SPECTROPHOTOMETRIC STUDY OF THE STOICHIOMETRY AND CONDITIONAL STABILITY CONSTANTS OF SOME TRIVALENT METAL ION COMPLEXES OF METHYLTHYMOL BLUE

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Abstract

Complexation reactions between methylthymol blue and Fe^{3+}, Al^{3+}, Ga^{3+}, In^{3+} and Tl^{3+} ions have been studied in buffer aqueous solutions of pH 5.0 at 25°C by a spectrophotometric technique. The conditional stepwise stability constants of the resulting 1:1 and 1:2 (metal-to-ligand) complexes were determined from the absorbance-mole ratio data at three different wavelengths of the visible spectra. The overall stabilities of the resulting complexes vary in the order $Al^{3+} > Fe^{3+} > Ga^{3+} \approx In^{3+} > Tl^{3+}$.

Introduction

Biological metal ion complexation is now of fundamental importance in the area of coordination chemistry. In particular, the design of highly selective chelating agents for trivalent metal ions such as Al^{3+}, Ga^{3+}, In^{3+}, Tl^{3+} and Fe^{3+} has received considerable attention [1-3]. The gallium and indium complexes of macrocyclic ligands are used as radiopharmaceutical agents [4]. Specific ligands for the coordination of Fe(III) are of interest as possible drugs for its removal from the body in cases of iron overload [5].

Methylthymol blue, 3,3'-bis[N, N'-di(carboxymethyl) aminomethyl] thymolsulphonaphthalein (MTB, Figure 1A) was first prepared, purified and introduced as an effective metallochromic indicator by Korbl [6,7]. Like its parent compound (i.e. thymolsulphonaphthalein), MTB behaves as an

Figure 1. Structures of MTB (A) and its 1:1 (B) and 2:1 (C) complexes with M^{3+} ions.
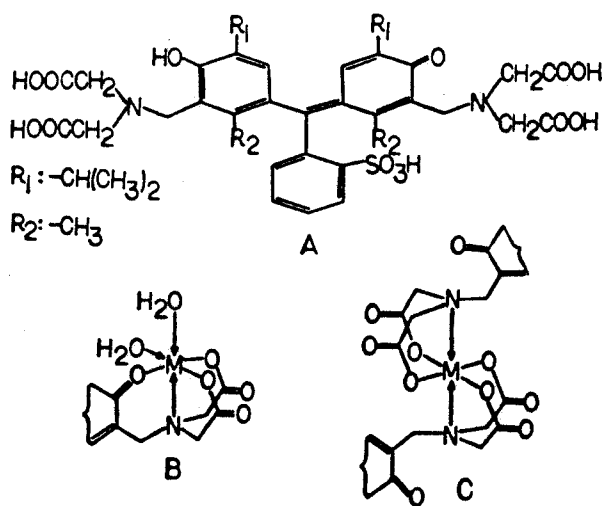
Keywords: Complexes; Conditional stability constants; Methylthymol blue; Spectrophotometry; Trivalent cations

J-base indicator with three colour changes: yellow
pH<6.5, pale blue at pH 6.5-8.5 and grey at pH
7-11.5. The solution turns dark blue at pH>12.7.
: reason for such colour changes has been ex-
ined by the presence of H-bonds and the alternating
mation of symmetrical and unsymmetrical
rotonated forms of the indicator [8,9]. The disso-
ion constants of the dyestuff have been reported
ore [8,10,11].

The yellow colour of MTB at pH 0 to 6 turns to
p blue upon complexation with many metal ions
luding alkaline earth, first series of transition met-
and heavy metal ions [9,12]. The stoichiometries
. stabilities of the resulting complexes in aqueous
ition have already been reported in the literature
[4].

In recent years, we have been involved in the study
complexation of some metallochromic indicators
h different metal ions [15-20] and their uses in the
ipetitive spectrophotometric investigation of the
wn ether complexes [21-24] and cryptates [25,26].
his paper, we report a spectrophotometric study of
complexation reactions between MTB and Fe^{3+},
$^+$, Ga^{3+}, In^{3+} and Tl^{3+} ions in aqueous buffer solu-
is of pH 5.0 at 25.00±0.05°C.

