



## THE EXPERIMENT OF REDUCING INTRAOCULAR PRESSURE IN NORMAL ANIMALS

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**Background:** Glaucoma is a high-incidence eye disease that affects vision. The main cause is that the aqueous humor produced in the eye cannot be discharged normally, resulting in increased intraocular pressure. Long-term high intraocular pressure will oppress the optic nerve and damage it, causing vision loss and even blindness. Lowering intraocular pressure through existing medications or surgical treatments can slow down the development of the disease and reduce the risk of blindness. The effect of drugs on lowering intraocular pressure in normal animals can be used as a pharmacodynamic evaluation index for evaluating new antihypertensive drugs. We will introduce the experiment on the effect of drugs on the intraocular pressure of animals with a case.

**Medicine:** Rhopressa® (0.02% netarsaudil), glaucoma drug by Aerie Pharmaceuticals, was approved by the U.S. FDA in December 2017 to treat open-angle glaucoma or high intraocular pressure. Rhopressa® is a new rho enzyme (ROCK) inhibitor that can block the transport of norepinephrine. The effect of Rhopressa® on lowering intraocular pressure was studied using rabbits, dogs and monkeys with normal intraocular pressure.

**Method:** 24 adult cyan blue rabbits, 14 beagle dogs, and 12 cynomolgus monkeys were used; each species of animals were randomly divided into 2 groups. One eye was given 30  $\mu$ L Rhopressa® drops and the opposite eye was given the same amount of saline. Rabbits and monkeys were dosed once a day for 3 consecutive days; dogs were given a single dose. ICARE® TONOVET Plus tonometer was used to measure intraocular pressure in conscious dogs and rabbits. Reichert 30 pneumatic tonometer was used to measure the intraocular pressure of conscious monkeys. The measurement time points for rabbits and monkeys were before dosing, and 0.5h, 2h, 4h, 6h, and 24h after the first and third doses (monkeys were measured 48h after the 3rd dosage). Dogs were measured before dosing and 1h, 2h, 4h, 6h, 8h and 24h after doses.



Figure 1. Rebound tonometer and the measurement of intraocular pressure of conscious rabbits, dogs and monkeys

(A. ICARE® TONOVET Plus tonometer; B. intraocular pressure measurement of rabbit; C. intraocular pressure measurement of dog; D. cynomolgus monkey on customized monkey chair with Reichert 30 pneumatic tonometer)

**Result:** Compared with saline, Rhopressa® significantly reduced the intraocular pressure of rabbits 2-6h after the first and the third doses ( $p < 0.05$ ). And intraocular pressure continued decreasing after the third dose. After the first dose, intraocular pressure decreased by as much as  $236 \pm 7.5\%$  (4h); after the third dose, by as much as  $25.7 \pm 8.3\%$  (2h). 2h-24h after the first and the third doses, intraocular pressure of monkeys decreased significantly. 6h after the third dose, intraocular pressure decreased by as much as  $37.1 \pm 12.1\%$ . Rhopressa® could reduce intraocular pressure for monkeys for a longer period of time than for rabbits. For beagle dogs, only slight reduction (without statistical significance) of intraocular pressure was observed 2h-6h after dosage.

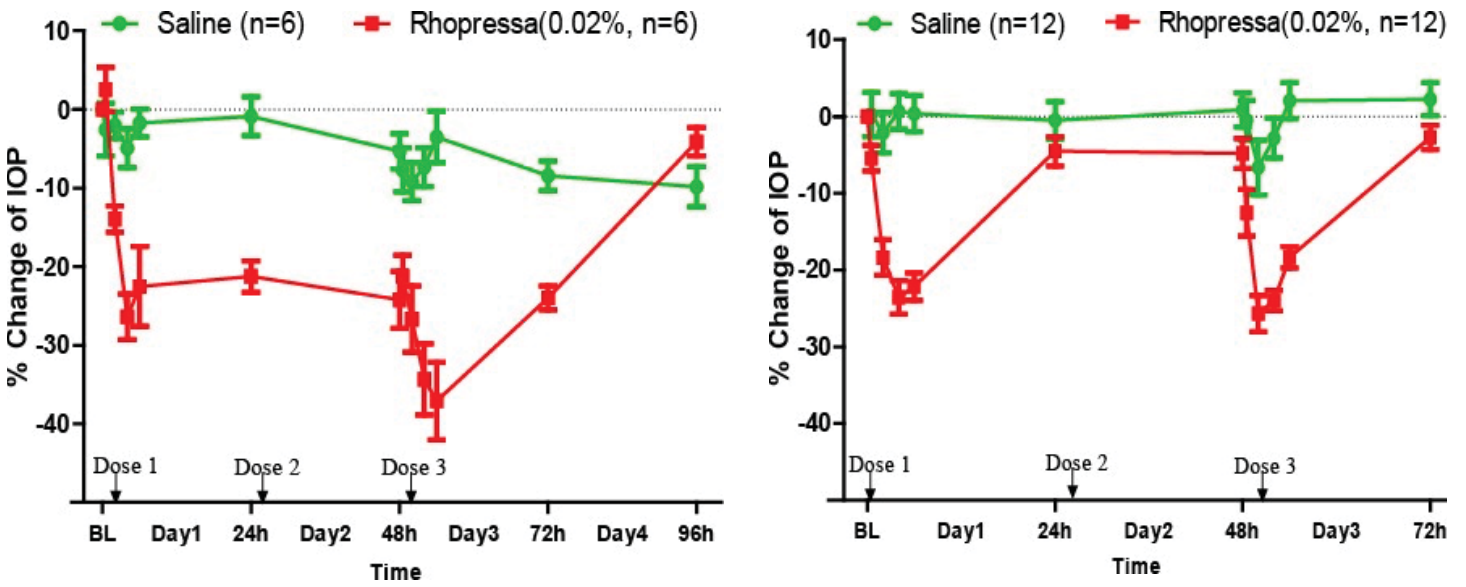


Figure 2. After-dosage intraocular pressure changes in cynomolgus monkeys (left) and cyan blue rabbits (right)

**Conclusion:** Rhopressa® can reduce intraocular pressure of normal cyan blue rabbits and cynomolgus monkeys. These two animals can be used as the preferred models for preclinical drug efficacy experiments of drugs similar to Rhopressa®.