cosmetics

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Review

Translating Heterogeneous Evidence into Specifications for Plant-Derived Cosmetic Ingredients

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Abstract

Plant-derived cosmetic ingredients sharing a botanical name can differ in plant parts, provenance, processing, native-extract contents, carriers, and intended uses. These differences affect composition, identity features, hazard profiles, analytical performance, and the transferability of evidence or finished-product limits. Authentication studies, phytochemical research, pharmacopoeias, safety guidance, and regulations address different parts of this problem. However, they provide no common procedure for translating heterogeneous evidence into an executable ingredient specification. This structured narrative review proposes a decision sequence that begins with the definition of the supplied ingredient and a decision-specific comparability domain. It then links each source of variation or harm to a critical attribute, analytical method, and evidence appraisal. The resulting output is an acceptance criterion, condition of use, or management measure. Numerical derivation stops when an essential material, analytical, or exposure bridge remains unresolved. Three cases examine *Centella asiatica* extract, expressed lemon peel oil, and pyrrolizidine-alkaloid contamination. They show how different evidence gaps lead to different outputs and data needs. The cases illustrate the framework but do not validate its performance or establish universal limits for plant-derived cosmetic ingredients.

Keywords: cosmetics; plant-derived cosmetic ingredients; ingredient specifications; structured narrative review; evidence transfer; comparability domain; analytical suitability

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1. Introduction

A plant-derived cosmetic ingredient is defined by both its botanical starting material and the operations used to produce the supplied form. Species, plant part, provenance, harvest conditions, extraction solvent and ratio, fractionation, drying, carrier, and storage can alter constituent distributions and native-extract content [1–4]. The same variables determine which anatomical, genetic, chromatographic, or spectrometric features remain measurable [5–7]. They also affect which hazards are plausible and whether a method developed in one matrix will perform adequately in another [5–7]. Intended use adds an

exposure boundary and may change the safety conclusion even when composition remains constant [8]. A common plant name is therefore insufficient to define the object of a specification.

Several bodies of evidence address discrete parts of this specification problem. Authentication studies examine identity, substitution, and adulteration using morphological, molecular, and chemical evidence [5,9,10]. Fingerprint and marker research characterizes composition and production-related variation while providing analytical precedents [7,11,12]. Pharmacopoeias and botanical-drug guidance set specifications for defined medicinal materials, whereas World Health Organization (WHO) documents describe general approaches to plant-material quality control [13–15]. Cosmetic safety guidance connects characterized ingredients with exposure and toxicological endpoints [8]. Legislation and national technical instruments impose prohibitions, restrictions, dossier requirements, or labelling duties within their respective jurisdictions and for defined regulated objects [16–20]. These sources perform different functions, and authority within one function does not establish applicability to another.

What remains missing is a transparent rule for moving between these evidence systems. Identity evidence for a starting plant may not establish the identity or composition of a purified extract. Likewise, a published analytical procedure is not necessarily suitable for release testing. Research or pilot-batch values do not by themselves define an acceptance criterion. A finished-product limit cannot be converted automatically into an ingredient limit. Each transition requires a claim-specific comparison of the material, processing history, matrix, measurand, method purpose, use, and exposure. If an essential link is unresolved, assigning a number can obscure uncertainty rather than control it.

This structured narrative review provides an explicit sequence for evaluating those transitions. Authority, meaning the legal, compendial, technical, or scientific role of a source, is assessed separately from applicability to the material and decision at hand. A decision-specific comparability domain is established before results are pooled or converted into acceptance criteria. The framework then connects each source of variation or harm to a controlled attribute and a fit-for-purpose method. Evidence appraisal then leads to an ingredient acceptance criterion, a numerical condition of use, or a non-numerical management measure. Each resulting output is paired with a lifecycle reassessment trigger. Numerical derivation ends when the necessary material, analytical, or exposure bridge cannot be supported.

Three cases illustrate how the sequence operates under different evidentiary constraints. The *C. asiatica* case considers how source, processing, triterpene composition, and method purpose inform consistency controls. Expressed lemon peel oil shows how a volatile identity profile, a non-volatile furocoumarin panel, product category, and sun exposure must be evaluated together. The pyrrolizidine alkaloid (PA) case examines how a recognized hazard may justify supply-chain and analytical controls even when target-specific dermal and aggregate-exposure evidence is incomplete. The examples illustrate the reasoning process but do not validate the framework or establish universal limits for plant-derived cosmetic ingredients. They also do not claim exhaustive coverage of all jurisdictions.

2. Review Design, Literature Search, and Evidence Appraisal

This structured narrative review evaluates claims concerning identity, comparability, critical attributes, analytical methods, acceptance criteria, conditions of use, exposure, and safety-related management measures for plant-derived cosmetic ingredients. It was not designed or reported as a systematic review and does not claim exhaustive coverage of all jurisdictions or relevant literature. No systematic-review reporting framework was applied or claimed. The Scale for the Assessment of Narrative Review Articles (SANRA)

guided reporting of the review rationale, search, referencing, and critical appraisal; no quantitative SANRA score was assigned [21].

PubMed was the only bibliographic database used. The review cut-off for both scientific-literature searches and regulatory-status assessment was 20 October 2026. Scientific-literature searches were conducted from 14 to 20 October 2026 and covered PubMed's full searchable record range through the cut-off. Formal modular searches were run on 19 October, followed by targeted supplementary searches and PubMed reference-list and cited-in tracking on 20 October. The formal and supplementary searches applied no language, publication-year, article-type, regional, or full-text-availability filters. Themes included botanical identity, authentication and adulteration; extraction, processing, matrix and batch variability; fingerprints, markers, method performance and analytical suitability; specification and quality control; exposure and safety; and the three case materials. A study was retained when it could define a source or target material, explain processing or matrix differences, support an analytical or control decision, or identify a limit to evidence transfer.

