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Review Article

The evolving landscape of biomimetic restorative dentistry: A review

Zoya Kidwai[1], Promila Verma[1]*, Rhythm Bains[1]

[1]Dept. of Conservative Dentistry and Endodontics, King George's Medical University, Lucknow, Uttar Pradesh, India

Abstract

A paradigm shifts from traditional dental procedures, biomimetic restorative dentistry (BRD) attempts to repair damaged teeth by imitating their natural structure, functionality, and appearance. This interdisciplinary field draws inspiration from biological processes to create innovative dental solutions that integrate seamlessly with natural tooth tissues. Unlike traditional methods that often involve extensive tooth reduction and the use of rigid, non-compatible materials, BRD prioritises the preservation of healthy tooth structure, leading to enhanced durability, longevity, and aesthetics of restorations. This review explores the fundamental ideas, variety of materials, cutting-edge clinical methods, and innovative uses of biomimetics in dentistry, including its function in tissue regeneration and the creation of intelligent materials. It also discusses the serious drawbacks and limitations of some recommended procedures, emphasizing the necessity of evidence-based validation to guarantee their widespread and successful application.

Keywords: Biomimetic Restorative Dentistry, Dental Adhesives, Caries Management, Aesthetic Dentistry, Smart Materials, Evidence-Based Practice.

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1. Introduction

1.1. What is biomimetic?

The term "*biomimetic*" is derived from the Latin words *"bio"* (life) and "*mimetic"* (imitating or copying), from nature and biological processes. It is an art and science of repairing unhealthy teeth with a restoration that imitates the physical appearance and chemical properties of natural teeth. *Otto Schmidt*, a biophysicist and biomedical engineer, coined the phrase "biomimetic" for the first time in the 1950s and described it as an interdisciplinary method that replicates natural processes using biologically produced materials. (**Figure 1**) Various synonyms have been used related to biomimicry including *bionics, bioinspiration, and biogenesis*.[1,2]

1.2. What sets it apart from conventional dentistry?

Traditional dentistry frequently requires extensive cavity preparation, resulting in the destruction of healthy tooth structure and the use of rigid restorative materials that don't have the properties of natural teeth, leading to tooth fracture instead of restoration. BRD, on the other hand, uses materials and techniques that closely resemble natural teeth in order to conserve the tooth structure as much as possible, which significantly lengthens its lifespan and durability.[3]

1.3. History

The term "*bionics*" was initially used for biomimetic. The term "*biomimetic*" was officially included in Webster's Dictionary in 1974. In 1997, *Jenine Benyus*'s book "*Biomimicry: Innovation Inspired by Nature*" sparked interest of the subject in several engineers and designers.[4] The historical roots of biomimetics in dentistry can be traced back to dental implants seen in pre-Columbian and Roman communities.[5] Apart from dentistry, biomimetics is employed in many different industries, including swimsuits that mimic the denticles of shark skin (**Figure 2**), needles that resemble mosquito wings, and wind turbine blades that are shaped like the fins of humpback whales.[6]

*Corresponding author: Promila Verma
Email: drzoyacpw10@gmail.com

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2. Discussion

2.1. Basic principles & Protocols of BRD

A paper titled "*Silent Revolution of Adhesive Dentistry*," by *Roulet J.*, contained the fundamental principles for BRD.[7] Japanese researchers made further progress by introducing novel technologies for predictable dentin bonding, which is achieved by following principles as discussed below.[8,9]

1. Maximum bond strength, which enables the restored teeth to operate and withstand stress like natural teeth. It is crucial for the longevity and functional integration of the restoration. [8,9]
2. A Long-term marginal seal, ensuring a tight seal at the edges of the restoration to prevent recurrent decay and microbial invasion, maintaining function over time.[10]
3. Retained pulp vitality: By achieving a highly bonded seal, biomimetic restorations aim for long-term function without recurrent decay, dental fractures, or pulp deaths, making the tooth three times more resistant to fracture compared to conventionally restored teeth.[11]
4. Reduced residual stress, aiming to minimize stress within the restoration, while still maintaining maximum bond strength to avoid problems like cuspal deformation, debonding, and sensitivity.[12]
5. Recommended Protocols: The protocols to adhere to these paradigms are: *stress-reducing protocols* and *bond-maximising protocols.*[13]

