TITRIMETRIC MICRO-DETERMINATION OF CETIRIZINE HYDROCHLORIDE USING POTASSIUM CAROATE

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Introduction. Cetirizine hydrochloride (Brand Name Zyrtec) is non-sedating an antihistamine with long acting activity that is FDA approved for the treatment of symptoms due to hay fever or other upper respiratory allergies such as runny nose, sneezing, itchy watery eyes [1,2]. Therefore, the development of new analytical methods for its quantification is very important. Cetirizine hydrochloride (CTZ, Fig. 1); is a piperazine derivative, (±)-[2-[4-[(4-Chlorophenyl) phenylmethyl]-1-piperazinyl] ethoxy] acetic acid), dihydrochloride [3].

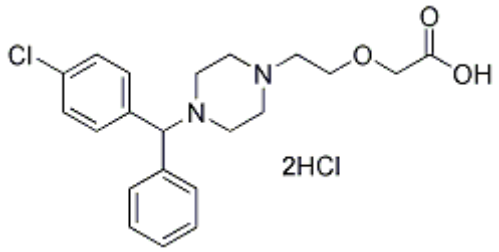

Fig. 1 Chemical Formula of Cetirizine hydrochloride

Cetirizine, marketed as a racemic mixture containing both Levocetirizine and Dextrocetirizine, is a member of the second generation H_1 antihistamines. Recently, its single R-enantiomer Levocetirizine has been approved by the FDA as the newest antihistamine [4,5]. Cetirizine is available over-the-counter in the US in the form of 5 and 10 mg tablets both chewable and non-chewable. The drug can be in the form capsules or a syrup [6].

The BP suggested a potentiometric titration method for determination of CTZ in its pure form; while it recommended an HPLC method for both cetirizine oral solution and tablets [7]. The USP suggested non-aqueous titration method using glacial acetic acid determination of CTZ also [8].

Different others analytical procedures were reported for its determination including HPLC [9-12], HPTLC [13], capillary electrophoresis [14] and spectrophotometry [15-16].

Aim. The present investigation an indirect titrimetric method is described for the determination of Cetirizine hydrochloride. The method involves the use of potassium peroxomonosulphate as the titrant. A known excess of either reagent is added and, after a specified time, the residual reagent is determined iodimetrically. The proposed method was applied to the analysis of pharmaceutical preparations containing the drugs, and the results obtained compared favourably with those obtained by pharmacopoeial methods.

Results and discussion. In the present investigation, potassium caroate was found to react quantitatively with CTZ in alkali medium to form the *N*-oxide. A stoichiometry of the reaction between potassium caroate and CTZ showed that for oxidation of 1 mol CTZ 1 mol of potassium caroate were required. The relationship between

the titration end-points obtained by the proposed method and the CTZ amounts was examined. The linearity between the amount of CTZ and titration end-point is apparent from the correlation coefficient. The correlation coefficient of 0.999 show that the reaction between potassium caroate and the studied CTZ proceeds stoichiometrically in a molar ratio of 1 : 1. To prove the validity and applicability of the proposed method, four replicate determinations at different concentration levels of CTZ was carried out. The within-day RSD values were within 2%.

