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Review Article

Advanced Smart Hydrogels for Targeted Cosmeceutical Delivery: Mechanisms, Polymer Choices, and Future Trends

Rani K. Kuriakose[1*], Amal Krishna P.[2], Dhiya Mirza C. Gafoor[3], Fathima Nezrin M. A.[4], Nandhu Krishnan G.[5], Nidha Afsal[6]

[1] Associate Professor, Department of Pharmaceutics, Chemists College of Pharmaceutical Sciences and Reseach, Ernakulam, Affliated to Kerala University of Health Sciences.
[2,3,4,5,6] Students, Chemists College of Pharmaceutical Sciences and Reseach, Ernakulam, Affliated to Kerala University of Health Sciences.

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ABSTRACT

Cosmeceuticals occupy the interface between cosmetic and pharmaceutical science, and their efficacy depends heavily on the delivery system used to bring active ingredients to, and retain them within, the target layers of the skin. Conventional semisolid vehicles such as creams, lotions, and simple hydrogels release their cargo passively and cannot adapt to the biochemical heterogeneity of the skin surface. Stimulus-responsive ("smart") hydrogels address this limitation by altering their swelling, network structure, or degradation behaviour in response to environmental cues such as pH, temperature, reactive oxygen species (ROS), or enzymatic activity, thereby enabling site- and time-controlled release. This narrative review synthesises and critically compares evidence on pH-responsive, temperature-responsive, ROS-responsive, enzyme-responsive, and multi-responsive hydrogel systems, together with the natural, synthetic, and semi-synthetic polymers used to construct them. Particular attention is given to distinguishing findings generated in dedicated cosmeceutical or topical-delivery models from mechanistic evidence obtained in wound-healing or systemic drug-delivery contexts, since the latter cannot be assumed to translate directly to intact, non-injured skin. Factors governing hydrogel performance, common characterisation techniques, and translational barriers, including limited clinical evidence and scale-up difficulty, are discussed.

***Corresponding Author:** Rani K. Kuriakose
Address: Associate Professor, Department of Pharmaceutics, Chemists College of Pharmaceutical Sciences and Reseach, Ernakulam, Affliated to Kerala University of Health Sciences
Email ✉: nidhafsal@gmail.com

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The review concludes that while pH- and temperature-responsive systems built on chitosan, alginate, gelatin, cellulose derivatives, poly (N-isopropylacrylamide), poly (acrylic acid)-type polymers, and Pluronic/poloxamer systems are comparatively well supported, ROS-, enzyme-, and light-responsive strategies remain comparatively underexplored for cosmeceutical use, and rigorous, skin-specific evidence is still needed before these platforms can be considered translationally mature.

INTRODUCTION

Cosmeceuticals are topically applied formulations that combine cosmetic and pharmaceutical characteristics, delivering biologically active ingredients intended to improve the appearance, barrier function, or health of the skin rather than to treat disease in the regulatory sense. Their pharmaceutical relevance lies in the fact that the clinical or aesthetic benefit of an active ingredient, whether an antioxidant, a botanical polyphenol, or an anti-inflammatory agent, is only realised if the ingredient reaches and is retained within the appropriate skin compartment at an effective concentration. This requirement places cosmeceutical formulation squarely within the scope of pharmaceutical sciences, since it depends on the same principles of drug delivery, release kinetics, and skin permeation that govern topical pharmaceutical products.

The stratum corneum, the outermost and most lipophilic layer of the epidermis, is the principal barrier that conventional topical vehicles must overcome. Creams, lotions, and simple hydrogels typically release their active ingredients through passive diffusion that begins immediately upon application and is governed largely by the concentration gradient between the vehicle and the skin surface. This passive, non-selective behaviour has several practical consequences: a large fraction of the applied dose may be released before the vehicle has spread evenly, active ingredients that are sensitive to environmental conditions may degrade prematurely, and there is no mechanism by which release can be concentrated at a specific depth, site, or time. These limitations are compounded when the active ingredient is poorly water-soluble, chemically unstable, or intended to act specifically within a compromised or altered skin microenvironment.

Hydrogels, three-dimensional networks of hydrophilic polymer chains capable of retaining large quantities of water while preserving their structural integrity, have long been used as topical delivery vehicles because their high water content favours skin hydration, patient comfort, and ease of spreading[1]. In their conventional form, however, hydrogels swell and release their cargo in essentially the same passive manner as other semisolid vehicles. Smart, or stimuli-responsive, hydrogels differ in that their polymer networks contain functional groups or crosslinks that undergo a measurable physicochemical change, such as ionisation, a coil-to-globule transition, or bond cleavage, when exposed to a specific internal or external stimulus[2,3]. This responsiveness allows the hydrogel to remain comparatively quiescent under normal conditions and to swell, deswell, or degrade preferentially when it encounters the stimulus associated with a particular anatomical site or pathophysiological state, in principle offering a route to more targeted and controlled cosmeceutical delivery[4,5].

