

## Biomimetics in dentistry – a review

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### ABSTRACT

Otto Schmitt in the 1950's coined the term "Biomimetics" while studying the nerves in a squid. He tried to copy and design an artificial device that could replicate the same process of synaptic impulse. It literally means to mimic life. It is the study of natural structural processes to try to mimic or replicate it artificially in an attempt to restore the same aesthetics or function.

Age, disease and traditional restorations can cause further problems to the existing tooth structure. As teeth do not have natural method of repair, biomimetic principles should be used to artificially repair the tooth to its natural functions and aesthetics. In biomimetic dentistry there are two aspects. One, the lost or missing dental tissue is restored, leading to the full return of function and aesthetics to the tooth. Or the material used can regenerate, replicate or mimic the missing dental tissue. This review will attempt to provide a better understanding of the relative position of the biomimetic materials in the context of the past and present dental materials.

**Key words:** Biomimetic material, Regeneration, Mineralization, Hydrogel, Peptides

### INTRODUCTION

Biomimetics is defined as the study of the formation, structure, or function of biologically produced substances and materials and biological mechanisms and processes especially for the purpose of synthesizing similar products by artificial mechanisms which mimic natural ones. A material fabricated by biomimetic technique based on natural process found in biological systems is called a biomimetic material (Kottoor, 2013).

The main principle of biomimetics is to return all prepared dental tissues to full function by a hard-tissue bond that allows functional stresses to allowing the entire crown to its final functional biologic and esthetic result (McMahon and Evron, 2011).

In dentistry there is no one biomaterial that has the same, mechanical, physical and optical properties as tooth structure (i.e., dentin, enamel, and cementum) and possesses the physiological characteristics of intact teeth in function. By using biomimetic therapeutic approaches, dental professionals can improve and become closer to natural biological structures and their function. There are two major perspectives to which the term "biomimetic" is applied: a purist perspective that focuses on recreating biological tissues and a descriptive perspective that focuses on using materials that result in a mimicked biological effect. Although different, both share a common goal of mimicking biology in restoration. A biomimetic material should match the part of the tooth that it's replacing in several ways, including the modulus of elasticity and function of the respective areas (e.g., pulp, dentin, enamel, dentoenamel junction). This review will attempt to

provide a better understanding of the relative position of the biomimetic materials in the context of the past and present dental materials.

**Biomimetics in restorative dentistry:** The physiological performance of intact teeth is the result of intimate and balanced relationships between mechanical, biological, functional and esthetic parameters. Natural teeth, through the superlative combination of enamel and dentin, make up the perfect and unmatched compromise between strength, rigidity and resilience (Magne and Belser, 2002).

Therefore a biomimetic approach to restorative dentistry would mean esthetic and functional restorative materials similar to the natural tooth and its individual layers of dentine and enamel. In 2006 Magne said "The goal of Biomimetics in restorative dentistry is to return all of the prepared dental tissues to full function by the creation of a hard tissue bond that allows functional stresses to pass through the tooth, making the entire crown into the final functional biologic and esthetic unit. The intact tooth in its ideal hues and shades, and more importantly in its intracoronary anatomy, location and mechanics in the arch, is the guide to reconstruction that determines success" (Magne, 2006).

### MATERIALS AND METHODS

We are aware that there may be some regeneration or stimulation of dentine with certain dental materials. There are also materials that can actually remineralise acid etched dentin. These materials would be classified as being "biomimetic". Other biomimetic materials are materials which are

used to restore the tooth which closely mimic enamel  
 The tooth structure itself is used as a guide to reconstruct the diseased or missing parts to its original strengths and properties. Adhesive bonding agents,

and dentin (Tay and Pashley, 2008).  
 glass ionomers, composites and ceramics are used to reconstruct and replicate these features in a natural tooth.

