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Review

Polyglutamate: Unleashing the Versatility of a Biopolymer for Cosmetic Industry Applications

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Abstract: Polyglutamic acid (PGA), a biopolymer comprising repeating units of glutamic acid, has garnered significant attention owing to its versatile applications. In recent years, microbial production processes have emerged as promising methods for the large-scale synthesis of PGA, offering advantages such as sustainability, efficiency, and tailored molecular properties. Beyond its industrial applications, PGA exhibits unique properties that render it an attractive candidate for use in the cosmetic industry. The biocompatibility, water solubility, and film-forming characteristics of PGA make it an ideal ingredient for cosmetic formulations. This article explores the extensive potential cosmetic applications of PGA, highlighting its multifaceted role in skincare, haircare, and various beauty products. From moisturizing formulations to depigmentating agents and sunscreen products, PGA offers a wide array of benefits. Its ability to deeply hydrate the skin and hair makes it an ideal ingredient for moisturizers, conditioners, and hydrating masks. Moreover, PGA's depigmentating properties contribute to the reduction in hyperpigmentation and uneven skin tone, enhancing the overall complexion. As the demand for sustainable and bio-derived cosmetic ingredients escalates, comprehending the microbial production and cosmetic benefits of PGA becomes crucial for driving innovation in the cosmetic sector.

Keywords: polyglutamic acid; microbial production; cosmetic applications; skincare

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1. Introduction

Polyglutamic Acid—An Overview

Polyglutamate, also known as poly-γ-glutamic acid (PGA), was first discovered in "natto", a type of fermented soybean. This biopolymer is derived from glutamic acid and is characterized by its unique structure, featuring anionic natural polymer chains linking α-amino groups and γ-carboxyl groups through amide bonds (Figure 1). The molecular weight (MW) of this homo-polyamide γ-PGA ranges from 50,000 to 2 million Daltons. The polymer composition can include a homopolymer derived from either L- or D-glutamic acid, or a heteropolymer combining both L- and D- enantiomers [1,2].

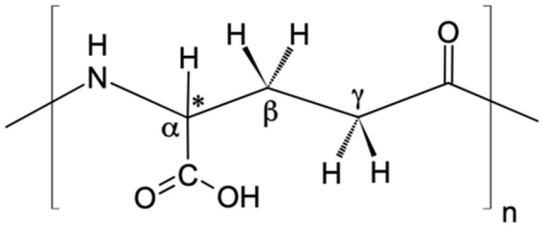

Figure 1. Chemical structure of polyglutamic acid.

Polyglutamate, or poly-γ-glutamic acid (PGA), is found in various natural sources, including specific micro-organisms and fermented foods [3]:

1. Micro-organisms: Certain bacteria, particularly strains of Bacillus species, are known to produce PGA as a part of their metabolic processes. *Bacillus subtilis* is one of the most well-studied producers of PGA. These bacteria synthesize PGA intracellularly and excrete it into the surrounding environment. PGA production by micro-organisms is often stimulated under conditions of stress or nutrient limitation, suggesting a role for PGA in microbial adaptation and survival.
2. Fermented Foods: PGA can also be found in certain fermented foods that undergo microbial fermentation processes. Fermented soybean products like natto, a traditional Japanese food, contain PGA produced by Bacillus subtilis during the fermentation of soybeans. Additionally, other fermented foods such as fermented soy sauce and Korean kimchi may also contain PGA as a result of microbial activity during the fermentation process.
3. Environmental Sources: Apart from microbial and food sources, PGA has also been detected in various environmental settings. For example, PGA-producing bacteria have been isolated from soil, water, and plant surfaces, indicating that PGA may play a role in microbial ecology and environmental interactions. The presence of PGA in environmental samples highlights its ubiquity and suggests its potential ecological significance beyond microbial metabolism.
4. Biotechnological Production: In addition to natural sources, PGA can also be produced through biotechnological processes using recombinant micro-organisms or enzymatic synthesis. This approach allows for the controlled and scalable production of PGA for various industrial and biomedical applications, including cosmetics, pharmaceuticals [4–6], and biodegradable materials [7–9].

Overall, polyglutamate, or PGA, is derived from a variety of natural sources, including specific micro-organisms involved in fermentation processes and environmental samples. Understanding the diverse sources of PGA is essential for exploring its potential applications in various fields and harnessing its beneficial properties for human health and biotechnological advancements.

Bacteria, particularly strains of *Bacillus* species such as *Bacillus subtilis* and *Bacillus licheniformis*, are major producers of polyglutamate, often secreting it as a protective capsule [2].

Bacteria produce polyglutamic acid (PGA) as a strategy to adapt to their environment and enhance their survival. Some reasons why bacteria produce PGA include the following:

Protection and Defense: PGA can act as a protective barrier around bacterial cells, shielding them from harsh environmental conditions such as extreme temperatures, pH fluctuations, and desiccation. This protective function helps bacteria withstand adverse conditions and enhances their chances of survival.

Biofilm Formation: PGA is a key component of bacterial biofilms, which are complex communities of micro-organisms encased in a matrix of extracellular polymeric substances (EPS). Biofilms provide bacteria with protection against antimicrobial agents, immune responses, and other environmental stresses. PGA contributes to the structural integrity and stability of biofilms, facilitating bacterial colonization on surfaces and promoting community interactions.

