

FOR VETERINARY USE ONLY



**A SMART DEFENSE  
AGAINST  
INFLAMMATION.**



**LONG-TERM VITALITY STARTS EARLY**

## INFLAMMATION DEFINED

Acute inflammation is the body's way of getting rid of foreign organisms and damaged tissues. It initiates tissue repair in order to return function to the affected site. This normal response often results in the classic signs of inflammation:

- HEAT

- REDNESS

- SWELLING

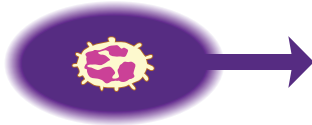
- LOSS OF FUNCTION

After an inflammatory stimulus, neutrophils migrate to the site of injury. Once there, neutrophils release a number of toxic substances, including destructive enzymes, reactive oxygen species and inflammatory mediators such as interleukin and tumor necrosis factor alpha (IL-1 $\alpha$ , IL- $\beta$ , IL-6, and TNF $\alpha$ ).

Normally, the body retains a delicate balance between the destructive effects necessary to resolve the infections and resultant collateral damage to healthy tissues. However, in some cases, the balance is upset and an inappropriate amount of tissue damage occurs. This is particularly true in cases of chronic inflammation when the inciting cause of inflammation has resolved, but the damaging effects of inflammation remain.

Inflammatory Stimuli

Neutrophil Migration



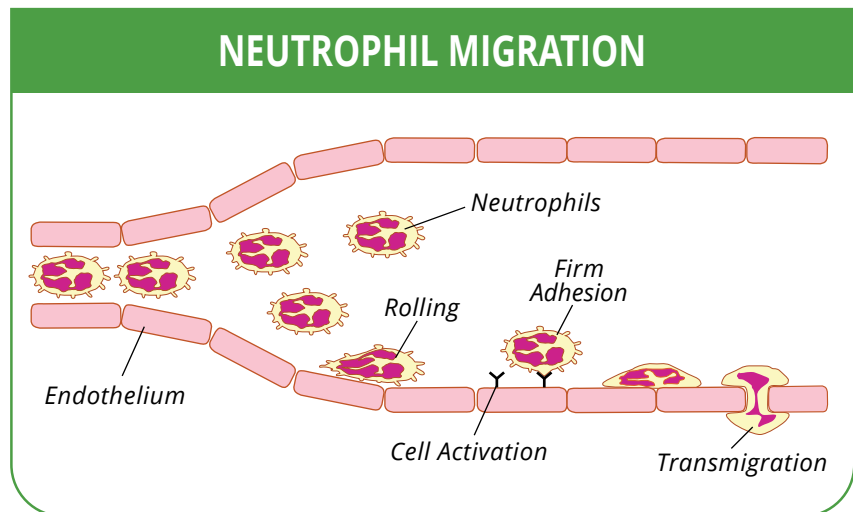
Pro-inflammatory mediators

Amplification

Arachidonic Acid

Inflammation

Discomfort



Ormrod DJ., *et al.* A Low Molecular Weight Component Derived from the Milk of Hyperimmunized Cows Suppresses Inflammation by Inhibiting Neutrophil Emigration. *Agents Actions* 37: 70-79; 1992.

Ormrod DJ., *et al.* Milk from Hyperimmunized Cows as a Source of a Novel Biological Response Modifier. *Agents Actions* 38: C146-C149; 1993.



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## *It's never been easier to help manage inflammation.*

Various dosage options and a full line of treat formulations make compliance easier for your clients.

Duralactin® products contain MicroLactin®, a protein that helps reduce inflammation at the cellular level. This makes them an ideal therapeutic option for helping maintain normal wellness.



