INJECTABLE POLYHIPE SCAFFOLDS FOR SOFT TISSUE REGENERATION

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Introduction

Polymerization of high internal phase emulsions (polyHIPEs) is a relatively new method for the production of high-porosity scaffolds. PolyHIPE has a big advantage for tissue engineered soft tissues since the architecture of the HIPE can be tuned by variable factors. It is desirable for scaffolds to possess high surface areas (>500 m^2/g), high porosities (>90%), and a high degree of pore interconnectivity to facilitate transport of nutrients and oxygen as well as cell migration and cell attachment. Previously studied polyHIPE systems require either toxic emulsion stabilizer or high cure temperatures which prohibit their use as an injectable polyHIPE scaffold. Here, we suggest the formation of stable injectable gelatin HIPE cross-linked with non-toxic genipin.

Proposed approach & Results

Making polyHIPE

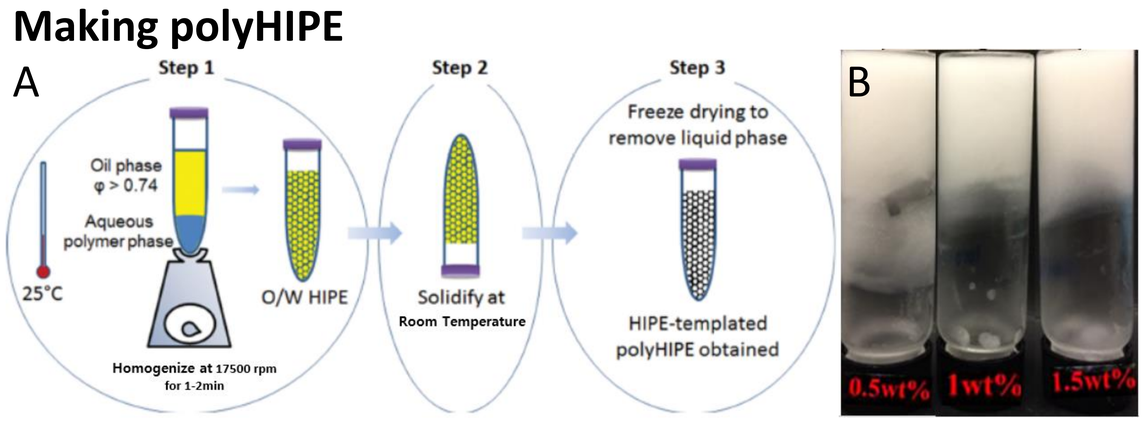
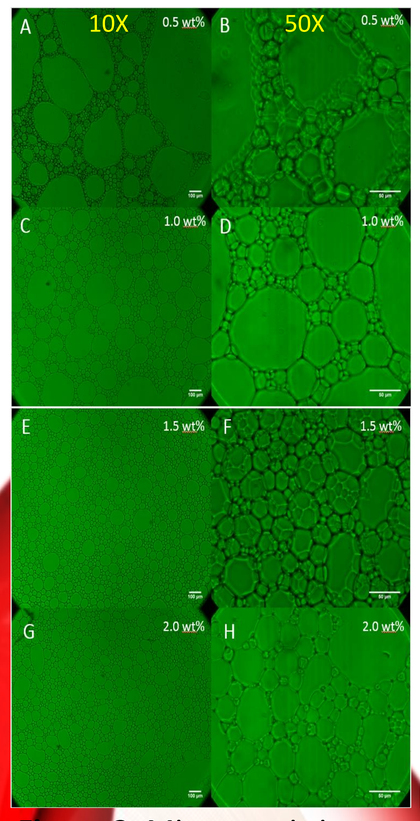


Figure 1. (A) The approach to prepare the high internal phase emulsions (HIPEs). The polymerization of the continuous phase and then drying lead to the porous PolyHIPE scaffold. (B) Photographs of HIPEs composed of 20 vol % distilled water as the external phase, 80 vol % hexane as internal oil phase. Emulsions are formed under room temperature stabilized by different concentrations of gelatin Type B with addition of 10ul 12.5% glutaraldehyde as cross-linker. Photographs were taken 1 day after preparation.

Characterization of HIPE



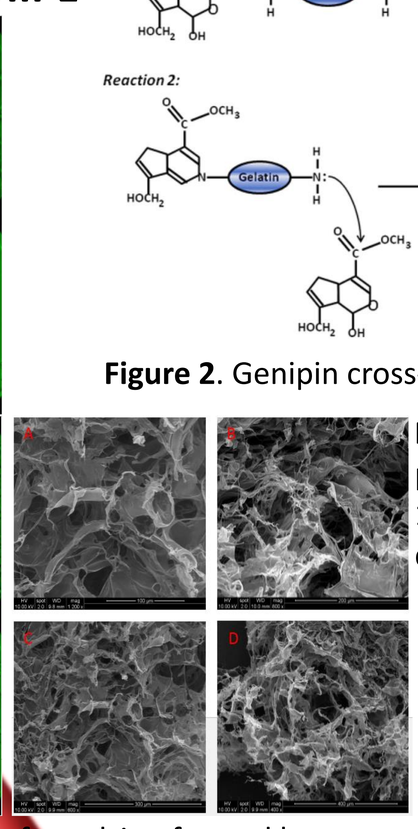


Figure 3. Microscopic image of emulsion formed by 0.5 wt% (A& B), 1.0 wt% (C&D), 1.5 wt% (E&F), and 2.0 wt% (G&H) gelatin polymer.

