L A T V I J A S Ķ Ī M I J A S Ž U R N Ā L S
2005, Nr. 4, 3.—269. lpp.

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SPECTROPHOTOMETRIC DETERMINATION OF BENZYDAMINE AND CHLORPHENOXAMINE HYDROCHLORIDES IN BULK AND PHARMACEUTICAL PREPARATIONS USING SULFOPHTHALEIN DYES

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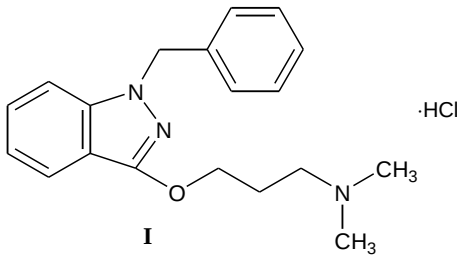
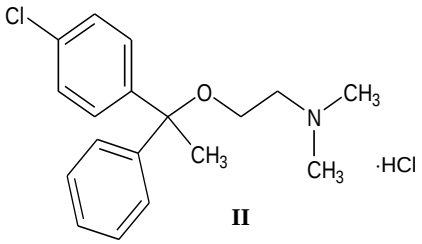
Benzydamine hydrochloride (BZH), **I** is hydrochloride of N,N-dimethyl-3-[1-phenylmethyl-1H-indazol-3-yl]oxy-1-propanamine (1-benzyl-3-(3-dimemethylaminopropoxy-1H-indazole, also named 1-benzyl-1H-indazol-3-yl 3-dimethylaminopropyl ether). It is a white crystalline powder, readily soluble in water, freely soluble in ethanol (95%), and in chloroform, practically insoluble in ether.



I

Benzydamine hydrochloride is a non-steroidal anti-inflammatory agent with analgesic, anti-exudative and local anesthetic activity. It is used topically on the skin in concentration of 3—5% in case of painful musculoskeletal and soft tissue disorder, also used as mouth wash or spray in concentration of 0.15% for relief of inflammatory conditions of mouth and throat.

Chlorphenoxamine hydrochloride (**II**) is hydrochloride of 2-[1-(4-chlorophenyl)-1-phenylethoxy]-N,N-dimethylethanamine (2-[(*p*-chloro-α-methyl-α-phenylbenzyl)oxy]-N,N-dimethylethylamine, also named β-dimethylaminoethyl (*p*-chloro-α-methyl-benzhydryl) ether).



II

Chlorphenoxamine hydrochloride is a white crystalline powder, readily soluble in water, alcohol, and its aqueous solutions are stable. Chlorphenoxamine

hydrochloride possesses antimuscarinic and antihistaminic properties. It has been used in cases of nausea, vomiting and vertigo, and was formerly used in the symptomatic treatment of parkinsonism. It has also been used in hypersensitivity reaction. Chlorphenoxamine hydrochloride is not official in either the USP XXIV or the BP 2002.

A few methods for the analysis of compounds **I** and **II** have been reported, including spectroscopic methods based on formation of coloured complexes [1—3]; other spectrophotometric methods that do not involve formation of coloured complexes [4—6]; IR spectroscopy [7], atomic absorption spectroscopy [8], cation exchange [9], high-performance liquid [10, 11] and thin-layer chromatography [12], potentiometry [13], polarography [14].

The aim of the present work is to develop three simple, rapid and sensitive extraction spectrophotometric methods for the assay of benzydamine hydrochloride and chlorphenoxamine hydrochloride. The methods are based on formation of ion-pair complexes of compounds **I** and **II** with dyestuffs such as bromophenol blue, bromocresol green, and bromocresol purple and subsequent extraction into chloroform under reaction conditions used.

EXPERIMENTAL

Apparatus. All the absorption spectra were taken using *Shimadzu* (UV-Visible 1601) spectrophotometer (Japan) with scanning speed of 400 nm/min, and band-width of 2.0 nm equipped with 10 mm matched quartz cells. The pH values of buffer solutions were measured using *Jenway* pH-meter (combined electrode).

Reagents. All the chemicals used were of analytical or pharmaceutical grade, and water was twice-distilled. Pure benzydamine hydrochloride (BZH) (Tantum and Tantum rose) and chlorphenoxamine hydrochloride (CPH) (Allergics and Emeral), were obtained from *Egyptian International Pharmaceutical Industrial Company* (*EPICO).* Stock solutions of pure benzydamine hydrochloride and chlorphenoxamine hydrochloride (100 $\mu g \cdot ml^{-1}$) were prepared by dissolving 10 mg of pure drugs in water and filling up to the mark in a 100 ml volumetric flask with water. Working solutions of lower concentrations were prepared by serial dilution.

