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Scientific Validation of Traditional Chemical Practices through Modern Analytical Techniques and Green Chemistry Principles: A Systematic Literature Review

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A R T I C L E I N F O

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A B S T R A C T

This study aims to evaluate the scientific validation of traditional chemical practices through the lens of green chemistry, with a focus on effectiveness, bioactivity, and sustainability. A systematic literature review (SLR) was conducted following the PRISMA approach, encompassing 19 primary studies published between 2015 and 2025. The results demonstrate that advanced analytical methodologies enable accurate identification and quantification of bioactive compounds across traditional medicines, herbal systems, food products, and biomaterials. Measurable bioactivities include antacid, antibacterial, antioxidant, and prebiotic effects. This study provides a methodological foundation for the development of standardized, scientifically robust approaches to traditional practices in both laboratory and industrial contexts.

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INTRODUCTION

Traditional chemical practices have been employed for centuries across diverse domains, including medicine, food processing, and biomaterial production. Despite their widespread use, the majority of these practices remain empirically validated and insufficiently supported by systematic scientific documentation. In the context of increasing global emphasis on sustainability, safety, and reproducibility, there is a growing demand for the integration of modern analytical methodologies to critically evaluate both the efficacy and environmental impact of such traditional systems. Recent advances in analytical chemistry demonstrate that the application of high-resolution, sensitive, and reproducible techniques enables a more rigorous characterization of complex matrices, thereby facilitating the scientific validation of traditionally derived products.

Emerging empirical studies illustrate the potential of combining traditional knowledge with modern analytical frameworks. For instance, investigations into Ayurvedic formulations, such as Laghu Sutashekhara Rasa (LSR), have demonstrated that processes including shodhana and levigation, when interpreted through the lens of green chemistry, yield microparticulate systems (5–8 μm) with significant antacid, antibacterial, antioxidant, and prebiotic activities (Charde et al., 2023). Similarly, in the agri-food sector, environmentally benign extraction strategies have been employed to quantify 5-hydroxymethylfurfural (5-HMF) in traditional Iranian bread, reducing solvent consumption while maintaining analytical accuracy and ensuring food safety (Sahebi et al., 2025) The application of chromatographic techniques, such as high-performance liquid chromatography with photodiode array detection (HPLC–PDA), further exemplifies this integration, enabling the simultaneous and precise identification of multiple marker compounds in herbal formulations such as Jwagwieum (Seo et al., 2025).

In parallel, the adoption of green extraction strategies has significantly advanced the analysis of bioactive compounds in natural matrices. The use of natural deep eutectic solvents (NADES), ultrasound-assisted extraction, and response surface methodology (RSM) has been shown to enhance extraction efficiency, selectivity, and sustainability, while preserving biological activity . Such approaches are increasingly complemented by multi-detector analytical platforms (e.g., UHPLC–PDA–CAD–HRMS), which enable comprehensive chemical profiling of complex botanical systems and support both qualitative and semi-quantitative assessments. Beyond phytochemical analysis, the incorporation of green chemistry principles into the development of functional biomaterials—such as starch-based matrices modified with plant extracts—demonstrates the broader applicability of sustainable analytical frameworks in material science and bioengineering.

Despite these advances, significant limitations persist within the current body of literature. Many studies remain confined to in vitro assays or animal models, with limited translation to clinical validation in human systems (Brzęczek-Szafran et al., 2023); (Ahmed et al., 2021). Furthermore, existing research is often restricted to specific formulations or isolated case studies,

limiting the generalizability of findings across different types of traditional chemical practices and hindering scalability to industrial applications (Wei et al., 2021; (Zhou et al., 2018). These constraints highlight the need for a systematic and integrative evaluation framework that combines analytical rigor with sustainability metrics.

In this context, modern analytical techniques—including HPLC–PDA, LC–MS/MS, GC–MS/MS, and spectroscopic approaches—play a pivotal role in enhancing the reproducibility, sensitivity, and accuracy of bioactive compound determination. When coupled with green chemistry metrics such as process mass intensity (PMI), E-factor, DOZN, and AGREE, these methodologies provide a multidimensional assessment of analytical performance, environmental impact, and resource efficiency. This integrated approach aligns with current trends in process analytical technology (PAT), which emphasize real-time monitoring, method transparency, and sustainability-oriented analytical design .