Nutrient Storage: Bacteria can utilize PGA as a reservoir for storing excess carbon and nitrogen. During periods of nutrient abundance, bacteria produce and accumulate PGA as a means of storing surplus energy and resources. Later, when nutrient availability becomes limited, bacteria can degrade PGA and utilize it as a source of carbon and nitrogen for growth and metabolism.

Virulence and Pathogenesis: In some pathogenic bacteria, PGA production is associated with virulence factors and contributes to the establishment and progression of infections. PGA can facilitate bacterial adherence to host tissues, evasion of host immune responses, and formation of biofilm-associated infections. By promoting bacterial coloniza-

tion and persistence within the host, PGA enhances the pathogenicity of certain bacterial species [10,11].

Environmental Adaptation: Bacteria inhabit diverse ecological niches with varying conditions, and the production of PGA allows them to adapt to different environments. PGA-producing bacteria are found in environments ranging from soil and water to the human body, highlighting the versatility of PGA as an adaptation mechanism.

Overall, the production of PGA by bacteria serves multiple functions that contribute to their survival, adaptation, and interaction with their surroundings. Understanding the roles of PGA in bacterial physiology and ecology is important for elucidating bacterial behavior in natural environments as well as in the context of human health and disease [12–14].

Managing the complexities of PGA biosynthesis can be challenging, particularly in controlling the molecular weight of the chains and the variability of the D/L ratio. These factors significantly influence the polymer's physical structure and behavior.

Polyglutamic acid (PGA) exhibits diverse applications due to its unique properties. For instance, PGA with lower molecular weight serves as a drug carrier and cryoprotectant, while the L-glutamic acid enantiomer, acting as a humectant, is preferred for cosmetic uses. The conformation of PGA can vary between an α-helix, a β-sheet, a helix-to-random coil transition, or an enveloped aggregate, depending on factors like pH and polymer concentration [15]. Given its versatility, PGA finds utility across multiple sectors, including food, cosmetics, pharmaceuticals, and agriculture. Cosmetics, defined as substances applied to external body parts, such as the skin, hair, nails, and mucous membranes within the oral cavity, are designed to enhance appearance, tactile sensation, and overall well-being. These products serve various functions, including cleansing, moisturizing, protecting, and enhancing the natural beauty of these tissues [1,2]. In cosmetics, its ability to retain moisture, form films, and stimulate collagen production is highly valued [16,17]. PGA is incorporated into skincare formulations to enhance hydration, reduce wrinkles, and strengthen the skin barrier against external stressors. In aesthetic procedures, it is used in dermal fillers to smooth wrinkles and other imperfections [18].

Furthermore, PGA has found utility in biomedicine for drug delivery and tissue engineering. It encapsulates and protects bioactive agents, ensuring controlled release and targeted delivery, owing to its biocompatibility and biodegradability. As a result, it can be easily assimilated by living organisms and naturally breaks down over time [19].

PGA's applications extend into agriculture and food science as well. It enhances nutrient uptake and retention in plants, promotes seed germination, and increases crop productivity. In the food industry, PGA serves as an edible and eco-friendly film-forming material for packaging [19].

In summary, polyglutamic acid (PGA) emerges as a versatile biopolymer with unique properties that make it adaptable to a wide range of industries.

2. Microbial Production of Polyglutamate

The fermentation process has emerged as a prominent technique for large-scale poly-γ-glutamic acid (PGA) production. Specific micro-organisms, notably *Bacillus* species such as *Bacillus subtilis* [20–30] and *Bacillus licheniformis* [31–34], are involved in the biosynthesis of PGA. Other PGA-producing bacteria, including *Bacillus paralicheniformis* [35], *Bacillus velezensis* [36,37], and *Bacillus tequilensis* [38], have also been identified. These micro-organisms naturally secrete PGA as an extracellular polymer, often forming protective capsules. Genetic manipulation of these strains has facilitated increased PGA production by exploiting their metabolic pathways [32,38].

During the fermentation process, selected microbial strains are cultivated under controlled conditions in either solid- or liquid-state mediums. The choice of growth medium, temperature, pH, aeration, and other conditions significantly impacts PGA yield. Various researchers have investigated different variables in the fermentation process [39,40].

Solid-state fermentation for PGA production has been explored by Tang et al. [20], Zhang et al. [21], and Liu et al. [36]. Optimal carbon and nitrogen sources and their

concentrations have been studied concerning culture media. For instance, Shi et al. [26] achieved a higher PGA concentration (54.4 g/L) using 60 g/L of sucrose and tryptone. Wang et al. [38] identified sucrose and ammonium sulfate as the best carbon and nitrogen sources, respectively, for improving PGA concentration.

