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Review Article

Marine/fish collagen matrix – a revolutionary breakthrough in management of gingival recession: A comprehensive review

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Abstract

"Gingival Recession" is the most commonly observed periodontal clinical problem chases significant challenges in clinical practice because of numerous negative effects in a patient such as impact on aesthetics, effect overall dental and oral health, dental caries and tooth sensitivity. Periodontal literature illustrated the gold standard conventional treatment modality like use of connective tissue grafts in the treatment of gingival recession cases. However, this traditional treatment technique is associated with several disadvantages like variable clinical outcomes and morbidity of the donor site. Hence, patient morbidity associated with graft harvesting is a major drawback of this treatment and has led to the invention of various biological substitute biomaterials. A 'quest' in biomaterial research has revolutionized several biomaterials in periodontal tissue regeneration and tissue medicine. Recent developments in biomaterials have introduced a novel biomaterial like "Marine Collagen Matrix" (MCM) as a revolutionary promising substitute for management of gingival recession. The aim of the present comprehensive review article is to explore the literature pertaining to the properties, applications, and clinical evidence about outcomes of the exciting domain 'marine collagen matrix' in periodontal regeneration of gingival recession defects, thereby showcasing its potential as a revolutionary breakthrough in the arena of periodontics.

Keywords: Gingival Recession; Marine/Fish Collagen Matrix (MFCM); Periodontal tissue regeneration; Root coverage treatment

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1. Introduction

Gingival Recession problems are one among the common periodontal condition, observed among all kind of population across the globe and associated with several psychological functional and aesthetic sequelae resulting in decreased self-esteem of the patient. The term 'Gingival Recession' is defined as 'a clinical condition in which there is apical migration of the gingival margin of the tooth thereby exposing the root surface.' This undesirable condition may exist either localised or generalized form irrespective of gender predilection. Gingival recession when occurs, not only compromises aesthetics, but also enhances the risk of root caries, dentin hypersensitivity, and continued loss of periodontal tissue.[1] The management of gingival recession has been revolutionized over the years, with a focus on obtaining predictable normal root coverage and periodontal tissue regeneration.[2-4] Conventional treatment strategies for gingival recession include different modalities like surgical techniques. In surgical techniques several tissue grafts and procedures are employed such as free gingival grafts, connective tissue grafts, and guided tissue regeneration. Among these, the 'gold standard' treatment modality in the management of gingival recession defects include connective tissue graft with coronally advanced flap technique.[2-4] Majority of researchers have illustrated with numerous clinical trials the most favourable results following this conventional technique such as appreciable aesthetics and long-term stability. However, there are few limitations associated with this treatment. Major limitations of using connective tissue graft are the sacrificing of a second surgical site (graft harvesting) that increases patient morbidity, problems with the availability of graft tissue when treating multiple recession defects, and prolonged treatment procedure.[2-11] To overcome these limitations, various soft tissue graft substitute biomaterials have been researched that

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could achieve enhanced comparable results to the conventional gold standard procedures.

Presently, periodontal tissue regenerative strategies that can enhance periodontal tissue repair have been investigated tremendously. This investigational research was aimed on use of combination of biomaterials, growth factors and stem cells to obtain periodontal tissue regeneration. Because this combination of biomaterial can provide templates to facilitate the regeneration of periodontal tissues.[12-14] Different types of biomaterials, such as synthetic organic materials and natural organic materials have been tried, tested in the laboratory for this purpose. These biomaterials include poly-lactic-co-glycolic acid and poly-lactic acid, collagen, silk fibroin, chitosan and alginate and all these showed variable findings emerged as a promising adjunct for the treatment of gingival recession.[12-15] Among the above listed biomaterial, collagen is an essential protein found in the extracellular matrix, and act as a biological scaffold, performing various functions like it facilitates vascular tissue growth and results in the deposition of oriented and organized fibres which increase the integrity of the newly formed tissue.[6,7,12-15]

