ABSTRACT

Formulations tested for ocular irritation using the Bovine Corneal Opacity and Permeability (BCOP) assay may be assigned a specific irritation label based on the resulting In Vitro Iritis Score (IVIS) and specific regulatory guidelines (e.g., OECD, EPA, and CLP) that provide cutoff values for classifications. The ability to reduce ocular irritation by slightly adjusting the physical properties of a formulation is highly desirable. Laboratory investigations found that increasing viscosity using increasing amounts of Carbopol® as a thickening agent reduced ocular irritation when mixed with a 1% NaOH solution in water. Following a 10-minute exposure in the BCOP assay, 1% NaOH was previously classified as a severe ocular irritant (IVIS=161.6). Increasing Carbopol® from 0.25% to 1.25% in a mixture with 1% NaOH decreased the IVIS score to a range of values between 75.3 and 18.3 and decreased ocular irritation across a range of irritation classifications from severe to mild irritation (n=3 corneas per treatment). Exposure to 1% Carbopol® alone exhibits minimal irritation (IVIS<13) and Carbopol® is consequently not considered to contribute to ocular irritation within the tested mixtures. Histopathology studies further support that exposure to 1% Carbopol® results in damage similar to negative control-treated corneas and that epithelial and stromal damage decreases as viscosity increases. Additionally, preliminary findings indicate that when a small amount of thickness is added to a complex formulation containing otherwise harsh ingredients, ocular irritation can be mitigated from a Category I label to a Category II label according to current EPA guidelines applicable to cleaning products containing surfactants and solvents. These results indicate that increasing viscosity may be an effective tool for reducing ocular irritation potential of a formulation. Viscosity, along with other physical properties, may therefore be used to inform decision making during product development, ultimately affecting downstream users in such areas as marketing, labeling, packaging, and distribution.

INTRODUCTION

In Vitro Ocular Irritation of Harsh Ingredients

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MATERIALS AND METHODS

RESULTS

CONCLUSIONS

The authors would like to acknowledge Jennifer R. Nash (IIVS) for histopathology evaluation.

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Preliminary Investigation on Reducing Ocular Irritation Potential of Harsh Ingredients By Increasing Formulation Viscosity

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Histology is able to provide useful information regarding the degree and depth of injury including identifying specific changes in the epithelium, stroma, and endothelium.

Figure 1: Ocular irritation of harsh ingredients diminishes as viscosity increases. The BCOP assay (n=3 corneas per sample) was performed for 1% NaOH solutions thickened with an increasing amount of Carbopol® to modify the viscosity of the solution. The 1% Carbopol® control solution demonstrates that the Carbopol® is not contributing to the irritation, whereas the 1% NaOH positive control solution indicates that the solution is corrosive based on the BCOP classification criteria.

Figure 2: Altering the viscosity of a cleaning prototype complex formulation can also attenuate ocular irritation. A cleaning prototype composed of surfactants and solvents was tested in the BCOP assay and met the EPA criteria for a Category I corrosive formula (IVIS>42.2). When the formula was thickened slightly (still remained a free-flowing liquid), the BCOP results were below the threshold for EPA Category I (IVIS<42).

Figure 3: Histopathology Evaluation. In 1% Carbopol® treated corneas, only upper epithelial damage was observed and stromal and endothelial observations were similar to the negative control treated corneas (A,B). As Carbopol® concentration decreased, the 1% NaOH mixture, an increase in the degree of damage to the corneas was observed as compared to Carbopol® only treated corneas (C-F). Epithelial changes including sloughing and detachment from the basement membrane, desaturation of the epithelial protein, and blanching of the nuclei in the epithelium were observed. The stromal membrane exhibited progressive damage with increasing stromal swelling and eventual loss of endothelial function (C-F).

The BCOP assay is a rapid, effective non-animal method to evaluate the ocular irritation potential of cleaning formulations.

Increasing viscosity may be an effective tool for reducing ocular irritation potential of a formulation. Viscosity, among other physical properties, may therefore be used to inform decision making during product development, ultimately affecting downstream users in such areas as marketing, labeling, packaging, and distribution.

CONCLUSIONS

1) Test a common, harsh ingredient (1% NaOH) independently using the BCOP assay and compare results when the ingredient is combined with increased amounts of a commonly used thickener (Carbopol®).
2) Add thickener to a complex formulation containing harsh ingredients and evaluate findings.

OBJECTIVES

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