

# **COLLAGEN – BASED HYDROGELS ENRICHED WITH BLUEBERRY ANTHOCYANINS AS EMERGING COSMECEUTICAL SYSTEMS FOR ANTI-AGING AND ACNE MANAGEMENT: A COMPREHENSIVE REVIEW**

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## **ABSTRACT**

Cosmeceuticals represent a rapidly growing segment at the interface of cosmetics and pharmaceuticals, which not only enhance appearance but also improve skin health through biologically active compounds. Among emerging topical delivery systems, collagen-based hydrogels have gained significant attention owing to their skin- mimetic properties, biocompatibility and high moisture-retaining capacity. Skin aging and acne formation are complex dermatological condition driven by oxidative stress, inflammatory response, microbial balance, ultraviolet exposure and progressive degeneration of skin collagen. Anthocyanins obtained from blueberries (*Vaccinium* species) exhibit potent antioxidant, anti-inflammatory and antimicrobial activities that are highly relevant to skin rejuvenation and acne control. Therefore, the naturally derived antioxidants have emerged as valuable agents for mitigating these pathological mechanisms.

This review critically examines the structure and barriers of the skin relevant to topical delivery, the biological role of collagen in maintaining skin integrity and the mechanisms underlying skin aging and acne pathogenesis. Collagen hydrogels as advanced topical delivery systems and the functional role of blueberry derived anthocyanins in enhancing their therapeutic efficacy. Recent formulation strategies, physicochemical properties, biological activities and evaluation parameters. Finally, current challenges, regulatory considerations and future perspective for translating collagen anthocyanin hydrogel systems into commercially viable cosmeceutical products are noted.

## **KEYWORDS**

Collagen hydrogels, Blueberry anthocyanins, anti-aging, acne, topical delivery systems, skin regeneration

## INTRODUCTION

Pharmaceutical cosmetics also known as cosmeceuticals, represent a unique blend of cosmetics and pharmaceuticals. They are designed to improve the appearance and health of skin, hair and nails. Ingredients often include vitamins, peptides, antioxidants and botanicals which are known for their healing hyperpigmentation. The pharmaceutical cosmetics market is expected to grow, driven by increasing demand for anti-aging and skin care products, rising awareness of skin health and wellness. Cosmeceuticals is a growing sector in cosmeceuticals and pharmaceuticals; this will also help in improving the skin health through biologically active ingredients. Rising the concerns relates to premature aging, acne and other skin damages have encouraged the exploration of delivery systems capable of enhancing efficacy and safety beyond conventional creams and lotions. Traditional topical solutions exhibit limited skin retention, reduced stability of sensitive bioactive and poor penetration of active compounds.

Hydrogels have attractive increasing interest as alternative topical platforms. Hydrogels are three-dimensional polymeric networks allow extensive water retention, prolonged skin contact and controlled release of incorporated substances. Collagen occupies a unique position due to its natural presence in human skin and its critical role in maintaining skin structure. Similarly, the growing interest in incorporating natural antioxidants into topical formulations to combat oxidative stress and inflammation which contributes to skin aging and acne. Blueberries are rich sources of anthocyanins which is a class of polymeric compounds known for their potent antioxidant, anti-inflammatory and antimicrobial properties. The integration of blueberry derived anthocyanins into collagen hydrogels offers a synergistic effect to skin rejuvenation and acne prevention.

Hydrogels offer numerous advantages over other preparations used in cosmetology and dermatology. Their high swelling capacity provides flexibility similar to natural tissues, and they can transition between gel and sol phases in response to various physical or chemical stimuli. The release of therapeutic substances from hydrogels can be triggered by changes in temperature, local pH, physical stimuli, or the presence of specific enzymes. Additionally, hydrogels can be customized by adjusting their pore size and surface properties to achieve precise and controlled drug release kinetics while tailoring their mechanical properties to meet specific application requirements.

