Other

UDC 665.58

Plonsak Rusana

Master Barber at The Gentry Barbershop,

Expert in Cosmetic ingredients

(Houston, TX)

ORCID: 0009-0006-9003-8898

THE RELATIONSHIP BETWEEN THE CHEMICAL COMPOSITION OF COSMETIC PRODUCTS AND THEIR BIOLOGICAL EFFECTS: A SCIENTIFIC APPROACH TO EFFICACY ASSESSMENT

Summary. *The article examines how the chemical composition of cosmetic formulations determines their biological activity at the skin level - from barrier restoration to sensitization risk. Hyaluronic acid, ceramides, surfactants, glycols, preservatives and emulsifiers are analyzed in terms of their mechanisms of action, formulation interactions and documented clinical effects.*

Key words: *cosmetic formulation, skin barrier, hyaluronic acid, ceramides, surfactants, preservatives, glycols, emulsification, contact allergy, acne cosmetica.*

A cosmetic product is a chemistry experiment applied to a biological surface daily, often for years, by someone who has no particular reason to think about what is in it. The ingredient list is there - required by law, standardized by INCI nomenclature - but the gap between knowing that a product contains propylene glycol and knowing what propylene glycol actually does to the stratum corneum at a given concentration, in the presence of the emulsifiers and surfactants sharing the formulation, is not something that INCI disclosure closes. What closes it is the science of how chemical composition translates to biological

effect - and that translation is neither straightforward nor well communicated to the people whose skin it concerns.

Hyaluronic acid has become one of the most recognizable active ingredients in modern skincare, which makes it a useful starting point precisely because its popularity has outrun accurate understanding of its mechanism. Al-Halaseh et al. (2022) reviewed the cosmetic use of hyaluronic acid and documented the molecular weight dependency that most product marketing does not mention: high molecular weight hyaluronic acid (above 500 kDa) forms a film on the skin surface that reduces transepidermal water loss and creates a temporary plumping effect through surface hydration, while low molecular weight fragments (below 50 kDa) penetrate deeper into the epidermis and interact with CD44 receptors to stimulate collagen synthesis and modulate inflammatory responses [1, p. 35]. Same molecule, different molecular weight, different depth of action, different biological outcome. A formulation that declares hyaluronic acid without specifying the molecular weight distribution is declaring something real and leaving out the part that determines what it actually does.

Ceramide products are sold on the basis that ceramides restore the skin barrier. Čuříková-Kindlová et al. (2021) tested this in vitro and found that the restoration effect depends on the ratio of ceramides to free fatty acids to cholesterol - the three lipid classes that make up the lamellar bodies of the stratum corneum - not on the presence of ceramides alone [2, p. 3]. The lamellar body is not a ceramide structure; it is a three-component structure, and substituting one component without the other two does not rebuild it. A product with ceramides and insufficient cholesterol produces a different barrier outcome than one formulated to replicate the natural lipid ratio. Both products list ceramides on the label. The label does not list the ratio, the cholesterol concentration, or the fatty acid chain length - the variables that actually determine whether the barrier recovers. The consumer reading the ingredient list has no way to distinguish between them.

Ceramide penetration is itself formulation-dependent. The ceramides in the stratum corneum are highly hydrophobic and require a delivery vehicle that can bring them into contact with the lipid matrix they are meant to supplement. The emulsion type - oil-in-water versus water-in-oil - affects both the skin feel and the penetration depth of lipophilic actives, and the interfacial properties of the emulsion system determine its physical stability and its behavior on contact with skin. Ravera et al. (2021) tracked what happens to emulsion droplets at the interface between the formulation and the skin surface - where the emulsifier film either holds the droplet intact long enough for penetration to occur, or breaks, releasing the dispersed phase onto the surface in a form that does not reach the stratum corneum [5, p. 4]. For a ceramide in an oil-in-water emulsion, this matters directly: if the emulsifier system cannot maintain droplet integrity on contact with skin, the ceramide separates before it penetrates. The emulsifier is not packaging - it is the mechanism that determines whether the active ingredient does anything at all.

