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Hydroxytriazenes as Indicator for Iron(III): Determination of Iron in Pharmaceutical Samples and Binary Metal Ions Mixtures

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With seven hydroxytriazenes as metallochromic indicators iron(III) could be determined even at very low concentration. The iron contents in pharmaceutical preparations could also be determined accurately.

INTRODUCTION

Hydroxytriazenes (R—N(OH)—N=N—R′ where R is alkyl or aryl group and R′ is aryl group) are well established analytical reagents[1–5]. However only a few of these have so far been used as metallochromic indicators for the complexometric determination of iron(III) by Jaimini *et al.*[6], Purohit *et al*[7], Majumdar and Chakraborti[8] and Golwalkar and Purohit[9]. Present work deals with the use of seven hydroxytriazenes as metallochromic indicators for the complexometric determination of iron(III). Attempt has also been made to use these hydroxytriazenes as metallochromic indicators for the determination of iron in iron containing formulations. Further all the seven hydroxytriazenes have also been used to determined both the components of synthetic binary mixtures of iron(III) with other metal ions, namely; nickel(II), cobalt(II) and copper(II).

EXPERIMENTAL

Preparation of hydroxytriazenes

Following seven hydrozytriazenes were synthesized and used in the present work.

Name of the Reagent	Reagent No.
3-Hydroxy-3-ethyl-1-*o*-hydroxyphenyltriazene	I
3-Hydroxy-3-*n*-propyl-1-*o*-hydroxyphenyltriazene	II
3-Hydroxy-3-phenyl-1-*o*-hydroxyphenyltriazene	III
3-Hydroxy-3-*p*-tolyl-1-*o*-carboxyphenyltriazene	IV
3-Hydroxy-3-phenyl-1-*m*-methoxyphenyltriazene	V
3-Hydroxy-3-isopropyl-1-*o*-hydroxyphenyltriazene	VI
3-Hydroxy-3-*p*-tolyl-1-*o*-hydroxyphenyltriazene	VII

Hydroxytriazene No I to V are already reported and as such they were synthesized following the methods reported in the literature[10–12]. Remaining two compounds have been synthesized for the first time by the procedures given below.

Preparation of 3-Hydroxy-3-Isopropyl-1-*o*-hydroxy-phenyltriazene

Isonitropropane (28.0 mL) was reduced by NH_4Cl-zinc dust (each 30.0 g) at 0–15°C to obtain isopropyl-hydroxylamine. Diazotised product of *o*-aminophenol (22.0 g) was rapidly mixed with aqueous alcoholic solution of isopropyl-hydroxylamine previously prepared and cooled to 0° to 5°C. Mixture was filtered under suction and left overnight at room temperature for the complete precipitation. Crude product so obtained was recrystallized twice with ethanol. Orange yellow plates were obtained [yield *ca* 16.0 g (43%), m.p. 148°C m.f. $C_9H_{13}N_3O_2$, Analysis % Found (Calcd.), C, 55.2 (55.3); H, 6.6 (6.5) and N, 22.4 (21.5)].

Preparation of 3-Hydroxy-3-*p*-tolyl-1-*o*-hydroxy-phenyltriazene

Aqueous alcoholic (3:1) solution of 0.8 mol (36.5 g) of *o*-nitrotoluene was reduced by ammonium chloride (15.5 g) and zinc dust (40.0 g) at temperature between 60°–65°C *p*-tolylhydroxylamine so obtained (24.0 g *i.e.*, 0.2 mole) was coupled with diazotised product of 0.2 mole (22.0 g) of *o*-aminophenol in the same way as described in the earlier preparation. Crude product was recrystallized twice with ethanol and orange yellow crystals were obtained (yield 20.0 g (43%) and m.p. 138°C m.f. $C_{13}H_{13}N_3O_2$, Analysis %, Found (Calcd.), C, 64.0 (64.1); H, 5.3 (5.3) and N, 17.1 (17.2).

