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Synthesis and spectrophotometric study of omeprazole charge transfer complexes with bromothymol blue, methyl orange and picric acid

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Abstract

Spectrophotometric determination of omeprazole through charge transfer complex has been described using bromothymol blue, methyl orange and picric acid. Formed complexes were investigated at 400, 420 and 373 nm in the concentration ranges of 7-56, 6-48 and 10-80 µg mL^{-1} respectively. The apparent molar absorptivity values have been determined. The data is discussed in terms of oscillator's strength, dipole moment, ionization potential, energy of complexes, resonance energy, association constant and Gibb's free energy changes. Benesi-Hildebrand plots have been constructed. Applicability of method was demonstrated by determining the omeprazole in pharmaceutical formulations which showed good percent recovery values. Commonly present excipients did not interfere during analysis. Solid charge transfer complexes were synthesized and characterized by IR and 1H NMR spectroscopy.

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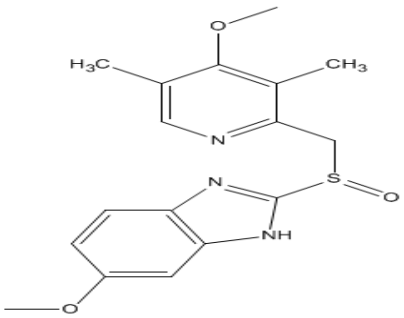
1. Introduction

Omeprazole (OME) (figure 1), a benzimidazole derivative, chemically 5-methoxy-2-{[(4-methoxy-3, 5-dimethyl-2-pyridinyl)methyl]sulfinyl}-1H-benzimidazole, is prescribed for the treatment of gastric and duodenal ulcers and reflux oesophagitis [1]. Its action mechanism is governed by interaction of OME with H^+/K^+ ATPase in the secretory membranes of the parietal cells, which leads to reduction of gastric acid secretion [2-4]. Several techniques have been reported in literature for the determination of OME in bulk drug, pharmaceutical formulation and body fluids including titrimetry [5], capillary electrophoresis [6], electrochemical [7], high performance liquid chromatography [8-9] with ultraviolet detection in biological fluids [10], employing electrochemical and coulometric detection [11], liquid chromatography–mass spectrometry [12], thin layer chromatography [13], high performance thin layer chromatography [14] and elemental analyses, IR, diffuse reflectance, magnetic moment, molar conductance and thermal analyses (TGA and DTA) techniques [15]. To date, several spectrophotometric methods have also been reported in literature for its determination including UV spectroscopy [16], manipulating ratio spectra [17], Vierordt's simultaneous equation method [18], chelation [19], colorimetric [20], ion-pair or charge transfer complex [21-25] and derivative spectrophotometry [26-29]. In the past era, a number of spectrophotometric methods for the determination of verapamil [30], gabapentin [31], quinolone antibiotics [32], metformin [33], ascorbic acid [34] and montelukast [35] have been developed by our research fellows. In the present study we aimed to describe rapid and accurate spectrophotometric methods based on charge transfer complexes of OME with bromothymol blue (BTB), methyl orange (MO) and picric acid (PA). The optimum reaction conditions of the developed methods have been established. The oscillator's strength (f), dipole moment (μ), ionization potential (I_p), energy of CT complex (E_{CT}) and resonance energy (R_N) have been evaluated. The association constant (K_c) and standard free energy changes ($\Delta G°$) have also been determined. The solid complexes were synthesized and characterized by IR and ^1H NMR spectroscopy.

Figure 1. Omeprazole



2. Materials and methods

2.1. Materials and analytical reagents

High purity reagents obtained from their sources were used. OME was obtained from Nabi Qasim Industries and pharmaceutical formulation Loprot® 20 mg was purchased from the local pharmacy (Karachi). The complexing reagents BTB and MO were purchased from Merck (Darmstadt, Germany) and PA from Sigma Aldrich Chemie GmbH. All the solvents used were of analytical grade and double distilled de-ionized water was used throughout the analysis.

2.2. Instruments

All the spectrophotometric measurements were carried out by using Shimadzu 1800 double beam UV–visible spectrophotometer version 2.32 software with quartz cells of 1.0 cm path length. The FT-IR spectra were obtained

from KBr discs using Shimadzu Prestige-21200VEC version 1.2 software and ^{1}H NMR spectra were measured on Bruker AMX 500MHz spectrophotometer using TMS as internal standard and MeOD as solvent.

2.3. Preparation of solutions

0.29×10^{-2} M stock solution of OME was prepared in methanol. Working standard solutions were prepared by suitable dilutions of stock standard solution. 0.16×10^{-2} M BTB, 0.30×10^{-2} M MO and 0.43×10^{-2} M PA were prepared fresh daily in double distilled deionized water. Phthalate buffer of pH ranging from 2.2-4.0 0.1M HCl were prepared in double distilled deionized water.