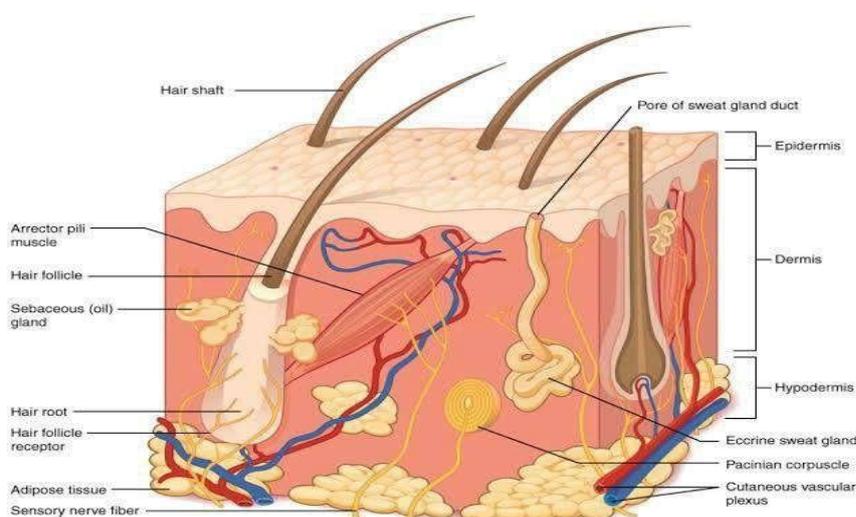
Blueberries are highly beneficial for the skin, abundance of antioxidants, particularly anthocyanins, which protect against oxidative stress and premature aging. Blueberries are rich in vitamin C, they stimulate collagen production, enhancing skin elasticity and reducing wrinkles. Their anti-inflammatory properties cure the irritated skin, minimize redness and help prevent acne. Additionally, blueberries promote hydration and even skin tone, contributing to a healthier, more radiant complexion. By neutralizing free radicals, they also shield the skin from UV damage and environmental pollutants, making them an essential ingredient for maintaining youthful and glowing skin.

This review aims to provide a comprehensive overview of collagen-based hydrogels enriched with blueberry anthocyanins, focusing on their biological relevance, formulation strategies, therapeutic mechanisms and future potential in cosmeceutical science.

## SKIN STRUCTURE AND ITS RELEVANCE TO TOPICAL DELIVERY

The skin is the largest organ of the human body and server as a protective barrier against all the environmental stress, pathogens and chemical agents. Structurally it consists of three major layers the epidermis, dermis and hypodermis. Among these layers the stratum corneum acts as the primary barrier to topical drug and cosmetic penetration.<sup>11</sup>

The stratum corneum is composed of differentiated keratinocytes or corneocytes embedded in a lipid matrix. this is highly organized structure restricts the permeation of hydrophilic and lipophilic substances. Penetration of topical agents occurs mainly through two pathways: the trans-epidermal route which involves the diffusion across the stratum corneum and the trans-appendageal route, which includes hair follicles and sweat glands.<sup>12</sup>



**Fig 1, Structure of skin**

Therapeutic substances can penetrate the skin through two main pathways: trans-epidermal and trans-appendageal. The trans-epidermal route involves the passage of molecules through the stratum corneum, a layer composed of multiple layers of large, polyhedral, non-nucleated cells. Intracellular penetration occurs either via corneocytes, which facilitate the transport of hydrophilic or polar substances, or through intercellular spaces that allow the diffusion of lipophilic or non-polar substances through the lipid matrix. In contrast, the trans-appendageal route involves the movement of substances through hair follicles and sweat glands.

Hydrogels provides unique advantages in overcoming skin barrier limitations. Their high-water content enhances skin hydration and it will disrupt the stratum corneum lipid layers, thereby improving permeability.<sup>23</sup> Their semi-solid consistency promotes adhesion to skin surface which extends the residence time and improved bioavailability of encapsulated actives.