2.2. Stress-reducing protocols: [13]

1. Indirect/Semi-direct restorations: help to reduce compressive stress on the remaining tooth structure by replacing lost dentin with a restorative material, primarily composites, which have an Elastic Modulus (EM) comparable to that of natural tooth, leading to even stress absorption. Indirect or semi-direct techniques are also used for occlusal and interproximal enamel replacements. This technique reduces the volume of restorative material shrinkage, thereby reducing residual stress.
2. Decouple with Time (DWT): minimises stress caused by polymerisation shrinkage on the developing adhesive bond between the dentin and composite by maintaining time intervals of no more than 30 minutes and keeping initial increments to a minimum thickness of < 2mm. This allows the adhesive bond to dentin to mature, reaching approximately 90% of its strength within the first 5 minutes post-application. A resin coating, typically 0.5 mm thick, is applied over dentin and the dentino-enamel junction (DEJ) after *Immediate Dentin Sealing (IDS)*. This DWT phase prevents the faster-setting enamel bond from prematurely influencing the slower-maturing dentin bond, creating a stress-free environment for the hybrid layer to stabilise. It also addresses challenges related to the *Hierarchy of Bondability*.
3. Restore the dentin with thin horizontal increments of composite (< 1 mm): This technique ensures that DWT is properly achieved and prevents composite flow from deep dentin areas during early stage of layer formation. It also mitigates "C-Factor" stress by maintaining a low proportion of bonded to unbonded surfaces, converting large-scale C-Factor stress into smaller, manageable "micro-C-Factor" stress. The *Hierarchy of Bondability* explains that if dentin and enamel are bonded simultaneously, the hybrid layer to dentin will be stressed as it is pulled towards the enamel due to faster bond formation to enamel (complete in 5 minutes) compared to dentin (maximum strength after 30 minutes).
4. Placing fiber inserts in extensive restorations: The fiber mesh placed along the pulpal floor and/or axial walls allow movement of the composite through micro-shifting of the woven fibers, permitting polymerisation shrinkage without stressing the developing hybrid layer. Materials like *Ribbond Fibre Reinforced Composite* mimic the elastic modulus of dentin and have low polymerisation shrinkage.
5. Use slow start and/or pulse activation polymerization techniques.
6. Selecting dentin-replacing composites with shrinkage rates below 3% and an elastic modulus ranging from 12 GPa to 20 GPa.
7. When restoring pulp chamber in non-vital teeth, opt for dual-cure composites with the chemical cure mode active during the initial five minutes: This gradual setting process of 4 to 5 minutes by chemical method allows sufficient time for the adhesive system to mature, forming a strong, stable hybrid layer.
8. Eliminating dentin cracks within 2 mm of the DEJ: This area called as the *"peripheral seal zone,"* should be devoid of all dentin cracks to a depth of 5 mm occlusally and 3 mm interproximally. Leaving cracked dentin can lead to crack propagation during functional stresses, making it advisable to remove as much compromised dentin as possible without pulp exposure.
9. Reducing onlay cusps to less than 2 mm thickness after removing decayed or cracked dentin, tensile stress converts into compressive stress on the hybrid layer, reducing the risk of debonding.
10. Verticalise occlusal forces to minimize tensile stress on both the restoration and the cervical area of the tooth by re-establishing anterior guidance using bonded composite on the lingual surfaces of maxillary canines and/or facial surfaces of mandibular canines. This strategy, known as the *compression dome concept* (**Figure 3**), transforms destructive lateral tensile forces into vertical compressive forces, which natural teeth are better designed to withstand, thereby enhancing restoration longevity and stability.[14,15]
11. Bond-maximising protocols: [13]

a. Creating a caries-free peripheral seal zone: Ensuring 2–3 mm of caries-free zone around the cavity without exposing the pulp, inside of the PSZ, caries removal in this zone is limited to a depth of 5 mm from the cavo-occlusal surface and 3 mm from the cavo-proximal margin.
b. Applying surface modification methods (*air abrasion, silane etc.)* on composite surfaces for bonding/cementation. These methods enhance adhesion to dentin and eliminate failures in the hybrid layer.
c. Enamel beveling prior to repair: Beveling enamel across enamel rods increases bond strength.
d. Deactivation of Matrix Metalloproteinases (2% chlorhexidine, etc.), helps to preserve 25% to 30% of adhesive bond strength over time. Deactivation is also achieved by *benzalkonium chloride* (e.g., Micro-Prime B by Danville), or a dentin adhesive with the *MPB monomer* (e.g., SE Protect by Kuraray)
e. Gold standard dentin bonding techniques: Proven dentin bonding systems that can achieve microtensile bond strengths of 25–35 MPa on enamel and 40–60 MPa on flat dentin surfaces are recommended. As per studies, Three-step total-etch and two-step self-etch systems offer best clinical outcomes.
f. Applying Immediate Dentin Sealing: enhances microtensile bond strength by up to 400% as the application and polymerization of the dentin bonding agents immediately after tooth preparation (before impression taking) offers significant benefits over conventional methods.
g. Resin coating following Immediate Dentin Sealing: This involves applying a flowable resin or low-viscosity restorative composite with an elastic modulus of roughly 12 GPa, which is same as deep dentin [(13)]. It ensures complete polymerisation of the adhesive system, even in cases of too thin adhesive layer which is compromised by pulpal fluid transudation and the air-inhibited layer. Once light-cured, this coating creates a stable interface, providing a "secure bond". Some dentin adhesives with high filler content and thicker consistency (approx. 80 microns) can also serve a similar function.
h. Elevation of the Sub-gingival box to a Supra-gingival margin: This technique aims to achieve a biomimetic microtensile bond strength > 30 MPa. When combined with IDS, resin coating, and the composite "dentin replacement," this deep margin elevation is known as the "bio-base," forming a highly bonded, stress-reduced foundation for indirect or semi-direct inlays or onlays. *(***Figure 4***)*

2.3. Materials utilised in biomimetic restoration

i. Glass Ionomer Cement (GIC): GIC possesses mechanical properties similar to dentin, along with the additional benefits of adhesion and fluoride release, making it ideal for many restorative situations. However, its relatively poor mechanical properties, limit its use as a final restorative material to low-stress areas, often requiring protection by resin composite or amalgam in high-stress areas.

