

Bio-adhesive Vaginal Foam: in-vitro and in-vivo adhesion profile

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Abstract Summary

Foamix's unique vaginal foam vehicle is an easy-to-use vaginal delivery system, which is simple to operate and requires minimal preparation. Vaginal foam is well tolerated, expands and spreads evenly over the entire vaginal cavity surface. It also effectively reaches the cervix. The vaginal foam is bioadhesive and does not leak following application and thus, it can retain an active agent intravaginally for a significant period of time.

Introduction

Vaginal topical foams are convenient to administer, provide accurate dosing and are compatible with daily activities. While semi-solid formulations, such as creams, lotions, gels and ointments are commonly used for delivery to the vaginal cavity, they are often reported to be messy, require frequent application and can be difficult to remove after use. Furthermore, application of topical gels and creams means several steps of operation. Solid formulations such as tablets, suppositories and pessaries also require frequent application, show poor retention in the vagina and exhibit insufficient spreadability over the vaginal cavity surface.

Intravaginal Foam

Foamix developed a series of intravaginal foams, which expand gently in the vaginal cavity and evenly cover the entire vaginal surface for efficient treatment. There are significant advantages of Foamix foams in intravaginal administration:

- Ready-to-use formulations with inexpensive disposable applicators facilitate compliance
- Excellent coverage of the intravaginal surface
- Can incorporate bioadhesives to reduce dosing frequency
- Easy and non-intimidating intravaginal insertion
- Accurate dosing (using metered dose valves)
- No dripping after treatment
- Pharmaceutical, non-irritating excipients

A variety of foam formulation platforms can be used for effective and safe delivery of intravaginal drugs:

- Oil-in-water emulsion foam (cream-like)
- Water-in-oil emulsion foam (occlusive-cream-like)
- Petrolatum based foam (ointment-like)
- Waterless hydrophilic foam (hydrophilic-ointment like)
- Oily foam (ointment-like, with or without water)
- Suspension foam