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 **Duralactin**®

## WHAT IS MICROLACTIN®?

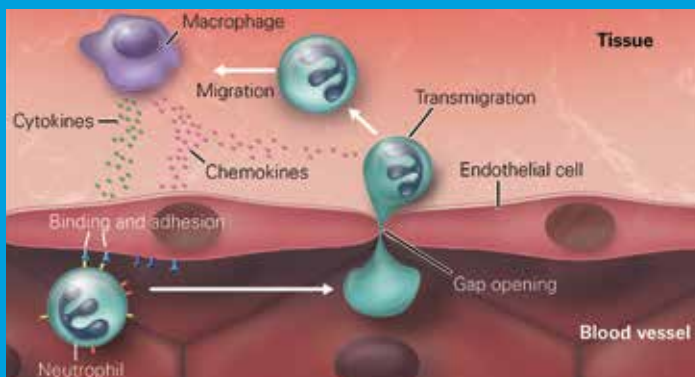
- MicroLactin® contains a natural component of milk known to help manage inflammation
- Scientists stimulate the production of this inflammation factor by frequently immunizing dairy cows with a polyvalent vaccine—a process known as hyperimmunization
- This hyperimmune milk factor (HIMF) is extracted from the cow's milk and concentrated to create MicroLactin®—the active ingredient in Duralactin® brand products

## HOW MICROLACTIN® WORKS

- **Inhibits and reverses neutrophil attachment** to the blood vessel wall via its effects on CD18 glycoprotein complex on the surface of neutrophils<sup>1,2,3</sup>—this keeps inactivated neutrophils within the bloodstream so they can't participate in the inflammatory response
- **Decreases the number of neutrophils present** at the inflammatory site
- **Maintains tight junctions** between cells so neutrophils can't transmigrate through blood vessel walls into inflamed tissues
- **Helps maintain proper action of macrophages**, a type of inflammatory cell<sup>4</sup>

## RELIEF WITH DURALACTIN® PRODUCTS

- Helps reduce inflammation with factors that inhibit neutrophil participation in the inflammatory response
- Reduce the number of neutrophils responding to the site of inflammation
- Does not have the side effects of other therapies
- One of the few therapies available for inflammation in cats
- 13 years of clinical use with very few side effects reported, and those reported have primarily been in animals sensitive to milk proteins
- Proven effective in multiple published studies,<sup>5,6,7</sup> including in-vivo and in-vitro



1 Beck LR, Fuhrer JP. Anti-inflammatory factor, method of isolation, and use. US Patent #5980953, Nov1999.

2 Beck LR, Fuhrer JP. Milk lymphocyte anti-adhesion factor, and its role as an anti-microbial. International Dairy Federation. 1993;62-72.

3 Woodman R, Fuhrer P, Beck L, Kubes P. The effects of hyperimmunized milk factor (HIMF) on neutrophil adhesion in vivo [Abstract]. Society for Leukocyte Biology, 29th National Meeting; Charleston, South Carolina. 1992.

4 Wilborn WH, Hyde BM, Beck LR, Fuhrer JP. Milk from hyperimmunized cows stimulates lysosomal activity in rat lung macrophages. Summary of presentation at The Lovelace Respiratory Research Institute Symposium on Respiratory Immunology; Santa Fe, NM. 1999.

5 The Use of MicroLactin® for Inflammatory Conditions in Equine Veterinary Practice Thomas R. Bello, DVM, PhD and Tammy Allen, RVT Journal of Equine Veterinary Science, Vol 25, No 9, Sept 2005

6 An Intensive Approach in the Treatment of Clinical Equine Protozoal Myeloencephalitis Thomas R. Bello, DVM, PhD and Tammy Allen, RVT Journal of Equine Veterinary Science, Vol 28, No 8, August 2008

7 Technical Brief: Canine Study Abstract Use of Client-specific Outcome Measures to Assess Treatment Effects in Geriatric Dogs with Orthopedic Disabilities; Controlled Clinical Evaluation of a Supplement D. Gingerich DVM, MS; J Strobel, PhD Veterinary Therapeutics, Vol 4, No 1, Spring 2003