Experimental Section

Reagent grade nitrate salts of Fe(III), Al(III),
(III), In(III) and Tl(III) (all from Fluka) were of the
hest purity available and used without any further
ification except for vacuum drying over P_2O_5. Ana-
cal reagent grade methylthymol blue (MTB, p.a.,
asodium salt, Fluka) was used as received. Triply
illed deionized water was used throughout. A so-
m acetate/acetic acid buffer of pH 5.0 solution
out 0.1 M) was used to maintain the pH of solu-
is.

All spectra were recorded on a Philips PUB 700
ctrophotometer and the absorbance measurements
e made with a Metrohm 662 probe type photom-
. In all measurements, the cell was thermostated at
)0±0.05°C using a Lo-Temprol 154 Precision Sci-
ific thermostat. Measurements of pH were made
h a Corning 113 pH-meter using a combined elec-
le.

Results and Discussion

In order to determine the stoichiometry and stabil-
of the MTB complexes with the trivalent metal
i used, the spectra of a series of solutions contain-
a constant concentration of the ligand at the fixed
of 5.0 and varying amounts of the metal ions were
tined. Sample spectra are shown in Figures 2 and

3. With the exception of the Tl^{3+}-MTB system, the
spectra show that the metal ions used can form two
complexes of 1:1 and 1:2 (metal-to-ligand) stoichi-
ometries with MTB. While MTB absorbs light at 440
nm, maximum absorption wavelengths for 1:1 and 1:2
complexes are located at about 490 and 595 nm, re-
spectively. In addition, there are two clear isosbestic
points in the corresponding spectra indicating the oc-
currence of two consecutive equilibria during the titra-
tion of MTB with M^{3+} ions used.

The stoichiometry of the complexes was further
examined by the method of continuous variations
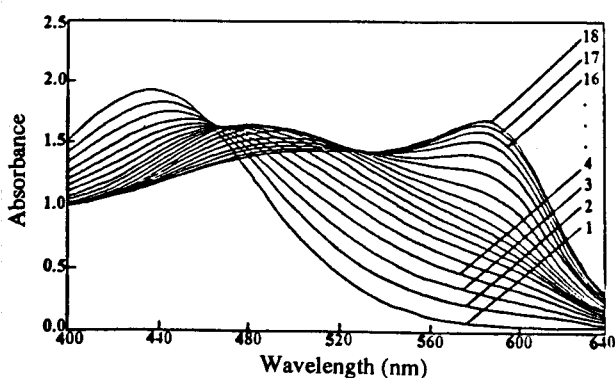[27,28]. A sample of the resulting plots is shown in

Figure 2. Visible spectra for titration of MTB (2.19 × 10^{-4} M)
with Ga^{3+} ion in aqueous solution at 25°C and pH= 5.0. Respec-
tive concentrations of Ga^{3+} ion (M) in different solutions are: 1,
0; 2, 1.28 × 10^{-5}; 3, 2.55×10^{-5}; 4, 3.83×10^{-5}; 5, 5.10× 10^{-5}; 6, 6.38
× 10^{-5}; 7, 7.65 × 10^{-5}; 8, 8.93 ×10^{-5}; 9, 1.02 × 10^{-4}; 10, 1.15 ×
10^{-5}; 11, 1.28 × 10^{-4}; 12, 1.40 × 10^{-4}; 13, 1.53 × 10^{-4}; 14, 1.66 ×
10^{-4}; 15, 1.79 × 10^{-4}; 16, 1.91 × 10^{-4}; 17, 2.04 × 10^{-4}; 18, 2.17 ×
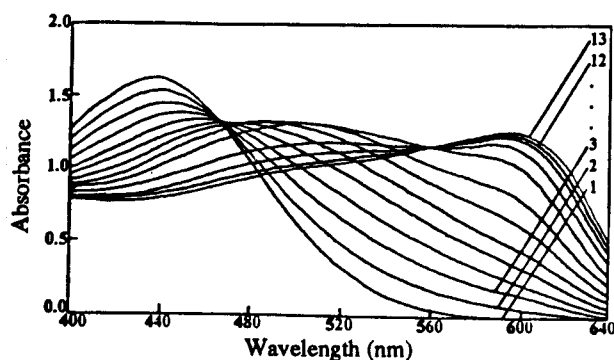10^{-4}.