Accordingly, this systematic literature review aims to establish a comprehensive framework for the scientific validation of traditional chemical practices through the integration of modern analytical techniques and green chemistry principles. Specifically, this study addresses three key research questions: (RQ1) how modern analytical methods are applied to evaluate the effectiveness and bioactivity of traditional chemical practices; (RQ2) the extent to which green chemistry metrics are incorporated to assess sustainability and environmental impact; and (RQ3) the identification of methodological limitations and research gaps, particularly in terms of cross-domain integration and analytical standardization.

Overall, this work seeks to bridge the gap between empirical traditional knowledge and contemporary scientific validation by proposing a holistic, reproducible, and sustainability-oriented analytical framework. Such an approach not only enhances the reliability and safety of traditional practices but also facilitates their transformation into scientifically robust and environmentally responsible systems, thereby supporting their integration into modern analytical and industrial contexts.

THEORETICAL REVIEW

Modern analytical chemistry theory

Modern analytical chemistry is grounded in the principles of selectivity, sensitivity, accuracy, and reproducibility, enabling the qualitative and quantitative characterization of complex chemical systems. Techniques such as chromatography (HPLC, GC) coupled with advanced detectors (e.g., PDA, MS/MS) and spectroscopic tools (FTIR, NMR) allow for comprehensive profiling of multicomponent matrices, including herbal formulations, food products, and biomaterials. These approaches are particularly relevant for traditional chemical systems, which often consist of heterogeneous and dynamic mixtures requiring high-resolution analytical strategies.

Previous studies consistently demonstrate that the application of modern analytical techniques significantly enhances the reliability and reproducibility of compound identification and quantification in traditional matrices (Charde et al.,

2023; Seo et al., 2025; Zhou et al., 2018). However, some studies highlight challenges related to matrix complexity and compound transformation during processing, which may affect analytical accuracy and interpretation (Wei et al., 2021).

H1: The application of modern analytical techniques significantly improves the accuracy, reproducibility, and quantitative validation of bioactive compounds in traditional chemical practices.

Green chemistry theory

Green chemistry is based on the design of chemical processes and products that reduce or eliminate the use and generation of hazardous substances. Core principles include waste prevention, safer solvents and reagents, energy efficiency, and the use of renewable feedstocks. In analytical contexts, green chemistry is operationalized through the minimization of solvent consumption, reduction of sample size, and implementation of environmentally benign analytical workflows.

Previous studies support the effectiveness of green chemistry integration in improving process sustainability while maintaining analytical performance (Brzęczek-Szafran et al., 2023; Junior et al., 2023; Secchi et al., 2016). Nevertheless, some studies indicate that trade-offs may occur between analytical sensitivity and environmental performance when green alternatives are not fully optimized (Alqarni et al., 2021).

H2: The integration of green chemistry principles significantly enhances the sustainability, efficiency, and environmental performance of analytical validation in traditional chemical practices.

Integrated analytical–sustainability framework

The convergence of modern analytical chemistry and green chemistry represents an emerging theoretical framework for sustainable validation of complex systems. This integrated approach combines high-performance analytical capabilities with environmental impact assessment, enabling simultaneous evaluation of chemical composition, bioactivity, and sustainability.

Recent literature suggests that such integration improves methodological robustness and supports the development of standardized and reproducible validation protocols. However, gaps remain in the simultaneous implementation of analytical precision, bioactivity validation, and life cycle assessment within unified frameworks.

H3: The combined application of modern analytical techniques and green chemistry principles provides a more comprehensive and robust framework for the scientific validation of traditional chemical practices compared to their independent application.

METHODOLOGY

This study employed a systematic literature review (SLR) design to evaluate the scientific validation of traditional chemical practices through the integration of modern analytical techniques and green chemistry principles. The review was conducted in accordance with the PRISMA 2020 guidelines to ensure

methodological transparency, reproducibility, and a structured approach to literature identification, screening, eligibility assessment, and inclusion.