Media supplementation has also been studied. Guo et al. [31] found that the addition of Fe^{2+} improved PGA concentration from 34.886 to 67.891 g/L. Glycerol supplementation was explored by Du et al. [32], who demonstrated that adding glycerol (70 g/L) enhanced PGA concentration from 9.7 g/L to 16.7 g/L, a finding supported by Richard et al. [27]. Moreover, PGA production has been studied with glutamic acid dependency. Xu et al. [25] concluded that *Bacillus subtilis* NX-2 cells are dependent on glutamic acid for PGA production, obtaining a maximum concentration of 30.2 g/L with 30 g/L of glutamic acid in the culture media. Kongklom et al. [41] found similar results, where the addition and concentration of glutamic acid affected PGA production. However, Moraes et al.'s investigation showed PGA production without the need for glutamic acid in culture media [37]. Researchers have also explored the use of agro-industrial residues as carbon and nitrogen sources, including dry mushroom residues [20], chicken manure [21], soybean cake [21], molasses [29,31,37], corn steep liquor [29], and soy sauce [30].

The influence of fermentation conditions (pH, aeration, agitation, and temperature) on PGA production has been studied [27,33]. Cromwick et al. [33] identified pH 6.5 as optimal for PGA production and observed an increase in PGA concentration (from 6.3 to 23 g/L) when the aeration rate was increased from 0.5 to 2 L/min.

Several authors have explored alternative fermentation modes, such as fed-batch culture [28,29,34,38]. Huang et al. [28] reported a 36% increase in PGA concentration using this approach.

After PGA production, recovery and purification from fermentation broths are critical steps. Commonly employed methods include filtration, precipitation, and chromatography for separation and purification purposes.

The table presented below (Table 1) provides a summary of various fermentation conditions investigated for poly-γ-glutamic acid (PGA) production.

Table 1. Different fermentation conditions and culture modes for producing microbial PGA by various micro-organisms in different culture media.

Micro-Organism	Culture Media	Fermentation Conditions	Results	References
Bacillus subtilis NX-2	95.6% *w*/*w* Glycerol Dry mushroom residues (DMR) Monosodium glutamate production residues (MGPR) [DSMR-to-MGPR ratio 12:8 (*w*/*w*)]	pH 7.0 35 °C 65% relative humidity 48 h	116.4 g/kg	[20]
Bacillus subtilis NX-2	30 g/L Glucose 30 g/L L-glutamic acid	37 °C 200 rpm 24 h	30.2 g/L 1.26 g/L/h	[25]
Bacillus subtilis ZC-5	62.35 g Chicken manure 25.15 g Soybean cake 15.09 g Crude extract of glutamic acid after isoelectric crystallization (CEGA)	37 °C >80% relative humidity 48 h	7%	[21]
Bacillus subtilis (natto) strain MR-141	6% Maltose 7% Soy sauce 3% Sodium L-glutamate 3% NaCI	pH 8 40 °C 0.1 vvm: 0–18 h 1 vvm: 18–90 h 400 rpm 90 h	35 g/L	[30]

Table 1. *Cont.*

Micro-Organism	Culture Media	Fermentation Conditions	Results	References
Bacillus subtilis subsp. *natto*	3% L-glutamic acid 2% Citric acid 1% $(NH_4)_2SO_4$	pH 7.0 37 °C 120 rpm 72 h	200 mg/L 10–50 kDa 17 kDa	[22]
Bacillus subtilis natto ATCC 15245	20 g/L L-glutamic acid 50 g/L Sucrose 50 g/L NaCl	pH 6.5 37 °C aeration rate 1 L/min 250 rpm 800 rpm, aeration rate 5 L/min to maintain DO > 40% 96 h	26–28 g/L 6.27×10^2 kDa	[24]
Bacillus subtilis IFO 3335	30 g/L L-glutamic acid 20 g/L Citric acid 20 g/L Glycerol 10 g/L $(NH_4)_2SO_4$	pH 7 37 °C 2 vvm 700 rpm 32 h	23 g/L 3.89×10^3 kDa	[23]
Bacillus subtilis IFO 3335	30 g/L L-glutamic acid 20 g/L Citric acid 10 g/L $(NH_4)_2SO_4$ 20 g/L Glycerol	pH 7 37 °C 2 vvm 700 rpm 30 h	23 g/L	[27]
Bacillus subtilis ZJU-7	30 g/L Glutamate 20 g/L Glucose	pH 6.5 37 °C 1.5 vvm 300–800 rpm to maintain DO > 10% glucose < 3 g/L: fed with glucose solution 46 h	101.1 g/L 2.19 g/L/h	[28]
Bacillus subtilis ZJU-7	60 g/L Sucrose 60 g/L Tryptone 80 g/L L-glutamic acid	pH 7 37 °C 200 rpm 24 h	54.4 g/L 1.24×10^3 kDa	[26]
Bacillus subtilis 242	100 g/L Cane molasses 30 g/L L-glutamate 2 g/L Corn steep liquor	pH 7 37 °C 1.5 vvm 200–600 rpm to maintain DO = 10% fed at 24 h and 34 h with cane molasses and glutamate 48 h	32.14 g/L 27.99 kDa	[29]
Bacillus velezensis CAU263	100 g/kg Sucrose 150 g/kg L-sodium glutamate	37 °C >70% relative humidity 48 h	155.1 g/kg 3.23 g/kg/h 3.8×10^3 kDa	[36]
Bacillus velezensis NRRL B—23189	200 g/L Molasses 12.5 g/L Citric acid 8 g/L $(NH_4)_2SO_4$	pH 6.5 27 °C 200 rpm 72 h	4.82 g/L	[37]

