Marine origin biopolymers on the development of hydrogels for articular cartilage tissue engineering: processing methodologies and main characteristics

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Introduction & Aims

In the recent decade, marine origin products have been growingly studied as building blocks complying to the constant demand from the biomedical sector for new materials regarding the development of improved devices for clinical applications and new therapeutical approaches [1, 2]. The advantages of marine products are the reduction or elimination of risks associated with zoonosis, as well as overcoming social/religious-related constraints when compares to the mammal sources for some compounds [3]. Moreover, their production methodologies are commonly associated to low-cost processes, corresponding in many cases to valorization of by-products, with inherent environmental and economic benefits [4].

In this project, marine proteins and polysaccharides are being combined using different processing methodologies, rendering hydrogels with a wide range of homogeneity degree, cohesiveness and rheological properties. The more compliant formulations regarding handling and structural stability are being further characterized, namely regarding their capacity to support cell culture and encapsulation, envisaging cartilage regeneration strategies, including less invasive approaches as injectable biomaterials.

Tissue Engineering: Strategies & Applications

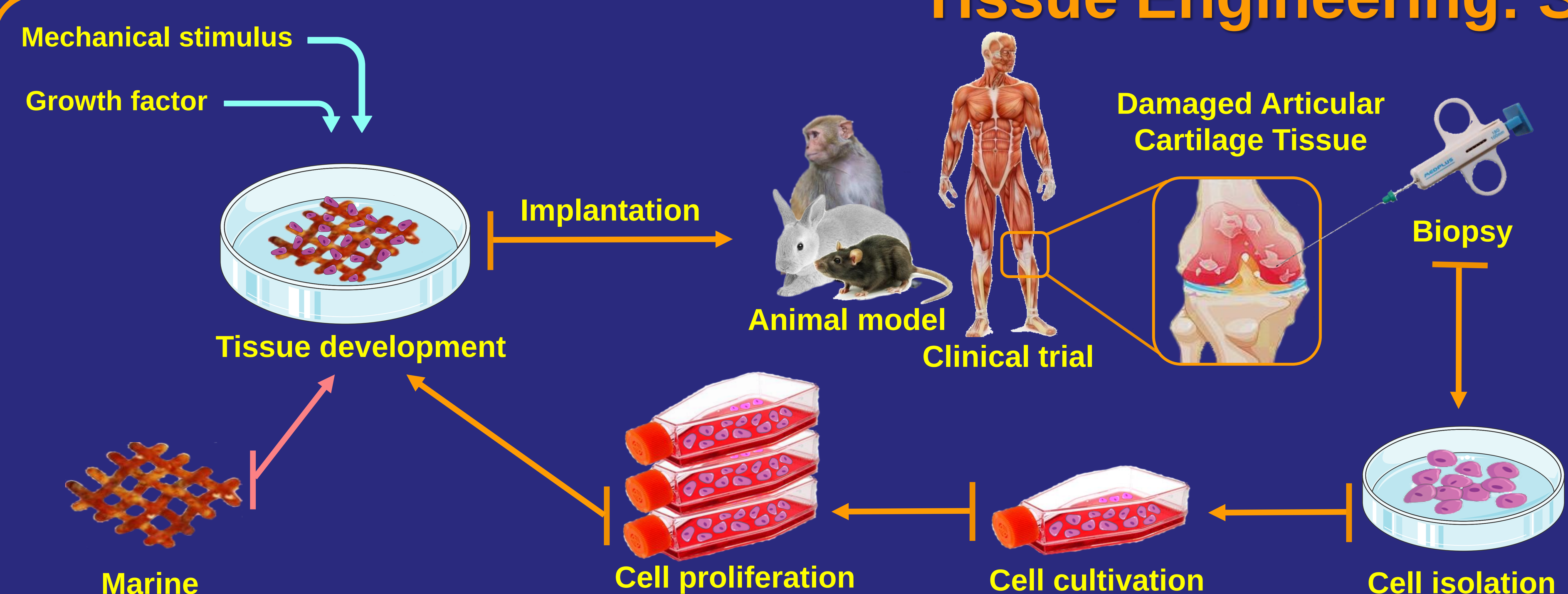

Figure 1. Schematic representation of the general strategy of tissue engineering regarding the treatment to regenerate the damaged cartilage tissue and recover the respective function.