Regulatory and normative documents were identified primarily through official regulatory websites, standards platforms, and document repositories. In China, sources included the National Medical Products Administration (NMPA), the National Institutes for Food and Drug Control (NIFDC), the State Administration for Market Regulation (SAMR), and the Standardization Administration of China (SAC). Other sources included EUR-Lex, the Scientific Committee on Consumer Safety (SCCS), the European Medicines Agency (EMA), the U.S. Food and Drug Administration (FDA), and WHO. Official-source searching and retrieval were performed mainly on 19 October 2026, with targeted regulatory-status checks completed on 20 October 2026. Regulatory status was assessed as of the review cut-off. We recorded the version, publication date, effective or implementation date, and access date. Requirements in force at the cut-off, published but not yet effective instruments, voluntary standards, technical guidance, and consultation drafts were distinguished. Legal requirements were applied only within their jurisdiction and regulated object; pharmaceutical and food documents were treated as technical precedents, not cosmetic requirements.

For each source, we extracted the material and plant part, provenance, process, carrier, matrix, batch or sample coverage, method purpose, analytes, performance, findings, and limitations. Authority and applicability were evaluated separately. Evidence was classified as directly applicable, conditionally applicable, not applicable, or insufficiently characterized. Quantitative transfer required compatibility in material, measurand, matrix, units, use, and exposure.

3. Defining the Ingredient and Its Comparability Domain

3.1. Defining the Supplied Ingredient

Specification development begins with a precise description of the supplied ingredient and of the external materials that may inform a particular decision. Establishing this scope at the outset prevents a shared species name, an analytical resemblance, or a published limit from being mistaken for material comparability. A botanical name identifies a taxon, not a chemically uniform article. Studies of *C. asiatica* make this distinction clear. Raw materials varied with plant part, collection site, and season; accessions grown under the same environmental conditions still showed different centelloside patterns; and controlled-cultivar studies continued to distinguish metabolite-production trends [2,22–24]. Reviews of extraction and field-to-market processing also identify solvent polarity, solid-to-liquid ratio, temperature, and purification as determinants of composition [4,25]. Although these studies consistently show that source and processing matter, their numerical

findings are not interchangeable because the plant parts, accessions, extraction conditions, and reporting bases differ.

Normative sources request related information for different purposes. NMPA Announcement No. 99 of 2026, published on 8 October 2026, set provision-specific implementation arrangements for revisions to the 2015 safety text. The applicable implementation date therefore had to be checked for each provision at the review cut-off. The recommended industry standard YY/T 10002—2026 had been published but was not yet effective. It was scheduled to take effect on 1 May 2027 and could not be treated as a standard in force on 20 October 2026. By contrast, the NIFDC Technical General Rules for Registration and Filing Dossiers of New Cosmetic Ingredients had been effective since 15 July 2026. They apply specifically to registration and filing dossiers for new ingredients and do not create a general release requirement for every existing ingredient [17–19,26]. EMA, FDA, and WHO documents likewise link the definition of the supplied ingredient to manufacturing and quality assessment within their medicinal or general botanical scopes [13–15]. Despite their different objects and status, these sources support the same technical conclusion: evidence cannot be interpreted without a defined material.

We propose that the minimum definition of the supplied ingredient should include the taxon and plant part; relevant provenance, cultivation, and harvest conditions; primary processing and subsequent manufacturing, including extraction solvent and selective purification where applicable; the input-to-output and native-extract basis; carriers; supplied form and composition; storage conditions relevant to stability; and intended cosmetic use. These fields identify the object of the specification and do not constitute a universal legal dossier. If the source, selective processing, carrier, or supplied composition cannot be reconstructed well enough for the intended decision, external evidence may identify candidate attributes, but it cannot support a shared numerical range or a transferred safety conclusion.

3.2. Processing State and Retained Identity Evidence

Processing determines which identity features remain observable. Whole or cut material may retain macroscopic anatomy, powders may preserve microscopic characters, deoxyribonucleic acid (DNA) methods may recover taxonomic sequence information, and chromatographic or spectrometric profiles may describe retained constituents [5,27,28]. Extraction, heating, purification, degradation, and high carrier content can remove, dilute, or transform these features. Morphology, DNA, and chemistry therefore answer complementary questions, and no single approach remains informative at every processing stage.

Comparative product studies illustrate why the analytical workflow must be considered alongside the method label. In commercial *H. perforatum* products, DNA metabarcoding, thin-layer chromatography (TLC), and high-performance liquid chromatography-mass spectrometry (HPLC-MS) yielded partly different information: chemical profiles supported assessment of the labelled material, whereas processing and formulation constrained the DNA results [29]. Extract-only Ayurvedic products could generate amplicons yet fail the final taxonomic-detection requirement, showing that primers, amplification, filtering, reference databases, and decision thresholds matter in addition to the processing history [30]. Reviews support the same qualified conclusion. DNA methods can reveal unexpected taxa, but non-detection after extensive processing does not demonstrate absence [9,31].

Studies that combine independent techniques also show the value, and the limits, of orthogonal evidence. DNA barcoding with chemical fingerprints improved discrimination in lavender raw material, as did independent molecular methods applied to flower ingredients, because the methods had different blind spots [32,33]. These findings support

complementary identity evidence; they do not imply that two methods are invariably required or that performance in raw material will transfer to an extract or oil. Adulteration forensics provides a further caution: methods directed at only a superficial feature may be deliberately circumvented [10].

The practical consequence is that an identity procedure should be confirmed in the supplied state before it is used for release. Confirmation should establish that the relevant feature survives processing, can be recovered, and distinguishes the target from plausible substitutes in that matrix, using suitable reference materials and controls. When direct features are lost, authenticated starting material and documented batch traceability can maintain the upstream identity link, supplemented by a justified chemical identity test or fingerprint in the supplied material. The resulting strategy should specify which claims are confirmed downstream, which depend on traceability, and which remain unresolved.

3.3. Establishing a Decision-Specific Comparability Domain

Comparability depends on the decision being made. A shared discriminatory sequence or anatomical feature may be sufficient for taxonomic identity, whereas a common marker range also requires similarity in plant part, process, composition, sample state, and reporting basis. Bridging a safety conclusion imposes additional requirements for comparable hazards, use, and exposure. Materials from the same species may therefore share identity evidence while remaining unsuitable for a common quantitative acceptance criterion or safety conclusion.

