Bergera koenigii (Murraya koenigii) Leaf Extract Face Serum for the Reduction of Hyperpigmentation and Dark Spots: *A Phytopharmaceutical Review and Formulation Approach*

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Abstract- Hyperpigmentary disorders — melasma, post-inflammatory hyperpigmentation (PIH), solar lentigines, and idiopathic dark spots — remain among the most common reasons patients with photo-exposed and darker skin types seek dermatological care, particularly across the Indian subcontinent. Conventional depigmenting actives such as hydroquinone, kojic acid, and synthetic tyrosinase inhibitors carry recognized concerns of cutaneous irritation, ochronosis, and limited long-term tolerability, sustaining interest in standardized herbal alternatives. Bergera koenigii L. (synonym Murraya koenigii (L.) Spreng., Rutaceae), the Indian curry leaf tree, is a rich source of pyranocarbazole alkaloids (mahanimbine, girinimbine, mahanine, koenimbine) and flavonoids (rutin, quercetin, kaempferol glycosides) with documented antioxidant, anti-inflammatory, antimicrobial, and wound-healing activity. This review consolidates the botanical, phytochemical, and pharmacological evidence relevant to cutaneous pigmentation and proposes a Quality-by-Design (QbD) based approach for developing a B. koenigii leaf extract face serum. A critical, and often overlooked, observation emerging from the literature is that the depigmenting potential of B. koenigii is extract-dependent: an aqueous leaf extract has been reported to inhibit mushroom tyrosinase, whereas a steam-distilled essential-oil fraction from the same species has been reported to activate tyrosinase several-fold. This contradiction carries direct formulation consequences and is addressed explicitly in the proposed extraction and quality-control strategy. The review further outlines candidate critical quality attributes, a representative formulation composition, evaluation parameters (physicochemical, in vitro antioxidant and tyrosinase-inhibition assays, dermal safety, and stability), and identifies the principal research gaps — extract standardization, seasonal/geographic alkaloid variability, and the absence of human clinical efficacy data — that must be resolved before B. koenigii can be confidently positioned as a depigmenting cosmeceutical active.

Index-Terms: Bergera koenigii; Murraya koenigii; curry leaf; hyperpigmentation; melasma; tyrosinase inhibition; carbazole alkaloids; herbal face serum; Quality by Design

I. INTRODUCTION

1.1 Hyperpigmentation: clinical burden and current therapeutic landscape

Cutaneous hyperpigmentation encompasses a spectrum of acquired pigmentary disorders — melasma, post-inflammatory hyperpigmentation (PIH), solar lentigines (age/sun spots), and idiopathic dark spots — that share a common downstream event: localized overproduction and accumulation of melanin. Surveys conducted across Indian cities report considerable heterogeneity in facial skin tone attributable to melasma, hyperpigmented spots, pigmented macules, and dark circles in a large majority of the population studied. Melasma in particular shows a markedly higher incidence in India than in several other populations, occurs roughly four times more often in women than men, typically affects individuals between 14 and 54 years of age, and has been reported in close to a third of middle-to-older aged women. PIH, arising after acne, eczema, or any cutaneous injury, is a particularly common presenting complaint in darker skin types because such skin tends to mount an exaggerated melanocytic response to inflammation.

First-line depigmenting agents — hydroquinone, kojic acid, arbutin, azelaic acid, tranexamic acid, and retinoids — act mainly by inhibiting tyrosinase, the rate-limiting enzyme of melanogenesis, or by interrupting melanosome transfer. While effective, several of these actives are limited by contact irritation, photosensitivity, allergic reactions, or, in the case of prolonged hydroquinone use, exogenous ochronosis. This safety profile, combined with a broader consumer shift toward "clean" and herbal personal-care formulations, has sustained sustained pharmaceutical and cosmetic interest in plant-derived tyrosinase inhibitors and antioxidants as gentler, adjunctive, or alternative depigmenting actives. Herbal face serums in general are now evaluated by the same physicochemical and safety criteria as conventional cosmeceuticals — pH, viscosity, spreadability, irritation potential, microbial stability, and in vitro antioxidant activity — reflecting growing scientific rigor in this segment of the herbal cosmetics market.

1.2 Rationale for Bergera koenigii as a candidate active

Bergera koenigii L. is the currently accepted botanical name for the plant long known as Murraya koenigii (L.) Spreng., the Indian curry leaf tree (family Rutaceae); the two names refer to the same species and are used interchangeably in the literature cited throughout this review. The leaves are a traditional culinary spice across South Asia and have a long history of ethnomedicinal use for digestive, dermatological, and antimicrobial indications. Phytochemically, the leaves are unusually rich in pyranocarbazole alkaloids — a class of compounds essentially unique to the genus Murraya/Bergera and a small number of related Rutaceae — together with flavonoids, phenolic acids, and an aromatic essential oil. Several of these constituents have documented antioxidant and anti-inflammatory activity, and at least one study has reported direct tyrosinase-inhibitory activity for an aqueous leaf extract, providing a plausible, literature-supported rationale for exploring B. koenigii as the active ingredient of a depigmenting face serum. At the same time,

as detailed in Section 4, the same plant has also been reported to yield a tyrosinase-activating fraction under a different extraction method — a finding with direct consequences for how any such serum should be formulated, and one that this review treats as a central design consideration rather than a footnote.

