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Determination of loratadine by UV molecular absorption spectrometry

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Abstract Loratadine (Ethyl 4-(8-chloro-5, 6-dihydro-11H-benzo [5, 6] cyclohepta [1, 2-b] pyridine-11-ylidine)-1-piperidinecarboxylate) is a last generation of H1-antihistamine drug used to treat allergies, and marketed for its non-sedating properties. At present, loratadine is studied by spectrophotometry, high-performance liquid chromatography and electrospray mass spectrometry.
This paper describes the development of a method for determination of loratadine by ultraviolet spectrophotometry: loratadine methanolic solution and complex ion tetraiodomercuriat $[HgI_4]^{2-}$ form a compound in the presence of hydrochloric acid. The 380nm maximum absorbance of the compound is proportional to its concentration in loratadine. The experiment establishes the appropriate working conditions (reaction environment, the optimal amount of reagent, the reaction time, etc.). The advantages of this sensitive method make it an efficient way to analyze loratadine from different types of samples.

Keywords: UV spectrometry, loratadine, potassium tetraiodomercuriat, macromolecules.

1. Introduction

Allergy is an altered reaction of an organism. This disease is an important national and international topic of study, because it is expanding due to increased global pollution and different synthetic chemicals as preservatives, artificial colorings, acidifications, taste correctors, etc., used in food industry at present.

Treatment of allergic disorders is complex. Pharmacotherapy is only one part of multiple measures that we took into consideration. Antiallergic treatment is *specific,* when it aims to reduce or remove an allergen or antibody and *nonspecific,* when it aims to reduce or remove the immediate consequences of antigen-antibody reaction (release and fixation mediators) or to control pathological phenomena, which occur in certain organs.

H1 antihistamines, bronchodilators, calcium antagonists and others (sodium thiosulfate, calcium salts, aminocaproic acid) activate upon the affected organs [1].

Antihistamines are competitive antagonists of histamine.

Loratadine and its metabolite, descarboetoxiloratadine, cetirizine (racemic mixture) and levocetirizine (active isomer) represent the latest generation of antihistamines [1].

Loratadine - *(Ethyl 4 - (8-chloro -5, 6 - dihydro-11H-benzo [5.6] cyclohepta [1,2-b] pyridine -11 - ylidine) -1 - piperidinecarboxylate)* or $C_{22}H_{23}ClN_2O_2$ [79794-75 -5], contains 98.5 to 101.5% dry substance. It is a crystalline, white or almost white powder,. It is practically insoluble in water, slightly soluble in acetone and methanol. It shows polymorphism [2].

At present, loratadine is studied by spectrophotometry, high-performance liquid chromatography, and electrospray mass spectrometry [3, 4]. There was found a sensitive method to determinate loratadine by bonding it to a complex ion in chlorine hydride. The macromolecular compound obtained is hardly soluble in water and can be determined by molecular absorption spectrometry in UV.

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2. Experimental

2.1. Equipment and materials:

Spectrometric measurements were done using a UV-VIS spectrophotometer Jasco V-630.

Grade of analytical purity of substances: Loratadine: reference substance, 98.5% pure (Sigma); Methanol (Merck); Hydrochloric acid 37% pure (Tunic Prod Bucharest); Potassium iodide (Merck); Mercury (II) chloride (Merck);

The following solutions were prepared:

- loratadine standard solution in methanol (1 mg/mL): 100 mg loratadine (reference substance) was dissolved in 100 mL methanol n volumetric flask; for experiments a working solution of 0.1mg/mL loratadine was prepared by diluting standard solution 1/10 with methanol;
- aqueous solution of potassium tetraiodomercuriat 0.017 M: 30 mL 0.1 N $HgCl_2$, (13.6 g $HgCl_2$ dissolved in distilled water to one liter) was mixed with 57mL solution KI 0.1 N (16.6 g KI dissolved in distilled water to one liter). The two substances were mixed drop by drop stirring continuously; the working solution ($4.857 \cdot 10^{-3}$M) was prepared by diluting the standard solution 4/10 (v/v) in distilled water.

The following reactions took place:

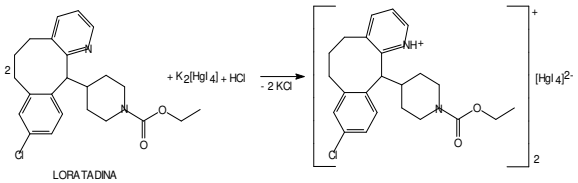
$$HgCl_2\ (aq) + 2\ KI\ (aq) \rightarrow 2KCl\ (aq) + HgI_2\ (pp)$$

$$HgI_2\ (pp) + 2KI\ (aq) \rightarrow K_2[HgI_4]\ (aq)$$

- aqueous solution 0.1 M and 0.05M HCl.

2.2. Analytical Method

Loratadine in methanolic solution reacts with complex ion tetraiodomercuriat $[HgI_4]^{2-}$ to form a compound, which is hardly soluble and very finely dispersed into reaction environment, in the presence of hydrochloric acid. The following reaction occurs:



The resulted compound shows maximum absorbance at 380 nm, being proportional to loratadine concentration.