Related literature illustrates this progressive increase in the required degree of similarity; Common ecological conditions did not eliminate accession-related variation in four centellosides [22]. Solvent choice altered recovery of triterpenes and phenolic groups [3], resin fractionation produced a triterpene-enriched preparation distinct from the crude extract [34], and formulation preparation changed apparent recovery of the target triterpenes [35]. Fermentation may further shift glycosides toward acidic triterpenoids [36]. The studies consistently identify composition as process-sensitive, yet they cannot define a single distribution because they examine different materials and transformations.

Analytical comparisons lead to a related conclusion. Quantitative nuclear magnetic resonance (qNMR) and liquid chromatography–tandem mass spectrometry (LC-MS/MS) measurements of green-tea catechins provided orthogonal quantitation but differed in calibration and interference profiles [37]. High-performance thin-layer chromatography (HPTLC) fingerprinting, high-performance liquid chromatography with diode-array detection (HPLC-DAD) profiling, and combined nuclear magnetic resonance/high-performance liquid chromatography (NMR/HPLC) studies showed that similarity depends on the selected features, sample preparation, and analytical platform [38–40]. Agreement between methods can strengthen an inference, but it does not establish equivalence between materials.

Here, the comparability domain comprises the materials eligible to share evidence for a stated decision. The comparison covers botanical origin, plant part, processing, carrier, matrix, composition, relevant hazards, analytical basis, and intended use. It also defines the sampling frame for representative batches, which must span the variation that the specification is intended to accept. Materials outside the domain require a justified bridge, separate grades, or their own evidence. Pooling incompatible materials merely enlarges the dataset by converting genuine differences into an artificial range.

3.4. Bridging External Evidence

Evidence bridging begins with the decision to be supported, whether identity, method suitability, a consistency range, a safety boundary, or a condition of use. Source

and target materials are then compared with respect to botanical origin, plant part, processing, carrier, composition, matrix, method purpose, and use. Any unresolved differences are recorded before the evidence is classified as directly applicable, conditionally applicable, not applicable, or insufficiently characterized. NIFDC dossier rules for new-ingredient registration and filing, together with medicinal quality guidance, provide precedents for defining materials and documenting relevance within their own scopes [13,14,18]. The four applicability categories used here are an operational proposal for this review; they do not determine the status of an existing cosmetic ingredient.

Evidence is directly applicable when no unresolved difference affects the stated decision. Evidence is conditionally applicable when a bounded difference can be managed through a restriction, stratification, or specified confirmation. Evidence is not applicable when an identified difference invalidates the intended claim. Evidence is insufficiently characterized when missing information prevents the comparison. These four categories are an operational classification proposed in this review, not a regulatory classification prescribed by the cited sources. They do not determine the legal status of an existing cosmetic ingredient.

The classification determines the next step. A matrix difference may call for method verification or validation, a proposed common range requires comparable production-batch evidence, and a safety bridge requires target-relevant information on hazard, route, and exposure. A remediation plan alone does not complete the bridge. Until the stated condition is met, the evidence supports only the narrower claim already demonstrated. That bounded conclusion then guides selection of attributes, methods, and an acceptance criterion, condition of use, or management measure.

4. From Critical Attributes to an Executable Specification

Sections 3.3 and 3.4 define the comparability domain and the four evidence-applicability categories. Section 4 applies those definitions to attribute selection, method confirmation, and control formation. In Figure 1, Steps 1–2 define the decision object, while Steps 3–6 select attributes and methods and appraise evidence. Step 7 forms an acceptance criterion, condition of use, or management measure; Steps 8–9 verify the control and trigger lifecycle reassessment.

4.1. Selecting Attributes That Change a Decision

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Q9(R1) links quality-risk decisions to knowledge, uncertainty, and decision importance [41]. EMA and FDA botanical-drug guidance links specifications to defined materials, manufacturing controls, and analytical evidence [13,14]. These pharmaceutical precedents are not cosmetic requirements. Their shared premise is that a specification test is justified only when it addresses a defined failure pathway.

An attribute is critical when loss of control could change identity, batch acceptance, permitted use, a safety conclusion, or an investigation. Plausible substitution calls for a discriminatory feature; selective extraction may require a compositional profile; cultivation or solvent history may support a residue or process marker; and credible contamination may justify a hazard panel. Multi-platform metabolomic studies show that complementary features can improve botanical discrimination, but not every detected feature is critical [42].

Each selected attribute should be linked to its variation or hazard source, the affected decision, the consequence of error, and the control point. Measurements without a credible pathway or decision consequence may support characterization, but they do not justify mandatory release testing.

