New Methods for Claritine Determination Based on Pt(IV) Complex Anions

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New ion-association complexes between claritine and $K_2[Pt(SCN)_6]$ were obtained and used thereafter for gravimetric, oxidimetric and spectrometric determination of this drug. The experimental data statistic processing proves that the proposed methods are accurate enough and not affected by systematic errors and could be used for analysis of pharmaceutical preparations.

Keywords: Claritin, platinum complexes,gravimetric, oxidimetric, spectrometric methods

Claritine is part of the antihistaminic drug family which block the histamine reaction in the body. The frequent symptoms are runny nose, itchy, watery eyes, sneezing, and cough [1-6]. Claritine is generically prescribed as loratadine and pseudoephedrine.

Loratadine, ethyl-4-(8-chloro-5,6 dihydro-11H-benzo[5,6] cyclohepta [1,2 *b*] pyridin-11-ylidene)-1-piperidine carboxylate, has the following structure (fig. 1).

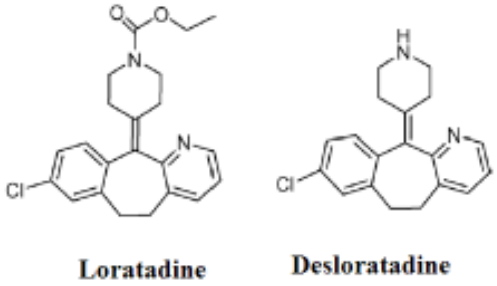

Fig.1. Strucural formula of loratadine and desloratadine

Claritine undergoes extensive first pass metabolism in the liver, forming an active metabolite desloratadine (DSL-descarboethoxy-loratadine) (fig.1). In the literature several methods have been descriebed for determination of Claritine in pharmaceutical preparation including UV spectrophotometry [7-10], colorimetry [11-13] spectro-fluorometry [8], atomic absorbtion spectrometry [13], polarography [14], densitometry [9, 15], capillary electrophoresis [16-18], and high performance liquid chromatography [7, 9, 10, 19].

We have observed that in acid medium Claritine quantitative precipitates with the anion $[Pt(SCN)_6]^{2-}$ as $(claritineH)_2[Pt(SCN)_6]$. This is the reason why we have elaborated three methods (gravimwetric, oxidimetric and spectrometric) for this drug determination as we have performed before for other drugs [20-22]. Furthermore, these methods which are not affected by sistematic errors, were used for claritine determination from pharmaceutical preparations with good results.

Experimental part

Reageants, equipment and methods

All reagents used were analytical grade: $K_2[Pt(Cl)_6]$, KSCN, Claritine, ICl, CCl_4, Ethanol are commercial available Fluka products. 20% HCl aqueosus solution was prepared from 37% HCl, Sigma-Aldrich product. 0.1N $KMnO_4$ aqueous solution, 0.1N $KBrO_3$ aqueous solution, 0.1N KIO_3 aqueous solution, and 5% NaOH aqueous solution were prepared from available Fluka reagents. 2% $K_2[Pt(SCN)_6]$ solution was prepared from $K_2[Pt(Cl)_6]$ and KSCN acccording to the methods of literature [23,24].

Pharmaceutical preparations containing loratadine include: Claritine tablets labeled to contain 10 mg LOR per tablet and Loratan D tablets labeled to contain 5mg LOR and 120 mg pseudoephedrine sulphate per tablet. All the pharmaceutical preparations were purchased from a local pharmacy.

Gravimetric determination of the Claritine after precipitation as (Claritine H)$_2$[Pt(SCN)$_6$]

2.4-24 mg Clartine was acidified with 5 mL 0.1M HCl and thereafter was precipitated with the $K_2[Pt(Cl)_6]$ analytical reagent in a 3% hidroalcoholic solution. A yellow precipitate was obtained, which was filtered in a G_4 crucible and washed 3-4 times with 10 mL hidroalcoholic solution until the filtrate becomes colorless.

