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REVIEW ARTICLE

The Therapeutic Role of Hyaluronic Acid in Veterinary Medicine: A Narrative Review of Clinical Applications

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ABSTRACT

Hyaluronic acid (HA), a natural glycosaminoglycan, has attracted much interest in veterinary medicine because of its viscoelastic, anti-inflammatory, and tissue-regenerating attributes. These physicochemical and pharmacological properties of HA are due to its unique structure. In recent years HA has been commonly used for its applications in various veterinary fields either alone or in a combination with other therapeutic agents. This review article discusses the extensive clinical uses of HA and its combination in different animal species with an emphasis on its therapeutic potential in the regulation of joint disorders, tendinopathies, ocular diseases, wound healing, auditory brainstem responses, oral and dental tissue healing, respiratory, gastrointestinal, urogenital, intramuscular disorders, and soft tissue augmentation. Both topical and intra-articular preparations have been demonstrated to enhance mobility, relieve pain and inflammation of visceral organs, and facilitate tissue repair in osteoarthritis, corneal ulcers, and skin wounds. HA's function in enhancing performance and surgical recovery is also becoming appreciated in veterinary medicine. The review points out recent evidence, routes of delivery, and safety profiles of HA-based therapies, highlighting its increasing value as a multifaceted therapeutic tool in veterinary clinical practice.

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INTRODUCTION

Hyaluronic acid (HA) is a mucopolysaccharide carbohydrate molecule, made up of thousands of sugars and naturally occurring in all living organisms (Buckley *et al.*, 2022). It can form conjugated molecules by binding with organic or other inorganic molecules. Although HA is primarily found in the pericellular and extracellular matrix, it can also be found inside cells (Parnigoni *et al.*, 2022). Karl Meyer and his colleague John separated a chemical compound from the vitreous corpus of cows' eyes in 1934. One of the two sugar molecules they discovered in the material was uronic acid. For ease of use, they suggested the term "hyaluronic acid." This special name, hyaluronic acid, comes from the Greek word hyalos, which means glass, with uronic acid (Meyer and Palmer, 1934). HA was first used commercially in bakery products by Endre Balazs in 1942, when it was considered a major food item (Buckley *et al.*, 2022). The term "hyaluronan" was first used in 1986 in accordance with the international nomenclature of polysaccharides. It was credited to Endre Balazs, who created it to refer to the various forms the molecule can take, including the acid form, hyaluronic acid, and the salts, like sodium hyaluronate, which form at physiological pH (Balazs *et al.*, 1986). After this, HA was isolated from many other sources and studied its physicochemical, pharmacological, and biological properties in many laboratories (Lierova *et al.*, 2022). It is the exceptional molecule that is not formed in the Golgi apparatus, and three HA synthases (Has1, Has2, and Has3) present in the cell membrane are responsible for its formation (Iaconisi *et al.*, 2023).

Since the 1930s, the majority of HA has been isolated from animal tissues, including the umbilical cord, cockscomb, and vitreous (Ucm *et al.*, 2022). It was also produced by fermentation with the aid of harmful microorganisms (Serra *et al.*, 2023). However, both sources and their methods are very authentic and have purified protocols to avoid toxin contamination, which can be costly and lead to cross-infections (Nordin *et al.*, 2023). The ability to produce HA from microbes has recently emerged, providing a more straightforward, cost-effective, raw material-unrestricted, and environmentally friendly method (Liu *et al.*, 2023). Usually, HA is synthesized primarily by the very diverse and heterogeneous gram-positive bacteria *Streptococcus equi* and *Streptococcus zooepidemicus* (Grabowski *et al*., 2025). Both use two different metabolic pathways (the UDP-glucuronic acid pathway and the UDP-N-acetylglucosamine pathway) to synthesize HA (Li *et al*., 2024). HA produced by *S. equi* has a lower molecular weight than compared of *S. zooepidemicus*. Furthermore, HA is biosynthesized by different modes of fermentation, including continuous, batch, repeated batch, and fed batch fermentation (Serra *et al*., 2023). The growth rate of *S. zooepidemicus* and the yield of HA are higher in continuous and fed-batch processes (Saharkhiz and Babaeipour, 2022). Scientists are using genetic engineering and nanotechnology by inserting genes and using distinct nanoparticles to increase the production of HA (Govindasamy *et al*., 2022).

HA is of immense therapeutic value in veterinary medicine owing to its unique physicochemical and biological characteristics (Marinho *et al*., 2021). HA maintains tissue hydration, elasticity, and tissue structural organization (Hejran *et al*., 2024). It is a good candidate for clinical therapy in animals because it is non-immunogenic, viscoelastic, and biocompatible (Valachová and Šoltés, 2021). HA is particularly relevant in treating osteoarthritis and joint diseases, as it functions as a lubricant and shock absorber in synovial fluid, decreasing inflammation and facilitating mobility (Varagani *et al*., 2024). Its use also in healing wounds hastens tissue repair by promoting cell migration and angiogenesis (Shi *et al*., 2023). In ophthalmology, it enhances ocular surface moisture and postoperative recovery (Mikalauskiene *et al*., 2021).

This review seeks to critically examine the therapeutic role of HA in veterinary medicine, focusing on its biochemical characteristics, mechanisms of action, and wide clinical use across animal species. The range of this narrative review includes existing evidence on the application of HA in the management of osteoarthritis, tendinopathies, neurosurgery, wound healing, ophthalmic therapy, auditory brainstem response, and dermatological disorders in veterinary practice. Focus is given to HA's lubricating, tissue-regenerating, and anti-inflammatory activities that justify its application as a bioactive substance in intra-articular injections, gels, and ophthalmic solutions. With a synthesis of existing research and clinical evidence, this review offers veterinarians, scientists, and drug developers comprehensive insights into HA's function in improving animal health, facilitating recovery, and enhancing the quality of veterinary medicine.

Structural and Pharmacological Properties of Hyaluronic Acid: HA is a glycosaminoglycan made up of consecutive units of β-1,4-d-glucuronic acid and β-1,3-N-acetyl-d-aminoglucose disaccharides (Wang *et al*., 2023; Wu *et al*., 2024). All glycosaminoglycans, such as HA, dermatan sulfate, chondroitin sulfate, heparan sulfate, keratin sulfate, and heparin, have a similar structure made up of disaccharide units with an amino sugar and aldose (Radhouani *et al*., 2022). But HA is distinct from other glycosaminoglycans in a number of respects. Owing to a lack of sulfation, HA is synthesized on the plasma membrane's inner surface, and it is able to attain extremely high molecular weights owing to non-covalently binding to the core proteins (Hintze *et al*., 2022). A structure diagram of HA's chemical structure is presented in Fig. 1.

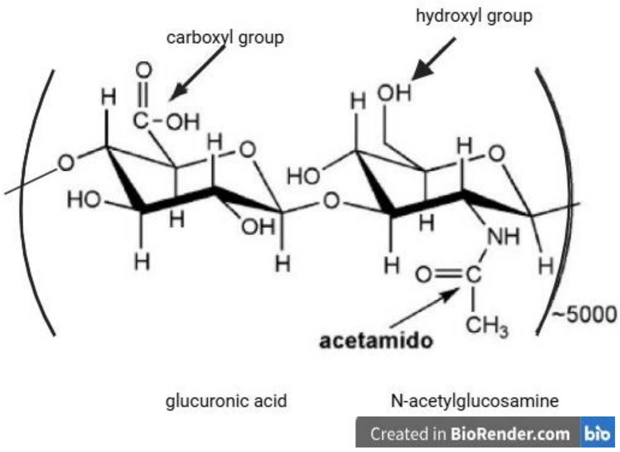

Fig. 1: Structure of hyluronic acid with –COOH and –OH functional groups (www.biorender.com).

