# Study of a liposomal formulation containing sirolimus for the treatment of dry eye disease

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The aim of this study was to develop and characterize a liposomal product containing sirolimus to be administered subconjunctivally for the treatment of non-responsive keratoconjunctivitis sicca (KCS) or dry eye.

Formulations were prepared using an ethanol injection method, and an adaptation of the heating method in pursuance of the most suitable methodology. Liposomes were loaded with either a high dose of 1 mg/ml of sirolimus or a less toxic dose of 0.4 mg/ml. The effects of critical process and formulation parameters were investigated. Liposomes were characterized in terms of size, zeta potential, polydispersity, differential scanning calorimetry, morphology, entrapment efficiency, phospholipid content, thermal stability and sterility. The formulation was evaluated clinically in dogs with spontaneous KCS.

Sterile liposomal dispersions with sizes ranging from 140 to 211 nm were successfully obtained. High entrapment efficiency of 93 - 98% was achieved. The heating method allowed an easier production of liposomes with high entrapment efficiency, to significantly shorten production time and the elimination of the use of alcohol. *In vivo* testing of the liposomal sirolimus formulations in the spontaneous KCS dog model have produced promising results, particularly with a sirolimus dose of 1 mg/ml, indicating the need for further development and study of proposed formulations in the treatment of canine KCS. Clinical improvement in tear production in dogs with spontaneous KCS treated with the 1mg/ml dose product was observed.