

Article

Standardized Ganoderic-Acid-Enriched Cream for Cutaneous Redness and Inflammatory Stress: Formulation Performance and Translational Evidence

Brandon Foutie¹, Zeynep Celik², Manon Richard³

1,2,3. National Standards Laboratory SA

Citation: Foutie B. Celik Z. Richard M. Standardized Ganoderic-Acid-Enriched Cream for Cutaneous Redness and Inflammatory Stress: Formulation Performance and Translational Evidence. American Journal Of Bioscience And Clinical Integrity 2026, 3(10), 10-16.

Received: 10th Sept 2026

Revised: 11th Sept 2026

Accepted: 24th Sept 2026

Published: 19th Oct 2026



Copyright: © 2026 by the authors. Submitted for open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>)

Abstract: Background: Cutaneous redness and irritation reflect interactions among epithelial stress, innate immune signaling, oxidative pressure and cytokine amplification. Ganoderma triterpenes, especially ganoderic acid A, have been studied across NF- κ B, MAPK, TLR4 and pyroptosis-related pathways, but cosmetic translation benefits from a chemically defined and physically stable topical matrix. Objective: To characterize a low-polysaccharide, ganoderic-acid-enriched cream and integrate its formulation data with current evidence relevant to soothing, inflammatory stress and erythema. Methods: A Ganoderma triterpene enriched material standardized to ganoderic acids A, C2 and D was produced by low-alcohol fractionation, resin separation, nanofiltration/diafiltration and low-temperature drying, and incorporated at 0.50% into a cream. Physicochemical release and stress-stability results were integrated with a structured PubMed evidence synthesis through September 2026. Results: The active material contained 2.9% ganoderic acid A, 1.05% C2, 0.75% D and 3.1% total polysaccharides on a dry basis; residual ethanol was 0.35%. The cream showed no visible phase separation, irreversible precipitation or substantial crystallization after centrifugation and temperature cycling. A 2026 systematic review/meta-analysis of Ganoderma triterpenes reported consistent preclinical suppression of inflammatory mediators, while topical ganoderic acid A reduced erythema and inflammatory signaling in a psoriasis model [1,2]. Human Ganoderma polysaccharide data showed lower erythema, and randomized topical botanical studies validate erythema as a responsive clinical endpoint [3-8]. Conclusion: The standardized triterpene profile and stable cream matrix provide a focused platform for evaluating redness and inflammatory-stress outcomes, with a mechanistic evidence chain centered on oxidative stress, NF- κ B/MAPK signaling and inflammatory mediator control.

Keywords: *Ganoderma; ganoderic acid A; triterpenes; inflammation; erythema; NF- κ B; MAPK; topical cream.*

1. Introduction

Visible redness is a final common phenotype produced by vascular, neurogenic and inflammatory processes in skin. Environmental stress can activate keratinocyte and innate immune pathways, generating reactive oxygen species and pro-inflammatory mediators that reinforce barrier discomfort and erythema. In topical research, objective erythema indices, UV-erythema models and investigator-rated redness have become useful endpoints for detecting anti-inflammatory effects [4-8].

Ganoderma triterpenes are particularly relevant to this biology because multiple compounds suppress inflammatory mediators and signaling nodes. A 2026 systematic review and meta-analysis of 23 preclinical Ganoderma triterpene studies found consistent reductions in NO, IL-6 and TNF- α , with MAPK and TLR4/NF- κ B repeatedly implicated [1]. Ganoderic acid A has also been studied in cutaneous inflammation, where topical exposure reduced erythema, scaling and skin thickening in an inflammatory skin model and was linked to inhibition of GSDMD-mediated pyroptosis [2].

The present work focuses on a cream whose active material is standardized to ganoderic acids A, C2 and D and constrained for residual polysaccharides and ethanol. This marker-based strategy is relevant to TIMEFLYS because it allows future redness studies to be anchored to a reproducible triterpene exposure instead of a nonspecific Ganoderma extract description.

2. Materials and Methods

2.1 Active-material and cream design

The triterpene material was prepared from authenticated red Ganoderma fruiting bodies by hydroalcoholic extraction, low-alcohol standing and solid-liquid separation, AB-8 resin fractionation, high-ethanol elution, ethanol-resistant nanofiltration/diafiltration and low-temperature drying. Batch blending was performed against marker-specific targets. The cream contained 0.50% enriched material, 4.00% caprylic/capric triglyceride, 4.00% squalane, 0.80% hydrogenated lecithin, 4.00% glycerin, 4.00% 1,3-propanediol and a conventional emulsifier/rheology system.

