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EYE DROPS OF FK506 AND FK506 PRODRUGS BASED ON CHITOSAN TO IMPROVE SOLUBILITY AND STABILITY

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ABSTRACT

Systemic administration of Tacrolimus(FK506) has potential in the treatment of local ophthalmic conditions involving cytokines, such as corneal graft rejection, autoimmune uveitis and dry eye syndrome. However, it is difficult to make tacrolimus ophthalmic formulation, because Tacrolimus(FK506) was so poor solubility in the water. Therefore, in order to improve water solubility of tacrolimus, three prodrugs such as FK506-G, FK506-S, FK506-S2 were synthesized using glucose, and sialic acid. The solubility of FK506 and prodrugs were determined 33.83ug/mL, 507.96ug/mL, 866.23ug/mL. This result is based on preparation of the eye drops. we manufactured emulsion eye drops and aqueous eye drops containing 0.05%(w/v) drug, which were measured solubility. Thus, the result of aqueous eye drops were 83.67ug/mL, 357.45ug/mL, 421.85ug/mL, 478.93ug/mL. Also, the mucoadhesive polysaccharide chitosan was evaluated as a potential component in ophthalmic delivery for enabling increased precorneal drug residence times. In case of FK506-S and FK506-S2, their solubility was decreased by adding chitosan. In addition, By measuring the pH is suitable for topical application of chitosan added and was analyzed. And suitability of the osmotic pressure was measured. The cytotoxic effects of blank eye drops and chitosan eye drops on Conjunctiva cell line were investigated using the MTT test.

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