The objective of this review is therefore twofold: (i) to consolidate the available botanical, phytochemical, mechanistic, and pharmacological evidence on B. koenigii leaves as it pertains to cutaneous pigmentation, and (ii) to propose a Quality-by-Design (QbD) based formulation approach for a B. koenigii leaf extract face serum, while explicitly identifying the evidence gaps that currently limit confident translational claims.

II. BOTANICAL PROFILE OF BERGERA KOENIGII

Table 1 summarizes the taxonomic classification of the plant, and Figure 1 illustrates the characteristic compound-leaf morphology used for macroscopic identification.

Taxonomic rank	Classification
Kingdom	Plantae
Order	Sapindales
Family	Rutaceae
Genus	Bergera (syn. Murraya)
Species	koenigii L. (syn. Murraya koenigii (L.) Spreng.)
Common names	Curry leaf tree, curry tree, kaloupilé, sweet neem (misnomer), kadhi patta (Hindi/Marathi), karivepallai (Tamil/Telugu)

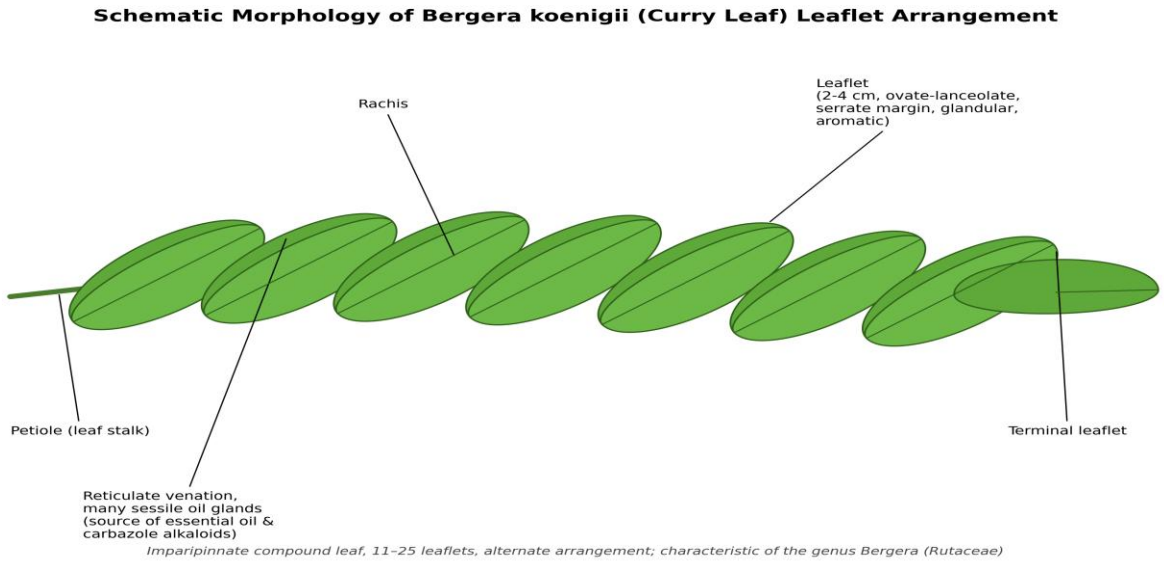

Figure 1. Schematic line diagram of the characteristic imparipinnate compound leaf of Bergera koenigii, showing leaflet arrangement and the sessile oil glands that are the principal source of essential oil and carbazole alkaloids. (Original schematic; an authenticated photographic plate of the fresh plant/leaf material should be inserted alongside this figure in the final manuscript.)

Bergera koenigii is a semi-deciduous aromatic shrub or small tree reaching up to about 6 m in height, with a short trunk and grey-to-brown bark. The leaves are alternate, imparipinnately compound, 20–30 cm long, bearing 11 to 25 ovate-lanceolate leaflets, each 2–4 cm long with a serrate margin, reticulate venation, and numerous sessile glandular dots that impart the characteristic curry-like aroma on crushing — the same glands that are the principal repository of the essential oil and carbazole alkaloids discussed in Section 3. The plant produces small white flowers in cymose panicles and small, ovoid, purplish-black berries when mature. It is native to and widely cultivated throughout the Indian subcontinent and parts of Southeast Asia, growing from the sub-tropical plains into lower temperate hill zones.

Beyond its culinary use, B. koenigii leaves, bark, and roots have a documented history in traditional and Ayurvedic medicine for the treatment of dysentery, diarrhoea, indigestion, nausea and vomiting, as an antidote for bites of poisonous animals and insects, and topically for various skin infections and inflammatory conditions — traditional indications that, notably, already anticipate the antimicrobial and anti-inflammatory pharmacology described in Section 5.

III. PHYTOCHEMISTRY

The bioactivity of B. koenigii leaves derives chiefly from three groups of secondary metabolites: (i) pyranocarbazole alkaloids, a chemotaxonomic hallmark of the genus; (ii) flavonoids and phenolic acids; and (iii) a terpene-rich essential oil. The relative proportions of these groups — and, critically, which group dominates a given extract — depend heavily on the plant part, extraction solvent, and extraction method used, a point that becomes central to the formulation discussion in Sections 4 and 6.