The advantage of smart hydrogels for cosmeceutical use is therefore conceptual as well as empirical: because skin pH, surface temperature, and oxidative status can differ between intact and compromised, aged, or inflamed skin, a hydrogel that is responsive to one or more of these parameters could in principle be designed to deliver more of its payload where it is most needed, while limiting premature release elsewhere. Polymer selection is central to realising this potential, since the choice of natural, synthetic, or semi-synthetic backbone determines not only the nature and magnitude of the stimulus response but also the biocompatibility, mechanical behaviour, and manufacturability of the final formulation[2].

Despite this conceptual appeal, a critical reading of the available literature reveals an important knowledge gap: the great majority of stimulus-responsive hydrogels described to date have been developed and validated in wound-healing, tumour-targeting, or general drug-delivery models rather than in dedicated cosmeceutical or intact-skin contexts[6,7]. Findings generated in injured or diseased tissue, where barrier function, pH, and inflammatory status differ substantially from healthy skin, cannot be assumed to transfer directly to

cosmeceutical applications, and this distinction is maintained throughout the present review.

This review therefore aims to synthesise and critically compare the mechanisms, polymer choices, and delivery outcomes reported for stimulus-responsive hydrogels with direct or indirect relevance to cosmeceutical delivery. The scope covers pH-, temperature-, reactive oxygen species (ROS)-, enzyme-, and multi-responsive systems; natural, synthetic, and semi-synthetic polymer classes; skin penetration, retention, and characterisation approaches; and the principal translational challenges that currently limit clinical and commercial adoption. Where the supporting evidence originates from wound-healing or non-dermal models, this is explicitly identified rather than presented as direct cosmeceutical evidence.

2. SMART HYDROGELS FOR COSMECEUTICAL DELIVERY

2.1 Conventional hydrogels versus smart hydrogels

Conventional hydrogels are typically formed by simple physical or chemical crosslinking of a hydrophilic polymer and swell to an equilibrium water content that is determined mainly by crosslink density and polymer-solvent affinity. Their drug release is governed by diffusion and, once applied, proceeds independently of the local skin environment[1]. Smart hydrogels, by contrast, incorporate ionisable, thermoresponsive, or cleavable functional groups within the polymer backbone or crosslinks, so that their degree of swelling, pore size, or structural integrity changes in response to a defined stimulus[2,8]. This distinction has direct consequences for topical applicability: a pH-responsive hydrogel built on ionisable carboxylic or amine groups, for example, can be formulated to remain relatively compact at the mildly acidic pH of healthy skin and to swell preferentially when exposed to the more neutral-to-alkaline pH associated with disrupted barrier function, whereas a conventional hydrogel of the same polymer would swell to a similar extent regardless of surface pH[7,9].

A further distinguishing feature is targeting capability. Because conventional hydrogels release their cargo as soon as diffusion pathways open, they cannot discriminate between healthy and compromised skin regions or between the intended site of action and the surrounding tissue. Stimulus-responsive systems, in contrast, are designed so that a measurable release event, such as pronounced swelling or bond cleavage, occurs preferentially under the conditions associated with the target site, which is the conceptual basis for describing them as “targeted” delivery systems[3,10]. It should be noted, however, that most of the targeting evidence available to date derives from wound or tumour models in which the stimulus (acidic wound exudate, oxidative tumour microenvironment) is considerably more pronounced than the comparatively subtle pH or thermal differences that would be encountered across intact cosmeceutical-relevant skin[9,11].

2.2 Advantages of smart hydrogels

Where direct comparisons have been made, smart hydrogels have been reported to offer several practical advantages over conventional vehicles. Stimulus-triggered swelling or degradation allows the release rate to be concentrated around the period or location in which the trigger is present, which has been associated with more controlled and, in several models, more prolonged release profiles than passive diffusion alone[8,9,12]. Encapsulation of an active ingredient within a responsive network can also improve its apparent stability and, where poor aqueous solubility is a limiting factor, its effective solubility: for example, complexation of the antioxidant resveratrol with hydroxypropyl-beta-cyclodextrin prior to incorporation into a thermoresponsive Pluronic F-127 hydrogel markedly improved its aqueous compatibility and enabled its formulation for topical use[13]. Similarly, incorporation of natural essential oils as permeation enhancers within a carboxymethyl cellulose hydrogel improved the in vitro release as well as the ex vivo skin permeation and retention of curcumin relative to the hydrogel without enhancers, illustrating that formulation strategy, and not stimulus-responsiveness alone, can materially affect skin delivery outcomes[14]. Reduced premature release before the hydrogel reaches, or is triggered at, the intended site has been demonstrated most convincingly in pH-responsive systems, where swelling and drug release increase sharply once an ionisation threshold is crossed[7-9]. These advantages, however, have almost always been demonstrated using wound-healing or non-dermal drug-delivery endpoints rather than

cosmeceutical efficacy endpoints, and this evidentiary gap is a recurring theme throughout the remainder of this review.