HA is a hydrophilic macromolecule with functional groups like –COOH and –OH. Due to this, it has high water solubility and can produce a highly viscous solution (Cheng *et al*., 2023). Under physiological pH conditions, each carboxyl group has a negative charge, which can be compensated by mobile cations like Na^+, K^+, Mg^{2+}, and Ca2+ (Bełdowski *et al*., 2021). As a result, HA has a negative charge and exists as a salt called sodium hyaluronate in water solutions. The hydrogen bonding with water molecules and HA's acetylamino/carboxyl groups is responsible for stabilizing the secondary and tertiary structures of such biopolymers (Cheng *et al*., 2023). In its specific conformation, HA possesses superior rheological properties, high hydrophilicity, and the power of binding and holding large amounts of water molecules (Yu *et al*., 2024).

HA has extraordinary viscoelastic properties because of its great molecular weight and hydrophilic nature (Snetkov *et al*., 2020). Its long, unbranched polysaccharide chains can become entangled and form a gel network in the presence of water, which helps yield elasticity (resistance to deformation) and viscosity (resistance to flow) (Jin *et al*., 2021). This viscoelastic property is crucial in synovial fluid, where HA serves as a lubricant and shock absorber (Mederake *et al*., 2022). HA's ability to bind a large amount of water up to 1,000 times its weight also makes it critical to tissue hydration, osmotic equilibrium, and cellular communication (Juncan *et al*., 2021). In injured or inflamed tissues, the water-retention capacity and capacity to preserve the extracellular matrix (ECM) structure of HA facilitate cell migration, proliferation, and repair, as well as modulate the immune response locally (Liu *et al*., 2024). These properties underlie the universal application of HA in medicine and cosmetics for restoring tissue function and moisture homeostasis (Salih *et al*., 2024; Chylińska and Maciejczyk, 2025).

HA has a crucial function in cell signaling via interaction with receptors such as CD44 (type I transmembrane glycoprotein) and receptors for hyaluronic acid-mediated motility (RHAMM) (Kesharwani *et al*., 2022; Minato *et al*., 2023). CD44 interaction with HA triggers signal transduction cascades that include kinases like HER2 and c-Src and govern cell proliferation and motility (Primeaux *et al*., 2022). During wound repair, CD44 facilitates internalization of products of HA degradation and induces fibroblast migration, whereas its binding with high molecular weight hyaluronic acid (HMWHA) contributes to the formation of a protective coat on the cell membrane, covering death receptors and inhibiting apoptosis (Aijaz *et al*., 2025).

RHAMM (CD168), a second receptor for HA, is involved in complementing CD44 signaling in wound healing and inflammation (Xu *et al*., 2024). RHAMM is present on the cell surface as well as intracellularly and binds to cytoskeletal proteins and stimulates signaling cascades containing Src, ERK1/2, and protein kinase C that initiate cell motility and proliferation (Berdiaki *et al*., 2023). Experiments have established that RHAMM acts synergistically with CD44, especially to create CD44–ERK1/2 complexes and promote downstream signaling (Moon, 2025). RHAMM activation further magnifies inflammatory signals, and RHAMM inhibition can inhibit fibrosis and chronic inflammation, which indicates a dual function in tissue pathology and repair (Bianchini *et al*., 2024).

Low molecular weight HA (LMWHA), interact with Toll-like receptors (TLR2 and TLR4), hence initiating inflammation (Lee *et al*., 2021). The HA fragments are damaged-associated molecular patterns (DAMPs) that induce the MyD88/NF-κB signaling pathway, the result of which is the synthesis of proinflammatory cytokines, including interleukin-1β, IL-8, tumor necrosis factor-alpha (TNF-α), and matrix metalloproteins (MMPs) (Marinho *et al*., 2021). Notably, though CD44 is implicated in HA-mediated signaling, LMWHA still elicits immune cell activation in CD44-deficient models through TLRs, underlining TLRs as crucial mediators of HA-induced inflammation (Yang *et al*., 2024). Conversely, HMWHA produces anti-inflammatory activities, as evidenced in osteoarthritis experiments, where it suppresses TLR and NF-κB expression and inhibits inflammatory cytokine release (Lee *et al*., 2021). These two contrasting activities of HA, according to its size in molecules, highlight its multifaceted role in coordinating inflammation and healing through separate receptor-mediated routes (Marinho *et al*., 2021).

Hyaluronic acid (HA) is delivered via various routes, such as topical, oral, intravenous (IV), intra-articular, intranasal, and subcutaneous routes, depending on its desired therapeutic use (Bravo *et al*., 2022; Song *et al*., 2023). Of these, intra-articular injection is most commonly employed in osteoarthritis therapy because it delivers the drug locally to synovial joints, which maximizes local bioavailability and limits systemic breakdown (Testa *et al*., 2021). Topical, subcutaneous, and oral applications are for skin wound healing, inflammation, and mucosal healing of the oral cavity (Joshi *et al*., 2024). HA does not have a long plasma half-life (2–6 minutes), and its bioavailability is restricted by fast degradation. Low oral bioavailability of HA arises from enzymatic degradation in the gut, though evidence indicates that LMWHA has limited systemic absorption and local anti-inflammatory activity (Gao *et al*., 2019). Improved stability, tissue targeting, and extended duration of action for HA in inflammatory and tissue repair applications are being realized by the development of nanocarrier systems and HA drug delivery systems (How *et al*., 2020). By using these routes, HA and HA products have been applied to treat different disorders and diseases in animals.

Applications in Veterinary Medicine: HA has gained significant importance in veterinary medicine due to its proinflammatory, anti-inflammatory, viscoelasticity, biocompatibility, biodegradability, cell signaling capability, and antioxidant activity (Di Mola *et al*., 2022; Ye *et al*., 2025). Mostly it is used for the treatment of osteoarthritis, in different species including horses, cats, and dogs, when intraarticular or intravenous injections are given at particular sites (Testa *et al*., 2021). İt improves joint lubrication, reduces pain, and slows cartilage degradation. In case of wound management, topical HA formulations are also utilized to promote hydration, reduce inflammation, and accelerate tissue regeneration (Ding *et al*., 2022). Similarly, HA-based eye drops are also used to treat eye infections, keratoconjunctivitis, and corneal ulcers in cats and dogs (Leonardi *et al*., 2024). Some of the important applications are shown in Fig. 2 and many of them discussed below.