Redox titration of Claritine after precipitation as (ClaritineH)$_2$[Pt(SCN)$_6$]

A sample of 2.4-24 mg Claritine was precipitated from an aqueous solution in the form of $(ClaritineH)_2[Pt(SCN)_6]$ complex salt. The precipitate was filtered off under vacuum through a Büchner funnel, afterwards washed 3 times with 8 mL water, until the filtrate was colouless. Precipitate and filter paper were transferred in a 250 mL Berzelius beaker, then the Büchner funnel was washed with 15 mL of water and, finally, with 15 mL of 3 % NaOH. The precipitate of Pt(IV) hydroxide become soluble by adding hydrocloring acid until the concentration of H_3O^+ ions was 1.7-2.0 M. Afterwards, 5 mL of CCl_4 and 10 drops of ICl indicator solution were added, then the mixture was trated with 0.1N solution of $KMnO_4$, $KBrO_3$ or KIO_3, respectively, under continouos stirring until organic layer became colorless.

Spectrometric determination of Claritine as (ClaritineH)$_2$[Pt(SCN)$_6$]

Samples containing 2.40-19.20 mg claritine were precipitated with $K_2[Pt(SCN)_6]$ as $(ClaritineH)_2[Pt(SCN)_6]$.

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The precipitate was afterwards dissolved in ethanol, the solution was poured in a 50 mL volumetric flask and diluted with ethanol to the mark and absorbance was plotted against drug concentration at selected λ_{max} = 570 nm. From these plots validity of Beer's Law was detected.

The statistical analysis of the experimental data (table 3) was achived using liniar regression method and the following equations [25, 26]:

$$\sum x^2 + \sum y^2 + 2\sum x \cdot y = 587.7935;\ \sum (x+y)^2 = 587.7935$$

$$\sigma_x = \sqrt{\frac{\sum x^2}{n} - (\bar{x})^2} = 3.666; \bar{x} = 7.2;$$

$$\sigma_y = \sqrt{\frac{\sum y^2}{n} - (\bar{y})^2} = 0.223; \bar{y} = 0.4387$$

$$r = \frac{\frac{\sum x \cdot y}{n} - \bar{x} \cdot \bar{y}}{\sigma_x \cdot \sigma_y} = 0.9998 \cong 1$$

Analysis of the pharmaceutical preparations

Claritine® and Loratan D tablets were used as real samples in order to verify the applicability of the three new methods of claritine determination. Ten tablets were after weighing finely powdered, and a portion of the tablet powder equivalent to 5 mg active substance was transferred quantitatively into a 25 mL volumetric flask and suspended in 20 mL acidulated water. After sonication for 15 min, the flask was made up to volume with water. The final solution was centrifuged (4000×*g*) for 15 min, and filtered. From this solutions, claritine was determined following the above mentioned procedures for gravimetric, oxidimetric and spectrometric dermination methods.

Table 1
GRAVIMETRIC DETERMINATION OF CLARITINE AS $(CLARITINE\ H)_2[Pt(SCN)_6]$

Claritin, mg taken in sample	Weighed $G_{complex}$, mg	Claritin found, mg	Statistical data
2.40	8.19	2.39	$\bar{x} = 12.01$
4.80	16.38	4.78	$s^2 = 6.33 \cdot 10^{-4}$
7.20	24.74	7.22	$s = 2.51 \cdot 10^{-2}$
12.00	41.19	12.02	$t_{n-1,\alpha} = 2.57$; α= 95%
14.40	49.13	14.34	$\bar{x} - ts < A < \bar{x} + ts$
19.20	65.64	19.16	11.95<12.01<12.07

Obs. n=6 determinations, s= standard deviation from the mean

Results and discussions

Claritine quantitative precipitates in acidic media with the anion $[Pt(SCN)_6]^{2-}$ as $(claritineH)_2[Pt(SCN)_6]$ ion-association complex which allowed us to develop new methods for this drug determination.

