REVIEW ARTICLE

Exploring the Potential Use of Bromelain in Cosmeceuticals: A Review

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Abstract

Pineapple (*Ananas comosus*) is a member of the Bromeliaceae family, predominantly found in tropical regions, including Indonesia. Bromelain, a proteolytic enzyme, is present throughout the pineapple plant, with higher concentrations found in the stem compared to the fruit. While bromelain has been extensively utilized in medical therapies, its applications have expanded into various industries, including food and beverage, textiles, and cosmetics. The growing interest in natural ingredients within the cosmetic industry has led to the emergence of cosmeceuticals products that combine cosmetic and therapeutic benefits. Cosmeceuticals are cosmetic products that contain biologically active ingredients with therapeutic benefits on the applied surface. Common treatments address issues such as acne, redness, hair damage, wrinkles, photoaging, skin dryness, hyperpigmentation, and uneven skin tone. This review article aims to discuss the potential benefits of bromelain as a cosmeceutical raw material.

Keyword: pineapple; bromelain; cosmeceuticals, antioxidant, antimicrobial, anti-inflammatory and wound healing, photoprotection, exfoliation, anti aging

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Introduction

The growing interest in natural ingredients within the cosmetic industry has led to the emergence of cosmeceuticals products that combine cosmetic and therapeutic benefits. Cosmeceuticals are increasingly sought after for their ability to address specific skin concerns while enhancing overall skin health. This trend reflects a broader consumer demand for safe, effective, and sustainable alternatives to synthetic chemicals in skincare formulations.

Plants have long been recognized for their medicinal properties, and many botanical extracts are now being explored for their potential as cosmeceuticals. These natural ingredients often contain a rich array of bioactive compounds, including antioxidants, anti-inflammatory agents, and antimicrobial substances, making them ideal candidates for developing innovative skincare products [1].

Among these natural ingredients, bromelain, a proteolytic enzyme derived from the pineapple plant (*Ananas comosus*) shows significant potential in the medical field, serving as an anti-edema agent, fibrinolytic, anti-cancer agent, anti-inflammatory, antibiotic, anticoagulant, and antithrombotic [2]. Furthermore, it may exhibit analgesic properties that aid in healing and minimizing post-operative pain and swelling [3]. Beyond its medicinal applications, bromelain is being explored in various other sectors, including food and beverage, textiles, and cosmetics [4].

Currently, cosmetics are not only utilized for beautification but also for therapeutic purposes addressing various skin conditions, leading to the emergence of the term "cosmeceuticals.". These products are used for treating various conditions, including acne, wrinkles, photoaging, skin dryness, hyperpigmentation, hair damage, and others. This review aims to explore the activity of bromelain derived from pineapple (*Ananas comosus*) and its potential applications in cosmeceutical formulations

Physicochemical Properties of Bromelain

Bromelain is a proteolytic enzyme typically associated with endopeptidases, found in the tissues of the Bromeliaceae family. The most notable plant in this family is pineapple (*Ananas comosus*), which thrives in several tropical and subtropical countries, including the Philippines, Thailand, Indonesia, Malaysia, Kenya, India, and China. Its chemical properties have been recognized since 1876, with efforts to isolate it beginning in 1894 [5,6]. The chemical structure of bromelain is illustrated in Figure1.

Biochemically, bromelain is a non-toxic enzyme with therapeutic potential, classified as a protease that breaks down proteins. Notably, the bromelain extract contains not only various thiol endopeptidases but also additional components like phosphatases, glucosidase, cellulases, peroxidases, glycoproteins, carbohydrates, several protease inhibitors, and organically bound calcium ions [7-9]. It is estimated that the extract comprises about 80% stem bromelain, 10% fruit bromelain, 5% ananain, along with other substances [10]

