a scientific insight

Glyde mobility joint health chews

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GLYDE®

what is it, and what's in it?

Glyde Mobility Chews is a great tasting joint supplement product for dogs with three proven ingredients, sustainably sourced from nature, that together can help relieve the signs of osteoarthritis (OA).

Glucosamine and **Chondroitin** are key building blocks of healthy cartilage that must be readily available in the bloodstream to protect and maintain good joint function especially in OA-affected patients.

Green Lipped Mussel (GLM) contains cartilage building blocks and multiple naturally occurring potent anti-inflammatory compounds including specific fatty acids that can assist in reducing stiffness and improving mobility in OA patients.

Features of OA in Clinical Practice

1. Joint Involvement

OA is a disease of the synovial joint. Cartilage, subchondral bone and the synovial membrane undergo metabolic and structural modifications as the disease progresses[1]. These changes to joint structures in OA are illustrated in Fig. 2 on page 2, and contrasted by Fig. 1 on page 2, representing the normal joint.

2. High Incidence

OA is one of the most widespread and insidious diseases faced in canine medicine, being a slowly progressive, degenerative and debilitating disease affecting 20% of the canine population over the age of one year[2] and 80% of dogs over the age of eight[3].

OA most commonly affects older dogs, with significant onset in younger dogs due to breed disposition, trauma or surgery.

3. Challenging Diagnosis

The development of clinical signs in OA are often unrecognised and hence most cases go untreated, especially in the early and mid-stages of the disease. Clinical signs of OA to look for in dogs include:

- **Reluctance to walk, climb stairs, play and jump**
- **Lameness, limping, slow cautious gait**
- **Limb weakness or stiffness after laying down**
- **Unexpected aggression or guarding behaviour due to pain**

4. Distinctive Pathophysiology

4.1 Normal Cartilage and Joint Structure

In the normal joint unaffected by OA, the articular cartilage, synovium and subchondral bone are all healthy, as represented in Fig. 1 below. The articular cartilage detailed view (LHS) shows the key structural components of normal articular cartilage and their even distribution throughout the matrix.

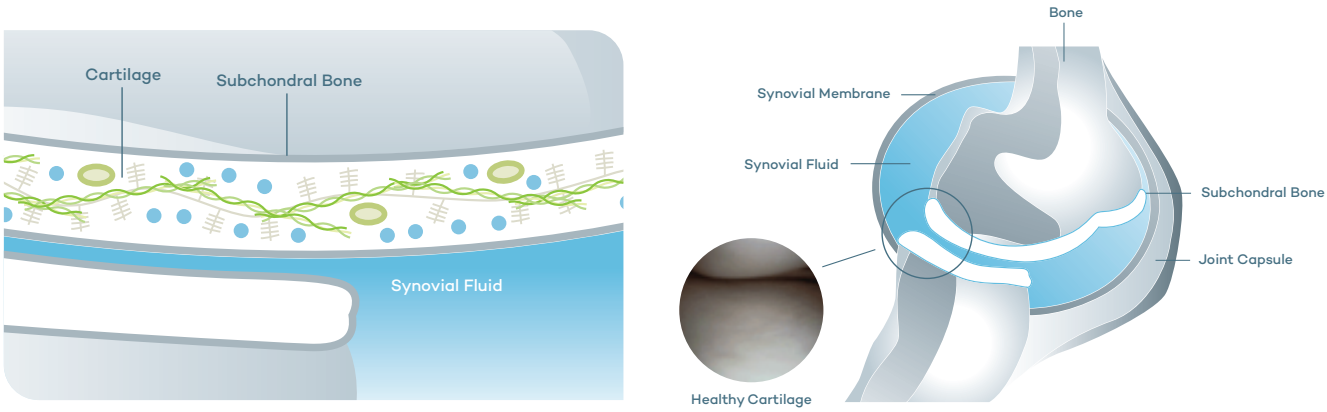


Figure 1: Diagram of the normal structures of a healthy synovial joint

4.2 Cartilage and Joint Structural Abnormalities in OA

In the OA-affected joint, the articular cartilage, synovium and subchondral bone all undergo structural and functional changes, as represented in Fig. 2 below. The articular cartilage detailed view (LHS) shows the abnormal distribution of key structural components throughout the matrix in OA.

