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SPECTROPHOTOMETRIC DETERMINATION OF ASTEMIZOLE IN TABLETS USING METHYLORANGE AND TROPAEOLIN 00

ASTEMIZOLÜN METİLORANJ VE TROPAEOLİN 00 KULLANILARAK TABLETLERDE SPEKTROFOMETRİK MİKTAR TAYİNİ

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Two simple and sensitive spectrophotometric methods have been developed for the determination of astemizole and its tablets. These methods were based on the formation of ion-pair complexes using methylorange and tropaeolin 00. The ion-pairs formed were densly colored and easily extracted with CH_2CI_2 for both of the reagents. Maximum absorbance was obtained at pH 4.0 for methylorange and pH 3.5 for tropaeolin 00 using citrate-phosphate buffer. Calibration curves were linear over the concentration range 1.0-7.0 $\mu g.mL^{-1}$ at λ_{max} 428 nm for methylorange (r = 0.9999) and λ_{max} 413 nm for tropaeolin 00 (r = 0.9999). Results obtained from the developed methods were compared statisti cally with the results obtained by UV-spectrophotometric method.

Astemizol ve tabletlerindeki miktar tayini için kolay ve hassas iki spektrofotometrik metod geliştirildi. Bu metodlar metiloranj ve tropaeolin 00 kullanılarak iyon-çifti kompleksi oluşumuna dayanmaktadır. Diklorometan ile her iki belirteç için koyu renkli, kolaylıkla ekstre edilebilen iyon-çiftleri oluşturuldu. Maksimum absorbanslar metiloranj için pH 4.0 ve tropaeolin 00 için pH 3.5 da sitratfosfat tamponu kullanılarak elde edildi. Kalibrasyon eğrileri 1.0 - 7.0 $\mu g.mL^{-1}$ konsantrasyon aralığında metiloranj için maksimum 428 nm (r= 0.9999) ve tropaeolin 00 için maksimum 413 nm dalga boyunda doğrusaldır (r=0.9999). Geliştirilen yöntemlerle elde edilen sonuçlar UV–spektrofotometrik yöntemle elde edilen sonuçlarla istatistiksel olarak kıyaslanmıştır.

Keywords: *Spectrophotometry; Astemizole; Methylorange;, Tropaeolin 00; Ion-pair extraction*

Anahtar Kelimeler: *Spektrofotometri; Astemizol; Metiloranj; Tropaeolin 00; İyon-çifti ekstraksiyonu*

Introduction

Astemizole [1] is a relatively new, potent and long-acting histamine H_1-antagonist devoid with central sedative and anticholinergic effects (1). Various methods as colorimetry (2-5) and HPLC (2, 6) have been published for the quantitation of astemizole in pharmaceutical dosage forms. Simultaneous determination of astemizole and its metabolites in biological fluids were carried out using TLC(7), HPLC(8) and RIA(9).

This report presents simple, sensitive and specific two spectrophotometric methods for **1** in its tablets based on the formation of ion-pair complexes using methylorange **(MO method)** [2] and tropaeolin 00 **(TP 00 method)** [3].

Materials and methods

Apparatus: A Shimadzu UV-160 A UV-visible spectrophotometer with 1 cm path length glass and quartz cells and WTW pH 526 pH meter with combined electrode were used.

Chemicals: Astemizole and its tablets (Histamizol®) were kindly supplied from Deva Pharmaceuticals (Istanbul, Turkey). The other chemicals and solvents used were of analytical reagent grade.

Stock solution of 1: 2.18 x 10^{-5} M of astemizole was prepared in CH_2Cl_2.

Reagent solution of 2 and 3: 2.99 x 10^{-4} M of methylorange and tropaeoline 00 solutions were prepared in distilled water, respectively.

*Preparation of calibration graph for **MO method**:* Suitable aliquots (0. 5 -1 mL) of the stock solution of **1** were transferred to marked tubes and diluted to 5 mL with CH_2Cl_2. 2mL of **2** and 2 mL of citrate-phosphate buffer (pH 4.0) were added and mixed for 2 min with a vortex mixer. The absorbance of the CH_2Cl_2 layer was measured at 428 nm against a blank solution prepared similarly. The calibration graph for astemizole with methylorange was plotted and regression equation was calculated.

*Preparation of calibration graph for **TP 00 method**:* Suitable aliquots (0.5 - 4 mL) of the stock solution of **1** were transferred to marked tubes and diluted to 5 ml with CH_2Cl_2. 2ml of reagent solution of **3** and 2 ml of citrate-phosphate buffer (pH 3.5) were added and mixed for 2 min with a vortex mixer. The absorbance of the CH_2Cl_2 layer was measured at 413 nm against a blank solution prepared similarly. The calibration graph for astemizole with tropaeolin 00 was plotted and regression equation was calculated.

