View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Elsevier - Publisher Connector

Arabian Journal of Chemistry (2016) xxx, xxx–xxx

King Saud University

Arabian Journal of Chemistry

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

Hydrophilic interaction chromatography (HILIC) for the determination of cetirizine dihydrochloride

Magdalena Paczkowska [a], Mikołaj Mizera [a], Artur Tężyk [b], Przemysław Zalewski [a], Jakub Dzitko [a,c], Judyta Cielecka-Piontek [a,*]

[a] *Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Poznan University of Medical Sciences, Grunwaldzka 6, 60-780 Poznań, Poland*
[b] *Department of Forensic Medicine, Poznan University of Medical Sciences, Święcickiego 6, 60-781 Poznań, Poland*
[c] *PozLab sp. z.o.o., ul. Parkowa 2, 60–775 Poznan, Poland*

Received 9 February 2016; accepted 24 May 2016

KEYWORDS

Cetirizine dihydrochloride;
Stability studies;
Hydrophilic interaction;
HPLC

Abstract A stability-indicating high-performance liquid chromatography (HPLC) of hydrophilic interactions was developed and validated for the determination of cetirizine dihydrochloride in bulk substance and in pharmaceutical dosage form. The separation was achieved on a Poroshell 120 Hilic (4.6 × 150 mm, 2.7 μm) column using a mobile phase composed of acetonitrile–0.1% formic acid (20:80 v/v) at a flow rate of 1.0 mL/min. The injection volume was 5.0 μL and the wavelength of detection was controlled at 235 nm. The method was validated by evaluating linearity, accuracy, precision, selectivity and robustness. Cetirizine dihydrochloride was the susceptible to the action of an oxidation factor. The product of its degradation under those conditions was identified with an EIS-Q-MS mass spectrometer. The hydrophilic interactions between the main analyte, its oxidation product, and the mobile and stationary phases were discussed with the support of a theoretical investigation.
© 2016 The Authors. Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Cetirizine dihydrochloride (CTZ), chemically known as [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl] ethoxy]-acetic acid dihydrochloride, is an antagonist of a H_1 receptor. CTZ is a racemic mixture of levocetirizine, showing biological antihistamine activity, and dextrocetirizine, with no such effect (Baltes et al., 2001). The difference in the molecular structures of the enantiomers affects their pharmacological properties, including an affinity to the receptor being 30 times greater for levocetirizine (Tillement et al., 2003). CTZ is used in the treatment of hay fever, allergies, angioedema, and urticaria. It belongs to the second-generation antihistamines that are less able to cross the blood–brain barrier and thus do not cause side effects such as sedation, drowsiness or decreased cognitive processing (Berger et al., 2006; Carson et al., 2010; Garg and Thami, 2007; Golightly and Greos, 2005; Howarth et al., 1999). In previous studies, spectrophotometric, HPTLC and HPLC methods have been applied for determining cetirizine hydrochloride (Arayne et al., 2005; Haghighi et al., 2013; Kaur et al., 2014; Khan et al., 2011; Rawool et al., 2013; Souri et al., 2013). So far only one report has presented a UHPLC procedure for CTZ determination, conducted in the presence of ambroxol hydrochloride and antimicrobial preservatives in liquid pharmaceutical formulations (Trivedi et al., 2011). All of those methods utilized classical stationary phases known from reversed-phase liquid chromatography. Moreover for the separation of cetirizine enantiomers were also proposed: HPLC method developed by Kang et al. (2010) and

* Corresponding author. Tel.: +48 618546649; fax: +48 618546652.
E-mail address: jpiontek@ump.edu.pl (J. Cielecka-Piontek).
Peer review under responsibility of King Saud University.

ELSEVIER Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.arabjc.2016.05.012
1878-5352 © 2016 The Authors. Production and hosting by Elsevier B.V. on behalf of King Saud University.
This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Please cite this article in press as: Paczkowska, M. et al., Hydrophilic interaction chromatography (HILIC) for the determination of cetirizine dihydrochloride. Arabian Journal of Chemistry (2016), http://dx.doi.org/10.1016/j.arabjc.2016.05.012

capillary electrophoresis (CE) obtained by Eeckhaut and Michotte (2006). Recently supercritical fluid chromatography was reported as fast method for chiral separation of racemic cetirizine and levocetirizine (Eom et al., 2016). However, it is worth noting that Pharmacopeia recommended potentiometric titration as a method for cetirizine determination, while chromatographic separation was signed as method for separation of A-F impurities of cetirizine (including levocetirizine) (European Pharmacopoeia; British Pharmacopoeia).

Currently, the interest in the application of hydrophilic interaction chromatography (HILIC) in the analysis of many polar drugs, metabolites and biological important compounds was observed (Nuijs et al., 2011). According to Buszewski and Noga (2012), the application of hydrophilic interaction liquid chromatography (HILIC) is a viable alternative to high-performance liquid chromatography in the analysis of many compounds. HILIC is also applicable to charged substances (Bertuzzi et al., 2010). It is also equally important that separation by this method, while analyzing hydrophilic and ionizable drugs, can be combined with mass spectroscopy (MS) resulting in a significantly increased sensitivity of determination (Sewell et al., 2012).

