RESEARCH ARTICLE

Mechanical properties improvement and bone regeneration of calcium phosphate bone cement, Polymethyl methacrylate and glass ionomer

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ABSTRACT

Advancement in nanoscience and biotechnology of bone materials and cement has been increasing over the past several decades. The combination of biomaterials with trace elements for bone cement has verified their better mechanical strength and biocompatibility response. Also, the ionic replacement has affected the chemical, physical and biological properties of the substance. Pyrophosphate has supported better absorption of calcium phosphates (CaPs) and bone formation. Bone cement is the ionomer of an important material in tooth repair application used in the tooth filling, tooth cover, and to fix adhesions of the tooth and crown. Nanoparticle additives (magnesium oxide (MgO), hydroxyapatite (HA), chitosan (CH), barium sulfate and silica) and alternate monomers can be effective with Polymethyl methacrylate (PMMA) granules and methyl methacrylate monomers (MMAs) to decrease the isothermal temperature. These materials can be used for the growth and development of bone cements. This paper aims to demonstrate a general and different view of the applications of CaP, PMMA, glass ionomer and bone repair cements in various methods under different experiments procedure.

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INTRODUCTION

Nowadays, prominent development is being observed in bone cement and hydroxyapatite (HA) biomaterials. Recent reports and researches about calcium phosphate (CaP) cements, acrylic bone cement (based on methyl methacrylate) and glass ionomer bone cements have been investigated in this review article. The reports indicate various experiments and methods in this regard, which include several results in the field of periodontal disease, bone or cavity defects due to trauma or cancer, surgical and spinal fusion for the clinical as well as orthopedic and dentistry applications [1-3]. This article aims to present a general and a different view of the applications of bone cement with calcium phosphate (CaP), Polymethylmethacrylate (PMMA), glass ionomer and bone repair in various methods with different experiments. The study performed to explain the effective parameters on the improvement of mechanical properties, applications and methods of fabricating calcium phosphate, polymethyl methacrylate, and glass ionomer bone cement [4-6].

CaP is a family of minerals containing calcium ions together with mineral phosphate anions. Some calcium phosphates also contain oxides and hydroxides. CaP cements are cementitious systems consisting of powder and liquid phases. They are designed to fill the weak parts of bones and join to the bones. Moreover, they can be injected into the bone directly through a needle. Calcium

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phosphate bone cement contains liquid (soluble or aqueous solution) and powder with one or more solid compounds of calcium or phosphate salts. Thus, as the powder and liquid are mixed with the proper ratio, they form a paste that is set at room temperature with one or more precipitates of other solid compounds. They are not only biocompatible, but also osteoconductive; i.e. after being placed in the bone defects, they complete the bone formation after their gradual absorption and simultaneous transformation into the new bone tissue [1].

Moreover, they may compete with the PMMA cements and apatite coatings for fixing the metal orthopedic prostheses and orthopedic implants [1], since they make good connections to metal and bone [2]. Because of not having the polymerization reaction, these cements do not generate heat, and hence, the problem of cell death, a major problem in the PMMA cements, is not observed. One of the features of this cement is the formation of a hydroxy-implant during the setting and operation, which hardens the cement. The self-setting calcium phosphate cement contains a mixture of fine Tetra-Calcium Phosphate (TTCP) and Di-Calcium Phosphate Aphanridis (DCPA), or Di-Calcium Phosphate Dehydrate (DCPD) as a solid phase [3]. The cement forms HA when these compounds are mixed with water solution. As the CaP cement has neutralized pH, concentration and only includes CaP, it is highly biocompatible and capable of promoting bone formation [4-8]. The documentary information indicates that the formation of hydroxyapatite (HA) can be increased due to the presence of phosphate in the solution component. Recently, a new CaP cement has been reported, which does not require TTCP. Hydroxyapatite (HA) is obtained in these cements by using the phosphate-containing solution or the solution with the high pH as the liquid phase [5]. HA is known to be biocompatible, non-toxic, non-disinfectant, and the most important mineral that makes up bones and teeth [6].

CaP cements can be moulded after mixing or during the setting, or they can simply be injected into the bone defects. When some CaP cement is pressurized, they are dissolved into a thin paste and the solid mass in the syringe tube. Therefore, a good selection of the paste is essential for dental and orthopedic application [6-9]. Moreover, by changing the production process or the raw materials such as using a smaller size of the granules powder, the mechanical properties and the setting times can be altered [7,8].

Effective parameters for improving the mechanical properties of calcium phosphate

The effective parameters for improving the mechanical properties of CaP cement is including the temperature, body fluids, and blood, as well as the effect of the additives and adding agents to the CaP cement. Ionic replacement affects the chemical, physical, and biological properties of materials [9]. Mechanical properties such as mechanical resistance, force, and strength are suitable for the clinical applications, especially in the cement containing strontium (Sr), which has shown proper performance. Mixing of calcium phosphate cement with different materials (gelatin, pyrophosphate, gelatin injection and soybean extract, addition of strontium and collagen by starchy method, strontium with chemical composition of $_{CaCO3}$ with $SrCO_3$) and injection of tricalcium phosphate with different concentrations of silica on bone cement and the injection of calcium phosphate itself in the benign tumors have shown different results.

