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THE USAGE OF SALTS OF CHAOTROPIC ANIONS FOR THE DEVELOPMENT OF HPLC METHOD FOR THE SIMULTANEOUS DETERMINATION OF CISPLATIN AND CARBOPLATIN IN MODEL MIXTURE

Mariana Druchok, Marjan Piponski, Mariana Horyn, Nadiya Zarivna, Liliya Logoyda

The aim of the work *was to develop an RP-HPLC method for the simultaneous determination of extremely polar and non-UV-absorbing chromophore molecules of cisplatin and carboplatin in a model mixture using salts of chaotropic anions, which can be used for single-analyte determination too.*

Material and methods. *HPLC analysis was performed using Agilent 1260 and Shimadzu LC-2050C with diode array detector (DAD).. Used chromatographic column Luna C18(2) (100 × 4.6 mm, 3 µm) purchased from Phenomenex. Cisplatin and carboplation (purity ≥99% (HPLC)) were supplied from Sigma-Aldrich Chemicals Co. (St. Louis, MO, USA). Used dosage forms: cisplatin «Ebeve» (0.5 mg/ml, Austria) and carboplatin «Ebeve» (10 mg/ml, Austria). All used reagents were HPLC gradient chromatography quality and purchased from Merck Darmstadt, Germany.*

Results and discussion. *Chaotropic agents enhance retention of basic molecules in acidic mobile phases on reversed-phase chromatographic columns and improve peak shape and symmetry. The chaotropic anions that increase interaction between the basic N-containing analyte and the alkyl chains of reversed-phase ligands, such as C-8 and C-18, are frequently employed to enhance and improve the performance of HPLC methods. The chromatographic analysis of cisplatin and carboplatin presented a unique challenge due to their inorganic structure. The experimentally established optimal chromatographic conditions are: mobile phase – 40 mM KPF6 buffer solution (pH 2.4) and ACN (95:5), chromatographic column – Luna C18 (100 × 4.6 mm, 3 µm), column temperature – 30°C, flow rate - 0.4 ml/min, detection wavelength – 210 nm. Linearity was assessed using five levels of each of the investigated drugs, where concentration varied in the range of 20–100 µg/mL. The proposed HPLC method is green, as confirmed by the most modern metrics for studying greenness (AGREE, MoGAPI, complex MoGAPI, AGSA, CaFRI and CACI).*

Conclusions*. In this work, thorough scientific research was carried out with the presentation of HPLC method development for the simultaneous determination of extremely highly polar molecules cisplatin and carboplatin in a model mixture using salts of chaotropic anions. In addition, two studied drugs were quantified using rapid, simple, cost-effective HPLC method approaches*

Keywords*: platinum-based drugs, high-performance liquid chromatography, assay, validation, greenness*

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1. Introduction

Carboplatin and cisplatin are platinum-based drugs with antitumor activity [1]. Their structural similarity and complexity in analysis by reverse-phase (RP) high-performance liquid chromatography (HPLC) are the main reasons for selecting platinum drugs as analytes for our study. Cisplatin and carboplatin are not used together in one dosage form; however, we have posed a complex task for their simultaneous determination due to their similar chemical structure, which contributes to the theory of chromatography. The chromatographic analysis of platinum-based drugs posed a unique challenge due to their inorganic structure. Its molecular composition features a central platinum atom flanked by two halogen atoms of chlorine and two amino groups, making it a strongly ampholytic molecule with both basic and acidic properties [2]. Pharmacopoeial methods regulate, and scientific articles present the use of ion-pair reagents or NH_2-bonded columns [3–10] in the analysis of platinum-based drugs. Among the approaches used to improve retention and separation in HPLC, the use of ion-pairing reagents is a common choice. However, the issues arising from their application motivate researchers to explore alternative methods to achieve reliable analytical results, such as the use of chaotropic anion salts. Chaotropic agents enhance retention and peak shape. The chaotropic interaction between the chaotrop anion and the N-containing area of the molecule of the analyte with the alkyl chains of RP ligands, such as C-8 and C-18, is frequently employed to enhance the performance of HPLC methods [11, 12].

In the scientific literature, there are no described methods for the simultaneous determination of carboplatin and cisplatin, as this is a complex task, yet it is relevant for quantitative determination in single-drug preparations, equipment rinses, wastewater analysis, therapeutic drug

monitoring, and other purposes. Furthermore, our work is relevant to the theory of liquid chromatography, as it demonstrates approaches to analyzing substances that pose challenges in conventional RP chromatography.

The aim of the work was to develop an RP-HPLC method for the simultaneous determination of extremely polar and non-UV-absorbing chromophore molecules of cisplatin and carboplatin in a model mixture using salts of chaotropic anions, which can be used for single-analyte determination too.

