

## Self-Healing Hydrogel Triggered by Magnetic Microspheres to Control Glutathione Release for Cartilage Repair

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**Abstract :** Osteoarthritis (OA) is among the most challenging joint diseases, and as far as we know, there is currently no exact and effective cure for it because it has low self-repair ability due to lack of blood vessels and low cell density in articular cartilage. So far, there have been several methods developed to treat cartilage disorder. The most common method is to treat the high molecular weight of hyaluronic acid (HA) injection, but it will degrade after a period of time, so the patients need to inject HA repeatedly. In recent years, self-healing hydrogel has drawn considerable attention because it can recover its initial mechanical properties after damaged and further increase the lifetime of the hydrogel. Here, we aim to develop a self-healable composite hydrogel combined with magnetic microspheres to trigger glutathione(GSH) release for promoting cartilage repair. We use HA-cyclodextrin (CD) as host polymer and poly(acrylic acid)-ferrocene (pAA-Fc) as guest polymer to form the self-healable HA-pAA hydrogel by host and guest interaction where various graft amount of pAA-Fc (pAA:Fc= 1:2, 1:1.5, 1:1, 2:1, 4:1) was conducted to develop different mechanical strength hydrogel. The rheology analysis showed that the 4:1 of pAA-Fc has higher mechanical strength than other formulations. On the other hand, iron oxide nanoparticle, poly(lactic-co-glycolic acid) (PLGA) and polyethyleneimine (PEI) were used to synthesize porous magnetic microspheres via double emulsification water-in-oil-in-water (W/O/W) to increase GSH loading which acted as a reductant to control the hydrogel crosslink density and promote hydrogel self-healing. The results show that the porous magnetic microspheres can be loaded with 70% of GSH and sustained release about 50% of GSH after 24 hours. More importantly, the HA-pAA composite hydrogel can self-heal rapidly within 24 hours when suffering external force destruction by releasing GSH from the magnetic microspheres. Therefore, the developed the HA-pAA composite hydrogel combined with GSH-loaded magnetic microspheres can be in-vivo guided to damaged OA surface for inducing the cartilage repair by controlling the crosslinking of self-healing hydrogel via GSH release.

**Keywords :** articular cartilage, magnetic microsphere, osteoarthritis, self-healing hydrogel

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