2.4. General procedure

2.4.1. Method for BTB and MO: Into two different series of 10 mL volumetric flaks, aliquots of OME solutions were transferred to get final concentration ranges 7-56 and 6-48 µg mL^{-1} for BTB and MO respectively. To each flask, 3.0 mL buffer of pH 3.2 (for BTB) and 3.6 (for MO) and also 3 mL BTB and MO were added in respective flask. The volume of mixture was completed with distilled water. The contents were transferred to a 50 mL separating funnel and extracted with 20 mL chloroform in two portions. The absorbance of extracted organic layer was measured against reagent blank treated similarly. The standard calibration graph was prepared by plotting absorbance of complexes vs. concentration of OME.

2.4.2. Method for PA: Aliquots of OME in the concentration range of 10-80 µg mL^{-1} was transferred to 10 mL volumetric flask. To this, 1.0 mL of PA was added and allowed to stand for few minutes for complete interaction. Then the volumes were made up to the mark with methanol and absorbance was measured against reagent blank treated similarly. The standard calibration graph was prepared by plotting absorbance of complexes vs. concentration of OME.

2.5. Pharmaceuticals formulation

Twenty tablets of Loprot® were finely triturated into pestle and mortar. The quantity of powder equivalent to 10 mg mL^{-1} of OME was separately dissolved in 100 mL methanol and shaken well for proper mixing. This solution was allowed to stand for 30 min and then sonicated for complete solubilization of drugs. The contents were filtered to separate the insoluble excipients and volume was completed with same solvent to get the solution of 1000 µg mL^{-1} OME. Then, the procedure was followed as described under the general procedure.

2.6. Synthesis of solid charge transfer complexes

Solid charge transfer complexes were synthesized by dissolving equimolar quantities (1:1) of OME and complexing agents in 10 ml methanol and refluxing the contents on water bath for 1.5 hrs. The contents were filtered to separate the unreacted substances. The excess solvent was evaporated to dryness. The resultant solid material was thoroughly washed to remove the remaining traces of reactant. These materials were then dissolved and re-crystallized in acetonitrile. Pure charge transfer complexes were characterized by UV-visible spectrophotometer, FT-IR and ^{1}HNMR spectroscopy.

3. Results and Discussions

3.1. Absorption spectra

Because of the presence of electron rich functional group, OME shows high electron density and thus behaves as powerful electron donor. Particularly, the amino group in its structure possesses lone pair of electron which participates in ion-pair complexation. BTB and MO are salt of sulfonic acid whereas PA is an acidic phenol. They are good acceptors which readily form electron donor acceptor complexes. The complexes are formed by transferring lone pair of electron from nitrogen in OME to electron deficient sulfonic group of BTB and MO and hydroxyl group of PA. Yellow, orange and dark yellow complexes appeared which absorbed in the visible region at 400, 420 and 373 nm apart from any of the reactant species. Figure 2 shows the electronic absorption spectra of all the complexes.

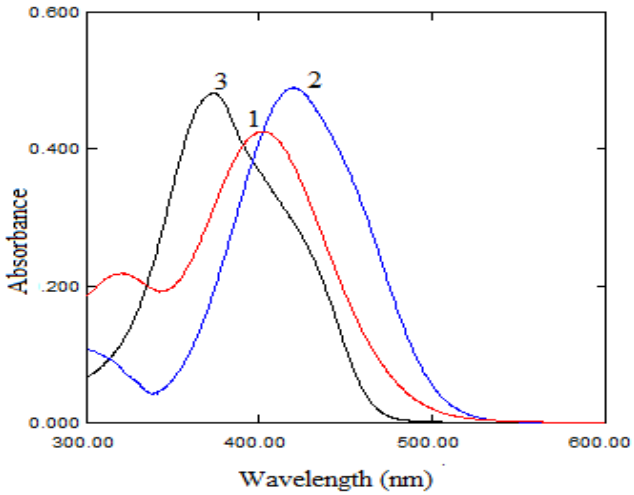


Figure 2. UV Spectra of OME complexes with (1)BTB, (2) MO and (3) PA

3.2. Optimization of reaction conditions

The reaction conditions suitable for the complexation were established by optimizing various parameters. One parameter was varied at a time while keeping others constant. Buffers of various pH were tried to find out the effect of pH on complexation. The maximum absorbance was obtained at pH 3.2 and 3.4 for BTB and MO respectively (fig. 3).

