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REVIEW ARTICLE

Utilization of Polymethyl Methacrylate and Hydroxyapatite Composite as Biomaterial Candidate for Porous Trabecular Dental Implant Fixture Development: A Narrative Review

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ABSTRACT:
Polymethyl Methacrylate (PMMA) and Hydroxyapatite (HA) utilization as single materials are rarely used as dental implant materials. There is a promising hope by combining these two materials as a dental implant fixture. Nevertheless, there is a limited information of PMMA/HA composite utilization as dental implant material. The aims of this narrative review is to describe the potential of PMMA/HA composite utilization as biomaterial candidate for porous trabecular dental implant fixture development. This narrative review finds the potential of PMMA/HA composite as biomaterial candidate for porous trabecular dental implant. The keywords "Biomaterial," "Dental Implant," "Hydroxyapatite," "Osseointegration," and "Polymethyl Methacrylate" were used in a web-based search of PubMed, NCBI, Scopus, ScienceDirect, and ResearchGate databases. PMMA is non-toxic, cost-effective, biocompatible, simple to manipulate, and has strong mechanical properties in the oral cavity. Furthermore, osteoblastic cell adhesion, development, and differentiation are aided by the use of HA as a biomaterial to induce bone formation. Nonetheless, due to its rapid absorption and degradation, single HA is seldom used as a dental implant material. Developing dental implant composite has been extensively studied, among them are the fabrication of PMMA/HA. PMMA/HA has fairly good physical characteristics with a compressive strength, good bioaffinity properties, biocompatible with bone cells. The osteoconductivity of HA enhance the bioactivity of the composite materials, thus making the dental implant to have an excellent osseointegration. We propose that there is a possibility of utilization of PMMA/HA composite as biomaterial candidate for porous trabecular dental implant fixture.

KEYWORDS: Biomaterial, Dental Implant, Hydroxyapatite, Osseointegration, Polymethyl Methacrylate.

INTRODUCTION:
Edentulism is one of global oral health concern due to its high prevalence. Edentulism also related to disturbance of stomatognathic function and facial aesthetic. It was estimated the prevalence of edentulism even worse in the developing countries.

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Self-reported edentulism in 50 years and older in the Southeast Asian countries were 22.2% in Malaysia and 14.6% in the Philippines based on *World Health Organization* survey in 2002-2004.[1-2] In Indonesia, the prevalence of edentulism was 15.7% in 50 years and older patient based on national community-based survey in 2014-2015.[3] The edentulism may serve as a risk factor of several oral and systemic disease such as diabetes mellitus, hypertension, osteoporosis, etc.[4-5] The disturbance stomatognathic fuctions may occurred after tooth loss such as the reduction of vertical height dimension, masticatory efficiency reduction, loss of facial aesthetic, and microflora composition changes in the oral cavity.[6] Furthermore, it may affect patient's Oral Health Related Quality of Life (OHRQoL).[7]

The rehabilitation of stomatognathic function due to edentulism can be done by means of dental implant modalities. The dental implant may enhance the maxillofacial aesthetic and stomatognathic function. Thus, it may reduce the risk factor of systemic and oral disease because of edentulism. However, the immediate and long term of dental implant therapy is quite challenging. There is an effort that can be done to increase the successful rate of dental implant through enhancing the osseointegration. The establishment of porous trabecular dental implant fixture may improve the osseointegration.[6] This is due to the wider contact of the material and bone tissue, which can increase the bone implant contact which leads to the success of the dental implant fixture that is implanted in the alveolar bone.[8]

Currently, most of the material used as dental implants is titanium. Although titanium has good biocompatibility properties and is considered the gold standard material for dental implants, some authors reported that there were clinical problems such as metal hypersensitive reactions, lack of bone cells recruitment and aesthetic constraints due to the metallic color around the neck of the titanium implants which caused a grayish color especially on thin mucosa. In addition, the price of titanium dental implants, which is relatively expensive, cannot be reached by everyone.[9-12] The exploration and utilization of Polymethyl Methacrylate (PMMA) and Hydroxyapatite (HA) may promising as biomaterial candidate as dental implant fixture in effort to enhance the osseointegration.[13] In the other hand, there are abundant of PMMA and HA as natural resources in Indonesia that can be used for the porous trabecular dental implant fixture raw material candidate. Thus, the aim of this narrative article is to describe the potential of PMMA and HA composite as biomaterial candidate for porous trabecular dental implant fixture development.

