AlphaVet Science™

SynoForte-VM™

NN.L7K2

SynoForte-VM™ is an oral hyaluronic acid and marine collagen supplement essential for joint function.

SynoForte-VM™ is specially formulated with a unique delivery system to ensure higher bioavailability.

INDICATIONS

- Supports lubricating and cushioning of the synovial joints

INGREDIENTS ACTIONS

- Anabolic
- Anti-arthritic
- Anti-edematous
- Antioxidant
- Chondroprotective
- Lubricant

PACKAGING 500 mL/bottle

STORAGE

- Refrigerate after opening
- Consume within six (6) months after opening
- Keep bottle cap tightly closed when not in use
- Keep out of reach of children

ADMINISTRATION Oral

DIRECTIONS

ADMINISTER ORALLY PER DAY			
LBS	**KG**	**MAINTENANCE DOSAGE**	
		mL	**Teaspoon(s)**
1-10	0.5-4.5	1.25	¼
11-20	5-9	2.5	½
21-40	9.5-18	5	1
41-75	18.5-34	7.5	1½
76-100	34.5-45.4	10	2
>100	45.4	12.5	2½

LOADING DOSE

- Administer the maintenance dose twice daily, morning and evening, for the first two weeks
- Syringe directly into the mouth for best results
- Can be added to animal's food
- Shake well before use
- For use in cats & dogs only

SynoForte-VM™ FORMULA

MEDICINAL INGREDIENTS PER 5 mL (1 TEAPOON)

Hyaluronic acid (Sodium hyaluronate).....30 mg

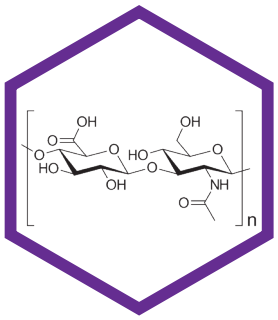
Hydrolyzed Collagen (Marine Collagen).....500 mg

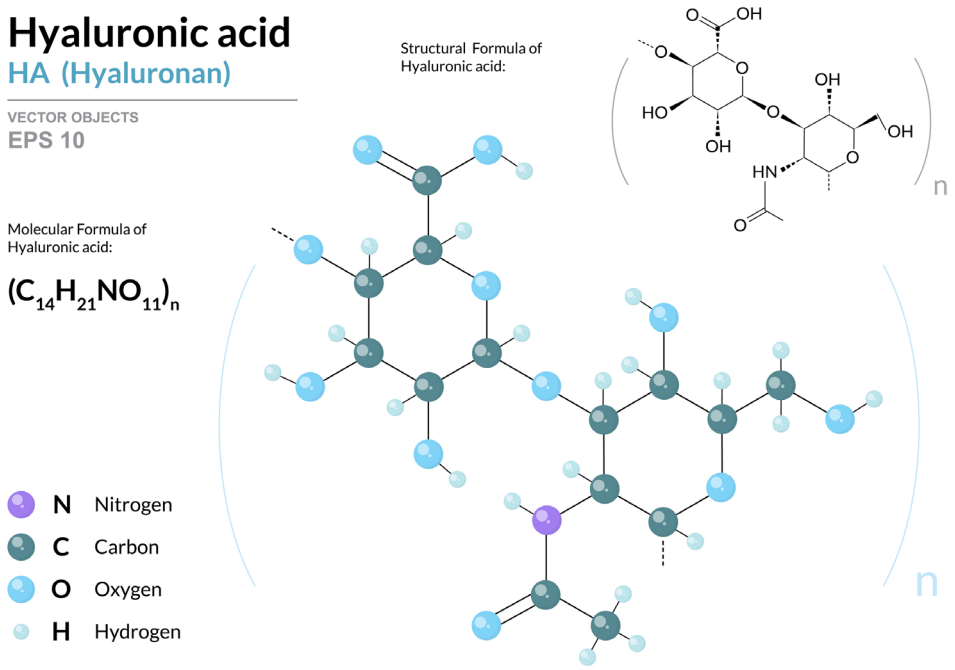
NON-MEDICINAL INGREDIENTS

Purified water, Citric acid, Potassium sorbate, Sodium benzoate

SynoForte-VM™ is manufactured under strict GMP standards and contains no corn, dairy, gluten, soy, wheat or yeast.

