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Determination of Mesalazine Using Ion Mobility Spectrometry in Pharmaceutical Samples

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Abstract
Ion mobility spectrometry is an analytical technique with main advantages such as high sensitivity, fast response and simplicity. The purpose of this work was to determine of mesalazine in different pharmaceutical samples using ion mobility spectrometry with a positive corona ionization source. After obtaining the best instrumental parameters (injection temperature: 230 ºC, cell temperature: 180 ºC, drift voltage: 6800 V, corona voltage: 2400 V, flow rate of drift gas: 600 mL/min and flow rate of carrier gas: 300 mL/min) the linear dynamic range was 1.0–70.0 ng with a determination coefficient, R^2=0.9881. The relative standard deviation values were lower than 6.0% (n=5) for the examined range (10.0–60.0 ng) of the drug. The limit of detection and limit of quantitation were 0.3 ng and 1.0 ng, respectively. The capability of the developed method was evaluated for the determination of mesalazine in tablet, capsule, and suppository as pharmaceutical samples. Satisfactory recovery results were obtained in the range of 98.0–103.8%.

Keywords
Ion mobility spectrometry; Mesalazine; Pharmaceutical samples; Tablet; Capsule, Suppository.

1. INTRODUCTION

Mesalazine [mesalamine or 5-aminosalicylic acid (5-ASA)] is a drug used to treat inflammatory bowel including ulcerative colitis and Crohn's diseases. It is generally used for mild to moderately severe diseases. This medicine is taken in the form of oral capsules, tablets, and suppositories and is excreted through urine and feces. Common side effects of mesalazine include headache, nausea, weakness, fatigue, abdominal pain, and fever. Moreover, serious side effects can contain pericarditis, as well as liver and kidney problems. For patients who have sulfa allergies, certain formulations may also cause problems. This drug acts through direct contact with the intestines [1–3].

Several methods have been reported for the determination of mesalazine by researchers, such as spectrophotometry [4, 5], high-performance liquid chromatography [6, 7], ultrahigh-performance liquid chromatography MS/MS [8], and voltammetric methods [9, 10]. According to the mentioned literature and other articles, most of these methods are laborious and also have limitations. Briefly, spectrophotometric methods are known for their simplicity and cost-effectiveness; however, they often suffer from lower figures of merit, such as sensitivity and selectivity. The chromatographic methods offer high separation power, but they typically require extensive sample preparation, organic solvents and also are time consuming. Therefore, it is still necessary to develop and introduce simple, low cost, green and rapid methods for mesalazine analysis.

Ion mobility spectrometry (IMS) is a gas phase ion separation technique that works under atmosphere pressure conditions. This technique has been used as a powerful analytical method to detect and determine trace analytes in various samples for several decades. The ion mobility spectrometer is typically comprised of five major components including (a) an injection port, (b) an ionization source, (c) an ion gate, (d) a drift region, and (e) a detector. Among the components of instrument, ionization sources are of the particular importance in IMS. One such source, with the following characteristics, is the corona discharge. The ionization process in IMS with corona discharge can be accomplished based on the proton or electron affinity of the compounds in positive or

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negative mode, respectively. Proton and electron transfer are common mechanisms, while other processes like charge transfer or adduct formation may also play a role depending on the nature and structure of analyte and ionization environment. Corona discharge has proven to be a reliable ionization source in IMS due to its main advantages such as simplicity, higher sensitivity, and an extended dynamic range. The wider dynamic range, compared to other ionization sources such as electrospray, radioactive, and chemical ionization, highlights the versatility of corona discharge, particularly in the analysis of compounds with different proton affinities. These advantages make corona discharge superior to other ionization sources for the certain applications. On the other hand, the matrix dependency and competitive nature of ionization in a corona discharge source are other important factors that must be considered. These factors can influence the ionization process and consequently the resulting spectra, particularly in complex matrices. A full description of the IMS technique and its advantages and applications were provided in books and articles [11–13]. Corona discharge ionization coupled to IMS has already been used for drug quantification [14–18].