**Table.1.Shows the similarity of these artificial materials to natural tooth substance: Physical Properties of Dental Hard Tissues and corresponding Biomaterials (Magne, 2006)**

	Elastic Modulus (GPa)	Thermal Expansion Coefficient (x 10 <sup>-6</sup> /°C)	Ultimate Tensile Strength (MPa)		Corresponding Material	Elastic Modulus (GPa)	Thermal expansion Coefficient (x10 <sup>-6</sup> /°C)	Ultimate Tensile Strength (MPa)
Enamel	82	17	10	→	Feldspathic ceramics	60-70	13-16	25-40
Dentin	14	11	40-105	→	Hybrid Composites	10-20	20-40	40-60
				→	Glass-ionomer Cements	4-10	35	4-5

From the table we can see that feldspathic ceramics are the closest to mimic enamel and hybrid composites are the closest to mimic dentin. However it has been also advised to use composites for small loss in tooth tissue and Glass ionomer cements as a base layer (van Dijken, 1994).

Composites resins are now displaying favorable properties and longevity on par to amalgam. The technique involves minimal preparation decreasing pulpal involvement and decreasing the prognosis of fractures. Therefore it preserves tooth vitality and substance. According to some authors composite can actually strengthen the remaining tooth structure when placed well within reduced c-factors and shrinkage (Morin, 1984).

Glass Ionomer Cements (GIC) is considered to be useful in deep class I or II cavities to fill up the base as lining material (Magne, 2006). They are also useful as buccal class V cavities. Composites can then be bonded over as a closed sandwich technique. GIC releases fluoride, is bactericidal, stimulates sclerotic dentin and also has properties similar to dentin. As such would fit the definition of biomimetic (Ngo, 2002). However as their tensile strength is poor they are not advocated in use of high occlusal stress and force. Biodentin is a new material that may replace GIC as a liner in deep fillings, but further research is needed. GIC is currently being the main material for advocates of minimum invasive dentistry which is under the umbrella of biomimetic restorative dentistry (Mount and Ngo, 2000).

**Biomimetics endodontics:** A biomimetic approach to restore tooth structure is based on regenerative endodontic procedures by application of tissue engineering which is new arena for the practioner. The

most important elements of tissue engineering are stem cells, a scaffold of extracellular matrix and morphogen (Craig, 2007).

**Biomimetic approaches for regeneration:**

**a. Stem cell therapy:** The simplest method to administer cells of appropriate regenerative potential is to inject the postnatal stem cells into the disinfected root canal system. Among the eight different post natal dental stem cells Stem cells from human exfoliated deciduous teeth (SHED), Dental pulp stem cells (DPSCs) and Stem cells from the apical papilla (SCAP) were more commonly used in the field of regenerative endodontics (Garcia and Murray, 2006).

DPSCs are the stem cells isolated from human dental pulp. The most important feature of DPSCs is their ability to regenerate a dentin-pulp-like complex that is composed of mineralized matrix with tubules lined with odontoblasts and fibrous tissue containing blood vessels arranged as that of dentin-pulp complex found in normal human teeth (Gronthos, 2002).

Stem cells from human exfoliated deciduous teeth (SHED) have become a captivative alternative for dental tissue engineering. The use of SHED for tissue engineering is more advantageous than the use of stem cells from adult human teeth because: (a) SHED have higher proliferation rate compared with stem cells from permanent teeth, which might allow the expansion of these cells in vitro before replantation. (b) SHED cells are taken from exfoliated deciduous teeth that is "disposable" and readily accessible in young patients. It also has an advantage of painless stem cell collection with minimal invasion and abundant cell supply (Miura, 2003).

A recent finding is the presence of a mesenchymal stem cells residing in the apical papilla of incompletely developed teeth. They are called stem cells from the apical papilla (SCAP). It is hypothesized that DPSCs are likely the source of replacement odontoblast cells, whereas SCAP appear to be the source of primary odontoblast cells that are responsible for the formation of root dentin (Bakopoulou, 2011). These cells are able to survive even during the process of pulp necrosis, as these cells are present in apical papilla which has collateral circulation.

