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Abstract:- Hyaluronic acid is naturally present in our human body. High amounts are present in eye secretion, skin and in joint spaces. Commercially, it is derived from bacterial fermentation or from cartilage of rooster combs. Its unique features of viscoelasticity, ability to retain water has made it an exemplary material for medical uses. It has wide range of usage from ophthalmology to orthopedics as well as in cosmetic dermatology. In dentistry and more so in periodontics, it has shown positive results in management of periodontal disease and surgical management of papillary loss. This short review elaborates and addresses the history, structure, functions and its numerous applications in medicine and dentistry.

Keywords:- *Hyaluronic Acid, Periodontics, Periodontal Disease, Orthopedics, Cosmetic Dermatology.*

I. INTRODUCTION

Hyaluronic acid (HA) is a biomolecule in a form of glycosaminoglycan. It is also known as sodium hyaluronate or hyaluronan or hylans, a high molecular weight glycosaminoglycan (GAG) composed of disaccharide non-sulfated units of D-glucuronic acid and N-acetylglucosamine in a repeated fashion [1].

This biomolecule is of considerable importance as it is one of the significant components of the extracellular matrix and has wide distribution in tissues, skin, synovial fluid, tendons, eyes, cartilage and also in some body fluids[2,3]. Its role is imperative, as it stimulates the cell migration during bone repair, adhesion and proliferation of undifferentiated mesenchymal cells and thus induces their differentiation into osteoblastic cells [4].

HA also participates in the healing of wound and reduces the post-operative inflammation and associated symptoms. In periodontology, commonly used property for aestheticprocedures is the hydrauling property of HA. And also, it has been widely employed in the treatment of gingival recessions, gingivitis, periodontal pockets and for implant procedures etc. [5].

II. HISTORY

Karl Meyer in 1934 discovered Hyaluronic acid and his colleague John Palmer, scientist at Columbia university, New York, isolated chemical substance from the vitreous jelly of coco's eyes. They proposed it as hyaluronic acid as it was derived from Greek word hylos meaning glass and it contained with two sugar molecules in which one among the two was uronic acid [6].

The first study of hyaluronan's medical application in humans was a vitreous substitution during an eye intervention done in 1950. In 1986, Balazs et. al distinguished hyaluronan from Hyaluronic acid and since HA is an acid, its physiological behaviour was shown to be more like that of sodium hyaluronate salt [5].

III. STRUCTURE (CHEMISTRY, MOLECULAR LEVEL, CELL RECEPTORS)

A biomolecule can exist in multiple conformational forms, due to different types of bonds between their individual elements. Extracellular matrix composition and organisation are tissue-specific and corresponds to a specific physiological and biochemical functional properties. In humans, Hyaluronic acid half-life in blood, epidermis& joints are 1-30 weeks, 1-2 days and 2-5 minutes respectively [7].

Hyaluronic acid (HA) a naturally occuring non-sulphated glycosaminoglycan which is made up of 4000-20,000,000daltons molecular weight that consists of polyanionic disaccharide units of glucuronic acid and N-acetyl glucosamine connected by alternating beta (1-3) and (1-4) bonds. It is a polysaccharide of linear fashion that is present in the extracellular matrix of connective tissue, vitreous humor, embryonic mesenchyma, skin and tissues of the body as most of the body cells efficiently of synthesizes Hyaluronan. Hyaluronan binds to cell bodies by the receptors present on the surface of the cell. As it attaches to extracellular matrix, it forms molecule and gets extruded immediately into the extracellular space.[8]

In a solution, hyaluronan molecule's framework can be stiffened by combination of disaccharide internal hydrogen bond and interactions. The hydrogen atoms are hydrophobic and non-polar, whereas the equatorial side chains form more polar hydrophilic face, thus represents the twisted ribbon structure. Hyaluronan solutions manifest abnormal rheological properties and it seems to be exceptionally lubricious and hydrophilic. In a solution, the hyaluronan polymer chain resembles the form of a random coil which is stretched. At low concentrations, polymer chains entangle with each other and at high concentrations, solutions have high pseudo plasticity. A 1% solution is in the form of jelly, which moves bodily under pressure, it moves easily and can also be injected through a small-bore needle. It has therefore been called as a "Pseudo-plastic" material. The incredible rheological properties of hyaluronan solution makes them paragon as lubricants. Evidence shows that hyaluronan separates tissue surfaces apart from each other. Even though Hyaluronan is highly lubricious, it fails in its efficacy in adhesion post-operative to orthopedic and abdominal surgeries. Thus, the hydrogen bonding in between the hydroxyl groups produces a polymer chain in the form of a stiffened helical pattern and coil structure is formed as an end product.[9]

IV. TISSUE DISTRIBUTION

Distribution of Hyaluronic acid in intracellular fluids and body tissues are ample, including

- Aqueous and vitreous humour,
- Synovial fluid
- Component of the hyaloplasm

V. BIOSYNTHESIS

The cellular synthesis of Hyaluronic acid is a unique controlled process. Most glycosaminoglycans are made in the cell's Golgi complex. Hyaluronan synthase, (HAS1, HAS2, HAS3) membrane protein produces Hyaluronic acid naturally. [10]