MATERIAL AND METHODS

Our team conducted an independent literature search using PubMed, NCBI, Scopus, ScienceDirect, and ResearchGate databases, using the keywords "Biomaterial," "Dental Implant," "Hydroxyapatite," "Osseointegration," and "Polymethyl Methacrylate." The following parameters were used to collect data: 1) observational studies and clinical trials; 2) English-language texts; (3) Publications from the previous ten years, from 2010 to 2020; 4) free and full-text access. To help support the main narrative review, any related studies were looked at.

Polymethyl Methacrylate:

Synthetic and natural polymers, has widely known as its application for medical implants.[14,15] However, in dentistry, polymer dental implants still have challenges to alternate titanium dental implants that has been used for long period of time. One of the synthetic polymers that many dental practitioner familiars with is polymethylmethacrylate (PMMA).[14,16]

PMMA has been commonly applied in dentistry as restoration, denture base, dental implant, as well as orthodontic appliances.[15] The excellent mechanical properties of PMMA makes it extensively studied, also its flexibility makes it easily manipulated. However, the lack of bioactivity such as osteoconductivity cause poor osseointegration between the materials and host tissue. The limitation, especially in bioactivity, makes the use of PMMA as dental implant still has not widely introduced. Some studies attempt to add some other materials to PMMA to overcome its drawbacks and produce an improved material.[16-18] Due to some limitations of this material, currently many studies are focusing on combining PMMA with other materials to improve its properties and on the same time adjusting to which kind of application it would be.

Chemical Properties of Polymethyl Methacrylate

PMMA is one of the organic polymers that is soluble in organic solvents like esters and ketones, and has insignificantly solubility in water. Even though there are no reaction with water, dimensional changes could still occur when PMMA frequently in contact with water. Chemical disturbances could cause impairment in its polymer structure (i.e. polymer chains), swelling and dissolution of the materials. In order to minimize the solubility in solvents, and also resist the dimensional changes, cross-linking process in PMMA is generally necessary.[17,18]

PMMA resistance to chemical reaction is important, concerning the outcome that might occur and affect its physical and mechanical performances. However, the use of PMMA in dentistry, particularly as denture base, has proven that PMMA is chemically stable in oral condition. The drawback in PMMA is that the possibility of residual monomer presence that could cause some harm, particularly to its biological properties. Efforts has been continuously conducted in order to increase its chemical resistance so it would overcome its challenge and widen the applications of PMMA in dental medicine use.

Physical Properties of Polymethyl Methacrylate:

PMMA is one of the acrylic polymers that has a good thermal stability and resistance in atmospheric condition. Several physical properties of PMMA are listed in Table 1. PMMA is a radioluscent and colorless material, make it easily modified to achieve the aesthetic requirement. However, the color stability is quite poor due to several factors such as increased water absorption and other molecules interferences. Color changes could also happen due to materials porosity and frequent contact with beverages such as coffee and tea.[17,19,20]

Absorption and solubility are properties in PMMA that often interfere the materials performance. Constant immersion in fluid would increase the water uptake and affect the dimensional stability of PMMA. Consequently, water uptake and solubility of the materials need to be minimized, which according to ISO 20795-1, absorption of a material should below 32 g/mm^3 and solubility is less than 1.6 g/mm^3. Available PMMA currently has satisfied this requirement by ISO 20795-1.[18]

Table 1. Physical properties of PMMA.[17,18,20]

Physical property	PMMA
Glass transition temperature (°C)	100 – 130
Density (g/cm^3)	1.2
Melting point (°C)	220 – 240
Sorption (mg/cm^2)	0.69
Solubility (mg/cm^2)	0.02 (water), 0.04 (hydrocarbons)
Color	Transparent, colorless

Mechanical Properties of Polymethyl Methacrylate:

Masticatory process required good mechanical properties of a material so it can perform under various kinds of stresses and still maintained intact. Important mechanical properties of PMMA, such as compressive strength, flexural strength, fracture toughness, and hardness showed in Table 2.[16,18,20,21] PMMA has mechanical properties that is valid, especially high in elastic modulus, but it has a poor fracture resistance and low elongation at break. The fatigue life would decrease because of water intake in prolonged time, decreasing its flexural strength. Flexural strength itself is quite important for a material to resist stresses, whether it is tensile, compressive, and shear stresses. Factors that would affect the flexural strength includes curing method, chemical composition, degree of polymerization, dimensions, and storage. Generally, heat cured PMMA has better mechanical values than self-cured PMMA. Modification, such as mixing with other materials, has been made to overcome the mechanical limitations and increase its flexural strength, impact strength, also rigidity.[6,14,16-18,20] Mentioned properties of PMMA such as solubility and sorption also affect mechanical stability of PMMA due to resulted dimensional changes. Resolving these problems certainly maintains the mechanical stabiltity of PMMA, thus the materials function is sustained.

Table 2. Mechanical properties of PMMA.[14,16]

Mechanical property	PMMA
Elastic modulus (GPa)	1.8 – 3.1
Flexural strength (MPa)	90 – 140
Compressive strength (MPa)	76 – 83
Tensile strength (MPa)	48 – 80
Hardness (VHN)	20
Surface hardness (Rockwell)	M92, M90-M100
Fracture toughness (MN/m$^{3/2}$)	2.53
Fatigue failure (MPa)	11
Impact strength (J)	0.98–1.27
Elongation at break (%)	1 – 5

Biological Properties of Polymethyl Methacrylate:

PMMA is non-toxic, cost-effective, biocompatible, easy to manipulate, and induce minimal to no inflammatory reactions. Biocompatibility in PMMA materials is quite an uncertain property. Evidently, the remaining problem in PMMA is residual monomer presence that could cause cytotoxicity and induce inflammation. Curing method, such as a heat cured PMMA would decrease the presence of monomer. In other words, heating process would increase the degree of polymerization of PMMA. Thus, a good biocompatibility in PMMA achieved when it is appropriately cured.[14,17,18]

PMMA is used in many medical applications as implant materials in treatments such as cranioplasty, rhinoplasty, and joint replacement.[14,15,17] Despite its lack of bioactivity, PMMA optimalization to enhance its biological performance has been conducted such as combining the PMMA with bioactive materials such as calcium phosphate ceramics. One of the major properties in implant materials including dental implants is its osteoconductivity to support osseointegration between materials and host tissues. Developing dental implant composite has been extensively studied. Among them are the fabrication of PMMA and HA.[17,22,23] The osteoconductivity of HA enhance the bioactivity of the composite materials, thus making the dental implant to have excellent osseointegration.

Hydroxyapatite:

Chemical properties of Hydroxyapatite:

Hydroxyapatite (HA) is an inorganic mineral with the apatite lattice structure (A10(BO4)6C2), where Ca, PO4, and OH define A, B, and C, respectively. The Ca/P mole ratio in pure HA is 1.67 since it contains 39.68 percent calcium and 18 percent phosphorus by weight. There are industrial HA goods with Ca/P ratios greater than or less than 1.67. The Ca/P ratio varies, indicating a phase transition between tricalcium phosphate (TCP) and calcium oxide (CaO). CaO is more abundant in HA with a Ca/P ratio greater than 1.67, and vice versa.[24,25] Fishbone, coral, bovine bone, eggshell, and seashells are widely used to make HA from natural sources. Because of the presence of trace ions in natural sources, HA derived from them is non-stoichiometric[.25,26,27] These ions, which include cations like Na+, K+, Mg2+, Sr2+, Zn2+, and Al3+, as well as anions like F-, Cl-, SO4 2-, and CO32-, help to encourage rapid bone regeneration.[28]

Biology properties of Hydroxyapatite:

HA is one of the inorganic compounds that make up the human body's hard tissues, such as bones, teeth, and dentin. Synthetic HA is a bone-like substance with excellent bonding properties. Several research findings suggest that synthetic HA has the ability to be used as an allograft and xenograft replacement for bones and teeth with good biocompatibility. Because of its bioactive and biodegradable properties, HA has been commonly used in biomedical implants and bone regeneration.[29]