**b. Pulpal implantation:** In pulp implantation, pulp tissue is produced by tissue engineering triad and is transplanted into cleaned and shaped root canal system. Rebecca *et al* had developed Dental pulp like tissue by using the tissue engineering triad, the Dental Pulp Stem Cells (DPSCs), Dentin Matrix protein 1 and a Collagen Scaffold, after subcutaneous transplantation in mice. Collagen was the scaffold, and dentin matrix protein 1 (DMP1) was the growth factor. The result concluded that the tissue engineering triad of DPSCs, DMP1 and a collagen scaffold, can induce an organized matrix formation similar to that of pulp tissue, which might lead to hard tissue formation (Prescott, 2008).

**c. Injectable scaffold delivery:** This procedure will allow tissue engineered pulp tissue to be administered in a soft three-dimensional scaffold matrix. Among the injectable biomaterials investigated so far, hydrogels are more attractive in the field of tissue engineering. Hydrogels are injectable scaffolds that can be delivered by syringe and are noninvasive and easy to deliver into root canal systems. In theory it is stated the hydrogel may promote pulp regeneration by providing a substrate for cell proliferation and differentiation into an organized tissue structure. Earlier hydrogels had limited control over tissue formation and development, but recent advances in formulation have dramatically improved their ability to support cell survival (Desgrandchamps, 2000).

**d. Gene Therapy:** Gene therapy is a method of delivering genes with the help of viral or non-viral vectors. The gene delivery in endodontics would be to deliver mineralizing genes into pulp tissue to promote tissue mineralization. Viral vectors are genetically altered to eliminate ability of causing disease, without losing infectious capacity to the cell. At present adenoviral, retroviral, adeno associated virus, herpes simplex virus, lentivirus are being developed. Nonviral delivery systems use plasmids, peptides, cationic liposomes, DNA-ligand complex, gene guns, electroporation, and sonoporation to address safety

concerns such as immunogenicity and mutagenesis (Roemer and Friedmann, 1992).

**e. Bioengineered tooth:** Research on whole tooth regeneration is also advancing using a strategy of transplanting artificial tooth germ and allowing it to develop in the adult oral environment.

Ikeda *et al* reported a fully functioning tooth replacement achieved by transplantation of a bioengineered tooth germ into the alveolar bone of a lost tooth region in an adult mouse (Ikeda, 2009). Bioengineered tooth, which was erupted had the correct tooth structure, hardness of mineralized tissues for mastication. However, the bioengineered tooth was smaller than the other normal teeth. In addition, the authors could not regulate the cusp position, crown width, and tooth patterning including anterior/posterior and buccal/lingual structures. However, in a more recent study Oshima *et al* showed that the crown widths and the cusp numbers of bioengineered molar could be regulated by cell manipulation method (Oshima, 2011). Tooth regeneration is an important stepping stone in the establishment of engineered organ transplantation, which is one of the eventual goals of regenerative therapy.

**Biomimetic mineralization:** A recently introduced technique of guided formation of an enamel-like fluorapatite layer on a mineral substrate has the potential to enable remineralization of superficial enamel defects and/or exposed dentin. The technique, BIMIN, utilizes the diffusion of calcium ions from solution into a glycerine enriched gelatin gel that contains phosphate and fluoride ions (Bush, 2004). When the conditioned gel is in direct contact with the exposed tooth surface, within 8 h, a firmly adhering mineral layer is formed on the tooth surface (Busch, 2004). Applying BIMIN in a clinical feasibility study, a deposition of fluorapatite mineral on dental enamel was recently demonstrated (Guentsch, 2010).

