Biomimicry: "The Nature Inspired Way" in Restorative Dentistry

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Abstract: ***Gathering inspiration from nature for the design of newer materials and products is a field gaining popularity nowadays .The ability to incorporate the "doing it nature's way" into the design of synthetic materials has advanced with time. There has been an increased interest among the scientific community to design systems that borrow the nature's mode. In a society familiar with dominating or improving nature, this respectful imitation introduces an era of science based not on what we can extract from nature, but on what we can learn from her . Broadly categorized as biomaterials, these are widely used in the field of Restorative dentistry because of its role in repair, regeneration and reconstruction. This review article highlights the concept of bio activity, its mechanism and compare and contrast various bio active materials.***

Keywords: Biomaterial, Biomimetic, Bioactive, Glass ionomer cement, Resin Dental composite

1. Introduction

The evolution of dentistry is closelyassociated with the advancements in dental materials.Nanotechnology aided in processing variety of nano structured materials with the complex arrangement of organic or inorganic molecular level constituents, simulating living tooth structure, allowing for innovative dental applications. As an expansion of nanotechnology applied to dental materials: the terms bioactive, bioinduction, and biomimetics are often defined separately [1], [2].

Biomaterial can be simply defined as a synthetic material used to replace part of a living system or to function in intimate contact with living tissue.Bioactive material is defined as a material that has the effect on or eliciting a response from living tissue, organism or cell such as inducing the formation of hydroxyapatite. Hench introduced some criteria for the evaluation of bioactivity of a material. Accordingly, a new classification was proposed in 1994, in which bioactive materials are divided into 2 groups [3]:

- **Class A**

This group consists of materials, which induce both intracellular and extracellular responses.They are not only able to bond to bone, but also bind to the soft tissues.
eg:45S5 Bioglass.

- **Class B**

These materials are osteoconductive and induce only extracellular responses.
eg. Synthetic hydroxyapatite implants.

The bioinductive property is the capability of a material for initiating a response in a biological system. Biomimetics is the study of formation, structure or function of biologically produced substances and materials (such as silk or conch shells) and biological mechanisms and processes (such as protein synthesis or mineralisation) for the purpose of synthesizing similar products by artificial mechanisms that mimic natural structures [4] (Websters Dictionary-1974). Biomimetics, (bios meaning life, mimesis meaning imitate) a name coined by Otto Schmitt in the 1950s for the transfer of ideas and analogues from biology to technology. Biomimetic dentistry is the practice of dentistry which applies the concept of Biomimetics. The primary goal of biomimetics refers to natural processing in a manner similiar to the natural process within the oral cavity, such as the calcification of a soft tissue precursor. The secondary meaning refers to the mimicking / recovery of the biomechanics of the original tooth by restoration [5].

Natural teeth through the optimal combination of Enamel and Dentin demonstrate the perfect & unmatched compromise between stiffness, strength & resilience. Ideally the restorative materials must match mechanical/ biological / optical properties closely to the tissue that is intended to get replaced. Biomimetics permits the repair of affected dentition imitating the characteristics of a natural tooth in terms of biological, esthetic, biomechanical, and functional properties [6]. A variety of bioactive formulations such as micro- and nano-hydroxyapatite (HA), tricalcium phosphate, mineral trioxide, casein-phosphate, and bioactive glasses have been introduced recently due to their excellent biocompatibility, biomimicry, bioactivity and remineralisation potentials.

Biomaterials can be classified into three different generations [7]. The first generation includes materials which focus not to provoke any foreign body reaction in the organism with maximum biochemical/biological inertness in contact with body fluids (Williams 2008). The second generations are the bioactive and biodegradable materials which show a positiveresponse of the living organism through the formation of a strong tissue-implant bond. The third-generation materials are responsible for stimulating cellular responses at molecular levels through the genetic activation of specific cell pathways.

2. Mechanisms of bioactivity

A bioactive restorative material display at least one or more of the following actions [8] :

- Remineralises and strengthens tooth structure through fluoride release and/or the discharge of other minerals.
- Forms an apatite-like material on its surface when immersed in body fluid or simulated body fluid (SBF) over time.
- Tissues repair and regeneration by promoting the normal healing mechanism.

