A REPORT ON RESEARCH VISIT TO UNIVERSITY OF BERGEN, NORWAY
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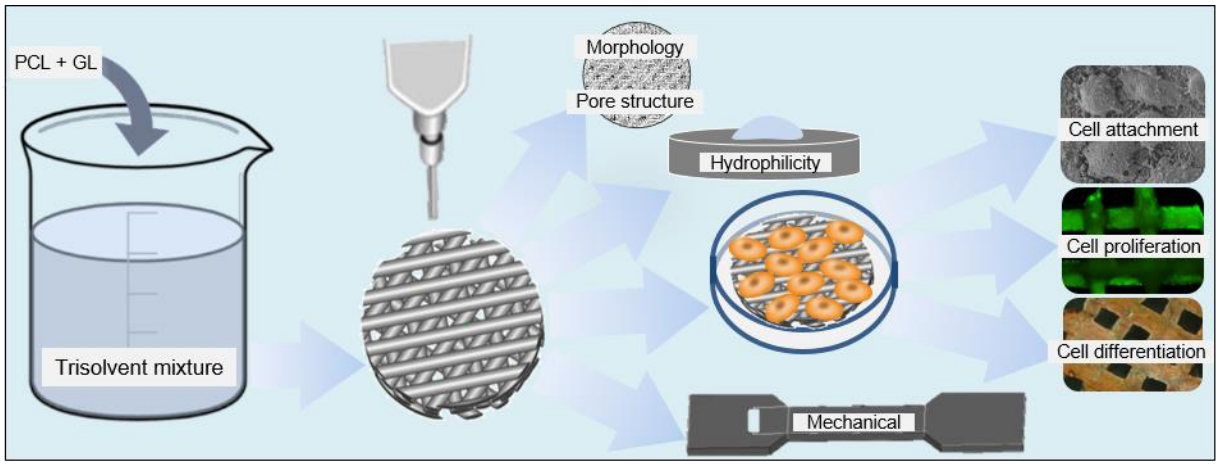
Tissue engineering approaches based on combining cells, degradable scaffolds and biological molecules that mimic natural healing have been tried in attempts to regenerate bone tissues. Various natural and synthetic biomaterials have been used to restore, maintain and improve the structure and function of bone. However, limiting factors are present in each biomaterial tested, either physical, chemical, biological or mechanical properties, that affect their use. As a result, blends and composite biomaterials have been designed for bone tissue engineering applications, combining natural and/or synthetic polymers with or without bioceramics. 3D printing and additive manufacturing have recently been used to fabricate complex structures and matrices with an interconnected pore structure and high mechanical strength, replacing or improving design, structure and fabrication of scaffolds previously produced by conventional techniques such as solvent-casting, gas foaming, and electrospinning. The fabrication of bone scaffolds *via* 3D printing allows customization and control of geometry, porosity, mechanical strength of the scaffolds.

During this visit, a novel scaffold involving poly(lactide-co-trimethylene carbonate) and hydroxyapatite was printed using 3D bioplotter. The printed scaffold was coated with silk fibroin solution in different ratio. Spin coating, spray coating and dip coating methods were adopted and the scaffolds were coated at HVL. The polymeric scaffolds were subjected to SEM analysis to identify the better coating technique and it was proven that 2% silk fibroin under dip coating was effective compared to the other techniques. Then the scaffolds were subjected to FTIR, XRD, TGA, AFM, micro-CT, hydrophilicity by contact angle and mechanical properties. In addition, the *in vitro* biodegradation and biocompatibility tests were performed. Then it was decided to undergo the *in vitro* and *in vivo* biological test

using rat bone marrow stem cells. Dr. Yassin and Mr. Nageeb will perform the bone regeneration studies and parameters like cell attachment, proliferation and differentiation performances by *in vitro* and *in vivo* studies.

Earlier, research work performed during my 1st and 2nd trip on 3D printing of polycaprolactone/gelatin was consolidated and converted as manuscript. The manuscript has been thoroughly reviewed by Prof. Kamal Mustafa, Prof. Dhayalan Velauthapillai and it has been communicated to a good impacted Journal. The results of the work are shown below.