Earlier studies have shown that cetirizine dihydrochloride is stable under conditions of base hydrolysis (1 M NaOH) and thermolysis (T = 43 K, RH = 76.4%), whereas strong affecting factors are required to degrade CTZ in an acidic environment (2 M HCl, T = 343 K). The greatest chemical instability of CTZ is observed on exposure to an oxidation factor (2% H_2O_2, T = 53 K), which is of particular practical importance indicating that excipients promoting an oxidative degradation path must be avoided (Khan et al., 2011).

Based on the above, the present study aimed to develop a rapid and sensitive HPLC–HILIC method for the determination of cetirizine dihydrochloride in the presence of its degradation product and excipients found in solid pharmaceutical dosage forms containing this compound. The method is useful for quality control of cetirizine dihydrochloride in biological fluids and in pharmaceutical matrix.

2. Experimental

2.1. Materials

Cetirizine dihydrochloride (purity > 98%, molecular weight: 461.81 g/mol, pKa (strongest acidic): 3.6, pKa (strongest basic): 7.79, log P: 1.70, solubility in water: 0.0658 mg/mL at 298 K) in bulk substance was applied by India PVT LTD, while pharmaceutical preparation 1: containing 10 mg of CTZ and excipients: microcrystalline cellulose, lactose monohydrate, colloidal silica, magnesium stearate; pharmaceutical preparation 2: containing 10 mg of CTZ and excipients: lactose monohydrate, microcrystalline cellulose, starch, crospovidone, magnesium stearate; and pharmaceutical preparation 3: containing 10 mg of CTZ and excipients: lactose monohydrate, microcrystalline cellulose, cornstarch, povidone, magnesium stearate, were commercially available preparations. Hydrochloric acid, sodium hydroxide solution, hydrogen peroxide and all other chemicals were obtained from P.O.Ch. (Poland). Acetonitrile of an HPLC grade was supplied by Merck KGaA (Germany) and formic acid (100%) by P.O. Ch. (Poland). High-quality pure water was prepared using an Exil SA 67120 Millipore purification system (France).

2.2. Chromatographic equipment and chromatographic conditions

The LC system (Dionex Thermoline Fisher Scientific, Germany) was equipped with a high pressure pump (UltiMate 3000), an autosampler (UltiMate 3000) and a DAD detector (UltiMate 3000). For data processing and acquisition, Chromeleon software version 7.0 from Dionex Thermoline Fisher Scientific (US) was used. As the stationary phase, a Poroshell 120 Hilic column, 2.7 μm particle size, 4.6 × 150 mm (Agilent Technology) was used. The mobile phase consisted of acetonitrile–0.1% formic acid (20:80 v/v). The flow rate of the mobile phase was 1.0 mL/min. The wavelength of the UV detector was set at 235 nm. The injection volume was 5.0 μL. A triple-quadrupole mass spectrometer model 6410B Triple Quad with an electrospray (ESI) interface (both from Agilent Technologies, USA) coupled with chromatograph Agilent 1200 was used for identification of degradation products of CTZ. The ESI source of the MS-detector was operated in a negative ionization mode. For nebulization a nitrogen stream at 40 psi (275.8 kPa) was applied. A drying gas, also nitrogen, was delivered at a flow rate of 8 L/min at 573 K. The electrospray needle voltage was 4000 V. The acquisition was carried out in the scan mode, and the spectra were collected in the range of m/z 40–600. The MassHunter workstation software (Agilent Technologies, USA) was used for the instrument control, data acquisition and data analysis. The identification of degradation products of CTZ based on application of an EIS-Q-MS mass spectrometer was possible by using the mobile phase which was composed of acetonitrile and 0.1% formic acid (20:80 v/v).

2.3. Preparation of analytical samples

2.3.1. Assay of in bulk substance

Solutions of CTZ were prepared by dissolving 10.0 mg of CTZ in 20.0 mL of distilled water (c = 0.5 mg/mL). Standard stock solution of CTZ was prepared by the same way (c = 0.5 mg/mL). Standard stock solution was kept during period of studies.

2.3.2. Assay of cetirizine dihydrochloride in tablets

The amount of accurately powdered tablets (pharmaceutical preparations 1, 2, 3) containing CTZ was pounded and transferred to 20.0 mL volumetric flasks, dissolved with about 20 mL of water, mixed in a ultrasound bath for 5 min and filtered. The final concentration of CTZ 0.5 mg/mL was achieved.

2.4. Method validation

The method was validated according to the International Conference on Harmonization Guidelines (1996). It comprised selectivity, linearity, accuracy, precision, limits of detection (LOD) and quantitation (LOQ). All measurements were performed triplicates.

2.4.1. Sample solutions

Sample solution of CZT was prepared by dissolving 10.0 mg of CTZ in 20.0 mL of distilled water. Pharmaceutical preparations 1, 2 and 3 (10 mg coated tablets), commercially available dosage form of CTZ were pounded, transferred into stopped flask and dissolved in 20.0 mL of distilled water.