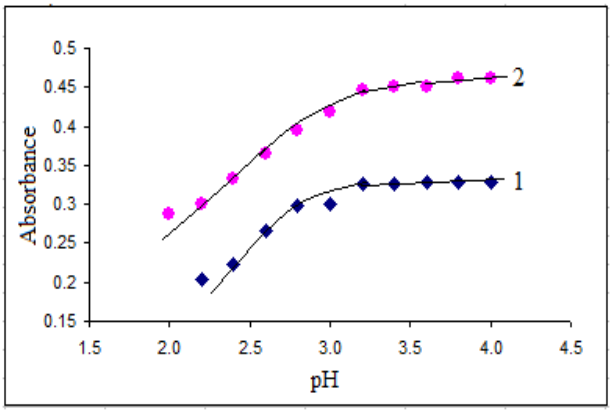


Figure 3. Effect of pH (1) BTB and (2) MO

The time required for the complete reaction was investigated from 0 min up to 5 min by taking absorbance after every min at room temperature. It was investigated that complexation occurs instantaneously and the absorbance remains constant after 0 min (figure 4). To determine the effect of reagent concentration, the concentration of donor was kept invariable and the concentration of acceptor was varied by varying the volume of stock solution. Above 2.4, 2.8 and

0.7 mL of BTB, MO and PA respectively, there was no effect on absorbance of complex, therefore, 3 mL BTB and MO, and 1 mL PA was found to be sufficient for complete complexation (figure 5). Selection of chloroform as appropriate solvent was carried out by testing different solvents like benzene, carbon tetra chloride, dichloromethane and chloroform. Double extraction was adequate for maximum recovery.

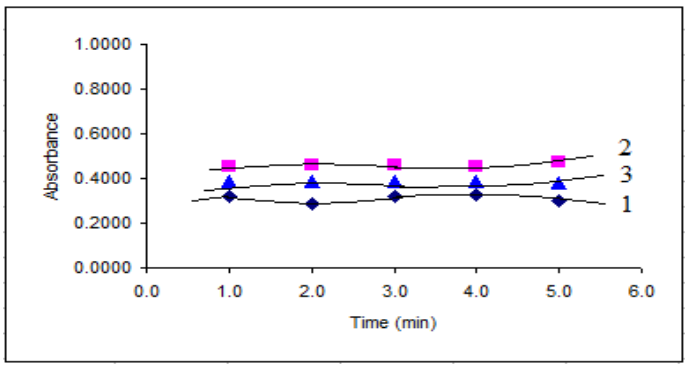


Figure 4. Effect of time on OME complexation with (1) BTB, (2) MO and (3) PA

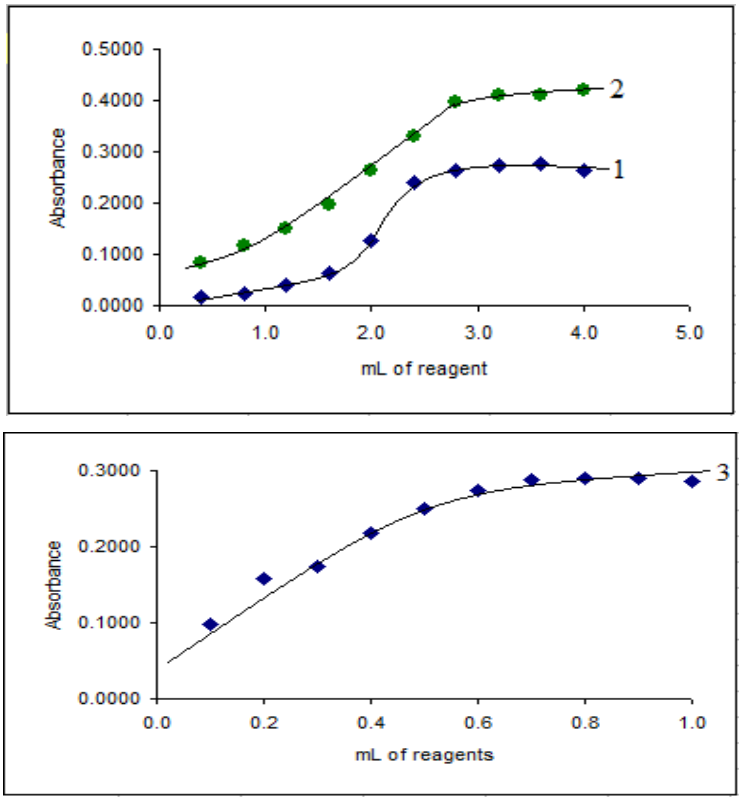


Figure 5. Effect of reagent concentration on OME complexes with (1) BTB, (2) MO and (3) PA

3.3. Stoichiometric ratio

Job's method of continuous variation was applied to determine the stoichiometry of OME complexes with BTB, MO and PA [36]. Equimolar solution of OME and all the acceptors were separately prepared in 100 mL volumetric flasks and absorbance of complex solutions of different ratios (0:10, 1:9, ……..10:0) (donor:acceptor) were measured. The

graph plotted between mole ratio of reagent vs. absorbance showed that OME interacts with each of acceptor in the ratio of 1:1 (figure 6).