## **MECHANISMS OF SKIN AGING AND ACNE PATHOGENESIS**

### **Skin Aging**

Skin aging is biological process resulting from the combined effects of intrinsic aging and extrinsic factors such as ultraviolet radiation, pollution and oxidative stress. The skin of skin aging is the progressive degradation of collagen and elastin fibres in the dermis leading to wrinkles, sagging and loss of elasticity<sup>2</sup>. Reactive oxygen species (ROS) generated by UV exposure and environment stress, which degrade collagen and other extracellular matrix components.<sup>6</sup> Anti-aging mechanisms for the skin involve multiple pathways that target cellular repair, regeneration, and protection to reduce or delay the visible signs of aging. Key mechanisms include:

#### **A. Collagen Production Stimulation:**

Ingredients like retinoids, peptides, and vitamin C boost collagen synthesis, improving skin elasticity and reducing wrinkles.

#### **B. Cell Turnover Enhancement:**

Retinoids and exfoliants (e.g., alpha-hydroxy acids) accelerate the shedding of dead skin cells and promote the formation of new, healthier cells.

#### **C. Antioxidant Protection:**

Compounds like vitamins C and E, coenzyme Q10, and polyphenols neutralize free radicals, minimizing oxidative stress and preventing collagen degradation.

#### **D. Hydration and Barrier Repair:**

Hyaluronic acid and ceramides improve skin hydration and strengthen the skin barrier, reducing dryness and enhancing plumpness.

#### **E. UV Protection:**

Sunscreens and antioxidants prevent photoaging by blocking or neutralizing the damaging effects of UV radiation.

Low fibroblast activity, impaired collagen synthesis and chronic inflammation further worsen the aging process. Effective anti-aging strategies therefore focuses on antioxidant protection, skin hydration, stimulation of collagen synthesis and restoration of skin barrier function<sup>20</sup>.

### **Acne Pathophysiology**

Acne vulgaris is a chronic inflammatory skin diseases which primarily affects the pilosebaceous unit. Its pathogenesis involves four key factors: increased sebum production, follicular hyperkeratinisation, proliferation of *Cutibacterium acnes* and inflammation.<sup>12</sup> Excess sebum creates an aerobic environment favourable for bacterial growth, leading to inflammatory mediator release and lesion formation. These insights have expanded therapeutic targets beyond conventional antimicrobial effects<sup>24</sup>.

**A. Increase in Sebum production:**

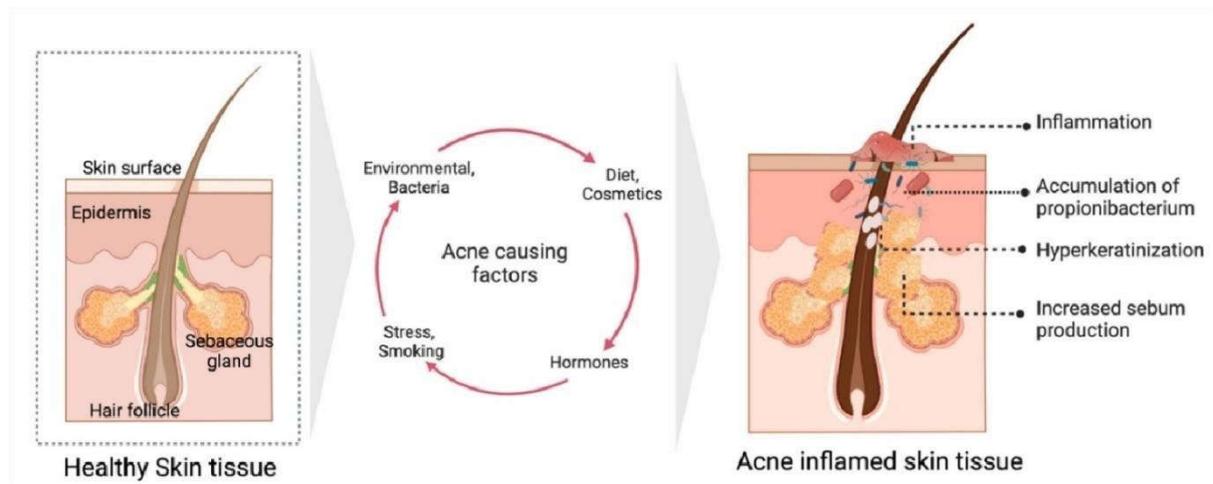
Acne is often caused by excess sebum (oil) production in the hair follicles. This overproduction is largely driven by hormones like testosterone and Insulin Growth Hormone (IGH-1). The more sebum produced, the more severe and frequent acne breakouts tend to be, making sebum production a key factor in acne vulgaris.

