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PURPOSE

Study on the permeability of excised ophthalmic tissues can evaluate the absorption property of drugs in different ophthalmic tissues by directional simulation of the osmotic environment of the dedicated tissues, and provide more possibilities for optimizing the corneal absorption pathway scheme and exploring the application of non-corneal absorption pathway. [1, 2]

OBJECTIVE(S)

Under current clinical background, local administration of conjunctival sac is the most common route of administration in ophthalmology. [3] Due to the absorption barrier formed by the special structure of the cornea, the bioavailability of drugs via the corneal absorption is low. [4] It is definitely challenging to improve the bioavailability of ocular topical drugs. Through this experiment, the permeability of ophthalmic tissues can be preliminarily evaluated, which is helpful for the development of ocular drugs.

METHOD(S)

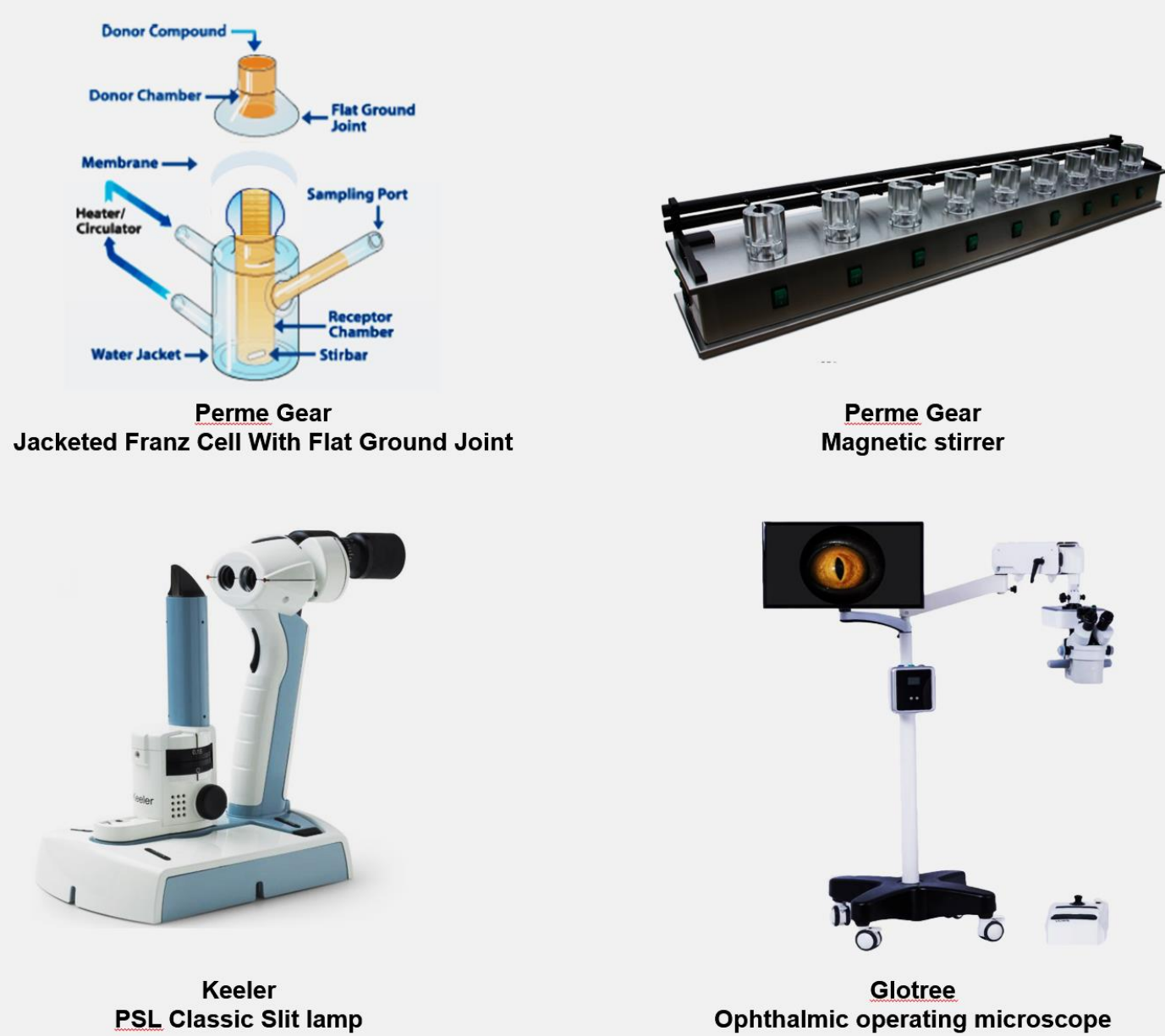


Figure 1. The main instruments of ophthalmic permeability platform.