Thus, bioactive materials might be categorized into three main categories as summarized in Table 1 [9]

Table1: Mechanism of action of Bioactive materials

	Mechanism of action	Dental Materials	Commercial examples
Bioactive materials	Remineralisation only	G.I cements and their derivatives	Riva Self Cure, Equia Forte and Activa bioACTIVE Restorative{Pulpdent}
	Deposition of Hydroxyapatite	Calcium aluminate cements	Ceramir
	Tissue Regeneration	Calcium silicate cements [MTA and other related Portland cements	Biodentine, I Root SP, BioRoot, Endoseal MTA and Theracal
		Calcium phosphate cements	Hydroset
		Calcium silicate / calcium phosphate combination cements	EndoSequence BC sealer

2.1 Remineralising bioactive materials

The remineralisation process is a natural repair mechanism to restore the minerals ions to the hydroxyapatite (HAP) crystal lattice [10]. It can occur either by the net remineralisation i.e. simple precipitation of mineral into the loose demineralised dentin matrix between collagen fibrils or by functional remineralisationie the chemical tight association of mineral to the dentin matrix structure. The former generates an increased mineral content, but may not necessarily provide an optimal interaction with the organic components of the dentin matrix. Fluoride enhances remineralisation as it accelerates the growth of the new fluorapatite crystals by bringing calcium and phosphate ions together. Although there is great mass of data on the positive effects of fluoride on enamel, no data have demonstrated the effectiveness of fluoride ions to induce mineralization of demineralised dentin and nucleation of new apatite crystallises within an apatite-free dentin [11].New bioactive materials reported have the ability to release calcium and, in some cases, phosphate which might provide better protection against demineralisation [12].

2.2 Bioactive materials that deposit Hydroxyapatite

Bioactive materials which create an apatite-like material on their surfaces when immersed in body fluid or simulated body fluid over time [13] .There are two chemical classes of these bioactive restorative materials: Calcium aluminates and Calcium silicates [14]. In order to get HA precipitation on a material surface; the ions must be present in high enough concentrations, the pH must be in the correct range, that is, alkaline, and a negatively charged surface is necessary [15]. Calcium aluminate based dental cement Ceramir C&B provided a good environment for HA growth [16]. This property, also observed in calcium silicate-based cements such as mineral trioxide aggregate (MTA), involves the calcium release and the pH raise in the vicinity that is essential for the stimulating effect of these materials on cellular events that form mineralised tissues. Variations in calcium aluminate formulations was suggested like the addition of bismuth oxide associated with a higher concentration of calcium chloride which enhanced odontoblast gene expression and function, offering a promising alternative to MTA for dentin-pulp complex regeneration [17].

2.3 Bioactive materials that promote tissue regeneration

Bioactive materials are not new to dentistry. Calcium hydroxide products considered as the oldest material that promotes tissues regeneration by promoting odontoblast differentiation, aid in the formation of dentin bridges, mineralize coronal pulp, and act as antimicrobial by increasing the pH [18]. The undesirable properties of calcium hydroxide are: high solubility, dissolution in tissue fluids, degradation upon tooth flexure, nonadherence to dentin and induction of dentin bridges containing tunnel like defects which may act as a portal of entry for microorganisms [19]. This has paved the way to seek out new materials for this therapy.

Calcium silicate cements may be defined as those that are composed (at least in part), of either di-/tri-/tetra- calcium silicate phases with a hydration process that is the sole or contributory mechanism for the setting reaction which results in the formation of leachate and crystalline phases that promote bioactivity [20]. Ca^{2+} ions released from Calcium silicate cements stimulate fibronectin synthesis, which might induce a differentiation of the dental pulp cells into mineralised tissue forming cells. The element uptakes from the materials into dentine may form tag like structures rich in Ca/P and Si, and the apatites formed may accumulate in the collagen fibrils, leading to the formation of a mineral-rich interfacial layer [21].

MTA's (calcium silicate based material derived from Portland cement) bioactivity is due to its ability to produce biologically compatible carbonated apatite [22] .Carbonated apatite represents the mineral phase of hard tissues such as bone, cementum, and dentin and is known as a biologic apatite which provides for high sealing ability and excellent biocompatibility . MTA-based materials stimulate formation of dentinal bridges faster and are of better quality than those of calcium hydroxide [23]. A white MTA ProRoot MTA that lacks the tetracalcium aluminoferrite (white mineral trioxide aggregate (WMTA) was introduced to overcome the discolouration associated with Pro root MTA / GMTA when used in pulpotomy or pulp capping procedures. Other drawbacks include cost; wash out during irrigation, delayed setting and difficult handling. Despite all these shortcomings, MTA rapidly became the gold standard for root-end restorations. HydroSetTM which was an apatite based calcium phosphate cement which is used as synthetic bone graft material. The setting reaction produces hydroxyapatite and octa calcium phosphate formation which have a positive impact on cell proliferation and bone formation [24].