In this work, the IMS method was investigated and developed for the determination of mesalazine. Corona discharge in positive mode was used to ionize the vaporized analyte molecules. Instrumental operating conditions of IMS such as temperature, voltage, and gas flow rate were investigated and optimized. The capability and application of the developed method were also evaluated to determine the drug analyte in different pharmaceutical samples. The analytical parameters of the proposed method showed that are comparable to those of previous methods. Moreover, IMS offers several practical advantages, including simplicity, rapid analysis, and the avoidance of costly instrumentation and toxic organic solvents.

2. EXPERIMENTAL

2.1. Chemicals

Mesalazine powder and methanol in analytical grade were purchased from Merck Co. Distilled water was prepared in-house.

2.2. Instrument and analytical procedure

An ion mobility spectrometer instrument equipped with a needle corona discharge ionization source (IMS−400, TOF Tech. Pars Company, Iran) was used in this project. A detailed description of the instrument was provided and seen in reference [19]. The IMS cell, including the ionization and drift regions, was placed in an oven with control systems for injection port (>230 ºC) and cell (50–200 ºC) temperatures. The ionization port and drift tube consisted of 16 Al rings which were separated from each other by thin Teflon insulators. These rings were connected using a series of resistors to generate a potential gradient. This instrument was also equipped with a needle–to–plate corona discharge ionization source for operation in positive and negative modes. A shutter grid was applied to generate an ion pulse to the drift region by the pulse generator. An analog–to–digital converter (Pico Scope, UK) was used to display the ion mobility spectra (response signal).

For the analytical procedure in the determination of mesalazine, the operating instrumental conditions of IMS in positive mode were investigated and optimized (i.e., drift and corona voltage, drift and carrier gas flow rate, injection and cell temperature, and pulse width, see Table 1). The stock solutions (100 µg/mL) and also the working standard solutions were prepared in distilled water. Then, 1 µL of each sample solution was injected into the IMS for analysis. The total peak area of the analyte (at a drift time of 6.2 ms) was integrated over the entire acquisition time (from the first to the final peaks) and was considered as the IMS response.

2.3. Preparation of pharmaceutical samples

In the present study, pharmaceutical samples including tablets, capsules, and suppositories were prepared according to the sample preparation procedures described below [20–22].

2.3.1. Tablet preparation

The determination of mesalazine in Asacol (800 mg, Haupt Pharma Wolfing: Germany) and Asafa (500 mg, Faran chemical company: Iran) tablet brands was done using the proposed method. For this purpose, three tablets (from each brand) were weighed and completely powdered in an agate mortar. Then, a specific amount of tablet powder containing 10 mg of mesalazine was taken and dissolved in the heated water (up to 40 ºC). After filtering, the obtained solution was transferred to a 100 mL volumetric flask and diluted to volume with distilled water to achieve a concentration of 100 µg/mL. This solution was diluted and used for injecting and analysis by IMS.

2.3.2. Capsule preparation

The determination of mesalazine in the Mesalover capsule (500 mg, Actoverco company: Iran) was also done using the proposed method. For this purpose, three capsules were weighed and the contents were completely powdered in an agate mortar. Then, a specific amount of the powder containing 10 mg of mesalazine was taken and used to prepare a solution

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of 100 µg/mL of mesalazine in the heated water (up to 40 ºC). This solution was diluted and used for injecting and analysis by IMS.