## **MAKE DURALACTIN® PRODUCTS PART OF YOUR TREATMENT AND WELLNESS PLANS**

- Prescribe as a primary supplement or as an adjunctive therapy
- Use in a variety of patients:
  - Young patients diagnosed with inflammation
  - Young patients to support normal activity and wellness
  - Patients prone to inflammation
  - Older patients (dogs and cats >7 years)
  - High-risk patients (hepatitis, renal, GI)
  - Patients not responding to other therapies
  - Patients experiencing adverse effects with other therapies
  - Patients with a selective palate

## **THE DURALACTIN® BRAND DIFFERENCE**

- A supplement unlike any other because it's for different types of inflammation—more than a joint supplement
- Not a COX inhibitors and does not have the side effects associated with other therapies
- Backed by 3 studies on target animals (Data on file)
- Does not have a loading dose for the first 4-6 weeks of use, leading to increased pet-owner compliance
- Provides once-a-day dosing
- Has strong palatability results
- Does not trigger additional neutrophils to the site of inflammation

## **DURALACTIN® BRAND PRODUCTS AND BENEFITS**

### **DURALACTIN® CANINE JOINT PLUS SOFT CHEWS**

- Can help manage inflammation and maintain healthy cartilage and joint function
- Contain MicroLactin®
- Available in a palatable soft chew that can be given alone or with food

### **DURALACTIN® CANINE CHEWABLE TABLETS**

- Can help manage inflammation
- Contain MicroLactin®
- Available in a palatable vanilla flavored tablet that can be given alone or with food

### **DURALACTIN® FELINE CAPSULES**

- Can help manage inflammation
- Contain MicroLactin®
- Available in a convenient capsule that can be given alone, with food or sprinkled over food

### **DURALACTIN® FELINE + FATTY ACIDS SOFT CHEWS**

- Can help manage inflammation and support healthy skin
- Contain MicroLactin® and Omega 3 (DHA) and Omega 6 (EPA) Fatty Acids
- Available in a palatable heart-shaped soft chew that can be given alone, with food, or crumbled onto food

### **DURALACTIN® FELINE L-LYSINE PASTE**

- Can help support respiratory and ocular health while managing inflammation
- Contains MicroLactin® and L-lysine
- Available in an economical palatable paste that can be given alone or with food



**PROOF POSITIVE FOR MICROLACTIN®**

**CANINE EFFICACY STUDY OF MICROLACTIN®\***

**Method:**

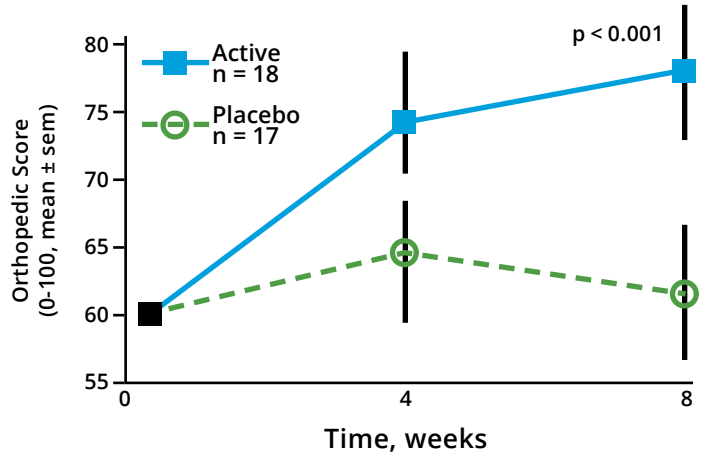
- Dog owner questionnaire to assess efficacy of a joint health supplement
- Large breed dogs, ages 7-12 years
- Randomized into placebo and active treatment groups