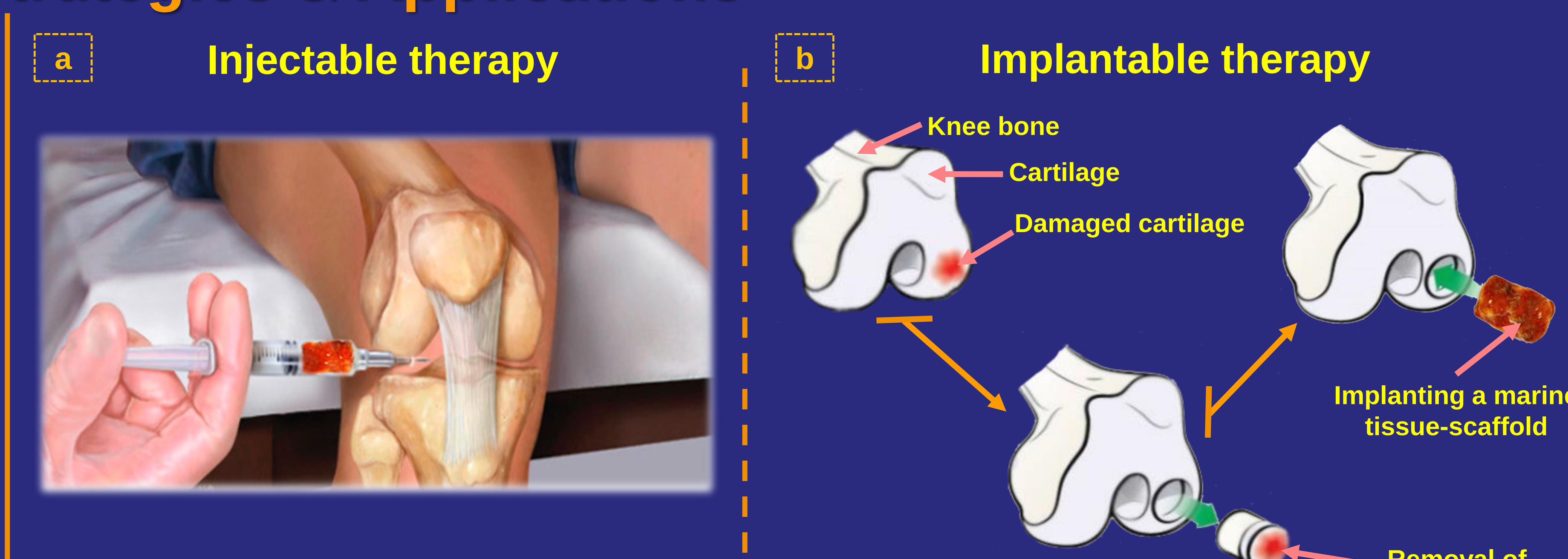

Figure 2. Schematic representation of two different treatments using marine biomaterials to regenerate the damaged cartilage tissue. The image a) represents the injectable therapies (less painful for the patient) and the image b) demonstrate the surgery procedure, its possible to remove the damaged tissue and implanted the new tissue-scaffold.