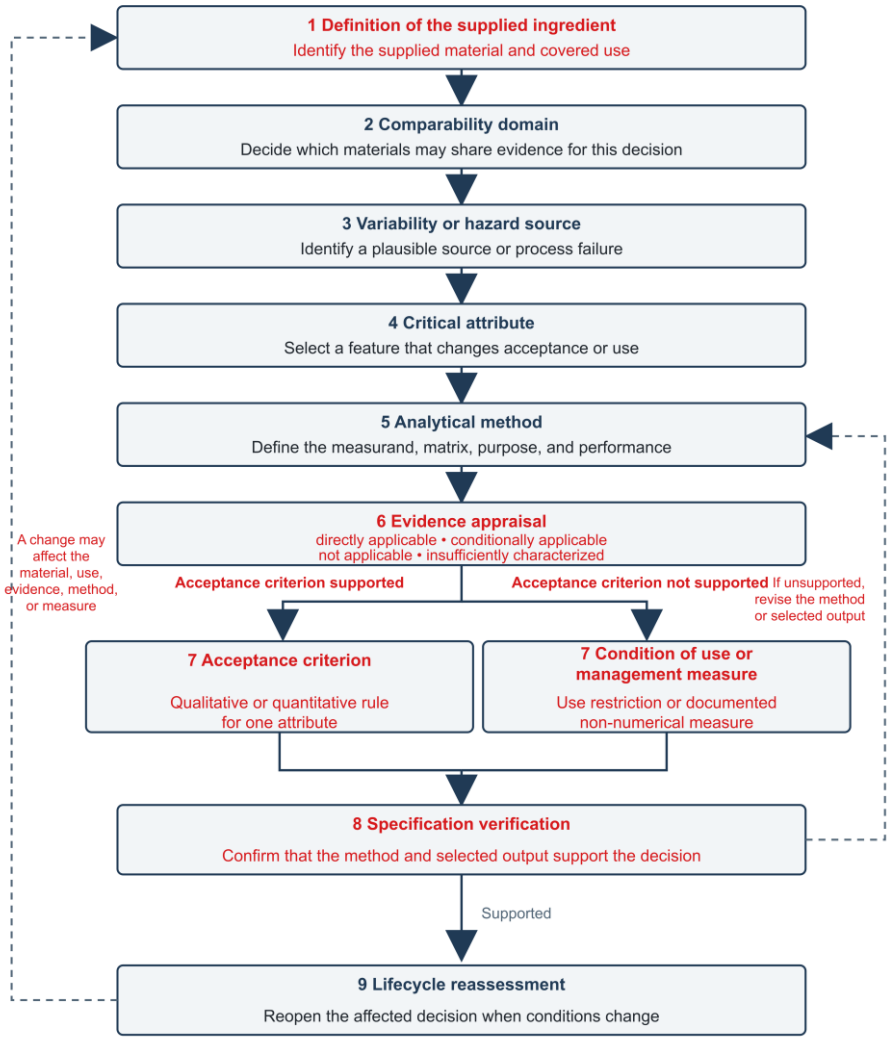


Figure 1. Proposed decision framework for an ingredient specification.

4.2. Assigning Marker Functions

Detecting a constituent does not support every conclusion for which that constituent might be used. WHO guidance and review literature distinguish several chemical-marker functions, and an empirical comparison of eight botanicals found that concentrations of commonly selected markers generally did not predict the tested in vitro activities [11,12,43]. Natural-product mixtures may also show synergy or antagonism that a single constituent cannot represent [44]. Taken together, these findings require the function of each marker to be stated explicitly, while leaving room for well-supported single-marker measurements.

An identity marker supports acceptance or rejection of an identity claim. The supporting evidence must show that the feature or profile distinguishes the target from relevant taxa, substitutes, and adulterants in the defined material. A widely distributed compound may contribute to a multivariate profile without being discriminating on its own. Its presence does not establish composition, consistency, function, or safety.

A consistency marker detects source or process drift within the comparability domain. Selection requires evidence that the marker or fingerprint reflects relevant variation. If a range is proposed, a suitable method and representative production-batch data are also needed. A fingerprint may identify similarity or an outlying batch, but it does not establish a toxicological boundary or cosmetic efficacy.

A function-related constituent supports a specified relationship between composition and the intended cosmetic function. This use requires evidence for the characterized ingredient and application, as well as evidence that the measured constituent is informative for that relationship. Detection or assay of the constituent alone does not demonstrate finished-product efficacy or permit transfer of a medicinal claim.

A hazardous constituent is measured to inform a defined safety decision, such as investigation, restriction, product testing, or release. Its selection requires a plausible source or contamination pathway and endpoint-relevant hazard evidence; any quantitative acceptance criterion also needs an applicable decision boundary. The resulting decision record should define the analytes, chemical forms, summation or equivalence rules, and reporting basis. Measurement of one hazardous constituent neither excludes other hazards nor demonstrates the safety of the entire mixture.

4.3. Selecting and Confirming Analytical Procedures

Method selection begins with the intended decision: screening, identity confirmation, batch release, trend monitoring, or safety control. That decision defines the measurand or qualitative feature, target matrix, reporting basis, working range, uncertainty, and required performance. ICH Q14, ICH Q2(R2), and Eurachem provide transferable analytical principles rather than cosmetic legal duties [45–47].

Target-matrix confirmation should test the performance needed for the stated decision. Identity procedures require recoverable and discriminatory features after processing; quantitative procedures require appropriate extraction recovery, selectivity, calibration, precision, and reporting in the supplied matrix [30,31,35,48–50]. These studies provide analytical precedents, not evidence that one procedure performs across all ingredient grades.

Hazard methods require the same decision-specific confirmation. Citrus furocoumarin and PA methods differ in analyte panels, chemical forms, extraction, calibration, and matrix [51–58]. A broader panel or lower detection limit adds value only when it matches the defined hazard and control decision.

Method provenance determines the available starting evidence, while the remaining gap determines whether verification, validation, or revalidation is needed. The method-use statement should record the supplied matrix, measurand or feature, purpose, range, performance, calculation and reporting basis, decision role, and remaining limitations. A citation alone is insufficient.

4.4. Forming the Specification and Recording Its Basis

In this framework, an ingredient specification is the complete documented control arrangement for the supplied ingredient, including release items and controls implemented elsewhere. An acceptance criterion is the qualitative or numerical decision rule for one attribute, accompanied by its method, units or features, sample-state basis, calculation, and conformity rule. A condition of use is a restriction at the formulation or use level, such as a maximum inclusion level. Management measures govern qualification, grade, supplier, sourcing, reporting, investigation, product testing, or batch handling.

Within the Section 3.3 comparability domain, representative commercial batches may support a consistency acceptance criterion; research and development batches primarily inform process understanding. Pooling requires an explicit material and statistical rationale. Analytical variation must be separated from batch variation, and atypical results investigated rather than absorbed by a wider criterion. The highest observed value describes occurrence, not a toxicological boundary.

For every specification item, the record should retain the source factor, controlled attribute, method, evidence status, acceptance criterion, condition of use, or management

measure, uncertainty, responsible party, and lifecycle reassessment trigger. This structure keeps applicable law separate from technical precedent, a range derived from representative batches, or an author-proposed control. It also identifies the evidence that is still missing when an acceptance criterion cannot yet be justified.

5. An Acceptance Criterion Cannot Yet Be Justified

Safety evidence must establish both the decision boundary and the stage at which the relevant risk can be controlled. The routes below distinguish requirements directed at ingredients, conditions directed at finished products, and hazard or toxicological information for which no applicable limit has been established.