Mechanical tests of calcium phosphate bone cement for bone recovery and repair

The mechanical properties studied on calcium phosphate cement include hardness, fatigue, Young's modulus, and tensile strength, compressive strength, bending strength, shear hydraulic strength, etc. CaP cement is used for the treatment and repair of the periodontal disease, bone or cavity defects due to trauma or cancer, surgery and spinal fusion, and is considered for the clinical, orthopedics and dentistry applications. Various studies have been conducted on the CaP cement for the bone treatment and bone regeneration

Luo et al. [10]worked on an implant consisting of a neutral and calcium-based mixture, including HA biochemical nanocrystals, to prepare for an abnormal injecting and bioresorbable bone paste based on calcium element. Injection and preparation of the sample took only five minutes. The radiographic and histologic results, and the analysis of implant sections with the paste showed that the amount of bone trabecula was well regenerated in the cortical and duct sections. The fracture of the tibial plateau was treated in two women with 32 and 42 years of age. This paste is placed in the metaphysical defect, and the bone is then healed. The isometric results indicated that the paste can be hardened even in the wet or

biological environments. The implant components are designed in such a way to create a paste material similar to the fatty and spongy tissue of the bone. Articular areas, bone regeneration and repair, as well as the fractures, show in the radiography that the implant and the healing process was clinically acceptable [10].

Pellenq et al. [11] proposed a real molecular model of cement hydrates using an atomistic simulation model with molecular hardness, strength and shear hydraulic response with regards to an *in vitro* evaluation of calcium-silicate (C-S-H). The ratio of calcium to silicon is 1.7 and C-S-H particles compaction is 2.6 g/cm^3. Their results showed that this experimental model was able to create a general microstructure between the structure of materials and the magnetic structure, indicating favorable effects on the creep and strength properties [11]. Sandra Pina et al. [12] worked on the formation of manganese (Mn), zinc (Zn) and strontium (Sr) as well as the bone replacement of cement for the clinical approaches. Accordingly, the ionic substitution has affected the chemical, physical and biological properties of materials. Properties of the mechanical resistance, force and strength are suitable for the clinical applications, especially for the cement containing strontium, which have shown sufficient properties overall mechanical performance. According to their research, the bone cement with an ionic composition (Sr-Mg-Zn) is an alternative to the clinical and orthopedic and dental applications such as the repair of bone lesions and periodontal problems [12].

Guimarães et al. [13] studied the histomorphometry transplantation and calcium phosphate bone modification. According to their research, calcium phosphateCaP is used as the bone replacement because of the biocompatibility properties of the CaP cement. Their aim in doing this study was to compare the histomorphometric and bone regeneration values using the bilateral HA, CaP cement and autogenous bone graft. Two cavities with a diameter of 5 mm were produced in the parietal bone of 72 rats. The test cavities GI.GII.GIII.GIV was filled with the CaP cement, bilateral ceramic HA, blood and bone graft. Animals were killed after 30, 60 and 90 days, and samples went under histomorphometry analysis. Then, they compared the test cavities with each other. Their results showed that the bone formation was more for the defects treated with autogenic bone graft over the 60 and 90 days in the GI.GII. GIII test groups. GI.GII cavities contained larger areas. During the test period, the GII evaluation illustrated the proper bone formation more than the GI cavity. Surgeons use bioceramics for the maxillofacial surgeries that require bone grafting [13]. Unuma et al. [14] studied the effect of temperature on the CaP cement with advanced in physical and mechanical behavior. Their reports showed that when the room temperature is similar to the biological temperature, it allows mixing of the CaP cement powder with gelatin (molecular weight of gelatin 100 KDa). The components of carbonic acid – phosphate is formed via the dissolution- precipitation in forming the HA. The reactions should be at room temperature when one or more molecules of CaP are coated with gelatin since the gelatin layer prevents dissolving of the oxidation. The gelatin temperature is increasingly deposited in the physiological temperature and the gelatin layer is eliminated rapidly. Gelatin is rapidly dissolved in the adjusted liquids at 310 K, reaching to the temperature of 293 K after cooling [14].

Grover et al. [15] suggested the effect of pyrophosphate on the absorption of CaP cement and bone formation. Hydrogenated crystals are mostly of nanocrystalline size in the bone. Normally, nanoscopic shows 100 nm in length, 4-6 nm in thickness, and width of 30-45 nm. HA and β-tricalcium phosphate (β-TCP) are micro-crystalized and therefore show a specific level of bone regeneration. The HA substitute of bone graft typically has a mechanical or biological similarity to the human bone. Due to the proper optimization of the cement formulations, there was the possibility to produce a substance composed of 28% by weight of amorphous calcium pyrophosphate with the low resistance of 25%; i.e. 2 MPa, that is the same amount for the trabecular bones and other non-mineral cement for the bones. Adaptable materials, such as the weak crystalline HA, may indicate the reducing degradation of orthophosphate cement. Periphosphate ions are identified as the strongest inhibitors of forming a little *in vivo* apatite. Modification of CaP biological materials with calcium pyrophosphate could effectively improve the rate of bone formation inside the body. Pyrophosphate was dissolved from the hardened ceramic materials, and an *in vivo* model showed that this was due to more rapid solubility via dissolution of the active pyrophosphatase enzymes. The obtained results show that this is the first substitute of the bone cements, which is related to

the mineralizing process in the form of the enzyme that supports the production of bones [15].

