

## ABOUT THE AUTHOR

Geeta Yadav, MD

Dr. Geeta Yadav is founder of FACET Dermatology in Toronto. She is a board-certified dermatologist who trained at University of Toronto, Johns Hopkins and the Northern Ontario School of Medicine. Dr. Yadav is an expert in both medical and cosmetic dermatology with a large and growing medical practice that specializes in atopic dermatitis, psoriasis, and skin cancer. She has a special interest in skin of color and has been quoted in numerous mainstream publications including the New York Times, Wall Street Journal, Allure, Vanity Fair and Cosmopolitan. She has a regular presence on Instagram, Facebook and LinkedIn and tries to use these platforms for education and awareness on a variety of topics.



**Affiliations:**

University of Toronto  
Women's College Hospital

## Three Essential Skincare Product Ingredients

### Introduction

According to a 2022 MarketWatch report, the global skincare market is estimated at \$63.8B USD (\$86.5B CDN)<sup>1</sup>. This high market value is evidenced by the plethora of consumer products currently available in the retail sector. The skincare landscape is vast, with a greater number of products available than seen previously. A significant number of skincare products are launched on a monthly basis, purportedly containing novel ingredients, and making bold efficacy claims such as improved skin brightening, collagen regeneration and deep hydration.

The myriad number of skincare product ingredients from which to choose can lead to a sense of being overwhelmed and confusion on the part of patients regarding the actual effectiveness of any given skincare product. This sense of confusion is further compounded by the rapid increase in and broad distribution of skincare-related consumer content created by skincare influencers on social media, only 4% of whom are board-certified dermatologists.<sup>2</sup> Although the majority of skincare social influencers are not, in fact, licensed dermatologists and may therefore not be qualified to disseminate skincare advice, nevertheless the clinical data demonstrates their ability to influence patients' treatment decisions.<sup>3</sup> Furthermore, when patients present their healthcare providers with treatment options they've sourced online, some of these providers may react negatively and be unwilling to explain the advantages and disadvantages of over-the-counter skincare treatments as an alternative to clinically-based solutions. These experiences may result in a sense of uncertainty on the part of patients regarding their providers' recommendations.<sup>4</sup>

For these reasons, it is critical for dermatologists to become aware of the skincare-related content their patients are researching online regarding treatment recommendations, particularly on the topic of ingredients contained in skincare formulations. It is the responsibility of healthcare providers to continue to educate patients, which will enable them to arrive at informed and well-researched decisions relating to their dermatologic health. This paper summarizes

clinical evidence-based findings on three of the most popular ingredients currently utilized in consumer skincare products: niacinamide, vitamin C and hyaluronic acid.

### Clinical Effects of Niacinamide

Vitamin B3 or niacin, performs a critical role in maintaining overall health, converting food into energy while supporting the skin, digestive and nervous systems. Niacinamide, the amide form of niacin, is contained in many topical skincare products, and has increasingly gained consumer interest as novel formulas have developed in recent years. Vitamin B3 is purported to provide the following dermatologic benefits: decrease hyperpigmentation; reduce facial redness; improve excess sebum production and pore size; increase skin radiance; and reduce signs of premature skin aging. Clinical trials comparing the effectiveness of niacinamide vs retinoids in achieving the above have demonstrated comparable results between the two components.<sup>5</sup>

Certain benefits attributed to niacinamide derive from its ability to induce enhanced exfoliation,<sup>6</sup> which enhances the skin's luminosity- the ability of the skin to reflect light. In addition to shedding the skin's surface components, it is theorized that niacinamide exfoliates the dead skin cells within the pore duct, thereby improving the flow of sebum, ultimately resulting in decreased sebum on the skin's surface.<sup>7</sup> This alteration in sebum production may result in decreased pore congestion, which minimizes the appearance of enlarged pores, a common characteristic in patients with a propensity for acne. Furthermore, niacinamide has been shown to have broad anti-inflammatory activity. Clinical studies have reported its efficacy in downregulating inflammatory reactions triggered by *Propionibacterium acnes*, the bacterium that causes inflammatory acne vulgaris.<sup>8</sup>

Niacinamide has demonstrated anti-aging benefits. Collagen synthesis decreases with age, causing a deceleration in cellular turnover.<sup>9</sup> Niacinamide's exfoliating properties aid in increasing cellular turnover, as does its ability to stimulate collagen synthesis and epidermal proteins.<sup>10</sup> These

mechanisms improve skin quality and texture, reducing the appearance of fine lines, wrinkles, and rough skin that is dull in appearance.

