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The transformation of titrimetric methods in pharmaceutical, herbal and food analysis: a literature review (2013–2026s)

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ABSTRACT: The development of analytical methods in the fields of pharmaceuticals, plant/herbal ingredients, and food shows a significant transformation from classical titrimetry toward more selective and efficient instrumental and digital techniques This study aims to evaluate method transformation, comparative validity, and the application of green analytical chemistry (GAC) principles in pharmaceutical, herbal, and food analysis based on a literature review. A non-systematic narrative literature review was conducted on 28 Scopus-indexed journal articles covering titrimetry, UV-Vis spectrophotometry, chromatography (HPLC and RP-HPLC), Karl Fischer, atomic spectrometry, as well as µPAD-based innovations, conductometry, and digital analysis. The synthesis showed that classical methods remain relevant because of their simplicity, low cost, and accessibility, but their selectivity may be limited in complex matrices. Instrumental methods generally provide improved precision, accuracy, and selectivity, particularly for multicomponent samples, whereas miniaturization and digitization enhance analytical efficiency and reduce resource requirements. However, explicit integration of GAC principles remained limited, with only 7 of the 28 reviewed studies demonstrating identifiable green analytical strategies. These findings indicate that analytical modernization does not necessarily result in greener methods. Overall, analytical method development is increasingly integrative, combining classical and instrumental approaches according to analytical requirements, matrix complexity, and sustainability considerations. This review therefore provides a structured evaluative framework for selecting and transforming analytical methods across pharmaceutical, herbal, and food matrices.

KEYWORDS: Analytical methods; food analysis; green analytical chemistry; herbal materials; pharmaceutical analysis.

▪ INTRODUCTION

The development of analytical methods in pharmaceuticals, plant/herbal ingredients, and food has evolved in response to increasing demands for accuracy, precision, selectivity, cost efficiency, and compliance with quality standards. Historically, classical methods based on titrimetry, including acid–base, redox, complexometric, and precipitation titrations, have provided an important foundation for quality control because of their procedural simplicity and well-established stoichiometric principles [1]–[5]. Studies on non-aqueous titrimetry for diuretic drug candidates demonstrate that classical methods can provide high linearity and precision when appropriately optimized [6]. Similarly, iodometric methods for amoxicillin and β-lactam antibiotics indicate that classical redox approaches remain applicable to pharmaceutical quality testing and can be combined with spectrophotometry to improve analytical flexibility [2], [7]. EDTA-based complexometric methods have also provided accurate results for minerals and electrolytes in pharmaceutical preparations and food products [3], [7], [8]. In herbal analysis, permanganometric titrimetry has been applied successfully to tannin determination [9], [10], while iodometric methods remain applicable to vitamin C determination in fruits and medicinal plants [11], [12]. Thus, titrimetry remains relevant, particularly in laboratories requiring simple, economical, and accessible analytical procedures.

However, increasing matrix complexity and the demand for higher selectivity have encouraged the adoption of instrumental approaches, including UV–Vis spectrophotometry, high-performance liquid

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chromatography (HPLC), coulometry, and atomic spectrometry [13]–[16]. Comparative analysis of acetylsalicylate demonstrates that spectrophotometry may provide higher precision than titrimetry under certain conditions, although limitations in absolute accuracy remain [13]. HPLC has demonstrated superior selectivity and reproducibility for pharmaceutical formulations, particularly when excipient interference is present [14]. In herbal analysis, RP-HPLC-UV and coulometric approaches enable the separation and quantification of individual organic acids, improving analytical validity compared with conventional acid–base titration [16]. Similarly, Karl Fischer analysis provides greater selectivity for moisture determination than loss on drying, particularly in plant materials containing volatile compounds [17], [18]. For sodium determination in food, comparisons of FAAS, FAES, ICP-AES, and thermometric endpoint titrimetry demonstrate that method selection should consider accuracy, cost, and analysis time [15]. The analysis of kombucha fermentation further shows that combining titration with HPLC can provide complementary information on total acidity and specific organic acids [19]. These findings indicate that instrumental methods do not necessarily replace classical approaches but can function complementarily to improve analytical reliability.

Recent developments have further incorporated miniaturization into analytical workflows, increasingly reflecting the principles of green analytical chemistry (GAC) [20]. Paper-based analytical devices have enabled redox titrimetric procedures for alcohol and antibiotic analysis to be adapted into portable systems with simplified procedures and reduced reagent requirements [7], [21]. Microfluidic paper-based analytical devices (μPADs) have also been applied to argentometric chloride determination without indicators or additional instrumentation, providing a distance-based detection strategy with reduced analytical requirements [22], [23], while broader developments in μPAD technology have demonstrated their potential as low-cost, portable, and easily fabricated analytical platforms [24]. Conductometric alternatives for chloride analysis provide a more environmentally friendly, faster, and cheaper approach while maintaining reliable analytical performance [25]. In addition, webcam-assisted EDTA complexometric titration for calcium determination in dairy products can improve endpoint objectivity and reduce dependence on visual judgment [26]. Integration of pH and conductivity measurements into titration systems has also demonstrated the potential to improve analytical performance in complex matrices [5]. These developments suggest that analytical modernization is increasingly directed not only toward precision and selectivity but also toward efficiency, accessibility, resource reduction, and sustainability [7], [21], [23], [26]

Despite these developments, the literature remains fragmented across specific analytes, matrices, and analytical technologies. Previous studies have independently addressed antibiotics and antihypertensive drugs [14], [21], vitamin C and plant secondary metabolites [9], [12], and minerals and electrolytes in pharmaceutical and food matrices [3], [15] Innovations such as simplified acid–base titration for determining the degree of deacetylation of chitosan have also not been integrated into a broader cross-matrix analytical framework [27]. In herbal analysis, geographical variation and processing conditions may alter phytochemical composition, emphasizing the need for robust and reproducible methods [9], [17]. Pharmaceutical excipients may interfere with analyte determination, making method selectivity an important consideration, particularly in multicomponent formulations [28]. Furthermore, although several studies incorporate elements of GAC, the integration of analytical performance, matrix complexity, method transformation, and sustainability remains insufficiently synthesized across pharmaceutical, herbal, and food applications [20], [24], [29]

Therefore, this study aims to evaluate the transformation and validity of analytical methods in pharmaceutical, herbal, and food analysis through a comparative literature review informed by GAC principles. Specifically, the review addresses three questions: (1) how classical analytical methods have transformed toward instrumental and digital approaches; (2) what advantages, limitations, and levels of validity distinguish classical from instrumental methods across pharmaceutical, herbal, and food matrices; and (3) how matrix complexity is addressed while incorporating GAC principles into analytical method development. By synthesizing the available evidence, this study proposes an integrated framework in which classical, instrumental, miniaturized, and digital methods are viewed as complementary components of a rational analytical strategy. This framework emphasizes that analytical method selection is an adaptive process guided by analytical performance, matrix characteristics, resource requirements, and sustainability considerations.

MATERIALS AND METHODS

This study employed a structured narrative literature review design to analyze the transformation and validity of analytical methods applied in pharmaceutical, herbal, and food matrices. The narrative review approach was selected because it enables a conceptual synthesis and comparative evaluation of analytical methods without the strict procedural constraints required in systematic reviews, while still maintaining transparency in the selection and analysis of literature sources.

A total of 28 peer-reviewed research articles published in international scientific journals were used as data sources. These articles were selected because they reported the application, modification, or evaluation of analytical methods relevant to the scope of this review. The overall review procedure followed several stages, including literature identification, full-text reading, data extraction, method categorization, and comparative thematic synthesis, as illustrated in Figure 1.

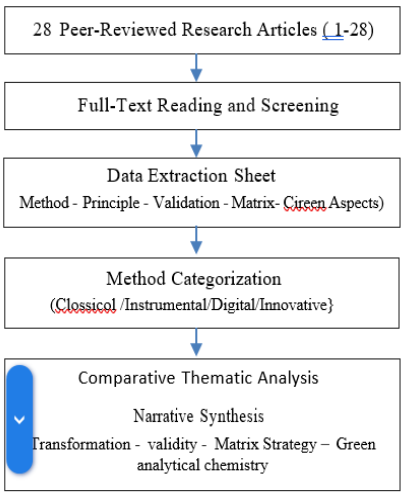

Figure 1. Structured narrative literature review process.