Gravimetric determination of Claritine

Gravimetric determination of Claritine ($G_{complex}$) was made after precipitation as $(claritineH)_2[Pt(SCN)_6]$. The gravimetric factor, f was 0.2919, considering the molecular weight of the complex $M_{Complex}$=1311g/mol.

The experimental results were statistically interpreted (table 1). We can see that this determination method of Claritine in not affected by systematic errors.

Redox titration of Claritine

Oxidimetric determination of Claritine by titration was made after its precipitation as $(ClaritineH)_2[Pt(SCN)_6]$. Three redox titrations methods, permanganometric, bromatometric and iodatometric methods based on redox reactions between SCN^- and the oxidizing agent MnO_4^-, BrO_3^-, and IO_3^-, respectively, have been developed [27, 28]. Iodine monochloride solution (ICl in CCl_4) was used as redox indicator.

The experimental data obtained by redox titration determinations of Claritine are presented in table 2.

Spectrometric determination of the claritine after precipitation as $(ClaritineH)_2[Pt(SCN)_6]$.

Spectrometric determination of Claritine was made after being converted into $(claritineH)_2[Pt(SCN)_6]$ ion-association complex. This one was soluble in ethanol and the maximum absorbtion of the resulting solution was in the visible region, at λ=570 nm. The Lambert-Beer's law was followed in the 0.01-0.9 mg/mL range. The statistic interpretation of the experimental data was accomplished by means of linear regression method and the obtained results are shown in the table 3. Based on the r value of 0.9904, we can state that this new spectrometric method

Table 2
OXYDIMETRIC DETERMINATION OF CLARITINE AS $(CLARITINE\ H)_2[Pt(SCN)_6]$

Claritine taken, mg	No.of det.	$\bar{x}$ mg	s	t_a	t_b	$t_{n-1,\alpha}$ (α=95%)
PERMANGANOMETRIC DETERMINATION						
2.4	10	2.392	$2.22 \cdot 10^{-2}$	$3.54 \cdot 10^{-4}$	$45.44 \cdot 10^{-3}$	2.26
12.00	10	12.011	$2.51 \cdot 10^{-2}$	$3.27.10^{-4}$	$48.47 \cdot 10^{-3}$	2.26
BROMATOMETRIC DETERMINATION						
4.8	10	4.790	$1.70 \cdot 10^{-2}$	$43.01 \cdot 10^{-4}$	$44.11 \cdot 10^{-3}$	2.26
16.8	10	16.813	$2.11 \cdot 10^{-2}$	$7.42 \cdot 10^{-4}$	$45.20 \cdot 10^{-3}$	2.26
IODATOMETRIC DETERMINATION						
7.2	10	7.191	$2.03 \cdot 10^{-2}$	$18.03 \cdot 10^{-4}$	$43.94 \cdot 10^{-3}$	2.26
19.2	10	19.212	$2.58 \cdot 10^{-2}$	$21.62 \cdot 10^{-4}$	$45.25 \cdot 10^{-3}$	2.26

Obs. 1 mL of oxidizer solution, 0.1N ($KMnO_4$, $KBrO_3$, KIO_3) is equivalent of 2.1272 mg claritin.

N	X (mg)	x^2	y	y^2	x·y	x + y	$(x + y)^2$
1	1.75	3.0625	0.029	0.000841	0.05075	1.779	3.164841
2	3.50	12.2500	0.059	0.003481	0.20650	3.559	12.666481
3	7.00	49.0000	0.117	0.013689	0.81900	7.117	50.651689
4	10.50	110.2500	0.176	0.030976	1.84800	10.676	113.976976
5	14	196.000	0.235	0.055225	3.29000	14.235	202.635225
6	17.50	306.2500	0.293	0.085849	5.12750	17.793	316.590849
Total	54,25	676.8125	0.909	0.190061	11.34175	55.159	699.686061