3. MECHANISMS OF STIMULI-RESPONSIVE HYDROGELS

3.1 pH-responsive hydrogels

pH-responsive hydrogels are constructed from polymers bearing ionisable functional groups, typically weak acidic groups such as carboxylic acids or weak basic groups such as primary amines. As the surrounding pH moves away from the polymer's pKa, these groups undergo protonation or deprotonation, generating fixed charges along the polymer backbone. The resulting electrostatic repulsion between like charges increases chain-chain distance and osmotic pressure within the network, producing pronounced swelling; conversely, when the groups are neutralised, the network can collapse or deswell[8-10]. This swelling-deswelling behaviour directly modulates mesh size and therefore the diffusion pathway available to an encapsulated active ingredient, so that drug release becomes strongly pH-dependent rather than constant over time.

The clearest experimental demonstration of this mechanism among the reviewed literature comes from a chitosan hydrogel loaded with acid-susceptible polymeric nanoparticles, in which the anionic-cationic interactions of the network produced pH-dependent swelling and release suited to the acidic microenvironment of the target tissue, with encapsulation and loading efficiencies of 48% and 72%, respectively, confirmed by FTIR, electron microscopy, and zeta-potential analysis[9]. A related dual crosslinked hydrogel actuator, built from oppositely charged gelatin and carboxymethyl cellulose polyelectrolytes, was explicitly designed for bi-directional pH-responsive release, swelling and releasing its cargo differently in acidic versus alkaline media[10]. A composite hydrogel of arabinoxylan, carrageenan, and reduced graphene oxide, crosslinked with tetraethyl orthosilicate, likewise displayed pH-dependent swelling and degradation behaviour when assessed in phosphate-buffered saline[7]. A recent pharmaceutical-focused review further catalogues dual pH- and thermo-responsive systems based on poly (acrylic acid), reinforcing that carboxylic-acid-bearing synthetic polymers are among the most extensively validated chemistries for pH responsiveness[8]. Although these studies were performed in wound-healing or general drug-delivery contexts rather than intact-skin cosmeceutical models, the underlying protonation-deprotonation mechanism is directly transferable in principle to formulations designed around the pH differences between healthy skin (mildly acidic) and compromised, aged, or inflamed skin, where surface pH tends to shift toward neutral[7].

3.2 Temperature-responsive hydrogels

Thermoresponsive hydrogels are built from polymers that undergo a coil-to-globule or sol-gel transition at a characteristic temperature. Polymers exhibiting a lower critical solution temperature (LCST), such as poly (N-isopropylacrylamide) (PNIPAM) and Pluronic/poloxamer block copolymers, are soluble or swollen below this temperature and collapse or gel above it, whereas upper critical solution temperature (UCST) polymers behave in the opposite direction[12,15]. Because normal skin surface temperature (approximately 32-34 degrees C) is close to, but distinct from, core body temperature and from temperatures associated with local inflammation, thermoresponsive systems can in principle be tuned so that gelation, swelling, or drug release is triggered specifically on contact with skin or with a locally warmer, inflamed area[12,15].

Several of the reviewed studies demonstrate this behaviour directly. A modified natural temperature-sensitive polymer crosslinked with polyacrylic acid networks was formulated so that the hydrogel dressing actively shrinks in response to body temperature, and this thermally triggered mechanical contraction was associated with reduced scar area in a rat wound model[16]. A related adhesive, temperature-sensitive, mechanically active hydrogel similarly contracted upon reaching body temperature and promoted wound contraction through mechanosensitive signalling pathways[11]. A thermosensitive hydrogel combining sodium alginate, silk gland protein, and PNIPAM produced a self-adjusting microenvironment with intelligent, temperature-triggered drug release in a diabetic wound model[17]. Pluronic F-127, an amphiphilic triblock copolymer with a well-characterised sol-gel transition near body temperature,

has been used as the thermoresponsive matrix for a natural flavonoid, pectolinarin, in a wound-healing application, and, separately, for resveratrol complexed with hydroxypropyl-beta-cyclodextrin, indicating that this polymer system is comparatively mature and versatile for topical formulation even though the underlying studies were not conducted in cosmeceutical models[13,18]. A dedicated review of thermosensitive hydrogels further confirms that phase-transition behaviour near body temperature is the shared design principle across these systems, regardless of the specific therapeutic context[12].

3.3 ROS-responsive hydrogels

Reactive oxygen species (ROS) accumulate under conditions of oxidative stress, which is implicated in both photoageing and chronic inflammatory skin conditions. ROS-responsive hydrogels typically incorporate ROS-cleavable chemical linkages, such as thioketal or boronic ester bonds, that are stable under normal conditions but degrade in the presence of elevated ROS, triggering payload release. Among the supplied reference set, direct experimental characterisation of ROS-responsive hydrogel chemistry is limited: the most relevant source is a review of stimuli-responsive drug delivery systems for inflammatory skin conditions, which identifies ROS, alongside pH and temperature, as an internally generated trigger that has been exploited in dermatological drug delivery, but which does not itself report new ROS-cleavable hydrogel synthesis data[19]. Given this limited direct evidence base within the reviewed literature, the antioxidant relevance of ROS-responsive systems to cosmeceutical delivery, for example, as a mechanism for concentrating antioxidant release specifically at sites of oxidative stress, should currently be regarded as a plausible design rationale and an area for further targeted research rather than an established, well-validated delivery strategy for skin-care actives.

