Charge Transfer Complexes of Antihistamines with Curcumin: Spectrophotometric Determination in Pharmaceutical Formulations

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Summary: An empirical spectrophotometric method for the determination of five antihistamines is carried out. The method is based on formation of a 1:1 charge transfer complex of promethazine, diphenhydramine, desloratadine, levocetirizine and loratadine with curcumin. Association between antihistamines and curcumin was confirmed by FT-IR spectroscopy. Method showed linear calibration curves over the range 20-140, 32-128, 18-126, 22-154 and 35-107 μg mL^{-1} respectively with correlation coefficient greater than 0.9981. The reliability of method was conferred by satisfactory recovery values greater than 98.45%. Moreover, the spectral characteristics including oscillator's strength, dipole moment, ionization potential, resonance energy and the thermodynamic parameters (association constant and Gibb's free energy changes) were investigated. The implementation of proposed method can help analysis of antihistaminic drugs in pharmaceutical formulations without interference of excipients.

Keywords: Charge transfer complexes, Antihistamines, Curcumin, Benesi–Hildebrand plot

Introduction

Antihistamines (Fig. 1), are useful therapeutic agent and one of the most frequently prescribed medicines world-wide for curing pruritus and urticaria (hives) associated with chronic idiopathic urticaria, non-nasal and nasal seasonal allergic rhinitis and for the perennial (non-seasonal) allergic rhinitis [1]. Another notable reason of their use is their anti-inflammatory activities as well as their averting effects in release of multiple inflammatory mediators [2]. The older antihistamines, such as diphenhydramine are very effective in blocking the actions of histamines, but their use has been limited by the adverse effects mainly associated with sedation and anticholinergic activity. The new generations of antihistamines developed since 1980's are essentially free from sedative and anticholinergic effects. Because the older antihistamines are free from serious life-threatening toxicity and newer drugs have even fewer side effects, antihistamines have so far been readily acceptable by physicians and assumed to be very safe. Literature shows the determination of antihistamines has been carried out by several analytical methods in both biological samples to be applied in pharmacokinetic studies as well as in pharmaceutical preparations. These methods includes liquid chromatographic method with both capillary isotachophoresis and UV isotachophoresis, non-aqueous titrimetric methods [3], fluorescence spectrophotometry [4], gas chromatography [5], high performance liquid chromatography [6], atomic absorption spectroscopy [7], reverse-phase high performance liquid chromatography [8] and so on.

The charge transfer complex is chemical association between donor and acceptor species. It plays an important role in bioelectrical fields [9], show vast application in chemistry such as they are used to modify coal tar pitch [10] and solvent polarity [11]. These complexes are employed as photo catalysts [12] and organic superconductors [13]. Regarding pharmaceutical chemistry, quantification of drug can be monitored by charge transfer complexes [4]. UV–Vis spectroscopy is highly sensitive and widely used method for the determination of charge transfer complexes. The complex formation is identified with a new absorption band in its UV–Vis spectrum that is useful for identification and analysis of the nature of donors and acceptors quantitatively and qualitatively [14]. The qualitative analysis becomes significant if drugs are used as donors in medicinal chemistry. Therefore, it is of much importance and interesting to study the charge transfer complexes of drugs with various σ or π-acceptors for qualitative and quantitative analysis

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of drugs in their pure form as well as in pharmaceutical formulations[15].

Present study has been targeted to develop the rapid and accurate spectrophotometric methods for the determination of five antihistaminic drugs; promethazine, diphenhydramine, desloratadine, levocetirizine, and loratadine. Since antihistamines do not have sufficient chromophoric groups, which enable this group of compounds to be determined directly by spectrophotometer, therefore the analysis has been carried out by preparing their charge transfer complexes with curcumin. Curcumin (diferuloylmethane) is a polyphenol extracted from Curcuma longa, generally named as turmeric. Over the last five decades, it has been indicated that curcumin is very effective in prevention and treatment of cancer. It is a powerful antioxidant with great therapeutic applications against many diseases such as inflammation, neurological, cardio-vascular, skin disorders[16]. Turmeric, particularly curcumin has carbonyl as well as hydroxyl moieties to facilitate complex formation with variety of electron deficient species[17]. Formation of curcumin complexes with different metals has been reported more often[18][19][20][21], but in the present work, it is first time that curcumin complexes have been synthesized with pharmaceutical drugs. The optimum reaction conditions of the developed methods have been established. Moreover, the oscillator strength (f) [22], energy of charge transfer complex (E_{CT}) [22], resonance energy (R_N) [22], dipole moment (μ) [22] and ionization potential (Ip) [14] were determined. In addition, the association constant (Kc) [22] and standard free energy changes (ΔG°) [22] have also been evaluated. Benesi-Hildebrand plots [23] for each complex have been constructed. Furthermore, solid charge transfer complexes were synthesized and characterized by FT-IR spectroscopy. Later on, the developed methods have been successfully applied for the determination of these aforementioned antihistamines in pharmaceutical formulation without interference of excipients.