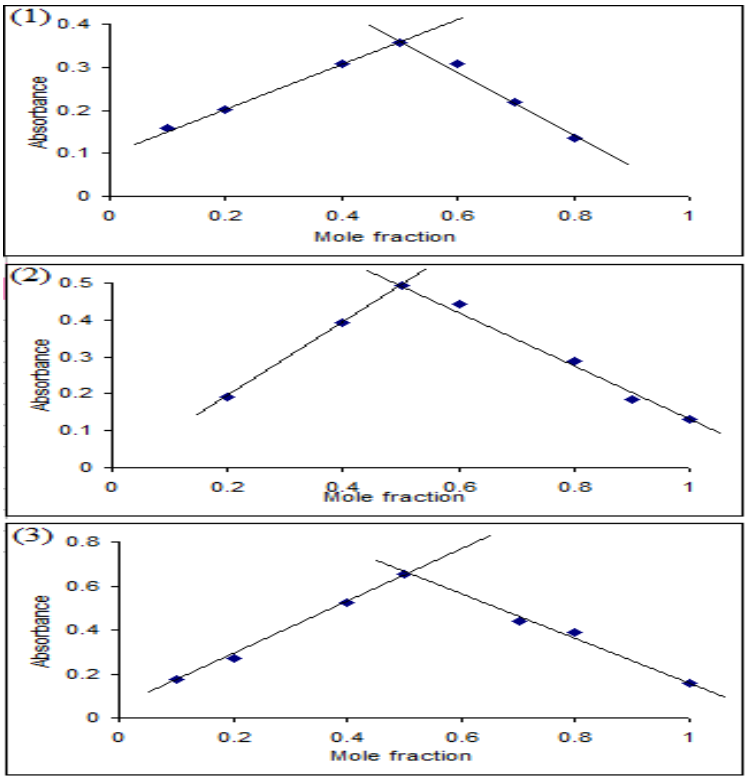


Figure 6. Job's plot for (1) OME-BTB, (2) OME-MO and (3) OME-PA

3.4. Analytical data

Under the established experimental conditions, calibration curves between concentration of OME in BTB, MO and PA complexes vs. peak area were plotted. Linear regression curve was obtained in the Beer's law range of 7-56, 6-48 and 10-80 µg mL^{-1} with correlation co-efficient greater than 0.998 in each case. Molar absorptivity values have been calculated which were found to be 5.10 x 10^3, 6.89 x 10^3 and 4.03 x 10^3 L. mol^{-1}. cm^{-1}. All the regression data including intercept, slope and correlation coefficient and also standard error and standard error of estimate are given in table 1.

Table 1. Optimum conditions and analytical parameters

Parameters	**BTB**	**MO**	**PA**
λ_{max} (nm)	400	420	373
Linearity range µg mL^{-1}	7-56	6-48	10-80
Molar absorptivity	5169	6892	4033
Slope	0.0155	0.0168	0.0105
Intercept	-0.0119	0.0941	0.0586
Correlation coefficient	0.9996	0.9997	0.9985
LoD ng mL^{-1}	211	292	107
LoQ µg mL^{-1}	0.639	0.884	0.324

3.5. Method validation

Linearity of developed analytical method was found to be in the concentration ranges 7-56, 6-48 and 10-80 µg mL^{-1} of OME with BTB, MO and PA and correlation coefficient greater than 0.998 for each method (table 1). Analyses were repeated for three days obtaining five measurements per day to evaluate inter-day and intra-day precision, which showed percent relative standard deviation 1.90, 0.96 and 1.91% respectively (table 2). Accuracy was analyzed by calculating percent recovery values and percent error in dosage formulation. The good recovery values in the range 98.46-101.75, 99.39-101.33 and 99.85-101.65% and error less than 1.75, 1.33 and 1.65% assure the accuracy of method (table 3). Sensitivity of method was established by determining the detection and quantitation limit. The LoD and LoQ values were calculated to be 211, 292, 107 ng mL^{-1} and 0.639, 0.884 and 0.324 µg mL^{-1} for BTB, MO and PA respectively (table 1).

