Determination of loratadine in pharmaceuticals by a spectrophotometric method

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Abstract. The spectrophotometric method for determination of loratadine using tetraiodomercurate has been applied in various pharmaceutical formulations. The results confirmed that recovery value is optimum and the method is valid, thus it can be used in quality control and evaluation of loratadine tablets, oral formulations of mixed composition, oral solutions, etc. The method is easy and simple to apply, does not require complicated equipment and spectrophotometric reading time is reduced, which allows a large number of analyzes in a relatively short time.

Keywords: loratadine, UV-Vis spectrometry, potassium tetraiodomercurate, formulations.

1. Introduction

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 drugs used to treat allergies, marketed for its non-sedating properties [1, 2]. At present, loratadine is quantified by spectrophotometry, high-performance liquid chromatography and electrospray mass spectrometry [3 - 5].

It was studied a spectrophotometric method for the determination of loratadine coupling with potassium tetraiodomercurate in an acid medium, the resulted compound showing an absorption maximum at 362 nm, compared to loratadine in methanol which shows a maximum absorption at 288 nm [1, 2, 6, 7].

Specific absorptivity coefficients of loratadine in methanol, solution respectively the reaction product are: $A^{1\%}_{1cm, 288nm}= 298$ and $A^{1\%}_{1cm, 362 nm}=1183$, so in this way the sensitivity of the determination of loratadine increased approximately 3-fold.

Optimal parameters method were established [8, 9] as follows: detection wavelength $\lambda = 362$ nm at maximum absorbance, the optimum concentration of potassium tetraiodomercurate 2×10^{-3}M, the reaction medium (1 mL 0.05M HCl was added to 5 mL sample), as well as stability of the samples (absorbance can be read after 10 minutes from the addition of the reagents, and the reaction product is stable for a further 10 min) [6]. In the UV-Vis spectrum of loratadine in methanolic solution, the absorption band is shifted to higher wave number in the presence of tetraiodomercurate.

Established method for the determination of loratadine in the form of ionic association loratadine $- [HgI_4]^{2-}$ was applied to in various pharmaceutical forms.

2. Experimental

Three pharmaceutical forms for internal use, namely: Tablets – Roletra, 10 mg loratadine, producer: RANBAXY LABORATORIES LTD. INDIA; Modified-release tablets – Clarinase, 5 mg/120 mg loratadine/ pseudoephedrine sulphate, producer: SCHERING PLOUGH LABO N. V., BELGIA and Syrup - Symphoral, 1 mg/mL, producer: GEDEON RICHTER SA ROMANIA, found on the Romanian market, were analyzed.

According to the prospectus, product Roletra 10 mg tablets contains 10 mg loratadine and the following excipients: lactose monohydrate, maize starch, magnesium stearate, purified water.

The package insert Clarinase, modified-release tablets referred to the following composition: 5 mg

loratadine and 120 mg pseudoephedrine sulfate, and the following ingredients: core - lactose monohydrate, maize starch, povidone, magnesium stearate; film coating - acacia, butyl parahydroxybenzoate, calcium sulfate dihydrate, carnauba wax, microcrystalline cellulose, oleic acid, gum arabic, flakes of soap, sucrose, talc, titanium dioxide, white beeswax, zein.

The product Symphoral syrup contains 1 mg / mL loratadine and the following inactive ingredients: propylene glycol, glycerin, citric acid, sodium benzoate, disodium salt of ethylen diaminotetracetic acid (EDTA), artificial flavor, sugar and water.

For application of the method, the following materials were used: loratadine (CRS European Pharmacopoeia) [4], methanol (Merck), chloroform (Merck), 37% hydrochloric acid (Tunic Prod. Bucharest), potassium iodide (Merck), mercury(II) chloride (Merck), double distilled water obtained with Millipore apparatus. The equipment used is UV-VIS spectrophotometer Jasco V-630 type series A040061148, program acquisition and data processing Spectra Manager, version 2, electronic analytical balance KERN & SOHN ABJ 220-4M, WTW pH meter and 500 TurboVap Vaporizer.