5.1. Selecting the Safety Assessment Route

The first step is to identify the object regulated or evaluated by the source. A requirement expressly directed at the supplied ingredient, or at a named constituent in that ingredient, may inform release within its stated jurisdiction, version, and scope. Regulation (EC) No 1223/2009 and the Chinese 2015 safety text illustrate how prohibitions, restrictions, product requirements, and substance-specific provisions attach to defined regulated objects [16–17,26]. Applying them still requires confirmation of the ingredient, product category, use, and text in force at the review cut-off. The mandatory national standard GB 7916—2026 had been published by 20 October 2026 but was not yet effective. It was scheduled to take effect on 1 January 2028 and could not be treated as a compliance requirement in force at the review cut-off [59].

A condition that applies to a finished cosmetic or product category constrains that product. It affects an ingredient only through a justified analysis of formulation and exposure. The SCCS Notes of Guidance provide the main cosmetic model used here for characterization, exposure, toxicology, and margin-of-safety reasoning [8]. Labelling obligations are recorded separately because consumer communication is not an ingredient acceptance criterion [20].

When a source identifies a hazard, provides toxicological data, or sets a medicinal or food limit without an applicable cosmetic limit, it frames the safety question rather than establishing a numerical ingredient requirement. Assessments by the EMA and the European Food Safety Authority (EFSA) of toxic 1,2-unsaturated pyrrolizidine alkaloids (PAs), for example, demonstrate hazard relevance in medicinal and dietary settings but do not create a cosmetic ingredient acceptance criterion [60-61]. Assessment must return to the characterized material, relevant endpoint, route, and intended use. Production-batch occurrence data describe what was observed; they do not independently establish a safe concentration.

5.2. Conditional Allocation from a Finished Cosmetic Product Limit

The simplest allocation model divides a finished-product concentration limit by the ingredient inclusion fraction, thereby assuming a direct and stable relationship between the two concentrations. That assumption fails if the product provision and ingredient assay address different analytes, chemical forms, or sums; if other ingredients contribute the same constituent; if processing causes formation, loss, migration, evaporation, or concentration; if product categories or exposure conditions differ; or if the method cannot resolve the decision level. Under these conditions, measurement and process uncertainty can outweigh the apparent precision of the calculation.

Aggregate-exposure models introduce a further constraint. Contributions from several products require compatible dose metrics, distributions of product use, retention and route assumptions, and a defensible treatment of concurrent use [62]. A formulation calculation cannot assume that an unquantified contribution from another source is zero. The

WHO risk-assessment toolkit similarly separates problem formulation, hazard characterization, exposure assessment, and risk characterization [63].

Accordingly, we propose allocation only when the conditions in Table 1 have been resolved for the specified formulation or product category. The inclusion fraction should refer to the supplied ingredient, including its carrier, on a basis compatible with the finished-product acceptance criterion. Contributions from other sources and any transformation during processing must be bounded. This is a risk-management approach, not a regulatory allocation procedure or a substitute for endpoint-appropriate safety assessment.

Table 1. Proposed conditions and outcomes for allocating a finished cosmetic product limit.

Allocation Condition	Evidence Required for the Proposed Allocation	Action If Unresolved
Measurand	The same analyte, chemical form, or defined sum, with compatible equivalence and summation rules.	Resolve the mismatch before allocation.
Concentration basis	Compatible units, sample state, denominator, and inclusion fraction expressed for the supplied ingredient.	Harmonize the bases and document every conversion.
Other sources	Bounded contributions from other ingredients, processing aids, packaging, and process-related sources.	Retain unknown contributions and assess the formulation or product.
Processing	Bounded formation, loss, migration, evaporation, degradation, or concentration.	Narrow the process domain or test the finished product.
Product and exposure	Covered category, route, retention, population, use pattern, and assumptions for aggregate exposure [8,62].	Obtain scenario-specific evidence or justify a narrower use.
Measurement	Representative sampling and adequate method capability at the decision level [46,47].	Improve the measurement or revise the supported decision.
Uncertainty	Measurement and process variation, residual contributions, the allocation factor, and the conformity rule.	Do not introduce an unexplained safety percentage.
Supported conclusion	When all necessary conditions are met, a bounded acceptance criterion may be derived. A condition of use requires separate safety justification.	Stop numerical allocation, document the gap, and select a separately justified management measure.

5.3. Evaluating Exposure, Toxicology, and Uncertainty

External exposure describes contact with an ingredient or constituent and depends on product amount, concentration, application area, frequency, duration, route, and retention. Systemic exposure also depends on absorption and, where relevant, metabolism. The Organisation for Economic Co-operation and Development (OECD) Test Guideline 428 provides an in vitro model for skin absorption, but evidence on dermal availability remains specific to the material, formulation, and test conditions [64]. Neither a concentration on skin nor a receptor-fluid result can be converted into systemic dose without a compatible basis.

Single-product exposure concerns a defined product and route. Aggregate cosmetic exposure combines relevant products and routes for the same ingredient or constituent, using compatible dose metrics and justified assumptions about concurrent use [8,62].

Non-cosmetic sources should be included only when the assessment requires them and their contributions can be expressed on a comparable basis. An unquantified source remains an uncertainty; it cannot be treated as zero.

For a threshold systemic effect, a suitable point of departure and a comparable estimate of systemic exposure may support a margin-of-safety assessment. Non-threshold, local, sensitization, phototoxicity, and genotoxicity endpoints require endpoint-specific evidence and dose metrics. Defined approaches such as OECD Guideline 497 apply only within their stated endpoint and applicability domains [65]. A systemic margin does not resolve local phototoxicity or sensitization.

Evidence for individual constituents and for the whole mixture is complementary, but the two are not interchangeable. A measured panel covers only the named analytes, whereas toxicity data for an extract apply to the characterized mixture that was tested. The threshold of toxicological concern (TTC) can support a bounded assessment only after exclusions, chemical-domain conditions, exposure, and endpoint relevance have been addressed [8,66]. Decision models based on a botanical history of use likewise require compositional comparability and cannot replace missing hazard data [67]. A recent cosmetic case combined in vitro tests, an in silico margin-of-safety analysis, the TTC, and history of use for one characterized extract [68]. Its conclusion remains specific to that ingredient and use.