Solutions of 5.0×10^{-4} $mol \cdot l^{-1}$ of bromocresol green (BCG), bromocresol purple (BCP) and bromophenol blue (BPB) (*Aldrich*) were prepared by dissolving an accurate weight of the dyes in few drops of acetone and then filling up to the mark with water in 100 ml volumetric flasks separately. A series of buffer solutions of CH_3COONa–HCl (pH 1.99—5.2) and CH_3COONa–CH_3COOH (pH 3.42—5.89), and NaH_2PO_4–Na_2HPO_4 (pH 6.0—8.0) were prepared by the following standard methods.

General procedures

Benzydamine hydrochloride (I)

Aliquot of compound **I** solution containing up to 2.0—28 $\mu g \cdot ml^{-1}$ of the drug was transferred into a series of 50 ml separating funnels, 2.0 ml of bromophenol blue, bromocresol green and bromocresol purple solutions (5.0×10^{-4} $mol \cdot l^{-1}$) were added followed by acetate buffer solution of pH = 3.1 (2.0 ml) when using bromophenol blue, pH = 3.3 (3.0 ml) when using bromocresol green and pH = 3.2 (2.0 ml) when using bromocresol purple. The formed ion pairs were extracted with 5.0 ml of $CHCl_3$ under shaking for 3.0 min. The two phases were allowed to separate and the chloroform layer was dried by running through anhydrous sodium sulphate. The absorbance of the extracted solutions was measured at the corresponding λ_{max} against extracted blank solution prepared similarly but without addition of the drug under study.

Chlorphenoxamine hydrochloride (II)

Aliquot of compound (**II**) solution containing up to 2.0—26 $\mu g \cdot ml^{-1}$ of the drug was transferred into a series of 50 ml separating funnels, 2.0 ml of bromophenol blue, bromocresol green or bromocresol purple solutions (5.0×10^{-4} $mol \cdot l^{-1}$) were added followed by acetate buffer solution of pH = 3.1 (2.5 ml) when using bromophenol blue, pH = 3.8 (2.0 ml) when using bromocresol green and pH = 3.2 (2.0 ml) when using bromocresol purple. The formed ion pairs were extracted with 5.0 ml of $CHCl_3$ under shaking for 3.0 min. The two phases were allowed to

separate and the chloroform layer was dried by running through anhydrous sodium sulphate. The absorbance of the extracted solutions was measured at the corresponding λ_{max} against extracted blank solution prepared similarly but without addition of the drug under study.

A calibration graph was constructed for each drug and the concentration of unknown samples was deduced by using of the calibration graph.

Procedure for Dosage Forms

Bulk samples were prepared by weighing and pulverizing 20 tablets or capsules, or sachets and finding the average weight of each one. An amount of the sample equivalent to about 10 mg of the drug was weighed and dissolved in 100 ml of water, shaken well and filtered through a sintered glass crucible (G_4). A 1.0 ml aliquot of the test solution was diluted to 100 ml in a volumetric flask. The drug content in this solution was obtained by applying the general procedure to aliquot containing 4.0 $\mu g \cdot ml^{-1}$ of the drug as described above and then followed by the standard addition method to confirm the obtained results.

RESULTS AND DISCUSSION

The nitrogenous drugs are present in positively charged protonated forms and anionic dyes of sulfophthalein group are present mainly in anionic form at pH ≥ 3.0. So when treated with an acid dye such as bromophenol blue, bromocresol green or bromocresol purple in acetate buffer solutions at pH ranged from 3.1 to 3.8, a yellow ion-pair complex which is extracted with chloroform is formed. The absorption spectra of the ion-pair complexes formed between benzydamine hydrochloride, chlorphenoxamine hydrochloride and each of sulfophthalein dyes (bromophenol blue, bromocresol green and bromocresol purple), were measured at 320—600 nm against a blank solution and are shown in Fig. 1, 2. The developed methods were applied to pharmaceutical preparations and the obtained results were evaluated statistically.

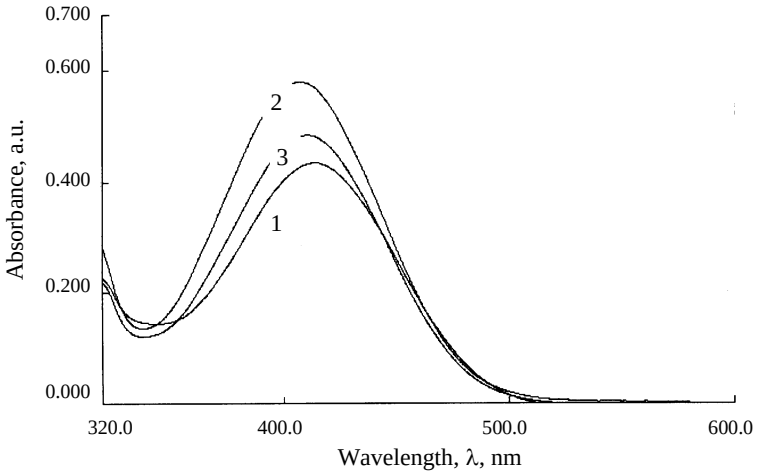


Fig. 1. Absorption spectra of benzydamine hydrochloride solution (4.0 $\mu g \cdot ml^{-1}$) with dyestuff: *1* — bromophenol blue, *2* — bromocresol green, *3* — bromocresol purple