Scheme illustrating the flow of work done on 3D printing of Polycaprolactone-Gelatin

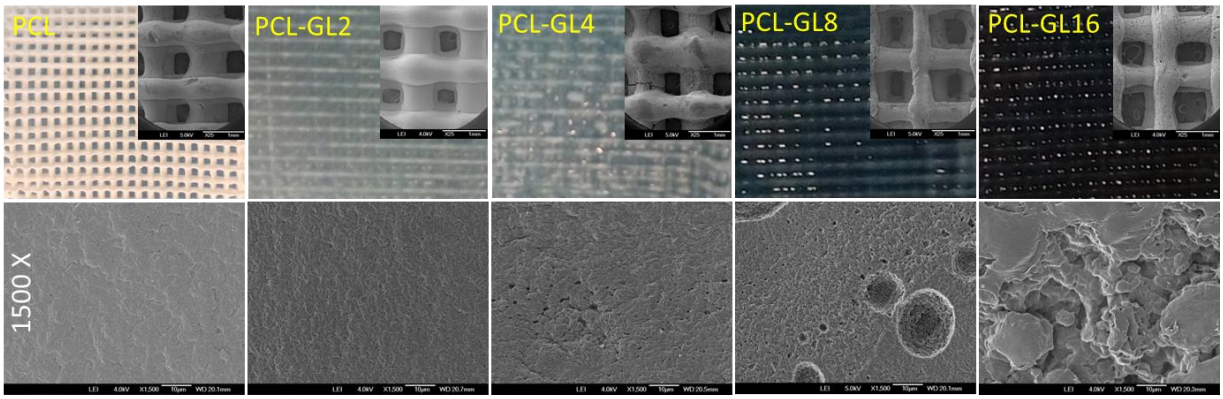


Figure 1. Optical images and SEM micrographs of the printed scaffolds characterizing their surfaces.

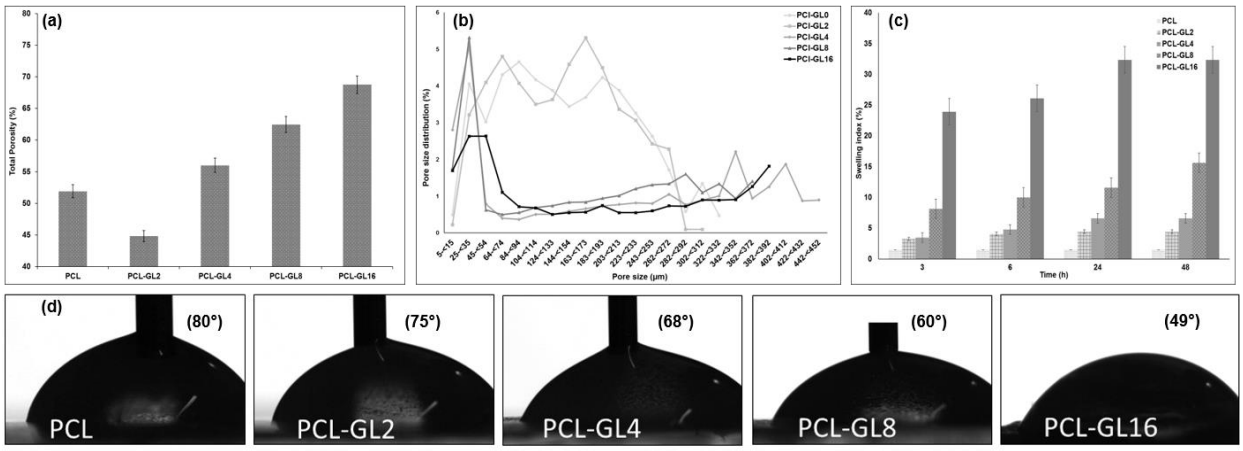


Figure 2. Effect of increasing gelatin (%) on the physical properties of the prepared blends showing, (a) total porosity; (b) pore size distribution; (c) swelling index; and (d) optical photographs for the contact angle measurements.

