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Extraction of Cetirizine Using Magnetic Nanoparticles of Hengam Island Sand and Determination by HPLC

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Abstract
In present work Hengam island sands were used for preparation of new magnetic nano-adsorbent. These sands have intrinsic magnetic properties due to possess specific compounds such as Fe_3O_4. It was modified by surface activator agent namely 3-(Glycidyloxypropyl)trimethoxysilane to produce effective nano-adsorbent. After preparation of this nano-adsorbent, Its physical and chemical properties was verified using several techniques such as FTIR, TGA/DTG, XRD and SEM. Nano-adsorbent was used as a solid phase to extraction of cetirizine from aqueous solutions and then its determination was done by HPLC. Effective analytical parameters such as pH of sample solution (pH=4), dosage of nano-adsorbent (100 mg), zero charge (pHz=5), breakthrough volume (500 mL) and contact time (15 min) were evaluated and optimized. Furthermore, figures of merit parameters such as precision (RSD=1.44%), limit of detection (LOD=1.1 µg L^{-1}) and linear dynamic range (LDR=0.01-250 mg L^{-1}) were obtained. Also for validation the accuracy of method, amount of cetirizine in two real samples were successfully determined.

Keywords
Hengam Island Sand; Modified Magnetic Nano-Particles; Cetirizine Extraction/Determination; HPLC.

1. INTRODUCTION

Cetirizine, the active component of ZYRTEC® tablets and syrup, is an orally active and selective H_1-receptor antagonist used for the treatment of allergy symptoms [1]. It is used in the treatment of perennial and seasonal allergetic rhinitis and also for chronic uticaria. Few methods have been used for quantitative determination of cetirizine. These methods include fluorimetry [2], spectrophotometry [3], titrimetry and conductimetry [4], gas chromatography [5], high-performance liquid chromatography [6,7], liquid chromatography [8,9] and ion-selective electrodes [10], based on the formation of ion-pair complex of cetirizine with tetraphenylborate. The solid-phase extraction (SPE) technique has increasingly become popular in comparison with the more traditional extraction methods because of its several major advantages such as: (i) simple to operate; (ii) high preconcentration factor; (iii) rapid phase separation and (iv) ability to combine with different detection techniques. Various solid phases including Chelex 100, Amberlite XAD resins, synthetic polymers, polyurethane foam and activated carbon have been used for the solid phase extraction of trace heavy metals in environmental samples prior to their instrumental analysis [11-17]. Surfactants are extensively used to stabilize drug delivery systems. Commonly they are molecules self-assembled in water or in oil, leading to the formation of a well-defined microstructure. Even a single surfactant can display a rich variety of structures that depends on several parameters, such as water content and temperature. Nevertheless, these microheterogeneous systems can interfere with drug separation and detection, and an adequate analytical method is needed to analyze the drug carried by these systems [18].

In the present study, Hengam island sand prepared and coated by surfactant modifier agent and after fully characterization, magnetic nano-material is utilized as SPE adsorbent for extraction of cetirizine from aqueous solution samples. Determination and quantification of the analyte was investigated by high performance liquid chromatography equipped with an ultra violet detector (HPLC-UV).

2. EXPERIMENTAL

2.1 Reagents and Materials

All reagent grades such as phosphoric acid, sodium di-hydrogen phosphate, di-sodium hydrogen phosphate, acetic acid, sodium acetate, acetonitrile, toluene and acetone were prepared from Merck Chemicals (Darmstadt, Germany).

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Chitosan, sodium carbonate and 3-(Glycidyloxypropyl)trimethoxysilane was obtained from Sigma-Aldrich (USA). Cetirizine syrup and tablet was purchased from Kimia-daro Pharmaceutical Co. (Tehran, Iran). Acetonitrile, acetone and methanol (all in HPLC grade) were purchased from Duksan Co. Ltd. (Ansan, South Korea). Hengam island sands was provided from Hengam, Qeshm Island, Hormozgan, Iran.