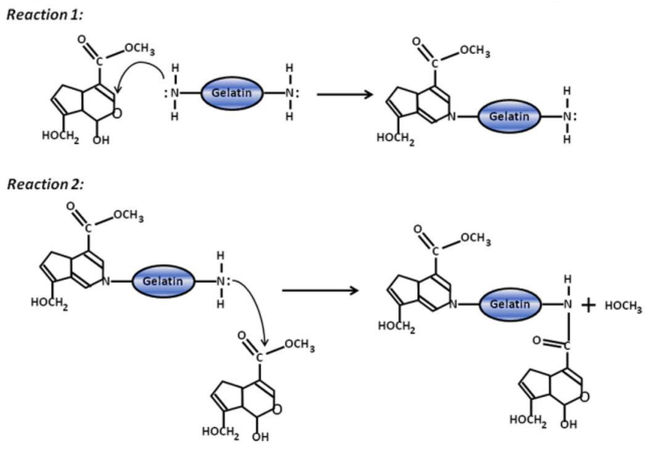


Figure 2. Genipin cross-linking reaction.

Figure 4. SEM image of polyHIPE scaffold formed by 1.5 wt% gelatin polymer with different magnification.

Injection test

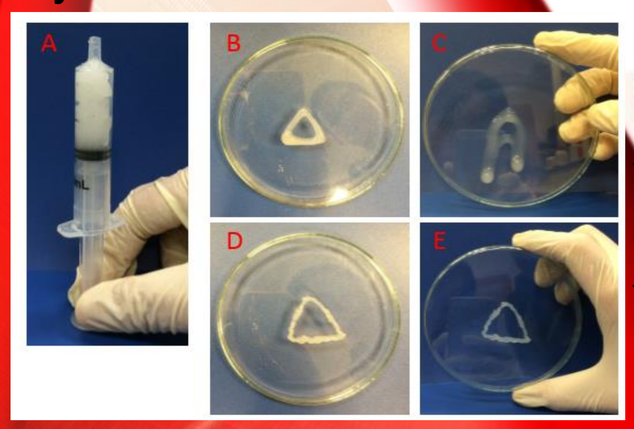


Figure 5.
(A) 1.5% gelatin HIPE in the syringe;
(B) HIPE without cross-linker injected out from the syringe on the glass wall;
(C) after B is heated over 50°C;
(D) HIPE with cross-linker injected out from the syringe,
(E) after D is heated over 50°C.

