Gold Nanorods-based Thermosensitive Hydrogel Produces Selective Long-lasting Regional Anaesthesia Triggered by Photothermal Activation of Transient Receptor Potential Vanilloid Type-1 Channels

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Background: Long-lasting regional anaesthesia and selective sensory block are useful in post-operative analgesia and treatment of pathological pain. Currently, duration of local anaesthetics is not satisfactory and their cardiac and central nervous systems toxicities have been widely reported. Previous studies have demonstrated that activation of TRPV1 channels facilitated the potency of a selective long-lasting regional anaesthetic drug QX-314 in vivo. Hydrogel is a solid jelly-like material. Gold nanorods is nanoparticles, which can be used for hyperthermia by exposure to near-infrared radiation.

Methods: We fabricated a gold nanorods and QX-314 containing hydrogel. The molecular weight of PECE hydrogel was adjusted to achieve a targeted phase transition temperature. Then, gold nanorods with a desired photothermal conversion efficacy and QX-314 were mixed with PECE hydrogel to produce a gold nanorods-QX-314/hydrogel nanocomposite. Biomaterials properties of this nanocomposite were determined and a rat model of sciatic nerve block was applied to evaluate the regional anaesthetic effect of this nanocomposite.

Results and Discussion: Both PECE hydrogel and GNRs-QX-314/PECE hydrogel nanocomposites showed the sol-gel transition within 2 min from room temperature (25°C) to physiological temperature. With exposure to near-infrared irradiation, the gold nanorods-QX-314/hydrogel nanocomposite can activate TRPV1 channels through photothermal conversion and release QX-314 at the same time. This gold nanorods and QX-314 loaded hydrogel exhibits a long-lasting regional anaesthetic effect with selective sensory function block. Sensory block duration of nanocomposite was significantly longer than 1% lidocaine (90.0±3.5 vs. 37.5±3.5 min, $P<0.001$). Motor block by the nanocomposite was observed for only 40% of rats with significantly shorter duration than its sensory block (42.5±4.1 vs. 90.0±3.5 min, $P<0.001$). With the 808 nm laser irradiation, the PECE hydrogel changes into sol phase to release QX-314 and thermal activate TRPV1 channel at the same time. The burst release of QX-314 from PECE hydrogel diffuses into cellular through TRPV1 channel and block voltage-dependent sodium channel to produce selective long-lasting regional anaesthesia.

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