2.3.3. Suppository preparation

Mesalazine was also determined in Mesalon suppository (500 mg, Aburihan company: Iran) using the proposed method. A 15 mL aliquot of a methanol:water (50:50 v/v) solvent mixture was added to the mesalazine suppository (1.7620 g) in a beaker, and then it was melted in a water bath at 40 ºC. In next step, the drug solution was placed on ice pieces to freeze the fat phase. For separating of fat content, the liquid phase was filtered through moistened cotton. The filtered liquid was collected in a 50 mL volumetric flask. The beaker was washed with solvent and it was added to the solution. Then, it was brought to volume with the same solvent. Finally, 1 mL from this solution was taken and transferred to a 100 mL volumetric flask and diluted to volume with the solvent (100 µg/mL). This solution was diluted and used for injecting and analysis by IMS.

3. RESULTS AND DISCUSSION

3.1. Optimizing IMS operational conditions

Mesalazine contains functional groups including NH_2, OH, and COOH with different free electron pairs. Consequently, it has the potential to be protonated by capturing a proton from hydronium or ammonium ions (as the main reactant ions), resulting in the appearance peak(s) in its ion mobility spectrum. The ion mobility spectra of mesalazine and reactant ions are shown in Fig. 1. The mesalazine spectrum exhibited two peaks at approximately 6.2 ms and 6.8 ms, appearing after the reactant ion peaks (<5.3 ms); which can be attributed to the formation of $[M+H]^+$ ions. The peak at 6.2 ms shows a higher amplitude and persists longer than the other peak. Therefore, it was selected for the determination of mesalazine.

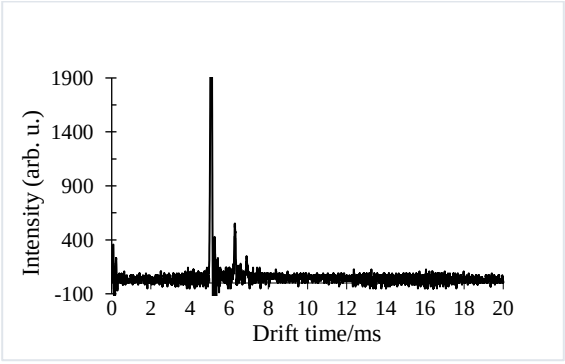

Fig. 1. Ion mobility spectra of mesalazine. The product ion peaks: at about 6.2 ms and 6.8 ms and reactant ion peaks: <5.3 ms.

To achieve the best sensitivity, the effective instrument parameters including corona and drift voltages, injection port and cell (oven) temperatures, carrier and drift gas flow rates, and pulse width were investigated and optimized. Among these, temperature (both injection and cell) played an important role in IMS studies. Factors such as the analyte adsorption or the specific design of IMS instrument can also influence on the relation between signal intensity and temperature. The temperature in injection port and cell were high, and therefore; the sample loss cannot be remarkable. But, since the adsorption effects cannot be entirely ruled out, the optimization of temperature was necessary to ensure and obtain the best possible performance in the IMS method. The effect of injection temperature on the signal intensity was studied in the range of 180–240 ºC, while the IMS cell temperature was maintained at 180 ºC. As seen in Fig. 2a, the signal intensity increased with temperature up to 230 ºC and then decreased at higher temperatures. This could be due to the thermal degradation of mesalazine and the decrease in ionization efficiency at higher temperatures. Therefore, 230 ºC was selected for future investigations. Similarly, the effect of the IMS cell temperature on signal intensity was studied in the range of 160–200 ºC (Fig. 2b), with the injection port set to 230 ºC. The results showed that the signal intensity improved as the IMS cell temperature increased up to 180 ºC and then remained constant. Therefore, 180 ºC was selected as the optimum cell temperature. Other operational conditions of IMS for the mesalazine determination were investigated and adjusted. The results are presented in Table 1. The operating conditions for the determination of mesalazine are comparable to those commonly used by other/our research groups employing corona discharge IMS [14–18].

Table 1. The operating instrumental conditions of ion mobility spectrometry (IMS).

