Assessment of Cosmetic Ocular Irritancy in Human Subjects
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Introduction
Ocular irritation testing represents an important step in the safety evaluation of cosmetic products. Increasing concern regarding the ethics of animal testing has prompted the development and use of numerous in vitro systems to approximate the irritancy potential of cosmetics designed for human application. While these systems are capable of determining potential tissue damage at a cellular level, human subjective responses to ocular cosmetic exposure, which may be more or less sensitive to particular irritants, cannot be accurately predicted from in vitro results. For the same reasons that the rabbit eye, despite the name of ocular tissues human eye, i.e. differences in corneal ultrastructure and in the sensitivity to eye irritants, cell lines cannot effectively simulate the human eye. Thus, the ideal system to use to test the ocular safety of cosmetics is the human eye, which is frequently disregarded due to its expense. However, in vitro systems have been shown to be capable of utilizing oculist instillation of test cosmetics into the human eye as a method to assess irritancy. Our studies have demonstrated that this methodology is safe and that obstructions related to subject compliance are minimized by the I.6.2 cm design of the test. Human ocular irritation provides a means of distinguishing effects of test materials on individual ocular tissues. Using this testing methodology in conjunction with our grading system, which is a more definitive irritation scoring system than the standard Draize scale, we are capable of categorizing test material irritation levels. The Kanengiser grading system records human subjective responses in addition to objective ocular irritation, which is scored in terms of area and density of tissue loss. As a result, the comprehensive nature of the Kanengiser grading method, we have demonstrated that differences in sensitivities exist among the ocular tissues. The three-point grading scale, assessing the areas of tissue loss in ocular tissues (cornes, palpebral, and bulbar conjunctiva, and caruncle), is capable of describing a range of tissue damage, encompassing minor lesions as well as severe tissue abrasions. This scoring system yields greater sensitivity and specificity than the Draize scale. Human subjective irritation scores demonstrate greater correlation with scores for corneal irritation assessed by the Kanengiser method that by the Draize method. While we have considered the cornea a predictive tissue with respect to corneal irritation, the cornea is highly representative of sensory correlation of ocular irritation with subjective corneal irritation scores with subjective reports of irritation provide further evidence of the significance of this tissue in predicting ocular irritancy.

Objective
The objective of this study was to introduce a method of assessing ocular irritancy in human subjects and to illustrate the significance of a new expanded grading system, designed by Kanengiser, for the precise evaluation of ocular lesions and quantitative assessment of ocular surface responses to cosmetic products (i.e. shampoos, soaps, sunscreens, eye, and facial cosmetics).

Methods
A total of 19 subjects, consisting of 12 males and 7 females, ranging in age from 31 to 69 years old, were included. A designated quantity of test material was administered to each eye. Ocular examinations were performed at scheduled intervals following product instillation.

Scoring scale

Subjective Ophthalmic Scoring Scale

Subj ective Irritation: (stinging, burning, itching, dryness, and/or foreign body sensation)

0 = None
1 = Slight
2 = Mild
3 = Moderate
4 = Severe

Objective Ophthalmic Scoring Scale (Slit Lamp Biomicroscope Examination)

Fluorescein Staining scores

0 = No evidence of staining
1 = Trace staining
2 = Mild staining
3 = Moderate staining
4 = Severe staining

Subjective Irritation

0 = None
1 = Slight
2 = Mild
3 = Moderate
4 = Severe

Objective Ophthalmic Scores (Slit Lamp Biomicroscope Examination)

Subjective and objective irritation scores were correlated using a Spearman rank order correlation test. The correlation coefficient (r), as well as the level of significance (p-value), was reported.

Results

Distribution of Fluorescein Staining

Distribution of Subjective Irritation

Figure 1: Incidence of Adverse Events in Human Ocular Instillation Tests

Figure 2: Subjective Irritation

Figure 3: Objective Ophthalmic Scores (Slit Lamp Biomicroscope Examination)

Figure 4: Objective Ophthalmic Scores (Slit Lamp Biomicroscope Examination) and Fluorescein Staining Observed During Ocular Irritation

Figure 5: Area Levels of Fluorescein Staining on Cornea (Kanengiser vs. Draize)

Figure 6: Objective Ophthalmic Scores (Slit Lamp Biomicroscope Examination) and Fluorescein Staining Observed During Ocular Irritation

The frequency of occurrence of adverse events is minimal in the human ocular instillation studies that we have performed. Of 190 human subjects, who participated in ocular irritation studies since 1996, only 1 subject experienced an adverse event. This event, which occurred prior to test material irritation, was unrelated to the test material or to the study procedures. Other evidence of the safety of this methodology is provided by the repeated willingness of subjects to enroll in future studies. As the resolution of all observed ocular irritation during the course of the studies.

Conclusion

Human ocular irritation testing represents a reliable, predictable and reproducible ocular irritation methodology to assess the irritancy potential of new products. Kanengiser’s ocular grading system is an efficient assay method for determining the corneal irritant potential of cosmetic products in human eyes.