Integral membrane protein can be indicated by secondary structure predictions and biomolecular modeling (IMP). An integral membrane protein is molecule that spans the biological membrane with which it is linked or which, is adequately embedded in the membrane to remain with it during biochemical purification. Linear polymers of disaccharides known as Hyaluronan is synthesized by the incremental addition of glucuronic acid and N-acetyl glucosamine by Hyaluronan synthase enzyme.[11]

VI. DEGRADATION

Hyaluronidase, β-d-glucuronidase and β-Nacetyl-hexosaminidase are the enzymes involved in degradation of HA. Hyaluronidase splits high molecular weight - HA into small oligosaccharides,β-d-glucuronidase and β-N-acetylhexosaminidase removes the nonreducing terminal sugars by degradation of oligosaccharides into fragments. Pro-angiogenic properties are exhibited by degraded outputs of HA, oligosaccharides and HA with low molecular weight. The tissue permeability of HA is increased by its decrease in the viscosity done by hyaluronidase.[11]

VII. FUNCTION

HA has many functions either directly or indirectly linked to cell functions such as proliferation of cell, recognition and locomotion which facilitate the healing of tissues. It holds both physiological and biological functions.[12]

VIII. ROLE OF HYALURONIC ACID IN MEDICAL FIELD

A.OPHTHAMOLGY:

During eye surgery, its plays a very appreciable role in the surgical site as it protects the corneal endothelium and helps in regeneration of the operated site to its anatomical form. Using exogenous HA in the intraocular environment has no detrimental effect, no post-surgical intra-ocular pressure and inflammatory sequelae and it rapidly gets eliminated by itself. HA's solutions simulates the viscosity of the innate tears and capable of adhering itself to the corneal epithelium. High molecular weight HA is used in ocular microsurgery, cataract, intraocular lens implantation, keratoplasty and vitreous retinal surgery.[13]

B.OSTEOARTHRITIS:

HA is used safely in knee and large joints. HA given on the mode of intraarticular injection relieves joint pain, reinstate viscoelasticity of synovial fluid, regularizes synthesis and endogenous HA's degradation is inhibited.[13]

C.HEALING:

Hyaluronic acid is used in any category of wounds such as metabolic ulcers, pressure sores, abrasions, donorsites and postoperative incisions, first- and second-degree burn.[13]

D.COSMETIC DERMATOLOGY:

The alterations in the metabolism and curtail content of HA is one of the causes of ageing of human skin, which may occur after the age of 50. The mercantile value of HA is high when compared to the polysaccharides as they can invade through the skin at an ease and restores the HA content. Topical application of HA in skin forms the viscoelastic film.[13] HA is used in Cosmetic dermatology as dermal filler, post-surgery it prevents the scar formation.[12]

IX. DENTAL APPLICATIONS OF HYALURONIC ACID

- Topical application of 0.2 % Hyaluronic acid thrice a day for a week in third molar surgery has shown to be helpful in the management of trismus and swelling during the postoperative period. [14]
- Low molecular weight HA has angiogenic effect. HA (1.33%) applied in internal or external surgical area will emphasize the healing of tissues.[15]

- Topical use of 0.2% HA is beneficial in recurrent aphthous ulcers, stomatitis, prosthesis induced mucosal irritations. [16]
- Combination of HA with synthetic bone graft in any sinus lift surgery and socket preservation procedure increases the growth and bone density.[7]
- When it is used as a matrix, helps in the rejuvenation of salivary glands, temporomandibular joint, enamel, root canal and oral mucosa. [7]
- HA is bacteriostatic in nature, it is applied in the surgical site during surgery in the form of gels and sponges which prevents the bacterial invasion thereby avoids post-surgical complication and boosts regeneration.[7]

X. ROLE OF HYALURONIC ACID IN PERIODONTICS

Hyaluronic acid is used as an adjuvant therapy in gingivitis, along with scaling and regular oral hygiene maintenance. it is applied in the form of gel or spray in the concentration of 0.2%, two times a day over a period of 3-5 weeks.The topical use Hyaluronic acid in chronic periodontitis in combination with complete scaling and root planing. [16] Hyaluronic acid binding proteins and CD44 surface receptors mediates cell adhesion, migration and differentiation and serves as a crucial component of periodontal ligament matrix.[14]Hyaluronic acid is used as rejuvenator in interdental papilla augmentation. Studies have shown that 0.2% HA reconstructs the lost interdental papilla, on multiple injections facilitates the expected results. This procedure is one of the non-surgical treatmentmodalityin the management of black triangles.[17,18,19]Kharidi Laxman Vandana et al., have conducted a study using different concentrations of HA in the management of Black triangle, wherein they proved that 5% HA shows 100% result in papillary enhancement other than any other concentrations.[15]. In implants, HA coated ones have shown to enhance osseointegration. [16]Gel based Hyaluronic acid hastens the ossification process in the case of infra-bony defects.[14]

XI. CONCLUSION

HA is commonly used in the fields of Dentistry and Medicine. It is not only used as an adjuvant but also applied for rejuvenation in several periodontal procedures, it holds the privilege of positive and favourable outcomes in healing, rejuvenation and inflammatory disease and also proved its excellence in various fields such as ophthalmology, dermatology, orthopedics etc., and its bioavailability is the most appreciable part and it eliminates itself from the human body which is the add on advantage of HA.

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