Figure 3. Visible spectra for titration of MTB (1.05 × 10^{-4} M)
with In^{3+} ion in aqueous solution at 25°C and pH= 5.0. Respective
concentrations of In^{3+} ion (M) in different solutions are: 1, 0; 2,
1.19 × 10^{-5}; 3, 2.38 × 10^{-5}; 4, 3.55 × 10^{-5}; 5, 4.71 × 10^{-5}; 6, 5.85 ×
10^{-5}; 7, 6.99 × 10^{-5}; 8, 8.12 × 10^{-5}; 9, 9.23 × 10^{-5}; 10, 1.03 ×10^{-4};
11, 1.14 × 10^{-4}; 12, 1.25 × 10^{-4}; 13, 1.36 × 10^{-4}.

Figure 4A. As it is evident, the plot shows two distinct inflection points at X_{Fe} of about 0.35 and 0.50, emphasizing the formation of both 2:1 and 1:1 (metal-to-ligand) complexes in solution, respectively. Similar behaviour was also observed in the case of Al^{3+}, Ga^{3+} and In^{3+} complexes with MTB. However, in the case of Tl^{3+}-MTB system both the titration spectra and continuous variations plot (Figure 4B) clearly showed the formation of just a 1:1 complex in solution. It should be noted that such a large spectral shift observed, from free MTB to its M^{3+} complexes, (i.e. about 155 nm) most probably results from deprotonation of the ligand from the H_4L^{2-} to the H_2L^{4-} form and from the corresponding changes in the conjugation of the dyestuff [29].

As seen from Figure 1A, MTB is a derivative of thymolsulphonaphthalein with two N, N' - di(carboxymethyl) aminomethyl groups attached to its 3, 3'-positions, each of which is capable of coordinating to a metal ion. It should be noted that, because of the steric hindrance of the bulky backbone of

sulphonphthalein, the coordination of both N, N' - di(carboxymethyl) aminomethyl groups to the same metal ion seems impossible. Thus, a possible structure for the six-coordinate 1:1 complex between the trivalent metal ions used and MTB is given in Figure 1B. In this case, the ligand acts as a tetradentate chelating agent [9]. On the other hand, in the presence of excess MTB, the highly charged metal ions would prefer to be coordinated with two MTB molecules, at the expense of the release of the coordinated water molecules into solution. A possible structure for the six-coordinate 1:2 (metal-to-ligand) complex of M^{3+} ions with MTB is shown in Figure 1C. In 1:2 complexes, it seems reasonable to assume that MTB tends to act as a tridentate ligand, so that each ligand would occupy three coordination sites of the central cation.

The conditional stepwise stability constants of the resulting 1:1 and 1:2 M^{3+}-MTB complexes were obtained at 25°C and pH 5.0 by absorbance measurements, at three different wavelengths of the corresponding visible spectra, of solutions in which varying concentrations of metal ions were added to fixed amounts of MTB in solution. It should be noted that since the measurements were made at a constant pH of 5.0, the possible contributions from the hydrolysis constants for $[M(OH)_m]^{(3-m)+}$ and the formation constants for $[M(OAc)_n]^{(3-n)+}$ in the overall stability of the resulting MTB complexes were not considered in the calculations. Incidently, all the stability constants obtained in this work are conditional constants.