Experimental Section

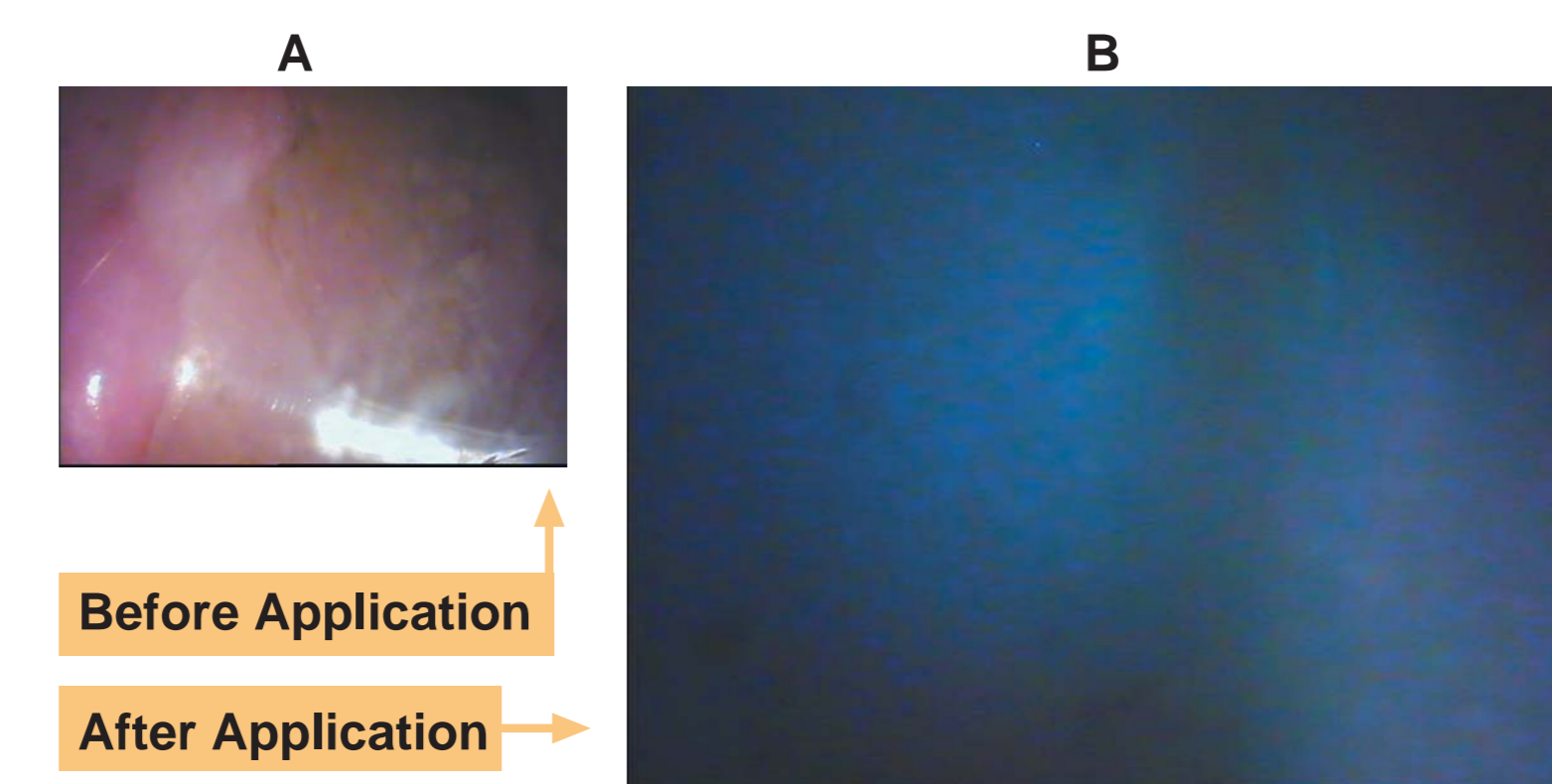
Intra-vaginal foam dosing female sheep

A vaginal foam with methylene blue pigment as a visualizing agent was administered to an adult female sheep. Expansion and distribution of the foam in the vagina and cervix were observed by colposcopy and recorded photographically.

The insertion of the foam applicator proved simple. Fifteen minutes after treatment, colposcopy observation was documented. The vaginal foam expanded effectively and the vaginal cavity and cervix surfaces were fully and uniformly covered: colposcopy revealed that the entire vaginal cavity and cervix area were still covered by the blue pigment, as demonstrated in Figure 1.

There was no overflow of the foam and no dripping after administration. No signs of irritation were noticed.

Figure 1: (A) Colposcopy before foam treatment; (B) Colposcopy 15 minutes post-administration: full and uniform coverage of the vaginal cavity and cervix surfaces.

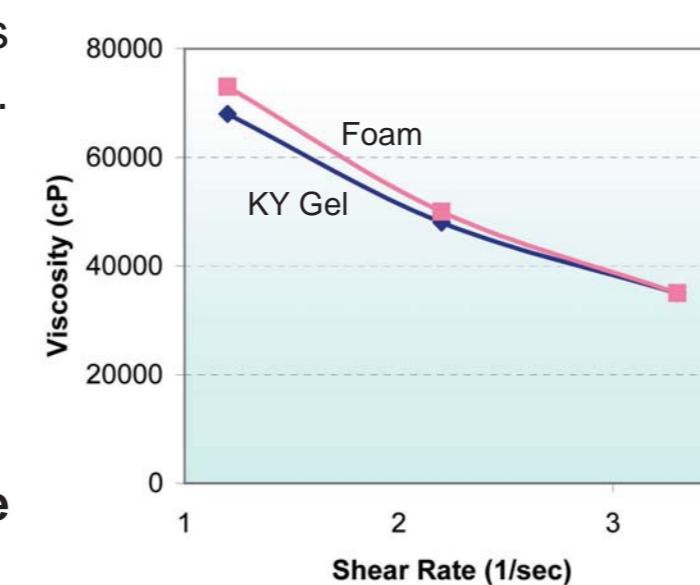


- Full & uniform coverage
- No leak

Lubrication: Foamix Vaginal Foam vs. KY™ Gel

The viscosity profile of Foamix foam was compared with the viscosity of KY™ Gel. As demonstrated in Figure 2, the lubricating effect of the vaginal foam is comparable to the "gold standard" in lubrication - KY™ Gel.