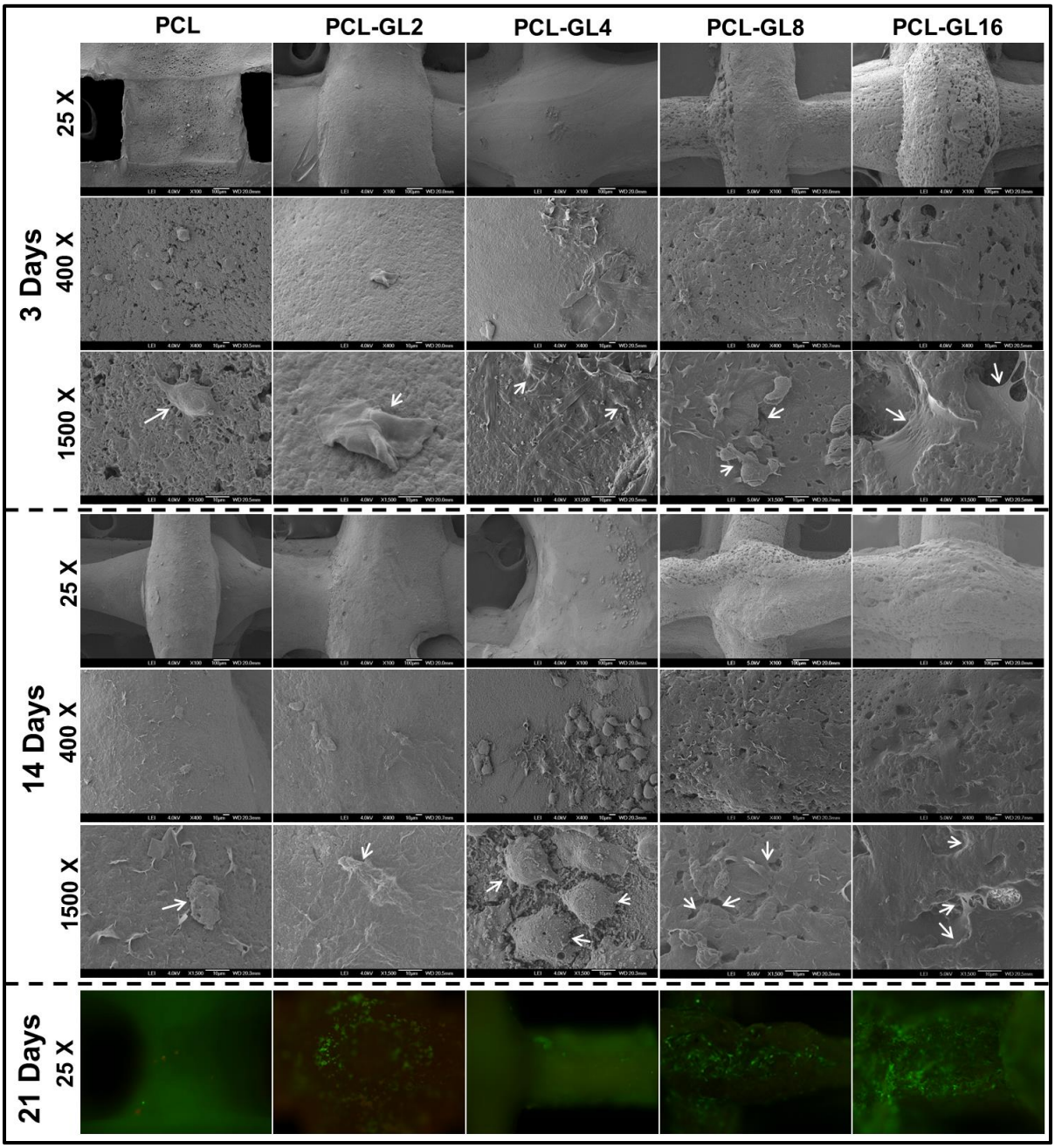


Figure 5. SEM and fluorescence micrographs for the attached BMSCs on the printed scaffolds. SEM at 25×, 400×, and 1500× magnifications after 3 and 14 days. Last row showing fluorescence micrographs at 25× for the live cells after 21 days. Cellular attachments are pointed with white arrows.

