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OVERVIEW OF PHYSIOLOGICAL FUNCTION PROPERTIES FOR HYALURONAN AND SYNOVIAL JOINT

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Abstract:

In this article we review main structural features of synovial joint and hyaluronan, important functional properties. We conducted a comprehensive literature search using the MEDLINE, EMBASE, and PubMed databases. This review describes hyaluronan properties and distribution, applications and its function in synovial joints for all studies published up to March, 2018. Synovial joints are one of the most common kind of joint in the body .A key architectural characteristic for a synovial joint that is not seen at fibrous or cartilaginous joints is the presence of a joint cavity. This fluid-filled area is the site at which the articulating surfaces of the bones contact each other. Likewise unlike fibrous or cartilaginous joints, the articulating bone surface areas at a synovial joint are not directly connected to each other with fibrous connective tissue or cartilage. This gives the bones of a synovial joint the ability to relocate smoothly versus each other, permitting enhanced joint range of motion.

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INTRODUCTION:

The individual skeletal system consists of both fused and personal bones sustained and supported by ligaments, tendons, and skeletal muscular tissues. Articular ligaments and ligaments are the major parts holding with each other the joint(s). In respect of activity, there are easily moveable, partly portable, and unmovable joints. Synovial joints, the openly moveable ones, permit a huge array of activity and include wrists, knees, ankles, shoulders, and hips [1].

A synovial joint is one of the most usual joint in mammals, and it enables more movement of verbalizing bones than other joints such as synarthroses, sutures, syndesmoses, or gomphoses. Structurally, a synovial joint is a solid organ which contain articular cartilage, perichondrium, subchondral bone and synovium, consisting of all cells in the marrow of the bone.The smooth and slippery lubricated surface of the articular cartilage covers the ends of bones, allowing the sliding of bones at the joint without rubbing each other. Load transfer with a minimum frictional coefficient and shock absorption is the major function of the articular cartilage during activity [2]. Articular cartilage is hyaline cartilage material, which is avascular, aneural, and alymphatic. The dense extracellular matrix (ECM) is sparsely populated by highly specialized cells called chondrocytes. ECM is largely made up of water (up to 80% of the wet weight) and collagen (as much as 60% of the dry weight, which 90% is kind II collagen) with other noncollagenous proteins and glycoproteins (10-15% of the damp weight) [2].The fibrils and fibers created by kind II collagen are linked with proteoglycan accumulations.

A healthy articular cartilage material sustains extensive and recurring physical tension, yet remarkably it can not self-heal or repair, despite the smallest injury.When damaged, the articular cartilage does not spontaneously fix due to a paucity of progenitor cells [3], a lack of capillary [3], a low cell-to matrix ratio (~ 5%) [4], [5], and reduced metabolic activity of fully grown chondrocytes [4], [5]. The very little unplanned repair work of cartilage material lesions results in a dynamic loss in joint functionality, together with the proceeding destabilization of tissue matrix [6].

In this article we review main structural features of synovial joint and hyaluronan, important functional properties.

METHODOLOGY:

We conducted a comprehensive literature search using the MEDLINE, EMBASE, and PubMed databases. This review describes hyaluronan properties and distribution, applications and its function in synovial joints for all studies published up to March, 2018. The following MeSH items or free words were taken: Joint, and hyaluronic acid, synovial joint. The references of searched studies were also reviewed to explore studies. No restrictions were made on the publication language.

DISCUSSION:

- **Structural Features of Synovial Joints**

Synovial joints are one of the most common joint in the body (Figure 1). A vital structural characteristic for a synovial joint that is not seen at fibrous or cartilaginous joints is the presence of a joint cavity. This fluid-filled room is the site at which the articulating surface areas of the bones get in touch with each other. Also unlike coarse or cartilaginous joints, the articulating bone surfaces at a synovial joint are not directly connected to every various other with coarse connective tissue or cartilage material. This gives the bones of a synovial joint the capability to relocate smoothly versus each various other, enabling raised joint movement.

Synovial joints are characterized by the presence of a joint cavity. The wall surfaces of this room are developed by the articular capsule, a fibrous connective tissue structure that is attached to each bone simply outside the location of the bone's expressing surface. The bones of the joint articulate with each various other within the joint cavity [1].

Rubbing within the bones at a synovial joint is avoided by the presence of the articular cartilage material, a layer of thin hyaline cartilage material that covers the whole surface of each bone. Nonetheless, unlike at a cartilaginous joint, the articular cartilages of each bone are not continual with each various other. Instead, the articular cartilage enabling to relocate against each other without harming the underlying bone tissue, imitates a Teflon covering over the articulating surface of the bone, Lining the internal surface area of the articular capsule is a thin synovial membrane. The cells of this membrane layer produce synovial liquid (synovia="a thick liquid"), a thick, slimy fluid that offers lubrication to even more lower friction in between the bones of the joint. This fluid additionally provides nutrients to the articular cartilage, which does not contain blood vessels. The bone’s capability to move efficiently versus each other within the joint cavity, and the liberty of joint activity, indicates that each synovial joint is functionally classified as a diarthrosis.

