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A Review on the use of Degenerative medicine as collagen-based biomaterials in tissue engineering

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ABSTRACT: Collagen is the most common and widely distributed class of proteins in human body. collagen based biomaterials are used in tissue engineering application. collagen sheets are used to stimulate human skin are used in the protection effect of ultraviolet cut films on skin when ozone hole appeared. Multiple crosslinking methods and different combination with other biopolymers are introduced to improve the tissue function. The capacity of collagen is that it is biodegradable, biocompatible and easily available. However, collagen is a protein but it is difficult to sterilize it without changing in its structure. The review shows a extensive overview in applications of collagen based biomaterials exhibited for tissue engineering application, various medicinal uses and aimed to provide some application in degenerative medicine from the animals and laboratory sources.

Key words: collagen, tissues, 3Dmodels, acellular matrix, biomaterials.

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1. Introduction: In the past centuries ,many innovations occurs in case of collagen base biomaterials from collagen matrices to bone regeneration and cross linking methods have produced and improve .collagen is now used in various research and medical applications and introduction on collagen molecule will represent by following some technical methods by collagen scaffold production method .Finally the recent progresses that have been developed in case of collagen base tissue engineering biomaterials will be practiced .Collagen is the structural protein in the extracellular space in various tissues in animal bodies .The main components of connective tissues are made up from 25% to 35% of the whole protein content of the body .collage consists of various amino acids bound together to form triple helix to form of elongated fibers .Depending on the degree of mineralization ,collagen tissues may be rigid and have a gradient from of cartilage .Gelatin is hydrolyzed collagen based biomaterials used in food industries for preparation of various cakes and pastries and in pharmaceutical industries for preparation of capsule shells and suppositories.

2.Types: On the basis of structural arrangements, collagens are classified into two types- 1. Fibrillar & 2. Non-fibrillar.

2.1 Fibrillar: In this type of collagen there are mainly four types:

Type-I: skin, tendon, bone.

TYPE-II: Cartilage (Mainly collageneous component of cartilage)

Type-III: Reticulate (Mainly components of reticular fiber)

Type-V: Cell surface, hair and placenta.

2.2 Non fibrillar:

a. Fibril associated collagens with interrupted tripple helix: Exp: Type- IX, Type-XII, Type-XIV, Type- XIX, Type-XXI.

b. short chain collagens: Exp: Type-VIII, Type-X.

C. Basement membrane: Type-IV.

d. Multiple tripple helix domains with interruption- Exp: Type-XV, Type-XVIII.

e. Membrane associated collagen with interrupted tripple helix: Exp: Type-XIII, Type-XVII.

f. Others: Exp: Type-VI, Type-VII.

3. LITERATURE STUDY:

1. Void Bone Filler :-

- The development collagen based composite scaffolds for bone regeneration.
  -By Dawei Zhang , Kaili Lin
- Bone grafts and biomaterials substitutes for bone defect repair.
  -By Wenhao Wang , Kelvin W.K. Yeung
- Critical size bone defect healing using collagen-calcium phosphate bone graft materials.
  - -By William Robert Walsh , Rema A , Oliver and Thomas Haider
- Bone tissue engineering :- Recent advances and challenges.
  -By Ani R Amini , Cato T.Laurencin and Syam P.Nukaverapu

2. De-mineralized bone matrices :-

- Review collagen based biometerials for wound healing.
  -by Sayani Chattopadhaya , Ronald T.Raines , Gary D.Glick
- Feasibility of silica-hybridized collagen hydrogels as three-dimensional cell matrices for hard tissue engineering –by Hye-Sun Yu , Eun-Jung Lee , Seog-Jin-Seo
- Biomineralized recombinant collagen based scaffold mimicking native bone enhances mesenchymal stem cell interaction and differenciation –by Ramirez-Rodriguez Gloriu Belen , Montasi Monika, Pansere Silvia.
- The mechanism of a chitosam – collagen composite folm used as biomaterial support for MC3T3 – E1 Cell differentiation – By Xiaoyan Wang , Gan Wang and Dongyi Zhang.

3. Drug delivery System :-

- Recent developments of collagen based materials for medical applications and drag delivery system.
- By K. Panduranga Rao
- A review on collagen based drug delivery system.
- By Dharmendra Kumar
- Collagen based drug delivery system for Tissue Engineering
- By Irina Titorencu
- Review on protein based drug delivery materials .
- By Dave Jao , Ye Xue, Jethro Medina and Xiao Hu.

4. Dental membrane

- Collagen as a Biomaterial in Dentistry. –By Jogendra Sai.
- Collagen membrane : a review -By Pintippa Bunyaratavey.

5. Dermatological fillers :-

- Collagen based Biomaterials for tissue engineering application.
- By Robert Gauvin
- Same as 2-i

6. Contact lenses :-

- Current development of collagen based biomaterials for tissue repair and regeneration .
- By Adam J.P Baver, JianZhao Liu.
- Surface treatment of collagen based biomaterials in medical application.
- By Jorge Andres Lopez , Garcia Zlinzon.

7. Tear duct plugs :-

- Comprehensive review of the literature on existing punctual plugs for the management of dry eye disease
- By Naz Jehangir , Greg Bevar.
- Clinical evaluation of the therapeutic effects of atelocollagen absorbable plunctul plugs.
- By Kaori Hirai, Yoji Takano

8. Tissue Scaffolds :-

- Future prospects for scaffolding methods and biomaterials in skin tissue engineering : A review - By Atul A.chawdhury
- The development of collagen based composite scaffolds for bone regeneration .
- By Dawei Zhang.