2. Recent advances in GICs:
    a. Bioactive glass reinforced GICs: The bioactivation of GIC's aims to enhance their mechanical characteristics and are considered bioactive due to chemical bonding with enamel, dentin, and bone via interactions between their polyacid and hydroxyapatite crystals. The original commercial bioactive GIC, like 45S5 or Bioglass, demonstrate antibacterial capabilities, though increased bioactive glass content can decrease compressive strength.[16]
    b. Reinforced GICs (Reactive glass fiber): Studies shows that adding glass fibers can significantly improve fracture toughness and energy release rate.[16]
    c. Hydroxyapatite Reinforced GIC: Incorporation of nano-hydroxyapatite (H.A.) particles enhances mechanical and antibacterial qualities, fluoride ion release, and aids in enamel remineralization.[16]
    d. Silica cement reinforced GIC: SiO2 supplementation aims to increase polysalt bridges in the glass matrix and improves transparency.[17]
    e. Zinc-based GIC: Developed as an alternative to aluminium-containing GICs, as aluminium can promote improper bone mineralisation. Zinc oxide functions same as alumina in the setting process. [17]
    f. Hydroxyapatite and zirconia-reinforced GICs: Zirconium and its oxide are used to reinforce and toughen brittle H.A. bioglass, increasing its hardness up to 5% concentration of nano-zirconia and decreases on further addition. [17]
    g. GIC incorporating Niobium pentoxide: When included in metal alloys, Niobium pentoxide, improves mechanical characteristics and exhibits biocompatibility and bioactivity, though higher niobium content can adversely impact mechanical properties.[18]
    h. Zirconomers: A newer restorative GIC, free of mercury hazard, offering strength and durability comparable to amalgam for high-stress posterior areas. Zirconia fillers of zirconomer provide structural stability, exceptional mechanical qualities, and continuous fluoride protection, making them perfect for the patients with high caries index.[19]
    i. Newer dental ceramics: Dental ceramics are capable of mimicking a tooth's natural appearance,

becoming increasingly popular with advances in computer-based dental technologies and digital workflows.

3. Lithium disilicate (LiDiSi): A recent dental ceramic with an elastic modulus (60-95 GPa) similar to natural enamel (72-125 GPa). It is preferred for larger defects. *(***Figure 5***)*
4. Recent advances:
    a. Bioactive Glass (BAG): used in various applications, including as a bonding and bone regeneration material, air polishing, periodontology, cariology, and desensitising toothpastes. BAG possesses antibacterial properties linked to pH both directly and indirectly.
    b. HX-BGC: is a novel BAG-ceramic available in powder form and contains SiO2-P2O5-CaO-Na2O-SrO, which acts by blocking dentinal tubules to decrease dentin permeability.
5. ORMOCERS (Organically Modified Ceramics): are a new type of packable restorative material. They are made up of inorganic silanated filler particles mixed with organic and inorganic copolymers. Unlike the organic dimethacrylate monomer matrix used in conventional composites, Ormocers, are made up of ceramic polysiloxane, which show less polymerisation shrinkage.[19]
    i. Resin Dental Composites (RDCs): Modern RDCs, with elastic moduli of 13–18 GPa similar to that of natural dentin (14–38 GPa), can effectively substitute dentin and reinforce remaining tooth structure in cases of mild to moderate tooth loss. (**Figure 6**)[20]
6. Recent Advances in RDCs:
    a. Rechargeable composites and adhesives with long term Calcium or Phosphate Ion release: These materials are able to continuously recharge and rerelease Ca and P ions to provide long-term caries inhibition. Furthermore, a rechargeable CaP bonding agent was created demonstrating sustained ion release over multiple cycles.[21]
    b. Antibacterial dental composites and bonding agents: developed to combat bacterial caries. Quaternary ammonium methacrylates (QAMs) and the MDPB (12-methacryloyloxy dodecyl pyridinium bromide) monomer have been incorporated into resin matrices to provide prolonged contact-inhibition against oral bacteria. Clearfil Protect Bond, a commercial product containing MDPB, shows substantial antibacterial activity and can eradicate residual germs from dentinal tubules.[21]
    c. **Cention N:** A recently introduced "alkasite" group restorative material (a subclass of composite resin) that is tooth-coloured and can be used with or without an adhesive. It is self-curing (and can be light-cured), based on UDMA, and contains alkaline glass fillers that are radio-opaque. It is capable of releasing ions such as fluoride, calcium, and hydroxide.[22]

Hence, an ideal restoration is a combination of two different restorative materials, with elastic modulus approximately same as that of natural enamel and dentin.

2.4. Properties of biomimetic restorative materials

2.4.1. Mechanical properties

The clinical efficacy of restorative materials is largely dependent on mechanical properties, particularly elastic modulus (EM) and surface hardness (SH).

2.4.2. Elastic modulus (EM)

The EM of dental restorative materials should ideally harmonise with the hard tissues of the teeth. Some RDCs may be approaching dentin's EM values, while GICs have considerably lower EM values than those of dentin and enamel (**Table 1**). Consequently, GICs are primarily used as luting agents, cavity liners, or for small cavities, especially in deciduous teeth. In contrast, modern indirect restorative materials like dental ceramics (e.g., IPS Emax Press, IPS Emax glass-ceramic) possess EM values (60-95 GPa), hardness and thermal expansion (**Table 1**) similar to enamel, making Ceramic veneers preferred choice for anterior dental damage due to even stress distribution and aesthetic advantages.