Parameter	Setting
Drift voltage (kV)	6.8
Corona voltage (kV)	2.4
Flow rate of drift gas (N_2, mL/min)	600
Flow rate of carrier gas (N_2,	300
Injection port temperature (ºC)	230
IMS cell temperature (ºC)	180
Pulse width (µs)	100
Polarity	Positive

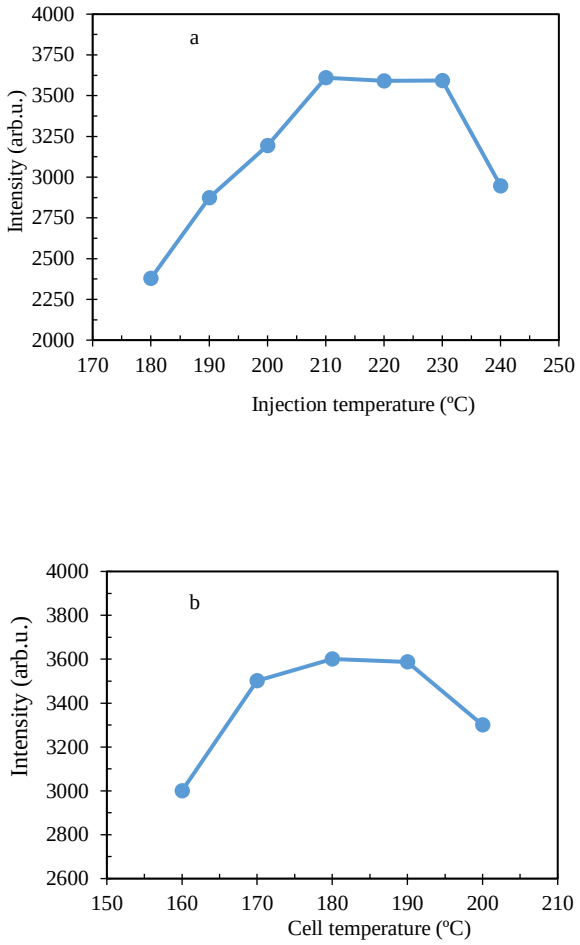

Fig. 2. The effect of injection (a) and cell (b) temperatures on peak intensity of IMS.

3.2. Analytical parameters

Under the optimized conditions (Table 1), the analytical parameters (including linear dynamic range (LDR), limit of detection (LOD), limit of quantification (LOQ), and relative standard deviation for precision (RSD)) of the developed IMS method for the determining mesalazine were obtained and are reported in Table 2. To plot the calibration curve, aliquots (1 µL) of the working standard solutions at different concentrations were injected into the IMS instrument. The calibration curve was found to be linear within 1.0–70.0 ng (with a determination coefficient close to one, R^2=0.9881; Fig. 3). The amounts of mesalazine in LDR covered the measured levels of analyte for the real samples. The LOD and LOQ values were calculated using equations $3S_b/m$ and 10 S_b/m, respectively; where S_b was the standard deviation of the blank signal and m was the slope of the calibration curve. The LOD was 0.3 ng and also LOQ was 1.0 ng. The RSD values (n=5, intra-day) were calculated at 10, 20, 50, and 60 ng (representing low, mid and high-range amounts of LDR) to evaluate the precision of the developed method. The RSD values were lower than 6.0%. The capability of the proposed method for determining mesalazine in pharmaceutical samples (tablet, capsule, and suppository) was evaluated, and the results were satisfactory, with recoveries ranging from 98.0–103.8% (Table 2). The absence of additional peaks or significant changes in the ion mobility spectra of the mentioned pharmaceutical samples in the presence of unwanted components, combined with satisfactory recovery results, indicated that they did not cause interference in the mesalazine determination. Therefore, the developed method was selective and robust for the purpose designed in this study. The analytical parameters of the proposed IMS method and other methods presented in previous studies are shown in Table 3. According to this Table, the LDR and recovery data were comparable to those reported in other literature. In addition, the proposed method was simple, fast and required no expensive equipment and hazardous solvents.