Biodentine is a bioactive and biocompatible dentin substitute that has a positive effect on vital pulp cells stimulating tertiary dentin formation [25]. It has better ease of handling, shorter setting time and high viscosity compared to MTA. However the main drawback using Biodentine is its water based chemistry and thus poor bonding as the bond is mainly micromechanical to the resin restoration [26] .To overcome this, Theracal - a light cured, resin modified tri calcium silicate was introduced which can be used in direct and indirect pulp capping, as a protective base/liner under composites, amalgams, cements, and other base materials [21]. As compared to Pro Root MTA and Dycal, it has low solubility and high calcium release [27].

Bioceramic sealers for obturation, also known as silicate based sealers/ MTA based sealers are constantly introduced in the market. Their composition includes mainly di- and tri-calcium silicates, calcium hydroxide, calcium phosphates and radiopacifier. When inserted inside root canal, the sealer diffuses into the dentinal tubules through chemical absorption of calcium and silicon ions which migrates from the sealer to the tooth, using natural moisture in the dentinal tubules to initiate the setting reaction. This interfacial interaction, results in the formation of a “mineral infiltration zone” where the alkaline caustic effect of the CSC’s hydration products degrades the collagenous component of the interfacial dentin. This degradation forms a porous structure that facilitates the permeation of high concentrations of Ca^{2+}, OH^-, and CO_3^{2-} ions, which in turn contributes to the formation of mineralized tissue and neutralization of lactic acid from osteoclasts [28].

3. Bioactive Glasses

Another group of bioactive materials include bioactive glasses and glass-ceramics which belong to the third generation of biomaterials. The bioactive glass - Bioglass® 45S5, exhibits the highest bioactivity index and is considered as the gold standard of bioactive materials. Bioactive silicate glasses undergo five-stage reactions [29], when in contact with body fluids leads to the formation of a hydroxylcarbonate apatite (HCA) on their surface which accounts for their higher osteoconductivity than bioactive ceramics, such as hydroxyapatite (HA). Nova Min ® is a fine Bioglass ® particulate with a particle size of 18 µm when exposed to water or body fluids causes the ions to precipitate and deposits hydroxylcarbonate apatite which will remineralise defect and occlude open tubules [30].

4. New concepts in Bioactive Restorative Materials

Newer concepts in bioactive restorative materials are emerging. Cention N is a recently introduced tooth coloured resin based self-curing “alkasite “restorative material [31] . Alkasite refers to a new category of filling material which utilises alkaline filler capable of releasing acid neutralising ions. Higher pH can be beneficial for remineralising tooth structure and possibly bacteriostatic. Current bioactive restorative materials have been modified by incorporating novel antimicrobial agentsparticularly, polymerizable QAMs, the quaternary ammonium compounds which produce an electric charge that may be used to repel bacterial attachment. Now the researches could successfully introduce newer biomimetic remineralisation products having the potential to create apatite crystals within completely demineralised collagen fibers. The new materials have been fabricated with polyamido amine (PAMAM) additions, which are polymers that induce the formation of HAP crystals with the equivalent structure, orientation, and mineral phase of the intact enamel in relatively short time.

4.1 Mechanical perspective of biomimetic restorative materials

Elastic modulus (EM) is considered to be an intrinsic characteristic of materials and it gives a clear picture about the stiffness of materials. Surface hardness (SH) of the restorative materials is determined so as to find their resistance to permanent surface indentation, which indirectly predicts the abrasion resistance and polishing ability of materials during their service in the oral environment.

Ideally, the restorative materials must match hardness and elastic modulus closely to the tissues that is intended to get replaced [6]. There is a gradual compositional change throughout the enamel as inner enamel has lower stiffness and hardness but higher creep and stress redistribution abilities than the outer enamel. The hardness and elastic modulus of dentin also varies from one micron to the other, however it may not be possible to mimic in restorative materials [32]. Table 1 shows the similarity of restorative materials to that of natural tooth [33].