Experimental

Materials and Reagents

Promethazine, diphenhydramine, desloratadine, levocetirizine and loratadine with purity greater than 98.34% were offered by Eros Pharmaceutical Pvt. Ltd. Pharmaceutical formulations Theoclate Avomine® 25 mg (Sanofi Aventis Pakistan), Dihydranil 120 mL syrup (Karachi Pharmaceutical Laboratories), Aloret 5mg (Pharma Health Pakistan Pvt. Ltd), T-Day™ 5 mg (Novartis Pharma), and Jardin 10 mg (High-Q Pharma) were procured from local pharmacy. 1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione (curcumin) and analytical grade methanol was acquired from Merck Darmstadt Germany.

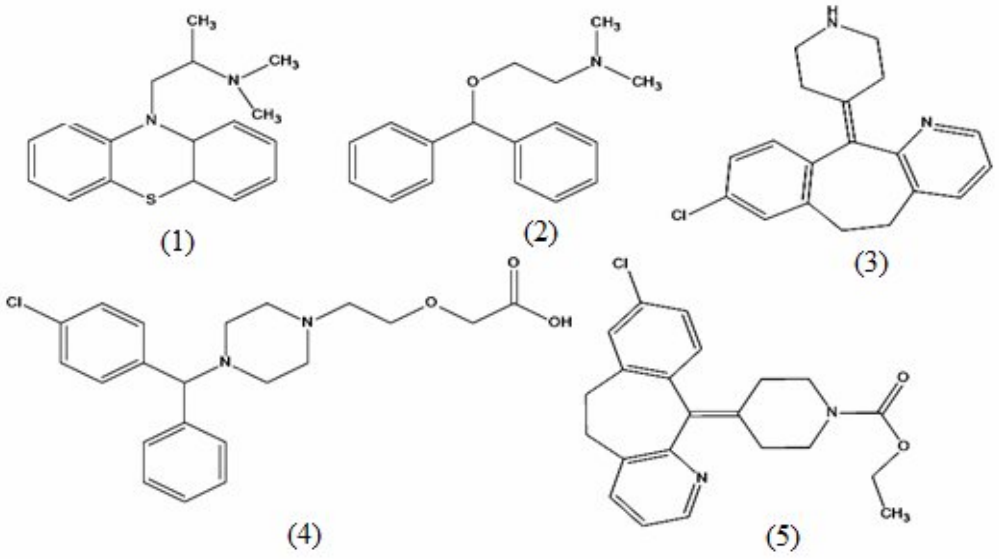


Fig. 1: Structural formulae of **(1)** promethazine, **(2)** diphenhydramine, **(3)** desloratadine, **(4)** levocetirizine and **(5)** loratadine.

Instruments

Quantitative analysis was conducted using Shimadzu model 1800 double beam UV-visible spectrophotometer available at Analytical Lab, Federal Urdu University of Arts, Science and Technology Karachi. Equipment was provided with 1 cm quartz cells connected with Pentium IV computer loaded with version 2.32 software. Attenuated total reflection (ATR) spectra recorded on Nicolet iS50 FT-IR with all-reflective diamond optics and software OMNIC 9.2.46 available at Physics Lab II, Department of Physics, NED University of Engineering and Technology

Preparation of stock solutions

An accurately weighed quantity equivalent to 100 mg of each antihistamine was transferred into a 100 mL volumetric flask separately, dissolved in 10 mL absolute methanol and diluted to the volume to obtain primary stock solution of 1 mg mL^{-1}. 0.1% reagent solution was obtained by dissolving 100 mg curcumin in 100 mL methanol.

Calibration standard solutions

Aliquots of stock solutions were transferred to 10 mL volumetric flasks separately to prepare seven standard solutions in concentration ranges 20-140, 32-128, 18-126, 22-154 and 35-107 µg mL^{-1} for promethazine, diphenhydramine, desloratadine, levocetirizine and loratadine respectively. 1 mL of 0.1% curcumin solution was added. All the solutions were allowed to stand for 5 min for complete complexation and then volumes were made up with methanol. Absorbance was measured against reagent blank. To determine the effect of curcumin concentration, variable volume of 2.71×10^{-6} M curcumin solution was added to constant volumes of histamine receptor antagonist and scanning against reagent blank.

Pharmaceutical formulation

Twenty tablets of each Theoclate Avomine®, Aloret, T-Day™ and Jardin formulation were delicately triturated into pestle and mortar and the powder equivalent to 10 mg of each antihistamine was dissolved in small volume of methanol and shaken well for proper mixing whereas 6.25 mL (equivalent to 10 mg) of Dihydranil was dissolved in small amount of methanol. All solutions were allowed to stand for one hour and then sonicated for complete extraction of analyte. The remains were filtered, properly washed and volumes were brought to 100 mL with same solvent. The procedure was then followed as described under the preparation of calibration curves.

