

A Comparative Evaluation of Lipid-based formulations for Dry-Eye Therapy using a corneal epithelial Cell Desiccation Model and Physicochemical Measurements

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SUMMARY

A new approach to dry eye treatment is the inclusion of both aqueous and lipid components in a single formulation to target multiple layers of the tear-film. While certain ingredients have beneficial properties in isolation, it must be determined whether the components combined within a given formulation are capable of exerting the desired effect. This study determined the potential beneficial effects of lipid-based products, which included 3 novel formulations (SG1, SG2 and AG2) and 2 marketed OTC products (Systane Balance [SB] and Refresh Optive Advanced [ROA]) on the tear film and ocular surface using multiple physicochemical measurements and a corneal epithelial cell model.

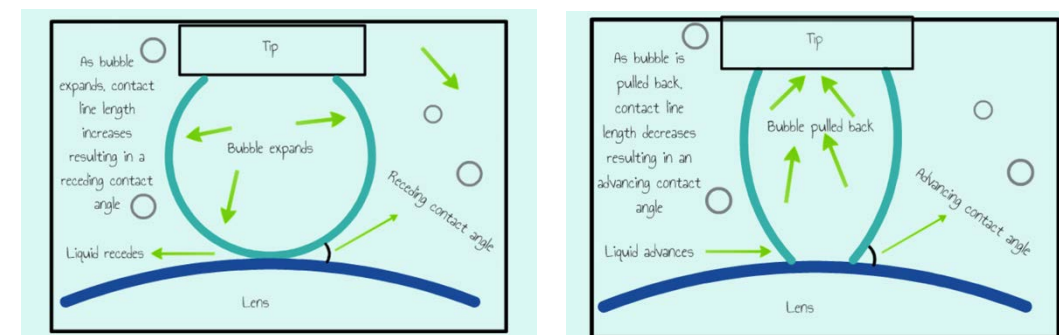
The two OTC products had low viscosities (SB: 2-3 cps; ROA: 10-12 cps) and only SB showed shear-thinning property. The three novel formulations had significantly higher viscosities and were markedly shear-thinning. All formulations had low surface tension and good wettability due to the presence of surfactants. SB and ROA were not significantly destabilized upon STF dilution and did not effectively release their component lipids to improve the compressibility of the TFL. In contrast, SG1, SG2 and AG2 showed destabilization by STF and released of lipid and addition to TFL. All three also provided protection to cells exposed to desiccating conditions whereas SB & ROA had minimal effect.

METHODS

Viscosity measurements were performed on a Brookfield viscometer using a cone and plate attachment at a shear rate of 15/sec. Shear thinning was determined using a TA AR2000 instrument using a double-gap concentric cylinder attachment and stress range from 0.1 to 5 Pa.

Surface tension measurements and wettability assessments were done using a Kruss-K 100 tensiometer and captive bubble method with Acuvue Oasys lenses respectively.

Figure 1. Wettability assessment using the Captive Bubble method



Destabilization of formulations in simulated tear fluid or STF was demonstrated using a dispersion analyzer, LUM, LumiSizer®. The samples were tested neat or after dilution with STF (1:1 ratio) and stressed for 4 hrs at speeds of 200-2000 RPM at 37°C. The % transmission was recorded throughout the analysis.

Lipid delivery was assessed by Langmuir Film-Balance model. A shallow trough with symmetrically moving barriers was used to compress a thin film of a synthetic meibum mixture (SM) on an aqueous subphase. The surface pressure (SP) of the film was monitored by an electrobalance coupled to the liquid surface by means of a small strip of chromatography paper (Wilhelmy plate). The resulting SP-Area isotherm described the SP of the film to increasing lateral compression (decreasing surface area). The ability of lipids to “disengage” from a vehicle and to move to the subphase surface was demonstrated by an improvement in the compressibility of the film.

Ability to protect human corneal epithelial cells from death under desiccating conditions was evaluated using cells pre-treated with formulation and then subjected to desiccation, after which cell viability was measured.