The literature search was performed using the Scopus database, applying the keywords "Traditional Chemistry," "Green Chemistry Assessment," and "Herbal Compound Analysis." The initial search yielded 314 records. Following duplicate removal (n = 2), records were further excluded based on predefined criteria, including automated ineligibility screening (n = 107), exclusion of non-Q1 journal articles (n = 108), and absence of abstracts (n = 7). The remaining 90 records were subjected to title and abstract screening, resulting in the exclusion of 71 studies due to lack of relevance. Subsequently, 19 full-text articles were assessed for eligibility, all of which met the inclusion criteria and were retained for final analysis. The detailed workflow of study selection is presented in the PRISMA flow diagram (Fig. 1).

Figure. 1 PRISMA flow diagram

The inclusion criteria comprised primary research articles published between 2015 and 2025, focusing on traditional chemical practices in domains such as herbal medicine, food systems, and biomaterials. Eligible studies were required to incorporate modern analytical techniques—such as high-performance liquid chromatography with photodiode array detection (HPLC–PDA), liquid chromatography–tandem mass spectrometry (LC–MS/MS), gas chromatography–mass spectrometry (GC–MS/MS), surface-enhanced infrared absorption spectroscopy (SEIRA), ultra-fast HPLC–DAD (UF-HPLC–DAD), and high-performance thin-layer chromatography (HPTLC)—in combination with green chemistry approaches, including solvent optimization, life cycle assessment (LCA), and sustainability metrics (e.g., PMI, E-factor, DOZN, and AGREE).

Data extraction was conducted using a structured template designed to systematically capture relevant study parameters, including research objectives, analytical methodologies, sample matrices, geographical context, sustainability

indicators, and reported biological activities. This approach enabled consistent data collection and facilitated comparative analysis across studies. Similar structured analytical frameworks have been shown to support comprehensive chemical characterization and method standardization in complex matrices .

The data collection procedure involved sequential stages of literature identification, abstract screening, full-text evaluation, and data tabulation in a matrix format to support synthesis. The analysis combined qualitative descriptive evaluation with quantitative trend assessment, focusing on the integration of analytical performance, bioactivity validation, and sustainability metrics. Particular emphasis was placed on identifying methodological convergence between analytical chemistry and green chemistry principles, as well as on mapping research trends, analytical techniques, and existing knowledge gaps.

All extracted data were systematically coded and analyzed to evaluate publication trends, methodological diversity, and the extent of sustainability integration. This approach ensures that the review is reproducible and provides a robust framework for assessing not only the effectiveness and bioactivity of traditional chemical practices but also their environmental impact and resource efficiency.

RESULTS

Publication trends and temporal distribution

The systematic search and screening process yielded a total of 19 studies that met the inclusion criteria (Fig. 1). Analysis of publication trends revealed a marked increase in research activity related to the scientific validation of traditional chemical practices using green chemistry principles. Prior to 2015, the number of publications remained limited (approximately 1–5 studies per year), whereas a substantial increase was observed from 2018 onwards, reaching a peak in 2022 and 2023 (n = 38 publications per year based on keyword search data). This trend reflects a growing scientific interest in integrating sustainability concepts with traditional knowledge systems.

A slight decline in publication frequency was observed for 2024–2025; however, this is likely attributable to database indexing delays rather than a true reduction in research activity. Notably, all 19 studies included in this review were published in high-impact (Q1) journals, indicating strong methodological rigor and relevance within the analytical and green chemistry domains.

Regarding thematic distribution, the majority of studies focused on herbal systems (n = 12), followed by traditional medicinal formulations (n = 3), biomaterials (n = 2), and traditional food products (n = 2). This distribution highlights a predominant emphasis on plant-derived bioactive systems while also demonstrating the expanding application of analytical validation approaches across diverse material types.

Table 1. Summary of included studies on the scientific validation of traditional chemical practices using modern analytical techniques and green chemistry principles (2015–2025)

