Novel ex vivo model to evaluate vaginal drug delivery formulations

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Abstract

Local treatment of vaginal diseases presents advantages over systemic treatments and interaction of drug delivery system with the biological tissue is a key factor for topical therapy success. Conventional permeation protocols using excised vaginal mucosa or even other tissues present several limitations. First, tissue may be impaired during dissection, leading to high variability. Second, they fail in distinguishing the performance of mucoadhesive or colloidal drug delivery systems from conventional ones, as static permeation models do not simulate formulation interaction with the tissue under physiological challenges as the vertical position or with the mucous layer that must be surpassed for efficient delivery. In fact, gravity and normal movements are considered the main challenges for formulation retention. As so, formulation mucoadhesiveness is highly desirable and the interaction with the mucous layer is highly sought by formulators. Dozens of studies have developed formulations capable of forming intermolecular bonds with the glycoproteins contained in the vaginal mucous. One of the greatest challenges in developing these drug delivery systems is to perform a proper screening, already in the bench, to select those formulations with greatest potential in vivo performance without the burden of in vivo studies. For this, our group has developed a novel simplified ex vivo vertical model, in which formulations are placed in porcine vaginas with the objective of mimicking a condition closer to the biological circumstance, specifically considering the possible leak from the vaginal canal in the vertical position. The results indicate the proposed method was capable of differentiating formulations performances and histological evaluation showed mucosa structures are preserved during this new assay. Therefore, the ex vivo method can be considered reliable for approaching the physiological situation in comparative studies.

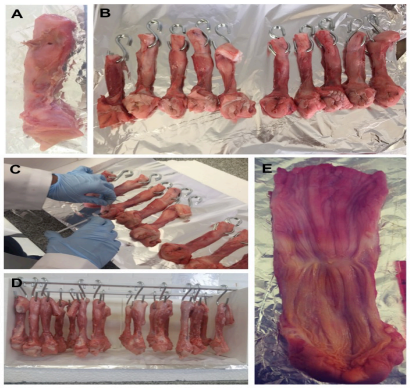


Figure 1. Representation of the protocol of hunging vaginas (A: Obtaining and cleaning material, B: preparation of the porcine vagina, C: insertion of formulations, D: Hanging vaginas and E: withdrawal of fragments.

Recent Publications

1. Gratieri T, Santer V, Kalia YN (2017) Basic principles and current status of transcorneal and transscleral iontophoresis. Expert Opinion on Drug Delivery. Doi: 10.1080/17425247.2017.1266334.
2. Silva AP, Silva NF, Andrade EHA, Gratieri T et al. (2017) Tyrosinase inhibitory activity, molecular docking studies and antioxidant potential of chemotypes of Lippia origanoides (Verbenaceae) essential oils. PLoS One 12: e0175598.
3. Borgheti-Cardoso LN, Angelo T, Gelfuso GM, Lopez RFV, Gratieri T (2016) Topical and Transdermal Delivery of Drug-Loaded Nano/ Microsystems with Application of Physical Enhancement Techniques. Current Drug Targets 17: 1545-1559.
4. Sa FAP, Taveira SF, Gelfuso GM, Lima EM, Gratieri T (2015) Liposomal voriconazole (VOR) formulation for improved ocular delivery. Colloids and Surfaces B 133:331-338.
5. Gratieri T, Yogeshvar KN (2013) Mathematical models to describe iontophoretic transport in vitro and in vivo and the effect of current application on the skin barrier. Advanced Drug Delivery Reviews 65:315-329.



Biography (150 word limit)

Tais Gratieri, Ph.D., has her expertise in development and evaluation of topical drug delivery systems for the eye, skin, nail and more recently the vaginal mucosa. During her Ph.D. in the University of São Paulo and a one-year period in the University of Saarbrücken, Germany, she validated a model for the study of topical ophthalmic formulations. She continued to work with ocular as well as skin topical drug delivery systems and physical drug enhancement techniques during her postdoc in the University of Geneva. Back to Brazil as Professor and head of the Laboratory of Food Drugs and Cosmetics (LTMAC) at the University of Brasilia, she maintains all these collaborations and focus on formulation development for the topical delivery of active natural extracts of the Amazonian Forest and the Cerrado Biome. In the year 2013 she received the local L'oreal-Unesco -Brazilian Sciences Academy Women in Science award.

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Session 3-7 Vaginal Route/Number
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