Optimization of the reaction conditions

The optimization of the reaction conditions of the proposed methods was carefully studied to achieve the complete reaction, highest sensitivity and maximum absorbance. Reaction conditions of formation of the ion-pair complexes were found by preliminary experiments varying pH of buffer solutions, nature of organic solvent, concentration of the sulfophthalein due and shaking time for the extraction of ion-pair complexes.

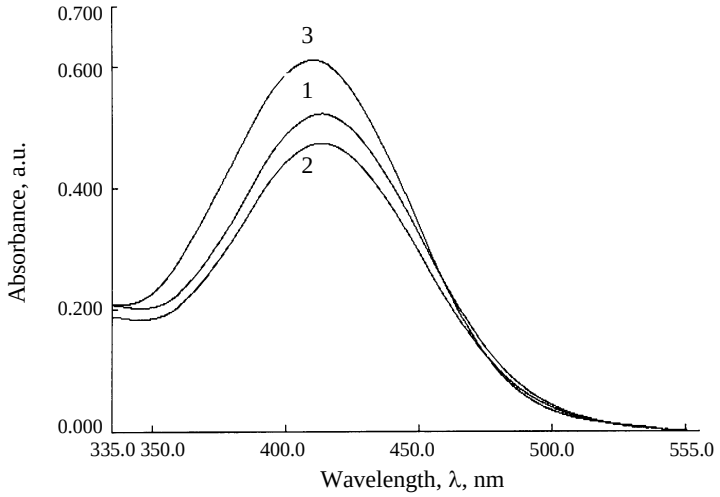


Fig. 2. Absorption spectra of chlorphenoxamine hydrochloride solution (4.0 μg·ml^{-1}) with dyestuff: *1* — bromophenol blue, *2* — bromocresol green, *3* — bromocresol purple

Effect of pH

The effect of pH was studied by extracting the coloured complex in the presence of various buffer solutions such as KCl–HCl (pH = 1.0—2.2), CH_3COONa–HCl (pH = 1.99—6.0), CH_3COONa–CH_3COOH (pH = 3.7—5.8) and potassium hydrogen phthalate – HCl (pH = 2.2—3.6). The maximum colour intensity was developed and constant absorbance values were found in CH_3COONa–HCl buffer solutions (see Fig. 3). It is evident that the absorbance of complexes with benzydamine hydrochloride was found to be maximal at pH 3.1, 3.3 and 3.2 using bromophenol blue, bromocresol green and bromocresol purple, respectively. As follows from Fig. 4, the absorbance of complexes with chlorphenoxamine hydrochloride is maximal at pH 3.1, 3.8 and 3.2 with bromophenol blue, bromocresol green and bromocresol purple, respectively. The optimum amount of buffer solution added to the aqueous layer of total volume of 5.0 ml was found to be 2.0 ml in case of benzydamine hydrochloride with bromophenol blue and bromocresol purple, and 3.0 ml with bromocresol green; 2.5 ml in case of chlorphenoxamine hydrochloride with bromophenol blue and 2.0 ml in case of chlorphenoxamine hydrochloride with bromocresol green and bromocresol purple that gave marginally the best results.

Effect of the extracting solvent nature

A number of organic solvents such as chloroform, dichloromethane, carbon tetrachloride, benzene and toluene were examined for extraction of the ion-pair complexes in order to provide an applicable extraction procedure. Chloroform was preferred for its selective extraction of ion-pair complexes from the aqueous solution, in addition, the reagents were not extracted in this solvent. Reproducible absorbance readings were obtained after a single extraction with 5.0 ml of chloroform. The overall extraction efficiency was 99.8%. Repeated extraction did not show any increase in the recovery percent.

Effect of shaking time

Shaking time of 1.0—5.0 min provided a constant absorbance and hence, time of 3.0 min was chosen as optimum shaking time throughout the experiments. The ion-pair complexes were quantitatively recovered in one ex-

traction only and were also stable for at least 12 h. Although the ion-pair complexes were formed instantaneously, constant absorbance readings were obtained after not less than 5.0 min of standing at room temperature (25±2 °C).