Table 1. Composition of the triterpene-standardized soothing cream.

Component	Mass %	Functional role
Ganoderma triterpene-enriched material	0.50	Core standardized active material
Caprylic/capric triglyceride	4.00	Active-material dispersing/emollient oil
Squalane	4.00	Emollient lipid phase
Hydrogenated lecithin	0.80	Lamellar-structure aid
Glycerin	4.00	Humectant
1,3-Propanediol	4.00	Humectant solvent
Glyceryl stearate citrate	1.00	Emulsifier
Cetearyl alcohol	0.80	Structurant
Polyacrylate Crosspolymer-6	0.20	Rheology modifier
Phenoxyethanol/ethylhexylglycerin (9:1)	0.80	Microbial control
Citric acid/sodium citrate buffer (1:2)	0.15	pH control
Purified water	79.75	Continuous phase

2.2 Physicochemical quality and stress stability

The active material was released against ganoderic acid A, ganoderic acids C2+D, total polysaccharides, moisture and residual-ethanol criteria. Finished-product stress testing used centrifugation at 3000 $\times$ g for 30 min and three cycles between -5 $^{\circ}$ C and 25 $^{\circ}$ C, with visual assessment of phase behavior and pH monitoring.

2.3 Evidence synthesis

PubMed-indexed studies available through September 2026 were identified using combinations of "Ganoderma," "ganoderic acid A," "triterpene," "inflammation," "NF- κ B," "MAPK," "pyroptosis," "skin," "erythema," "topical," and "clinical trial." Priority was given to Ganoderma

triterpene and ganoderic-acid studies, followed by human Ganoderma skin studies. Randomized topical botanical anti-inflammatory studies were used to define human erythema and tolerability endpoints and were retained as methodological benchmarks, analytically separated from formulation-specific efficacy.

3. Results

3.1 Standardized chemistry and formulation integrity

The released enriched material contained 2.9% ganoderic acid A, 1.05% ganoderic acid C2, 0.75% ganoderic acid D, 1.80% combined C2+D and 3.1% total polysaccharides on a dry basis. Moisture was 4.0% and residual ethanol was 0.35%. Incorporation at 0.50% produced a cream that remained physically stable after the defined stress protocol, with pH changing from 5.32 to 5.37. This stable dispersion is important for inflammatory-stress research because precipitation or phase separation could alter actual skin exposure independently of the intrinsic activity of the triterpenes.

Table 2. Standardized active profile and finished-product stress performance.

Attribute	Observed result	Interpretation
Ganoderic acid A	2.9% dry basis	1-5%
Ganoderic acid C2	1.05% dry basis	component of C2 + D
Ganoderic acid D	0.75% dry basis	component of C2 + D
Ganoderic acids C2 + D	1.80% dry basis	0.5-3.0%
Total polysaccharides	3.1% dry basis	≤5.0%
Moisture	4.0%	≤6.0%
Residual ethanol	0.35%	≤0.50%
Finished-cream stress test	No phase separation / irreversible precipitation / substantial crystallization	3000×g, 30 min + three -5°C/25°C cycles
Cream pH	5.32 → 5.37	within pH 5.0-5.8

3.2 Ganoderma triterpenes and inflammatory signaling

The strongest class-level synthesis is the 2026 systematic review/meta-analysis of Ganoderma triterpenes [1]. Across 23 preclinical studies, triterpenes consistently lowered inflammatory mediators; pooled in-vitro analyses showed significant reductions in NO, IL-6 and TNF- α , and the review identified MAPK and TLR4/NF- κ B as recurrent pathways. These findings are consistent with isolated-compound studies. Ganoderic acid A suppressed IL-1 β -driven NO, PGE2, iNOS, COX-2, TNF- α and IL-6 in human cells through NF- κ B regulation [9], while Ganoderma triterpenoids and sterols have shown related effects on NF- κ B, p38 MAPK and inflammatory mediator production [10,11].

Cutaneous evidence is especially relevant. In a 2025 inflammatory skin model, ganoderic acid A applied topically reduced erythema, scaling, skin thickening and inflammatory cytokines, with inhibition of GSDMD-mediated pyroptosis proposed as a key mechanism [2]. Ganoderma ethanol extracts have also protected keratinocytes against free-radical injury and supported re-epithelialization [12]. Together, these results position epithelial stress control and inflammatory-signal attenuation as plausible upstream events for a soothing cosmetic phenotype.