**Results:**

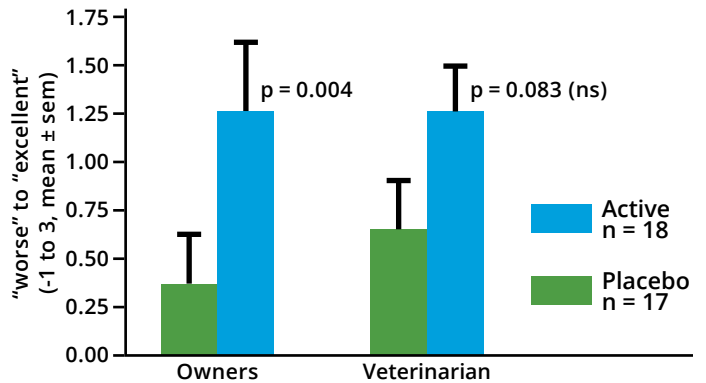
- 68% of the MicroLactin®-treated dogs showed an overall clinical improvement versus only 35% of the placebo group
- The degree of overall improvement was significantly higher ( $P < .05$ ) in the MicroLactin®-treated group than in the control group at 4 and 8 weeks
- The standardized and client-specific questionnaire scores improved significantly ( $P < .05$ ) in the MicroLactin®-treated group but not in the control group
- Treatment with MicroLactin® had a large effect on the case-specific questionnaire results and on the overall improvement seen by owners
- MicroLactin® was well tolerated by the observed dogs



**IMPROVEMENT IN ORTHOPEDIC DISABILITY INDEX IN DOGS**



**OVERALL GLOBAL RESPONSE AS SEEN BY DOG OWNERS AND BY VETERINARIANS**



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\*Derived from study by DA Gingerich DVM, MS; JD Strobel, PhD Veterinary Therapeutics, Vol 4, No 1, Spring 2003. Use of Client-specific Outcome Measures to Assess Treatment Effects in Geriatric Dogs with Orthopedic Disabilities: Controlled Clinical Evaluation of a Supplement

## STUDIES: NEUTROPHIL AND EDEMA ACCUMULATION

These studies indicate that HIMF decreases neutrophil migration and tissue swelling (edema) in the inflammatory response. HIMF can both prevent and treat inflammation.

### Method:

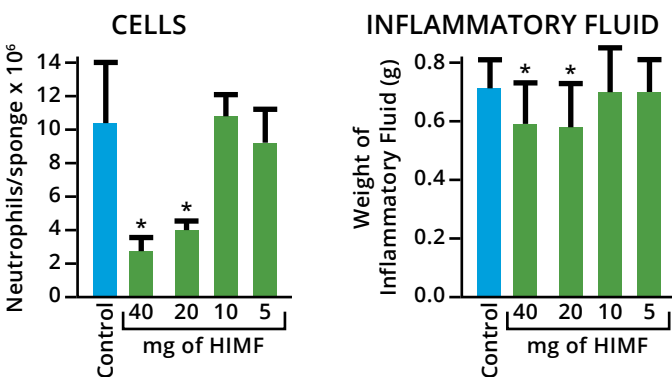
#### Subcutaneous Sponge Implants:

- Polyurethane sponges were implanted under the skin of rats
- The subcutaneous (SQ) sponges act as foreign material to trigger inflammation
- Hyperimmune milk factor (HIMF) was given intravenously at various doses
- After removing the sponges, neutrophils and amount of fluid (edema) were measured

### Results:

#### After sponge removal:

- Sponges from rats receiving the 20 and 40 mg doses contained dramatically fewer neutrophils and a mildly less fluid than sponges from the rats that did not receive medications (see below)
- Sponges from rats given 5 or 10 mg did not show a significant difference from the control group. The number of neutrophils was also significantly decreased when HIMF was given 30, 60, and 120 minutes after the implant.



The effect of hyperimmune milk factor (HIMF) on neutrophil migration and fluid accumulation in subcutaneous sponges. \* = p < 0.01, n = 6. Graphs borrowed from Ormrod DJ, Miller TE. A low molecular weight component derived from the milk of hyperimmunized cows suppresses inflammation by inhibiting neutrophil emigration. Agents and Actions. 1992;37:73. Figure 5.