Table 2. Precision of method

OME-BTB		**OME-MO**		**OME-PA**	
Conc µg mL^{-1}	**%RSD**	**Conc µg mL^{-1}**	**%RSD**	**Conc µg mL^{-1}**	**%RSD**
7	1.12	6	0.85	10	0.40
14	1.13	12	0.52	20	1.77
21	0.67	18	0.38	30	0.83
28	0.84	24	0.75	40	0.31
35	0.24	30	0.34	50	0.34
42	0.17	36	0.29	60	0.63
49	0.58	42	0.29	80	0.72
56	1.12	48	0.04	90	0.43

Table 3. Accuracy of method

OME-BTB		**OME-MO**		**OME-PA**	
% Rec	**% Err**	**% Rec**	**% Err**	**% Rec**	**% Err**
98.46	1.54	99.39	0.61	100.66	-0.66
101.75	-1.75	100.98	-0.98	101.59	-1.59
99.23	0.77	100.63	-0.63	101.65	-1.65
98.55	1.45	101.33	-1.33	100.61	-0.61
99.73	0.27	100.68	-0.68	100.68	-0.68
100.23	-0.23	99.45	0.55	99.85	0.15
100.42	-0.42	100.52	-0.52	100.68	-0.68

3.6. Effect of interference

Before analysis in pharmaceutical formulation, the effect of excipients, adjutants or additives usually present in dosage formulation were individually monitored by spiking OME in lactose monohydrate (10%), cellulose (10%), sucrose

(15%), starch (15%) and talc (10%). It was observed that the commonly present excipients do not interfere during analysis (table 4).

Table 4. Recovery of OME in presence of different excipients

Excipient	OME-BTB	OME-MO	OME-PA
	% Recovery		
Lactose Monohydrate	99.75	99.20	99.87
Cellulose	98.33	100.86	99.07
Sucrose	99.75	99.31	100.65
Talc	99.50	100.02	99.57
Starch	98.94	100.22	98.67

3.7. Pharmaceutical formulation

The applicability of method was ascertained by determining the OME in its dosage formulation. All the three suggested procedures were successfully applied. Five replicate determinations were made. Satisfactory recovery data in the range 98.46-101.75, 99.39-101.33 and 99.85-101.65% for BTB, MO and PA and small values of percent error were obtained indicating the reliability of method (table 3). The assay results were in good agreement with the label claim. Excipients commonly used in pharmaceutical formulation did not found to interfere during the assay.

3.8. Spectral characteristics of CT complexes

The experimental transition dipole moment (μ) and oscillator strength (f) of newly formed CT complexes were determined by formulae given in equation (1) and (2) [37-38];

$\mu = 0.0958\ (\varepsilon_{max}.\nu_{1/2}/\nu_{max})^{1/2}$ (1)

$f = (4.319 \times 10^{-9})\ \varepsilon_{max}.\nu_{1/2}$ (2)

where ε_{max} is molar extinction coefficient at maximum absorbance, ν_{max} is wave number in cm^{-1} and $\nu_{1/2}$ is the band-width at half absorbance in cm^{-1}. Relatively large values of oscillator strength indicate the strength of complexes. The ionization potential (Ip) of free donor was calculated by using the equation (3) [39].

$I_p = 5.76 + 1.53 \times 10^{-4}\ \nu_{CT}$ (3)

where ν_{CT} is the wave number in cm^{-1} corresponding to the charge transfer band of complex formed between donor and acceptor. Resonance energy of CT complex in the ground state was determined by Brieglab and Czekalla equation (4) given bellow [40]:

$\varepsilon_{max} = 7.7 \times 10^{-4}/ [h\nu_{CT}/ R_N-3.5]$ (4)

The energy of CT complexes was calculated by applying the relationship given in equation (5) [38]:

$$E_{CT}=1243.667/\lambda_{CT} \quad (5)$$

where λ_{CT} represents wavelength at maximum absorbance for charge transfer band. All the spectral data including dipole moment, oscillator strength, ionization potential, resonance energy and energy of CT complexes are presented in table 5. The association constant was determined by employing Benesi-Hildebrand equation [41].

$[A_o]/A = 1/K\ [D_o].\ \varepsilon + 1/\varepsilon$ (6)

where, K is the association constant, A represents absorbance, ε is molar extinction coefficient and $[A_o]$ and $[D_o]$ corresponds to initial concentrations of acceptors and OME respectively. The values for Kc are given in table 5.

Further investigation was made by plotting the values of $1/D_0$ versus A_0/A, which showed linear curve in all the cases. Table 6 presents the values and the graphs are displayed in figure 7.

