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Glaucoma is a chronic eye disorder affecting more than 1% of the world population and is characterised by sustained elevation in intraocular pressure (IOP). The long-term elevation in IOP is a potential risk for the irreversible damage to the eye, finally resulting in blindness. The drug therapy of glaucoma is therefore, aimed at reducing the IOP through various mechanisms. The search for new drugs for the treatment of glaucoma is steadily accelerating, mainly because of the advancement in the knowledge of physiological and biochemical processes of the aqueous humor dynamics. The conventional drugs of the past decade improved pharmaceutically with respect to their ocular bioavailability. The new drug delivery system has reduced the frequency of drug dosing from four times a day to once in a day. This has improved not only the patient compliance but also has reduced the fluctuations in IOP. Recently several new promising drugs have emerged such as apraclonidine and brimonidine (α2-adrenoceptor agonists), dorzolamide - a water soluble, topically effective carbonic anhydrase inhibitor and latanoprost a prostaglandin F2α-derivative. These new drugs are steadily replacing the conventional drugs like timolol, pilocarpine and physostigmine.

Angiotensin converting enzyme inhibitors have recently attracted attention as a new class of drugs for the treatment in glaucoma. There are few
reports suggesting effectiveness of enalaprilat, ramiprilat and captopril in lowering IOP in animals as well as in patients with glaucoma (Lotti et al., 1990; Constad et al., 1988). The evidence for the presence of the ACE system in the eye has also been reported (Sramek et al., 1992). Wagner et al. (1996) demonstrated the gene expression for various components of the renin angiotensin system in various ocular tissues. Meyer et al. (1995) provided an evidence for the importance of the AT1-receptors in the microcirculation in the ocular tissues. However, the mechanism of action for the ACE-inhibitors in lowering IOP has not been definitely known. The three possibilities that can be put forth as the possible mechanism for ACE inhibitors are: (i) Autonomic effects, (ii) involvement of prostaglandins and (iii) Angiotensin converting enzyme inhibition.

Autonomic effects of ACE inhibitors have been known for a long time. These include facilitation of vagal bradycardia (Rechtmann and Majewski, 1993), inhibition of response to sympathetic spinal outflow (Antonacci et al., 1980) and inhibitor of vasconstrictor response to noradrenaline (Okuno et al., 1979). Large number of such reports have shown that parasympathetic action of the ACE inhibitors are mainly responsible for the absence of tachycardia while reducing the blood pressure. The parasympathomimetics such as pilocarpine and physostigmine are among the popular agents for glaucoma. The likelihood of this property of ACE inhibitors, as a possible mechanism for IOP lowering effect, needs to be investigated.
Lotti et al. (1990) proposed the involvement of prostaglandins in the ocular hypotensive effect of enalaprilat. The conclusion was based on the findings that indomethacin blocked the IOP-lowering effect of enalaprilat. ACE inhibitors are also the inhibitors of kininase-II and thus prevent the breakdown of bradykinin. The increased bradykinin levels promote prostaglandin synthesis. Prostaglandins, especially PGF$_{2\alpha}$ is known to increase uveoscleral outflow of aqueous humor (Crawford and Kaufmann, 1987). Further, Lotti et al. (1990) studied the effect of enalaprilat in African Green monkeys. There are large interspecies variations with respect to uveoscleral outflow. Uveoscleral outflow in monkeys amounts to 30-34% of the total aqueous outflow as against 10-14% in humans and in rabbits (Bill and Phillips, 1971). Thus, though the proposition by Lotti et al. (1990) sounds logical, the mechanism needs to be confirmed in the other species with low uveoscleral outflow rate under physiological conditions.

Although, the role of RAS in ocular tissue has been documented, the exact physiological importance of this system is not known. It can be presumed that it plays a significant role in aqueous humor dynamics (Percicot et al., 1995; Denis et al., 1995), ocular blood circulation (Meyer et al., 1995; Rockwood et al., 1987) and in retinal neuronal function (Ferrari-Dileo et al., 1988). It is possible that ACE inhibition may be one of the important mechanisms in lowering IOP.
In the light of above, present investigation was undertaken to study the ocular hypotensive action of some ACE inhibitors such as enalaprilat, enalapril, ramiprilat, ramipril and fosinopril in rabbits. Attempts were made to elucidate the mechanism of action considering three possibilities - parasympathetic effects, involvement of prostaglandins and the inhibition of ACE.