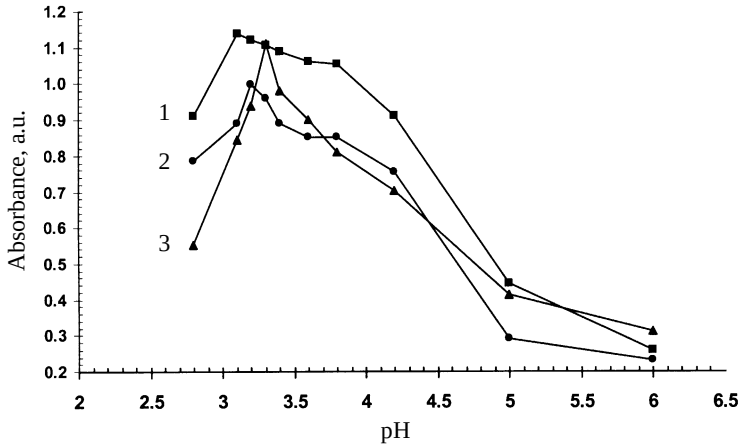


Fig. 3. Effect of pH on the absorbance of benzydamine hydrochloride using 5.0×10^{-4} mol·l^{-1} solutions of: *1* — bromophenol blue, *2* — bromocresol purple, *3* — bromocresol green

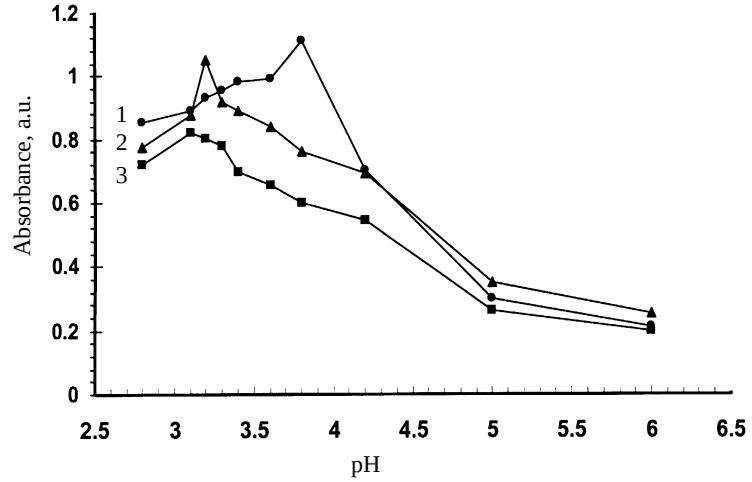


Fig. 4. Effect of pH on the absorbance of chlorphenoxamine hydrochloride using 5.0×10^{-4} mol·l^{-1} solutions of: *1* — bromocresol green, *2* — bromocresol purple, *3* — bromophenol blue

Effect of reagent concentration

The effect of the dye concentration on the intensity of the colour developed at the selected wavelength and constant drug concentration was examined using different amounts (0.5—5.0 ml) of 5.0×10^{-4} mol·l^{-1} solution of reagents. As can be seen in Fig. 5, 6, the maximum absorbance in each case, was found with 2.0 ml of 5.0×10^{-4} mol·l^{-1} solution of the dyestuff, beyond which the absorbance was decreased. Therefore 2.0 ml of each dyestuff were chosen for ion pair formation throughout the experiments.

Effect of sequence of addition

Although the sequence of mixing of the reaction components is not a fundamental factor, the most favourable sequence is *drug–reagent–buffer–*

chloroform for the highest and stable absorbance. The complexes obtained using this sequence of addition remain stable at least for 12 h.

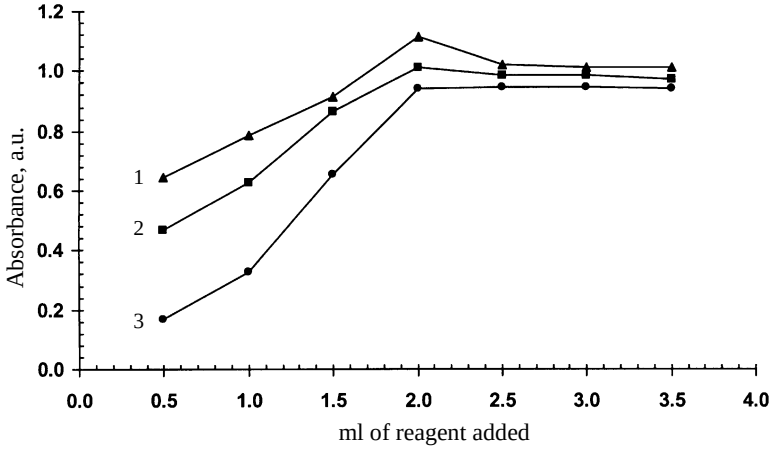


Fig. 5. Effect of reagent concentration on the absorbance of benzydamine hydrochloride using 5.0×10^{-4} mol·l^{-1} solutions of sulfophthalein dyes: *1* — bromocresol green, *2* — bromocresol purple, *3* — bromophenol blue