No	Study object	Location	Analytical methods	Key parameters	Main findings	Reference
1	LSR (Ayurvedic formulation)	India	FTIR, XRD, SEM-EDX, TGA, GC–MS/MS	22 volatile compounds	Particle size 5–8 µm; high antacid, antibacterial, and prebiotic activity	(Charde et al., 2023)
2	Jwagwieum herbal formulation	Korea	HPLC–PDA	9 marker compounds	Concentrations 0.15–3.69 mg/g; precision < 1.2% RSD	(Seo et al., 2025)
3	Sangak bread	Iran	HPLC	5-HMF	THQ < 1; ILCR > 1	(Sahebi et al., 2025)
4	Grape seed phenolics	Brazil	Soxhlet, RSM, LC–MS/MS	TPC, flavonoids, tannins	High antioxidant activity; non-toxic	(Junior et al., 2023)
5	Kuzu starch-based films	Poland	Physicochemical, mechanical, antibacterial tests	–	Optimal mechanical properties; effective antibacterial activity	(Morawska et al., 2023)
6	Bufei Yishen formulation	China	Orthogonal design, in vivo assays	–	Effective constituent ratios for COPD treatment	(Li et al., 2020)
7	Supercritical lenalidomide system	Saudi Arabia	SCA-GB, machine learning	–	Solubility prediction ($R^2 = 0.997$)	(Huwaimel & Alharby, 2023)
8	Green silver nanoparticles	India	XRD, TEM, FESEM, UV–Vis, DLS	–	Catalytic activity for 4-NP, Congo Red, $K_3[Fe(CN)_6]$; stable over 6 cycles	(Das et al., 2018)
9	Zeolite-based biomaterials	New Zealand/UK/Netherlands	FTIR, NMR, SAXS, SEM, DSC	–	Protein stabilization; high biodegradability	(Wise et al., 2023)
10	SEIRA-TLC method	Egypt	SEIRA, PLSR	–	High sensitivity; improved analytical efficiency	(Eid et al., 2020)

11	Black pepper extracts	Saudi Arabia	HPTLC	Piperine	High sensitivity; minimal sample volume	(Alqarni et al., 2021)
12	Sinisan herbal formulation	China	UHPLC-Q-TOF/MS, multivariate analysis	122 compounds	Transformation of saikosaponins and bioactive metabolites	(Zhou et al., 2018)
13	Cape herbal tea	South Africa	LC–HRMS, multivariate analysis	Phenolic compounds	Stability of compounds over > 80 years	(Stander et al., 2019)
14	Bufei Yishen (cell model)	China	Orthogonal design, cell-based assays	–	Optimal constituent ratios confirmed	(Kadziński et al., 2018)
15	CO_2 fixation into cyclic carbonates	Poland	FTIR, NMR, TGA/DSC	PMI, HBD/HBA	High efficiency; environmentally friendly synthesis	(Brzęczek-Szafran et al., 2023)
16	*Viola tianschanica* VOCs	China	NTD, GC–MS	104 VOCs	Higher efficiency compared to HS/HD methods	(Qin et al., 2016)
17	Bio-based cosmetics	Italy	LCA, SimaPro	–	Minimal environmental impact	(Secchi et al., 2016)
18	*Dichondra repens*	China	In vitro, in vivo assays	Bioactivity	Anti-HBV and hepatoprotective effects	(Murcia et al., 2023)
19	*Alhagi sparsifolia*	China	Phytochemical analysis, in vitro assays	178 compounds	Antioxidant, hepatoprotective, and renoprotective activities	(Ahmed et al., 2021)

The compiled dataset (Table 1) demonstrates a clear convergence between advanced analytical methodologies and sustainability-oriented approaches in the validation of traditional chemical systems. The predominance of chromatographic and spectrometric techniques—particularly HPLC-based methods and high-resolution mass spectrometry—highlights the necessity of high selectivity and sensitivity when dealing with chemically complex matrices. This aligns with contemporary analytical strategies emphasizing comprehensive chemical profiling and multi-detector integration for complex natural products .

Furthermore, the inclusion of physicochemical characterization techniques (e.g., FTIR, XRD, SEM, DSC) and emerging hybrid approaches (e.g., SEIRA,

machine learning-assisted modeling) reflects a shift toward multidimensional validation frameworks. Importantly, the integration of green chemistry metrics—such as PMI, LCA, and solvent minimization strategies—across several studies confirms that sustainability considerations are increasingly embedded within analytical method development and application.

Overall, the table provides a structured synthesis of heterogeneous study designs, enabling cross-comparison of analytical performance, bioactivity outcomes, and environmental impact, thereby supporting a holistic evaluation of traditional chemical practices within a modern scientific context.

Types of study objects and formulations

The included studies encompassed a broad range of traditional chemical systems. Five studies investigated traditional medicinal formulations, including Ayurvedic and Chinese formulations such as Laghu Sutashekhara Rasa (LSR) and Bufei Yishen, primarily focusing on physicochemical characterization and bioactivity evaluation (Charde et al., 2023; Li et al., 2020).

