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Review Article

Bioactivity: A New Buzz in Dental Materials

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Abstract

The rapidly emerging domain of bioactivity is an area of great focus as it is intriguing and exciting topic in dental field. Bioactive restorative materials continue to show interesting potential offer significant benefits for both dentist and patient. Such promising materials can form an apatite-like surface layer along the materials tissues interface when exposed to inorganic phosphates solution. Their applications in dentistry include remineralization of hard tissues, maintenance of long-duration dental bonded restorations and healing of bony defects. This article clarifies the concept, developments and assessment of bioactivity and highlights the still untapped aspects that bioactive materials could promise for.

Keywords: *Bioactive; Bioactivity; Remineralization; Dental Materials; Apatite Layer; Tissues Regeneration*

Introduction

The bioactivity now considered as the latest buzz in all field of dentistry, especially in dental biomaterials specialty. It is highlighted as s significant topic of interest in the production of novel restorative materials.

What is bioactivity?

In generally, Bioactivity means any materials that have effect on, inducing a response or interaction with the living tissues or cells, such as encouraging of the hydroxyapatite formation [1]. Larry Hench in 1969 was the first to use the term bioactive materials in describing a new material for bone reconstruction that could be able to form a bond to body tissues. Hench developed a completely synthetic material named bioglass composed mainly from calcium silico-phosphate glass that not rejected by body and chemically bonds to bone [2]. The early concept of bioactivity was limited to a biomaterial that elicits a specific biological response at the material tissue interface which results in the formation of a bond between them. Since then, the concept of bioactive materials has expanded extremely [3]. In 1994 he classifies biomaterials into osteoproductive and osteoconductive. Osteoconductive materials permits bone growth on its biocompatible interface that occurs when a material could be elicits an extracellular response only along its interface. However, osteoproductive materials permit colonization of osteogenic stem cells along its bioactive surface. Bioactivity arises when a material could be elicits combination of an intracellular and extracellular response through its interface [4]. Bioactive dental materials not considered as a new idea. Adhesion of dental materials to tooth structure by an apatite-like material by aid of fluoride releasing materials or recently by action of calcium phosphate releasing materials considered as the first trend for bioactivity. As there is materials have been widely used over many years that demonstrated various levels of bioactivity. These materials are used mainly for repair, reconstruction and regeneration of dental insults. For example, glass ionomer have been described as bioactive material due to their ability to remineralization of tooth structure, in addition to continuous dynamic release of fluoride which delay the secondary caries around the restoration margins [5]. Likewise, cal-

cium hydroxide, which have used for decades has the ability to be dissociated into calcium and hydroxyl ions, which in turn cause cascade of events that encourage deposition of reparative dentin and tooth remineralization [6]. Thus, these activities make glass ionomer and calcium hydroxide one of the firstly known bioactive dental materials. Bioactive dental materials could be defined as materials that form a layer of an apatite-like material at the tissue materials interface upon exposure to inorganic phosphates solution [7].

Mechanisms of bioactivity

A bioactive restorative material includes at least one or more of the following behavior [8-10]:

1. Remineralization of the hard tissues through fluoride and or other minerals release.
2. Apatite-like formation along the material tissue interface upon immersion in liquid that mimics the normal physiological fluids.
3. Tissues repair and regeneration by promoting the normal healing mechanism.

Thus, bioactive materials could be categorized into three main categories as summarized in table 1.

	Mechanism of action	Dental materials	Commercial examples
Bioactive materials	Remineralization only	G.I. cements and their derivative	Riva Self Cure, Equia Forte and Activa BioACTIVE Restorative (Pulpdent)
	Deposition of hydroxyapatite	Calcium aluminates cements	Ceramir
	Tissue regeneration	Calcium silicates cements (MTA and other related Portland cements)	Biodentine, iRoot SP, BioRoot, Endoseal MTA and TheraCal
		Calcium phosphates cements	HydroSet
		Calcium silicates/calcium phosphates combination cements	EndoSequence BC Sealer

Table 1: *Schematic representation of some examples of bioactive dental materials categorized according to their mechanism of action.*

Remineralizing bioactive materials

Remineralizing materials only e.g. glass ionomer and their modifications. Remineralization could be defined as the natural repairing process for non-cavitated lesions. It depends on calcium and phosphate ions, by help of fluoride, to promote deposition of a new mineral into crystal voids. In normal conditions caries progress is very slow under normal physiological conditions at pH7, where saliva is supersaturated with calcium and phosphate ions. However, if the pH is lowered, a higher concentration of calcium and phosphate is essential to reach the saturation. The critical pH of hydroxyapatite is approximately 5.5 and that of fluorapatite is approximately 4.5. Below the critical pH, demineralization occurs while beyond critical pH, remineralization occurs. Fluoride assists remineralization by carrying calcium and phosphate ions together and incorporating them into the remineralized surface [11].