2.2 Instruments

HPLC-UV analysis was performed on a Knauer (Germany) system equipped with a UV visible detector (K-2600, Knauer, Germany) and pump (K-1001, Knauer, Germany) and a Knauer injector consisting of a 20 µL loop. Separation was conducted on an analytical C_{18} column (10 µm particle diameter, 4.6 mm i.d.×25 cm) (Knauer, Germany) at room temperature. The mobile phase of the acetonitrile/phosphate buffer solution (10 mmol L^{-1}) at a ratio of 15/85 (V/V) with final pH of 4 were used in the isocratic mode at a flow rate of 1.5 mL min^{-1}. A Fourier transform infrared (FTIR) spectrometer (Thermo, Nickolet 10, and Australia) and powder X-ray diffraction (XRD) (D5000, Siemens, Germany) were applied to characterize the prepared nano-particles. Scanning electron mmicroscopy (SEM) MIRA3 FEG–SEM (Tescan, The Czech Republic) was utilized for morphologic survey. A pH meter (Metrohm-692, Herisau-switzerland) and digital balance (AND, DR-200) were used to the pH adjustment and balancing, respectively.

2.3 Synthesis/extraction of Fe_3O_4 particles from Hengam island sand

Firstly, prepared Hengam island sand was washed several times with acetone and distilled water to removing of the impurities and then, after two days dried at 50 C°. Dried sand particles were crushed using bullet mill several times (to obtain very fine nano particles) and then magnetic nano particles of sand were separated by the help of strong magnet.

2.4 Preparation of nano/Fe_3O_4-SiO_2 by natural magnetic nano particles

In order to increase the selectivity of magnetic nano-particles and prepare it to adsorb of cetirizine, a surface activation process is necessary. A main goal of this process is activation of functional groups on adsorbent to increase the interaction with analyte. For this purpose, in 250 mL of round-bottom flask 3 g of magnetic nano particles prepared in the previous step mixed with 95 mL of anhydride toluene. Then, at reflux condition, 5 mL of 3-(Glycidyloxypropyl)trimethoxysilane was added and mixing was continued at 85-90 C° for 72 h. Finally, modified nano-particles was separated using magnet and washed several times with toluene and then at 70 C° dried for 24 h.

2.5 Synthesis of nano/Fe_3O_4-SiO_2-Chitosan as nano-adsorbent

In Erlenmeyer flask 100 mL, 1 gram of chitosan was dispersed in the 50 ml of acetate buffer at pH of 5 and mixed. Then, 2 gram of nano/Fe_3O_4/-SiO_2 particles added and was mixed for 24 h at temperature of 40 C° (warm bath). After it, 0.2 gram of sodium carbonate was added and then mixing process was repeated for 24 h. Finally, solution was cooled at room temperature and upper solution was decanted and sedimented solid was washed several times with acetate solution and then distilled water, then Solid was dried at 50 °C for 6 h. The mechanism of presented synthesis was showed in the Fig. 1.

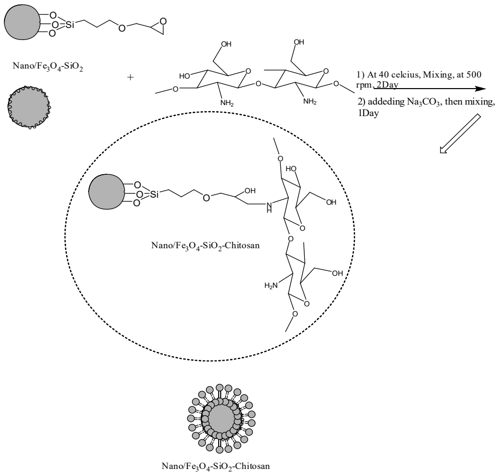

Fig. 1. Synthesis mechanism of nano/Fe_3O_4-SiO_2-Chitosan.

2.6 Chromatographic conditions

The mobile phase was acetonitrile-water (1:1), the pH of this mobile phase was adjusted to 3.0 with phosphoric acid (85 %). Before delivering into the system it was filtered through 0.45 µm filter and degassed using a vacuum. The analysis was carried out under isocratic conditions using a flow rate 2.0 ml min^{-1} at room temperature. Chromatograms were recorded at 205 nm using a detector. Injector with a 10 µL sample loop introduced the samples.

