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# **GIAVAL® ovule**

Medical Device Class IIb

 Mark 0477

**Intended use:** Adjuvant in treatment of acute or chronic vulvaginitis, cervicitis, cervical erosion, leucorrhoea and vulvar itching.

## **WHY WE MADE IT?**

The vaginal epithelium is particularly sensitive to the **effects of circulating estrogens in women**: this sensitivity may lead to several problems and disorders such as *vulvaginitis*, *cervicitis* and *vulvar itching* which can even have a major impact on a woman's life. More than 70% of women (note. CENSIS information) suffer from these kind of **discomforts from the age of 20 onwards**. Furthermore, during the menopause, when there is a drastic reduction in estrogens, the vaginal epithelium strongly modifies its structure, with progressive and worsening atrophic changes. But that is not all: the use of **contraceptives, pregnancy, breast-feeding** or even the use of certain drugs can determinate the appearance of typical symptoms and discomforts related to the health of the epithelium itself.

To treat and mitigate the above mentioned disorders, **Innate's R&D developed** its solution represented in the product Giaval®, a vaginal ovule with a peculiar formulation particularly enriched by **Hyaluronic Acid**.

HA is an endogenous **polysaccharide** that represents an important part of the extra-cellular matrix of the skin and cartilage. This substance is able to attract and retain large amounts of water molecules and has a key role due to its **properties in the formation and maintenance of extra-cellular matrix** **turgidity**, skin moistening in the case of inflammation and preservation of tissue homeostasis.

Moreover, Hyaluronic Acid is widely effective in the treatment of skin diseases due to the **preservation of tissue consistency**, helping the physiological process of cellular migration and also contributes in the **regeneration process of damaged tissues**. HA can also play a key defensive role supporting mucosa protection against pathogens.

Finally, hyaluronic acid, with its **film forming power**, helps to restore the tissue and normalize the damaged surface. Thanks to all these properties Giaval® ovules ensures **protective action for the vaginal mucosae**, creating the conditions to **help in scarring, reepithelization and restoring of the normal hydration of vagina**, avoiding in this way the proliferation of pathogens.



**Efficacy in vitro test (Report number: S.VT.078-MS02 2018/3894 of 27/12/2018):**

### **TEST FOR EFFICACY IN RIEPITELIZATION of GIAVAL®**

To demonstrate the capability of Giaval® to act as an adjuvant in **repairing, regenerating and epithelialization activity** a study was executed considering a constructed human vaginal model, in which tissue integrity was altered by using a surfactant (Sodium dodecyl sulfate 0.1% for 4 hours).

The experimental model used in the test is a reconstructed human vaginal epithelium (Strelab, batch 1.812 VAG 01), constructed starting from vaginal cells (A431 P33 17) seeded on polycarbonate filter with air-liquid interface.

The experimental design included the following **experimental conditions**:

- CTR-: undamaged and untreated vaginal epithelium
- CTR+: damaged and untreated vaginal epithelium
- TREATED: vaginal epithelium damaged and treated with Giaval®

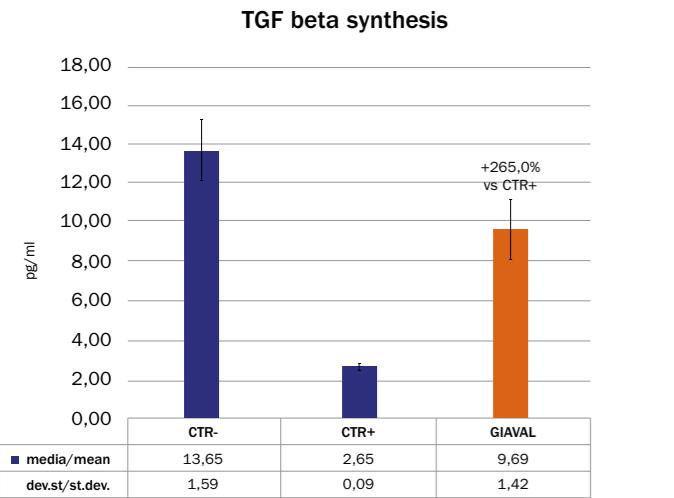
The treatment of the tissue with the Giaval® was prolonged for 48 hours. At the end of the testing period the following biological parameters were considered:

- TGFalpha synthesis
- KDAF (SFN, Stratifin) synthesis
- Mucopolysaccharides synthesis

TGFalpha, TGFbeta and KDAF represent proteins involved in the proliferating and repairing process in the vaginal epithelium *in vivo*; Mucopolysaccharides are elements capable to attract water according to their chemical nature and contribute to the hydration of the tissue.