Bioactive materials that deposit hydroxyapatite

Some bioactive materials have the ability to precipitate on their surface an appetite-like material when immersed in physiological body fluid by time in addition to promoting remineralization by adding minerals to tooth structure e.g. calcium aluminates [12].

Bioactive materials promote tissues regeneration

Other bioactive materials in addition to their ability to promote remineralization and precipitation of hydroxyapatite layer, they also have a capability to regenerate new tissues. Calcium hydroxide products considered as the oldest material that promotes tissues regeneration by enhancement of dentin bridge formation and their ability to promote wound healing when used as a vital pulp capping material. However, their inadequate physical properties limited their use. Thus, novel bioactive materials promote stimulate the regeneration of

live tissue dentin, pulp, blood vessels and bone with advanced properties have been developed such as calcium phosphate cement (CPC) and calcium silicate based cement e.g. mineral trioxide aggregate (MTA) and other related Portland cement calcium silicate products [13,14].

Dental applications of bioactive materials

The level of evolution will include extended applications across all dental material categories, including permanent fillings, adhesives, dental and bone cements, bone grafts, substitute and scaffold, cavity liners and bases, endodontic sealers and pulp capping, preventive measures and patient home care [1,15].

Assessment of bioactivity

No single test could be performed to test the bioactivity potentiality, but there are a several methods could be done to get an idea about the predicted bioactivity potentiality of the tested materials which includes:

In vitro assessment:

In vitro assessment methods of bioactivity is valuable prior to doing *in vivo* bioactivity experiments and can significantly decrease the number of animals needed for *in vivo* evaluation. In addition, to avoid the complication and high cost of *in vivo* test, several *in vitro* experiments have been used to predict the *in vivo* bioactivity of the materials [16].

Changes in pH give a preliminary indication of ions released from the bioactive specimens to be examined. This will give an insight on the behavior of the bioactive material when come in contact with physiological solution. Thus, ions release test is useful for assessment of bioactivity as calcium and phosphorus ions release is the basic steps involved in minerals dissolution and deposition on bioactive materials [17]. Calcium and phosphorus ion release could be detected using inductively coupled plasma (ICP) [18]. Subsequent dissolution of bioactive material leads to supersaturation of physiological solution with calcium and phosphorus ions with consequent apatite nucleation, growth and precipitation of calcium phosphate apatite layer on the surface [19].

Currently, there is still challenging for in vitro bioactivity assessment of bioceramics as a primary basic step. Two commonly methods have been used to evaluate the in vitro bioactivity of bioceramics. First method depends on evaluation of the ability of apatite-formation of bioceramics after immersion for a period of time in simulated body fluids (SBF) which was first introduced by Kokubo., *et al* [16].

The SBF solution (originally named as simulated physiological solution) has ions concentration match that of human blood plasma (Table 2) [16]. The SBF could be used either to evaluate in vitro bonding ability of a material to bone or to coat a material surface with a biomimetic coating [20]. Kokubo's method is carried out by maintaining SBF solution pH and temperature similar to blood plasma, as it has been found that this is essential for deposition of an apatite mineral. Free calcium and phosphate ion concentrations reduce as mineralization progresses. Thus, the SBF solution needs to periodically replace (usually every 3 to 4 days) to ensure optimum of these concentrations [20]. Several studies confirmed this correlation between apatite layer formation on various materials in SBF in the *in vitro* test and *in vivo* reality [16,21].

	Ion concentration [mmol]								pH
	Na^+	K^+	Mg^{2+}	Ca^{2+}	Cl^-	HCO_3^-	HPO_4^{2-}	SO_4^{2-}	
Blood plasma	142.0	5.0	1.5	2.5	103.0	27.0	1.0	0.5	7.2 - 7.4
SBF	142.0	5.0	1.5	2.5	147.8	4.2	1.0	0.5	7.4

Table 2: *Ion concentrations of SBF and human blood plasma [16].*

Finally, to characterize the deposited calcium phosphate mineral, elemental composition of the surface could be analyzed via energy dispersive x-ray spectroscopy (EDX) connected with scanning electron microscope (SEM) or by using X-ray photoelectron spectroscopy (XPS). X- ray diffraction (XRD) could be also used to identify the calcium phosphate mineral phase, but it is restricted to crystalline mineral deposits only [20,22].

