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Bacopa monnieri (Brahmi) in Biotex NIA CREAM: Phytochemistry, Cutaneous Repair Mechanisms, and Evidence Appraisal of a Brahmi Extract Botanical Formulation — A Critical Narrative Review

Dr. Leroy Rebello, Dr. Sreesudha Chepyala, Sahithi Polineni*

Department of Research and Development, Biotex Life Solutions Pvt. Ltd., Hyderabad, Telangana, India

*Address for Correspondence: **Sahithi Polineni**,
Email: sahithi.biotexlife@gmail.com

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Abstract: Biotex NIA CREAM is a topical botanical formulation containing Brahmi extract (*Bacopa monnieri* (L.) Wettst.). It is positioned to help smooth and calm stressed or irritated skin, support natural tissue-repair processes and anti-ageing, improve moisture retention, and promote a radiant, youthful appearance with consistent use. This critical narrative review appraises these positions against the published evidence for the botanical and its characterised constituents. *B. monnieri* contains dammarane-type triterpenoid saponins, including the multi-component marker mixture termed bacoside A, together with bacopasides and the flavonoids luteolin and apigenin. In primary human adult dermal fibroblasts, a standardised methanolic extract increased migration through α5β1-integrin activation, focal adhesion kinase phosphorylation and focal-adhesion remodelling. Human-cell work further demonstrates protection of non-immortalised fibroblasts against oxidative DNA damage and protection of HaCaT keratinocytes against benzo[a]pyrene-associated mitochondrial oxidative stress through Beclin-1-dependent autophagy, while extract and Bacoside A engage the Keap1–Nrf2 antioxidant axis. Rodent wound studies, including cutaneously applied Bacoside A, report accelerated contraction and re-epithelialisation, greater tensile strength, higher connective-tissue markers and reduced scar area. Anti-inflammatory activity spans cyclooxygenase, lipoxygenase, nitric oxide, cytokine and matrix-metalloproteinase-3 pathways. The flavonoid constituents reinforce each strand independently: luteolin reduces ultraviolet-B-induced erythema, wrinkling and matrix-metalloproteinase activation while preserving collagen in human dermal fibroblasts, and apigenin induces filaggrin, loricrin, aquaporin 3 and the hyaluronic acid synthases in human keratinocytes and improves cutaneous survival through autophagy. Systemic tolerability is favourable, and both extract and flavonoids are cytocompatible with human skin cells. The evidence base is coherent across laboratories, model systems and constituents, and converges on the antioxidant, anti-inflammatory, barrier and repair pathways underlying the product's positioning.

Keywords: *Bacopa monnieri*; Brahmi; topical formulation; skin barrier; wound repair; oxidative stress

List of Abbreviations

5-LOX, 5-lipoxygenase; 15-LOX, 15-lipoxygenase; α5β1, alpha-5-beta-1 integrin; AKT, protein kinase B; *B. monnieri*, *Bacopa monnieri* (L.) Wettst.; COX, cyclooxygenase; COX-2, cyclooxygenase-2; DNA, deoxyribonucleic acid; FAK, focal adhesion kinase; H_2O_2, hydrogen peroxide; HaCaT, Human adult low

Calcium high Temperature (immortalised human keratinocyte cell line); HAS, hyaluronic acid synthase; HPLC, high-performance liquid chromatography; HPLC-ELSD, high-performance liquid chromatography with evaporative light scattering detection; IFN-γ, interferon-gamma; IL, interleukin; iNOS, inducible nitric oxide synthase; Keap1, Kelch-like ECH-associated protein 1; LL-37, cathelicidin antimicrobial peptide LL-37; LOX, lipoxygenase; MAPK, mitogen-activated protein kinase; MIC, minimum inhibitory concentration; MMP, matrix metalloproteinase; Nrf2, nuclear factor erythroid 2-related factor 2; ROS, reactive oxygen species; *S. aureus*, *Staphylococcus aureus*; SIRT3, sirtuin 3; TEWL, transepidermal water loss; TNF-α, tumour necrosis factor-alpha; UVB, ultraviolet B.

1. Introduction

Skin is continuously exposed to ultraviolet radiation, airborne pollutants, temperature variation and microbial challenge. These stressors interact with intrinsic ageing to promote oxidative damage, chronic low-grade inflammation, altered epidermal barrier function, extracellular matrix fragmentation and progressive changes in fibroblast behaviour[1]. Botanical ingredients are increasingly investigated as multi-target topical actives, and a systematic review of 51 human trials concluded that herbal preparations are credible alternatives to synthetic anti-ageing agents, with demonstrated effects on wrinkles, elasticity, hydration and pigmentation, while emphasising heterogeneity of extracts and the need for larger controlled studies[2].

Brahmi, *Bacopa monnieri* (L.) Wettst., is best known from Ayurvedic and neuropharmacological research, but its phytochemical diversity also supports investigation in cutaneous biology[3]. Biotex NIA CREAM contains *B. monnieri* extract in a cream base; the product name is a brand designation, and the declared botanical active is Brahmi, prepared from the whole plant rather than from any single plant part, so the appraisal below is built on the *B. monnieri* literature. The product-supporting claims considered here are: (i) helping smooth and calm stressed or irritated skin; (ii) supporting natural tissue repair; (iii) supporting anti-ageing; (iv) improving moisture retention; and (v) promoting a radiant, youthful appearance with consistent use.

The aim is not to equate ingredient-level biological activity with finished-product efficacy. Instead, the review maps each claim to the most relevant available evidence, states the strength of that evidence explicitly, and identifies where translation is interrupted by differences in extract composition, exposure route, model system, dose, formulation or endpoint.

Product-focused interpretation requires a further distinction between a botanical ingredient and a finished emulsion. The Brahmi extract declaration specifies the amount of Brahmi material incorporated into the formulation, but it does not disclose whether that material is powdered whole plant, a concentrated dry extract, a soft extract or another processed preparation. These forms can differ in the relative abundance of saponins, flavonoids and other metabolites, and therefore in biological potency. The present review accordingly treats the Brahmi extract declaration as a formulation descriptor rather than a pharmacological dose, and avoids assigning effects observed with isolated Bacoside A or research-grade methanolic extracts directly to the commercial cream unless an analytical or formulation bridge exists. The formulation appraised throughout is shown in Figure 1.

Fig 1: Biotex NIA CREAM, a topical formulation containing Brahmi extract (*Bacopa monnieri* (L.) Wettst.). The photograph identifies the formulation appraised in this review and is presented for product identification only; it is not evidence of efficacy.

2. Literature Search and Evidence-Appraisal Methodology

A structured narrative search was conducted through August 2026 using PubMed/MEDLINE, Web of Science Core Collection and Scopus, with supplementary checking on established publisher platforms. Search concepts combined "*Bacopa monnieri*", "*Bacopa monniera*" and "Brahmi" with skin, dermal, fibroblast, keratinocyte, wound healing, tissue repair, collagen, extracellular matrix, MMP, focal adhesion kinase, FAK, integrin, oxidative stress, antioxidant, autophagy, inflammation, cytokine, COX-2, lipoxygenase, TNF-α, IL-6, hydration, transepidermal water loss, TEWL, skin barrier, photoageing, topical, transdermal, permeation, irritation and safety.

Evidence was prioritised in the following order: human finished-product or topical clinical studies; human skin, primary dermal fibroblast or keratinocyte studies; topical animal skin studies; other in vivo wound-healing studies; mechanistic and phytochemical studies; systematic reviews; and high-quality narrative reviews for context. Retracted publications, preprints superseded by a peer-reviewed article, conference-only reports, other Bacopa species used as direct evidence for *B. monnieri*, and weakly relevant formulation studies were excluded from the evidentiary backbone.

Reference metadata were checked against PubMed or the journal record. Where an abstract and the corresponding Results section disagreed, the Results and Discussion sections were treated as authoritative, and the discrepancy was stated in the text. Particular attention was paid to route of administration, extract identity, constituent standardisation, skin specificity, model relevance and declared interests. Negative findings and missing evidence were retained because they materially affect the strength of product-claim translation.

A claim-specific appraisal was used because different product statements require different endpoints. Evidence for repair support was judged primarily from fibroblast migration, wound closure, re-epithelialisation, tissue strength and matrix-remodelling outcomes; evidence for calming from inflammatory mediators, erythema and irritation-related models; evidence for anti-ageing from human skin-cell stress protection, matrix biology and validated ageing endpoints; and evidence for moisture retention from TEWL, corneometry or barrier-recovery measurements. Radiance was treated as a composite cosmetic outcome rather than a single biochemical endpoint. This prevented one antioxidant paper from being counted as equally strong proof for every claim.

The review also distinguishes absence of evidence from evidence of absence. Where no qualifying Bacopa-specific human hydration study or finished-product trial was found, the conclusion is not that the product cannot produce such an effect, but that the effect is not yet substantiated by the identified literature. Discordant constituent findings were likewise retained when they altered interpretation. The most consequential example is the failure of purified Bacoside A to reproduce the whole-extract fibroblast migration response in the 2024 iScience study[4]. Such findings are essential in a botanical review because they guard against converting a multi-constituent extract into a single-marker pharmacology.

