IN VITRO EVALUATION OF THE PROTECTIVE EFFECT OF SODIUM HYALURONATE AGAINST TOXICITY INDUCED BY ANTI-GLAUCOMATOUS FORMULATIONS

María Silvia Passerini[1], Giselle Rodriguez[1], Jeremias Galletti[2]

1.Poen Laboratories, Medical Affairs, Buenos Aires, Argentina, 2.National Medicine Academy of the city of Buenos Aires, Innate Immunity Laboratory, Experimental Medicine Institution/CONICET, Buenos Aires, Argentina.

Purpose

Several studies have shown that topical anti-glaucomatous medication may reduce the viability of corneal epithelial cells. The purpose of this study is to assess the in vitro toxicity induced by antiglaucomatous medication and to evaluate the protective effect of sodium hyaluronate (SH) in these cases.

Methods

The HEC-2 cell line (human corneal epithelium) was employed. Cell monolayers were exposed to twelve preservative-free (PF) anti-glaucomatous formulations and their vehicles for 30 minutes; we repeated this procedure and added previously PF-SH 0.4% for 30 minutes. Fresh culture media was included after washing and metabolic activity was evaluated by reducing resazurin after 3 hours. Subsequently, data were analyzed by one-way and two-way ANOVA and the results are shown as mean ± SD of 3-6 replicates each.

Results

Most anti-glaucomatous formulations significantly decreased cell viability (Figure 1). However, most vehicles didn't cause a significant cell viability reduction (Figure 2). In those cases, we attribute the toxic effect specifically to the active ingredients of each formulation.

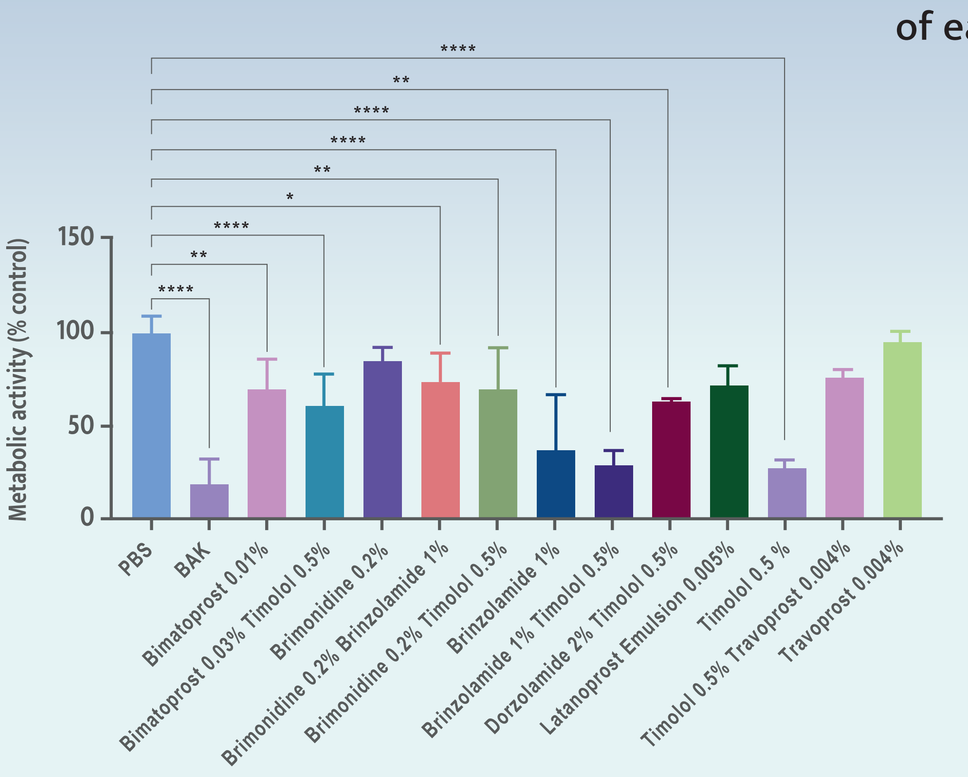

Figure 1. PF Anti-glaucomatous formulations. Cell viability significantly decreased vs PBS in presence of most of the evaluated formulations (*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001).

