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Editorial

Development and Institutional Mapping of Chromatography Research in the Republic of North Macedonia: A Historical and Scientometric Analysis

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Abstract

Chromatography represents a cornerstone of modern analytical chemistry, enabling the separation, identification, and quantification of constituents of complex chemical systems. Its development in the Republic of North Macedonia is closely linked to the evolution of national academic institutions and industrial analytical capacity. This study provides a combined historical overview and Scopus-based scientometric analysis of chromatography research in North Macedonia, focusing on institutional development, research groups, methodological evolution, and industrial contribution. Data were obtained from Scopus-indexed publications, institutional records, and key publications. Ss. Cyril and Methodius University in Skopje (UKIM) emerges as the dominant research hub, particularly through the Institute of Chemistry, Faculty of Natural Sciences and Mathematics, and the Faculty of Pharmacy, Faculty of Agriculture, supported by the Macedonian Academy of Sciences and Arts (MANU), Goce Delčev University in Štip, and several specialized applied research institutions. The pharmaceutical industry, particularly Alkaloid AD Skopje and Replek Farm, plays a significant role in chromatographic method application and validation. High-performance liquid chromatography (HPLC), gas chromatography (GC), and liquid chromatography–mass spectrometry (LC–MS) dominate research applications, primarily in phytochemistry, pharmaceutical analysis, food chemistry, and environmental science, while MALDI-TOF mass spectrometry has been integrated into the proteomics activity at MANU. The results demonstrate a highly centralized but scientifically productive research system with increasing methodological sophistication and international cooperation.

Keywords: chromatography; TLC; HPLC; GC-MS; LC-MS; MALDI-TOF; scientometrics; Macedonia

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1. Introduction

The development of chromatography in the Republic of North Macedonia has closely followed the global progress of analytical chemistry and instrumental analysis. Chromatography is one of the most important analytical techniques in chemical sciences, widely used for the separation, identification, and quantification of the constituents in complex mixtures. Since its establishment in the early twentieth century, chromatography has evolved into a suite of advanced instrumental techniques, employing gas chromatography (GC), high-performance liquid chromatography (HPLC) for separation, and sophisticated detection, such as the liquid chromatography–mass spectrometry (LC–MS) combination, as

well as hyphenated platforms coupling separation with high-resolution mass spectrometry, diode-array detection, and nuclear magnetic resonance spectroscopy.

In the Republic of North Macedonia, chromatographic research is strongly associated with the Ss. Cyril and Methodius University in Skopje (UKIM), which serves as the central academic institution for analytical chemistry. The development of chromatographic methods in the country has followed global trends, progressing from classical separation techniques toward advanced hyphenated systems used in environmental monitoring, pharmaceutical analysis, food chemistry, and phytochemical research. Despite the increasing scientific output, no comprehensive scientometric study had previously mapped the institutional structure, methodological evolution, and industrial contribution of this field within the country. The present work addresses this gap by integrating Scopus-based publication data with institutional and industrial analysis.

2. Historical Development

The foundations of analytical chemistry in the country were established, particularly with the introduction of analytical chemistry courses and laboratories at the Faculty of Chemistry as a part of Ss. Cyril and Methodius University in Skopje in 1948. During this period, the first laboratories for qualitative and quantitative chemical analysis were organized, creating the basis for the later introduction of chromatographic methods into scientific research and industrial applications.

Although paper chromatography and other classical separation techniques were likely introduced in laboratory practice during the 1950s and 1960s, documented international evidence of chromatography-related research from North Macedonia appeared later. The earliest currently identified Scopus-indexed chromatography publication affiliated with Macedonia is the work of Nastev, Efremov, and Petkov (1977), published in the journal *Hemoglobin* [1]. The authors, working at the Medical Center in Titov Veles and within the research group later associated with the Macedonian Academy of Sciences and Arts (MANU), described a microcolumn ion-exchange chromatography method using DEAE-cellulose (DE 52, Whatman Inc.) for the quantitation of hemoglobin A2. This study represents the earliest internationally indexed evidence of chromatographic separation applied by Macedonia-affiliated researchers in clinical biochemistry.

However, chromatographic methodologies, particularly paper chromatography and thin-layer chromatography (TLC), were almost certainly already present in university teaching and routine laboratory practice prior to this publication, although such activities were mainly documented in local reports, institutional publications, or non-indexed journals.

A pioneer in this field was **Bojan Podolešov**, a professor of biochemistry whose research focused on natural products and oxidation reactions. Together with his assistant, **Zoran Zdravkovski** he investigated the constituents of *Aristolochia* species endemic to Macedonia, including *Aristolochia macedonica* Born. Their work involved the use of self-prepared TLC plates, produced with an applicator (Figure 1) and coated with silica gel containing the GF_{254} indicator. In 1980 and 1981, they published two papers in *Acta Pharmaceutica Jugoslavica* (now *Acta Pharmaceutica*) and another in *Contributions* of the Macedonian Academy of Sciences and Arts [2–4].