Kovtun et al. [16] analyzed the performance of the living tissue as well as the gelatin injection and soybean extract on the HA foam. In this study, the inter-physical performance of gelatin-based hydroxy and the foam apatite soybean extract of the non-foam CaP cement cultured is proposed for a bone defect of the distal femoral section of rabbit's bone. According to their reports, bone formation and degradation of materials after 4, 12, and 20 weeks were studied using histological and biomechanical methods. The foams adjust the living tissue after being injected. They used XRD and implantation histology images. One of the advantages of using gelatin on the other foam agents is its properties. The addition of gelatin increased the continuity and expansion of osteoblastic cells in CaP under laboratory conditions and increased osteogenic differentiation and proliferation. Compared to the non-foam CaP cement, cellular foam degradation was significantly increased and was associated with the formation of a new bone. Both foams showed excellent compatibility. According to their results, foam with soybean extracts contributes to bone formation and increases mechanical performance [16].

He et al. [17] investigated the bone cement for vertebroplasty and balloon kyphoplasty. Osteoporotic vertebral compression fracture (OVCF) has gradually been transformed into a serious health problem in the world. Two minimally invasive operations, i.e. vertebroplasty (Vp) and balloon kyphoplasty (Bkp) have been developed to reduce the mortality rate of patients and improve their quality of life. According to the reports released by He et al., both Vp and Bkp require injection of bone cement into the patient's vertebrae to fix the broken vertebra. In this regard, bone cement plays an important role in the treatment as the stabilizing agent. In general, two major categories of bone cement have been introduced, which are non-degradable acrylic cements and degradable CaP cements. Due to the lack of mobility, acrylic cement is not suitable for the selected materials of Vp and Bkp and are not used for wider applications. With regards to the unique bio decomposition, ductility and low shrinkage, CaP cement plays an important role in the development of the next generation in Vp and Bkp. A sample of CaP cement (SR-CPC) can simultaneously form and absorbed by the bone, showing the potential application for the bone cement to strengthen the bones and heal the fractures [17].Huang et al. [18] worked on the physical, chemical properties and biocompatibility of silica and injection of tricalcium phosphate (TCP) on the bone cement. Based on their studies, silica has an important role in the mineralization extraction and its composition has increased the biocompatibility of the orthopedic implants. Various concentrations (0%, 10%, 20%, and 30%) of silica were investigated in their study. The Si-a-TCP was obtained after refining the prepared powders at 1400°C. The results show that the increase in sodium content has increased the apatite precipitation rate. The in vitro cellular testing indicates that silica-enriched cement increases the proliferation and differentiation of hDpC. The destruction of bTCP and osteoporosis make the cement containing silica the best material for the bone repair [18].

Zhou et al. [19] also investigated the preparation and the new specification of CaP with the injected Sr and collagen. For this report, CaP was prepared by adding Sr and collagen, and the modified starch method was used in that regard in which the collagen is a very active bioactive substance. The Sr containing CaP cement was rapidly decomposed by increasing the Sr concentration. Three types of Sr containing CaP cement (5%, 10%, and 20%) were studied too. The obtained results showed that CaP-containing 5% Sr cement had a maximum compressive strength of 36 MPa. Therefore, the CaP cement containing 5% Sr was used. The compressive strength of cement was reduced by increasing the ratio of liquid cement to the solid bone. Various parameters such as the injection time, solidification time, microstructure, phase composition, compressive strength, anti-elasticity and tissue properties of the materials were investigated. The results showed that the used biomaterial can be injected with proper mechanical and physical performance. The highest compressive strength of cement was obtained with a liquid to solid ratio of 0.3. The cement mechanical resistance was measured 48 ± 2.3 MPa. When the ratio of liquid to solid bone cement was 0.6, and the compressive strength of bone cement decreased to 21 ± 2.5 MPa. Analysis of the tissue repair showed that the bone was modified after 16 weeks. This material is used for bone defects in orthopedic and maxillofacial surgeries [19].

Ichihara et al. [20] suggested the CaP cement injection in a benign tumor in the hand exoskeleton of two people. Based on their report, bone repair

usually occurs after the fracture and healing of the benign bone tumors. There were no previous clinical reports on exoskeleton regeneration [20]. In this report, they examined two clinical cases of exoskeleton regeneration after CaP injection in the benign tumor in the hands of two people. The benign tumor bone was completely removed in two cases and CaP injection was performed mechanically. This article showed that CaP was capable of rebuilding the trabecular bone. CaP cement is one of the best solutions for ossification [20].

