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# The Increasing Need for Preservative-free Topical Formulations for Chronic Ocular Therapy: Dry Eye Disease and Glaucoma

Alejandro Rodriguez-Garcia
Tecnologico de Monterrey, Escuela de Medicina
Monterrey, Mexico

**COLUMN ARTICLE**

Dry eye disease (DED) accounts for a large number of patients (prevalence estimated range, 5 to 35%) seen daily on general ophthalmology clinics [1]. The disease is frequently long lasting, more prevalent in women and increases with age [2]. Long-term use of lubricant eyes drops is the mainstay therapy for the symptomatic relief of patients suffering from DED. Nowadays approximately 70% of lubricant eye drops available worldwide require preservatives in their formulation in order to make them stable and sterile [3]. Ophthalmic formulations are usually preserved in three different kinds of compounds: detergents, oxidizing, and ionic-buffered preservatives [4]. The detergent benzalkonium chloride (BAK), the most commonly used preservative in ophthalmic drops causes disruption of the tear film, increase tear evaporation and osmolarity, as well as damage to ocular surface epithelial cells [5]. The duration of therapy, the type and number of different medications required for treatment, as well as the number of drops per day needed to obtain therapeutic efficacy are directly related to the potential for serious ocular surface disease (OSD) due to cumulative toxicity [6]. It seems paradoxical that in our attempt to improve the signs and symptoms of DED and hence, improve the quality of life of patients suffering from this common condition, we are frequently applying lubricant eye drops preserved with substances that potentiate toxicity to the cornea and conjunctiva.

The situation seems even worse for patients on anti-glaucoma therapy. In recent years, the awareness of quality of life and OSD related to anti-glaucoma medications has become a major issue for ocular surface and glaucoma specialists [7,8]. The prevalence of clinically significant OSD signs in glaucoma patients may be as high as 70.3% [9,10]. Risk factors correlated with severity of OSD in long-term anti-glaucoma therapy include, patient age, number of daily drops, treatment changes for ocular intolerance, intraocular pressure, and glaucoma severity [11]. At the end, OSD has a significant negative effect on therapeutic compliance for this progressive and irreversible blinding disease [8].

Topical drug administration will remain the basis of treatment for ophthalmic diseases in the future. Therefore, considering the evidence on the increased prevalence of preservative-related OSD of ophthalmic formulations and the awareness of its impact in patient´s compliance and quality of life, the pressing need for pharmaceutic research, development, and innovation on preservative-free drops must not delay. Current strategies applied by the pharmaceutical industry include, reduction of preservatives concentration, oxidizing preservatives, longer duration of therapeutic effect (depots), sustained-release drug devices, preservative-free unit-dose vials, and multi-dose preservative-free dispensers. The latter are based in different technologies focused on preventing the backflow, airtight sealing, and antibacterial filtering. In conclusion, preservative-free sterile formulations will be the future trend to avoid hazardous chemicals from active pharmaceutical ingredients. The challenge for ophthalmic pharmacists is to preserve chemical formulations from bacterial contamina-

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tion, but without any additives or preservatives. This need opens a wide range of possibilities to innovate.

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