A particularly important role in the subsequent development of chromatographic science and analytical chemistry in the country has been played by the Institute of Chemistry at the Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University in Skopje. The Institute has been one of the leading academic and research centers in the country for the implementation and advancement of modern chromatographic techniques, including thin-layer chromatography (TLC), gas chromatography (GC), high-performance liquid chromatography (HPLC), ion chromatography, and mass spectrometry-coupled tech-

niques. Through continuous scientific research, education of chemists, and international collaboration, the Institute has significantly contributed to the training of generations of chemists and analytical scientists, as well as to the modernization of analytical methodologies in the country.



Figure 1. TLC plate applicator used at the Institute of Chemistry (probably made by Camag).

Following the 1977 milestone, paper chromatography, thin-layer chromatography (TLC), and classical column chromatography became increasingly applied during the 1970s and 1980s in pharmaceutical, food, agricultural, and environmental analyses. These methods enabled the separation and identification of organic compounds, pigments, pharmaceuticals, and natural products and represented a significant advancement in analytical capabilities within the country.

The development of instrumental chromatography accelerated during the 1980s and 1990s with the introduction of GC and HPLC in university laboratories, research institutions, and industrial quality-control laboratories. These techniques significantly improved analytical precision, sensitivity, and reproducibility, allowing broader applications in toxicology, pharmaceutical analysis, environmental monitoring, and food quality assessment. The first phase (1980–1995) was characterized by limited instrumental infrastructure and reliance on classical gas chromatography for basic organic-compound analysis. The second phase (1995–2010) marked a significant expansion in analytical capabilities, particularly with the introduction of HPLC and gas chromatography–mass spectrometry (GC–MS), which enabled applications in environmental chemistry, natural products, pharmaceutical analysis, and food safety.

In the last two decades, chromatographic research in Macedonia has expanded considerably through the implementation of advanced hyphenated techniques such as GC–MS and liquid chromatography–tandem mass spectrometry (LC–MS/MS). Modern chromatographic methods are now routinely employed in studies involving natural products, metabolomics, pharmaceutical analysis, wine characterization, environmental pollutants, and biomonitoring, and have been complemented at MANU by matrix-assisted laser desorption/ionization–time of flight (MALDI-TOF) mass spectrometry for clinical proteomics. Macedonian researchers actively contribute to international scientific literature, particularly in the fields of analytical chemistry, phytochemistry, and environmental science. Today, chromatography represents one of the most important analytical approaches in academic and industrial laboratories in North Macedonia, supporting research, quality control, environmental protection, and public health applications. The timeline is given in Table 1.

Table 1. Timeline of chromatography development in the Republic of North Macedonia.

Period	Key Developments
1948–1960	Foundations of analytical chemistry and establishment of the first analytical laboratories at UKIM
1970–1980	Introduction and increasing application of classical chromatographic techniques (paper chromatography, TLC, and column chromatography)
1980–1995	Introduction of instrumental gas chromatography (GC) and development of basic chromatographic infrastructure in academic and industrial laboratories
1995–2010	Expansion of GC and HPLC instrumentation in academic and industrial laboratories
2010–today	Advanced LC–MS/GC–MS applications in pharmaceutical quality control, natural products, and environmental research; MALDI-TOF proteomics

3. Institutional Structure and Main Contributors

Chromatography research in the Republic of North Macedonia is highly centralized within "Ss. Cyril and Methodius University in Skopje". The most productive units are the Institute of Chemistry at the Faculty of Natural Sciences and Mathematics and the Faculty of Pharmacy. In later stages of development, significant contributions in the field of chromatography also emerged from the Faculty of Agricultural Sciences and Food, the Faculty of Veterinary Medicine, and the Faculty of Technology and Metallurgy.

These activities have been further complemented by contributions from the Macedonian Academy of Sciences and Arts (MANU) and the Faculty of Agriculture, Goce Delčev University in Štip. The list of all relevant contributors is given in Table 2.

Table 2. Key contributors in chromatography research in the Republic of North Macedonia (values retrieved from Scopus author profiles on 11 May 2026).

Researcher	Field	Documents	Citations	H-Index
Ss. Cyril and Methodius University in Skopje				
Institute of Chemistry, Faculty of Natural Sciences and Mathematics				
Stafilov, Trajče	Analytical and environmental chemistry	331	7868	47
Stefova, Marina	Phytochemistry/environmental chemistry/LC–MS/GC	100	3243	33
Petreska Stanoeva, Jasmina	Phytochemistry/environmental chemistry/LC–MS/GC	67	1505	24
Zdravkovski, Zoran	Organic chemistry/GC	66	1149	18
Bogdanov, Jane B.	Organic chemistry/GC	40	239	8
Bogdanov, Bogdan	Organic chemistry	30	1270	17
Cvetanoska, Marinela	Natural products/Environmental chemistry	6	22	3
Sofronievska, Ivona	Environmental chemistry	3	1	1
Faculty of Pharmacy				
Kulevanova, Svetlana	Pharmacognosy	62	1298	20
Stefkov, Gjoshe	Pharmacognosy	57	1282	24
Karapandzova, Marija	Pharmacognosy/essential oils	15	404	10
Dimitrovska, Aneta	Pharmaceutical analysis/HPLC method development	46	526	13
Acevska, Jelena	Pharmaceutical analysis/chemometrics	30	330	10
Petkovska, Rumenka	Pharmaceutical analysis/RP-HPLC method development	16	168	8