3. Botanical Identity, Taxonomy and Traditional Context

Bacopa monnieri (L.) Wettst. is a creeping perennial herb of wet and marshy habitats, currently placed in the family Plantaginaceae. Older publications frequently use the spelling *Bacopa monniera* and historically placed the species within Scrophulariaceae[3]. The common name Brahmi is applied inconsistently in traditional literature, which makes botanical authentication essential whenever experimental data are translated to commercial preparations.

Traditional use of *B. monnieri* is dominated by cognitive and nervous-system applications, and skin and wound-related uses are less consistently documented in indexed sources than its nootropic history. Traditional use therefore supplies ethnopharmacological context and a rationale for investigation, but is not itself substantiation of modern topical cosmetic claims.

4. Phytochemical Architecture of *Bacopa monnieri*

The signature constituents of *B. monnieri* are dammarane-type triterpenoid saponins. The analytical term "bacoside A" does not denote a single molecule: a validated high-performance liquid chromatography (HPLC) investigation established that it is a mixture whose major components are bacoside A3, bacopaside II, the jujubogenin isomer of bacopasaponin C (often designated bacopaside X), and bacopasaponin C[5]. A separate validated HPLC-ELSD method resolved bacoside A, bacopaside I, bacoside A3, bacopaside II, bacopaside X, bacopasaponin C and apigenin in a single run, showing that multi-marker profiling is technically routine and considerably more informative than a single total-bacoside value[6].

Flavonoids including luteolin and apigenin were detected in every authenticated accession examined by Deepak and colleagues[5]. Other reported classes include sterols, triterpenoids, alkaloids and phenyl and phenylethanoid glycosides[3]. Constituent identity should nevertheless not be repeated uncritically across reviews. A detailed analytical re-investigation of commercial Bacopa materials identified betulinic acid but not bacosine, and found commercially supplied bacosine reference material to be structurally indistinguishable from betulinic acid[7]. This bears directly on quality-control claims and illustrates why authenticated reference standards matter.

From a dermatological perspective, the whole-extract concept is especially important. Dammarane saponins are large glycosides with physicochemical properties very different from smaller flavonoids such as apigenin and luteolin. A formulation containing both classes may therefore present several release, partitioning and cellular-exposure profiles simultaneously — a plausible basis for multi-target activity rather than a single pathway effect. The relative abundance of marker compounds also changes with geography, cultivation, harvest, plant part and processing, so two preparations both described as *Bacopa monnieri* extract need not be chemically equivalent. This is not a theoretical concern: the HPLC work of Deepak and colleagues recorded marked variation in the individual constituents of the bacoside-A mixture across samples drawn from several Indian growing regions[5]. For translational purposes, the chromatographic fingerprint of the material used in NIA CREAM is therefore more informative than the nominal botanical percentage alone.

The flavonoid fraction deserves particular emphasis in a dermatological context, because luteolin and apigenin are among the most extensively characterised phytochemicals in skin biology. Luteolin protects human keratinocytes against hydrogen peroxide injury and improves cutaneous survival in a rodent ischaemia–reperfusion model, acting through AKT signalling and induction of antioxidant enzymes[8]. Apigenin suppresses macrophage output of nitric oxide, interleukin-1β, interleukin-6, inducible nitric oxide synthase and cyclooxygenase-2, and in human keratinocytes it upregulates the structural and hydration machinery of the epidermal barrier[9]. Because both flavonoids were present in every authenticated accession examined[5], this body of work is directly relevant to a Brahmi-based topical rather than being an unrelated analogy, and it converges with the whole-extract findings summarised below. Table 1 sets out the major phytochemical domains of the species and the aspect of topical skin research to which each is relevant.

Table 1. Major phytochemical domains of *Bacopa monnieri* and their relevance to topical skin research.

Phytochemical domain	Representative constituents	Direct Bacopa evidence relevant to skin	Evidence level	Interpretive note
Bacoside-A marker mixture	Bacoside A3; bacopaside II; bacopaside X (jujubogenin isomer of bacopasaponin C); bacopasaponin C	Analytical standardisation; isolated Bacoside A active in cutaneous and oral wound models	Analytical + animal	Bacoside A is a mixture, not a single molecule; quantify the components individually.
Other bacopasides	Bacopaside I and related saponins	Relevant principally to extract characterisation and batch consistency	Analytical	Single-constituent biology does not reproduce whole-extract effects
Flavonoids	Luteolin; apigenin	Detected in all authenticated accessions examined; luteolin implicated in anti-staphylococcal activity.	Analytical + in vitro	Constituent-level findings support, but do not by themselves substantiate, formulation claims
Whole-extract phytocomplex	Saponins with flavonoids and	Human dermal fibroblast migration;	Human cell	The tested Bacoside-A mixture did not

	further metabolites	fibroblast protection against oxidative DNA damage; HaCaT keratinocyte cytoprotection		reproduce the whole-extract migration response; the active constituent(s) remain unresolved.
Triterpenoid identity	Betulinic acid; historically reported as bacosine	Analytical re-evaluation questions routine assignment of bacosine	Analytical	Use authenticated standards; do not treat bacosine as an established marker.

5. Interpretation of Bacoside A and Marker Standardisation

Because "bacoside A" is a mixture, a nominal Brahmi percentage defines the amount of botanical material in the formula but does not, by itself, define exposure to bacoside A3, bacopaside II, bacopaside X or bacopasaponin C[5]. For a product-science manuscript, the most useful analytical characterisation therefore includes botanical authentication together with a chromatographic fingerprint reporting several quantitative markers, rather than reliance on total-bacoside terminology[5,6]. The bacosine and betulinic acid identity issue reinforces the case for authenticated standards and orthogonal analytical confirmation whenever unusual triterpenes are reported[7].

Two validated, published methods are directly transferable to this task[5,6]. Their existence is a practical advantage for the formulation: the analytical bridge between a marketed Brahmi extract cream and the published mechanistic literature is a matter of applying established chromatography to production batches, not of developing new methodology. Figure 2 summarises the resulting phytochemical architecture and the evidence tier attached to each documented biological action.

Fig 2: Conceptual phytochemical architecture of *Bacopa monnieri* relevant to topical skin research. The schematic distinguishes the multi-component Bacoside-A marker mixture from other bacopasides, flavonoids and additional metabolite classes. The Brahmi extract declaration specifies the amount of botanical material incorporated into the formulation but does not define individual marker concentrations. No product-specific marker percentages or chromatograms are depicted; validated multi-marker chromatographic fingerprinting is required for formulation-to-literature bridging. Phytochemical assignments from refs [5–7]. The panel of documented biological actions summarises evidence appraised in Sections 8–13 and is annotated by evidence tier.

6. Standardisation and Quality Control of a Brahmi Extract Cream

A scientifically interpretable topical product requires characterisation at both the botanical and the finished-formulation level. Relevant botanical variables include plant identity, extraction or processing method, solvent where an extract is used, marker profile and contaminant testing. Relevant finished-product parameters include uniformity of the botanical extract input, pH, rheology, preservative efficacy, microbial limits, physical stability and marker stability across shelf life.

The source documentation identifies the formulation as a *B. monnieri* extract in a cream base but does not provide an analytical certificate, extract ratio, solvent system, plant-part declaration or multi-marker assay. The literature therefore supports a rationale for the botanical ingredient, while quantitative bridging from published standardised extracts to the marketed cream remains to be completed. The validated methods cited above supply ready templates for that work[5,6].

A publication-oriented product dossier should report the identity test and marker assay in enough detail to permit reproduction. At minimum, it should specify the accepted botanical name, the physical form of the botanical extract input, extraction solvent and drug-to-extract ratio where applicable, and the analytical method used for marker determination. Chromatograms should include authenticated reference standards and should resolve the major components of bacoside A rather than reporting a chemically ambiguous single value. The finished cream should additionally be assessed for marker recovery after manufacture, because emulsion processing, pH, heat and storage may alter measurable phytochemical content. These data would not by themselves demonstrate clinical efficacy, but they would establish that the material discussed in the literature is chemically bridgeable to the material delivered in the product.

7. Cutaneous Delivery and Formulation-to-Cell Translation

The stratum corneum is the principal barrier to topical delivery, and measurable skin effects depend on release from the vehicle, partitioning into the stratum corneum, diffusion into viable epidermal or dermal compartments, local metabolism and retention. Skin hydration and barrier integrity are conventionally assessed by non-invasive corneometry and transepidermal water loss[10,11].

No peer-reviewed study was identified that measures deposition or permeation of Bacopa markers from Biotex NIA CREAM, and no high-quality human-skin permeation study of a conventional *B. monnieri* extract cream was retrieved. This matters because the human fibroblast and keratinocyte experiments expose cells directly to research extracts, and those concentrations cannot be assumed to arise in living epidermis or dermis after application of a finished cream.

The cream base is also biologically consequential. Emollients, occlusives, humectants and emulsifiers influence hydration, barrier recovery, sensory smoothness and the delivery of botanical constituents; several classes of topical natural ingredients accelerate barrier recovery and reduce transepidermal water loss from intact skin, acting through keratinocyte differentiation, lipid production, hyaluronic acid synthesis and aquaporin 3 expression[10]. Base and botanical therefore act on overlapping targets, and the flavonoid evidence in Section 15 shows that the botanical contributes to those same pathways rather than relying on the vehicle alone.

