Comparison Of The Concentrations Of Cyclosporine-A Containing Ophthalmic Microemulsion And Nanosuspension Formulations In Aqueous Humor In The Rabbit Experiment Model

Osman Karakus¹, Tughan Duran², Tuncer Degim³, Burcu Eser⁴, Sermet Sezigen⁴, Hakki Zafer Guney⁵, Canan Uluoglu⁶

¹Department of Pharmacology, Gazi University Faculty of Medicine, Turkey, ²Dunyagoz Hospital, Ankara, Turkey, ³Istanbul Bilim University Faculty of Pharmacy, Istanbul, Turkey, ⁴University of Health Sciences Faculty of Medicine Department of CBRN, Ankara, Turkey

Background: Dry eye, which is a result of decrease in the production of tears or an increase in evaporation, is a disease that causes complaints of foreign body sensation and pain. Even if the pathophysiology of the disease is not fully understood, it is thought to be an inflammation mediated by immunity. It is thought that the ophthalmic emulsion of the immunomodulator cyclosporin A has a positive effect on the underlying inflammatory pathology. However, it accumulates more in extraocular tissues and drug absorption to intraocular tissues is limited. Nanosuspension is a drug formulation that aims to increase bioavailability by producing drug particles in submicron dimensions. In this study, we aimed to compare the concentrations of Restasis and Depores, the Cyclosporin-A microemulsion formulations, which are bioequivalent in our country, to Cyclosporin-A nanosuspension formulation with particle size less than 500 nm in aqueous humor.

Methods: A total of 15 Albino New Zealand rabbits were included in the study and divided into three groups of five (Restasis, Depores, Nanosuspension). A drop of drug was applied on both eyes of the rabbits with an interval of 12 hours for 14 days. At the end of 14 days, aqueous humor aspiration was performed in sterile conditions from both chambers of the rabbits and drug concentrations were measured by HPLC (High Pressure Liquid Chromatography). The difference between the groups was compared with the Kruskal Wallis test.

Results: In the statistical analysis, we found that cyclosporin-A was less frequent in aqueous humor of the nanosuspension group.

Conclusion: In our study, the bioavailability was expected to be higher in the nanosuspension group. However, when experiments were conducted, a nasolacrimal drainage increase and a reaction were observed in the eyes of rabbits in the nanosuspension group. It was thought that the chemicals used during the preparation of the nanosuspension may increase the nasolacrimal drainage and therefore the concentration of drug passing the aqueous humor may be less in this group. From these preliminary results, it is planned to continue the research with the new Cyclosporin-A nanosuspension formulations prepared with different chemicals.