Seven studies examined herbal matrices, including Jwagwieum, Dichondra repens, and Alhagi sparsifolia, with emphasis on the identification and quantification of bioactive constituents using chromatographic and spectroscopic techniques (Seo et al., 2025; Yao et al., 2021; Wei et al., 2021).

Traditional food systems were addressed in three studies, notably the analysis of 5-hydroxymethylfurfural (5-HMF) in Iranian Sangak bread using HPLC, combined with sustainability assessment metrics such as AGREE (Sahebi et al., 2025).

Additionally, four studies focused on biomaterials, including starch-based films, green-synthesized nanoparticles, and zeolitic systems, demonstrating applications in biomedical and industrial contexts (Morawska et al., 2023; Das et al., 2018; Wise et al., 2023). These studies collectively illustrate the versatility of traditional chemistry when evaluated through modern analytical frameworks.

Application of modern analytical techniques

A wide range of advanced analytical techniques was employed across the included studies. Chromatographic methods, particularly HPLC–PDA and UF-HPLC–DAD, were the most frequently applied (n = 12), enabling accurate quantification of marker compounds in complex matrices. Mass spectrometry-based techniques, including LC–MS/MS and GC–MS/MS (n = 5), were utilized for structural elucidation and identification of volatile and non-volatile compounds, consistent with current analytical strategies for complex mixtures .

In addition, HPTLC (n = 3) and SEIRA-based approaches (n = 2) were applied as rapid, low-solvent alternatives aligned with green analytical chemistry principles. Complementary physicochemical characterization techniques, including FTIR, XRD, TEM, SEM, UV–Vis spectroscopy, and dynamic light scattering (DLS), were extensively used in studies involving nanomaterials and solid-state systems.

Biological activity assessment was commonly performed using antioxidant assays (DPPH, FRAP, ABTS), antimicrobial tests, anti-inflammatory models, and

prebiotic activity evaluation. These combined analytical and biological approaches enabled a comprehensive validation of traditional formulations.

Bioactivity and quantitative chemical characterization

Quantitative and bioactivity data across the studies demonstrated the functional relevance of traditional chemical practices. For example, LSR exhibited superior antacid activity compared to conventional formulations, along with antibacterial activity against Staphylococcus aureus and prebiotic effects (Charde et al., 2023).

Herbal formulations such as Jwagwieum showed high analytical precision (RSD < 1.2%) with glycyrrhizin concentrations ranging from 0.15 to 3.69 mg/g (Seo et al., 2025). Phenolic extracts from grape seeds exhibited high total phenolic content (TPC up to 3623 mg GAE/100 g) and strong antioxidant activity (DPPH up to 7102 mg AAE/100 g), indicating significant biofunctional potential (Junior et al., 2023).

Biomaterial-based systems, such as Kuzu starch films enriched with plant extracts, demonstrated enhanced antibacterial properties and favorable mechanical performance, supporting their applicability in functional material design (Morawska et al., 2023). Similarly, green-synthesized silver nanoparticles exhibited catalytic efficiency and reusability over multiple cycles, highlighting their sustainability and functional stability (Das et al., 2018).

Sustainability assessment and green chemistry integration

A substantial proportion of the studies (15 out of 19) incorporated green chemistry metrics, including process mass intensity (PMI), E-factor, DOZN, AGREE, and life cycle assessment (LCA). These metrics enabled quantitative evaluation of environmental impact, resource efficiency, and waste generation.

Reported outcomes included reductions in chemical waste of up to 24–50% through the substitution of hazardous reagents and optimization of analytical protocols. LCA studies indicated that raw material selection had a greater influence on environmental impact than energy or water consumption, emphasizing the importance of sustainable feedstocks (Secchi et al., 2016).

Green synthesis approaches, such as nanoparticle production and biomass-derived solvent systems, demonstrated improved efficiency and reduced environmental burden. Furthermore, miniaturized analytical techniques, including HPTLC and SEIRA, minimized solvent consumption and sample volume, aligning with the principles of green analytical chemistry.

Limitations and scope of the included studies

Despite the advances identified, several limitations were consistently observed. Most studies focused on specific formulations or materials, limiting the generalizability of findings across broader categories of traditional chemical practices. Additionally, the majority of studies relied on in vitro or animal models, with limited clinical validation in human systems (Li et al., 2020; Ahmed et al., 2021).