5.4. Selecting and Documenting the Safety-Related Output

The appropriate output depends on where the risk can be bounded reliably. A defined hazard boundary and a suitable measurement in the supplied ingredient may support an ingredient acceptance criterion. If safety depends on the inclusion proportion, a condition of use, such as a maximum use level, can constrain the formulation only when the hazard, exposure, composition, and contributions from other sources justify that level. Both are numerical decisions and require explicit treatment of uncertainty and a conformity rule.

When formulation or processing determines the relevant hazard concentration, finished-product testing may implement or verify the control. The test still requires the correct measurand, demonstrated performance in the matrix, representative sampling, and an applicable decision boundary. If the evidence does not support a number, management measures may include supplier qualification, a defined grade, source restrictions, process controls, reporting, targeted monitoring, or a case-specific safety assessment. Each management measure must address the documented uncertainty, and use may need to be withheld until the relevant gap is closed.

The decision record should state the acceptance criterion, condition of use, or management measure, implementation point, covered uses, assumptions, responsibilities, residual uncertainty, and lifecycle reassessment trigger. When outputs are combined, their functions remain distinct, and product testing does not convert a product requirement into an ingredient acceptance criterion. Section 6 applies these choices to the three cases.

6. Illustrative Applications and Common Implementation Requirements

6.1. Case Selection and Comparison

The cases were selected because their controlling uncertainties occur at different stages. For *C. asiatica*, the main question is compositional consistency within a manufacturing grade. Expressed lemon peel oil raises a phototoxicity question governed by oil grade, formulation, and use on sun-exposed skin. The PA case concerns a recognized hazard, a plausible but unconfirmed contamination pathway in the target supply chain, and

an incomplete cosmetic-exposure bridge. Table 2 compares the resulting decisions. The cases examine the reasoning process rather than the performance of the framework.

Table 2. Comparison of three illustrative ingredient decisions.

Comparison Field	*Centella asiatica* Extract	Expressed Lemon Peel Oil	PA Contamination
Defined scenario and decision difficulty	Dried hydroethanolic aerial-part extract with defined native-extract content and carrier. The decision concerns a composition range for one manufacturing grade.	Defined grade of expressed *Citrus* × *limon* peel oil in a leave-on product used on sun-exposed skin. Phototoxicity control depends on use.	Hydroalcoholic *H. perforatum* aerial-part extract. The suspected contamination pathway is external, and the cosmetic-exposure bridge is incomplete.
Comparative scientific finding	Plant part, accession, solvent, enrichment, fermentation, and formulation alter triterpene patterns [2,3,22,35,36].	Volatile profiles inform identity; non-volatile oxygenated heterocycles require a separate panel; phototoxicity depends on analyte composition and test and use conditions [52,69–71].	Medicinal and food evidence supports hazard recognition and analyte selection, while occurrence, source attribution, matrix performance, and dermal transfer remain separate questions [55,56,60,72,73].
Decision at review cut-off (20 October 2026)	Use authenticated source, a fingerprint, and a four-triterpene panel for grade development and monitoring. Numerical release limits require representative production batches.	Define the oil grade and use separate methods for volatile identity and furocoumarin safety. Evidence available by the review cut-off does not support conversion of a product value into an oil value.	Combine supplier and field management measures with a named PA/N-oxide screening panel and case-specific safety review. No universal cosmetic threshold can be inferred.
Evidence needed to advance	Method confirmation in the target grade, stability data, and representative batches spanning the declared source and process variation.	The applicable product provision, method performance in the target oil and finished product, analyte and summation definitions, other-source contributions, processing, and exposure.	Occurrence and source data from the target supply chain, recovery and calibration in the target extract, relevant dermal availability, cosmetic use, and aggregate exposure.
Boundary and stopping point	Do not pool incompatible plant parts, extracts, enriched fractions, or carriers. Consistency does not establish efficacy or safety.	Do not treat a finished-product value or industry proposal as an automatic oil acceptance criterion. Derivation stops when an allocation condition remains unresolved.	Food or medicinal values and analytical detection do not establish target-specific dermal or cosmetic safety.
Lifecycle reassessment trigger	A change in starting material, cultivation, extraction, enrichment, carrier, marker trend, stability, or batch coverage.	A change in oil grade, hazard-reduction process, analyte panel, formulation, use, product law, or industry-standard status.	A change in weed pressure, supplier, PA/N-oxide profile, process, formulation, use, dermal evidence, or exposure evidence.

6.2. Centella asiatica Extract

The target material is a dried hydroethanolic extract of authenticated *C. asiatica* aerial parts, with a specified native-extract content, carrier, and topical use. Evidence from raw materials points in the same direction but is quantitatively heterogeneous. Puttarak and Panichayupakaranant reported effects of plant part, location, and season on pentacyclic

triterpenes, whereas Kunjumon et al. found different ratios of four centellosides among accessions grown under common conditions [2,22]. In the latter dataset of 50 dried aerial-part accessions, reported concentrations ranged from 0.04% to 2.41% for asiaticoside, 0.15% to 5.27% for madecassoside, and 0.02% to 0.72% for madecassic acid; asiatic acid was below the HPTLC detection level in 28 samples. These values document variation on the study basis and are not proposed as limits for the processed target extract. Studies of greenhouse cultivars and Yunnan germplasm likewise distinguished chemical profiles despite more controlled growth or combined phenotypic and genetic characterization [23,24]. Collectively, the studies identify source and accession as sources of variability without defining an acceptance criterion for the target extract.

Processing studies explain why raw-material ranges cannot be carried forward unchanged. Solvent selection altered the recovery of major triterpenoids and other compound groups [3]. Hydroethanolic extraction followed by resin fractionation yielded a triterpene-enriched fraction distinct from the crude extract [34], while fermentation shifted the balance toward acidic triterpenoids [36]. A targeted liquid chromatography-mass spectrometry (LC-MS) study of *C. asiatica* extracts and formulations found matrix-dependent analytical recovery [35]. Its formulation data, however, do not establish recovery in the target cosmetic grade. Separate work showed that release from cold-processed topical vehicles also depended on formulation [74]. The common finding is process sensitivity, with differences attributable to solvent, enrichment, biotransformation, carrier, and measurement basis.