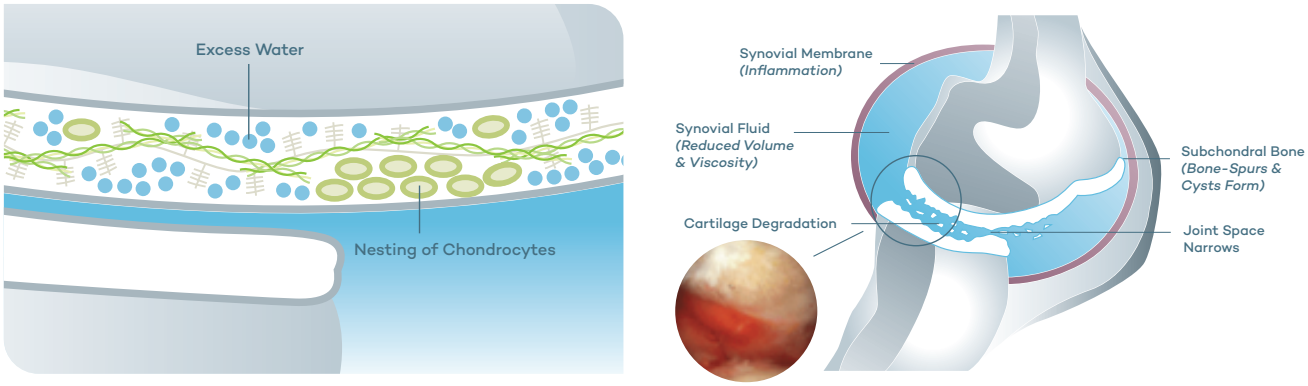


Figure 2: Diagram of structural pathology in the diseased synovial joint

5. Progressive Pathogenesis

At the cellular level, OA is characterised by the production of phenotypically abnormal chondrocytes which rapidly multiply and become metabolically very active, forming nests within the cartilage matrix.

Chondrocyte nesting leads to cartilage breakdown and inadequate cartilage renewal. The resultant cartilage erosion can lead to discomfort or even overt joint pain. The cellular pathways to joint pathology in OA are set out below:

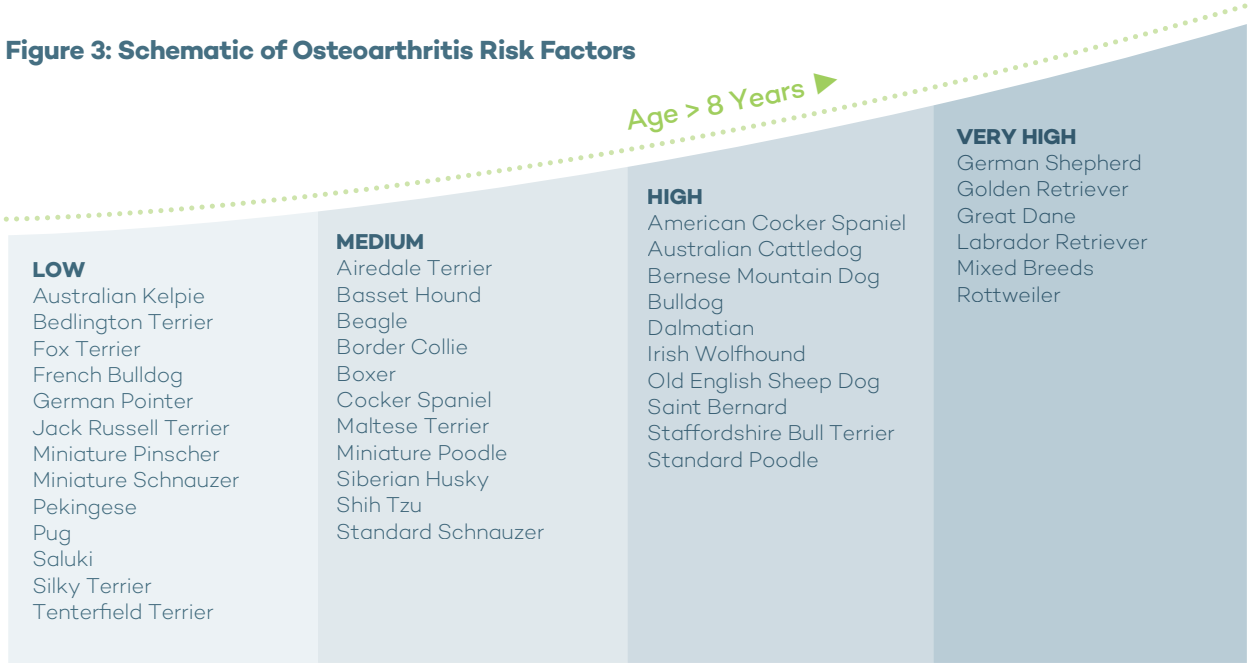
- Proteoglycans and collagen produced within affected cartilage are abnormal and break down faster than they can be produced
- Chondrocytes attempt to compensate by producing more proteoglycans and cartilage, which can result in cartilage hypertrophy
- The breakdown of proteoglycans leads to chondromalacia where excess water content results in characteristic cartilage stiffening
- Microfractures and fibrillation in chondromalacia lead to roughening and cracking of normally smooth cartilage surface, predisposing affected cartilage to erosion
- Severe cartilage erosion exposes underlying bone, exacerbating pain and lameness