Methodologies

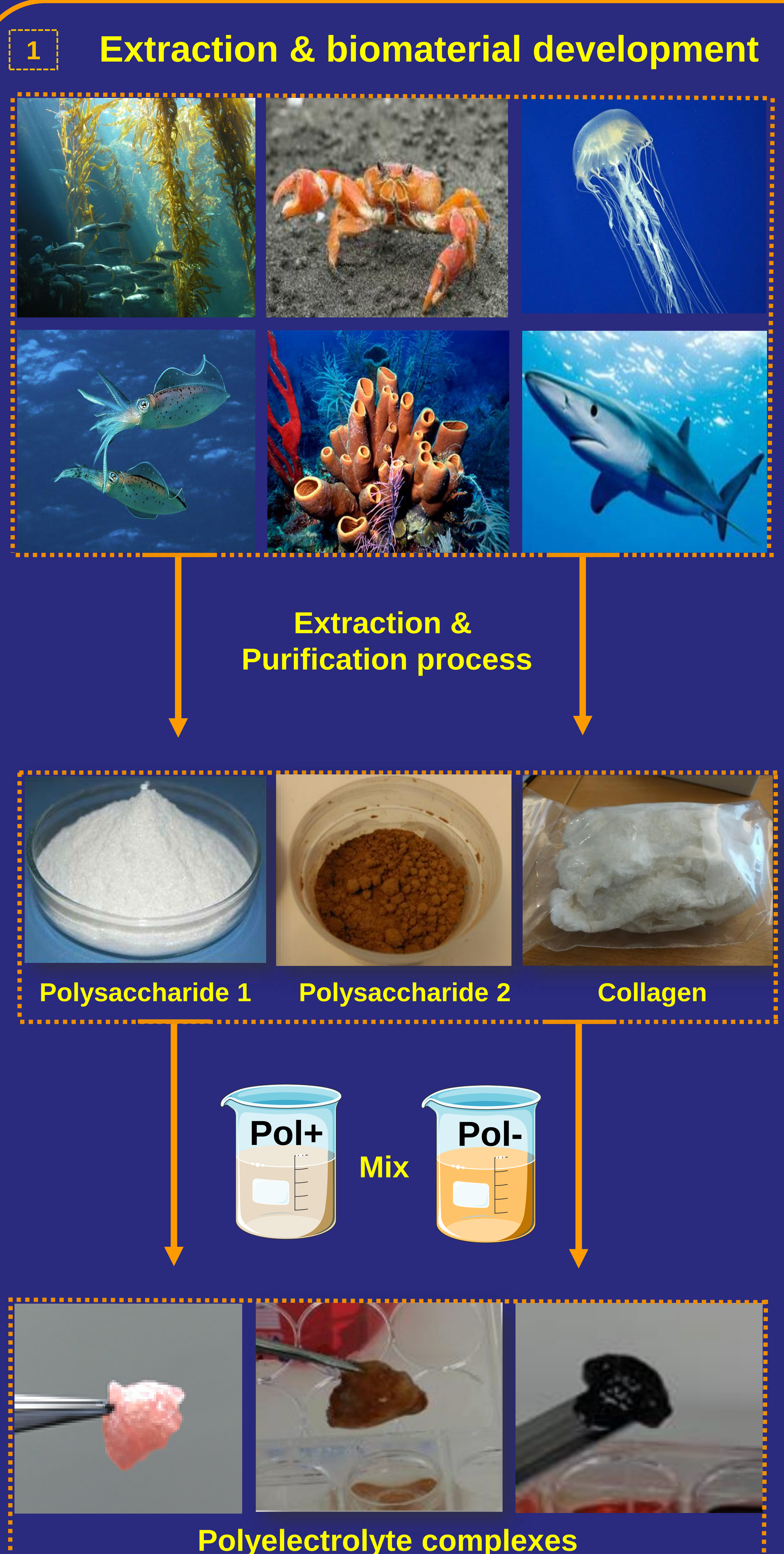

Figure 3. Schematic representation of the biopolymers extraction from different marine sources and the development of new biomaterials using polyelectrolyte procedures which promote the natural cross-linking.

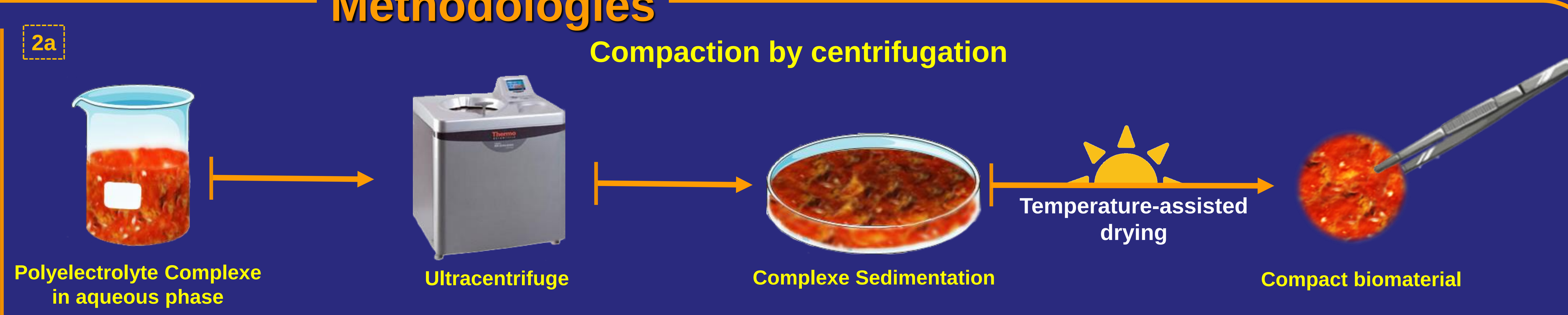

Figure 4. Schematic representation of the compaction procedure by centrifugation. The process compacts the polymers and removes the wastewater, create a biomaterial membrane.