Information from each article was systematically recorded using a data extraction sheet developed for this study. The extracted variables included the type of analytical method, underlying analytical principle, reported validation parameters (such as linearity, precision, accuracy, detection limits, and robustness), analytical matrix (pharmaceutical, herbal, or food samples), and any reported aspects related to green analytical chemistry. Articles were included if they reported the development, validation, or application of analytical methods relevant to pharmaceutical, herbal, or food matrices.

The collected information was subsequently organized according to the type of analytical method and application matrix to facilitate comparative evaluation. The extracted data were then analyzed using a comparative thematic analysis approach to identify key patterns in the literature, including the transformation of classical analytical methods into instrumental or digital approaches, differences in validation characteristics between methods, strategies for addressing matrix complexity, and the integration of green analytical chemistry principles, illustrated in Figure 2.

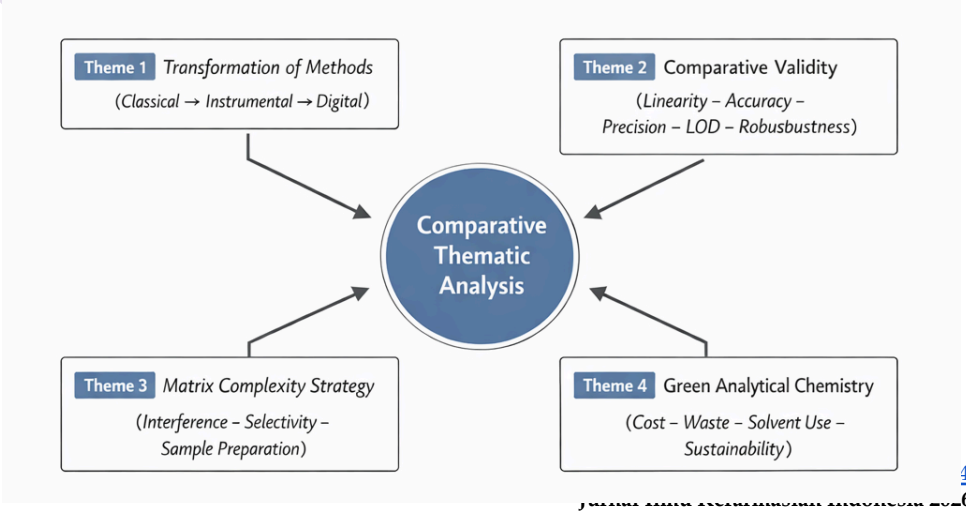

Figure 2. Comparative thematic analysis framework.

Finally, the findings from the selected articles were synthesized narratively by comparing methodological characteristics and reported validation outcomes across studies. This approach allowed the identification of methodological trends and conceptual relationships between analytical techniques applied in different analytical matrices.

▪ RESULTS

Distribution of types of analysis methods used in 28 articles

Table 1. Research mapping of titrimetric methods in pharmaceutical, herbal and food analysis for the period 2015–2026.

No	Research title	Research sample	Author	Year	Main ınsight	Theory used research	Research method	Research results	Limitations	Correlation with research
1	Novel and Validated Non-Aqueous Titrimetric Method for Determination of Perspective Potassium-Sparing Diuretic Drug Candidate in Pure Form and Pharmaceutical Formulation	4-GBA (diuretic candidate) in pure form and pharmaceutical formulations	Ivanov A., Smirnov I., Murashko T., Trusova M., Stepanova E.	2021	Development of a validated non-aquadest titrimetric method for weak base compounds	Non-aqueous acid-base theory; potentiometry	Titration of $HClO_4$ in glacial acetic acid; potentiometric and visual detection	Linearity $r^2 > 0.99$; recovery 98–103%; RSD ≤ 2%	Limited to one compound; not compared to chromatographic methods	Relevant for the development of simple methods in the analysis of drugs and herbal compounds that have weak acid/base properties.
2	New Applications for Amoxicillin Determination in Pure Form and Pharmaceuticals Based on Iodate-Iodide Mixture	Amoxicillin bulk and pharmaceutical preparations	Qarah N.A.S., Abdulrahman S.A.M., Algethami F.K., Basavaiah K., El-Maaiden E.	2020	Combination of titrimetry and iodometric-based spectrophotometry	Iodometric redox theory; Beer-Lambert law	Iodometric titration and UV-Vis spectrophotometry (370 nm and 570 nm)	Sensitive method; adequate LOD and LOQ; suitable for QC	Requires strict control of reaction conditions	Very relevant for the analysis of pharmaceuticals and food/herbal materials that have reducing groups.
3	Quantification of Iron(II) in Supplements Using Redox Titration and UV–Visible Spectroscopy	Iron supplements (OTC)	Quiñones R., Knott H., Frost L., Bartram M., Clark T., Westfall T.D., Buxó J.A.	2024	Comparison of classical and instrumental methods with statistical analysis	Teori redoks Fe^{2+}/Fe^{3+}; komplek s Fe-phenanthroline; Beer-Lambert	Titration of $KMnO_4$ and UV-Vis	No significant difference (t-test, F-test); comparable results	Educational focus; not full industry validation	Relevant for mineral analysis in fortified foods and supplements
4	Lab on Paper: Assay of Beta-Lactam Pharmaceutica	Amoxicillin and ampicillin (Kenyan	Myers N.M., Maina M.W., Were	2019	Development of paper-based	Iodometric back titration theory; beta-lact	Base degradation → reaction I_3^- →	Error 4–5%; able to detect substand	Lower precision than HPLC	Relevant for rapid screening of herbal/food ingredients

No	Research title	Research sample	Author	Year	Main ınsight	Theory used research	Research method	Research results	Limitations	Correlation with research
	ls by Redox Titration	market samples)	P.M., Karwa R., Pastaki a S.D., Sharp J.C., Luther J.L., Cooper A., Bliese S., Oberho f N., Aldulai mi D., Lieber man M.		iodome tric assay for detectio n of substan dard drugs	am degradat ion	back titration of thiosulfat e	ard drugs at 40–60% concentra tion		or substandard pharmaceut ical products
5	Determination of Iron in Some Selected Iron Containing Tablets Using Redox Titration	Fe (ferrous fumarate) tablets	Balarab e M.A., Folasha de A.Z.	2019	Determ ination of Fe levels using perman ganome try	Redox theory $Fe^{2+} \rightarrow Fe^{3+}$ by $KMnO_4$	Permang anometri c titration	There is variation in actual vs label levels	There is no complete statistical validation	Relevant for Fe mineral analysis in tablet preparation s
6	Novel Titrimetric Method for the Determination of Rosuvastatin in Pure Form	Pure rosuvasta tin	Khagga B.S., Ghanu kota S., Mogili S.	2023	EDTA comple xometri c method for drug analysis	Comple xometric theory (EDTA); Eriochro me Black T indicator	EDTA-M g titration at pH 12–13	Percenta ge content 103.05%	There is no inter-day precision testing or recovery testing.	Relevant for the analysis of compounds that can form metal complexes in herbal and food matrices.
7	Comparative Quantitative Study of Acetyl Salicylic Acid in Aspirin Samples Using Spectrophoto metry and Volumetric	Commerc ial aspirin tablets (14 samples)	Khaled Hreeba et al.	2025	Compa rison of titrimet ric vs spectro photom etric accurac y for ASA	Acid-bas e neutraliz ation theory, Beer-La mbert law	Back titration and UV-Vis	Spectrop hotometr y is more precise; variation s in levels between brands	The accuracy of both methods is still limited	Relevant for drug analysis and simple method validation on pharmaceut ical and food matrices
8	First Step Analysis in Quality Control – Volumetric Analysis	Raw materials and pharmace utical products	Moham ad Taleuzz aman and S.J. Gilani	2017	Titrimet ry as an initial QC method	Principle s of titrimetr y (acid-bas e, redox, complex ometry)	Review of volumetr ic methods	Cheap and fast method for initial QC	Low selectivity compared to HPLC	It is important to initial screening of herbal and food materials before further analysis.