Beyond their articulating surface areas, the bones are connected with each other by ligaments, which are solid bands of coarse connective tissue [6].These

strengthen and sustain the joint by anchoring the bones with each other and avoiding their splitting up. Ligaments enable typical motions at a joint, however restrict the variety of these movements, therefore preventing too much or uncommon joint movements. Ligaments are identified based on their relationship to the coarse articular capsule. An extrinsic ligament is situated beyond the articular pill, an innate ligament is integrated to or integrated into the wall of the articular capsule, and an intracapsular ligament lies inside of the articular capsule.

At most of the synovial joints, support is supplied by the muscle groups and their tendons that act throughout the joint [2].A tendon is the thick connective tissue framework that attaches a muscle mass to bone. Automatically body will enhance the total strength of contraction of the muscle mass crossing that joint, when forces acting on joint increases, thus allow the muscle and its tendon to work as a "dynamic ligament" to stand up to forces and sustain the joint. This sort of indirect support by muscles is crucial at the shoulder joint, for instance, where the ligaments are fairly weak [3].

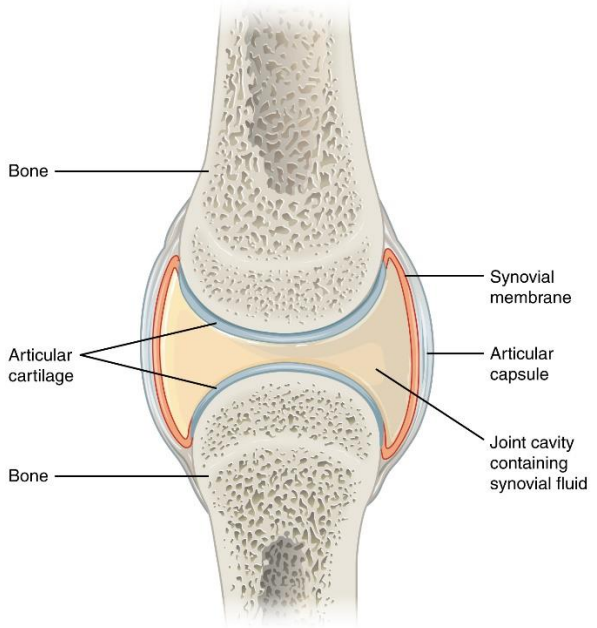

Figure 1. Synovial Joints. Synovial joints allow for smooth movements between the adjacent bones. The joint is surrounded by an articular capsule that defines a joint cavity filled with synovial fluid. The articulating surfaces of the bones are covered by a thin layer of articular cartilage. Ligaments support the joint by holding the bones together and resisting excess or abnormal joint motions.

- **Hyaluronan**

In 1934, Karl Meyer and his coworker John Palmer separated a previously unidentified chemical substance from the vitreous body of cows' eyes. They found that the compound contained two sugar particles, one of which was uronic acid. For convenience, for that reason, they proposed the name "hyaluronic acid". The popular name is originated from "hyalos", which is the Greek word for glass + uronic acid [7].At the time, they did not recognize that the substance which they had actually discovered would confirm to be among the most interesting and helpful natural macromolecules. HA wased initially made use of readily in 1942 when Endre Balazs made an application for a patent to utilize it as a replacement for egg white in bakery products [8].

The term "hyaluronan" was presented in 1986 to comply with the worldwide nomenclature of polysaccharides and is credited to Endre Balazs [9] who created it to inclusive the different forms the molecule can take, e.g, the acid form, hyaluronic acid, and the salts, such as sodium hyaluronate, which forms at physical pH [10] HA was consequently isolated from many various other sources and the physicochemical structure properties and biological function of this polysaccharide were researched in countless laboratories [11].This work has been summarized in a Ciba Foundation Symposium [10] and a current review [12], [13], [14].

Hyaluronan (Figure 2) is a distinct biopolymer made up of duplicating disaccharide systems created by N-acetyl-d-glucosamine and d-glucuronic acid. Both sugars are spatially related to sugar which in the β-configuration permits all of its bulky teams (the hydroxyls, the carboxylate moiety, and the anomeric carbon on the adjacent sugar) to be in sterically beneficial equatorial placements while all the little hydrogen atoms inhabit the much less sterically beneficial axial placements. Therefore, the framework of the disaccharide is vigorously very stable. HA is likewise unique in its size, rising to numerous million Daltons and is synthesized at the plasma membrane layer rather compared to in the Golgi, where sulfated glycosaminoglycans are included in protein cores [15-17].