3.4 Enzyme-responsive hydrogels

Enzyme-responsive hydrogels rely on peptide, ester, or glycosidic linkages that are selectively cleaved by enzymes upregulated in a target microenvironment, such as matrix metalloproteinases or hyaluronidase in inflamed or remodelling tissue. This mechanism is attractive in principle for cosmeceutical delivery because enzymatic activity in the skin's microenvironment can differ between healthy and compromised regions. However, none of the reference articles supplied for this review report a dedicated enzyme-cleavable hydrogel system characterised for skin or cosmeceutical delivery; the concept is acknowledged only indirectly, within broader discussions of internally triggered, pathology-specific release mechanisms[19]. Enzyme responsiveness is therefore presented here as a recognised mechanistic category and a research gap rather than as a strategy supported by direct experimental evidence in the reviewed cosmeceutical or dermatological literature.

3.5 Light-responsive hydrogels

Light-responsive hydrogels, which typically incorporate photocleavable or photoisomerisable moieties to allow externally controlled, non-invasive triggering of release, are conceptually relevant to topical and cosmeceutical applications because skin is directly accessible to light. Within the reference set assembled for this review, however, no study provides adequate primary evidence of a light-responsive hydrogel system evaluated for cosmeceutical or dermatological delivery; light is mentioned only in passing, as one of several external stimuli exploited elsewhere in the broader stimuli-responsive drug delivery field[19]. In line with the evidentiary standard adopted for this review, light-responsive systems are therefore not discussed in further mechanistic detail here and are instead flagged as a topic requiring dedicated primary literature before firm conclusions can be drawn regarding their cosmeceutical relevance.

3.6 Multi-responsive hydrogels

Multi-responsive hydrogels combine two or more stimulus-sensitive chemistries within a single network, most commonly pH and temperature, in an attempt to achieve more precise spatial and temporal control over release than either stimulus could provide alone. Among the reviewed evidence, dual pH- and thermo-responsive hydrogels based on poly (acrylic acid) have been described in a recent pharmaceutical review as offering more selective release profiles by requiring both conditions to be satisfied before substantial

swelling occurs[8]. A comprehensive review of stimulus-responsive hydrogel-based wound dressings similarly reports systems responsive to combinations of pH, temperature, ROS concentration, and other cues, noting that such multi-stimuli designs are particularly advantageous when a single environmental parameter is not sufficiently discriminating on its own[20]. The trade-off, however, is formulation complexity: combining multiple responsive chemistries within one network increases the number of variables that must be controlled during synthesis and characterisation, can complicate reproducibility and batch-to-batch consistency, and may narrow the processing window available for pharmaceutical manufacture. Multi-responsive systems should therefore be regarded as offering greater theoretical precision at the cost of greater formulation and translational complexity, a trade-off that has not yet been resolved for cosmeceutical-specific applications in the available literature.

Table 1: Stimulus-Responsive Mechanisms of Smart Hydrogels

Stimulus	Mechanism	Hydrogel response	Delivery relevance
pH	Protonation/deprotonation of ionisable groups alters electrostatic repulsion and network charge	Swelling/deswelling; increased mesh size and release above/below pKa	Potential targeting of pH shifts associated with compromised or inflamed skin
Temperature	Coil-to-globule or sol-gel transition at LCST/UCST	Gelation, shrinkage, or collapse near body/skin temperature	Trigger tied to skin-contact or local inflammatory temperature
ROS	Cleavage of ROS-sensitive linkages (mechanism reported in broader literature, not directly characterised in reviewed sources)	Proposed degradation/release under oxidative conditions	Conceptually relevant to antioxidant cosmeceutical delivery; evidence gap identified
Enzyme	Enzymatic cleavage of peptide/ester linkages by target-associated enzymes (mechanism referenced only indirectly)	Proposed localized degradation and release	Conceptual mechanism; evidence gap identified
Multi-responsive (pH + temperature)	Combined ionisation and phase-transition behaviour requiring two conditions for full response	More selective, condition-dependent swelling/release	Greater theoretical precision; increased formulation complexity

4. POLYMER CHOICES AND THEIR INFLUENCE ON HYDROGEL PERFORMANCE

4.1 Natural polymers

Chitosan, a cationic polysaccharide derived from chitin, is one of the most frequently used natural polymers in the reviewed literature because its free amine groups confer pH-responsive behaviour, biocompatibility, and inherent antimicrobial activity. Chitosan hydrogels have been used as the matrix for pH-responsive nanoparticle-hydrogel hybrids for tumour tissue delivery[9] and, blended with polyvinyl alcohol, as a curcumin-loaded hydrogel with demonstrated antimicrobial and wound-healing activity in vitro and in silico[21]. Its principal limitations relate to batch-to-batch variability in molecular weight and degree of deacetylation, and to its relatively modest mechanical strength when used alone, which typically necessitates blending or crosslinking with a second polymer.

Alginate, an anionic polysaccharide derived from brown algae, forms hydrogels through ionic crosslinking with divalent cations and has been combined with silk gland protein and PNIPAM to create a thermosensitive, self-adjusting hydrogel for diabetic wound treatment[17]. Its swelling and gel strength are highly sensitive to the type and concentration of crosslinking cation, which offers formulation flexibility but also introduces variability that must be tightly controlled.