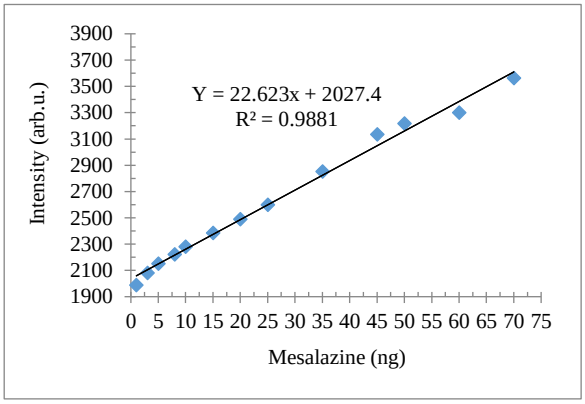

Fig. 3. Calibration curve for mesalazine by IMS method.

Table 2. The analysis results of mesalazine in pharmaceutical samples using IMS.

Pharmaceutical samples	Amount claimed (mg)	Amount obtained (mg)	Recovery (%)
Asacol 800 (Tablet)	800	830.4	103.8
Asafa 500 (Tablet)	500	491.5	98.3
Mezalover 500 (Capsule)	500	502	100.4
Mezalon 500 (Suppository)	500	490	98.0

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Table 3. Comparison of the IMS analytical parameters of mesalazine with other methods.

Method	LDR (µg/mL)	RSD (%)	LOD (µg/mL)	LOQ (µg/mL)	Recovery (%)	Ref.
RP-HPLC	20–50	2 >	0.2	1.8	99.7	7
HPLC	20–100	3 >	–	–	–	23
RP-HPLC	2–10	2 >	0.1	0.4	95.0–105.0	26
Indirect spectrophotometry	0.2–36	0–0.3	–	–	100.0	24
Spectrophotometry	0.1–11	–	0	0.1	99.0	25
Spectrophotometry	2.5–37.5	1 >	–	–	99.0–101.0	4
Spectrophotometry	2–25	0.1–0.3	–	–	99.5–101.5	5
Spectrophotometry	0.4–12	0–3	0.1	0.3	100.1–103.4	2
IMS	1.0–70.0	4.8–5.4	0.3	1.0	98.0–103.8	Present work

4. CONCLUSIONS

This work demonstrates the capability of IMS for the determination of mesalazine in pharmaceutical samples. The literature review revealed that most previously reported methods were laborious and had limitations such as requiring expensive equipment, high time and solvent consumption, and also the need for derivatization process. The proposed method offers significant advantages, including: low organic solvent consumption, low cost, low LOD, relatively wide LDR, high sensitivity and fast. Potential limitations such as reproducibility were considered among the main aspects of the proposed method. It was successfully applied to determine mesalazine in tablet, capsule, and suppository formulations, yielding excellent recovery results ranging from 98.0 to 103.8%.

Declaration of interest

There are no conflicts to declare. The authors report no conflicts of interest. Also, the authors are responsible for the writing and content of this article.

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REFERENCES

[1] K. Kanala, N. T. Hwiza, B. R. Chandu, K. Mukkanti, and P. Katakam, An open-label, randomized, crossover bioequivalence study of mesalazine 400 mg tablets in indian healthy volunteers under fasting conditions, *Der Pharm. Lett.* 5 (2013) 465–471.

[2] E. S. Salih, and M Al-Enizzi, Spectrophotometric assay of mesalazine in pharmaceutical preparations via oxidative coupling reaction with off-cresol and sodium metaperiodate, *J. Edu. Sci.* 29 (2020) 279-292.

[3] J. Mayberry. The history of 5-ASA compounds and their use in ulcerative colitis-trailblazing discoveries in gastroenterology, *J. Gastrointest Liver Dis.* 22 (2013) 375–377.

[4] S. A. Al-Zakaria, Spectrophotometric determination of mesalazine, *Raf. J. Sci.* 28 (2018) 127–134.