Table 5. Spectrophotometric results

Complex	f	μ	Ip	E_{CT}	R_N	Kc x10^2 (lit/mol)	ΔG° (KCal)
OME-BTB	1.82	1.35	11.22	4.44	1.27	6.57	3.84
OME-MO	8.75	2.96	9.01	2.64	0.75	3.36	3.44
OME-PA	1.89	1.38	9.86	3.33	0.95	2.38	3.24

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

Complex	D (M) x 10^{-4}	A (M) x 10^{-3}	Abs	1/D x 10^4	A/Abs x 10^{-2}
OME-BTB	0.4	1.60	0.2109	2.46	0.76
	0.6	1.60	0.3127	1.64	0.51
	0.81	1.60	0.4195	1.23	0.38
	1.01	1.60	0.5272	0.98	0.30
	1.42	1.60	0.7519	0.70	0.21
OME-MO	0.52	3.05	0.3995	1.91	0.77
	0.69	3.05	0.4891	1.43	0.63
	0.87	3.05	0.5993	1.15	0.51
	1.04	3.05	0.7008	0.95	0.44
	1.22	3.05	0.8020	0.82	0.38
OME-PA	0.58	4.36	0.2515	1.73	1.74
	1.16	4.36	0.4744	0.86	0.92
	1.45	4.36	0.5741	0.69	0.76
	1.74	4.36	0.7014	0.58	0.62
	2.32	4.36	1.1121	0.43	0.39

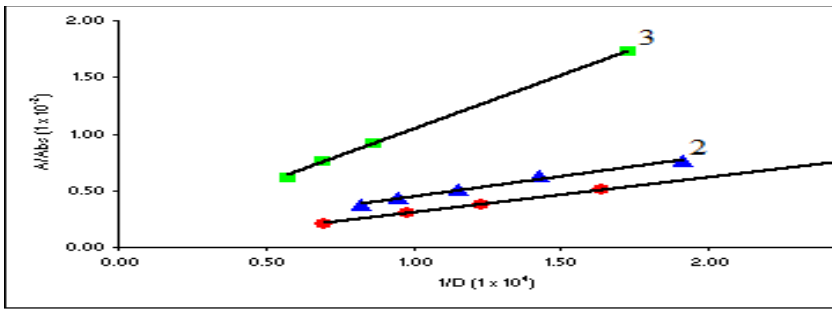


Figure 7. BH plot for OME complexes with (1) BTB, (2) MO and (3) PA

The standard free energy changes (ΔG°) associated with OME complexation reactions were established from association constants by applying equation (7) [42]. The values of ΔG° for each complex are given in table 5.

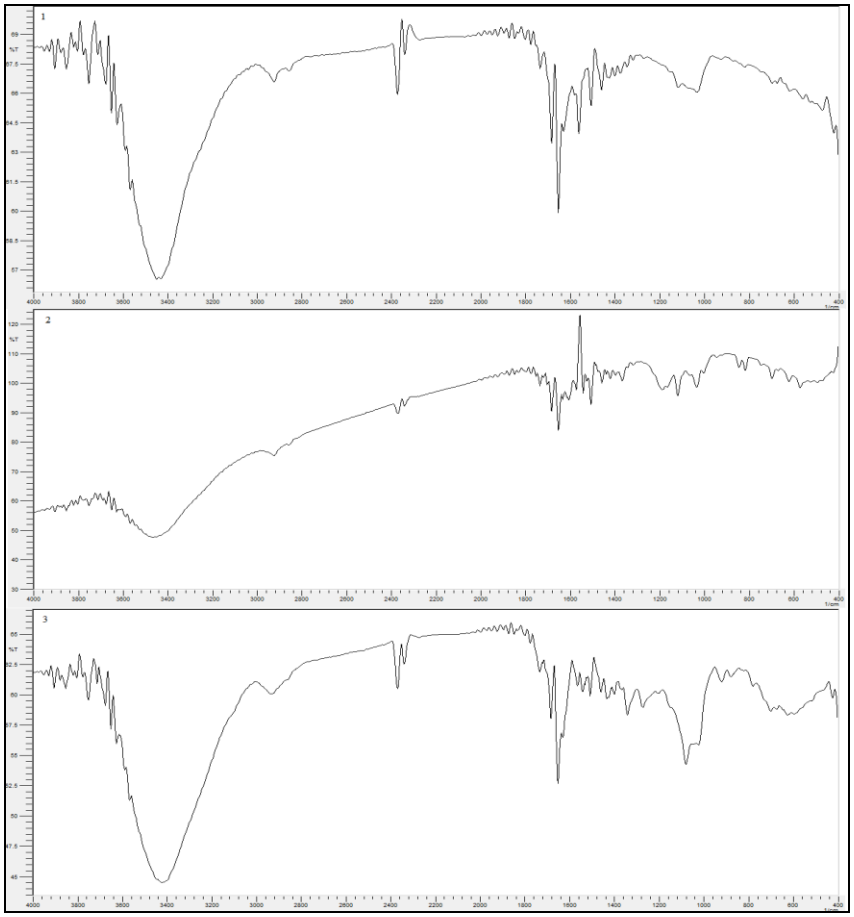
$$\Delta G° = -2.303RT \log K_C \qquad (7)$$

where ΔG° is the free energy change of complex, R is gas constant, T is temperature and K_c is association constant of OME-acceptor complexes.