Assay procedure for tablets: Tablet powder equivalent to 10 mg of astemizole was accurately weighed and transferred into a 100 mL calibrated flask. After addition of 40 mL CH_2Cl_2, the mixture was shaken mechanically for 30 min and diluted to volume with CH_2Cl_2 and filtered. 1 mL of the filtrate was diluted to 10 mL with the same solvent. 3 mL of this solution was withdrawn and diluted to 5 mL with CH_2Cl_2 and proposed methods were (**MO method and TP 00 method**) applied to the resulting solution for the analysis of astemizole in tablets. The amount of astemizole in tablets was calculated from the regression equation of the calibration curve.

Results and Discussion

Optimum conditions of the ion-pairs with respect to solvent, pH, time and reagent amount were investigated. The ion-pairs formed were densely colored and easily extracted with CH_2Cl_2 for both of the reagents. The absorption spectrum in CH_2Cl_2 showed a maximum at λ_{max}: 428 nm for [2] and λ_{max}: 413 nm for [3]. Maximum absorbances were obtained at pH 4.0 for [2] (Fig. 1) and pH 3.5 for [3] (Fig. 2) using citrate-phosphate buffer and these final solutions were stable at room temperature in the dark for at least 24 h for [2] and 6 h for [3]. The stoichiometric balances were found to be 1:2 (astemizole: methylorange and astemizole: tropaeolin 00) by Job's curve.

The optimum molar ration of reagents to astemizole were found to be 6 for [2] (Fig. 3) and 4 for [3] (Fig. 4) by molar ration method, respectively.

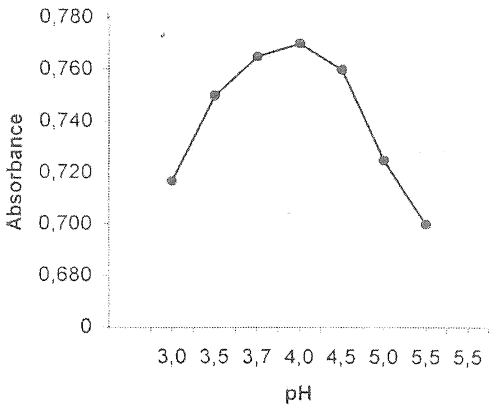

Fig. 1 Effect of pH on the reaction of astemizole with methylorange.

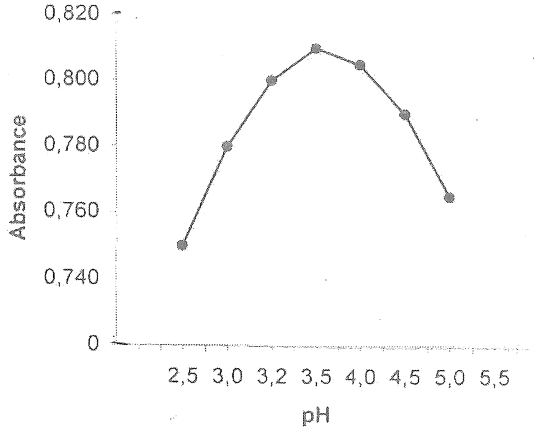

Fig. 2 Effect of pH on the reaction of astemizole with tropaeolin 00.

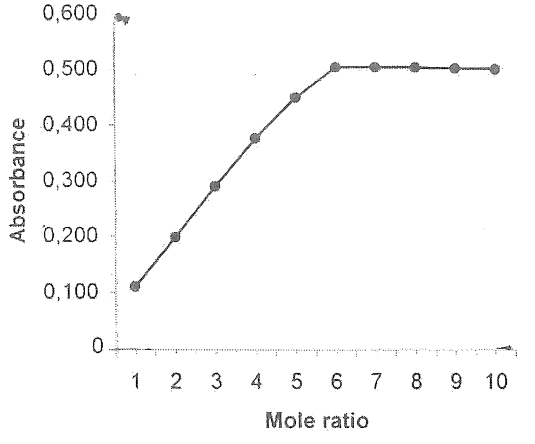

Fig. 3 Effect of reagent concentration on the reaction of astemizole with methylorange.

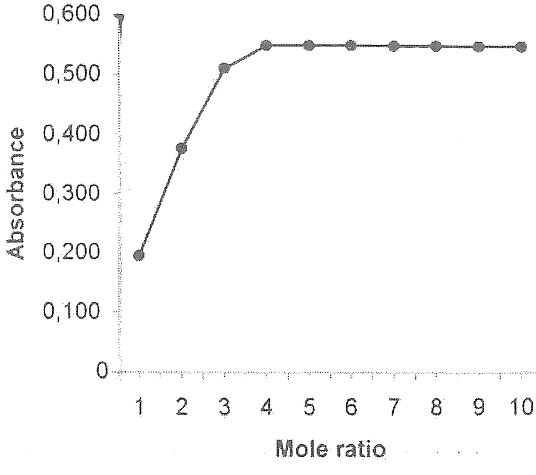

Fig. 4 Effect of reagent concentration on the reaction of astemizole with tropaeolin 00.