2.4.2. Selectivity

The selectivity of determination of CTZ was examined for non-degraded and degraded samples as well as in the presence

Please cite this article in press as: Paczkowska, M. et al., Hydrophilic interaction chromatography (HILIC) for the determination of cetirizine dihydrochloride. Arabian Journal of Chemistry (2016), http://dx.doi.org/10.1016/j.arabjc.2016.05.012

of excipients (microcrystalline cellulose, lactose monohydrate, colloidal silica, magnesium stearate, starch, cornstarch, povidone and crospovidone). The selectivity was examined after stress conditions in aqueous solutions after oxidation (2% H_2O_2 at 353 K).

In order to evaluate the selectivity of proposed HPLC method in determination of CTZ in bulk substance and in pharmaceutical dosage forms in the presence of excipients (microcrystalline cellulose, lactose monohydrate, colloidal silica, magnesium stearate, starch, cornstarch, povidone and crospovidone) degradation studies in aqueous solutions after oxidation (2% H_2O_2 at 353 K) were performed. The identification of degradation products of CTZ was carried in the same conditions.

2.4.3. Precision

Precision of the assay of CTZ was determined in relation to repeatability (intra-day) and intermediate precision (inter-day). In order to evaluate the repeatability of the method, six samples were determined during the same day for three concentrations of CTZ. Intermediate precision was studied comparing the assays performed on two different days.

2.4.4. Accuracy

The accuracy of the method was determined by recovering CTZ from the placebo. The recovery test was performed at three levels: 80%, 100%, and 120% of the nominal concentration of CTZ during degradation studies. Three samples were prepared for each recovery level. The solutions were analyzed and the percentage of recoveries was calculated from the calibration curves.

2.4.5. The limit of detection (LOD) and quantification (LOQ)

LOD and LOQ parameters were determined from the regression equations of CTZ. LOD = 3.3 S_y/a, LOQ = 10 S_y/a, where S_y is a standard error and a is the slope of the corresponding calibration curve.

2.4.6. Robustness

The impact of the composition of the mobile phase (percentage of acetonitrile in the mobile phase 20 ± 5 v/v), pH of mobile phase (formic acid concentration, 3–0.05%), the flow rate (1.0 ± 0.1 mL/min), absorption wavelength (235 ± 5 nm) and column temperature (25 ± 10 °C) on the peak area and shape of CTZ were determined.

2.5. Theoretical studies

Molecular electrostatic potential (MEP) of optimized structures of CTZ and its degradation product were obtained with density functional theory calculations using Becke's three-parameter hybrid functional (B3LYP) with 6-31++(d,p) basis set. All *ab initio* calculations were carried out by Gaussian 03 package. GaussView application was utilized to present the MEP maps (Frisch et al., 2009). Modeling and visualization of fragment of stationary phase were made using molecular mechanics MMFF94 method implemented in ChemBio3D. Prediction of pKa values was carried out by ePik software.

3. Results and discussion

The HPLC procedure was developed in regard to stability-indicating assay of CTZ in bulk substance and pharmaceutical dosage forms. The chromatographic separation of CTZ and its degradation products were achieved on a Poroshell 120 Hilic column, 2.7 μm particle size (4.6 × 150 mm) at 25 °C. A mixture of acetonitrile and 0.1% formic acid (20:80 v/v) with a flow rate of 1.0 mL/min was used as a mobile phase. The wavelength of detection was set at 235 nm. The chromatograms of non-degraded and degraded samples CTZ are shown in Fig. 1. On chromatograms of degraded samples of CTZ, peaks originating from degradation product were observed at retention times from about 1.65 (Fig. 1). The degradants and excipients were not interfering with the main peaks. As a result of exploiting hydrophilic interactions in the determination of CTZ by using HPLC in this work, it was possible to obtain shorter retention times for CTZ (t_R = 1.79 min) compared to values received with HPLC (t_R = 3.8 min and t_R = 7.0 min) (Kaur et al., 2014; Souri et al., 2013). The use of a hydrophilic interactions in HILIC ensuring a high selectivity of CTZ determination in the presence of oxidation products without using phosphate buffers allowed an analysis of degradation products by means of an EIS-Q-MS mass spectrometer. Buszewski noted that the advantage of coupling HILIC with an MS detector is a tenfold increase in sensitivity as against HPLC-MS systems due to the presence of a higher organic content in the mobile phase (20% in this study) leading to rapid solvent evaporation during electrospray ionization (Buszewski and Noga, 2012).

The method was also validated for linearity, inter- and intra-day accuracy and precision, robustness, system suitability, LOD, LOQ and recovery for the assay of CTZ in bulk substance and in the pharmaceutical preparations. The calibration plots were linear and in CTZ column load range 0.50–3.00 μg/mL. They were described by the equations $y = ax$. The b values, calculated from the equation $y = ax + b$, were insignificant because of being lower than the critical value $t_b = b/S_b$ (Table 1). Precision of the proposed method was characterized by relative standard deviation (RSD, %) which was calculated for six consecutive measurements at three concentration levels 80%, 100% and 120% of standard solutions during the system suitability test. All values that characterize the inter-day precision of determination of cetirizine dihydrochloride were less than 2% and meet the criteria required for the precision of the method. The accuracy of the developed HPLC method was evaluated by analyzing content of cetirizine dihydrochloride in bulk substance and in pharmaceutical preparations. Although the content of organic fraction in the mobile phase was low for the HILIC application in our studies, the high sensitivity of determination analytes was achieved. The average values of the recoveries and precision are collected in Table 2.