2.4.3. Surface hardness (SH)

The SH of restorative materials should closely resemble that of enamel, as restoration surfaces are directly exposed to masticatory stresses and wet conditions. Dentin has an SH of 0.71 to 0.92 GPa, while that of enamel ranges from 2.23 to 7.18 GPa.[23,24] Because of their significantly lower SH compared to dental enamel, RDCs and GICs are more susceptible to surface wear and failure. Dental ceramics, however, have an SH equivalent to or less than that of enamel. They tend to function mechanically better than direct RDCs and GICs, but underlying adhesives' strength and flexibility are also critical factors in reducing masticatory stresses and averting restoration failure.

2.4.4. Adhesive properties

Bonding agents, often known as dental adhesives, are essential for achieving predictable results in biomimetic restorations. A "monoblock" is created when the restorative material and tooth form a perfect connection but no interface allowing functional stress to dissipate through the tooth structure and restoring its ideal mechanical and biological function. Proper selection and use of modern adhesives are essential to seal the interface, prevent long-term sensitivity, pain, bacterial leakage, and pulpal damage. Adhesives significantly contribute to the tooth's ability to withstand functional pressures and preserve natural tooth structure, aligning with the biomimetic goal of tooth conservation by avoiding excessive tooth cutting for mechanical retentive features.

2.4.5. Aesthetic properties

Dental composites have excellent aesthetics addressing concerns such as discolourations, misaligned teeth, and diastemas.[32] Modern RDC kits offer a range of tints and opacities that match the translucency and shades of natural enamel and dentin, allowing for highly aesthetic restorations. Clinical studies confirm excellent colour match of posterior RDC restorations even after 10 to 17 years.[33,34] GICs, however, are generally disregarded for anterior repairs due to their poor aesthetic qualities. Porcelain veneers, a mainstay in cosmetic dentistry since the 1980s, offer minimally invasive preparation and exceptional aesthetics. Indirect porcelain restorations (veneers, crowns, bridges) provide excellent morphological and optical qualities (colour, hue, translucency, fluorescence) closely resembling natural enamel (**Figure 7**) with a range of surface features like pits, fissures and stains to match natural dentition.[35]

Table 1: Modulus of elasticity (MOE) of tooth-colored restorative materials and tooth hard tissues.

Restorative Materials	**Elastic Modulus (GPa)**	**References**
Enamel	72.0–125.0	23
	80.9 ± 6.6	24
Dentin	14.0–38.0	23
	20.5 ± 2.0	24
Resin-Based Dental Composites (RDCs) (Micro hybrid)	18.3 ± 1.2	25
	11.3 ± 0.5	26
Restorative Materials	**Elastic Modulus (GPa)**	**References**
RDC (nano filled)	13.7 ± 0.6	27
	9.4 ± 0.7	27
RDC (hybrid)	6.9 ± 0.5	27
RMGIC	2.1 ± 0.4	28
Conventional GIC	1.8 ± 0.01	29
Dental Ceramics Emax Press	82.3	13
IPS Emax® Press glass-ceramic material	95	30
IPS Emax	60.6 ± 1.6	31

2.4.6. Biocompatibility

A key biological characteristic for the materials used in the oral cavity. The majority of biomimetic restorative materials currently available in the market are biocompatible, e.g. RDC. Usage tests of GICs showed mild pulp reactions and little to no inflammatory response that too after four weeks. Dental porcelains, on the other hand, are highly biocompatible and bioinert, demonstrating incredible durability and insolubility without triggering any negative biological reactions. Scientific literature generally highlights minimal biological adverse effects of dental ceramics compared to direct restorative materials.[36,38]

