



Anivestin™ is a specially formulated, natural plant-based composition, clinically researched to provide faster relief for joint discomfort and support for oral health in companion animals, as assessed by veterinarians and owners alike. It is composed of medicinal plant extracts standardised to two specific bioflavonoids with a long history of safe consumption.



PRODUCT PROFILE SHEET

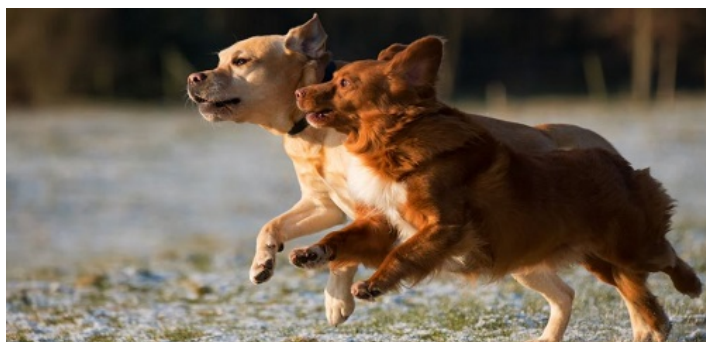
What makes Anivestin™ Unique?

The Anivestin™ plant extracts are standardised for two distinct types of bioflavonoids that the manufacturer, Unigen (USA), discovered to inhibit the pro-inflammatory enzymes COX and LOX, and neutralize inflammatory reactive oxygen species (ROS). Anivestin™ is a plant-based supplement, derived from the roots of *Scutellaria baicalensis* and heartwood of *Acacia catechu*, clinically proven to alleviate joint discomfort and support oral health in companion animals.

The discovery

Over 1230 medicinal plants from Unigen's PhytoLogix® library were screened to identify natural substances with COX and LOX dual inhibitory activity. The Anivestin™, bioflavonoids, baicalin from *Scutellaria baicalensis*, and catechins from *Acacia catechu* (*Senegalia catechu*) were identified as the active components of the most effective extracts tested both in-vitro and in-vivo.

The combination of these two extracts produced a synergistic analgesic and anti-inflammatory effect in-vivo with regards to both onset and duration.



Product Advantages

- ✓ **Animal-Friendly Concept**
- ✓ **Scientifically studied plant-based composition**
Multiple peer review publications
- ✓ **Multiple Pet health concerns supported with one ingredient**
Supports joint health and promotes oral hygiene for companion animals
- ✓ **Fast onset of action**
Faster relief for joint discomfort in companion animals
- ✓ **Discovered through screening of the unique Unigen's PhytoLogix® library**
- ✓ **Safe**

Research

1. Pre-clinical Studies

Extensive pre-clinical data has shown the beneficial effects of Anivestin™ related to alleviating joint discomfort. The bioflavonoid components of Anivestin™ were discovered as inhibitors of the pro-inflammatory COX and LOX enzymes.¹ The IC50 for inhibition of COX-1 by Anivestin™ was calculated to be 0.2 µg/mL/unit of enzyme and the IC50 for inhibition of COX-2 was calculated to be 0.4 µg/mL/unit of enzyme.

Anivestin™ is also an effective inhibitor of the LOX pro-inflammatory pathway. The IC50 of Anivestin™ for inhibition of the LOX pathway was 25 µg/mL in the LPS stimulated THP-1 cells. Chondrocytes and inflammatory cells, e.g., neutrophils and macrophages, produce high amounts of ROS such as superoxide anion, H₂O₂, and HO that are causally linked to cartilage degradation.² Importantly, Anivestin™ is a potent antioxidant having an oxygen radical absorbance capacity (ORAC) much greater than that of commonly used antioxidants such as Citrus Bioflavonoids.

Three experimental systems were utilized to evaluate Anivestin™ for regulation of gene expression³: human peripheral blood monocytes (hPBMCs), the human monocytic cell line 28SC, and the mouse macrophage cell line RAW 264.7. Anivestin™ significantly decreases pro-inflammatory IL-1β, IL-6, and COX-2 gene expression in human PBMCs. Anivestin™ significantly decreases LPS-induced gene expression for TNF-α, IL-1β and NFκB in human 28SC monocytic cells.