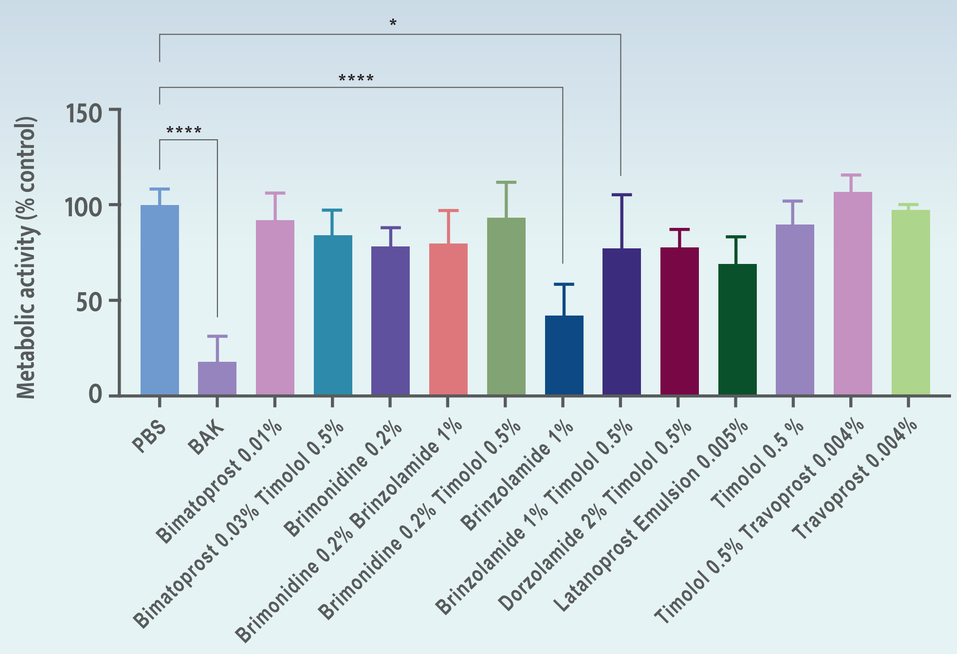

Figure 2. PF Vehicles of anti-glaucomatous formulations. No significant changes in cell viability vs PBS were observed after incubation with most vehicles (*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001).

PF-SH 0.4% significantly counteracted the toxic effect induced by anti-glaucomatous formulations containing: Bimatoprost 0.01%, Bimatoprost 0.03% + Timolol 0.5%, Brimonidine 0.2% + Timolol 0.5%, Brinzolamide 1%, Brinzolamide 1% + Timolol 0.5% and Dorzolamide 2% + Timolol 0.5%.

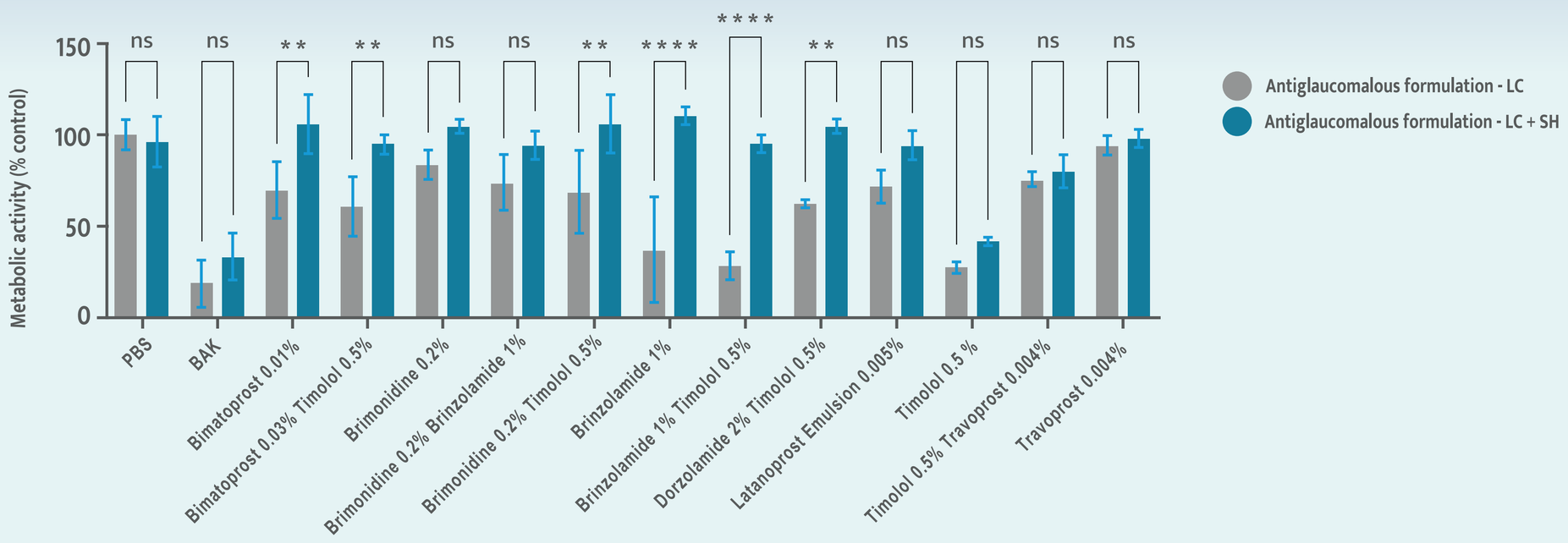

Figure 3. Anti-glaucomatous formulations with and without PF-SH. Cell viability increased significantly in presence of SH (*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001).

Conclusion

- Most of the evaluated anti-glaucomatous formulations decreased cellular viability.
- The fact that most of the vehicles did not cause toxicity suggests that anti-glaucomatous active ingredients may produce this effect.
- PF-SH 0.4% demonstrated a protective effect against formulation-induced toxicity containing the following drug classes: prostaglandins, β-blockers, α-adrenergic agonists and carbonic anhydrase inhibitors.
- The protection provided by PF-SH 0.4% could be the result of the improvement of the physiological conditions of the general cell culture, regardless of the drug class.

This study was funded by: POEN Laboratories.

Queries: investigación@poen.net.ar