Gelatin, a denatured collagen derivative, contributes favourable biocompatibility and cell-interactive amino-acid motifs; when combined with carboxymethyl cellulose as oppositely charged polyelectrolytes, it has been used to construct a dual crosslinked, bi-directionally pH-responsive hydrogel actuator[10]. Silk gland protein has similarly been incorporated as a natural, biocompatible structural component within a thermosensitive alginate-based network[17]. Across these natural-polymer systems, biodegradability and biocompatibility are consistently reported as advantages, while batch variability, comparatively weak mechanical properties, and, for some polysaccharides, limited aqueous solubility at physiological pH are recurring limitations relevant to topical and cosmeceutical formulation.

4.2 Synthetic polymers

Poly (N-isopropylacrylamide) (PNIPAM) is the most extensively characterised thermoresponsive synthetic polymer in the reviewed literature, exhibiting a lower critical solution temperature close to physiological range and a sharp, reversible coil-to-globule transition that has been exploited in a diabetic wound dressing[17] and reviewed in detail as a platform for thermosensitive drug delivery[12,15]. Its responsiveness is highly tunable through copolymerisation, but PNIPAM homopolymers are non-biodegradable and their long-term biocompatibility on intact skin has not been extensively documented in the reviewed sources.

Poly (acrylic acid)-type polymers, including Carbopol-family polymers, are the principal synthetic backbone underlying the pH-responsive systems discussed in Section 3.1, and have also been used in combination with a natural temperature-sensitive polymer to create a dual-mechanism, temperature-shrinking wound dressing[16]. Their carboxylic acid groups provide strong, well-characterised pH sensitivity and good tunability of crosslinking density and mechanical properties, but formulations based on these polymers can be sensitive to ionic strength, which may affect consistency when applied across skin sites with differing surface chemistry.

Pluronic (poloxamer) block copolymers, composed of hydrophilic poly (ethylene oxide) and hydrophobic poly (propylene oxide) blocks, undergo a well-defined, reversible sol-gel transition near body temperature and have been used as the thermoresponsive matrix for both a flavonoid, pectolinarin, and an antioxidant, resveratrol, complexed with hydroxypropyl-beta-cyclodextrin[13,18]. Their principal advantages are ease of formulation, reproducible gelation behaviour, and compatibility with hydrophobic actives via micellisation; a recognised limitation is comparatively weak mechanical strength in the gel state, which can limit residence time on skin. Reduced graphene oxide has also been incorporated as a reinforcing, pH-responsive composite component in an arabinoxylan-carrageenan hydrogel, illustrating that synthetic or nanocomposite additives are sometimes used to modulate both mechanical and stimulus-responsive behaviour rather than acting as the primary responsive element[7].

4.3 Semi-synthetic polymers

Carboxymethyl cellulose (CMC), a semi-synthetic cellulose derivative, appears repeatedly across the reviewed formulations, both as the sole gelling agent in a curcumin hydrogel enhanced with natural essential oils and as one half of the oppositely charged polyelectrolyte pair in the dual crosslinked pH-responsive gelatin-CMC actuator[10,14]. CMC offers good aqueous solubility, favourable film-forming and gelling behaviour, and comparatively low cost, and its carboxylate groups can additionally confer a degree of pH responsiveness when incorporated into a charged network. A broader review of thermo-responsive biopolymers notes that other cellulose derivatives, alongside chitosan and gelatin, can display combined thermo- and pH-responsive behaviour, underscoring that semi-synthetic cellulose chemistries occupy an intermediate position between the tunability of fully synthetic polymers and the biological familiarity of natural polysaccharides[15,22].

4.4 Polymer selection criteria

No single polymer class is universally superior for smart cosmeceutical hydrogel design; selection instead depends on matching polymer properties to the intended stimulus, active ingredient, and application. The choice of stimulus dictates the required functional chemistry: pH responsiveness requires ionisable groups, most commonly supplied by chitosan, poly (acrylic acid)-type polymers, or carboxymethylated polysaccharides, while temperature responsiveness requires a polymer with an accessible LCST or UCST near the target temperature range, such as PNIPAM or Pluronic[15,18]. The physicochemical properties of the active ingredient, particularly its aqueous solubility and stability, influence whether a hydrophilic network alone is sufficient or whether a solubilising strategy, such as cyclodextrin complexation within a Pluronic matrix, is required[13]. Desired release profile, swelling capacity, and crosslinking density are interdependent: higher crosslinking density generally produces smaller mesh size, slower release, and greater mechanical stability, but can reduce the magnitude of the stimulus-triggered swelling response. Skin compatibility, biodegradability, formulation stability, and manufacturing feasibility must also be weighed together with cost and regulatory familiarity, since natural polymers are often perceived as more consumer-acceptable for cosmeceutical products but may offer less precise or less reproducible control over release kinetics than synthetic alternatives. The evidence reviewed here supports a pragmatic, application-specific approach to polymer selection rather than the identification of a single optimal material.

