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Topical Dermatological Potential of *Tagetes erecta* L. Flower Extract: Phytochemistry, Skin-Relevant Mechanisms, Dermatological Evidence, and Translational Relevance to BIOPANACEA™ Cream — A Narrative Review

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Abstract: *Tagetes erecta* L. (Asteraceae), the African or Aztec marigold, is a carotenoid- and polyphenol-rich species of increasing relevance to cosmetic formulation science. Its flowers are an established commercial source of lutein and lutein esters and also contain zeaxanthin, quercetagetin, patuletin-related compounds, syringic acid and β-amyrin. This narrative review evaluates the skin-relevant evidence for *T. erecta* flower extract across antioxidant defence, inflammatory regulation, extracellular-matrix preservation, melanogenesis, antimicrobial activity, repair biology, photoprotection-related mechanisms, topical formulation performance and human skin compatibility. Literature was identified through structured searches of PubMed/MEDLINE, Scopus, Web of Science and Google Scholar with citation chaining, prioritising authenticated flower-derived material published through August 2026. Direct flower-extract evidence demonstrates free-radical scavenging, inhibition of lipid peroxidation, tyrosinase, elastase, hyaluronidase and MMP-1, and regulation of inflammatory cytokines, neutrophil migration and macrophage efferocytosis. A polyphenol-enriched flower fraction suppresses α-melanocyte-stimulating-hormone-induced melanogenesis through the cAMP–CREB–MITF–tyrosinase axis. Topical flower preparations show antibacterial and repair-relevant activity, and have been formulated into gels, creams, nanoemulsion gels, nanostructured lipid-carrier creams, chitosan films and hydrogels. Two small human topical investigations, together with human irritation testing, provide delivery-system-specific translational evidence. Lutein and zeaxanthin add a complementary xanthophyll rationale supported by human carotenoid studies, although constituent and whole-plant findings cannot be assumed to represent any given flower extract. Collectively, the evidence provides a coherent ingredient-level basis for the topical use of *T. erecta* flower extract and supports its incorporation as the principal botanical active in BIOPANACEA™ Cream, interpreted according to botanical authentication, cultivar, extract composition and delivery system, and not equated with finished-product clinical proof.

Keywords: *Tagetes erecta*; marigold flower extract; lutein; zeaxanthin; quercetagetin; melanogenesis; skin ageing; cosmeceutical.

1. INTRODUCTION

Human skin functions simultaneously as a permeability barrier, immune organ, sensory interface and mechanically resilient tissue. Its visible appearance and physiological performance are influenced by oxidative stress, ultraviolet and environmental exposure, inflammatory signalling, pigmentary regulation, extracellular matrix turnover, microbial interactions and the efficiency of tissue repair. These processes are

interdependent: reactive oxygen species can activate inflammatory and matrix-degrading pathways; persistent inflammation can increase oxidative burden; and repeated ultraviolet exposure can accelerate degradation of collagen, elastin and hyaluronan while also perturbing pigmentation. This biological convergence has encouraged interest in topical botanical extracts that contain several classes of bioactive molecules capable of acting across more than one cutaneous pathway.

Tagetes erecta L., a member of the Asteraceae family, is native to Mexico and has subsequently become widely cultivated across Asia, Africa and other regions for ornamental, industrial and medicinal purposes[1,2]. The plant is known as cempasúchil in Mexico and is also commonly described as African marigold, Aztec marigold or marigold. Its flowers are particularly important as a commercial source of the xanthophyll carotenoid lutein, while modern phytochemical studies also demonstrate a substantial polyphenol fraction[1,3,4]. This combination makes the flower scientifically relevant to dermatology and cosmeceuticals because carotenoids and phenolic compounds represent chemically distinct antioxidant systems and may contribute complementary biological effects.

The term "marigold" requires botanical precision. *T. erecta* is not *Calendula officinalis*. Although both plants belong to Asteraceae and both may be encountered in traditional skin-care literature, they belong to different genera and have different phytochemical profiles. Evidence generated with *C. officinalis* therefore cannot be used as direct evidence for *T. erecta*. The same caution applies within the *Tagetes* genus: data from *T. minuta*, *T. patula* or *T. lucida* may provide contextual information but should not be treated as direct support for a *T. erecta* flower extract unless clearly identified as such[2].

BIOPANACEA™ Cream is considered in this review as a topical formulation containing *T. erecta* flower extract in a cream base. The scientific question is therefore not whether every traditional claim made for "marigold" is valid, but whether authenticated *T. erecta* flower material has a sufficiently coherent body of phytochemical, mechanistic, preclinical, formulation and human evidence to support its use as a topical botanical active. The present review addresses that question by prioritising flower-specific studies and by distinguishing ingredient-level evidence from evidence generated with particular delivery systems or finished products.

Fig 1: BIOPANACEA Cream product image and formulation context. The product is considered in this review as *Tagetes erecta* L. flower extract in a topical cream base.

The objective of this narrative review is to synthesise the available evidence on *T. erecta* flower phytochemistry and its skin-relevant biological activities, with particular emphasis on antioxidant defence, inflammatory regulation, extracellular matrix preservation, melanogenesis, antimicrobial activity, repair-supportive biology, photoprotection-related mechanisms, topical formulation and human skin compatibility. Particular attention is given to lutein and zeaxanthin because they provide a distinct xanthophyll-based mechanism that complements the better-known polyphenol fraction. The review concludes with an evidence-calibrated interpretation of how this literature relates to BIOPANACEA Cream (Figure 1), while retaining a clear distinction between biological plausibility, formulation-specific efficacy and finished-product clinical proof.

2. LITERATURE SEARCH AND EVIDENCE-SYNTHESIS APPROACH

A structured narrative-review approach was used. Searches were undertaken across PubMed/MEDLINE, Scopus, Web of Science and Google Scholar, supplemented by backward and forward citation tracking. Search combinations included "*Tagetes erecta*", "African marigold", "Aztec marigold" and "cempasúchil"

together with terms related to skin, topical application, cream, cosmeceutical, fibroblast, antioxidant, inflammation, wound healing, collagen, elastase, hyaluronidase, MMP-1, tyrosinase, melanogenesis, antimicrobial activity, photoprotection, SPF, ultraviolet radiation, lutein, zeaxanthin and skin ageing. Literature available through August 2026 was considered.

Priority was given to studies that authenticated *T. erecta* and used flowers, petals, inflorescences or clearly defined flower-derived fractions. Chemically characterised extracts, skin-relevant biochemical and cellular models, topical formulations, dermal animal models and human topical studies were weighted more heavily than nonspecific reports. Studies of isolated lutein and zeaxanthin were included as constituent-level supportive evidence because these xanthophylls are established components of *T. erecta* flowers; however, their findings were not treated as direct proof of the efficacy of any unspecified *T. erecta* extract. Evidence from other *Tagetes* species, leaves, whole-plant preparations and essential oils was used only for context when necessary and was not allowed to substitute for flower-specific evidence.

The synthesis was intentionally evidence-graded. Biochemical enzyme assays were interpreted as mechanistic evidence; cell and animal studies as preclinical evidence; topical formulation studies as translational evidence; and human topical studies as the most directly relevant evidence for cosmetic use. The question asked of BIOPANACEA Cream was deliberately narrow: whether the botanical ingredient is scientifically supportable at ingredient level, rather than whether the finished formulation has demonstrated clinical efficacy. No claim of formulation-specific efficacy is made unless the cited study evaluated that formulation.

3. BOTANICAL IDENTITY, TRADITIONAL RELEVANCE AND PLANT-PART SPECIFICITY

T. erecta is an annual herbaceous species in the Asteraceae family with conspicuous yellow, orange or reddish inflorescences. The species originated in Mexico and occupies an important cultural and medicinal position in Mesoamerican history, while modern cultivation has expanded globally[1,5]. Historical sources and ethnopharmacological reviews describe a wide range of uses for *Tagetes* species. For *T. erecta* specifically, the flowers carry a documented ethnomedical association with cutaneous complaints: Indian ethnobotanical survey work records their use for skin ailments among the Buksa community of Uttarakhand[6], and the anti-wrinkle literature cites a comparable traditional indication as the rationale for investigating the flower[7]. Such use should be understood as ethnomedical context rather than clinical proof, but it provides a historically coherent rationale for modern examination of skin-related biological activity.

Plant-part specificity is essential. The flower is chemically distinct from the leaf, aerial essential oil and root. The petals are especially enriched in carotenoid pigments, whereas essential-oil profiles are dominated by volatile terpenoid chemistry and may raise a different set of efficacy and safety considerations. For a flower-extract cream, therefore, the most relevant evidence is derived from petals, flowers, flower extracts and flower-derived fractions. This distinction also prevents the inappropriate transfer of activities associated with essential oils or unrelated *Tagetes* species to BIOPANACEA Cream.