No	Research title	Research sample	Author	Year	Main ınsight	Theory used research	Research method	Research results	Limitations	Correlation with research
9	Titrimetric Assay of Some Antihistamines with PFC Reagent	Antihistamines (CPH, FFH, PMH, PM)	Ajay K. Pandey and D. Dwivedi	2018	Iodometric method using PFC	Oxidation–reduction theory, stoichiometry	Redox titrimetry	Accurate, precise (SD and CV validated)	Limited to certain compounds	Relevant for the analysis of oxidizable plant bioactive compounds
10	A Comparative Review of Methods for Estimation of Some Antihypertensive Drugs	Antihypertensive drugs (TEL, CAP, IRB, VAL, etc.)	Ayad K. Fadhil et al.	2021	Comparison of HPLC, CE, UV, titrimetry	Titrimetry and chromatography theory (HPLC, HILIC, ZIC-HILIC)	Comparative review of methods	The most precise and selective HPLC	Expensive costs and instruments	Relevant for the development of analytical methods for complex compounds in food and herbs
11	Influence of Organic Acids Excipients: Comparative Analysis of Aspirin	Aspirin tablets (6 brands)	Anthony O. Ochieng	2025	The effect of acid excipients on the analysis results	Matrix interference theory and stability	Titrimetry, UV-Vis, HPLC	HPLC is most accurate; titrimetry overestimates	Simple methods are less robust	Highly relevant for food/herbal analysis with complex matrices
12	Combining pH and electrical conductivity measurements to improve titrimetric methods to determine ammonia nitrogen, volatile fatty acids and inorganic carbon concentrations	24 digestate samples from the anaerobic digestion unit	C. Charnier, E. Latrille, L. Lardon, J. Miroux, J.P. Steyer	2016	Integration of pH and conductivity measurements improves titrimetric accuracy.	Acid-base equilibrium theory, buffer capacity, ionic conductivity	Sensor-based titrimetry (SNAC: pH + conductivity)	$R^2 \approx 0.94–0.95$; lower error than classical methods	Requires complex mathematical models and calibration	Relevant for the development of modern titrimetric methods in food and environmental analysis
13	Using Classical EDTA Titrations To Measure Calcium and Magnesium in Intravenous Fluid Bags	IV bag Ca gluconate and Mg sulfate	I.W. Kimaru, A.T. Coriglia no, F. Zhao	2018	EDTA titration is effective for pharmaceutical electrolyte quality control	Complexometric theory (EDTA–metal chelation)	Complexometric titration according to USP	Determine Ca and Mg levels accurately	Limited to divalent metals	Relevant for pharmaceutical quality control
14	Tannin Concentration of Gyrinops Tea Taken From Different Agarwood Plantation and Different	Gyrinops versteegii leaves (3 locations, 2 processing methods)	I.G.A.S. Wangiyana, Supriadi, A. Nikmatullah, Sunarpi	2021	Location and drying affect tannin levels	$KMnO_4$–Indigo carmine redox reaction	Permanganometric titrimetry	Dried leaves from Kekait have the highest tannin content	Not compared with instrumental methods	Relevant for standardization of herbal ingredients and phytochemi

No	Research title	Research sample	Author	Year	Main ınsight	Theory used research	Research method	Research results	Limitations	Correlation with research
	Processing Method		, L. Mulyaningsih							cal analysis of food
15	Water Content Determination in Different Varieties of Cannabis Flowers	>40 varieties of medical Cannabis	M. Miloshevska, I. Slaveska Spirevska, N. Nakov, G. Stefkov, A. Dimitrovska, J. Acevska	2023	Karl Fischer is more selective than LOD	Karl Fischer redox reaction	Semi-micro Karl Fischer titration	Moisture content 3.8–8.5%; selective and rapid method	Need homogenization and special tools	It is important to validate the water content of herbal and pharmaceutical ingredients.
16	Qualitative and Quantitative Determination of Organic Acids in Crude Herbal Drugs and Medicinal Herbal Preparations	Rosaceae fruits (hawthorn, rosehip, etc.)	E.V. Sergunova, A.A. Sorokina, D.O. Bokov, A.I. Marakhova	2019	Combination of modern methods improves the precision of organic acid analysis	Acid-base theory, redox, reverse phase chromatography	Coulometry, potentiometry, RP-HPLC-UV	HPLC is more selective and precise than classical titration.	Requires expensive instrumentation	Highly relevant for the analysis of herbal bioactive components
17	Water Determination in Plants by Karl Fischer with Extraction	Various parts of the plant (bark, roots, rhizomes, seeds, etc.)	C. Ma, J. Aplin, N. Lo, T.T. Xu, V.S.K. Goldman, S. P., P.R.R. Vadaparthi	2026	KF with formamide extraction is more accurate and more environmentally friendly	Karl Fischer reaction and extraction principles	KF direct titration with extraction (DTE)	Valid (accuracy, repeatability, robustness)	Need to optimize the extraction process	Supporting green analytical chemistry for herbal & food
18	Spectrophotometric and Titrimetric Analysis of Phytoascorbate	16 types of plants (fruit & leaves)	A.K. Tantray, S.A. Dar, S. Ahmad, S.A. Bhat	2017	DNPH spectrophotometry is more sensitive than titration	DNPH derivatization and iodine/DCIP redox reactions	Spectrophotometry and redox titration	DNPH produces higher levels of vitamin C	Titration is less sensitive	Relevant for vitamin analysis in food & herbs
19	Assay of sodium in food: comparison of different preparation methods and	Tomato sauce (ketchup), low-sodium sauce, spiked sample	Ploegaerts, Desmet, Van Krieken	2015	Evaluation of 12 sodium analysis protocols in food	Atomic spectroscopy (FAAS, FAES, ICP-AES), thermo	Sample preparation (dispersion, wet digestion, dry ashing) +	All methods are accurate (recovery ~100%); TET and dry	ICP-AES is expensive; some methods take a long time	Relevant for validation of mineral analysis methods in food and herbal ingredients

No	Research title	Research sample	Author	Year	Main ınsight	Theory used research	Research method	Research results	Limitations	Correlation with research
	assay techniques					metric titrimetry (TET)	FAAS, FAES, ICP-AES, TET	ashing–FAAS are the most efficient.		
20	Titration and HPLC Characterization of Kombucha Fermentation	21-day fermented kombucha	Miranda, Lawton, Tachibana, Swartz, Hall	2016	Monitoring fermentation kinetics through acid analysis	Acid-base theory, Gran Plot, liquid chromatography (HPLC)	Potentiometric titration and HPLC (standard addition)	Total acid increased linearly (1.5 mM/day); method validation by t-test	Non-selective titration of specific acids	Relevant for analysis of herbal fermentation products and validation of quantitative methods
21	Determination of Vitamin C content in Citrus Fruits and in Non-Citrus Fruits by Titrimetric Method	Orange, lemon, grapefruit, mango, papaya	Tareen, Mengal, Masood, dkk.	2015	Determination of vitamin C levels using the iodimetric method	Redox theory (ascorbic acid–iodine)	Iodometric titration	Highest vitamin C in oranges (12.78 mg/100 mL)	Results are influenced by maturity and extraction method.	Relevant for phytochemical analysis of plant and herbal materials
22	A facile approach for the determination of degree of deacetylation of chitosan using acid-base titration	Chitosan various grades	Dutta, Priyanka	2022	Simple titration method with new equation for DD of chitosan	Acid–base theory; 13C-NMR validation	HCl–NaOH titration and NMR validation	DD 77–91%, as per specification and NMR validated	Strict control of normality and sample preparation is required.	Relevant for the analysis of pharmaceutical excipients and herbal biomaterials
23	Redox titration on foldable paper-based analytical devices for alcohol determination in whiskey	44 whiskey samples (original and confiscated)	Nogueira, Lemes, Chagas, dkk.	2019	Development of µPAD for portable alcohol analysis	Redox theory (permanganometry)	Redox titration on paper-based devices	Linear 0–50% (R^2=0.992); LOD 2.1%	Limited reagent stability (~40 min)	Relevant for the development of portable analytical methods in food/herbs/pharmaceuticals
24	Indicator-Free Argentometric Titration for Distance-Based Detection of Chloride Using Microfluidic Paper-Based Analytical Devices	Tap water, standard chloride solution	Longfei Cai; Zhuang Ouyang; Jiahong Song; Liye Yang	2020	Developing a µPAD-based indicatorless argentometric titration with zone length-based detection	Precipitation theory ($Ag^+ + Cl^- \rightarrow AgCl$), argentometry, distance-based detection	µPAD-based laboratory experiment; measurement of color band length after UV exposure	LOD 1.7 mg/L Cl^-; results equivalent to conventional titration	Limited to insoluble silver salt-forming analytes; UV optimization required	Relevant for the development of simple, portable, and low-cost analytical methods on food and herbal matrices containing chloride or inorganic ions.

