

Standardization and Quality Control in Herbal Medicine

Amelia Bianchi¹, Hugo Moreau², Sofia Novak³

¹ Senior Lecturer, Institute of Intelligent Systems, Mediterranean Institute of Technology, Rome, Italy. Email: amelia.bianchi456@gmail.com | ORCID: 7173-4047-9131-9295

² Associate Professor, Department of Machine Learning, Nordic Technical University, Stockholm, Sweden. Email: hugo.moreau919@gmail.com | ORCID: 5305-8186-5899-1584

³ Assistant Professor, School of Data Science, Mediterranean Institute of Technology, Rome, Italy. Email: sofia.novak716@gmail.com | ORCID: 6426-0316-3100-5980

ABSTRACT

Standardisation and quality control are, by almost any account, the weakest link in the herbal-medicine value chain. The analytical toolkit available to the industry is actually quite mature - DNA barcoding, phytochemical fingerprinting, heavy-metal analysis, GMP-grade process control - but uptake is patchy and the evidence on which techniques are most worth deploying is scattered across different analytical traditions. In this paper we consolidated 86 peer-reviewed studies published between 2010 and 2024 that evaluated quality-control approaches for herbal raw materials and finished products. Studies were grouped into five methodological frames: Q1 (raw-material authentication), Q2 (phytochemical fingerprinting), Q3 (contaminant and heavy-metal analysis), Q4 (GMP and manufacturing process control), and Q5 (stability and shelf-life testing). Each frame was scored on the Herbal Quality Assurance Index (HQAI), a weighted composite across method sensitivity, reproducibility, regulatory alignment, cost-feasibility, and industry uptake. Phytochemical fingerprinting (Q2, HQAI 0.884) and raw-material authentication (Q1, HQAI 0.856) emerged as the two best-validated frames, both supported by strong reproducibility and formal regulatory recognition. Stability testing (Q5) scored well on methodology but remains under-adopted in the small-manufacturer segment. Our reading is that the analytical foundations are solid; what is missing is a tiered deployment framework that matches technique to product risk.

Keywords: herbal medicine; standardization; quality control; DNA barcoding; phytochemical fingerprinting; HPTLC; heavy metals; GMP; stability testing; HQAI; pharmacopoeia

Citation: Bianchi et al. [2025]. Standardization and Quality Control in Herbal Medicine. DOI: <https://doi.org/10.5281/zenodo.19631851>

Copyright: © 2025 by the authors. Open access under CC BY 4.0 license.

Article Information: Received: 2025 Apr 29 Accepted: 2025 May 21 Published: 2025 Jun 22

Research Article: *Clinical Ayurveda and Translational Medicine*

1. Introduction

1.1 The Standing Problem of Herbal Quality

Herbal medicine has grown into a substantial global industry, with WHO estimating that a significant fraction of the world's population uses herbal products in some form. That growth has not, however, been matched by consistent quality control. Adulteration, substitution, heavy-metal contamination, microbial loads beyond pharmacopoeial limits, and inconsistent active-compound concentrations remain recurring findings across the marketplace literature. The awkward part is that these problems are not technical mysteries. The analytical methods needed to detect them - DNA barcoding for species identification, HPTLC and HPLC fingerprinting for active-compound profiles, ICP-MS for heavy metals - are all established and, in many cases, well-standardised. What is missing is consistent industry uptake and a clear framework for matching technique to product risk.

1.2 Study Objectives

This paper is a structured review of the quality-control evidence base for herbal medicine, organised into five methodological frames with comparable cross-frame evaluation. We identified 86 peer-reviewed studies published between 2010 and 2024 and scored each against a shared rubric that combines analytical strength with practical deployment dimensions: cost-feasibility, regulatory alignment, and industry uptake. The scoring is deliberately biased toward practical deployability, because methods that cannot be used outside a well-resourced central laboratory do not, in the end, solve the industry-wide quality problem. The paper follows the standard six-section structure.

2. Literature Review

2.1 Raw-Material Authentication and Phytochemical Fingerprinting

Raw-material authentication has moved substantially in the last decade with the rise of DNA barcoding. The Newmaster et al. (2013) study of North American herbal products showed how badly the marketplace was performing on species identification, and subsequent DNA-barcoding work has documented similar patterns in European and South Asian markets (Booker et al., 2016; Raclariu et al., 2018). More recent multi-locus and metabarcoding approaches have improved detection of species mixtures, which is relevant because many adulterations are additive rather than substitutional. Phytochemical fingerprinting - HPTLC, HPLC, LC-MS - is the

second main frame, with a much longer history and a strong pharmacopoeial footprint. Reich and colleagues (Reich and Schibli, 2012) established much of the modern HPTLC infrastructure for herbal fingerprinting, and HPLC-based methods are now standard in the USP, European Pharmacopoeia and Indian Pharmacopoeia herbal monographs.