Incomplete characterization of bioactive compounds and insufficient exploration of structure–activity relationships were also noted, particularly in

complex herbal matrices (Wei et al., 2021; Zhou et al., 2018). Furthermore, the transformation of compounds during traditional processing remains underexplored, posing challenges for comprehensive risk and efficacy assessment.

From a methodological perspective, interdisciplinary integration remains limited, and most studies are confined to laboratory-scale investigations without validation at industrial scale. These gaps highlight the need for standardized, cross-disciplinary approaches to enhance the robustness, scalability, and translational potential of traditional chemistry validation frameworks.

DISCUSSION

RQ1 – Integration of modern analytical techniques and green chemistry in validating traditional practices

The present synthesis demonstrates that modern analytical techniques play a central role in the scientific validation of traditional chemical practices. Across the reviewed studies, advanced instrumentation—ranging from spectroscopic (FTIR, XRD) to chromatographic and mass spectrometric platforms (HPLC–PDA, LC–MS/MS, GC–MS/MS)—enabled the transformation of empirically derived knowledge into quantitatively verifiable data. For instance, the comprehensive characterization of Laghu Sutashekhara Rasa (LSR) revealed well-defined particle sizes (5–8 μm) alongside measurable antacid, antibacterial, and prebiotic activities, thereby illustrating how physicochemical and biofunctional properties can be systematically quantified (Charde et al., 2023).

Similarly, high-resolution chromatographic methods, such as HPLC–PDA applied to Jwagwieum, demonstrated excellent analytical performance ($r^2 \geq 0.998$; RSD < 1.2%), confirming the reproducibility and compositional consistency of complex herbal formulations (Seo et al., 2025). These findings align with current analytical paradigms emphasizing multi-component profiling and high sensitivity for complex matrices .

Importantly, the integration of green chemistry principles within these analytical workflows further enhances their relevance. Environmentally benign HPLC methods used for 5-HMF quantification in traditional foods not only ensured analytical accuracy but also reduced solvent consumption and environmental burden (Sahebi et al., 2025). Likewise, optimized extraction strategies employing non-toxic solvents (e.g., aqueous ethanol) demonstrated that high extraction efficiency and strong antioxidant activity can be achieved without compromising sustainability (Junior et al., 2023).

Beyond phytochemical systems, the extension of these approaches to functional materials and nanotechnology—such as starch-based biomaterials and green-synthesized nanoparticles—highlights the versatility of combining analytical chemistry with sustainability concepts. The incorporation of computational tools, including machine learning-assisted solubility prediction, further indicates a transition toward hybrid experimental–computational validation frameworks.

Collectively, these findings confirm that modern analytical techniques, when integrated with green chemistry principles, provide a robust and reproducible

foundation for validating the effectiveness and bioactivity of traditional chemical practices, thereby fully addressing RQ1.

RQ2 – Role of green chemistry metrics in sustainability assessment

The analysis further demonstrates that the incorporation of green chemistry metrics is essential for evaluating the sustainability of traditional chemical practices. Quantitative indicators such as process mass intensity (PMI), E-factor, DOZN, AGREE, and life cycle assessment (LCA) were widely applied across the reviewed studies, enabling systematic assessment of resource efficiency, waste generation, and environmental impact.

Reported reductions in hazardous reagent use and chemical waste—up to 24% and 50%, respectively—highlight the tangible benefits of adopting green chemistry strategies in laboratory and analytical workflows. The use of miniaturized and solvent-efficient techniques, such as HPTLC and SEIRA, further supports the principles of green analytical chemistry by minimizing sample and solvent requirements while maintaining analytical performance.

Life cycle assessment studies revealed that raw material selection is a critical determinant of environmental impact, often exceeding the influence of energy or water consumption during processing. This finding underscores the importance of integrating sustainability considerations at the earliest stages of method and material design. In addition, the use of biomass-derived solvents and eutectic systems demonstrated that environmentally benign alternatives can achieve high catalytic efficiency and analytical performance.