Result and Discussion

Antihistamines are found to be the top choice for controlling some early and late-phase allergic indications in eyes, nose and pharynx [1]. Most of them limit chemotaxis of inflammatory cells hence, act efficaciously as anti-inflammatory drugs [24]**.** These histamines receptors antagonist are the first choice of study for many scientists these days. In the present study, ion pair complexes of five antihistamines with curcumin have been studied. Curcumin is the main bioactive ingredient of turmeric that has tremendous medicinal importance like it has the preventive action against Alzheimer [20]**,** also possesses antioxygenation, antibiosis and antitumor activities [25]. Separately, it shows yellowish orange colour with λ_{max} 427 nm in methanol. Here we report the determination of antihistamines in bulk drug and pharmaceutical formulation to investigate the spectrophotometric characteristics of all five charge transfer complexes. Out of five newly formed charge transfer complexes, desloratadine and levocetirizine with curcumin appeared as deep red and pale yellow respectively, whereas promethazine, loratadine and diphenhydramine had yellowish-orange colour nearly similar to each other. The complexes showed absorption maxima at 419, 423, 431, 429 and 424 nm for promethazine, desloratadine, levocetirizine, diphenhydramine and loratadine respectively. Comparing the pure curcumin and promethazine with the formed complex shows the maximum absorption shifted from 421 to 436 confirming the formation of complex (Fig. 2). The proposed reaction is illustrated in Scheme-1.

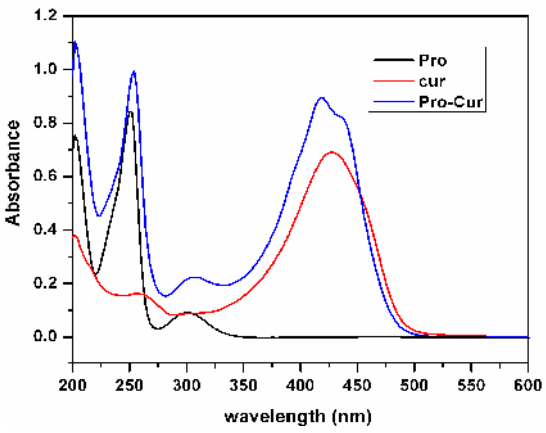
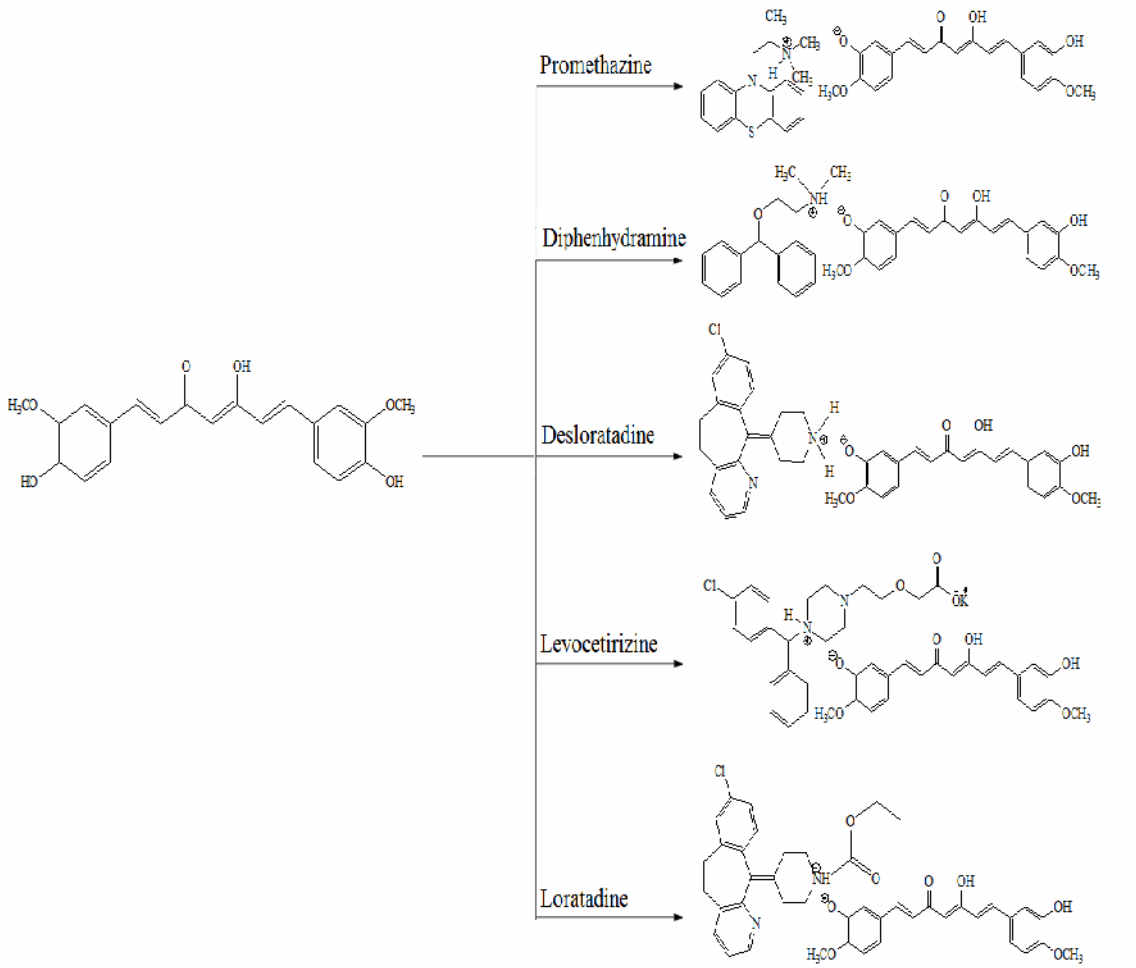


Fig. 2: Absorption spectrum of promethazine complex compared with the spectra of pure promethazine and curcumin.