2. Planning of the research

Methodology of research of HPLC method for the simultaneous determination of cisplatin and carboplatin in a model mixture using salts of chaotropic anions includes:

1. Study of the recommendations of British Pharmacopoeia (BP), United States Pharmacopoeia (USP) and European Pharmacopoeia (Ph.Eur.), analysis of scientific literature.

2. Previous studies have confirmed the possibility of using chaotropic anion salts in the HPLC analysis of platinum-based drugs.

3. Selection the optimal chromatographic conditions and HPLC method development (mobile phase composition, column type and temperature, flow rate, detection).

4. The application of the proposed HPLC method for the simultaneous determination of cisplatin and carboplatin in a model mixture.

5. Validation of the HPLC method for the determination of cisplatin and carboplatin.

6. Evaluation of the greenness study of the developed HPLC method by using tools AGREE, MoGAPI, complex MoGAPI, AGSA, CaFRI and CACI.

3. Materials and methods

Objects of study, solvents and equipment.

HPLC analysis was performed using Agilent 1260 and Shimadzu LC-2050C with diode array detector (DAD). Chromatographic data acquisition and post-run analysis integration were performed using LabSolutions software. A digital pH meter (Mettler-Toledo, model LE438, Switzerland) was used for pH measurements. An ultrasonic bath (Elmasonic Easy 40 H, Germany) was used for degassing the mobile phase and dissolving the samples. RADWAG AS 200/C precision analytical balances were used for accurate weighing. Used chromatographic column Luna C18(2) (100 × 4.6 mm, 3 μm) purchased from Phenomenex.

Cisplatin and carboplation (purity ≥99% (HPLC)) were supplied from Sigma-Aldrich Chemicals Co. (St. Louis, MO, USA). Used dosage forms: cisplatin «Ebeve» (0.5 mg/ml, Austria) and carboplatin «Ebeve» (10 mg/ml, Austria).

All the used reagents: acetonitrile (ACN), 85% m/v o-phosphoric acid (o-H_3PO_4), *potassium hexafluorophosphate (*KPF_6), and potassium dihydrogen phosphate (KH_2PO_4) were HPLC gradient chromatography quality and were purchased from Merck Darmstadt, Germany.

Chromatographic conditions.

Isocratic chromatographic separation was performed on a Luna C18(2) (100 × 4.6 mm, 3 μm) maintained at 30 ± 2°C. The mobile phase consisted of 40 mM KPF_6 (pH 2.4) buffer та ACN (95:5). The mobile phase was degassed ultrasonically prior to use. The flow rate was 0.5 mL/min, and the injection volume was 5 μL. UV detection was performed at 210 nm with a total run time of only 5 min.

Procedure for preparation of standard stock solutions.

Dissolve the substance in the solvent mixture and dilute with the solvent mixture, mobile phase, thus resulting test solution to 0.1 mg/ml. Calibration curves were constructed in the coordinates of the dependence of peak areas and the analyte concentration in μg/mL (range – 20–100).

4. Research results

4. 1. Previous studies confirming the possibility of using chaotropic anion salts in the HPLC analysis of platinum-based drugs

The theory of the interaction enhancement between the analyte and the C-18 or C-8 column ligand suggests that chaotrops allow for better exposure of hidden buried hydrophobic areas of molecules to their surfaces, thereby enhancing the attractive hydrophobic forces between the nitrogen-containing analyte and the alkyl-bound phase. The resulting effect of these interactions is increased retention times and retention capacities of the separating molecules. It has been proven that the interactions are more intense when ACN is used in the mobile phase, which forms thicker multilayer structures on the stationary phase than when methanol is used. Another important feature of using the salts of chaotropic anions in the separation of nitrogen-containing molecules on C18 and C8 columns is the improved symmetry of the peaks.

Mobile-phase conditions utilizing ACN and water reveal that the PF_6^- ion achieves the highest retention due to its pronounced lipophilic nature within the Hoffmeister series. This ion exhibits a significant degree of charge delocalization coupled with high polarizability, enabling robust dispersive (van der Waals) interactions [11]. These characteristics make it particularly adept at interacting with ACN. While other anions share similar traits, their capacity for dispersive interactions is less pronounced compared to PF_6^-. At ACN concentrations of up to 20% v/v, all ions demonstrate maximum retention as a global conclusion, as a beneficial role of chaotropic anions in refining and optimising HPLC methods for the analysis of active pharmaceutical ingredients (APIs) of basic compounds containing nitrogen atoms, which comprise approximately 90% of pharmaceutical molecules. It is well-documented and confirmed that their presence in the mobile phase during HPLC separation enhances interactions between analytes and hydrophobic reverse-phase alkyl ligands in stationary phases, thereby prolonging retention times. Considering previous studies and research conducted by our scientific group, mobile phases using a 40 mM KPF_6 (pH 2.4) buffer solution pH 2.4 and ACN in ratios of 90:10 and 95:5, and a C18 chromatographic column (Luna C18 (100 × 4.6 mm, 3 μm)) have been tested [12]. Only one method of spectrophotometric determination of cisplatin and carboplatin is re-

ported in the scientific literature, and there is no developed RP-HPLC method for their simultaneous determination [13].