3. Results and Discussions

To establish the appropriate working conditions there were made the following studies: (i) the determination of the optimum detection wavelength; (ii) determination of the optimal volume of potassium tetraiodomercuriat solution; (iii)determination of the required HCl quantity for the reaction (iv) reaction stability in time.

(i) The determination of the optimum detection wavelength

In order to set up the detection wavelength the method uses 0.04 mg/mL loratadine (one mL sample), to which 1 mL potassium tetraiodomercuriat reagent (stock solution) and 1 mL 0.05 N HCl were added. The recipient was filled up with 5 mL distilled water. 10 minutes after the mix was done, the absorption spectrum was recorded in 1 cm cuvette against blank prepared in the same conditions (**Fig. 1**). The absorption spectrum of a sample of 0.01 mg/mL loratadine in methanol was also recorded.(**Fig**. **2**).

As it can be seen, the maximum level of absorption is at 380 nm wavelength and specific absorbance $A^{1\%}_{1cm,\ 380\ nm}$ nm = 1183. Loratadine in methanol indicates an absorption at maximum 288 nm with specific absorbance $A^{1\%}_{1cm,\ 288nm}$ = 298.

There can be seen that specific absorption at 380 nm is 3 times bigger than the specific absorption of loratadine in methanol at 288 nm.

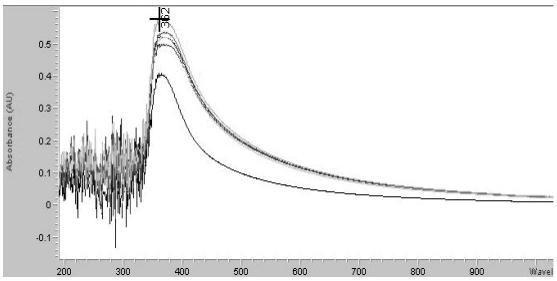


Fig. 1 - Absorption spectra of new loratadine-$[HgI_4]^{2-}$macromolecular compound

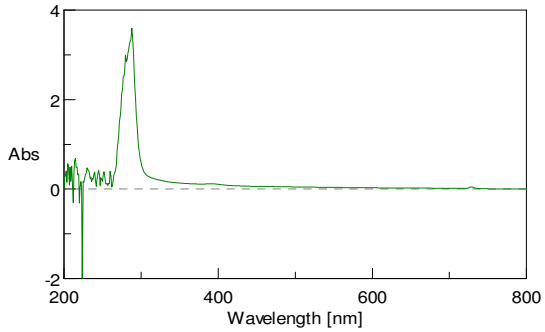


Fig. 2 - Absorption spectra of loratadine in methanol 0.01 mg / mL, λ_{max} = 288nm

The experiment was made at 380 nm wavelength for all determinations.

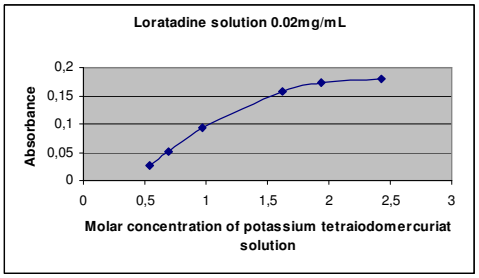
(ii) Determination of the optimal volume of potassium tetraiodomercuriat solution

The experiment was made using 2 samples of loratadine with 0.02 mg / mL, and 0.08 mg / mL concentration, respectively (1 mL sample), which meant the lowest and the highest level of concentration, respectively. To each sample 1 mL potassium tetraiodomercuriat solutions in different concentrations was added (stock solution was diluted as follows: 1:1, 1:1,5, 1:2, 1:4, 1:6, 1:8); they were acidified with 1 ml 0.05 M HCl. The samples were completed with distilled water up to 5 mL. The outcome reaction was measured by molecular absorption spectrometry in UV. Ten minutes after preparation, the absorbance was measured at wavelength λ = 380 nm against a blank prepared in the same conditions in 1 cm cuvette. Absorbance depending on concentration of potassium tetraiodomercuriat solution is given in **Fig. 3.**

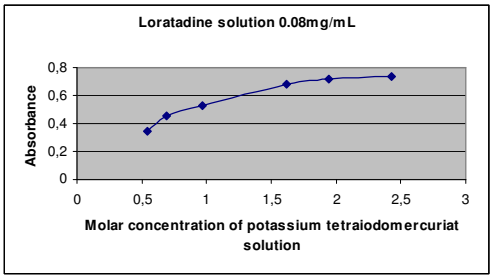
As it can be seen, for further analysis the optimal concentration of potassium tetraiodo mercuriat is the following: $1.9428*10^{-3}$M.

(iii) Determination of HCl quantity required for the reaction

Several attempts were made in order establish the acidity required for reaction. The concentration of hydrochloric acid solutions ranges from 0.01 M to 1M. Concentration and volume of potassium tetraiodomercuriat solution, and the time of reaction were the parameters, which remained constant. The absorbance of each prepared sample was registered (**Fig. 4**) and the optimal quantity of HCl required by a successful reaction was selected.



