Role and Evolution of Scaffold in Periodontal Regeneration- A Narrative Review

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Abstract
The goal of periodontal regeneration is to repair the periodontium along with its lost structural and functional integrity as a result of periodontal disorders. Scaffolds play an essential role in periodontal tissue engineering because they offer a three-dimensional framework for cell attachment, proliferation, differentiation, and extracellular matrix synthesis. The perfect scaffold should be mechanically stable, biocompatible, biodegradable, and capable of replicating the natural periodontal microenvironment while promoting the regeneration of intricate tissues, including cementum, periodontal ligament, and alveolar bone.
Collagen, chitosan, alginate, polylactic acid, and polycaprolactone are among the natural and synthetic biomaterials that have been investigated for scaffold production. Multiphasic and functionally graded scaffolds that more closely resemble the hierarchical architecture of periodontal tissues have been made possible by advancements in scaffold design, including electrospinning, 3D printing, and nanotechnology-based techniques. Additionally, incorporating stem cells, growth factors, and bioactive compounds into 3D-printed scaffolds has shown encouraging results in fostering tissue regeneration. More investigation will confirm its function and optimise its advantages in periodontal regeneration.

Keywords : Scaffold, Periodontal Regeneration, Tissue Engineering, 3D Printing, Scaffold biomaterials

Introduction
Periodontal disease is a common, prevalent inflammatory condition that causes breakdown of tooth-supporting tissues, leading to tooth loss if not treated. Regeneration of periodontal tissues, including alveolar bone, periodontal ligament, and cementum, is one of the biggest challenges in periodontal treatment[1], as traditional methods cannot fully regenerate these tissues[2].
Tissue engineering has emerged as a solution to this challenge, with scaffolds playing a vital role in this process[3]. Initially, Scaffolds were designed to provide mechanical support to tissues; however, over time, their design evolved into complex, bioactive systems capable of delivering cells, growth factors and therapeutics precisely[4].

Concept of Tissue Engineering
Tissue engineering is a field that focuses on regenerating, repairing or replacing damaged organs and tissues by combining elements from biology, materials science, and engineering[5]. It involves the use of cells, scaffolds and bioactive substances to support the formation of functional tissue that integrates with the host system.

Applications of Tissue Engineering in Health

1. Regenerative Therapy

Tissue engineering is majorly used to restore or replace damaged tissues and organs. Scaffolds, growth factors, and stem cells can help generate new functional tissues.

example

Dermal replacements for individuals with burns.

Regeneration of cartilage and bone in orthopaedic procedures.

Regeneration of nerves for spinal cord or peripheral nerve injuries.

Regeneration of periodontal tissues in dentistry[6].

2. Organ Replacement and Transplantation

Tissue engineering offers a solution to the shortage of donor organs.

Researchers are developing constructs for bioartificial organs, like liver and kidney models.

3D bioprinting allows for the creation of organ-like structures layer by layer using cells from patients, reducing the risk of immune rejection.

3. Healing of Injuries and Skin Regeneration

Engineered skin substitutes such as Dermagraft and Apligraf are used for chronic wounds, burns, and diabetic ulcers.

These substitutes speed up healing and minimise scarring by mimicking the natural structure of skin.

4. Cardiac Restoration

Vascular engineered grafts and heart valves can replace damaged blood vessels or valves.

Cardiac patches aid in the regeneration of heart tissue after a myocardial infarction.

5. Restoration of the Nervous System

Efforts are ongoing to restore neurons and neural networks for spinal cord injuries, Parkinson's disease, and stroke.

Role of Tissue Engineering in Periodontics

Periodontal disease destroys essential tooth-supporting structures such as cementum, periodontal ligament (PDL), and alveolar bone. Tissue engineering aims not only to halt disease progression but also to restore the lost periodontal tissues.

Various tissue engineering approaches employed in periodontics include the following:

1. Guided tissue regeneration (GTR) using membranes and scaffolds[6].
2. The introduction of stem cells, such as periodontal ligament stem cells (PDLSCs), and stem cells from human exfoliated deciduous teeth (SHED).
3. The addition of growth factors like PDGF, BMP-2, and enamel matrix derivatives (EMDs).
4. The use of biomimetic scaffolds that replicate the natural periodontal environment.

Scaffolds are essential in applying tissue engineering methods in periodontal treatment.

What is a scaffold?