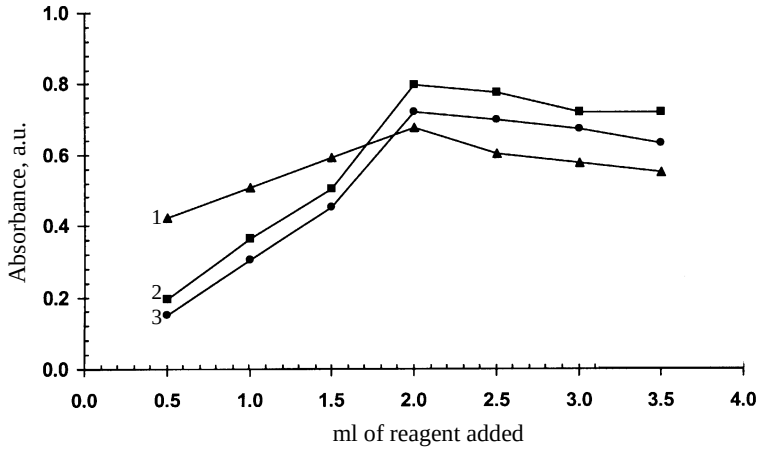


Fig. 6. Effect of reagent concentration on the absorbance of chlorphenoxamine hydrochloride using 5.0×10^{-4} mol·l^{-1} solutions of sulfophthalein dyes: *1* — bromocresol purple, *2* — bromocresol green, *3* — bromophenol blue

Composition of ion pairs

In order to establish molar ratio between benzydamine hydrochloride or chlorphenoxamine hydrochloride, on one side and dyestuff used on the other, Job's method of continuous variation was applied. In this method, 5.0×10^{-4} mol·l^{-1} solutions of drug and dyestuff were mixed in varying volume ratio in such a way that the total volume of each mixture was the same. The absorbance of each solution was measured and plotted against the mole fraction of the drug. This procedure showed that 1:1 complex was formed through the electrostatic attraction between the positively charged BZH^+, CPH^+ ions and negatively charged BPB^-, BCG^- and BCP^- ions. The extraction equilibrium can be represented as follows:

$$BZH^+_{aq} + D^-_{aq} \rightleftarrows BZH^+D^-_{aq} \rightleftarrows BZH^+D^-_{org},$$

where BZH^+ and D^- represent the protonated benzydamine hydrochloride and the anion of the dye, respectively, and the subscript "aq" and "org" refer to the aqueous and organic phases, respectively. In a similar way, chlorphenoxamine hydrochloride reacts with the dyestuff. Stability constants (–log *K*), were calculated and recorded in Table 1 applying the data obtained from the continuous variation method [15].

Table 1

Quantitative parameters, results of statistical analysis of calibration graphs and analytical data in the determination of benzydamine hydrochloride and chlorphenoxamine hydrochloride by bromophenol blue, bromocresol green and bromocresol purple

Parameter	Benzydamine hydrochloride			Chlorphenoxamine hydrochloride		
	BPB	BCG	BCP	BPB	BCG	BCP
pH	3.1	3.3	3.2	3.1	3.8	3.2
λ_{max}, nm	409	408	407	412	412	414
Stability, h	12	12	16	24	12	12
Beer's law validates limits, $\mu g \cdot ml^{-1}$	2—28	1—26	1—28	1—22	1—28	1—29
Ringbom concentration, $\mu g \cdot ml^{-1}$	2—24	2—22	2—24	2—20	2—24	2—26
Molar absorptivity, $l \cdot mol^{-1} \cdot cm^{-1} \times 10^4$	3.60	3.70	3.86	5.03	4.09	4.19
Sandell's sensitivity	0.0096	0.0093	0.0089	0.0068	0.0083	0.0081
Detection limits, $\mu g \cdot ml^{-1}$	0.0310	0.0190	0.0225	0.0250	0.0130	0.0204
Quantification limits, $\mu g \cdot ml^{-1}$	0.0700	0.0350	0.0750	0.0550	0.0690	0.0660
Regression equation[a]						
Slope	0.1045	0.1145	0.1074	0.1149	0.1087	0.1160
Intercept	0.0061	0.1112	0.0501	–0.0077	0.0716	0.0550
Relative standard deviation of slope	0.0021	0.0093	0.0022	0.0016	0.0057	0.0063
Relative standard deviation of intercept	0.0011	0.0020	0.0019	0.0025	0.0042	0.0079
Correlation coefficient, *r*	0.9985	0.9986	0.9975	0.9994	0.9989	0.9986
Relative standard deviation, %[b]	0.5612	0.5425	0.9016	0.9316	0.5755	0.5817
Range of error	0.5886	0.5689	0.9457	0.9772	0.6036	0.6115

[a] $A = a + bC$ (where C stands for the concentration of drug, $\mu g \cdot ml^{-1}$).
[b] average of six determinations.