Flower colour, cultivar, maturation stage, geographic origin, drying conditions and extraction method influence phytochemical composition. Red and orange cultivars may differ from yellow cultivars in their xanthophyll profile, and solvent polarity strongly affects recovery of phenolic compounds. Consequently, "*T. erecta* flower extract" should be treated as a class of preparations rather than a chemically uniform substance. This variability becomes especially important when translating literature into product claims, because an aqueous paste, a hydroalcoholic extract, an ethyl acetate fraction, a polyphenol-enriched fraction and a carotenoid-rich oleoresin are not pharmacologically interchangeable.

The magnitude of this variability is supported by comparative analytical studies. Li and colleagues examined 11 Chinese marigold cultivars and found marked differences in phenolic, flavonoid and lutein-ester content together with antioxidant activity[8]. Park and colleagues identified seven carotenoids across *Tagetes* cultivars—violaxanthin, lutein, zeaxanthin, α-carotene, β-carotene, 9-cis-β-carotene and 13-cis-β-carotene—and confirmed that lutein was the predominant carotenoid while individual carotenoid concentrations varied by cultivar[9]. More recent work has extended this observation to genetic and developmental control of carotenoid accumulation. Qiu and colleagues demonstrated that flower-colour-associated differences in *T. erecta* reflect differential expression of carotenoid-biosynthetic and cleavage genes[10], while Eghlima and Seyed Hajizadeh quantified substantial cultivar-to-cultivar variation in lutein and zeaxanthin across *T. erecta* and *T. patula* material[11]. These data strengthen the argument that botanical identity alone is insufficient for chemical equivalence and that cultivar and analytical standardisation are central to translational interpretation.

4. PHYTOCHEMICAL ARCHITECTURE OF TAGETES ERECTA FLOWERS

4.1 Xanthophyll carotenoids: lutein and zeaxanthin

The best-known phytochemical feature of *T. erecta* flowers is their xanthophyll content. Commercial marigold flower extracts have long been used as natural sources of lutein. In a detailed chromatographic characterisation of a saponified commercial *T. erecta* flower extract, Hadden and colleagues reported that 93% of pigments detected at 450 nm were utilisable pigments; all-trans and cis forms of lutein together with lutein esters accounted for approximately 88%, while all-trans and cis zeaxanthin isomers accounted for approximately 5%[3]. These figures should not be generalised to every cultivar or extraction process, but they clearly establish zeaxanthin as a genuine constituent of the flower rather than a theoretical extrapolation from other plant sources.

The native carotenoid architecture is considerably more complex than a simple 'lutein extract'. Comprehensive LC-MS/MS profiling by Rodrigues and colleagues identified 56 carotenoids in non-saponified marigold material, including free carotenoids, monoesters and diesters; esters of zeaxanthin, violaxanthin, auroxanthin, zeinoxanthin and β-cryptoxanthin were characterised in addition to the dominant lutein esters[12]. This finding is especially relevant to topical formulation because esterification changes lipophilicity, stability and partition behaviour. It also provides stronger phytochemical justification for discussing zeaxanthin as part of the *T. erecta* xanthophyll system rather than treating it as an incidental minor pigment.

Lutein and zeaxanthin are C40 oxygenated carotenoids, or xanthophylls, with extended conjugated double-bond systems. Their chemical structures enable quenching of electronically excited species and interaction with reactive intermediates. Lutein and zeaxanthin differ in terminal-ring double-bond configuration, which affects molecular behaviour but not their shared classification as xanthophyll antioxidants. In native flower tissues, lutein occurs extensively in esterified forms; extraction and saponification can therefore alter the analytical profile and the proportion reported as free lutein.

Cultivar-level studies corroborate this broader xanthophyll profile. Park et al. directly quantified lutein and zeaxanthin together with several additional carotenoids in *T. erecta* and *T. patula* cultivars[9], and a 2026 comparative analysis reported lutein concentrations of 2.44–6.42 mg/g dry weight and zeaxanthin concentrations of 1.05–2.48 mg/g dry weight across ten *Tagetes* cultivars[11]. Because the latter investigation included two *Tagetes* species, these concentration ranges should not be assigned to BIOPANACEA or to *T. erecta* universally. Their value is instead to demonstrate the scale of biological variability and the need to distinguish confirmed presence from product-specific quantitative standardisation.

From a dermatological perspective, the lutein–zeaxanthin pair is relevant because oxidative stress and photo-oxidation are major upstream drivers of skin damage. Human studies of lutein and zeaxanthin administered topically and/or orally have shown changes in skin surface lipids, hydration, elasticity, photoprotective activity and lipid peroxidation, while oral supplementation trials have also reported effects on overall skin tone and minimal erythemal dose[5,13]. These studies do not establish that a *T. erecta* cream will reproduce the same outcomes, because dose, delivery and bioavailability differ. They do, however, provide biologically credible constituent-level support for the xanthophyll fraction of the flower.

4.2 Polyphenols, flavonoids and phenolic acids

The flower is not simply a lutein source. Burlec and colleagues profiled *T. erecta* flowers and documented multiple polyphenolic constituents, emphasising that the plant contains a chemically meaningful non-carotenoid fraction[4]. Phrutivorapongkul and colleagues used bioassay-guided fractionation of an ethyl acetate flower extract and isolated quercetagetin, a flavonoid with strong radical-scavenging and tyrosinase-inhibitory activity[14]. More recent UPLC-QTof/MS work on a polyphenol-enriched fraction identified patulitrin, quercetagetin, kaempferol, patuletin and isorhamnetin among prominent constituents[15].

Earlier anti-ageing work also identified syringic acid and β-amyrin in standardised *T. erecta* flower material. The methanol extract inhibited hyaluronidase, elastase and MMP-1, and both syringic acid and β-amyrin contributed to enzyme-inhibitory activity[7]. The importance of these observations is not that any one molecule explains the entire extract, but that several chemically distinct constituents converge on skin-relevant endpoints. This supports a multicomponent model in which xanthophylls provide lipophilic antioxidant capacity while polyphenols contribute radical-scavenging, enzyme-modulating and signalling-related effects.

4.3 Extraction-dependent variability

The extraction method is a major determinant of biological activity. Ethyl acetate fractions can concentrate relatively lipophilic phenolic compounds, hydroalcoholic extracts recover a broader polarity range, and highly polar aqueous extracts capture a different chemical spectrum. In the 2013 appraisal study, ethyl acetate extract showed the strongest activity and highest phenolic content among the tested extracts[14]. The 2021 cosmeceutical study compared aqueous, 50% ethanolic and 95% ethanolic flower extracts and concluded that especially the 95% ethanolic preparation had potential for cosmeceutical development[16]. These differences make it inappropriate to assume that all *T. erecta* extracts are equivalent simply because they originate from the same flower.

Harvest stage and extraction technology further modify the recovered phytochemical profile. Siddiqa and colleagues compared *T. erecta* flowers at different blooming stages and extraction conditions and found that ultrasound-assisted extraction of full-bloom material produced the highest reported total carotenoid content in their experimental series, together with high DPPH and ABTS activity; HPLC-DAD quantified gallic acid, quercetin, lutein and zeaxanthin in the optimised extract[17]. Taken together with cultivar-comparison studies[8-11], this work shows that the phrase "flower extract" conceals meaningful chemical variability generated before the ingredient ever enters a cream base. The principal constituent classes and their skin-relevant interpretation are summarised in Table 1, and the two-arm phytochemical architecture is shown schematically in Figure 2.

Table 1. Principal phytochemical classes in *Tagetes erecta* flowers and their skin-relevant interpretation.

Constituent/class	Evidence of occurrence	Skin-relevant rationale	Interpretation
Lutein/lutein esters	Dominant xanthophyll fraction in many flower extracts; cultivar and processing variability documented [3,8-12,17]	Singlet-oxygen quenching; lipid-phase antioxidant support; photobiological relevance	Strong phytochemical evidence; constituent-level skin evidence
Zeaxanthin	Established xanthophyll; free/esterified forms and cultivar-dependent variation documented [3,9-12,17]	Antioxidant and photobiological support; complements lutein	Strong occurrence evidence; concentration is cultivar/process dependent
Quercetagetin	Isolated from flower extract	Radical scavenging; tyrosinase inhibition	Direct *T. erecta* mechanistic evidence
Patulitrin / patuletin / isorhamnetin/kaempferol	Identified in polyphenol-enriched flower fraction	Melanogenesis-related and antioxidant mechanisms	Direct phytochemistry plus preclinical mechanism
Syringic acid	Quantified in standardised flower extract	Hyaluronidase/elastase/ MMP-related relevance	Direct anti-ageing enzyme evidence
β-Amyrin	Detected and quantified in standardised flower extract	Matrix-enzyme inhibitory relevance	Direct mechanistic evidence
Other phenolics	Variable among extracts	Radical scavenging and inflammatory modulation	Extract dependent