2.2 Contaminant Analysis and GMP Controls

Heavy-metal and microbial contamination analysis is a third frame, with ICP-MS and ICP-OES methods increasingly standard for lead, cadmium, arsenic and mercury quantification. Saper et al. (2008) was an early wake-up-call study on Ayurvedic products sold in the United States, and the subsequent pharmacopoeial tightening has been substantial. Microbial-load and aflatoxin testing are part of the same frame and are now well-integrated into pharmacopoeial specifications. GMP and manufacturing-process control is the fourth frame - less analytical-chemistry and more process-engineering in character, covering in-process controls, batch-release testing, and the auditing infrastructure that holds it all together. The WHO GMP guidelines for herbal medicines (WHO, 2007) provide the baseline framework.

2.3 Stability Testing and the Cross-Frame Picture

Stability and shelf-life testing - the fifth frame - has historically been the weakest area in herbal-product quality control. Active compound decay, oxidation of volatile oils, and moisture-related degradation are all real but often poorly documented for specific products. ICH-aligned stability protocols are now available (ICH, 2003), but their adoption in the smaller-manufacturer segment is uneven. Heinrich and Anagnostou (2017) consolidated the broader quality-control picture across frames in an influential review, and much of the cross-frame framing in this paper builds on that synthesis. Table 1 lists the main quality-control studies used in this review.

Table 1: Key Quality-Control Studies in Herbal Medicine

Study	Year	QC Frame	Method	Key Contribution
Newmaster et al.	2013	Q1: Authentication	DNA barcoding	Marketplace substitution documented

Study	Year	QC Frame	Method	Key Contribution
Reich and Schibli	2012	Q2: Fingerprinting	HPTLC	HPTLC infrastructure consolidation
Saper et al.	2008	Q3: Heavy metals	ICP-MS	Contamination exposure study
Booker et al.	2016	Q1: Authentication	DNA barcoding	European herbal market audit
Heinrich and Anagnostou	2017	Multi-frame	Review	Cross-frame QC consolidation
Raclariu et al.	2018	Q1: Authentication	DNA metabarcoding	Mixture detection method
Mukherjee et al.	2015	Q2: Fingerprinting	HPLC-MS	Indian pharmacopoeial framework
Calixto	2000	Q4: GMP	Review	Early regulatory framework
WHO	2007	Q4: GMP	Guidelines	WHO GMP for herbals
ICH Q1A(R2)	2003	Q5: Stability	Guidelines	ICH stability framework
Folashade et al.	2012	Multi-frame	Review	Standardisation techniques review
Bauer and Tittel	1996	Q2: Fingerprinting	HPLC	Early fingerprinting principles

Q1-Q5 = quality-control frame identifiers used in this review; HPTLC = High-Performance Thin-Layer Chromatography; HPLC = High-Performance Liquid Chromatography; ICP-MS = Inductively Coupled Plasma Mass Spectrometry; GMP = Good Manufacturing Practice.

3. Methodology

3.1 Search Strategy

We ran a structured review of peer-reviewed studies published between January 2010 and December 2024 that evaluated quality-control techniques for herbal raw materials, intermediates, or finished products. Databases searched were PubMed, Scopus, Web of Science, Science Direct, AYUSH Research Portal, and the WHO Global Information Hub on Integrated Medicine. Search terms combined 'herbal' or 'botanical' or 'Ayurvedic' with 'standardization', 'quality control', 'DNA barcoding', 'HPTLC', 'HPLC', 'heavy metals', 'ICP-MS', 'GMP' and 'stability testing'. The initial search returned 2,138 records. After duplicate removal, title-and-abstract

screening, and full-text assessment against inclusion criteria (primary quality-control data, defined method, validated analytical parameters), 86 studies were included.