Table 1: Physical Properties of Dental Hard Tissues and corresponding Biomaterials (Magne, 2006)

	Elastic Modulus (GPa)	Thermal Expansion Coefficient (x 10 -6/°C)	Ultimate Tensile Strength (MPa)		Corresponding Material	Elastic Modulus (GPa)	Thermal expansion Coefficient (x10 -6/°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

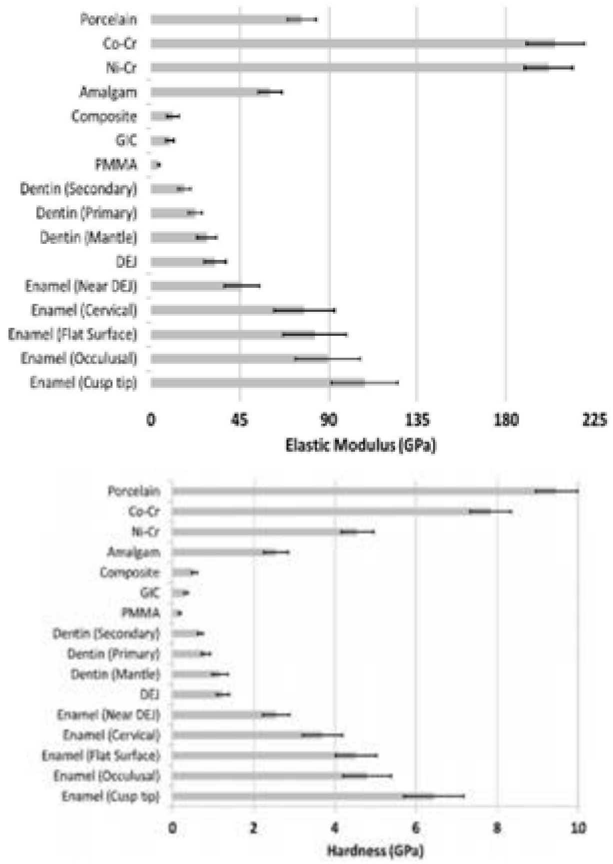

Fig 1 shows a comparison of elastic moduli (GPa) and surface hardness (GPa) of dental tissues and a range of dental restorative materials.

GICs exhibit lower EM and surface hardness compared to enamel, dentin, and RDCs. Composites due to their low elastic modulus appear to be challenged by stresses albeit scientific literature suggests that some of the RDCs are meeting the EM values of dentin .So in the context of mismatched EM between enamel and the direct restorative materials, more stresses may be transferred to teeth which may lead to either tooth damage or failure of restoration [32].In contrast, elastic modulus and SH of dental ceramics meets the limits of natural tooth enamel. The afore mentioned fundamental concepts of materials science clearly give way to dental ceramics undisputedly placing them as the therapeutic ambassador for modern biomimetic dentistry [34].

4.2 Antibacterial restorative materials

An antibacterial bioactive material is a material that has the ability to kill bacteria or suppress their growth or their ability to reproduce, by stimulation of the host living tissue to produce an unfavorable environment. The key factor of antimicrobial effects of bioceramic dental materials is directly related to the biomineralization ability, initiated by calcium silicates components on hydration with tissue body fluids produces calcium silicate hydrogel and calcium hydroxide, thereby elevating local pH. Calcium hydroxide (CH) reacts with calcium phosphate compounds to form hydroxyapatite, releasing water, which participates again in the reaction cycle to continue a rapid production of more calcium silicate hydrogel and CH. The continuous release of CH further elevates the pH creating an alkaline environment, which is not well tolerated by bacteria, which might be responsible for their antibacterial activity. Besides the antibacterial properties, It's necessary that biomaterials have the capacity to alter the biofilm structural formation. Addition of antibacterial agents (ions like Fl^-)to dental materials more specifically in endodontics may provide or enhance antibiofilm activity, without influencing mechanical properties[28].

5. Conclusion

The new class of bioactive materials differentiates itself by the ability to release calcium and precipitate hydroxyapatite on its surface. Although these bio materials are in their infancy, long-term efficacy is needed based on improvements of mechanical and physical properties. Hopefully future materials will create circumstances for increased tooth-like attributes due to properties of adhesion, remineralization, and integration. These responses have a large impact on the mechanical and esthetic outcomes, thereby prolonging the clinical durability of the bioactive materials. Regeneration of the lost tooth structure rather than replacement during treatment will ensure better prognosis and higher rate of success. Hence the future in dentistry would involve the use of such biomimetic materials which could successfully replace lost dentine, cementum and even the pulp tissue.

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