4. 2. Selection the optimal chromatographic conditions and HPLC method development

The parameters of the suitability of the chromatographic system were satisfied by the approach using the mobile phase – a buffer solution of 40 mM KPF_6 (pH 2.4) and ACN (95:5 and 90:10) (**Fig.1, 2**, **Table 1, 2**). 90-10 ratio showed unsatisfactory suitability parameters of the chromatographic system (low number of theoretical plates (NTP) and resolution less than 2.0). 95-5 ratio showed excellent separation.

The key factor in the speed of chromatography and analysis, respectively, was the flow rate. We have been tested 0.4–1.0 ml/min. Typical chromatograms under the conditions of studying the choice of flow rate are presented in **Fig. 3, 4**. As can be seen from the figures, all flow rates are satisfactory. The slower the mobile phase moves, the longer the chromatography time. For further studies, we chose a flow rate of 0.4 ml/min. We will show in detail the results of the change in the flow rate on the parameters of the chromatographic system suitability, further in the study of robustness (validation) of the analytical method.

We have conducted a temperature selection of the column. The chromatograms obtained at 30°C and 35°C are presented in **Fig. 5**. Both studied temperatures are optimal.

The experimentally established optimal chromatographic conditions are: mobile phase – 40 mM KPF_6 buffer solution (pH 2.4) and ACN (95:5), chromatographic column – Luna C18(2) (100 × 4.6 mm, 3 µm), column temperature – 30°C, flow rate – 0.4 ml/min, detection wavelength – 210 nm.

Table 1

System suitability parameters for Fig.1

Peak	Ret. time, min	Area	Height	Area%	Tailing F.	k’	NTP(USP)	HETP (USP)	Resolution (USP)
Cisplatin	1.209	169222	42451	51.275	1.415	0.000	1554	96.504	–
Carboplatin	1.376	160805	36334	48.725	1.276	0.138	2624	92.384	1.287

Table 2

System suitability parameters for Fig.2

Peak	Ret. time, min	Area	Height	Area%	Tailing F.	k’	NTP(USP)	HETP(USP)	Resolution (USP)
Cisplatin	1.235	172462	43184	51.942	1.400	0.000	2690	88.735	–
Carboplatin	1.796	159564	37453	48.058	1.356	0.454	3062	48.986	4.489

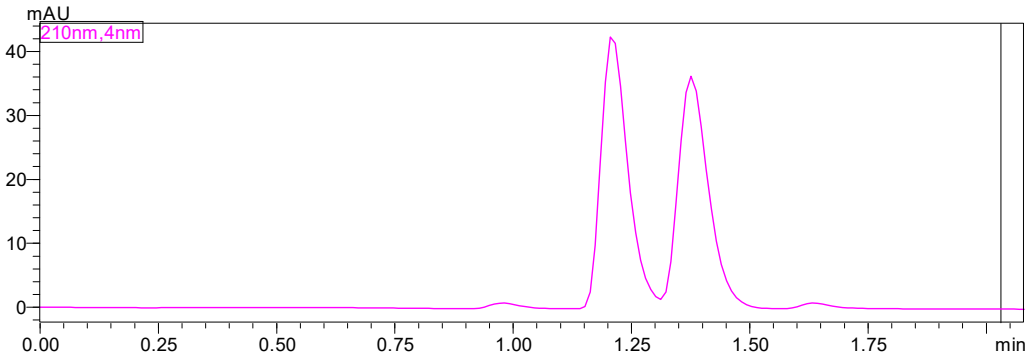


Fig. 1. The chromatogram of cisplatin (0.1 mg/ml) and carboplatin (0.1 mg/ml) on Luna C18(2) column (100 × 4.6 mm, 3 µm) with 10% ACN and 90% KPF_6 buffer 40 mM pH 2.4, flow rate 1 mL/min and detection at 210 nm

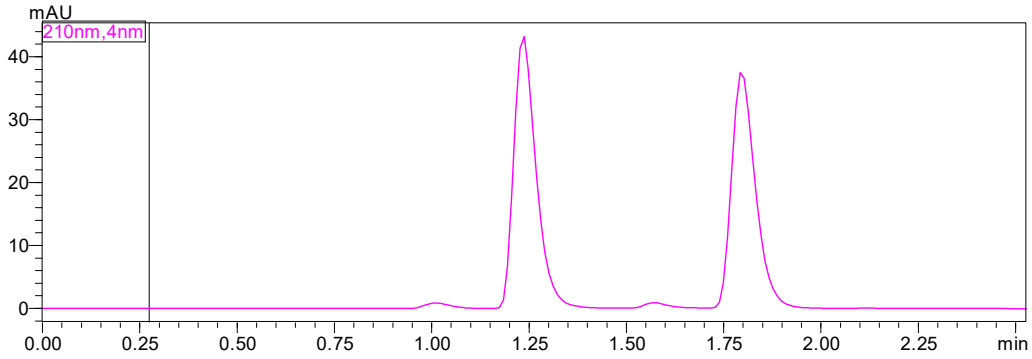


Fig. 2. The chromatogram of cisplatin (0.1 mg/ml) and carboplatin (0.1 mg/ml) on Luna C18 column (100 × 4.6 mm, 3 µm) with 5% ACN and 95% KPF_6 buffer 40 mM pH 2.4, flow rate 1 mL/min and detection at 210 nm