**B. Hyper proliferation of Propionibacterium acnes (P. acnes):**

Another major cause of inflammatory acne is the overgrowth of Cutibacterium acnes (formerly Propionibacterium acnes). This bacterium thrives in the oil-rich, oxygen-poor environment of sebaceous follicles. C. acnes break down sebum into fatty acids, which contribute to the formation of comedones (clogged pores) and skin inflammation.

**C. Inflammation acne:**

When the immune system detects the overgrowth of *C. acnes* bacteria, it triggers inflammation. *C. acnes* itself are highly inflammatory, attracting immune cells like lymphocytes, neutrophils, and macrophages to the area. This leads to damage and rupture of the hair follicle, releasing bacteria, fatty acids, and lipids into the deeper layers of the skin (dermis). This process results in inflammatory acne lesions like pustules, nodules, cysts, and papules. Neutrophils also produce reactive oxygen species (ROS), further damaging the follicle and contributing to inflammation. These inflammatory lesions are distinct from non-inflammatory acne, which are smaller and contain less pus.



**Fig 2, Pathophysiology of acne**

## COLLAGEN AS A FUNCTIONAL BIOPOLYMER IN COSMECEUTICALS

Collagen is the most abundant structural protein in the human body, accounting for almost 25-30% of total protein content. It plays a crucial role in maintaining skin strength, elasticity and hydration. Structurally, collagen consists of three polypeptides chains arranged in a triple helix configuration providing a good tensile strength.<sup>2</sup>

Several types of collagens are relevant to skin health, mainly type I and type III which are predominant in dermis. Collagen used in cosmeceuticals are mainly obtained from marine,

bovine, porcine or recombinant origins. Marine collagen has gained assurance due to its high biocompatibility, lower risk of disease transmission and favourable safety profiles.<sup>13</sup>

Collagen itself has a mild antimicrobial property, helping reduce acne-causing bacteria. It can absorb and retain large amounts of water, ensuring deep hydration of the skin. They can be infused with anti-aging agents like peptides, hyaluronic acid or antioxidants. The gel-like consistency of collagen hydrogels provides a soothing, cooling effect, which can reduce puffiness and inflammation associated with aging. Collagen promotes tissue regeneration and speeds up the healing of acne lesions, minimizing scars and post-inflammatory hyperpigmentation. They are lightweight and non-greasy, ensuring they do not clog pores or contribute to acne formation. Some collagen hydrogels incorporate antioxidants, protecting the skin from free radical damage and UV-induced aging. The hydrogel matrix ensures a slow, sustained release of these actives, providing long-lasting effects.

More than hydration collagen facilitates sustained release of bioactive, protect sensitive compounds from degradation and provide a cooling effect. Its ability to wound healing, improve elasticity and enhance skin barrier repair makes it ideal for advanced cosmeceutical systems.<sup>6</sup>

## **COLLAGEN HYDROGELS: PROPERTIES AND ADVANTAGES**

Collagen hydrogels are three-dimensional, cross-linked polymeric networks which has the capacity to retain large amount of water. By modifying its polymeric concentration, crosslinking density and formulation conditions we can able to change its physicochemical properties. Collagen hydrogels provide a major advantage in cosmeceutical application include high biocompatibility, hydration, mechanical flexibility and controlled release of active ingredients.

