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 using selected carbopol-934 (C-934) as mucoadhesive to reduce the extensive 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% formulations ophthalmic gels containing different concentrations of C-934 as 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 TONOPEN® XL applanation 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 ΔIOP. 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-934 mucoadhesive concentration. © 2009 Wiley-Liss, Inc. and the American Pharmacists Association J Pharm Sci 99:119–127, 2010

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