When MTB reacts with a metal ion, M^{3+}, it may form either a 1:1 complex (model I) or both 1:1 and 1:2 (metal-to-ligand) complexes (model II). The mass balance equations of the two possible models in solution, shown in Table 1, can be solved in order to obtain equations for the free ligand concentration, [L], (Table 2). The observed absorbance of solution is given by

$$A_{obs} = \varepsilon_L[L] + \varepsilon_{1:1}[M\text{-}L] + \varepsilon_{1:2}[M\text{-}L_2] \quad (1)$$

where ε values are the molar absorptivities of the species denoted. For evaluation of the conditional stability constants from the absorbance vs. C_M/C_L mole ratio data, a non-linear least-squares curve fitting program KINFIT was used [30]. The program is based on the iterative adjustment of calculated values of absorbance to observed values by using either the Wentworth matrix technique [31] or the Powell procedure [32]. Adjustable parameters are the conditional stepwise stability constants of the complexes present in solution and the corresponding molar absorptivities (i.e. two and four adjustable
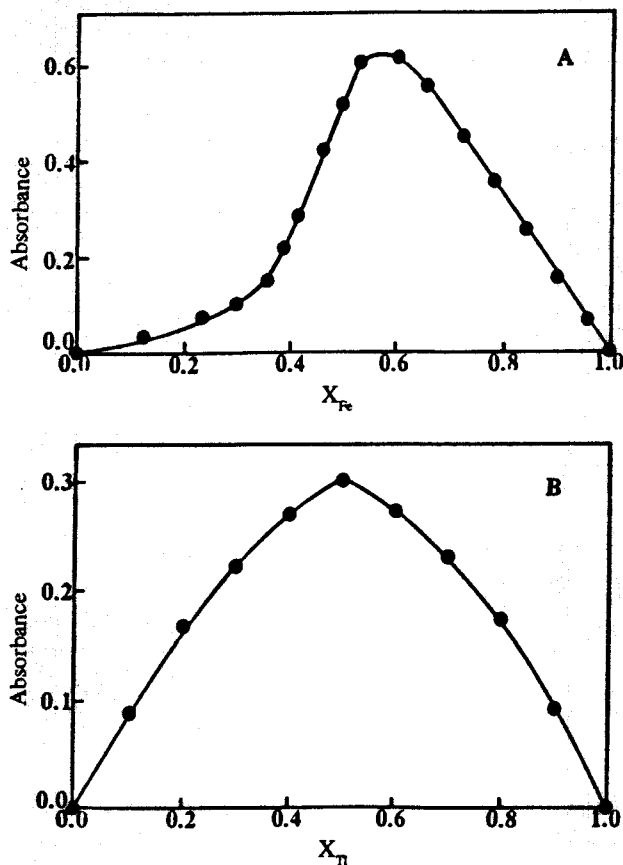
Figure 4. Continuous variations plots for Fe^{3+}-MTB (A) and Tl^{3+}-MTB (B) systems. $C_M + C_L = 1.0 \times 10^{-4}$ M in (A) and $C_M + C_L = 5.0 \times 10^{-5}$ M in (B).

Table 1. Mass-balance equations used in computer program KINFIT for evaluation of spectro-photometric data

Model	Reactions	Formation constants	Mass-balance equations
I	$M + L = ML$	$K_1 = [ML]/[M][L]$	$C_M = [M] + [ML]$ $C_L = [L] + [ML]$
II	$M + L = ML$	$K_1 = [ML] / [M] [L]$	$C_M = [M] + [ML] + [ML_2]$
	$ML + L = ML_2$	$K_2 = [ML_2] / [ML]$	$C_L = [L] + [ML] + 2 [ML_2]$

Table 2. Solution of the mass-balance equations given in Table 1 in terms of the free ligands concentration [L]

Model	Solution
I	$K[L]^2 + (1 + K_1(C_M - C_L)) [L] - C_L = 0$
II	$K_1 K_2 [L]^3 + (K_1(1 + K_2(2C_M - C_L))) [L]^2 + (1 + K_1(C_M - C_L)) [L] - C_L = 0$

Table 3. Conditional stepwise and overall stability constants of Fe^{3+}, Al^{3+}, Ga^{3+}, In^{3+} and Tl^{3+} complexes with methylthymol blue at pH 5.0 and 25°C

