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In vitro and in vivo Release Profile of a Minimally Invasive Triamcinolone Biodegradable Controlled Release Microspheres System (RETAAC) for Intravitreous Use

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Purpose: To study a triamcinolone (TA) biodegradable microspheres system (RETAAC) for intraocular use proportionating a prolonged drug release with minimal surgical implantation manipulation. **Methods:** TA and polylactic-co-glycolic acid (PLGA) were dissolved in acetone to obtain the relationship TA/PLGA 1:1 and 1:2. The TA loading efficiency and quantitative analysis were determined by high performance liquid chromatography. The TA microspheres were characterized by scanning electronic microscopy and by diameter measurements. For *in vitro* studies amounts of microspheres equivalent to 1mg of TR were incubated in phosphate buffer and the analytical concentrations of TA released were determined against the time. For the *in vivo* studies amounts of microspheres equivalent to 1mg/0.1mL of TA were injected into the vitreous cavity of sixty albino rabbits utilizing a 27-gauge syringe. The TA concentration was determined in the aqueous and vitreous humors up to 120 days. To assess toxicity serial electron microcopy and electrophysiology examinations were performed. **Results:** The RETAAC showed a uniform particle size distribution (1μm $\pm$.0.1). The encapsulated TA in the microspheres was about 39,53 $\pm$ 1,80%; 33,01 $\pm$ 1,80 %; for 1:1 and 1:2 TA/PLGA microspheres, respectively. It was verified that the PLGA amounts in the structural material of microparticle play an important role on the rate of TA release. The time required for release of all free TA was 3 hs while for TA/PLGA 1:1 microspheres was 144 hs and for 1:2 TA/PLGA was 366 hs. The results of the *in vivo* experiments shown that the free TA do not remain above the active for more than 24 days in both, aqueous and vitreous humors. For encapsulated TA/PLGA 1:1, the theoretical intravitreal therapeutic level of 25μg/ml remained for up to 120 days. No toxicity was observed. **Conclusions:** RETAAC demonstrated a more sustained *in vitro* and *in vivo* release profile than its free form. Taken together with its minimally invasive delivery requirements, this new system may characterize an optimized approach, overcoming most of the implantation barriers faced with the conventional pellet system.