig. 1: Absorption curves of desloratadine (25), fexofenadine HCl (1.125), etodolac (1), moxepril HCl (17.5), thiocolchicoside (25) µg ml^{-1} with $KMnO_4$

Table 1: Characteristic parameters for the reaction of studied drugs with $KMnO_4$

Parameter	Desloratadine	Fexofenadine HCl	Etodolac	Moexipril HCl	Thiocolchicoside
λ max (nm)	607	607	607	607	607
Beers law limits (ig/ml)	2.5-25	0.25-1.125	0.1-1	2.5-25	5-25
Vol and NaOH molarity	2ml-0.3M	1ml-0.3M	1ml-0.3M	2ml-0.2M	1.5ml-0.3M
Vol and conc of $KMnO_4$	4ml-0.0726%	3.5ml-0.0726%	2.5ml-0.0726%	3ml-0.0726%	3ml-0.0726%
Time (min)	15	20	15	20	15
Regression equation**					
Slope (b)	0.0286	0.5863	0.9923	0.04	0.0398
Intercept (a)	0.031	0.1322	0.1199	-0.0333	0.0386
Correlation coefficient (r^2)	0.9999	0.9999	0.9998	0.9998	0.9998
LOD µg/ml	0.7	0.51	0.78	0.96	0.55
LOQ µg/ml	2.33	1.72	2.60	3.19	1.85
Sandell sensitivity $\mu g.cm^{-2}$	0.03	0.001	0.001	0.028	0.022
ε ($\times 10^5$) $L.mol^{-1}.cm^{-1}$	0.10	4.5	3.6	0.19	0.24

*Average of three experiments

**A=a + bc

Table 2: Application of the standard addition technique to the spectrophotometric determination of the studied drugs I-IIwith $KMnO_4$ in pharmaceutical dosage forms*

Desa® tablets				Fastel® tablets				Rapido® capsules			
Claimed taken Mg/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 %**
2.5		2.50	100.00	0.25	-	0.25	100.15	0.25		0.25	100.84
	2.5	2.50	100.00		0.125	0.13	100.69		0.25	0.25	100.85
	5	5.02	100.35		0.25	0.254	101.52		0.375	0.37	99.53
	10	10.05	100.52		0.375	0.38	100.88		0.5	0.49	99.22
	12.5	12.33	98.60		0.5	0.50	100.22		0.625	0.62	99.02
	15	14.88	99.18		0.625	0.62	99.28		1	0.99	99.42
	17.5	17.57	100.40								
	20	19.81	99.04								
	22.5	22.53	100.16								
	25	25.40	101.61								
Mean			99.78				100.52				99.61
Variance			0.54				0.69				0.52
S.D.			0.73				0.83				0.72
S.E.			0.24				0.37				0.29

*Average of three experiments

Table 3: Application of the standard addition technique to the spectrophotometric determination of the studied drugs (III-V) with KMnO4 in pharmaceutical dosage forms*

Etodolac® tablets				Primox® tablets				Relax® capsules			
Claimed taken Mg/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 %
0.1	---	0.09	96.85	5							
	---	5.08	101.5	5							
		4.95	99.09								
	0.2	0.19	99.31		5	5.08	101.5		2.5	2.49	99.69
	0.3	0.29	98.79		7.5	7.47	99.66		5	4.98	99.59
	0.4	0.39	99.29		10	10.05	100.5		7.5	7.47	99.56
	0.5	0.49	98.58		12.5	12.5	100		10	10.18	101.81
	0.6	0.60	100.12		15	14.97	99.83		12.5	12.54	100.34
					20	19.9	99.5		15	14.97	99.87
									17.5	17.42	99.53
									20	20.01	100.02
									22.5	22.29	99.07
Mean			99.22				100.17				99.94
Variance			0.35				0.55				0.61
S.D.			0.59				0.74				0.78
S.E.			0.27				0.33				0.26

*Average of three experiments

Effect of diluting solvent

Several organic solvents such as methanol, ethanol, distilled water, acetone and acetonitrile were investigated. Distilled water was found to be the most appropriate solvent for all the investigated drugs to give the highest absorbance and more stability since $KMnO_4$ oxidizes other solvents such as methanol and ethanol giving manganate ion.

Effect of interfering species

Experiments showed that there was no interference from the additives and excepients e.g. lactose, glucose, fructose, magnesium stearate and starch.

Effect of order of addition

The sequence of addition of reactants was very important. Addition of drug followed by NaOH and then KMnO4 was recommended to obtain stable, high color intensity.

Method validation

Under the described experimental conditions, standard calibration curves for desloratadine, fexofenadine HCl , etodolac , moxepril HCl and thiocolchicoside with $KMnO_4$ were constructed by plotting absorbance against concentration.