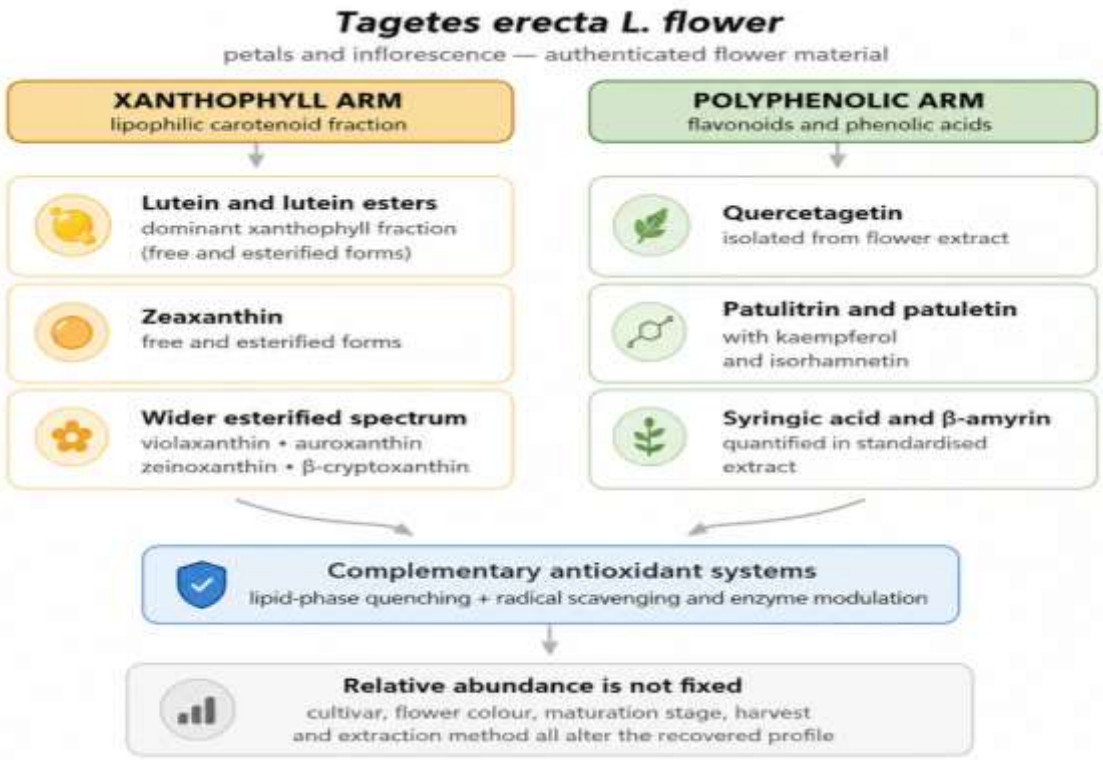

Fig 2: Phytochemical architecture of *Tagetes erecta* flowers relevant to topical dermatology. A xanthophyll arm dominated by lutein/lutein esters and including zeaxanthin is complemented by a polyphenolic arm containing quercetagetin, patulitrin/patuletin, kaempferol, isorhamnetin, syringic acid and related constituents. Relative abundance varies with cultivar, flower colour, maturation, extraction and processing.

5. ANTIOXIDANT DEFENCE AND CUTANEOUS OXIDATIVE STRESS

Oxidative stress is a unifying mechanism across photoageing, pollution-related skin stress, inflammatory amplification and barrier dysfunction. Reactive oxygen species generated by ultraviolet radiation, visible light, environmental oxidants and normal cellular metabolism can oxidise membrane lipids and proteins, alter redox-sensitive signalling and promote matrix-degrading pathways. An antioxidant botanical is therefore most relevant when evidence exists at more than one level: direct radical scavenging, lipid protection, cytocompatibility and downstream biological effects.

T. erecta flower extracts satisfy several of these criteria. Phrutivorapongkul and colleagues demonstrated DPPH radical-scavenging and TBARS-related antioxidant activity, with quercetagetin showing particularly strong DPPH activity relative to reference antioxidants in their experimental system[14]. Burlec and colleagues confirmed antioxidant activity in chemically profiled flower extracts and simultaneously assessed cytotoxicity, supporting the concept that antioxidant effects were observed within a broader phytochemical context rather than from a single isolated assay[4]. The 2021 cosmeceutical study likewise evaluated antioxidant and skin-ageing-related activities across extracts and identified the highly ethanolic preparation as particularly promising for cosmetic development[16].

The xanthophyll fraction adds a complementary mechanism. Lutein and zeaxanthin are lipophilic enough to associate with membrane environments and have the physical chemistry required for quenching excited-state species. In human skin, combined topical/oral lutein and zeaxanthin administration has been associated with improved antioxidant-related parameters and reduced lipid peroxidation[13]. For BIOPANACEA Cream, the defensible interpretation is therefore that *T. erecta* flower chemistry contains both polyphenolic and xanthophyll antioxidant systems. It is not defensible to claim a defined lutein or zeaxanthin dose unless the actual extract has been analytically standardised for those constituents.

Human dermal-fibroblast data provide an additional bridge between antioxidant chemistry and skin-ageing biology, although the material used was a whole-plant rather than a flower preparation. Kang, Rhie and Kim evaluated a methanol extract prepared from whole *T. erecta* plants and reported concentration-dependent DPPH, ABTS and superoxide-dismutase-like antioxidant activities. At 100 µg/mL, the extract increased type-I procollagen synthesis by 83.7% in non-irradiated fibroblasts, and in

ultraviolet-A-irradiated fibroblasts reduced MMP-2 activity by 36.5% and MMP-1 mRNA expression by 69.5% while increasing laminin-5 mRNA expression by 181.2% relative to the corresponding controls[18]. The same concentration reduced fibroblast viability by approximately 20%, so the highest-dose values should be read with that in mind. Because the extract was prepared from whole plants, these findings are treated here as species-level supportive evidence rather than as direct flower-extract evidence; the authors themselves attribute part of the difference between their flavonoid values and those of a Thai marigold flower extract to differences in cultivar, plant part and extraction solvent[18]. The results do not establish clinical wrinkle reduction, but they strengthen the cellular rationale linking *T. erecta* antioxidant activity to matrix preservation and dermal structural support.

A further translational point is that antioxidant activity measured in an extract does not automatically survive formulation. Oxidation-prone carotenoids may degrade with light, oxygen or heat, while polyphenols can interact with emulsifiers or partition away from the biologically relevant phase. The 2014 NLC cream study and later conventional cream work are therefore useful because they show that flower-derived activity can be incorporated into topical dosage forms rather than remaining only a test-tube phenomenon[19,20].

6. ANTI-INFLAMMATORY AND INFLAMMATION-RESOLVING ACTIVITY

Inflammation is central to visible erythema, barrier disturbance, post-environmental stress and many pathological dermatoses. For cosmetic interpretation, the key issue is not to convert anti-inflammatory assay results into disease-treatment claims, but to ask whether *T. erecta* can plausibly support a calmer cutaneous environment.

The strongest mechanistic evidence is provided by Vaz and colleagues, who investigated a hydroalcoholic *T. erecta* flower extract in neutrophil and macrophage systems and in an in vivo model of acute inflammation[21]. In cell-based work, the extract restrained the directed movement of neutrophils and lowered the levels of TNF, IL-1β, CXCL1 and IL-6 recovered from lipopolysaccharide-stimulated neutrophils and macrophages, along with nitric oxide. It increased neutrophil CD62L expression in a pattern associated with impaired adhesion and enhanced macrophage efferocytosis of apoptotic neutrophils. Efferocytosis was accompanied by increased IL-10 and decreased TNF, suggesting an effect not only on inflammatory mediator production but also on resolution-associated macrophage behaviour[21].

The in vivo component of the same study showed reductions in neutrophil migration, protein exudation and inflammatory cytokine release in carrageenan-induced inflammation[21]. Although the in vivo extract was administered orally rather than topically, the work is valuable mechanistically because it demonstrates that the flower extract can influence multiple stages of an inflammatory response. It should be described as evidence of anti-inflammatory biological potential rather than proof of treatment for a specific skin disease.

The flower flavonoid quercetagetin also has skin-cell evidence that is mechanistically relevant, although it must be classified as constituent-level support rather than direct proof for the complete flower extract. In HaCaT human keratinocytes, quercetagetin suppressed inflammatory chemokines induced by IFN-γ and TNF-α[22]. Subsequent work showed inhibition of macrophage-derived chemokine/CCL22 and STAT1 phosphorylation, with upregulation of SOCS1 and TGF-β1-related signalling[23]. Because quercetagetin has been isolated directly from *T. erecta* flowers[14], these studies deepen the biological plausibility of the polyphenolic anti-inflammatory arm while remaining analytically distinct from whole-extract experiments.