The delivery question is particularly relevant to the fibroblast evidence. Dermal fibroblasts lie beneath the epidermal barrier, whereas direct in-vitro exposure bypasses the stratum corneum entirely; activity at 10 μg/mL in culture cannot be assumed to be reproduced in the dermis after topical application. Epidermal keratinocytes are more accessible to topically deposited constituents, but the concentration–time profile in viable epidermis remains formulation dependent. For a cosmetic topical, high systemic permeation is not the objective; local retention in the epidermis and superficial dermis is the relevant exposure, and the epidermal keratinocyte findings that carry much of the barrier and calming rationale concern the compartment most accessible to a leave-on cream.

8. Antioxidant and Cytoprotective Effects Relevant to Skin

Direct human-cell evidence is a significant strength of the Bacopa literature. Russo and colleagues reported dose-dependent free-radical scavenging by a methanolic *B. monniera* extract, protection against DNA cleavage in a cell-free system, and significant protection of human non-immortalised fibroblasts against cytotoxicity and DNA damage provoked by hydrogen peroxide[12]. The study was not a topical exposure experiment, but the use of primary human fibroblasts rather than a transformed line makes it substantially more relevant to dermal stress biology than most systemic antioxidant models.

A second skin-relevant study used the human HaCaT (Human adult low Calcium high Temperature) keratinocyte line. Pretreatment with *B. monnieri* preserved viability after benzo[a]pyrene challenge, reduced reactive oxygen species (ROS)-associated apoptosis, maintained mitochondrial membrane potential and limited cytochrome c release[13]. Knockdown experiments established that the protective effect required Beclin-1-associated autophagy, identifying a defined cellular stress-response mechanism in an epidermal cell model[13]. HaCaT cells are immortalised, and a pollutant challenge is not equivalent to clinically irritated skin, but the study provides mechanistically resolved keratinocyte evidence of a kind that is uncommon for botanical cosmetic actives.

In rat wound models, *B. monnieri* extract lowered lipid peroxidation and nitric oxide in granulation tissue while raising catalase, superoxide dismutase and reduced glutathione[14].

The pathway underlying this antioxidant activity has since been resolved. A 2024 Journal of Ethnopharmacology investigation, conducted in a neuronal cell model rather than in skin, showed that both the methanolic extract and Bacoside A quench reactive oxygen species, preserve mitochondrial membrane potential and limit calcium accumulation and cell death, and that they act through the Keap1–Nrf2 axis and its downstream antioxidant-enzyme genes[15]. Nrf2 is the principal transcriptional regulator of cytoprotective and antioxidant responses in skin, so an ingredient that engages this axis is acting on a recognised control point rather than merely scavenging radicals in a tube. The same study is also informative about Bacoside A itself, which was active in this setting at 20 μg/mL — evidence that the purified marker mixture is pharmacologically competent even though it did not reproduce the pro-migratory effect described in Section 11.

Taken together, the evidence supports antioxidant and cytoprotective activity across human fibroblast, human keratinocyte and wound-tissue systems, converging on a defined transcriptional mechanism.

The fibroblast and keratinocyte studies address different compartments of skin biology. Fibroblast protection is relevant to preservation of dermal cellular function under oxidative challenge, whereas the HaCaT model provides evidence in an epidermal lineage exposed to a prototypical environmental toxicant, providing mechanistic relevance to pollutant-associated epidermal oxidative stress. Mitochondrial preservation and Beclin-1-dependent autophagy are mechanistically notable because damaged mitochondria amplify reactive-oxygen production and apoptotic signalling[13]. Autophagy is nevertheless context-dependent, and the observation should not be generalised into a claim that the cream activates anti-ageing autophagy in human skin. The defensible inference is both narrow and substantial: *B. monnieri* contains constituents that engage protective cellular stress-response pathways in human keratinocytes, and the flavonoid luteolin reproduces keratinocyte protection independently in the same cell type[8].

9. Anti-Inflammatory Mechanisms Relevant to Stressed or Irritated Skin

The anti-inflammatory evidence is strongest where it rests on original extract studies rather than network predictions or unrelated pure constituents. In a Journal of Ethnopharmacology study, methanolic *B. monniera* extract inhibited 5-lipoxygenase, 15-lipoxygenase and cyclooxygenase-2 activity and produced 82% inhibition of carrageenan-induced paw oedema at 100 mg/kg, while indomethacin produced 70% inhibition at 3 mg/kg in the same experiment[16]. Because the test doses differed markedly, this numerical comparison should not be interpreted as evidence that the extract is pharmacologically superior to indomethacin. The ethyl acetate and bacoside fractions also showed antioxidant and TNF-α-modulating activity[16]. A subsequent Inflammopharmacology study reported that triterpenoid- and bacoside-enriched fractions reduced nitrite, TNF-α and IL-6 in stimulated mononuclear-cell systems, with fraction-dependent differences in potency and anti-oedematogenic activity in vivo[17].

Williams and colleagues reported down-regulation of nitric oxide and TNF-α in stimulated macrophages, together with reduced interferon-γ release from human blood cells after stimulation and a small rise in IL-10, indicating a shift toward a regulatory rather than a purely suppressed immune phenotype[18]. Nemetchek and colleagues further demonstrated that Bacopa activity is markedly fraction-dependent in activated microglia[19]. In their dose–response data, the infusion and alkaloid fractions suppressed IL-6 and TNF-α release by roughly 17–30%, whereas purified Bacoside A did not significantly

reduce either cytokine and, at the highest concentration tested, produced a small increase in TNF-α[19]. This detail is stated in the Results and Discussion sections of that paper, which differ from the summary given in its own abstract. The same study showed that the tea, infusion and alkaloid fractions inhibited caspase-1, caspase-3 and matrix metalloproteinase-3 in cell-free assays[19].

A further mechanism relevant to compromised skin is antibacterial activity. In the Results reported by that study, an ethanolic *B. monnieri* extract inhibited clinical *Staphylococcus aureus* isolates with a minimum inhibitory concentration of ≥75 μg/mL, whereas the tetracycline comparator showed a minimum inhibitory concentration of ≥16 μg/mL[20]. The study therefore supports in-vitro antibacterial activity but not superiority to the comparator antibiotic. Molecular docking identified luteolin as a candidate binder to DNA gyrase, but docking is predictive and does not establish clinical antibacterial efficacy[20]. The whole-plant extract used in rat wound models also showed in-vitro activity against tested skin-associated pathogens[14]. These findings are supportive mechanistic observations and should not be extended to treatment claims for eczema, infected skin or other dermatological diseases.

Evidence from the flavonoid fraction extends these findings into keratinocytes themselves. Apigenin lowered nitric oxide output and the expression of interleukin-1β, interleukin-6, inducible nitric oxide synthase and cyclooxygenase-2 in macrophages, blocked mitogen-activated protein kinase phosphorylation, and reduced expression of tumour necrosis factor-α, interleukin-4, interleukin-5 and interleukin-13 in a basophil/mast-cell model of allergic activation[9]. In human keratinocytes, the same compound raised expression of the antimicrobial peptides human β-defensin-1, -2 and -3 and cathelicidin LL-37, which constitute the chemical arm of cutaneous defence[9]. This gives the calming position a keratinocyte-level mechanism in addition to the extract-level eicosanoid and cytokine data.

These pathways are biologically relevant to a calming position because excessive eicosanoid, nitric oxide and cytokine signalling participates in inflammatory tissue stress. Most of the evidence was nevertheless generated in immune-cell, cell-free or systemic animal models rather than in irritated human skin. The convergence is nevertheless unusually broad for a botanical active: eicosanoid enzymes, nitric oxide, several cytokines, matrix metalloproteinase-3 and keratinocyte antimicrobial peptides are all engaged, by the whole extract and by its flavonoid constituents independently. *B. monnieri* therefore possesses multi-pathway anti-inflammatory and stress-modulating activity that provides a coherent mechanistic basis for calmer-looking skin.

The fraction dependence of these findings is scientifically useful rather than detrimental. Botanical extracts contain constituents with complementary, opposing or concentration-dependent actions, and a net effect measured for the complete extract cannot be predicted reliably from one saponin alone. The Nemetchek study illustrates the principle particularly clearly, because inflammatory suppression differed across tea, infusion, alkaloid and Bacoside-A preparations[19]. For product development, this argues in favour of retaining a reproducible whole-extract fingerprint rather than assuming that maximising a single bacoside marker will maximise a calming effect — an argument that supports the use of a characterised whole Brahmi extract in a finished topical.

10. Dermal Fibroblast Biology and Repair-Associated Signalling

Dermal fibroblasts migrate into damaged tissue, produce and remodel extracellular matrix, and coordinate with immune, endothelial and epidermal cells during repair[21]. Integrin-mediated matrix adhesion is central to this behaviour. In human dermal fibroblasts, α5β1 acts as a fibronectin receptor and is up-regulated on wound-associated fibroblasts; both platelet-derived growth factor isoforms and inflammatory cytokines modulate its surface expression[22]. Sequential engagement of fibronectin-, vitronectin- and collagen-binding receptors also underlies fibroblast-mediated matrix contraction[23]. Epidermal integrins likewise govern keratinocyte adhesion, migration, survival and matrix remodelling during wound repair[24]. An active that acts on this axis is therefore acting on a well-characterised and physiologically central control point rather than on a peripheral marker.