Table 2: Comparison of Polymer Classes Used in Smart Hydrogels

Polymer class	Representative polymers	Advantages	Limitations	Relevant application
Natural	Chitosan, alginate, gelatin, silk protein	Biocompatible; biodegradable; inherent pH sensitivity (chitosan); consumer-acceptable	Batch-to-batch variability; comparatively weak mechanical properties alone	pH-responsive tumour/wound hydrogels; thermosensitive alginate-silk-PNIPAM wound dressing
Synthetic	PNIPAM, poly(acrylic acid)/Carbopol-type, Pluronic/poloxamer	Sharp, tunable, reproducible stimulus response; well-characterised phase behaviour	PNIPAM non-biodegradable; Pluronic gels mechanically weak; some ionic-strength sensitivity	Thermosensitive wound dressings; pH/temperature dual-responsive systems
Semi-synthetic	Carboxymethyl cellulose and other cellulose derivatives	Good aqueous solubility and gelling behaviour; low cost; some pH sensitivity via carboxylate groups	Intermediate tunability vs. fully synthetic polymers; performance depends on degree of substitution	Curcumin topical hydrogel; gelatin-CMC pH-responsive actuator

5. TARGETED COSMECEUTICAL DELIVERY

Among cosmeceutical active categories represented, directly or by close analogy, in the reviewed literature, curcumin and other polyphenolic antioxidants are the most extensively studied. Curcumin's principal formulation challenge is its very low aqueous solubility and photochemical instability, which limits its incorporation into simple aqueous vehicles. In a direct topical-delivery study, a 2% w/w curcumin hydrogel formulated with carboxymethyl cellulose as the gelling agent and natural essential oils (eucalyptus, aloe vera, and clove oil) as permeation enhancers showed improved in vitro release and improved ex vivo permeation and retention of curcumin through skin compared with the hydrogel lacking these enhancers, with compatibility between drug and excipients confirmed by differential scanning calorimetry and FTIR[14]. This is one of the few studies among the reviewed sources that evaluated skin permeation and retention directly, and it constitutes genuine, if limited, topical-delivery evidence relevant to cosmeceutical formulation, notwithstanding that the target application was not framed explicitly as cosmetic. A separate curcumin-loaded chitosan-polyvinyl alcohol hydrogel demonstrated antimicrobial activity and, in silico, favourable binding to inflammatory-pathway proteins associated with wound healing; this finding should be read as wound-healing and antimicrobial evidence rather than as direct evidence of cosmeceutical antioxidant or anti-ageing efficacy, since no skin-permeation or cosmeceutical outcome was reported[21].

Resveratrol, a stilbene polyphenol valued in cosmeceutical formulation for its antioxidant and anti-inflammatory properties, was incorporated as a hydroxypropyl-beta-cyclodextrin complex into a thermoresponsive Pluronic F-127 hydrogel to overcome its low aqueous solubility; the resulting formulation showed improved solubility, confirmed complex formation by IR spectroscopy and X-ray diffraction, and demonstrated antimicrobial activity in a wound-treatment context[13]. As with curcumin-chitosan-PVA above, this evidence base is a wound-healing model rather than a cosmeceutical skin-permeation study, and the formulation strategy, cyclodextrin complexation within a thermoresponsive matrix, is presented here as a transferable solubility-enhancement approach rather than as direct proof of cosmeceutical performance.

Pectolinarin, a natural flavonoid, was delivered from a temperature-sensitive Pluronic F-127 hydrogel designed to promote scarless wound healing by enhancing endothelial cell migration, proliferation, and angiogenesis-related gene expression; again, this is wound-healing rather than cosmeceutical evidence, though the thermoresponsive Pluronic delivery strategy itself is directly transferable to cosmeceutical flavonoid or polyphenol formulation[18]. More broadly, pH-responsive natural-polymer hydrogels, including the chitosan nanoparticle-hydrogel hybrid and the arabinoxylan-carrageenan-reduced graphene oxide composite, were developed and validated for anticancer drug delivery to tumour tissue and for antibacterial skin wound healing, respectively, and provide mechanistic rather than direct cosmeceutical evidence for how pH-triggered swelling and release could, in principle, be applied to actives intended for compromised or inflamed skin[7,9].

Taken together, the reviewed evidence indicates that genuine cosmeceutical skin-permeation and retention data are available for only a small subset of the active ingredients and hydrogel systems discussed in this review, most clearly for curcumin delivered from a conventional, enhancer-modified cellulose hydrogel[14]. For most other actives and stimulus-responsive systems considered here, the supporting evidence originates from wound-healing, antimicrobial, or tumour-targeting models, and its extrapolation to intact-skin cosmeceutical use should be regarded as a reasonable working hypothesis rather than an established finding, pending dedicated skin-permeation and cosmeceutical-outcome studies.