Dentin is a mineralized tissue consisting of apatite (the mineral phase), collagen and other proteins, and water (Perdigao, 2010). Remineralization of dentin can occur either by simple precipitation of calcium phosphates into the loose demineralized dentin matrix between collagen fibrils (net remineralization), or by the chemical tight association of mineral to the dentin matrix structure (functional remineralization) (Gandolfi *et al.*, 2011). By and large, the sequences of amino acids in collagen and acid-hydrolyzed gelatin are identical. Phosphate ions of the apatite surface should be attracted to the positively charged N-terminal end of the peptides. The peptides originating from the gelatin of BIMIN may orient perpendicular to

the substrate and parallel to each other. Polar regions on the molecules attract ions, which mineralize to apatite, template by the ordered gelatin. This leads to the growth of fluorapatite crystals perpendicular to the surface. The long axis of the apatite crystals and gelatin peptides preferentially orient themselves parallel to each other (Busch et al., 2003). Thus the introduced experimental biomaterial may lead to (at least superficial) functional remineralization in existing dentin structures, with an additional mineralization of an enamel-like fluorapatite layer.

Biomimetic remineralization of dentin has been investigated with different methods using ion-containing solutions or ion leaching silicon-containing materials. Gandolfi et al. recently reported the use of bioactive “smart” composites containing reactive calcium-silicate. Ning et al. in 2011 introduced an experimental method for biomimetic mineralization of hydroxyapatite. They used agarose gel containing Na<sub>2</sub>HPO<sub>4</sub> that covered an acid-etched dentin sample. Comparable to a sandwich-technique, the gel was then covered by a layer of agarose without phosphate ions, masked by a CaCl<sub>2</sub> solution. The system was immersed in a water bath at 37 °C, replenished on multiple occasions, and resulted in densely packed hydroxyapatite crystals that covered the dentin surface and occluded the dentinal tubules after 10 days of biomimetic mineralization.

**Biomimetic self-assembling peptides:** P11-4 is a rationally-designed self-assembling peptide. Self-assembling peptides undergo well-characterized hierarchical self-assembly into three-dimensional fibrillar scaffolds in response to specific environmental triggers, offering a new generation of well-defined biopolymers with a range of potential applications (Brunton et al., 2013).

P11-4 switches from a low viscosity isotropic liquid to an elastomeric nematic gel at pH <7.4 and in the presence of cations, conditions assumed to be found within a caries lesion. In a number of *in vivo* and *in vitro* experiments, the assembled P11-4 fibres were shown to be highly biocompatible with low immunogenicity. Following P11-4 self-assembly, the anionic groups of the P11-4 side chains would attract Ca<sup>++</sup> ions, inducing *de novo* precipitation of hydroxyapatite (Brunton et al., 2013).

The earliest clinical sign of enamel caries is the appearance of a ‘white spot’ lesion on the tooth surface. At this stage, clinicians generally elect to monitor lesion appearance, possibly after the use of topical fluorides, to determine whether the lesion will progress or not, in which case a restoration would then

be placed. Non-surgical intervention promoting defect biomineralization or regeneration at the white spot lesion stage would remove the need to ‘wait and see’ and avoid the ultimate excavation of the tooth to place a restoration (Brunton et al., 2013).

Infiltration of early (‘white spot’) caries lesions using low viscosity monomeric P11-4 would result in triggered self-assembly within the lesion, generating a subsurface bioactive scaffold capable of recapitulating normal histogenesis by inducing mineral deposition *in situ*.

Peptide treatment significantly increased net mineral gain due to a combined effect of increased mineral gain and inhibition of mineral loss (Brunton et al., 2013).

## CONCLUSION

Replacement of diseased or lost tooth structure with biocompatible restorative materials is currently the technique of today but each of these procedures has their own limitations and drawbacks. Regeneration of the lost tooth structure rather than replacement will ensure better prognosis and high success rate. Hence the future dentistry would involve the use of biomimetic materials which could successfully replace lost enamel, dentin, cementum and even the pulp tissue.

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