[5] A. Sasmita Kumari, S. Alok, D. Srikanta, S. Padhy, and A. M. Mathrusri, Spectrophotometric methods for the determination of mesalamine in bulk and pharmaceutical dosage forms, *Pharm. Educ. Res.* 1 (2010) 63–67.

[6] J. Balaji, and M. Shivashankar, Development and validation of reverse-phase high performance liquid chromatography procedure for estimation of 5-aminosalicyclic acid in rectal suppositories, *IOP Conf. Serie: Mater. Sci. Eng.* 263 (2017) 022025.

[7] N. K. Sahoo, M. Sahu, P. S. Rao, and G. Ghosh, Validation of stability indicating RP-HPLC method for the estimation of mesalamine in bulk and tablet dosage form, *Pharm. Methods* 4 (2013) 56–61.

[8] J. Banda, R. Lakshmanan, R. P. Katepalli, U. K. R. Venati, Ramesh Koppula, and V. V. S. Shiva Prasad, Determination of mesalazine, a low bioavailability olsalazine metabolite in human plasma by ultra-high performance liquid chromatography–ms/ms, *J. Chromatogr. B.* 1008 (2016) 1–10.

[9] M. Štěpánková, R. Šelešovská, L. Janíková, and J. Chýlková, Voltammetric determination of mesalazine in pharmaceutical preparations and biological samples using boron-doped diamond electrode, *Chem. Pap.* 71 (2017) 1419–1427.

[10] A. B. Teradale, S. D. Lamani, P. S. Ganesh, B. E. K. Swamy, and S. N. Das, CTAB immobilized carbon paste electrode for the determination of mesalazine: A cyclic voltammetric method, *Sens. Bio-Sens. Res.* 15 (2017) 53–59.

[11] G. A. Eiceman, and Z. Karpas, Ion Mobility Spectrometry, Boca Raton, FL: CRC, 2005; 5th ed.
[12] C. S. Creaser, J. R. S. Griffith, C. J. Bramwell, S. Noreen, C. A. Hill, and C. L. P. Thomas, Ion mobility spectrometry: a review. Part 1. Structural analysis by mobility measurement, *Analyst* 129 (2004) 984–994.
[13] A. Sheibani, M. Tabrizchi, and H. S. Ghaziaskar, Determination of methadone in human hair by headspace extraction and ion mobility spectrometry, *Anal. Lett.* 43 (2011) 667–675.
[14] F. Shamsi, A. Sheibani, and M. Reza Shishehbore, Biological application of dispersive magnetic solid phase extraction using Fe3O4@Cuo&GO nanocomposite and ion mobility spectrometry: Determination of aspirin, *Iran. J. Anal. Chem*. 10 (2023) 80-88.
[15] A. Dehghani-Talgerdouie, A. Sheibani, and M. Reza Shishehbore, Pharmaceutical and bio-analytical applications of ion mobility spectrometry for determination of clopidogrel (Plavix), *Anal. Bioanal. Chem.* 8 (2021) 445-451.
[16] Y. Valadbeigi, V. Ilbeigi, A. Afgar, and M. Soleimani, Comparison of the positive and negative modes of corona discharge ion source for direct determination of aspirin in urine by ion mobility spectrometry, *Inter. J. Mass Spect.* 470 (2021) 116699.
[17] M. Behpour, M. Maghsoudi, and S. Nojavan, Analysis of methamphetamine, methadone, tramadol, and buprenorphine in biological samples by ion mobility spectrometry after electromembrane extraction in tandem with slug flow microextraction, *J. Chromatogr. A.* 1978 (2022) 463355.
[18] F. Shamsi, A. Sheibani, and M. Reza Shishehbore, Determination of bupropion by off-line coupling Fe3O4@CuO&GO nanocomposite and ion mobility spectrometry with application to biological samples, *Anal. Sci.* 39 (2023) 1521–1529.
[19] M. Tabrizchi, T. Khayamian, and N. N. Taj, Design and optimization of a corona discharge ionization source for ion mobility spectrometry, *Rev. Sci. Instrum.* 71 (2000) 2321–2328.
[20] T. Aziz Alaa and H. Sultan Saad, Spectrophotometric Determination of Mesalazine in Pharmaceutical Preparations by Oxidative Coupling Reactions with m-Aminophenol and 2,6-Dihydroxybenzoic Acid, *Baghdad Sci. J*. 16 (2019) 1010–1016.
[21] N. A. Chaudhari, and N. S. Ranpise, Determination of mesalamine in bulk and suppository dosage forms through the development and validation of stability-indicating RP-HPLC method, *Curr. Pharm. Anal.* 20 (2024) 433–443.
[22] E. Zawada, E. P. Chaber, A. Somogi, and T. Pawinski. Development and validation of bromatometric, diazotization and vis-spectrophotometric methods for the determination of mesalazine in pharmaceutical formulation, *Acta Polo. Pharm.* 74 (2017) 401–404.
[23] V. Darak, A. Karadi, S. Raju, and A. L. Ganure, Development and validation of high-performance liquid chromatography method for determination of mesalazine in tablet dosage form, *Pharm. Sci. Monitor*. 3 (2012) 74–81.
[24] E. A. Hamdoon, Indirect spectrophotometric determination of mesalazine via chromate-1,5-diphenyl carbazide complex, *Raf. J. Sci.* 27 (2018) 69–78.
[25] A. S. Ahlam, and H. M. Dawood, Spectrophotometric determination of mesalazine via oxidative coupling reaction, *Systec. Rev. Pharm.* 11 (2020) 922–929.
[26] A. Awasthi, A. Kumar, R. Kumar, S. Vishwas, R. Khursheed, and J. Kaur, RP-HPLC method development and validation for simultaneous estimation of mesalamine and curcumin in bulk form as well as nanostructured lipid carriers, *S. Afr. J. Bot.* 151 (2022) 529–537.