Hyperpigmentation, a primary characteristic in aging skin, may respond to treatment by niacinamide, as can melasma. By inhibiting melanosome transfer from melanocytes to keratinocytes, niacinamide can significantly decrease hyperpigmentation and increase the skin's luminosity.<sup>11</sup> In a clinical trial comparing the results of treating melasma with hydroquinone vs niacinamide, the latter reported efficacy with the absence of significant side effects, and was well tolerated.<sup>12</sup>

Over-the-counter skincare products formulated with niacinamide may be an effective resource for patients with skin barrier dysfunction. Ceramides are structurally and functionally critical to a healthy skin barrier. A clinical trial demonstrated that niacinamide increases ceramide synthesis, resulting in reduced transepidermal water loss (TEWL) and improved resistance to potentially harmful topical agents. The same study showed that niacinamide strengthens the skin barrier through improved keratinocyte differentiation, reducing TEWL and increasing the moisture content in the stratum corneum.<sup>13</sup>

In making patient recommendations regarding products containing niacinamide, consideration of its concentration is a primary concern, as is the formula as a whole. The studies cited in the above article utilized formulas with niacinamide concentrations ranging from 2% to 5%, although concentrations of up to 10% have not demonstrated any side effects associated with stinging or redness. Patient tolerability of niacinamide varies, therefore clinicians are advised to begin a protocol initiating treatment with a lower concentration to determine how the patient's skin will react. Efficacy of niacinamide is increased when using products that contain both niacinamide and retinol.<sup>14</sup>

### **Clinical Effects of Vitamin C**

Vitamin C, also known as L-ascorbic acid, is present in high concentrations in human skin.<sup>15</sup> However, it cannot be intentionally produced—and with consumption of vitamin C-rich foods and oral supplements, very low quantities are bioavailable or active in the skin,<sup>16</sup> making topical application of L-ascorbic acid necessary to achieve skincare benefits.<sup>17</sup> Vitamin C possesses anti-oxidative properties and has been shown to prevent UV radiation damage, as well as providing photoprotection, depigmentation and collagen synthesis.<sup>18</sup>

Clinical trials have reported reduced vitamin C levels in mature and photoaged skin,<sup>19</sup> as well as in skin

exposed to extreme oxidative stress.<sup>20</sup> The free radicals emitted by UV radiation are highly damaging to the skin, and have the effect of degrading collagen, decreasing new collagen production, and increasing the accumulation of elastin. This causes hyperpigmentation, wrinkling and rough skin texture.<sup>21</sup> Topical application of vitamin C can reduce collagen damage<sup>21</sup> and inhibit elastin synthesis,<sup>22</sup> reducing the appearance of photodamage.<sup>23</sup> While sunscreen is critical for protection against photo damage, combining it with vitamin C delivers additive protection.<sup>24</sup> Studies have demonstrated that combining vitamin C with vitamin E and ferulic acid can increase the efficacy of vitamin C eight-fold.<sup>17</sup>

Beyond its ability to provide photoprotection and thus decrease photodamage, vitamin C may exhibit an antipigmentary effect by interrupting the process of melanogenesis.<sup>18</sup> Vitamin C inhibits the production of tyrosinase, the enzyme responsible for triggering melanin production, decreasing melanocyte activity and reducing pigmentation.<sup>18</sup> However, it may be more effective when paired with other skin-brightening agents, such as licorice root extract.<sup>25</sup>

Intrinsic and extrinsic aging lead to collagen degradation and a reduced rate of collagen production. Vitamin C is essential to collagen synthesis, promoting it through two mechanisms: 1) by acting as a cofactor for the enzymes that stabilize and crosslink collagen; and 2) by increasing the levels of procollagen mRNA.<sup>25</sup> Clinical studies have reported this behaviour in both young and old fibroblasts,<sup>26</sup> supporting the use of vitamin C as preventative and corrective treatment for patients of all ages.