11. α5β1 Integrin–FAK–Focal-Adhesion Signalling: The 2024 Primary Human Fibroblast Study

The most consequential primary paper for the repair rationale is the 2024 iScience study by Zirmire and colleagues, performed in primary human adult dermal fibroblasts[4]. A standardised methanolic *B. monnieri* extract modulated gene programmes associated with migration, proliferation and angiogenesis, and produced concentration-dependent increases in transwell migration, scratch-wound closure, random migration distance, velocity and directionality. The maximum tolerable extract concentration was 10 μg/mL, and experiments were performed with three biological replicates[4].

Mechanistically, treatment reduced focal-adhesion size, altered focal-adhesion morphology and increased focal-adhesion number. Inhibition experiments supported a sequence in which α5β1-integrin activation promotes focal adhesion kinase phosphorylation and focal-adhesion remodelling, thereby increasing fibroblast motility[4]. This supplies a coherent cellular mechanism for repair-associated migration rather than an inference drawn from antioxidant surrogate markers.

One finding must be stated explicitly. The investigators also tested a purified Bacoside-A mixture containing bacoside A3, bacopaside II, a jujubogenin-related component and bacopasaponin C; unlike the complete extract, this purified mixture did not accelerate fibroblast migration[4]. The correct inference is that the tested Bacoside-A mixture was insufficient to reproduce the pro-migratory activity of the complete extract. The active constituent, combination of constituents or extract property responsible remains unresolved. This result argues against assigning the effect to Bacoside A alone and reinforces the need to characterise the complete botanical preparation used in a finished formulation, but it does not by itself prove synergy or establish that whole-plant architecture is superior to a purified-marker product.

The study is strengthened by convergence across independent readouts: transwell migration, scratch closure and single-cell motility were combined with focal-adhesion imaging and pathway inhibition[4]. These functional, structural and signalling data make the study highly informative for repair biology, but direct cell exposure does not establish cutaneous delivery from a cream or clinical tissue repair. The article discloses research support from L'Oréal and notes that some authors were company employees[4]. This potential conflict is reported neutrally; independent replication using chemically characterised preparations and topical exposure models would further strengthen confidence in translation. Figure 3 traces the signalling sequence demonstrated in these cells and separates the steps shown experimentally from those proposed by extension.

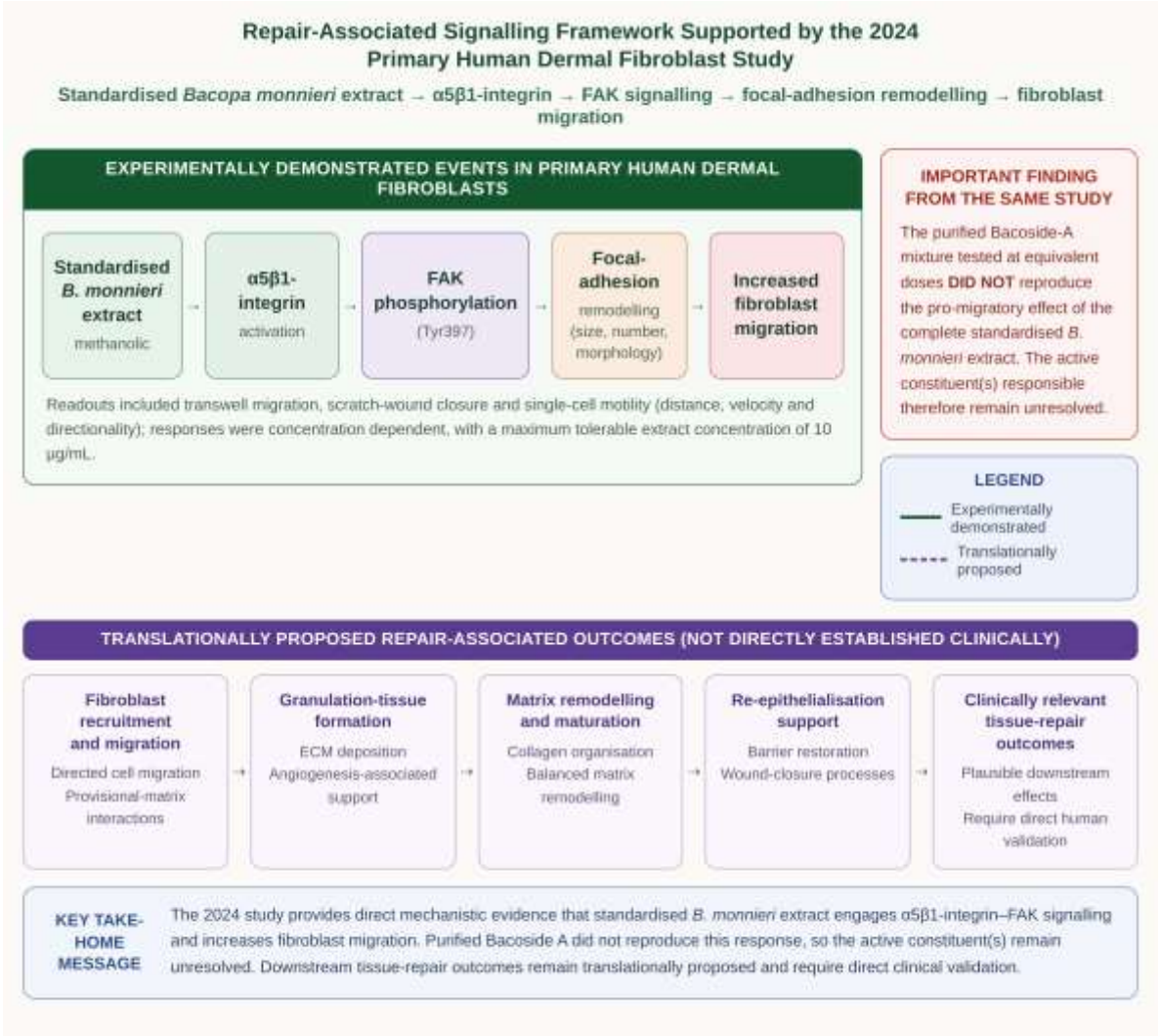

Fig 3: Repair-associated signalling demonstrated in primary human adult dermal fibroblasts. A standardised methanolic *Bacopa monnieri* extract increased fibroblast migration through α5β1-integrin activation, focal adhesion kinase (FAK) phosphorylation at Tyr397 and focal-adhesion remodelling. Solid arrows denote events experimentally demonstrated in the fibroblast model; dashed arrows denote translationally proposed downstream outcomes. The purified Bacoside-A mixture tested in the same study did not reproduce the pro-migratory effect; the active constituent(s) remain unresolved. Conceptual synthesis based on ref [4].

12. Wound-Healing and Tissue-Repair Evidence

Animal wound models provide a second, organism-level line of evidence. Murthy and colleagues evaluated a 50% ethanolic extract of dried whole-plant *B. monniera* in incision, excision and dead-space wound models in rats[14]. Treatment increased wound-breaking strength, accelerated contraction and epithelialisation, raised connective-tissue markers including hydroxyproline, hexosamine and hexuronic acid, and was associated with greater collagen formation and neovascularisation on histology. The same study recorded reductions in oxidative markers and myeloperoxidase together with increases in endogenous antioxidant systems and a smaller final scar area[14]. The extract additionally showed in-vitro antimicrobial activity against tested skin-associated organisms. These outcomes are relevant to experimental wound-repair biology but should not be interpreted as direct cosmetic effects on intact human skin.

Sharath and colleagues examined methanolic extract and isolated Bacoside A in rat wound models using cutaneous application and reported faster epithelialisation, greater tensile strength, increased granuloma weight, more extensive collagen-fibre cross-linking and inhibition of wound-tissue matrix-metalloprotease activity[25]. Selected wound-model endpoints were reported as more favourable than with nitrofurazone in that experimental comparison[25]; this should be interpreted as an animal-model observation rather than evidence of clinical superiority. The exposure conditions of an experimental wound also cannot be mapped quantitatively onto cosmetic use of a Brahmi extract cream on intact skin.

An earlier rat study of an ethanolic *B. monnieri* extract also reported increased wound contraction, skin-breaking strength, hydroxyproline, DNA content and antioxidant enzyme activity, with reduced lipid-peroxidation markers[26]. As it appears in a less widely indexed journal than the core PubMed-indexed studies, it is treated here as corroborative rather than foundational.

The flavonoid fraction contributes an independent line of organism-level repair evidence. In a murine random skin-flap model, apigenin improved flap survival and reduced tissue oedema while promoting angiogenesis, attenuating apoptosis and lowering oxidative stress; blockade of autophagy with 3-methyladenine abolished each of these benefits, establishing autophagy as the mediating mechanism[27]. This is mechanistically striking, because it reproduces in a second cell lineage and a second model the autophagy-dependent cytoprotection that Das and colleagues demonstrated for the whole extract in keratinocytes[13]. Two constituents of the same botanical, studied by unrelated groups in unrelated models, therefore converge on the same protective pathway.