6. Known Risk Factors

The onset of OA can be triggered in several ways, including:

- Breed predisposition including conformational factors (Fig. 3 below)
- Obesity
- Excessive force to the joint leading to anatomical malformation
- Idiopathic defects in the articular cartilage or subchondral bone
- Post-surgical inflammation or realignment of articular surfaces
- Mechanical wear from an active lifestyle over multiple years

Figure 3: Schematic of Osteoarthritis Risk Factors



Treatment Options

Until recently the management of OA has been symptomatic, aimed at reduction of pain and improvement of joint function.

The ideal OA treatment should "preserve the joint function, improve quality of life and exhibit a good safety profile".[1]

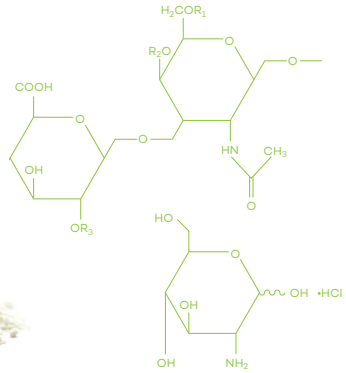
Treatment options include; oral non-steroidal anti-inflammatory drugs (NSAIDs); "disease-modifying" pentosan polysulfate therapies such as ZYDAX INJECTION; and nutraceutical supplements such as GLYDE MOBILITY CHEWS. Each of these products has a pivotal role to play in managing the complex disease that is OA.

NSAIDs: Non-steroidal anti-inflammatory drugs are most commonly used in short term symptom management. NSAIDs are known to cause gastrointestinal ulceration and bleeding as an adverse effect and are contraindicated in the presence of renal insufficiency or dehydration.[2] Thus, there is wide and growing interest in nutraceuticals as an alternative for long term and ongoing disease management.

Pentosan Polysulfate Sodium - ZYDAX INJECTION: Pentosan Polysulfate Sodium (PPS) is a semisynthetic highly sulfated polysaccharide with a linear xylan (pentosan) backbone. Xylan is a hemicellulose derived from beech pulpwood. PPS possesses anti-inflammatory, antiarthritic and chondroprotective activities[4]. The beneficial effects of PPS in joint disease are due to the following actions: anti-inflammatory activity; inhibition of neutrophil migration into the joint; stimulation of hyaluronic acid synthesis by synovial fibroblasts, resulting in increased volume and viscosity of synovial fluid; stimulation of proteoglycan synthesis by chondrocytes; and fibrinolytic activity, resulting in improved circulation to subchondral bone and periarticular structures. The use of Zydax has been shown to inhibit aggrecanase activity and thus reduce the progress of OA by slowing the destruction of proteoglycans[5].

Glucosamine and Chondroitin: Glycosaminoglycans such as chondroitin sulfate and glucosamine are natural compounds in the Symptomatic Slow Acting Drugs for Osteoarthritis (SYSADOA) class that are demonstrated to possess disease modifying potential. The combination of chondroitin sulfate and glucosamine was shown to be efficient for pain relief and function improvement in OA patients with moderate to severe stifle pain[6]. Most studies[1,6,7] recommend the use of pharmaceutical grade products rather than food supplements and insist on the importance of formulation and quality in order to benefit patients with OA.[1] Numerous clinical studies[1,4,7] have demonstrated that the targeted administration of selected micronutrients at effective dose rates leads to a more effective reduction of OA symptoms, with less adverse events.

