Ternary Complexes of some Sulphadrugs and Salicylaldhyde with Cu^{2+} and Fe^{3+} - A Spectral Study

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Sulphamethazine (SMZ), sulphathiazole (STZ) and Tolbutamide (TA) form 1:1 and 1:2 complexes with Cu^{2+} and Fe^{3+}. The bonding sites are the oxygen of sulphonamide group and heterocylic nitrogen atom of aryl moiety. Cu^{2+} and Fe^{3+} ions form ternary complexes with salicylaldhyde as the primary ligand and SMZ, STZ and TA as secondary ligands. The spectrophotometric data indicate the formation of 1:1:1 ternary complexes. Stability of binary and ternary complexes were found to be in the order: SMZ > STZ > TA.

Metal ions participate in most of the biological reactions actively and biological systems are dominated by different ligands. Studies of metal ligand model systems are proved useful in understanding the roles of metal ions in biological systems [1-2]. Sulphonamide group is well known for its antibacterial actions and are found to inhibit the growth of many bacteria [3]. Complex formation of Cu^{2+} and Fe^{3+} with salicylaldehyde as the primary ligand and sulphamethazine (SMZ), sulphathiazole (STZ) and tolbutamide (TA) as secondary ligands has been reported here.

EXPERIMENTAL

Stock solution of metal nitrate (0.05 $mol.dm^{-3}$), sulphadrugs (from the Nile company) (0.02 $mol.dm^{-3}$) and salicylaldehyde (Aldrich) (0.002 $mol.dm^{-3}$) were prepared in absolute ethanol. The stoichiometry of the complex solution was determined spectrophotometrically using both molar ratio [4] and continuous variation methods [5]. The spectral measurements were made with freshly prepared solutions on UV- visible recording spectrophotometer (shimadzu UV -240).

Conductometric titration were carried out at room temperature (30°C) using WPA. C.M. 25 conductivity meter and an immersion cell using 25.0 ml of 1.0×10^{-3} $mol.dm^{-3}$ metal ion solution with 1.0×10^{-2} $mol.dm^{-3}$ of ligand solution in 0.5 ml increment.

RESULTS AND DISCUSSION

Absorption Spectra of Ligand & Binary Complex

Spectra of the ligand was recorded against alcohol as the blank. In the study of the complex, the spectra of the metal + ligand solution in ethanol was taken with solution of the ligand at the same concentration in ethanol as blank. Typical electronic absorption spectra the free ligands and their 1:1 metal ligand solutions are recorded in Fig.1 . The entire spectral data are collected in Table 1. The spectra consist mainly of three bands for compounds SMZ

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Table 1

Spectral data of the Free ligand and Complexes

Maximum Wavelength (λ_{max} in nm) and extinction coefficient ($\varepsilon x10^{-3}$ in $mol^{-1}.cm^2$) sh = shoulder

Free Ligands		Binary Complexes				Ternary Complexes			
		Cu(II)		Fe(III)		Cu(II)		Fe(III)	
λ_{max}	$\varepsilon x10^{-3}$	λ_{max}	$\varepsilon x10^{-3}$	λ_{max}	$\varepsilon x10^{-3}$	λ_{max}	$\varepsilon x10^{-3}$	λ_{max}	$\varepsilon x10^{-3}$
Ligand SMZ									
205	28.5	230	4.0	-	-	-	-	-	-
212sh	26.0	240	4.0	240	48.75	280	3.38	290	5.25
270	31.5	310	1.65	285	25.0	390	1.88	360	2.88
Ligand STZ									
205	27.0	220	4.31	210	9.95	-	-	-	-
268	23.25	270	2.67	240sh	3.6	275	6.06	275	6.0
295	26.25	-	-	270	4.0	395	2.25	365	3.0
Ligand TA									
210	41.50	230	8.8	215	5.5	-	-	-	-
-	-	260sh	1.2	225sh	3.63	280	613	285	6.13
-	-	-	-	240sh	2.06	395	1.88	360	2.75