Intact cornea and sclera of healthy male New Zealand White rabbits were used and placed on the Franz diffusion cell for the experiment, respectively. The commercial available drug 0.3% gatifloxacin eye drops and gel were used as the test drugs. Samples were collected at predetermined time points (0.5, 1, 1.5, 2, 2.5, 3, 3.5 and 4 h). The cornea was weighed at the endpoint of the experiment to calculate the corneal hydration levels (HL) to evaluate the cornea status. [5] The change curve was drawn according to the cumulative permeability of drugs, and the permeability of different dosage forms of drugs with the same concentration in different eye tissues was evaluated by Q_n and P_{app} .

RESULT(S)

Table 1. Comparison of permeability parameters of gatifloxacin in different dosage forms on cornea and sclera.

Tissue	Q_n ($\mu\text{g}/\text{cm}^2$)		P_{app} ($\times 10^{-6}\text{cm/s}$)	
	Eye drops	Gel	Eye drops	Gel
Cornea	244.49 $\pm$ 16.95	122.02 $\pm$ 10.49	5.66 $\pm$ 0.39	2.82 $\pm$ 0.24
Sclera	799.74 $\pm$ 187.45	292.03 $\pm$ 30.11	18.51 $\pm$ 4.34	6.76 $\pm$ 0.70

(Data presented as mean $\pm$ SD, n=3 per group)

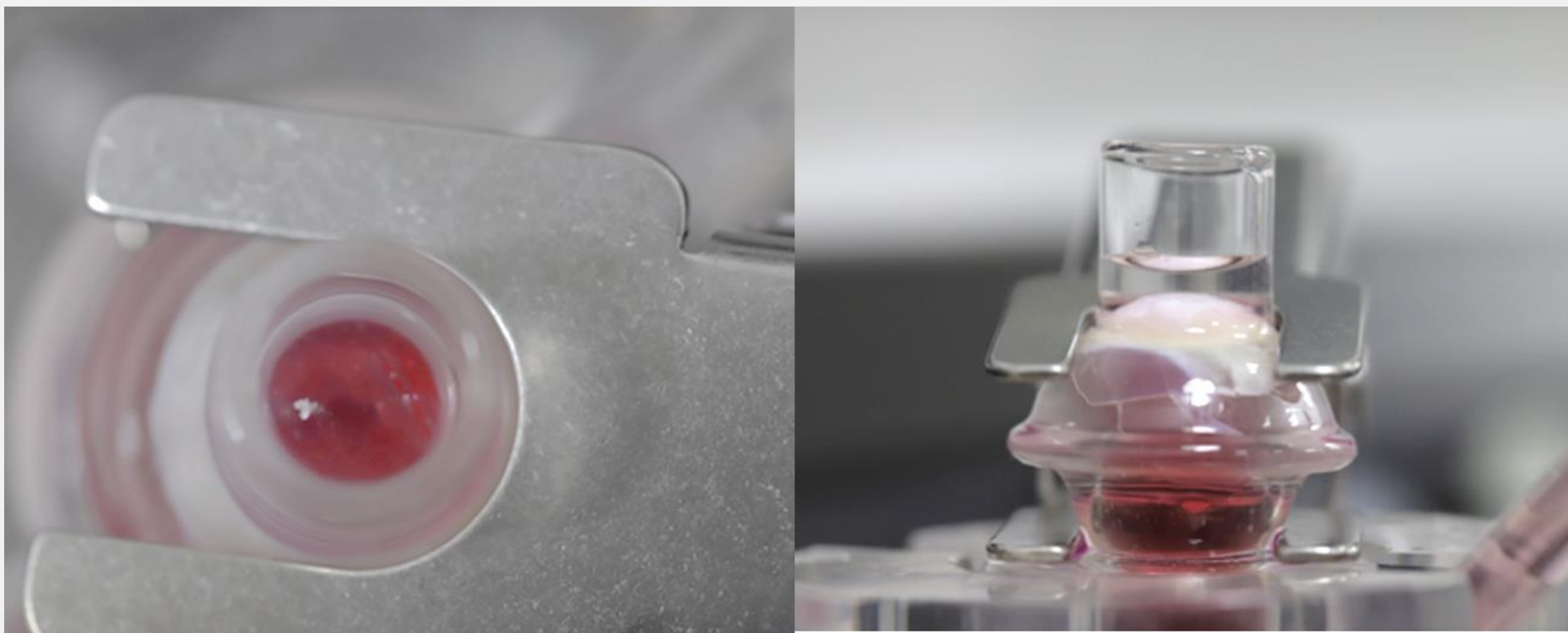


Figure 2. Experimental endpoint cornea (left) and sclera (right).