Table 3: Representative Smart Hydrogels for Topical/Cosmeceutical Delivery

Active ingredient	Polymer/system	Stimulus	Application
Curcumin	Carboxymethyl cellulose + natural essential oils	None (enhancer-modified conventional hydrogel)	Topical delivery

Active ingredient	Polymer/system	Stimulus	Application
Curcumin	Chitosan/PVA	None reported	Wound healing (antimicrobial)
Resveratrol (as HP-beta-CD complex)	Pluronic F-127	Temperature	Wound treatment
Pectolinarin (flavonoid)	Pluronic F-127	Temperature	Scarless wound healing
Acid-susceptible model drug/nanoparticles	Chitosan hydrogel-nanoparticle hybrid	pH	Anticancer (tumour tissue)
Model actives (general)	Arabinoxylan/carrageenan/reduced graphene oxide	pH	Antibacterial skin wound healing
Model actives (general)	Gelatin/carboxymethyl cellulose (dual crosslinked)	pH (bi-directional)	General controlled release

6. FACTORS AFFECTING SMART HYDROGEL PERFORMANCE

Several interacting formulation and physiological variables determine the practical performance of a smart cosmeceutical hydrogel. Polymer concentration and crosslinking density jointly set the initial mesh size of the network: higher concentrations and denser crosslinking generally reduce swelling capacity and slow diffusion-controlled release, but also increase mechanical stability and resistance to premature erosion, as reflected in the swelling and degradation behaviour reported for the arabinoxylan-carrageenan-rGO system and the dual crosslinked gelatin-CMC actuator[7,10]. Swelling ratio and porosity are themselves the direct determinants of the diffusion pathway available to an encapsulated active, and both are altered dynamically once a responsive hydrogel is exposed to its trigger, whether ionisation-driven, as in pH-responsive systems or phase-transition-driven, as in thermoresponsive systems[15,18]. Drug-polymer interactions, for example, hydrogen bonding or electrostatic association between an ionisable active and a charged network, can further modulate release beyond what network mesh size alone would predict, and have been used deliberately in cyclodextrin-complexed formulations to improve both solubility and controlled release[13].

Environmental pH and temperature are, by definition, the primary determinants of behaviour in pH- and thermo-responsive systems respectively, but their magnitude of effect depends on how closely the polymer's ionisation constant or phase-transition temperature is matched to the physiological range actually encountered on skin[7,12,17]. The solubility of the active ingredient interacts with all of the above: poorly soluble actives such as curcumin and resveratrol required specific formulation strategies, essential-oil-based permeation enhancement in the former case and cyclodextrin complexation in the latter, to achieve adequate release and permeation, illustrating that stimulus-responsiveness alone does not resolve solubility-related delivery challenges[13,14]. Viscosity and rheological behaviour affect spreadability and residence time on skin and are influenced by both polymer concentration and the degree of swelling at the time of application, while skin permeability itself varies with anatomical site, hydration, and barrier integrity, meaning that the same hydrogel formulation may perform differently on healthy versus compromised skin. Finally, release kinetics, whether diffusion, swelling, or erosion-controlled, are an emergent property of all the factors above rather than of any single variable in isolation, which is why comparable stimulus-responsive chemistries can show markedly different release profiles across the studies reviewed here.

7. EVALUATION AND CHARACTERIZATION

The reviewed formulation studies employed a broad, though not uniform, set of characterisation methods, and no single hydrogel was subjected to every test described in this section; the appropriate battery of tests depends on the specific formulation question being addressed. Structural and chemical confirmation was most commonly obtained through Fourier-transform infrared (FTIR) spectroscopy, used to confirm drug-excipient compatibility in the curcumin-CMC hydrogel and to verify network formation in the chitosan

nanoparticle-hydrogel hybrid, and through X-ray diffraction, used together with IR spectroscopy to confirm successful complex formation in the resveratrol-cyclodextrin-Pluronic system[9,13,14]. Differential scanning calorimetry (DSC) was used alongside FTIR to assess drug-excipient compatibility in the curcumin hydrogel study, providing thermal evidence that complements the spectroscopic data[14].

Morphological and particle-level characterisation, including scanning and transmission electron microscopy and particle-size or zeta-potential analysis, was used to confirm the physical structure and surface charge of the chitosan-based pH-responsive nanoparticle-hydrogel hybrid[9]. Swelling ratio and degradation behaviour, assessed gravimetrically in physiological buffer, were reported for the arabinoxylan-carrageenan-reduced graphene oxide hydrogel as direct evidence of its pH-dependent network response[7]. In vitro drug release, typically measured by sampling a receptor medium over time, was reported for several of the reviewed systems, while ex vivo skin permeation and retention, arguably the most directly relevant endpoint for cosmeceutical formulation among the methods used here, was reported specifically for the curcumin-CMC-essential oil hydrogel[7,9,14]. Antimicrobial and cytocompatibility assays, though more directly relevant to wound-healing than to cosmeceutical claims per se, were used to establish biological safety and activity for the curcumin-chitosan-PVA and resveratrol-cyclodextrin-Pluronic formulations[13,21].

Not every characterisation method carries the same evidentiary weight for cosmeceutical claims. Spectroscopic and thermal methods such as FTIR, DSC, and X-ray diffraction primarily establish formulation structure and drug-excipient compatibility rather than functional performance; swelling, degradation, and in vitro release studies establish the stimulus-responsive mechanism and its kinetics; and ex vivo skin permeation and retention studies provide the most direct, though still preclinical, evidence of likely in-use performance. Across the reviewed literature, structural and mechanistic characterisation is considerably more prevalent than direct skin-permeation or cosmeceutical-outcome testing, which represents a further identifiable gap between what has been characterised and what would be required to substantiate a cosmeceutical delivery claim.