No	Research title	Research sample	Author	Year	Main ınsight	Theory used research	Research method	Research results	Limitations	Correlation with research
25	Instrument-free Argentometric Determination of Chloride via Trapezoidal Distance-Based Microfluidic Paper Devices	Biological fluids (serum, urine, sweat), drinking water, river water	Mohammad Rahbar; Brett Paull; Mirek Macka	2019	The trapezoidal channel design improves the sensitivity of distance-based detection.	Argentometry (Mohr Method), AgCl precipitation, paper microfluidics	µPAD with trapezoidal channel design; color zone length measurement	LOD 0.05 mM; higher sensitivity than square channel	Optimization of channel geometry and reagent concentration is required.	Provides the basis for the design of portable analytical devices for microfluidic-based pharmaceutical and food analysis.
26	Vitamin C Determination in Foods. Titrimetric Methods – A Review	Fruits, vegetables, fortified food products	Sofia Popescu; Tania-Ștefania Chiș; Miruna Georgiana Chiricuță; Antonia-Claudia Vârlan; Luminita Pîrvulescu; Ariana Velciov	2024	Comprehensive review of titrimetric methods for vitamin C	Redox theory (AA ↔ DHAA), iodimetry, DCPIP titration	Literature study (review article)	The titrimetric method is economical and suitable for routine analysis.	Interference with other reducing compounds; lower sensitivity than HPLC	Relevant for the analysis of herbal and food ingredients containing antioxidants
27	Conductimetry: a Rapid Alternative Technique for Chlorides Determination in Cheese	Molido Nariñense Cheese with NaCl variation	Jessica Aguirre-Londoño; Víctor Alexander Aristizabal-Ferreira; Sandra Patricia Castro-Narváez; Juan Sebastián Ramírez-Navas	2019	Conductometry can replace potentiometry for chloride analysis.	Ionic conductivity theory; argentometric precipitation as a comparison	Comparative experiment (potentiometry vs. conductometry)	Significant correlation; faster and more environmentally friendly method	Limited to cheese matrix; validation of other matrices required	Provides an alternative approach to the analysis of inorganic ions in food and pharmaceutical materials.
28	Application of the Semi-Automatic Titration Method Using	Milk, yogurt, cream, cottage cheese	Alexander Shyichuk; Dorota	2025	RGB camera can be used as an	Complexometry (Ca-EDTA), calcein	Semi-automatic titration with webcam;	Very high linearity (R^2=0.9999); RSD 0.3–2.9%	Limited to colored analytes/color-based indicators	Highly relevant for innovation of pharmaceut

No	Research title	Research sample	Author	Year	Main ınsight	Theory used research	Research method	Research results	Limitations	Correlation with research
	a Webcam for the Determination of Calcium in Milk and Dairy Products		Ziółkowska; Iryna Shyychuk; Maria Kowalska		EDTA titratıon endpoint detector	and HNB indicators, RGB image analysis	color signal analysis (RGB and Hue)			ical and food analysis methods based on low-cost digital detection.

The analytical methods identified across the 28 reviewed studies (Table 1) were classified into five main categories: classical titrimetry, UV–Vis spectrophotometry, chromatography and advanced instrumental techniques, Karl Fischer titration for moisture analysis, and innovative approaches based on miniaturization and digitization. Classical acid–base, redox, complexometric, and precipitation titrations remain applicable to routine quantitative analysis because of their simplicity and accessibility. The reviewed studies also show increasing consideration of reagent consumption, waste generation, energy requirements, and environmental impact alongside analytical performance.

The reviewed studies demonstrate multiple pathways of analytical modernization. UV–Vis spectrophotometry was used independently or in combination with titrimetric methods, while HPLC, RP-HPLC-UV, atomic spectrometry, and Karl Fischer titration provided instrumental approaches for pharmaceutical, herbal, and food analysis. Classical titrimetric procedures were further integrated with paper-based and microfluidic platforms, conductometric detection, and webcam-assisted endpoint determination. The incorporation of pH and conductivity measurements enhanced conventional titration systems, while acid–base titration supported by ^13C-NMR demonstrated the use of an independent instrumental technique for method validation. Overall, these studies indicate that analytical development increasingly combines classical procedures with instrumental, miniaturized, and digital approaches. Quantitatively, 16 studies employed titrimetric methods as primary or complementary approaches, whereas 13 employed modern instrumental methods, reflecting overlap between methodological categories and indicating that classical and modern techniques function as complementary rather than mutually exclusive approaches.

Among the 28 reviewed studies, UV–Vis spectrophotometry was applied either independently or in combination with titrimetric methods (e.g., Studies 2, 7, 9, and 12). Chromatographic techniques, including HPLC, RP-HPLC-UV, and HILIC, and atomic spectrometric techniques, including FAAS, FAES, and ICP-AES, were reported in several studies (Studies 13–17). Karl Fischer titration was used for moisture-content determination (Studies 18–19). Further developments included paper-based analytical devices (PADs and μPADs), conductometric detection, and webcam-assisted endpoint determination (Studies 20–24). Study 25 integrated pH and conductivity measurements into an SNAC titration system, while Study 26 used acid–base titration supported by ^13C-NMR spectroscopy for method validation. Overall, 16 studies employed titrimetric approaches as primary or complementary methods, whereas 13 employed modern instrumental approaches as primary or complementary methods.

Objects and analysis matrices in reviewed articles

The 28 reviewed studies covered three main categories of analytical objects: pharmaceutical ingredients, herbal and plant materials, and food products, as illustrated in Figure 3. Pharmaceutical studies included diuretic drug candidates, amoxicillin and other β-lactam antibiotics, iron supplements, rosuvastatin, antihistamines, antihypertensive drugs, aspirin, and electrolytes in intravenous fluids. Herbal and plant studies addressed tannins in Gyrinops leaves, moisture in Cannabis flowers and plant materials, organic acids in herbal simplicia, vitamin C, and fruits. Food-related studies included sodium in food, kombucha fermentation, vitamin C, chloride in cheese and water samples, calcium in milk, and alcohol in beverages. μPAD-based studies also examined chloride in water and biological fluids. Overall, 12 studies focused on pharmaceutical matrices, 8 on herbal and plant materials, and 9 on food products, with some studies involving more than one matrix category. All reviewed studies involved real samples or matrices rather than relying exclusively on pure standards.

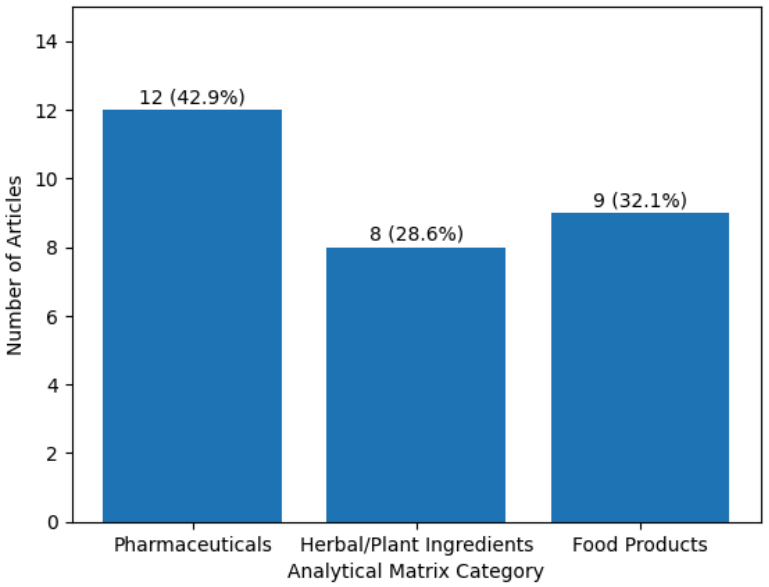

Figure 3. Distribution of analytical objects and real matrices in the reviewed studies (n = 28).

Reported validation parameters

The reported validation parameters included linearity, precision, accuracy (recovery), limits of detection and quantification (LOD and LOQ), repeatability, robustness, and statistical tests such as t-test, F-test, and ANOVA, as summarized in Figure 4. Study 6 reported linearity with a coefficient of determination close to 1 and RSD <2%. Studies 7 and 16 used t-test, F-test, and/or ANOVA at a 95% confidence level to compare analytical methods, with Study 7 reporting no statistically significant difference between the compared methods. Study 12 compared precision between titrimetry and spectrophotometry, while Study 13 evaluated analytical methods based on precision, selectivity, and cost efficiency. Studies 9 and 17 reported repeatability and robustness for Karl Fischer methods, and Study 16 reported recoveries close to 100% for different sodium determination techniques. For detection capability, Study 21 reported a detection limit of 1.7 mg/L for chloride, whereas Study 22 reported an LOD of 0.05 mM. Study 24 demonstrated an R^2 of 0.9999 and RSD values of 0.3–2.9%. Some studies, including Studies 3 and 27, did not report complete validation parameters and instead provided label-level or comparative data.

