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CHROMIUM (III) COMPLEXES ANIONS IN THE CHEMICAL ANALYSIS ANAFRANILE DETERMINATION

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ABSTRACT

Some new gravimetric, oxidimetric and spectrophotometric methods for the determination of anafranile as anafranile H[Cr(NCS)$_4$(amine)$_2$] have been described. Statistical treatment of the experimental data shows that the methods employed are sufficiently accurate and are not affected by systematic errors

KEYWORDS: Cr(lll), anafranile determination, complex salts

RESUMO

O presente trabalho descreve alguns métodos gravimétricos, espectrofotométricos e de oxidação novos para a determinação da afranila como afraniloH[Cr{NCS}$_4$(amino)$_2$]. Tratamento estatístico dos dados experimentais mostra que os métodos desenvolvidos tem precisão adequada e não são afetados por erros sistemáticos.

PALAVRAS CHAVE: Cromo(III), determinação de afranila, sais complexos

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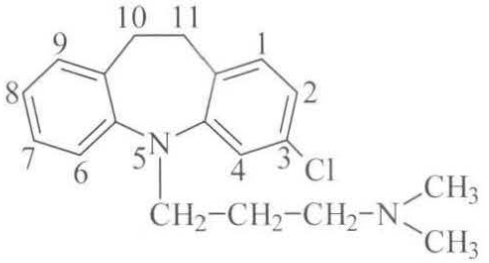
INTRODUCTION

Anafranile (3-chlor-5-[3-(dimetilamine)-propil]-10,11-dihydro-5H-dibenzo [b,f] azepinehydrochlorate), chlomipramine hydrochlorate (3-chlorine-imipramide) is an antihistamine, anticholinergic, tricyclic antidepressive medicine. It is given in the form of tablets of 10, respectively 25mg anafranile hydrochlorate/tablet.

The structural formula of this drug is:



Anafranile is obtained through a similar method to that described for antideprin [1]. In the literature it does not mention many methods for determining this drug [2].

We have observed that in acid medium, anafranile precipitates quantitatively with Reinecke's salt and its analogous, of type $NH_4[Cr(NH_4)(amine)_2]$, where the amine is: aniline, toluidine, Et_2PhP, imidazole, cystamine etc., in the form of anafranile·$H[Cr(NH_4)(amine)_2]$. For this reason we could elaborate three methods for determining this drug by gravimetric, oxidimetric and spectrometric methods [3].

Anafranile compounds with Reinecke salt and its analogous are red-violet coloured, hardly soluble in water but easily soluble in acetone, DMF, DMSO, etc. The solutions obtained allowed us to make the spectrophotometric determination of this substance.

EXPERIMENTAL PROCEDURE

Synthesis of reagent $NH_4[Cr(NH_4)(amine)_2]$ was made according to the method of Ion Ganescu [4], starting with $K_3[Cr(NCS)_6]$ anhydrous and N-respective base.

The elementary analysis of anafranile complexes with complex anions of Cr(lll), type $[Cr(NCS)_4(amine)]$ was as follows:

- anafranile·$H[Cr(NH_4)(amine)_2]$

M=786.42

%Cr: calc. 6.61, found 6.57

%N: calc. 10.68, found 10.62

%S: calc. 16.31m found 16.26.

- anafranile·$H[Cr(NCS)_4(Et_2PhP)_2]$

M=880,57

%Cr: calc. 5.90, found 5.87

%N: calc. 9.54, found 9.74

%S: calc. 14.54, found 14.48.

- anafranile·$H[Cr(NCS)_4(pilocarpine)_2]$

M=880,57

%Cr: calc. 5.12, found 5.07
%N: calc. 11.02, found 10.98
%S: calc. 12.60, found 12.54.
- anafranile·H[Cr(NCS)$_4$(scopolamine)$_2$]
M=1199,88
%Cr: calc. 4.33, found 4.29
%N: calc. 9.33, found 9.28
%S: calc. 10.67, found 10.61.
- anafranile·H[Cr(NCS)$_4$(cystamine)$_2$]
M=880,56
%Cr: calc. 5.90, found 5.87
%N: calc. 22.26, found 22.15
%S: calc. 14.54, found 14.48.

RESULTS AND DISCUSSION

New complexes salts of anafranile with thiocyanatochromic complexes of type anafranile·H[Cr(NCS)$_4$(pilocarpine)$_2$]

A sample of 0.01-0.02 moles of anafranile was treated with distilled water up to 50-80mL, subsequently, a solution 3% of thiocyanatochromic complex salt was added until the above solution of the precipitate was red-violet. The reactions mixture was allowed to stay for 15-20 minutes and then was filtered, washed with distilled water and dried. The experimental results are presented in Table 1.