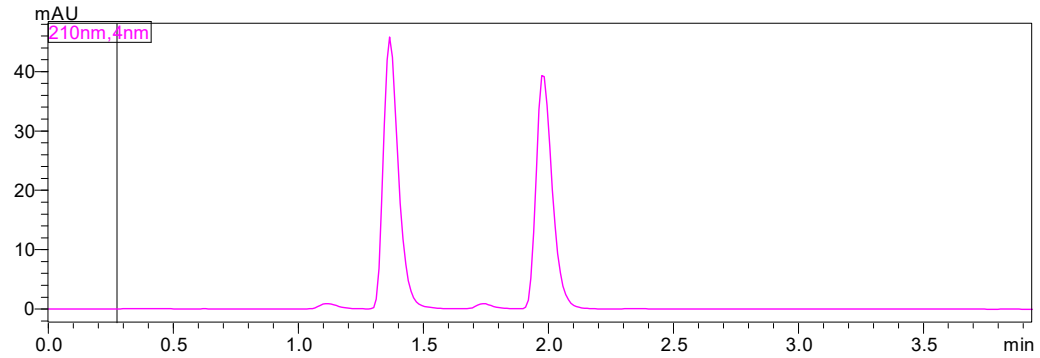


Fig. 3. The chromatogram of cisplatin (0.1 mg/ml) and carboplatin (0.1 mg/ml) on Luna C18 column (100 × 4.6 mm, 3 µm) with 5% ACN and 95% KPF_6 buffer 40 mM pH 2.4, flow rate 0.9 mL/min and detection at 210 nm

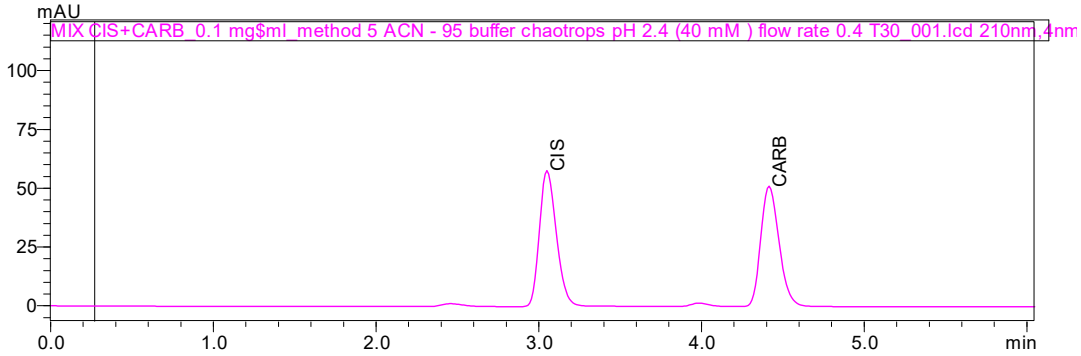


Fig. 4. The chromatogram of cisplatin (0.1 mg/ml) and carboplatin (0.1 mg/ml) on Luna C18(2) column (100 × 4.6 mm, 3 µm) with 5% ACN and 95% KPF_6 buffer 40 mM pH 2.4, flow rate 0.4 mL/min and detection at 210 nm

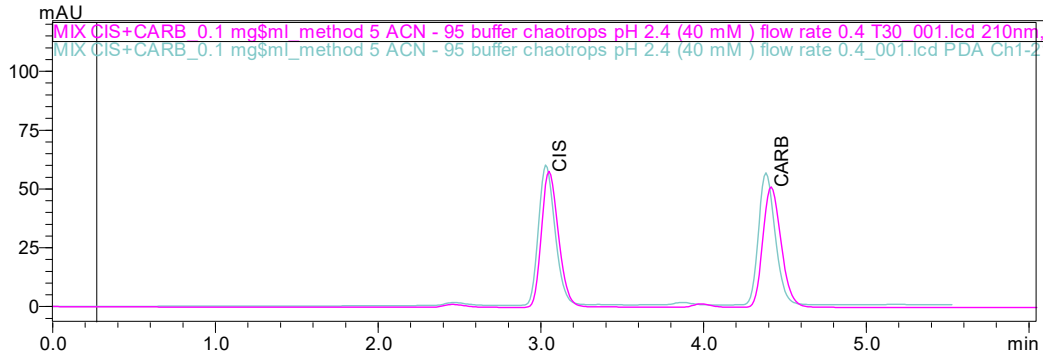


Fig. 5. The chromatogram of cisplatin (0.1 mg/ml) and carboplatin (0.1 mg/ml) on Luna C18(2) column (100 × 4.6 mm, 3 µm) with 5% ACN and 95% KPF_6 buffer 40 mM pH 2.4, flow rate 0.4 mL/min, temperature (pink) 30°C and (blue) 35°C, detection at 210 nm