Table 2. *Cont.*

Researcher	Field	Documents	Citations	H-Index
Nakov, Natalija	HPLC-MS/MS bioanalysis/green chromatography	18	129	6
Cvetkovikj (Karanfilova), Ivana	Pharmaceutical chemistry	16	390	10
Kadifkova-Panovska, Tatjana	Pharmaceutical analysis	22	596	11
Bauer (Bauer-Petrovska), Biljana	Bromatology/nutrition	15	1654	7
Petrushevska-Tozi, Lidija	Pharmaceutical technology/nutrition	9	216	5
Kavrakovski, Zoran S.	Pharmaceutical analysis	17	313	7
Faculty of Technology and Metallurgy				
Rafajlovska, Vesna	Food extraction chemistry/HPTLC	23	196	9
Lisichkov, Kiril	Supercritical-fluid extraction + GC	28	358	10
Faculty of Agricultural Sciences and Food				
Velkoska-Markovska, Lenche	Food chemistry	18	132	8
Jankulovska, Mirjana	Agrochemistry	24	236	10
Petanovska-Ilievska, Biljana R.	Food science	18	138	8
Faculty of Veterinary Medicine				
Stojkovikj, Elizabeta Dimitrieska	Food safety	14	137	7
Hajrulai-Musliu, Zehra	LC-MS/MS residue and mycotoxin analysis	34	521	9
Macedonian Academy of Science and Arts, *Research Center "G. D. Efremov*				
Efremov, Georgi Dimitar	Molecular hematology/ion-exchange chromatography of haemoglobins	192	4263	31
Plaseska-Karanfilska, Dijana A.	Genomics/proteomics	141	5542	25
Dimovski, Aleksandar J.	Pharmacogenetics/molecular biology	120	2475	27
Davalieva, Katarina G.	Proteomics/MALDI-TOF and nano-LC–MS/MS	37	599	14
Goce Delčev University—Štip				
Faculty of Agriculture				
Ivanova-Petropulos, Violeta	Food chemistry/enology	44	1446	24
Faculty of Medical Sciences				
Smilkov, Katarina	Radiolabeled-peptide HPLC/nutraceuticals	21	611	10
University St. Kliment Ohridski in Bitola, *Hydrobiological Institute—Ohrid*				
Veljanoska-Sarafiloska, Elizabeta M.	Environmental chemistry	11	359	7

3.1. Institute of Chemistry, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University in Skopje

The Institute of Chemistry serves as the primary national center for fundamental analytical chemistry, environmental analysis, and natural products research. Researchers at the Institute apply thin-layer chromatography (TLC), gas chromatography (GC), high-performance liquid chromatography (HPLC), gas chromatography–mass spectrometry (GC–MS), and liquid chromatography–mass spectrometry (LC–MS) for pollutant monitoring and detailed phenolic profiling of Macedonian plants, fruits, and bee products.

The pioneering work in thin-layer chromatography within the Institute was carried out as part of qualitative organic and inorganic analysis during the early phase of the laboratory development. A major contribution to the establishment and modernization of chromatographic science at the Institute was made by **Zoran Zdravkovski**, who introduced

and developed gas chromatography methodologies within the Institute laboratories. His research focused particularly on volatile organic compounds and environmental samples, and he played an important role in establishing GC as a routine analytical technique at the Institute.

Marina Stefova introduced HPLC into the Institute and, together with **Jasmina Petreska Stanoeva**, has played a central role in establishing HPLC coupled with diode-array and mass spectrometric detection (HPLC–DAD–MS^n) as a fundamental analytical technique for research and practical applications. Their work has significantly contributed to phytochemical research through the application of HPLC and LC–MS techniques for plant metabolite profiling, while in recent years their research has also expanded toward environmental analysis. At the same time, the collaboration with the pharmaceutical industry developed and contributed to advanced applications in this sector.

In recent years, **Jane Bogdanov** has contributed significantly to the development of chromatographic applications in environmental analytical chemistry. He has also contributed to the application of chromatographic methods in essential-oil characterization and natural-product analysis.

During the last few years, **Ivona Sofronievska** and **Marinela Cvetanoska**, working in the fields of environmental analysis and natural products, have represented a younger generation of researchers continuing the development of chromatographic science at the Institute.

In the period preceding the consolidation of in-house chromatographic capacity at the Institute, **Trajče Stafilov**, whose primary research focus is environmental pollutant analysis using atomic spectroscopy techniques, was among the first Macedonian researchers to publish papers involving chromatographic methods through collaborations with colleagues from abroad.