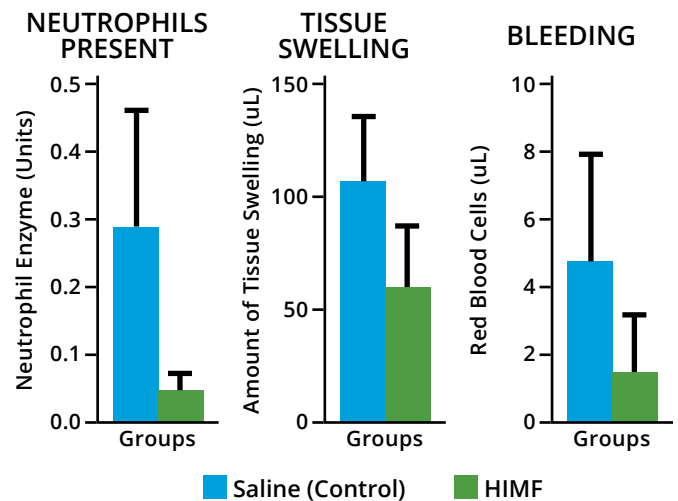
### Method:

#### Reverse Passive Arthus Reaction:

- In the reverse passive Arthus reaction (RPA), rats are injected with a protein found in egg whites (antigen) and rabbit antibodies to that protein
- At injection site, antibodies bind to the antigens and create an intense inflammatory reaction

### Results:

- Reduced the number of neutrophils present at the sites of inflammation by up to 81%
- Decreased the volume of edema present at sites of inflammation by up to 44%
- Worked effectively when given prior to and after an inflammatory stimulus to block excess neutrophils from traveling to site of inflammation



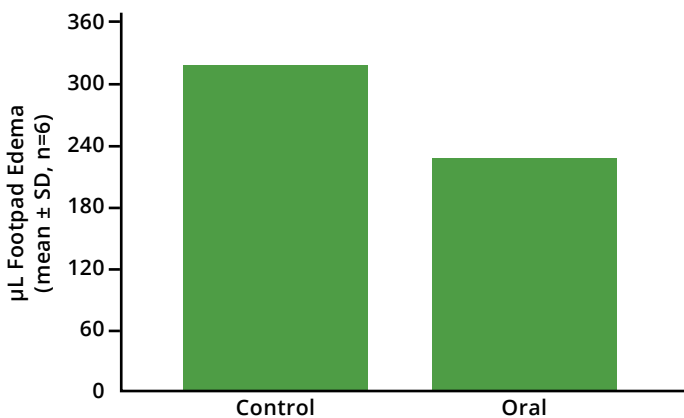
The effect of 20 mg of intravenous (IV) hyperimmune milk factor (HIMF) on the number of neutrophils, amount of tissue swelling, and bleeding seen at the injection sites of a reverse passive Arthus reaction in rats. A significant decrease in neutrophil number, tissue swelling, and bleeding were present (p < 0.01, n = 6 per group). Data collected from Beck LR, Fuhrer JP. Anti-inflammatory factor, method of isolation, and use. US Patent #5980953. Nov1999.

## STUDY: CARRAGEENAN-INDUCED INFLAMMATION

Scientists test the efficacy of inflammation treatments by injecting an inflammatory substance called carrageenan into the paws of laboratory rats and then measuring the resulting edema.

Utilizing this experimental technique, researchers have repeatedly<sup>1,2,3,4</sup> shown that the active factors found in MicroLactin®:

- Inhibits the inflammation triggered by carrageenan
- Work effectively when given orally
- Block excess neutrophils from traveling to site of inflammation to improve action of phagocytic inflammatory cells (neutrophils and macrophages)



Effect of oral hyperimmune milk factor (HIMF) vs. control (no treatment); tissue swelling caused by carrageenan in the rat paw.