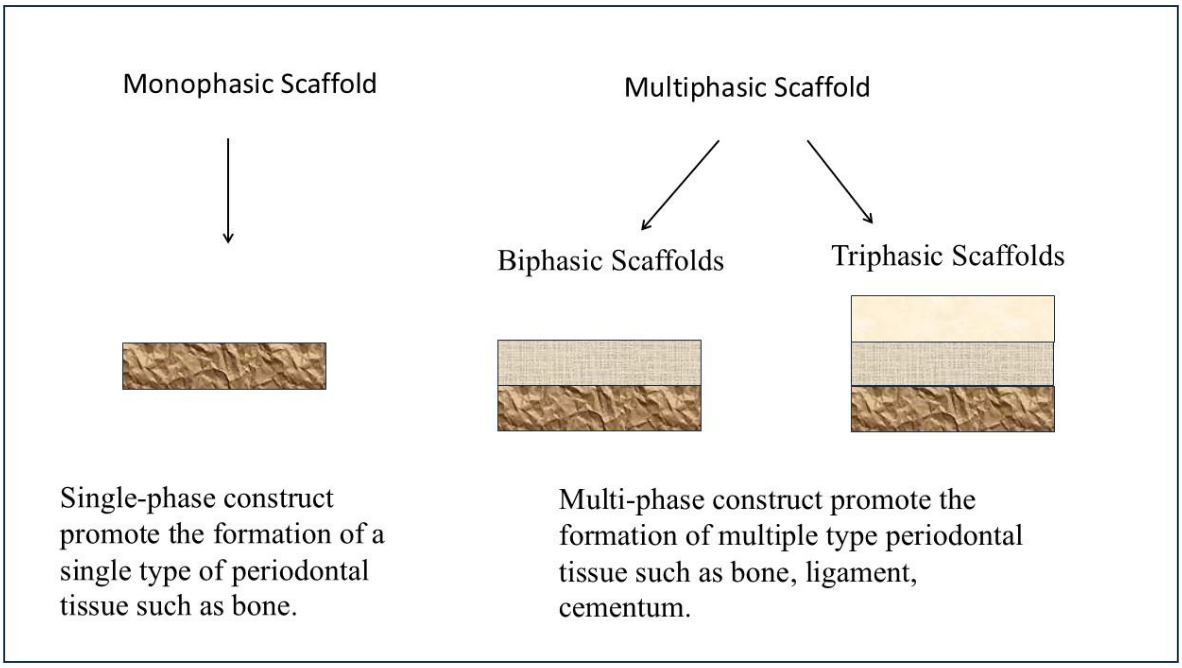
A scaffold is a three-dimensional, porous, and permeable structure made from natural or synthetic biomaterials meant for temporary or permanent placement at a tissue injury site. It is biocompatible and functions as a supportive matrix that encourages the adhesion, migration, proliferation, and differentiation of progenitor or stem cells[7]. In periodontal regeneration, scaffolds provide a structural framework that mimics the native extracellular matrix (ECM), guiding the formation of new tissue[8].

Evolution of Scaffolds in Periodontal Regeneration

To achieve 3D tissue regeneration, scaffolds in periodontal treatment have progressed from simple, monophasic materials to advanced, multi-phasic, and bioactive systems[9]. This evolution allows for guided regeneration of various periodontal tissues, including the cementum, periodontal ligament, and alveolar bone.

Monophasic scaffolds are single-phase constructions that maintain a consistent chemical composition, structure, and material characteristics throughout[10]. Their main purpose is to support general tissue. However, they may need additional treatments like growth factors or cell transplantation to be effective, as they cannot distinguish between bone, ligament, and cementum.

Fig 1: Schematic representation of monophasic and multiphasic scaffolds



Periodontal regeneration requires coordinated, spatially organised healing of soft and hard tissues, which limits the effectiveness of standard monophasic scaffolds in guiding cells to renew these tissues in an organised manner. Multiphasic scaffolds tackle this by creating defined tissue zones within the scaffold (e.g., bone vs ligament), providing tailored material properties for each zone (e.g., stiffness, porosity), and delivering specific bioactive components to each area[11].

Multiphasic scaffolds consist of multiple distinct sections, each designed to promote the regeneration of specific periodontal tissues, such as cementum, periodontal ligament, and alveolar bone. [12].