Scheme-1: Reaction pathway of promethazine, diphenhydramine, desloratadine, levocetirizine, and loratadine with curcumin.

Optimization of experimental conditions

Several analytical parameters and their effects were studied by varying single parameter at a time while others as kept constant to set the optimum reaction conditions for proposed method. Different analytical solvents were examined such as methanol, acetonitrile, acetone, dimethyl sulfoxide and water, however methanol was found to give maximum absorbance with high sensitivity. Optimum reaction time was established by monitoring the complexation within time span of 1.5 minutes. It was observed that the complete colour formation was occurred promptly right after mixing the reagents together at ambient temperature (25 ± 2°C) and there was no effect on absorbance with the passage of time (Fig. 3). It was found that 1.5 mL of curcumin for each of promethazine, desloratadine, levocetirizine, diphenhydramine and loratadine was consumed for complexation, thus 1.5 mL of curcumin was sufficient for complete complexation of studied antihistamines with curcumin.

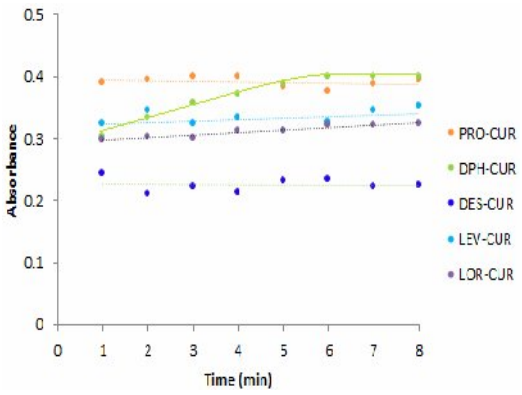


Fig. 3: Effect of time on absorbance.

Stoichiometric ratio of complexes

The setting up of stoichiometric ratio of antihistamines and curcumin has been undergone with the help of Job's plot of continuous variation [26]**.** On this account, equimolar solutions of curcumin and studied antihistamines were prepared and they were brought to react in different ratios. The graph between mole fractions of each drug vs. absorbance revealed that antihistamines react with curcumin in the ratio of 1:1 (Fig. 4).

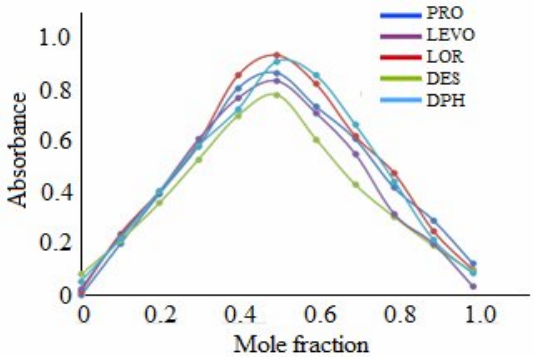


Fig. 4: Job's Plot for charge transfer complexes of promethazine, diphenhydramine, desloratadine, levocetirizine and loratadine complexes with curcumin.

Linearity

Standard calibration curves for each complex were plotted with the series of 20-140, 18-126, 22-154, 32-128 and 35-107 µg mL^{-1} for promethazine, desloratadine, levocetirizine, diphenhydramine and loratadine respectively. The value of correlation coefficient in each case was greater than 0.998 that shows good linearity. Regression data including slope and intercept are given in Table-1. The analogous molar absorptivity values have been calculated and are determined as: 2105, 2573, 2523, 2013 and 4072 $L.mol^{-1}$ cm^{-1} respectively.

Precision

Table-1: Optimum conditions and analytical parameters.

Parameters	PRO	DPH	DES	LEV	LOR
λ_{max} (nm)	419	429	423	431	424
Linearity range (µgmL^{-1})	20-140	32-128	18-126	22-154	35-107
Molar absorptivity	2105	2013	2573	2523	4072
Slope	0.007	0.009	0.008	0.006	0.013
Intercept	0.006	0.105	0.005	0.015	0.3217
Correlation coefficient	0.998	0.994	0.997	0.996	0.981
Standard error	1.797	1.428	0.404	2.036	1.665
Standard error estimate	1.962	1.662	0.406	2.339	1.405
LOD ngmL^{-1}	1.3	0.78	0.57	2.47	0.41
LOQ µgmL^{-1}	3.93	2.36	1.72	7.5	1.24

To assess inter-day and intra-day precision, six replicates of each complexes in the range 20-140, 18-126, 22-154, 32-128 and 35-107 µg mL^{-1} for promethazine, desloratadine, levocetirizine, diphenhydramine and loratadine respectively were analysed for three days of method validation. Precision was reported in terms of %RSD which was found to be 0.06-1.35, 0.08-0.75, 0.11-0.85, 0.07-1.00 and 0.05-0.63 respectively. The results indicate that the methods have good repeatability and reproducibility (Table-2).