Table 1. New complex salts of type anafranile·H[Cr(NCS)$_4$(pilocarpine)$_2$].

Crt no.	Combination	Molecular Weight calculated	Yield %	Microcrystalline character	Analysis %	
					Calc.	Found
1	A·H[Cr(NCS)$_4$(NH$_3$)$_2$]	614.29	97	Red-violet Microcrystals	Cr:8.46 S:20.88 N:13.67	8.42 20.81 13.62
2	A·H[Cr(NCS)$_4$(aniline)$_2$]	786.42	98	"	Cr:6.61 S:16.31 N:10.68	6.57 15.69 10.26
3	A·H[Cr(NCS)$_4$(benzylamine)$_2$]	814.42	96	"	Cr:6.38 S:15.75 N:10.31	6.34 15.69 10.26
4	A·H[Cr(NCS)$_4$(imidazole)$_2$]	736.58	93	"	Cr:7.06 S:17.41 N:15.21	7.02 17.36 15.15
5	A·H[Cr(NCS)$_4$(benztriazole)$_2$]	839.46	95	"	Cr:6.19 S:15.28 N:16.68	6.16 15.22 16.61
6	A·H[Cr(NCS)$_4$(urotropine)$_2$]	880.56	96	"	Cr:5.90 S:14.54 N:22.26	5.87 14.48 22.15

A= anafranile; Cr as Cr_2O_3; N-gas-volumetric.

Gravimetric determination

A sample of 2.1-21 mg anafranile in the form of hydrochlorate was diluted with distilled water to a volume of 50 mL and then precipitated with reagent $NH_4[Cr(NCS)_4(amine)_2]$, where amine is aniline and Et_2PhP, in hydroalcoholic solution (2%). After 15-20 minutes, the precipitate was filtered by using a G4 filter crucible, washed two-three times with 10 mL distilled water until the filtrate flowed colorless, dried in a drying oven at 105-110°C for an hour and after that it was weighed with an analytical balance. [5,6] The experimental results are shown in Table 2.

Table 2. The gravimetric determination of anafranile after precipitation in the form of anafranile·$H[Cr(NCS)_4(aniline)_2]$ (A) and anafranile·$H[Cr(NCS)_4(Et_2PhP)_2]$ (B).

Anafranile mg taken	Form of determination							
	A				B			
	Weighed $G_{complex}$	Anafr. mg found	Error		Weighed $G_{complex}$	Anafr. mg found	Error	
			mg	%			mg	%
2.1	5.20	2.08	-0.02	0.95	5.85	2.09	-0.01	0.48
4.2	10.54	4.22	+0.02	0.48	11.81	4.22	+0.02	0.47
8.4	20.96	8.39	-0.01	0.12	23.57	8.43	+0.03	0.36
12.6	31.53	12.62	+0.02	0.16	35.12	12.56	-0.04	0.32
16.8	42.06	16.84	+0.04	0.24	47.07	16.83	+0.03	0.18
21.0	52.57	21.05	+0.05	0.24	58.87	21.05	+0.05	0.24
M_A=786.42; f_A=0.4004 $\overline{X}$=8.41 $S^2=6.33\cdot10^{-4}$ $S=2.51.10^{-2}$ t=0.4 $t_{n-1,\alpha}$=2.26; α=95% $\overline{X}$ -ts<A<$\overline{X}$ +ts 8.39<8.40<8.41					M_A=880.57; f_B=0.3576 $\overline{X}$=16.81 $S^2=7.66\cdot10^{-4}$ $S=2.51.10^{-2}$ t=0.36 $t_{n-1,\alpha}$=7.26; α=95% $\overline{X}$ -ts<A<$\overline{X}$ +ts 16.79<16.80<16.81			

Oxidimetric determination

A sample of 2.1-21 mg anafranile was treated with HCl as described above, then precipitated with thiocyanatochromic reagents; the precipitate was filtered with filter paper using a 5 diameter Büchner funnel and it was washed with 10 mL distilled water until the filtrate flowed colourless. The paper with the respective precipitate was transferred moved in a high- shaped Berzelius glass of 500 mL to which 20 mL solution of NaOH 5% are added. The glass containing the precipitate is boiled on a gas burner sieve when green-coloured $Cr(OH)_3$ appears. $Cr(OH)_3$ is destroyed with HCl so that its normal condition in each sample should be 1.7 N. Then 5 mL CCl_4 and

110 drops ICl [7] are added, it is titrated with a solution 0.1 N $KMnO_4$, $KBrO_3$ and KIO_3 under continuous stirring until the violet layer of CCl_4 discolors. The experimental results are shown in Table 3.

