In situ cross-linkable thermogel based on methcrylated and thiolated N-acyl glycol chitosan for sustain delivery of insulin

Hyemin Oh, Daeun Kim, Ik Sung Cho, Chanyang Joo, Sudipta Mallick, Kang Moo Huh1*,

Department of Polymer Science and Engineering, Chungnam National University, 99 Daehak-ro, Yuseong-gu, Daejeon 34134, Republic of Korea

Thermo-gelling polymers have been widely used as in-situ forming hydrogel systems for various biomedical applications because additional requirement of organic solvents, chemical cross-linkers and additives can be avoided to form hydrogel.[1] However, reported weak mechanical strength and low physical stability have limited its practical applications. To address this problem, thermosensitive N-hexanoyl glycol chitosan (HGC) derivatives, methacrylated HGCs (M-HGCs) and thiolated HGCs (SH-HGCs) were synthesized to develop in situ cross-linkable thermogel system. The thermosensitivity of M-HGCs and SH-HGCs could be optimized by varying the degree of each substitution (hexanoylation, methacrylation, and thiolation). The mixture solutions of M-HGC and SH-HGC (M/SH-HGC) in PBS could form thermogels at physiological temperature due to their intrinsic thermo-responsive sol-gel transition nature. Additionally, the chemical crosslinking between methacrylate and thiol group enhanced the mechanical properties of M/SH-HGC thermogels. Their physico-chemical properties were characterized by ^{1}H-NMR, FT-IR, SEM and rheometer. Compared to the corresponding thermogels, M/SH-HGC thermogels showed enhanced mechanical properties due to the synergistic effect of dual cross-linking system. The cytotoxicity tests of M/SH-HGC in lungs fibroblast (LF) cells showed negligible toxicity and in-situ cross linking step also did not affect cell viability. Moreover, the MSH-HGC thermogel system showed sustained release of Insulin for up to 1 week *in vitro*. So, this in-situ crosslinkable thermogel system has promising possibilities as a biomaterial for various biomedical applications, due to their irreversible and tunable thermo-gelling properties.

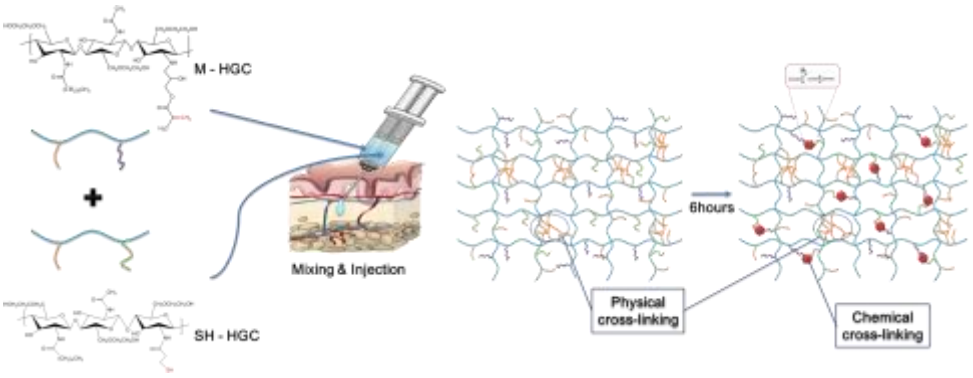

Figure 1: Schematic illustration of in-situ cross-linkable system.

References
[1] Thrimoorthy, P. *Biomaterials* **2010**, *31*, 8107-8120. *Injectable, dual cross-linkable polyphosphazene blend hydrogels*.

Biographic Details

Name Hyemin Oh
Title: Master Student
Affiliation, Country: Chungnam National University, Republic of Korea
Phone: +821039930524 Fax: +82428218910 E-mail: hyemin0love@naver.com
Research interests: drug delivery system, stem cell, biomaterials