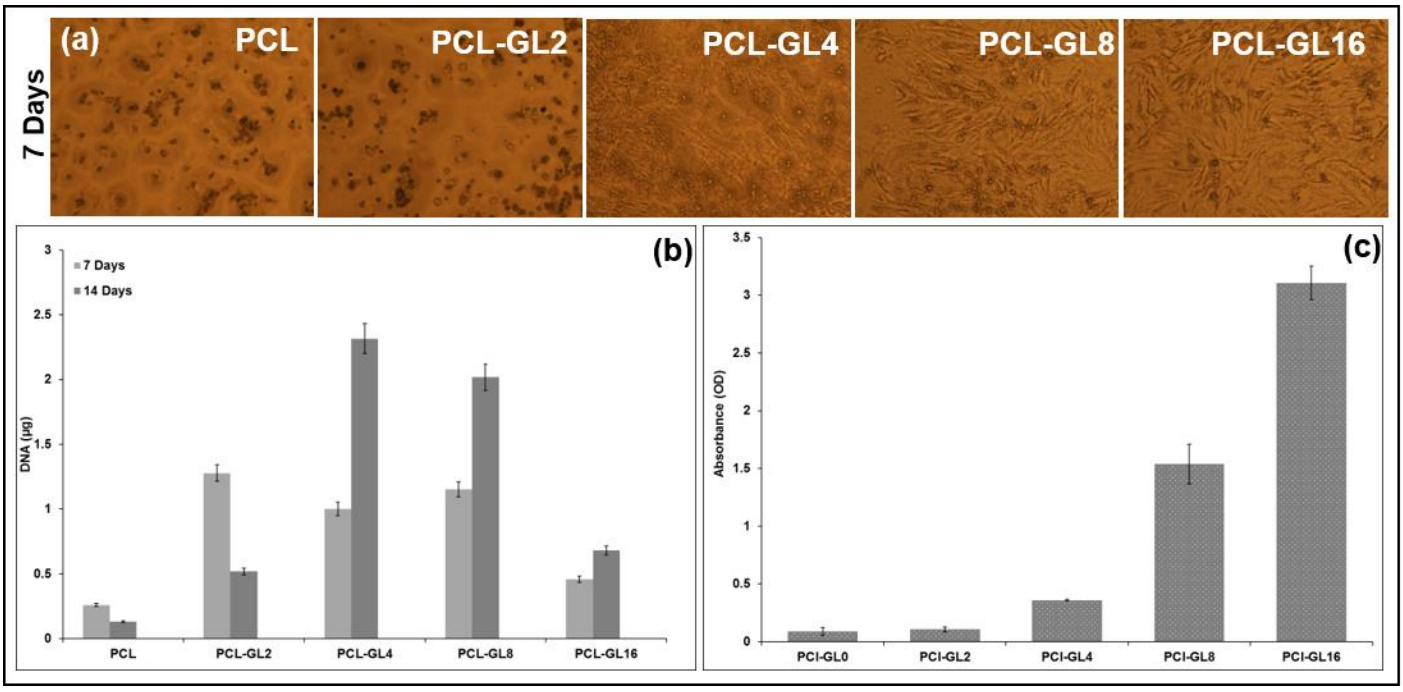


Figure 6. Biological characterization of the printed scaffolds seeded with BMSCs. (a) Microscopic images at 10× showing the effect of the scaffold extraction media on the attachment of BMSCs on low adherent plates at 7 days, (b) Proliferation of cells on the scaffolds evaluated by DNA quantification (7 and 14 days). (c) Optical density (quantification) of the extracted Alizarin red stain from the scaffolds.