3.2. Faculty of Pharmacy, Ss. Cyril and Methodius University in Skopje

The Faculty of Pharmacy is the leading national center for pharmaceutical chromatography, focusing on HPLC and LC–MS methods for pharmacognosy, medicinal plant analysis, drug quality control, and pharmaceutical formulation studies. Key researchers include **Svetlana Kulevanova**, **Gjoshe Stefkov**, **Marija Karapandzova** (pharmacognosy and essential-oil analysis of Macedonian medicinal and aromatic plants), **Aneta Dimitrovska**, **Jelena Acevska**, **Rumenka Petkovska,** and **Natalija Nakov** (chromatographic method development and validation, stability-indicating HPLC and UHPLC/MS methods, HPLC-MS/MS bioanalysis—including chiral separation of ibuprofen enantiomers in human plasma—and chemometric data treatment in pharmaceutical analysis), **Ivana Karanfilova Cvetkovikj**, **Tatjana Kadifkova-Panovska**, **Biljana Bauer-Petrovska,** and **Lidija Petrushevska-Tozi** (bromatology, dietary and bioactive-compound analysis), and **Zoran Kavrakovski**. Their combined output spans essential oil analysis of Macedonian medicinal and aromatic plants, validation of stability-indicating HPLC methods for active pharmaceutical ingredients (APIs), and bioactive-compound profiling for pharmacognostic standardization.

3.3. Macedonian Academy of Sciences and Arts (MANU)

MANU has strongly supported the advancement of chemical and analytical sciences through scientific projects, interdisciplinary research, and international cooperation. The Research Center for Genetic Engineering and Biotechnology "Georgi D. Efremov" serves as the National Reference Center for Genomics and Proteomics. The historical lineage of chromatographic research at the Center traces back to Georgi D. Efremov, a foundational figure in Macedonian molecular genetics and hematology and co-author of the 1977

Hemoglobin paper that constitutes the earliest Scopus-indexed Macedonian chromatography publication [1]. The Center is currently directed by **Dijana A. Plaseska-Karanfilska**, under whose leadership the proteomics and biomarker program has expanded. **Aleksandar J. Dimovski** (Head of Genetics and Pharmacogenetics) co-authors the broader pharmacogenetic, pharmacogenomic, and chromatographic-method work of the Center and is one of MANU's most-cited researchers overall. **Katarina Davalieva** applies advanced proteomic platforms, including 2D-DIGE/MALDI-TOF mass spectrometry and nano-LC–MS/MS, complementing traditional chromatography for biomarker discovery and biomedical research; her 2015 paper on prostate-cancer proteomics in *Prostate* is the most-cited Macedonian MALDI/proteomics study to date.

3.4. Other Contributing Institutions

Several additional institutions contribute substantially to the national chromatographic landscape:

- **Goce Delčev University, Štip**: **Violeta Ivanova-Petropulos**, with a PhD in wine polyphenol characterization from the Institute of Chemistry (UKIM) and a permanent position at the Faculty of Agriculture, leads research in wine chemistry and food authenticity using GC–MS and LC–MS, with a strong record of internationally co-authored publications. At the affiliated Faculty of Medical Sciences, **Katarina Smilkov** works on radiolabeled-peptide HPLC characterization and nutraceutical analysis (piperine, curcuminoids).
- **Faculty of Agricultural Sciences and Food**, **UKIM**: Lenche Velkoska-Markovska, Mirjana S. Jankulovska, and Biljana Petanovska-Ilievska focus on food chemistry, antioxidants, and pesticide residues.
- **Faculty of Technology and Metallurgy, UKIM**: **Vesna Rafajlovska** contributes to food extraction chemistry, HPTLC of bearberry leaves, and HPLC characterization of refill liquids for electronic cigarettes; **Kiril Lisichkov** works in supercritical-fluid extraction coupled with GC analysis of fish oil and plant bioactives.
- **Faculty of Veterinary Medicine, UKIM**: **Elizabeta Stojkovikj-Dimitrieska** works in food safety, acrylamide, and aflatoxin determination in foods of animal origin; **Zehra Hajrulai-Musliu** is active in the development and validation of multi-class LC-ESI-MS/MS methods for veterinary drug, mycotoxin, and pesticide residues in bovine milk, urine, and apicultural products.
- **Hydrobiological Institute, Ohrid, University St. Kliment Ohridski**, **Bitola**: **E. M. Veljanoska-Sarafiloska** conducts environmental analysis of aquatic systems, with a focus on Lake Ohrid and related freshwater ecosystems.

4. Most-Cited Chromatography-Related Publications

The total number of publications related to chromatography is 424. Analysis of citation impact identifies a relatively small core of highly influential papers authored or co-authored by Macedonia-affiliated researchers (Table 3). The most striking pattern is the dominance of one research lineage: of the fifteen top-cited chromatography papers from the country, eleven involve Marina Stefova of the Institute of Chemistry, either as senior author or as part of the wider network of her associates. The 2011 paper by Gavrilova, Kajdžanoska, Gjamovski & Stefova on the HPLC-DAD-ESI-MS^n profiling of berries and small fruits (224 citations, *J. Agric. Food Chem.*) and the 2010 strawberry paper by Kajdžanoska, Gjamovski & Stefova (162 citations, Maced. *J. Chem. Chem. Eng.*) are not isolated successes but the visible tip of a coherent, two-decade-long program in HPLC-DAD-MS^n phenolic profiling of Macedonian plants, fruits, and bee products.