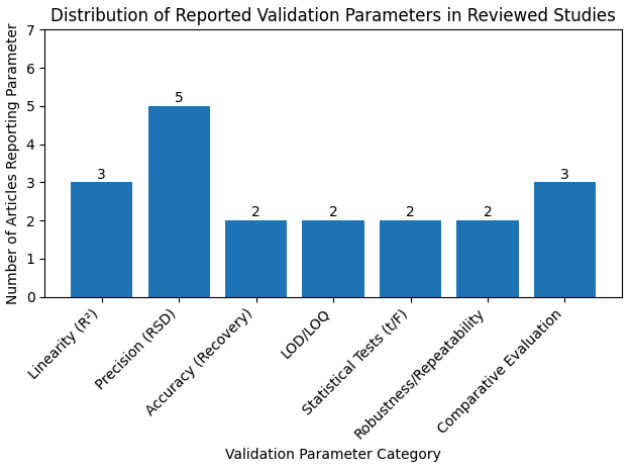

Figure 4. Distribution of reported validation parameters in the reviewed studies.

Forms of transformation of analysis methods

The transformation of analytical methods reported in the literature can be classified into four main forms, as illustrated in Figure 5.

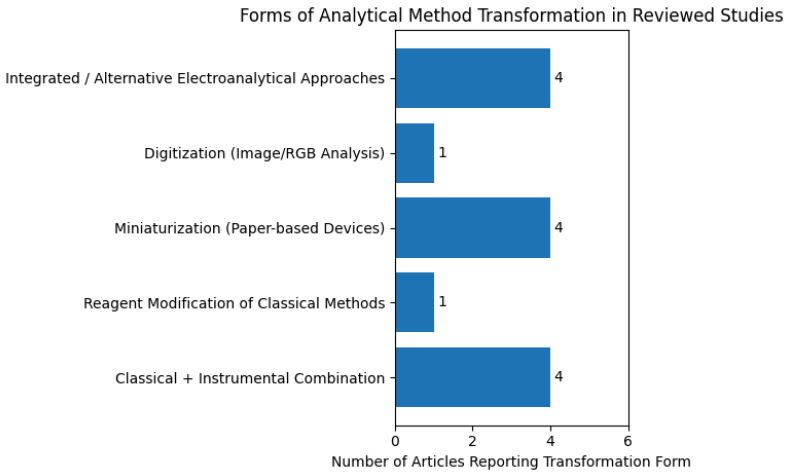

Figure 5. Forms of analytical method transformation reported in the reviewed studies.

The reviewed studies demonstrated several forms of methodological transformation. First, classical titrimetric methods were combined with instrumental techniques, including spectrophotometry and HPLC. Second, classical procedures were modified through changes in reagents, such as the use of pyridinium fluoro chromate (PFC) in antihistamine titration. Third, titrimetric procedures were miniaturized using paper-based devices. Fourth, titration endpoint detection was digitized using webcams and RGB image analysis. Other transformations included the integration of pH and conductivity measurements within a single titration system, the use of conductometry as an alternative detection approach to conventional precipitation titration, and the application of coulometry for the quantification of organic acids. Modification of Karl Fischer analysis through formamide extraction was also reported. Overall, 11 of the reviewed studies demonstrated transformations of classical analytical procedures toward improved selectivity, efficiency, portability, or objectivity.

Matrix complexity and interference

A total of nine reviewed studies reported matrix interference or environmental factors that could affect analytical results, as illustrated in Figure 6. These factors included interference from organic acid excipients in aspirin analysis, geographical and processing-related variation in tannin content, differences in selectivity between titrimetric and RP-HPLC methods for herbal simplicia, and the influence of volatile compounds on loss-on-drying results. Other reported issues included interference from reducing compounds in vitamin C titration, the inability of titration to distinguish individual organic acids, the need for further validation of conductometric methods across different food matrices, and the dependence of webcam-based results on lighting conditions. Overall, the findings indicate that matrix composition, sample characteristics, and measurement conditions can influence analytical results across the reviewed methods.

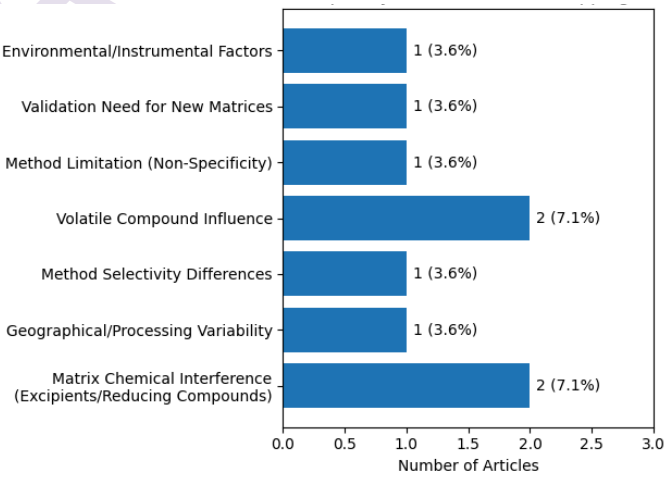

Figure 6. Matrix complexity and interference categorization mapping in the reviewed studies (n = 28).

Aspects of green analytical chemistry

Among the 28 reviewed studies, seven (25.0%) explicitly demonstrated elements consistent with green analytical chemistry (GAC), primarily through reagent reduction, miniaturization, and improved operational efficiency, as illustrated in Figure 7. The reported green strategies included replacing azeotropic toluene distillation with formamide extraction, reducing reagent volumes and chemical waste through paper-based analytical devices, reducing silver nitrate consumption through conductometric approaches, and minimizing the use of additional indicators through digital image analysis. Sensor integration also improved analytical efficiency without increasing reagent consumption. Overall, these findings show that GAC-related strategies were applied across both classical and instrumental analytical approaches.

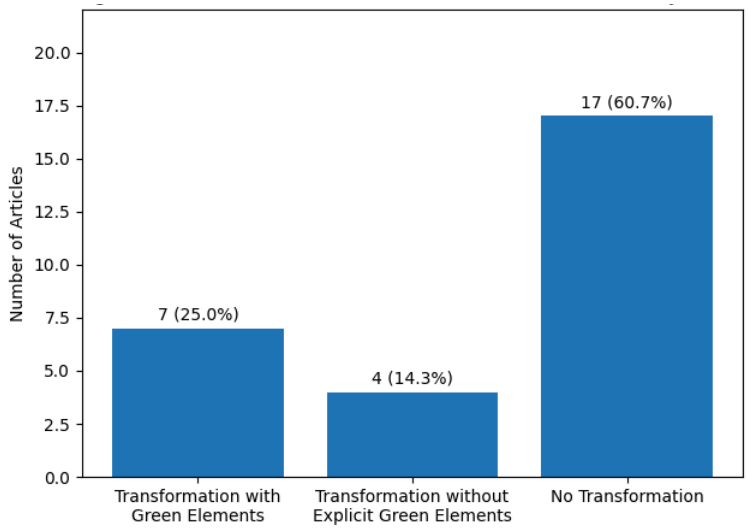

Figure 7. Integration of methode transformation and green sustainability (n=28)

Among the 11 studies that demonstrated methodological transformation, seven explicitly incorporated elements consistent with green analytical chemistry, whereas the remaining studies primarily focused on improving selectivity, analysis time, or instrumental integration without reporting measurable reductions in reagent consumption or waste generation. Some studies did not explicitly use the term green analytical chemistry but reported practices consistent with selected green principles, such as reduced reagent volumes, shortened analysis time, miniaturization, or simplified analytical procedures. Overall, the findings indicate that methodological transformation and GAC-related practices did not always occur simultaneously, with some innovations improving analytical performance without explicitly incorporating environmental considerations.

▪ DISCUSSION

Transformation of classical methods towards ınstrumental and digital approaches

The synthesis findings show that the transformation of analytical methods in the fields of pharmaceuticals, herbal ingredients, and food does not take place in a substitutional manner, but integrative and evolutionary (Figure 2). The literature demonstrates that classical titrimetry methods remain a key foundation in many studies, mainly due to their clear stoichiometric principles, low cost, and ease of operation [1–5]. The development of non-aqueous titrimetry for diuretic drug candidates suggests that optimization of solvents and titrants can result in high linearity and precision that meet validation criteria [6]. In the analysis of antibiotics and antihistamines, modification of redox reagents such as iodate-iodide and PFC demonstrates that classical methods can be extended in scope without dependence on complex instruments [2], [6], [21]. Even in iron analysis, redox titration shows statistical equivalence with UV–Vis spectrophotometry based on t- and F- test [3], [8]. These findings suggest that classical methods are still scientifically competitive in certain contexts.