Green Lipped Mussel: GLM is a natural, environmentally sustainable product from the sea that has an exceptional ability to aid the body in halting the progression of joint and connective tissue disease and promote the regeneration and healing of arthritic and injured joints. GLM contains a unique mixture of natural anti-inflammatory agents, immune modulators and many of the essential building blocks needed in homeostasis and repair of collagen, proteoglycans and synovial fluid found variously in the joints, ligaments and tendons. In clinical studies[8], GLM was associated with significant reductions in joint pain, swelling and inflammation, and with improvements in joint mobility and exercise tolerance.



Glucosamine Hydrochloride | Chondroitin Sulfate (Bovine) | Green Lipped Mussel

How does Glyde work?

Ingredients:

- Glucosamine HCl - ***reduces cartilage degradation***
- Chondroitin Sulfate - ***helps rebuild cartilage***
- Green Lipped Mussel (GLM) - ***clinically proven anti-inflammatory***

Action:

Glucosamine provides building blocks for the biosynthesis of cartilage extracellular matrix and may provide mild anti-inflammatory effects[9] while chondroitin sulfate inhibits destructive enzymes in joint fluid and cartilage. The combination of the 2 ingredients also contributes to the synthesis of glycosaminoglycans (GAGs) and proteoglycans (PGs), which are important building blocks for the formation of cartilage[1].

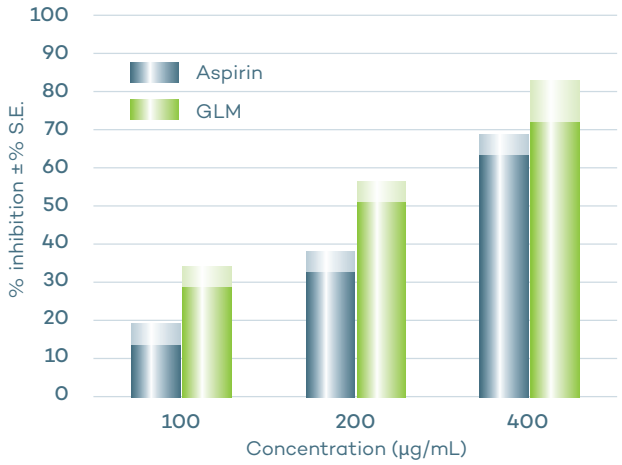
Several controlled studies in dogs diagnosed with degenerative joint disease have shown that dogs treated with glucosamine and chondroitin sulfate had better physical performance and lesser muscle atrophy than untreated control dogs[10].

In a recent meta-analysis, both glucosamine and chondroitin were shown to offer some improvement in the signs of OA; however, only glucosamine PLUS chondroitin showed clinically significant improvement from baseline function [1,11,12].

GLM is a rich source of nutrients including glycosaminoglycans such as chondroitin sulfates, vitamins, minerals and OMEGA-3 series Polyunsaturated Fatty Acids (PUFAs). The eicosatetraenoic acids (ETAs) of GLM have considerable anti-inflammatory activity and, *in vitro*, the extracted lipids were shown to possess significant cyclo-oxygenase (COX) and lipoxygenase (LOX-5) inhibitory activity; hence, GLM appears to be working on the same inflammatory pathways as the newer NSAIDs[6].

In contrast to NSAIDs, GLM was not gastro-toxic in disease-stressed rats at 300 mg/kg orally and did not appear to affect platelet aggregation in humans or rats. GLM was shown to be a reproducible and relatively stable source of bioactive lipids with much greater potency than plant or other marine oils typically used as nutritional supplements to ameliorate signs of inflammation[13].

Anti-Inflammatory Activity
Inhibition of superoxide production by activated neutrophils



Glyde contains building blocks for cartilage and a wide range of anti-inflammatory compounds that protect and repair cartilage. The use of glucosamine and chondroitin sulfate in combination leads to the production of proinflammatory mediators such as Nitric Oxide (NO) and Prostaglandin (PGE2) two mediators responsible for the cell death of chondrocytes and inflammatory reactions[7]. Incorporating glucosamine and chondroitin into a multimodal management plan can improve long-term joint function for patients with OA[14]. These building blocks, along with the anti-inflammatory effects of GLM, can slow the development of clinical arthritis and help repair existing damage from arthritis while contributing to OA pain relief. Importantly, the ingredients in Glyde are considered to be safe with no serious side effects even under long term use.