3.3 Human evidence context for erythema and tolerability

Human Ganoderma evidence is available from a 2026 study of β -glucan-rich Ganoderma polysaccharides. The tested material reduced wrinkles, improved hydration and brightness, and diminished erythema; in a heat-patch challenge, erythema severity was reduced by as much as approximately 48% [3]. Because the study material was polysaccharide-rich, it provides human Ganoderma skin context for tolerability and erythema biology and complements the triterpene evidence base; formulation-specific effects can be addressed through subsequent direct evaluation of the standardized cream. Broader randomized topical botanical trials demonstrate that erythema can be quantitatively responsive to plant-derived anti-inflammatory preparations, including UV-erythema and rosacea models [4-8].

Table 3. Evidence hierarchy for Ganoderma triterpenes, cutaneous inflammatory signaling, and erythema endpoints.

References	Evidence type	Principal observation	Relevance
------------	---------------	-----------------------	-----------

[1]	Systematic review/meta-analysis of 23 preclinical Ganoderma triterpene studies	Consistent reductions in NO, IL-6 and TNF- α , mainly via MAPK and TLR4/NF- κ B	Triterpene-class inflammatory evidence
[2]	Ganoderic acid A; topical and systemic psoriasis model	Lower erythema, scaling, skin thickening and inflammatory cytokines; GSDMD-pyroptosis pathway	Direct cutaneous GAA mechanism
[9],[13]	Ganoderic acid A review + human-cell inflammation model	NF- κ B, MAPK, TLR4/Nrf2 context; reduced inflammatory mediators	Mechanistic triangulation
[10],[11]	Ganoderma triterpenoids/sterols in inflammatory cell models	Reduced iNOS, COX-2, IL-1 β , IL-6, TNF- α and NF- κ B/p38 activity	Ganoderma inflammatory signaling
[12],[14]	Ganoderma topical/keratinocyte studies	Anti-inflammatory/antioxidant activity and free-radical protection	Topical biological context
[3]	Ganoderma polysaccharide; human skin study	Reduced erythema, with up to ~48% reduction in heat-patch erythema severity	Human Ganoderma redness context; different active class
[15]-[17]	Ganoderma skin/homeostasis reviews	Multi-target anti-inflammatory, antioxidant and barrier biology	Contextual synthesis
[4]-[8]	Human randomized topical botanical studies	Objective erythema and inflammatory endpoints respond to anti-inflammatory topical regimens	Clinical endpoint benchmarking
[18]	Ganoderma topical cream formulation study	Skin-compatible pH, stable cream matrix and biological activity	Formulation translation

Mechanistic evidence chain for triterpene-associated soothing and redness modulation

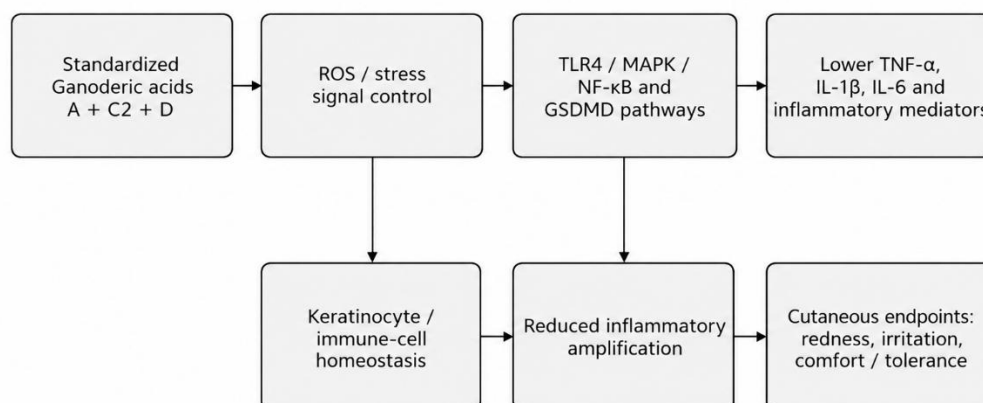


Figure 1. Mechanistic evidence chain connecting a standardized ganoderic-acid profile with inflammatory-stress and redness endpoints. The figure integrates triterpene-specific, *Ganoderma* skin, and clinical endpoint literature [1-18].

4. Discussion

4.1 From chemical standardization to inflammatory mechanism

The triterpene content of *Ganoderma* preparations is highly sensitive to raw-material identity and processing. A defined ganoderic acid A/C2/D profile is therefore more informative for mechanism-oriented work than an undifferentiated “*Ganoderma* extract” label. The present process also limits polysaccharides to 5% or less, reducing one major compositional source of variability when the primary hypothesis concerns triterpenes. This distinction matters because human *Ganoderma* skin data currently include polysaccharide-rich products, whereas the most direct anti-inflammatory evidence for ganoderic acids is mechanistic and preclinical [1-3,9-17].