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The collagen hydrogels have extracellular matrix which promotes cell adhesion, proliferation and tissue regeneration. They have a cooling and soothing effect that reduces irritation and inflammation in skin, making them suitable for sensitive and acne-prone skin.<sup>2</sup>

## **BLUBERRY ANTHOCYANINS AS NATURAL ANTI-AGING AND ANTI-ACNE AGENTS**

Blueberries (*Vaccinium* species) are rich in anthocyanins, water soluble flavonoid pigments which are responsible for imparting the colour. Anthocyanins have strong antioxidant activity by scavenging free radicals and inhibiting oxidative stress induced cellular damage.<sup>13</sup> They also possess anti-inflammatory and antimicrobial properties, which particularly beneficial for aging and acne-prone skin. Anthocyanins, the pigments that give blueberries their vibrant blue, are more than just eye-catching compounds.



**Fig 3, Blueberries**

These powerful antioxidants play a significant role in promoting healthy skin. By neutralizing harmful free radicals, anthocyanins shield the skin from environmental stressors like UV radiation and pollution, which can accelerate aging. Moreover, their anti-inflammatory properties can soothe irritated skin, making them beneficial for conditions such as acne, eczema, and psoriasis. Beyond their antioxidant and anti-inflammatory effects, anthocyanins contribute to improved skin hydration. They can help the skin retain moisture more effectively, leaving it feeling supple and plump. This increased hydration can also contribute to a more youthful appearance. Additionally, anthocyanins may help even out skin tone by inhibiting the production of melanin, the pigment responsible for dark spots and hyperpigmentation.

Anthocyanins stimulate collagen synthesis, inhibit melanogenesis and protect skin cells from UV induced damage. While the potential skin benefits of anthocyanins are promising, it's important to note that further research is needed to fully understand their effects. As with any skincare concern, consulting with a dermatologist is crucial for personalized advice and recommendations.<sup>30</sup> Their antimicrobial activity against skin pathogens further supports their use in acne management. However, anthocyanins are sensitive to environmental factors such as light, heat and pH which is suitable delivery systems to preserve their bioactivity.<sup>33</sup>

## **SYNERGISTIC INTEGRATION OF ANTHOCYANINS INTO COLLAGEN HYDROGELS**

The incorporation of blueberry derived anthocyanins into collagen hydrogels offers synergistic therapeutic advantages. Anthocyanin from blueberry show strong antioxidant and anti-inflammatory effects that mitigate UV-induced oxidative stress and inflammation in skin cells, helping to prevent photoaging. The hydrogel matrix stabilizes anthocyanins, minimizes premature degradation and enable gradual release at the skin surface. This integration allows simultaneous targeting of dermal aging processes and acne-related inflammation, positioning collagen anthocyanin hydrogels as multifunctional cosmeceutical platforms.

Encapsulating blueberry anthocyanins in a collagen hydrogel encourage collagen's structural support and intrinsic pro-regenerative effect with anthocyanins ability to reduce reactive oxygen species, suppress inflammatory pathways and inhibit collagen breakdown. This combination can rebalance collagen homeostasis that is, increased collagen synthesis and decreased degradation leading to improved dermal matrix density, wrinkle reduction and better recovery from photoaging compared with either component alone.

## **EVALUTION PARAMETERS REPORTED FOR COLLEGEN-BASED HYDROGELS**

Studies on collagen hydrogels commonly evaluate parameters such as pH, viscosity, spreadability, homogeneity, antimicrobial activity and stability. Skin compatible pH typically 5-7 is essential to prevent irritation. A proper viscosity ensures ease of application and controlled release, which good spreadability enhances customers satisfaction. Antimicrobial testing against common skin pathogens provides insight into acne preventive potential.

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