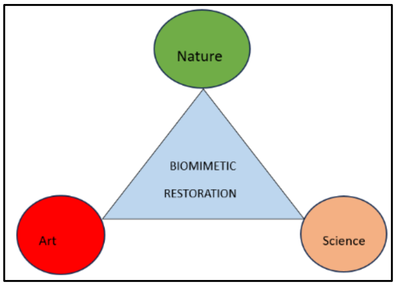

Figure 1: Triad of biomimetic restoration

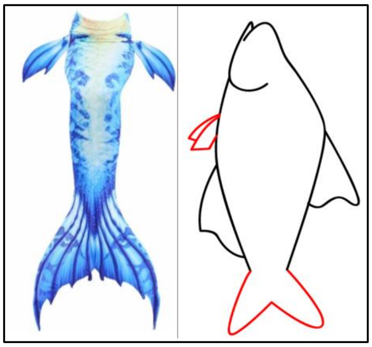

Figure 2: Diagram depicting swimsuits design inspired by fish fins

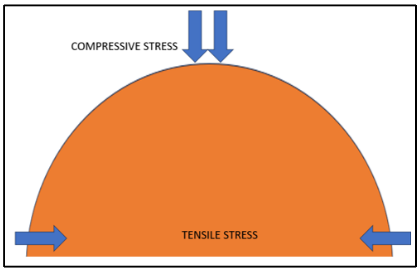

Figure 3: Depicting compression dome concept

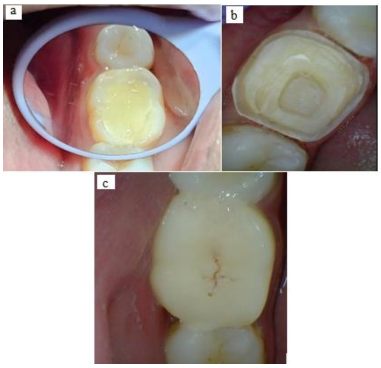

Figure 4: A,B,C depicting Placement of preparation margins more occlusally to reduce tensile stresses. **A:** Large defective restoration on Mandibular molar; **B:** Tooth Preparation for endocrown; **C:** Endocrown on mandibular molar

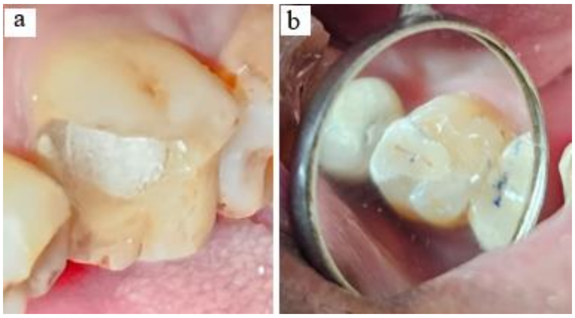

Figure 5: a: Large defect on molar; **b:** Corrected using LiDiSi inlay

Figure 6: Class IV restorations with angle build up using composite resin

Figure 7: Aesthetic rehabilitation of tooth no. 11 by indirect LiDiSi Veneer and 21 by resin dental composites (RDC)

2.5. Clinical approaches and techniques in biomimetic dentistry

The primary goal of biomimetic restorative dentistry is to restore the biomechanics of the original tooth, thereby optimising the function of hard tissues (cementum, dentin, and enamel). This approach aims to preserve the tooth's morphology, biology, and ability to act as a cohesive unit against functional stresses.

1. Caries Removal Protocols:[39] Biomimetic principles guide caries removal to preserve healthy dentin. Researchers differentiate between two layers of caries:
2. Infected dentin (outer layer): It is highly infected, acidic and demineralised, can be removed without anaesthesia as the collagen framework cannot remineralise.
3. Affected dentin (inner layer): It is slightly infected and partially demineralised, sensitive to removal without anaesthesia, as collagen fibrils remain intact and can remineralise.

Selective caries removal [40] is a minimally invasive technique that removes infected dentin while preserving affected dentin for remineralisation. It preserves remineralisable dentinal structure and primary odontoblasts that form tertiary dentin, reducing cariogenic bacterial load near the pulp and extends tooth life. The main challenge lies in clinically distinguishing carious dentin and deciding the extent of removal.

2.6. Technology that guides us to determine caries removal endpoint and the peripheral seal zone:[41]

1. DIAGNOdent: determines the number of bacteria in a caries lesion by reading bacterial products called porphyrins.
2. Caries detector dye (CDD): helps distinguish between affected and infected areas by staining them differently based on molecular weight.
3. Combining DIAGNOdent and CDD: Can create a bacteria-free lesion without removing affected dentin in the peripheral zone.
4. Anatomical measurement using perioprobe: aids in predictable caries removal within the peripheral seal zone by excavating the outer carious red zone. Excavation should stop near the pulp (> 5 mm from the occlusal surface or > 3 mm from the DEJ) and the CDD still stains red, to prevent pulp exposure.

The peripheral seal zone (PSZ) is a 2-3mm wide circumferential, caries-free area around pulp horns. Its main benefits are pulp preservation in deep caries cases, creation of a bondable surface for restorations, and reducing the need for root canal treatments.

2.7. Step-by-step technique to achieve caries end point and PSZ:[42]

1. The pulp vitality test is done using endo ice, if the response is positive, caries removal is done; if negative or no response, inform the patient of root canal treatment.
2. Anesthetise and then isolate the tooth with a rubber dam.
3. Access the carious lesion after removing any failed restoration.
4. Stain with red CDD, wait for 10 seconds, then rinse.
5. Starting near the DEJ, use 1mm round diamond bur to create the PSZ, removing red-stained outer caries and pink-stained inner caries.
6. Repeat staining and removal until the caries removal end point in PSZ is stain-free.
7. After removing red areas and leaving pink areas between pulp horns, evaluate pink areas with DIAGNOdent to confirm a bacteria-free PSZ.
8. If tissues in deep pulp horns still stain red and the perioprobe indicates depth within 5mm from the occlusal surface or 3mm from the DEJ, stop excavation to prevent pulp exposure.