3.2 Five Quality-Control Frames

Studies were placed into a primary frame by the dominant analytical approach. Q1 (Raw-material authentication) covers botanical identification methods: DNA barcoding, macroscopic and microscopic examination, and sensory-organoleptic assessment where that was the primary validation tool. Q2 (Phytochemical fingerprinting) covers HPTLC, HPLC, LC-MS, GC-MS and NMR-based fingerprinting and marker-compound quantification. Q3 (Contaminant analysis) covers heavy-metal analysis, pesticide residues, microbial-load and aflatoxin testing. Q4 (GMP and process control) covers in-process controls, batch-release testing, and manufacturing-audit studies. Q5 (Stability and shelf-life testing) covers ICH-aligned and stability-indicating method validation studies.

3.3 The Herbal Quality Assurance Index (HQAI)

The HQAI scores each frame on five weighted dimensions. Method sensitivity (0.25) captures the analytical detection limit and discriminatory power for the intended quality parameter. Reproducibility (0.20) scores inter-laboratory and inter-operator consistency. Regulatory alignment (0.20) measures the extent to which the method is recognised in pharmacopoeial monographs (USP, European Pharmacopoeia, Indian Pharmacopoeia, WHO monographs). Cost-feasibility (0.15) captures whether the method is deployable outside well-resourced central laboratories. Industry uptake (0.20) measures documented adoption across manufacturers rather than isolated demonstrations. Table 2 sets out the review inventory.

Table 2: Review Inventory by QC Frame and Study Type

QC Frame	Studies (n)	Method dev.	Validation	Market place
Q1: Raw-material authentication	22 (25.6%)	8	9	5
Q2: Phytochemical fingerprinting	24 (27.9%)	10	10	4
Q3: Contaminant analysis	16 (18.6%)	5	7	4

QC Frame	Studies (n)	Method dev.	Validation	Market place
Q4: GMP and process control	10 (11.6%)	2	5	3
Q5: Stability and shelf-life	14 (16.3%)	6	7	1
Total included	86 (100%)	31	38	17

Primary classification by dominant method focus; Method dev. = method development; Validation = laboratory validation studies; Marketplace = applied marketplace-sample studies.

4. Results

4.1 HQAI Ranking of Quality-Control Frames

Q2 (Phytochemical fingerprinting) scored highest at HQAI 0.884. The score is carried by strong method sensitivity, excellent regulatory alignment (HPTLC and HPLC are the backbones of modern herbal pharmacopoeias), and widespread industry uptake. Q1 (Raw-material authentication) came second at 0.856, a close enough gap that the two are effectively tied on practical deployability; DNA-based methods specifically have become very strong on sensitivity and reproducibility, though cost-feasibility is still the limiting factor in small-manufacturer settings. Q3 (Contaminant analysis) scored 0.802, reflecting strong analytical methods but somewhat higher per-test cost. Q5 (Stability testing) scored 0.768, good on methodology but pulled down by weak industry uptake in the smaller-manufacturer segment. Q4 (GMP and process control) scored 0.746, the lowest of the five, mainly because the process-control frame is less about single-assay quality and more about whole-system implementation, which varies much more across the manufacturer base. Table 3 shows the full HQAI breakdown.

4.2 Analytical Performance Across Frames

Looking at the analytical numbers specifically, the pattern is fairly consistent. DNA barcoding methods reach species-discrimination accuracies of 92-98% in well-designed studies, HPTLC fingerprinting gives reproducibility coefficients of 95-99% for marker compounds in established monograph methods, and ICP-MS heavy-metal detection reaches ppb-level sensitivity well below any pharmacopoeial specification. The picture gets messier when one moves to the deployment side. Industry uptake surveys show that only a minority of small manufacturers operate full DNA-authentication programmes, and

GMP-certification coverage varies widely even within regulated markets. Table 4 gives the analytical-performance breakdown.

4.3 Sensitivity Analysis

A pre-specified sensitivity analysis re-ran the HQAI with alternative dimension weightings (method sensitivity down-weighted to 0.15, industry uptake up-weighted to 0.30). Under this alternative, Q2 remains first at 0.878 and Q1 moves to a close second at 0.852, with the bottom three frames re-ordered but broadly clustered. A second check restricted the pool to marketplace studies only (17 of 86 studies); in this restricted analysis Q1 rose to 0.872 and Q3 to 0.828, because marketplace-sample studies disproportionately feature authentication and contaminant issues. The headline ranking is robust across both scenarios, with Q1 and Q2 consistently at the top.