3.1 Carbazole alkaloids

More than twenty carbazole alkaloids have been isolated from various parts of B. koenigii, the most extensively studied being mahanimbine, girinimbine, mahanine, isomahanine, mahanimbicine, koenimbine, murrayanine, murrayazoline, and murrayazolidine. Mahanimbine and koenimbine are reported as the two most dominant carbazole alkaloids in the leaf. Structurally, mahanine, isomahanine, and mahanimbine share a 23-carbon pyranocarbazole skeleton with four methyl groups, while girinimbine has an 18-carbon skeleton with three methyl groups. Several of these alkaloids — euchrestine B, bismurrayafoline E, mahanine, mahanimbicine, and mahanimbine — have been specifically highlighted for strong radical-scavenging activity, and girinimbine in particular has been the subject of a dedicated pharmacological review describing

potent anti-inflammatory and antioxidant effects, including inhibition of pro-inflammatory cytokines and nitric oxide production.

3.2 Flavonoids and phenolic acids

High-resolution mass spectrometric profiling (HPLC-ESI-QTOF-MS) of B. koenigii leaf extracts has identified rutin, quercetin, ferulic acid, hyperoside, kaempferol-7-O-glucoside, and morin as major flavonoid/phenolic constituents, with the ethyl acetate and methanolic extracts showing the highest total flavonoid and phenolic content. These compounds are well-characterized antioxidants in their own right and are independently reported in the cosmetic-ingredient literature as skin-conditioning and whitening agents, reinforcing their relevance to a depigmenting formulation.

3.3 Essential oil

Hydro- or steam-distillation of the leaves yields an aromatic essential oil rich in mono- and sesquiterpenes, traditionally noted for skin-moisturizing properties. As discussed in Section 4.3, however, this volatile fraction has also been specifically reported to activate tyrosinase, which distinguishes its dermatological relevance sharply from that of the polar (aqueous/alcoholic) leaf extract.

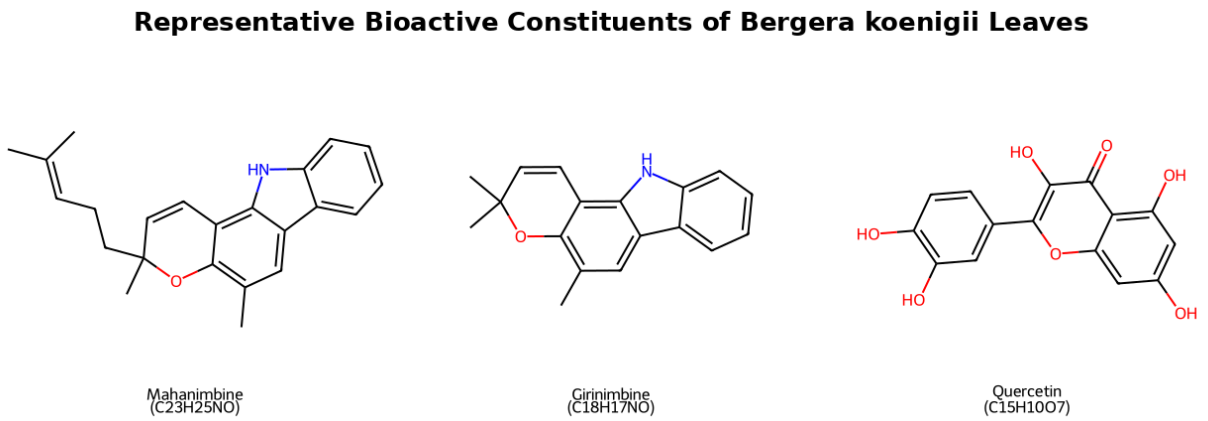

Figure 2. Two-dimensional structures of representative bioactive constituents of Bergera koenigii leaves: the pyranocarbazole alkaloids mahanimbine and girinimbine, and the flavonol quercetin (structures generated from validated PubChem-deposited SMILES; molecular formulae confirmed against literature mass-spectral data).

Table 2 summarizes the principal phytoconstituents discussed above together with their reported bioactivity relevant to this review.

Constituent	Class	Reported activity relevant to pigmentation/skin
Mahanimbine	Pyranocarbazole alkaloid	Antioxidant; major leaf alkaloid; antimicrobial, antidiabetic activity reported

Constituent	Class	Reported activity relevant to pigmentation/skin
Girinimbine	Pyranocarbazole alkaloid	Potent antioxidant and anti-inflammatory action (↓ cytokines, ↓ NO); gastroprotective, cardioprotective
Mahanine	Pyranocarbazole alkaloid	Strong radical scavenger; pro-oxidant/cytotoxic at higher (anticancer-research) doses — relevant safety caveat for topical use
Koenimbine / koenigin	Carbazole alkaloid	Among the dominant leaf alkaloids; contributes to overall antioxidant pool
Rutin, quercetin, kaempferol-7-O-glucoside, hyperoside, morin	Flavonoids	Free-radical scavenging (DPPH/ABTS); reported skin-whitening/conditioning use in cosmetic formulations generally
Ferulic acid	Phenolic acid	Antioxidant; common co-formulant in commercial brightening serums
Essential oil (terpenes)	Volatile oil	Skin-moisturizing; the steam-distilled fraction specifically has been reported to ACTIVATE tyrosinase (see Section 4.3)