4.2 NF-κB/MAPK, oxidative stress and pyroptosis as convergent nodes

NF-κB and MAPK signaling integrate oxidative and inflammatory inputs and regulate cytokines, iNOS and COX-2. The repeated observation that *Ganoderma* triterpenes modulate these pathways across models [1,9-11,13] provides a coherent mechanistic axis. The GSDMD findings in cutaneous inflammation add a second layer: controlling inflammatory cell-death signaling may reduce cytokine amplification and visible erythema [2]. These pathways are biologically compatible with a non-therapeutic topical soothing hypothesis focused on cosmetic redness, comfort and skin tolerability.

4.3 Why human erythema studies remain important

Erythema is measurable but context-dependent. UV challenge, heat-patch provocation, sensitive-skin models and rosacea studies differ in vascular and inflammatory drivers. The human *Ganoderma* polysaccharide study shows that *Ganoderma*-derived materials can affect erythema in skin [3], while controlled studies of other botanical anti-inflammatory preparations demonstrate robust methods for vehicle comparison and objective erythema quantification [4-8]. For the present triterpene-rich cream, these studies support a future protocol using standardized provocation, instrumental erythema measurement, symptom scoring and barrier co-endpoints.

4.4 Role of the cream matrix

The active material is introduced through a triglyceride/lecithin premix and then dispersed into a squalane-containing emulsion. This design supports triterpene distribution and minimizes visible crystallization. The final formula also includes humectants and emollients that can improve comfort independently of anti-inflammatory signaling; future vehicle-controlled studies should therefore preserve the same base cream on both sides or arms so that the incremental contribution of the standardized triterpene fraction can be resolved.

5. Study Considerations and Future Directions

The present study was designed to define the chemical and formulation platform first, then connect it to the strongest available mechanistic and human-context evidence. Building on this

foundation, a double-blind vehicle-controlled study can evaluate the TIMEFLYS triterpene cream in healthy volunteers using a mild UV- or heat-erythema challenge, with erythema index/a* value, subjective stinging, hydration and TEWL followed over 24-72 hours. A longer sensitive-skin cohort could then examine basal redness, comfort and reactivity over 4-8 weeks. Such a sequence would extend the current evidence chain from standardized chemistry to controlled human cutaneous response.

6. Conclusion

A low-polysaccharide Ganoderma triterpene active material standardized to ganoderic acids A, C2 and D was formulated into a stress-stable cream. Ganoderma triterpene literature consistently converges on oxidative-stress, NF- κ B/MAPK and inflammatory-mediator control, while topical ganoderic acid A has shown reductions in erythema-associated inflammatory phenotypes in a cutaneous model. Human Ganoderma and randomized botanical studies provide a clinically meaningful framework for redness measurement and tolerability. Together, the chemistry, formulation and evidence base establish a clear pathway for direct evaluation of soothing, redness and inflammatory-stress outcomes in human skin.

