

Evaluation of the Self-Emulsifying Properties of PCCA Ellage™

Part 1: Microscopic Evaluation

SUMMARY: The self-emulsifying properties of PCCA Ellage were evaluated under the microscope and compared to VersaBase® Cream and PCCA Plasticized™. Upon mixture with VFS and incubation at 37°C, PCCA Ellage created a spontaneous emulsion and the resulting droplets decreased in size with prolonged incubation. On the contrary, there were no changes in the properties for VersaBase Cream and PCCA Plasticized. PCCA Ellage exhibited its self-emulsifying properties even in the presence of small amounts of VFS, a very important finding taking into account the variable amounts of vaginal fluids in women.

Introduction & Methodology:

PCCA Ellage Anhydrous Vaginal is an innovative proprietary base with self-emulsifying properties that creates a spontaneous emulsion when it comes into contact with water from vaginal fluids. This emulsion releases the active ingredients from the base to the mucosa. Once the active ingredients are released, the emulsifier system in the base also holds the drugs to the surface and increases the contact time. This novel and promising technology, named Self-Emulsifying Drug Delivery Systems (SEDDS), has the potential to maximize drug solubility and bioavailability [1-2].

Initially, two laboratory tests were performed at PCCA R&D to evaluate the SEDDS, in particular the formation of droplets, for PCCA Ellage in comparison with other test products. Initially, PCCA Ellage, VersaBase Cream and PCCA Plasticized were mixed gently with Vaginal Fluid Simulant (VFS) in a 1:2 ratio (w/v). Following 5 min of incubation at 37°C, a sample of each vial was observed under a light microscope with a total magnification of 100x. Afterwards, 10 µL of VFS at 37°C were placed on glass slides and added were equal volumes of the same test products (1:1 ratio). The mixtures were spread with a pipette tip, incubated at 37°C for 1 min and 5 min, and protected with a cover slip for microscopic evaluation at a magnification of 100x (10x objective lens and 10x ocular lens).

Afterwards, a third laboratory test was performed at PCCA R&D to evaluate the formation of droplets with increasing volumes of VFS, as the research by Rohrer *et al.* [3]. PCCA Ellage was mixed gently with VFS (90:10, 75:25 and 50:50 ratios) and, following 5 min of incubation at 37°C, a sample of each mixture was observed under a light microscope with a total magnification of 10x.

Results & Discussion:

PCCA Plasticized, as expected, did not mix with the VFS because it is an anhydrous gel. VersaBase, on the other hand, is an emulsifying cream and, as such, it made a homogeneous emulsion upon gentle mixing with VFS. PCCA Ellage showed a similar behavior to VersaBase Cream, as shown in Figure 1.

Under the microscope, it was observed that the original PCCA Ellage and PCCA Plasticized do not have any droplets, as expected, whereas VersaBase Cream contains a large number of droplets sized around or under 10 µm. Following mixture with VFS and incubation (1-5 min), there were no significant changes for VersaBase Cream. Likewise, there were no significant changes for PCCA Plasticized as the oil and water phases were kept separated, as shown in Figure 2. PCCA Ellage, on the contrary, developed droplets when mixed with the VFS and these droplets decreased in size from 1 min to 5 min of incubation at 37°C. This phenomenon is the process of self-emulsifying which is a unique property of PCCA Ellage. This process took place also when the active pharmaceutical ingredients (APIs) amitriptyline 2% and baclofen 2% were incorporated into PCCA Ellage (Figure 2).

The self-emulsifying properties for PCCA Ellage are observed even in the presence of small amounts of VFS. As shown in Figure 3, droplets were developed in all three mixtures (90:10, 75:25 and 50:50 ratios for PCCA Ellage:VFS). This property is very important in the clinical practice taking into account the variable amounts of vaginal fluids in women. When these fluids are low, depending on the menstrual cycle or in the presence of vaginal dryness, PCCA Ellage is expected to exhibit its self-emulsifying properties *in vivo* upon application to the vaginal mucosa.

