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## Topical losartan inhibits corneal scarring fibrosis and collagen type IV deposition after Descemet's membrane-endothelial excision in rabbits

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The article "Topical losartan inhibits corneal scarring fibrosis and collagen type IV deposition after Descemet's membrane-endothelial excision in rabbits" is an experimental study that evaluates the potential of losartan to inhibit the process of fibrosis in an experimental model of fibrosis in rabbits.

Losartan, an angiotensin-converting enzyme (ACE)-2 inhibitor, also has inhibitory effects on tumor growth factor  $\beta$  (TGF- $\beta$ ). It is a safe drug for human use, as one of the first-choice drugs for systemic arterial hypertension, with millions of users worldwide and very few reported side effects. Despite this huge population making systemic use of losartan and other ACE inhibitors, there are no reports associating the use of ACE inhibitors with the reduction of fibrosis or haze in more diverse scenarios.

The study design and methods seem appropriate, although the process of posterior corneal fibrosis is somewhat different from that in the anterior region, and the effect of chronic corneal edema due to the lack of endothelium may interfere with the application of the results for use in humans, where other mechanisms of fibrosis may act.

The authors found that, for the experimental model of posterior corneal fibrosis, the use of topical losartan 0.4 mg/mL was associated with lower scores of opacity and fibrosis markers such as TGF- $\beta$  and type IV collagen.

Interestingly, the oral use of losartan at the maximum veterinary dose, which is much higher than that usually used systemically in adult humans, had no inhibitory effect on opacity and fibrosis markers and no adjuvant effect, a result suggesting that penetration of the drug through the cornea and aqueous humor probably does not reach therapeutic levels.

Clinical application of the these findings should be viewed with caution, for several reasons: the findings in rabbits are not always transferable to humans; the study did not address the long-term effects of the treatment; and the study did not address whether there will be a recurrence of the fibrosis process after suspension of the medication, the systemic effects of topical use, and the effects of the association of topical losartan with other medications already used for the treatment and modeling of corneal healing, such as corticosteroids and mitomycin C.

In summary, whereas the evidence from the study is intriguing and promising, it is not strong enough to support the conclusion that losartan is effective in inhibiting fibrosis and haze in the cornea. Further research, particularly in humans, is needed to better understand the potential benefits and limitations of losartan for this use.

Sampaio LP, Hilgert GSL, Shiju TM, Murillo SE, Santhiago MR, Wilson SE. Topical losartan inhibits corneal scarring fibrosis and collagen type IV deposition after Descemet's membrane-endothelial excision in rabbits. Exp Eye Res. 2022 Mar;216:108940. doi: 10.1016/j.exer.2022.108940.

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