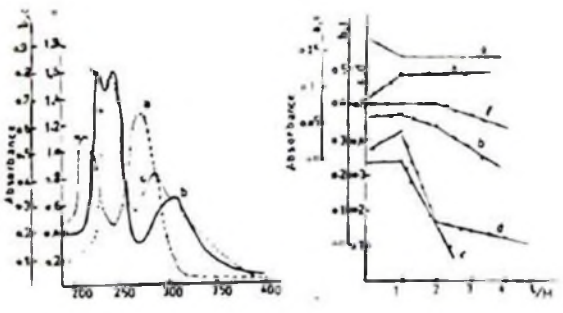
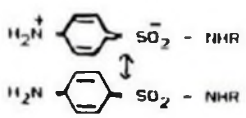


Fig 1 Absorption Spectra of 1:1 metal: SMZ Chelates
a [Free SMZ] = 2 x 10^{-4} M
b [Cu^{2+} - SMZ] = 1.6x10^{-4} M
c [Fe^{3+} - SMZ] = 2 x 10^{-4} M

Fig 2 Metal Chelate Study by Mole - Ratio Method
a SMZ - [Cu] = 2x10^{-4} M; l = 300 nm
b SMZ - [Fe] = 1.6x10^{-4} M; l = 300nm
c STZ - [Cu] = 1.2x10^{-4} M; l = 267 nm
d STZ - [Fe] = 1 x10^{-4} M; l = 290 nm
e TA - [Cu] = 1.8x10^{-4} M; l = 280 nm
f TA - [Fe] = 1.6x10^{-4} M; l = 260 nm

& STZ and one band for compound TA. The peak at shorter wavelength (at 205 nm for SMZ and STZ or at 210 nm for TA) can be assigned to π - π^* transition of the benzenoid system [6]. The second band in the UV region (within the wavelength 268 nm and 270 nm for STZ and SMZ respectively) may be used to gain information about the extent of electron delocalization in sulphonamides. A number of hypotheses have been presented suggesting the following resonance structure [7,8].

Sulphonamides



The spectra of complex solutions show that the band of both Fe^{3+} and Cu^{2+} complexes [7] are split into several components. These split components are observed for the shorter as well as for the longer wavelength. The lower energy split in the longer wavelength band have been related to binuclear nature of copper and iron complexes [9,10]. This behaviour may be due to (L-M^{n+}) charge - transfer band [11], indicating co-ordination of the ligand to metal as a result of the high positive charge of the co-ordinated metal ion.

The stoichiometry of the chelate formed in solution, with these ligands was investigated using molar ratio and continuous variation methods (Fig.2). In all cases the blank was a solution of the ligand of the same concentration as in the solution of the chelate. The results reveal the posible formation of 1:1 Cu^{2+} complex

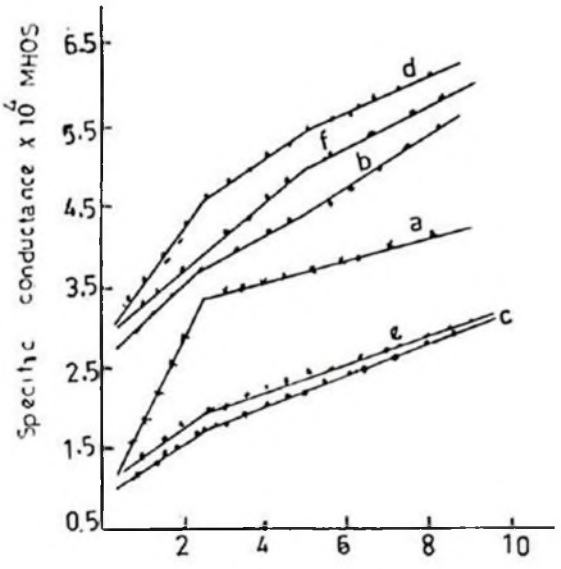


Fig 3 Conductometric Titration
25 ml of 10^{-3} M metal ion with 10^{-2} M Sulpha drugs.
a SMZ - [Cu] b SMZ - [Fe]
c STZ - [Cu] d STZ - [Fe]
e TA - [Cu] f TA - [Fe]