The second method is to investigate the in vitro cell growth response to bioceramics [23-25]. Combination between Kokubo's method and cell experiments for in vitro bioactivity assessment of bioceramics may be the superior option, because the novel bioceramic has the ability for both induction of apatite deposition in SBF and stimulation of cell response [8].

In vivo assessment

Assessment of bioactivity *in vivo* could be done utilizing a bone defect animal model and measuring the interfacial bond strength at the interface [26,27]. In addition, further investigation could be done by examination of the cell interactions with host tissues at the biomaterial tissue interface using a number of techniques, such as histological examination, SEM images and micro computed tomography (micro CT) observation which is considered as a non-destructive 3-D imaging technology [27-29].

Clinical studies

Clinical non-destructive assessment of bioactivity includes clinical examinations by the radiographs, image analysis system, computed tomography (CT) scan and magnetic resonance imaging (MRI) images [30-34].

Conclusion

Bioactivity refers to a unique property of a material that elicits a cellular response, such as the formation of hydroxyapatite. As compared to inert materials, bioactive materials are capable to produce growth factors and encourage natural mineralization. These response has a large impact on the mechanically and esthetically outcomes, thereby clinical durability of the bioactive material.

Bioactive materials offer better alternative to the conventional dental materials, providing a potential benefits over non-bioactive materials include the following:

1. Possess a remineralizing and reinforcement effect on hard dental tissue.
2. Protecting tooth structure from the harmful effects of all types of acids due to the increased pH level which provided by mineral saturation.
3. Chemically bonding to hard dental tissues which in turn help to decrease sensitivity originated by bonding technique defects.
4. Releasing of calcium and phosphorus ions from their composition, forming a mineral comparable to that of natural hydroxyapatite.
5. They are effective in decreasing matrix metalloproteinases formation, hence eliminating the collagen destruction.
6. Effective materials in healing of intrabony defects.

Thus, the benefits of these promising products appear to be of significant value in producing long durable restoration and help to repair damaged hard dental structure while decreasing the chance for recurrent decay occurs around existing restorations.

Conflict of Interest

No competing interests were disclosed.

Bibliography

1. S Sonarkar and R Purba. "Bioactive materials in conservative dentistry". *International Journal of Contemporary Dental and Medical Reviews* (2015): 1-4.

2. JR Jones. "Reprint of: Review of bioactive glass: From Hench to hybrids". *Acta Biomaterialia* 23.S (2015): S53-S82.

3. LL Hench, *et al*. "Bonding mechanisms at the interface of ceramic prosthetic materials". *Journal of Biomedical Materials Research* 5.6 (1971): 117-141.

4. LL Hench. "Bioactive Ceramics: Theory and Clinical Applications". *Bioceramics* (1994): 3-14.

5. J Hicks., *et al*. "Fluoride-releasing restorative materials and secondary caries". *Dental Clinics of North America* 46.2 (2002): 247-276.

6. S Desai and N Chandler. "Calcium Hydroxide-Based Root Canal Sealers: A Review". *Journal of Endodontics* 35.4 (2009): 475-480.

7. SR Jefferies. "Bioactive and biomimetic restorative materials: A comprehensive review. part i". *Journal of Esthetic and Restorative Dentistry* 26.1 (2014): 14-24.

8. C Wu and Y Xiao. "Evaluation of the In Vitro Bioactivity of Bioceramics". *Bone and Tissue Regeneration Insights* 2 (2009): 25-29.

9. D Fernando., *et al*. "Bioactive glass for dentin remineralization: A systematic review". *Materials Science and Engineering C* 76 (2017): 1369-1377.

10. MI Garchitorena Ferreira. "Bioactive materials in dentin remineralization". *Odontoestomatologia* 18.28 (2016): 11-18.

11. F Goldstep. "Proactive intervention dentistry: a model for oral care through life". *Compendium of Continuing Education in Dentistry* 33.6 (2012): 394-416.