IV. MECHANISTIC BASIS: MELANOGENESIS AND PROPOSED SITES OF PHYTOCHEMICAL ACTION

4.1 Overview of cutaneous melanogenesis

Melanin, the principal determinant of skin colour, is synthesized within melanosomes of epidermal melanocytes through a cascade initiated by ultraviolet (UV) radiation, inflammatory mediators, and hormonal stimuli. These triggers increase secretion of α-melanocyte-stimulating hormone (α-MSH), which binds the melanocortin-1 receptor (MC1R) on melanocytes, raising intracellular cyclic AMP (cAMP) and activating protein kinase A (PKA) and the transcription factor CREB. Phosphorylated CREB upregulates microphthalmia-associated transcription factor (MITF), the master regulator of melanogenesis, which in turn drives transcription of tyrosinase and tyrosinase-related proteins 1 and 2 (TRP-1, TRP-2). Tyrosinase is the rate-limiting enzyme of the pathway, converting tyrosine to L-DOPA and then to dopaquinone, the precursor of eumelanin and pheomelanin. UV exposure additionally generates reactive oxygen species (ROS) that independently sensitize this cascade. Newly synthesized melanin is transferred via melanosomes to surrounding keratinocytes, producing the visible pigmentation of melasma, PIH, solar lentigines, and related disorders. Figure 3 depicts this pathway together with the three plausible sites at which B. koenigii phytoconstituents could intervene, based on the pharmacological evidence reviewed below.

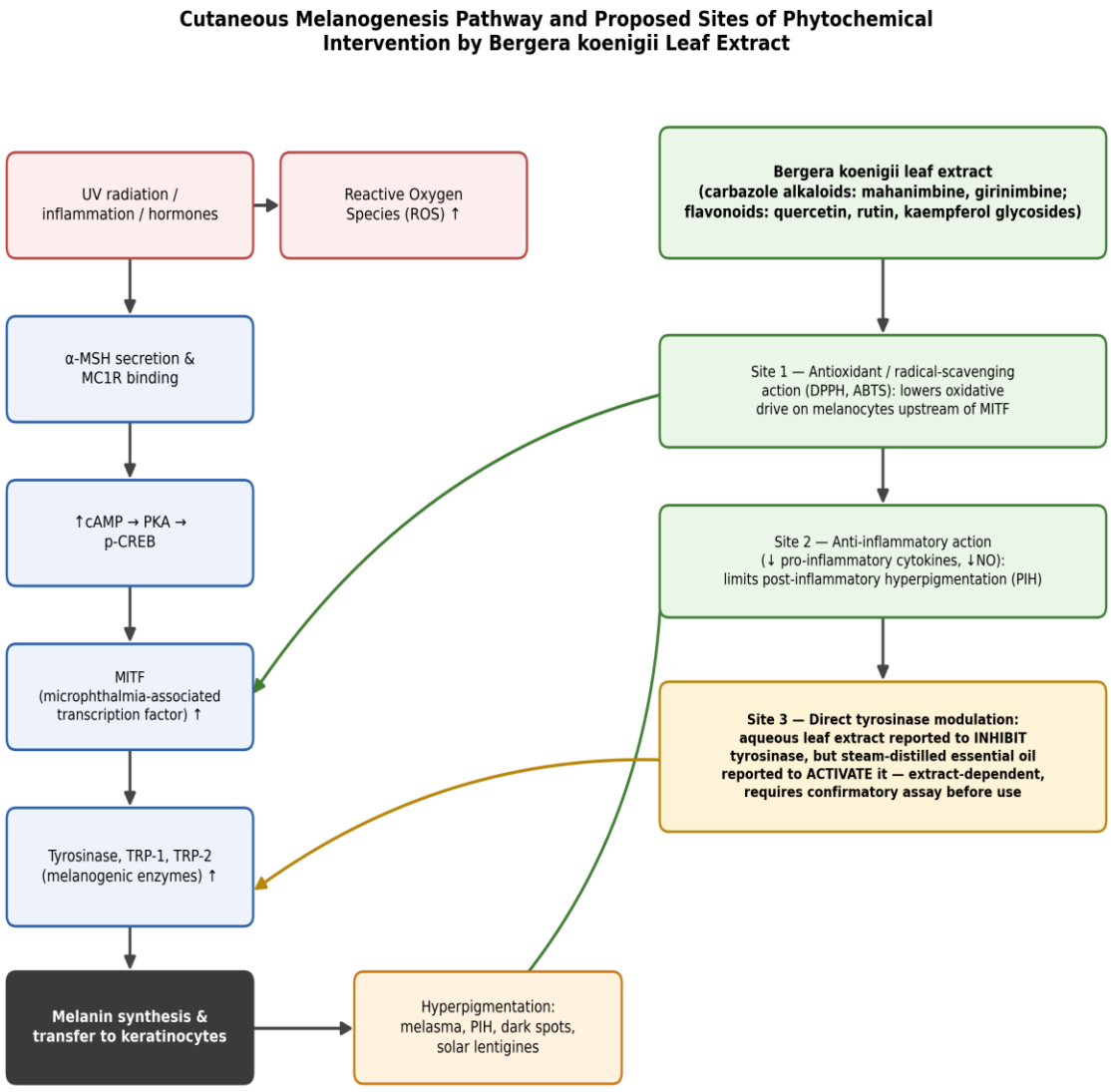

Figure 3. Simplified cutaneous melanogenesis pathway (left) and the three candidate sites at which Bergera koenigii leaf constituents may act (right), based on the pharmacological evidence summarized in Sections 4.2–4.3. Site 3 is flagged because the available evidence is extract-dependent and partially contradictory (see Section 4.3).