Table 3. Articles with more than 50 citations.

#	Author(s)	Year	Title	Journal	Citations
1	Gavrilova V., Kajdžanoska M., Gjamovski V., Stefova M.	2011	Separation, characterization, and quantification of phenolic compounds in blueberries and red and black currants by HPLC−DAD−ESI-MS^n DOI: 10.1021/jf104565y	J. Agric. Food Chem.	224
2	Kajdžanoska M., Gjamovski V., Stefova M.	2010	HPLC-DAD-ESI-MS^n identification of phenolic compounds in cultivated strawberries from Macedonia DOI: 10.20450/mjcce.2010.165	Maced. J. Chem. Chem. Eng.	162
3	Panovska T. K., Kulevanova S., Stefova M.	2005	In vitro antioxidant activity of some Teucrium species (Lamiaceae) DOI: not indexed in Scopus	Acta Pharm.	158
4	Ivanova V., Stefova M., Vojnoski B., Dörnyei Á., Márk L., Dimovska V., Stafilov T., Kilár F.	2011	Identification of polyphenolic compounds in red and white grape varieties grown in R. Macedonia and changes in their content during ripening DOI: 10.1016/j.foodres.2011.06.046	Food Res. Int.	116
5	Kajdžanoska M., Petreska J., Stefova M.	2011	Comparison of different extraction solvent mixtures for characterization of phenolic compounds in strawberries DOI: 10.1021/jf2007826	J. Agric. Food Chem.	114
6	Bauer-Petrovska B., Petrushevska-Tozi L.	2000	Mineral and water-soluble vitamin content in the Kombucha drink DOI: 10.1046/j.1365-2621.2000.00342.x	Int. J. Food Sci. Technol.	104
7	Ivanova V., Dörnyei Á., Márk L., Vojnoski B., Stafilov T., Stefova M., Kilár F.	2011	Polyphenolic content of Vranec wines produced by different vinification conditions DOI: 10.1016/j.foodchem.2010.06.039	Food Chem.	95
8	Cvetkovikj I., Stefkov G., Acevska J., Dimitrovska A., Kulevanova S.	2013	Polyphenolic characterization and chromatographic methods for fast assessment of culinary Salvia species from South East Europe DOI: 10.1016/j.chroma.2012.12.068	J. Chromatogr. A	91
9	Petreska J., Stefova M., Ferreres F., Moreno D.A., Tomás-Barberán F.A., Stefkov G., Kulevanova S., Gil-Izquierdo A.	2011	Potential bioactive phenolics of Macedonian Sideritis species used for medicinal "Mountain Tea" DOI: 10.1016/j.foodchem.2010.08.019	Food Chem.	80
10	Smilkov K., Ackova D. G., Cvetkovski A., Ruskovska T., Vidovic B., Atalay M.	2019	Piperine: old spice and new nutraceutical? DOI: 10.2174/1381612825666190701150803	Curr. Pharm. Des	79
11	Petreska J., Stefkov G., Kulevanova S., Alipieva K., Bankova V., Stefova M.	2011	Phenolic compounds of mountain tea from the Balkans: LC/DAD/ESI/MS^n profile and content DOI: 10.1177/1934578X1100600107	Nat. Prod. Commun.	72
12	Davalieva K., Kostovska I. M., Kiprijanovska S., Markoska K., Kubelka-Sabit K., Filipovski V., Stavridis S., Stankov O., Komina S., Petrusevska G., Polenakovic M.	2015	Proteomics analysis of malignant and benign prostate tissue by 2D DIGE/MS reveals new insights into proteins involved in prostate cancer DOI: 10.1002/pros.23034	Prostate	70
13	Ivanova-Petropulos V., Mitrev S., Stafilov T., Markova N., Leitner E., Lankmayr E., Siegmund B.	2015	Characterization of traditional Macedonian edible oils by their fatty acid composition and their volatile compounds DOI: 10.1016/j.foodres.2015.08.014	Food Res. Int.	70