2. Clinical Studies

Anivestin™ for companion animals joint discomfort support

A multi-site, double-blind, randomized, direct-comparator trial comparing chewable tabs FlexileRx (a trade name product containing 250mg of Anivestin™) to a combination of chondroitin sulfate (400mg), glucosamine hydrochloride (500mg), and manganese ascorbate formulation, (CosequinDS), was performed over a two-month period. Sixty-nine dogs were randomized into two groups: 33 were assigned to the FlexileRx group, and 36 to the CosequinDS group.



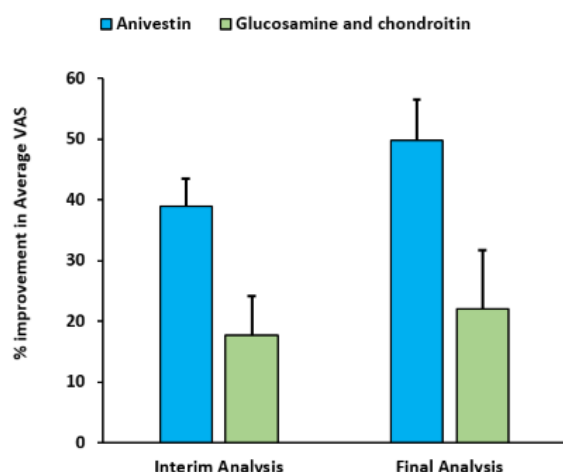
The FlexileRx and CosequinDS groups were equivalent in demographics for weight, age, and initial pain scores. Pain scores were assessed by veterinarians and owners.⁴

In this clinical study, Anivestín™ showed statistically significant improvement in pain scores over the combination formulation (Cosequin®DS) using both the veterinarian and owner visual analog scale (VAS) assessments.

At both the interim (28 days) and final analysis (56 days), Anivestín™ was more than twice as effective as Cosequin®DS at relieving pain. Adverse events were generally mild in both groups. This study demonstrates that Anivestín™ is a relatively fast-acting therapy for reduction of pain scores in dogs with OA.

Graphic 1

Veterinarian/owner Assessment Using Visual Analog Scale of OA



Anivestín™ for companion animal oral care

Anivestín™ was evaluated for its oral care effect on ligature-induced periodontal disease in beagle dogs. Disease model was induced in 20 male and female dogs. After a 12-week induction of periodontitis, animals were assigned to a placebo, positive control (doxycycline), and two treatment groups consisting of five animals each.

The placebo group was only administrated to normal dog chow (25 g/kg/day). In the doxycycline treatment group, animals were fed a normal diet (25 g/kg/day) and doxycycline (5 mg/kg) was orally administrated every day.

Treatment of Anivestín™ was done by feeding the regular diet formulated with 0.1% and 0.2% of the bioflavonoid by weight. Clinical indices such as plaque index (PI), gingival index (GI), clinical attachment level (CAL), probing pocket depth (PPD), and bleeding on probing (BoP) were measured every two weeks for 12 weeks.⁵

Anivestín™ administered to beagle dogs for 12 weeks at 0.1% and 0.2% resulted in statistically significant reductions in gingivitis, pocket depth, loss of attachment, and

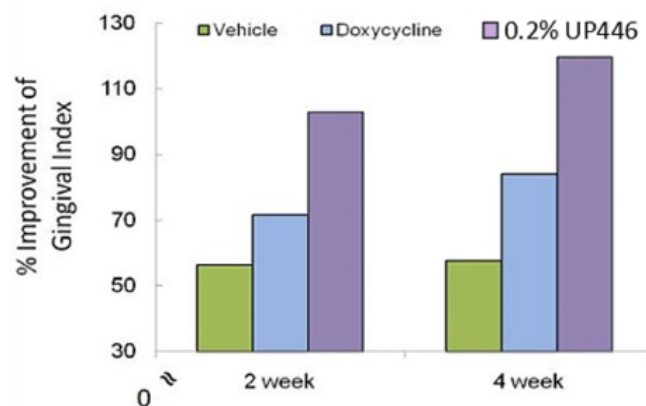
gum bleeding. For example, when Anivestín™ was formulated at 0.2% in the diet, the reductions in gingival indices were higher than to that of doxycycline treated dogs.