Nevertheless, matrix complexity encourages the use of instrumental techniques such as HPLC, RP-HPLC, and ICP-AES to improve selectivity and precision [14]–[16], [21], [28]. In aspirin analysis, comparative analytical approaches demonstrate differences in precision and accuracy between instrumental and titrimetric methods [13], [28]. In the analysis of kombucha fermentation, the combination of titration and HPLC allows the quantification of total acidity and identification of specific acids [19]. For herbal ingredients, RP-HPLC-UV can provide improved selectivity for the determination of individual organic acids [16]. Karl Fischer analysis offers greater selectivity for moisture determination than loss on drying, particularly in plant materials containing volatile compounds [17]. These findings suggest that instrumental methods are often used as complementary or confirmatory approaches rather than as complete substitutes for classical methods.

Further developments are seen in the miniaturization and digitization of classical methods. Paper-based devices (PADs and µPADs) allow redox and precipitation analysis with minimal reagent consumption [7], [22], [24], [37], [38], [41]. Distance-based argentometric detection provides competitive detection limits without additional instrumentation [22]. The integration of webcams into complexometric titration reduces endpoint subjectivity and improves precision[16]. Conductometry, as an alternative to precipitation titration, also shows a strong correlation with standard methods [6], [25]. The integration of pH and conductivity sensors in SNAC systems demonstrates that physicochemical parameters can be combined to improve accuracy [5]. Overall, these findings confirm that analytical method transformation is adaptive and innovative while maintaining the fundamental principles of classical analytical chemistry.

The significance of this finding lies in clarifying that the development of analytical methods does not mean abandoning classical methods, but rather adapting them to meet modern demands. The present study contributes to the field of analytical methods by compiling a methodological evolution map that demonstrates continuity between traditional techniques and modern technologies. This perspective is particularly relevant to analytical laboratories seeking practical and sustainable approaches, where simple and cost-effective methods can remain valuable for reliable quality control across pharmaceutical, herbal, and food matrices [34], [40], [42]. The conceptual contribution of this research is to strengthen an integrative paradigm for the development of pharmaceutical, herbal, and food analytical methods.

Advantages, limitations, and validity of methods

The synthesis demonstrates that classical methods excel in simplicity, cost efficiency, and ease of implementation [1], [28], [31], [40]. Non-aqueous titrimetry and complexometric methods show acceptable precision and recovery [4], [6], [10]. In the analysis of vitamin C and iron, titrimetric methods provide valid and reproducible results [11], [43]. However, the main limitation of classical methods is their lower selectivity in complex matrices, especially when excipients or interfering components are present [40], [42]–[45]. In aspirin analysis, organic acid excipients caused overestimation of the analyte level by titrimetry[13], [28]. In tannin analysis, geographical and processing variations affect quantification results [9]. These findings demonstrate that the validity of classical methods is highly dependent on matrix characteristics and homogeneity.

In contrast, instrumental methods such as HPLC and RP-HPLC show high selectivity due to the separation stage before detection [14], [16], [19], [21], [28]. Atomic spectrometry techniques for sodium analysis provide high accuracy, with recovery close to 100% [1], [15]. Karl Fischer analysis provides selective determination of water, particularly in plant materials containing volatile compounds [17], [18]. UV–Vis spectrophotometry can provide higher sensitivity or precision than in some analyses [15], [28]. However, instrumental methods have limitations, including higher costs, instrument maintenance requirements, and operational complexity [26], [30], [36], [42], [45]. Furthermore, spectrophotometric methods remain susceptible to spectral interference, particularly in complex matrices [13], [43].

From a critical standpoint, method validity should be assessed contextually according to the analyte and matrix rather than as an absolute measure [42], [44]. A critical synthesis of the reviewed literature indicates that a tiered approach—using titrimetry for routine or preliminary analysis and instrumental methods for confirmation or complex matrices—is a rational strategy supported by the literature [40], [42], [44], [46]. The significance of these findings is that method selection should consider analytical performance, efficiency, matrix characteristics, and resource requirements [40], [42], [44]. The contribution of this research is to clarify a comparative evaluation framework for classical and instrumental methods based on empirical evidence from the reviewed studies.

Matrix complexity and green analytical chemistry

The findings suggest that matrix complexity is a major factor affecting analytical accuracy[19], [31], [47]. Excipient interference in pharmaceutical formulations [28], variations in plant composition due to geographical and processing factors [42], and the presence of volatile compounds in herbal ingredients are concrete examples reported in the literature. In kombucha fermentation, titration cannot distinguish individual organic acids and therefore requires HPLC confirmation [19]. In vitamin C analysis, other reducing compounds can interfere with the redox reaction [12], [43] These findings demonstrate that controlling matrix complexity is essential for method validity.

The literature also shows the application of green analytical chemistry principles through miniaturization and reduction of hazardous reagents. µPADs and PADs reduce reagent volumes and chemical waste [20]-[22]. Conductometry reduces the use of silver nitrate consumption [43]. The use of formamide in Karl Fischer is a more environmentally friendly alternative to toluene distillation [19]. Digitizing titration endpoints with webcams reduces dependence on visual recognition and operator judgment [26]. The integration of pH and conductivity sensors in SNAC systems improves the robustness of titrimetric analysis while maintaining the practical advantages of titration for small-scale monitoring [5]. Such methodological improvements are consistent with the broader GAC emphasis on analytical efficiency and resource use [44]. These findings suggest that sustainability principles are increasingly being integrated into analytical method development.

The significance of these findings is to strengthen the relevance of green analytical chemistry in pharmaceutical and food analysis [44]–[46], [48]. The study contributes by integrating empirical evidence that methodological innovations can improve efficiency while maintaining analytical performance [14], [49]. This perspective is particularly relevant to modern laboratories seeking to reduce environmental impact without compromising analytical quality[36], [47].

Research implications

The theoretical implication of this research is to strengthen an integrative paradigm for analytical method development by combining classical principles with modern technologies. The practical implication is a tiered approach in which method selection is guided by matrix complexity, analytical performance, and validation requirements. Paper-based and miniaturized analytical platforms further demonstrate the potential to improve accessibility, reduce analytical scale, and support more resource-efficient workflows [37], [50]. Similarly, developments in green liquid chromatography illustrate how analytical performance can be maintained while reducing solvent consumption and environmental impact [51]. The continued application of simple and economical titrimetric procedures also demonstrates that classical methods remain relevant when appropriately adapted to analytical needs [49]. These findings provide a basis for analytical chemistry curricula that balance classical and instrumental methods and support the design of pharmaceutical and food testing laboratories that consider both analytical quality and sustainability. Overall, this integrative interpretation moves beyond a merely descriptive comparison and advances a structured evaluative framework for method selection across different analytical matrices.

Research limitations

The present study uses a non-SLR literature review design and therefore does not apply a systematic selection protocol or meta-analysis. The analysis is based on 28 predetermined articles, so relevant studies outside the selected literature were not assessed. Furthermore, the synthesis was conducted using a comparative narrative approach without meta-statistical analysis. Variations in validation parameters across studies also limit direct numerical comparisons. Nonetheless, the analysis is based on the empirical evidence presented in Table 1, which summarizes the 28 reviewed articles.

Taken together, these limitations highlight an important conceptual gap: although recent analytical research increasingly incorporates green and sustainable approaches, the evaluation of analytical methods requires consideration of analytical performance, applicability, and environmental impact in an integrated manner [52]. This study addresses this gap by providing an integrative framework for evaluating the transformation and validity of pharmaceutical, herbal, and food analytical methods while incorporating green analytical chemistry considerations.