Quantification

The Beer–Lambert law limits, molar absorptivity, Sandell sensitivity, regression equations and correlation coefficients obtained by linear least-squares treatment of the results are given in the Table 1. The detection and quantification limits were calculated from the standard deviation of the absorbance measurements obtained from a series of 13 blank solutions for each procedure. The limits of detection (k = 3.0) and of quantification (k = 10) were established according to the IUPAC definitions [16].

In order to determine the accuracy and precision of the proposed methods, solutions containing three different concentrations of benzydamine hydro-

chloride and chlorphenoxamine hydrochloride were prepared and analysed in six replicates. The analytical results obtained from this investigation are summarized in Table 2. The percentage standard deviation (≤ 0.9316) and the percentage range of the error at 95% confidence level (≤ 0.9457) can be considered as satisfactory. The performance of the methods was assessed by calculating the *t*- and *F*-values compared with the official method [17], and reported methods [2]. The mean values were obtained in Student's *t*- and *F*-tests at the 95% confidence level for five degrees of freedom [18]. The results show that the calculated *t*- and *F*-values did not exceed the theoretical ones.

Table 2

Accuracy and precision of the proposed methods

Ion pair	Amount of the drug		Recovery, %	RSD[b], %	Relative error, %	Confidence limits[c]
	Taken, $\mu g \cdot ml^{-1}$	Found[a], $\mu g \cdot ml^{-1}$				
BZH–BPB	2.0	2.05	102.50	1.5622	1.6390	2.05±0.033
	4.0	3.96	99.00	1.4421	1.5130	3.96±0.059
	6.0	6.04	100.66	1.3290	1.3943	6.04±0.084
BZH–BCG	2.0	1.97	98.50	0.9221	0.9674	1.97±0.019
	4.0	3.88	97.00	1.2200	1.2590	3.88±0.049
	6.0	5.86	97.67	1.0900	1.1436	5.86±0.067
BZH–BCP	2.0	2.02	101.00	1.3516	1.4180	2.02±0.028
	4.0	3.98	99.50	0.9548	1.0017	3.98±0.039
	6.0	5.95	99.10	0.3214	0.3372	5.95±0.020
CPH–BPB	2.0	2.03	101.50	0.9431	0.9894	2.03±0.020
	4.0	4.04	101.00	0.5223	0.5479	4.04±0.022
	6.0	5.98	99.66	0.6972	0.7315	5.98±0.043
CPH–BCG	2.0	1.99	99.50	1.5500	1.6262	1.99±0.032
	4.0	4.04	101.00	1.2400	1.3010	4.04±0.052
	6.0	6.20	103.30	0.5670	0.5948	6.20±0.036
CPH–BCP	2.0	2.01	100.50	1.0330	1.0838	2.01±0.021
	4.0	4.10	102.50	0.7666	0.8043	4.10±0.032
	6.0	5.85	97.500	1.1630	1.2202	5.85±0.071

[a] average of six determinations;
[b] relative standard deviation for six determinations;
[c] 95% confidence limits and five degrees of freedom.

Analytical Applications

The proposed methods were successfully applied to determine benzydamine hydrochloride and chlorphenoxamine hydrochloride in dosage forms using standard addition method in which the variable amounts of the pure drug were added to the previously analyzed portions of pharmaceutical dosage forms. Results are shown in Table 3 and confirm that the proposed methods are not liable to interference by tablet filters usually used with the drugs. Therefore, the methods could be used easily for the routine analysis of pure drugs and their dosage forms. The proposed procedures were applied to various dosage forms, viz., tablets, capsules and sachets. The results are recorded in Table 4, and

compared statistically with the official method in the BP [17], and the reported methods [2].