A comparison of validation parameters obtained in the present study with those reported previously demonstrated that the newly developed method is far more sensitive, provides a wider range of linear relation between analyte concentration and a detector signal, and allows receiving lower limits of quantitation and detection. With regard to %RSD reflecting the intra-day precision of the methods compared, HPLC procedures proved superior whereas no significant differences were found in inter-day precision. The accuracy

Please cite this article in press as: Paczkowska, M. et al., Hydrophilic interaction chromatography (HILIC) for the determination of cetirizine dihydrochloride. Arabian Journal of Chemistry (2016), http://dx.doi.org/10.1016/j.arabjc.2016.05.012

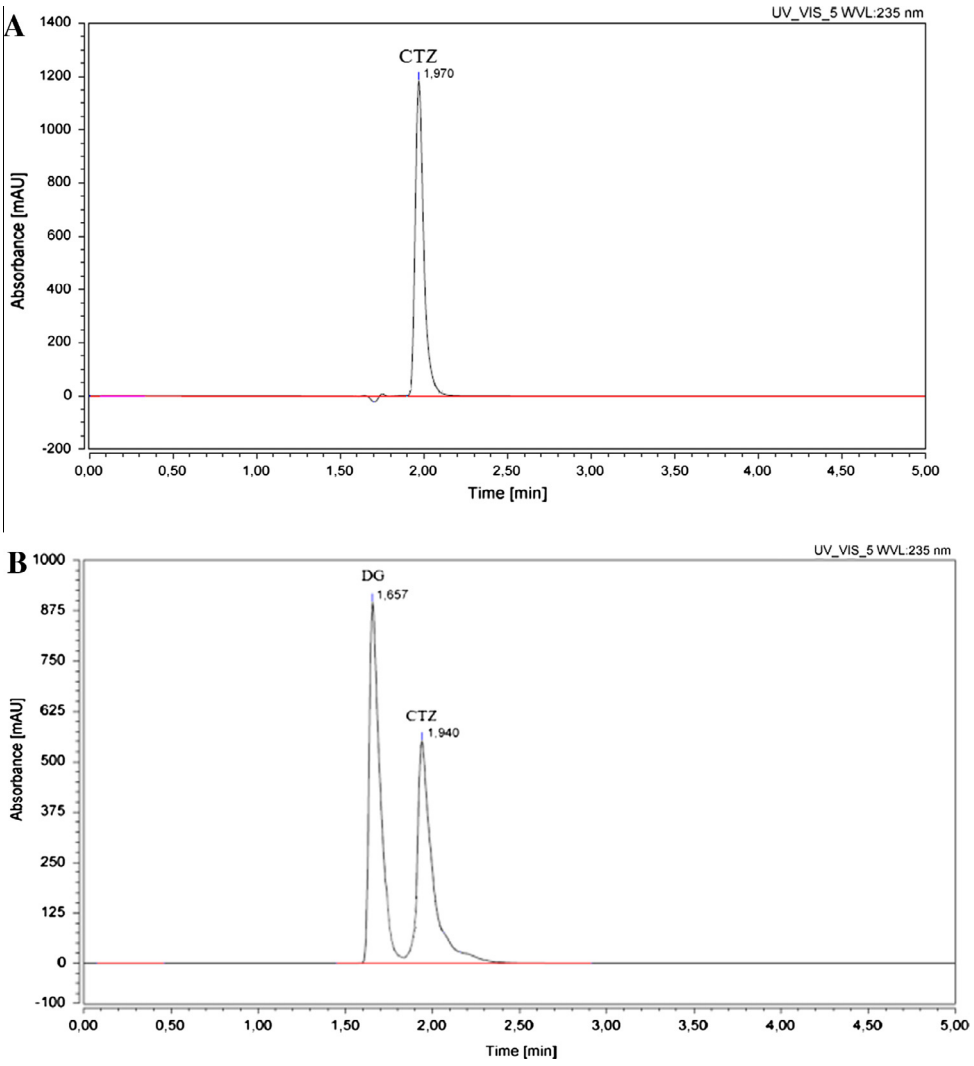

Figure 1 The chromatograms of non-degraded samples of CTZ in a bulk substance (A) and degraded samples of CTZ in bulk substance under oxidizing conditions (2% H_2O_2, $T = 53$ K, $t = 40$ min) (B).

Table 1 Validation parameters of linearity of CTZ in a bulk substance and pharmaceutical preparations.