Recent formulation studies are consistent with this mechanistic picture. Kamal and colleagues evaluated flower extracts for protein denaturation and red-cell membrane stabilisation alongside photoprotection-related assays, reporting concentration-dependent anti-inflammatory activity[24]. A 2026 flower-extract cream study similarly reported antioxidant activity, red-cell membrane stabilisation, and inhibition of protein denaturation in vitro[20]. These assays are surrogates and do not establish clinical efficacy in psoriasis, despite the disease-oriented framing of the papers. For a cosmetic cream, their more appropriate use is to support the proposition that *T. erecta* flower extract can retain inflammation-relevant activity in topical formulation.

7. EXTRACELLULAR-MATRIX PRESERVATION AND ANTI-AGEING RELEVANCE

Visible skin ageing reflects both intrinsic processes and cumulative environmental exposure. Matrix metalloproteinases, elastase and hyaluronidase contribute to degradation or altered turnover of collagen, elastin and hyaluronan. Botanical inhibition of these enzymes is therefore a useful mechanistic screen for

anti-ageing potential, although the concentrations required in biochemical assays may not be achieved in intact human skin.

Maity and colleagues directly investigated standardised *T. erecta* flower extract for hyaluronidase, elastase and MMP-1 inhibition[7]. The methanol extract showed inhibitory activity against all three targets, and syringic acid and β-amyrin were isolated and evaluated as contributing constituents. This study is especially important because it ties authenticated flower chemistry to enzymes that map directly onto extracellular-matrix preservation rather than relying on a generalised antioxidant argument.

Vallisuta and colleagues independently examined ethanol and ethyl acetate flower extracts and reported elastase inhibition significantly greater than the negative control, together with tyrosinase inhibition and an absence of cytotoxicity in the two cell lines tested[25].

The human fibroblast study by Kang and colleagues broadens this evidence from isolated enzyme inhibition to cellular matrix regulation, with the important qualification that it used a whole-plant methanol extract. That extract increased type-I procollagen synthesis while suppressing MMP-1 expression and MMP-2 activity and increasing laminin-5 expression[18]. This combination is relevant to skin ageing because it addresses both matrix synthesis and matrix degradation within the same cellular system, but because the material was not flower-derived, it supports the species rather than the specific flower preparation considered here. At the constituent level, lutein has independently been shown in dermal fibroblasts to suppress MMP-1 expression and MMP-2 protein and to influence cellular responses to UVA/UVB exposure[26]. The lutein study is supportive rather than direct *T. erecta* evidence, but it is biologically coherent with the flower's xanthophyll composition.

The most translational evidence comes from the 2014 study in which ethyl acetate extract and a semi-purified antioxidant-rich fraction were incorporated into nanostructured lipid carriers and then into cream[19]. In 25 healthy volunteers treated twice daily for eight weeks, the NLC-containing preparations were reported as non-irritating on patch testing, and instrumental wrinkle parameters were significantly reduced relative to untreated and vehicle-treated areas for all measured parameters. The comparison against cream containing the corresponding unencapsulated material was more limited: superiority was demonstrated only for the semi-purified antioxidant-rich fraction and only for the roughness parameters Ra and Rz, whereas the ethyl acetate arm showed no significant difference on any parameter[19]. The study therefore supports the topical anti-wrinkle potential of a specific *T. erecta* delivery system, but the effect cannot be automatically transferred to a conventional cream because nanostructured lipid carriers can alter stability, partitioning and cutaneous delivery.

A separate 2014 human study evaluated a nanoemulsion gel containing ethyl acetate *T. erecta* flower extract on the forearms of 30 healthy volunteers for eight weeks[27]. The formulation was non-irritating on patch testing, increased skin hydration, and significantly reduced wrinkle volume, Ra and Rz relative to the vehicle-treated area, while the surface parameter did not differ significantly. In-vitro Franz-cell permeation work in the same study, performed on excised rat skin, found that most of the recovered quercetagetin was retained in the skin rather than crossing into the receptor phase; the retained fraction was, however, dominated by the stratum corneum, with comparatively little reaching the viable epidermis and dermis[27]. This is a reservoir observation in an animal membrane and should not be read as a human cutaneous bioavailability measurement. Together with the NLC-cream study[19], this gives the review two distinct human topical anti-wrinkle datasets, while simultaneously demonstrating why delivery-system specificity must remain explicit.

The anti-ageing evidence is therefore convergent rather than singular: antioxidant chemistry addresses upstream oxidative stress; direct enzyme studies address elastase, hyaluronidase and MMP-1; and a small human study demonstrates that a specifically engineered *T. erecta* cream can change instrumental wrinkle parameters. This is sufficient to support a scientifically positive anti-ageing narrative at ingredient level, provided the manuscript avoids the stronger claim that BIOPANACEA has itself been clinically proven to reduce wrinkles.

8. MELANOGENESIS, TYROSINASE AND EVEN-LOOKING SKIN TONE

Melanogenesis is regulated by melanocyte signalling pathways that converge on the transcription factor MITF and melanogenic enzymes including tyrosinase. Tyrosinase catalyses rate-limiting steps in melanin synthesis, making it a common screening target for botanical cosmetic ingredients.

Two earlier *T. erecta* flower studies demonstrated tyrosinase-related activity. Phrutivorapongkul and colleagues reported that both the flower extract and isolated quercetagetin inhibited tyrosinase, with quercetagetin showing greater inhibitory activity than α- and β-arbutin in their L-tyrosine assay and activity within the range of the study comparators in the L-DOPA system[14]. Vallisuta and colleagues also

reported tyrosinase inhibition by ethanol and ethyl acetate flower extracts, but with IC50 values of 1,078 and 1,467 µg/mL, respectively, which indicate measurable activity rather than high potency[25].

A major advance came from the 2024 Phytomedicine study of a polyphenol-enriched *T. erecta* flower fraction[15]. UPLC-QTof/MS identified patulitrin, quercetagetin, kaempferol, patuletin and isorhamnetin. In α-MSH-stimulated B16F10 cells and zebrafish larvae, the fraction reduced melanogenesis and modulated the cAMP–CREB–MITF–tyrosinase pathway. Molecular docking suggested possible interactions with MC1R, but direct binding studies did not support direct receptor binding, leading the authors to interpret the effect mainly through intracellular cAMP-linked signalling[15]. Patulitrin and patuletin were identified as prominent contributors to anti-melanogenic activity.

This evidence supports a careful cosmetic interpretation: *T. erecta* flower extract has mechanistic potential to support a more even-looking skin tone by modulating melanogenesis-related pathways. It does not establish treatment of melasma or other pigmentary disease, and the degree to which these mechanisms operate in a conventional cream depends on extract standardisation and delivery to the epidermal compartment.

9. ANTIMICROBIAL ACTIVITY AND REPAIR-SUPPORTIVE BIOLOGY

9.1 Antimicrobial activity

Microbial control is relevant to topical formulation because disruption of the epidermal barrier can increase exposure to opportunistic organisms, and microbial products can amplify inflammation. Direct flower evidence is available. Meetong and colleagues prepared ethanolic *T. erecta* flower extracts and identified a water-insoluble fraction with the highest flavonoid content and useful antibacterial activity against *Staphylococcus aureus*. That fraction retained activity after incorporation into a topical gel, demonstrating that antibacterial action could survive formulation[28]. Activity against *Pseudomonas aeruginosa* was evaluated but was less prominent, illustrating that antimicrobial effects are organism-dependent.

The 2021 caprine wound study also found that an aqueous *T. erecta* flower paste was active against *S. aureus* in the context of dermal wound management[29]. More recently, *T. erecta* flower extract has been incorporated into chitosan hydrogels that showed antimicrobial activity against *Escherichia coli*, *S. aureus* and *Candida albicans* together with acceptable L929-cell viability[30]. Chitosan itself is biologically active and contributes to hydrogel performance, so this study should be interpreted as evidence that *T. erecta* can function within an antimicrobial wound-dressing system rather than as proof that the flower extract alone accounts for the entire effect.

Additional flower-specific evidence strengthens the link between inflammatory control and repair biology. In a study comparing *Clerodendrum infortunatum* leaves with *T. erecta* flowers, Kumar and colleagues evaluated an ethanolic flower extract using antioxidant, cytotoxicity, lipoxygenase-inhibition-guided fractionation and proliferation assays; the *T. erecta* flower extract and its active fractions showed substantial lipoxygenase inhibition and repair-relevant proliferative activity, and cycloisolongifolene-8,9-dehydro-9-formyl, a metabolite common to the active fractions of both plants, was identified as a candidate contributor to the anti-lipoxygenase effect[31]. This study is useful because lipoxygenase activity sits at the interface of inflammatory lipid signalling and tissue repair, although the isolated metabolite should not be treated as the sole mediator of the whole extract.

9.2 Wound-repair-relevant activity

The caprine full-thickness wound study provides direct topical evidence for repair-supportive activity[29]. Sixteen surgical wounds were created in eight Black Bengal goats and treated with aqueous *T. erecta* flower paste or normal saline control. The marigold-treated wounds showed reduced inflammatory features, greater wound contraction and histological architecture that more closely approached normal cutaneous tissue. These findings are biologically meaningful because they connect the flower with an integrated dermal process rather than a single enzyme or antioxidant assay.

