Benzalkonium Chloride as an Ophthalmic Preservative: Examining Harmful Implications, Toxic Inhibition, and Potential Alternatives

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Whether a simple eye-wash or an anti-glaucoma solution, ophthalmic medications have employed benzalkonium chloride (BAK) as a preservative since the 1950's. Currently, BAK remains the most common ophthalmic preservative, but has recently been identified to cause acute toxic effects on the ocular surface through 1) detergent interactions with the cell membrane and 2) cellular damage by reactive oxygen species (ROS) hyperproduction. Thus, to address the issues of safety and compliance that BAK poses for countless patients, this study focused on inhibiting the two aforementioned mechanisms of BAK toxicity and identifying alternative preservatives for future use. Specifically, the efficacy of carboxymethyl cellulose (CMC), an anionic polymer, in inhibiting BAK's detergent-induced toxicity and the efficacy of a-tocopherol (TOC), a vitamin E, in inhibiting BAK's ROS-induced effects were examined. Additionally, methyl paraben (MP), which belongs to the generally safer class of oxidizing preservatives, was proposed as a less toxic alternative to BAK. To quantify toxicity, MTT assays were performed on Chang's immortalized conjunctival cells, comparing each group to the 0% viable control of formalin (10% paraformaldehyde). Both CMC and TOC significantly reduced BAK toxicity in vitro ($p<0.05$ at all BAK concentrations). MP also possessed a significantly superior safety profile to BAK's ($p<0.05$ at all BAK and MP concentrations), suggesting the applicability of oxidizing preservatives. Both inhibition of BAK and alternative oxidizing preservatives provide viable means of addressing BAK ocular toxicity. In the future, the focus will be on seeking effective yet innocuous-to-human preservatives and increasing their availability to eliminate BAK from ophthalmic pharmaceuticals.