Table 1. *Cont.*

Micro-Organism	Culture Media	Fermentation Conditions	Results	References
Bacillus licheniformis CGMCC3967	Sugarcane molasses (9% soluble solids) 0.7 g/L $FeSO_4 \cdot 7H_2O$ 80 g/L Monosodium glutamate	pH 7.2–7.3 37 °C 1.2 vvm 450 rpm 72 h	76.848 g/L 1.07 g/L·h	[31]
Bacillus licheniformis WBL-3 mutant	10 g/L Citric acid 20 g/L L-glutamic acid 70 g/L Glycerol	pH 6.5 37 °C aeration rate 1.5 L/min 600–800 rpm to mantain DO > 20% 96 h	29.4 g/L	[32]
Bacillus licheniformis ATCC 994514	20.0 g/L L-glutamic acid 12.0 g/L Citric acid 80.0 g/L Glycerol	pH 6.5 37 °C 250 rpm and aeration rate 1.0 L/min: 0–20 h 800 rpm and aeration rate 2.0 L/min: 20–48 h	23 g/L	[33]
Bacillus licheniformis ATCC 9945	75 g/L L-glutamic acid 12 g/L Citric acid 80 g/L Glycerol 7 g/L NH_4Cl	pH 6.5 30 °C 250 rpm 72 h	12.64 g/L 98 kDa	[41]
Bacillus licheniformis ATCC 9945A	20 g/L L-glutamic acid 12 g/L Citric acid 80 g/L Glycerol 7 g/L NH_4Cl	pH 6.5 37 °C 2 vvm 1000 rpm 42 h	35 g/L	[34]
Bacillus tequilensis BL01 engineering strain	30 g/L Glucose 10 g/L Sodium citrate 5 g/L $(NH_4)_2SO_4$	pH 6.5 37 °C aeration rate 10 NL/min 400–700 rpm to mantain DO > 5% sugar < 10 g/L: fed with sucrose solution citric acid < 5 g/L: fed with citric acid solution 30 h	25.3 g/L 2.06×10^3 kDa	[38]
Bacillus paralicheniformis NCIM 5769	50% Sucrose 7% L-glutamic acid monosodium salt monohydrate 1% Citric acid monohydrate 1.5% Ammonium nitrate	pH 7.5 28 °C 1 vvm 250 rpm 72 h	284 g/L 3.94 g/L/h 785 kDa	[35]

3. The Potential of Polyglutamate in Cosmetic Applications

Polyglutamic acid (PGA) is emerging as a potent ingredient in cosmetic formulations, with Regulation (EC) No. 1223/2009 defining cosmetics as products utilized for personal grooming, hygiene, and aesthetic enhancement. This classification encompasses substances applied to various external body parts, including the skin, hair, nails, lips, external genital organs, teeth, and mucous membranes within the oral cavity [14,42].

Cosmetics are formulated to enhance the visual appearance, tactile sensation, and overall well-being of the skin, hair, and nails. These products serve multiple functions such as cleansing, moisturizing, protecting, and enhancing the natural beauty of these tissues. PGA's versatile capabilities have garnered significant attention in the cosmetic industry. Its ability to moisturize the skin, improve skin elasticity, and act as a whitening agent make it an intriguing candidate for incorporation into various cosmetic products. Thus, PGA has been proposed for use in moisturizing creams, anti-aging solutions, and depigmentation formulations [14,42].

Researchers have conducted numerous studies to explore the efficacy of PGA in cosmetic applications, with highly promising results. These studies contribute to the growing body of evidence supporting PGA's potential as a valuable ingredient in cosmetic formulations aimed at enhancing skin health and appearance [14,43].

Polyglutamic acid (PGA) exhibits remarkable versatility in forming films, making it a valuable component in various applications. When dissolved in water, PGA molecules have the ability to self-assemble and form cohesive films on different surfaces. These films possess unique properties that make them suitable for a wide range of uses. PGA films are known for their excellent water solubility and biodegradability, making them environmentally friendly alternatives to traditional plastics. They can be used as coatings to protect surfaces from moisture or as barriers to prevent the penetration of gases and other substances. In the cosmetic industry, PGA films are often utilized in skincare products as occlusive layers to enhance the efficacy of active ingredients and improve skin hydration [11,14,44,45].

Moreover, PGA films have been explored for their potential in drug delivery systems. By encapsulating active compounds within PGA films, controlled release formulations can be developed, allowing for targeted and sustained delivery of therapeutic agents. This application is particularly promising in the pharmaceutical industry for the development of transdermal patches and wound dressings [46,47].

Additionally, PGA films can be engineered to have specific mechanical properties, such as flexibility and strength, depending on the processing conditions and additives used during film formation. This versatility makes PGA films suitable for various industrial applications, including packaging materials, agricultural coatings, and biomedical devices [48–51]. Overall, the films formed from PGA offer a wide range of possibilities in terms of functionality and application, making them a promising material for innovation in multiple industries [52,53].

In fact, the biocompatibility, water solubility, and film-forming characteristics make it an ideal ingredient for cosmetic formulations. Its ability to retain moisture and form protective barriers on the skin enhances skincare and haircare products, offering hydration, protection, and improved texture. Additionally, PGA's compatibility with other ingredients allows for synergistic effects, further amplifying its efficacy in cosmetic applications. Overall, PGA's efficacy stems from its versatile properties, making it a valuable component in various products aimed at enhancing beauty and well-being [14,42,54].