At these conditions, linear correlations were observed between absorbance and concentration of astemizole over the range of 1.0 – 7.0 $\mu g.ml^{-1}$ for both of the reagents (Fig. 5 and 6). (A = 0.1310 c – 0.005, r = 0.9999 for [2] and A = 0.1391 c – 0.004, r = 0.9999 for [3].)

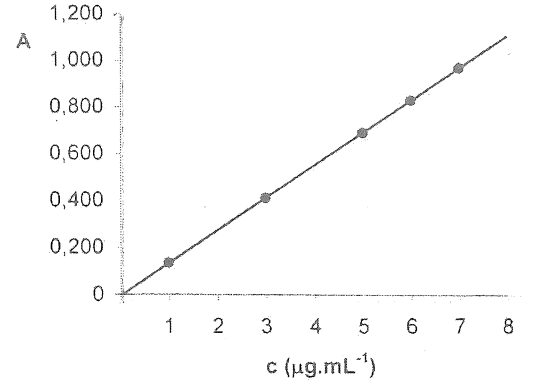

Fig. 5 Calibration curve of astemizole with methylorange.

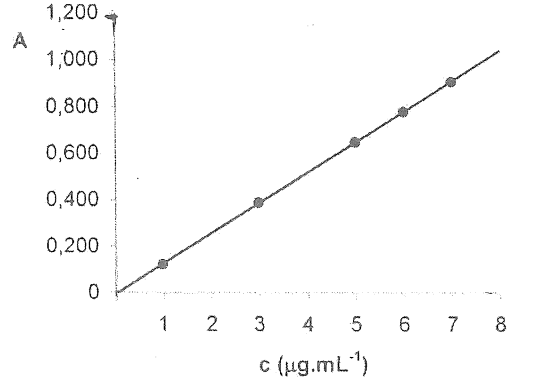

Fig. 6 Calibration curve of astemizole with tropaeolin 00.

The proposed methods were applied to commercially available tablets. Different tablet additives such as lactose, starch, magnesium stearate, carboxy-methylcellulose did not interfere. The results were compared with those obtained by UV-spectrophotometric method(10). Statistical comparisons in terms of t- and F-tests for these methods

are given in the table. There were no significant differences between the proposed methods and UV-spectro photometric method with respect to the mean values and standart deviations.

Results showed that these methods have good accuracy and precision and they can be recommended for routine pharmaceutical analysis of astemizole.

Table Comparison of the results obtained by spectrophonometric (MO method and TP 00 method) and UV-spectrophotometric methods for the determination of astemizole in tablets (each tablet contains 10 mg of astemizole).

Statistical values	Proposed methods		UV-spectrophotometric method
	MO	TP 00	
Mean (mg)	10.04	10.05	10.07
Recovery ± standard deviation (%)	100.4 ± 0.36	100.5 ± 0.32	100.70 ± 0.32
Confidence limit	9.72 – 10.36	9.76 – 10.34	9.78 – 10.36
t-test of significance*	1.53	0.99	
F-test of significance*	1.21	1.02	

* n=6 p=0.05 t=2.23 F=5.05

References

1. Reynolds, J.E.F.: Martindale, The Extra Pharmacopoeia, 30 th Ed., pp930 The Pharmaceutical Press 1993
2. El Walily, A.M., El Gindy, A., Wahbi, A.M.: STP Pharma Prat. 5 (5) 403 (1995)
3. Abdelmageed, O.H.: Bull. Pharm. Sci. Assiut Univ. 19, 53 (1996)
4. Al-Warthan, A.A., AI-Obaid, A.M.: J. Pharm. Biomed. Anal. 14 (5) 579 (1996)
5. Meyyanathan, S.N., Ravisankar, S., Suresh, B.: East. Pharm. 37 (438) 125 (1995)
6. Suryanarayana, M.V., Venkataraman, S., Reddy, M.S., Reddy, B.P., Sastry, C.S.P., Krupadanam, G.L.D.: Talanta 40 (9) 1357 (1993)
7. Mangalan, S., Patel, R.B., Gandhi, T.P., Chakravarthy, B.K.: J. Chromatogr. 567 (2) 498 (1991)
8. Woestenborghs, R., Embrechts, L., Heykants, J.: J. Choromatogr. 278 (2) 359 (1983)
9. Woestenborghs, R., Geuens, I., Michiels, M., Hendriks, R., Heykants, J.: Drug Dev. Res. 8 (1-4) 63 (1986)
10. Deva Pharmaceuticals, Istanbul, Turkey (Personel çommunication).

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