Table 3. Oxidimetric determination of anafranile after precipitation in the form of anafranile·H[Cr(NCS)$_4$(pilocarpine)$_2$] (A) and anafranile·H[Cr(NCS)$_4$(scopolamine)$_2$]. (B).

Anafr.mg taken	Det. no.	$\overline{X}$ mg	S	t_a	t_b	$t_{n-1,\alpha}$ α=95%
Permanganometric determination						
2.1	10	2.109	$2.81 \cdot 10^{-2}$	$6.978 \cdot 10^{-4}$	$18.46 \cdot 10^{-2}$	2.57
16.8	10	16.83	$2.77 \cdot 10^{-2}$	$6.978 \cdot 10^{-4}$	$14.46 \cdot 10^{-2}$	2.57
Bromatometric determination						
4.2	10	4.211	$2.52 \cdot 10^{-2}$	$28.69 \cdot 10^{-4}$	$18.51 \cdot 10^{-2}$	2.57
12.6	10	12.613	$2.77 \cdot 10^{-2}$	$23.11 \cdot 10^{-4}$	$18.36 \cdot 10^{-2}$	2.57
Iodatometric determination						
8.4	10	8.411	$2.51 \cdot 10^{-2}$	$26.06 \cdot 10^{-4}$	$18.03 \cdot 10^{-2}$	2.57
21.0	10	21.011	$2.52 \cdot 10^{-2}$	$22.89 \cdot 10^{-4}$	$18.45 \cdot 10^{-2}$	2.57

1 mL solution 0.1N ($KMnO_4$, $KBrO_3$, KIO_3) is equivalent to 1.312 mg anafranile.

This method is very responsive because 1 mole of SCN^- consumes six equivalents of oxidizer:

$$SCN^- - 6e^- + 4H_2O \rightarrow SO_4^{2-} + HCN + 7H^+$$
$$5SCN^- + 6MnO_4^- + 13H^+ \rightarrow 6Mn^{2+} + 5SO_4^{2-} + 5HCN + 4H_2O$$
$$2SCN^- + 3IO_3^- + 4H^+ \rightarrow 2SO_4^{2-} + 3I^+ + 2HCN + H_2O$$
$$2SCN^- + 3BrO_3^- + 4H^+ \rightarrow 2SO_4^{2-} + 3Br^+ + 2HCN + H_2O$$

The method is accurate, rapid and, according to statistical data, it is not affected by systematic errors.

Spectrophotometric determination

A sample of 2.15-2.17 mg anafranile in the form of hydrochloride are precipitated with reagent NH_4[Cr(NCS)$_4$(cystamine)$_2$] in hydroalcoholic solution 2%. The precipitates was filtered with a G_4 crucible, it was washed two-three times with 10 mL distilled water until the filtrate flowed colourless and then it was dissolved in acetone. The red-violet solution is moved to a volumetric flask balloon and was completed with acetone up to the mark. The absorbance of this solution was measured at 540 nm. [9,10] The experimental results are shown in Table 4.

$$y - \bar{y} = r\frac{\sigma_x}{\sigma_y}(x - \bar{x})\,;\ y=0.0605049x + 0.000674$$

$$x - \bar{x} = r\frac{\sigma_x}{\sigma_y}(y - \bar{y})\,;\ x=16.4925664y + 0.0093486$$

The concentration domain, where the Lambert-Beer law is followed, lies between 0.086 mg and 0.6868 mg anafranile.

The molar extinction coefficient is ε=1333.4048 $Lcm^{-1}mole^{-1}$. The calibration curve for spectrophotometric determination of anafranile in the form of anafranile·H[$Cr(NCS)_4(cystamine)_2$] is presented in figure 1.