4. 3. Validation of the HPLC method for the determination of cisplatin and carboplatin

Validation of the proposed method was performed following ICH guidelines, assessing its linearity, accuracy, precision and robustness [14].

Linearity was assessed using five levels of each of the investigated drugs, where concentration varied in the range of 20–100 µg/mL (**Fig. 6, 7, Table 3**). **Fig. 6, 7** provide an overview of the relevant regression equations, correlation coefficients, concentration ranges, slope values, and intercepts for the analysed data. The findings reveal that both compounds exhibit robust linear relationships across the concentration range of 20–100 µg/mL, demonstrated by correlation coefficients (r^2) surpassing 0.9983. This high degree of correlation underscores the excellent linearity of the analytical method. Additionally, the combination of these elevated r^2 values and minimal intercepts further supports the reliability and precision of the method's linearity throughout the specified range. Low limit of detection (LOD) of carboplatin was 4.12 µg/ml, and for cisplatin – 5.18 µg/ml. Low limit of quantification (LOQ) of carboplatin was 12.48 µg/ml, and for cisplatin – 15.71 µg/ml.

The accuracy and precision of the HPLC method were thoroughly assessed through a series of tests using laboratory-prepared mixtures containing predefined concentrations at three specific levels: 20, 60, and 100 µg/mL. The percentage recoveries obtained ranged impressively

from 99.42% to 100.45%, accompanied by negligible standard deviations (**Table 3**). These results strongly support the method's notable accuracy and its ability to reliably measure pharmaceutical concentrations. For evaluating repeatability, the same concentrations of 20, 60, and 100 µg/mL were tested three times in a single day. The observed relative standard deviation (RSD) values consistently fell below 1.0% for all tested drugs, further underscoring the high repeatability of the method as shown in **Table 3**. Additionally, intermediate precision was examined by conducting measurements over three consecutive days using triplicate analyses of the same drug concentrations. The results presented in **Table 3** reveal that RSD values did not exceed 1.0%, which confirms the method's exceptional consistency and intermediate precision in multi-day testing scenarios.

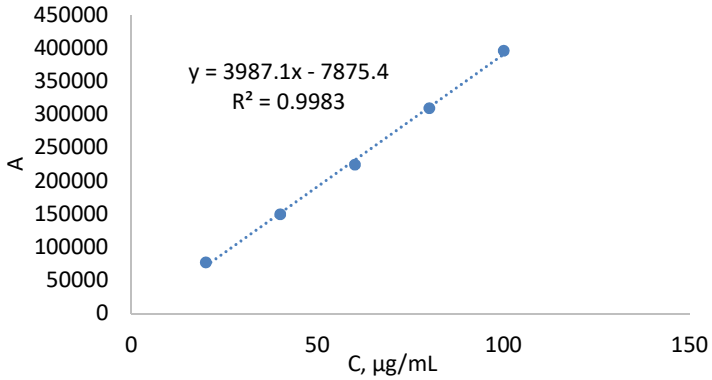


Fig. 6. Linearity of cisplatin's determination

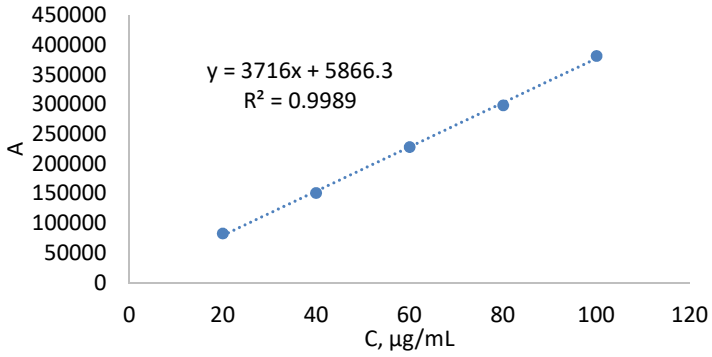


Fig. 7. Linearity of carboplatin's determination

Table 3

Regression and validation parameters of the proposed HPLC method

Parameters		Cisplatin	Carboplatin
Wavelength (nm)		210	
Linearity range (µg/mL)		20–100	
Regression equation		$y^* = b\,x^{**} + a$	$y^* = b\,x^{**} + a$
Slope (b)		3987.1	3716
Intercept (a)		–7875.4	5866.3
Coefficient of determination (R^2)		0.9983	0.9989
Accuracy (%R)		99.42 ± 0.89	100.45 ± 0.64
Precision (%RSD)	Repeatability	0.784	0.851
	Intermediate precision	0.874	0.907

Table 4 illustrates that the percentage recoveries ranged from 99.30% to 100.45%, confirming that the excipients in the drug formulations did not interfere with the analysis of APIs.