3.9. Spectroscopic data

FT-IR: The IR spectra of CT complexes (figure 8) showed changes in band intensities and frequencies as compared to free donor and acceptor spectra which clearly indicate the interaction between OME and acceptors. The characteristic N-H peak of OME shifted from 3392 cm^{-1} to 3400 cm^{-1} in BTB, MO and PA complexes declaring the participation of N-H bond in complexation. The-OH of sulfonic group in BTB and MO and also the OH of PA interact with N-H of OME and ion pair complexes are formed. The IR frequencies and their band assignments of OME and its complexes are given in table 7.

Figure 8. IR spectra for (1) OME-BTB (2) OME-MO and (3) OME-PA



^{1}H NMR: The ^{1}H NMR of free donor and acceptor were studied in MeOD solvent at room temperature. OME showed intense peak at δ5.38 ppm attributing to the proton of N-H bond in 5-membered ring, which shifted to δ5.01, 5.37 and 5.09 ppm for BTB, MO and PA complexes respectively. Table 8 represents the chemical shift values of OME and its CT complexes

Table 7. Infrared frequencies and their assignments

OME	OME-BTB	OME-MO	OME-PA	Assignment
3392	3444	3425	3450	ν(N-H)
2943	2960, 2850	2924	2924	ν(C-H)
1654	1654	1654	1654	ν(C=N)
1620		1546	1583	ν(C=C)
	1500, 1541	1508	1541	ν(N-H)
1458	1462	-	1495	ν(C-H) deformation
1300	-	1369	1359	ν(C-N)
1205, 1076	-	-	1218, 1077	ν(C-O)
-	1161	-	-	ν(C-Br)
1018	1344, 1098	1035	1018	ν(S=O)
1170	1180	-	1176	ν(C-H) in plane
872		817	832	δ_{rock} CH_2
-	650	620	-	ν(S-O)
-	-	-	720	ν(NO_2)

Table 8. ^{1}H NMR spectra

Assignment	OME	OME-BTB	OME-MO	OME-PA
(s, CH_3)	δ 2.15	δ 1.98	δ 1.89	δ 2.45
(s, CH_3)	δ 2.23	δ 2.16	δ 2.14	δ 2.55
(s, OCH_3)	δ 3.82	δ 3.82	δ 3.78	δ 3.78
(s, OCH_3)	δ 3.84	δ 3.86	δ 3.84	δ 3.94
(s, CH_2)	δ 4.10	δ 4.03	δ 4.10	δ 4.10
(s, NH)	δ 5.38	δ 5.01	δ 5.37	δ 5.09
Aromatic	δ 6.90-7.50	δ 6.80-7.30	δ 6.81-6.84 δ 7.80-7.94	δ 6.9-7.5
CH (pyridine)	δ 8.53	δ 8.12	-	δ 9.05
(d, $4CH_3$)	-	δ 1.00	-	-
(s, CH_3)	-	δ 1.82	-	-
(s, CH_3)	-	δ 2.24	-	-
(m, 2CH)	-	δ 3.29	-	-
(s, $2CH_3$)	-		δ 3.09	-

On the basis of IR and ^{1}H NMR, the proposed structure of OME complexes are given in figure 9.