Accuracy

Accuracy of the method was established in terms of percent recovery values and percent error in dosage formulation i-e Theoclate Avomine®, Aloret, T-Day™, Dihydranil and Jardin. It was evaluated in the linearity range 20-140, 18-126, 22-154, 32-128 and 35-107 µg mL^{-1} for promethazine, desloratadine, levocetirizine, diphenhydramine and loratadine respectively. The method showed good %recovery values 99.35-100.32, 100.34-100.66, 98.45-100.68, 100.00-101.08 and 99.87-100.82 respectively indicating the reliability of method. (Table-3).

Sensitivity

Sensitivity of method was established by studying the limit of detection and quantitation. Calculation for LOD and LOQ for the proposed method has been calculated by the following equations [14]:

$$LOD = \frac{3s}{k}$$

$$LOQ = \frac{10s}{k}$$

where: s is the standard deviation of replicate determination values, k is the sensitivity, i-e, the slope of the calibration graph. In agreement with the mentioned formulae, the LOD and LOQ obtained for the absorbance were calculated for promethazine, diphenhydramine, desloratadine, levocetirizine and loratadine, these values were found to be as 0.13, 0.78, 0.57, 2.47, 0.41 µg mL^{-1} and 3.39, 2.36, 1.72, 7.5, 1.24 µg mL^{-1} respectively.

Interference of Excipients

Accurately weighed 2.5 g pyrrolidine, lactose, talc, magnesium stearate and starch were separately transferred into 25 mL volumetric flask and small amount of methanol was added, the contents were sonicated for complete mixing, then the volume was finally brought to the mark with the same solvent and filtered. Each excipient solution was introduced with 100% drug solutions and absorbance was recorded to

determine the recovery. It was observed that the commonly encountered excipients did not affect the present recovery of drug confirming the selectivity of method (Table-4).

Spectral characteristics

From the absorption spectra of each complex, different spectral characteristics including transition dipole moment (μ) [22] were calculated using the formulae f = (4.319 x 10-9) $\varepsilon_{max}.\nu_{1/2}$ and μ = 0.0958 $(\varepsilon_{max}.\nu_{1/2}/\nu_{max})_{1/2}$. The ionization potential (Ip) [14] of free donor in methanol medium was determined using the equation Ip = 5.76 + 1.53 x 10^{-4} ν_{CT}. Resonance energy (R_N) [22] and energy of charge transfer complexes (E_{CT}) [22] were calculated by employing the equations ε_{max} = 7.7.10^{-4}/ [$h\nu_{CT}$/ R_N-3.5] and E_{CT} = 1243.667/λ_{CT} respectively, where ε_{max} is the molar extinction coefficient at maximum absorbance, $\nu_{1/2}$ is the band-width at half absorbance in cm^{-1}, ν_{max} and ν_{CT} are wave number in cm^{-1} and λ_{CT} is the wavelength of charge transfer band. The standard free energy changes (ΔG°) [22] associated with antihistamines complexes were calculated from the association constants by applying equation ΔG° = −2.303 RT log Kc, where R is the gas constant (1.987 cal mol^{-1} deg^{-1}), T is temperature in Kelvin and Kc is the association constant of drug-acceptor complexes. The obtained data is summarized in Table-5.

The association constant of the complexes was determined by using Benesi-Hildebrand equation [14], $[A_0]/A = 1/K [D_0]. \varepsilon + 1/\varepsilon$ for cells with 1 cm optical path length, where, $[A_0]$ and $[D_0]$ are the initial concentrations of the acceptor and donor respectively, A is absorbance of definite charge transfer band, ε is molar extinction coefficient and K is the association constant. The concentration of acceptor is much greater than that of donor. On plotting the values of $[A_0]/A$ against $1/ [D_0]$, sharp straight lines were obtained as shown in (Fig. 5). The data obtained throughout this calculation is given in Table-6.

Table-2: Precision of proposed method.

PRO-CUR			DPH-CUR			DES-CUR			LEV-CUR			LOR-CUR		
	%RSD			%RSD			%RSD			%RSD			%RSD	
Conc	Inter Day	Intra Day	Conc	Inter Day	Intra Day	Conc	Inter Day	Intra Day	Conc	Inter Day	Intra Day	Conc	Inter Day	Intra Day
20	1.32	0.75	32	1.00	0.37	18	0.75	0.37	22	0.85	0.43	35	0.63	0.31
40	0.19	0.19	48	0.62	1.68	36	0.00	0.00	44	0.23	0.23	47	0.41	0.24
60	1.35	0.14	64	0.00	0.14	54	0.25	0.00	66	0.39	0.13	59	0.12	0.12
80	0.10	0.10	80	0.19	0.10	72	0.26	0.10	88	0.11	0.11	71	0.00	0.10
100	0.09	0.95	96	0.14	0.78	90	0.08	0.08	110	0.00	0.08	83	0.08	0.08
120	0.26	0.06	112	0.07	0.13	108	0.17	0.06	132	0.39	0.28	95	0.18	0.07
140	0.06	0.06	128	0.11	0.53	126	0.20	0.10	154	0.00	0.67	107	0.05	0.06

Table-3: Accuracy of proposed method.