A complementary biomaterial study, reported as a conference proceedings paper, loaded an ethyl acetate *T. erecta* flower extract into a chitosan film and evaluated cytocompatibility and wound-repair-related behaviour[32]. The extract was non-toxic to L929 fibroblast-like cells across the concentrations tested, and the optimised loaded film showed greater cell migration in a scratch assay than a povidone-iodine positive control, together with activity against Gram-positive and Gram-negative bacteria. Because chitosan itself can contribute to wound-dressing performance, the result cannot be attributed exclusively to

the flower extract; nevertheless, it adds a distinct cellular-migration endpoint to the repair evidence base and supports the feasibility of incorporating the botanical into wound-contact materials.

The evidence remains preclinical and should not be converted into a clinical wound-healing claim for a cosmetic cream. Nevertheless, when combined with anti-inflammatory, antioxidant and antibacterial evidence, the wound model supports the narrower concept that *T. erecta* flower chemistry can create conditions compatible with repair. For BIOPANACEA Cream, terminology such as "repair-supportive", "supports skin recovery" or "helps maintain skin integrity" is scientifically more defensible than "heals wounds".

10. PHOTOPROTECTION-RELATED ACTIVITY AND THE ROLE OF LUTEIN–ZEAXANTHIN

Ultraviolet exposure initiates photochemical reactions that generate reactive oxygen species, alter membrane lipids and proteins, activate inflammatory pathways and accelerate matrix degradation. Photoprotection can therefore be considered at two different levels: direct attenuation of incident radiation and downstream control of photo-oxidative damage. *T. erecta* flower chemistry is relevant to both concepts, but the evidence must be interpreted carefully.

Kamal and colleagues evaluated multiple solvent extracts of *T. erecta* flowers for phytochemical composition, antioxidant capacity, critical wavelength, in-vitro SPF and inflammation-related assays[24]. The study reported critical wavelengths above 370 nm across tested concentrations and high spectrophotometric SPF values under the experimental conditions. These results support the photoprotection-related potential of the extracts but do not establish the labelled SPF of a finished cream. In-vitro absorbance calculations can be strongly influenced by extract concentration, optical properties and assay geometry; regulatory sunscreen claims require standardised finished-product testing.

Lutein and zeaxanthin provide a second layer of photobiological rationale. In a double-blind placebo-controlled human study, Palombo and colleagues evaluated these xanthophylls administered orally, topically or in combination and reported improvements across skin physiological parameters including surface lipids, hydration, photoprotective activity, elasticity and lipid peroxidation, with the combined route producing the largest overall antioxidant effect[13]. A later oral study of lutein and zeaxanthin isomers reported improvement in overall skin tone and an increase in minimal erythemal dose over 12 weeks[33]. Because these are constituent studies, they demonstrate that lutein–zeaxanthin biology is relevant to human skin; they do not prove that an unspecified *T. erecta* cream achieves the same tissue exposure.

The constituent-level photobiological evidence extends beyond the combined lutein–zeaxanthin study. In a randomised, double-blind, placebo-controlled crossover study in which 65 healthy volunteers were allocated across four treatment groups, Grether-Beck and colleagues found that oral lutein inhibited ultraviolet-induced upregulation of HO-1, ICAM-1 and MMP-1 messenger RNA in human skin when it was taken in the first treatment period, although its effect was significantly smaller than that of a lycopene-rich tomato nutrient complex in the second sequence[34]. In a separate randomised double-blind placebo-controlled trial in 30 healthy women, 12 weeks of lutein supplementation increased minimal erythema dose and produced an estimated 22% increase in photoprotective activity, although the investigators did not demonstrate a corresponding skin-regeneration effect[35]. These oral studies cannot be used as evidence that topical BIOPANACEA produces the same exposure or response, but they strengthen the biological relevance of lutein as a cutaneous photoprotective constituent and simultaneously illustrate the need to separate oxidative photoprotection from claims of tissue regeneration or sunscreen efficacy.

For BIOPANACEA Cream, the strongest scientifically defensible message is therefore "supports protection against oxidative consequences of environmental exposure" rather than "provides SPF" or "acts as a sunscreen". If the actual *T. erecta* ingredient is shown analytically to contain lutein and zeaxanthin, these constituents strengthen the mechanistic basis for that positioning.

At the cellular level, lutein also reduced MMP-1 expression and MMP-2 protein in dermal fibroblasts and was evaluated in UVA- and UVB-exposed fibroblast systems[26]. This provides a mechanistic connection between the xanthophyll arm and the extracellular-matrix arm of the review. The convergence of direct *T. erecta* phytochemistry[3,9-12,17], direct flower-extract matrix evidence[7,18], and independent lutein skin biology[26,34,35] is stronger than any one line of evidence alone, while still requiring formulation-specific caution.

11. TOPICAL FORMULATION SCIENCE AND TRANSLATIONAL DELIVERY

The skin is not an aqueous test system. The stratum corneum restricts penetration, and a compound's solubility, lipophilicity, molecular size, ionisation, vehicle partitioning and chemical stability influence whether it remains on the surface, partitions into the barrier or reaches deeper epidermal compartments. Consequently, formulation is not a neutral carrier of botanical activity; it is part of the pharmacotechnical mechanism.

Several *T. erecta* studies demonstrate feasibility across different topical platforms. The 2014 NLC study entrapped ethyl acetate extract and a semi-purified fraction in lipid nanoparticles before incorporation into cream[19]. A separate nanoemulsion-gel study incorporated ethyl acetate flower extract into a nanoscale emulsion and documented skin retention of quercetagetin together with an eight-week human evaluation[27]. The 2023 gel study demonstrated that an antibacterial flower fraction could retain activity after incorporation into a gel[28]. Chitosan film and hydrogel studies further show that flower extract can be incorporated into wound-contact biomaterials with retained cytocompatibility, migration-related and antimicrobial performance[30,32]. The 2026 cream study formulated ethanolic flower extract into a conventional cream and documented retained antioxidant and in-vitro anti-inflammatory activity[20]. Collectively, these systems demonstrate formulation feasibility while also emphasising that release and cutaneous disposition are delivery-system dependent.

These formulation studies reinforce two points. First, *T. erecta* flower actives are compatible with topical dosage forms. Second, delivery technology influences outcome. An NLC cream cannot be assumed equivalent to an ordinary emulsion; a chitosan hydrogel contributes its own biological and release properties; and an extract dissolved in a solvent-rich gel may partition differently from the same extract in a lipid cream. When interpreting the human anti-wrinkle study, the beneficial effect must therefore be attributed to the studied *T. erecta*–NLC formulation rather than generalised to every cream containing marigold flower extract.

A cream base nevertheless provides rational advantages for a product such as BIOPANACEA. Emulsion systems can prolong contact with the skin, provide emolliency, reduce surface roughness and, depending on composition, decrease transepidermal water loss. These vehicle effects should be separated conceptually from the biological effects of *T. erecta*. Hydration and softness may be primarily formulation-driven, while antioxidant, enzyme-inhibitory, anti-inflammatory, pigmentation-related and antimicrobial activities arise from the flower extract. This distinction allows the finished product to be positioned positively without misattributing all effects to a single botanical ingredient.

12. HUMAN SKIN COMPATIBILITY AND DIRECT HUMAN TOPICAL EVIDENCE

Human evidence for *T. erecta* in skin care is limited but now comprises more than a single efficacy-oriented formulation study. The 2014 NLC cream investigation included patch-test skin-irritation testing and an eight-week instrumental wrinkle evaluation in 25 healthy adults; the test preparations were non-irritating, and the NLC formulations reduced wrinkle-related parameters relative to untreated and vehicle-treated areas, with a significant advantage over the corresponding non-NLC cream only for the semi-purified fraction and only for Ra and Rz[19]. In a separate study, a nanoemulsion gel containing ethyl acetate flower extract was applied to the forearms of 30 healthy volunteers for eight weeks; it was non-irritating, increased skin hydration, and improved wrinkle volume, Ra and Rz relative to the vehicle-treated area, with no significant change in the surface parameter[27]. These studies are small and formulation-specific, but together they materially strengthen the translational evidence tier because they demonstrate human topical performance in two different delivery systems.

Mekjaruskul and colleagues subsequently evaluated aqueous, 50% ethanolic and 95% ethanolic flower extracts for cosmeceutical activities and human skin irritation[16]. Their study integrated total phenolic measurement, syringic acid analysis, antioxidant and skin-ageing-related assays with a human irritation component and concluded that the flower extracts—particularly the 95% ethanolic preparation—were promising for development of cosmeceutical skin products. This work strengthens the safety narrative because it links biological activity to direct skin-compatibility testing rather than assuming tolerability from traditional use.