4.2 Site 1 and Site 2: indirect, upstream support — antioxidant and anti-inflammatory action

The strongest and most consistent evidence for B. koenigii in this context is indirect rather than a direct enzyme-inhibitory effect. Ethyl acetate and alcohol:water extracts of the leaves show pronounced free-radical scavenging activity against DPPH and ABTS radicals, attributable to their

high flavonoid and phenolic content; such antioxidant action would be expected to blunt the UV/ROS-driven arm of the melanogenesis cascade upstream of MITF (Site 1 in Figure 3), an action shared conceptually with other plant-derived antioxidants (e.g., sesamol, hesperidin) already validated in melanocyte and animal models. Separately, girinimbine — one of the most studied leaf alkaloids — has been specifically shown to inhibit pro-inflammatory cytokine release and nitric oxide production, supporting a plausible role in limiting post-inflammatory hyperpigmentation, which is mechanistically driven by cutaneous inflammation rather than UV exposure alone (Site 2). Both of these mechanisms are biologically credible and consistent with the plant's traditional use for inflammatory skin conditions, but neither has yet been demonstrated directly in a pigmentation-specific cell or animal model (e.g., α-MSH-stimulated B16F10 melanocytes) using a B. koenigii extract; the supporting data currently come from general antioxidant/anti-inflammatory assays rather than melanogenesis-specific endpoints.

4.3 Site 3: direct tyrosinase modulation — a critical, extract-dependent contradiction

The most pharmacologically direct evidence is also the most internally inconsistent, and this inconsistency has direct, practical implications for serum formulation. On one hand, a comparative enzyme-inhibition study of three M. koenigii leaf extracts (ethyl acetate, methanol, and water) found that only the aqueous extract inhibited mushroom tyrosinase, even though the ethyl acetate and methanolic extracts had the higher antioxidant and total phenolic content. On the other hand, a separate study evaluating the steam distillate (essential oil) of M. koenigii leaves against mushroom tyrosinase reported the opposite effect: the distillate activated tyrosinase by approximately three-fold relative to control, following mixed/non-competitive activation kinetics — the largest activation observed among the six plant distillates tested in that study.

Taken together, these two findings indicate that the depigmenting potential of B. koenigii is not an intrinsic, fixed property of the plant but is extraction-method and polarity dependent: the polar aqueous fraction (rich in flavonoids/phenolics) appears to inhibit tyrosinase, while the volatile, non-polar essential-oil fraction (rich in terpenes) appears to activate it. This is, to our knowledge, the most important single consideration for anyone formulating a B. koenigii face serum intended to reduce pigmentation, and it is treated as such throughout the formulation approach proposed in Section 6: the working extract must be a polar (aqueous or hydro-alcoholic) leaf extract with the volatile oil fraction deliberately minimized or removed, and the chosen extract batch should be confirmed for tyrosinase-inhibitory (not activating) activity by an in vitro assay before any depigmenting claim is attached to the finished product. Neither of the two cited studies tested a face-serum-relevant topical concentration range or a melanocyte cell-based model, so this conclusion, while directionally clear, should be treated as a formulation safeguard rather than a settled efficacy finding.

Separately, and consistent with feasibility, a published international patent application describes M. koenigii leaf/stem extracts (prepared in a betaine–propanediol–water solvent system) for use in cosmetic compositions explicitly including whitening/pigmenting agents, alongside antioxidant, anti-inflammatory, and anti-ageing claims. This indicates industrial recognition of the plant's cosmetic potential, though patent disclosures describe intended use and composition rather than independently verified clinical efficacy, and should be read accordingly.

V. SUPPORTING PHARMACOLOGICAL EVIDENCE RELEVANT TO SKIN HEALTH

Beyond the pigmentation-specific evidence discussed above, B. koenigii leaves and their isolated alkaloids have a broader pharmacological profile that is indirectly relevant to a face-serum application — particularly for managing the inflammatory and microbial triggers that precede PIH, and for general antioxidant skin protection. Table 3 summarizes the principal supporting activities and, where relevant, their caveats.