PRO		DPH		DES		LEV		LOR	
% Rec	% Err	% Rec	% Err	% Rec	% Err	% Rec	% Err	% Rec	% Err
98.70	1.30	100.22	-0.22	100.88	-0.88	99.03	0.97	100.73	-0.73
100.11	-0.11	101.72	-0.72	101.51	-1.51	100.13	-0.13	100.41	-0.41
100.78	-0.78	100.00	0.00	100.29	-0.29	100.45	-0.45	100.14	-0.14
99.88	0.12	100.19	-0.19	100.22	-0.22	99.94	0.06	100.00	0.00
99.90	0.10	100.00	0.00	100.05	-0.05	100.00	0.00	99.96	0.04
100.15	-0.15	100.08	-0.08	100.15	-0.15	99.72	0.28	99.96	0.04
99.97	0.03	100.07	-0.07	100.22	-0.22	100.00	0.00	100.06	-0.06

Table-4: Recovery of antihistamines in presence of different excipients.

Excipients	PRO	DPH	DES	LEV	LOR
	% Recovery				
Pyrrolidone	99.35	100.65	100.66	98.54	100.55
Lactose	100.32	101.08	100.34	100.40	100.82
Talc	100.00	100.00	100.28	100.68	100.21
Magnesium stearate	99.82	100.38	100.34	100.00	100.17
Starch	99.71	100.27	100.48	100.00	99.87

Table-5: Spectrophotometric results.

Complex	F	μ	Ip	E_{CT}	R_N	Kc x10^2 (lit/mol)	ΔG° (KJ)
PRO	0.50	6.77	9.29	2.87	0.82	1073	17275
DPH	0.56	7.21	9.27	2.85	0.81	1100	17336
DES	0.75	8.24	9.35	2.92	0.83	983	17058
LEV	0.53	6.99	9.30	2.88	0.82	935	16934
LOR	1.24	10.69	9.29	2.87	0.82	929	16918

Table-6: The values of $[A_0]$/Abs and 1/ $[D_0]$ for antihistamines complexes.

Complex	D (M) x 10^{-3}	A (M) x 10^{-3}	Abs	1/D x 10^{3}	A/Abs x 10^{-2}
PRO	0.070	1.357	0.153	14.22	0.887
	0.141	1.357	0.309	7.11	0.439
	0.211	1.357	0.426	4.74	0.319
	0.281	1.357	0.568	3.56	0.239
	0.352	1.357	0.677	2.84	0.200
DPH	0.125	1.357	0.998	7.98	0.881
	0.188	1.357	1.998	5.32	0.430
	0.251	1.357	2.998	3.99	0.298
	0.313	1.357	3.998	3.19	0.227
	0.376	1.357	4.998	2.66	0.192
DES	0.058	1.357	0.154	17.27	0.881
	0.116	1.357	0.316	8.63	0.430
	0.174	1.357	0.455	5.76	0.298
	0.232	1.357	0.598	4.32	0.227
	0.290	1.357	0.707	3.45	0.192
LEV	0.057	1.357	0.135	17.68	1.005
	0.113	1.357	0.25	8.84	0.543
	0.170	1.357	0.446	5.89	0.304
	0.226	1.357	0.54	4.42	0.251
	0.283	1.357	0.695	3.54	0.195
LOR	0.091	1.357	0.998	10.94	0.742
	0.123	1.357	1.998	8.15	0.552
	0.154	1.357	2.998	6.49	0.287
	0.185	1.357	3.998	5.39	0.232
	0.217	1.357	4.998	4.61	0.180

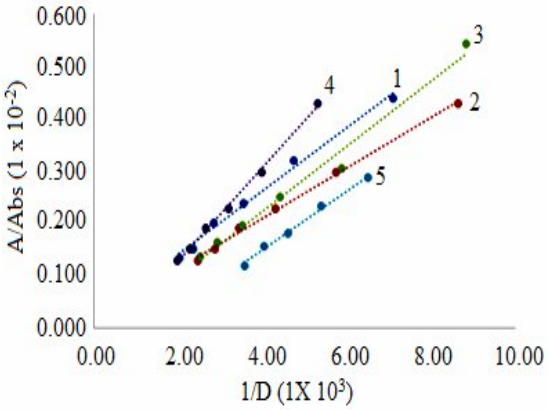


Fig. 5: Benesi-Hildebrand plots for promethazine[1], diphenhydramine[4], desloratadine[2], levocetirizine[3] and loratadine[5] complexes with curcumin.

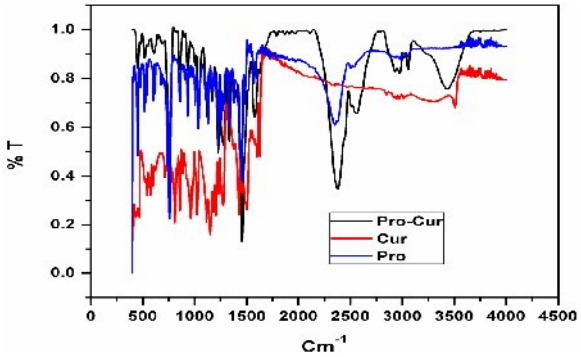


Fig. 6: FT-IR spectra of promethazine-curcumin complex compared with that of promethazine and curcumin alone.