Table 4

Quantitative determination of cisplatin and carboplatin in its pharmaceutical dosage form by HPLC method

Drug	Pharmaceutical taken (µg/mL)	Pharmaceutical found* (µg/mL)	Pure added (µg/mL)	Pure found ** (µg/mL)	%Recovery
Cisplatin	100	100.09	20	20.09	100.45
			60	60.18	100.30
			100	99.82	99.82
Mean					100.19
Carboplatin	100	100.17	20	19.86	99.30
			60	60.16	100.27
			100	100.24	100.24
Mean					99.94

The robustness was evaluated by introducing slight variations to the chromatographic parameters, specifically adjusting the flow rate and column temperature (±2°C). As summarized in **Table 5**, these minor changes showed no significant impact on T or Rt/Rs, demonstrating the robustness of the HPLC method.

4. 4. Evaluation of the greenness study of the developed HPLC method by using tools AGREE, MoGAPI, complex MoGAPI, AGSA, CaFRI, BAGI, and CACI

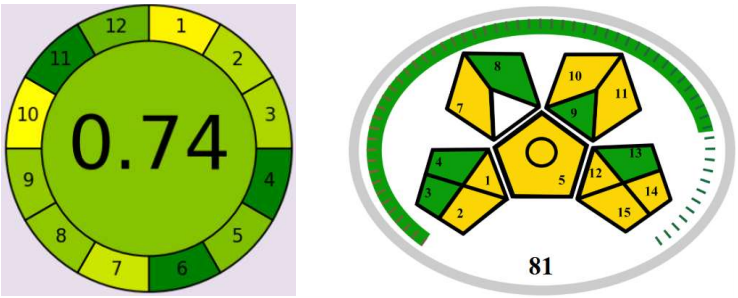
The study of greenness was conducted using tools Analytical GREEnness (AGREE), Modified Green Analytic Procedure Index (MoGAPI) and Complex MoGAPI, Analytical Green Star Area (AGSA), Carbon Footprint Reduction Index (CaFRI), Click Analytical Chemistry Index (CACI) [15–20] (Fig. 8–10).

The development of the HPLC method was meticulously guided by green analytical chemistry principles. This is clearly reflected in aspects such as the adoption of chromatographic analysis using ACN, H_3PO_4, and KPF_6, as well as the elimination of derivatisation steps. These features set our proposed method apart from earlier HPLC approaches that relied on more hazardous solvents. Furthermore, the solvent waste was kept minimal, approximately 2 ml, due to a flow rate of 0.4 ml/min, which considerably enhances the method's environmental friendliness (aligned with operation 7, evaluated using the AGREE tool). Overall greenness score using AGREE tool was 0.74 (Fig. 8, *a*), MoGAPI – 81 (Fig.8, *b*), complex MoGAPI – 81 (Fig. 9, *a*), AGSA – 77.78 (Fig. 9, *b*), CaFRI – 82 (Fig. 10, *a*), CACI – 79 (Fig. 10, *b*). The tools AGREE, MoGAPI, complex MoGAPI, AGSA, CaFRI and CACI found that the proposed HPLC method is «green».

Table 5

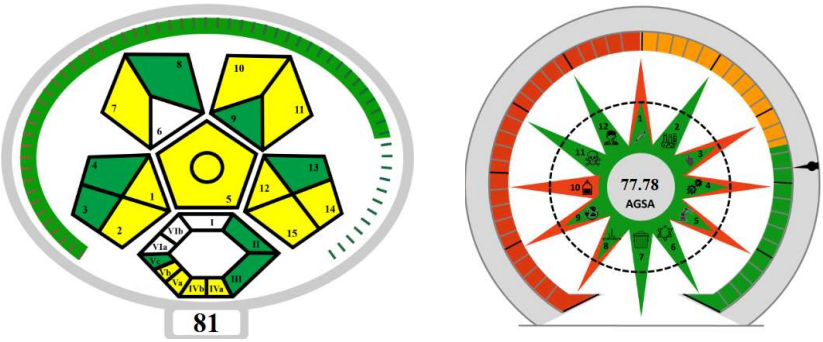
Robustness results for the determination of cisplatin and carboplatin by the proposed HPLC method