2.8. Clinical applications

Restoration techniques typically involve different restorative materials according to the degree of tooth damage and desired aesthetics. For example, most dental ceramics and hybrid RDCs can mimic enamel and dentin, respectively. RDCs are typically proposed for teeth with moderate damage, as they require less tooth preparation, reducing the chance of pulpal involvement and fracture, and can reinforce remaining tooth structure in low-configuration factor defects. Bonded porcelain restorations are advised for severe tooth damage, such as wear or fractures. Alumina ceramics offer high compressive strength, good wear behaviour, and strong fracture resistance.[17,42] GICs, being antibacterial and biomimetic are used in pedodontia for deep class I or II cavities and for class V cavity restoration. However, their low tensile strength generally contraindicates their use in load-bearing posterior dentition.[42]

2.9. Biomimetic mineralization of enamel and dentin: A current approach

Biomimetic mineralization imitates the natural mechanics of tooth mineralization. The synthesis of enamel-like apatite structures using biomimetic techniques in physiological settings is considered a promising restorative alternative. Positive results have been documented with proteins and protein analogues, glycerin-enriched gelatin, bioactive ingredients, ethylenediaminetetraaceticsacid, and agarose hydrogel models for enamel biomimetic mineralisation.[43]

In dentin, several systematic studies describe approaches like using bioactive materials and non-collagenous protein (NCP) analogues for biomimetic mineralisation of dentin, showing effectiveness in intrafibrillar and interfibrillar remineralisation of dentin collagen fibrils.[44]

1. Recent Studies on Enamel Biomimetic Remineralisation Systems: While clinical trials are ongoing, various combinations of biomimetic systems, primarily ACP (Amorphous Calcium and Phosphate)-based systems, have shown promise in treating caries lesions:
2. Electrospun hydrogel mat of ACP/PVP (poly (vinyl pyrrolidone)) nanofibers: facilitates in situ transformation of spherical ACP into a continuous layer of crystalline fluoride hydroxyapatite (approx. 500 nm thick) on the enamel surface.[45]
3. Nano-sized HAP (Hydroxyapatite) particles (20 nm): Strongly adsorbed to enamel, they reinforce acid-etched enamel surfaces and repair initial submicrometer erosions.[46]
4. Anionic peptide P11-4: This self-assembling peptide (Ace-Gln-Gln-Arg-Phe-Glu-Trp-Glu-Phe-Glu-Gln-Gln-NH2) supports de novo mineralisation and nucleates hydroxyapatite similar to natural enamel formation. It forms scaffold-like structures with negative charge domains mimicking biological macromolecules. Single application to class V lesions showed improvement persisting for 180 days.[47]
5. Anionic OPA (oligopeptide amphiphilic) (C18H35O-Thr-Lys-Arg-Glu-Glu-Val-Asp): Synthesised by Li et al. to initiate hydroxyapatite nucleation and encourage biomimetic mineralisation of demineralised enamel, with apatite crystals developing on etched enamel after treatment.[48]
6. 8DSS peptide: Research demonstrates that this eight-repetition aspartate-serine-serine peptide enhances demineralised enamel surface characteristics and promotes mineral deposition. It led to higher mineral content, improved mechanical qualities (hardness, elastic modulus), and uniform nanocrystallisation of calcium phosphate carbonate, reducing surface roughness.
7. PAMAM-based dendrimers: Poly (amidoamine) (PAMAM) and phosphate-terminated dendrimers (PAMAM-PO3H2) restore mineral density to acid-etched human dental enamel. Alendronate-conjugated PAMAM dendrimer (ALN-PAMAM-COOH) induces in situ remineralisation of enamel due to its HA-anchoring and remineralisation capacity.[50]
8. Amelogenin-releasing agar hydrogel: Repeated application of this hydrogel, containing calcium, phosphate, and fluoride, to etched enamel in multispecies oral biofilm models demonstrated steady increases in enamel hardness.[45]
9. CS-AMEL hydrogel: A novel amelogenin-containing chitosan hydrogel that significantly enhances in situ regrowth of apatite crystals and creates a strong enamel–restoration interface, both of which are critical for longevity of restorations. Amelogenin assemblies within the hydrogel stabilise Ca–P clusters, organising them into linear chains that fuse with enamel crystals to form co-aligned, enamel-like crystals with antibacterial properties from chitosan.[51]
10. Leucine-rich amelogenin peptide (LRAP): By promoting the selective linear formation of enamel crystals along the c-axis, this 59-residue splice version of amelogenin exhibits promise for biomimetic dental enamel regeneration. It stabilises ACP and guides its transformation into well-organised bundles of apatite crystals.[52]
11. Chitosan-based systems: a) Hybrid synthetic chitosan (C.S.) systems induce morphological changes in HAP. C.S. macromolecules act as a matrix for the ordered embedding of amelogenin-HAP nanocrystals.
    a. HAP@ACP core-shell nanoparticles, guided by glycine, promote organised, oriented mineral crystal bundles. Amelogenin-guided chimaeric peptide-mediated nanocomplexes of carboxymethyl chitosan/amorphous calcium phosphate (CMC/ACP) can crystallise into enamel-like particles with great mechanical qualities.[53-55]
12. Other enamel biomimetic systems: Include agarose hydrogel, glycerine-enriched gelatin, and CS-EMD hydrogel. Fluoride-substituted hydroxyapatite microcrystals with ordered enamel-like structures have been formed using CS-HAP on human enamel with EDTA as a mediating agent.[56]

2.10. Recent studies on dentin biomimetic remineralisation

Polymer-induced liquid-precursor (PILP) approach developed by Gower et al. [57], this approach relies on process-directing agents that create nanodroplets rich in calcium phosphate ions. These nanodroplets release ions into collagen fibrils, promoting amorphous calcium phosphate development that crystallises into dentin-like, orientated apatite crystals. The following are the biomimetic systems available in the market:

2.10.1. Resin doped with calcium phosphate microfillers and carboxymethyl chitosan (CMC-CAP)

These resins enhance bonding endurance and encourage biomimetic remineralisation of caries-damaged dentin by promoting quick and thorough intrafibrillar crystallisation. CMC's capacity to stabilise and guide mineralisation precursors is exceptional, leading to a stronger resin-dentin connection.[58]

2.10.2. PAMAM and rechargeable composite with amorphous calcium phosphate nanoparticles

Restored pre-demineralised dentin hardness to that of healthy dentin, leading to full dentin remineralisation, likely due to enhanced nucleation templates, Ca and P ion recharge/rerelease, and acid neutralization.[59]

1. Collagen cross-linking with glutaraldehyde: Has the potential to stimulate dentin biomimetic remineralisation, enhancing mechanical and biostable characteristics. The aldehyde group binds calcium and cross-links collagen, providing nucleation sites for calcium phosphate crystals.[60]
2. Modification of self-etch adhesive: with carriers loaded with polyaspartic acid Si-ACP particles, experimental primers with biomimetic analogues, and adhesives containing ion-releasing components like polydopamine, CPP-ACP, BAG, CaSi, ZnO, CaP have shown potential in reducing collagen degradation and encouraging mineral precipitation within the hybrid layer.[61]

2.10.3. Biomimetic principles applied to cosmetic dentistry

In cosmetic dentistry, the biomimetic approach assumes that an undamaged tooth's optimal colour, tone, intracoronal architecture, mechanics, and arch position serve as a guide for reconstruction. This field is rapidly evolving with "smart materials," which are seen as the future of biomimetic restorative dentistry.

2.10.4. Smart materials

Smart materials can detect and react to changes in their surroundings (stress, temperature, moisture, pH) and revert to their initial state after stimulus removal. There are two types of smart materials:

1. Passive smart materials: Release ions in response to external changes, e.g., GIC, Compomer. Smart GIC can exhibit thermal expansion or contraction in response to thermal stimuli.
2. Active smart materials: Take action in response to risky environmental variations, e.g., smart composites and smart GIC. In 1998, ion-releasing composite material was introduced by Ariston PHC (also known as Smart Composites) which marked a new technique in restorative dentistry. These light-activated, nanofilled healing substances contain amorphous calcium phosphate as a filler, releasing hydroxyl, fluoride, and calcium ions when pH drops below 5.5. These ions are deposited as apatite crystals, similar to seen in teeth and bone.[62]
3. Giomer: is a composite resin and glass ionomer hybrid. Pre-Reacted Glass Ionomer (PRG) technology is used in it, creating a stable glass-ionomer phase floating in a resin matrix. The high degree of fluoride release and giomer recharging is attributed to the presence of pre-reacted hydrogel.
4. Ceromers: Combines composite resin technology with ceramic benefits. The ceramic (inorganic phase) provides aesthetics, abrasion resistance, and stability, while the resin (organic phase) improves polishability, bonding to luting resin, low brittleness, and decreased fracture susceptibility.[63]
5. Compomers: Contain fluoride compounds that, in the presence of moisture or acidic environments, can release free fluoride

2.11. Limitations and challenges in biomimetic dentistry

2.11.1. Cost

BRD often incurs higher costs due to advanced materials and technologies that mimic natural tooth anatomy, morphology, and function. While these materials provide superior results and preserve tooth function, their cost is a challenge for economically challenged patients, leading them to use of less effective but more affordable conventional treatments. This need to adopt recent but costly procedures, coupled with the expense of materials, practitioner expertise, and geographic location (especially in urban clinics), can lead to financial strain, increased patient anxiety, and reduced confidence in dental services.

2.11.2. Training

Adopting BRD requires specialised training beyond traditional dental education, significantly influencing treatment choices. Dentists trained in biomimetic techniques prioritise conservative restorations like bonding and fiber reinforcement over full-coverage crowns. This approach preserves dentin, minimises tooth structure reduction, and strengthens the dentin-resin bond, particularly for endodontically treated teeth. Biomimetic procedures allow for future restorability, unlike full-coverage crowns that impair remaining tooth volume, even if they may produce restorations with failure rates comparable to full-coverage crowns. Among experienced dentists, biomimetic training is still less common while newly graduated dentists choose full-coverage restorations due to a lack of thorough exposure to partial coverage therapies (inlays, onlays), as this is a technique-sensitive procedure.

2.11.3. Accessibility

The adoption of BRD is constrained by the high expense of specialised training and advanced technologies, particularly in rural areas or resource-constrained practices. While advancements like digital workflows (like CAD/CAM and 3D printing) and innovative materials (e.g. zirconia ceramics and nano-filled composites) have improved patient outcomes, efficiency, and aesthetics by providing same-day restorations adding to patient's convenience, their high cost and training requirements remain barriers to its widespread usage. Similarly, laser technology, offers precision and a quicker recovery. To make them more affordable, available, and incorporated into routine procedures, extensive research and development are required with proper implementation.

