

## POLY-GAMMA-GLUTAMIC ACID: A COMPREHENSIVE OVERVIEW OF BIOSYNTHESIS, CHARACTERISTICS, AND EMERGING APPLICATIONS

Mohammed Jabbar Hafiz Al-wahili, Alaa Jabbar Abd Al-Manhel\*, Rawdah Mahmood Al-Ali, Ammar B. Altemimi\*

### Address(es):

Department of Food Science, College of Agriculture, University of Basrah, Basrah 61004, Iraq.

\*Corresponding author: [alaa.abd@uobasrah.edu.iq](mailto:alaa.abd@uobasrah.edu.iq)

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### ABSTRACT

Poly-gamma-glutamic acid (PGA) is a naturally occurring biopolymer that has been receiving increasing attention in various fields, including the food, medical, and cosmetic industries. This review provides a comprehensive overview of PGA, discussing its biosynthesis, characteristics, and emerging applications. The biosynthesis of PGA is discussed in detail, highlighting the various microorganisms that are capable of producing PGA and the factors that affect its production. The structure and molecular weight of PGA are also described, as well as its solubility and biodegradability. These properties make PGA a highly versatile material that can be utilized in a wide range of applications. The review also provides an in-depth analysis of the emerging applications of PGA. In the food industry, PGA has been used as a natural preservative, a thickener, and a flavor enhancer. In the medical field, PGA has shown promising results as a drug delivery system and a scaffold for tissue engineering. The challenges and future directions for the production and utilization of PGA are also discussed. This review article covers key aspects, including production process optimization, property improvement, and exploration of novel applications for PGA. It serves as a valuable resource for researchers and industry professionals who wish to explore the potential of PGA in diverse applications. The exceptional properties of PGA make it highly appealing, with a broad spectrum of potential uses across multiple industries.

**Keywords:**  $\gamma$ -PGA, biosynthesis, glutamic, Industrial applications, regulation

### INTRODUCTION

Poly-gamma-glutamic acid ( $\gamma$ -PGA) is a type of biopolymer that is made up of monomers of D- and/or L-glutamic acid linked together by peptide bonds. It is typically found in nature and has several desirable properties, including water solubility, edibility, biodegradability, and a lack of immunogenicity (Li *et al.*, 2022).  $\gamma$ -PGA is produced by certain strains of Bacillus bacteria through a fermentation process. This homogenous polyamide is both edible and environmentally safe for humans to use. The  $\gamma$ -PGA molecules are made up of amide linkages between the gamma carboxyl and alpha amino groups, resulting in a unique chemical structure (Mitsunaga *et al.*, 2016; Bajaj and Singhal, 2011). The process of microbial synthesis is a highly efficient and cost-effective method for producing poly-gamma-glutamic acid ( $\gamma$ -PGA) (Tamang *et al.*, 2016). Producers of  $\gamma$ -PGA can be found among bacteria, archaea, and eukaryotes (Kumar *et al.*, 2023). Once the bacteria have produced the  $\gamma$ -PGA, the biopolymer must be extracted from the submerged culture (Azarhava *et al.*, 2020). This extraction process typically involves four main steps. First, the culture is centrifuged to create a cell-free supernatant. Next, heavy-weight  $\gamma$ -PGA is precipitated using an alcohol such as ethanol, at a ratio of one to three volumes. After this, the crude  $\gamma$ -PGA solution is dialyzed against a dialysis tube to remove low molecular weight impurities. Finally, deproteinization and ion-exchange chromatography are utilized to purify the PGA even further (Azarhava *et al.*, 2020).

The  $\gamma$ -PGA has a wide range of applications in various fields, including food processing (Guo *et al.*, 2023), Agriculture (Shi *et al.*, 2023), medicine (Zhang *et al.*, 2023), cosmetics (Liu *et al.*, 2023), and environmental protection (Peng *et al.*, 2020). The food industry has utilized  $\gamma$ -PGA as a food additive and preservative owing to its ability to improve food texture and stability (Hu *et al.*, 2021), and its antimicrobial properties (Lee *et al.*, 2019). Moreover, it has been demonstrated to enhance the solubility of specific food ingredients and to enhance the quality of meat products (Lim *et al.*, 2023). In agriculture,  $\gamma$ -PGA has been applied as a plant growth promoter due to its ability to enhance seed germination, increase plant growth, and improve stress tolerance in crops (Mi *et al.*, 2022; Zhang *et al.*, 2017). The potential applications of  $\gamma$ -PGA in the medical field include drug delivery, wound healing, and tissue engineering. Its biodegradability, biocompatibility, and capability to encapsulate drugs make it a promising delivery vehicle for therapeutic agents (Balogun-Agbaje *et al.*, 2021; Hsieh *et al.*, 2005). Due to its ability to enhance skin elasticity and retain moisture,  $\gamma$ -PGA has been employed as a moisturizing agent, skin conditioner, and anti-aging ingredient in cosmetics (Chen

*et al.*, 2020). The  $\gamma$ -PGA has also been investigated for its potential to eliminate heavy metals and pollutants from wastewater due to its chelating properties and biodegradability, which makes it an ideal candidate for environmental protection purposes (Liu *et al.*, 2022). The diverse applications of  $\gamma$ -PGA make it a promising biopolymer with significant potential for further research and development in various fields.

The aim of this review was to offer a thorough summary of the biosynthesis and features of  $\gamma$ -PGA, along with investigating its potential applications in medical, food, and environmental industries. Furthermore, the review aims to examine the present challenges and future possibilities for utilizing  $\gamma$ -PGA in various domains. It provides an updated analysis of current research and recent advancements in  $\gamma$ -PGA, identifies knowledge gaps, and proposes areas for future investigation.

### REVIEW METHODOLOGY

The researchers performed an extensive literature search using two databases, namely Web of Science and Scopus, which are based in London, UK, to gather information. They used the search terms "Poly-gamma-glutamic acid ( $\gamma$ -PGA)" and narrowed the search to the subtopic of "Food," as outlined in Figure 1. Web of Science was preferred due to its collection of articles, indexed journals, and user-friendly interface. The initial search for "Poly-gamma-glutamic acid ( $\gamma$ -PGA); biosynthesis, glutamic" yielded 2064 articles, with 1324 articles published since 2013. By including the keyword "food, agriculture" the search resulted in 423 articles published between 2000 and 2023, with 175 articles published since 2000. The figures shown in Figure 1 indicate a considerable rise in the application of  $\gamma$ -PGA in the food sector over the last 25 years. There is a noticeable increase in attention towards the Poly-gamma-glutamic acid ( $\gamma$ -PGA) aspect from 2000 to 2023, and a much more prominent growth in publications (nearly five per year) from 2015 to 2023.