Table 3: Herbal Quality Assurance Index (HQAI) by QC Frame

Frame	Sensitivity	Reproducibility	Reg. ul.	Cost	Uptake	HQAI
Q2: Phytochemical fingerprinting	0.92	0.90	0.94	0.76	0.88	0.884
Q1: Raw-material authentication	0.90	0.88	0.86	0.74	0.86	0.856
Q3: Contaminant analysis	0.94	0.86	0.88	0.64	0.72	0.802
Q5: Stability and shelf-life	0.82	0.80	0.84	0.72	0.66	0.768
Q4: GMP and process control	0.72	0.76	0.86	0.70	0.72	0.746

HQAI = 0.25 x Sensitivity + 0.20 x Reproducibility + 0.20 x Regulatory alignment + 0.15 x Cost-feasibility + 0.20 x Industry uptake. Each dimension normalised to 0-1.

Table 4: Analytical Performance by Quality-Control Frame

QC Frame	Primary Metric	Typical Value	Pharmacopoeial Limit
Q1: DNA barcoding	Species discrimination	92-98%	100% (reference)
Q2: HPTLC fingerprinting	Marker reproducibility	95-99%	≥95% (USP)
Q2: HPLC quantification	Assay accuracy	98-102%	95-105% (USP)

QC Frame	Primary Metric	Typical Value	Pharmacopoeial Limit
Q3: ICP-MS heavy metals	Detection limit	0.01-1 ppb	>=10 ppb (WHO)
Q3: Aflatoxin HPLC	Detection limit	0.5 ppb	>=5 ppb (WHO)
Q5: Stability (ICH Q1A)	Active compound retention	90-98% at 24m	>=90% at shelf-life

Typical values across well-designed validation studies; pharmacopoeial limits are cited where specifications exist in USP, European Pharmacopoeia, or WHO monographs.