2.7. Analytical procedure

The extraction process by magnetic nano-adsorbent was conducted as follows: In the conical tube 10 mL of 100 mg L^{-1} cetirizine solution was added and using solutions such as HCl, NaOH, acetate or phosphate buffer (0.1 M), pH was adjusted and then 100 mg of nano-adsorbent was added. The tube was stirred in the vortex for defined time in order to the adsorption was occurred. After that the magnetic nano-adsorbent was separated from aqueous solution by the external magnet. Then the nano-adsorbent is sonicated in proper desorption solvent for 5 minutes to desorb extracted cetirizine from the adsorbent surface and 20 µL of sample was injected into the HPLC-UV system.

3. RESULT AND DISCUSSION

Effective analytical parameters on the absorbance of cetirizine onto nano-adsorbent are containing pH of sample solution, dosage of cetirizine, amounts of nano-adsorbent, point of zero charge (pzc) and furthermore figures of merits such as limit of detection (LOD), linear dynamic range (LDR), precision (RSD) and isotherms studies were examined and obtained. Finally, ability of method in to determination of cetirizine in some real sample was evaluated.

3.1 Characterization of nano-adsorbent synthesized

Synthesized nano-adsorbent was checked by several techniques such as FTIR, XRD, TGA/DTG and SEM.

In the Fig. 2, FTIR analysis of nano-adsorbent was showed and results indicated that absorption band in 516.18 Cm^{-1} related to Fe-O or Fe-O-Fe bond vibration, 877.91 Cm^{-1} related to Ca-O band vibration, 1130.41 Cm^{-1} related to Si-O band vibration, 1648.0 Cm^{-1} related to O-H bending band vibration, 2816.76 Cm^{-1} related to O-H dimer band vibration and 3555.99 Cm^{-1} related to O-H stretching band vibration.

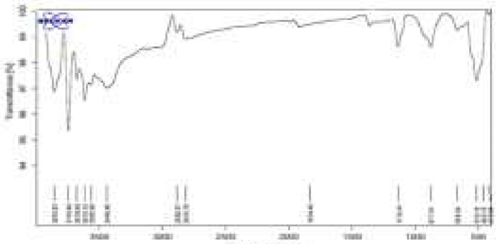

Fig. 2. FTIR spectrum of nano-adsorbent (nano/Fe$_3$O$_4$-SiO$_2$-Chitosan).

XRD pattern of nano-adsorbent has been showed in Fig. 3. Diffraction angels at 2θ of 29.28°, 35.45°, 39.43°, 40.65° and 47.40° related to the calcite phase and angles of 23.90°, 33.01°, 35.45°, 47.40° and 49.24° related to the hematite (Fe$_3$O$_4$) phase. Furthermore, diffraction angles of 29.28°, 33.01°, 34.45°, 47.40° and 49.24° related to the quartz phase in the nano-adsorbent.

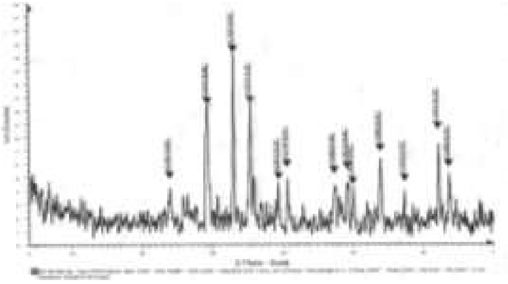

Fig. 3. XRD pattern of nano-adsorbent synthesized.

Thermal gravimetric analysis was done on the nano-adsorbent and spectrum was shown in Fig. 4. Results showed that the in the temperature of 200 C° about 5% mass was decreased that related to the loss of water in the sample. In the temperature of 313 C° amount of 25% mass was decreased and related to decompose or separate of chitosan from nano-adsorbent. Final loss in mass was occurred in the upper temperature and because of get out of other organic compounds.

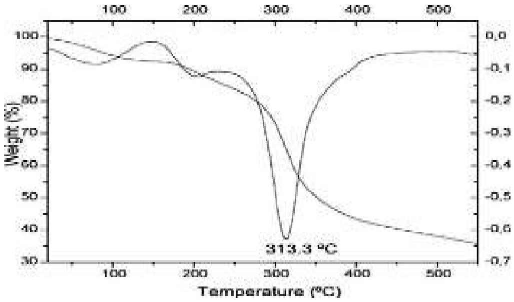

Fig. 4. TGA/DTG analysis of nano-adsorbent synthesized.