There were ranges of 26.9–49.8%, 55.1–92.9%, and 44.6–107.4% reductions in gingivitis were observed for the dogs treated with Doxycycline, Anivestín™ at 0.1% and 0.2%, respectively.

This data suggests the potential use of Anivestín™ alone or as an adjunct with other oral hygiene preparations for periodontal disease in companion animals.

Graphic 2

Anivestín™ (UP446) at 0.2% was more effective than the antibiotic doxycycline at reducing gum inflammation measured by Gingival Index



Product Safety

Anivestín™ was found to be safe in wide ranges of animal species. Acute toxicity, repeated toxicities lasted up to 6 months; pharmacological, reproductive, developmental and genotoxicity studies have demonstrated the safety of Anivestín™.

Product Range

Ingredient	Active Content	Grade	Mesh Size
Anivestín	Min 56% Baicalin Min 8% Catechins	Powder	NLT 80% thru 80 mesh

Product Pack Size

The packing size for Anivestín™ is 25kg.

Product Applications

Anivestín™ can be used in treats, chews and wet foods. We suggest you use a strong flavour to cover the bitter taste when formulating for cats.



Product Dosage

Cats and Dogs

Considering 500mg/day as the daily recommended dosage of Uninvestin™ for humans, the daily equivalent dosage for Aninvestin™ for dogs/cats can be calculated using the 1.8 conversion factor from FDA guidelines: Animal Dose in mg/kg = Human dose (mg/kg) x 1.8.

Based on the above, Unigen recommends the following dosages:

Body Weight	Aninvestin™ Suggested Dosage
5kg	60mg
10kg	120mg
20kg	240mg
40kg and above	480mg



Horses

For horses, please see below the following recommendations.

Racing Horses:

We recommend 3.5 grams the evening before the event and 2.5 grams 2 -3 hours before the event.

Horses (General) based on duration of the treatment:

Duration	Aninvestin™ Suggested Dosage
Instant Impact (4 days)	3.5 grams per day
7-day course	3.5 grams per day
28 day course (4 weeks)	3.5 grams per day

Horses (General) based on body weight:

Body Weight	Aninvestin™ Suggested Dosage
450 kilos or above	3.5 grams per day
Below 450kg	1.75 grams per day

The Phytologix® Technology Platform



Aninvestin™'s unique formulation was discovered and developed through Unigen's proprietary Phytologix® Technology Platform. This proprietary informatics database contains comprehensive botanical profiles on over 12,000 plants and data on more than 15,000 extracts and 300,000 HTP fractions. Unigen scientists used these profiles to identify plants whose actives delivered the most effective health benefits.

About

UNiGEN

Unigen focus on identifying and studying the unique bioactive natural products of medicinal botanicals and then developing them into research-driven, proprietary standardized extracts for use in nutraceutical, cosmetic, and pharmaceutical finished products.

References

1. Burnett BP1, Q. Jia, Y. Zhao, R.M. Levy. 2007. A medicinal extract of Scutellaria baicalensis and Acacia catechu acts as a dual inhibitor of cyclooxygenase and 5-lipoxygenase to reduce inflammation. *J Med Food*. 10(3):442-51.
2. Tiku ML, Gupta S, Deshmukh DR. Aggrecan degradation in chondrocytes is mediated by reactive oxygen species and protected by antioxidants. *Free Radic Res*. 1999 May;30(5):395-405.
3. Tseng-Crank J., S. Sung, Q. Jia, et al. 2010. A medicinal plant extract of Scutellaria Baicalensis and Acacia catechu reduced LPS-stimulated gene expression in immune cells: a comprehensive genomic study using QPCR, ELISA, and microarray. *J Diet Suppl*. 7(3). 253-72.
4. Burnett BP, Stenstrom KK, Baarsch MJ, et. al. "A Flavonoid Mixture, Dual Inhibitor of Cyclooxygenase and 5-Lipoxygenase Enzymes Shows Superiority to Glucosamine/Chondroitin for Pain Management in Moderate Osteoarthritic Dogs." *International Journal of Applied Research* 7.18&2 (2009): 1-12.
5. Yimam M, Brownell L, Do SG, Lee YC, Kim DS, Seo K, Jeong M, Kim S, Jia Q. Protective Effect of UP446 on Ligature-Induced Periodontitis in Beagle Dogs. *Dent J (Basel)*. 2019 Mar 28;7(2):33