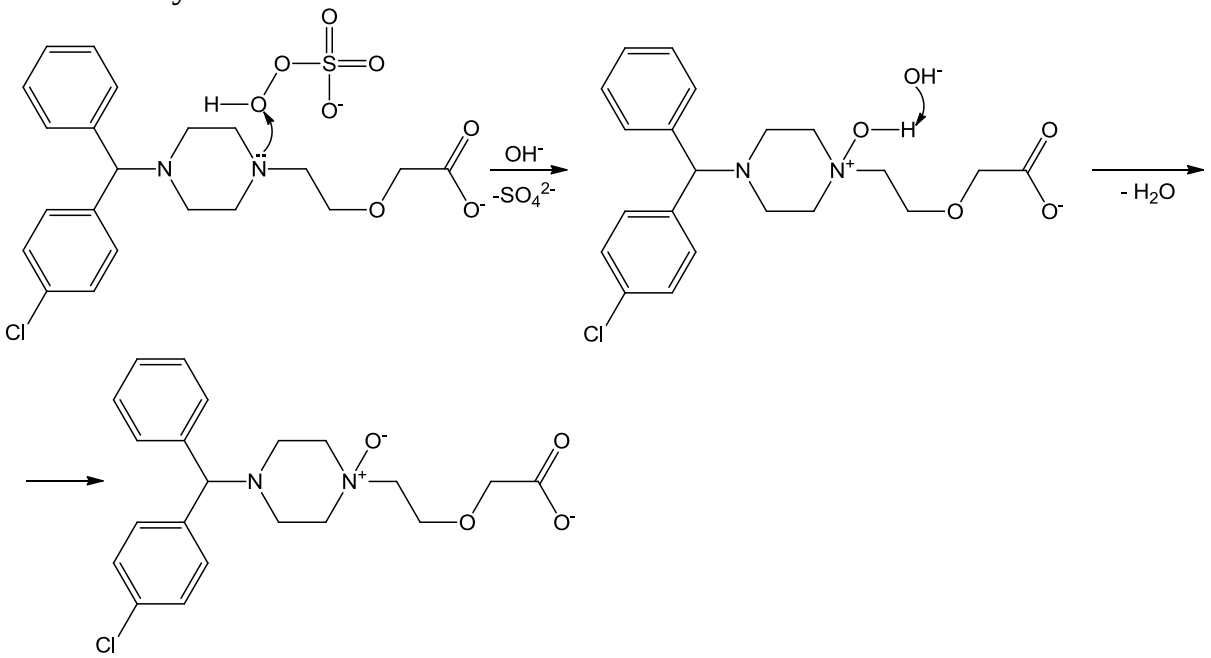

Fig. 3 Scheme of *N*-oxidation of CTZ potassium caroate

The method was successfully applied to the assay of CTZ in tablets Cetirizine-Astrafarm on 10 mg (ASTRAPHARM Ltd, Ukraine) and the results were statistically compared with those of a reference method. No interference was observed from common tablet adjuvants. The accuracy and reliability of the methods were further ascertained by recovery experiments via the standard-addition technique.

Conclusion. The developed analytical method is simple, accurate and economic and can be used in quality control laboratories.

References

1. Sweetman SC (ed) (2011) Martindale, the complete drug reference, 37th edn. The Pharmaceutical Press, London
2. Corsico, A.G., Leonardi, S., Licari, A. et al. Focus on the cetirizine use in clinical practice: a reappraisal 30 years later. Multidiscip Respir Med 14, 40 (2019). https://doi.org/10.1186/s40248-019-0203-6
3. O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 334
4. Sweetman SC (ed) (2011) Martindale, the complete drug reference, 37th edn. The Pharmaceutical Press, London
5. Kathyyn B, Hengameh R. Chiral Switch Drugs for Asthma and Allergies: True Benefit or Marketing Hype. Pediatr Allergy Immunol Pulmonol, 2013; 26: 157-160.

6. Mashkovsky M.D. Medicines. 16th ed., Rev., Rev. and additional, Moscow: New Wave: Publisher Umerenkov, 2020.1216 p.
7. British Pharmacopoeia (2013) Vol II, The stationary office, electronic version, London, pp 305, 1227, 1099
8. United States Pharmacopeial Convention. USP 35- NF 30. Rockville, MD: The Convention; 2012.
9. Karakuş S, Küçükgüzel I, Küçükgüzel SG (2008) Development and valida‑tion of a rapid RP‑HPLC method for the determination of cetirizine or fexofenadine with pseudoephedrine in binary pharmaceutical dosage forms. J Pharm Biomed Anal 46:295–302
10. Sunil K, Yogesh K, Abhijeet K (2013) Simultaneous estimation of cetirizine hydrochloride, phenylpropanolamine hydrochloride and paracetamol by RP‑HPLC method. Int J Pharm Life Sci (IJPLS) 4:3122–3132
11. Suryan AL, Bhusari VK, Rasal KS, Dhaneshwar SR (2011) Simultaneous quantitation and validation of paracetamol, phenylpropanolamine hydrochloride and cetirizine hydrochloride by RP‑HPLC in bulk drug and formulation. Int J Pharm Sci Drug Res 3:303–308
12. Aly Fatma Ahmed, EL-Enany Nahed, Elmansi Heba and Nabil Amany Simultaneous determination of cetirizine, phenyl propanolamine and nimesulide using third derivative spectrophotometry and high-performance liquid chromatography in pharmaceutical preparations Chemistry Central Journal (2017) 11:99 DOI 10.1186/s13065-017-0326-9
13. Makhija SN, Vavia PR (2001) Stability indicating HPTLC method for the simultaneous determination of pseudoephedrine and cetirizine in phar‑maceutical formulations. J Pharm Biomed Anal 25:663–667
14. Azhagvuel S, Sekar R (2007) Method development and validation for the simultaneous determination of cetirizine dihydrochloride, paracetamol, and phenylpropanolamine hydrochloride in tablets by capillary zone electrophoresis. J Pharm Biomed Anal 43:873–878
15. Wankhede SB, Lad KA, Chitlange SS (2012) Development and validation of UV‑spectrophotometric methods for simultaneous estimation of cetirizine hydrochloride and phenylephrine hydrochloride in tablets. Int J Pharm Sci Drug Res 4:222–226
16. Aly, F.A., El-Enany, N., Elmansi, H., Nabil, A., 2017. Simultaneous determination of cetirizine, phenyl propanolamine and nimesulide using third derivative spectrophotometry and high-performance liquid chromatography in pharmaceutical preparations. Chemistry Central Journal 11:99. doi:10.1186/s13065-017-0326-9