Activity	Key finding	Relevance / caveat
Antioxidant / free-radical scavenging	Alcohol:water and ethyl acetate leaf extracts show high DPPH/ABTS scavenging, correlating with total phenolic/flavonoid content	Supports Site 1 (upstream ROS suppression); well replicated across multiple studies
Anti-inflammatory	Girinimbine reduces pro-inflammatory cytokines and nitric oxide; aqueous extract with tannins/alkaloids shows anti-inflammatory activity in classical models	Supports Site 2 (PIH mitigation); evidence is mostly from non-cutaneous inflammation models
Antimicrobial / anti-biofilm	Methanolic leaf extract inhibits growth and biofilm formation of Streptococcus mutans; essential oil active against several bacteria and fungi including Candida albicans	Plausible adjunct benefit for acne-associated PIH, though tested organisms are oral/dermatophyte models, not validated acne pathogens specifically
Wound healing	Combination of carbazole alkaloids, essential oil, and crude extract enhanced subcutaneous wound healing in a rat model	Supports a barrier-repair rationale for a serum positioned for PIH following skin injury/acne

Activity	Key finding	Relevance / caveat
Cytotoxic / antiproliferative (alkaloids, esp. mahanine)	Mahanine and related alkaloids show dose-dependent cytotoxicity and pro-oxidant activity in multiple cancer cell lines; mahanine has undergone formal acute/chronic toxicity evaluation in the context of oncology drug development	Important safety caveat: these are systemic, high-dose, disease-context findings, not topical cosmetic data — they underscore the need for a defined, conservatively low topical concentration and dedicated dermal safety testing rather than an assumption of "natural = automatically safe"
Photoprotective / UV-protective	No dedicated SPF or UV-protection study on B. koenigii leaf extract was identified in the literature reviewed	Acknowledged gap; antioxidant activity may mitigate UV-induced oxidative stress but does not substitute for a sunscreen, and the serum should not be marketed as photoprotective without dedicated testing

VI. PROPOSED FORMULATION APPROACH FOR A BERGERA KOENIGII LEAF EXTRACT FACE SERUM

Building on Sections 3–5, this section proposes a structured, Quality-by-Design (QbD) based approach for translating the available phytopharmacological evidence into a stable, evaluable face-serum prototype. The approach follows the general physicochemical and safety-evaluation conventions established for herbal face serums in the recent formulation literature, while incorporating the extract-selection safeguard identified in Section 4.3.

6.1 Extract selection and standardization

- Extraction method: a polar hydro-ethanolic (e.g., 50–70% ethanol–water) maceration or Soxhlet extraction of shade-dried, authenticated B. koenigii leaves is recommended over steam distillation, so that the active fraction is dominated by the flavonoid/phenolic and polar-alkaloid pool associated with tyrosinase inhibition, and the volatile essential-oil fraction linked to tyrosinase activation is deliberately minimized.
- Standardization marker(s): the extract should be standardized against a quantifiable marker — total phenolic content (Folin–Ciocalteu) and/or mahanimbine content by validated HPLC — so that batch-to-batch variability (see Section 8.2) does not translate into inconsistent product performance.

- Mandatory confirmatory bioassay: each standardized extract batch intended for the serum should be confirmed for in vitro mushroom-tyrosinase inhibition (not activation) before release, using a standard L-DOPA oxidation assay, given the contradictory literature described in Section 4.3.

6.2 Representative formulation composition

Table 4 outlines a representative aqueous-gel-based serum composition, drawing on excipient categories and concentration ranges that are standard practice in the herbal face-serum formulation literature.

Phase / role	Representative ingredient(s)	Indicative function
Active	Standardized B. koenigii hydro-ethanolic leaf extract (~1–5% w/w, to be optimized by CCD/response-surface study)	Primary depigmenting / antioxidant / anti-inflammatory active
Gelling agent	Carbopol 940/934 or guar gum (0.5–2% w/v)	Imparts serum viscosity and spreadability
Humectant	Glycerin (3–5% w/v)	Moisture retention, improves skin feel
Antioxidant co-adjuvant	Vitamin E (tocopherol, 0.1–0.5% w/v)	Protects formulation and skin from oxidative degradation; synergizes with extract
Preservative	Sodium benzoate / phenoxyethanol (within regulatory limits)	Microbial stability
pH adjuster	Citric acid / triethanolamine, as needed	Maintains pH in the 5.0–6.0 range compatible with skin
Vehicle	Purified/distilled water, q.s.	Aqueous base

6.3 QbD-based development workflow

Figure 4 outlines the proposed stepwise development workflow, beginning from the Quality Target Product Profile (QTPP) and proceeding through risk assessment, formulation design, and finished-product evaluation to a documented control strategy.