Cation	Ionic radius[a]	Wavelength	$\log K_1$	$\log K_2$	$\log \beta_2$
Fe^{3+}	0.87	480	7.46±0.02	5.34±0.05	
		540	7.53±0.01	4.76±0.05	
		620	7.45±0.06	5.26±0.10	
		Mean value	7.48±0.07	5.12±0.07	12.60±0.10
Al^{3+}	0.68	435	6.84±0.04	6.59±0.04	
		510	6.82±0.03	6.62±0.04	
		525	6.85±0.06	6.62±0.04	
		Mean value	6.84±0.04	6.61±0.04	13.45±0.06
Ga^{3+}	0.76	470	4.92±0.03	4.64±0.04	
		533	4.83±0.06	4.83±0.07	
		585	4.80±0.02	4.70±0.02	
		Mean value	4.85±0.04	4.72±0.04	9.57±0.06
In^{3+}	0.94	463	5.47±0.03	4.22±0.02	
		505	5.50±0.07	4.06±0.06	
		558	5.64±0.02	3.39±0.10	
		Mean value	5.53±0.04	3.89±0.06	9.42±0.07
Tl^{3+}	1.03	440	3.75±0.03		
		610	3.62±0.01		
		Mean value	3.69±0.02		

[a]Data taken from Ref. 35.

parameters for models I and II, respectively).

For models I and II, the free ligand concentrations, [L], were calculated by means of a Newton-Raphson procedure. Once the value of [L] had been obtained, the concentrations of all other species involved were calculated from the corresponding mass-balance equations given in Table 1, by using the estimated values of the stability constants at the current iteration step of the program. Refinement of the parameters was continued until the sum-of-squares of the residuals between calculated and observed values of the absorbance for all experimental points were minimized. The output of the program KINFIT comprises the refined parameters, the sum-of-squares and the standard deviation of the data.

With the exception of Tl^{3+}-MTB, all the absorbance-mole ratio data were best fitted to model II (Tables 1 and 2), which further supports the formation of both 1:1 and 1:2 complexes in solution. Sample computer fits of the mole ratio data for Fe^{3+}-MTB are shown in Figure 5 and all the resulting conditional stability constants for complex species present in solution are summarized in Table 3. It is interesting to note that the existence of two inflection points at metal-to-ligand mole ratios of about 0.5 and 1 (Figures 5A and 5B) are also indicative of the formation of both 1:2 and 1:1 adducts in solution, respectively. However, the mole ratio data for Tl^{3+}-MTB system were only fitted to model I, which was constructed based on the formation of a single 1:1 complex in solution.

The data given in Table 3 clearly show that for the case of each M^{3+}-MTB system studied, the conditional stepwise stability constants evaluated from the computer fitting of absorbance-mole ratio data at three different wavelengths (two wavelengths in the case of thallium complex) are in excellent agreement with each other. This is indicative of the high degree of reliability of the method used for the determination of the K_1 and K_2 values. Comparison of the stability data revealed that while the overall stability constant (log β_2) for the MTB complexes decreases in the order $Al^{3+}>Fe^{3+}>Ga^{3+}\approx In^{3+}>Tl^{3+}$, the stepwise stability constants vary differently as:

log K_1: $Fe^{3+}>Al^{3+}>In^{3+}>Ga^{3+}>Tl^{3+}$

log K_2: $Al^{3+}>Fe^{3+}>Ga^{3+}>In^{3+}$

The observed trends of stabilities of the MTB complexes with Al(III), Ga(III), Tl(III) and Fe(III) cations would not seem to follow a predictable pattern. This is most probably due to some mix combination of different constitutional factors such as effective ionic radii of cations, metal ion electron negativity and steric fac-