Control release

Sample preparation

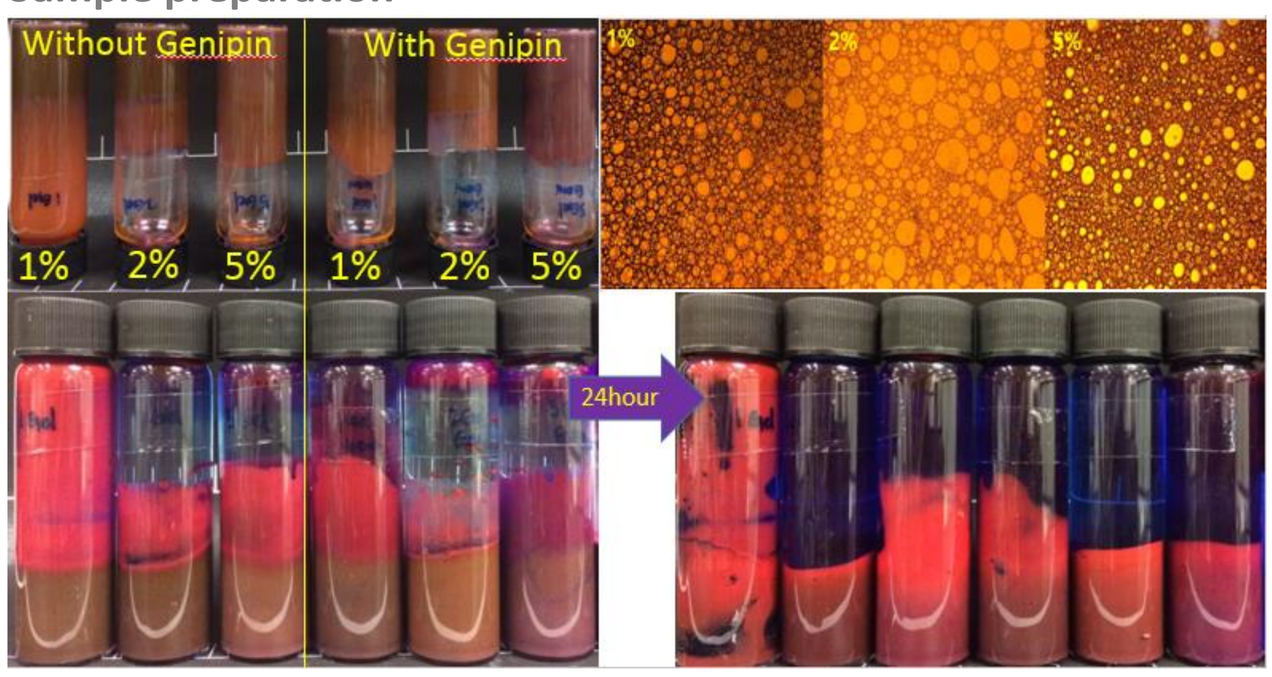


Figure 6. (A) Photographs of HIPEs composed of 20 vol % 1:1000 Bromthymolblau dissolved distilled water as the external phase, 80 vol % 1:1000 Nile Red 99% dissolved in toluene as internal oil phase. (B) Samples with 5mL DW: 5ml Ethanol placed on the top of 5mL emulsion as acceptor for the control release from 0 hr to 24 hr.

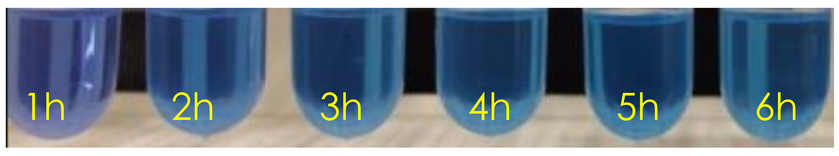


Figure 7. 1mL sample was taken every hour from acceptor layer to detect absorption by UV-spectrometer to calculate release % as a function of time.

Control release Result

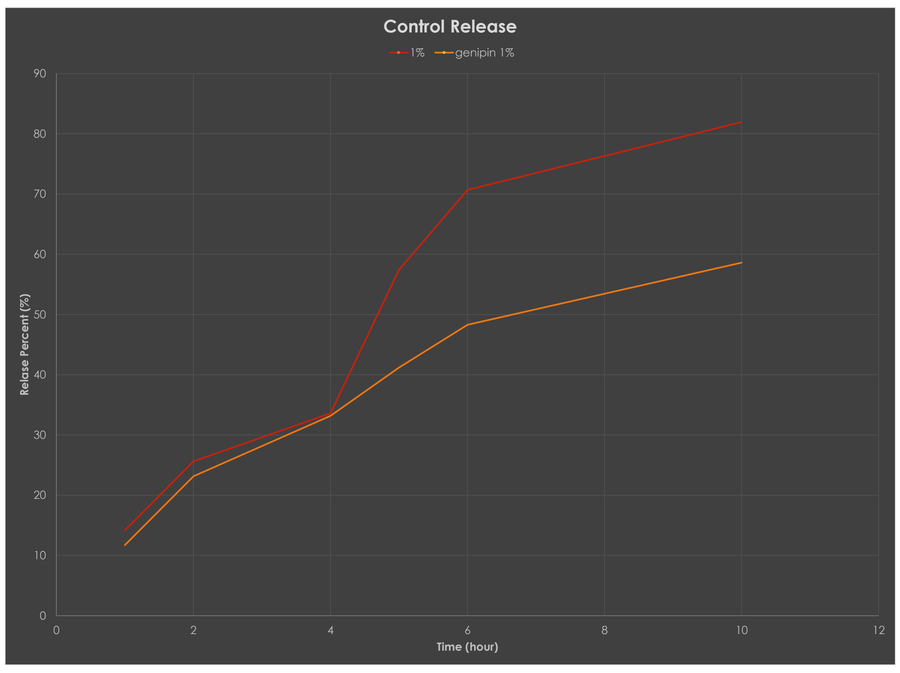


Figure 8. Release percent % calculated by time from the 1% samples shown in Figure 6.

Conclusion

- Biocompatible gelatin HIPE could be prepared extremely simply by homogenization and addition of cross-linker (Figure 1).
- The average pore diameter decreased as the gelatin concentration increased (Figure 3). More successful isolated emulsion with less aggregation is stabilized with higher wt% of gelatin polymer.
- 1.5% gelatin HIPE has pore diameter of 100-200 um which fulfills the requirement for a good small droplets for bioavailability (Figure 4).
- HIPE was injectable under room temperature and was stable at high temperature after the gelation (Figure 5).
- Control release with genipin cross-linker showed slower rate of release than the control (Figure 8).

Acknowledgement

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References

Solorio, Luis et al. "Gelatin Microspheres Crosslinked with Genipin for Local Delivery of Growth Factors." *Journal of tissue engineering and regenerative medicine* 4.7 (2010): 514–523. *PMC*. Web. 28 Mar. 2016.