

# A Mechanistic Evaluation of Drug Availability from Imvexxy<sup>®</sup> (Estradiol) Vaginal Inserts

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## Objective

Imvexxy<sup>®</sup> (estradiol) vaginal “inserts” are small, light pink, tear-shaped inserts for manual placement into the vagina. This study aimed to evaluate the performance characteristics of these vaginal inserts and the impact on availability of estradiol in the vaginal mucosa.

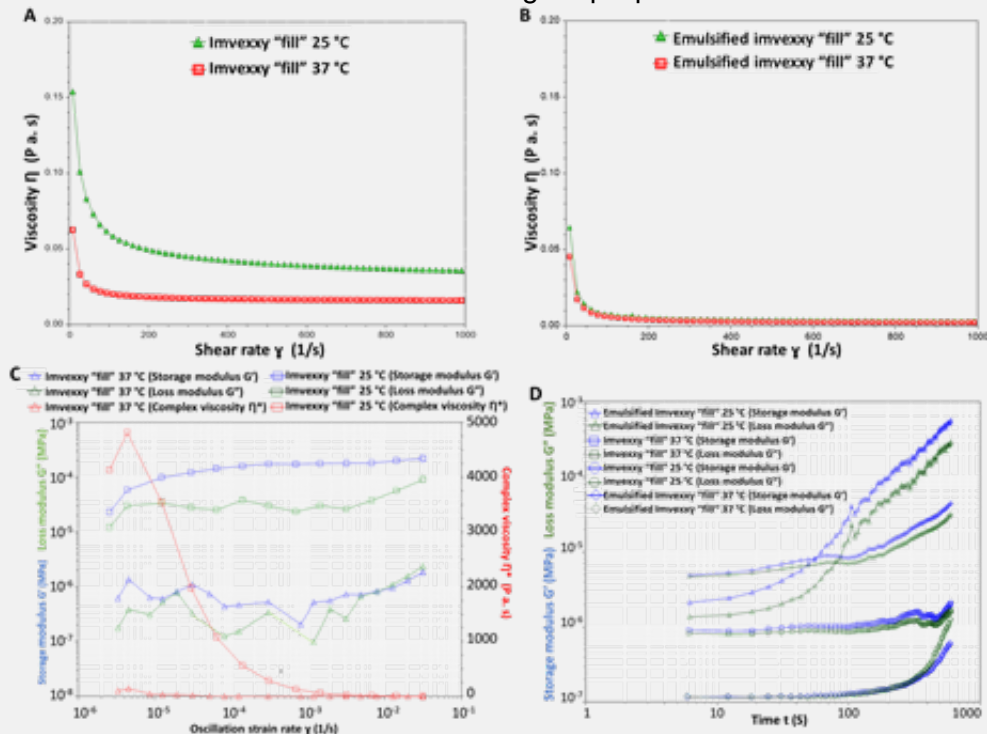
## Methods

The rheological properties of the “fill” formulation alone and following emulsification of the “insert” in the simulated vaginal fluid (SVF), were evaluated at 25°C and 37°C. The disintegration time of the “shell” of the insert was assessed at various agitation rates and using different volumes of SVF. The disintegration time was recorded as the first appearance of the “fill” formulation in the SVF. Estradiol dissolution from the insert was assessed using a mini-USP II apparatus at 37°C. Additionally, the mechanical properties of the “shell” were evaluated by a texture analyzer, and the differential scanning calorimetry (DSC) was used to characterize the thermal behavior of the “fill”.

## Results

### □ Rheology properties

- The viscosity of the “fill” tends to decrease with an increase in the shear rate and temperature
- The impact of the emulsified shell on the rheological properties were assessed.



**Fig 1.** Effect of temperature (A, B, C) and presence of the disintegrated “shell” (D) on the rheological profiles of the “fill” of the drug product.

- Emulsification of the “insert” in the SVF resulted in higher viscosity, storage and loss moduli values compared to the “fill” of the drug product.

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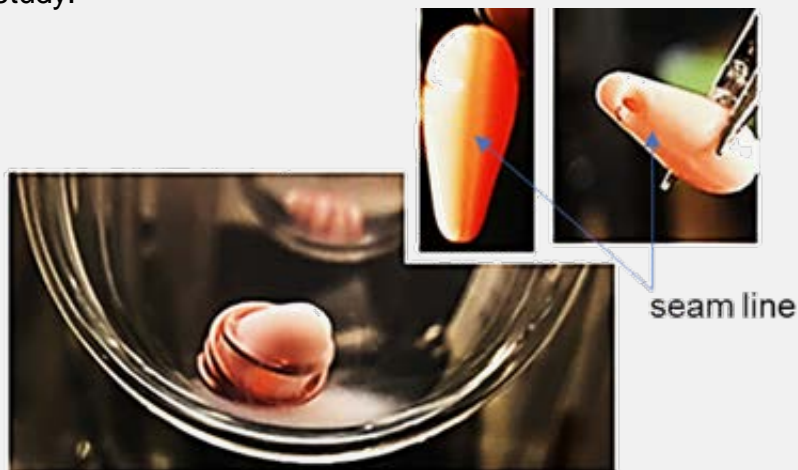
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## Results