Madecassoside, asiaticoside, madecassic acid, and asiatic acid are proposed as a linked consistency panel. These constituents represent the principal glycoside and aglycone pairs commonly used to characterize centelloid composition, and their joint pattern can reveal extraction selectivity or a change in conversion state [2,48,75]. The EMA assessment of medicinal *C. asiatica* preparations provides a precedent, specific to its source status, for evaluating these constituents; it does not establish a range for cosmetic grades [76]. The proposed panel serves consistency assessment, not proof of efficacy. A fingerprint supplies broader compositional context, whereas a single ratio or total may conceal reciprocal changes. Target-grade characterization may identify additional decision-relevant constituents.

Published methods provide candidates while defining the limits of the available evidence. Mass-spectral fingerprinting with standard-based quantitation separates qualitative characterization from constituent measurement [48]. LC-MS studies of extracts and formulations demonstrate the importance of extraction recovery and matrix effects [35]. A recent six-triterpene high-performance liquid chromatography (HPLC) method shows the value of resolving isomers in the commercial products studied [49]. Structural fingerprint libraries may improve peak assignment [50]. None of these publications, however, establishes precision, recovery, stability, and discrimination for the defined carrier-containing grade.

6.3. Expressed Lemon Peel Oil

The target material is expressed lemon (*Citrus* × *limon*) peel oil used in a leave-on product on sun-exposed skin. Cold expression retains a volatile fraction useful for identity and a non-volatile oxygenated-heterocycle fraction that may contain phototoxic furocoumarins. A gas chromatography (GC) volatile profile and a liquid chromatography (LC)-based furocoumarin panel therefore serve different control purposes. Work on the authentication of cold-pressed citrus oils also shows that non-volatile profiles can help distinguish grades, although the analytes used for authenticity need not be the same as those included in the safety panel [51,69].

Analytical studies broadly agree on the need for a defined panel, but the reported quantity depends on the analytical definition. Frérot and Decorzant showed that HPLC with ultraviolet (UV), fluorescence, or mass detection provides different selectivity for furocoumarins; an apparent UV total is therefore not a self-defining measure of "total furocoumarins" [52]. In one lemon-oil sample, bergapten was reported at 18.50 parts per million (ppm), whereas the sum of the 15-target panel was 2919.6 ppm by atmospheric-pressure chemical ionization mass spectrometry (APCI-MS) [52]. The contrast shows how strongly the numerical result depends on analyte definition, and neither value is a finished-product limit. An ultra-high-performance liquid chromatography–tandem mass spectrometry (UHPLC-MS/MS) method covering 25 oxygenated heterocycles in cold-pressed grapefruit oils reports R^2 values above 0.99, analyte-specific quantification limits of 2×10^{-7} to 5×10^{-6} mg/g, and interday precision of 2.16% to 6.90% [53]. Those performance values apply to the grapefruit-oil method described in the abstract. Solid-phase extraction coupled with LC-MS (SPE-LC-MS) work in natural cosmetics provides a separate precedent for the finished-product matrix [54]. Grapefruit oil, lemon oil, and finished cosmetics remain distinct in composition and analytical recovery.

Phototoxicity evidence is equally dependent on the tested material and conditions. An older lemon-oil study relates composition to phototoxic response and reports bergapten concentrations of 4–87 ppm in the oils examined [70]. Tests of essential oils intended for cosmetic use also found differences in phototoxic potential [77]. A recent 3T3 neutral-red-uptake study illustrates an endpoint-specific screening method and the need to address solubility and test applicability for botanicals [71]. Together, these studies inform hazard identification and test selection, not a universal safe concentration for every oil and use.

International Fragrance Association (IFRA) guidance describes use categories and the implementation of industry standards, but its status and amendment must be distinguished from law [78]. Any legally applicable finished-product condition for the intended category would retain its product scope. Conversion to an oil acceptance criterion would require resolution of the analyte definition, contributions from other sources, processing, matrix, inclusion fraction, exposure, method capability, and uncertainty described in Section 5.2.

6.4. PA Contamination

The target material is a hydroalcoholic aerial-part extract of *H. perforatum*, with a suspected contamination pathway involving co-harvested PA-producing weeds. EMA medicinal documentation recognizes contamination of herbal materials by toxic 1,2-unsaturated PAs as a control problem [60]. The National Institute for Public Health and the Environment (RIVM) assessment states that St John's wort is not naturally a PA source and interprets findings in some preparations as likely contamination from other plants [79]. These sources justify investigation of a plausible pathway but do not establish contamination in the target cosmetic supply chain.

Analytical evidence must distinguish occurrence from source attribution. Food studies demonstrate multi-analyte LC-MS/MS strategies and show that DNA metabarcoding may provide clues to the contributing plants [55,56]. One food-matrix method used 30 reference analytes, comprising 16 PAs and 14 corresponding N-oxides. This is an example of a defined panel rather than a universal analytical total. Recent reviews and UHPLC-MS/MS studies further show that the panel, inclusion of free bases and N-oxides, availability of standards, surrogate calibration, extraction, and matrix all influence the result [57,58]. PA profiles also differ between comfrey roots and leaves, and quantitation becomes less certain when authentic standards are unavailable [80]. These findings support

a named PA/N-oxide panel with explicit calibration and summation rules. They do not establish method performance in the target hydroalcoholic extract.

Related reports describe limited dermal availability of lycopsamine from a comfrey cream and assess percutaneous absorption of selected retronecine-type PAs through human skin [72,73]. The comfrey-cream abstract reports that 0.6 ± 0.4% of the applied lycopsamine dose appeared in receptor fluid after 24 h; a theoretical worst-case estimate of 4.9% was strongly influenced by the detection-limit assumption. The preparations, analytes, dose bases, and exposure conditions differ from the target extract and intended cosmetic use. The studies show that dermal transfer can be measured and may be limited in particular systems, but they do not provide a universal absorption fraction or cosmetic limit. EFSA dietary risk values cannot be transferred without route- and exposure-specific justification [61].