Preparation of Solutions

(i) *Metal Ions*: Stock solution of iron(III) (0.01 M) was prepared by dissolving requisite quantity of ferrous ammonium sulphate in water, oxidizing it with nitric acid and making up to the desired volume. Stock solutions (0.01 M) of copper(II), cobalt(II) and nickel(II) were prepared by dissolving requisite quantities of AR Grade (BDH), sulphates of these metal ions in double distilled water which were standardized by usual methods[13]. Weaker solutions were prepared by appropriate dilution.

(ii) *Reagents*: A 0.1% (w/v) ethanolic solution of each reagent was prepared by dissolving requisite quantity of hydroxytriazene in ethanol. Fresh solutions were prepared from time to time.

(iii) *pH adjustment*: Mixtures of proper volumes of 0.1 M acetic acid and 0.1 M sodium acetate solutions were prepared and used as buffers to maintain desired pH of metal ion solutions.

(iv) *Digestion of pharmaceutical samples*: Mineralization of pharmaceutical samples was done by treating the appropriate quantity of sample with concentrated HNO_3 and evaporating it to dryness. The process was repeated twice and the residue was finally dissolved in minimum quantity of dil. HNO_3.

RESULTS AND DISCUSSION

Optimum Conditions of Titration

The optimum conditions of pH and temperature for titration were established by carrying out a series of titrations between centinormal iron(III) solution and equimolar EDTA solution in different temperature ranges between 20°–50°C and in different pH ranges between 2 to 5 using each of the seven hydroxytriazenes as indicators. All the seven hydroxytriazenes used as indicators gave satisfactory results in entire temperature range studied *i.e.* 20°–50°C. However ideal pH range for them was found to be 3 to 3.5 where colour change at the end point was sharpest and most perceptible.

Procedure for titration of iron(III) solution

A 10.0 mL of iron(III) solution containing 5.58 mg to 0.11 mg of it was taken in a conical flask. A 5 mL of sodium acetate-acetic acid buffer was added to maintain the pH between 3 to 3.5. Four to five drops of 0.1% indicator (hydroxytriazene) were added. Instantaneous development of intense bluish-violet colour took place with each of the seven hydroxytriazenes. In case of reagents Nos. II and III a slight turbidity appeared which was removed by adding 2–3 mL of alcohol. The solution was titrated with EDTA solution (equimolar to iron(III) solution) very slowly for colour change at the end point from bluish-violet to light yellow. An average of five determinations has been tabulated in Table 1.

TABLE–1
COMPLEXOMETRIC DETERMINATION OF IRON(III)

Iron(III) taken in mg	Iron(III) found in mg using indicator No. (% error)						
	I	II	III	IV	V	VI	VII
5.580	5.552 (+0.5)	5.580 (–)	5.608 (+0.5)	5.552 (–0.5)	5.580 (–)	5.552 (–0.5)	5.580 (–)
2.790	2.776 (–0.5)	2.790 (–)	2.790 (–)	2.817 (+0.96)	2.790 (–)	2.790 (–)	2.776 (–0.5)
1.116	1.116 (–)	1.110 (–0.53)	1.116 (–)	1.110 (–0.53)	1.116 (–)	1.116 (–)	1.110 (–0.53)
0.558	0.558 (–)	0.560 (+0.35)	0.560 (+0.35)	0.555 (–0.53)	0.558 (–)	0.560 (+0.35)	0.555 (–0.53)
0.279	0.279 (–)	0.280 (+0.35)	0.277 (–0.71)	0.279 (–)	0.280 (+0.35)	0.277 (–0.71)	0.279 (–)
0.111	0.111 (–)	0.111 (–)	0.111 (–)	0.110 (–0.9)	0.112 (+0.9)	0.112 (+0.9)	0.112 (+0.9)

Interference studies

For interference studies iron(III) solution containing 5.58 mg was titrated with EDTA solution under optimum conditions in presence of varying quantities of each of the 20 foreign ions using each of the seven indicators. It was found that results were identical for all the seven indicators. Thus in the determination of

5.58 mg of iron(III), presence of even 5 mg of four ions, namely, Zn(II), Hg(II), $S_2O_3^{2-}$ and F^- seriously interfered. However Co(II) and Cu(II) were tolerated up to 20 mg; Zr(IV), SO_3^{2-} Ni(II) and Mg(II) up to 50 mg and Na(I), Ca(II), Ba(II), Cl^-, Br^-, I^-, NO_2^-, acetate, CO_3^{2-} and SO_4^{2-} were tolerated up to 100 mg.