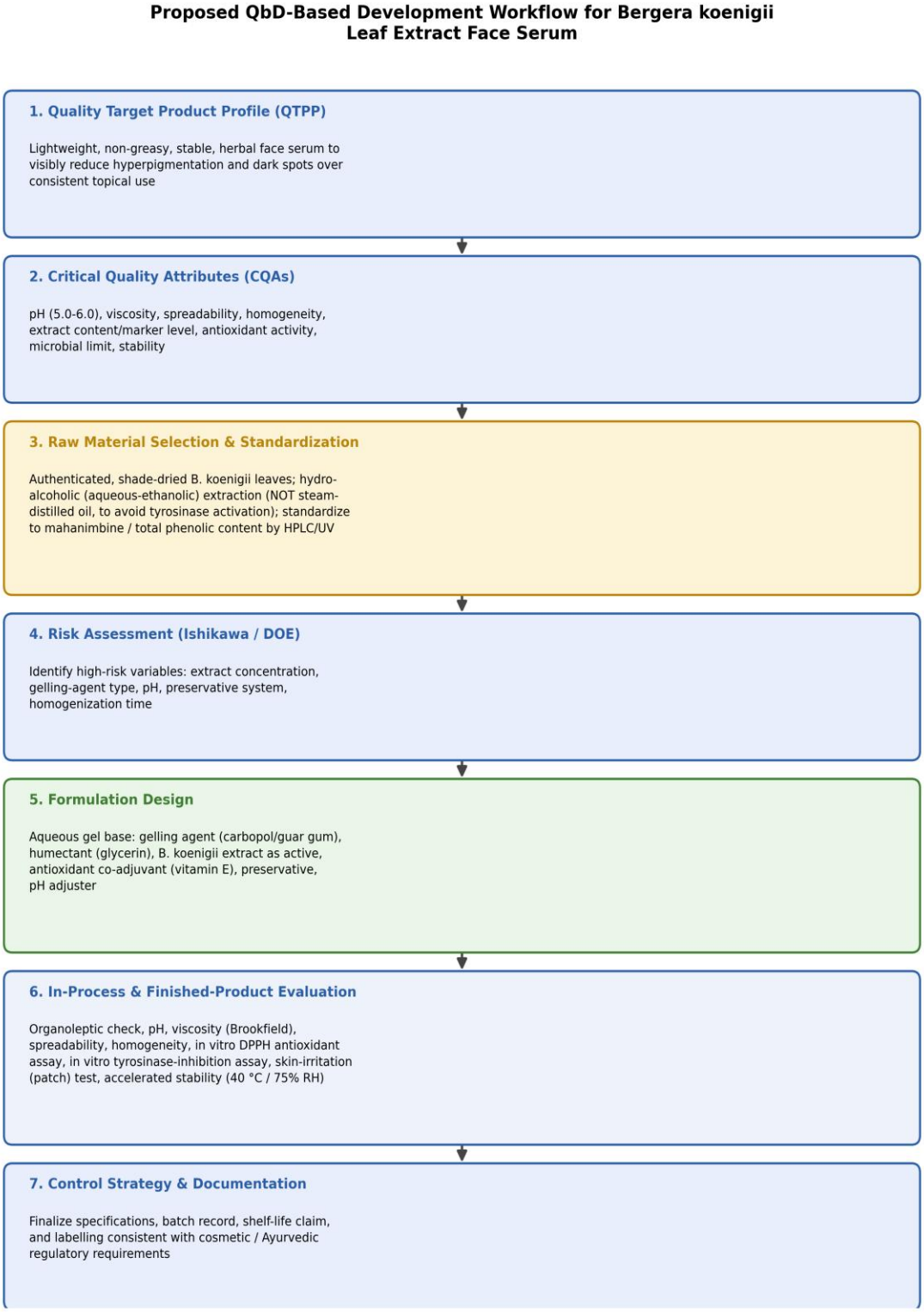

Figure 4. Proposed seven-step Quality-by-Design (QbD) workflow for development of the Bergera koenigii leaf extract face serum, incorporating the extraction-method safeguard identified in Section 4.3 at the raw-material-standardization step.

6.4 Evaluation parameters

Consistent with current herbal-serum evaluation practice, the finished prototype should be assessed against the parameters in Table 5.

Parameter	Method / acceptance consideration
Organoleptic properties	Visual assessment of colour, odour, homogeneity, and phase separation
pH	Digital pH meter; target 5.0–6.0 to match skin surface pH
Viscosity	Brookfield viscometer at defined spindle/rpm; assessed for application-appropriate consistency
Spreadability	Standard parallel-plate spreadability method
Homogeneity	Visual/microscopic check for absence of particulate matter or extract aggregates
In vitro antioxidant activity	DPPH and/or ABTS radical-scavenging assay on the finished serum
In vitro tyrosinase-inhibition assay	L-DOPA/L-tyrosine oxidation assay against mushroom tyrosinase; mandatory release check given Section 4.3
Dermal safety	Human repeat-insult patch test / HET-CAM or reconstructed human epidermis irritation model before any human-use claim
Microbial limit testing	Total viable count and pathogen-specific tests per pharmacopoeial limits for topical products
Stability	Accelerated stability (e.g., 40 °C/75% RH) and refrigerated/room-temperature controls over at least 90 days, monitoring pH, viscosity, colour, and marker-compound content

VII. EXISTING COSMETIC AND PATENT LANDSCAPE

“Murraya koenigii Leaf Extract” and “Murraya koenigii Stem Extract” already appear as listed INCI ingredients in commercial personal-care products, though current commercial use is concentrated in hair-care formulations (oils, shampoos) rather than dedicated facial depigmenting serums. An international patent application (WO2021156556A1) describes M. koenigii leaf/stem extracts, prepared using a betaine–propanediol–water solvent system, for use in cosmetic compositions spanning antioxidant, anti-inflammatory, anti-ageing, and — notably — whitening/pigmenting applications, with the phenolic acid, flavonoid, and alkaloid content of several extract variants characterized. This indicates that the cosmetic-industry feasibility of B.

koenigii as a skin-active ingredient is already recognized at the patent level. A dedicated, clinically substantiated face serum specifically marketed for hyperpigmentation/dark-spot reduction using this plant as the primary active does not appear to be established in the literature or commercial landscape reviewed, representing a genuine, currently unoccupied product opportunity — conditional on resolving the evidence gaps identified in Section 8.

