Development of Biocompatible Porous Hydrogels via Aqueous Two-Phase System: A Comparative Study of Poly(ethylene oxide), Polysarcosine, and Glucomannan

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Hydrogels have become essential in tissue engineering applications like injectable systems and 3D bioprinting due to their biocompatibility and ECM-mimicking properties. Their porous, interconnected structure supports cell growth, nutrient transport, and cell migration—key features for replicating native ECM function [1]. Various of fabrication strategies have been explored to achieve such porosity in hydrogels. Among these strategies, aqueous two-phase systems (ATPS) have gained attention as a biocompatible method. ATPS involves forming of two immiscible aqueous phases, that can be precisely controlled through polymer concentration, molecular weight, and solution viscosity. In this approach, one polymer forms the hydrogel matrix via crosslinking, and the second phase functions as a pore-forming agent. This second phase is typically removed after gelation because it does not interact with the hydrogel matrix [2]. Polyethylene oxide (PEO) is commonly used as a pore-forming agent for hydrogels due to its water solubility, low toxicity, and minimal interference with crosslinking, enabling the formation of well-defined pore structures [3]. However, its reported immunogenicity has led to the search for safer alternatives. In this study, we explore aqueous two-phase systems (ATPS) using polysarcosine and glucomannan as alternative porogens, comparing them with PEO. We assess how each affects hydrogel porosity, phase separation, and suitability for biological applications.

A biocompatible ATPS was developed for the fabrication of porous hydrogels using polysarcosine and glucomannan. The construction of the porous hydrogel involved the use of methacryloyl and tyramine functionalized polymers, including hyaluronic acid methacryloyl (HA-MA), poly(N^5-2-hydroxyethyl-L-glutamine) methacryloyl (PHEG-MA), hyaluronic acid tyramine (HA-TYR), and a combination of HA-MA with PHEG-MA. The polymer precursors were photocrosslinking under the blue light using Ru(II) complex/$(NH_4)_2S_2O_8$ or Riboflavin/L-Arginin as photoinitiators. The resulting hydrogels were analyzed based on several factors, including the gelation time, gel yield, swelling, pore size, and morphology. The findings of this study underscored the efficacy of the ATPS system as a more compatible approach to producing porous hydrogels for biocompatible applications.

Keywords: Hydrogels,Two phase systems , biocompaility.

References

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