**Purpose:** Chronic inflammatory eye diseases, such as allergic conjunctivitis or dry eye are treated either with cyclosporine or tacrolimus as ophthalmic suspension. Marinomed aims to develop eye drops containing tacrolimus dissolved with the help of the Marinosolv technology, called Tacrosolv. Marinosolv allows the solubilization and thereby improvement of the bioavailability of practically insoluble drugs, such as tacrolimus, as dissolved drugs permeate faster into tissues. A set of experiments with formulations containing tacrolimus concentrations of up to 500 μg/ml dissolved in Marinosolv was conducted to investigate the permeation into cornea and conjunctiva of dissolved tacrolimus in comparison to the application of a tacrolimus suspension.

**Methods:** Porcine eyes were incubated ex vivo up to 60 minutes at room temperature after a single 50 μl topical application of 33, 66, 100, and 500 μg/ml Tacrosolv — 1.7, 3.3, 5.0, 25.0 μg tacrolimus — compared to 1000 μg/ml Talymus — 50 μg tacrolimus — a marketed eye drop suspension. Tissue concentrations in cornea and conjunctiva were evaluated by LC-MS/MS.

**Results:** The content of tacrolimus in the conjunctiva showed a linear relation to the applied concentration of Tacrosolv.

After application of 33 μg/ml Tacrosolv, a tissue concentration of 205±87 ng/g conjunctiva tissue was found, which is at 10-fold higher than the effective serum concentration of 2-20 ng tacrolimus/ml in patients undergoing organ transplantation. After application of 500 μg/ml Tacrosolv, a tissue concentration of 4571±1347 ng/g conjunctiva was found, which is 2.6-fold higher than the concentration in eyes treated with Talymus.

Tacrolimus content in the cornea showed a dose dependent increase and a peak concentration at 100 μg/ml of 1498 ng/g cornea, when treated with Tacrosolv. Application of 500 μg/ml Tacrosolv resulted in a tissue content of 791 ng/g in the cornea compared to 524±200 ng/g after a single application with Talymus.

**Conclusions:** The results demonstrated a concentration-dependent permeation of tacrolimus with the help of Marinosolv in both conjunctiva and cornea. A maximum concentration of 100 μg/ml in Tacrosolv should be sufficient to treat inflammatory anterior eye diseases, based on previous studies where a concentration of 2-20 ng/ml tacrolimus might be considered as the minimal effective concentration for controlling immune-mediated eye diseases.