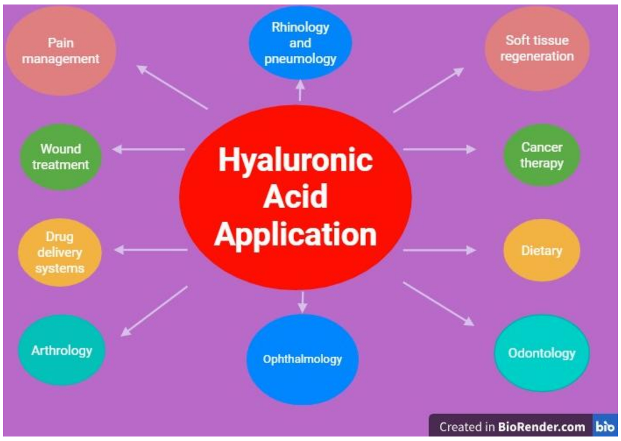

Fig. 2: Various veterinary uses of hyaluronic acid for better performance and disease treatment (www.biorender.com).

Orthopedic Applications: In veterinary medicine, HA has become a principal component in the management of orthopedic disorders, especially in the treatment of osteoarthritis and joint dysfunctions (Guerra-Gomes *et al*., 2025). HA acid in joint diseases is administered in the intra-articular site, where it reduces friction between articular surfaces, reduces inflammation, increases joint mobility, and diminishes chronic pain (Cao *et al*., 2021). In canines and equines, HA injections are widely used for the treatment of osteoarthritic joints, synovitis, and traumatic joint injuries (Lee *et al*., 2019; Pirri *et al*., 2024). HA administrations cause inhibition of pro-inflammatory cytokines and enzymes such as IL-1 and 6, TNF-α, and MMPs (Ferreira *et al*., 2022). Moreover, HA increases chondrocytes (cartilage cells) viability and contributes to cartilage matrix synthesis, thus supporting long-term joint health (Strecanska *et al*., 2022). In addition to intra-articular injections, HA is also used in post-surgical protocols to enhance tissue healing, repair, and limit fibrosis (Chen *et al*., 2025). HA may also be used with other regenerative therapies such as platelet-rich plasma or stem cells to potentiate therapeutic outcomes (Goulian *et al*., 2025).

In one of the studies conducted by Kim *et al*. (2022), a clinical trial was performed on dogs suffering from osteoarthritis to check the effectiveness of high molecular weight HA and intra-articular mesenchymal stem cells (MSCs). Both groups showed mild clinical improvement, but the dogs treated with HA exhibited significantly better results in terms of weight distribution and overall joint function. In another study, the efficacy of intra-articular HA was evaluated on osteoarthritic dogs having hip dysplasia. Experimental dogs were given HA alone and HA in combination with ozone gas. The results showed improvements in lameness and orthopedic scores. However, the combination of the therapies demonstrated better kinetics results (Silva Júnior *et al*., 2020).

Mostly, HA is introduced intra-articular, but to check the better effects of HA, it was given orally. For this purpose, dogs having cranial cruciate ligament rupture were given HA orally before the surgery and after the surgical resolution of the ligament. The results showed a marked increase in some of the biomarkers indicated that postoperative oral administration of HA is effective for the management of stifle osteoarthritis in dogs (Serra Aguado *et al*., 2021). A similar type of study was conducted by Lee *et al*. (2019) and demonstrated that intra-articular administration of HA and HA-platelet rich plasma (HA-PRP) effectively diminishes the clinical signs of osteoarthritis in dogs having cranial cruciate ligament resection. Both treatments showed a significant effect on joint function and reduced pain. More importantly, the group treated by HA-PRP showed superior and long-term benefits, such as limb function and increased cartilage preservation.

Besides canine treatment, HA has also been used in horses for the treatment of osteoarthritis and osteochondritis. Pereira *et al*. (2024) conducted a study on male and female sports horses with osteochondritis disease in Brazil. Horses were treated with HA, PRP, and Ringer's lactate solution (control) after arthroscopy. After 30 days, improvement in term of thickening of the joint capsule was observed in all three treatments. A similar type of study was conducted on horses having arthogenic lameness. Horses were treated with a single intra-articular injection of HA with corticosteroid. The study showed reduced lameness and a quick response in horses treated with HA. No severe adverse effects were seen, indicating HA alone or in combination as a safe and effective alternative (Fürst *et al*., 2020). These findings concluded that HA in combination with PRP and steroids is more effective than HA alone for managing osteoarthritis and preserving joint integrity. The mechanism of HA against osteoarthritis is shown in Fig. 3. Various other studies have also been demonstrated in *Table 1*.

Tendon Surgery and Tendinopathies: HA has shown promising therapeutic results in the management of tendon rupture, tendon injuries, and tendinopathies in veterinary medicine (Oliva *et al*., 2021). The unique biological and pharmacological properties make HA a unique agent in both surgical and non-surgical approaches to tendon repair and regeneration (Müller *et al*., 2015). During tendon surgery, one of the major postoperative complications is the formation of peritendinous adhesion, which can severely affect tendon gliding and their functions (Jia *et al*., 2023). When HA is applied at the tendon repair site, it acts as a physical barrier and modulator of the healing environment, and reduces adhesion formation (Zhou and Lu, 2021). Furthermore, HA also produces anti-adhesive effects that reduce fibrin deposition and decrease inflammatory cell infiltration (Mei *et al*., 2021). In addition, the lubrication-enhancing ability of HA helps to maintain tendon gliding movement and prevent friction-induced damage. These effects are beneficial in flexor tendon repair in various species, including dogs and race horses, where restored mobility is essential for functional recovery (Jann *et al*., 2016).

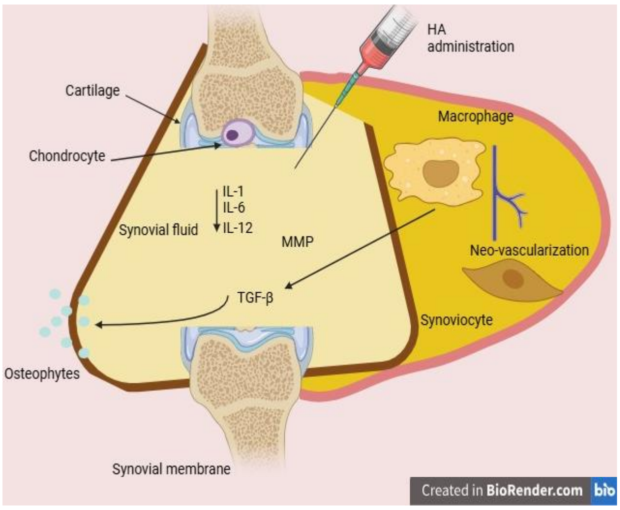

Fig. 3: Intra-articular administration of hyaluronic acid and hyaluronic acid formulation against osteoarthritis (www.biorender.com).

Clinical and experimental studies have concluded that HA-coated biomaterials and devices are used not only to improve healing outcomes but also to minimize the complications of scarring and fibrosis. In addition, the HA formulation in injectable form has also shown efficacy in reducing chronic tendon inflammation and promoting regeneration in overuse-related tendinopathies (Concoff *et al*., 2017). A research study was conducted on adult horses having full-thickness forelimb tendon lesions. The lesions were surgically excised and implanted with cross-linked carboxymethyl hyaluronic acid-thiol (xCMHA-S) gels in the right tendon. The treated tendon showed complete lesion recovery, and histological scores were significantly better in treated tendons with decreased inflammation, neovascularization, and cell density (Jann *et al*., 2016). A similar type of study was conducted by Ohana *et al*. (2024) on horses having Achilles tendinopathies (IAT). All horses were treated with ultrasound-guided HA injections, and symptoms were assessed by Victorian Institute of Sports Assessment-Achilles (VISA-A). Results have shown significant improvement with VISA-A scores. No adverse side effects were observed, emphasizing the safety of the procedure. In equines, another study was conducted by Özaydın et al. (1996) that evaluated the anti-inflammatory properties of HA-based sodium hyluronate on acute and chronic aseptic tendinits and tenosynovitis. Sodium hylurонate was administered intrasynovially, and both clinical and laboratory results were evaluated. The results showed full healing with a single administration of sodium hyaluronate.