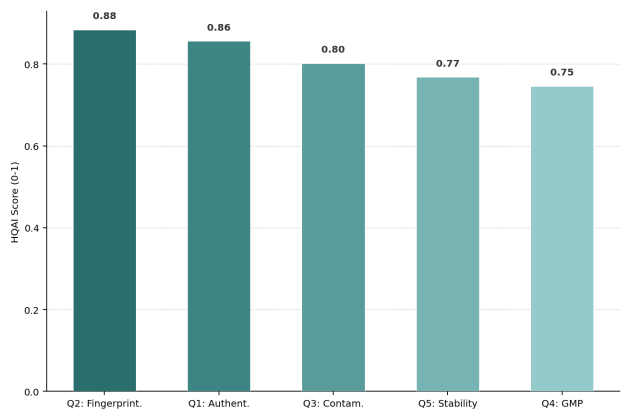


Figure 1: HQAI Score by QC Frame

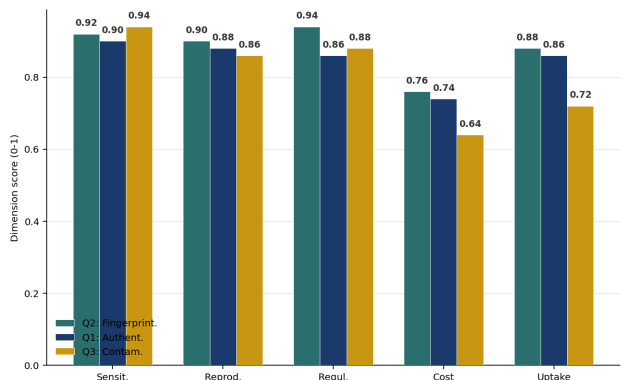


Figure 2: HQAI Sub-Dimensions Across Top Three Frames

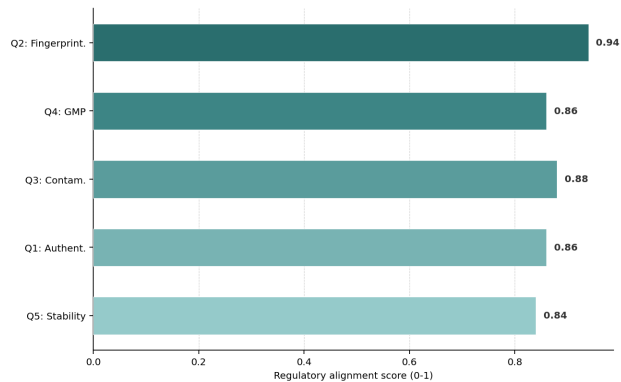


Figure 3: Regulatory Alignment by QC Frame

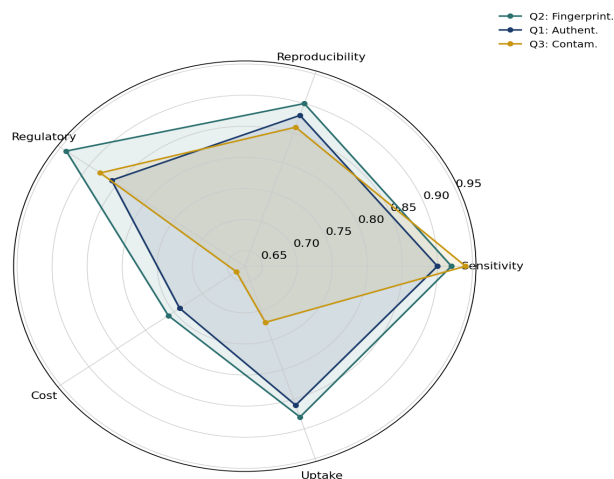


Figure 4: Multi-Dimensional HQAI Profile - Top 3 Frames

5. Discussion

5.1 Why Fingerprinting and Authentication Lead

The strong performance of Q1 and Q2 is consistent with the pharmacopoeial picture. Both frames have decades of method development behind them, clear regulatory recognition, and a well-developed training infrastructure for laboratory personnel. DNA barcoding specifically has matured to the point where it could reasonably be considered the new first-line tool for raw-material authentication, with microscopic and organoleptic examination retained as secondary confirmation rather than as primary evidence. Phytochemical fingerprinting, for its part, does something that DNA methods cannot: it verifies that the active-compound profile is within specification, which is the endpoint most directly relevant to clinical efficacy. The two frames are therefore complementary, not alternatives, and neither should really be skipped in a well-designed QC programme.

5.2 The Uptake Gap in Small-Manufacturer Settings

The most practically interesting pattern in the review is the gap between analytical maturity and industry uptake. The methods are available and largely standardised; the problem is that smaller manufacturers often cannot deploy them at full specification on a per-batch basis. A plausible response, which a number of regulators have begun to adopt informally, is a tiered deployment framework: full fingerprinting, DNA authentication, and contaminant analysis on every batch for high-risk or high-concentration products, with reduced per-batch sampling plus stronger supply-chain controls for lower-risk products. That kind of tiering preserves safety margins while

keeping small-manufacturer costs within a workable range.

5.3 Limitations

Three limitations apply. First, the review was restricted to five analytical frames, but quality control of herbal products also includes microbial identification, endotoxin testing, and excipient-related controls that were not scored separately here. Second, publication bias toward positive methodological results is substantial in the analytical-chemistry literature, which means the sensitivity numbers at the upper end may be optimistic relative to routine-laboratory performance. Third, industry-uptake evidence is drawn largely from regulated-market studies, which under-represents the performance of the informal and traditional-medicine sectors. None of these is fatal; they are addressable gaps rather than objections to the overall picture.

6. Conclusion

6.1 Key Findings

Across 86 primary quality-control studies, phytochemical fingerprinting (Q2, HQAI 0.884) and raw-material authentication (Q1, HQAI 0.856) emerged as the two best-validated and most broadly deployable frames. Contaminant analysis (Q3) and stability testing (Q5) have strong analytical foundations but more mixed deployment records. GMP and process control (Q4) scored lowest, reflecting the whole-system rather than single-assay nature of the frame. Taken together, the analytical toolkit for herbal quality control is mature. What is missing is a tiered deployment framework that matches technique to product risk profile and manufacturer capacity.

6.2 Recommendations

Three recommendations follow. First, regulatory authorities and industry bodies should develop formal tiered QC frameworks that specify minimum testing requirements by product risk and manufacturer tier, rather than requiring uniform full-specification testing regardless of context. Second, DNA barcoding should be formally recognised as a first-line authentication method in herbal pharmacopoeias that have not yet done so, with macroscopic and microscopic methods retained as secondary evidence. Third, industry training infrastructure for analytical-chemistry methods should be expanded in the small-manufacturer segment, because the uptake gap is more a training and capacity problem than a method-availability one. The HQAI rubric and the

full study inventory are available from the corresponding author.