	Bulk substance	Pharmaceutical preparations		
		1	2	3
Retention time (min)	1.970	1.977	1.980	1.980
Range of linearity (μg/mL)	0.50–3.00	0.50–3.00	0.50–3.00	0.50–3.00
Regression equation (y)				
Slope ($a \pm S_a$)	25.32 ± 0.28	20.57 ± 0.45	21.19 ± 0.24	23.53 ± 0.39
Correlation coefficient (r)	0.9999	0.9996	0.9999	0.9998
LOD (μg/mL)	0.0373	0.0737	0.0384	0.0553
LOQ (μg/mL)	0.1131	0.2236	0.1164	0.1475

S_a standard deviation of slope; S_b standard deviation of intercept, t, calculated values of Student's t test, $t_{\alpha,f} = 2.1709$ critical values of Student's test for degrees of freedom $f = 11$ and significance level $\alpha = 0.05$.

of the HPLC method involving hydrophilic interactions was slightly worse compared to a HPLC procedure with a C18 column used as a stationary phase (Kaur et al., 2014; Souri et al., 2013; Trivedi et al., 2011).

The robustness of the HPLC–HILIC procedure was evaluated after changing the mobile phase composition (acetonitrile volume, 20 ± 5 v/v), mobile phase pH (formic acid concentration, 3–0.05%), flow rate (1.0 ± 0.1 mL/min), absorption

Table 2 Results for the determination of CTZ in a bulk substance and pharmaceutical dosage forms.

	Bulk substance	Pharmaceutical preparations		
		1	2	3
Column load, μg	RSD, %			
Intra-day precision				
4.0 (80%)	0.09	0.21	0.67	0.57
5.0 (100%)	0.51	1.14	0.24	0.17
6.0 (120%)	0.83	1.25	0.08	0.87
Inter-day precision				
4.0 (80%)	0.08	1.49	0.28	0.46
5.0 (100%)	0.01	0.48	1.23	1.25
6.0 (120%)	0.12	1.11	0.75	0.39
Accuracy, %				
4.0 (80%)	100.13	79.74	93.61	83.04
5.0 (100%)	100.06	80.97	93.89	84.77
6.0 (120%)	100.06	82.20	94.42	84.92

Table 3 System suitability tests of the HPLC-DAD for CTZ determination under oxidizing factor (2% H_2O_2, $T = 53$ K, $t = 30$ min).

Parameter	CTZ	DP
Relative standard deviation of peak area %	0.09	0.17
Relative standard deviation of retention time (min) %	0.03	0.03
Peak purity	99.79	99.52
Resolution	1.28	1.35
Asymmetry (tailing factor)	1.54	1.79
Number of theoretical plates	2775	3036

Resolutions were calculated between two adjacent peaks in no-degraded and degraded samples.
DP – degradation product.

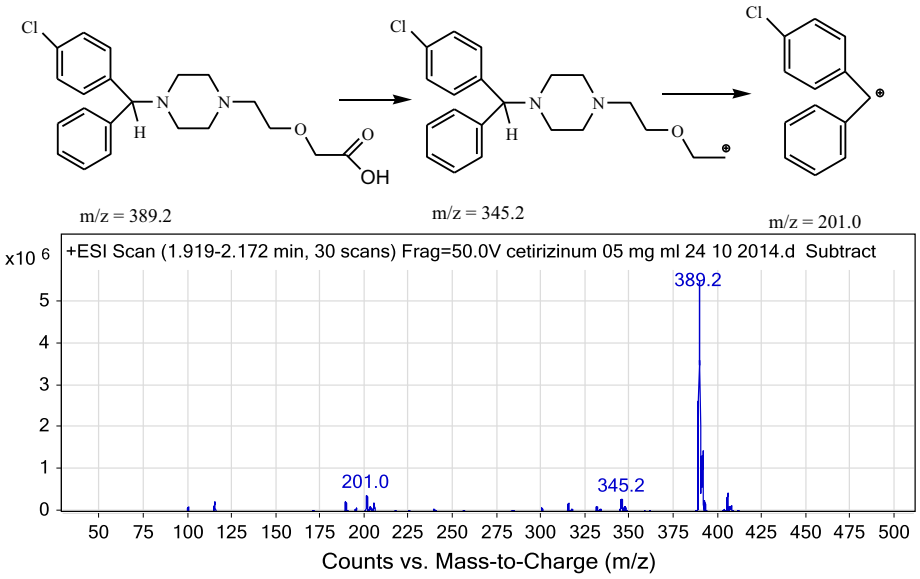

Figure 2 Degradation pathways of cetirizine hydrochloride during oxidation.

wavelength (235 ± 5 nm) and column temperature (298 ± 10 K). No statistically significant differences were established for the parameters studied in the investigation of robustness as their deviation did not exceed the permissible range of ±2%. System suitability was examined in regard to the relative standard deviation for peak areas and peak times, peak resolution, peak asymmetry and the number of theoretical plates (Table 3).