Table 2

Formation Constants (ß) & Free Energy Changes (DG° in k.cal/mol at 25°) of the Complexes

Method	Cu^{2+}(1:1)		Fe^{3+} (1:1)		Fe^{3+} (1:2)	
	β	ΔG°	β	ΔG°	β	ΔG°
SMZ complexes						
M.R.	$6.11x10^5$	7.408	$2.14x10^7$	9.386	$1.8x10^{15}$	19.533
C.V.	$2.8x10^5$	7.476	$2.84x10^7$	10.230	$2.52x10^{15}$	21.139
STZ complexes						
M.R.	$2.2x10^5$	6.840	$1.70x10^7$	9.258	$1.12x10^{15}$	19.270
C.V.	$1.6x10^5$	7.168	$1.2x10^7$	9.750	$1.23x10^{15}$	20.712
TA complexes						
M.R.	$4.6x10^4$	5.970	-	-	$3.15x10^8$	10.881
C.V.	$7.4x10^4$	6.683	-	-	$3.55x10^8$	11.735

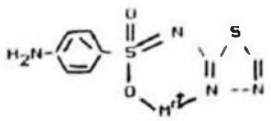
ß±(1.5 - 2.1%); ΔG° ± (0.009 - 0.12%)

with all ligands and 1:1 or 1:2 Fe^{2+} complexes. The apparent formation constant (K_f) of the complex species in solution were calculated from the spectrophotometric data. The K_f values are collected in Table 2 together with ΔG^* values.

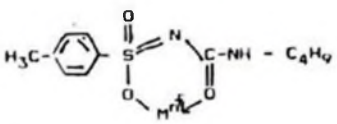
The results of conductometric titration of the metal ions with the ligands (Fig.3) are in accordance with those obtained from the spectrophotometric methods. The observed gradual increase of conductance on increasing ligand ion concentration is due to the replacement of hydrogen of sulphonamide group (SO_2NH_2 group) of ligand by the metal ions forming metal-ligand complexes. It is evident from the results shown in Table 2, that stability constant values of the metal chelate decrease in the following order SMZ > STZ > TA.

The formation constant of the 1:1 (M-L) chelates decrease as the valency of the metal (Fe^{3+} > Cu^{2+}).

The inramolecular charge transfer (C.T.) takes place within the chelated ligand as indicated below [12] :



STZ Complex



TA Complex

Accordingly, the longer wavelength band observed in the spectra of all chelates is ascribed to an intramolecular C.T transition within the six member chelate ring formed.

Table 3

Validity of Beer's law of Sulphadrugs Chelates

Ligand	Amt (mg/50ml)	ppm	λ_{max}	$\varepsilon_{max} \times 10^{-3}$
Cu Complexes				
SMZ	$(0.2 - 10) \times 10^{-5}$	0.18 - 9.16	310	2.27
STZ	$(0.4 - 10) \times 10^{-5}$	0.37 - 9.11	270	1.91
TA	$(2.0 - 8.03) \times 10^{-5}$	1.83 - 7.35	262	1.41
Fe Complexes				
SMZ	$(0.2 - 12) \times 10^{-5}$	0.11 - 6.71	310	3.73
STZ	$(0.4 - 11.9) \times 10^{-5}$	0.22 - 6.7	290	3.4
TA	$(1.0 - 11.6) \times 10^{-5}$	0.92 - 6.5	260	3.36

λ_{max} in nm; ε_{max} in mol^{-1}. cm^2

The spectrophotometric method can be applied for the micro-determintion of the metal ions; A constant concentration of the ligand (colouring agent) is mixed with different concentration of the tested metal ion. The molar absorptivity values of the formed chelate are high (Table 3). This value would suggest the validity of the method for the micro-determination of the elements under investigation. It is found that, the minimum amount which can be measured for each the metal ions runs in the following order SMZ > STZ > TA.

This behaviour is in line with general order of stability of the chelates studied here.