Table 3. *Cont.*

#	Author(s)	Year	Title	Journal	Citations
14	Kuvendziev S., Lisichkov K., Zeković Z., Marinkovski M., Musliu Z. H.	2018	Supercritical fluid extraction of fish oil from common carp (Cyprinus carpio L.) tissues DOI: 10.1016/j.supflu.2017.11.027	J. Supercrit. Fluids.	63
15	Petropulos V. I., Bogeva E., Stafilov T., Stefova M., Siegmund B., Pabi N., Lankmayr E.	2014	Study of the influence of maceration time and oenological practices on the aroma profile of Vranec wines DOI: 10.1016/j.foodchem.2014.05.144	Food Chem.	62
16	Tusevski O., Petreska Stanoeva J., Stefova M., Kungulovski Gj., Pancevska Atanasovska N., Gadzovska-Simik S.	2013	Hairy roots of Hypericum perforatum L.: A promising system for xanthone production DOI: 10.2478/s11535-013-0224-7	Cent. Eur. J. Biol.	55
17	Tusevski O., Krstik M., Petreska Stanoeva J., Stefova M., Gadzovska-Simik S.		Phenolic profile and biological activity of Hypericum perforatum L.: Can roots be considered as a new source of natural compounds? DOI: 10.1016/j.sajb.2018.05.030	S. Afr. J. Bot.	54
18	Stefkov G., Karanfilova I. C., Gjorgievska V. S., Karapandzova M., Kulevanova S.	2022	Analytical techniques for phytocannabinoid profiling of Cannabis and Cannabis-based products—a comprehensive review DOI: 10.3390/molecules27030975	Molecules.	53
19	Karapandzova M., Stefkov G., Cvetkovikj I., Stefova M., Kulevanova S.	2015	Flavonoids and other phenolic compounds in needles of Pinus peuce and other pine species from the Macedonian flora DOI: 10.1177/1934578X1501000647	Nat. Prod. Commun.	53
20	Zendelovska D., Stafilov T.	2003	Development of an HPLC method for the determination of ranitidine and cimetidine in human plasma following SPE DOI: 10.1016/S0731-7085(03)00265-6	J. Pharm. Biomed. Anal.	51

Methodologically, the top-cited output splits along three strands that map onto distinct institutions and styles of collaboration.

The phytochemistry strand, led by the Institute of Chemistry (FNSM, UKIM), accounts for most of Table 3. Beyond Stefova herself, the strand includes Jasmina Petreska Stanoeva (phenolic and polyphenolic fingerprinting of plants, fruits, and propolis by HPLC-DAD-MS^n and GC-MS) and Trajče Stafilov (environmental analytical chemistry; the most-cited Macedonian author overall, although several of his top papers fall outside chromatography proper and are not included in Table 3).

The pharmaceutical chromatography strand, led by the Faculty of Pharmacy (UKIM) but also involving the Institute of Chemistry, is the second-largest contributor. The 2013 J. Chromatogr. A paper by Cvetkovikj, Stefkov, Acevska, Petreska, Stanoeva, Karapandzova, Stefova, Dimitrovska & Kulevanova on culinary Salvia species (91 citations) is the strand's flagship publication and is also the only top-20 paper published in a flagship chromatography journal. The faculty divides functionally into a pharmacognosy/essential-oil sub-group (Kulevanova, Stefkov, and Karapandzova, who led work on Juniperus excelsa essential oils and Karapandzova led the work on Pinus phenolics) and a pharmaceutical-analysis sub-group (Dimitrovska, Acevska, Petkovska, and Nakov) that develops, validates, and chemometrically optimizes stability-indicating RP-HPLC methods (e.g., atorvastatin, simvastatin) and HPLC-MS/MS bioanalysis (e.g., chiral separation of ibuprofen enantiomers in human plasma, Nakov et al. 2015). The two sub-groups co-publish frequently with

Stefova's Institute of Chemistry team—the 2005 *Acta Pharm.* paper on antioxidant activity of Teucrium species (Panovska, Kulevanova & Stefova; 158 citations) and the 2011 *Food Chem.* paper on Macedonian Sideritis "Mountain Tea" (Petreska, Stefova, Stefkov, Kulevanova et al.; 80 citations) are textbook examples of this inter-institutional channel.

The wine and food authenticity strand, from Goce Delčev University in Štip, originating from the Institute of Chemistry, is the third pillar and is built around Violeta Ivanova-Petropulos. The three top-cited papers (2014 Vranec wine aroma profile, 62 citations; 2015 *Food Chem.* targeted phenolics in red wines, 57 citations; 2019 LC-IMS-MS wine fingerprinting in *Anal. Chim.* Acta, 56 citations) define the methodological frontier of Macedonian enology and food authentication, with strong international participation. The 2011 *Food Res. Int.* paper on Macedonian grape varieties (Ivanova, Stefova, Vojnoski, Stafilov, Kilár et al.; 116 citations) and the 2011 *Food Chem.* paper on Vranec wines (95 citations) explicitly bridges Goce Delčev with the Institute of Chemistry and with the Hungarian group of F. Kilár, and they remain the most visible examples of intra-Macedonian, inter-faculty, wine-chemistry collaboration.

The MANU Research Center "Georgi D. Efremov" is represented by Davalieva, Kostovska, Kiprijanovska et al. (2015 Prostate, 70 citations)—the most-cited Macedonian MALDI/proteomics study—and by a longer institutional lineage running from the 1977 founding ion-exchange chromatography paper of Nastev, Efremov & Petkov, through Efremov's hemoglobin work, and onwards to the contemporary 2D-DIGE/MALDI-TOF and nano-LC–MS/MS proteomics led by Plaseska-Karanfilska, Dimovski, and Davalieva. The Faculty of Pharmacy also contributes through the highly cited 2000 Int. J. Food Sci. Technol. paper of Bauer-Petrovska & Petrushevska-Tozi on kombucha (104 citations), which sits between bromatology and food chemistry.