CONCLUSION

A critical synthesis of 28 reviewed articles indicates that analytical method development in pharmaceutical, herbal, and food analysis is evolutionary and integrative rather than a complete replacement of classical methods by modern instrumental techniques. Acid–base titrimetry, redox, complexometry, and precipitometry remain relevant because of their simplicity, cost efficiency, and ease of implementation, particularly in routine testing and resource-limited laboratories. In contrast, instrumental methods such as UV–Vis spectrophotometry, HPLC, RP-HPLC, ICP-AES, and Karl Fischer offer greater selectivity and precision for complex matrices containing interferents. Method transformation is also reflected in miniaturization and digitization through µPADs, conductometry, pH–conductivity integration, and webcam-based endpoint detection, supporting reagent reduction and analytical efficiency in line with green analytical chemistry principles. Overall, method validity depends on the analyte and matrix context, supporting a tiered, evidence-based strategy that combines classical and instrumental approaches. The main contribution of this review is a structured comparative framework integrating methodological transformation, empirical validity, matrix complexity, and sustainability to guide analytical method selection across pharmaceutical, herbal, and food matrices.

Future research should focus on standardizing robustness and reproducibility, particularly for miniaturized and digital methods, and on experimentally validating tiered analytical strategies across diverse matrices. Further development should incorporate green analytical chemistry through reduced use of hazardous solvents and reagents. Simple digital technologies can also be integrated with classical methods to improve endpoint objectivity and precision without substantially increasing operational costs. Research should further examine how natural matrix complexity affects analytical accuracy under different conditions. These directions can strengthen the integration of analytical validity, operational efficiency, and environmental sustainability in pharmaceutical, herbal, and food analysis.

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REFERENCES

[1] M. R. Gama, W. R. Melchert, and M. Wr, "An overview of the Brazilian contributions to Green Analytical Chemistry," *An. Acad. Bras. Cienc.*, vol. 91, pp. 1–33, 2019.

[2] N. A. S. Qarah, S. A. M. Abdulrahman, F. K. Algethami, and K. Basavaiah, "New Applications For Amoxicillin Determination In Pure Form and Pharmaceutical," *Quim. Nova*, vol. 43, no. 1, pp. 44–49, 2020, doi: 10.21577/0100-4042.20170455.

[3] M. Auwal Balarabe and A. Zainab Folashade, "Determination of Iron in Some Selected Iron Containing Tablets Using Redox Titration," *World J. Appl. Chem.*, vol. 4, no. 3, p. 42, 2019, doi: 10.11648/j.wjac.20190403.13.

[4] M. Taleuzzaman, "First Step Analysis in Quality Control -Volumetric Analysis," *Glob. J. Pharm. Pharm. Sci.*, vol. 1, no. 3, pp. 1–3, 2017, doi: 10.19080/gjpps.2017.01.555564.

[5] C. Charnier, E. Latrille, L. Lardon, J. Miroux, and J. P. Steyer, "Combining pH and electrical conductivity measurements to improve titrimetric methods to determine ammonia nitrogen, volatile fatty acids and inorganic carbon concentrations," *Water Res.*, vol. 95, pp. 268–279, 2016, doi: 10.1016/j.watres.2016.03.017.

[6] M. T. Alexey Ivanov, Ivan Smırnov, Tatyana Murashko and Elena Stepanova, "Novel and Validated Non-aqueous Titrimetric Method For Determination Of Perspective Potassium-Sparing Diuretic Drug Candidate In Pure Form and Pharmaceutical Formulation," *Malaysian J. Anal. Sci.*, vol. 25, no. 1, pp. 95–104, 2021, [Online]. Available: https://mjas.analis.com.my/mjas/v25_n1/pdf/Ivanov_25_1_9.pdf

[7] S. A. Nogueira *et al.*, "Talanta Redox titration on foldable paper-based analytical devices for the visual determination of alcohol content in whiskey samples," *Talanta*, vol. 194, no. August 2018, pp. 363–369, 2019, doi: 10.1016/j.talanta.2018.10.036.

[8] R. Quin *et al.*, "Quantification of Iron(II) in Supplements Using Redox Titration and UV − Visible Spectroscopy," *J. Chem. Educ.*, vol. 101, no. 12, pp. 5484–5491, 2024, doi: 10.1021/acs.jchemed.4c01090.

[9] I. G. A. S. Wangiyana, Supriadi, A. Nikmatullah, Sunarpi, and L. Mulyaningsih, "Tannin Concentration of

Gyrinops Tea Taken Form Different Agarwood Plantation and Different Processing Method," *IOP Conf. Ser. Earth Environ. Sci.*, vol. 913, no. 1, pp. 1–8, 2021, doi: 10.1088/1755-1315/913/1/012068.

[10] I. W. Kimaru, A. T. Corigliano, and F. Zhao, "Using Classical EDTA Titrations to Measure Calcium and Magnesium in Intravenous Fluid Bags," *J. Chem. Educ.*, vol. 95, no. 12, pp. 2238–2242, 2018, doi: 10.1021/acs.jchemed.8b00412.

[11] H. Tareen *et al.*, "Determination of vitamin c content in citrus fruits and in non-citrus fruits by titrimetric method, with special reference to their nutritional importance in human diet," *Biol. Forum – An Int. J.*, vol. 7, no. 2, pp. 367–369, 2015.

[12] A. K. Tantray, S. A. Dar, S. Ahmad, C. Aabid, K. Tantray, and S. A. Bhat, "Spectrophotometric and titrimetric analysis of phytoascorbate," *J. Pharmacogn. Phytochem.*, vol. 6, no. 61, pp. 27–31, 2017, [Online]. Available: http://www.phytojournal.com/archives/2017/vol6issue1/PartA/6-1-13-137.pdf

[13] K. Hreeba, "Comparative Quantitative Study of Acetyl Salicylic Acid in Aspirin Samples Using Spectrophotometry and Volumetric," *AlQalam J. Med. Appl. Sci.*, vol. 8, no. 2, pp. 832–835, 2025, doi: 10.54361/ajmas.258240.

[14] A. K. Fadhil, M. J. M. Hassan, and A. S. Rasheed, "A comparative review of methods for estimation of some antihypertensive drugs in pharmaceutical production," *Egypt. J. Chem.*, vol. 64, no. 11, pp. 6301–6321, 2021, doi: 10.21608/ejchem.2021.76547.3750.

[15] G. Ploegaerts, C. Desmet, and M. Van krieken, "Assay of sodium in food: Comparison of different preparation methods and assay techniques," *J. Food Compos. Anal.*, vol. 45, pp. 66–72, 2016, doi: 10.1016/j.jfca.2015.09.017.

[16] E. V. Sergunova, A. A. Sorokina, D. O. Bokov, and A. I. Marakhova, "Qualitative and quantitative determination of organic acids in crude herbal drugs and medicinal herbal preparations for quality control in Russian Federation by modern physicochemical methods," *Pharmacogn. J.*, vol. 11, no. 5, pp. 1132–1137, 2019, doi: 10.5530/pj.2019.11.176.

[17] M. Miloshevska, I. S. Spirevska, N. Nakov, G. Stefkov, A. Dimitrovska, and J. Acevska, "Water content determination in different varieties of Cannabis flowers," *Maced. Pharm. Bull.*, vol. 69, no. 1, pp. 67–75, 2023, doi: 10.33320/maced.pharm.bull.2023.69.01.006.

[18] C. Ma *et al.*, "Water Determination in Plants by Karl Fischer with Extraction," *J. AOAC Int.*, no. October 2025, pp. 1–6, 2026, doi: 10.1093/jaoacint/qsaf108.

[19] B. Miranda, N. M. Lawton, S. R. Tachibana, N. A. Swartz, and W. P. Hall, "Titration and HPLC Characterization of Kombucha Fermentation: A Laboratory Experiment in Food Analysis," *J. Chem. Educ.*, vol. 93, no. 10, pp. 1770–1775, 2016, doi: 10.1021/acs.jchemed.6b00329.

[20] G. Peris-pastor, C. Azorín, J. L. Bened, A. Chisvert, and G. J, "Miniaturization as a smart strategy to achieve greener sample preparation approaches : A view through greenness assessment," *Trends Anal. Chem.*, vol. 170, 2024, doi: 10.1016/j.trac.2023.117434.

[21] N. M. Myers *et al.*, "Lab on paper: Assay of beta-lactam pharmaceuticals by redox titration," *Anal. Methods*, vol. 11, no. 37, pp. 4741–4750, 2019, doi: 10.1039/c9ay01547g.

[22] L. Cai, Z. Ouyang, J. Song, and L. Yang, "Indicator-Free Argentometric Titration for Distance-Based Detection of Chloride Using Microfluidic Paper-Based Analytical Devices," *ACS Omega*, vol. 5, no. 30, pp. 18935–18940, 2020, doi: 10.1021/acsomega.0c02143.