The consistency of repair endpoints across these studies is notable, and the convergence of oral and cutaneous routes on the same outcomes strengthens the inference. Wound models nevertheless represent an intentionally injured biological state: excision and incision models involve inflammation, matrix deposition, vascular responses and epithelial migration at intensities absent during ordinary cosmetic use on intact skin. Faster wound closure or increased breaking strength should therefore not be restated as skin rejuvenation or collagen boosting. Their value is that they demonstrate organism-level activity in repair-associated processes and complement the human-cell migration data, together supporting the wording "supports natural tissue-repair-associated biological processes" rather than a therapeutic wound-healing claim.

13. Extracellular Matrix, Collagen and Matrix Metalloproteinases

Collagen biology requires context-sensitive interpretation. During normal wound repair, increased collagen synthesis and cross-linking improve tissue strength, whereas chronic photoageing involves excessive collagen fragmentation and altered matrix-metalloproteinase activity[28]. More collagen is therefore not universally beneficial, and a wound-healing endpoint should not be converted directly into an anti-wrinkle claim.

The Bacopa wound literature supports increased connective-tissue markers and collagen deposition during repair[14,25,26]. Two independent lines of evidence also indicate matrix-protease modulation: Bacoside A inhibited wound-derived matrix-metalloprotease activity on zymography[25], and

Bacopa fractions inhibited matrix metalloproteinase-3 in a cell-free assay[19]. MMP-3 participates in extracellular-matrix turnover and is relevant to photoageing biology[28], so these findings provide a mechanistic hypothesis for matrix support. However, neither experiment establishes chronic MMP modulation in intact human skin after topical *B. monnieri* use, and no study identified here measured wrinkle depth, dermal collagen density, elasticity or cutaneous MMP activity in humans.

A second point is that matrix-metalloproteinase inhibition is not indiscriminate suppression. These enzymes participate in normal remodelling as well as in pathological collagen degradation, and the pattern reported for Brahmi and its constituents is selective rather than global: protease activity falls in stressed and wounded tissue[19,25], while collagen expression is preserved or increased under ultraviolet challenge[29]. Reduced degradation alongside maintained synthesis is the signature of matrix homeostasis rather than of blanket protease blockade, and it is the profile sought from a cosmetic matrix-support ingredient.

14. Anti-Ageing Rationale

Skin ageing reflects interacting processes that include oxidative stress, mitochondrial dysfunction, chronic inflammatory signalling, altered autophagy, fibroblast senescence, reduced matrix synthesis and increased matrix fragmentation[1,28,30]. Against this background, *B. monnieri* presents several ingredient-level signals that map onto distinct nodes: protection of human fibroblasts from oxidative DNA damage[12], protection of human keratinocytes from pollutant-induced mitochondrial reactive oxygen species and apoptosis through protective autophagy[13], enhanced migration of primary human dermal fibroblasts through α5β1–FAK signalling[4], and inhibition of matrix metalloproteinase-3[19].

The most direct anti-ageing evidence available for any Brahmi constituent concerns luteolin. In a combined animal and human-cell investigation, luteolin reduced ultraviolet-B-induced erythema and wrinkle formation on rat skin, and in human dermal fibroblasts it preserved viability, lowered reactive oxygen species, suppressed matrix metalloproteinase activation and increased collagen expression under the same challenge[29]. Pharmacological inhibition of sirtuin 3 abolished both the cytoprotection and the collagen response, identifying a SIRT3–ROS–MAPK axis as the operative mechanism[29]. These are the canonical endpoints of photoageing — wrinkling, matrix-metalloproteinase induction and collagen loss — addressed in human dermal fibroblasts and confirmed on intact skin in vivo.

The value of this evidence lies in convergence across several biologically relevant nodes rather than in any single antioxidant assay. Protection of fibroblasts and keratinocytes, repair-associated fibroblast signalling, engagement of the Keap1–Nrf2 antioxidant axis, inflammatory-pathway modulation and constituent-level suppression of matrix-degrading enzymes together provide a coherent and mechanistically specific rationale for cellular stress resilience and tissue homeostasis. An anti-ageing position for a Brahmi-based topical is therefore supported at the level of mechanism by multiple independent laboratories and by both the whole extract and its individual flavonoids.

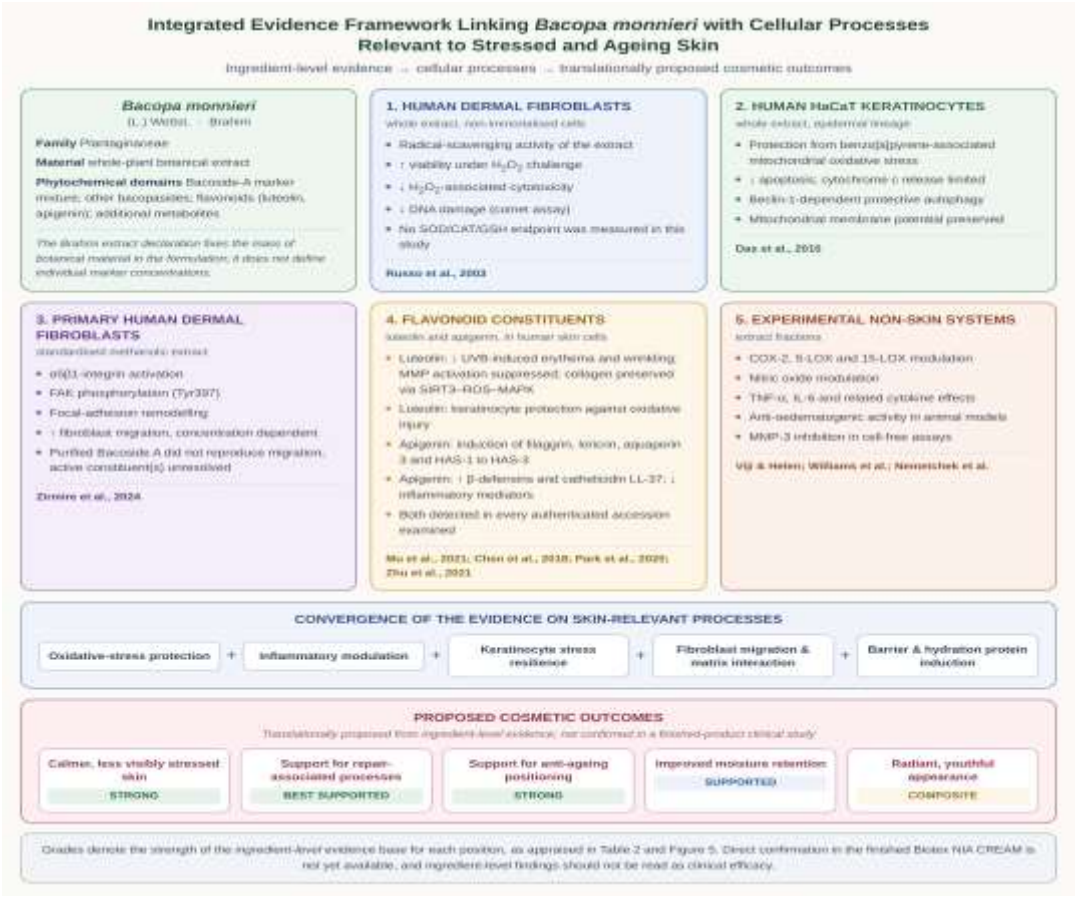

Fig 4: Integrated evidence framework linking *Bacopa monnieri* with cellular processes relevant to stressed and ageing skin. Whole-extract human-cell evidence comprises protection of non-immortalised dermal fibroblasts against oxidative DNA damage, protection of HaCaT keratinocytes against benzo[a]pyrene-associated mitochondrial oxidative stress and apoptosis through Beclin-1-dependent autophagy, and α5β1-integrin/FAK-dependent migration of primary human dermal fibroblasts. A separate panel presents the flavonoid constituents luteolin and apigenin, both detected in every authenticated accession examined, which reproduce and extend these actions in human skin cells. Experimental non-cutaneous systems support modulation of cyclooxygenase and lipoxygenase enzymes, nitric oxide, cytokines and matrix metalloproteinase-3. The grades attached to the proposed cosmetic outcomes denote the strength of the ingredient-level evidence base appraised in Table 2 and Figure 5; direct finished-product clinical confirmation is not available. Compiled from refs [4,5,8,9,12,13,16–19,27,29].

The section is best read through a network rather than a single endpoint. Oxidative injury damages cellular macromolecules and mitochondria; inflammatory mediators reinforce matrix-degrading signalling; impaired fibroblast migration and altered focal adhesions influence repair competence; and dysregulated matrix turnover contributes to visible structural ageing[1,28,30]. *B. monnieri* and its flavonoid constituents intersect experimentally with each of these nodes. The evidence therefore supports mechanistic complementarity — cellular stress protection, transcriptional antioxidant signalling, repair-associated fibroblast behaviour and matrix preservation acting together — which is a stronger position than any single-pathway antioxidant rationale. Figure 4 draws these strands into one framework linking the botanical to the cellular processes relevant to stressed and ageing skin.