Attenuated total reflection spectra

The ATR Spectroscopic studies have been under gone for the complexes formed to overlay the structures of the newly formed complexes. All the studied antihistamines contain tertiary nitrogen which shows no band in the region of 3400 cm^{-1}. However, compression of the spectrum of formed complex with that of promethazine and curcumin alone indicates twin peak in the region 2920-3070 cm^{-1} attributing to quaternary nitrogen (Fig. 6). The recorded infra-red frequencies and their band assignments are assembled in Table-7.

Application of the proposed method

Theoclate Avomine®, Aloret, T-Day™, Dihydranil and Jardin were processed with the proposed method by five replicate determinations in order to evaluate the reliability. Good accuracy and precision ratified the effective application of method even in the presence of excipients. The method was proved to be convenient, sensitive, accurate, sanctioning good precision for all investigated drugs with good recoveries and less error in the range 0.03-1.30, 0.05-1.51, 0.06-0.97, 0.07-0.72 and 0.04-0.73% indicating the reliability of method. Present excipients showed no interference during the assay. Thus, the proposed analytical method can be pragmatic for routine analysis in forensic medicines, clinical laboratories and quality control laboratories.

Table-7: Infrared frequencies and their assignments.

PRO-CUR	DPH-CUR	DES-CUR	LEV-CUR	LOR-CUR	Assignment
3421.7	3500-3400	3500-3300	3500-3400	3500-3300	ν(C-OH)
-	-	-	1741		ν(COO^-)
-	-	-	-	1701	ν(N-COOR)
1643	1610	1633	1629	1566	ν(C=C)
1640	1625	1570	1645	1566	Alpha-beta unsaturated ketone
-	-	1633	-	-	ν(NH_2)
1566	1500	1512	1552	1512	ν(N-H)
1454	1460	1435	1442	1433	ν(C=C) (Ar)
1334	1282	1285	1317	1224	ν(C-N)
-	1103	1180	1136	1114	ν(C-O)
-	-	-	1024	-	ν(C-Cl)
-	-	1095	-	1028	ν(C-Cl) Ar
2924	2902	2915	2933	2930	R_3-$^+$NH

Conclusion

We have described a spectrophotometric method to determine five antihistaminic drugs (promethazine, desloratadine, levocetirizine, diphenhydramine and loratadine) via analysing their charge transfer complexes with curcumin in active pharmaceutical ingredients. The solid charge transfer complexes of all five antihistamines were synthesized and characterized by the FTIR spectroscopy which confirms the association between donor and acceptors hence proving the formation of complexes. The method is low-cost, simple and reproducible for the purpose of studying antihistamines. Statistical parameter and recovery data explains the precision and accuracy of method. Furthermore, spectral characteristics transition dipole moment (μ), ionization potential (Ip) of free donor in methanol medium, resonance energy (RN), energy of charge transfer complexes (E_{CT}) and thermodynamic parameters have been determined. Benesi-Hildebrand plots for each complex were constructed.

References

1. L. Bielory, K. W. Lien, and S. Bigelsen, Efficacy and Tolerability of Newer Antihistamines in the Treatment of Allergic Conjunctivitis, *Drugs*, **65**, 215 (2005).
2. G. Coruzzi, M. Adami, E. Guaita, I. J. P. de Esch, and R. Leurs, Antiinflammatory and antinociceptive effects of the selective histamine H4-receptor antagonists JNJ7777120 and VUF6002 in a rat model of carrageenan-induced acute inflammation, *Eur. J. Pharmacol.*, **563**, 240 (2007).
3. K. Basavaiah and V. S. Charan, Titrimetric and spectrophotometric assay of some antihistamines through the determination of the chloride of their hydrochlorides, *Farmaco*, **57**, 9 (2002).
4. S. N. H. Azmi, S. S. K. Al-Hadhrami, B. M. R. Al-Marhoubi, S. S. S. Al-Sulaimi, and Z. D. S. Al-Shamoosi, Development and validation of fluorescence spectrophotometric method: Quantitation of chlorpheniramine maleate in pharmaceutical formulations, *J. Mol. Liq.*, **243**, 750 (2017).
5. P. Adamowicz and M. Kała, Simultaneous screening for and determination of 128 date-rape drugs in urine by gas chromatography-electron ionization-mass spectrometry, *Forensic Sci. Int.*, **198**, 39 (2010).
6. M. Rambla-Alegre, J. Peris-Vicente, J. Esteve-Romero, M. E. Capella-Peiró, and D. Bose, Capillary electrophoresis determination of antihistamines in serum and pharmaceuticals, *Anal. Chim. Acta*, **666**, 102 (2010).
7. N. El-Kousy and L. I. Bebawy, Determination of some antihistaminic drugs by atomic absorption spectrometry and colorimetric methods, *J. Pharm. Biomed. Anal.*, **20**, 671 (1999).
8. V. Choudhari, A. Kale, S. Abnawe, B. Kuchekar, V. Gawli, and N. Patil, Simultaneous determination of montelukast sodium and levocetirizine dihydrochloride in pharmaceutical preparations by ratio derivative spectroscopy, *Int. J. PharmTech Res.*, **2**, 4 (2010).
9. I. M. Khan, A. Ahmad, and M. Oves, Synthesis, characterization, spectrophotometric, structural and antimicrobial studies of the newly charge transfer complex of p-phenylenediamine with π acceptor picric acid, *Spectrochim. Acta - Part A Mol. Biomol. Spectrosc.*, **77**, 1059 (2010).
10. N. Miyajima, T. Akatsu, T. Ikoma, O. Ito, B. Rand, Y. Tanabe, and E. Yasuda, Role of charge-transfer complex with iodine in the modification of coal tar pitch, *Carbon N. Y.*, **38**, 1831 (2000).
11. S. Bhattacharya, M. Banerjee, and A. K. Mukherjee, Study of the formation equilibria of electron donor-acceptor complexes between fullerene and methylbenzenes by absorption spectrometric method, *Spectrochim. Acta - Part A Mol. Biomol. Spectrosc.*, **57**, 1463 (2001).
12. D. Y. Wu, L. B. Zhao, X. M. Liu, R. Huang, Y. F. Huang, B. Ren, and Z. Q. Tian, Photon-driven charge transfer and photocatalysis of p-aminothiophenol in metal nanogaps: a DFT study of SERS, *Chem. Commun.*, **47**, 2520