4. Overview & use:

Collagen based bio-materials are used in various cases of tissue engineering applications, trans-dermal drug delivery and used in cases of burns and wounds.

1.Bone void fillers:

Collagen is used as a main carrier protein in case of bone void filler and encourages bone growth.

There are two major substances that required for void bone filler: (I) calcium sulphate , (II) calcium phosphate.

(I)calcium sulphate:- At first, it was use to treat cavities of bone, in Germany by Dr. dressman[1]. He used this therapy on those patient who suffering from large bone defects, grafting them with beta calcium sulphate hemi hydrate and he got good result with complete bone regeneration and found that calcium sulphate was excellent biocompatible in nature[1].

(II)Calcium phosphate:- The chemical structure of Calcium phosphate is –[HA; $Ca_{10}(PO_4)_6(OH)_2$]. It's structure is similar to mineral phase of bone and it shows excellent biocompatibility . HA is very bioactive thus bone can easily binds with it.

This study was done on proximal tibia of 30 rabbits and demonstrate that HA and calcium phosphate gives 52% bone formation after 4 weeks and 90% bone formation after 24 weeks.

In this review, we conclude that if collagen fibres can mixed with calcium sulphate then it will be more bioactive in nature and act as more active void bone filler.

If we mixed beta calcium sulphate hemi hydrate with collagen fibre sheet , then it will give complete bone regeneration and relief patient from bone degradation.

2.De-mineralized Bone Matrix:- De-mineralized bone matrix is collected from animal sources. The inorganic minerals present on the bone matrix is removed and organic collagen matrix is collected[2]. By removing bone mineral, it posses more biologically active proteins more biologically active protein. By demineralization process , demineralized bone matrix become more biologically active than un-demineralized bone matrix.

Demineralized bone matrix was prepared from the long bone (In mid shafts) of Holstein calf foetus. The soft tissues were then removed and the bones were cut into 1cm pieces with a stryker saw and store in a zoo proof ethanol in air dried condition. Further the bones were decalcified using 0.6 mol/lit. nitric acid analysed by absorption spectrophotometer to determine the percentage of calcium per gram dry weight. After demineralisation, the bones were placed in phosphate buffer solution over night. After adjusting the pH (pH -7.3) they were placed in ethanol and allow to evaporate over night and store at 4^0 C[2].

In this review, we conclude that if after preparation of demineralised bone matrix, if we used gelatin powder with this bone matrix , it will become more powerful and give more action as a demineralised bone matrix.

3.Drug Delivery System: Collagen based biomaterials are used for the delivery of the drug. For this kind of delivery system, at first gelatin is taken gelatin is prepared by degradation of collagen and injectable microspheres are prepared based on gelatin; which is further used for ophthalmic preparation[3].

From the first few eras, various innovation occurred in the field of collagen based biomaterials. Various cross linking method and production have evolved and improved, such as bone regeneration scaffolds, injectable collagen matrix[4].

Collagen is being converted to lattice like gels from compacted solids. For this nature, collagen is a very useful suture material in surgery.

In this review, we conclude that if collagen scaffolds are mixed with wool fat and main constituent (ex- zinc sulphate) then a very powerful paste base will form. By this way, we can prepare various kind of sticky paste for external use.

4. Dental Membranes: Collagen based biomaterials are used for preparation collagen membrane. Collagen membrane can be made from type-I bovine collagen. They are used in dental applications by inhibit the rapid growth of skin when implant bone which take longer time to regenerate[5]. Collagen membranes do not required surgical removal as they are naturally absorbed by the body. They can raised the attachment of new connective tissue and prevent the excessive loss of blood by clotting[6].

5. Dermatological Filler: Collagen can also used as a good dermatological soft tissue filler as they are non-immunogenic in nature[6].

6. Contact lenses: Collagen based ophthalmic shields act as contact lenses. They contain formulated drugs and gradually dissolved on cornea by absorbing the collagen in the body.

7. Tear Duct Plugs: Tear duct plugs are small collagen based devices inserted into tear ducts to block the drainage[7]. This increases the eyes tears film and surface and moisture to relieves dry eyes. The other names of the tear duct plugs are punctum plugs, lacrimal plugs and occluders.

8. Tissue Scaffolds: The main function of tissue engineering is to recovery of damaged tissues by combining body cells with porous scaffold biomaterials. This scaffolds act as templates for regenerating tissue growth. Tissue engineers used porous collagen sponges to support the growth of numerous tissues. Collagen sponges are developed with embedded materials to encourage cartilage differentiation[8].

9.Collagen Hydrolysate: orally administered collagen hydrolysate has been shown to be absorbed intestinally and to accumulate in cartilage[9]. Collagen hydrolysate ingestion stimulates a statistically significant increase in synthesis of extracellular matrix macromolecules by chondrocytes ($p < 0.05$ compared with untreated controls). These findings suggest mechanisms that might help patients

affected by joint disorders such as OA. Four open-label and three double-blind studies were identified and reviewed; although many of these studies did not provide key information-such as the statistical significance of the findings--they showed collagen hydrolysate to be safe and to provide improvement in some measures of pain and function in some men and women with OA or other arthritic conditions.

5. Conclusion:

collagen base biomaterial are the most important material for tissue engineering and regenerative medicine .Presence of its important biocompatibility and low immunogenesity , collagen is now the protein that is most important for biomaterial preparation.it can be extracted from various tissues sources and in combination with other molecule .There is another use in the laboratory as a tissue replacement material, dental membranes, contact lenses, tear duct plugs and others medical application .

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