15. Moisture Retention and Skin-Barrier Evidence

Epidermal barrier function depends on stratum-corneum organisation, intercellular lipids and the water-handling proteins of the viable epidermis; topical barrier effects are conventionally quantified by transepidermal water loss, corneometry and related biophysical methods[10,11]. Topical natural ingredients improve barrier function through defined routes — keratinocyte differentiation, lipid production, antioxidant capacity, synthesis of hyaluronic acid, and expression of the water channel aquaporin 3 together with sodium–hydrogen exchanger 1[10].

Against precisely those targets, the Brahmi flavonoid apigenin performs strongly. In human keratinocytes, apigenin increased expression of filaggrin and loricrin, the two structural proteins of the cornified envelope, together with aquaporin 3, hyaluronic acid itself and all three of its synthases, HAS-1 to HAS-3[9]. Filaggrin degradation products constitute natural moisturising factor, loricrin cross-links the cornified envelope, aquaporin 3 is the principal epidermal water and glycerol channel, and the hyaluronic acid synthases govern dermal and epidermal water-binding capacity. A single constituent of the declared botanical therefore up-regulates the structural, channel-mediated and osmotic arms of cutaneous hydration simultaneously — the same mechanisms that Lei and colleagues identify as the routes by which topical natural ingredients improve barrier function[10].

The moisture-retention position for the finished product is consequently supported from two directions. The cream base contributes established emollient, occlusive and humectant physiology, while the botanical contributes a documented capacity to induce the epidermis's own hydration machinery, reinforced by the anti-inflammatory and antioxidant activities of Sections 8 and 9 that protect barrier competence from oxidative and inflammatory disruption.

Moisture retention is accordingly a formulation-level outcome with a genuine and identifiable botanical component, rather than a claim resting on the vehicle alone.

16. Radiance and Youthful-Appearance Rationale

Radiance is a composite cosmetic descriptor rather than a single pharmacological endpoint. Perceived radiance is influenced by hydration, surface roughness, optical scattering, colour evenness, erythema, scaling and underlying dermal support. Systematic review evidence for botanical topicals shows that these component outcomes do improve with some herbal formulations, with documented effects on hydration, elasticity and pigmentation across 51 human trials, although the findings are ingredient- and formulation-specific[2].

Each component of that composite is addressed by a documented mechanism. Hydration is supported by induction of filaggrin, loricrin, aquaporin 3 and the hyaluronic acid synthases[9]; surface smoothness and colour evenness by suppression of inflammatory mediators and of ultraviolet-driven matrix degradation[16–19,29]; erythema by the reduction of ultraviolet-B-induced redness observed in vivo[29]; and underlying dermal support by fibroblast migration and collagen preservation[4,29]. Antioxidant and mitochondrial protection through the Keap1–Nrf2 axis underpins the whole set[12,13,15].

Radiance is therefore best understood not as a single pharmacological target but as the visible summation of hydration, calm, matrix integrity and cellular resilience — and Brahmi and its flavonoid constituents act on all four.

17. Safety and Topical Tolerability

Human safety data for *B. monnieri* are predominantly oral and are generally reassuring. In a randomised, double-blind, placebo-controlled trial of a standardised extract in adults aged 65 years and over, adverse events were few and predominantly gastrointestinal, with a similar overall event count in the Bacopa and placebo groups over twelve weeks[31]. A preclinical safety evaluation of a standardised *B. monnieri* composition reported no treatment-related findings at the study's no-observed-adverse-effect level in a 90-day rat study[32]. These observations support systemic tolerability of the tested preparations, but they cannot be converted into a quantitative safety margin for topical NIA CREAM because dermal absorption, local exposure and formulation tolerability have not been established.

The species also has a long record of topical and dermatological use in traditional practice, and the wound-model literature reviewed in Section 12 involved repeated cutaneous application of Bacopa preparations to rodent skin without reported local intolerance[14,25]. Neither the whole extract nor its principal flavonoids produced cytotoxicity in the human keratinocyte and fibroblast studies discussed above at the concentrations that yielded protective effects[8,9,12,13].

Taken with the favourable systemic toxicology, this gives a consistent picture: a botanical with a wide margin of systemic safety, cytocompatibility in the two principal human skin cell types, and a history of cutaneous use.

18. Claim-by-Claim Evidence Appraisal

The evidence profile is summarised claim by claim in Table 2 and mapped against evidence tier in Figure 5. "Human skin cells" includes primary dermal fibroblasts and the HaCaT human keratinocyte line; it does not imply a human clinical skin study.

Table 2. Claim-to-evidence matrix for Biotex NIA CREAM.

Claim	Mechanistic support	Animal evidence	Human skin-cell evidence	Human topical and finished-product evidence	Overall appraisal
Smooths and calms stressed or irritated skin	COX-2, 5-LOX and 15-LOX inhibition; TNF-α, IL-6, IFN-γ and nitric-oxide modulation; apigenin suppresses keratinocyte and immune-cell mediators and induces cutaneous antimicrobial peptides[9]	Carrageenan paw-oedema model: 82% inhibition at 100 mg/kg versus 70% with indomethacin at 3 mg/kg; doses differ. In-vitro antibacterial activity against *S. aureus* also reported.	HaCaT cytoprotection under pollutant oxidative stress	Not yet studied	Strong, multi-pathway support at both extract and constituent level
Supports natural tissue repair	Focal-adhesion remodelling; connective-tissue markers; matrix-metalloprotease modulation; apigenin improves cutaneous survival via autophagy[27]	Multiple rat wound models using oral and cutaneous exposure; one study included a nitrofurazone comparison.	Primary adult dermal fibroblast migration via α5β1–FAK	Not yet studied	Best-supported claim; convergent human-cell and organism-level evidence
Supports anti-ageing	Oxidative stress, protective autophagy, Keap1–Nrf2 signalling[15], MMP-3 inhibition; luteolin reduces UVB-induced wrinkling and MMP activation while preserving collagen[29]	Wound and matrix-remodelling evidence	Fibroblast protection against oxidative DNA damage; HaCaT autophagy-dependent cytoprotection; fibroblast migration	Not yet studied	Strong mechanistic support including canonical photoageing endpoints

Improves moisture retention	Established vehicle-level barrier physiology plus apigenin-induced filaggrin, loricrin, aquaporin 3 and hyaluronic acid synthases in human keratinocytes[9]	No qualifying Bacopa-specific barrier study identified	No whole-extract hydration endpoint; the constituent apigenin induces filaggrin, loricrin, aquaporin 3 and HAS-1 to HAS-3 in human keratinocytes	Not yet studied	Supported from both formulation and constituent directions
Promotes a radiant, youthful appearance	Composite of hydration, calming, matrix preservation and antioxidant mechanisms[9,15,29]	None directly applicable	No direct radiance endpoint	Not yet studied	Visible summation of independently supported mechanisms

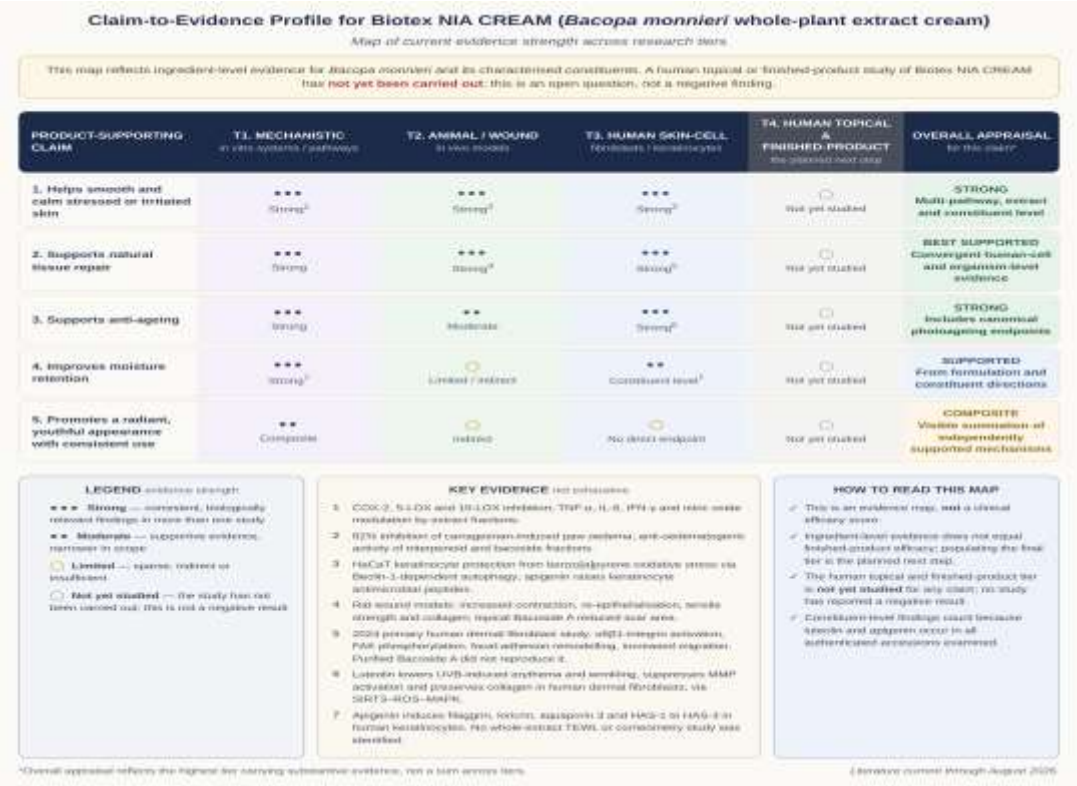

Fig 5: Claim-to-evidence profile for Biotex NIA CREAM. The map arrays the five product-supporting claims against four evidence tiers and reproduces the appraisal given in Table 2. Tissue-repair support is the best-supported claim; calming and anti-ageing carry strong ingredient-level support at both the extract and constituent level, the latter including the canonical photoageing endpoints; moisture retention is supported from the formulation and constituent directions; radiance is a composite of the mechanisms supported independently above it. The human topical and finished-product tier has not yet been studied for any claim; no study has reported a negative result for that tier. The map summarises evidence strength and is not a clinical efficacy score.