Hyaluronic Acid $(C_{14}H_{21}NO_{11})_n$





Hyaluronic acid, also known as hyaluronan or hyaluronate, is an anionic, non-sulfated glycosaminoglycan. It consists of alternating N-acetyl-D-glucosamine and D-glucuronic acid monosaccharide units (Saari et al., 1993). It is distributed widely throughout connective, epithelial and neural tissues, and in the aqueous and vitreous humour (Martindale, 1996). Hyaluronic acid is unique among glycosaminoglycans in that it is non-sulfated and forms in the plasma membrane instead of the Golgi apparatus (Frasher et al., 1997).

Found naturally in the synovial joints, it owns a key role in musculoskeletal structure as a cushioning and lubricating agent between joint surfaces against mechanical and chemical damage while providing rigidity to vertebrae (Tsukasa, 2006). Hyaluronic acid has been used for more than four decades in the management of osteoarthritis in dogs, horses, and humans. Hyaluronic acid produces anti-arthritic effects via multiple mechanisms involving receptors, enzymes, and other metabolic pathways (Gupta et al., 2019).

Physiological and pharmacological mechanisms and effects of hyaluronic acid (Gupta et al., 2019):

Physiological

- Maintenance of viscoelasticity
- Restores rheological properties and metabolism of fibroblasts
- Maintenance of lubrication

Pharmacological

- Scavenges ROS/RNS and exerts an antioxidative effect.
- Exerts anti-inflammatory effect.
- Reduces the production of MMPs (MMP-1, MMP-3, and MMP-13).
- Reduces the production and activity of IL-1β.
- Inhibits synthesis of PGE2 and bradykinin.
- Mitigates synovial hypertrophy and increases the number of synovial fibroblast-like cells while decreasing macrophages, lymphocytes, mast cells, and adipocytes.
- Regulates fibroblast proliferation.
- Inhibits the migration and aggregation of leukocytes and macrophages.
- Alters the behavior of immune cells.
- Enhances the synthesis of chondrocytes, hyaluronic acid, and proteoglycan.
- Improves the viscoelasticity and enhances lubricating potential.
- Improves joint function and mobility, and reduces stiffness.
- Interacts with hyaluronic acid receptors on or around the free nerve endings, thereby producing analgesia.

Canine-Studies of oral hyaluronic acid and combinations

Studies-Canine	Study Title	Study Summary
Serra Aguado et al., 2021	Effects of Oral Hyaluronic Acid Administration in Dogs Following Tibial Tuberosity Advancement Surgery for Cranial Cruciate Ligament Injury.	Fifty-five canine patients participated in this prospective, randomized, double-blind clinical study. The canine patients received oral hyaluronic acid (27 mg or 52 mg once daily) for ten weeks. The study concluded that oral hyaluronic acid administration in canine patients with cranial cruciate ligament injury leads to improvements in osteoarthritis biomarkers, namely higher synovial fluid hyaluronic acid concentrations and reduced synovial fluid paraoxonase-1 concentrations.
Martello et al., 2022	Efficacy of a dietary supplement in dogs with osteoarthritis: A randomized placebo-controlled, double-blind clinical trial.	The randomized, placebo-controlled, double-blinded trial investigated the effects of a dietary supplement containing a mixture of Boswellia serrata, chlorophyll, green tea extract, glucosamine, chondroitin sulfate, hyaluronic acid in 40 osteoarthritis canine patients. The study concluded that the combination was beneficial in alleviating pain and reducing the clinical signs in canine patients with osteoarthritis.

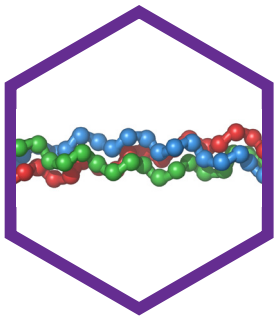
TOXICOLOGY

Toxicity of hyaluronic acid has not been documented in dogs and cats when administered orally in therapeutic doses.