References

- [1] Guedes Pozzobon R, Rutckeviski R, Siqueira de Lima L, Oliveira CS, Ribeiro Smiderle F. Anti-Inflammatory Potential of Ganoderma lucidum Triterpenes: A Systematic Review and Meta-Analysis of Preclinical Evidence. *Pharmaceuticals* (Basel). 2026;19(1):188. doi:10.3390/ph19010188. PMID:41599785.
- [2] Xiao C, Chen J, Zhou X, Liu H. Ganoderic acid A alleviate psoriasis by inhibiting GSDMD-mediated pyroptosis. *Tissue Cell*. 2025;97:103078. doi:10.1016/j.tice.2025.103078. PMID:40818170.
- [3] Huang CF, Chang JF, Yang HS, Hsu CP, Lin CC. In Vitro and In Vivo Evaluation of the Skincare Bioactivity of β -1,3;1,6-Glucans-Rich Ganoderma lucidum Polysaccharides. *Molecules*. 2026;31(10):1740. doi:10.3390/molecules31101740. PMID:42197294.
- [4] Draelos ZD. Efficacy, Tolerance, and Safety of a Novel Botanical Anti-Inflammatory Moisturizer in Rosacea: Results From a Double-Blinded, Randomized Controlled Trial. *J Cosmet Dermatol*. 2026;25(5):e70910. doi:10.1111/jocd.70910. PMID:42163060.
- [5] Seiwerth J, Tasiopoulou G, Hoffmann J, et al. Anti-Inflammatory Effect of a Novel Topical Herbal Composition (VEL-091604) Consisting of Gentian Root, Licorice Root and Willow Bark Extract. *Planta Med*. 2019;85(7):608-614. doi:10.1055/a-0835-6806. PMID:30690691.
- [6] Reuter J, Jocher A, Hornstein S, Schulte Mönzing J, Schempp CM. Sage extract rich in phenolic diterpenes inhibits ultraviolet-induced erythema in vivo. *Planta Med*. 2007;73(11):1190-1191. doi:10.1055/s-2007-981583. PMID:17713873.
- [7] Reuter J, Jocher A, Stump J, Grossjohann B, Franke G, Schempp CM. Investigation of the anti-inflammatory potential of Aloe vera gel (97.5%) in the ultraviolet erythema test. *Skin Pharmacol Physiol*. 2008;21(2):106-110. doi:10.1159/000114871. PMID:18253066.
- [8] Hoffmann J, Wölfe U, Schempp CM, Casetti F. Tannins from *Potentilla officinalis* display antiinflammatory effects in the UV erythema test and on atopic skin. *J Dtsch Dermatol Ges*. 2016;14(9):917-922. doi:10.1111/ddg.12792. PMID:27607036.
- [9] Zheng S, Ma J, Zhao X, Yu X, Ma Y. Ganoderic Acid A Attenuates IL-1 β -Induced Inflammation in Human Nucleus Pulposus Cells Through Inhibiting the NF- κ B Pathway. *Inflammation*. 2022;45(2):851-862. doi:10.1007/s10753-021-01590-0. PMID:34739636.
- [10] Wu YL, Han F, Luan SS, Ai R, Zhang P, Li H, Chen LX. Triterpenoids from Ganoderma lucidum and Their Potential Anti-inflammatory Effects. *J Agric Food Chem*. 2019;67(18):5147-5158. doi:10.1021/acs.jafc.9b01195. PMID:30995041.
- [11] Xu J, et al. Anti-inflammatory effects of Ganoderma lucidum sterols via attenuation of the p38 MAPK and NF- κ B pathways in LPS-induced RAW 264.7 macrophages. *Food Chem Toxicol*. 2021;150:112073. doi:10.1016/j.fct.2021.112073. PMID:33631283.
- [12] Abate M, Pepe G, Randino R, et al. Ganoderma lucidum Ethanol Extracts Enhance Re-Epithelialization and Prevent Keratinocytes from Free-Radical Injury. *Pharmaceuticals* (Basel). 2020;13(9):224. doi:10.3390/ph13090224. PMID:32872510.

- [13] Sui Q, Zhu C, Shi S, et al. Ganoderic acid A: an in-depth review of pharmacological effects and molecular docking analysis. *J Ethnopharmacol.* 2025;349:119868. doi:10.1016/j.jep.2025.119868. PMID:40316150.
- [14] Taofiq O, Heleno SA, Calhelha RC, et al. The potential of *Ganoderma lucidum* extracts as bioactive ingredients in topical formulations, beyond its nutritional benefits. *Food Chem Toxicol.* 2017;108(Pt A):139-147. doi:10.1016/j.fct.2017.07.051. PMID:28760544.
- [15] Yin Z, Yang B, Ren H. Preventive and Therapeutic Effect of *Ganoderma* (Lingzhi) on Skin Diseases and Care. *Adv Exp Med Biol.* 2019;1182:311-321. doi:10.1007/978-981-32-9421-9_14. PMID:31777026.
- [16] Zhao H, Wu K, Zhang S, Cheng H, Kong F, Liu Y. Multidimensional Research Progress of *Ganoderma Lucidum* Active Components in Regulating Skin Homeostasis. *Mini Rev Med Chem.* 2026. doi:10.2174/0113895575459119260729112156. PMID:42634533.
- [17] Ahmad R, Riaz M, Khan A, et al. *Ganoderma lucidum* (Reishi) an edible mushroom; a comprehensive and critical review of its nutritional, cosmeceutical, mycochemical, pharmacological, clinical, and toxicological properties. *Phytother Res.* 2021;35(11):6030-6062. doi:10.1002/ptr.7215. PMID:34411377.
- [18] Dikmen Kucuk S, Jabet P, Groso A, Collet G, Daniellou R, Karadeniz B. Cosmetic potential of *Ganoderma lucidum* (Reishi) extract in a topical cream formulation. *Int J Cosmet Sci.* 2026;48(4):828-840. doi:10.1111/ics.70079. PMID:41657122.