Safety must nevertheless remain formulation-specific. The Asteraceae family contains species capable of producing contact allergy, and older *Tagetes* research identified butenylbithiophene, α-terthienyl and hydroxytremetone as contact allergens in selected marigold cultivars in sensitisation experiments[36]. α-Terthienyl isolated from *Tagetes* species has also produced UVA-dependent phototoxicity in an experimental guinea-pig model after topical exposure[37]. These findings do not establish that a characterised *T. erecta* flower cream contains these compounds at sensitising or phototoxic concentrations, nor do they negate the encouraging human irritation data for specific

extracts[16,19,27]. Rather, they reinforce the importance of plant part, cultivar, extraction method, volatile/thiophene content and finished-product compatibility testing. Representative direct and translational skin-related studies are summarised in Table 2.

Table 2. Representative direct and translational skin-related studies of *Tagetes erecta* flower preparations.

Study	Preparation/model	Key skin-relevant findings	Evidence level	Interpretation for the review
Maity et al. [7]	Standardised flower methanol extract; enzyme assays	Inhibition of hyaluronidase, elastase and MMP-1; syringic acid and β-amyrin characterised.	Direct mechanistic	Supports extracellular matrix preservation rationale.
Phrutivorapongkul et al. [14]	Flower extracts and isolated quercetagetin	Antioxidant activity and tyrosinase inhibition.	Direct mechanistic	Supports antioxidant and even-looking-tone mechanisms.
Leelapornpisid et al. [19]	NLC-loaded flower extract cream; 25 healthy volunteers, 8 weeks	Non-irritating; wrinkle parameters improved versus untreated and vehicle areas; advantage over non-NLC cream only for the semi-purified fraction, on Ra and Rz.	Human topical	Strong translational support, but delivery-system specific.
Leelapornpisid et al. [27]	Nanoemulsion gel; 30 healthy volunteers, 8 weeks	Non-irritating; increased hydration; improved wrinkle volume, Ra and Rz versus vehicle (surface parameter unchanged); quercetagetin retained in skin in a rat in-vitro permeation model.	Human topical	Independent human topical support; nanoemulsion specific.
Kang et al. [18]	Human dermal fibroblasts; whole-plant methanol extract (not flower-derived)	Type-I procollagen increased; MMP-1 expression and MMP-2 activity reduced; laminin-5 expression increased.	Species-level cellular	Strengthens matrix/healthy-ageing rationale beyond enzyme screening; plant part differs from the flower extract under review.
Mekjaruskul et al. [16]	Aqueous and ethanolic flower extracts; human irritation evaluation	Cosmeceutical activities integrated with direct human skin-compatibility testing.	Human compatibility / translational	Supports tolerability of specific characterised preparations.

Sultana et al. [29]	Topical flower paste; caprine full-thickness wound model	Reduced inflammatory features, greater wound contraction and improved histological architecture.	Animal dermal	Supports repair-relevant biology; not a human wound-healing claim.
Meetong et al. [28]	Flavonoid-rich flower fraction in topical gel	Retained antibacterial activity, particularly against *Staphylococcus aureus*.	Formulation / antimicrobial	Supports microbial balance and topical-formulation feasibility.
Vaz et al. [21]	Hydroalcoholic flower extract; neutrophils, macrophages and in vivo inflammation	Reduced inflammatory mediators and neutrophil migration; promoted macrophage efferocytosis and IL-10-related resolution.	Strong preclinical	Principal evidence for inflammation-regulatory positioning.
Sanjaya et al. [15]	Polyphenol-enriched flower fraction; B16F10 cells and zebrafish	Reduced α-MSH-induced melanogenesis via cAMP–CREB–MITF–tyrosinase signalling.	Preclinical mechanistic	Supports even-looking-tone/melanogenesis rationale.
Kamal et al. [20]	Ethanolic flower extract incorporated into conventional cream	Antioxidant and in-vitro anti-inflammatory activity retained after formulation.	Formulation	Supports feasibility of conventional cream delivery; not clinical efficacy.

13. INTEGRATED CUTANEOUS MECHANISM

The literature supports an integrated rather than single-target model. *T. erecta* flower extract can be conceptualised as a two-arm phytochemical system: a lipophilic xanthophyll arm dominated by lutein and containing zeaxanthin, and a polyphenolic arm containing quercetagetin, patulitrin, patuletin, kaempferol, isorhamnetin and other phenolics[3,4,15]. These arms converge on redox balance but also contribute distinct mechanisms.

At the oxidative level, polyphenols and xanthophylls can reduce radical and photo-oxidative burden. At the inflammatory level, the hydroalcoholic flower extract has been shown to suppress pro-inflammatory mediators, reduce neutrophil chemotaxis and promote macrophage efferocytosis[21]. At the extracellular matrix level, standardised flower extract inhibits elastase, hyaluronidase and MMP-1[7]. At the pigmentary level, flower extracts and constituents inhibit tyrosinase, while a polyphenol-enriched fraction suppresses α-MSH-driven cAMP–CREB–MITF–tyrosinase signalling[14,15,25]. At the tissue-integrity level, topical flower preparations demonstrate antibacterial and repair-supportive activity[28,29].

These mechanisms are biologically interconnected. Lower oxidative stress can reduce redox-sensitive inflammatory and matrix-degrading signalling. Reduced inflammatory burden can support barrier recovery and lessen secondary oxidative stress. Lower microbial burden can decrease inflammatory

stimulation in compromised skin. Modulation of melanogenesis can influence visible tone without requiring a disease-treatment claim. In this way, the flower's chemistry provides a coherent mechanistic explanation for cosmetic outcomes such as calmer-looking skin, protection from oxidative stress, support of skin recovery, a more even-looking tone and maintenance of smoother, healthier-looking skin. These converging pathways are represented in Figure 3.

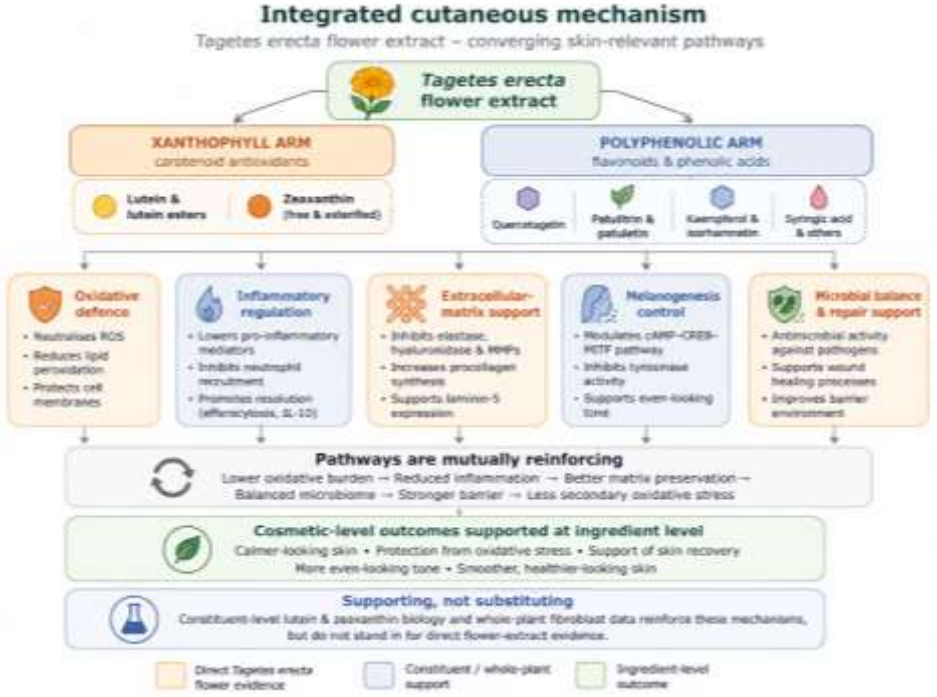

Fig 3: Integrated cutaneous mechanism supporting the topical relevance of *Tagetes erecta* flower extract. The flower provides complementary xanthophyll (lutein, lutein esters and zeaxanthin) and polyphenolic arms. These converge on oxidative defence, inflammatory regulation, extracellular-matrix preservation, melanogenesis control and microbial/repair-supportive pathways. The figure should visually distinguish direct *Tagetes erecta* evidence from constituent-level supportive evidence.

14. EVIDENCE CONVERGENCE ACROSS DERMATOLOGICAL BENEFIT DOMAINS

The preceding sections can be consolidated into a domain-by-domain view of how much evidential weight each proposed benefit actually carries. Table 3 sets out that hierarchy, distinguishing direct flower-extract evidence from constituent-level, whole-plant and formulation-specific findings, and Figure 4 represents the same material as a convergence map. Read together, they show that the evidence is strongest for antioxidant defence, inflammatory regulation and extracellular-matrix preservation, moderate for pigmentation, antimicrobial and repair-supportive domains, and weakest — by design — for any statement about the finished product itself.

Table 3. Evidence hierarchy for major skin-relevant benefit domains.