The above benefits support the value of incorporating vitamin C into patients' daily skincare regimen. However, while many currently available over-the-counter skincare products claim vitamin C as an active ingredient, their efficacy depends entirely on the form of vitamin C used in the formula. While vitamin C esters represent the most stable molecules with which to formulate skincare products, they are not as effective as ascorbic acid.<sup>27</sup> Ascorbic acid is the most bio-active form of vitamin C; however, it is the most unstable as well.<sup>17</sup> Skincare products must be developed according to the highest clinical standards in order to ensure optimal, verifiable results. One study showed that the most efficacious skincare products containing vitamin C are formulated with a pH level of 3.5 or below, and that enhanced delivery occurs at a pH level of 2.0.<sup>27</sup> Furthermore, their concentration of ascorbic acid must be high as well—concentrations of 15 to 20 percent have demonstrated the highest degree of efficacy.<sup>27</sup>

## Clinical Effects of Hyaluronic Acid

Hyaluronic acid (HA) is a glycosaminoglycan that is found throughout the human body, primarily in the dermis. More than 50% of the body's HA is found in the skin.<sup>28</sup> The functions of HA include hydration<sup>29</sup> and an ability to occupy a significant amount of space in relation to its mass.<sup>30</sup> HA can hold up to 6,000 times its weight in water<sup>31</sup> within the body. Intrinsic skin aging, affected by hormonal age-related changes, can lead to a myriad of characteristics of mature skin, including dryness and collagen degradation resulting in loss of skin volume.<sup>32</sup> Due to HA's hydrophilic and high level of biocompatibility, it has gained popularity for use in injectable fillers to restore lost subcutaneous volume caused by dermal atrophy in aging skin,<sup>30</sup> as well as in topical formulas designed to help diminish dryness.

Topical forms of HA, typically serums and moisturizers, are recognized in dermatology as an essential component in achieving the appearance of well-hydrated, healthy skin. However, it is important to note that the majority of the body's HA content is located in the dermis, rather than in the epidermis.<sup>33</sup> Water present in the dermis cannot penetrate beyond the lipids in the stratum granulosum. Additionally, lipids block the diffusion of aqueous material through the epidermis.<sup>32</sup>

### Molecular weight of hyaluronic acid

In consideration of this, dermatologic products containing HA will demonstrate efficacy solely where they are applied—in the stratum corneum. The stratum corneum is impermeable by HA that possess a high molecular weight.<sup>34</sup> Low molecular weight HA is the only form capable of penetrating the stratum corneum, and permeating the deeper dermal layers.<sup>35</sup> However, exogenous HA is rapidly cleared by the body.<sup>36</sup> An important caveat for practitioners to note is that low molecular weight HA does not equate to hydration in the skin's upper layers. As a humectant, while HA is a water-attracting substance, water vapour comprises only approximately 0.4% to 2% of atmospheric gasses<sup>37</sup>. Rather, HA binds to water molecules, drawing and retaining water reserves from the skin to create an appearance of increased hydration; however, its ultimate effect is further dehydration. A clinical trial sponsored by Massachusetts General Hospital and the Estée Lauder Companies Inc. examining the efficacy of a particular HA skincare product under humid conditions<sup>38</sup> demonstrated that the product resulted in over-estimated hydration values and resulted in a net dehydration effect. Furthermore, low molecular weight HA is a pro-inflammatory molecule.<sup>33</sup>

While the application of high molecular weight HA may provide temporary dermatologic benefits, additional robust clinical trials are necessary to assess its sustained efficacy. The clinical trials cited herein suggest that HA should not comprise a mandatory step in one's skincare regimen; and that overuse of HA may have deleterious effects. The medical literature indicates that a higher degree of hydration may be achieved by supplementing the body's natural reserves of HA through increased dietary intake of HA.<sup>39</sup> An injectable form of HA may deliver positive hydration effects. Clinical studies of an injectable HA gel, Juvéderm Volite, which is not a dermal filler, have reported effectiveness in augmenting skin smoothness for up to six months, and skin hydration for up to nine months.<sup>40</sup>

### Summary

Patients' interest in increased access to research of skincare ingredients as a result of brand marketing and social media activities must be supported by credible, evidence-based clinical information which dermatologists are in the optimal position to provide. With the significant amount of clinical trial data available on niacinamide, vitamin C and HA, dermatologists have a responsibility to provide patients with informed professional insights. This will foster improved clinician-patient relationships and assist patients in developing a skincare routine that is both efficacious and valuable to them.

### Correspondence:

Dr. Geeta Yadav

Email: [hello@facetdermatology.com](mailto:hello@facetdermatology.com)

### Financial Disclosures:

#### Consultancy/Speaker/Advisory Board honorarium:

AbbVie, Amgen, Aralez, Arcutis, Bausch Health, Bioderma, BMS, Byrdie, Galderma, Incyte, Janssen, Johnson & Johnson, Leo, Lilly, L'Oreal, Medexus, Novartis, Pfizer, Sanofi-Regeneron, Sun Pharma, UCB.

#### Grants, Research or Clinical Trials:

UCB, Bausch Health, AbbVie, Janssen.



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