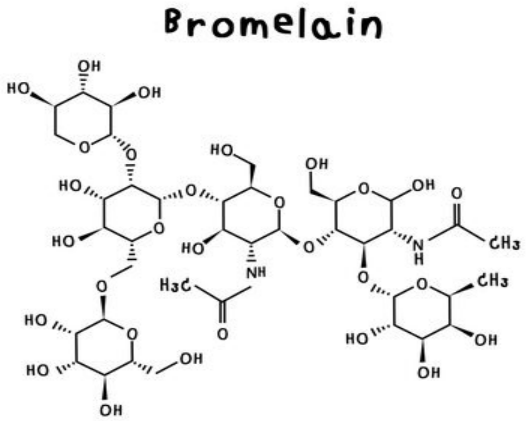

Figure 1: Chemical structure of Bromelain

Two types of enzymes are identified based on their source: stem bromelain (SBM) with the EC number EC 3.4.22.32, and fruit bromelain (FBM) with EC number EC 3.4.22.33. While their names might imply they are variations of the same enzyme, research indicates that SBM and FBM differ in biological activity, structure, and physicochemical properties [5,11]. SBM is primarily used in the pharmaceutical, medical, and food industries because it is more economically viable to extract from the pineapple stems, where enzyme concentration is higher, and the extraction and purification process is cheaper [12].

The molecular weight for SBM ranges from 26 to 37 kDa, while FBM's molecular weight ranges from 24.5 to 32 kDa [4]. Notable biochemical analyses of SBM extracts have been provided by Herrach et al. (1995) [13], which utilized two-step cation-exchange chromatography to isolate nine key proteolytically active components. Among these, fractions F4 (24.4 kDa) and F5 (24.5 kDa) are the primary components, both approximately 50% glycosylated and stabilized by disulfide bridges and hydrogen bonds.[14] The most active protease in the SBM extract appears to be fraction F9 (ananain; 23.5 kDa), which constitutes about 2% of the total proteins and is not glycosylated [14].

Differences in the performance of SBM and FBM are also evident in their optimal pH levels and temperature ranges, which influence the activity of pineapple extracts. For SBM, the ideal pH is between 6 and 7, and the optimal temperature is 50–60 °C [15-17]. In contrast, FBM has an optimal pH range of 3–8 and performs best at temperatures between 37 and 70 °C [18,19].

Bromelain is distributed throughout the pineapple plant, with the highest concentration found in the stem, making it one of the most abundant sources of bromelain. Other parts, such as the skin, core, and crown, have also been investigated for their bromelain content. The efficacy of bromelain is largely attributed to its thiol protease activity. It is classified as either stem bromelain or fruit bromelain, depending on its source. The proteolytic activity of stem bromelain is relatively higher than that of fruit bromelain [20]. Both forms undergo complex glycosylation influenced by factors such as enzyme availability, amino acid sequence, and protein conformation. Thus, it is crucial to identify effective extraction and purification methods. The most studied and promising methods include micropropagation, reverse micelle systems, membrane filtration, and aqueous two-phase extraction. Additionally, researchers are leveraging advancements in recombinant DNA technology for large-scale production and purification of recombinant bromelain.

Bromelain Activity

Antioxidant

Antioxidants are compounds capable of donating one or more electrons to free radicals, thereby preventing degenerative diseases. Antioxidant activity is typically assessed using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) method, compared to a standard like vitamin C, and measured using a visible spectrophotometer. Bromelain, as a proteolytic enzyme, exhibits antioxidant properties by inhibiting lipid peroxidation and scavenging free radicals [21]. Studies Saraswaty et al, 2017 [22]. indicate that pineapple skin extract possesses antioxidant potential at concentrations of 0.05 - 0.8%, achieving IC50 values of 0.8 - 1.3 mg/mL. Further research noted that at a concentration of 0.3%, ethanolic extract of pineapple skin inhibited free radical activity by 63.8% [23].

Another study by Hossain et al, 2011 [2]. extracted total polyphenols from pineapples using various solvents, finding the highest polyphenol content in methanol correlating with the highest antioxidant activity. Key polyphenols identified included gallic acid, catechin, epicatechin, and ferulic acid in pineapple skin. While interactions among polyphenols showed no synergistic effects, additive effects were observed in combinations of ferulic acid-epicatechin and ferulic acid-gallic acid using antioxidant activity assays [24].

Several researchers have reported that pineapple skin is a potential source of bioactive compounds, including vitamin C, carotenoids, phenolic compounds, and flavonoids, all of which have been linked to antioxidant activity and various biological activities [25]. However, the concentration of these bioactive compounds can vary significantly based on factors such as cultivar, pre- and post-harvest treatments, and methods used for raw materials and extraction preparation [26]. Other studies confirm the antioxidant activity of pineapple skin extracts [27]. Chlorogenic acid and ferulic acid in pineapple water extract are believed to play crucial roles as reducing or antioxidant agents [28].