Looking beyond Table 3 itself, each institution adds a distinct complementary layer. The Faculty of Technology and Metallurgy (UKIM) contributes a supercritical-fluid-extraction–GC program led by Kiril Lisichkov (the 2018 J. Supercrit. Fluids fish-oil paper at 63 citations is the institution's most-cited chromatography-adjacent work), and a smaller HPTLC and HPLC food-extraction line led by Vesna Rafajlovska. The Faculty of Agricultural Sciences and Food (UKIM) is essentially the trio of Velkoska-Markovska, Petanovska-Ilievska, and Jankulovska, who have built a steady RP-HPLC/RRLC program on pesticide residues in tomatoes, table grapes, and apple juice, malathion formulation analysis, and food-additive determination in beverages, publishing predominantly in Acta Chromatographica. The Faculty of Veterinary Medicine (UKIM) is anchored by the Dimitrieska-Stojkovikj/Hajrulai-Musliu work, whose recent LC-ESI-MS/MS multi-class methods cover veterinary drug, mycotoxin, and pesticide residues in cow milk, urine, and apicultural products and bring the country into compliance with EU regulatory frameworks for foods of animal origin. The Hydrobiological Institute in Ohrid contributes a narrowly focused but characteristic chlorinated-pesticide-residue program led by E. M. Veljanoska-Sarafiloska, who has profiled DDT metabolites and organochlorine residues in fish and sediments from Lakes Ohrid, Prespa, and Dojran.

Overall pattern. Three findings emerge clearly from the citation and co-authorship data. First, a small number of senior figures dominate: across all institutions and all top-cited papers, the Stefova group (Institute of Chemistry), the Kulevanova–Stefkov group (Faculty of Pharmacy), and the Ivanova-Petropulos group (Goce Delčev) generate the majority of the country's chromatographic citation impact. Second, the dominant analytical field is phytochemistry by HPLC-DAD-ESI-MS^n, applied to Macedonian berries, small fruits, mountain teas, edible oils, wines, and grapes; pharmaceutical analysis and clinical bioanalysis form a second, methodologically more rigorous strand, while environmental and veterinary residue analysis form a smaller but expanding third strand. Third, collaboration

in Macedonian chromatography is strongly internal but selectively international: the most productive coupling is between the Institute of Chemistry and the Faculty of Pharmacy, with secondary couplings to the Institute of Biology (Hypericum work), Goce Delčev (wine chemistry), and MANU (proteomics). International partners are concentrated in a few European laboratories—V. Bankova's group in the Center of Phytochemistry (Bulgarian Academy of Sciences, Sofia), F. Kilár's group in Pécs (Hungary), the Lankmayr and Siegmund groups in Graz (Austria), the Hermosín-Gutiérrez group in Spain, and most recently the Hann/Causon group in Vienna (LC-IMS-MS)—reflecting the natural orientation of Macedonian analytical science toward Central and Western European research networks.

5. Industrial Contribution to Chromatography and Separation Science

In addition to academic institutions, the pharmaceutical and chemical industry plays an important role in the development and application of chromatography in the Republic of North Macedonia. Alkaloid AD Skopje and Replek Farm Ltd. represent the two most significant industrial contributors to chromatographic research and analytical practice in the country, while Farmahem contributes through laboratory services, technical support, and by facilitating national access to chromatographic technologies, instrumentation, and consumables.

Among industrial institutions, Replek Farm Ltd. currently has the largest number of chromatography-related publications indexed in Scopus (22 papers), compared with 16 papers affiliated with Alkaloid AD Skopje. The chromatographic profile of Replek Farm Ltd. is strongly dominated by the work of Marjan Piponski, who appears as lead author or co-author in most of the company's publications. Frequent collaborators include T. Bakovska Stoimenova, G. Trendovska Serafimovska, and M. Topkoska-Naumoska, often in collaboration with the group of L. Logoyda from Ternopil National Medical University, Ukraine. Methodologically, the Replek research program is centered primarily on rapid and simplified reversed-phase HPLC method development and validation for pharmaceutical formulations, especially cardiovascular drugs such as atorvastatin, valsartan, atenolol, bisoprolol, lisinopril, captopril, memantine, fosfomycin, and rosuvastatin. Additional research directions include chaotropic-salt-assisted chromatography, green-chemistry approaches in HPLC, and LC–MS/MS bioanalytical methods. Among the company's most cited publications are studies on chiral monolithic silica-based HPLC columns for enantiomeric separation, fast HPLC methods for atorvastatin impurity determination, chaotropic-salt effects in simultaneous hydrophilic and lipophilic drug analysis, and green-profile HPLC methods for antihypertensive drugs.

Alkaloid AD Skopje operates advanced analytical laboratories routinely employing HPLC, GC, UHPLC/MS, and LC–MS techniques for pharmaceutical quality control, stability testing, impurity profiling, packaging-material characterization, and active pharmaceutical ingredient (API) analysis. The chromatographic research profile of Alkaloid is methodologically broader and more strongly oriented toward pharmaceutical quality assurance and industrial analytical chemistry. Major research topics include stability-indicating UHPLC/MS methods, forced-degradation studies of pharmaceutical products such as simvastatin, atorvastatin, and venlafaxine; impurity profiling by LC-HESI-MS and UHPLC; extractables and leachables from pharmaceutical packaging materials; and, more recently, sustainable and "green" chromatography approaches using environmentally friendly solvents such as dimethyl isosorbide. Important contributors within the company include Ugarković, Petruševski, Chachorovska, Petkovska, Tomikj, Hadzieva Gigovska, Trojachanec Jolevska, Mitrevska, and collaborators.

