Marine origin methacrylated gelatine (mGelMA)-based hydrogels and its application in tissue engineering

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INTRODUCTION

Marine organisms are constituted by materials with a vast range of properties and characteristics that may justify their potential application within the biomedical field and have been receiving increasing attention as they are free from the transmissible diseases associated with the use of mammalian resources, as well as the fact that they enable high production at a low cost.[1, 2]

Gelatine (Figure 1) is derived from the fibrous protein collagen, which is the principal constituent of animal skin, bone, and connective tissue, by denaturation and often partial hydrolysis.[3] It is applied in many industrial sectors, from food to pharma, and particularly in biomedical context can be utilized in tissue engineering/regenerative medicine for the development of scaffolds.[4]

Gelatine can be combined with methacrylic anhydride to give origin to methacrylated gelatine (GelMA), enabling the formation of hydrogels and 3D printing upon photocrosslinking.[5]

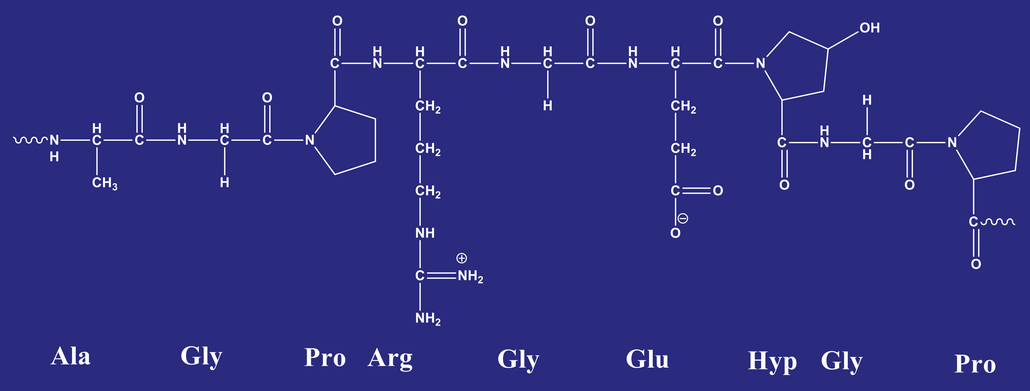

Figure 1 – Typical structure of gelatine.

AIMS

Since methacrylation occurs mainly with gelatine from mammals, the aim of this project is to develop an effective method for the production of marine origin methacrylated gelatine. To accomplish this, the first goal is the isolation of gelatine from fish skin (obtained as by-product from industry), as valorization strategy with environmental and socio-economic benefits, and the second goal is to establish an effective methacrylation methodology.

The ultimate objective of this work is to extend the application of fish gelatine to tissue engineering, particularly as component of (bio)inks for 3D bioprinting.

METHODS

Production of gelatine from cod fish skins

- Pretreatment with sodium hydroxide (0.04M)
- Wash with acidic solutions, namely, sulfuric acid (0.12M) and citric acid (0.005M)
- Extraction with hot water, promoting the partial hydrolysis of native collagen, involving the breaking of the triple-helix structure into random coils (figure 2).[6]

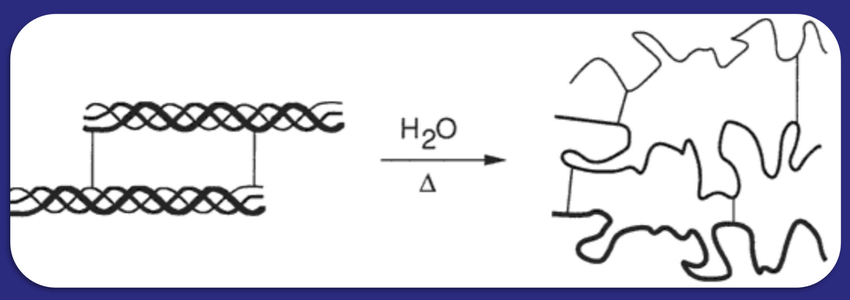

Figure 2 – Denaturation of collagen to obtain gelatine.

Physical and chemical characterization

- SDS-Page
- isoelectric point determination
- amino acid analysis
- characterization of rheological properties

Functionalization of gelatine with methacrylate groups

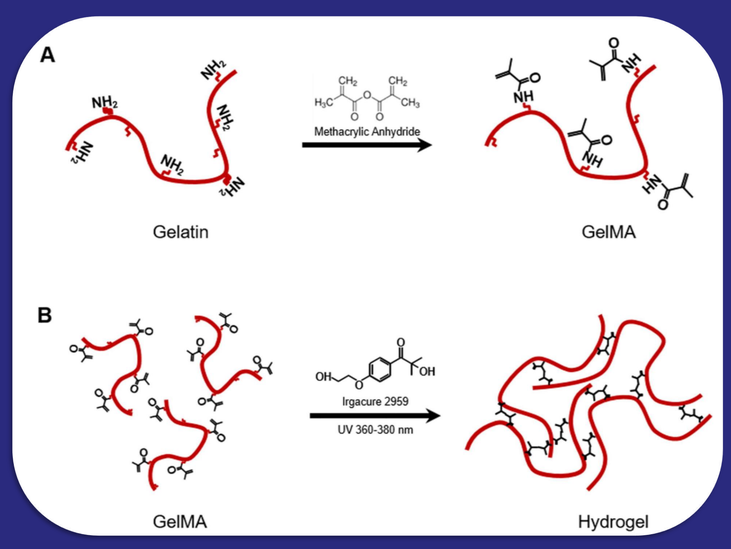

Figure 3 – (A) Gelatine will be reacted with methacrylic anhydride to introduce a methacryloyl substitution group on the reactive amine and hydroxyl groups of the amino acid residues. **(B)** GelMA photocrosslinking to form a hydrogel matrix under UV irradiation. The free radicals generated by the photoinitiator initiated chain polymerization with methacryloyl substitution.[7]

FUTURE PRESPECTIVES

The establishment of effective and reproducible methods for the gelatine extraction will represent a strategy for sustainable valorization of fish skins (industrial by-products).

The isolated compounds can be alternatives to their mammal counterparts, finding application in high-value products for the health, cosmetic and industrial biomaterials sectors.

For the future, the survival and proliferation of cells in culture onto or into the developed multicomponent hydrogels will be investigated, to support the use of mGelMA as component of (bio)inks enabling the biofabrication of 3D constructs for personalized tissue regeneration.

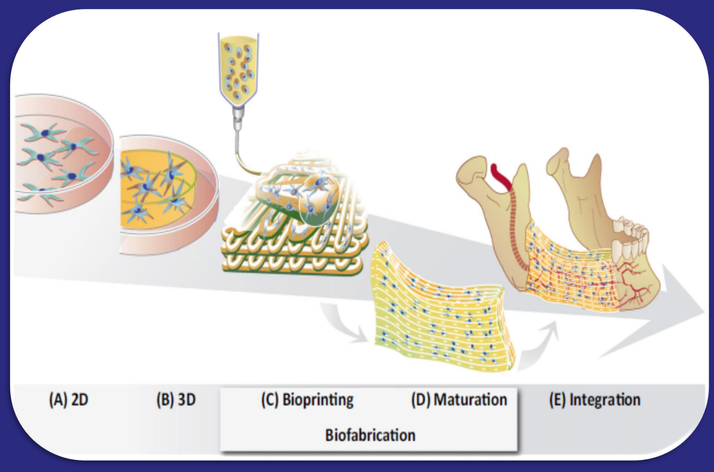

Figure 4 – Evolutionary stages from 2D Cell Culture to the Development of 3D Tissue Analogs.

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Acknowledgments

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