In another study, pineapple crowns yielded 0.26% raw dry bromelain with a total protein content of 44.10% and an IC50 of 3624 µg/mL of raw bromelain, equivalent to 1590.18 µg/mL of total protein [29]. Additionally, the flesh extract exhibited antioxidant effects with an IC50 value of 0.1 µg/mL, classifying it as a potent antioxidant.

Antimicrobial

Research by Okoh et al, 2019 examined the antibacterial activity of skin extracts, revealing significant inhibition against Staphylococcus aureus and Pseudomonas aeruginosa [28]. This indicates that pineapple skin contains potential antimicrobial components that could be useful in cosmetics for treating skin infections. In other study also highlight the antibacterial effects of pineapple flesh against various bacterial strains, suggesting its potential for incorporation into cosmeceutical formulations [30].

In other study, the purified bromelain from peel, stem and crown was used to create a facewash formulation towards pathogens frequently associated with skin infections. Common skin pathogens like Staphylococcus aureus and Propionibacterium acne were found highly sensitive to its action [31].

Additionally, bromelain from pineapple is reported to possess antifungal properties. In a study, bromelain derived from pineapple exhibited antifungal effects against Candida albicans, indicating its potential for addressing fungal infections in cosmetic applications [32].

Anti-inflammatory and wound healing

Bromelain has been recognized for its anti-inflammatory properties, contributing to its use in cosmetic formulations targeting inflammation and skin irritation. These properties may benefit formulations designed for sensitive skin, as bromelain can help reduce inflammation and promote healing [33].

The analysis of the healing process, from a macroscopic point of view, shows that the protein extract obtained from pineapple peel plays an important role in the recovery from acute cutaneous lesions in rats, resulting in a reduction in the width of the lesion and accelerating the healing process, which reinforces its therapeutic potential [34].

Bromelain exerts potent anti-inflammatory effects by modulating various inflammatory mediators, including cytokines, chemokines, and prostaglandins. It inhibits the production of proinflammatory cytokines such as interleukin-1 beta (IL-1β), tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6) [35-42].

Additionally, bromelain suppresses the nuclear factor-kappa B (NF-κB) signaling pathway, a key regulator of inflammation and immune responses; by inhibiting NF-κB activation, bromelain reduces the expression of inflammatory genes and attenuates the inflammatory cascade [43]. Bromelain's proteolytic activity facilitates the breakdown of proteins involved in edema formation and swelling. By degrading extracellular matrix proteins and reducing the accumulation of fluid in tissues, bromelain may help alleviate inflammation-associated edema [44,45]

Photoprotection

Repeated exposure to solar ultraviolet (UV) radiation can lead to serious health risks, UVA and UVB rays penetrate the epidermis, resulting in ROS production, activation of signaling pathways, and damage to DNA, proteins, and lipids, which can disrupt the skin's defense mechanisms [46]. Recent studies have also identified the potential of bromelain as an anti-UV agent, providing protection against UV-induced skin damage. It demonstrated that bromelain can help mitigate the adverse effects of UV radiation, positioning it as a valuable ingredient in sun protection formulations [47].

In another study, revealed that pineapple peel extracted into Dichloromethane (DCM) fraction is possible to develop natural sunscreen formulation with Sun Protection Factor (SPF) value 29 ± 74 [48].

Exfoliation

Exfoliation is the process of removing impurities and keratinised cells from the skin's surface, and thinning and making the stratum corneum uniform, to facilitate the penetration/permeation of cosmetically active ingredients, resulting in healthier-looking skin with an improved aesthetic appearance [49]. Enzymatic peels use proteolytic enzymes (proteases) that break down proteins. Enzymes are macromolecules that accelerate chemical reactions with considerable advantages over chemical catalysts, mainly because of their specific action and ecological qualities. Bromelain digests the proteins of dead cells in the upper layer of the skin, resulting in their replacement by younger skin cells from the lower layers. It also helps to reduce post-injection bruising and swelling [50,31].

Anti-aging

The connection between bromelain and aging is a growing area of interest, although direct studies on this topic are still limited. Cellular senescence refers to a state where cells stop dividing but remain alive, contributing to aging and the onset of age-related diseases. Senescent cells release a senescence-associated secretory phenotype (SASP), which includes pro-inflammatory cytokines, chemokines, and proteases that can lead to tissue dysfunction and various diseases [51].