12. JF McCabe, *et al*. "Smart materials in dentistry". *Australian Dental Journal* 56.1 (2011): 3-10.

13. C Tziafa., *et al*. "Dentinogenic responses after direct pulp capping of miniature swine teeth with Biodentine". *Journal of Endodontics* 40.12 (2014): 1967-1971.

14. GJ Tanomaru M and Viapiana R. "From MTA to New Biomaterials Based on Calcium Silicate De MTA a nuevos biomateriales basados en Silicato de Calcio". *International Journal of Dental Sciences* 18.1 (2016): 18-22.

15. M Bhushan., *et al*. "Bioactive Materials: A Short Review". *Journal of Orofacial Research* 5.4 (2015): 138-141.

16. T Kokubo and H Takadama. "How useful is SBF in predicting in vivo bone bioactivity?" *Biomaterials* 27.15 (2006): 2907-2915.

17. T Kokubo., *et al*. "Solutions able to reproduce in vivo surface-structure changes in bioactive glass-ceramic A-W3". *Journal of Biomedical Materials Research* 24.6 (1990): 721-734.

18. CN Carvalho., *et al*. "Ions release and pH of calcium hydroxide-, chlorhexidine- and bioactive glass-based endodontic medicaments". *Brazilian Dental Journal* 27.3 (2016): 325-331.

19. AA Zadpoor. "Relationship between in vitro apatite-forming ability measured using simulated body fluid and in vivo bioactivity of biomaterials". *Materials Science and Engineering C: Materials for Biological Applications* 35 (2014): 134-143.

20. K Kepa., *et al*. "In vitro mineralization of functional polymers". *Biosurface and Biotribology* 1.3 (2015): 214-227.

21. M Kolafová., *et al*. "In vitro bioactivity test of real dental implants according to ISO 23317". *International Journal of Oral and Maxillofacial Implants* 32.6 (2017): 1221-1230.

22. X Chatzistavrou., *et al*. "Bactericidal and bioactive dental composites". *Frontiers in Physiology* 9 (2018): 103.

23. Y Xie., *et al*. "Responses of human bone marrow-derived stromal cells to calcium silicate coatings with different chemical stability". *Materials Science Forum* 761 (2013): 117-120.

24. C Prati and MG Gandolfi. "Calcium silicate bioactive cements: Biological perspectives and clinical applications". *Dental Materials* 31.4 (2015): 351-370.

25. DA Mohamed., *et al*. "The Effect of Three Different Biomaterials on Proliferation and Viability of Human Dental Pulp Stem Cells (In-vitro Study)". *Open Access Macedonian Journal of Medical Sciences* 5.5 (2017): 657-663.

26. AS Fawzy and MA Amer. "An in vitro and in vivo evaluation of bioactive titanium implants following sodium removal treatment". *Dental Materials* 25.1 (2009): 48-57.

27. PSP Poh., *et al*. "Fabrication and in vitro characterization of bioactive glass composite scaffolds for bone regeneration". *Biofabrication* 5.4 (2013): 45005.

28. CT Badea and D Panetta. "High-Resolution CT for Small-Animal Imaging Research". *Comprehensive Biomedical Physics* 2 (2014): 221-242.

29. P Benjasuwantep., *et al*. "The remineralization effect of bioactive glass on enamel caries-like lesions in primary teeth". *Southeast Asian Journal of Tropical Medicine and Public Health* 48.5 (2017): 1127-1132.

30. A Garrocho-Rangel., *et al*. "Bioactive Tricalcium Silicate-based Dentin Substitute as an Indirect Pulp Capping Material for Primary Teeth: A 12-month Follow-up". *Pediatric Dentistry* 39.5 (2017): 377-382.

31. NAP Van Gestel., *et al*. "Clinical Applications of S53P4 Bioactive Glass in Bone Healing and Osteomyelitic Treatment: A Literature Review". *BioMed Research International* (2015): 684826.

32. Y Iijima. "Early detection of white spot lesions with digital camera and remineralization therapy". *Australian Dental Journal* 53.3 (2008): 274-280.

33. E Suominen and J Kinnunen. "Bioactive glass granules and plates in the reconstruction of defects of the facial bones". *Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery* 30.4 (1996): 281-289.

34. MC Tanner., *et al*. "Evaluation of the clinical effectiveness of bioactive glass (S53P4) in the treatment of non-unions of the tibia and femur: Study protocol of a randomized controlled non-inferiority trial". *Trials* 19.1 (2018): 299.

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