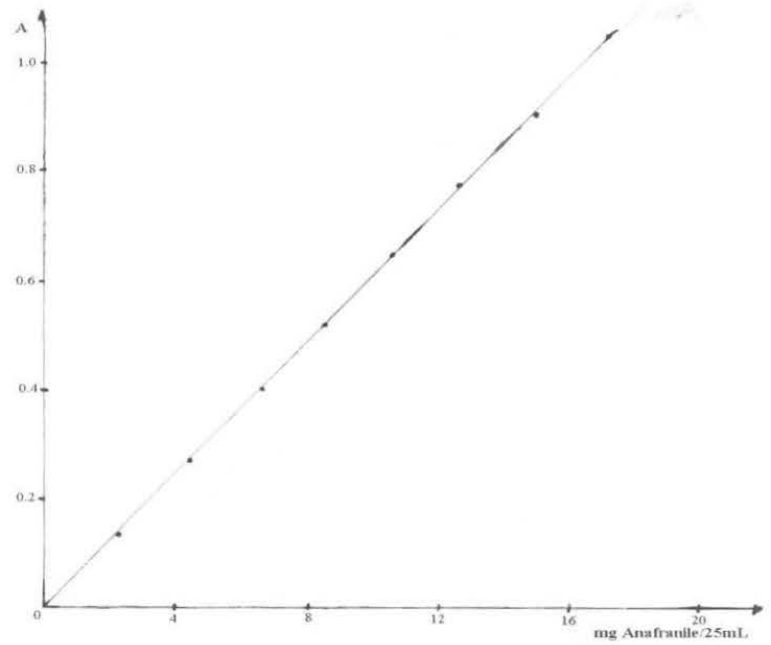


Figure 1. Determination of anafranile in the form of anafranile·H[$Cr(NCS)_4(cystamine)_2$].

The variation of absorbance with wave length is presented in Figure 2 and the variation of colour depending with time is presented in Figure 3.

Table 4. Spectrophotometric determination of anafranile, after precipitation, in the form of anafranile H[Cr(NCS)$_4$(cystamine)$_2$].

Crt. no.	x mg	x^2	y	y^2	xy	x+y	$(x+y)^2$
1	2.15	4.6225	0.13	0.0169	0.2795	2.28	5.1984
2	4.29	18.4041	0.26	0.0676	1.1154	4.55	20.7025
3	6.44	41.4736	0.39	0.1521	2.5116	6.83	46.6489
4	8.59	73.6164	0.52	0.2704	4.4616	9.10	82.8100
5	10.73	115.1329	0.65	0.4225	6.9745	11.38	129.5044
6	12.88	165.8944	0.78	0.6084	10.0464	13.66	186.5956
7	15.02	225.6004	0.91	0.8281	13.6682	15.93	253.7649
8	17.17	294.8089	1.04	1.0816	17.8568	18.21	331.6041
Total	77.26	939.5532	4.68	3.4476	56.914	81.94	1056.8288

From these data statistically processed [8,11], we verified the calculations as follows:

$\Sigma x^2 + \Sigma y^2 + 2\Sigma xy = 1056.8288$

$\Sigma (x+y)^2 = 1056.8288$

We can notice that the two values are equal. This means that the method is reproducible and precise.

The standard deviations and the regression coefficient were calculated as follow:

$$\sigma_x = \sqrt{\frac{\sum x^2}{n} - \bar{x}^2} = 4.92; \quad \bar{x} = 9.6575$$

$$\sigma_y = \sqrt{\frac{\sum y^2}{n} - \bar{y}^2} = 0.298; \quad \bar{y} = 0.585$$

$$r = \frac{\frac{\sum xy}{n} - \bar{x}\bar{y}}{\sigma_x \sigma_y} = 0.99894 \approx 1$$

The value of $r \approx 1$ shows that the results obtained with this method are reproducible and the error is negligible.

The equations show the dependence between absorbance and concentration of active product in the sample (mg), deducted by linear regression method are:

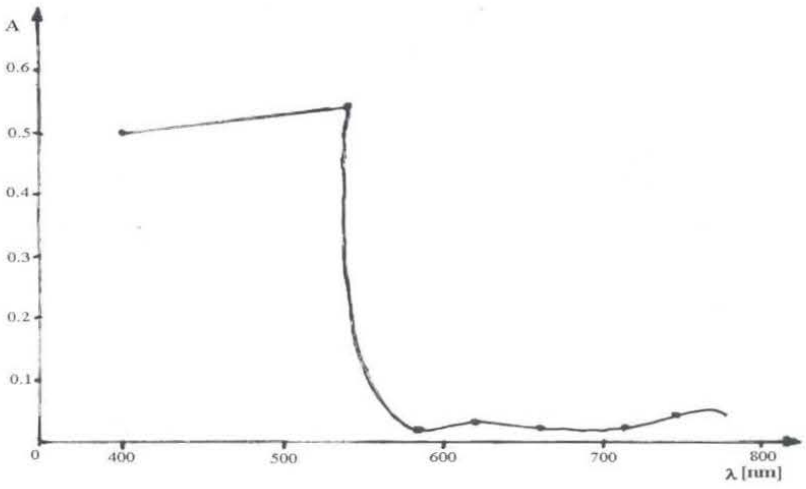


Figure 2. Variation of absorbance of anafranile complex with wave lenth.