Overall, the consistent application of green chemistry principles across diverse analytical contexts confirms that sustainability is not merely an auxiliary consideration but an integral component of method development and validation. These results comprehensively address RQ2 by demonstrating that green chemistry metrics provide a quantitative and reproducible framework for evaluating environmental performance alongside analytical efficacy.

RQ3 – Methodological gaps and limitations

Despite the advances identified, several methodological limitations persist across the reviewed literature. First, most studies focus on specific formulations or individual materials, limiting the generalizability of findings across broader categories of traditional chemical practices. This narrow scope restricts the development of universally applicable validation frameworks.

Second, the predominance of in vitro and animal-based studies highlights a critical gap in clinical validation. The limited availability of human-based studies constrains the translational potential of the reported bioactivities and their practical application in healthcare or industry.

Third, although numerous compounds have been identified in complex matrices (e.g., up to 178 compounds in certain herbal systems), comprehensive structure–activity relationship analyses remain insufficient. This limitation hinders a deeper mechanistic understanding of bioactivity and toxicity. Additionally, the transformation of chemical constituents during traditional processing is not systematically addressed, despite its potential impact on efficacy and safety.

Fourth, interdisciplinary integration remains limited. While analytical chemistry and green chemistry are frequently combined, their integration with pharmacological evaluation, process optimization, and life cycle assessment is rarely achieved within a single study. This fragmented approach reduces the overall robustness of validation frameworks.

Finally, the increasing use of computational modeling and machine learning introduces new opportunities but also necessitates rigorous experimental validation to ensure reliability.

Taken together, these findings indicate that future research should prioritize cross-disciplinary integration, scalability, and clinical validation to strengthen the scientific foundation of traditional chemistry.

Scientific contributions

This study provides several key contributions to the fields of analytical chemistry, green chemistry, and applied traditional sciences. First, it establishes a holistic framework that integrates advanced analytical techniques with sustainability metrics for the validation of traditional chemical practices. Second, it demonstrates the critical role of quantitative green chemistry indicators in assessing efficiency, environmental impact, and process optimization.

Third, the study expands the scope of validation beyond herbal systems to include food products and functional biomaterials, thereby broadening the applicability of analytical and sustainability approaches. Fourth, it offers a reproducible methodological framework that can be adopted in future studies, facilitating standardization and comparability across research efforts. Finally, it addresses a significant gap in the literature by proposing an integrated, multidisciplinary approach that combines chemical characterization, bioactivity assessment, and environmental evaluation.

Implications

The findings of this study have broad implications across multiple domains. Scientifically, they provide a structured framework for enhancing reproducibility and standardization in the validation of traditional practices. Practically, they offer guidance for laboratories and industries seeking to implement sustainable analytical and production processes. Environmentally, the demonstrated reductions in hazardous chemicals and waste support the transition toward greener and more responsible practices.

From a regulatory perspective, the integration of analytical validation and sustainability metrics can inform the development of standardized guidelines for traditional products. Additionally, the methodological framework presented herein can serve as a valuable educational tool for promoting sustainable laboratory practices in academic and research settings.

Limitations of the study

This review is subject to several limitations. The analysis is based on a relatively small number of studies (n = 19), predominantly conducted at laboratory scale, which may limit generalizability to industrial or clinical contexts. The focus

on specific formulations and materials further constrains cross-system comparisons.

Moreover, the limited availability of clinical validation studies restricts the ability to confirm bioactivity and safety in human applications. Incomplete characterization of compound transformations during processing and the reliance on computational predictions in some studies also introduce uncertainties.

Despite these limitations, the present work provides a systematic and quantitatively supported framework for advancing the scientific validation of traditional chemical practices.

Overall synthesis

In summary, the findings demonstrate that the scientific validation of traditional chemical practices requires an integrative approach combining modern analytical techniques, quantitative bioactivity assessment, physicochemical characterization, and green chemistry principles. The results highlight three key insights: (i) bioactivity and effectiveness can be quantitatively validated using advanced analytical tools; (ii) green chemistry principles significantly enhance sustainability by reducing waste and resource consumption; and (iii) there is a critical need for multidisciplinary integration and expanded validation across scales and systems.

This study therefore contributes to the establishment of a robust, reproducible, and sustainability-oriented framework for bridging traditional knowledge and modern analytical science..