In order to the evaluation morphologies of nano-adsorbent, scanning electron microscopy (SEM) analysis was accomplished (Fig. 5a,b). Results showed that the particle size of adsorbent was 30-48 nm and has cylindrical shapes with homogeneous distribution.

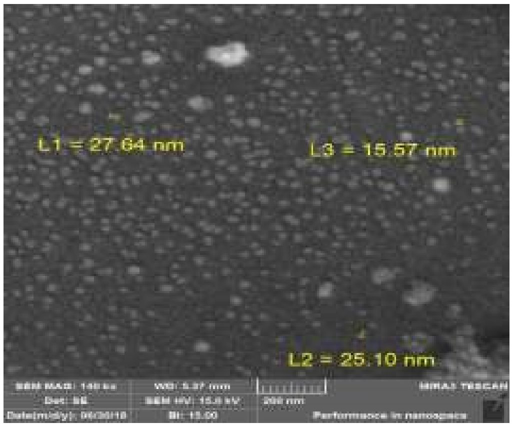

Fig. 5a. SEM of nano-adsorbent at scale of 200 nm

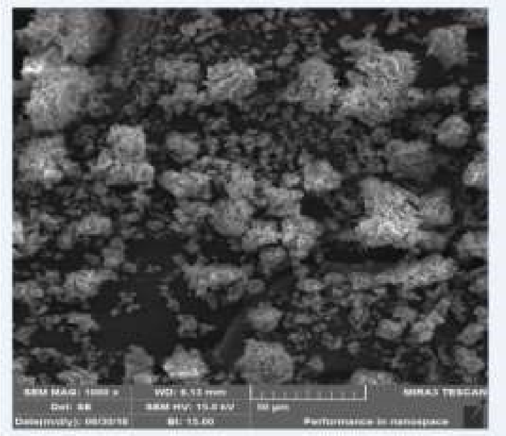

Fig. 5b. SEM of nano-adsorbent at scale of 50 µm

3.1 Determination of point of zero charge (pzc)

The point of zero charge (pzc), in physical chemistry, is a concept relating to the phenomenon of adsorption, and it describes the condition when the electrical charge density on a surface is zero [19]. For this purpose, results showed in Fig. 6. It was found that a pH of 5 was selected as zero charge because have no any charge. In the lower amounts of 5, the surface charge on the nano-adsorbent is positive and at upper of it the surface charge is negative. Given that the cetirizine structure has become negative charge in the aqueous solution, it is expected that adsorption of cetirizine on nano-adsorbent take place in the acidic media.

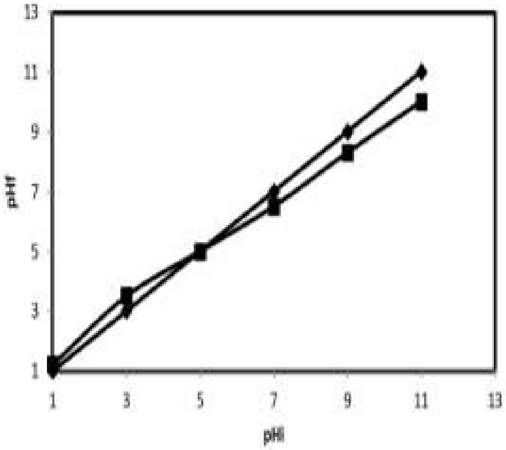

Fig. 6. Point of zero charge for nano-adsorbent.

3.2 Effect of pH

Effect of pH on the amounts of extraction depends on type of functional groups in the structure of analyte. Several solutions containing 10 mL of 100 mg L^{-1} cetirizine solution in the pH range of 1.0 to 9.0 were prepared and analytical procedure was carried out. Results showed in the Fig. 7. As can be seen maximum amount of extraction was take place at pH of 4 because of the best interaction between cetirizine and functional groups of the adsorbent at this point.

