Redox-active PMNT–PEG–PMNT Polymer for Rheumatoid Arthritis Treatment – Preparation and ESR Studies

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Abstract

Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder primarily affecting the joints, causing pain and stiffness, leading to destruction of the articular cartilage with subsequent severe morbidity and disability. It is characterized by a chronic infiltration of inflammatory cells into the synovial membrane and the development of a pannus tissue. It is also well established that free radicals/reactive oxygen species (ROS) play an important role in RA inflammation. Although 1% of the population suffers from RA and new treatment approaches have significantly delayed disease progression and improved the quality of life for many patients, there is still a continued need for the development of new therapeutic strategies for its treatment. Available therapeutics show many side effects so in the long run they may impair many disorders. Because chronic inflammation continues in this disease, long term and continuous suppression of ROS are important trials. Current strategies are to design nanosystem for delivery of therapeutic agents specifically to the site of inflammation, therefore avoiding potential systemic and off-target unwanted effects. In order to suppress excessively generated reactive oxygen species in inflamed area, we developed a nitroxide radical-containing injectable hydrogel (RIG) system and conducted evaluation of anti-RA drug loading efficiency, viz., we have synthesized poly[4-(2,2,6,6-tetramethylpiperidine-N-oxyl)aminomethyl-styrene]-b-poly(ethylene glycol)-b-poly[4- (2,2,6,6-tetramethylpiperidine-N-oxyl)aminomethyl-styrene] (PMNT-PEG-PMNT) triblock copolymer possessing ROS scavenging TEMPO moieties as side chains of PMNT segment. Along with anionic poly(acrylic acid), it forms polyion complexes to become flower type micelle (ca. 79 nm), with nanoreservoir core for charged drugs. It can be further injected as mildly viscous solution, exhibiting in situ thermo-irreversible gelation under physiological condition, leading to long term retention of drug at local site. Electron paramagnetic resonance (EPR) or electron spin resonance (ESR) spectroscopy is a technique for studying materials with unpaired electrons. These sensitive and specific method is a great tool for studying radical-containing materials, such as polymer mentioned previously. Here, we show ESR studies of PMNT-PEG-PMNT triblock copolymer as well as its preparation and application.

References

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Figures

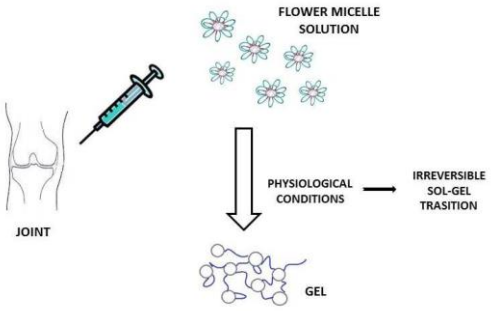

Figure 1. Nitroxide Radical-containing Injectible Hydrogel (RHG) System