VIII. RESEARCH GAPS AND CHALLENGES

8.1 The tyrosinase activation/inhibition contradiction

As discussed in Section 4.3, the single most important unresolved question is whether a standardized, formulation-relevant B. koenigii leaf extract reliably inhibits tyrosinase under conditions representative of topical use. The two relevant studies used different solvents (water vs. steam-distilled oil), different plant material, and neither tested a face-serum-relevant concentration in a melanocyte-based or human model. Before any depigmenting claim can be made with confidence, a single, well-characterized extract (as proposed in Section 6.1) needs to be tested head-to-head against both mushroom and cellular (e.g., B16F10 melanocyte) tyrosinase assays, ideally alongside a positive control such as kojic acid or arbutin.

8.2 Seasonal and geographic variability in alkaloid content

Carbazole alkaloid content in B. koenigii leaves varies substantially with geography and season: one systematic study found mahanine content ranging from roughly 2.7% in north-eastern (sub-tropical) plant material to over 40% in southern (tropical) material, with content peaking between September and December. This degree of natural variability poses a significant standardization challenge for any commercial extract and reinforces the necessity of marker-compound-based release testing (Section 6.1) rather than reliance on raw plant material alone.

8.3 Absence of clinical efficacy data

All pigmentation-relevant evidence reviewed here is preclinical — cell-free enzyme assays, in vitro antioxidant assays, or, at most, traditional-use observation. No randomized controlled human trial evaluating a B. koenigii-based topical formulation for melasma, PIH, or dark spots was identified. By contrast, contemporary depigmenting serum development (e.g., trials of 2-MNG-containing or trihydroxybenzoic-acid/α-arbutin serums) routinely uses objective endpoints such as colorimetric melanin index, standardized photography, and dermatologist/subject global assessment over 8–16-week periods; a B. koenigii serum prototype would need to be evaluated on a comparable basis before efficacy claims could be substantiated.

8.4 Dermal safety of an alkaloid-rich topical extract

Mahanine and related carbazole alkaloids are pharmacologically potent compounds under active investigation as pro-oxidant, cytotoxic anticancer leads, with formal acute and chronic (14–180

day) toxicity evaluation reported in that context. While these data derive from oral/systemic administration at doses and endpoints relevant to oncology drug development rather than topical cosmetic use, they are a useful reminder that "herbal" does not equate to "inherently safe at any concentration," and they reinforce the need for a conservatively low active concentration in the proposed serum together with dedicated dermal irritation/sensitization testing (Section 6.4) before human use.

8.5 Formulation stability of the actives

Carbazole alkaloids and flavonoids are susceptible to oxidative and photochemical degradation; their stability within an aqueous gel base over the product's intended shelf life has not been specifically studied and should be a dedicated focus of the stability programme outlined in Section 6.4, alongside microbiological and physicochemical stability.

IX. FUTURE PROSPECTS

- Nanocarrier-based delivery: encapsulation of the standardized extract in phytosomes, liposomes, or nanoemulsions — an approach already validated for other polyphenol-rich face serums — could improve dermal penetration, photostability, and shelf-life of the carbazole alkaloid/flavonoid actives.
- Combination with broad-spectrum sunscreen: given that UV exposure is a principal upstream driver of melanogenesis (Figure 3) and that no dedicated photoprotective data exist for B. koenigii (Section 5), pairing the serum with, rather than substituting for, a broad-spectrum sunscreen is the more defensible positioning until photoprotective data are generated.
- Mechanistic confirmation in melanocyte models: α-MSH-stimulated B16F10 or human melanocyte assays evaluating melanin content, tyrosinase activity, and MITF/TRP-1/TRP-2 expression would directly resolve the Site 3 contradiction described in Section 4.3 and substantiate (or refute) the proposed mechanism.
- Controlled clinical evaluation: an 8–16-week randomized, controlled study using colorimetric/Mexameter melanin-index measurement, standardized photography, and validated subject/investigator global assessment scales — following designs already established for other depigmenting serums — would be the appropriate next step toward a substantiated efficacy claim.

X. CONCLUSION

Bergera koenigii leaves present a phytochemically rich and traditionally well-supported, but mechanistically incompletely resolved, candidate active for a depigmenting face serum. The plant's antioxidant and anti-inflammatory pharmacology provides plausible, if indirect, support for limiting UV- and inflammation-driven hyperpigmentation, and a patent-disclosed cosmetic precedent confirms industrial interest. However, the literature also contains a genuine and

formulation-relevant contradiction: a polar aqueous extract has been reported to inhibit tyrosinase, while a steam-distilled essential-oil fraction from the same plant has been reported to activate it. This review has treated that contradiction as a central design constraint — favouring a standardized, polar hydro-ethanolic extract with the essential-oil fraction minimized, and recommending mandatory confirmatory tyrosinase-inhibition testing of each extract batch — rather than glossing over it. With this safeguard built into the proposed QbD-based formulation approach, together with resolution of the standardization, safety, and clinical evidence gaps identified in Section 8, B. koenigii leaf extract represents a scientifically credible, if not yet clinically proven, candidate for further development as a herbal face serum for hyperpigmentation and dark-spot reduction.

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