Benefit domain	Key evidence	Evidence level	Interpretive position
Antioxidant defence	Direct DPPH/TBARS and chemically profiled flower-extract studies; human fibroblast antioxidant data; lutein/zeaxanthin constituent evidence [4,8,13,14,16-18]	Strong mechanistic; supportive human constituent evidence	One of the strongest ingredient-level domains
Inflammatory regulation	Neutrophil/macrophage flower-extract work; in vivo acute inflammation; quercetagetin keratinocyte support; formulation-level	Strong preclinical	Supports calming/inflammatory -balance language

	anti-inflammatory assays [20-24]		
Matrix/anti-ageing	Hyaluronidase/elastase/MMP-1 inhibition; human fibroblast procollagen/MMP/laminin data; two human topical anti-wrinkle studies [7,18,19,27]	Moderate translational	Supports healthy-ageing/anti-wrinkle plausibility, formulation dependent
Pigmentation	Tyrosinase inhibition; α-MSH-stimulated cAMP–CREB–MITF–tyrosinase pathway data [14,15,25]	Moderate preclinical	Supports even-looking-tone language
Antimicrobial	*S. aureus* activity; topical gel; chitosan hydrogel systems [28-30]	Moderate preclinical/translational	Supports microbial-balance/skin-integrity rationale
Repair support	Caprine topical wound model; LOX/proliferation study; chitosan film/hydrogel migration and formulation evidence [29-32]	Moderate preclinical	Use repair-supportive rather than wound-healing clinical claim
Photoprotection relevance	In-vitro critical wavelength/SPF plus lutein–zeaxanthin human skin and lutein RCT evidence [13,24,26,34,35]	Moderate mechanistic/translational	Do not equate with sunscreen efficacy
Hydration/softness	Cream vehicle plus lutein/zeaxanthin constituent literature [13,27]	Formulation dependent	Primarily vehicle effect unless measured in finished product
Finished BIOPANACEA efficacy	Ingredient-level convergence across the domains above	Indirect	Not equivalent to product-specific clinical proof

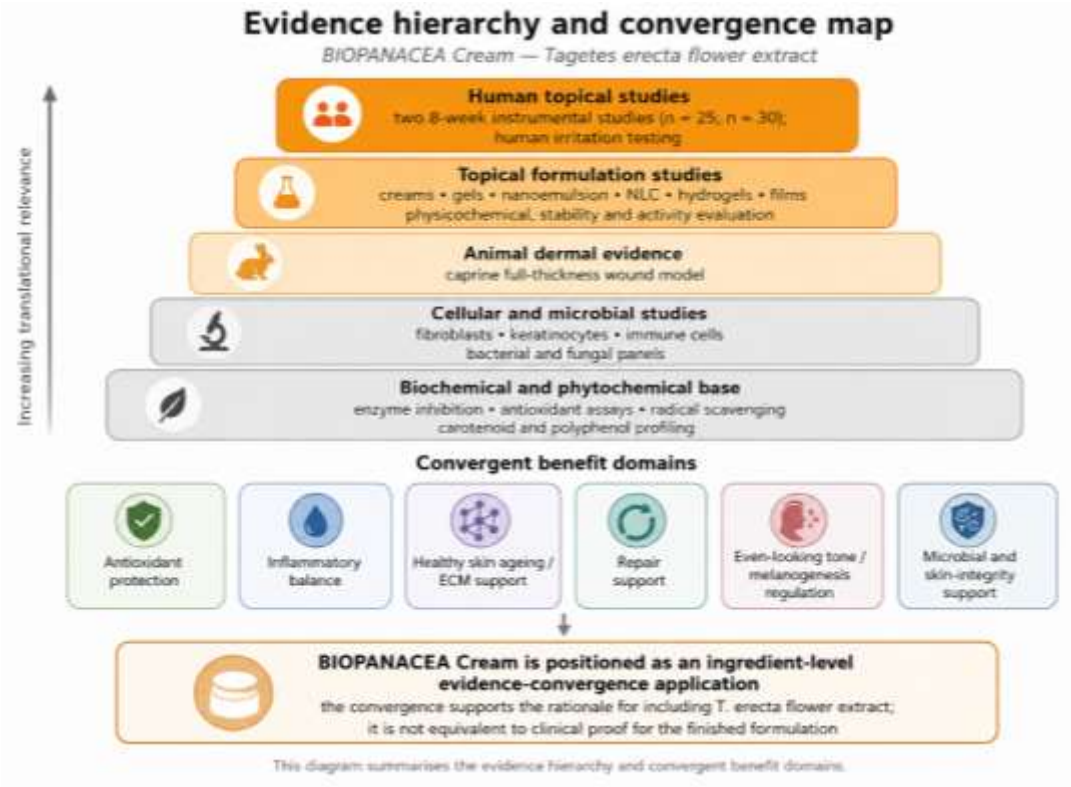

Fig 4: Evidence hierarchy and convergence map for BIOPANACEA Cream. Phytochemical characterisation and biochemical assays form the evidence base; skin-relevant cellular and microbial studies, animal dermal evidence and topical formulation studies provide increasing translational relevance; human topical studies occupy the highest current tier. The convergent benefit domains are antioxidant protection, inflammatory balance, healthy skin ageing/extracellular-matrix support, repair support, even-looking tone/melanogenesis regulation and microbial/skin-integrity support. BIOPANACEA should be represented as an ingredient-level evidence-convergence application rather than a clinically proven finished product.

15. TRANSLATIONAL RELEVANCE TO BIOPANACEA CREAM

BIOPANACEA Cream can be scientifically framed as a topical cream centred on *T. erecta* flower extract. That ingredient is supplied against a certificate of analysis identifying the botanical source as *Tagetes erecta* L. The point is stated explicitly because the trade designation "marigold extract" is applied in commerce to material of both *Tagetes* and *Calendula* origin, and because the two genera are not phytochemically interchangeable; botanical authentication rather than common name should therefore govern the interpretation of the evidence summarised in this review. The literature provides a favourable ingredient-level rationale because several independent evidence streams converge on skin-relevant processes. The strongest positioning is built around antioxidant defence, inflammatory balance, maintenance of extracellular-matrix integrity and repair-supportive biology. Pigmentation regulation, antimicrobial activity and environmental-stress support provide additional, but more context-dependent, domains.

For antioxidant claims, the evidence is particularly coherent. The flower contains a well-established xanthophyll fraction as well as antioxidant polyphenols, and direct extract studies repeatedly demonstrate radical-scavenging or lipid-oxidation-related effects[3,4,14]. For calming or stressed-skin claims, the neutrophil/macrophage study offers detailed mechanistic support that is stronger than generic statements about "anti-inflammatory herbs"[21]. For healthy-ageing claims, the combination of direct matrix-enzyme inhibition and a small human anti-wrinkle formulation study gives the ingredient a meaningful translational basis[7,19].

Zeaxanthin should be visible in the scientific narrative, but proportionally. In a representative commercial flower extract, it was a minor xanthophyll relative to lutein, and its concentration varies with cultivar and processing[3]. Therefore, zeaxanthin should be described as an established constituent of *T. erecta* flowers and as part of the xanthophyll antioxidant architecture. Unless BIOPANACEA or its

botanical raw material is analytically standardised for zeaxanthin, the manuscript should not state a specific zeaxanthin concentration or imply that zeaxanthin is the dominant active.

The cream base also deserves appropriate credit. A topical emulsion can independently contribute moisturization, softness, spreadability and prolonged contact. Such formulation effects are complementary to the botanical activity and do not weaken the ingredient narrative. On the contrary, separating vehicle effects from extract effects improves scientific credibility. The cream can be described as providing an emollient topical environment while delivering a flower extract with antioxidant, inflammation-regulatory, matrix-related, pigmentation-related and antimicrobial biological potential.

The most defensible product language is therefore supportive rather than therapeutic: "supports antioxidant defence", "helps calm the appearance of stressed skin", "supports skin recovery and integrity", "helps maintain smoother and healthier-looking skin", "supports an even-looking skin tone" and "helps protect against oxidative contributors to premature visible ageing". Terms such as "treats psoriasis", "heals wounds", "cures infection" or "provides SPF" exceed the ingredient-level evidence and should not be inferred from laboratory or animal studies. The mapping from evidence domain to defensible wording is set out in Table 4.

Table 4. Evidence-to-claim translation for BIOPANACEA Cream.