Healthy skin sits at a surface pH between 4.5 and 5.5. That range is not incidental. The serine proteases that process barrier lipids and the antimicrobial peptides that defend the skin surface both operate within it, and both lose activity as pH rises. An alkaline cleanser - anything above pH 7 - raises skin surface pH measurably, and that elevation persists for several hours after rinsing. During that window, barrier lipid processing slows and the skin is more susceptible to penetration of whatever comes next in the routine. This effect does not require the cleanser to be chemically irritating; pH alone produces it. Al-Halaseh et al. (2022) found that the uptake of low molecular weight hyaluronic acid fragments and their binding to skin surface receptors also varies with pH across the physiological range [1, p. 36]. A hyaluronic acid serum formulated at pH 6.5 behaves differently at the receptor level than the same concentration at pH 4.5 - and that difference is predictable from the chemistry, technically addressable in formulation, and routinely left unaddressed.

The sequential application of multiple products - the routine rather than the individual product - introduces a complexity layer that single-product efficacy and safety assessments do not address. A person who applies a vitamin C serum at pH 3.5, followed by a niacinamide moisturizer, followed by a sunscreen with an occlusive finish, has created a multi-product system whose combined pH, penetration enhancement, and ingredient interaction profile is not predictable from any individual product's assessment. Glycol-containing products earlier in the routine can act as penetration enhancers for actives applied subsequently; surfactant exposure from a morning cleanser can leave the barrier in a transiently disrupted state that modifies the penetration of everything applied in the next two to four hours. Ravera et al. (2021) analyzed emulsion stability under dynamic conditions and found that emulsion behavior on contact with a surface - including the skin - differs substantially from its behavior in a sealed container, with coalescence and phase separation possible on application depending on the formulation's interfacial film strength [5, p. 8]. A product that is stable in the bottle may not behave as a stable emulsion on skin, and the biological consequence depends on what separates and what the separated fractions do at the barrier surface. Routine-level interaction assessment is not standard practice in cosmetic safety evaluation - and the gap between what single-product testing captures and what routine use actually produces is where a significant portion of unexplained consumer reactions live.

Surfactants are the component of cosmetic formulations most likely to be experienced as a problem. Salomon and Giordano-Labadie (2022) reviewed the dermatological evidence on surfactant irritation and allergy and identified the critical distinction between irritant contact dermatitis - a dose-dependent, non-immunological response to surfactant-induced barrier disruption - and allergic contact dermatitis, which requires sensitization and involves an immunological reaction that is not dose-dependent in the same way [6, p. 678]. Both are real clinical problems, and both are predictable from the chemistry. Anionic

surfactants such as sodium lauryl sulfate disrupt the lipid matrix of the stratum corneum efficiently - which is why they are effective at removing sebum and make-up - and at sufficient concentration or frequency of exposure they disrupt it beyond what barrier recovery can manage. The irritation potential is concentration-dependent, frequency-dependent and modified by the other ingredients in the formulation, particularly humectants and skin-identical lipids that can partially offset the barrier disruption.

The acnegenicity of cosmetic ingredients is a specific subset of the biological effect question that matters enormously in practice and receives inadequate attention in ingredient safety assessments not designed for acne-prone skin. Ghani et al. (2021) investigated makeup ingredients and their relationship to acne cosmetica - comedone formation triggered by topical cosmetic use rather than endogenous hormonal factors - and found that comedogenicity ratings developed in animal models do not reliably predict clinical outcomes in human acne-prone skin [4, p. 476]. The mechanism of comedogenicity involves follicular occlusion and altered keratinization, and the relevant variables include not only the comedogenic potential of individual ingredients but the concentration at which they are present, the molecular size of the ingredient relative to the follicular opening, and the sebum production level of the individual skin. An ingredient rated comedogenic in a rabbit ear model at high concentration may not produce comedones in a human formulation at the concentration it is actually used. The inverse - that a low-rated ingredient can trigger acne cosmetica in a susceptible individual at formulation concentration - is equally documented.

Glycols occupy a structural position in cosmetic formulations that makes their biological effects particularly context-dependent. Yu and Goh (2024) reviewed glycols as solvents for dermal formulations and documented the range of functions they perform: solubilizing poorly water-soluble actives, acting as humectants that draw water from the dermis into the epidermis, functioning as penetration enhancers that transiently disrupt the lipid organization of the stratum

corneum to increase the permeability of co-formulated actives, and serving as antimicrobial co-preservatives that reduce the required concentration of the primary preservative system [7, p. 3]. The penetration enhancement function is the one most consequential for safety assessment. A glycol that increases the permeability of the stratum corneum to co-formulated actives increases it non-selectively - it also increases the skin's exposure to any irritant or sensitizing ingredient present in the same formulation. Propylene glycol, butylene glycol and pentylene glycol each have different penetration enhancement profiles, different humectancy, and different rates of contact sensitization, and selecting among them is a formulation decision with direct consequences for the biological activity of everything else in the product.