Parameters		Tailing factor (*T*)	Cis-platin	Carbo-platin	Resolution (*Rs*)	Cis-platin	Carbo-platin
Flow rate (ml/min)	0.4	Tailing factor (*T*)	1.219	1.211	Retention time (*Rt*)	–	6.627
	0.6		1.290	1.278		–	5.358
	0.8		1.354	1.313		–	4.799
Temperature (°C)	30	Tailing factor (*T*)	1.219	1.211		3.031	4.384
	35		1.223	1.215		3.030	4.385



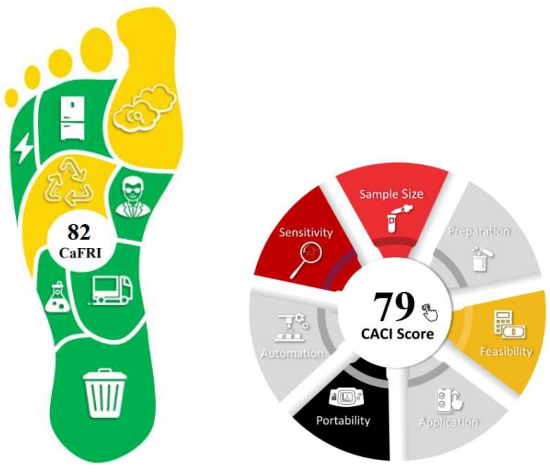
a *b*

Fig. 8. Greenness metric assessment of the developed RP-HPLC method: *a* – AGREE (overall greenness score of 0.74); *b* – MoGAPI (overall score of 81)



a *b*

Fig. 9. Greenness metric assessment of the developed RP-HPLC method: *a* – MoGAPI (overall greenness score of 81); *b* – AGSA (overall score of 77.78)



a *b*

Fig. 10. Greenness metric assessment of the developed RP-HPLC method: *a* – CaFRI overall greenness score of 82); *b* – CACI (overall score of 79)

5. Discussion of research results

Platinum-based drugs are effective antitumor agents. Their pharmaceutical analysis is complicated due to their chemical structures. The chromatographic analysis of cisplatin and carboplatin presented a unique challenge due to their inorganic structure. The molecule's core features a central platinum atom flanked by two halogen atoms (chlorine) and two amino groups, creating a strongly ampholytic compound with both acidic and basic properties. Its lack of an organic carbon skeleton, functional groups, or UV-absorbing chromophore makes it nearly invisible under UV detection and results in weak retention on alkyl RP C8 or C18 columns, typically preferred for achieving optimal peak resolution and precise separation. The task of simultaneous determination of cisplatin and carboplatin is complicated too, for example, for the analysis of wastewater or bioanalytical purposes (therapeutic drug monitoring, pharmacokinetics, or bioequivalence). In world pharmacopoeias, there are monographs on cisplatin and carboplatin using the HPLC method, NH_2-bonded columns, and/or ion-pairing reagents (Fig. 11) [3].

We have reproduced and verified in our laboratory the pharmacopeial method presented in Fig. 11. The pharmacopeial method proved inconvenient due to the use of two opposing ion pairs, making it less cost-effective. Motivated by the presence of 2-amino groups, we decided to explore an alternative approach involving chaotropic agents and chaotropic anions through two different experiments, utilising both columns and chaotropes. An important aspect of using salts of chaotropic anions in reverse-phase C18 or C8 separation of nitrogen-containing molecules is their ability to enhance peak symmetry and improve retention. Based on prior studies and investigations carried out by our research team, mobile phases composed of a 40 mM KPF_6 buffer solution (pH 2.4) combined with ACN in proportions of 90:10 and 95:5, along with the use of a C18 chromatographic column (Luna C18, 100 × 4.6 mm, 3 µm), have been evaluated. We have studied the choice of composition of the mobile phase, type of column, temperature, and flow rate. The optimal chromatographic conditions determined through experimentation are as follows: the mobile phase consists of a 40 mM KPF_6 buffer solution (pH 2.4) mixed with acetonitrile in a 95:5 ratio. The analysis employs a Luna C18 column (100 × 4.6 mm, 3 µm particle size) maintained at a temperature of 30°C, with a flow rate of 0.4 ml/min and detection carried out at a wavelength of 210 nm. The range of application of the analytical method for both analytes was 20–100 µg/ml. Regression for cisplatin was $y = 3987.1x - 7875.4$ ($R^2 = 0.9983$), for carboplatin – $y = 3716x + 5866.3$ ($R^2 = 0.9989$). LOD carboplatin was 4.12 µg/ml, and cisplatin was 5.18 µg/ml. LOQ carboplatin was 12.48 µg/ml, cisplatin –15.71 µg/ml. The developed HPLC method is green, as confirmed by the most

modern metrics for studying greenness (AGREE, MoGAPI, complex MoGAPI, AGSA, CaFRI and CACI).