Below, in the graphics, being summarized the results:

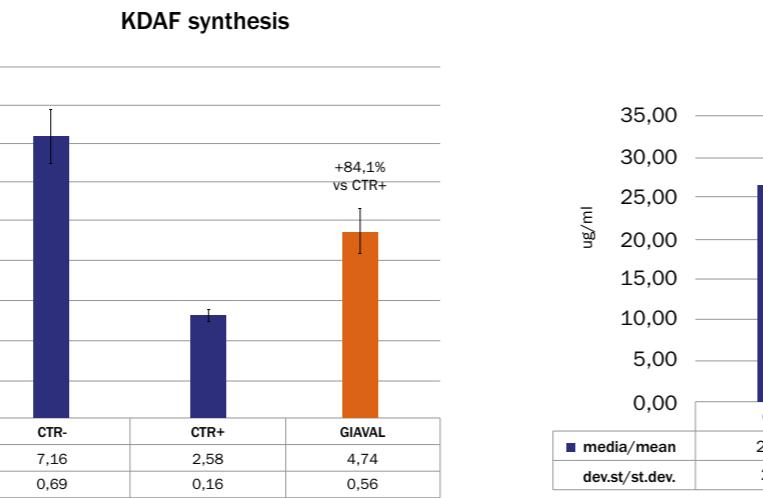
Figure 1



In the figure 1 and in the table above the data of the TGFbeta dosage at the end of the incubation period are reported and compared with CTR- and CTR+; Statistical analysis highlights a significant increase of the TGFbeta production in the tissue treated with GIAVAL Batch 806619 respect CTR+.

Results: According to the applied experimental protocol, the results obtained and displayed in the figures demonstrate that **the treatment of the vaginal epithelium with GIAVAL® has significantly and positively helped in modulating all the markers considered. Based on such evidence it being confirmed the contribution of Giaval® to local reepithelization.**

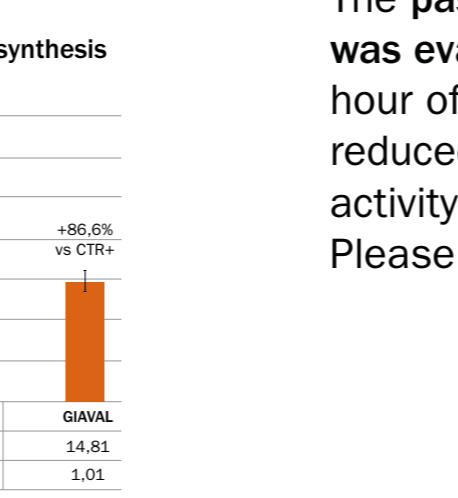
Figure 2



In the figure 2 and in the table above the data of the KDAF (Stratifin) dosage at the end of the incubation period are reported and compared with CTR- and CTR+; Statistical analysis highlights a significant increase of the KDAF (Stratifin) production in the tissue treated with GIAVAL Batch 806619 respect CTR+.

Results: According to the applied experimental protocol, the results obtained and displayed in the figures demonstrate that **the treatment of the vaginal epithelium with GIAVAL® has significantly and positively helped in modulating all the markers considered. Based on such evidence it being confirmed the contribution of Giaval® to local reepithelization.**