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اندازه‌گیری مزالازین با روش طیف‌سنجی تحرک یونی در نمونه های دارویی

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چکیده

طیف‌سنجی تحرک یونی یک تکنیک تجزیه‌ای با مزایای اصلی مانند حساسیت بالا، پاسخ سریع و سادگی است. هدف از این کار، تعیین میزان مزالازین در نمونه‌های دارویی مختلف با استفاده از طیف‌سنجی تحرک یونی مجهز به منبع یونش کرونا با قطبیت مثبت بود. پس از دستیابی به بهترین پارامترهای دستگاهی (دمای تزریق: °C ۲۳۰ ، دمای سل: °C ۱۸۰، ولتاژ شناوری: ۶۸۰۰V، ولتاژ کرونا: ۲۴۰۰V، سرعت جریان گاز شناوری: ۶۰۰mL/min و سرعت جریان گاز حامل: ۳۰۰ mL/min)، محدوده خطی دینامیکی ۱/۰ تا ۷۰/۰ ng با ضریب تعیین R^2 =۰/۹۸۸۱ به دست آمد. مقادیر انحراف استاندارد نسبی برای محدوده بررسی شده دارو (۱۰/۰ تا ۶۰/۰ ng) کمتر از ۶ درصد (n=5) بود. حد تشخیص و حد تعیین روش به ترتیب ۰/۳ و ۱/۰ ng محاسبه شد. قابلیت روش توسعه یافته برای تعیین مزالازین در نمونه‌های قرص، کپسول و شیاف ارزیابی شد که نتایج بازیابی رضایت‌بخشی در محدوده ۹۸/۰ تا ۱۰۳/۸ درصد به دست آمد.

کلید واژه ها

طیف‌سنجی تحرک یونی، مزالازین، نمونه‌های دارویی، قرص، کپسول، شیاف.