Ioannidou et al. [21] analyzed the porous texture of the cement hydrates. Their studies showed that the comparison of data in a volumetric test in certain ranges for 3 samples indicated that nanoparticle experiments were mainly susceptible to the adhesive side of the matter (η <0.6) [21]. Oh et al. [22] worked on the performance of Chronos injection and its replacement in the CaP cement. Their research showed radiography provides a good clinical outcome for the bone defect after internal fixation and proximal tibia fracture. Chronos injections give the patient a remarkable result in improving knee performance and reducing the foot pain [22]. Habraken et al. [23] investigated CaP for biological applications. According to their reports, human bone includes 70% of CaP mineral. They proposed to investigate the extraordinary developments in the CaP studies in the past 15 years, especially in the field of biomineralization, which is a bioactive factor for delivering the ions. Their reports show that the appropriate biological behavior and easily preparation procedure with low costs was utilized [23].

Luo et al. [24] studied the mechanical properties of brushite and apatite, as the two main types of CaP cement. They aimed to evaluate the mechanical properties and cement formulation of empirical brushite and apatite cement compared to the commercial brushite and apatite. They also aimed to evaluate the tensile and bending strength on both sides of the cement in wet and dry conditions. Their results showed that the conventional cement with mechanical and empirical properties is better than the commercial cement. The high compressive strength of 6.5 ± 57.2 MPa (before drying) and 6 ± 69.5 MPa (after drying) were found for the testing cement. This cement also has a tensile strength (0.8 ± 10) and a double-sided moisture-bending strength (1.8 ±30.7). The dry CaP cement has a higher moisture content than the moist cement under the same conditions [24]. Canillas et al. [25] suggested CaP for the applied biomedical cases. Their studies showed that CaP was advanced with new techniques in biomaterials science, medicine, or tissue engineering. Whereas bioceramic materials have been selected based on their biocompatibility and mechanical properties for the damaged bone replacement, CaP is an appropriate solution for bone tissue regeneration [25]. Lode et al. [26] investigated the calcium phosphate cement containing Sr for the bone defects and osteoporosis. According to them, the CaP bone cement containing strontium used a biocompatible oil as a carrier fluid in contact with the aqueous medium. Strontium was used with the chemical composition of $CaCO_3$ and $SrCO_3$, and replacement of one of the $CaCO_3$ cement material components with $SrCO_3$ was used for the strontium ions in the cement. The replacement resulted in improving the mechanical properties, better radiography contrast and stimulation of cell proliferation as well as the osteogenic cells *in vitro* compared to a controlled cement with no Sr elements. Their results indicated that the CaP cement containing Sr is for the clinical regeneration of bone defect associated with the osteoporosis. Nowadays, the clinical operations have s with minimally invasive surgical (MIS) techniques. The developed cement application kyphoplasty is a MIS technique used to restore osteoporosis vertebral compression fracture [26]. Dolci et al. [27] offered a new and useful bone tissue delivery system. Bisphosphonates are used due to their biocompatibility and less toxicity, as compared with many polymers. An α-CaP cement with alendronate was produced by the spray technology. The composition of alendronate and cement is limited because alendronate can remove calcium from calcium, thus preventing cement regulation. According to the reports, solid-state specimens showed that alendronate's capsule did not change its crystalline structure. Alendronate Loaded MPS increased the duration of adjustment and hardening reaction, resulting in a complete conversion of CaP alpha-chloride to reverse HA calcium. *In vitro* test results in cement with alendronate loaded MPS showed that the system allows the drug release over a controlled period of time. Alendronate CaP cement is very important for the treatment and minimizes the side effects of the infusion of bisphosphonates. The results of their study indicate that the combination system is suitable for a variety of narcotics, such

as antibiotics, anticoagulant drugs and cancer drugs that help improve bone tissue [27]. Ajaxon et al. [28] considered the fatigue function from the CaP cement with high mechanical resistance and decomposability. They examined the effects of the environment and changes in the ratio of liquid to powder during the fatigue life. In increasing the maximum level of compression or the ratio of the liquid to the powder, its survival probability decreases. According to their study, the probability of survival of the investigated materials for the liquid to powder ratio is the maximum compressive stress of 30 MPa. In the PBS environment, the high strength cement resistance has a 100% likelihood of survival in case a pressure of 5 MPa is used. This level of compression is in the range of the quasi-static strength of human bone, which is twice as much as the measured loads in the spine of the living tissue. This fact indicates that this material is for particular applications in orthopedic field. The cement can drastically destroy under the pressures that are substantially lower than the quasi-static strength of the materials (at least 30% of the semi-static energy). The results of this study show the importance of fatigue testing on CaP bone cement. Fatigue behaviour of the decomposable CaP cement has been very important in the clinical application [28].