RESULTS

Table 1. Viscosity of OTC and experimental products

Sample ID	Spindle	Viscosity cP
SG2	CP-52	96
AG2	CP-40	87.8
SG1	CP-40	38.4
ROA	CP-40	12.57
SB	CP-40	3.98

Figure 2. Rheology of Lipid-Based Formulations

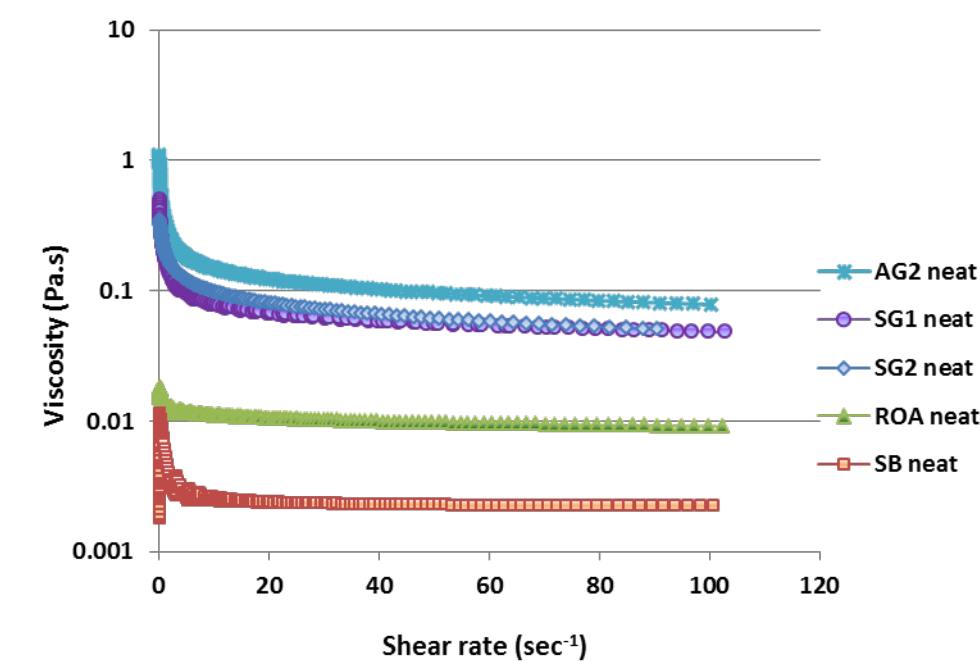


Figure 3. Lumisizer Analyses of Lipid-Based Formulations

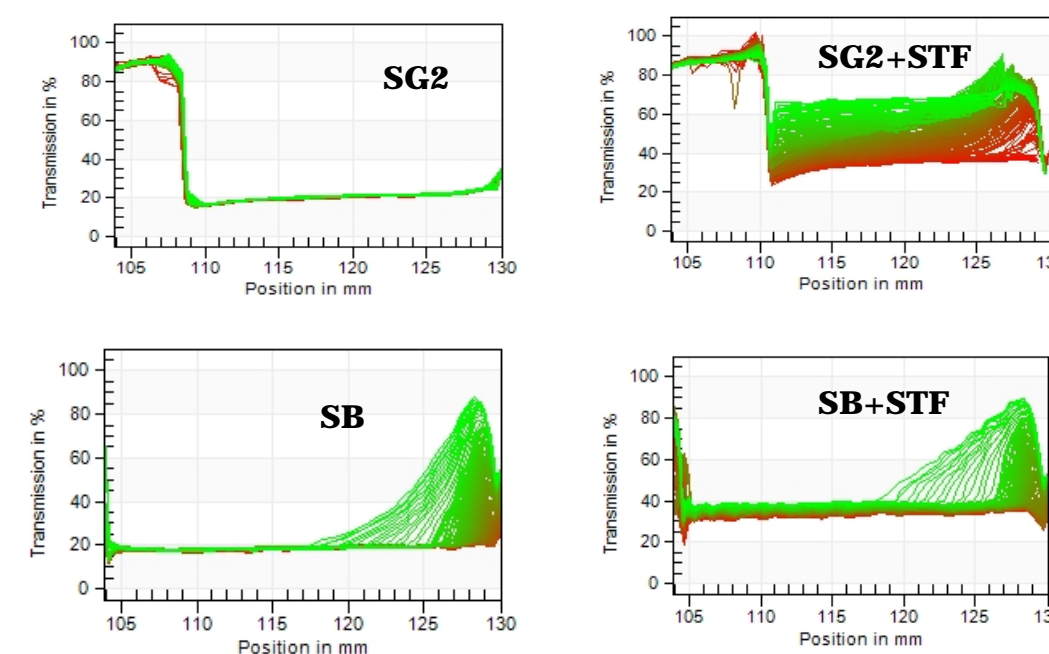