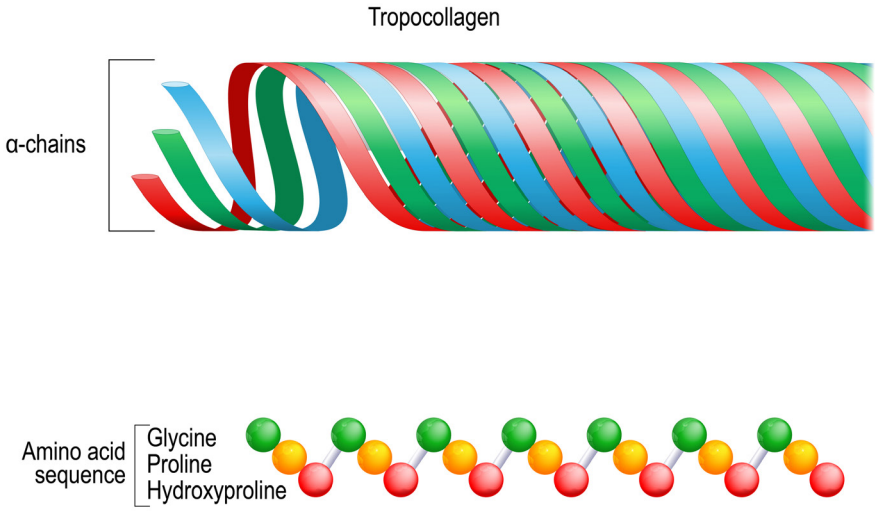
Hyaluronic acid was not toxic in a wide range of acute animal toxicity studies, over several species and with different exposure routes (Becker et al., 2009).

DRUG INTERACTIONS

Validated interactions studies do not exist for oral hyaluronic acid preparations. Clinical interactions with other drugs have not been reported.



Hydrolyzed Collagen (Marine Collagen)



Marine collagen has gained extensive recognition in the recent past as an appropriate alternative to mammalian collagen. It is processed from different marine sources and their by-products, such as skin, scales, and bones. During fish processing operations, such as skinning and filleting, the removal of collagen-containing materials can account for up to 30% of the total fish by-products. Collagen is the main structural protein in skin, representing up to 70% of dry weight depending on the species, age and season (Blanco et al., 2017).

Marine collagen has been extracted mainly from fish skin and is a rich source of type I collagen (Silva et al., 2014; Sotelo et al., 2016; Raman & Gopakumar, 2018). Analysis of Marine collagen by SDS-PAGE (sodium dodecyl sulfate-polyacrylamide gel electrophoresis) has indicated the absence of a disulfide bond, which is a characteristic of type I collagen (Noitup et al., 2005). Type I collagen forms more than 90% of the organic mass of bone and is the essential collagen of tendons, skin, ligaments, cornea, and most interstitial connective tissues. It provides tensile stiffness for tendons and fascia in organs (Hashim et al., 2015).

Marine collagen promotes the gene expression of alkaline phosphatase, osteocalcin, and bone sialoprotein in vitro (Capati et al., 2016). In clinical trials over the past decade, the beneficial effect of orally administered collagen in osteoarthritic dogs has demonstrated its effectiveness in decreasing lameness and increasing vitality in affected animals (Schunck et al., 2017). Collagen supplementation is an important treatment possibility to avoid cartilage damage over time while supporting the therapeutic process after osteoarthritis inception (Gencoglu et al., 2020).