Table 1: Hyaluronic acid and its various combinations used against osteoarthritis in canines, felines, equines, and animal models

Molecular weight of HA	Condition of bone	Site for treatment	Form of HA used	Alone/combination	Combination agent	Route for administration	Observed effects	Species	References
Medium	Bone cysts	Proximal radius	HA gel	Combination	MSCs + PRP	Local	Reduced cystic lesions	Horse	(Canonici *et al.*, 2023)
High	Navicular bone syndrome	Navicular region	HA injectable	Combination	MSCs+ PRP	Intra-articular	Decreased lameness, better gait	Horse	(Marsh *et al.*, 2012)
High	Joint infection recovery	Tarsal joint	HA injectable	Combination	Antibiotics + salt	Intra-articular	Faster recovery and anti-inflammatory effect	Horse	(Riley *et al.*, 2024)
High	Subchondral cystic lesion	Hock joint	HA injection	Combination	Sodium hyluronate	Intra-articular	Promoted cartilage synthesis	Horse	(Pérez-Nogués *et al.*, 2024)
High	Ligament injury with OA	Suspensory ligament	HA solution	Combination	Stem cells	Peri-ligament injection	Reduced inflammation, improved strength	Horse	(Trebinjac & Gharairi, 2020)
Medium	OA due to joint wear	Fetlock joint	Reticulated HA	Combination	Ozone gas	Intra-articular	Improved joint mobility	Horse	(Oliva *et al.*, 2021)
High	Post-surgical bone healing	Mandible	HA film	Combination	Antibiotics	Topical dressing	Reduced infection and enhanced healing	Dog	(Kim *et al.*, 2001)
Medium	Periosteal defect	Cannon bone	HA-coated scaffold	Combination	Mesenchymal stem cells (MSCs)	Implanted	Induced bone regeneration	Horse	(Luque *et al.*, 2025)
High	Hypertrophic osteodystrophy	Radius and ulna	HA	Combination	HA salt + vitamin C	Surgical site	Regeneration of the growth plate region	Dog	(Aleksiewicz *et al.*, 2013)
Medium	Osteoarthritis	Chondrocytes	HA hydrogel	Combination	HA + chitosan nanoparticles	Intra-articular	Enhanced cartilage regeneration	Horse	(De Angelis *et al.*, 2021)
High	Bilateral hip osteoarthritis (OA)	Hip joint	Intra-articular HA	Combination	HA + triamcinolone	Intra-articular	Reduced inflammation, pain relief	Dog	(Franklin and Franklin, 2021)
Low	Osteoarthritis	Hip joint	HA nanoparticles	Combination	Curcumin	Local	Antioxidant and regenerative effect	Bovine	(Astaneh *et al.*, 2024)
Medium	Hip dysplasia	Hip joint	HA solution	Combination	PRP	Intra-articular	Improved joint function	Dog	(Silva Júnior *et al.*, 2020)
Low	Subchondral bone repair	Carpal and metacarpal joint	HA nanoparticles	Combination	Mesenchyme Stem Cells	Local injection	Enhanced subchondral bone density	Horse	(Reis *et al.*, 2024)
Not specified	Distraction osteogenesis	Femur	HA paste	Combination	Chitosan + calcium sulfate	Surgical site	Increased osteo-integration	Dog	(Cho *et al.*, 2002)
Not specified	Bone density loss	Vertebrae	HA-calcium matrix	Combination	Calcium sulfate	Local	Increased bone mineralization	Cat	(Muhamad *et al.*, 2021)
High	Osteoarthritis	Bones	HA coating	Combination	Bone marrow stem cells	Intra-articular	Controlled infection, bone healing	Rats	(Assi *et al.*, 2024)
Medium	Joint surface wear	Knee joint	Cross-linked HA	Combination	MSCs	Intra-articular	Repair of articular surface	Cat	(Pozzi *et al.*, 2021)
High	Osteoarthritis	Carpal joint	HA hydrogel	Combination	Triamcinolone acetonide	Intra-articular	Structural joint protection	Dog	(Alves *et al.*, 2020)
Medium	Chronic OA	Stifle joint	Stabilized HA	Combination	Polysulfated glycosaminoglycans	Intra-articular	Joint lubrication and anti-inflammatory	Horse	(Frisbie *et al.*, 2009)
Not specified	Fracture healing	Radius-ulna	HA with hydrogel	Combination	Hydrogel scaffold	Local	Accelerated callus formation	Dog	(Kim *et al.*, 2001)
Low	Post-fracture healing	Femur	HA gel	Combination	Corticosteroides	Topical/implant	Enhanced bone regeneration	Cat	(Alves, 2021)
High	Bone defect	Tibia and femur	HA scaffold	Alone	Single	Intra-articular	Stimulated osteogenesis	Dog	(Lee *et al.*, 2019)
High	Degenerative joint disease	Elbow joint	Cross-linked HA gel	Combination	HA + Salt	Intra-articular	Reduced stiffness	Cat	(Abbas *et al.*, 2023)
Low	Elbow dysplasia	Elbow joint	HA-based microspheres	Combination	Chondroitin sulfate	Intra-articular	Slowed disease progression	Dog	(McCarthy *et al.*, 2007)
Low	Osteoarthritis	Bones and joints	Injectable HA	Alone	Mesenchymal stem cells (MSCs)	Peri-surgical injection	Shortened healing time	Dog	(Kim *et al.*, 2022)
Medium	Hip dysplasia	Knee joint	Topically HA	Alone/ Combination	-	Intra-articular	Reduced disorder progression	Dogs	(Martins *et al.*, 2022)

In mice, a study was conducted to determine the efficacy of commercially available HA in the prevention of peritendinous adhesions in the course of tendon healing in rabbits with ruptured Achilles tendons. HA decreased the adhesion formation, augmented healing and improved tensile strength (Kurt *et al*., 2018). Another study was conducted to evaluate the effect of HA and bone marrow plasma on the healing of the tenotomized Achilles tendon in dogs. Ultrasonography showed almost normal tendon structure in both treated groups. Both treated groups showed no adverse effects (Mohammed *et al*., 2024).

The physicochemical, hygroscopic, and biological properties of HA within the tendons remain unexplored, and its clinical use for tendinopathies is still debated. However, the preclinical and clinical studies showed good efficiency against tendinopathies due to its biocompatible, mucoadhesive, hygroscopic, and viscoelastic properties (Mei *et al*., 2021). Furthermore, clinical studies also showed its effect against tendinopathies, including rotator cuff, epicondylitis, Achilles, and patellar tendinopathies (Oliva *et al*., 2021).