Figure 4. Wettability assessment on Acuvue Oasys lenses

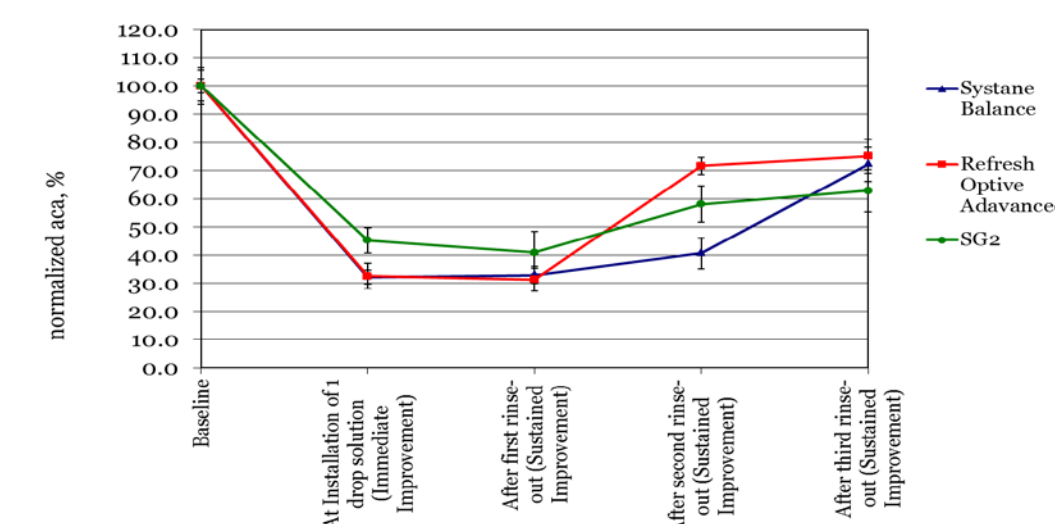


Figure 5. Release of lipids from formulations

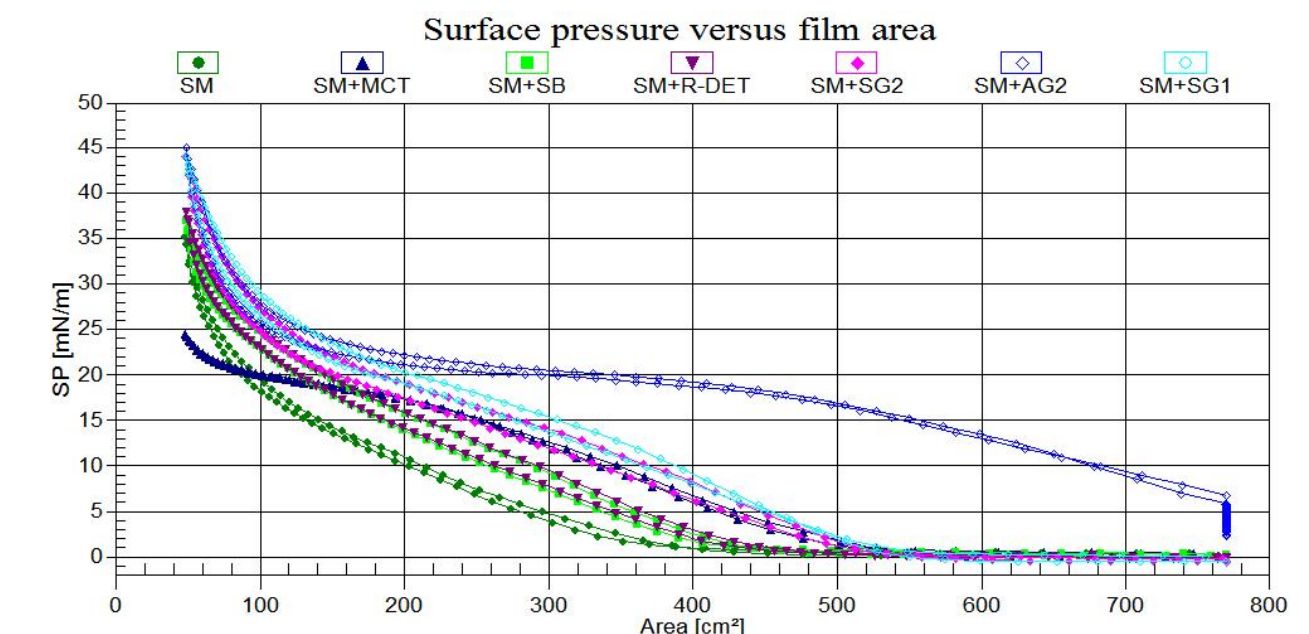
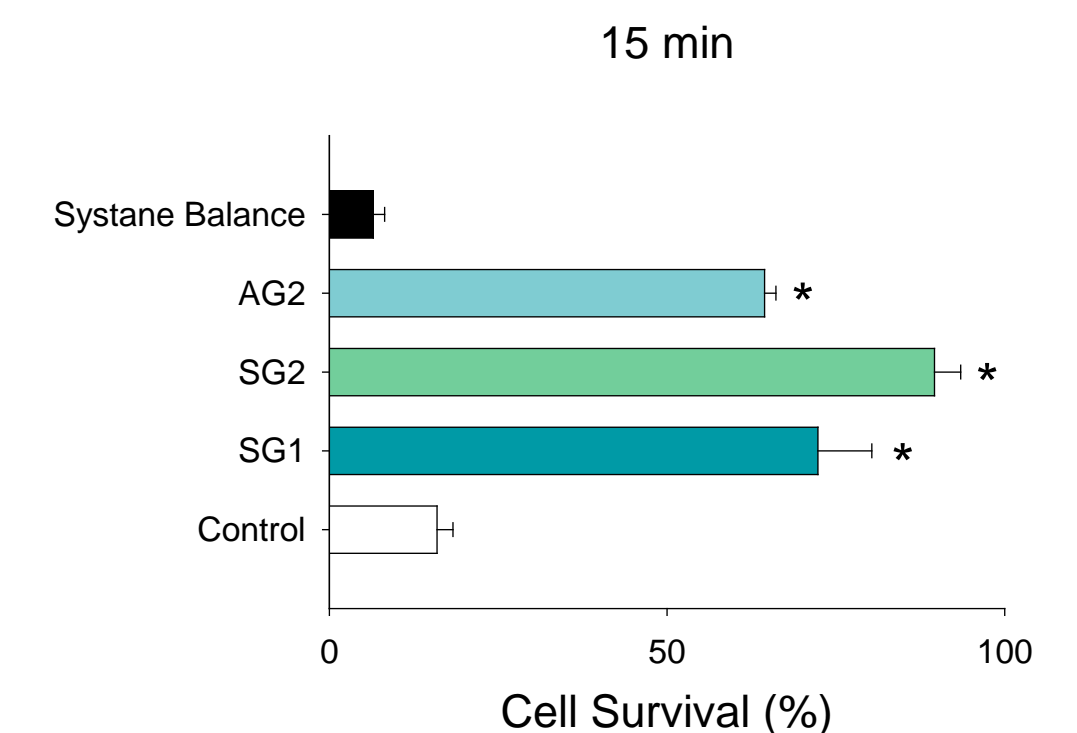


Figure 6. Protection of HCEpiC against desiccation induced death



CONCLUSIONS

Based on the in vitro physicochemical properties and desiccation-induced corneal cell death model, novel OTC dry eye formulations have properties which may be beneficial to the ocular surface, including long retention, release of lipids to the STF and protection of corneal cells from desiccation. Marked differences in responses were evident between formulations tested despite them all including both an aqueous and lipid component. Clinical evaluation of the novel products is warranted.