Table 3

Results of determination of benzydamine hydrochloride (I) and chlorphenoxamine hydrochloride (II) in pharmaceutical formulations applying standard addition technique

Pharmaceutical formulations analyzed	Content of drug, mg	Taken, $\mu g \cdot ml^{-1}$	Added, $\mu g \cdot ml^{-1}$	Found[a] using the reagent, $\mu g \cdot ml^{-1}$		
				BPB	BCG	BCP
Tantum	3.0 mg of **I**	4.0	0.0	4.05	4.01	4.09
			2.0	6.10	5.80	5.93
			3.0	6.90	6.85	7.07
			5.0	8.90	8.95	8.82
Sachets	500 mg of **I**	4.0	0.0	4.02	4.01	4.02
Tantum Rose			4.0	8.20	8.02	8.01
			7.0	10.78	11.10	10.95
			8.0	12.18	11.90	12.03
Emeral	30.0 mg of **II**	4.0	0.0	4.01	4.01	4.03
			3.0	6.95	7.02	7.20
			5.0	8.85	8.90	8.88
			7.0	10.86	11.05	11.01
Allerjex	30.0 mg of **II**	4.0	0.0	3.95	3.90	4.03
			1.0	5.02	5.07	4.95
			5.0	8.91	8.95	8.90
			8.0	11.90	12.10	12.09

[a] average of six determinations.

Table 4

Determination of studied drugs in dosage forms by the proposed and official methods

Formulations	Labeled, mg/tablet	Proposed methods									Official method
		Recovery[a], %			*t*-test			*F*-value			Recovery, %
		BPB	BCG	BCP	BPB	BCG	BCP	BPB	BCG	BCP	
Tantum	3.0	99.33	100.50	98.30	1.003	0.461	0.276	3.010	2.910	2.130	101.60
Tantum rose	500	99.99	102.50	99.00	1.285	0.281	0.577	1.646	3.010	2.880	100.50
Emeral	30	102.50	98.10	98.50	0.505	0.929	0.929	2.630	1.630	1.610	100.50
Allerjex	20	101.90	102.30	101.60	0.254	1.012	0.751	1.241	1.890	2.070	99.30

[a] average of six independent analysis.

The percentage recoveries were found to be close to 100% (Table 4). The high percentage recoveries indicate that there is no interference from ingredients and excipients that might be found in different formulations. Consequently, the

methods are simple, rapid and stability indicating assay. The results obtained from the proposed procedures were compared with those obtained using official and reported methods. The accuracy (*t*-value) and the assessment of the precision (*F*-test) for six degrees of freedom and 95% confidence level were calculated and the results indicated that there is no significant difference between the characteristics of the proposed methods and those of the official BP or reported methods (Table 4). Moreover, the proposed methods provide more stable results (at least for 12 h) than the official method.

Conclusions. It is clear that sulfophthalein dyes such as bromophenol blue, bromocresol green, and bromocresol purple are highly sensitive reagents for determination of benzydamine hydrochloride and chlorphenoxamine hydrochloride. The proposed methods were successfully utilized for determining these drugs in bulk, as well as in pharmaceutical preparations and proved highly sensitive, accurate, precise, simple and with higher tolerance limits. Student's *t*- and *F*-tests for the proposed methods gave lower values relative to the theoretical ones indicating high accuracy and precision with no significant differences when compared to the official method. Therefore these reagents can be safely used for quality control of benzydamine hydrochloride and chlorphenoxamine hydrochloride in pure state and in their dosage forms.

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BENZIDAMĪNA UN HLORFENOKSAMĪNA HIDROGĒNHLORĪDU SPEKTROFOTOMETRISKA NOTEIKŠANA TĪRĀ VEIDĀ UN FARMACEITISKOS PREPARĀTOS, LIETOJOT SULFOFTALEĪNA GRUPAS KRĀSVIELAS

K O P S A V I L K U M S

Izstrādātas trīs vienkāršas, jutīgas un precīzas spektrofotometriskas metodes benzidamīna hidrogēnhlorīda (pretiekaisuma līdzeklis) un hlorfenoksamīna hidrogēnhlorīda (pretalerģijas līdzeklis) noteikšanai tīrā veidā un farmaceitiskos preparātos. Metodes balstās uz ārstniecisko vielu ekstraģēšanu hloroformā jonu pāru veidā ar sulfoftaleīnu grupas krāsvielām — bromfenolzilo, bromkrezolzaļo un bromkrezolpurpuru acetāta buferšķīdumu klātbūtnē pie pH 3,1; 3,3 un 3,2 benzidamīna hidrogēnhlorīda gadījumā un pie pH 3,1; 3,8 un 3,2 hlorfenoksamīna hidrogēnhlorīda gadījumā (attiecīgi ar bromfenolzilo, bromkrezolzaļo, bromkrezolpurpuru). Izveidotos jonu pāru kompleksus ekstraģē hloroformā un mēra gaismas absorbciju benzidamīna hidrogēnhlorīdam pie 409, 408 vai 407 nm (attiecīgi kompleksiem ar bromfenolzilo, bromkrezolzaļo un bromkrezolpurpuru), hlorfenoksamīna hidrogēnhlorīdam pie 412, 412 vai 414 nm (attiecīgi kompleksiem ar bromfenolzilo, bromkrezolzaļo un bromkrezolpurpuru). Atrasti optimālie apstākļi kompleksveidošanās norisei. Bēra–Lamberta likums ir spēkā koncentrācijām 2,0—28; 1,0—26 un 1,0—28 $\mu g \cdot ml^{-1}$ benzidamīna hidrogēnhlorīda kompleksiem ar bromfenolzilo, bromkrezolzaļo un bromkrezolpurpuru, attiecīgi; 1,0—22; 1,0—28; 1,0—29 $\mu g \cdot ml^{-1}$ hlorfenoksamīna kompleksiem ar bromfenolzilo, bromkrezolzaļo un bromkrezolpurpuru, attiecīgi.