3.1. The Potential of Poly-γ-Glutamic Acid as a Moisturizing and Anti-Aging Agent

Extensive research has delved into exploring the moisturizing potential of poly-γ-glutamic acid (PGA), comparing it with other polymers like hyaluronic acid and collagen. Studies consistently position PGA as an exceptional moisturizing agent, potentially owing to its capacity to stimulate the production of natural moisturizing factors (NMFs) such as pyrrolidone carboxylic acid (PCA), lactic acid, and urocanic acid [28]. These NMFs, synthesized within the deeper layers of the stratum corneum, play a pivotal role in maintaining skin health by ensuring hydration, preventing excessive dryness, and facilitating the natural exfoliation process crucial for smooth and healthy skin [55–59].

Research by Guan-Huel Ho et al. [60], has focused on incorporating gamma-polyglutamate into cosmetics and personal care items to develop cost-effective solutions with superior moisturizing attributes. Their studies evaluated the effectiveness of water retention af-

ter applying various cosmetic formulations to volunteers' skin, with propylene glycol and hyaluronic acid used as control and reference substances, respectively. The results showcased that gamma-polyglutamate formulations exhibited enhanced water retention (45%) for up to 120 min, surpassing both the control (40%) and the reference (36%). Moreover, PGA formulations demonstrated superior effectiveness in enhancing skin hydration compared to glycerol formulations (13.5 vs. 7.5). Importantly, the application of PGA formulations did not cause irritation or rashes, indicating the safety of poly-γ-glutamic acid for human skin [60].

Further studies, such as those conducted by Shin-An Yang et al. [61,62], explored the formulations of cosmetic products containing poly-γ-glutamic acid within specific concentrations and molecular weights. Their results demonstrated that PGA formulations promoted cell growth in fibroblast and keratinocyte cells, indicating biocompatibility and potential wound-healing properties. Additionally, PGA exhibited a significant photoprotective effect against light-induced damage and improved skin texture, elasticity, and collagen content over time [62–65].

Additional investigations by Na-Ri Lee et al. [36], unveiled PGA's potential as a moisturizing agent in facial and hand creams, showing promising results in terms of hydration and antibacterial activity against Gram-positive bacteria. Furthermore, studies by Wen Liangliang [66] shed light on the collaborative impact of PGAs with different molecular weights on skin hydration and barrier enhancement. Results suggested that polyglutamic acid of varying molecular weights could effectively stimulate the production of NMFs and enhance skin barrier function synergistically [67–69].

The impact of different molecular weights of polyglutamic acid (PGA) on the condition of the skin is a subject of interest in cosmetic research. PGA molecules can vary significantly in their molecular weight, and this variation plays a crucial role in determining their effects on the skin [70,71].

Skin Hydration: Studies have shown that PGA of varying molecular weights can influence skin hydration differently. Higher-molecular-weight PGAs tend to form a more occlusive barrier on the skin surface, reducing transepidermal water loss (TEWL) and enhancing skin hydration by preventing moisture evaporation. On the other hand, lower-molecular-weight PGAs may penetrate deeper into the skin layers, where they can bind to water molecules and increase skin hydration from within [10,71].

Barrier Function: The skin barrier is essential for maintaining skin health and protecting against external aggressors. Different molecular weights of PGA can impact the skin barrier function in distinct ways. Higher-molecular-weight PGAs may form a protective film on the skin surface, reinforcing the skin barrier and preventing the entry of harmful substances. Lower-molecular-weight PGAs, meanwhile, may have the ability to penetrate the skin more effectively, where they can interact with skin cells to promote barrier repair and regeneration [72,73].

Stimulation of NMFs: Natural moisturizing factors (NMFs) are substances present in the skin that help maintain hydration levels and support skin barrier function. Studies suggest that PGA of varying molecular weights can stimulate the production of NMFs in the skin. Higher-molecular-weight PGAs may trigger the synthesis of NMFs on the skin surface, while lower-molecular-weight PGAs may penetrate deeper into the skin to promote the production of NMFs within the epidermal layers [10,74].

Overall, the use of PGA with different molecular weights in skincare formulations allows for tailored approaches to address specific skin concerns. By selecting PGA molecules of the appropriate molecular weight, cosmetic formulators can optimize skin hydration, improve barrier function, and promote overall skin health effectively.

Collectively, these findings endorse the use of PGA as an active ingredient in moisturizing and anti-aging creams, underscoring its ability to retain skin moisture, improve elasticity, and promote overall skin health without causing adverse reactions [11,75].

Poly-γ-glutamic acid (PGA) demonstrates significant potential as a moisturizing and anti-aging agent in skincare formulations. Here are some key details about its potential in these areas:

Moisturizing Properties:

PGA possesses an exceptional water-binding capacity, enabling it to attract and retain moisture in the skin. This hydration helps to keep the skin supple, soft, and plump, reducing the appearance of fine lines and wrinkles.

The ability of PGA to stimulate the production of natural moisturizing factors (NMFs) such as pyrrolidone carboxylic acid (PCA), lactic acid, and urocanic acid further enhances its moisturizing properties. These NMFs play a crucial role in maintaining skin hydration and preventing dryness.