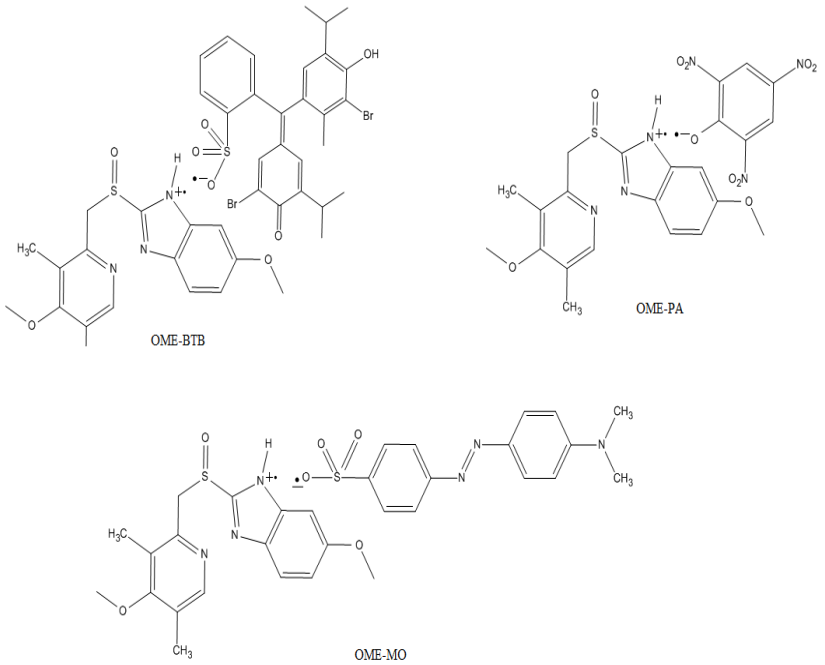


Figure 9. Proposed sructure of complexes

3.10. Advantages over reported methods

For the determination of OME, several techniques have been applied and articles have been reported for its determination in bulk drug, commercial formulations, biological and clinical samples. Different reported spectrophotometric methods have been compared in table 9. All of the previously reported methods are relatively less sensitive, time consuming or require the expensive reagents. In comparison, present study describes simple and more sensitive UV/ visible spectrophotometric method based on CT complex formation of OME with economic reagents like bromothymol blue, methyl orange and picric acid. Easy methodology is applied and results are calculated without employing any complicated equations. Moreover, none of the reported methods explicate the spectral characters of OME and its complexes. Here, we reported the oscillator's strength, dipole moment, ionization potential, energy of complexes, resonance energy, association constant and Gibb's free energy changes and constructed the Benesi-Hildebrand plot in each case. The interday and intraday precision and percent recovery values were evaluated. Results of analysis were validated successfully. These methods were fruitfully employed for OME determination in pharmaceutical formulations. Commonly present excipients did not show interference during analysis. Solid CT complexes were synthesized and characterized by spectroscopic techniques for structure elucidation.

Table 9: Reported spectrophotometric methods for OME

S. No.	Reagents used	Methodology	λ_{max} (nm)	Linear range µg mL^{-1}	LOQ µg mL^{-1}	Time (min)	Remarks	Ref.
1	-	Vierordt's equation	269	5-30	0.029	-	Complicated equation applied	18
2	-	EXRSM[a]	302	1–20	NA	-	Sensitivity is not given	17
	-	RDSM[b]	265 290					
	-	MCR[c]	277					
3	-	UV method	300	5-45	NA	-		16
4	BPB[d]	Ion-pair	408	5-30	NA	1		21
	Orange G		503	50-250				
5	4% methanol-ammonia	First derivative	307	1.61-17.2	1.126	NA		26
6	-	First derivative	313	10-30	0.49	NA		28
7	-	Second derivative	310	0.2-40	NA	-		29
8	TCNQ[e]	Charge transfer	843	3.40-14	NA	30		24
9	I_2	Charge transfer	362	0.25-3.0	0.08	45	Expensive reagents, Much analysis time	22
	DDQ		418	0.5-25	0.14	5		
10	Fe (III)	Chelation	411	15-95	0.70	15	Less sensitive Much analysis time	19
	Cr (III)		339	10-60	1.98	10		
	Co (III)		523	15-150	0.22	35		
11	-	Second derivative	306.2	2-40.2	0.033	-	Derivative spectrophotometric technique is non robust.	27
	-	Orthogonal function	306	0.5-3.5				
	-	Intact vs. deg. in NaOH	256	0.5-4.0				
	-	Intact vs. deg. in HCl	280	0.7-4.0				
12		First derivative	290.4	5-20	NA	NA		25
		Second derivative	320.6	5-20				
		Third derivative	311.6	5-20				
	Chloranil	Charge transfer	377	10-50				
13	MBTH[f]	Colorimetric	660	1.0-10	0.074	20	Much analysis time	20
	Chloramine-T		420	2.0-32	0.104	10		
	Celestine blue		540	0.4-2.4	0.023	5		
	Folin-Ciocalteau reagent		770	0.8-10	0.039	10		
14	I_2	Charge transfer	378	NA	NA	20		23
15	BTB	Charge transfer	400	7-56	0.211	<5	Sensitive, economic reagent, less analysis time	Present
	MO		420	6-48	0.292			
	PA		373	10-80	0.107			

[a]EXRSM = Extended ratio subtraction ; [b]RDSM = Ratio difference spectrophotometry; [c]MCR = Mean centering of ratio spectra; [d]BPB = Bromophenol blue

[e]TCNQ = Tetracyanoquinodimethane ; [f]MBTH = 3-methyl-2-benzothiazolinone hydrazone

4. Conclusion

Charge transfer complex of OME with BTB, MO and PA were analyzed in aqueous medium. Developed method was found to be simple and rapid and did not require expensive reagents or chemicals. However, the sensitivity of method is high. Linear calibration curves were obtained with R^2>0.998. The method showed great sensitivity and accuracy. Spectral characteristics including ionization potential, oscillator's strength, dipole moment and energy of complexes have been calculated. Besides, the solid CT complexes were synthesized and characterized by IR and ^{1}H NMR spectroscopy. Developed method was efficiently employed for OME determination in dosage formulation without obstruction of excipients.

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