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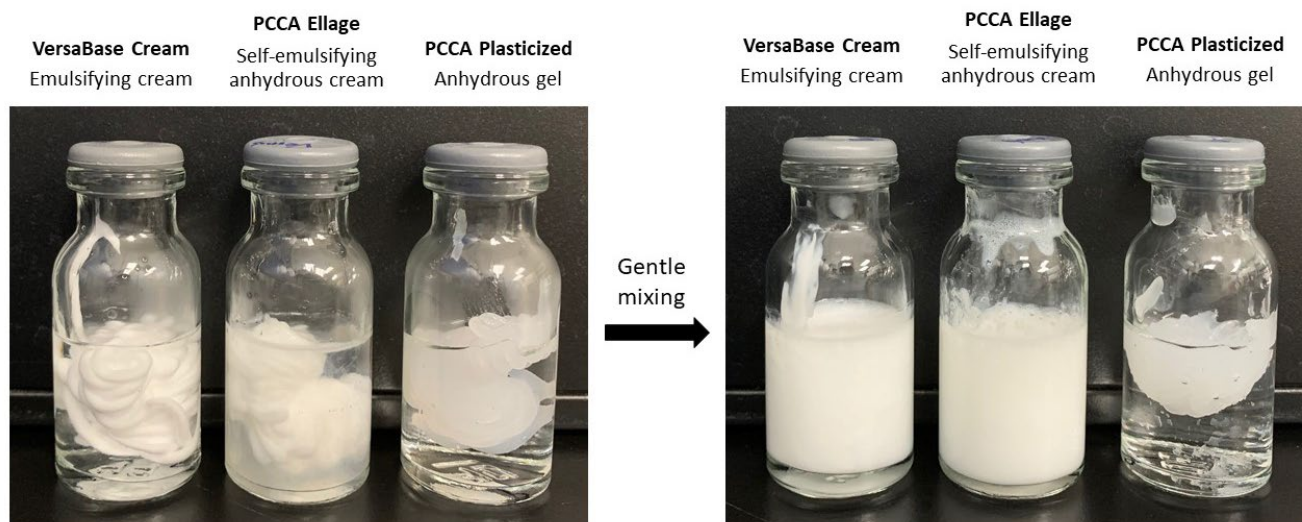


Figure 1. Mixture of PCCA proprietary bases with VFS (1:2 ratio).

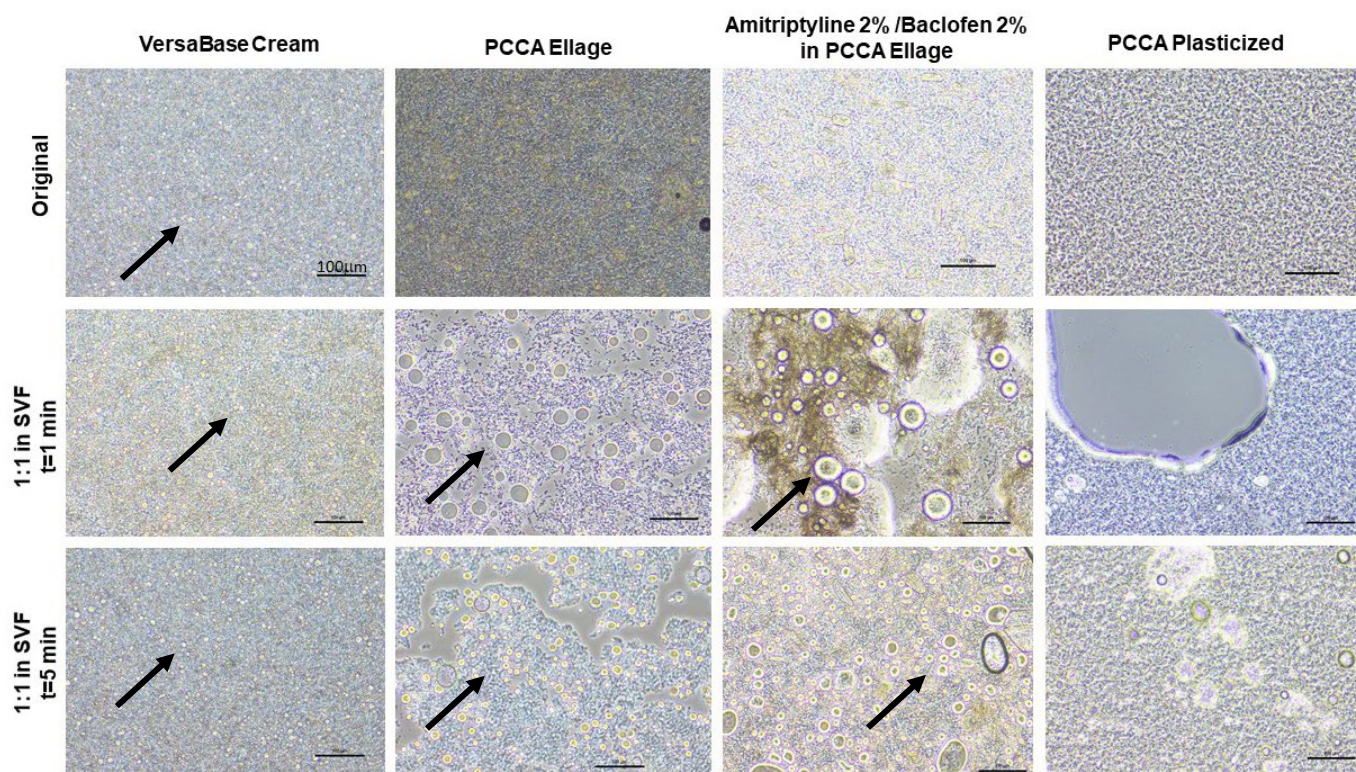


Figure 2. Microscopic evaluation of droplet size formation (100x) for VersaBase Cream, PCCA Plasticized and PCCA Ellage, with and without APIs (selected droplets highlighted with arrows).