PGA's water-soluble nature allows it to form a protective barrier on the skin's surface, minimizing water loss and improving overall skin hydration levels [76].

Anti-Aging Benefits:

Studies have shown that PGA can stimulate collagen production in the skin, leading to improved skin firmness, elasticity, and smoothness. Collagen is a structural protein that helps maintain the skin's youthful appearance by providing support and structure.

PGA's antioxidant properties help to neutralize free radicals, which are molecules that can damage skin cells and contribute to premature aging. By protecting the skin from oxidative stress, PGA helps to prevent the formation of wrinkles, fine lines, and other signs of aging [77,78].

PGA has been found to promote cell growth and regeneration in the skin, accelerating the turnover of old, damaged skin cells and promoting the growth of new, healthy cells. This renewal process helps to improve skin texture, tone, and overall radiance [79,80].

Overall, poly-γ-glutamic acid shows promise as a multifunctional ingredient in skincare formulations, offering both moisturizing and anti-aging benefits. Its ability to hydrate the skin, stimulate collagen production, and protect against oxidative damage makes it a valuable addition to skincare products aimed at promoting youthful, healthy-looking skin [7,9,81–83].

3.2. The Potential of Poly-γ-Glutamic Acid as a Depigmenting Agent

The potential of poly-γ-glutamic acid (PGA) as a skin lightening agent has been a subject of focused investigation. Researchers have found that PGA exhibits the ability to inhibit the activity of the enzyme tyrosinase, which plays a key role in regulating melanin production [55]. The ability of poly-γ-glutamic acid (PGA) to inhibit the activity of the enzyme tyrosinase can vary in percentage depending on factors such as concentration, experimental conditions, and the specific study being referenced [84,85].

In a study by Liu et al. [38], the inhibitory effects of PGA of various molecular weights on tyrosinase enzyme activity and melanogenesis were explored. Their findings revealed that PGA could effectively inhibit tyrosinase activity and melanogenesis in B16 melanoma cells. Notably, the polymer was observed to decrease levels of reactive oxygen and nitric oxide species while increasing the activity of catalase in these cells. The authors suggested that low-molecular-weight PGA could be particularly promising as a depigmenting agent, as it demonstrated the ability to suppress melanogenesis without stimulating B16 cell proliferation. This suggests a potential role for PGA in addressing hyperpigmentation concerns and promoting even skin tone.

3.3. Poly-γ-Glutamic Acid's Potential in Sunscreens

In the realm of cosmetics, sunscreens play a crucial role in safeguarding skin health and preserving its youthful appearance. They serve as a vital defense against sun-induced damage, premature aging, and other undesirable effects, significantly contributing to the overall vitality and aesthetics of the skin [86–88].

Recognizing the importance of sunscreen safety, Guo Tian [39] embarked on the development of a novel formulation incorporating polyglutamic acid sunscreen peptides. This

innovation stemmed from concerns regarding the potential toxicity associated with traditional small-molecule sunscreens. These molecules, characterized by their low molecular weight, possess the ability to penetrate the skin, raising the possibility of adverse effects. Guo Tian's invention addresses this concern by designing sunscreen peptides with a higher molecular weight, thereby minimizing the risk of skin absorption and toxicity [89,90].

Despite the higher molecular weight, the sunscreen peptides retain their efficacy in absorbing UV radiation, aligning with the UV absorption range of conventional small-molecule sunscreens. This ensures that their protective capabilities against harmful UV rays remain uncompromised, offering a viable and safer alternative for shielding the skin from the sun's detrimental effects. By prioritizing safety without compromising effectiveness, this innovative formulation represents a significant advancement in sunscreen technology, promising enhanced skin protection and peace of mind for consumers [91].

3.4. Exploring Poly-γ-Glutamic Acid's Potential in Treating Skin Damage

The concept of skin damage encompasses a wide array of conditions, spanning from the adverse effects of allergies and inflammation to the regenerative processes involved in wound healing. In this context, the potential use of poly-γ-glutamic acid (PGA) as an active agent in treating skin damage has been extensively explored.

Moon Hee Sung et al. [60] conducted research highlighting PGA's ability to ameliorate allergic responses. Their findings indicated that PGA effectively prevented the permeability of inflammatory cells, a critical step in attenuating allergic manifestations. Sensory tests involving 15 children with atopic dermatitis further validated these findings, with the use of PGA-infused shampoo providing noticeable relief for 8 of the children.

In parallel, research by Zeng Rong provided insights into PGA's anti-inflammatory potential. Gel film formulations incorporating crosslinked PGA demonstrated significant efficacy in suppressing the expression of TNF-α, a key regulator of inflammatory reactions [32]. This underscores the multifaceted utility of PGA, suggesting its potential as a modulator of crucial molecular mechanisms associated with skin inflammation.

Moreover, PGA has shown promise in wound healing applications [61], which entail sequential stages including hemostasis, inflammation, proliferation, and tissue reconstruction. Studies have revealed PGA's effectiveness in promoting the growth of fibroblasts and collagen production, thus positioning it as a viable option for wound healing interventions. Wai-Ching Liu et al. [92] explored the use of PGA hydrogels for wound healing treatment, observing accelerated wound contraction, formation of new blood vessels, collagen fibers, granulation tissues, hair follicles, and capillaries.