Moreover, another study was conducted *in vitro* and *in vivo* to assess the cell compatibility and therapeutic potential of collagen-based HA substrate for anterior cruciate ligament (ACL) treatment in dogs. The result showed better attachment and proliferation of cells for collagen-based HA as compared to the silk matrix alone by promoting tissue granulation, with increased fibroblasts and collagen fibers. It also enhanced angiogenesis, and histology showed monocyte presence with no giant cells, indicating biocompatibility. Overall, the collagen-based HA substrate promoted cell growth and improved tissue regeneration and vascularization in ACL repair (Seo *et al.*, 2010). These findings suggest that HA and HA-based formulations show better output as compared to other therapies.

Neurosurgical and Neuroregenerative Applications: HA and HA-coated nerve guidance tubes and hydrogels are increasingly applied in peripheral nerve injury and surgery. These HA substrates act as physical scaffolds that fill nerve gaps, increase axonal growth, and cause regular alignment of regenerating fibers (Djoudi *et al.*, 2022). One of the most important neurosurgical properties is the anti-adhesive property to inhibit fibroblast proliferation and collagen deposition at the surgical site (Park *et al.*, 2020). HA forms a hydrated and viscoelastic barrier that reduces perineural fibrosis, preserves nerve gliding, reduces compression, and prevents scar formation in both primary and revision surgeries (Chylińska and Maciejczyk, 2025). Furthermore, HA hydrogels maintain hydration, stimulate inflammation, and promote cellular migration. These activities generate a conducive microenvironment for better nerve regeneration (Gao *et al.*, 2024). Their interactions with cell surface receptors, including CD44 and RHAMM, induce Schwann cell activity, angiogenesis, and increase dendritic and axonal growth (Ouasti *et al.*, 2020). Recently, a study on rats demonstrated the effect of three-dimensional, modified HA scaffolds loaded with neurotrophic factors (GDNF) for brain tissue reconstruction after traumatic injury. The HA-based scaffolds showed no cytotoxicity in hippocampal cultures. They promoted early neuronal process outgrowth and histologic studies showed improved tissue morphology, increased motor activity, and greater regenerative potential (Mishchenko *et al.*, 2022). In another study, Hüseynoğlu *et al.* (2012) evaluated the effect of silicone tubes and HA-based silicon tubes on sciatic nerve regeneration after incision and reconstruction in rats. Peripheral nerve injury can lead to scar formation, which in turn hinders axonal recovery, while silicon tubes decrease scar formation and HA-based silicone tubes offer additional anti-adhesive benefits and nerve conduction velocities. A similar type of study elaborated that silicone tubes (ST) alone and HA-based silicon tubes (ST+HA) prevent fibrosis and sciatic nerve tissue regeneration in Wistar rats. ST and ST+HA groups showed normal gait and better nerve morphology. HA in combination caused a smoother anastomosis and less adhesion, and its long-term use increased myelination and improved axonal structure, which will lead to better nerve generation (Özaydın *et al.*, 2014).

In another study conducted by Xu et al. (2024) demonstrated the effects of a hydrogel without HA and a hydrogel scaffold incorporated with MSCs for peripheral nerve repair in rats. The hydrogel without HA promoted a microenvironment by enhancing macrophage polarization and supporting angiogenesis, while MSCs incorporated HA-based hydrogels enhanced gene expression of Schwann cells, increased myelination, and axonal regeneration. These findings suggest that HA and HA-based biomaterials are very effective for tissue regeneration, axonal growth, and tissue repair after surgery.

Wound Healing and Dermatological Applications: HA plays an important role in wound healing by binding with a significant amount of water, maintaining a moist wound environment, which is important for optimal cell migration and their proliferation (Ding *et al.*, 2022). HA forms a hydrated complex with the extracellular matrix, which provides a scaffold that supports the attachment and movement of cells involved in tissue repair, including fibroblasts and keratinocytes (Ribeiro *et al.*, 2024). Moreover, it binds with cell surface receptors, cause cell migration to the wound site, accelerates the regeneration of damaged tissues, and cause restoration of normal skin texture. It also stimulates the inflammatory response by activating immune cells and the release of cytokines, which prevents excessive inflammation (Naor, 2016).

Besides this, HA is also involved in angiogenesis (formation of new blood vessels) (Xue *et al.*, 2022). In addition, it affects the remodeling phase of wound healing by regulating collagen deposition and fibroblast function (Lin *et al.*, 2023). This regulation promotes an organized ECM arrangement and limits fibrosis, which results in scarless tissue repair (Cialdai *et al.*, 2022). This combination is not only beneficial for superficial and deep wound healing, but also improves the aesthetic outcomes, including burns, chronic ulcers, and surgical incisions (Özaydın and Aydın, 2023; Vinci *et al.*, 2024). A recent research study evaluated the role of HA in synovial fluid (SF) for reducing scar formation in incisional skin wounds in mice. Histopathological analysis showed that the SF containing HA had fewer inflammatory cells and reduced granulation tissues, indicating faster progression to the healing phase. These results suggest that HA in SF promotes efficient tissue repair and helps minimize fibrosis (Aydın *et al.*, 2022). Another study evaluated the role of HA from synovial fluid (SF) in improving the healing of Limberg and elliptical rotation flaps in mice. SF administration significantly enhanced epithelialization and showed a regulatory role in angiogenesis. SF as a source of HA demonstrated potential to enhance wound healing in flaps involving tissue loss (Çantay *et al.*, 2021).

In dogs, open cutaneous wounds were treated with commercially available HA-containing dressing and they were are effective (Ferrari *et al.*, 2015). Another study conducted by Iacopetti *et al.* (2020) compared the healing effect of HA, manuka honey (MH), and acemannan gel (AG) on surgically excised wounds in sheep. Histological and molecular analysis demonstrated that HA improved all phases of healing, stimulated skin regeneration, and promoted rapid, physiological wound closure. In another study, the effect of crosslinked HA-based biomaterials was conducted in enhancing wound healing in various species, including rats, dogs, and horses. The main compound, thiolated carboxymethyl HA, was used, which promoted keratinocyte proliferation and improved wound healing. In rats, it results in forming a thicker epidermis, but in horses, it improved the healing outcomes, but the healing process was slower as compared to rats (Yang *et al*., 2011). A similar type of study was conducted to evaluate the effectiveness of topically applied HA serum and chitosan-based gel in the treatment of skin wound healing in dogs. Clinical, histological, and tensile strength demonstrated that the HA serum-treated wound showed greater wound contraction, improved tensile strength, and better histological repair scores as compared to the chitosan gel-treated group. The study concluded that HA serum is much effective than chitosan-based gel in enhancing skin wound healing and tissue repair in dogs (Morsy *et al*., 2023). Overall, the findings suggest that HA and HA-based substances are very effective in wound healing and cosmetic improvement.

Applications in Ear Surgery: HA plays an important role in promoting wound healing and tissue repair in external and middle ear surgeries. It promotes wound healing in tympanic membrane perforations and induces keratin formation that provides a scaffold for epithelial migration (Daou and Bassim, 2020). Various studies have shown the promising effects of topically applied HA and grafts enriched with HA in the treatment of tympanic membrane perforation. In one of the experimental studies, researchers evaluated the therapeutic potential of mesenchymal stem cells (MSCs) delivered via hyaluronate-based laminas for the treatment of delayed-healing tympanic membrane (TM) perforations in an animal model. The HA-based lamina served as a biocompatible scaffold, supporting cell adhesion and retention at the injury site. MSCs combined with the HA lamina promoted significantly enhanced TM regeneration compared to HA alone or untreated controls. Histopathological examination showed better epithelial continuity, organized collagen fiber deposition, and improved revascularization in the MSC-treated group (Shahal *et al*., 2022).