Tablets samples were prepared as follows: it was determined the average weight (0.1026 g for tablets and 0.9365 g for modified-release tablets) by weighing 20 tablets. The weighed tablets were brought into a mortar and were triturated to obtain a fine, homogeneous powder. A quantity of powder equivalent to 3-5 mg loratadine was weighed. The weighed powder and 20 mL of chloroform were brought into a 100 mL volumetric flask. For the extraction of loratadine in the formulation it was used chloroform whereas loratadine is readily soluble and excipients listed in the prospectus is sparingly soluble in mentioned solvent. The resulting suspension was filtered through quantitative filter paper and the filtrate was brought into vaporizer to completely remove the solvent. The residue was brought into 100 mL methanolic solution. Three samples were prepared for tablets (**Table 1**) and three samples for modified release tablets (**Table 2**) according to the procedure described above.

Table 1. Tablets sample preparation for applying spectrophotometric method.

No.	Weighed quantity of powder from tablets (g)	Corresponding amount loratadine (g)	Concentration of the solution in methanol (μg/mL)
1	0.0307	0.003	30
2	0.0410	0.004	40
3	0.0513	0.005	50

Table 2. Modified-release tablets sample preparation for applying spectrophotometric method.

No.	Weighed quantity of powder from tablets (g)	Corresponding amount loratadine (g)	Concentration of the solution in methanol (μg/mL)
1	0.5619	0.003	30
2	0.7492	0.004	40
3	0.9365	0.005	50

Syrup samples were prepared as follows: syrup volume corresponding to 5-7 mg loratadine and 10 mL of chloroform was brought into the extraction funnel. After vigorous stirring for 10 minutes, and the rest to the total separation of the two phases, chloroform component was collected in a flask with a stopper. The operation was repeated 4-5 times. Loratadine solution in chloroform was brought into the vaporizer for complete removal of solvent. The substance thus separated was processed similarly to that obtained from tablets and have prepared three such samples (**Table 3**).

Method. Nine samples were made from each formulation (three for each loratadine solution of each formulation) as follows: 1 mL of a solution of the loratadine formulation, 1 mL potassium tetraiodomercurate 2×10^{-3} M and 1 mL of 0.05 M hydrochloric acid were brought in a measuring cylinder. It was completed to 5 mL with double-distilled water. After 10 minutes, the absorbance was measured at a wavelength of 362 nm in 1 cm cuvette, against a blank prepared under the same conditions.

Table 3. Syrup sample preparation for applying spectrophotometric method.

No.	The volume of syrup taken over (mL)	Corresponding amount loratadine (g)	Concentration of the solution in methanol (μg/mL)
1	5	0.005	50
2	6	0.006	60
3	7	0.007	70

The method was developed and validated. Calibration was performed on the concentration range of 10-100 μg / mL, in our previous research [6, 7].

3. Results and Discussions

The concentration of Tablets Roletra analyzed samples was calculated using the equation of the calibration and the results presented in **Fig. 1** were expressed in μg / mL and as a percentage of the theoretical concentration.
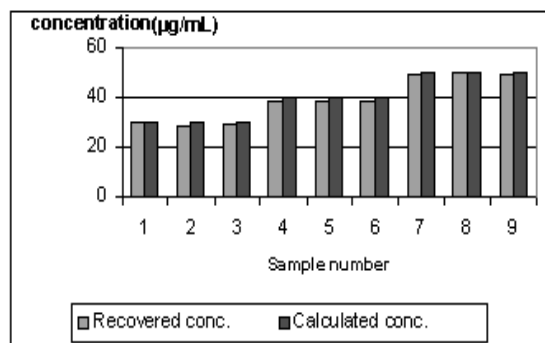

Figure 1. The variation of the calculated concentration to the concentration found in the analysis of loratadine tablets.

For the determination of loratadine in Tablets Roletra, recovering average is 97.908 with confidence interval $\mu = 97.908 \pm 3.38$ (**Table 4**). The presented results confirmed that recovery conforms and the method is valid and can be used in quality control and evaluation of loratadine tablets.

It is noted that the two concentration values (concentration recovered and calculated

concentration) are very close so the method is effective for this type of samples (**Fig. 1**).