## STUDY: INTRAVITAL MICROSCOPY

### Hyperimmune milk factor (HIMF) inhibits neutrophil attachment.

Through the use of intravital microscopy,<sup>5,6,7</sup> researchers can watch as neutrophils adhere to the endothelium—a critical step in an inflammatory cell's migration from the blood into inflamed tissues.

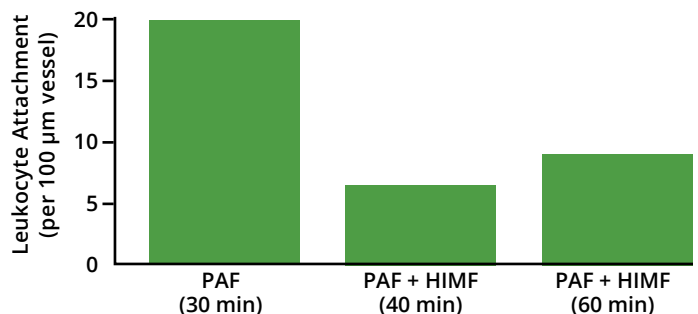
#### Method:

Researchers induced inflammation with platelet-activating factor (PAF).

#### Results:

Researchers observed that when given intravenously, the hyperimmune milk factor (HIMF) which is found in MicroLactin®:

- Inhibited neutrophil attachment to endothelial cells by 80-90%
- Completely blocked neutrophils from passing through endothelial walls into inflamed tissues (compared to a 12-time increase in the untreated control group)
- Reversed neutrophil adhesion to endothelial cells when given after the inflammatory stimulant



The effect of platelet-activating factor (PAF) and 40 mg of hyperimmune milk factor (HIMF) on the number of neutrophils attached to 100 µm vessel wall. The vessel was treated with PAF alone for 30 minutes. After 30 minutes, HIMF was added. Ten minutes after HIMF was added, there was a large reduction in the number of attached neutrophils. This is not a typical effect of anti-inflammatory treatments. Graph adapted from Beck LR, Fuhrer JP. Anti-inflammatory factor, method of isolation, and use. US Patent #5980953. Nov1999, Figure 27A.

1 Beck LR, Fuhrer JP. Anti-inflammatory factor, method of isolation, and use. US Patent #5980953. Nov 1999.  
 2 Beck LR. Method of treating inflammation using bovine milk. US Patent #4284623. Aug 1981.  
 3 Ormrod DJ, Miller TE. The anti-inflammatory activity of a low molecular weight component derived from the milk of hyperimmunized cows. Agents and Actions. 1991;32(3/4):160-166.  
 4 Ormrod DJ, Miller TE. A low molecular weight component derived from the milk of hyperimmunized cows suppresses inflammation by inhibiting neutrophil emigration. Agents and Actions. 1992;37:70-79.

5 Beck LR, Fuhrer JP. Milk lymphocyte anti-adhesion factor, and its role as an anti-microbial. International Dairy Federation. 1993;62-72.  
 6 Woodman R, Fuhrer P, Beck L, Kubes P. The effects of hyperimmunized milk factor (HIMF) on neutrophil adhesion in vivo [Abstract]. Society for Leukocyte Biology, 29th National Meeting; Charleston, South Carolina. 1992.  
 7 Beck LR, Fuhrer JP. Anti-inflammatory factor, method of isolation, and use. US Patent #5980953. Nov 1999.



## STUDY: MAINTAINING TIGHT JUNCTION FUNCTION

Studies indicate that the active factor found in MicroLactin® can protect tight junctions between epithelial cells. This explains the decrease in the number of inflammatory cells seen at inflammatory sites in treated animals.

In order for inflammatory cells to enter inflamed tissues, they need to pass through gaps between endothelial cells. Normally these cells are held close together via junctional complexes, which contain tight junctions.