Spectral Study of Ternary Complexes

The visible spectra of SMZ, STZ and TA or SA exhibit an absorption band at about 270 nm. But the spectrum of the metal + ligand solution against a solution of the same concentration of the ligand as blank shows an apparent new band at 360 nm for Fe^{3+}/SA/SMZ or Fe^{3+}/SA/TA, 365 nm for Fe^{3+}/

SA/STZ, 390 nm for Cu^{2+}/SA/SMZ, 395 nm for Cu^{2+}/SA/STZ or Cu^{2+}/SA/TA. The later band is presumably due to the formation of a mixed - ligand complex with metal. The relations obtained are characterized by a maximum at a point corresponding to mole fraction equal to 0.5 for continuous variation method and 1.0 for molar ratio method. This suggests the stoichiometry of 1:1:1 for the ternary complex. The apparent stability constants (K_f) of the complexes are determined using the equation

$$\beta = \frac{A/A_{max}}{(1 - A/A_{max})^2 C}$$

where A_{max} is the limiting absorbance corresponding to the concentration of ML at full colour development, A is the abasrbance corresponding to the concentration of the complex molecules existing in equilibrium and C is the initial concentraion of the metal ion. In all cases the blank solution for spectral measurements was a solution of salicylaldhyde and sulphadrugs of the same concentration as in the ternary complex solution. Fig.4 and 5 are representive. The values of β_1 and ΔG° are collected in Table 4. The results indicate the formation constant values of the (1:1:1) complex decrease in the following order SMZ > STZ > TA

This order is in accordance with the decrease in basicity of these ligands (pK's = 8.5, 8.35 and 6.35 respectively). The bonding in the mixed ligand complexes occurs through oxygen atoms of both sulphonamide group of sulphadrugs and aldehyde group of salicylaldehyde. The

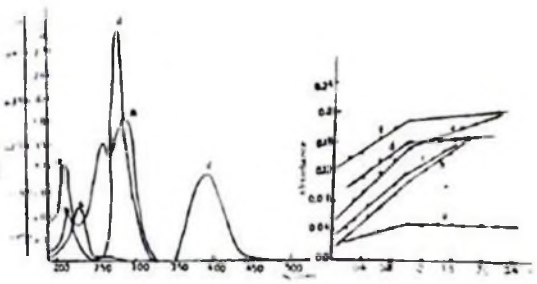
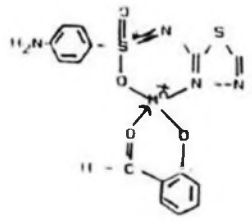


Fig 4 Absorption Spectra of 1:1:1 Cu: STZ SA Chelates
a [Free STZ]: b [Cu^{2+} - STZ]
c [Cu^{2+} - SA]: d [Cu^{2+} - STZ - SA]
Fig 5 Mole - Ratio Method of Ternary Complexes
a [Cu]- TA - SA]; b [Cu] STZ - SA; c [Cu]- SMZ - SA
d [Fe]-SMZ- SA; e [Fe] - STZ - SA; f [Fe]- TA - SA

Table 4

Formation Constants (ß) & Free Energy Changes (ΔG° in k.cal/mol at 25°) of 1:1:1 Mixed Ligand Complexes

Method	Cu(II)		Fe(III)	
	ß	ΔG°	ß	ΔG°
SMZ complexes				
M.R	$2.09X10^6$	8.092	$6.29X10^7$	9.985
C.V.	$1.8X10^6$	8.009	$7.74X10^7$	10.101
STZ Complexes				
M.R.	$2.84X10^6$	8.263	$1.51X10^7$	9.192
C.V.	$2.65x10^6$	8.224	$1.01x10^7$	8.968
TA Complexes				
M.R	$1.04X10^6$	7.704	$6.68X10^6$	8.738
C.V	$1.68x10^6$	7.97	$7.09x10^6$	8.772
ß±(1.5 - 2.1%);			$\Delta G^\circ \pm$ (0.009 - 0.12%)	



SMZ TernaryComplex

structure of the ternary complexes can be represented schematically as above

The values of formation constants with respect of metal ions are in the order: Fe^{3+} > Cu^{2+}. This is the same order for both binary and ternary complexes. Obviously the metal of higher valancy forms stronger complex.

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