6.5. Common Implementation Requirements

Representative batches should cover the comparability domain, including relevant variation in source, harvest, supplier, process, carrier, storage, and season. Development, stability, and routine commercial batches serve different purposes and should be identified accordingly. Any proposed acceptance criterion needs a statistical and process rationale, separation of analytical variability from batch variability, and a rule for investigating atypical results. The extremes of a small dataset neither define future production nor relax a safety boundary.

Taken together, the three cases show that the available evidence supports different outputs of control rather than a common numerical endpoint. For *Centella asiatica*, it supports authenticated sourcing, process documentation, chromatographic fingerprinting, and a four-triterpene consistency panel. For expressed lemon peel oil, it supports separate control of volatile identity and furocoumarin-related safety. For PA contamination, it supports supply-chain management measures and screening based on an explicitly defined PA/N-oxide panel, followed by case-specific safety assessment when contamination is confirmed. None of the three evidence packages yet justifies a grade-specific numerical release limit or maximum use level. Such a limit should be considered only after the relevant gaps in target-matrix method performance, representative batch or occurrence data, applicable product conditions, and exposure relevance have been resolved. The common method record should cover sampling, sample-state basis, measurand or profile, recovery or discrimination, working range, precision, quantification capability where relevant, uncertainty, and the conformity rule. Even a reliable chemical result cannot supply missing exposure evidence or validate the framework.

Lifecycle reassessment is triggered by changes in identity, source, processing, carrier, composition, stability, hazard information, exposure, method performance, supplier, or source status. Depending on the change, the response may involve comparative batches, additional method confirmation, revised limits, use restrictions, product testing, or a new safety assessment. An atypical result should initiate an investigation rather than an automatic widening of the specification.

7. Discussion

Existing systems address different components of the specification problem. Authentication reviews and forensic studies determine what a material is and how substitution can be detected [5,6,10]. Fingerprint, marker, and multi-platform research identifies measurable chemical features and shows how orthogonal evidence may strengthen discrimination [7,38,42]. Pharmacopoeial and botanical-drug guidance develops controls for defined medicinal materials [13,14], whereas SCCS guidance addresses cosmetic exposure

and toxicology [8]. The framework presented here links these outputs within a single decision process for a specified cosmetic ingredient.

Its purpose lies in making several normally implicit judgements explicit and sequential. Comparability is defined for the decision at hand, not for a botanical name alone. Authority is assessed separately from applicability, preventing a legally binding product condition, a pharmacopoeial method, and a scientific observation from being treated as equivalent. Marker functions are assigned separately for identity, consistency, function, and hazard. The possible outputs are then distinguished as acceptance criteria, conditions of use, or management measures. If a material, analytical, or exposure bridge remains unresolved, the sequence stops before an apparently precise number is produced.

These operations change practical decisions. They prevent dossiers organized by common name from pooling incompatible extracts and require a published method to demonstrate performance in the supplied matrix before release use. They also keep batch consistency distinct from efficacy and safety, and prevent mechanical division of a finished-product restriction into an ingredient limit. In the *C. asiatica* case, the immediate task becomes generation of target-grade batch evidence rather than importation of research ranges. For lemon oil, identity by GC is separated from safety measurement by LC, and the numerical question remains at the appropriate product and exposure boundary. In the PA case, the unresolved exposure bridge becomes a defined set of supplier, occurrence, analytical, and safety tasks.

Implementation entails additional work. Manufacturers need a reconstructable definition of the supplied ingredient, authenticated reference materials, method transfer or validation, representative batches, and coordinated responsibility for legal, analytical, and safety decisions. Analytical complexity alone does not guarantee decision value. A broad metabolomic or DNA dataset may increase the interpretive burden without improving release decisions if discrimination, uncertainty, and action rules remain undefined. A focused panel may be sufficient when the failure pathway and decision boundary are clear. The framework consequently seeks the least evidence sufficient for the stated decision while preserving the specific gap that prevents the next one.

The approach is vulnerable to several forms of misuse. The supplied ingredient may be defined retrospectively from test results; analytical similarity may be treated as evidence of process equivalence; one marker may be assigned several functions without separate support; a range may be based on a small or biased batch set; or legal and industry sources may be used without version control. A narrow panel may also create false reassurance by excluding unrecognized hazards, while product testing may be used to compensate for an inadequately characterized ingredient. Traceable assumptions, claim-specific bridges, separate status records, and lifecycle reassessment are intended to expose these failure modes.

The framework has not been validated against a commercial ingredient dataset or through multi-institutional application; the cases illustrate the reasoning process rather than validating framework performance. Several precedents originate in medicinal or food contexts and require fresh appraisal for cosmetic matrices and exposure scenarios. This structured narrative review is not a systematic review, and its searches do not guarantee coverage of every relevant source or jurisdiction. Future evaluation should examine assessor agreement, resource requirements, method-transfer success, decision changes, and detection of unacceptable batches using supplier, transfer, stability, and safety records.

8. Conclusions

Heterogeneous evidence can support an ingredient specification only after the supplied material and the comparability domain relevant to the decision have been defined.

Within that domain, each source of variation or harm must be connected to a decision-relevant attribute, a fit-for-purpose method, the status of the supporting evidence, an acceptance criterion, condition of use, or management measure, and a lifecycle reassessment trigger.

Legal requirements, standards, pharmacopoeial methods, guidance, scientific studies, and batch observations serve different purposes. Their use depends on the jurisdiction and regulated object, as well as compatibility in material, processing, matrix, method purpose, intended use, and exposure. A missing bridge narrows the claim that can be supported and prevents quantitative transfer.

An ingredient acceptance criterion is warranted when the attribute and decision boundary can be measured reliably in the supplied ingredient. A condition of use is appropriate when formulation and exposure connect the ingredient to a safety boundary. If the evidence does not support a numerical decision, a management measure addressing supplier, grade, process, use, testing, or case-specific safety assessment should target the identified gap. The three cases show that the same decision sequence can produce different outputs while keeping the remaining evidence needs visible.

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