(2011).
13. J. S. Miller, A. J. Epstein, and W. M. Reiff, Ferromagnetic molecular charge-transfer complexes, *Chem. Rev.*, **88**, 201 (1988).
14. N. Sultana, Charge Transfer Complexes of Gamma Aminobutyric Acid-Analogue, A Neurotransmitter: Synthesis and Spectrophotometric Determination, *J. Bioanal. Biomed.*, **5**, 13 (2013).
15. S. N. Ali, N. Sultana, and M. S. Arayne, Synthesis and Spectrophotometric Study of Omeprazole Charge Transfer Complexes with Bromothymol Blue , Methyl Orange , and Picric Acid, **9**, 21749 (2015).
16. K. I. Priyadarsini, Photophysics, photochemistry and photobiology of curcumin: Studies from organic solutions, bio-mimetics and living cells, *J. Photochem. Photobiol. C Photochem. Rev.*, **10**, 81 (2009).
17. A. Qayoom, S. A. Kazmi, and S. N. Ali, Turmeric powder as a natural heavy metal chelating agent: Surface characterisation, *Pakistan J. Sci. Ind. Res. Ser. A Phys. Sci.*, **60** (2017).
18. A. Bagchi, P. Mukherjee, S. Bhowmick, and A. Raha, International Journal of Drug Development and Synthesis , Characterization and Antibacterial Activity of a Novel Curcumin Metal Complex, **7**, 11 (2015).
19. P. R. S, B. S, J. Daisy, and M. P. V, Reactive Centers of Curcumin and the Possible Role of Metal Complexes of Curcumin as Antioxidants, *Univers. J. Phys. Appl.*, **9**, 6 (2015).
20. M. A. Subhan, K. Alam, M. S. Rahaman, M. A. Rahman, and R. Awal, Synthesis and Characterization of Metal Complexes Containing Curcumin ($C_{21}H_{20}O_6$) and Study of their Anti-microbial Activities and DNA-binding Properties, *J. Sci. Res.*, **6**, 97 (2013).
21. X. Z. Zhao, T. Jiang, L. Wang, H. Yang, S. Zhang, and P. Zhou, Interaction of curcumin with Zn(II) and Cu(II) ions based on experiment and theoretical calculation, *J. Mol. Struct.*, **984**, 316 (2010).
22. M. S. Refat, A. Elfalaky, and E. Elesh, Spectroscopic and physical measurements on charge-transfer complexes: Interactions between norfloxacin and ciprofloxacin drugs with picric acid and 3,5-dinitrobenzoic acid acceptors, *J. Mol. Struct.*, **990**, 217 (2011).
23. N. Rahman, N. A. Khan, and S. N. H. Azmi, Validated Spectrophotometric Methods for the Determination of Amiodarone Hydrochloride in Commercial Dosage Forms Using *p*-Chloranilic Acid and 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone, *Anal. Sci.*, **20**, 1231 (2004).
24. R. L. Thurmond, E. W. Gelfand, and P. J. Dunford, The role of histamine H1 and H4 receptors in allergic inflammation: the search for new antihistamines, *Nat Rev Drug Discov*, **7**, 41 (2008).
25. Y. M. Song, J. P. Xu, L. Ding, Q. Hou, J.-W. Liu, and Z.-L. Zhu, Syntheses, characterization and biological activities of rare earth metal complexes with curcumin and 1,10-phenanthroline-5,6-dione., *J. Inorg. Biochem.*, **103**, 396 (2009).
26. C. Y. Huang, Determination of binding stoichiometry by the continuous variation method: The job plot, *Methods Enzymol.*, **87**, 509 (1982).