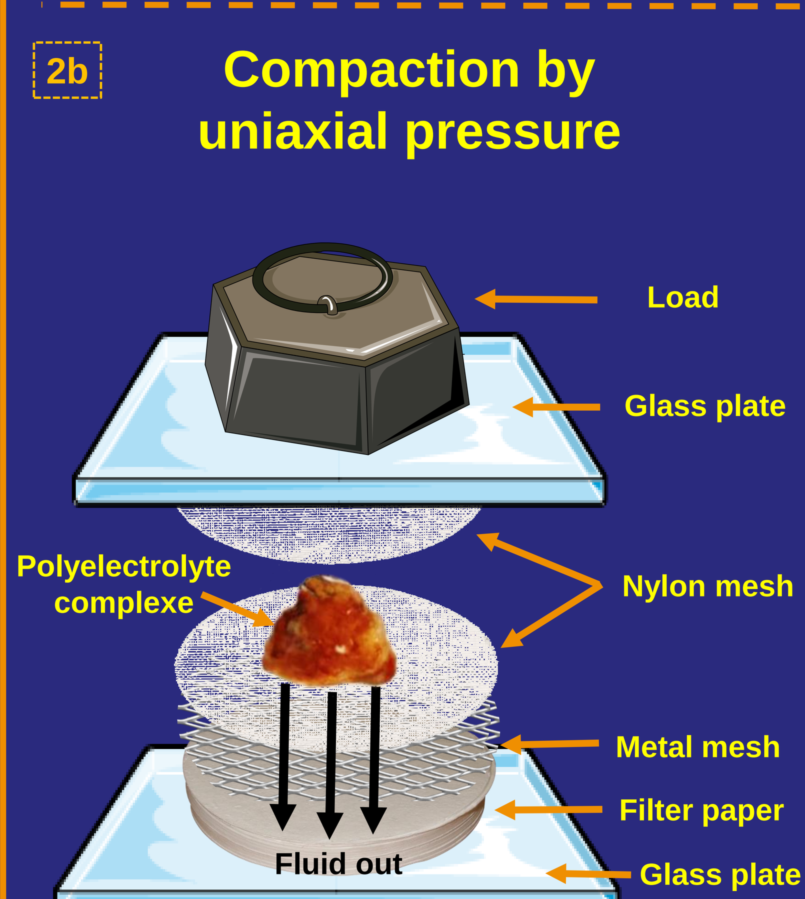

Figure 5. Schematic representation of the compaction procedure by uniaxial pressure. The load press the biomaterial forcing the wastewater to flow out, promoting natural cross-linking between polymers.

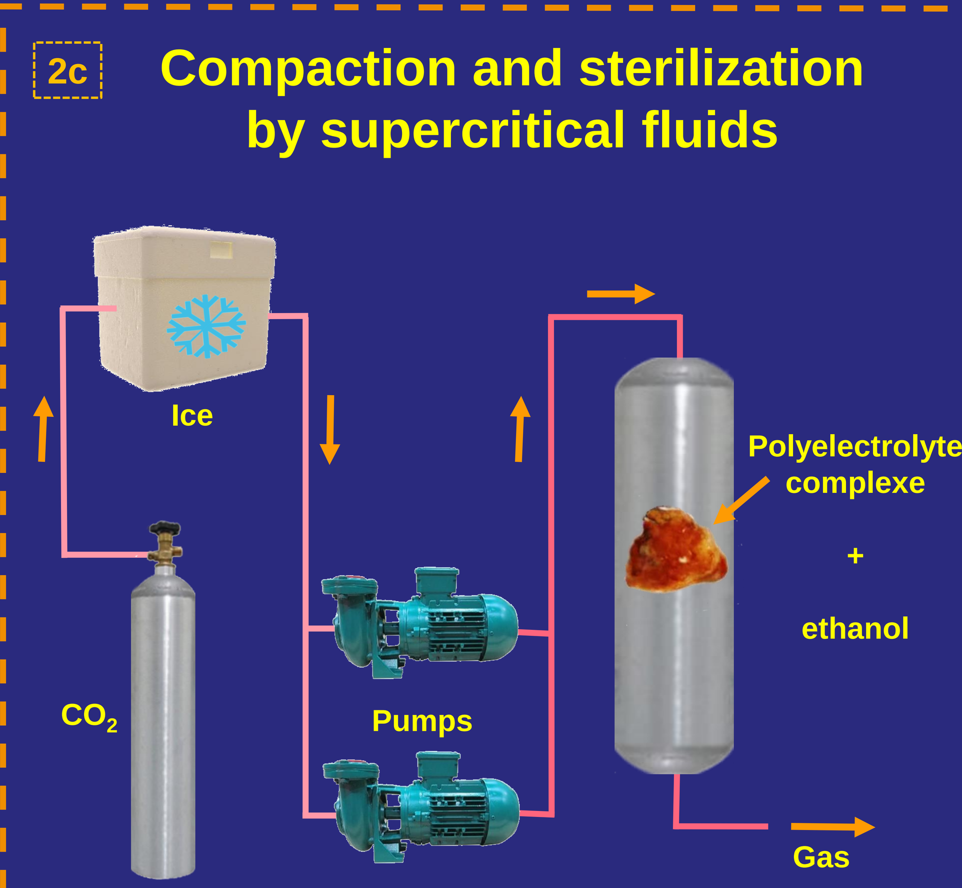

Figure 6. Schematic representation of the compaction procedure by supercritical fluids. The ethanol forcing the wastewater flow out (compact the material which promote the cross-linking) and sterilizes the biomaterial at the same time.