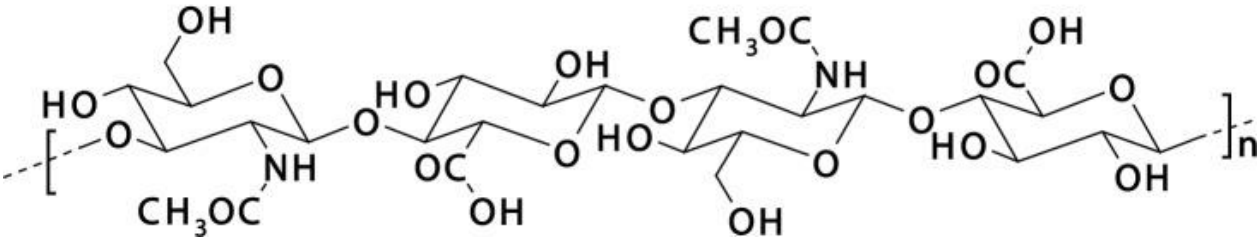

Figure 2.Structural formula of hyaluronan – the acid form.

The foundation of a HA particle is tensed by a combination of the chemical framework of the disaccharide, interior hydrogen bonds, and communications with the solvent in a physical solution. The axial hydrogen atoms establish a non-polar, relatively hydrophobic face while the equatorial side chains develop a more polar, hydrophilic face, for that reason generating a twisting ribbon structure. Solutions of hyaluronan are exceptionally lubricious,show very unusual rheological properties and very hydrophilic.The hyaluronan polymer chain in the solution takes form of a broadened, arbitrary coil. These chains ensnare with each other at extremely low concentrations, which might add to the unusual rheological residential properties At higher concentrations, remedies have a very high yet shear-dependent viscosity. A 1% solution, when it is put under pressure it relocates quickly and can be administered via a small-bore needle, but resembles jelly. It has been called a "pseudo-plastic" material because of that reason. The amazing rheological buildings of hyaluronan solutions make them ideal as lubricants. There is proof that hyaluronan divides most tissue surface areas that slide along each various other. The very lubricious properties of hyaluronan have actually been shown to decrease postoperative adhesion formulation following abdominal and orthopedic surgical procedure.As mentioned, the polymer in solution presumes a stiffened helical arrangement, which could be associated to hydrogen bonding in between the hydroxyl teams along the chain. As a result, a coil structure is formed that traps about 1000 times its weight in water [18-20].

- **Properties of hyaluronan**

Hyaluronan networks

The physico-chemical properties of hyaluronan were examined thoroughly from 1950 onwards [21].

The molecules act in remedy as very moisturized arbitrarily kinked coils, which start to at concentrations of less than 1 mg/mL. The complexity point could be seen both by sedimentation analysis [22] and viscosity.More lately Scott and his team have provided proof that the chains when ensnaring also interact with each various other and kind stretches of dual helices to make sure that the network comes to be mechanically extra firm [23].

Rheological residential properties.

Solutions of hyaluronan are viscoelastic and the viscosity is significantly shearing reliant [24].Above the complication factor the viscosity boosts quickly and exponentially with concentration (~ c3.3) and an option of 10 g/l could have a thickness at low shear of ~ 106 times the viscosity of the solvent. At high shear the viscosity might go down as much as ~ 103 times.elasticity of the system increases with increasing molecular weight and focus of hyaluronan as anticipated for a molecular network. The rheological residential or commercial properties of hyaluronan have been attached with lubrication of joints and tissues and hyaluronan is frequently found in the body in between surfaces that move along each various other, for instance cartilage surface areas and muscle bundles [25].

Water homeostasis

A fixed polysaccharide network supplies a high resistance to mass circulation of solvent [26].This

was shown by Day (1950) who showed that hyaluronidase treatment gets rid of a solid obstacle to water circulation through a fascia. Thus HA and other polysaccharides prevent too much liquid fluxes with tissue areas. Furthermore, the osmotic pressure of a hyaluronan remedy is non-ideal and raises greatly with the focus. In spite of the high molecular weight of the polymer the osmotic pressure of a 10 g/l hyaluronan solution is of the exact same order as an l0 g/l albumin service. The exponential relationship makes hyaluronan and various other polysaccharides exceptional osmotic buffering substances- modest changes in focus cause marked adjustments in osmotic pressure. Circulation resistance along with osmotic buffering makes hyaluronan an excellent regulatory authority of the water homeostasis in the body.