They are typically biphasic or triphasic. Biphasic scaffolds have separate areas for bone and periodontal ligament[13].

This involves creating a scaffold using two technologies: electrospinning to create a finer fibrous layer that resembles the periodontal ligament and 3D printing to build a structurally supporting layer of bone.

Triphasic scaffolds add a third component aimed at cementum regeneration[14].

Scaffold biomaterials used in periodontal regeneration

Table 1: Classification of Scaffold biomaterials used in periodontal regeneration

Naturally derived	**Synthetic**
1.Ceramics –	Synthetic polyesters –
Hydroxyapatite (HA)	
Beta tricalcium phosphate (TCP)	Polyglycolic acid (PGA)
	Polylactic acid (PLA)
2. Polymers –	Polycaprolactone
Collagen, fibrin, albumin, hyaluronic acid,	
cellulose, chitosan, polyhydroxyalkanoates,	PLGA a copolymer of PGA and PLA
alginate, agarose, polyaminoacids	

Ceramics, which are biocompatible and osteoconductive, are ideal for bone regeneration[15].

- **Hydroxyapatite (HA):** mimics the mineral composition of natural bone.
- **Beta-tricalcium phosphate (β-TCP):** A calcium-phosphorus compound that degrades naturally and can act as a bone replacement material. Natural polymers are favoured for their biocompatibility, biodegradability, and ability to encourage cell adhesion and growth.

Synthetic polyesters are appreciated for their mechanical strength, structural stability, and degradation properties, making them suitable for various scaffold applications.

Polyglycolic acid (PGA) is among the first synthetic polymeric scaffolds developed. Although it does not dissolve in water, it hydrolyses quickly in physiological conditions[15].

Polylactic acid (PLA), derived from lactic acid, is more hydrophobic and resistant to hydrolysis than PGA, which offers added stability.

Poly lactic-co-glycolic acid (PLGA) is known for its excellent biocompatibility, mechanical and structural characteristics, and predictable degradation rates[15].

Emerging Technology 3D- printed scaffolds

In tissue engineering, three-dimensional (3D) printing has become a transformative technology, allowing the creation of scaffolds with precise anatomical details, controlled porosity, and consistent structure[16]. These scaffolds can be customised using patient-specific data through computer-aided design (CAD) and computer-assisted manufacturing (CAM).

Methods like stereolithography (SLA) and selective laser sintering (SLS) facilitate the layer-by-layer assembly of biomaterials like polycaprolactone (PCL), β-TCP, and HA. 3D-printed scaffolds have shown promising results in guided bone regeneration, sinus augmentation, and socket preservation, aiding the recovery of alveolar bone and periodontal tissue[17].

Their sophisticated biphasic and multiphasic designs resemble natural tissue interfaces, promoting the regeneration of multiple tissues, including bone, periodontal ligament, and cementum.

Future Perspectives and Innovations

The future of scaffolds for periodontal regeneration is moving toward smart, multifunctional, and patient-specific materials[17]. Current innovations focus on stimuli-responsive scaffolds that release drugs or growth factors in response to environmental changes, such as pH or inflammation[18]. Along with these advancements, nanofibrous scaffolds mimic the extracellular matrix, promoting cell attachment and tissue formation. [19]. Scaffolds that incorporate stem cells may also enhance tissue and defect repair[20]. Biodegradable and immune-modulating scaffolds are in the early stages of research as well[21]. The combination of these technologies is expected to improve periodontal therapy in the near future.

Conclusion

Recent advancements in biomaterials and 3D printing have opened up new possibilities for periodontal regeneration through specialised membranes and multiphasic scaffolds. These methods enhance control over scaffold composition, design, and spatial placement, potentially allowing for closer mimicking of the complex structure of periodontal tissues.

However, there are still a lot of obstacles to overcome before these technologies are regularly being applied in clinical settings. It is essential to address issues related to biological integration, scaffold stability, material qualities, and long-term functional results. Overall, 3D-printed scaffolds represent a promising avenue for periodontal tissue regeneration, but their clinical use will depend on robust biological data and consistent clinical evaluation.