Canine and Feline-Studies of collagen and combinations

Studies-Canine	Study Title	Study Summary
Deparle et al., 2005	Efficacy and safety of glycosylated undenatured type-II collagen (UC-II) in therapy of arthritic dogs.	Arthritic canine patients receiving 1 mg or 10 mg undenatured type-II collagen/day for 90 days showed significant declines in overall pain and lameness after physical exertion. Supplementation with 10 mg showed more significant improvement than 1 mg. Undenatured type-II collagen had no adverse effects and was well-tolerated.
D'Altilio et al., 2007	Therapeutic Efficacy and Safety of Undenatured Type II Collagen Singly or in Combination with Glucosamine and Chondroitin in Arthritic Dogs.	This placebo-controlled study demonstrates that daily treatment of arthritic dogs with undenatured type II collagen or in combination with glucosamine and chondroitin markedly alleviates arthritic-associated pain. The therapy was well-tolerated and had no side effects.
Martí-Angulo et al., 2014	Efficacy of an oral hyaluronate and collagen supplement as a preventive treatment of elbow dysplasia.	The study evaluated the efficacy of oral hyaluronate and collagen supplements for 20 months as a preventive treatment of elbow dysplasia in 105 Labrador dogs. Symptoms of dysplasia at 12 months differed between the treated (12.5%) and control (61.5%) animals and were significantly different at 20 months ($p < 0.05$). Differences in lameness and swelling of the elbows between groups were seen after 12 months. Treatment with oral hyaluronate and collagen protected dysplasia and significantly improved symptoms of elbow dysplasia.
Beynen et al., 2010	Oral Administration of Gelatin Hydrolysate Reduces Clinical Signs of Canine Osteoarthritis in a Double-Blind, Placebo-Controlled Trial.	In this double-blind, placebo-controlled trial of 15 arthritic dogs, administration of 10 g of gelatin hydrolysate improved activity (vitality) and reduced stiffness and lameness.
Blair & Bonavaud, 2017	Palatability and Tolerability of a Novel Joint Supplement in the Cat.	Administration of 10 mg of undenatured type-II collagen in feline patients was well-tolerated based on physical examination

Comblain et al., 2017	A Randomized, Double-Blind, Prospective, Placebo-Controlled Study of the Efficacy of a Diet Supplemented With Curcuminoids Extract, Hydrolyzed Collagen and Green Tea Extract in Owner's Dogs With Osteoarthritis.	A randomly allocated, double-blind, prospective, placebo-controlled study was performed on 42 osteoarthritic dogs to evaluate the efficacy of an oral hydrolyzed collagen mixture containing antioxidant polyphenols. Dogs (n=23) receiving hydrolyzed collagen mixture for three months showed less pain at manipulation. The ability of canine patients to rise and stand from a lying-down position significantly improved compared to the control group.

TOXICOLOGY

Toxicity of marine collagen has not been documented in dogs and cats when administered orally in therapeutic doses.

Note: Due to the increased consumption of marine collagen peptides (MCP) preparation as ingredients in functional foods and pharmaceuticals, an oral chronic toxicity assessment is a requirement. In experimental conditions, no higher risk of chronic toxic effects was observed in MCP-treated rats at the diet concentrations of 2.25%, 4.5%, 9% and 18% (wt/wt) than in the rats fed with basal rodent diet (Liang et al., 2012).

DRUG INTERACTIONS

Validated interactions studies do not exist for oral marine collagen preparations. Clinical interactions with other drugs have not been reported.

PRECAUTIONS

- An examination from a veterinarian is recommended before using this product.
- Safe use in pregnant animals or animals intended for breeding has not been proven.
- If animal's condition worsens or does not improve, stop product administration and consult your veterinarian.
- Not recommended in autoimmune diseases in dogs and cats.
- Consult your veterinarian for potential drug interactions.
- Administer during or after the animal has eaten to reduce the incidence of gastrointestinal upset.
- Off-label use of this product in ruminants is not recommended.
- Oral use only.
- Do not use if security seal is broken.

WARNINGS

- To be used in dogs and cats only.
- Keep out of the reach of children and animals.
- In case of accidental overdose, contact a health professional immediately.

ADVERSE REACTIONS

- No side effects have been reported for the oral use of hyaluronic acid and marine collagen in dogs and cats.

Note: Parenteral hyaluronic acid can cause erythema, swelling, pain, itching, discoloration and tenderness at the site of administration. In Shar-pei dogs it can cause thrombosis (Gupta et al., 2019).

CONTRAINDICATIONS

- Contraindicated in known hypersensitivity to hyaluronic acid.

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ILLUSTRATION

Collagen: Tropocollagen molecule. Available at https://en.wikipedia.org/wiki/Collagen.

Hyaluronic acid: Hyaluronan. Available at http://en.wikipedia.org/wiki/Hyaluronan.

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