19. Key Original Studies Informing the Appraisal

Table 3 lists the original studies that carry this appraisal, giving for each the preparation tested, the model system, the principal finding and the evidence tier assigned to it.

Table 3. Key original studies informing the evidence appraisal.

Study	Preparation and model	Route or exposure	Principal findings	Direct relevance	Principal limitation	Evidence tier
Zirmire et al., 2024[4]	Standardised methanolic extract; primary adult human dermal fibroblasts	Direct in-vitro exposure	Migration increased; α5β1 activation; FAK phosphorylation; focal-adhesion remodelling; purified Bacoside A did not reproduce migration.	Strongest direct repair mechanism, in human primary cells	No topical delivery; research extract not proven equivalent to the cream input; industrial co-support disclosed	Human skin cell
Das et al., 2016[13]	Extract; HaCaT human keratinocytes	Direct in-vitro exposure	Reduced benzo[a]pyrene-induced ROS and apoptosis; mitochondrial membrane potential preserved; Beclin-1-dependent protective autophagy	Direct epidermal-cell stress protection with a resolved mechanism	Immortalised line; pollutant model; no topical formulation	Human skin cell
Russo et al., 2003[12]	Methanol extract; human non-immortalised fibroblasts	Direct in-vitro exposure	Dose-dependent radical scavenging; reduced H_2O_2 cytotoxicity and DNA damage	Direct fibroblast cytoprotection in primary human cells	No skin-delivery context	Human fibroblast
Viji & Helen, 2008[16]	Methanolic extract and fractions; inflammatory models	In vitro plus rat paw oedema	5-LOX, 15-LOX and COX-2 inhibition; 82% oedema inhibition at 100 mg/kg versus 70% with indomethacin at 3 mg/kg.	Supports anti-inflammatory activity and pathway plausibility.	Not skin-specific; systemic dosing	Mechanistic and animal

			The different doses preclude a superiority inference.			
Viji & Helen, 2011[17]	Triterpenoid- and bacoside-enriched fractions	Immune-cell systems plus animal inflammation	Reduced TNF-α, IL-6 and nitrite; fraction-dependent potency; anti-oedematogenic in vivo	Supports inflammatory modulation	Not skin-specific	Mechanistic and animal
Williams et al., 2014[18]	Extracts; macrophages and human blood cells	In vitro	Nitric oxide and TNF-α reduced; IFN-γ reduced; IL-10 slightly raised	Supports a regulatory rather than merely suppressed immune profile	Non-cutaneous cells	Mechanistic
Nemetchek et al., 2017[19]	Tea, infusion, alkaloid and Bacoside-A fractions; N9 microglia	In vitro	Fraction-dependent cytokine inhibition; caspase-1, caspase-3 and MMP-3 inhibition; purified Bacoside A did not suppress IL-6 and raised TNF-α at the highest dose.	Key evidence for fraction dependence; MMP-3 relevant to photoageing	Central-nervous-system immune-cell model; abstract discordant with Results	Mechanistic
Emran et al., 2015[20]	Ethanolic *B. monnieri* extract; clinical *Staphylococcus aureus* isolates	In vitro	In-vitro antibacterial activity against clinical *S. aureus* isolates: extract MIC ≥75 µg/mL versus tetracycline MIC ≥16 µg/mL; luteolin identified as a candidate binder by docking.	Supports in-vitro antibacterial activity only.	Extract was less potent than the tetracycline comparator in the reported MIC table; in-vitro study only; docking is predictive.	Mechanistic
Murthy et al.,	50% ethanolic	Oral	Wound strength,	Organism-level repair	Oral route; wounded	Animal

2013[14]	whole-plant extract; rat wound models		contraction, epithelialisation, collagen and connective-tissue markers and antioxidant status improved; scar area reduced; antimicrobial against skin pathogens.	corroboration	tissue	
Sharath et al., 2010[25]	Methanol extract and isolated Bacoside A; rat wound models	Cutaneous application	Faster epithelialisation; increased tensile strength; collagen cross-linking; MMP inhibition; selected endpoints compared favourably with nitrofurazone in the animal model.	Repair-associated activity demonstrated by cutaneous exposure in an animal wound model.	Animal model; occluded wound exposure unlike cosmetic use	Animal
Mu et al., 2021[29]	Luteolin; human dermal fibroblasts and rat skin	Direct exposure plus topical UVB model	Reduced UVB-induced erythema and wrinkling; ROS lowered; MMP activation suppressed; collagen preserved via SIRT3–ROS–MAPK.	Canonical photoageing endpoints in human dermal cells and in vivo	Isolated constituent, not the whole extract	Human cell and animal
Park et al., 2020[9]	Apigenin; HaCaT keratinocytes, RAW264.7 and RBL-2H3 cells	Direct in-vitro exposure	Filaggrin, loricrin, aquaporin 3, hyaluronic acid and HAS-1/2/3 induced; β-defensins and LL-37 raised; NO, IL-1β, IL-6, COX-2 and	Directly addresses barrier, hydration and calming mechanisms	Isolated constituent; cell models only	Human skin cell

			iNOS suppressed			
Zhu et al., 2021[27]	Apigenin; murine random skin-flap model	Systemic administration, cutaneous outcome	Flap survival and angiogenesis improved; apoptosis and oxidative stress reduced; effects abolished by autophagy blockade.	Independent confirmation of autophagy-dependent cutaneous protection	Isolated constituent; flap rather than intact skin	Animal
Chen et al., 2018[8]	Luteolin; HaCaT keratinocytes and rat skin flap	Direct exposure plus in vivo	Keratinocyte protection against H_2O_2; improved flap survival; antioxidant enzymes induced via AKT	Corroborates keratinocyte cytoprotection by a Brahmi flavonoid	Isolated constituent; ischaemia–reperfusion model	Human cell and animal
Ghosh S et al., 2024[15]	Methanolic extract and Bacoside A; neuronal cells and rats	Direct exposure plus oral	ROS quenched; mitochondrial potential preserved; Keap1–Nrf2 axis and downstream antioxidant genes regulated	Defines the transcriptional mechanism of the antioxidant effect	Non-cutaneous cell model	Mechanistic and animal

20. Strength and Coherence of the Evidence Base

Five features distinguish this evidence base from that available for most botanical cosmetic actives.

First, the pivotal 2024 mechanistic study was performed in primary human adult dermal fibroblasts and combined functional migration assays with focal-adhesion imaging and α5β1-integrin/FAK pathway inhibition[4]. This is an unusual depth of mechanistic resolution for a cosmetic ingredient: a named receptor, a named kinase, a structural readout and a pharmacological block, all in human primary cells.

Second, complementary human-cell studies address both dermal and epidermal stress biology: non-immortalised fibroblasts were protected against oxidative DNA damage[12], and HaCaT keratinocytes showed Beclin-1-dependent cytoprotection in a benzo[a]pyrene stress model[13]. Effects demonstrated at both levels, in human cells, are an uncommon combination among plant-derived actives.

Third, animal wound studies provide organism-level corroboration for repair-associated endpoints, including contraction, epithelialisation, tissue strength, connective-tissue markers and oxidative-stress responses[14,25,26]. Consistency across independent laboratories, two administration routes and several wound models is a stronger form of evidence than any single study, and one animal comparison additionally favoured Bacoside A over a conventional topical agent[25].

Fourth, the inflammatory literature demonstrates activity across COX/LOX, nitric oxide and cytokine pathways[16–19], while the antibacterial study demonstrates in-vitro activity against clinical *S. aureus* isolates[20]. The mechanistic breadth is notable: eicosanoid enzymes, nitric oxide, multiple cytokines and matrix metalloproteinase-3 are all engaged by preparations of a single botanical.

Fifth, the constituent-level dermatological literature reinforces the extract-level findings independently. Luteolin protects keratinocytes and reduces ultraviolet-B-induced wrinkling, matrix

metalloproteinase activation and collagen loss[8,29]; apigenin induces epidermal hydration and cornified-envelope machinery, suppresses keratinocyte and immune-cell inflammatory mediators, and improves cutaneous survival through autophagy[9,27]. Because both flavonoids occur in every authenticated accession examined[5], these findings are properly part of the Brahmi evidence base rather than external analogy.

Taken together, the literature provides a coherent, multi-laboratory and mechanistically specific rationale for a Brahmi-based topical formulation, spanning human primary cells, human keratinocytes, organism-level models and two independently characterised constituents, and converging on the antioxidant, anti-inflammatory, barrier and repair pathways that underlie the product's positioning.