Bromelain, a complex mixture of proteolytic enzymes from the pineapple plant, has been investigated for its diverse biological activities, including anti-inflammatory, immunomodulatory, and potential anticancer effects. Although research specifically examining bromelain's impact on cellular senescence is sparse, its known properties suggest several ways it could influence aging. These include its anti-inflammatory effects, immunomodulatory capabilities, and proteolytic activity. Research indicates that bromelain can modulate inflammation, which is closely related to the onset and persistence of cellular senescence. By potentially reducing inflammation, bromelain might indirectly influence the senescence-associated secretory phenotype, thereby alleviating the negative impacts of senescent cells on tissue function [51-54].

Bromoprotease reduces skin aging by operating according to a similar process as trypsin, albeit milder and more selective. It regulates the epidermal growth factor (EGF) signaling pathway, hydrolyzes dead skin cells on the skin's

Table 1: The formulation of bromelain as cosmetics modified from various formulations

Dosage form	*Part of plant*	*Formulation*	*Eficacy*	*Reference*
Cream	stem	Bromelain, stearic acid, olivem 1000, caprylic capric triglyceride, liquid paraffin, propylene glycol, xanthan gum, glycerin, methyl paraben, tween 60, sorbitol, propylene glycol, vitamin E, aquademin	Anti-inflammatory (in vitro)	[57]
Body scrub	Peel and core	Glycerin, Stearic acid, cetyl alcohol, triethanolamine, ispropyl, propylparaben, aquademin	Natural exfoliator	[58]
Gel	Stem	Bromelain, carbopol 940, Triethanolamine, propylen glycol, glycerin, DMDM Hydantoin	Wound healing	[59]
	Fruit	Pineapple fruit extract, HPMC, Propylene glycol, methyl paraben, propyl paraben, natrium metabisulfite, dinatrium EDTA, aquadest	Natural exfoliating	[62]
Body wash	Stem	Pineapple stem extract, stearic acid, adaps lanae, triethanolamine, glycerin, parfume, aquadest	Anti fungi	[60]
Face wash	Peel, crown, core, fruit and stem	Bromelain, turmeric, aloevera gel, xanthan gum, tea tree oil, NaOH, Sodium lauryl sulfate, sodium stearate, pripylene glycol	Anti acne	[31]
Sunscreen	Peel	Bromelain, stearic acid, liquid paraffin, triethanolamine, aquadest, nipagin, ethanol, ctearyl alcohol, cera alba, cetyl alcohol, propylene glycol	Sunscreen	[61]
Topical cream nanoemulsion	Core	Pineapple core extract, lecithin, propylene glycol, tween 80, olive oil, virgin coconut oil, oleic acid, vitamin E, methylparaben, propylparaben,	Anti-inflammation	[63]

surface, and removes proteins from the stratum corneum, thus promoting the regeneration of healthier skin cells [55]. The mechanism of action for elastin involves the selective hydrolysis of damaged tissues, which can selectively identify and decompose damaged or aged elastin, speeding up the skin repair process. To reduce skin stains, bromelain decreases melanin synthesis by affecting tyrosinase activity, which is mainly involved in regulating the microphthalmia-associated transcription factor (MITF) signaling pathway. MITF plays a crucial role in regulating tyrosinase expression in pigmentation cells [56].

Application and Development of Bromelain Formulations in Cosmetic Preparations

Over recent years, the demand for natural and bioactive ingredients in cosmetics has grown, leading to the increasing inclusion of bromelain in skincare formulations. The application of bromelain in cosmetics is rooted in its ability to break down protein molecules, which can help in exfoliating dead skin cells, thereby promoting smoother and brighter skin. Furthermore, its anti-inflammatory properties make it an excellent ingredient for products targeting sensitive or acne-prone skin. Its enzymatic action has also been explored in formulations intended for the treatment of hyperpigmentation, as it is believed to support skin regeneration and lightening. Here are the key applications of bromelain in cosmetics in table 1.

Conclusion

Bromelain is a natural enzyme complex with diverse potential therapeutic effects, ranging from anti-inflammatory and digestive properties to immune modulation, aging, and wound healing. While research on bromelain continues to expand, further well-designed clinical trials are needed to elucidate its mechanisms of action, optimal dosing regimens, and benefit for skin. Bromelain's diverse properties make it a valuable ingredient in cosmetic formulations. From exfoliation to anti-inflammatory benefits, its applications can enhance the effectiveness of various skincare products. As consumer interest in natural and effective ingredients grows, bromelain is likely to become increasingly prominent in the cosmetic industry, providing innovative solutions for skin health.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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