Figure 2: Viscosity of vaginal formulation with Hydroxyethylcellulose vs. KY™ Gel



Vaginal foams adhesiveness

Bioadhesiveness is an important feature of vaginal preparations, as it affects the adhesion of the preparation to the vaginal mucosal surface, thereby influencing drug residence at the target site of treatment. Vaginal foams with (a) mixture Hypromellose and Carbopol; (b) Sodium Carboxymethylcellulose; and (c) Hydroxyethylcellulose, were prepared and pressurized in aluminum monoblock canisters.

Texture Analyzer, Brookfield LFRA®, was used in order to compare the bioadhesive effect of various adhesive polymers.

Adhesive forces were measured with LFRA® Texture Analyzer, for foams with the selected polymers, in comparison with Dalacin® Cream, which is known for its bioadhesive property.

As exemplified in Figure 3 and Table 1, the adhesive force of the various foams were in the same range as the commercial cream preparation.

Figure 3: A typical foam texture analysis histogram; Foam vs. Dalacin®. Adhesive force is measured as the "Pull" force (in grams).

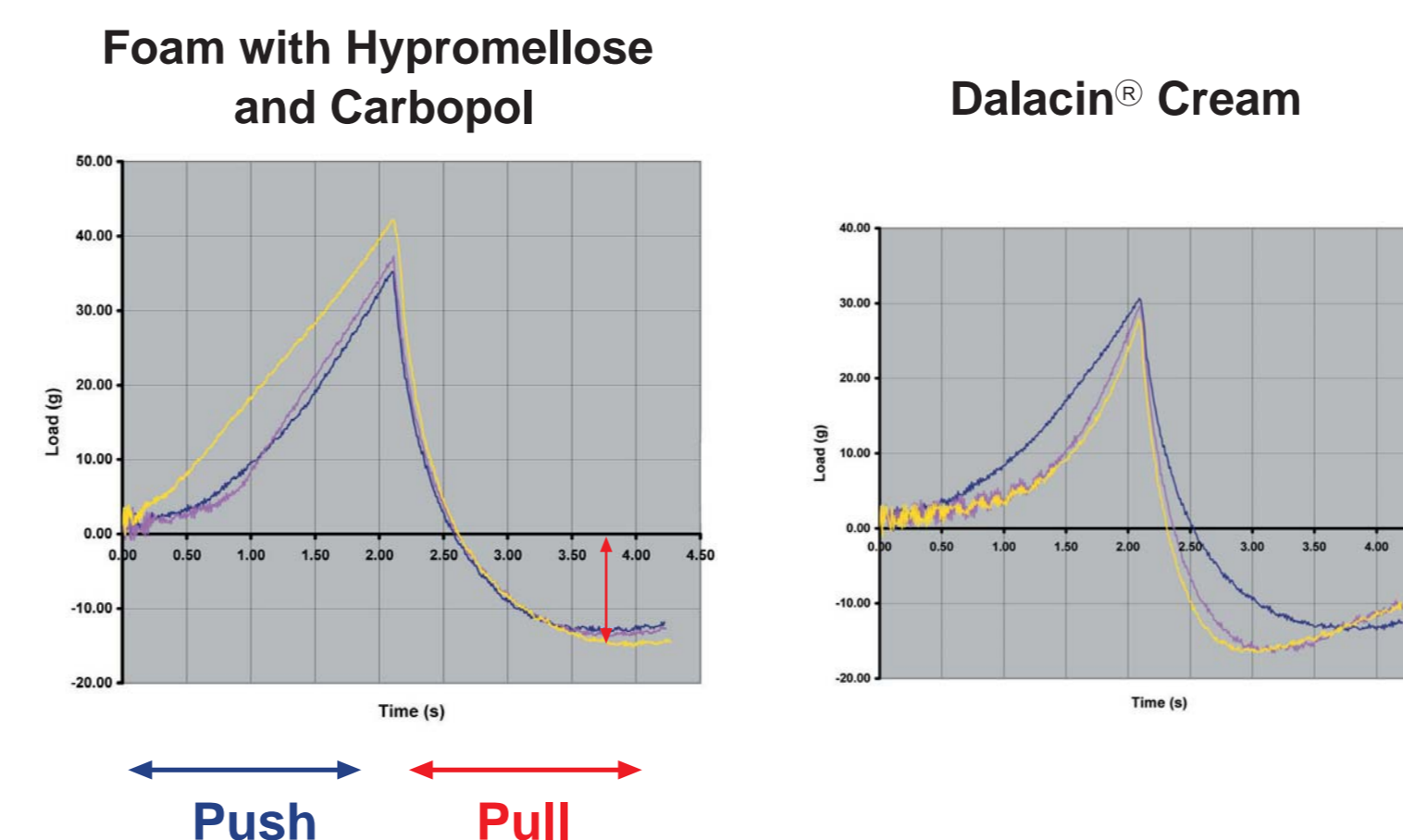


Table 1: Foam adhesive force (in grams)

Product	Adhesive force (g)
Foam with Hypromellose and Carbopol	8 - 18
Foam with Sodium Carboxymethylcellulose	12 - 18
Foam with Hydroxyethylcellulose	18 - 35
Dalacin (reference product)	15

Conclusion

1. Vaginal Foam expands uniformly throughout the vaginal cavity and covers the vaginal surface including difficult to reach areas such as the Cervix.
2. The vaginal Foam is patient friendly and easy to use.
3. Vaginal Foam is an ideal delivery system for vaginal drugs, providing optimal drug distribution throughout the vaginal cavity.
4. Vaginal Foam is bioadhesive, and thus has a potential for improved drug absorption and bioavailability.

References

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About Foamix

Foamix Ltd. develops proprietary topical foam products for the delivery of active agents in dermatology, gynecology, wound care and burn care.