What does Glucosamine Do?

- Main building block for healthy joints
- Reduces pain, improves joint function and mobility and reduces OA progression in humans[1]
- Reduces joint space narrowing in the knee, a measure of progression of OA in humans[2]
- Inhibits cartilage degradation[6]
- Precursor of glycosaminoglycan production[7]
- Upregulates glycosaminoglycan synthesis[8]
- Increases proteoglycan production[15]
- Suppresses neutrophilic inflammation in the arthritic joint[10]
- Good bioavailability and absorption[2]
- Clinically significant improvement in the signs of OA when only used in conjunction with chrondroitin[11]

What does Chondroitin do?

- Another main building block for healthy joints
- Reduces pain, improves joint function and mobility and reduces OA progression[1]
- Inhibits synovial membrane inflammation[13]
- Predominant glycosaminoglycan used by chondrocytes to produce proteoglycans[14]
- Upregulates glycosaminoglycan synthesis[8]
- Maintains viscosity of synovial fluid[16,17]
- Good bioavailability and absorption[2]
- Clinically significant improvement in the signs of OA when only used in conjunction with glucosamine[11]

What does GLM do?

- Inhibits inflammation[18]
- Inhibits COX-1, COX-2 and LOX and other inflammatory pathways[19-21]
- Scavenges free radicals and prevents lipid peroxidation and inflammation[19,22]
- Reduces production of inflammatory cytokines[19,23,24] TNF-α, IFN-γ, IL-1, IL-2, IL-6
- Reduces histamine-induced inflammation[25]
- Shown to contain GAGs, among one of the main building blocks of healthy cartilage[8]

Therapeutic doses of 3 proven ingredients in Glyde

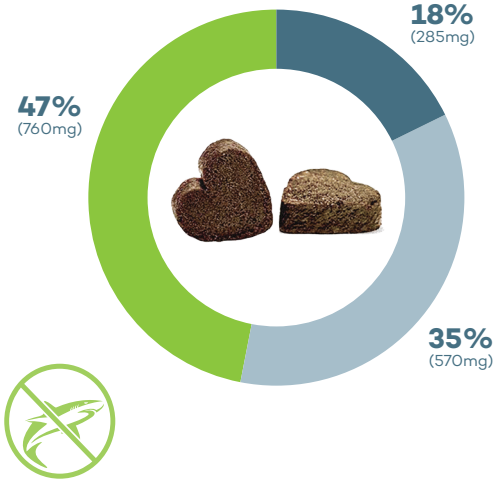
Glyde Mobility Chews are formulated to provide each of the 3 ingredients at the dosage level that is best supported by the available evidence. As referenced above and in the reference publication list below, Glyde Mobility Chews have been carefully formulated to deliver the most evidence-based ingredient combination at the most appropriate and effective dose rates. Glyde Mobility Chews are manufactured to the highest pharmaceutical quality standards in-house by Parnell in our own FDA and APVMA accredited pharmaceutical manufacturing facility.

Many nutraceutical products are formulated as OTC "diet supplements" to accommodate a low price point without regard to the available clinical and scientific evidence that would support their proportions and concentrations of ingredients. Hence when assessing OA nutraceuticals, it is important to establish that your patients are not at risk of under-dosing in one or all of the key ingredients.

Outside the 3 proven ingredients of Glyde Mobility Chews, many different "novel" ingredients of supplement products simply don't have any independent published support for their use - at any dose rate.

Glyde Mobility Chews are truly ***Everything you need, and Nothing you don't*** when it comes to OA management.

Glyde Chews
Optimal dose of active Ingredient*



Decreases inflammation
Green Lipped Mussel
(a potent source of Eicosatetraenoic Acid)

Chondroprotectives
Chondroitin
Glucosamine

*per 3 gram chew

Dosage Guide	Number of Chews Daily	
Body Weight (kg)	Initial treatment 4-6 weeks	Maintenance Treatment
5-10	1 chew	½ chew
11-20	2 chews	1 chew
21-30	3 chews	1 ½ chews
31-40	4 chews	2 chews
Over 40	5 chews	2 ½ chews

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