Obs.samples of 25 mL

Table 3
SPECTROMETRIC DETERMINATION OF CLARITINE AS $(CLARITINEH)_2[Pt(SCN)_6]$

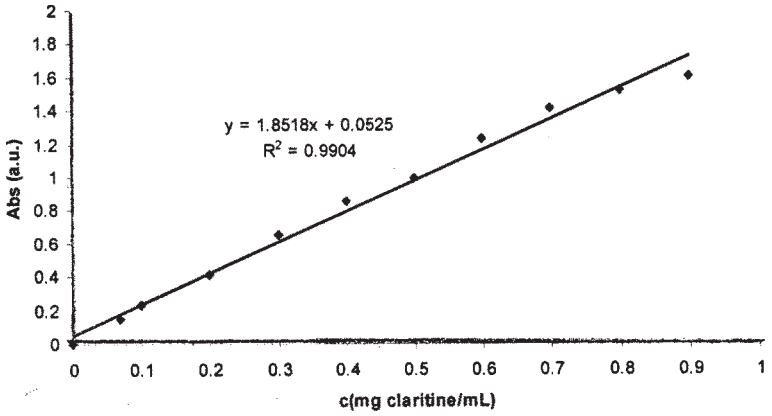

Fig.2. Calibration curve for the spectrometric determination of claritine as $(claritineH)_2[Pt(SCN)_6]$

Preparation	Taken, mg	Found (± standard deviation), mg		
		Gravimetric	Oxidimetric ($KMnO_4$)	Spectrometric
Claritine tablets (loratadine (10 mg)/tablet)	2.5	2.5 ± 0.08213	2.5 ± 0.05689	2.5 ± 0.00964
	5	5 ± 0.06541	5 ± 0.05525	5 ± 0.00891
	10	10 ± 0.02489	10 ± 0.01291	10 ± 0.00715
Loratan D tablets (loratadine (5 mg) + 120 mg pseudoephedrine sulphate))	2.5	2.5 ± 0.09741	2.5 ± 0.04982	2.5 ± 0.01028
	5	5 ± 0.07321	5 ± 0.06581	5 ± 0.00128
	10	10 ± 0.03691	10 ± 0.04781	10 ± 0.00365

Table 4
APPLICATION OF GRAVIMETRIC, OXIDIMETRIC AND SPECTROMETRIC METHODS FOR PHARMACEUTICAL PREPARATIONS ANALYSIS

is enough accurate and it is not affected by systematic errors. The linear dependence of the absorbance versus the concentration of Claritin and the ecuation of the reggresion curve are shown in the figure 2. The molar extinction coefficient was $\varepsilon=2744.35\ L \cdot cm^{-1} \cdot mol^{-1}$.

Application of gravimetric, oxidimetric and spectrometric methods for pharmaceutical preparations analysis

The $K_2[Pt(SCN)_6]$ reagent was successfully applied for determination of claritine in Claritine® and Loratan D tablets. The results obtained are presented in table 4 and prove that the new gravimetric, oxidimetric and spectrometric methods that we have developed are enough accurate and reproducible to be used for claritidine determination from pharmaceutical preparations.

Conclusions

Determination of Claritine can be performed by different new procedures based on gravimetric, spectrometric and redox titration methods. This research involved the development of three simple, sensitive, cheep methods using $K_2[Pt(SCN)_6]$ reagent, via formation of ion-association complex with claritine. They are successfully applied for this drug determination in pure and in Claritine and Loratan D tablets.