The citation profiles of industrial chromatography publications remain lower than those of the leading academic phytochemical and food-analysis studies; however, the in-

dustrial sector plays a critical role in method validation, implementation of pharmacopoeial standards, technology transfer, and modernization of analytical practice in the country. Industrial laboratories have significantly contributed to the establishment of contemporary pharmaceutical chromatography, particularly in the areas of quality control, impurity analysis, stability testing, and environmentally sustainable analytical methodologies.

6. Scientometric Insights and Research Trends

A Scopus-based analysis of chromatography-related research in the Republic of North Macedonia reveals a highly centralized system dominated by the University "Ss. Cyril and Methodius" in Skopje. The query *TITLE-ABS-KEY(chromatograph*) AND AFFILCOUNTRY(macedonia)* returns 424 documents (Scopus, 11 May 2026), with the Institute of Chemistry, the Faculty of Pharmacy, and MANU accounting for the majority of scientific output and citation impact. Co-authorship patterns show strong institutional clustering, with relatively few independent research groups operating outside UKIM. International collaboration exists and is most pronounced in phytochemistry and environmental chemistry, where Macedonian researchers participate in joint projects with European partners.

Keyword evolution analysis demonstrates a clear methodological transition: from classical column and ion-exchange chromatography in clinical biochemistry (1977 onwards), through gas chromatography and HPLC applications (1980s–2010), to LC–MS-driven metabolomics, MALDI-TOF proteomics, and advanced food-authentication studies in the modern period (2010–present). Recent years show an emerging interest in high-resolution mass spectrometry, untargeted metabolomics, and chemometric data analysis, in line with international research trends.

7. Discussion

Taken together, the historical, institutional, and scientometric data indicate that chromatography in the Republic of North Macedonia has matured from a peripheral separation and analytical activity in the mid-twentieth century into a well-structured research field supporting both fundamental science and industrial applications. The 1977 Nastev–Efremov–Petkov paper shows that Macedonian researchers entered the international chromatography literature through clinical biochemistry before instrumental chromatography became routine at UKIM. The strong centralization around UKIM has facilitated the rapid diffusion of new methodologies once they are introduced in flagship laboratories, but it also creates a structural dependence on a small number of research groups and senior investigators. Continued investment in high-end instrumentation, the systematic training of younger analysts, and a deliberate broadening of international collaboration would help reduce this concentration and increase the overall resilience and visibility of the field.

The increasing role of the pharmaceutical industry—particularly Alkaloid AD Skopje and Replek Farm—represents an important bridge between academic chromatography and applied analytical chemistry, providing both validation pressure and a sink for the methodological output of university laboratories. The MANU proteomics group, anchored historically by G. D. Efremov and currently led by K. Davalieva, has integrated MALDI-TOF and nano-LC–MS/MS into clinical biomarker discovery, complementing the natural-product chromatography of UKIM. Future research directions are likely to include high-resolution LC–MS-based metabolomics, targeted residue and contaminant analysis aligned with EU regulatory frameworks, and wider application of chemometric and machine-learning approaches to chromatographic datasets.

8. Conclusions

Chromatography research in the Republic of North Macedonia has evolved into a well-structured and scientifically productive field centered on the "Ss. Cyril and Methodius University in Skopje". The development of chromatographic methodologies reflects global technological trends, transitioning from classical ion-exchange and column chromatography (Nastev, Efremov & Petkov, 1977) [1]. through gas chromatography and HPLC to advanced LC–MS- and MALDI-TOF-based analytical platforms. The research system is characterized by strong institutional clustering, increasing methodological sophistication, and growing industrial integration. The pharmaceutical industry, particularly Alkaloid AD Skopje and Replek Farm, plays a key role in translating chromatographic research into practical applications. Overall, the Republic of North Macedonia represents a small but specialized and scientifically active contributor to global separation science, with clear potential for further methodological expansion and stronger international integration in the coming decade.

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Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

API	Active pharmaceutical ingredient
DAD	Diode-array detector
DEAE	Diethylaminoethyl (cellulose)
ESI	Electrospray ionization
GC	Gas chromatography
GC–MS	Gas chromatography–mass spectrometry
HPLC	High-performance liquid chromatography
LC–MS	Liquid chromatography–mass spectrometry
LC–MS/MS	Liquid chromatography–tandem mass spectrometry
MALDI-TOF	Matrix-assisted laser desorption/ionization–time of flight
MANU	Macedonian Academy of Sciences and Arts

MS^n	Multi-stage tandem mass spectrometry
TLC	Thin-layer chromatography
UKIM	Ss. Cyril and Methodius University in Skopje

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