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Assessment of Organotypic EpiVaginal™ Tissue Model to Screen Irritation Potential of Chemicals

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A predictive test system for assessing the vaginal irritation of chemicals and formulations will have far reaching application in industries involved in feminine care products. The vaginal mucosa is commonly exposed to chemicals or therapeutic agents that can cause irritation/inflammation and increase the susceptibility to infections such as HIV-1 and HSV-2. Hence, chemical/formulation or therapeutic agent induced vaginal irritation is a concern for industrial and academic toxicologists. Traditionally, testing has been performed using the rabbit vaginal irritation (RVI) assay. In the current study, we investigated use of the organotypic, highly differentiated EpiVaginal tissue as a non-animal alternative. EpiVaginal tissues were exposed to N=6 chemicals at 3 concentrations for 1, 3, and 6 hrs. The effects of single or repeat application on tissue viability (MTT assay), barrier disruption (measured by trans-epithelial electrical resistance, TEER, or sodium fluorescein, FL, leakage), and inflammatory cytokine release (IL-1a, IL-1b, IL-6, and IL-8) were examined. When compared to untreated controls, two irritating test articles, benzalkonium chloride and nonoxynol-9, reduced tissue viability to <40%, reduced TEER to <60%, increased FL leakage by 11-24%, and increased IL-1a and IL-1b release by >100%. Four other non-irritating materials had minimal effects on these parameters. Assay reproducibility was confirmed by testing the chemicals using three different tissue production lots (coefficient of variation, CV <10%) and by using tissues derived from cells of three different donors (CV <12%). In conclusion, decreases in MTT and TEER and increases in FL and cytokine release appear to be useful endpoints for preclinical toxicity screening of chemicals/formulations. The assay method will be cost effective and reduce the use of laboratory animals for experimentation. In the future, the in vitro test method could also be useful to assess toxicity of medical devices, perform drug permeation studies, and serve as an in vitro alternative test for the RVI assay.

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