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Opinion Article

Photoresponsive Plasmonic Nanocomposites for Controlled Drug Release in Retinal Disorders

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DESCRIPTION

Posterior segment eye diseases, including age-related macular degeneration and diabetic retinopathy, remain significant causes of vision loss worldwide. Current treatment modalities often involve frequent intravitreal injections, creating substantial burden for patients and healthcare systems while increasing risks of injection-related complications. We have developed photo-responsive plasmonic nanocomposites capable of on-demand, controlled release of therapeutic agents within the vitreous humor following a single administration, with subsequent light-triggered activation using safe, trans-corneal illumination. These nanocomposites consist of gold nanorods embedded within a thermosensitive polymer matrix containing anti-Vascular Endothelial Growth Factor (anti-VEGF) antibodies, creating a system responsive to near-infrared light that penetrates ocular tissues without causing photochemical damage.

The nanocomposites were synthesized through a thermally induced phase separation process, creating a porous matrix approximately 200 μm in diameter with uniform distribution of gold nanorods throughout the structure. The plasmonic nanorods, with aspect ratios carefully tuned to exhibit absorption maxima at 810 nm, function as efficient photo-thermal transducers that convert near-infrared light to localized heat. The surrounding polymer matrix consists of a poly(N-isopropylacrylamide) derivative exhibiting a volume phase transition at approximately 39°C-slightly above ocular temperature but readily achievable through moderate photothermal heating. This transition causes temporary matrix contraction, creating pressure gradients that facilitate controlled release of the incorporated anti-VEGF antibodies. Surface modification with poly (ethylene glycol) chains prevents protein adsorption and cellular adhesion, while incorporation of fluorescent reporters enables non-invasive monitoring of implant integrity and drug release through standard ophthalmic imaging techniques.

In vitro characterization demonstrated precise control over release kinetics, with approximately 25% of the incorporated antibody released following each 5-minute illumination session (810 nm, 200 mW/cm^2) with minimal passive leakage (<5% over 30 days) in the absence of light activation. The released antibody maintained full structural integrity and binding efficacy as confirmed by enzyme-linked immunosorbent assays and cell-based VEGF inhibition studies. Thermal modeling and experimental validation confirmed that the temperature increases remained localized to the immediate vicinity of the nanocomposite, with surrounding vitreous temperature elevations limited to less than 2°C during typical activation parameter well below thresholds associated with thermal damage to ocular tissues.

In vivo evaluation in a rabbit model of choroidal neovascularization demonstrated successful implantation through a standard 25-gauge intravitreal injection system, with optical coherence tomography confirming stable positioning within the vitreous cavity. Transcorneal illumination using a slit-lamp adapted with an 810 nm diode laser successfully triggered antibody release, with vitreous sampling confirming antibody concentrations within the therapeutic range following each activation session. Serial fundus photography and fluorescein angiography demonstrated significant regression of neovascular lesions following four weekly activation sessions, with efficacy comparable to monthly intravitreal injections of equivalent anti-VEGF antibody doses.

CONCLUSION

Safety assessment through electroretinography and histopathological analysis revealed no evidence of retinal toxicity or inflammatory responses throughout the 6-month observation period. Intraocular pressure remained within normal limits, and comprehensive ophthalmic examination showed no evidence of cataract formation, vitreal opacities, or other adverse effects. Biodegradation studies demonstrated gradual dissolution of the polymer matrix over approximately 8 months, with complete clearance of all components through normal ocular outflow pathways. This photoresponsive plasmonic nanocomposite

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represents a promising approach for reducing treatment burden in chronic retinal disorders, potentially enabling several months of therapy from a single intravitreal procedure with non-invasive, on-demand control over drug release kinetics.