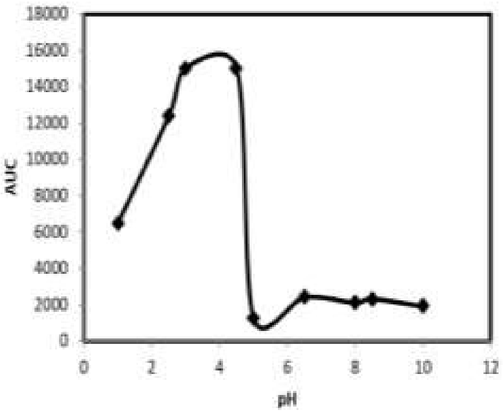

Fig. 7. Effect of pH on the extraction of cetirizine.

3.3 Effect of contact time

Contact time between analyte and adsorbent has effect on the extraction efficiency. To obtain the best time of extraction, several times between 0.5-30 min was examined. Results showed that with increasing the time, extraction efficiency was increased. As can be seen, 15 min was selected as the optimum time (Fig. 8).

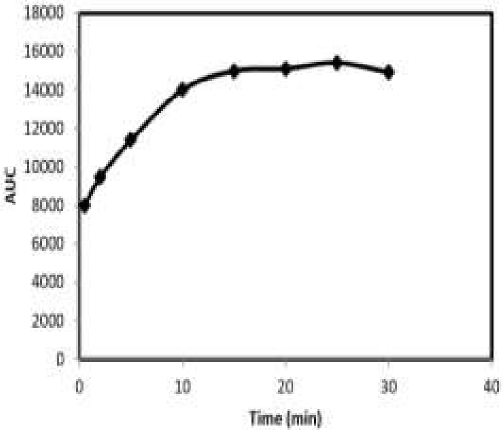

Fig. 8. Effect of contact time on the extraction of cetirizine

3.4 Effect of nano-adsorbent amount

Amount of adsorbent has direct relationship within amount of active sites to adsorb of analyte and it expected that change with the amount it. Several amounts of nano-adsorbent were examined in the range of 25-250 mg and results showed in the Fig. 9. It was be found that with increasing in the amounts of nano-adsorbent, extraction amounts was increased and 100 mg of it has ability to maximum extraction of cetirizine.

At amounts more than of 100, the extraction efficiency was constant.

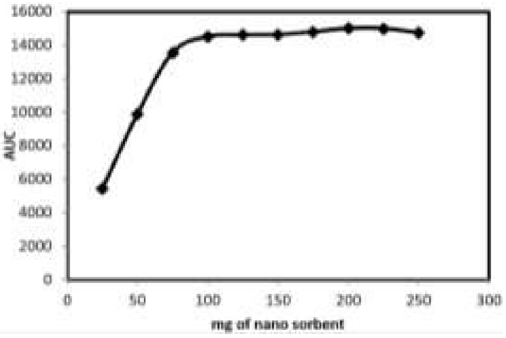

Fig. 9. Effect of nano-adsorbent dosage on the extraction of cetirizine.

3.5 Calculation of figures of merits

The suitability of the proposed method for quantitative analysis was investigated by determination of cetirizine recovery from aqueous samples, and the obtained results clearly show that the matrix effects are negligible (Table 1). Analytical accuracy was assessed from the recovery of cetirizine spiked to various samples. The recovery was 99.6–102.7%. The limit of detection (LOD) is defined as the lowest concentration of the analyte that produces a response detectable above the noise level of the system; it was calculated as $3s_b$+m, where s_b is the standard deviation of blank as three injections and m is the slope of calibration curve. The quantitative characteristics of the proposed method such as calibration curve equations, correlation coefficients, limit of detection (LOD), and linear dynamic ranges (LDR) were studied**.** The high correlation coefficients (> 0.997) and low detection limit (1.1 μg L^{-1}) with a wide LDR (0.01 - 250 mg L^{-1}) are important characteristics of the proposed method (Fig. 10). In order to examine the enrichment factor of analyte, three replicate extractions were carried out at optimal conditions from aqueous solutions containing 100 μg L^{-1} of cetirizine. To obtain the final concentration of cetirizine in the extractant phase, it was injected to HPLC and the area of the resulting signal was used to determine its concentration from a calibration graph obtained from the direct injections of varying concentration of the standard solutions of sample under the same experimental conditions. Further experiments have been performed to assess the repeatability of the method. Thus, seven replicate determinations of cetirizine at different concentrations in various water samples have been carried out by using the proposed method and the relative standard deviations were calculated. These results showed that the RSD% of the method was about 1.44 % (n = 7), which indicated that the proposed method has a good reproducibility.