The biological applications of nanotechnology have advanced significantly over the last few decades. Nanomaterials have been used in a variety of dental applications, including tissue regeneration, polymeric composite reinforcement, endodontics, and implant coatings. Surface modification of dental implants has been done with HA nanocrystals/particles The wet chemical method can be used to make either microcrystalline HA (sintering at 1100°C for 60 minutes) or nanocrystalline HA (hydrothermal treatment at 200°C for 24 hours) HA nanocrystals powder. In the case of nanocrystalline HA coating, HA powder deposited on the implant surface at room temperature resulted in greater osteoblast adhesion and more calcium deposition than typical HA coating.[30]

As compared to other materials, metallic implants made of titanium and its alloys have the highest biocompatibility. Depending on the applications and pattern of osteogenesis, these implants are usually grouped with bio-inert materials and ceramics such as zirconia, titania, and alumina. For tightening and compact packaging, some applications needed good bio-interaction, or a strong bond with natural bone. Biocompatibility is ideal for calcium phosphate-based biomaterials like TCP and HA. Mechanical strength, ductility, ease of fabrication, and biocompatibility are all necessary properties for this type of fixation technique.[31] Because of their desirable biological properties, such as biocompatibility, bioaffinity, bioactivity, osteoconduction, osseointegration, and osteoinduction in some settings, HA bioceramics have been commonly used as artificial bone replacements.[32 – 34]

Since HA only contains calcium and phosphate ions, no adverse local or systemic toxicity has been identified in any research. When newly developed bone is inserted, a carbonated calcium-deficient apatite layer at the bone implant interface attaches directly to HA.[35,36] The HA surface promotes osteoblastic cell adhesion, development, and differentiation, and new bone is deposited as the adjacent living bone is gradually replaced. In addition, cytokines with the ability to bind and concentrate bone morphogenetic proteins (BMPs) *in vivo* can be delivered via HA scaffolds.[37]

A bioactive material dissolves slightly, but before it interacts with tissues at the atomic level, it forms a biological apatite, which results in chemical bonds being formed directly with bones. The bioresorbable materials are used as scaffolds and filling materials. The essence of the material, such as porosity, influences these reactions. The use of HA with a Ca/P ratio of 1.0–1.7 is nontoxic, and no foreign body reaction has been observed. The healing process is similar to that of a fracture. 30 A chemical bond is formed between bioactive materials. Roughness and porosity of the biomaterial are thought to be essential factors in bonding.[38]

Blood vessel development requires a pore size of approximately 50 m, while osteoid growth requires a pore size of approximately 200 m. Bone ingrowth was also visible in the pore dimensions, which were respectively 100 m and 50 m.[39] The following are the pore sizes and their effects: 1 m is responsible for bioactivity, protein interaction, and cell attraction; 1–20 m contributes to cellular and bone ingrowth orientation and directionality; 100–1,000 m aids in mechanical strengthening and functionality; >1,000 m affects the form and aesthetics of the implant.[40]

The bioactivity of graft replacements is regulated by the degree of porosity, which controls the rate of bone regeneration, the local environment, and the equilibrium of new bone at the repair site. Pore interconnectivity, geometry, topography, and porosity all influence osteogenesis, which facilitates the osteoconductivity or inductivity capacity of bone grafts in a synergistic manner. The excellent biocompatibility, possible osteoinductivity, and high affinity for drugs, protein, and cells make these tissue engineering applications very much functional.[41]

Mechanical Properties of Hydroxyapatite:
HA has weak mechanical properties in its bulk form, such as low fatigue resistance, brittleness, low strength, and durability. The bending power of HA is less than 100 MPa, which is significantly less than that of natural bone. Porosity, which can take the form of micropores (less than 1 m diameter) caused by incomplete sintering or macropores (greater than 100 m diameter) produced to enable bone growth, has an impact on tensile and compressive strength as well as fatigue resistance. The Weibull modulus (m) of HA implants in physiological solutions is low (m = 12), suggesting low reliability under tensile loads.[42]