Another study aimed to evaluate the efficacy of concentrated growth factor (CGF) and HA in promoting the healing of acute tympanic membrane (TM) perforations. Complete healing was observed in 100% of rats in both the CGF and HA groups, with mean healing times of 12.11 and 15.05 days, respectively. In contrast, spontaneous healing occurred in 89% of the control group, with a significantly longer mean closure time of 17.11 days. The findings suggest that both CGF and HA significantly accelerate TM healing and could serve as practical, cost-effective, and minimally invasive options for managing tympanic membrane injuries, especially in chronic cases (Sarı *et al*., 2021). In the same year, Yilmaz *et al*. (2021) investigated the healing potential of two materials in the treatment of the right traumatic tympanic membrane in rats. Rats were treated with Vivosorb (Vv), without HA, and a commercial product, Epifilm (Ep) with HA. The results showed that Ep achieved a 100% closure rate, while Vv achieved an 85.7% closure rate. However, HA-based Ep caused less fibrosis and inflammation as indicated by lower fibroblastic and neovascularization scores. Overall, Ep is a more favorable option in treating perforations of the right tympanic membrane of the ear. Moreover, another study was conducted to evaluate the effects of a novel hydrogel composed of HA-based methacryloyl (HAMA), gelatin methacryloyl (GelMA), and ECM from α-1, 3-galactosyltransferase to treat perforations of the TM in pig ears. *In vitro* tests demonstrated better biocompatibility and cell viability. The HA-based hydrogel promoted tympanic membrane regeneration with promising structural results and chondrogenic potential (Wang *et al*., 2021).

HA-based materials are also used as packing material and have shown better results in terms of reduced adhesion, less new bone formation, and improved mucosal healing as compared to commercially available sponges (Graça *et al*., 2020). Although these differences were not statistically significant, some studies favored HA-based packing material. Deniz *et al*. (2019) conducted a research study on rats having mucosal trauma to compare the efficacy of HA-based Spongostan and Spongostan soaked with dexamethasone. Both materials were used as packing material in the middle ear. Results of the study showed that HA-based Spongostan caused higher threshold elevations. Histology of the tissues revealed less inflammation, decreased residual material, limited new bone formation, and reduced adhesion. Another study conducted by Jang *et al*. (2008) to determine the anti-adhesive effects of HA-based Seprafilm and MeroGel in a guinea pig having middle ear mucosal damage. Results showed better results for Merogel in terms of reduced adhesion and fibrosis. Better hearing was observed in the Seprafilm and MeroGel groups.

Studies also demonstrated that HA-based biomaterials facilitate cochlear gene vector delivery by increasing the permeability of the round window membrane. This gene-related delivery assists in treating hereditary deafness. HA-based biofilms have also promoted faster re-epithelialization of the mastoid cavity and reduced secretions in animal models. This approach may improve the healing process as compared to traditional skin flaps that can cause bacterial infections (Dhawan and Cui, 2022). In one of the studies, it was demonstrated that HA-based bilayer polymer films showed less acute and chronic toxicity and inflammation. On the other hand, they showed better biodegradation and increased connective tissue proliferation (Naumenko *et al*., 2023). Overall, these findings suggest that HA alone and HA-based biomaterials are very effective in ear surgery in wound healing, control of granulation tissues, scar formation, and infections. The protective effect of HA and HA-based gels is shown in Fig. 4.

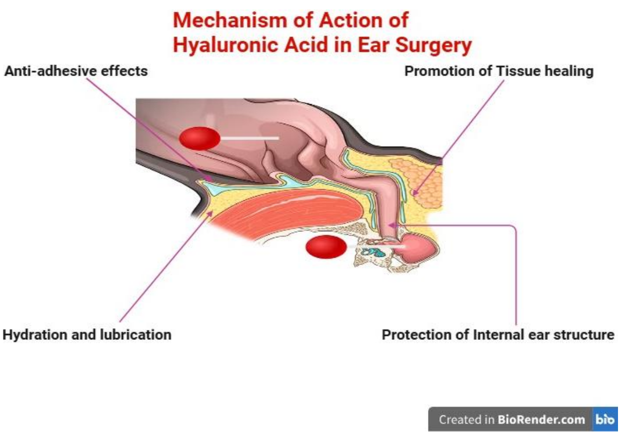

Fig. 4: The protective effects of hyaluronic acid and hyaluronic acid-based gels after ear surgery (www.biorender.com).

Ophthalmologic Applications: HA plays an important role in ophthalmology due to its physicochemical properties, including its high water-binding capacity and viscoelastic nature. These properties help to maintain ocular surface hydration and structural integrity (Wang *et al*., 2023). Mostly, HA is used individually in the form of eye drops or as artificial tears, but in combination, HA is used in surgical settings (Hynnekleiv *et al*., 2024). When used in eye drop form, it forms a protective, lubricating film over the surface of the cornea, hence reducing friction during blinking. It also protects epithelial cells from mechanical and environmental stress (Chang *et al*., 2021).

The mucoadhesive nature of the HA allows it to stay longer on the ocular surface and increases tear film stability. This is very helpful in relieving dry eye symptoms and also accelerates the healing of minor corneal abrasions (Guarise *et al*., 2023). In surgery, such as cataract extraction and vitreoretinal surgery, HA maintains space within the anterior chamber and protects the corneal endothelium from instrumental damage or trauma (Hussain *et al*., 2021). It also stabilizes the ocular tissues during manipulation. It also possesses anti-inflammatory and antioxidant effects, triggering CD44 receptors that lead to cell proliferation, migration, and extracellular matrix remodeling (Salathia *et al*., 2023). Various studies have been conducted to evaluate the effects of these HA and HA-based substrates and gels against corneal damage, and they have proved their effectiveness. Recently a study compared the effect of ocular surface retention time (OSRT) of cross-linked HA, linear HA, and saline in dogs by using fluorescent labelling. Results demonstrated that cross-linked HA and linear HA showed significantly prolonged contact with the ocular surface as compared to saline-treated dogs. Cross-linked HA also showed a two-phase retention pattern, which includes broad surface coverage followed by localization in the tear meniscus and medial canthus. These findings suggest that HA-based substrates provide better lubrication and may be a promising vehicle for sustained release ocular drug delivery (Grego *et al*., 2024).