Procedure for Titration for Binary Mixtures of Fe(II)-Ni(II), Fe(III)-Co(II) and Fe(III)-Cu(II)

A method was developed to determine both the components of binary mixtures of Fe(III)-Ni(II), Fe(III)-Co(II) and Fe(III)-Cu(II) using each of the seven hydroxytriazenes as indicators and that too without the use of any masking or demasking agent. An aliquot (10–15 mL) of synthetic binary mixture containing 2.79 to 5.58 mg of iron(III) and 2.93 to 5.89 mg of other metal ion was taken in a conical flask. Its pH was maintained between 3 to 3.5 by adding 5 to 7 mL of acetic acid sodium acetate buffer. Four to five drops of 0.10% alcoholic solution of one of the indicators were added. Instantaneous development of intense bluish-violet colour took place. The solution was titrated directly with centinormal EDTA solution for light green end point in case of iron(III)-nickel(II) mixture, light blue end point in case of iron(III)-copper(II) mixture and light pink end point in case of iron(III)-cobalt(II) mixture. Iron(III) in the binary mixture was determined by direct titration. After this direct titration addition of EDTA was continued till its volume was 2 to 3 mL more than what was theoretically required for total amount of both the metal ions of the mixture. The resultant solution was back titrated with standard iron(III) solution for bluish-violet end point to determine excess EDTA from which the amount of other metal ion was calculated. The determination of iron with other metal ion in steps was possible on account of large difference in stabilities of iron(III), cobalt(II), nickel(II) and copper(II) complexes with EDTA *e.g.*, Fe(III)-EDTA ($\log K_1 = 25.42$), Ni(II)-EDTA ($\log K_1 = 18.66$), Co(II)-EDTA ($\log K_1 = 16.31$) and copper(II)-EDTA ($\log K_1 = 18.87$). Thus in the first step iron(III) was titrated directly, and in the second step in the same solution other metal ion was titrated. Results (average of five determinations) are given below in Table 2.

Application

Determinations of iron in pharmaceutical samples

A method was developed to determine iron volumetrically in iron containing pharmaceutical preparations using each one of the seven hydroxytriazenes as indicators. Preparations selected for this purpose were; Fefol (Eskayef-Banglore); Softeron (Aristo pharmaceutical-Raisen (M.P.)); Raricap (Ethnor-Bombay); Tonoferon Syrup (East India pharmaceuticals works-Calcutta) and Hematrine [Sandoz (India)-Thane]. Requisite quantity of preparations (tab/cap/syrup) was taken which gave 5.58 mg of iron per 100 mL of final solution. Mineralization of pharmaceutical samples was done by the method as described earlier. An aliquot (10 to 15 mL) of this final solution was titrated with centinormal EDTA solution under the optimum conditions of the titration using each of the seven

hydroxytriazenes as indicators. Results obtained (worked out per tablet/capsule/5 mL of syrup) are given in Table 3.

TABLE–2
DETERMINATION OF CONSTITUENTS OF BINARY MIXTURE

Indicator No.	Fe(III)-Ni(II)		Fe(III)-Co(II)		Fe(III)-Cu(II)	
I	2.79*	2.93	5.58	5.89	4.18	4.72
	2.77$	2.93	5.88	5.86	4.18	4.74
	−0.71#	—	—	−0.5	—	+0.42
II	2.79	2.93	5.58	5.89	4.18	4.72
	2.84	2.93	5.55	5.89	4.20	4.70
	+1.75	—	−0.53	—	+0.47	−0.42
III	2.79	2.93	5.58	5.89	4.18	4.72
	2.79	2.99	5.60	5.83	4.16	4.72
	—	+2.04	+0.36	−1.01	−0.47	—
IV	2.79	2.93	5.58	5.89	4.18	4.72
	2.84	2.90	5.55	5.89	4.18	4.72
	+1.75	−1.02	−0.53	—	—	—
V	2.79	2.93	5.58	5.89	4.18	4.72
	2.79	2.99	5.58	5.89	4.18	4.72
	—	+2.04	—	—	—	—
VI	2.79	2.93	5.58	5.89	4.18	4.72
	2.79	2.93	5.58	5.89	4.18	4.72
	—	—	—	—	—	—
VII	2.79	2.93	5.58	5.89	4.18	4.72
	2.79	2.90	5.58	5.86	4.18	4.74
	—	−1.05	—	−0.50	—	+0.42