Network communications with other macromolecules

The hyaluronan network retards the diffusion of other molecules [26].It can be revealed that it is the steric obstacle which limits the motions and not the viscosity of the option. The larger the molecule the much more it will be impeded. In vivo hyaluronan will as a result work as a diffusion obstacle and regulate the transportation of other materials with the intercellular areas. Moreover, the network will omit a specific volume of solvent for other molecules; the larger the molecule the much less space will certainly be available to it [26].A solution of 10 g/l of hyaluronan will exclude concerning fifty percent of the solvent to serum albumin. Hyaluronan and various other polysaccharides for that reason take part in the dividers of plasma proteins in between the vascular and extravascular areas. The excluded quantity phenomenon will additionally impact the solubility of other macrom
olecules in the interstitium, change chemical balances and maintain the structure of, for instance, collagen fibers.

Medical applications of hyaluronic acid.

The viscoelastic matrix of HA can work as a strong biocompatible support product and is therefore frequently utilized as growth scaffold in surgery, wound healing and embryology. Furthermore, administration of purified high molecular weight HA into orthopaedic joints could restore the preferable rheological properties and ease several of the symptoms of osteoarthritis [27], [28], [17].The success of the medical applications of HA has resulted in the production of a number of effective commercial items, which have been extensively reviewed formerly.

Table 1 summarizes both the medical applications and the generally used commercial preparations containing HA made use of within this area. HA has also been thoroughly examined in ophthalmic, nasal and parenteral medicine delivery. Additionally, more unique applications including pulmonary, implantation and gene distribution have also been suggested. Typically, HA is believed to work as either a mucoadhesive and preserve the medicine at its site of action/absorption or to modify the in vivo release/absorption rate of the therapeutic representative. A summary of the drug distribution applications of HA is revealed in Table 2.

Table 1. Summary of the medical applications of hyaluronic acid [29].

Disease state	**Applications**
Osteoarthritis	Lubrication and mechanical support for the joints
Surgery and wound healing	Implantation of artificial intraocular lens, viscoelastic gel
Embryo implantation	Culture media for the use of In vitro fertilization

Table 2. Summary of the drug delivery applications of hyaluronic acid [30].[31].

Route	**Justification**	**Therapeutic agents**
Ophthalmic	Increased ocular residence of drug, which can lead to increased bioavailability	Pilocarpine, tropicamide, timolol, gentimycin, tobramycin,arecaidine polyester, (S) aceclidine
Nasal	Bioadhesion resulting in increased bioavailability	Xylometazoline, vasopressin, gentamycin
Pulmonary	Absorption enhancer and dissolution rate modification	Insulin
Parenteral	Drug carrier and facilitator of liposomal entrapment	Taxol, superoxide dismutase, human recombinant insulin-like growth factor, doxorubicin
Implant	Dissolution rate modification	Insulin
Gene	Dissolution rate modification and protection	Plasmid DNA/monoclonal antibodies

Cosmetic uses of hyaluronic acid

HA has been thoroughly used in cosmetic products as a result of its viscoelastic properties and excellent biocompatibility. Application of HA consisting of cosmetic items to the skin is reported to hydrate and restore elasticity, thereby accomplishing an antiwrinkle impact, albeit until now no strenuous scientific evidence exists to corroborate this claim. HA-based cosmetic formulas or sunscreens might likewise can protecting the skin versus ultraviolet irradiation as a result of the cost-free radical scavenging properties of HA [32].

HA, either in a supported form or in combination with other polymers, is utilized as a part of commercial skin fillers (e.g. Hylaform ®, Restylane ® and Dermalive ®) in plastic surgery. It is reported that shot of such items into the dermis, could minimize facial lines and wrinkles in the lengthy term with less side-effects and far better tolerability compared with making use of collagen [33].The primary side-effect could be an allergic response, perhaps due to impurities existing in HA [34].

CONCLUSION:

Synovial joints are very common joint type in the body.A main characteristic for a synovial joint that is not seen at fibrous or cartilaginous joints is the presence of a joint cavity. This fluid-filled area is the site at which the articulating surfaces of the bones contact each other. The articulating bone surface areas at a synovial joint are not directly connected to each other with fibrous connective tissue or cartilage, like fibrous or cartilaginous joints. This gives the bones of a synovial joint the ability to relocate smoothly versus each other, permitting an enhanced joint range of motion.

Hyaluronan is a high-Mr polysaccharide and a significant element of synovial tissue and fluid as well as other soft connective tissues. Entangled networks at dilute concentrations (< I mg/mL) formed and endows its solutions with unique rheological properties. Physiological functions of hyaluronan (lubrication, water homeostasis. macromolecular filtering, exclusion, etc.) have been ascribed to the properties of these networks. Normally, hyaluronan has important duties in body functions according to organ type in which it is distributed. The most basic explanation for its existence would be that a flow of hyaluronan through the joint is had to maintain the joint cavity open and thereby permit extended movements of the joint.

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