Aprēķinātas metožu raksturlielumu — šķietamās molārās absorbcijas, jutības (pēc Sendela), korelācijas koeficientu, noteikšanas un linearitātes robežu — vērtības. Ieteiktās metodes sekmīgi lietotas benzidamīna un hlorfenoksamīna hidrogēnhlorīdu analīzei individuāliem savienojumiem un farmaceitiskos preparātos. Farmaceitiskiem preparātiem parasto piedevu traucējošo ietekmi nenovēroja. Iegūtie rezultāti uzrādīja labu sakritību ar oficiālo, kā arī citu pazīstamo analīzes metožu rezultātiem.

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СПЕКТРОФОТОМЕТРИЧЕСКОЕ ОПРЕДЕЛЕНИЕ ГИДРОХЛОРИДОВ БЕНЗИДАМИНА И ХЛОРФЕНОКСАМИНА В ИНДИВИДУАЛЬНОМ ВИДЕ И В ФАРМАЦЕВТИЧЕСКИХ ПРЕПАРАТАХ С ПРИМЕНЕНИЕМ СУЛЬФОФТАЛЕИНОВЫХ КРАСИТЕЛЕЙ

Р Е З Ю М Е

Для определения гидрохлорида бензидамина (противовоспалительное средство) и гидрохлорида хлорфеноксамина (антиаллергическое средство) в индивидуальном виде и в составе фармацевтических форм предложено три простых, чувствительных и точных спектрофотометрических метода. Методы основаны на экстракции лекарств в хлороформе в виде ионных пар со сульфофталеиновыми красителями — бромфеноловым синим, бромкрезоловым зеленым и бромкрезоловым пурпуровым в присутствии ацетатного буферного раствора при pH 3,1; 3,3 и 3,2 в случае

гидрохлорида бензидамина (для комплексов с бромфеноловым синим, бромкрезоловым зеленым и бромкрезоловым пурпуровым, соответственно) или при pH 3,1; 3,8 и 3,2 в случае гидрохлорида хлорфеноксамина (для комплексов с бромфеноловым синим, бромкрезоловым зеленым и бромкрезоловым пурпуровым, соответственно). Образующиеся ион-парные комплексы экстрагируют хлороформом и измеряют светопоглощение при 409, 408 и 407 нм для комплексов гидрохлорида бензидамина с бромфеноловым синим, бромкрезоловым зеленым и бромкрезоловым пурпуровым, соответственно, и при 412, 412 или 414 нм для комплексов гидрохлорида хлорфеноксамина с бромфеноловым синим, бромкрезоловым зеленым и бромкрезоловым пурпуровым, соответственно.

Установлены оптимальные условия протекания реакций комплексообразования. Найдено, что светопоглощение подчиняется закону Бера–Ламберта в диапазонах концентраций 2,0—28; 1,0—26 и 1,0—28 мкг·мл$^{-1}$ для комплексов гидрохлорида бензидамина с бромфеноловым синим, бромкрезоловым зеленым и бромкрезоловым пурпуровым, соответственно, и 1,0—22; 1,0—28 и 1,0—29 мкг·мл$^{-1}$ для комплексов хлорфеноксамина с бромфеноловым синим, бромкрезоловым зеленым и бромкрезоовым пурпуровым, соответственно. Вычислены значения характеристических параметров разработанных методов — кажущегося молярного поглощения, чувствительности по Сенделлу, коэффициентов корреляции, пределов обнаружения и количественного определения. Предлагаемые методы успешно применены для определения гидрохлоридов бензидамина и хлорфеноксамина в индивидуальном виде и в фармаевтических формах. Присутствие добавок, характерных для фармацевтических препаратов, определению не мешает. Результаты, полученные применением предлагаемых методов, имеют хорошую сходимость с результатами, полученными официальным и другими известными методами.

Iesniegts 30.05.2005