* Metal taken in ag; $ Metal found in mg; # % Error.

TABLE–3
DETERMINATION OF IRON IN PHARMACEUTICAL SAMPLES

Name of Medicine	Amount of iron present in mg per tablet/cap/syp	Amount of iron found in mg using (% Error) indicator No.					
		I	II	III	IV	V	VI
Softeron	54.00	54.27 (+0.5)	54.00 (–)	54.00 (–)	54.27 (+0.5)	54.27 (+0.5)	53.73 (–0.5)
Raricap	25.00	24.87 (–0.5)	25.00 (–)	25.12 (+0.5)	24.87 (–0.5)	25.12 (+0.5)	25.00 (–)
Fefol	55.00	55.55 (+1)	54.45 (–1)	55.27 (+0.5)	54.72 (–0.5)	55.00 (–)	55.00 (–)
Hematrine	32.38	32.38 (–)	32.70 (+1)	32.38 (–)	32.38 (–)	32.31 (–0.5)	32.54 (+0.5)
Tonofaren Syrup	250.00	250.00 (–)	248.75 (–0.5)	250.00 (–)	250.00 (–)	248.75 (–0.5)	250.00 (–)

Conclusion

All the seven hydroxytriazenes studied are equally good for determination of iron(III), in binary mixture or alone. Both the constituents of binary mixture of Fe(III)-Ni(II), Fe(II)-Co(II) and Fe(III)-Cu(II), could easily be determined using each of the hydroxytriazenes as indicator. Contents of pharmaceutical samples could also be determined. The study thus leads to development of hydroxytriazenes as good indicators for iron(III).

REFERENCES

1. D.N. Purohit, *Talanta*, **14**, 363 (1967).
2. D. Chakroborty and A.K. Majumdar, *J. Indian Chem. Soc.*, **54**, 258 (1977).
3. R.L. Dutta and R. Sharma, *J. Sc. and Ind. Res.*, **40**, 715 (1981).
4. D.N. Purohit, Nizamuddin and Arun M. Golwalkar, *Rev. Anal. Chem. (Israel)*, **8**, 76 (1985).
5. D.N. Purohit, M.P. Tyagi, Rita Bhatnagar and I.R. Bishnoi, *Revs. Anal. Chem. (Israel)*, **11**, 259 (1992).
6. J.P.C. Jaimini, D.N. Purohit and N.C. Sogani, *Z. Anal. Chem.*, **203**, 181 (1964).
7. D.N. Purohit, J.P. Jaimini and N.C. Sogani, *J. Inst. Chemists (India)*, **38**, 123 (1966).
8. A.K, Majumdar and D. Chakroborti, *Anal. Chem. Acta*, **55**, 450 (1971).
9. A.M. Golwalkar and D.N. Purohit, *Ciencia E Cultura (Brazil)*, **38**, 552 (1986).
10. A.K. Mukherjee, "Studies of some organic compounds containing nitrogen as chelating agents", Ph.D. Thesis, University of Rajasthan, Jaipur (1971).
11. J.K. Humad, "Hydroxytriazenes in the determination of Zinc, Cadmium, and Molybdenum". Ph.D. Thesis, Sukhadia University, Udaipur (1984).
12. D.N. Purohit and J.K. Humad, *Ciencia E Cultura (Brazil)*, **38**, 358 (1986).
13. F.A. Flaschka, EDTA Titrations, Pergamon Press, New York (1964).

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