Chi Bo et al. [93] investigated the potential applications of multi-polyglutamic acid cross-linked polymers in skin repair. Their comprehensive experiments evaluated the antioxidant attributes, biocompatibility, and blood compatibility of these polymers, revealing significant moisturizing, antioxidant, and tissue compatibility properties. These findings suggest the broad applicability of cross-linked polyglutamic acid polymers in various skin tissue-related applications.

Furthermore, Mei-Hua Huang et al. [94] explored a novel approach to wound care by developing sodium alginate/polyglutamic acid hydrogels for use as wound dressings. The hydrogel exhibited non-toxicity against fibroblast and pulmonary cells, promoted blood coagulation and platelet adhesion, and demonstrated notable fluid retention, making it suitable for moist wound healing.

In conclusion, the multifaceted potential of poly-γ-glutamic acid (PGA) in addressing various aspects of skin damage is increasingly evident through rigorous scientific investigations. This underscores its potential as a versatile therapeutic agent in the field of dermatology and wound care.

3.5. The Potential of Poly-γ-Glutamic Acid in Haircare

The versatility of poly-γ-glutamic acid (PGA) extends beyond skincare into the realm of hair care, offering promising benefits for enhancing hair health and appearance. This

biopolymer's unique characteristics, including its humectant properties, moisture retention abilities, and biocompatibility, position it as a compelling candidate for addressing various hair-related concerns. The multifaceted advantages of PGA in hair care have garnered significant attention, prompting thorough investigations and cementing its role in this domain [81,95].

An innovative study by Hasebe Kohei et al. [46] introduced a novel cosmetic product that combined polyhydric alcohol with poly-γ-glutamic acid (PGA), designed for application on both hair and skin. While polyhydric alcohol is renowned for its humectant and hydrating effects, its application to hair has often been associated with discomfort due to stickiness and tingling sensations. To overcome these drawbacks, researchers formulated blends of polyhydric alcohols and PGA. Subsequent sensory evaluations and safety assessments revealed no instances of skin irritation or inflammation post-application. Moreover, these formulated blends effectively alleviated the stickiness and tingling sensations commonly experienced with polyhydric alcohols when applied to hair, while demonstrating notable moisturizing benefits for both hair and skin. Thus, this research underscored the potential of incorporating polyhydric alcohol and PGA into cosmetic formulations to address hair and skin care needs simultaneously [96–99].

Furthermore, studies have explored PGA's potential in stimulating cell growth and promoting healing processes, particularly in the management of alopecia. Alopecia, characterized by hair loss, poses significant challenges with physical and psychological ramifications. Choi et al. [100] found that high-molecular-weight PGA exhibited inhibitory effects on the 5-alpha reductase enzyme, suggesting its potential utility in addressing androgenetic alopecia in men. Notably, PGA demonstrated efficacy in promoting hair growth, with more than 50% of shaved skin exhibiting hair regrowth within four weeks, outperforming the control group treated with minoxidil. These findings highlight the promising role of PGA in addressing hair loss concerns, offering potential solutions for individuals grappling with alopecia.

3.6. The Potential of Poly-γ-Glutamic Acid in Dental Care

The exploration of Gamma-PGA-based toothpastes represents a significant area of research, offering promising avenues for innovative, natural, and effective oral care solutions. The inclusion of PGA in toothpaste formulations holds immense potential due to its multifaceted benefits, ranging from its anti-allergenic properties to its whitening and oral health-enhancing effects, thereby making it a compelling ingredient for modern oral care products. A seminal study by Qiao Changsheng et al. [101] delved into the development of an oral hygiene toothpaste aimed at nurturing the oral cavity, enhancing teeth whitening, restoring oral microbial balance, and preventing oral health issues. Beyond these primary objectives, the innovation also boasted additional advantages, including prolonged action time and the non-toxic nature of glutamic acid, a byproduct of PGA degradation.

The formulated toothpaste exhibited notable efficacy in promoting oral health and hygiene, contributing to the maintenance of overall oral well-being. By addressing various aspects of oral care, such as microbial balance, teeth whitening, and oral cavity nourishment, the PGA-infused toothpaste emerged as a comprehensive solution for individuals seeking effective and natural oral care alternatives.

Moreover, the extended action time of the toothpaste ensured sustained benefits, providing prolonged protection and oral care support throughout the day. Importantly, the non-toxic nature of glutamic acid, derived from PGA degradation, underscored the safety profile of the toothpaste formulation, further enhancing its appeal as a reliable and health-conscious oral care option.

Overall, the study shed light on the potential of Gamma-PGA-based toothpastes to revolutionize oral care practices, offering a holistic approach to oral hygiene that combines effectiveness, safety, and natural ingredients [102,103].

3.7. Polyglutamic Acid Skincare Products in the Market

According to a report by the QYResearch Group [104], the global polyglutamic acid (PGA) market reached a value of approximately USD 441.19 million in 2023. Projections suggest a Compound Annual Growth Rate (CAGR) of 7.41% from 2023 to 2029, leading to an estimated market valuation of around USD 677.54 million by 2029. This growth trend is primarily fueled by the increasing demand for PGA across various industries, particularly in skincare.