Ajaxon et al. [29] analyzed the elastic, tensile and cracking properties of the calcium phosphate bone cement by a measurement method. In this investigation, they studied the mechanical properties of three different types of calcium phosphate cement (apatite, monetite, and brushite). The results indicate that the use of compression may in some cases cause compressive strength of up to 40%. Also, these measurements may reduce the elastic modulus by 62% compared to digital measurements. Using a very different digital image, the considered rate was found 24.3 ± 2.3 GPa for brushite cement, 13.5 ± 1.6 GPa for apatite, and 7.1 ± 1 GPa for monetite cement. The Poisson ratio was determined 0.26 ± 0.02 for brushite, 0.21 ± 0.02 for apatite and 0.20 ± 0.03 for monetite, respectively. All the considered calcium phosphate bone cements indicate the rates 0.17% to 0.19% at the beginning of interference to cracking. Cholesterol and cadmium protein of CaP cement is mainly reported to be higher than before. Their obtained results show that the elastic modulus from digital images is significantly higher as compared to the results of the displacement measurements made by the testing authorities of the material. Also, the Poisson ratio, establishing the pressure as well as the elasticity can be determined by the digital image tools. Their results showed that the aim of the material behavior prediction for the simulated clinical scenarios is quite important in the computational models [29].

Preparation of calcium phosphate bone cement

CaP Cement is prepared according to different chemical formulas with calcium and phosphorous based on definite rates. This composition can be prepared by mixing the tetra CaP powder and anhydrous di-calcium phosphate with Na_2HPO_3 solution [30]. Since, the CaP bone cement is used in the body, it should be tested for environmental corrosion, substrate adhesion testing and also its compressive strength. Since the base of CaP bone cement is of calcium and phosphate, it has the properties of a bioceramic composite material, the brittleness of which causes it not to have appropriate torsional and compressive strength. The ultimate strength of the stiff calcium phosphate cements depends on the degree of conversion of the cement, the cement porosity, the type of cured product, the size of the crystal, or the use of filler particles. The use of low modulus cements can reduce the effect of stiffness of the conventional cement, which reduces the hardness of the vertebrae, and thus maintaining better bone strength. Gelatin and soy significantly increase the elasticity of cement paste [31-40]. Gelatin causes continuity and expansion of osteoblastic cells in calcium phosphate [14], [19]. Bonding of bioactive ions, e.g. of magnesium, zinc, fluoride and strontium, which show better biological performance and mechanical properties, increase the bone metabolism [12], [19], [26]. Long duration of the cement setting (carrying with CaP cement) can be due to the inability of cement to maintain the health conditions. Hence, the required setting time should be fast.

Conclusion in bone healing and repair using calcium phosphate bone cement

Calcium phosphate cement can be used for the treatment of periodontal disease, bone or cavity defects due to trauma/cancer, surgery and spinal fusion, and for clinical, orthopedic and dental applications. It is better to use the biologically active ions, e.g. of magnesium, zinc, fluoride and strontium, to improve the mechanical properties and biological function [12], [19], [26]. Gelatin

Table 1. Different crystals that can precipitate in calcium phosphate cement during setting

COMPOSITION	CHEMICAL FORMULA	Ca/P
Di-Calcium phosphate dehydrate (DCPD)	$CaHPO_4.2H_2O$	1.00
Octacalcium phosphate (OCP)	$CaH_2(PO_4)_6.5H_2O$	1.33
Amorphous calcium phosphate (ACP)	$Ca_3(PO_4)_2.3H_2O$	1.50
Hydroxyapatite (HA)	$Ca_{10}(PO_4)_6(OH)_2$	1.67

polymer can be used to integrate and expand the osteoblastic cells regarding its natural properties [14], [19]. Gelatin can be used to increase the elasticity of cement paste [16]. To reduce the stiffness of cement, it can be use as a cement with a low modulus or the brushite cement, which has a soft texture [40-48].

The effective suggestion of previous researchers on improving mechanical properties of calcium phosphate bone cement

It has been suggested by previous researchers that CaP cement is widely available and affordable for injuries [23]. They have suggested that the CaP cement is not ideal for the clinical applications regarding its weak properties for injection. Moreover, due to its weak adhesion, it is easily destructed by bleeding of the surgical area. These disorders largely restrict their use in the clinical practices for dental and orthopedic approaches. Therefore, it has been proposed to add bioactive ions, for example of magnesium (Mg), zinc (Zn), calcium fluoride (CaF_2) and strontium (Sr), and by injecting or adding gelatin or gelatin-soy, to convert this cement into an ideal bone cement for the clinical, orthopedic, and other medical applications [49-56]. b-TCP consists of several bone graft replacements that are commercially available. However, since it is not formed under the environmental conditions, it is not widely used for the post-trauma restoration. The nature of metastasis from salt indicates that the hydrolysis is poorly formed. More appropriate results can be achieved by adding magnesium salts and recommended salts with the cement, to prevent prolonged contraction [18]. With the help of suitable substances such as pyrophosphates, a specific environmental reaction can be reached by replacing the ceramic bone graft with another proper substance rather than taking an action in the implant site [15]. In subsequent generations of cement for BkP and VP, sufficient injection, coherence and radiopacity should be provided for the adequate mechanical strength and porosity to allow blood circulation in the body, as well as cell migration, increased bone growth, excellent osteoconductivity, and bone resilience to promote the new bone formation, degradability and intermediate environmental conditions for the absorption of the cement materials to correspond to the bone formation [17].