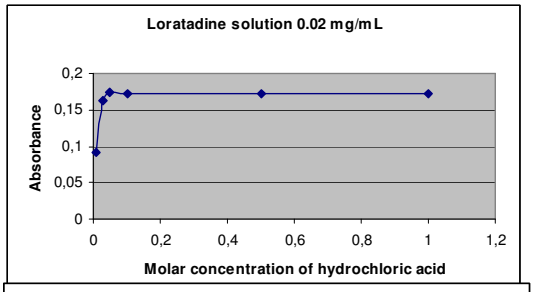
a)



b)

Fig. 3 – Absorbance depending on molar concentration of potassium tetraiodomercuriat solution: a) 0.02mg/mL loratadine; b) 0.08mg/mL loratadine

a)



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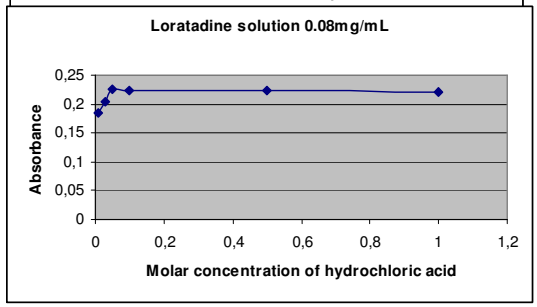
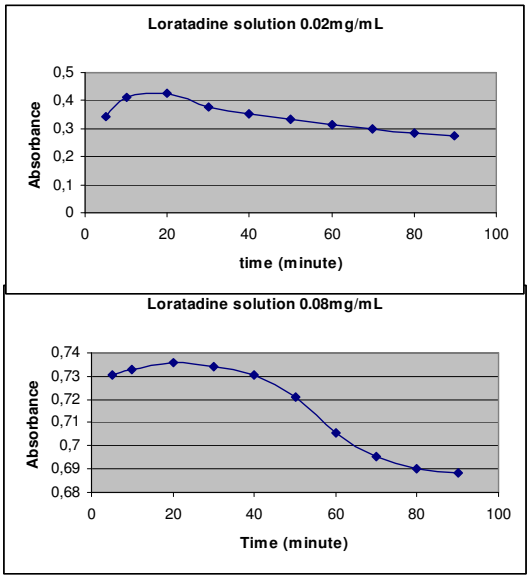


Fig. 4 - Absorbance depending on molar concentration of hydrochloric acid: a) 0.02mg/mL loratadine; b) 0.08mg/mL loratadine

(iv) Reaction stability in time

The experiment requires two samples of loratadine, with different concentrations: 0.02 mg / mL and 0.08 mg / mL. Volumes and concentrations of potassium tetraiodomercuriat solutions or hydrochloric acid remain constant. The absorbance of samples at λ = 380 nm is measured several times from 5 minutes to 90 minutes.

The peak evolution in time is shown in **Fig. 5**: There can be seen that absorbance reaches its peak value at 10 minutes after the reaction started.



a)

b)

Fig. 5 – The variation of absorbance in time: a) 0.02mg/mL loratadine; b) 0.08mg/mL loratadine

Procedure

All solutions were mixed: 1 mL of loratadine with 1 mL potassium tetraiodomercuriat $1.9428*10^{-3}$M and 1 mL 0.05 M HCl. The flask was filled up to 5 mL, by adding distilled water. Once the new compound formed, the substance became opalescent. After 10 minutes, the absorbance at wavelength of 380 nm in 1 cm cuvette was measured against a blank prepared in the same conditions.

4. Conclusions

The experiment sets up a method of determining turbidity of a hardly soluble compound resulted from mixing loratadine with potassium tetraiodomercuriat in acid environment, compound that shows maximum absorption at 380 nm in methanol in comparison with maximum absorption of loratadine, which is at 288 nm.

The optimal working conditions are: the concentration of potassium tetraiodomercuriat is $1.9428*10^{-3}$M, the acidity of the reaction is acquired by adding 1 mL 0.05 M HCl solution, and absorbance can be read 10 minutes after reagents are added.. Reaction outcome is stable for about 10 minutes. After this period, the precipitated particles in suspension get down on the bottom of recipient.

Specific absorptive coefficients for loratadine in methanol solution, and the reaction outcome, are: $A^{1\%}_{1cm,\ 288nm}$ =298, and $A^{1\%}_{1cm,\ 380nm}$ = 1183. This method increases the sensitivity of loratadine determination almost 3 times.

The next stage of our study is to optimize and validate the presented method.

By simple working technique, the study proves that this sensitive method is an efficient way to analyse loratadine from different types of samples.

5. References

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[1]. A. N. Cristea, *Farmacologie*, Ed. Medicala, Bucuresti (2000)

[2]. ***** European Pharmacopoeia 6.0, pag 2286 – 2288.

[3]. Y. H.Lu,., H. M.Wen,., W.Li, Y. M.Chi and Z. X. Zhang, Journal of chromatographic science **42**(5) 234-236 (2004)

[4]. C. A. Muller, W. Weinmann, S. Dresen, A. Schreiber and M. Gergov, Journal: Rapid communications in mass spectrometry, **19**(10) 1332-1338 (2005)