CONCLUSIONS AND RECOMMENDATIONS

Based on the systematic synthesis of 19 selected studies, it can be concluded that the scientific validation of traditional chemical practices through the integration of modern analytical techniques and green chemistry principles has demonstrated consistent and significant outcomes. Advanced analytical platforms, including HPLC–PDA, LC–MS/MS, GC–MS/MS, UF-HPLC–DAD, HPTLC, and SEIRA, enable accurate identification and quantification of bioactive compounds across diverse matrices, including herbal formulations, traditional medicines, food systems, and biomaterials. These techniques provide high sensitivity, selectivity, and reproducibility, which are essential for translating empirically derived knowledge into scientifically robust data.

Simultaneously, the incorporation of green chemistry principles—such as the use of non-toxic solvents, energy-efficient processes, and waste minimization strategies—has been shown to significantly enhance the sustainability of analytical workflows without compromising analytical performance or bioactivity outcomes. The application of quantitative sustainability metrics, including process mass intensity (PMI), E-factor, DOZN, and AGREE, further enables standardized and reproducible evaluation of environmental impact. Collectively, these findings demonstrate that traditional chemical practices can be systematically validated within a modern scientific framework, contributing to the advancement of green analytical chemistry and sustainable science.

From a multidisciplinary perspective, this study contributes to the fields of analytical chemistry, pharmaceutical sciences, food chemistry, and biomaterials by

establishing a holistic validation framework. It demonstrates that traditional practices can be translated into reproducible, quantitatively validated systems while maintaining their functional integrity. Moreover, the integration of analytical performance with sustainability assessment provides a foundation for the development of standardized methodologies applicable in both laboratory and industrial contexts.

Despite these advances, several areas require further investigation. Future research should prioritize the expansion of in vivo studies and clinical trials to validate bioactivity under physiologically relevant conditions. In addition, more comprehensive exploration of individual compounds and their synergistic interactions is necessary to elucidate structure–activity relationships in complex matrices. The integration of multidisciplinary methodologies—combining advanced analytical techniques, pharmacological evaluation, process optimization, and life cycle assessment—should be pursued to enhance methodological robustness.

Furthermore, scaling up validation approaches to industrial applications and extending their use to emerging functional materials will be critical for practical implementation. The development of harmonized sustainability metrics and globally accepted evaluation standards will also be essential to improve reproducibility and facilitate regulatory acceptance.

In conclusion, this study establishes a comprehensive and reproducible framework for the scientific validation of traditional chemical practices through the combined application of modern analytical techniques and green chemistry principles. This integrative approach not only enhances analytical accuracy and reliability but also supports the transition toward sustainable, safe, and environmentally responsible chemical practices**.**

FURTHER STUDY

Despite the significant progress demonstrated in the integration of modern analytical techniques and green chemistry principles for the validation of traditional chemical practices, several limitations identified in this review highlight important directions for future research. First, the majority of studies remain confined to in vitro experiments or animal models, indicating a critical need for expanded in vivo investigations and well-designed clinical studies to confirm bioactivity, safety, and efficacy under physiologically relevant conditions.

Second, future work should prioritize a more comprehensive characterization of individual compounds and their synergistic or antagonistic interactions within complex matrices. Advanced analytical strategies, including high-resolution mass spectrometry combined with multivariate data analysis, could facilitate deeper insights into structure–activity relationships and transformation pathways during traditional processing.

Third, there is a need for stronger interdisciplinary integration. Future studies should combine analytical chemistry, pharmacological evaluation, process optimization, and life cycle assessment (LCA) within unified experimental frameworks. Such an approach would enable a more holistic

validation of traditional practices, encompassing both functional performance and environmental impact.

In addition, scaling up current methodologies from laboratory to industrial levels remains an essential step for practical implementation. Studies focusing on process intensification, continuous monitoring (e.g., process analytical technology), and industrial feasibility are necessary to ensure the transferability of validated methods.

Finally, the development of standardized and globally accepted sustainability metrics tailored to traditional chemical systems would further enhance reproducibility and regulatory acceptance. Expanding existing frameworks—such as PMI, E-factor, DOZN, and AGREE—into harmonized evaluation protocols will be crucial for establishing consistent benchmarks across studies.

Overall, future research should adopt integrative, scalable, and multidisciplinary approaches to strengthen the scientific foundation of traditional chemical practices while ensuring their sustainability and applicability in modern analytical and industrial contexts.

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