References

1. BUDAVARI, S., "The Merck Index—An Encyclopedia of Chemicals, Drugs and Biologicals", 12th ed., Merck and Co., NJ, 1996, p. 953.
2.*** Farmacopeea Romana, Ed.a-X-a, Ed.Medicala Bucuresti, 1993
3.*** European Pharmacopea, 4 –th Edition, Council of Europa,
4.*** The United State Rharmacopea, 25 th Edition, United State Pharmaceutical Convention, Inc.Rockville, 2002.
5.*** British Pharmacopea, voll, International Edition London, HMSO, 2001
6 . DAESCU, C., Chimia si Tehnologia medicamentilor, Ed.Did.si Ped., Bucuresti, 1994, p.167.
7.MABROUK.,MM, EL-FATATRY,H.M,HAMMAD,S, WAHBI ,A.A.M., J. Pharm. Biomed. Anal. ,**33** ,2003, 597–604.

8. MABROUK, M.M, EL-FATATRY, H.M.,HAMMAD,S , WAHBI,A.A.M, J. Pharm. Biomed. Anal. ,**33**, 2003, 597–604.
9. EL-RAGEHY, N.A, BADAWY,A.M., KHATEEB,S.Z., J. Pharm. Biomed. Anal., **28**, 2002,1041–1053.
10. RADHAKRISHNA.,T, NARASARAJU, A, RAMAKRISHNA,M, SATYANARAYANA,A,. J Pharm. Biomed. Anal. ,**31**, 2003 ,359–368..
11. RAJPUT,S.J., VYAS,A.G., Indian Drugs, **35** ,1998, 352–355.
12. BASAVAAH,K, CHARAN, V.S.,ScienceAsia ,**28** ,2002, 359–364.
13. EL-KOUSY,N., BEBAWY, L.I.,J. Pharm. Biomed. Anal. ,**20** ,1999, 671–679
14. SQUELLA,J.A., STURM,J.C.,, DIAZ,M.A., PESSOA,H., VERGARA-NUNEZ,L.J.,Talanta,**43**, 1996, 2029–2035
15. INRAYANTO, G.,DARMAWAN,L. , WIDJAJA,S, NOORRIZKA,G., J. PlanerChromatogr. TLC**,12** ,1999, 261–264.
16. FERNANDEZ,H., RUPEREZ,F.J., BARBAS, C.,J. Pharm. Biomed. Anal. **31** ,2003,499–506.
17. MIKUS,P,. KUBACAK,P, VALASKOVA,I.,, E. Havr´anek, Pharmazie**, 59** ,2004,260–262.
18. CAPELLA,M.E., BOSSI,A, ESTEVE-ROMERO,J, Anal. Biochem., **352**, 2006, 41–49.
19. RUPEREZ, F.J.,FERNANDEZ,H. , BARBAS,C. , J. Pharm. Biomed. Anal. **29** ,2002,35–41.
20. GANESCU, I., BRATULESCU, G., MAGEARU, V., PAPA, I., GANESCU, A., Anal.Univ.Buc., Chimie, XIII, **vol. I-II**, 2004, p.58.
21. GANESCU,I, BRATULESCU,G., PAPA,I., GANESCU,A.,CIRTINA ,D.,Acta Chim.Slov.,**49,**2002,p.181
22. GANESCU, I., PAPA,I., GANESCU,A.,MIRCIOIU, C, ALDEA, V., Farmacia, (Buc)., **XLIX(4),** 2001, p.62
23. GANESCU,I.,VARHELYI, Cs., Rev.Roum.Chim.,**32**,1987, p.771.
24.GANESCU,I.,VARHELYI,Cs.,ZSAKO,J.,Rev.Roum.Chim., **34,**1989,p.225
25. BATUNER, L.,POZIN M.,Metode matematice in tehnica, Ed.Acad.,Buc.,1956,p.486
26. CEAUSESCU, D., Metode statistice expeditive in chimia analitica, Ed.Mirtan, Timisoara, 1992,p.82
27.GANESCU,I., GANESCU,A, PAPA,I.,CHIRIGIU L.,Rev. Chim. (Bucharest), **51**, no. 9, 2000, p.697
28.GANESCU,I., GANESCU,A, PAPA,I., CHIRIGIU L, PREDA,D., BARBU,A.,Rev. Chim., (Bucharest), **52**, no. 6, 2001,p.304

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