Table 4. Statistical data.

Average	97.90863
Minimum	96.31579
Maximum	100.0789
Standard deviation (SD)	1.464
Relative standard deviation (RSD) (%)	0.488
Degrees of freedom	8
Error Probability 5%	0.05
t student value [10]	2.31
Confidence Interval	97.908 ± 3.38

The concentration of the Tablets Clarinase samples was calculated using equation of the calibration and the results presented in **Fig. 2** were expressed in μg / mL and as a percentage of the theoretical concentration.

Recovered concentration values overlap with calculated concentrations, so the method proved to be reliable in Clarinase tablets that contain two active ingredients and a significant number of excipients (**Fig. 2**).
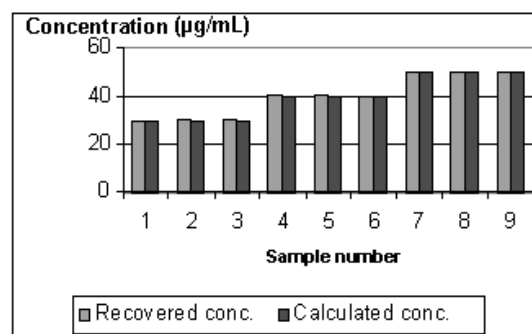

Figure 2. The variation of the calculated concentration to the concentration found in the analysis of Clarinase tablets.

For the determination of loratadine in Clarinase Tablets, recovery is 100.7122 mean with confidence interval $\mu = 100.7122 \pm 2.57$ (**Table 5**). The presented results confirmed that recovery is optimal and the method is valid and can be used in quality control and loratadine dosage of oral formulations with mixed composition.

Table 5. Statistical data

Average	100.7122
Minimum	99.17763
Maximum	102.3684
Standard deviation (SD)	1.115609
Relative standard deviation (RSD) (%)	0.372
Degrees of freedom	8
Error Probability 5%	0.05
t student value [10]	2.31
Confidence Interval	100.7122 ± 2.57

The concentration of Symphoral syrup samples was calculated using the equation of the calibration and the results presented in **Fig. 3** were expressed in μg / mL and as a percentage of the theoretical concentration.
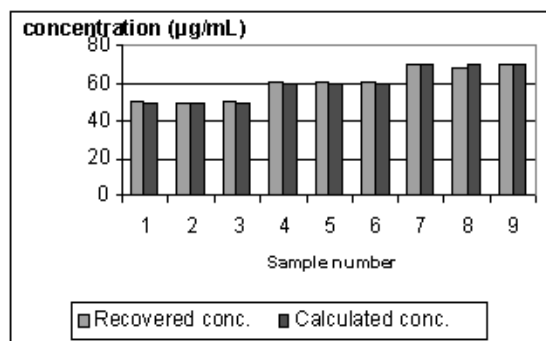

Figure 3. The variation of the calculated concentration to the concentration found in the analysis of Symphoral syrup

Table 6. Statistical data

Average	100.4817
Minimum	98.15789
Maximum	101.7895
Standard deviation (SD)	1.0282
Relative standard deviation (RSD) (%)	0.3427
Degrees of freedom	8
Error Probability 5%	0.05
t student value [10]	2.31
Confidence Interval	100.48 ± 2.37

The method is specific for the syrup as well because values of recovered concentrations and calculated concentrations are similar and other components of the pharmaceutical preparation does not change the results (**Fig. 3**).

Recovery average is 100.48 with confidence interval of μ= 100.48 ± 2.37 (**Table 6**) for loratadine determination in Symphoral syrup, so the method is efficient and can be used in quality control and determination of loratadine in oral solution.

Compared to other spectrophotometric methods presented in the literature [1, 2, 5], this method has proven to be fast, with low limits of detection and quantification, far below the admissibility limit for the analysis and control of drugs.

4. Conclusions

The test method is suitable for the intended purpose, namely for determining low concentrations of loratadine in drug control tests for various pharmaceutical preparations.

For the determination of loratadine in all three formulations analyzed, it was obtained a mean recovery and a confidence interval corresponding norms. The method is easy and simple to apply on different formulations since no interference of excipients occurs.

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