Acrylic bone cements (with methyl methacrylate basis)

Polymers with large molecules that are made by smaller molecules called monomers. Polymers can be divided into three categories for the medical applications such as synthetic polymers, elastic polymers for surgical applications, and adhesives for medical applications. Polymethyl methacrylate, as a kind of polymers, is mainly used for the biomedical applications [31]. PMMA bone cement is made of a polymethyl methacrylate, which consists of two parts. The liquid section is composed of methyl methacrylate (MMA), as the activator, and hydroquinone as an inhibitor. This cement with 90% of polymethyl methacrylate (PMMA) is formless and completely transparent. The rest of the materials in it are mainly crystalline barium sulfate or zirconia oxide, which distinguishes the product in a non-transparent state. The PMMA microscopic structure is combined with two-component, a part of the small PMMA particles before polymerization, which is supplied as a powder fibre, and the other part is MMA liquid monomer. Both materials are added in the catalyst operation Table 1, which begins with polymerization of the monomer liquid. The formless polymers such as PMMA are fragile and hard plastics in the room temperature. PMMA is attacked by mineral acids, but it is resistant to the alkalis, water and organic salt solutions. PMMA is affected by the tensile and viscoelastic deformation. PMMA has used since

1960 as an extraction polymer of bone cement in the orthopedic approaches to fill the irregular space between the prosthesis and the bone during complete replacement of the hip joint to maintain the prosthesis in place. They are used to fix the artificial joints, securing orthopedic operations, and to transfer the mechanical loads from the implant to the bone. They are used in almost 50% of the orthopedic implants for stabilization [31].

Effective parameters in improving the mechanical properties of polymethyl methacrylate bone cement

Acrylate polymer, commonly known as acrylic or polyacrylate belongs to a group of polymers that can be called as plastics. This is due to the transparency and resistance to fracture and stretching properties of this material. Polyacrylates are made of acrylic acid, methacrylic acid and their esters [31]. Nanoparticle additives (Magnesium oxide, Hydroxyapatite, chitosan, barium and silica sulfates) and alternative monomers can be used with the PMMA particles and methyl methacrylate monomers (MMA) to reduce the isothermic temperature. By measuring the temperature variations on different bone cements with different concentrations of nanoparticles and monomers, the maximum curing temperature was for another sample of PMMA with the MMA monomer. However, examples with higher concentrations of nanoparticles had the highest temperatures compared to the PMMA sample with only MMA monomers. Moreover, adding 3MPMA to the monomer reduced the max. curing temperature of the samples, but adding GMA to the monomer reduced the impasting time of the samples [32].Since, the hip and knee joints have very complicated biomechanics and support extensive loads, the acrylic bone cement must comply with international standards (ISO 5833) to preserve the biological safety and durability of the implant [33].

Mechanical tests of polymethyl methacrylate bone cement for bone repair and recovery

The mechanical properties of PMMA bone cement mainly depend on the properties of the granules, which are the principle solid part of the cement. Since, the cement is under the cyclic loads, the other mechanical properties including the dynamic properties are also needs to be investigated [33]. Due to the chemical reactions during the polymerization and strong exothermic regulator reactions, severe contraction of cement after polymerization, intolerance of hardness between bone and cement, the toxic effect of monomer in the local tissue damage needs to be considered. Specific problems occur at the interfaces caused by various tensile modules of materials 110 GPa for titanium, 2.2 GPa for PMMA and 20 GPa for bone [31]. The tests used on the PMMA bone cement include hardness tests, CSM Nano Indentation tester applied for determining the mechanical properties such as elastic module and plastic tensile stress behavior or the creeping behavior, pushout test to determine the bonding strength of bones and implants [34, 57-62], flexural strength test, flexural modulus, fracture toughness, impact resistance and small-punch test for restoring the mechanical properties of the acrylic bone cements and the nano-composite materials [35-36]SEM is also used to investigate the radiation dose in the fracture behavior of this material [37-38].