Polyglutamic acid (PGA) has garnered rising popularity in skincare due to its exceptional hydrating and moisturizing properties. It serves as an active ingredient in skincare products aimed at improving skin hydration, refining texture, and enhancing overall appearance. PGA is frequently incorporated into serums and moisturizers for its ability to retain water, ensuring sustained skin hydration. Its inclusion in makeup primers and setting sprays helps create a smooth makeup base and prolongs makeup wear while preserving skin moisture. Moreover, PGA's efficacy in enhancing skin texture and moisture makes it a valuable component in anti-aging products targeting fine lines and wrinkles.

One notable skincare product featuring PGA is Charlotte's Magic Serum Crystal Elixir, which underwent testing on 209 individuals aged 18–80 over a 4-week period. User trial results revealed positive outcomes, with 93% reporting younger-looking skin, 97% experiencing intense hydration, 91% noticing refined pores, 91% observing reduced lines and wrinkles, 94% experiencing firmer skin, and 91% noting lifted contours. Clinical studies, conducted over 8 weeks with 31 participants aged 18–80, further demonstrated significant benefits, including a 172% increase in skin hydration after 1 h, a 43% reduction in water loss after 1 h, 24 h moisturization, a 122% improvement in skin elasticity, a 49% increase in firmness, a 34% reduction in wrinkles, and a 39% decrease in pore appearance [105].

Another noteworthy raw material is Twainmoist by Sollice Biotech (Toulouse, France), known for its significant effects on the skin when incorporated into cosmetic formulations. This ingredient has been shown to elevate hyaluronic acid levels and enhance natural moisturizing factors. Clinical efficacy tests have demonstrated its effectiveness in increasing skin hydration and firmness, reducing water loss, and even decreasing wrinkle depth by up to 35% [106].

The table provided below (Table 2) outlines several skincare products containing PGA currently available in the cosmetic market.

Table 2. Skincare products containing PGA available in the cosmetic market and their functions.

Trademark	Skin Care Product	Benefits
REN Clean Skincare	Perfect Canvas Smooth, Prep And Plump Essence	Offers anti-pollution defense for fortified skin barrier; acts as skin primer.
Dr. Jart	Cicapair Tiger Grass Re. Pair Serum	Soothes redness, moisturizes, protects from environmental stressors; minimizes pore visibility.
TULA SKINCARE	24-7 Ultra Hydration Triple-Hydra Complex Day & Night Serum	Aids in smoothing wrinkles and fine lines.
dermalogica	Circular Hydration Serum	Promoting long-lasting hydration.
111Skin	The Hydration Concentrate	Moisturizes and prevents excess water loss through skin.
The INKEY List	Polyglutamic Acid Serum	Promotes hydration and reduces the visibility of fine lines.
The INKEY List	Polyglutamic Acid Dewy Sunscreen Spf30	Offers full UVA and UVB protection against sun's rays.
Collistar	Hyaluronic And Polyglutamic Acid	Offers multi-level hydration.

Table 2. *Cont.*

Trademark	Skin Care Product	Benefits
Charlotte Tilbury	Charlotte's Magic Serum Crystal Elixir	Enhances hydration, elasticity, and firmness; diminishes wrinkles and pores.
Viviology	Ceramide Moisturiser	Moisturizing, soothing and calming product.
KATE SOMERVILLE	Dermalquench Wrinkle Warrior Advanced Hydrating And Plumping Treatment	Combats wrinkles, sagging, uneven tone; ensures unmatched hydration.
Sollice Biotech	Twainmoist®	Delivers hydration, firmness, and vitality.
Good Molecules	B5 Hydrating Body Serum	Preserves moisture, fortifies skin barrier.

4. Conclusions

In conclusion, the integration of polyglutamic acid (PGA) in the cosmetic industry represents a promising frontier, owing to its remarkable biocompatibility, water solubility, and film-forming properties. These characteristics render PGA an attractive ingredient for a wide array of cosmetic formulations, offering significant potential for innovation and product development.

Looking ahead, the trajectory of PGA research encompasses a multifaceted approach aimed at maximizing its utility and efficacy in cosmetic applications. Further optimization of fermentation processes, exploration of novel microbial strains, and advancements in genetic engineering techniques present opportunities for enhancing PGA production yields. By refining these methodologies, manufacturers can meet the escalating demand for PGA in skincare, haircare, and other cosmetic products.

In the realm of cosmetic applications, comprehensive studies are essential to elucidate PGA's performance across various formulations, ensuring its stability and compatibility with other cosmetic ingredients. Understanding the synergistic interactions between PGA and other components can unlock its full potential, enabling the creation of innovative and effective skincare and haircare solutions.

Moreover, as sustainability becomes increasingly pivotal in the cosmetics industry, future research endeavors should prioritize environmental considerations and sustainable practices. Aligning PGA production processes with eco-friendly principles not only mitigates environmental impact but also resonates with consumer preferences for sustainable and responsibly sourced ingredients.

Navigating the intersection of biotechnology and cosmetics, the ongoing exploration of PGA's capabilities holds significant promise for meeting industry demands for sustainable, effective, and eco-conscious cosmetic ingredients. By leveraging PGA's unique properties and advancing scientific understanding, the cosmetic industry can continue to innovate and evolve, offering consumers products that are both efficacious and environmentally responsible.

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