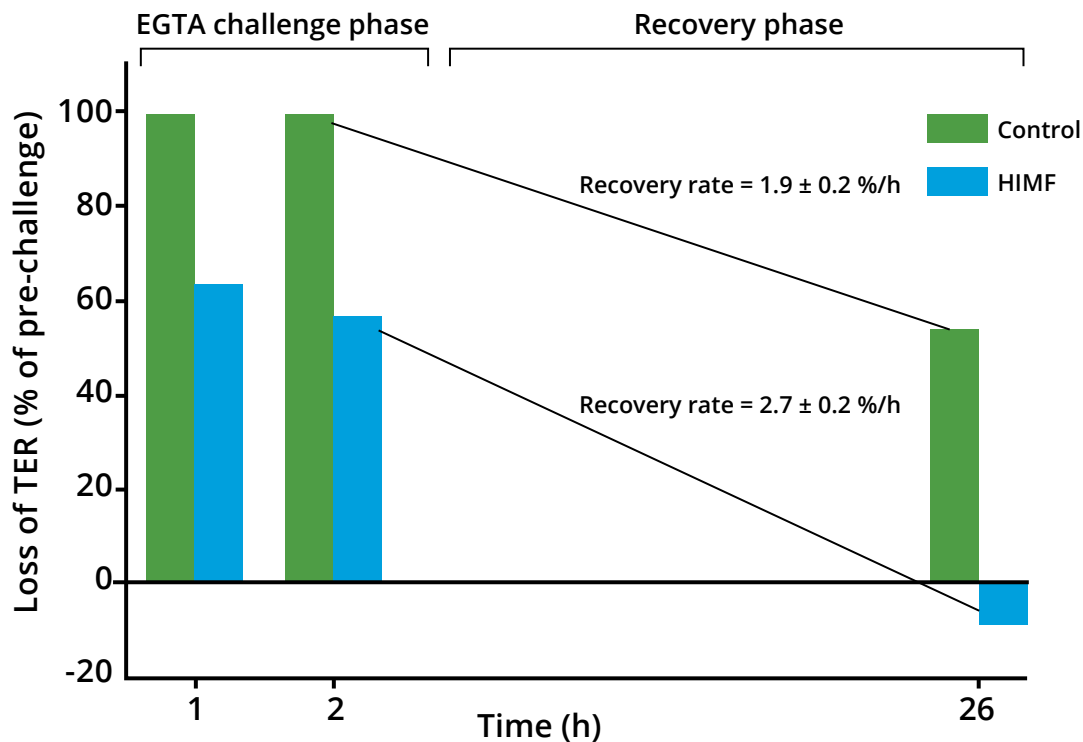
### Method:

Stelwagen and Ormrod measured the transepithelial electrical resistance (TER) of in vitro epithelial cells in order to test the permeability of in vitro epithelial tight junctions.

### Results:

Epithelial cells treated with the active factor found in MicroLactin®:

- Showed stronger tight junctions than untreated control cells
- Stimulated the production of tight junction
- Accelerated the recovery rate of tight junctions
- Decreased the permeability of tight junctions



The effect of hyperimmune milk factor (HIMF) on transepithelial electrical resistance (TER)—an indicator of intact tight junctions. Tight junctions open under the influence of EGTA. HIMF prevented the loss of TER significantly more than the untreated control group. Also, the HIMF-treated cells recovered their TER faster than the control group. \*\* =  $p < 0.01$  Graph borrowed from Stelwagen K, Ormrod DJ. An anti-inflammatory component derived from milk of hyperimmunized cows reduces tight junction permeability in vitro. *Inflammation Research*. 1998;47:384-388.

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Item Number	Product Name
100522704	Duralactin® Canine Joint Plus Soft Chews (60 ct.)
100522703	Duralactin® Canine Joint Plus Soft Chews (90 ct.)
100521850	Duralactin® Feline + Fatty Acids Soft Chews (60 ct.)
3002932	Duralactin® Canine Chewable Tablets (60 ct.)†
3004948	Duralactin® Canine Chewable Tablets (180 ct.)†
3003829	Duralactin® Feline Capsules (60 ct.)
100504080	Duralactin® Feline L-lysine (32.5 ml syringe)†

†Not available in New Mexico



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