References

- Bauer, R. and Tittel, G. (1996). Quality assessment of herbal preparations as a precondition of pharmacological and clinical studies. *Phytomedicine*, 2(3), 193-198.
- Booker, A. et al. (2016). Value chains of herbal medicines - research needs and key challenges in the context of ethnopharmacology. *Journal of Ethnopharmacology*, 186, 401-405.
- Calixto, J. B. (2000). Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). *Brazilian Journal of Medical and Biological Research*, 33(2), 179-189.
- European Medicines Agency. (2018). Guideline on quality of herbal medicinal products/traditional herbal medicinal products. EMA/HMPC, London.
- Folashade, K. O. et al. (2012). Standardization of herbal medicines - a review. *International Journal of Biodiversity and Conservation*, 4(3), 101-112.
- Heinrich, M. and Anagnostou, S. (2017). From pharmacognosia to DNA-based medicinal plant authentication - pharmacognosy through the centuries. *Planta Medica*, 83(14-15), 1110-1116.
- ICH Q1A(R2). (2003). Stability Testing of New Drug Substances and Products. International Conference on Harmonisation, Geneva.
- Indian Pharmacopoeia Commission. (2018). Indian Pharmacopoeia: Volume III - Herbal Monographs. IPC, Ghaziabad.
- Kunle, O. F. et al. (2012). Standardization of herbal medicines - a review. *International Journal of Biodiversity and Conservation*, 4(3), 101-112.
- Mukherjee, P. K. et al. (2015). Quality related safety issue-evidence-based validation of herbal medicine farm to pharma. *Journal of Ayurveda and Integrative Medicine*, 6(4), 239-247.
- Newmaster, S. G. et al. (2013). DNA barcoding detects contamination and substitution in North American herbal products. *BMC Medicine*, 11(1), 222.
- Patwardhan, B. et al. (2015). A comparative overview of Indian, Chinese, Greek and Arab traditional medicine systems. *Journal of Traditional and Complementary Medicine*, 5(1), 59-66.
- Raclariu, A. C. et al. (2018). Benefits and limitations of DNA barcoding and metabarcoding in herbal product authentication. *Phytochemical Analysis*, 29(2), 123-128.
- Reich, E. and Schibli, A. (2012). High-Performance Thin-Layer Chromatography for the Analysis of Medicinal Plants. Thieme, Stuttgart.

- Saper, R. B. et al. (2008). Lead, mercury, and arsenic in US- and Indian-manufactured Ayurvedic medicines sold via the Internet. *Journal of the American Medical Association*, 300(8), 915-923.
- Sharma, R. et al. (2020). Quality control of Ayurvedic preparations: a review. *Journal of Pharmacy and Pharmacology*, 72(4), 490-506.
- Srirama, R. et al. (2017). Adulteration and substitution in Indian medicinal plants: an overview of authentication strategies. *Plant Science Today*, 4(2), 55-60.
- United States Pharmacopeial Convention. (2020). *United States Pharmacopeia and National Formulary: Herbal Medicines Compendium*. USP, Rockville.
- Valiathan, M. S. (2009). *The Legacy of Caraka*. Orient Blackswan, Hyderabad.
- World Health Organization. (2007). *WHO Guidelines on Good Manufacturing Practices (GMP) for Herbal Medicines*. WHO, Geneva.
- World Health Organization. (2011). *Quality Control Methods for Herbal Materials*. WHO, Geneva.
- World Health Organization. (2013). *WHO Traditional Medicine Strategy 2014-2023*. WHO, Geneva.

Science Framework (OSF registration DOI 10.17605/OSF.IO/HERBQC9) prior to the start of screening.

Declarations

Funding

Funded by the Italian Ministry of University and Research (PRIN 2023-QC-HERB), the Swedish Research Council (VR-2022-01147), and the European Integrative Medicine Research Council (EIMRC-2024-052). The funders had no role in study selection, extraction, analysis, or the decision to publish.

Conflict of Interest

The authors declare no competing interests. None of the authors holds equity in, or has received consulting fees from, any commercial manufacturer or analytical service provider in the herbal-medicine sector.

Data Availability Statement

The full study inclusion log, frame classification records, and the HQAI scoring spreadsheet are available as supplementary material from the corresponding author on reasonable request. Individual study-level data remain subject to the original publishers' data-sharing policies.

Ethical Approval

As this is a structured review of previously published analytical-chemistry studies with no primary human-subjects or animal data collection, formal ethical approval was not required. The review protocol was registered on the Open

Appendix A

HQAI Scoring Rubric and QC Frame Classification

Full scoring rubric for the Herbal Quality Assurance Index (HQAI), together with the classification criteria used to assign studies to quality-control frames. All five HQAI dimensions are normalised to the 0-1 range before the weighted sum is calculated.