The sol-gel of chondroitin-4-sulfate -based Pluronic hydrogels as injectable biomaterials

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ABSTRACT

The paper researched 10 wt% Pluronic F68 and 15 wt% Pluronic F127 with 5 wt% chondroitin-4-sulfate(CS) in Phosphate-buffered saline(PBS) in order to design physical hydrogels with good stability at 37°C. Pluronic hydrogels with 5 wt% CS are thermoreversible, and it is very fast to answer the thermal stimulus by rheology.

INTRODUCTION

Injectable hydrogels are environment responsive sol-gel transition behavior in solution, therefore, we pay more attention for versatile applications for macromolecular drug delivery and tissue engineering. Among the injectable hydrogel, PEO-PPO-PEO triblock copolymers also known as the Pluronics, is widely used as injectable carriers. However, Pluronic hydrogel injected into the body, the formed in situ Pluronic hydrogel structure was quickly disintergrated at the local site due to rapid dilution with the body fluid. Pluronic hydrogel formed physically crosslinked hydrogels in human body, the limit of its use due to the unstable. So, researchers have been many efforts to modify or blend the PEO-PPO-PEO copolymer structure in order to enhance their stability.[1,2] Chondroitin-4-sulfate based hydrogels will be a versatile platform for a wide range of application in drug delivery when an injection is required.[3] The structure of chondroitin sulfate is shown in Figure 1, according permeability coefficient to Table 1.[4]

Table 1. The name and permeability coefficient of chondroitin sulfate.

Letter identification	Systematic name	Permeability coefficient (x 10^{-6}) (n=3) (cm/sec)
Chondroitin sulfate A	chondroitin-4-sulfate	10.1 (± 0.6)
Chondroitin sulfate C	chondroitin-6-sulfate	7.94 (± 7.35)
Chondroitin sulfate D	chondroitin-2,6-sulfate	0.00 (± 0.00)
Chondroitin sulfate E	chondroitin-4,6-sulfate	3.63 (± 2.07)

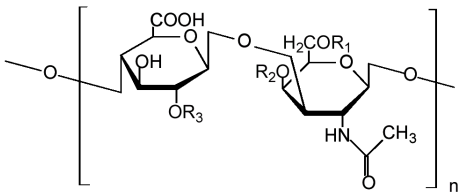

Figure 2. The structure of one unit in a chondroitin sulfate chain.

MATERIALS

Pluronic F127 and Pluronic F68 were purchased from Sigma -Aldrich. Chondroitin-4- sulfate (CS) were purchased

from Alfa Aesar and Phosphate-buffered saline(PBS) from Amesco, respectively.
All chemicals were used without further purification. All solutions and gels were prepared with doubly distilled water.

METHODS

The formulations were prepared by dissolving different amounts of Pluronic F127 and Pluronic F68 with 5 wt% Chondroitin-4-sulfate solution by mixing under continuous stirring at 4 °C until a clear solution. The clear solution form the gel under room temperature.

RHEOLOGY

The rheology experiments include temperature sweep and viscometry which were carried out with a Kinexus pro (Malvern) rheometer. For all measurements parallel plate tools (40 mm diameter) were used and all samples were measured directly after polymerization without further swelling. The temperature sweep measurements were performed at heating rate of 1°C/min. The shear stress was varied between 0.01 and 100 Pa.

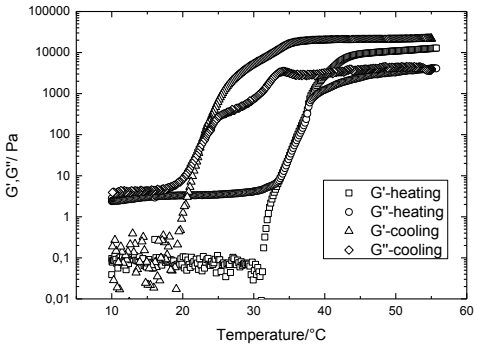

Figure 2.Temperature ramp of 10 wt% Pluronic F68 and 15 wt% Pluronic F127 and 10 wt% F68 with the addition of 5 wt% chondroitin-4-sulfate. The temperature sweep measurements were performed at heating and cooling rate of 1°C/min.

We blend of CS and Pluronic hydrogel in PBS solutions and successfully obtained the physical hydrogel which is close to the body temperature. The rheological measurements of Pluronic hydrogel blended with chondroition-4-sulfate showed that the gelation temperature of the Pluronic is closed to body temperature by the addition of 5 wt%. As showed in Figure 2, the viscoelastic moduli showed a sharp increase near the gel point, G' increases more than 4 orders of magnitude and reaches a constant level (12 000 Pa), which were very sensitive to the sol−gel transition process was obtained. Kyung et al.[5] found The CP solution underwent a sol–gel transition around 25 °C at which the storage modulus (G′) approaches 10^4 Pa, highlighting the potential of this material as an injectable scaffold for cartilage regeneration.

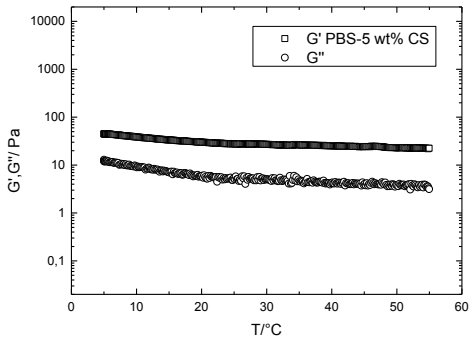

Figure 3.Temperature ramp of 5 wt% chondroitin-4-sulfate in PBS. The temperature sweep measurements were performed at heating rate of 1°C/min.

Figure 3 described CS that undergo a temperature induced phase transition in Pluronic solution providing an important basis for enhancing their stability. The G' is higher than G'' when CS concentration increased to 5 wt% in PBS. It means CS formed the weak gel in PBS.

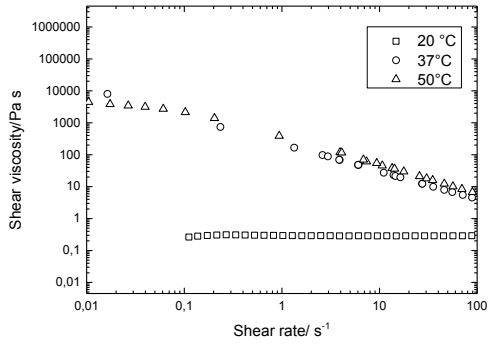

Figure 4. Shear rate dependence of the viscosity of 10 wt% Pluronic F68 -15 wt% F127 Pluronic with 5 wt % CS in PBS.

We examined the effect of chondroitin sulfate on the viscosity of different solutions through their rheological flow behavior. The viscosity of the solution containing 5 wt% chondroitin -4-sulfate in a flow was constant at all shear rates examined (0,01–100 s^{-1}) at room temperature.

However, the viscosity of solutions of hydrogel plus chondroitin sulfate decreased in a shear rate-dependent manner, exhibiting shear thinning behavior.

CONCLUSION

The rheological properties of the gels were intended for the local administration of drugs by injection. We studied the effect of Pluronic hydrogel with branched polysaacharides on the rheological properties. Indeed, the heteroglycans's polysaacharides strengthened the network due to their interactions with multiblock copolymers of PEO-PPO-PEO in PBS by sol-gel gelation, resulting the Pluronic hydrogel with 5 wt% CS was totally the reversible thermos-reversible properties. It was easy to injectable through needles due to the shear thinning behavior of the gels.

ACKNOWLEDGMENTS

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