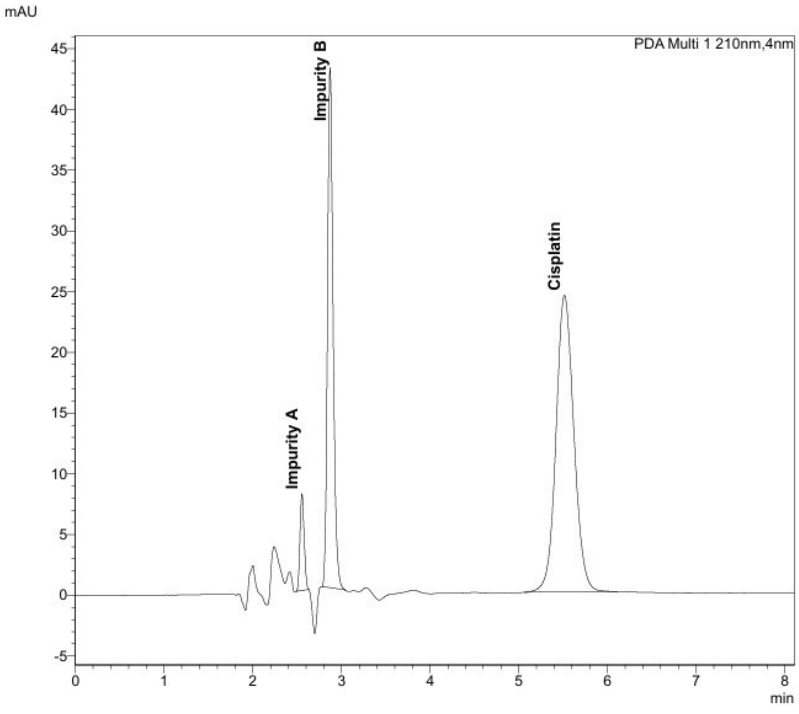


Fig. 11. Chromatogram which was reproduced in our lab with column 250 × 4 mm, 5 µm Merck LiCHrospher C-8e using anionic and cationic ion-pairing agents according to pharmacopeial monography described in BP2025 and USP2024 (chromatographic column Superspher Select B 250 × 4.6 mm, 4 µm)

Compared to the pharmacopoeial method [3], by eliminating the need for ion-pairing agents and dedicated columns for ion-paired separations, our HPLC method improves usability and enables comprehensive validation of challenging molecular structures, such as cisplatin and carboplatin, enhances peak symmetry and improves retention, and performs green analysis. The proposed HPLC method also allows the quantitative determination of relative compounds.

Practical relevance. The proposed method can be used for routine pharmaceutical analysis. The method may be modified for monitoring these substances' environmental effects in sewage, which would help determine how they affect the environment.

Study limitations. The proposed strategy can not be transferred to LC-MS.

Prospects for further research. The next stage of research is planned to develop a HPLC-DAD method for the simultaneous determination of cisplatin and carboplatin in blood plasma using salts of chaotropic anions, by improving the sensitivity of this method with lower particle filed columns, especially with solid-core based technology and improving the UV-detection signal with changes of DAD-options, quartz-cell dimensions, and selecting the most retentive column RP-matrix, thus counting a higher Number of Theoretical Plates of the column.

6. Conclusion

In this work, thorough scientific research was carried out with the presentation of an HPLC method development for the simultaneous determination of cisplatin and carboplatin in a model mixture using salts of chaotropic anions. In addition, two studied drugs were quantified using rapid, simple, cost-effective HPLC method approaches. These studies and experiments demonstrated the advantages of utilising various chaotropic salts to regulate the interaction strengths between analytes and bonded ligands on a reverse-phase RP column. This approach facilitates the development of rapid and cost-effective HPLC methods, particularly for weakly retained, highly polar molecules that elute near the void volume or void time of RP columns. By eliminating the need for ion-pairing agents and dedicated columns for ion-paired separations, this method enhances usability and supports comprehensive validation of challenging molecular structures, such as cisplatin and carboplatin, which can be further improved with longer columns with smaller particle sizes that increase separation power to higher Number of Theoretical Plates of column and DAD-adjusted parameters and UV-quartz cell diameter and lengths.

Conflict of interest

The authors declare that they have no conflict of interest in relation to this research, whether financial, personal, authorship or otherwise, that could affect the research and its results presented in this article.

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Data availability

Manuscript has no associated data.

Use of artificial intelligence

The authors confirm that they did not use artificial intelligence technologies when creating the current work.

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Authors' contributions

Mariana Druchok: Funding acquisition; Investigation; Methodology; Software; Validation; Writing – original draft; **Marjan Piponski:** Conceptualization; Writing – review & editing; **Mariana Horyn:** Formal Analysis; Visualization; **Nadiya Zarivna:** Formal Analysis; Visualization; **Liliya Logoyda:** Conceptualization; Data curation; Funding acquisition; Project administration; Software; Supervision; Validation; Writing – review & editing

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