CONFLICT OF INTEREST: Nil

REFERENCES

1. Jhawar B, Kujur S, Gupta V, Kumari P, Chanreiphy H. Unfolding the journey of scaffold. International Journal of Preventive and Clinical Dental Research. 2022 Oct 1;9(4):99-102.
2. Figueiredo TD, Do Amaral GC, Bezerra GN, Nakao LY, Villar CC. Three-dimensional-printed scaffolds for periodontal regeneration: A systematic review. Journal of Indian Society of Periodontology. 2023 Sep 1;27(5):451-60.
3. Costa PF, Vaquette C, Zhang Q, Reis RL, Ivanovski S, Hutmacher DW. Advanced tissue engineering scaffold design for regeneration of the complex hierarchical periodontal structure. Journal of clinical periodontology. 2014 Mar;41(3):283-94.
4. Mishra M, Mishra P, Shambharkar V, Raut A. Scaffolds in periodontal regeneration. J. Pharm. Biomed. Sc. 2016 May 25;6:10-7.
5. Daar AS, Greenwood HL. A proposed definition of regenerative medicine. Journal of tissue engineering and regenerative medicine. 2007 May;1(3):179-84.
6. Shimauchi H, Nemoto E, Ishihata H, Shimomura M. Possible functional scaffolds for periodontal regeneration. Japanese Dental Science Review. 2013 Nov 1;49(4):118-30.
7. Lin Z, Rios HF, Cochran DL. Emerging regenerative approaches for periodontal reconstruction: a systematic review from the AAP Regeneration Workshop. Journal of periodontology. 2015 Feb;86:S134-52.
8. Chen FM, Jin Y. Periodontal tissue engineering and regeneration: current approaches and expanding opportunities. Tissue Engineering Part B: Reviews. 2010 Apr 1;16(2):219-55.
9. Farzin A, Bahrami N, Mohamadnia A, Mousavi S, Gholami M, Ai J, Moayeri RS. Scaffolds in dental tissue engineering: A review. Arch. Neurosci. 2019;7:1-5.
10. Yamada S, Shanbhag S, Mustafa K. Scaffolds in periodontal regenerative treatment. Dental Clinics of North America. 2022 Jan 1;66(1):111-30.

11. Ivanovski S, Vaquette C, Gronthos S, Hutmacher DW, Bartold PM. Multiphasic scaffolds for periodontal tissue engineering. Journal of dental research. 2014 Dec;93(12):1212-21.
12. Vaquette C, Saifzadeh S, Farag A, Hutmacher DW, Ivanovski S. Periodontal tissue engineering with a multiphasic construct and cell sheets. Journal of dental research. 2019 Jun;98(6):673-81.
13. Vaquette C, Fan W, Xiao Y, Hamlet S, Hutmacher DW, Ivanovski S. A biphasic scaffold design combined with cell sheet technology for simultaneous regeneration of alveolar bone/periodontal ligament complex. Biomaterials. 2012 Aug 1;33(22):5560-73.
14. Lausch AJ, Chong LC, Uludag H, Sone ED. Multiphasic collagen scaffolds for engineered tissue interfaces. Advanced Functional Materials. 2018 Nov;28(48):1804730.
15. Dagar M, Chaudry K, Shukla P, Joshi CS, Shiwach R, RR N. Scaffolds in periodontal regeneration- A brief review. Journal of Orofacial and Health Sciences. 2025 Jul 18;11(3):93-102.
16. Asa'ad F, Pagni G, Pilipchuk SP, Giannì AB, Giannobile WV, Rasperini G. 3D-printed scaffolds and biomaterials: review of alveolar bone augmentation and periodontal regeneration applications. International Journal of Dentistry. 2016;2016(1):1239842.
17. Chen G, Ushida T, Tateishi T. Scaffold design for tissue engineering. Macromolecular Bioscience. 2002 Feb 1;2(2):67-77.
18. Gelmi A, Schutt CE. Stimuli-responsive biomaterials: scaffolds for stem cell control. Advanced Healthcare Materials. 2021 Jan;10(1):2001125.
19. Do AV, Khorsand B, Geary SM, Salem AK. 3D printing of scaffolds for tissue regeneration applications. Advanced healthcare materials. 2015 Aug;4(12):1742-62.
20. Gupte MJ, Ma PX. Nanofibrous scaffolds for dental and craniofacial applications. Journal of dental research. 2012 Mar;91(3):227-34.
21. Antmen E, Vrana NE, Hasirci V. The role of biomaterials and scaffolds in immune responses in regenerative medicine: macrophage phenotype modulation by biomaterial properties and scaffold architectures. Biomaterials science. 2021;9(24):8090-110.