[23] M. Rahbar, B. Paull, and M. Macka, "Analytica Chimica Acta Instrument-free argentometric determination of chloride via trapezoidal distance-based micro fl uidic paper devices," *Anal. Chim. Acta*, vol. 1063, pp. 1–8, 2019, doi: 10.1016/j.aca.2019.02.048.

[24] S. Boobphahom *et al.*, "Recent Advances in Microfluidic Paper-Based Analytical Devices toward High-Throughput," *Molecules*, vol. 25, no. 13, 2020, doi: 10.3390/molecules25132970.

[25] J. Aguirre-Londoño, V. A. Aristizabal-Ferreira, S. P. Castro-Narváez, and J. S. Ramírez-Navas, "Conductimetry: A rapid alternative technique for chlorides determination in cheese," *Univ. Sci.*, vol. 24, no. 2, pp. 307–322, 2019, doi: 10.11144/Javeriana.SC24-2.cara.

[26] A. Shyichuk, D. Ziółkowska, I. Shyychuk, and M. Kowalska, "Application of the Semi-Automatic Titration Method Using a Webcam for the Determination of Calcium in Milk and Dairy Products," *Molecules*, vol. 30, no. 17, pp. 1–22, 2025, doi: 10.3390/molecules30173553.

[27] J. Dutta and Priyanka, "A facile approach for the determination of degree of deacetylation of chitosan using acid-base titration," *Heliyon*, vol. 8, no. 7, p. e09924, 2022, doi: 10.1016/j.heliyon.2022.e09924.

[28] A. O. Ochieng, "Influence of Organic Acids Excipients : A Comparative Analysis Study of Aspirin in Analgesic Drug Formulation," *Adv. Int. J. Res. E-ISSN*, vol. 6, no. 5, pp. 1–9, 2025, doi: 10.63363/aijfr.2025.v06i05.1490.

[29] M. Mehta, D. Mehta, and R. Mashru, "Recent application of green analytical chemistry : eco - friendly approaches for pharmaceutical analysis," *Futur. J. Pharm. Sci.*, 2024, doi: 10.1186/s43094-024-00658-6.

[30] M. Koel, "Do we need Green Analytical Chemistry?," *R. Soc. Chem.*, pp. 1–21, 2015, doi: 10.1039/C5GC02156A.

[31] F. A. Esteve-turrillas, S. Garrigues, and M. De Guardia, "Trends in Analytical Chemistry Green extraction techniques in green analytical chemistry : A 2019 – 2023," *Trends Anal. Chem.*, vol. 170, no. September 2023, p. 117464, 2024, doi: 10.1016/j.trac.2023.117464.

[32] L. Yin *et al.*, "Green analytical chemistry metrics for evaluating the greenness of analytical procedures," *J. Pharm. Anal.*, vol. 14, no. 11, p. 101013, 2024, doi: 10.1016/j.jpha.2024.101013.

[33] J. Plotka-Wasylka, "A new tool for the evaluation of the analytical procedure: Green Analytical Procedure Index," *Talanta*, pp. 1–16, 2018, doi: 10.1016/j.talanta.2018.01.013.

[34] A. B. Eldin, O. A. Ismaiel, W. E. Hassan, and A. A. Shalaby, "Green Analytical Chemistry : Opportunities for Pharmaceutical," *J. Anal. Chem.*, vol. 71, no. 9, pp. 861–871, 2016, doi: 10.1134/S1061934816090094.

[35] B. J. Al-shatti and N. F. Al-tannak, "Green chemistry and its implementation in pharmaceutical analysis," *Rev. Anal. Chem.*, vol. 42, no. 1, pp. 8–27, 2023, doi: 10.1515/revac-2023-0069.

[36] J. Jurjeva and M. Koel, "Talanta Open Implementing greening into design in analytical chemistry," *Talanta Open*, vol. 6, no. June, p. 100136, 2022, doi: 10.1016/j.talo.2022.100136.

[37] A. Bandopadhyay and P. Kumar, "Physical Journal Paper based microfluidic devices : a review of fabrication," *Eur. Phys. J. Spec. Top.*, vol. 232, no. 6, pp. 781–815, 2023, doi: 10.1140/epjs/s11734-022-00727-y.

[38] L. Shayne *et al.*, "Advances in Microfluidic Paper-Based Analytical Devices for Food and Water Analysis," *micromachines*, vol. 7 No.5, pp. 1–21, 2016, doi: 10.3390/mi7050086.

[39] C. Cannavacciuolo, S. Pagliari, R. Celano, L. Campone, and L. Rastrelli, "Trends in Analytical Chemistry Critical analysis of green extraction techniques used for botanicals : Trends , priorities , and optimization strategies-A review," *Trends Anal. Chem.*, vol. 173, no. February, p. 117627, 2024, doi: 10.1016/j.trac.2024.117627.

[40] D. Ballesteros-vivas, B. Socas-rodríguez, J. A. Mendiola, E. Ibáñez, and A. Cifuentes, "Green food analysis : Current trends and perspectives," *Green Sustain. Chem.*, vol. 31, no. i, pp. 1–8, 2021, doi: 10.1016/j.cogsc.2021.100522.

[41] E. Noviana *et al.*, "Micro fl uidic Paper-Based Analytical Devices : From Design to Applications," *Chem. Rev.*, 2020, doi: 10.1021/acs.chemrev.0c01335.

[42] N. W. Muyumba, S. C. Mutombo, H. Sheridan, A. Nachtergael, and P. Duez, "Quality control of herbal drugs and preparations : The methods of analysis , their relevance and applications," *Talanta Open*, vol. 4, p. 100070, 2021, doi: 10.1016/j.talo.2021.100070.

[43] S. Popescu, T.-Ștefania Chiș, M. G. Chiricuță, A.-C. Vârlan, L. Pîrvulescu, and A. Velciov, "Vitamin C determination in foods. Titrimetric methods – A review," *J. Agroaliment. Process. Technol.*, vol. 2024 (30), no. 4, pp. 471–476, 2025, doi: 10.59463/japt.2024.2.49.

[44] M. Saura-cayuela, S. Lara-torres, and I. Pacheco-fernández, "Green Analytical Chemistry Green materials for greener food sample preparation : A review," *Green Anal. Chem.*, vol. 4, no. January, p. 100053, 2023, doi: 10.1016/j.greeac.2023.100053.

[45] F. Pena-pereira and S. Pedersen-bjergaard, "The ten principles of green sample preparation," *Trends Anal. Chem.*, vol. 148, 2022, doi: 10.1016/j.trac.2022.116530.

[46] T. Jankech *et al.*, "Analytica Chimica Acta Current green capillary electrophoresis and liquid chromatography methods for analysis of pharmaceutical and biomedical samples (2019 – 2023) – A review," *Anal. Chim. Acta*, vol. 1323, no. February, p. 342889, 2024, doi: 10.1016/j.aca.2024.342889.

[47] M. Koel and M. Kaljurand, "Application of the principles of green chemistry in analytical chemistry *," vol. 78, no. 11, pp. 1993–2002, 2016, doi: 10.1351/pac200678111993.

[48] M. Herrero, "Towards green extraction of bioactive natural compounds," *Anal. Bioanal. Chem.*, vol. 416, no. 9, pp. 2039–2047, 2024, doi: 10.1007/s00216-023-04969-0.

[49] Bhavya sri Khagga, Srija Ghanukota, and Sumakanth Mogili, "Novel titrimetric method for the determination of rosuvastatin in pure form," *World J. Biol. Pharm. Heal. Sci.*, vol. 13, no. 2, pp. 001–004, 2023, doi: 10.30574/wjbphs.2023.13.2.0054.

[50] F. Pena-pereira *et al.*, "Miniaturized analytical methods for determination of environmental contaminants of emerging concern e A review," *Anal. Chim. Acta*, vol. 1158, 2021, doi: 10.1016/j.aca.2020.11.040.

[51] H. Shaaban and T. Górecki, "Talanta Current trends in green liquid chromatography for the analysis of pharmaceutically active compounds in the environmental water compartments," *Talanta*, vol. 132, pp. 739–752, 2015, doi: 10.1016/j.talanta.2014.09.050.

[52] R. H. O. Samar H. Elagamy a,*, Adri´an Fuente-Ballesteros b, Hemanth Kumar Chanduluru c,*, "Systematic review of recent metrics (2020 – 2025) for greenness , applicability , and analytical performance with guidelines for practical use," *Results Chem.*, vol. 20, 2026, doi: 10.1016/j.rechem.2026.103048.