Evidence domain	Scientifically supportable product-oriented wording	Wording to avoid without direct finished-product evidence
Antioxidant	Supports antioxidant defence and protection from oxidative stress	Prevents all UV damage; clinically proven antioxidant treatment
Inflammatory balance	Helps calm the appearance of stressed or irritated-looking skin	Treats eczema/psoriasis/dermatitis
Skin ageing	Supports smoother, healthier-looking skin and protection against oxidative contributors to visible ageing	Clinically proven wrinkle reversal
Repair	Supports skin recovery and integrity	Heals wounds
Pigmentation	Supports an even-looking skin tone	Treats melasma or hyperpigmentation disorders
Antimicrobial	Supports a skin environment resistant to microbial stress	Treats bacterial or fungal infection
Photoprotection	Supports protection from oxidative consequences of environmental exposure	Sunscreen / SPF claim without finished-product testing

16. LIMITATIONS OF THE CURRENT EVIDENCE

The current literature is scientifically useful but heterogeneous. The first limitation is extract variability. Studies have used aqueous pastes, aqueous extracts, hydroalcoholic extracts, ethanolic extracts, ethyl acetate extracts, semi-purified fractions, polyphenol-enriched fractions and carotenoid-rich preparations. These materials differ in chemical composition and cannot be treated as interchangeable doses of a single substance. The lutein-to-zeaxanthin profile is also not constant; the approximately 88% lutein/lutein-ester and 5% zeaxanthin distribution reported in one commercial extract is a compositional example, not a universal specification[3]. Comparative studies across cultivars demonstrate substantial variation in phenolics, flavonoids, lutein, zeaxanthin and total carotenoids[8,9,11], while developmental, flower-colour and extraction studies show that gene expression, blooming stage and processing further modify carotenoid accumulation and recovery[10,17]. Accordingly, the presence of lutein and zeaxanthin is well supported, but a defined quantitative claim for BIOPANACEA requires analytical characterisation of the actual ingredient.

The second limitation is plant-part heterogeneity. Not every study described in the literature as a "marigold" or "*T. erecta*" investigation used flower material. The human dermal-fibroblast work that provides the most detailed cellular matrix data was performed with a methanol extract of whole plants rather than flowers, and its authors expressly attribute part of the difference between their flavonoid values and those reported for a flower extract to plant part, cultivar and solvent[18]. Because petals are the compartment enriched in xanthophylls and the flower is chemically distinct from leaf, aerial and root tissue, whole-plant findings are treated in this review as species-level support and are not counted as direct evidence for a flower-extract cream.

The third limitation is formulation heterogeneity. Human anti-wrinkle evidence was generated with both NLC and nanoemulsion delivery systems, while other studies used conventional creams, gels, chitosan films, hydrogels or raw flower paste[19,20,27-30,32]. Delivery technology changes stability, release, residence time and penetration. A positive result with NLCs or nanoemulsions therefore cannot be assumed to occur at the same magnitude in a conventional cream. Conversely, successful conventional and polymeric formulations demonstrate feasibility but not pharmacokinetic or clinical equivalence.

Fourth, the human clinical dataset remains small despite being stronger than is typical for many botanical ingredients. Two eight-week topical anti-wrinkle studies enrolled 25 and 30 healthy volunteers, respectively, and each evaluated a specialised delivery system[19,27]. The 2021 cosmeceutical paper included human irritation testing but was not a large randomised efficacy trial[16]. Most of the mechanistic strength therefore continues to come from biochemical, cellular or animal work. The two topical human studies improve translational confidence, but they do not establish the clinical magnitude of effect of an unrelated finished cream.

Fifth, the publication venues of the human efficacy evidence deserve explicit comment. Both eight-week topical studies appeared in the same journal, which was covered by Scopus at the time of publication but has since been discontinued from that index, is not indexed for MEDLINE, and assigned no digital object identifier to either article[19,27]. Neither study was randomised, blinded or prospectively registered, neither reports a sample-size justification, and neither presents a numerical table of the wrinkle data underlying its efficacy claim. These are genuine constraints on evidential weight. They do not invalidate the observations, which are internally consistent with the mechanistic and formulation literature, but they are the reason this review treats the human tier as supportive translational evidence rather than as confirmatory clinical proof.

Sixth, several endpoints are surrogate measures. DPPH scavenging, TBARS assays, tyrosinase inhibition, protein-denaturation assays, red-cell membrane stabilisation, and spectrophotometric SPF are useful for screening but do not directly measure clinical outcomes in intact human skin. The 2026 photoprotection study, for example, reported strong in-vitro SPF and critical-wavelength values, but these data should not be interpreted as a regulatory SPF claim for a finished cream[24].

Seventh, wound-repair evidence is predominantly non-human or biomaterial based. The caprine model demonstrates a biologically integrated topical effect, but wound contraction and histological repair in goats are not equivalent to efficacy in human acute or chronic wounds[29]. Lipoxygenase-guided fractionation and proliferation assays add mechanistic support[31], while chitosan film and hydrogel studies add cytocompatibility, migration-related, release and antimicrobial endpoints[30,32]. However, both polymer platforms contribute their own physical and biological effects, so wound-contact performance cannot be attributed solely to *T. erecta*.

Eighth, disease-oriented framing in some recent studies requires restraint. Studies labelled as psoriasis-relevant or anti-psoriatic largely measured in-vitro antioxidant, photoprotective or anti-inflammatory endpoints rather than clinical disease improvement[20,24]. These studies are valuable for mechanistic and formulation evidence but should not be used to claim that *T. erecta* cream treats psoriasis.

Ninth, safety is preparation specific. Human irritation studies are encouraging[16,19,27], but they cannot exclude sensitisation in all users or all extract types. The broader *Tagetes* literature has identified contact-allergenic thiophenes and hydroxytremetone in selected cultivars and has demonstrated UVA-dependent phototoxicity of isolated α-terthienyl in experimental skin models[36,37]. These older studies should not be generalised to a characterised flower extract without compositional evidence, but they justify retaining a balanced sensitisation/phototoxicity discussion rather than treating traditional use as a substitute for safety characterisation. Finally, BIOPANACEA itself is represented in this review as a formulation context. Ingredient-level evidence supports the rationale for including *T. erecta* flower extract, but the magnitude of benefit of the finished cream cannot be inferred from studies of other extract types and delivery systems.

17. CONCLUSION

T. erecta L. flower is a scientifically credible dermatological botanical with a distinctive combination of xanthophyll carotenoids and polyphenolic constituents. Lutein and lutein esters dominate many flower carotenoid preparations, while zeaxanthin is an established secondary xanthophyll whose abundance varies with cultivar, developmental stage and processing[3,8-12,17]. Comprehensive carotenoid profiling demonstrates that the native flower matrix contains a wider esterified xanthophyll spectrum than lutein alone[12]. The polyphenol fraction includes quercetagetin, patulitrin/patuletin, kaempferol, isorhamnetin and related compounds, with additional constituents such as syringic acid and β-amyrin contributing to skin-relevant mechanisms[4,7,14,15].

Across the evidence base, *T. erecta* flower extracts demonstrate antioxidant activity, regulation of inflammatory mediators and leukocyte behaviour, inhibition of elastase, hyaluronidase and MMP-1, cellular modulation of procollagen, MMP-1/MMP-2 and laminin-5, modulation of tyrosinase and melanogenesis pathways, antibacterial activity and repair-supportive effects[7,14,15,18,21,25,28,29,31,32]. Quercetagetin keratinocyte studies and lutein fibroblast/human photobiology studies provide coherent constituent-level support for inflammatory, matrix and photoprotective mechanisms without replacing direct flower evidence[22,23,26,34,35]. Topical formulation studies show that flower-derived activity can be carried into creams, gels, nanoemulsions, lipid nanocarriers, films and hydrogels, while two small human anti-wrinkle studies and human irritation testing support skin compatibility and translational potential for specific preparations[16,19,20,27,28,30,32].

Taken together, this convergence provides a coherent ingredient-level scientific basis for the use of *T. erecta* flower extract as the principal botanical active in BIOPANACEA Cream. The strongest support lies in antioxidant defence, inflammatory balance, extracellular-matrix preservation and repair-supportive biology, with additional evidence for pigmentation regulation, antimicrobial activity and photoprotection-related mechanisms. The product should be positioned in accordance with this evidence hierarchy: positively, but without equating mechanistic and formulation studies with finished-product clinical proof.

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Conflicts of interest: All authors are employees of Biotex Life Solutions Pvt. Ltd., which develops and manufactures BIOPANACEA Cream, the formulation discussed in Section 15. The authors declare this affiliation as a potential competing interest. The literature search strategy and the evidence-grading framework described in Section 2 were defined before the synthesis was written and were applied uniformly, including to findings that do not support the product positioning; the limitations of the evidence base are set out in full in Section 16. The authors declare no other competing interests.

Author contributions: All authors contributed to the conceptualisation of the review, the literature search, appraisal of the primary sources and drafting of the manuscript. All authors read and approved the final version and accept accountability for its content.

Ethics statement: Not applicable to this narrative review; no new human or animal experiments were performed for this article.

Data availability: No new datasets were generated. All information synthesised in this review is derived from the cited literature.

Use of artificial intelligence: Generative artificial-intelligence tools were used to assist with literature searching and with language and formatting. All scientific content, extraction of data from primary sources, interpretation and conclusions were verified by the authors, who take full responsibility for the accuracy and integrity of the work. No artificial-intelligence tool is listed as an author.

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