

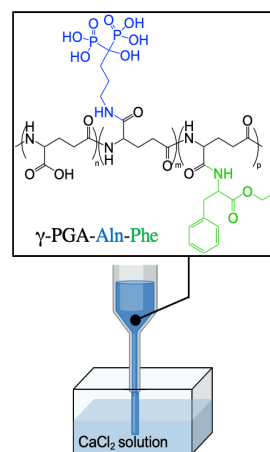
## Synthesis of Alendronic acid and Phenylalanine conjugated Poly( $\gamma$ -Glutamic) acid for 3D bioprinting

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**Keywords:** poly( $\gamma$ -glutamic) acid, alendronic acid, phenylalanine, 3D bioprinting, tissue engineering

Tissue damage and organ shortage continue to be major problems across the world. In the past decade, to meet the tremendous need for tissues and organs, tissue engineering was developed with the aim of fabricating artificial tissues. Three-dimensional (3D) bioprinting technologies are one of the emerging technologies, having high potential to fabricate complex and sophisticated 3D tissue constructs. Regarding the fabrication of 3D structures, one of the challenging aspects is the bioinks' properties. Since the printed materials are required to have cell adhesion, cytocompatibility and printability, the key challenge is to provide bioink that meets all of these requirements.

In this study, poly( $\gamma$ -Glutamic) acid ( $\gamma$ -PGA) was chosen as the main polymeric backbone for the bioink.  $\gamma$ -PGA has high water solubility, biocompatibility, and biodegradability, however, it cannot form a gel or self-supporting structure alone. Inspired by previous studies, a highly stretchable hydrogel conjugating of alendronic acid (Aln) on a biodegradable polymer backbone was successfully formed via ionic crosslinking between the negatively charged bisphosphonate groups and positively charged calcium ions present in a calcium chloride solution<sup>1</sup>. Due to its rapid crosslinking, the stability and ability to extrude this hydrogel using a bioprinter are hard to control. Herein,  $\gamma$ -PGA based hydrogel composed of bisphosphonate moieties and L-Phenylalanine (Phe) group ( $\gamma$ -PGA-Aln-Phe) was synthesized (**Figure 1**) Aln having bisphosphonate moieties will allow crosslinking to occur in solutions containing calcium ions. At the same time, the presence of the hydrophobic Phe groups will enhance polymer assembly by their hydrophobic interaction in aqueous solution<sup>2</sup>. In this conference, we will discuss the effect of grafting degree of Aln and Phe for printability against calcium ion concentration in the bath solution.



**Figure 1.** Schematic of  $\gamma$ -PGA-Aln-Phe polymer extrusion in calcium chloride solution

<sup>1</sup>M. Nakamoto et al., *Mater. Today Bio.* **2022**, *14*, 100225.

<sup>2</sup>M. Matsusaki et al. *Chem. Lett.* **2004**, *33*, 398-399.