Marine/fish collagen is one of novel biomaterial derived from fish or other marine sources. Extensive review of literature search revealed it as a promising biocompatible, biodegradable, and sustainable biomaterial which has potential in the domain of regenerative medicine and tissue engineering and has recently engulfed with magnificent potential in periodontal therapy. It is experimented, investigated and hypothesized by various researchers that collagen obtained from marine sources has structural similarity and better physiologic and biochemical properties in comparison to collagen obtained from terrestrial sources. Moreover, marine collagen is also proved valuable biomaterial with less immunogenicity and absence of the risk of developing zoonotic diseases.[8] Therefore, the purpose of this review article is to showcase a comprehensive overview pertaining to the role of marine collagen matrix in management of gingival recession, validating its potential to revolutionize the arena of clinical periodontology.

2. Review of Literature

In Human body ‘Collagen’ comprises about one third of all total proteins and is the primary component of the extracellular matrix found in different connective tissues such as tendons, ligaments, cartilage, bones and skin.[16] The major role of collagen is that it gives basic structural support to all organs by providing elasticity, firmness and strength as these are highly essential factors needed for favourable tissue repair and regeneration.[16-18] In health sector, collagen is mainly used for biological applications like for making wound cover dressings, haemostatic agent, absorbable sutures and in tissue engineering and biomaterial development. However, animal sourced collagen is associated with various drawbacks. It can cause or transmit few animals’ related diseases like bovine spongiform encephalopathy and foot-and-mouth disease. As result, research field is exploring as well as experimenting for the development of marine/fish collagen as a natural alternative for mammalian collagen.[16-20] Another important reason for the preference of developing marine collagen is that about 75% of total fish weight is made of collagen, suggesting that there is an abundance of this type of collagen available from fish. Moreover, about three fourth of a fish, including its fins, skeletal system, head and skin thrown out during fish processing. Hence, the disposal of discarded by-products from fish processing can cause environmental pollution or threat to its sustainability or can be economically burdensome.[15-21] all these facts (and being an environmentally friendly material) led to the development of marine/fish collagen as a unique biomaterial for experimental research procedures. As a result, marine collagen is tremendously engineered in larger quantities to mimic the extracellular matrix of human tissues, thereby act as a scaffold to supports cell proliferation, migration and tissue regeneration.[6-10,12-15]

Table 1: Biological properties of marine/fish collagen matrix[8,12-20]

Properties	Purpose
Biocompatibility	Marine/fish collagen is well-tolerated by human tissues, minimizing the risk of adverse immune reactions.
Osteo-conductivity and angiogenesis	Marine collagen promotes bone formation and facilitates blood vessel growth as it is essential for periodontal regeneration.
Biodegradability	It gradually undergoes degradation following its application thereby promoting for natural tissue regeneration and does not require its removal.
Sustainability	As marine/fish collagen is extracted from marine by-products, it is reported as an easily available and eco-friendly material and also found alternative to mammalian collagen.

2.1. Biological properties of marine/fish collagen matrix

Marine/Fish collagen is a kind of collagen extracted from marine sources such as fish, sponges and jellyfish.[6-8,16-21] Marine collagen mainly consists of type I collagen, which is the most abundantly seen collagen in the human body and which is also considered as the primary structural component of the periodontal ligament and gingival connective tissues. Because of its main clinical features like its bioavailability and high solubility, and as it almost similar to human collagen, marine/fish collagen is considered as an ideal material for biomedical applications in health science.[6-10,12-15] The main clinical properties of marine/fish collagen are elaborated in

2.2. Role of marine/fish collagen matrix in the treatment of gingival recession[8,12,13]

Marine/fish collagen being a type I collagen act as a primary bioactive scaffold to promote the regeneration of gingival tissues. Following application of marine collagen in the gingival recession defects, this natural collagen serves as a temporary structure and thereby facilitates the migration of endothelial cells, fibroblasts and epithelial cells. Additionally, the porous structure of the collagen matrix facilitates the infiltration of these tissue cells leading to the formation of new blood vessels, which is essential for tissue regeneration.[8,12] Moreover, fish/marine collagen matrix release bioactive signalling peptides that stimulate cellular activities such as angiogenesis and collagen synthesis, subsequently enriching tissue repair.[13]