Figure 3



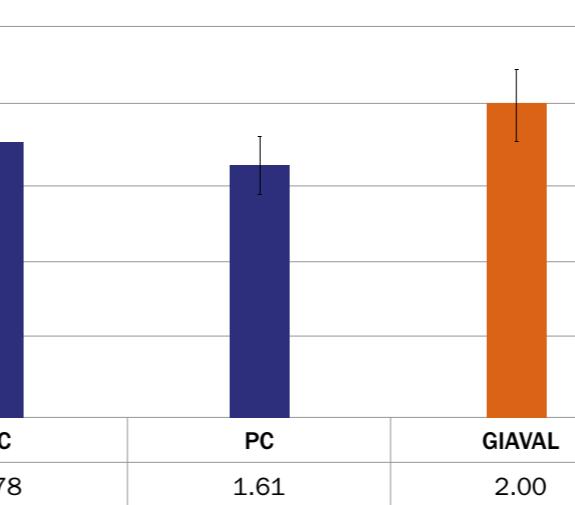
In the figure 3 and in the table above the data of the mucopolysaccharides dosage at the end of the incubation period are reported and compared with CTR- and CTR+; Statistical analysis highlights a significant increase of the mucopolysaccharides production in the tissue treated with GIAVAL Batch 806619 respect CTR+.

## TEST FOR BARREL ACTIVITY of GIAVAL® (REPORT NUMBER VS 03-22 OF 09/02/2022)

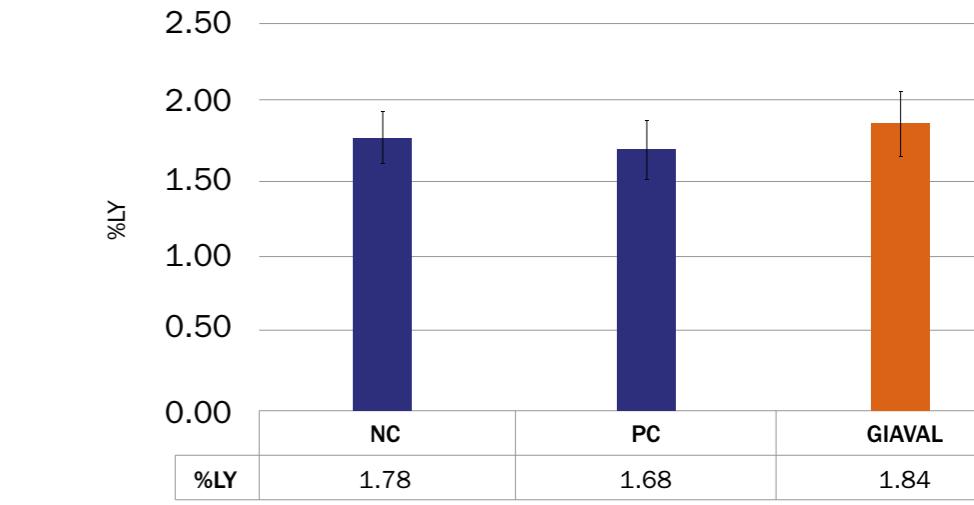
A test with the intent to evaluate the barrel action of the product was done using a caffeine based solution. The **passage through a barrier** was tested and compared versus the negative control. **Film forming property was evaluated after 1 hour of exposure** and immediate readout while film persistency was evaluated after one hour of exposure and after a gentle washing with 0,9% saline solution. In both cases the product significantly reduced the passage of the caffeine compared to the negative control demonstrating therefore the barrier activity of Giaval®.

Please note that LY stands for Lucifer Yellow Flux (paracellular).

### VS 03-22 LY FILM FORMING PROTOCOL



### VS 03-22 LY FILM PERSISTENCY PROTOCOL



## EXPECTED CLINICAL BENEFITS

The expected clinical benefits of Giaval® are identified in helping the **resolution or reduction of signs and symptoms of vaginitis at the end of treatment**. Specifically, important identifying data are so-called **subjective symptoms** such as burning, pain, itching, vaginal dryness, dyspareunia and dysuria. These are accompanied by so-called **objective symptoms**: leucorrhoea, vulvar erythema, vulvar oedema and the presence of abrasions or erosions. The **reduction or complete disappearance** of these types of symptoms is an indication of the effectiveness of the product Giaval®.

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## GIAVAL ovule



10 ovules per box (2 blisters of 5 ovules each)

**Format:** 2,7 gr vaginal ovule

**Indication of use:** one ovule per day for 10 (mild symptoms) or 15 days (severe symptoms)

Package leaflet in each box