During general anesthesia, tear production is less in animals, which can cause ocular dryness and potential corneal damage during instrumental surgeries. HA is used in tear production in healthy animals under general anesthesia before surgery. In one of the studies, 1% HA ophthalmic gel was used to produce tears in healthy sheep under general anesthesia (Pavel *et al*., 2024). In one of the case studies, HA filler injections were used to correct entropion in a 3-year-old English Bulldog and a 5-month-old Chow Chow. HA was administered into the eyelid tissues by the layered feathering technique. The treatment caused immediate correction of eyelid position, effectively revealed clinical signs, and maintained eyelid alignment for 6 to 8 months. This administration highlights that HA has a therapeutic and structural support role in managing non-surgical entropion (Lee and Kim, 2021). In another study, HA-containing drops were used in managing canine keratoconjunctivitis sicca (KCS) in dogs. Initially, all dogs were treated with carbomer-based gel and showed no significant improvement in ocular signs. Then, dogs were switched to HA-based drops, which noticeably reduced conjunctival hyperemia and ocular discomfort scores (Williams *et al*., 2012). Some of the researchers used HA and HA-based nanoparticles as a drug delivery vehicle to deliver the drug to the target site (Hussein and Abdullah, 2022). For example, arginine-HA-based nanoparticle (ADHA NPs) loaded with dexamethasone are used for the dry eye in dogs. The arginine containing positive charge forms ionic cross linking with HA, which leads to sustained drug release and possesses strong mucoadhesive property. The result of the study demonstrated that ADHA NPs retained water for a longer period of time and made cells more compatible. They also protected cellular integrity and enhanced tear production twofold when applied *in vivo*. With up to 12 hours of ocular retention, these NPs offer a promising strategy for sustained and effective dry eye treatment (Mishra *et al*., 2025). In summary, HA and HA-based substrates are used to treat KCS and corneal lesions by lubricating, healing, protecting, and modulating inflammation on the ocular surface. The ophthalmological application of HA and HA-based formulations is shown in Fig. 5.

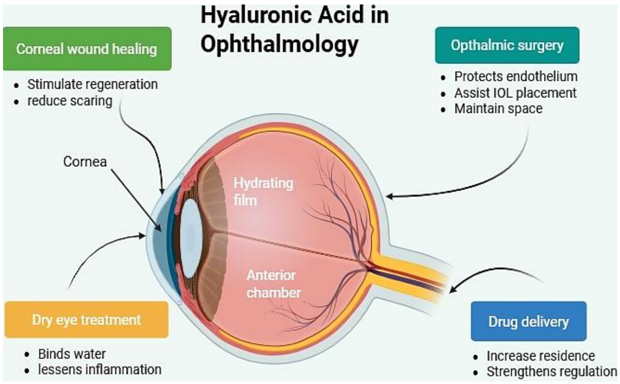

Fig. 5: Ophthalmological application of hyaluronic acid and hyaluronic acid-based formulation (www.biorender.com).

Oral and Dental Applications: Periodontitis is a chronic inflammatory disease that involves dysbiotic plaque biofilms (Di Stefano *et al*., 2022) and the progressive destruction of the structures that support the teeth, which are mainly characterized by clinical attachment loss (CAL), alveolar bone loss (ABL), gingival bleeding (GB), and periodontal pocketing (Ray, 2023). This disease was countered with the application of HA, which has many structural and functional roles within tissues, such as extracellular and cellular interactions, growth factor interaction, and tissue lubrication (Bhati *et al*., 2022). HA is actually responsible for forming associations with collagen, fibrin, and other matrix molecules. Its early response to tissue includes the formation of a temporary matrix rich in hyaluronan and fibrin protein, which is vital for the influx of fibroblasts and endothelial cells into the wound site and the subsequent formation of granulation tissue (Roman *et al*., 2023). No matter, HA bounds to cells or to extracellular matrix components, its hydrophilic nature creates an environment permissive for the migration of cells to new tissue sites, whereas its free radical scavenging and protein exclusion properties offer protection to cells (Mohammad *et al*., 2023). A study was carried out by Lee *et al*. (2022) on oral wound healing by taking a rat as a tongue wound model. It was noticed that both HA gel and HA film significantly improved the wound healing of rats as compared to the control group. HA film was particularly effective in enhancing epithelial repair and could offer both therapeutic and practical advantages in clinical oral wound management. Another study was conducted by Shirakata *et al*. (2022), who investigated the histological effects of cross-linked HA with or without collagen matrix on periodontal wound healing in dogs. The findings of the study were quite promising, suggesting that treatment with cross-linked HA achieved significantly greater results in new bone formation and connective tissue attachment as compared to those with open flap debridement.

A similar type of study was conducted and demonstrated that HA with cross-linked collagen matrix showed better output in enhancing periodontal regeneration (Shirakata *et al*., 2021). One more study that was conducted by Ghanbari *et al*. (2008) to evaluate the effectiveness of HA-based *Curcuma longa*-ghee formation for the healing of the gingival tissues in beagle dogs. The results were taken at two intervals after surgery, and it was noted that HA-based *Curcuma longa*-ghee was more effective in enhancing gingival healing and reducing inflammation in wounds. Various effects of HA and HA-based formulation in oral and dental applications are shown in Fig. 6.

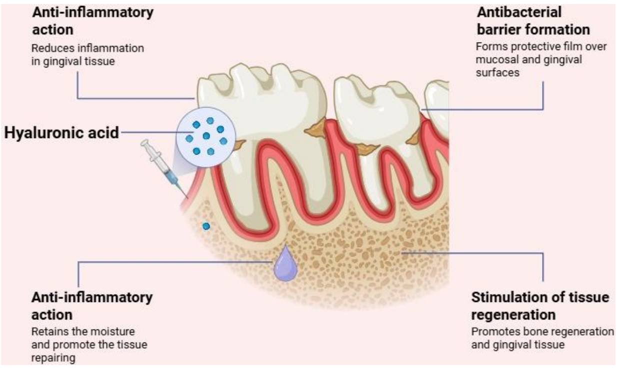

Fig. 6: Various effects of hyaluronic and hyaluronic acid-based formulations in oral mucosa and dental tissues (www.biorender.com).

Other Potential Applications: HA has shown promising experimental applications across various organ systems, including the respiratory, gastrointestinal, and urogenital tracts, as well as in subcutaneous and intramuscular tissue support. In the respiratory system, HA is being investigated for its anti-inflammatory and protective roles in diseases like asthma and chronic obstructive pulmonary disease (COPD) (Garantziotis *et al*., 2016), where inhaled HA may help reduce oxidative stress, stabilize the epithelial barrier, and enhance mucociliary clearance (Máiz Carro and Martínez-García, 2020). In conditions such as cystic fibrosis and bronchiectasis, nebulized HA is explored to improve mucus hydration and clearance. A study conducted by Johnson *et al*. (2018) investigated the therapeutic potential of HMWHA in a mouse model having allergic asthma. Results of the experiment showed that HMWHA administration significantly reduces airway inflammation and hyper-responsiveness. The findings suggest HMWHA may be an effective treatment for allergic airway inflammation. Another study investigated the effects of hyaluronan synthase 2 (HAS2) overexpression in a mouse model of chronic allergic airway disease. Mice with targeted HAS2 expression showed increased airway fibrosis, including HA accumulation and collagen deposition, but surprisingly, they had reduced airway hyper-responsiveness despite similar inflammation levels (Walker *et al*., 2017). Additionally, its ability to prevent post-surgical adhesions and reduce fibrosis is under study. In the gastrointestinal tract, HA-based formulations are used experimentally to alleviate chemotherapy or radiation-induced oral mucositis by promoting mucosal healing and reducing pain (Mohammed *et al*., 2023). HA also showed potential in the medication of gastric ulcers and inflammatory bowel diseases, where it may aid in mucosal regeneration and exert anti-inflammatory effects (Kotla *et al*., 2022). A study was conducted and evaluate the oral delivery of various HA formulations in rats, revealing that it influences mucoadhesion and absorption. Intermediate free HA (f-HA) and mixed HA (m-HA) showed strong adhesion in the jejunum, while crosslinked nanoparticles (n-HA) penetrated deepest into intestinal tissue, suggesting potential for systemic delivery. All formulations except high molecular weight f-HA were absorbed into the bloodstream. The results highlight n-HA for systemic targeting and intermediate/mixed-HA for intestinal therapies (de Souza *et al*., 2020). Another study compared the anti-adhesive effects of HA/carboxymethylcellulose (HA/CMC) with flunixin meglumine and flunixin meglumine alone in the abdomen of the rabbits. Histological and microscopic observations showed the lowest adhesion scores for the HA-based formulation as compared to flunixin meglumine. The finding suggests that HA/CMC is more effective in reducing postoperative intraabdominal adhesion (Köm, 2013). A similar study was conducted to compare the effect of natural SF with a chemical solution, i.e., dimethyl sulfoxide (DMSO), in preventing peritoneal adhesion in rabbits. The result demonstrated that natural SF reduced adhesion in the paritoneum as compared to DMSO. This finding suggests HA is a better anti-adhesive agent in tissue healing (Kılıç et al., 2013).