2.3. Clinical applications/outcomes of marine collagen in periodontal regeneration

Compared to calf collagen, marine-derived collagen has proved to be a much safer alternative biomaterial as calf collagen is associated with risks of transmitting bovine spongiform encephalopathy and other diseases. Because of reduced risk of zoonotic disease transmission and the easily available reservoir of industrial fish waste from which collagen can be extracted and processed, fish or marine collagen has conquered great attention recently for periodontal regeneration.[16-18]

Marine by-products are important sources of valuable inorganic and organic materials and hence used for various industrial purposes such as in cosmetics, pharmaceuticals and nutraceuticals.[15-22] Large number of studies have proved that found that hydrolysed fish collagen exhibits biologically active characteristics such anti-oxidative, immunomodulatory, anti-bacterial, anti-inflammatory and angiotensin-converting enzyme inhibitory properties.[23-25] Therefore, the adequate clinical application of marine collagen can not only limit the quantity of bio waste to protect the environment, but can also increase the economic weightage of fish by-products.

A previous Chinese study experimented a cross-linked collagen gel along with acid-soluble collagen which was extracted from skin of salmon fish. The investigators examined the growth rate and differentiation capacity of human periodontal ligament fibroblasts cultured on this salmon collagen gel. In the experiment, the growth rate was observed to be higher when these cells were cultured on the salmon collagen gel compared with that in cells cultured on the porcine collagen gel. Additionally, the human periodontal ligament fibroblasts cultured on the salmon collagen gel showed an enhanced ALP activity compared to those cultured on the porcine collagen gel. It was also evident in the experiment that a greater mRNA expression of ALP, collagen type I and osteocalcin in the salmon collagen gel group.[19]

Another Japanese study explored the efficacy of a scaffold prepared from salmon collagen-coated ePTFE.[20] The results of the research showed that the outgrown cells penetrated the coated mesh fibre networks and formed complex multicellular layers. Moreover, an increased higher ALP activity in response to osteogenesis induction was also observed. In addition, an in-vitro mineralization was tremendously increased in the primary tissue segment regions, along with some micro-mineral deposits formed on the coated-fibre networks. These observations suggested that the scaffold made of three-dimensional mesh consisting of salmon collagen-coated fibres undoubtedly accelerated the biological mineralization and osteogenesis of human periosteal sheets.[20] Apart from above mentioned clinical trials, marine collagen matrix has been experimented in various periodontal procedures as mentioned in **Table 2**.

Table 2: Clinical applications of marine/Fish collagen matrix in various periodontal procedures

Periodontal procedure	Application of marine/fish collagen
Root coverage periodontal procedures	Marine/fish collagen matrix act as a scaffold for gingival tissue regeneration, promotes the formation of new connective tissue and epithelium over exposed root surfaces following surgery.
Guided tissue regeneration (gtr) procedures	Marine collagen when used in combination with barrier membranes, enhances the regeneration of periodontal tissues.
Soft tissue augmentation procedures	Marine/fish collagen can be used to increase the thickness of normal gingival tissue thereby reducing the risk of future gingival recession occurrence.

2.4. Advantages of marine collagen matrix over traditional methods

Minimally Invasive: Application of marine/fish collagen avoids the necessity of a second surgical site thereby minimizes patient and tissue morbidity and postoperative complications.

Biocompatibility: Marine collagen is proved as eco-friendly and well-tolerated by the human body. The low immunogenic property of marine collagen decreases the risk of adverse reactions.

Sustainability: As marine collagen is derived from renewable natural sources, it is established as an eco-friendly bio-material.

Ease of Use: It is easy to handle the marine collagen matrix and it can be applied to different defect shapes and sizes.

Reduced Morbidity: Compared to other auto grafts used for gingival recession, marine collagen matrix doesn't require a secondary surgical site. Hence there are no postoperative pain and complications.

Biodegradability: The matrix gradually undergo degradation. As a result, it does not require its surgical removal following its application for clinical procedures.