Preservatives are where the chemistry-to-biology translation has produced the most extensively documented population-level consequences. Dréno et al. (2019) conducted a safety review of phenoxyethanol - one of the most widely used preservatives following the regulatory restriction of parabens - and examined its toxicological profile across use conditions [3, p. 16]. Phenoxyethanol is effective as a broad-spectrum preservative at concentrations up to 1% in leave-on and rinse-off products; it penetrates the stratum corneum, it is absorbed systemically to a small degree, and its sensitization rate in the general population is low by historical standards. The review found the available evidence consistent with safe use at established concentrations - while also noting that the evidence base for some use conditions, particularly products applied to broken or compromised skin and products used in infants, is thinner than for standard adult leave-on application. That qualification matters clinically because phenoxyethanol is present in many products marketed for sensitive or eczematous skin - the population most likely to have compromised barrier function and most likely to experience enhanced penetration of everything the formulation contains.

The broader preservative picture is one of sequential substitution without full resolution of the underlying problem. When formaldehyde-releasing

preservatives fell out of favor due to sensitization data, isothiazolinones expanded to fill the gap. When isothiazolinone sensitization rates climbed in the following decade - particularly for methylchloroisothiazolinone and methylisothiazolinone - phenoxyethanol, benzyl alcohol and the organic acid preservative systems expanded. Each substitution addressed a documented problem with the previous preservative and introduced a new set of unknowns about sensitization in populations not yet extensively exposed to the replacement. The lesson of this pattern is not that cosmetic preservation is unsolvable but that preservative safety is a population-level, time-dependent problem that ingredient-level assessment at point of approval does not fully capture. A preservative can pass all pre-market safety evaluations and still produce meaningful sensitization rates once it reaches the scale of exposure that mass-market cosmetic use represents.

The interaction between these ingredient categories - active, emulsifier, surfactant, glycol, preservative - is where formulation chemistry becomes most consequential and most difficult to predict from ingredient-level data alone. A ceramide formulation that includes a glycol penetration enhancer will deliver the ceramide more effectively to the stratum corneum; it will also deliver the preservative system more effectively, increasing the skin's exposure to the preservative per application relative to a formulation without the penetration enhancer. A surfactant-based cleanser that compromises the barrier increases the penetration of everything applied afterward - including the toner, serum and moisturizer in the consumer's routine - regardless of whether those subsequent products are considered safe in isolation. The biological effect of a cosmetic product cannot be extracted from the biological effect of the formulation as a whole, applied in sequence with other products, on a skin barrier that varies in integrity across individuals and across time.

The regulatory framework governing cosmetic ingredient safety was built around individual ingredients assessed in isolation, and it has not yet systematically incorporated what formulation science has established about

interaction effects, delivery vehicle dependency and barrier-modifying co-ingredients. Čuříková-Kindlová et al. (2021) used reconstructed skin models to study barrier recovery under controlled conditions - demonstrating that the recovery trajectory depends on the specific lipid ratio in the test formulation, not simply on the presence of ceramides as an ingredient class [2, p. 7]. This kind of in vitro formulation-level testing is technically available and scientifically validated. Its adoption as a standard component of cosmetic efficacy substantiation - rather than as a research tool used selectively by manufacturers with the resources and interest to apply it - requires regulatory expectations to shift. The science has moved faster than the standards that shape what manufacturers are required to demonstrate before making efficacy claims or placing products in the market. That gap is not theoretical; it is the distance between a ceramide product that restores the barrier and one that says it does.

The scientific approach to efficacy and safety assessment that this situation calls for is one that treats the formulation as the unit of analysis rather than the individual ingredient. Efficacy claims attached to a single listed active - hyaluronic acid, ceramides, vitamin C - are meaningful only in the context of the delivery vehicle that determines whether that active reaches the intended depth, at the intended concentration, with the intended residence time. Safety assessment that evaluates each ingredient against its own threshold, without modeling the combined exposure and barrier-modifying effects of the full ingredient mixture, misses interactions that are mechanistically predictable and clinically documented. The tools to do better exist - computational interaction modeling, in vitro barrier models, ex vivo skin testing - and their systematic application to finished formulations rather than isolated ingredients is the gap between where cosmetic science currently is and where accurate efficacy and safety prediction requires it to be.

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