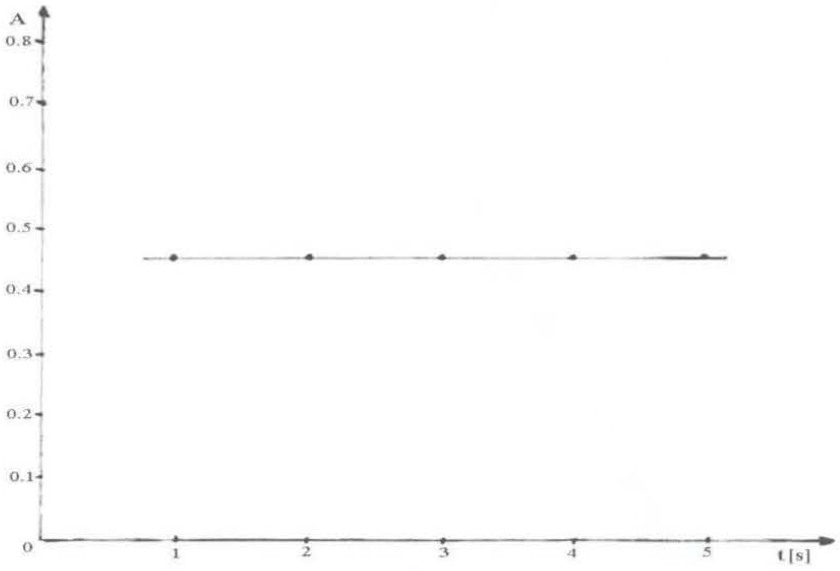


Figure 3. Variation of colour with depending on time.

Determination of anafranile in tablets

Twenty tablets of anafranile containing 10 mg anafranile hydrochlorate/tablet were pulverized in a mortar. From the resulting powder, well homogenized, 0.10-

0.15g were weighed on the analytical balance and were treated as mentioned above. The precipitate, washed, in order to remove the excess reagent, was transferred quantitatively to a 100 mL flask by using acetone and is completed under the same conditions described for the standard curve (λ=540nm). The quantity of anafranile in each sample was determined with the help of the standardization curve presented in Figure 1.

CONCLUSIONS

Anafranile can be determined quantitatively in the form of thiocyanatochromic complexes, gravimetrically, oxidimetrically and spectrophotometrically.

Every experimental result was statistically processed. The results showed that the methods developed were not influenced by systematic errors, were quite rapid and accurate. We recommended these methods to all laboratories for analysis and control of drugs.

REFERENCES

1. C.Dăescu, *Chimia şi tehnologia medicamentelor* (in Romanian), Ed.Didactică şi Pedagogică, Bucharest, Romania, p 64, 1994.
2. *** Farmacopeea Română (in Romanian), 10th edition, Bucharest, Romania (Supplement of 1981).
3. I.Gănescu, I.Papa, A.Gănescu, G.Brătulescu and D.Cirtina, *Acta Chim. Slov.*, *49*, 181 (2002).
4. I.Gănescu, *Studia Univ.Babeş-Bolyai Chem.*, *13*, 15 (1967).
5. I.Gănescu, I. Papa, A. Gănescu, V. Aldea, L. Chirigiu et V. Popescu, *Farmacia (Bucharest)*, 71 (2000).
6. I.Gănescu, Al.Popescu, L.Chirigiu and I.Papa, *Anal.Univ.Buc.*, *Vll*, 33 (1998).
7. G.Desmuch, M.Ioshi, *Z.anal.Chem.*, *142*, 275 (1969).
8. L.Batuner, M.Pozin, *Metode matematice în tehnică* (in Romanian), Ed.Tehn.,Bucharest, Romania, p 486, 1956.
9. I.Gănescu, I. Papa, A. Gănescu and L. Chirigiu, *Rev.Chim. (Bucharest)*, *9*, 697(2000).
10. M.Pleniceanu, M.Mureşanu, I.Gănescu, O.Rusu, *Indian Journal of Chem.*, 40A, 486, (2001).
11. M.Steibach, *Prelucrarea statistică în medicină şi biologie* (in Romanian), Ed. Academiei, Bucharest, Romania, p 223, 1961.