Aesthetic Outcomes: Marine/fish collagen matrix facilitates the regeneration of natural gingival tissue, thereby enhances aesthetic outcome.

Versatility: It can be combined/used with other biomaterials and growth factors to accelerate its regenerative properties.

Reduced Inflammation: Marine collagen has some anti-inflammatory properties thereby reduces periodontal inflammation.

3. Discussion

Gingival recession, gingivitis and periodontitis are the most prevalent periodontal problems damaging the supporting structures of the teeth, such as the gums, periodontal ligament, and alveolar bone, ultimately leading to tooth loss bringing panic in patients. Conventional treatments for the management of these irreversible conditions consists of scaling and root planning, use of antibiotics, probiotics, autologous blood products and surgical procedures. As all these materials and techniques are associated with their own drawbacks and limitations, regenerative medicine invented novel biomaterials like marine/fish collagen matrix as a promising tool for periodontal tissue regeneration.[25-28]

Introduction of marine/fish collagen matrix represents a marvellous advancement in the treatment of gingival recession defects. Because of its unique properties, like biocompatibility, sustainability, and ease of use, marine collagen has found a valuable substitute to conventional grafting procedures. As research showed the complete potential of marine collagen in periodontal regeneration, it is not too far from reality to prove it a boon for the treatment of gingival recession thereby offering patients a less invasive and more effective treatment option.[26-28]

3.1. Promising clinical evidence of marine/fish collagen matrix

In the periodontal literature, there is insufficient evidence to provide data on combined efficacy of different biomaterials and techniques used in the treatment of gingival recession defects.[28] Therefore, based on this hypothesis it is essential to evaluate whether marine collagen matrix when used as a carrier for autologous blood components such as platelet rich fibrin or plasma could have synergistic activity to expedite wound healing and regeneration when used in the management of gingival recession defects. To make this fact tested, Krishnaraj et al in 2023[15] explored the efficacy of marine collagen matrix (MCM) impregnated with injectable platelet-rich fibrin (I-PRF) along with modified coronally advanced flap (CAF) in the treatment of Miller's class I and II recession defects. In their research, six patients with ten gingival recession defects in maxilla were treated with coronally advanced flap in addition to marine collagen matrix and injectable PRF. Authors evaluated clinical parameters, visual analogue score and aesthetic scores in these six patients at baseline and till six months post-operatively. There was significant root coverage observed at three- and six-month follow-ups periods. Results of the study suggested that I-PRF-impregnated marine collagen matrix act as a bioactive carrier can promote soft tissue regenerative outcome. However, considering limitations of this study, further research including huge sample sizes with longer follow-up periods highly warranted to explore the synergistic effects of marine collagen matrix combined with other drugs or growth factors for the application in various domains of periodontal procedures.[28]

4. Clinical Challenges and Future Perspectives

Although marine collagen matrix has shown outstanding results, there are challenges encountered with the use of marine collagen matrices. Its various biological and physical properties like durability, faster degradation rate, low mechanical strength and the long-term stability need to be further studied. Additionally, further research is essential to understand the molecular mechanisms behind the bioactive effects of marine collagen and also to draw its new standardized protocols and formulations to accelerate its regenerative potential. Regarding cost factor, the production and processing of marine collagen looks more expensive, thereby reducing its widespread utilization in all clinical procedures.

Therefore, it is evident that advanced understanding of the modification methods used for enhancing the physico-chemical-biological properties of marine collagen is highly warranted along with need for the development of advanced manufacturing technologies. Hence, currently the attractive scope of marine collagen in stem cell therapy appears to be a dream rather than a reality. Further research including in-vivo research is also essential to show how marine collagen modulates mesenchymal stem cells and manipulates periodontal stem cells and embryonic stem cell physiology.[12,20-25]

5. Conclusion

Marine/Fish collagen matrix definitely represents a revolutionary breakthrough in the arena of clinical periodontics pertaining to management of gingival recession defects. Despite all the clinical challenges posed, marine collagen showcases a great promise in the field of periodontal tissue regeneration.

6. Source of Funding

None.

7. Conflict of Interest

None.

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