By incorporating drugs in foam, we create premium products with improved convenience, higher compliance and better efficiency of treatment.

We currently collaborate with 8 pharmaceutical companies on 10 projects in the development of proprietary foam drugs; and we have our own in-house pipeline of dermatological and gynecological drugs in foam presentation.

Foamix Product Pipeline

BetaFoam™ Emollient & BetaFoam™ Oily Alcohol-Free Betamethasone valerate 0.12% in Foamix's proprietary Emollient Foam and Oil Foam bases. Easily applied to sensitive skin and mucosal areas. Most suitable for treating superficial inflammation, such as psoriasis and atopic dermatitis.

AcycloFoam™ Acyclovir in Foamix's Emollient Foam base. An easy-to-apply product for the treatment of sensitive skin and mucosal areas. Most suitable for treating genital herpes.

MetroMouse™ Metronidazole in Foamix's Emollient Foam base. Most suitable for treating acne-rosacea.

TerbiFoam™ Terbinafine in Foamix's Emollient Foam base. An easy-to-apply product for the treatment of dermal mycoses, e.g., athlete's foot and other dermatophyte infections.

PerFoam™ Permethrin 1% and 5% in Foamix's Emollient Foam base. Ideal for applications to the scalp and pubic area. Most suitable for treating head lice (1%), pubic lice and scabies (5%).

Urea Foam™ Moisturizing, easily spread and highly absorbable 10%, 20% and 40% Urea emollient Most suitable for the treatment of dry, scaly skin, including ichthyosis vulgaris and xerosis.

DicloFoam™ Diclofenac 1% in Penetrating Emollient Foam base. A superior product for treating osteoarthritis, joint & back pain. Diclofenac 3% in Emollient Foam base. A superior product for treating actinic keratoses.

Ammonium Lactate Foam Moisturizing, easily spreadable and highly absorbable ammonium lactate 12% emollient foam. This delicate alcohol-free foam product is ideal for the treatment of dry, scaly skin, including ichthyosis vulgaris.

MupiFoam™ The only stable Mupirocin Foam available. Cosmetically elegant, this foam is suitable for treating skin infections such as impetigo.



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