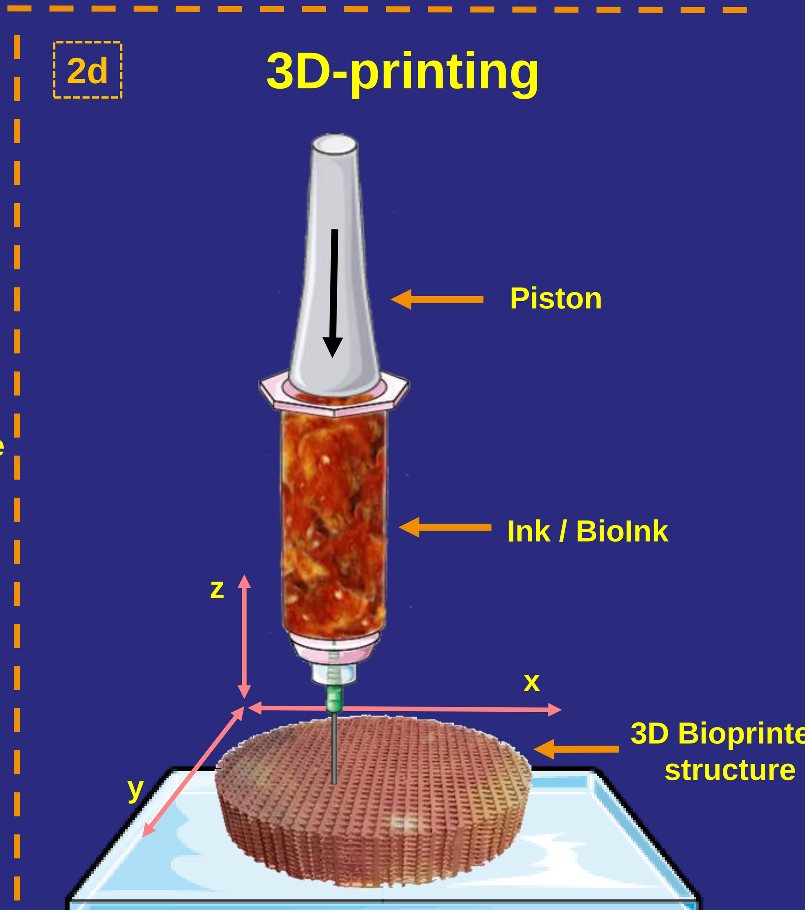

Figure 7. Schematic representation of the construction of three-dimensional (3D) bioprinting structure (artificial tissue-scaffold model) for tissue implantation.

Figure 8. Schematic representation in left demonstrates the procedure to developed biomaterials in cryo-environment. The low temperatures promote the natural cross-linking between polymers. The image in right, show the microscopy of Live/dead assay (Calcein-PI) and the cell morphology assessment (Phalloidin-DAPI) during three-time points after culturing.

Result: The structures provide a good microenvironment for cellular viability during the culture time.

Future Perspectives

The marine origin materials under study are an economically viable alternative to mammal-origin materials, supporting the production of biomaterials having similar biocompatibility, physical-chemical and biological properties regarding its use on therapeutic approaches.

The development of these biomaterials using different methodologies can respond to the requirements of personalized treatments, including cartilage regenerative procedures in biomedical approaches.

References:

[1] Silva, T. H. *et al.* (2012). Materials of marine origin: a review on polymers and ceramics of biomedical interest. 57, 276−306.

[2] Sumayya & Muraleedhara Kurup (2018). Marine macromolecules cross-linked hydrogel scaffolds as physiochemically and biologically favourable entities for tissue engineering applications. 28(9), 807-825.

[3] Iswariya *et al.* (2018). Isolation and characterization of biocompatible collagen from the skin of Puffer fish (*Lagocephalus inermis*). 26(5), 2086-2095.

[4] Ferraro et al. (2016). The "sisters" α-hélices of collagen, elastina and keratin recovered from animal by-products. 51, 65-75.

Acknowledgments:

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