Table 1. Recovery of cetirizine from real samples.

Real sample	Added cetirizine (μg mL^{-1})	Founded cetirizine (μg mL^{-1})	Recovery (%)
Cetirizine tablet, 10 mg	0.000	(0.86) ± 0.993	
	0.462	(1.26) ±1.460	100.34
	3.694	(2.22) ±4.817	102.77
Cetirizine tablet, 5 mg	0.000	(1.80) ± 0.956	–
	0.462	(0.88) ±1.413	99.64
	3.694	(3.40) ±4.746	102.06

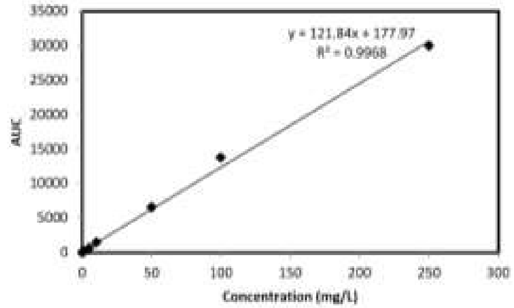

Fig. 10. Linear calibration curve for determination of cetirizine.

4. CONCLUSION

Nano/Fe_3O_4-SiO_2-Chitosan as natural adsorbent based on magnetic nanoparticles of Hengam Island was prepared for the first time and used for the extraction of cetirizine from aqueous sample solutions. Simplicity of nano-adsorbent synthesis, fast, selective and easy extraction process is the advantages of the new proposed sample treatment method for extraction of cetirizine from aqueous and real samples.

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استخراج سیتریزین با استفاده از نانوذرات مغناطیسی شن جزیره هنگام و اندازه‌گیری با استفاده از کروماتوگرافی مایع با کارایی بالا

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چکیده

در کار حاضر از شن جزیره هنگام برای تهیه نانوجاذب جدید مغناطیسی استفاده شده است. نانوجاذب مغناطیسی تهیه شده ذاتاً به دلیل داشتن ترکیبات ویژه مخصوصاً اکسید آهن (III) یعنی Fe_3O_4 دارای خاصیت مغناطیسی بوده و به کمک عامل فعال کننده سطح به نام ۳-(گلایسی دیلوکسی پروپیل) تری متوکسی سیلان برای تولید یک نانوجاذب مؤثر اصلاح شده است. تهیه نانوجاذب مغناطیسی به همراه خصوصیات فیزیکی و شیمیایی به طور موفقیت‌آمیزی به کمک تکنیک‌های مادون قرمز تبدیل فوریه FTIR، آنالیز گرماسنجی تفاضلی/گرماسنجی حرارتی دیفرانسیلی TGA/DTG، پراش اشعه ایکس XRD و تصویر برداری میکروسکوپی الکترونی SEM تأیید شد. نانوجاذب به عنوان فاز جامد برای استخراج داروی سیتریزین از محلول‌های آبی استفاده بکار برده شد. تعیین میزان دارو به کمک کروماتوگرافی مایعی با کارایی بالا انجام شد. پارامترهای تجزیه ایی مؤثر مانند pH محلول نمونه (۴)، میزان جاذب (۱۰۰ میلی‌گرم)، نقطه بار صفر (۵)، حجم رسوخ (۵۰۰ میلی‌لیتر) و مدت زمان تماس (۱۵ دقیقه) ارزیابی و بهینه شدند. علاوه بر این، ارقام شایستگی روش مانند دقت RSD (۱/۴۴٪)، حد تشخیص LOD (۱/۱ $\mu g\ L^{-1}$) و گستره خطی روش LDR (۰/۰۱–۲۵۰ $mg\ L^{-1}$) بدست آمد. همچنین به‌منظور اعتباربخشی و صحت روش، مقدار سیتریزین در دو نمونه حقیقی ارزیابی و از نقطه نظر بازیابی نتایج رضایت‌بخش حاصل شد.

واژه‌های کلیدی

شن جزیره هنگام؛ نانوذرات مغناطیسی اصلاح‌شده؛ اندازه‌گیری/استخراج سیتریزین؛ کروماتوگرافی با کارایی بالا.