Corneal hydration levels (HL) is a sensitive index to measure corneal *in vitro* integrity. The degree of hydration has a great influence on drug permeability. If the corneal epithelium and endothelium are damaged, it will cause swelling of the interstitial layer and corneal.

According to calculation of the corneal hydration level, the result indicated that there was no corneal injury before the experiment ($81.7\% \pm 0.77\%$, HL ranges are typically $76\% \sim 83\%$). [5]

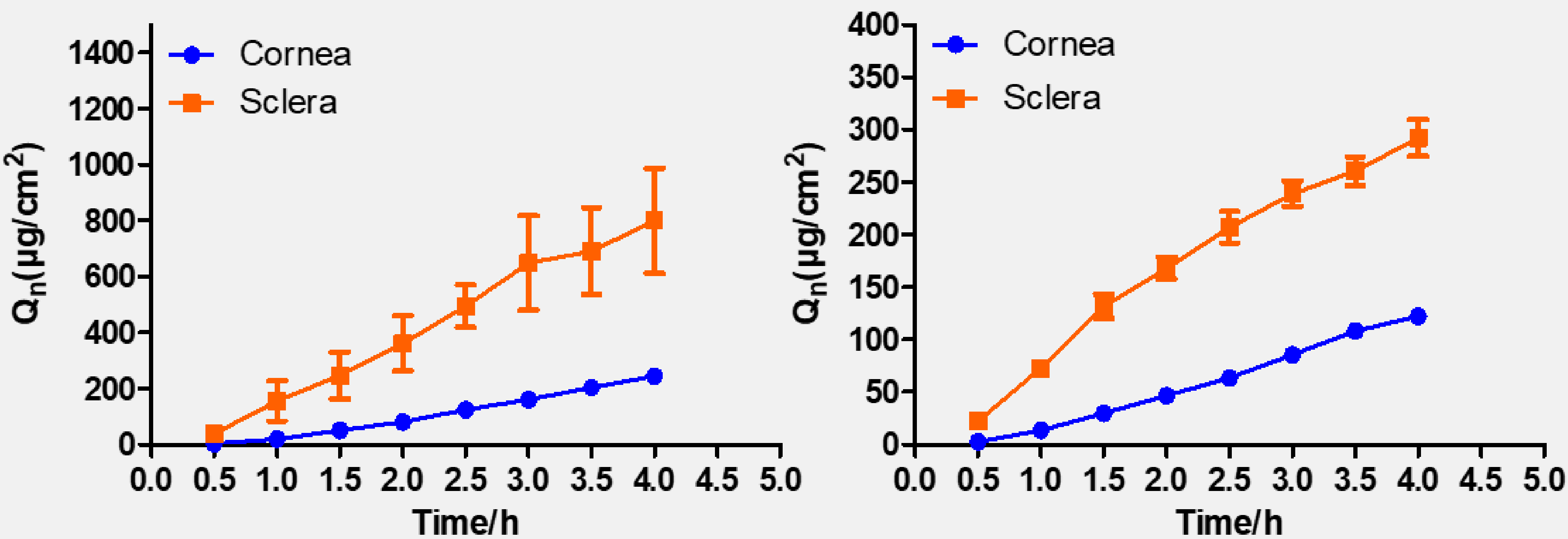


Figure 3. The cumulative permeability (Q_n) of gatifloxacin eye drops (left) and gels (right) in cornea or sclera of rabbits.

CONCLUSION(S)

The P_{app} in cornea and sclera in the eye drops group was higher than that of in the eye gel group. Previous studies have shown that excipients could prolong the drug release and retention in target tissues, but it may affect the rate at which the drug penetrates through the ophthalmic tissue. [3] The Q_n and P_{app} of sclera group were significantly higher than these of cornea group. Therefore, the development of new ocular delivery modes (such as periocular injection) has potential advantages. The preliminary evaluation of ophthalmic tissue permeability has important screening and evaluation value for the preclinical study of ophthalmic drug.

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