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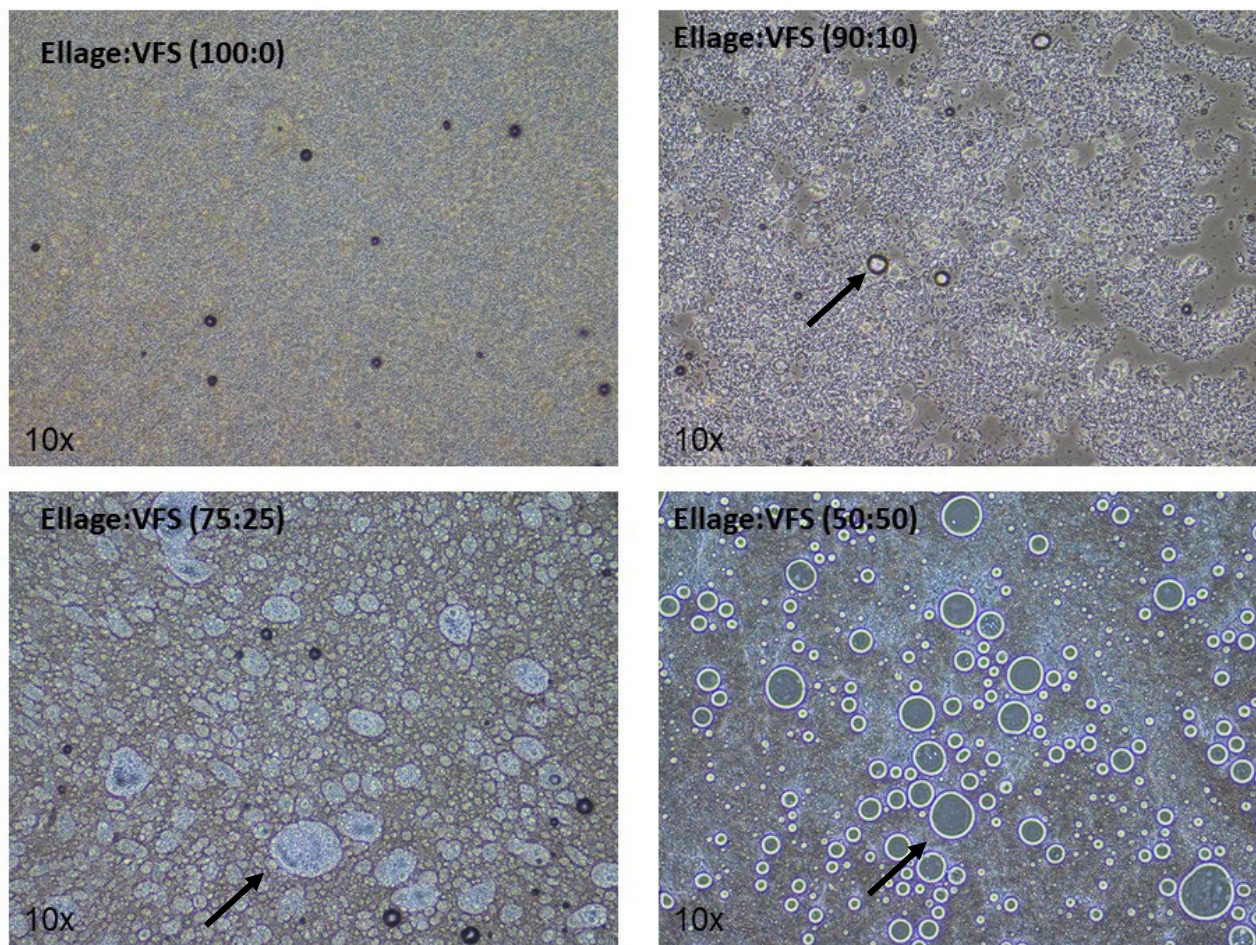


Figure 3. Microscopic evaluation of droplet size formation (10x) for PCCA Ellage with increasing volumes of VFS (selected droplets highlighted with arrows).

References:

- [1] Vasconcelos, T., Marques, S. and Sarmiento, B. (2018) 'Measuring the emulsification dynamics and stability of self-emulsifying drug delivery systems'. *European Journal of Pharmaceutics and Biopharmaceutics*, 123 (1-8). doi: 10.1016/j.ejpb.2017.11.003.
- [2] Dokania, S. and Joshi, A.K. (2015) 'Self-microemulsifying drug delivery system (SMEDDS) – challenges and road ahead'. *Drug Delivery*, 22 (6), p.675-90. doi: 10.3109/10717544.2014.896058.
- [3] Rohrer, J., Zupančič, O., Hetényi, G., Kurpiers, M. and Bernkop-Schnür, A. (2018) 'Design and evaluation of SEDDS exhibiting high emulsifying properties'. *Journal of Drug Delivery Science and Technology*, 44, p.366-72. doi: 10.1016/j.jddst.2018.01.013.