



**USE OF THE RECONSTRUCTED EPIVAGINAL TISSUE MODEL TO SCREEN IRRITATION POTENTIAL OF FEMININE HYGIENE PRODUCTS**

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The vaginal mucosa is commonly exposed to chemicals and therapeutic agents that may result in irritation/inflammation that can make women susceptible to infections such as HIV-1 and HSV-2. Hence, chemical/formulation or therapeutic agent induced vaginal irritation is a concern for toxicologists. Traditionally, testing of such materials has been performed using the rabbit vaginal irritation (RVI) assay. In the current study, we investigated whether the organotypic, highly differentiated EpiVaginal tissue could be used as a non-animal alternative. The EpiVaginal tissue was exposed to a single application of six chemicals at three concentrations and the effects on tissue viability (MTT assay), barrier disruption (measured by trans-epithelial electrical resistance, TEER, and sodium fluorescein, NaFI, leakage), and inflammatory cytokine release (Interleukin, IL-1a, IL-1 $\beta$ , 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% and TEER to <60% and increased NaFI leakage by 11-24% and IL-1a and IL-1 $\beta$  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 production lots and by using tissues derived from cells of three different donors; coefficients of variation were <12%. In conclusion, decreases in MTT and TEER, and increases in NaFI and IL-1a and IL-1 $\beta$  release appear to be useful endpoints for preclinical toxicity screening of chemicals, formulations, and medical devices and should be investigated further as an in vitro alternative for the current RVI assay.

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