tors resulting from differences in the chelating character of MTB in the formation of 1:1 and 1:2 complexes. From the resulting stability data, it seems unlikely that
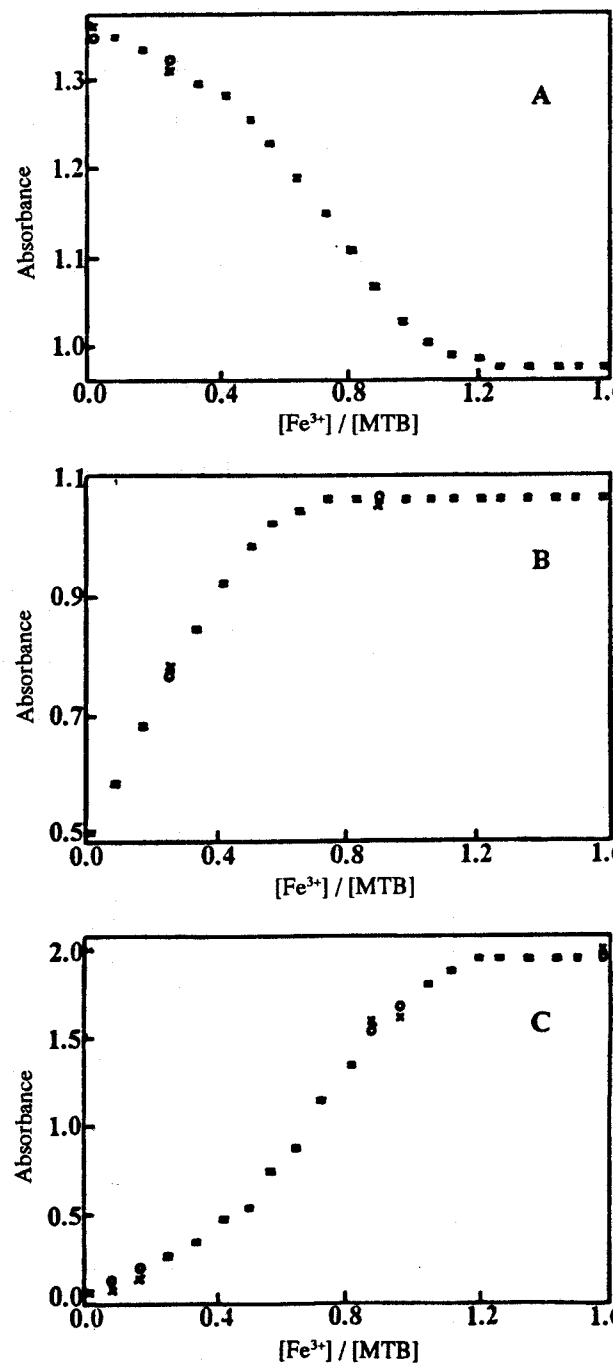

Figure 5. Computer fit of absorbance-mole ratio data obtained from the complexation of Fe^{3+} with MTB at various wavelengths: (A) 480 nm, (B) 540 nm, (C) 620 nm; (x) experimental points; (o) calculated points; (=) experimental and calculated points are the same within the resolution of the plot.

observed sequences in the formation constants can entirely related to the size of metal ions used. tile Ga^{3+} ion, with some larger ionic size than Al^{3+}, ms a much weaker MTB complex in comparison h aluminium ion, the overall stability of its MTB nplex is comparable with that of In^{3+} ion which has nuch larger ionic size than Ga^{3+} ion. Such unusual naviour in In^{3+} complex can be most probably re- :d to its suitable size for 1:1 complex formation h MTB, as a tetradentate ligand in this case.

On the other hand, the overall stability of the MTB nplex of Fe^{3+} ion, with about the same ionic size as $^{3+}$ ion, is more than three orders of magnitude her than that of Ga^{3+} -MTB complex. A possible son for such a large difference in the overall stabili- ; of Fe(III) and Ga(III) complexes is the differences the preferred orientations of MTB's oxygen and ni- gen donor groups in the coordination spheres of the ions as well as the forced distortion of the preferred ahedral orientation in the 1:2 (metal-to-ligand) nplex toward a triangular prismatic structure [33,]. Finally, the effect of a much larger ionic radius of $^{l+}$ ion in its preferred 1:1 complex formation and in huge decreased stability (some 10 orders of magni- le in comparison with Al^{3+} complex), indicates that rd-COO⁻ groups of MTB are not suited for effective ordination to large metal ions.

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