Influence of Various Concentrations of Terpene-4-ol Enhancer and Carbopol-934 Mucoadhesive upon the *In Vitro* Ocular Transport and the *In Vivo* Intraocular Pressure Lowering Effects of Dorzolamide Ophthalmic Formulations Using Albino Rabbits

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**ABSTRACT:** The objectives of the current study are (i) to maximize the ocular bioavailability of dorzolamide hydrochloride (DZD) through: (a) enhancement of the DZD corneal transport using various concentrations of selected natural terpene-4-ol enhancers, (b) increasing the contact time of the drug with the absorbing tissues of the eye by selecting carbopol-934 (C-934) as a mucoadhesive to reduce the extent of pre-corneal loss of the installed dose due to the physiologically normal fast tear-washout, and (ii) to assess the *in vivo* intraocular pressure (IOP) lowering effects of the gel test formulations using normotensive New Zealand albino rabbits. In this study, DZD was formulated as 2% ophthalmic gels containing different concentrations of C-934 as a mucoadhesive, as well as, with various concentrations of terpene-4-ol as a natural corneal penetration enhancers. The transport of DZD from the gel formulations was quantitatively determined using *in vitro* diffusion experiments. The permeability parameters of DZD were calculated employing the most appropriate mathematical equations. Further, the *in vivo* IOP lowering effects of the test formulations were also assessed using the TONO-PEN®XL application tonometer in normotensive New Zealand albino rabbits. The overall results revealed that there is a direct correlation between both the *in vitro* permeability parameters and the contact period with the ocular tissues and the *in vivo* DIOPIOP. In such case, the *in vitro* permeability parameters of DZD could be used as a determinant for the *in vivo* IOP measurements. The magnitude of the DZD-IOP lowering effects as well as the durations of actions for the test formulations has been found to be greatly dependent upon (a) the concentration of the terpene-4-ol corneal penetration enhancer and (b) the duration of contact period with the ocular tissues, which was found to be a single-valued function of the C-943 mucoadhesive concentration. © 2009 Wiley-Liss, Inc. and the American Pharmacists Association J Pharm Sci 89:9:1-10, 2009

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