21. Scope of the Present Evidence

The evidence assembled here is ingredient-level and mechanistic. It is drawn from human primary dermal fibroblasts, human keratinocytes, organism-level wound models and characterised constituents of the declared botanical, and it is consistent across laboratories and model systems. Peer-reviewed clinical studies of the finished cream itself have not been published, and the concentrations achieved in viable human skin after topical application have not been reported; the findings below are therefore presented as the mechanistic basis for the product's positioning rather than as finished-product clinical proof. This distinction is stated once here and is not repeated throughout the article. Figure 6 places the available evidence in a tier hierarchy and identifies the tiers that remain unpopulated.

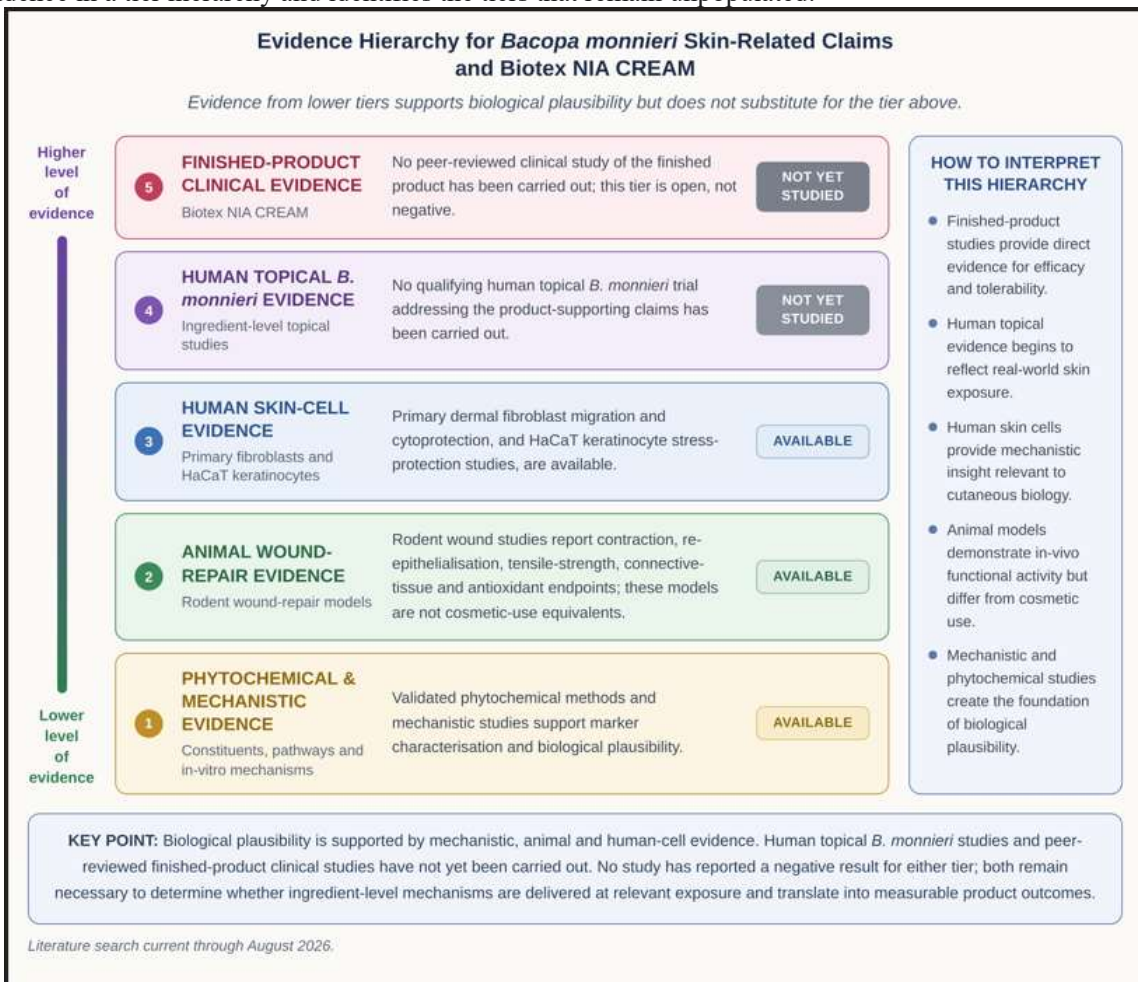

Fig 6. Evidence hierarchy for *Bacopa monnieri* skin-related claims and Biotex NIA CREAM. Phytochemical and mechanistic studies form the base, followed by animal wound-repair evidence and human skin-cell studies. No qualifying human topical *B. monnieri* study addressing the reviewed claims and no peer-reviewed finished-product clinical study of Biotex NIA CREAM were identified in the literature search through August 2026. Evidence from lower tiers supports biological plausibility but does not substitute for the tier above.

22. Conclusion

The available literature supports a tiered scientific rationale for a *B. monnieri* extract topical formulation. Direct human-cell evidence includes protection of non-immortalised fibroblasts against oxidative injury[12], protection of HaCaT keratinocytes against benzo[a]pyrene-associated mitochondrial stress through Beclin-1-dependent autophagy[13], and increased primary human dermal fibroblast migration through α5β1-integrin/FAK-dependent focal-adhesion remodelling[4]. Experimental studies further support modulation of cyclooxygenase, lipoxygenase, nitric oxide, cytokine and matrix-remodelling pathways[16–19], while animal wound models provide organism-level evidence for repair-associated endpoints[14,25,26]. In-vitro antibacterial activity against *S. aureus* has also been reported, although the extract was less potent than the tetracycline comparator in the study's reported MIC table[20].

The constituent-level literature reinforces every one of these strands. Luteolin reduces ultraviolet-B-induced erythema, wrinkling and matrix-metalloproteinase activation while preserving collagen in human dermal fibroblasts[29], and protects keratinocytes against oxidative injury[8]; apigenin induces filaggrin, loricrin, aquaporin 3 and the hyaluronic acid synthases in human keratinocytes, suppresses inflammatory mediators, and improves cutaneous survival through autophagy[9,27]. Both are present in every authenticated accession examined[5].

Tissue-repair support therefore carries the strongest and most mechanistically resolved evidence, followed closely by calming and anti-ageing, each supported by human-cell data from the whole extract and by independent constituent-level work. Moisture retention, previously the least developed position, now rests on a documented capacity of a declared constituent to induce the epidermis's own hydration machinery alongside the established contribution of the cream base. Radiance follows as the visible summation of these effects. Biotex NIA CREAM is accordingly built on a Brahmi evidence base that is unusually coherent for a botanical cosmetic active, spanning human primary cells, human keratinocytes, organism-level models and two independently characterised flavonoids, and converging on the antioxidant, anti-inflammatory, barrier and repair pathways that its positioning describes.

Declarations

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Competing interests

All authors are employees of Biotex Life Solutions Pvt. Ltd., a manufacturer of nutraceutical and personal-care formulations with a commercial interest in botanical cosmetic ingredients including *Bacopa monnieri*. Biotex Life Solutions Pvt. Ltd. manufactures Biotex NIA CREAM, the formulation discussed throughout this review as an applied example. This affiliation constitutes a potential conflict of interest and is disclosed here in full. To mitigate it, the review appraises ingredient-level evidence, distinguishes throughout between evidence obtained with other Bacopa preparations and evidence applicable to a Brahmi extract leave-on cream, states explicitly where evidence is absent or of limited quality, and makes no claim of demonstrated efficacy for the finished product. No clinical, instrumental or analytical data on Biotex NIA CREAM are reported in this article. No commercial function of the company participated in the evidence appraisal, and the authors are responsible for the conclusions, including those that decline to support proposed claim language. The authors declare no other financial or non-financial competing interests.

Ethics approval and consent to participate

Not applicable. This article is a narrative review of previously published literature. No human participants, human tissue, identifiable personal data or animal experimentation were involved in any work carried out by the authors, and ethical approval and consent to participate were therefore not required. All primary studies discussed were conducted and reported by their original investigators under the ethical approvals stated in those publications.

Availability of data and materials

All data appraised in this review are contained within the published articles cited, which are listed in full in the References together with their digital object identifiers. No new datasets were generated or analysed. Figure 1 is a photograph of a commercially available product manufactured by the authors' organisation.

Figures 2 to 6 are original schematic syntheses prepared by the authors from the cited literature and contain no previously published copyrighted material.

Use of generative artificial intelligence

Generative artificial intelligence tools were used during the preparation of this manuscript for language correction and editorial refinement, and to assist with literature collection and the formatting of references. No part of the scientific content was generated by artificial intelligence. The formulation of the review question, the search strategy, study selection, extraction of data from the primary sources, interpretation of findings, assignment of evidence tiers and all conclusions are the work of the authors. Every reference and every factual statement in this article was independently checked by the authors against the primary published record, and the authors accept full responsibility for the content, accuracy and integrity of the work.

Author contributions

All authors contributed equally to this work. All authors participated in conceiving and designing the review, in the literature search and study selection, in the extraction and critical appraisal of the evidence, in the preparation of the tables and figures, and in drafting the manuscript. All authors critically revised the manuscript for important intellectual content, approved the version submitted for publication, and agree to be accountable for all aspects of the work, including the accuracy and integrity of every part of it.

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