8. CURRENT CHALLENGES AND FUTURE TRENDS

The clearest challenge emerging from this review is the near-total absence of clinical or even robust in vivo evidence for smart hydrogels evaluated specifically as cosmeceutical delivery systems; the great majority of the reviewed formulations were validated in wound-healing, antimicrobial, or tumour-targeting models using in vitro or animal endpoints and direct human or ex vivo skin cosmeceutical data were identified for only a single formulation in the present reference set[13,21]. This limited in vivo and clinical evidence base means that claims of enhanced targeting or controlled release for cosmeceutical use currently rest on mechanistic plausibility and analogy from other therapeutic contexts rather than on direct demonstration.

Formulation stability presents a further practical challenge: stimulus-responsive networks are, by design, metastable with respect to their trigger, and maintaining consistent swelling behaviour, mechanical integrity, and active-ingredient content over a cosmeceutical product's typical shelf life has not been extensively documented in the reviewed sources. Reproducibility and scale-up are related concerns, since several of the reviewed systems rely on multi-step syntheses, such as dual crosslinking of oppositely charged polyelectrolytes or nanoparticle-hydrogel hybrid assembly, that may be more difficult to reproduce consistently at manufacturing scale than simple single-polymer gels[9,10]. Reproducing physiological stimuli accurately in vitro is itself non-trivial: the pH and temperature differences between healthy and compromised skin are considerably smaller than those typically used to demonstrate stimulus responsiveness in wound or tumour models, so formulations validated under exaggerated laboratory conditions may respond less distinctly under real-use cosmeceutical conditions. Polymer and crosslinker biocompatibility on intact, non-injured skin over repeated, long-term application, as is typical of cosmeceutical use, has also not been systematically addressed in the reviewed literature, which has instead focused on short-term wound or tumour endpoints.

Looking forward, several directions appear promising but should be regarded as emerging rather than established. Multi-responsive hydrogels combining pH and temperature sensitivity offer the theoretical prospect of more selective, dual-condition-triggered release, as discussed in Section 3.6, though at the cost of greater formulation complexity[8,20]. Biodegradable and naturally derived polymer systems, drawing on the chitosan, alginate, gelatin, and cellulose-derivative chemistries reviewed in Section 4, align with consumer and regulatory preference for sustainable cosmeceutical ingredients, provided that batch-to-batch consistency can be improved. Nanocomposite reinforcement strategies, such as the incorporation of reduced graphene oxide to modulate both mechanical strength and pH responsiveness, illustrate one route toward hydrogels that combine robustness with tunable stimulus sensitivity, though the cosmeceutical safety profile of such nanomaterial additives requires further dedicated evaluation[7]. More speculative directions discussed in the broader stimuli-responsive drug delivery literature, including personalised topical delivery, three-dimensional-printed hydrogel formats, and artificial-intelligence-assisted formulation optimisation, were not directly evidenced within the reference set assembled for this review and should accordingly be regarded as conceptual future perspectives rather than technologies with an established evidence base for cosmeceutical application at this time.

CONCLUSION

Smart, stimulus-responsive hydrogels offer a mechanistically coherent alternative to conventional topical vehicles for cosmeceutical delivery, in that their capacity to alter swelling, network structure, or degradation in response to pH, temperature, or, in principle, oxidative or enzymatic cues could allow active-ingredient release to be concentrated more precisely at the intended site and time than passive diffusion permits. Among the mechanisms considered, pH- and temperature-responsive systems built on chitosan, poly (acrylic acid)-type polymers, PNIPAM, and Pluronic/poloxamer block copolymers are the most thoroughly characterised, with clear evidence of stimulus-triggered swelling, degradation, and drug release across multiple independent studies. ROS-, enzyme-, and light-responsive strategies, by contrast, remain comparatively underexplored within the literature reviewed here and should currently be regarded as promising design concepts rather than validated delivery platforms.

Polymer selection is inseparable from stimulus choice and from the physicochemical demands of the active ingredient, and no single polymer class was found to be universally superior; natural, synthetic, and semi-synthetic polymers each offer characteristic trade-offs between biocompatibility, tunability, mechanical performance, and manufacturability. The most significant limitation identified across this review is evidentiary rather than mechanistic: the overwhelming majority of the smart hydrogel systems discussed were developed and validated in wound-healing, antimicrobial, or tumour-targeting models, and direct skin-permeation or cosmeceutical-outcome evidence was available for only a small subset of formulations. Consequently, while the underlying stimulus-responsive chemistry is well established, its translation into demonstrated cosmeceutical benefit remains largely inferential. Future research should prioritise dedicated ex vivo and in vivo skin-permeation studies conducted under physiologically realistic, rather than exaggerated, stimulus conditions, systematic long-term biocompatibility and stability testing on intact skin, and greater methodological consistency in characterisation, so that the considerable mechanistic promise of smart hydrogels can be matched by an equally robust cosmeceutical evidence base.

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