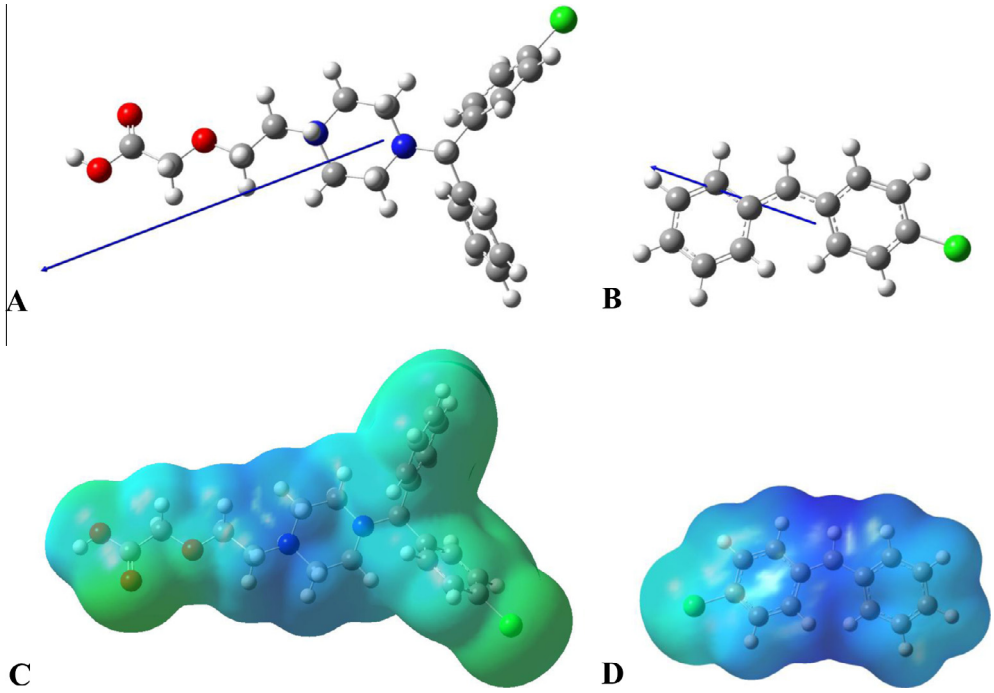

Figure 3 Dipole moment vectors of CTZ (A) and degradation product (B). Electrostatic potential maps of CTZ (C) and its degradation product (D).

The action of an oxidation factor (2% H_2O_2) caused changes within the bond connecting the phenyl and the piperazine rings resulting in the formation of a degradation product with a partition coefficient different from that of the analyte. The mass fragmentation of the CTZ during oxidation is shown in Fig. 2. The resulting oxidation product of cetirizine has not been previously reported as its impurity (European Pharmacopoeia; British Pharmacopoeia). As demonstrated, the degradation product of CTZ oxidation meets the criteria of Lewis base being an electron donor and thus can be assumed to interact with negatively charged silanols from the stationary phase. By contrast, CTZ is a polar compound with a tendency to form hydrogen bonds and numerous physical interactions (e.g. an ion–dipole or a dipole-induced dipole) as a consequence of being an electron acceptor. According to Yoshida, the fact of obtaining similar retention times (t_R = 1.65 min vs t_R = 1.95 min) for two different compounds, CTZ and its degradation product during separation confirms the occurrence of both hydrogen bonding (Lewis acidity/basicity) and dipole–dipole interactions (dipole moments and compound polarizability) in separation based on application of HILIC column (Yoshida, 2004). The order of elution results from a shift in the partition equilibrium toward the immobilized water layer on the stationary phase for the more hydrophilic analyte; therefore, cetirizine dihydrochloride was eluted after its degradation product.

Based on parameters of molecular electrostatic potential (MEP), which are useful descriptors in indicating sites for electrophilic/nucleophilic reactions and hydrogen bonding, a proposition was made as to which molecular domains of cetirizine dihydrochloride and its oxidation product participated in hydrophilic interactions with the stationary phase. In order to model behavior of CTZ and its degradation

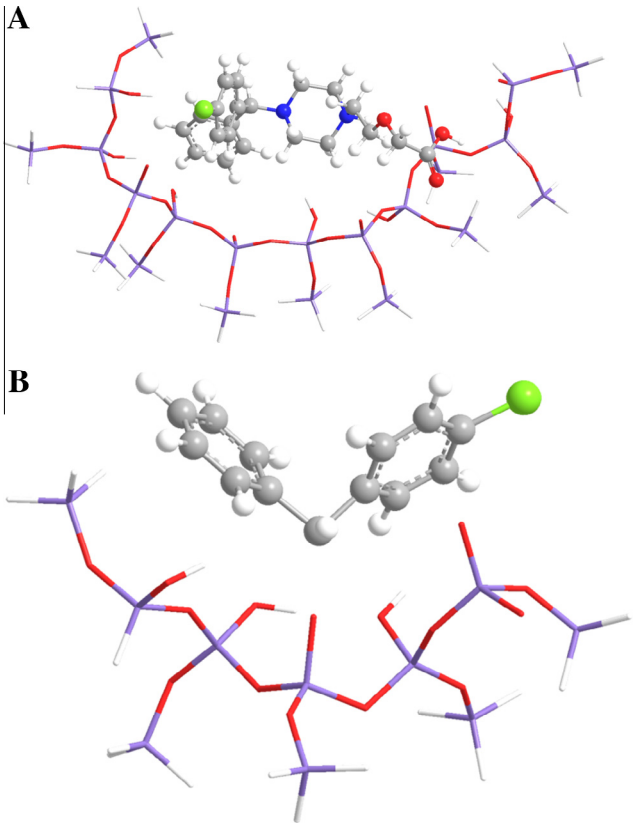

Figure 4 Model of CTZ – silanol stationary phase system (A) and model of degradation product – silanol stationary phase system (B).