In the urogenital tract, intravesical instillation of HA is studied for restoring the glycosaminoglycan (GAG) layer of the bladder in interstitial cystitis and bladder pain syndrome (Poletajew *et al*., 2024), while HA-based vaginal gels are used to combat dryness and atrophy in postmenopausal or cancer-treated patients by improving tissue hydration and elasticity (Nappi *et al*., 2022). A study conducted by Moon *et al*. (2003) examined the safety of injectable HA gel for glans penis augmentation in rabbits and dogs. Minimal inflammation and gradual fibrosis were observed in rabbits, with no signs of inflammation. In dogs, HA implants remained stable for 6 months with only mild inflammation in one case. No systemic side effects or foreign body reaction occurred, suggesting that HA gel is a safe and effective bio-implant for the soft tissues. Moreover, its application in urethral repair is being evaluated due to its regenerative properties.

In the context of subcutaneous and intramuscular tissue support, HA is widely used in aesthetic medicine as a dermal filler to restore volume and improve contouring (Cassuto *et al*., 2021). HA hydrogels are also being tested for their ability to support fat grafting, promote angiogenesis, and accelerate soft tissue healing, reflecting their versatile bioactivity and biocompatibility across multiple biomedical fields. The above studies depict that

HA and HA-based formulations are very effective for respiratory, gastrointestinal, and urogenital damage and diseases.

Advantages, Limitations, and Clinical Practice Guidelines: In veterinary medicine, HA is a key drug substance, particularly in the case of the treatment of joint disease (Chang *et al*., 2021). Its ability to enhance joint health is its primary advantage. HA acts as an effective lubricant by rendering synovial fluid more viscous, reducing joint friction, and enhancing motion (Pereira *et al*., 2024). Animals that suffer from diseases such as osteoarthritis will specifically benefit from this. HA possesses potent anti-inflammatory properties along with its lubricating properties. It helps to control the inflammatory response, which can lower pain and swelling associated with joint disease (Goulian *et al*., 2025). HA is a valuable agent in a host of surgical and dermatological procedures because its benefits extend beyond joint therapy (Oliva *et al*., 2021). It helps to heal wounds by stimulating tissue repair and inhibiting the development of scar tissue.

There are disadvantages to the use of hyaluronic acid in veterinary medicine alongside the benefits. One of the key problems is inconsistent efficacy, so that outcomes could vary significantly based on the specific animal and the condition treated (Daou and Bassim, 2020). It can be challenging for veterinarians to predict a successful outcome given this variability. Side effects can also occur; they tend to be mild but may also involve pain at the site of injection or, in some cases, allergic reactions (Bayer, 2020). To ensure maximum therapeutic effect with a reduction in possible risks, these factors necessitate the stringent selection and observation of the patient.

Clinical practice guidelines have been developed to redress these challenges and ensure safe and effective use of HA. The guidelines favor an evidence-based practice by helping veterinarians determine the optimum situations for giving HA injections. As proper administration is critical to maximal therapeutic effects and reducing the risk of side effects, the importance of proper application methods is also emphasized. Also, there is a wide range of commercial preparations of differing molecular weights and concentrations for use on the market. Due to the wide range, veterinarians have to select the most appropriate formulation for every case with great care. The decision often lies in contrast to the extreme expense of these drugs, whose prices differ widely and which can impact availability for both professionals and owners.

Future Perspectives: Future uses of hyaluronic acid (HA), a vital element in veterinary regenerative medicine, will be propelled by advanced bioengineering and nano-technology. To extend its therapeutic application, the next generation of HA products is being made. For instance, incorporating nanotechnology means creating HA-based orthopedic and dermatological nanostructured products. In a similar manner, HA-based electrospun nanofibers are employed in replicating the extracellular matrix, ideal for localized drug delivery and tissue transplantation. In addition, hydrogel technology advances are yielding HA hydrogels with outstanding mechanical properties that are well-suited for directed tissue restoration and healing. HA is being applied beyond traditional joint lubrication into more sophisticated regenerative treatments due to these bioengineering advancements.

Despite these promising advances, much remains unclear in the literature. To better leverage HA's therapeutic effects, a more comprehensive understanding of its mechanistic interactions with cells and immune-pathways is needed. To evaluate the efficacy of different HA formulations in diverse animal species and in a variety of therapeutic applications, comparative studies are also essential. A more robust evidence base for its application will be developed in response to these research recommendations. This will enable the development of consistent policies and procedures in veterinary practice, ensuring the effective and consistent use of HA.

HA's initial role as a simple joint lubricant is being eclipsed by an increasingly fluid role in veterinary regenerative medicine. Since it boosts joint function and reduces pain, more and more is being used to manage diseases such as osteoarthritis. HA-based dressings are applied in wound healing to generate the optimal moist environment, which significantly accelerates the healing process. These applications show how versatile HA is and how it might be an integral part of future veterinary practice. In order for HA to be able to fulfill its potential and sidestep the challenge of being standardized in a large number of clinical situations, additional research and development are needed.

Conclusions: Hyaluronic acid, which is valued due to its unique structural and pharmacological properties, has great therapeutic potential in veterinary medicine. Due to its viscoelastic behavior, biocompatibility, and ability to modify inflammatory and cellular processes, it is an exceedingly versatile agent from a scientific perspective. HA is essential in the healing of wounds, eye disease, and musculoskeletal conditions as it not only serves as a lubricant and pressure absorber for joints but also stimulates tissue repair. With advances in bioengineering and regenerative medicine yielding next-generation products such as hydrogels and nanostructured devices, the future for HA in veterinary medicine is promising. There remain gaps in research despite these advances, particularly regarding understanding its molecular mechanics and performing cross-species comparisons. Completing these gaps is necessary to formalize its use and unlock its full potential, ultimately turning HA from a simple lubricant into a critical element of cutting-edge regenerative medicine that maximizes the health and well-being of animals.

Data Availability: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflict of Interest: The authors declare that there is no conflict of interest.

Authors contribution: İÖ: Conceptualization, Methodology, Data Curation, Writing - Original Draft, Supervision. MC and EK: Literature Review, Data Analysis, Visualization, Writing - Review & Editing. All authors have read and approved the final version of the manuscript.

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