Effects of (-)-carveol and HPMC on the in vitro ocular transport and the in vivo intraocular pressure lowering effects of dorzolamide formulations in normotensive New Zealand rabbits

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Abstract
The objective of the current study was to maximize the ocular bioavailability of the carbonic anhydrase inhibitor, dorzolamide hydrochloride (DZD) via (a) enhancement of DZD corneal transport using terpene enhancers, (b) reducing pre-corneal loss of the installed dose via increased formulation viscosity, and (c) assessment of the in vivo intraocular pressure (IOP) lowering effects of test formulations using rabbit. DZD was formulated as a 2% ophthalmic solution containing different concentrations of HPMC as a viscosity improving agent (VIA), and (-)-carveol as a corneal penetration enhancer. The transport of DZD from test formulations was quantitatively determined using in vitro diffusion experiments, the permeability parameters were mathematically calculated, and the in vivo IOP lowering effects were assessed using a Tono-Pen XL® tonometer. The results revealed a good correlation between the in vitro permeability parameters and the in vivo ΔIOP. The magnitude of the DZD-IOP lowering effects and durations of actions for DZD formulations were dependent on (a) the concentration of (-)-carveol, and (b) the contact period with ocular tissue which was found to be a single-valued function of the HPMC as VIA. Drug Dev Res 70, 2009. © 2009 Wiley-Liss, Inc.