# CHITOSAN-COATED PLGA NANOPARTICLES OF TRIAMCINOLONE ACETONIDE: FORMULATION OPTIMIZATION FOR OCULAR DRUG DELIVERY

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**Background:** Age-related Macular Degeneration (AMD) is a disease of the posterior segment the eye and the most common cause of vision loss in elderly people. There is a rapid increase in the disease population partly due to ageing (~20% of Europe's population are now over 65). The number of Europeans suffering from early and late-stage AMD will have increased to 21.5 and 4.8 million, respectively, by 2040. The existing treatment regimen involves repeated intravitreal injections of anti-VEGF (vascular endothelial growth factor) agents. Such injections are reportedly associated with serious side effects such as retinal detachment, retinal haemorrhage and endophthalmitis. Therefore, there is an urgent need for the development of a non-invasive treatment option for AMD, in order to reduce or eliminate the need for frequent intravitreal injections, enhance therapeutic efficacy and improve patient compliance. The present study aims to develop a topically applied nanoparticulate system exhibiting extended drug release for the treatment of AMD. The corticosteroid encapsulated into the nanoparticulate system has the potential to help in managing this complex disease.

**Methods:** Triamcinolone acetonide (TA)-loaded chitosan-coated poly (lactic-co-glycolic acid) (PLGA) nanoparticles were prepared using the thin-film hydration technique. The particle size, zeta potential and polydispersity index (PDI) of the nanoparticles were analyzed using dynamic light scattering. High-performance liquid chromatography was used to quantify TA to determine encapsulation efficiency and percentage drug release. The stability of nanoparticles was assessed using thermogravimetric analysis (TGA) and dynamic scanning calorimetry (DSC) techniques.

**Results:** The particle size of uncoated and chitosan-coated PLGA nanoparticles ranged from 411 ± 2.83 nm to 456 ± 67.89, with an encapsulation efficiency of 63.13% ± 6.44% and 24.16 ± 10.29. The zeta potential of uncoated PLGA nanoparticles was -4.1 ± 1.36 mV which increased to +44.05 ± 5.02 mV following chitosan coating indicating the formation of uniform and stable particles with polydispersity indices ranging from 0.08 and 0.19. TGA and DSC results indicated that nanoparticles were thermally stable and in a mono-dispersed form. The *in-vitro* TA release from the nanoparticles was 27.48 ± 0.65% in 32 hours, subsequently reaching a plateau suggesting the controlled release of the drug. The cytotoxicity study on human corneal epithelial cell lines revealed the components and the nanoparticles resulted in at least 90% cell viability, an important first step in demonstrating biocompatibility.

**Conclusions:** The polymer matrix of PLGA aids in controlled diffusion of encapsulated drug, while the mucoadhesive property of chitosan, along with the lipophilic nature of TA may help in better permeation across the barriers of the eye. The size of the nanoparticles in conjunction with the biodegradable and biocompatible properties of the polymers used suggest the prepared chitosan-coated PLGA nanoparticles might be promising for topical ocular drug delivery.