### Disintegration time

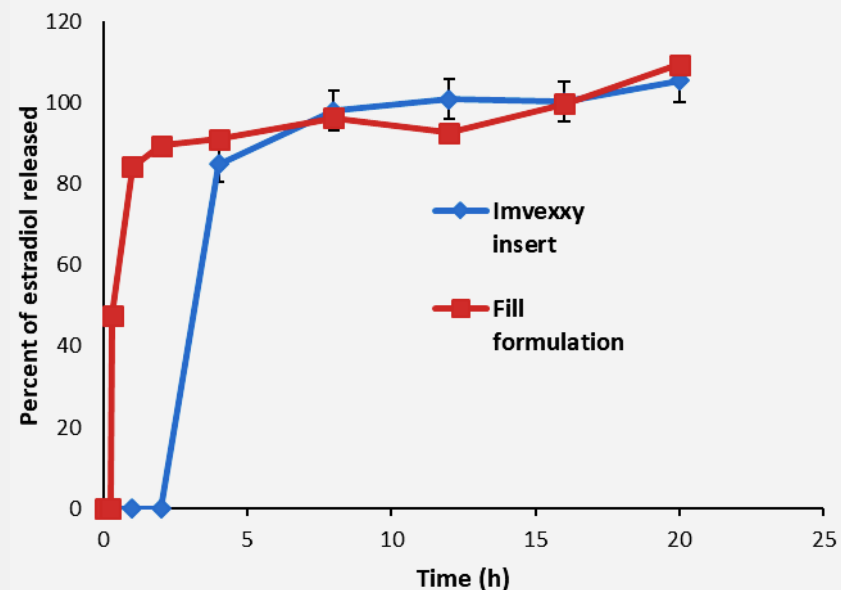
- Disintegration of the “shell” occurred at the seam line.
- The disintegration time ranged from 2-60 minutes depending on the study conditions.
- The disintegration time was found to be inversely proportional to the volume of the SVF and the agitation rate used in the study.



**Fig 2.** Disintegration of the “shell” in the SVF.

### Dissolution data

- A 90-minute lag time was observed in the dissolution of estradiol from the drug product compared to dissolution of estradiol from the “fill” of the drug product.



**Fig 3.** Dissolution profiles of estradiol from the “fill” (in red) and from Imvexxy<sup>®</sup> (estradiol) inserts (in blue) using USP II apparatus (n=3 replicates; mean ± SD)

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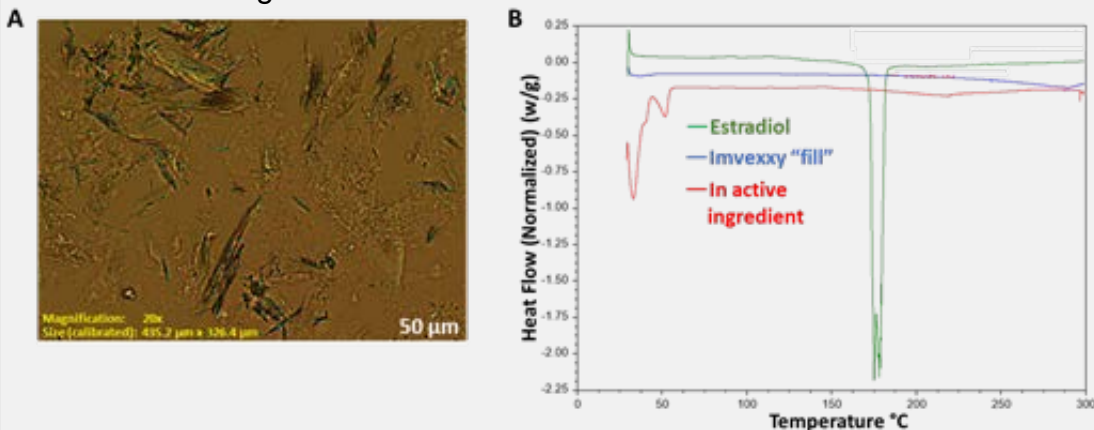
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## Results

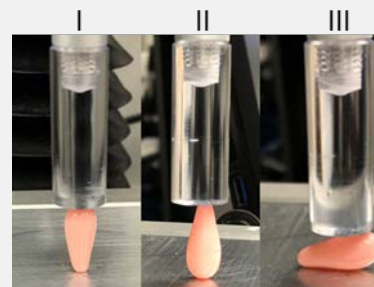
### Morphology and DSC analysis

- DSC data indicated that estradiol is solubilized in the “fill.”
- Crystals of an inactive ingredient were observed at room temperature and were no longer visible at 60°C.



**Fig 4.** Polarized light optical images at 200x magnification of the “fill” (A), and DSC thermogram of estradiol, an inactive ingredient, and “fill” of the drug product (B).

### Mechanical properties



**Fig 5.** The maximum compression force were evaluated by a texture analyzer. Row I, II and III show the insert positioned vertically with the smaller end down, smaller end up and longitudinally respectively.

**Table 1.** Maximum compression forces (n=3, mean ± SD)

Orientation	Compression force (kg)
Vertically (small end down)	5.4 ± 0.25
Vertically (small end up)	5.3 ± 0.46
Longitudinally	9.3 ± 1.73

## Conclusions

- The study evaluated various characteristics of Imvexxy® (estradiol) vaginal inserts in order to understand factors that could influence drug availability at the site of administration in the vagina.
- The preliminary data indicated that “shell” disintegration and emulsification of the “fill” in vaginal fluid may impact the availability of the drug through the vaginal mucosa. Studies are underway to further characterize the drug product.

## Acknowledgment

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