Please cite this article in press as: Paczkowska, M. et al., Hydrophilic interaction chromatography (HILIC) for the determination of cetirizine dihydrochloride. Arabian Journal of Chemistry (2016), http://dx.doi.org/10.1016/j.arabjc.2016.05.012

product in proximity of silanol groups, theoretical calculations were performed. Both CTZ and degradation product were subjected to pKa calculations which resulted in protonated form of CTZ in pH = 6.5 (±0.74). The protonation took place on nitrogen of piperazine ring and causes increased polarity of molecule. Dipole vectors computed for optimized geometries of protonated CTZ (Fig. 3A) and degradation product (Fig. 3B) were presented. Vector values are 13.26 Debye and 5.78 Debye for CTZ and degradation product, respectively. Electrostatic potential was visualized on ESP maps (Fig. 3C and D). Blue color indicates positive charge, which is mostly susceptible on interactions with negatively charged stationary phase. High electric dipole moment of CTZ confirms higher polarity, and thus stronger retention relatively to degradation product. Simplified model of absorption of analyte on silanol groups was done in order to measure binding energy of silanol – CTZ and silanol – degradation product systems. Application of force fields method allowed modeling of aforementioned systems with preservation of dipole effects. Models of structures are presented (Fig. 4). Calculated binding energies were −946.71 kJ/mol and −773.45 kJ/mol for silanol-CTZ and silanol-degradation product systems, respectively. Binding of silanol-CTZ is 1.2 times stronger than silanol-degradation product binding energy what stays in agreement with previous investigations of dipole moment and ESP maps.

4. Conclusion

The proposed HPLC method exploiting hydrophilic interactions can be recommended for the determination of cetirizine dihydrochloride in the presence of its oxidation product in bulk substance and in solid pharmaceutical dosage forms. Theoretical calculations confirmed differences in hydrophilic interactions of the analytes determined the various times of their elution.

Acknowledgments

This study was supported by grant from the Ministry of Science and Higher Education (Diamentowy Grant DI 2012 024342).
This research was supported in part by PL-Grid Infrastructure.

References

Arayne, M.S., Sultana, N., Siddiqui, F.A., 2005. Determination and quantification of cetirizine HCl in dosage formulations by RP-HPLC. Pak. J. Pharm. Sci. 18, 7–11.

Baltes, E., Coupez, R., Giezek, H., 2001. Absorption and disposition of levocetirizine, the eutomer of cetirizine, administered alone or as cetirizine to healthy volunteers. Fundam. Clin. Pharmacol. 15, 269–277.

Berger, W., Hampel Jr, F., Bernstein, J., Shah, S., Sacks, H., Meltzer, E.O., 2006. Impact of azelastine nasal spray on symptoms and quality of life compared with cetirizine oral tablets in patients with seasonal allergic rhinitis. Ann. Allerg. Asthma. Im. 97, 375–381.

Bertuzzi, T., Agosti, B., Gualla, A., Pietri, A., 2010. LC–MS–MS determination of sanguinarine and chelerythrine using a HILIC column. Chromatographia 72, 969–973.

British Pharmacopoeia, Volume I & II, Monograph: Cetirizine Hydrochloride.

Buszewski, B., Noga, S., 2012. Hydrophilic interaction liquid chromatography (HILIC) – a powerful separation technique. Anal. Bioanal. Chem. 402, 231–247.

Carson, S., Lee, N., Thakurta, S., 2010. Drug Class Review: Newer Antihistamines. Oregon Health & Science University.

Eeckhaut, A., Michotte, Y., 2006. Chiral separation of cetirizine by capillary electrophoresis. Electrophoresis 27, 2376–2385.

Eom, H.Y., Kang, M., Kang, S.W., Kim, U., Suh, J.H., Kim, J., Cho, H.D., Jung, Y., Yang, D.H., Han, S.B., 2016. Rapid chiral separation of racemic cetirizine in human plasma using subcritical fluid chromatography-tandem mass spectrometry. J. Pharm. Biomed. Anal. 5, 380–389.

European Pharmacopoeia, Monograph 1084: Cetirizine Dihydrochloride.

Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M. A., Cheeseman, J.R., Scalmani, G., Barone, V., Mennucci, B., Petersson, G.A., Nakatsuji, H., Caricato, M., Li, X., Hratchian, H. P., Izmaylov, A.F., Bloino, J., Zheng, G., Sonnenberg, J.L., Hada, M., Ehara, M., Toyota, K., Fukuda, R., Hasegawa, J., Ishida, M., Nakajima, T., Honda, Y., Kitao, O., Nakai, H., Vreven, T., Montgomery Jr., J.A., Peralta, J.E., Ogliaro, F., Bearpark, M., Heyd, J.J., Brothers, E., Kudin, K.N., Staroverov, V.N., Kobayashi, R., Normand, J., Raghavachari, K., Rendell, A., Burant, J.C., Iyengar, S.S., Tomasi, J., Cossi, M., Rega, N., Millam, J.M., Klene, M., Knox, J.E., Cross, J.B., Bakken, V., Adamo, C., Jaramillo, J., Gomperts, R., Stratmann, R.E., Yazyev, O., Austin, A.J., Cammi, R., Pomelli, C., Ochterski, J.W., Martin, R.L., Morokuma, K., Zakrzewski, V.G., Voth, G.A., Salvador, P., Dannenberg, J.J., Dapprich, S., Daniels, A.D., Farkas, Ö., Foresman, J.B., Ortiz, J. V., Cioslowski, J., Fox, D.J., 2009. Gaussian 09, Revision E.01. Gaussian Inc, Wallingford CT.

Garg, G., Thami, G.P., 2007. Comparative efficacy of cetirizine and levocetirizine in chronic idiopathic urticaria. J. Dermatol. Treat. 18, 23–24.

Golightly, L.K., Greos, L.S., 2005. Second-generation antihistamines: actions and efficacy in the management of allergic disorders. Drugs 65, 341–384.

Haghighi, S., Shapouri, M.R., Amoli-Diva, M., Pourghazi, K., Afruzi, H., 2013. HPTLC-densitometric determination for cetirizine and montelukast analysis in combined tablet dosage forms. Iran. J. Pharm. Res. 12, 303–309.

Howarth, P.H., Stern, M.A., Roi, L., Reynolds, R., Bousquet, J., 1999. Double-blind, placebo-controlled study comparing the efficacy and safety of fexofenadine hydrochloride (120 and 180 mg once daily) and cetirizine in seasonal allergic rhinitis. J. Allergy Clin. Immunol. 104, 927–933.

Kang, S.W., Jang, H.J., Moore, V.S., Park, J.Y., Kim, K.A., Youm, J. R., Han, S.B., 2010. Enantioselective determination of cetirizine in human plasma by normal-phase liquid chromatography-atmospheric pressure chemical ionization-tandem mass spectrometry. J. Chromatogr. B 878, 3351–3357.

Kaur, P., Bansal, G., Saranjit, S., 2014. Stress degradation studies on cetirizine dihydrochloride and development of degradation pathways. Int. J. Pharm. Chem. Sci. 3, 2277–5005.

Khan, M.I., Murtaza, G., Awan, S., Iqbal, M., Waqas, M.K., Rasool, A., Fatima, U., Hassan Bin Asad, M.H., Kahlid, A., Usman, F., Najam-us-Saqib, Q., Khan, S.A., Farzana, K., Mahmood, S., Hussain, I., 2011. Development and validation of stability indicating assay method of cetirizine hydrochloride by HPLC. Afr. J. Pharm. Pharacol. 5, 143–149.

Nuijs, A.L.N., Tarcomnicu, I., Covaci, A., 2011. Application of hydrophilic interaction chromatography for the analysis of polar contaminants in food and environmental samples. J. Chromatogr. A 1218, 5964–5974.

Rawool, N.D., Venkatchalam, A., Singh, K.H., 2013. Development and validation of a rapid RP-HPLC method for the simultaneous estimation of cetirizine and pseudoephedrine in pharmaceutical dosage forms. Int. Curr. Pharm. J. 5, 54–60.

Sewell, P.A., Wang P.G., Weixuan (Eds.), 2012. Hydrophilic Interaction Liquid Chromatography (HILIC) and Advanced Applications. Chromatographia, vol. 75, pp. 951.

Souri, E., Hatami, A., Ravari, N., Alvandifar, F., Tehrani, M., 2013. Validating a stability indicating HPLC method for kinetic study of cetirizine degradation in acidic and oxidative conditions. Iran. J. Pharm. Res. 12, 287–294.

Tillement, J.P., Testa, B., Brée, F., 2003. Compared pharmacological characteristics in humans of racemic cetirizine and levocetirizine, two histamine H1-receptor antagonists. Biochem. Pharmacol. 66, 1123–1126.

Trivedi, R., Patel, M., Jadhav, S.B., 2011. A rapid, stability indicating RP_UPLC method for simultaneous determination of ambroxol hydrochloride, cetirizine hydrochloride and antimicrobial preservatives in liquid pharmaceutical formulation. Sci. Pharm. 79, 525–543.

Validation of analytical procedures, Proceeding of the International Conference of Harmonisation (ICH), 1996. Commission of the European Comminities.

Yoshida, T., 2004. Peptide separation by Hydrophilic-Interaction Chromatography: a review. J. Biochem. Biophys. Meth. 60, 265–280.

Please cite this article in press as: Paczkowska, M. et al., Hydrophilic interaction chromatography (HILIC) for the determination of cetirizine dihydrochloride. Arabian Journal of Chemistry (2016), http://dx.doi.org/10.1016/j.arabjc.2016.05.012