Application of polymethyl methacrylate bone cement to repair and recovery

PMMA bone cement loaded with antibiotics is widely used as an agent for reducing the incidence of periprosthetic joint infections (PJI) [39]. This cement is also used to fix prosthesis in the human body in the orthopedic surgeries. Several kinds of research have been done on the PMMA bone cement regarding bone repair and recovery, some of which are as follows: One of the methods that can improve the mechanical properties of PMMA bone cement is adding fibre reinforcing particles to increase the hardness of the cement and its strength [41]. Fatigue features and strengthening of PMMA are improved with carbon fibre, particles of hydroxyapatite, stainless steel fibre, titanium fibre, zirconia particles and fibre, etc. [31]. Khandaker et al. [32] showed that PMMA bone cement produced an isothermic reaction that damaged the bone tissue around it during the orthopedic surgery. Nanoparticle additives (magnesium oxide (MgO)¸ hydroxyapatite (HA)¸ chitosan¸ barium and silica sulfates) and alternative monomers could be used with PMMA granules and methyl methacrylate monomers (MMA) to reduce the isothermic temperature. The aim of this study was measuring the temperature variations on different bone cement with different concentrations of nanoparticles and monomers and considering the maximum curing temperature for another PMMA sample with the MMA monomer. However, there were samples with higher concentrations of nanoparticles that

had the highest temperatures compared to the PMMA sample, which had only MMA monomers. Moreover, adding the 3 PMMA to the monomer reduced the max. curing temperature of the samples, while GMA addition to the monomer reduced the impasting time of the samples [32]. Russo et al. [35] worked on a primary analysis of mechanical and antibacterial activities of the bone cement based on the loaded PMMA with gold nanoparticles, which improves the performance and antimicrobial activity. The mechanical analysis provided interesting information on the effect of Au-NP on a bone cement based on PMMA. It was specifically found that the inclusion of 0.25% of the Au-NPs weight significantly improved the performance of punch performances without negative changes of the bone cement compressive properties. This primary study shows some of the important features in optimizing the Au-NPs-loaded bone cement, which should improve the mechanical performance of the cement. On decreasing the thickness of the biofilm layer and the ratio of live-to-death bacteria to the dead, several critical characteristics were identified in the earlier studies for this article to maintain the bone cement performance [35]. Salehi et al. [39] specified the release of daptomycin from a daptomycin-xylitol-loaded cement sample as a function of xylitol particle loading. The PMMA bone cements loaded with antibiotics are widely used as an agent for reducing the incidence of periprosthetic joint infections (PJI). Reports on daptomycin with the average dose indicate that the releasing speed of that from the cylindrical specimens is low. It has been shown that the use of portages, such as dextrose, glycine, or xylitol particles in the powder is an effective way to increase the releasing speed of daptomycin. The release of daptomycin from the bone cement sample may occur with a condition that causes the initial explosion of antibiotics. This mechanism is unaffected, when xylitol, daptomycin and dry powder are mixed, although there are constant increases in the related models with the releases [39].

Morejón et al. [40] studied on polymer particles with particle size distribution and molecular weight that allows the formulation of bone cement according to international standards. Polyvinylpyrrolidone (PVP) and polyvinylpyrrolidone-hydroxyapatite compounds were studied as stabilizers of the system. Benzoyl peroxide was the initiator of the reaction and the copolymer granules characterized by various analytical techniques. It was shown that the two studied stabilizers (PVP and PVP-HA mixtures) were effective in obtaining the granules during the polymerization process. Only the PVP provides granules with a uniform distribution in the range of commercial cement size of 30 - 10 μm. Regarding the PVP-HA stabilizer, the obtained distribution was two-dimensional (2D) and the granule size was greater than 100 μm [40].

Morejón et al. [40] worked on obtaining the polymer particles with particle size distribution and a molecular weight that allow the bone cement formulation to perform according to the international standards. PMMA granules were synthesized for this study. Polyvinylpyrrolidone and polyvinylpyrrolidone-hydroxyapatite (PVP-HA) compounds were studied as the stabilizers of the system. Benzoyl peroxide was the initiator of the reaction. The copolymer granules were characterized by various analytical techniques. Polyvinylpyrrolidone alone was the best stabilizer. It was shown that the two stabilizers studied (PVP and PVP-HA mixtures) are effective in obtaining the granules during the polymerization process. Only the PVP provides granules with a uniform distribution in the range of commercial cement size: 30 - 10 μm. Regarding the PVP-HA stabilizer, the obtained distribution was two-dimensional and the granule size was greater than 100 μm [40].

The combination of MWCNT with the orthopedic bone based on PMMA is the case, in which a high degree of MWCNT Polymer matrix interaction has shown that the fracture resistance increases during mechanical loading. Also, it has been reported that MWCNT-PMMA bone cement increases the viscosity and decreases the polymerization temperature. Reducing the temperature during the polymerization can reduce the thermal necrosis of the in vivo cell. Moreover, reducing the bone cement exotherm reduces the remaining stresses within the cement mantle as a result of over-contraction [63-70]. Adequate studies are required for using MWCNT in the PMMA bone cement. Specifically, precise investigation of the biologic compatibility of MWCNT composite cement is also required. This consideration needs the connection of human osteoblasts to MWCNT-PMMA bone cement and ultimately leads to the *in vivo* cell activity. This is a clearer indication of the composition of several MWCNT composite cement in the body. Initial studies prove a quite high potential of MWCNT systems for the