Table 4: Determination of desloratadine, fexofenadine HCl, etodolac, moxepril HCl and thiocolchicoside by $KMnO_4$ method compared with reported or reference methods

Drug	$KMnO_4$ method		Reference or reported method
Desloratadine	Mean ±R.S.D	99.81± 0.699	99.76 ± 1.03[3]
	Variance	0.49	1.06
	Student-t-test	0.12 (2.14)*	-
	f-test	2.16 (3.58)*	-
	n	9	7
Fexofenadine HCl	Mean ±R.S.D	100.04 ± 0.489	100 ± 0.85[14]
	Variance	0.24	0.72
	Student-t-test	0.11 (2.2)*	-
	f-test	3 (4.12)*	-
	n	8	5
Etodolac	Mean ±R.S.D	100.12 ±0.685	100.48 ± 0.846[26]
	Variance	0.47	0.72
	Student-t-test	0.814(2.23)*	-
	f-test	1.53(4.53)*	-
	n	7	5
moxepril HCl	Mean ±R.S.D	99.87 ± 0.849	99.86±0.66[31]
	Variance	0.72	0.44
	Student-t-test	0.03 (2.13)*	-
	f-test	1.64(3.37)*	-
	n	7	10
Thiocolchicoside	Mean ±R.S.D	100.44±0.52	100.16±0.38[39]
	Variance	0.27	0.14
	Student-t-test	1.05(1.78)*	-
	f-test	1.87(2.81)*	-
	n	9	5

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

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.

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

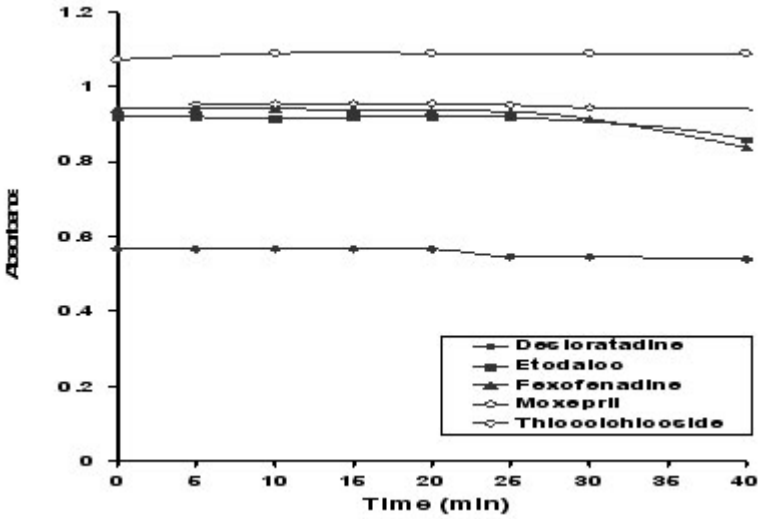

Fig. 2: Stability of the reaction product formed between 0.0726 % w/v $KMnO_4$ and: 17.5 µg ml^{-1} desloratadine, 1.375µg ml^{-1}fexofenadine HCl, 0.8 µg ml^{-1}etodolac, 25 µg ml^{-1} moxepril HCl , 25 µg ml^{-1}thiocolchicoside

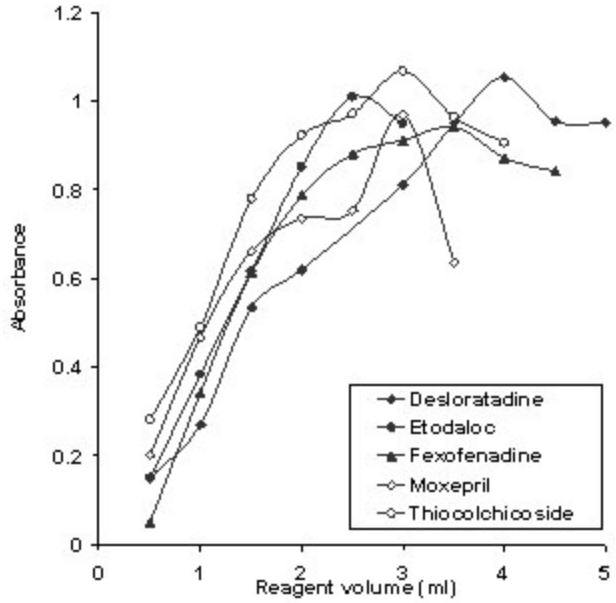

Fig. 3. Effect of volume of 0.0726 % w/v $KMnO_4$ on absorbance of 25 µg ml^{-1} desloratadine, 1.375µg ml^{-1}fexofenadine HCl, 1µg ml^{-1} etodolac, 25 µg ml^{-1} moxepril HCl, 25 µg ml^{-1}thiocolchicoside

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 as shown in (Tables 2, 3). The results obtained were compared with the reported methods [3, 14, 26, 31, and 39]. No significant differences were found between the proposed methods and reference methods. 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).

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