These disadvantages prohibit HA from being used in load-bearing applications. Bulk HA and other CaP bioceramics are currently used in polymer bioactive ceramic composites as powders, small unloaded implants, dental implants (with reinforcing metal posts), low-loaded porous implants, and bioactive phases in polymer bioactive ceramic composites. Repair of bony defects, periodontal defect repair, alveolar ridge augmentation, ear implants, eye implants, maxillofacial reconstruction, spine fusion, bone space fillers, implant coatings, adjuvant to uncoated implants, and so on are some of the other HA applications.[43]

The success or failure of an implant is determined by the production of good mechanical strength between the implant and the bone, known as osseointegration. Metal implants do not bind to bone well and do not encourage bone formation. Furthermore, such implants corrode and release metal ions into the body. As a result, coating metal implants with bioactive ceramics such as HA not only prevents degradation, but also accelerates tissue growth within the pores.[44] Bone ingrowth (biological fixation) occurs in the porous implants, and attachment occurs by direct chemical bonding with the bone (bioactive fixation). HA-coated implants improve the adhesion of structural prostheses and thereby minimize particle release from the metal, resulting in a significant reduction in the number of cases of rejection.[45] Low porosity, high cohesive strength, good adhesion to the substrate, a high degree of crystallinity, high chemical purity, and phase stability are all desirable characteristics in a HA coating for orthopedic implants. In most HA coatings, the crystallinity level is about 65–70 percent.[46]

Polymethyl Methacrylate and Hydroxyapatite Composite for Dental Implant Osseointegration:
Polymethyl methacrylate (PMMA) and Hydroxyapatite (HA) have been widely used in the field of dentistry, one of which is their involvement in dental implant materials. PMMA is a form of polymer that can be developed into a candidate for dental implant biomaterials. The use of PMMA as a dental implant biomaterial has been widely studied. PMMA can be used as a dental implant biomaterial because this material has properties as an insulator against thermal and electrical and is resistant to biodegradation.[47] In addition, several studies of these biomaterials suggest that PMMA has biocompatible properties and shows characteristics in supporting the attachment of mesenchymal stem cells and osteoblasts.[48-51] However, PMMA has poor characteristics in supporting this material as a dental implant fixture, which is a lower mechanical strength and a higher modulus of elasticity compared to alloys and ceramics so that it can affect this material in accepting masticatory loads.[52]

HA particles have a relatively high compressive strength with a tensile strength similar to that of human bones.[47,52] Besides, HA as ceramic also has insulation properties against thermal and electricity and is non-corrosive.[52] Based on several studies, single HA is rarely used as a dental implant material because this material can be absorbed and degraded by the host so that this material is more often used as a graft material.[53,54]

In the study of dental implant biomaterials, PMMA and HA as single materials are rarely used as dental implant materials. However, a study shows that there is a promising hope by combining these two materials as an implant fixture. The composite that combines PMMA and HA has fairly good physical characteristics with a compressive strength value of 178-381 MPa which shows a value similar to bone.[55] In addition, this study also shows that PMMA / HA composites have good bio affinity properties and are biocompatible with bone cells. Previous studies have also shown that PMMA / HA composites can increase the interfacial shear strength in rabbit bone and can improve chemical resistance and mechanical properties. However, one of the obstacles is the discovery of gaps between the biomaterial and the surrounding bone because PMMA does not have bioactivity properties so that it can affect osseointegration in the use of this material.[12,56]

The establishment of porous trabecular dental implant fixture may improve the osseointegration.[6] This is due to the wider contact of the material and bone tissue, which can increase the bone implant contact which leads to the success of the dental implant fixture that is implanted in the alveolar bone.[8] Materials such as HA are often used as coating materials to improve the success of dental implants implanted into bone. A study showed that coating using HA on implant materials derived from metal can improve corrosion resistance of the original material and increase osseointegration because HA has good bioactivity properties against bone cells so that it can promote osteoblast cell adhesion.[57] In addition, a clinical study was also conducted in evaluating HA coating of dental implants. The results of this study indicate that coating using HA can increase the survival rate of implants implanted in bone, thus indicating that there is good osseointegration in implants coated with HA.[58]

CONCLUSION:

Based on our review, we suggest that Polymethyl Methacrylate and Hydroxyapatite composite may potential as biomaterial candidate for porous trabecular dental implant. Further study still required to investigate this composite biomaterial *in vitro* and *in vivo*.

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CONFLICT OF INTEREST:

The authors declare no conflict of interest.

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