2.12. Limitations of protocols in BRD (41)

2.12.1. Establishing a caries-free peripheral seal zone

BRD aims to preserve a softened dentin layer near the pulp. However, the use of caries-detecting dyes often leads to excessive removal of demineralised tissue, increasing the risk of pulp exposure, especially in deep cavities, which contradicts BRD's minimally invasive principles. Consequently, the visual-tactile approach is preferred for deep cavities to strike a balance between conservation and efficient caries eradication.

2.12.2. Aluminium oxide air abrasion

Extensively used in BRD for cleaning cavity surfaces, removing residues, and improving bonding via micromechanical retention. A comprehensive analysis suggests that it does not outperform alternatives like no treatment, bur preparation, or acid etching in terms of bond strength, with laboratory tests yielding inconsistent findings. Therefore, more research is needed to determine optimal air abrasion parameters and assess its clinical advantages through randomised controlled trials.

2.12.3. Bevel enamel in posterior restorations

BRD recommends a 45° bevel in proximal boxes to align with enamel prisms and enhance bonding, and a mini bevel for occlusal margins to improve bonding, aesthetics, marginal adaptation, and remove weakened enamel. However, the use of enamel beveling in occlusal cavities has decreased since the 1990s, and microleakage tests have been criticized stating no advantages of beveling over butt joint preparations.

2.12.4. Deactivate matrix metalloproteinases (MMPs)

Laboratory research suggests that chlorhexidine (CHX) applied to acid-etched dentin may reduce bond strength (BS) by blocking MMPs, which degrade collagen in the hybrid layer. Nevertheless, clinical trials with follow-up periods of up to three years, revealed no appreciable variations in restoration lifespan or retention rates in non-carious cervical lesions treated with or without CHX.

2.12.5. Immediate dentin sealing (IDS) and resin coating

IDS and delayed dentin sealing produce almost similar results in terms of the post-operative sensitivity or longevity of indirect restorations, as per recent RCTs and Systematic Reviews.

2.12.6. Decouple with time (DWT)

This protocol is based on the idea that composite shrinks towards mineralised, dry walls and away from moist, organic ones due to the "hierarchy of bondability". However, a literature review found no strong scientific evidence (RCTs) supporting this concept. This protocol appears unrealistic in clinical practice and lacks strong scientific backing; it should not be recommended without RCT validation.

2.12.7. Place fiber inserts on pulpal floor and/or axial walls to minimise stress

BRD promotes fiber-reinforced composites (e.g., EverX and Ribbond) to reduce polymerisation shrinkage stress and improve fracture resistance in restoring severely compromised teeth. However, no clinical trials have compared fiber-reinforced composites with traditional alternatives like fiber posts or endocrowns.

3. Conclusion

The field of biomimetic restorations has witnessed significant progress and continues to evolve beneficially. With the correct knowledge and application of available resources—materials, technology, and protocols—promising outcomes can be achieved, benefiting both the patient and the restorative dentist.

The future of restorative dentistry should encourage the regeneration of dental tissues and enable their self-healing rather than relying on inert materials that only covers cavity preparations. While the most biomimetic methods for remineralising enamel and dentin are supported by preliminary laboratory data, their clinical application holds immense promise for restorative dentistry. Significant advancements in the restorative area are anticipated with the development of novel biomimetic processes for dentin adhesion, integration, and sealing. Extensive research is focused on creating new materials or modifying existing ones to produce biomimetic restorative biomaterials.

Numerous processing technologies, including nanotechnology, advanced manufacturing techniques, and biomaterial functionalisation, have been investigated. Over the past decade, substantial breakthroughs have been made in the qualities of biomimetic restorative materials that mimic natural tissues. However, the development of biomimetic restorative materials is still in its early stages. Comparably, Biomimetic tissue engineering has grown exponentially in the last decade, transitioning from a theoretical phase to a rapidly evolving subject; nonetheless, more research is essential to convert these advancements into practical clinical applications.

Given the significant obstacles that researchers and clinicians must overcome, it might take over a decade before biomimetic materials become a part of our daily dental practice. Breakthroughs in genetics, molecular biology, cell biology, and materials science are expected to make new alternative therapy modalities accessible for clinical use. These approaches will likely regulate the soft tissues of periodontium, regenerate dentin, enamel, and pulp, and perform restorative treatments, demonstrating in the near future, how biological regeneration reinforces and completes the tooth structure.

There is also great potential for the development and application of intelligent, biomimetically driven dental restoratives from laboratory to clinical dentistry. However, further research would be necessary to understand the molecular and metabolic processes behind biomineralisation. Potential applications for novel biomaterials include intrinsically disordered proteins, creative biomimetic cell-free templates, and effective peptide-based remineralisation techniques. Furthermore, more research is required to determine the precise roles of various chemicals and biomimetic agents in tooth tissue regeneration.

However, a lot of multidisciplinary research effort is being done to create biomimetic materials, with the ultimate goal of achieving fully regenerated dental tissues (pulp, cementum, dentin, and enamel) that possess mechanical, biological, and mineralised nanostructural characteristics similar to those of natural tooth tissues.

4. Author Contribution

1. Dr Zoya Kidwai: Writing – original draft.
2. Promila Verma: Supervision.
3. Dr Rhythm Bains: Validation, Writing – review editing.

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6. Conflict of Interest

None.

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