Table 2. Weight average molecular weight (*w*) of the commercial bone cement

CEMENT	SP*	$\overline{M}_W$
CMW (Vila, 1992)	GR	1.06 x 105
CMW (Khorosani,1992)	GR	1.43 x 105
Palacos R (Topoleski et al., 1990)	EO	5.2 x 105
Palacos R (Harper, 1996	EO	8.7 x 105
Palacos R (Morejón, 1995)	EO	7,7 x105
Simplex P (Haas, 1975)	GR	1.98 x105
Simplex P (Topoleski et al., 1993)	GR	1.94 x105
Simplex P (Morejón, 1995)	GR	1.96 x105
LVC-Zimmer (Topoleski et al., 1993)	GR	9.32 x104
Rostal (Vila, 1992)	EO	3.24 x 105

SP*: Sterilization Process. GR: Gamma Radiation, EO: Ethylene Oxide

biomedical and bioengineering applications as the composite scaffolding covering structure, although most of these materials are in the in vitro scale and laboratory tests [42]. Dunne et al. [42] investigated that, as the total amount of Total Joint Replacement (TJRs) increases each year, PMMA bone cement is still needed for most TJR methods, even with the reported decreasing amount of that. It has been proven that several factors contribute to damage the "aseptic" for the cement implants. Thus, there is a critical need for the development of new and emerging technologies for the treatment of chronic diseases, which can result in less tissue damage, help tissue regeneration, and provide quicker recovery of the patients.

López et al. [43] aim to evaluate the thermal analytical properties such as adjustment time, maximum temperature and enthalpy of polymerization of PMMA/Ca^{+2} bone cement in addition to their chemical properties. Polymerization reactions do not change the crystalline structure of the forces, which is very important for improving the biocompatibility. Moreover, PMMA is used because of its proper biological stability and good mechanical properties. The remaining monomers were analyzed using H-NMR spectroscopy and showed low values (mol 1%>). The setting time varied between 3.6 to 8 minutes and the maximum temperature varied between 62°C and 110°C. The obtained values are ten times lower than the MMA base monomers in the case of enthalpy polymerization, and the resulting oscillation is between 1 and 8 kJ/mol [43].

Morejón et al. [40] worked on obtaining the polymer particles with particle size distribution and a molecular weight that allow the bone cement formulation to perform according to the international standards. PMMA granules were synthesized for this study. Polyvinylpyrrolidone and polyvinylpyrrolidone-hydroxyapatite (PVP-HA) compounds were studied as the stabilizers of the system. Benzoyl peroxide was the initiator of the reaction. The copolymer granules were characterized by various analytical techniques. Polyvinylpyrrolidone alone was the best stabilizer. It was shown that the two stabilizers studied (PVP and PVP-HA mixtures) are effective in obtaining the granules during the polymerization process. Only the PVP provides granules with a uniform distribution in the range of commercial cement size: 30 - 10 μm. Regarding the PVP-HA stabilizer, the obtained distribution was two-dimensional and the granule size was greater than 100 μm [40].

Morejon et al. [33] examined the effect of sterilization by ethylene oxide or gamma radiation on bonacryl bone cement, determining how the sterilization methods affect the molecular weight of the polymer as well as its quasi-static mechanical properties. The results showed that gamma radiation changes the molecular weight of PMMA, as outlined in the following Table 2. Although the compression and bending strength did not alter by the sterilization process, the setting time, the maximum temperature and the mechanical

properties were also under the international standard (ISO 5833) [33]. Preparation of bioactive bone cement with the required proper mechanical properties that can lead to bone growth is considered by Qiang. The extracted bone cement from PMMA cannot create an adhesive chemical bond to create a stable cement interface. The improved bioactive bone cement with the porous surface was analyzed in this study to determine the specification, mechanical properties and its behavior in a simulated body fluid. In laboratory conditions, the cellular responses of the samples were also investigated in terms of cellular continuity, proliferation, and differentiation of osteoblasts. The bond strength of bone implants was also assessed using the tensile tests. For the other achievements of this project, it can be said that the modified bone cement with low environmental activity fillers is suitable for the required performance and mechanical properties, but it does not properly affect its biological properties. Also, the degree of dependency, proliferation, and the osteogenic distinction from the preosteoblastic cells increased. The results of the tensile test showed that a higher level is obtained in the bond strength using the improved bone cement due to the formation of apatite layer and bone implantation after implant bone graft [34].

Russo et al. [35] studied the primary aspects of mechanical and antibacterial activities of the bone cement based on the loaded PMMA with gold (Au) nanoparticles, which improves the performance and antimicrobial activity. The mechanical analysis provided interesting information on the effect of Au-NP on a bone cement based on PMMA. It was specifically found that the inclusion of 0.25% of the Au-NP weight significantly improved the performance of punch performances without negative changes of the bone cement compressive properties. This primary study shows some of the important features in optimizing bone cement Au-NP -loaded, which should improve the mechanical performance of the cement. On decreasing the thickness of the biofilm layer and the ratio of live-to-death bacteria to the dead, several critical characteristics were identified in the earlier studies in this article. Thus, the optimization of nano-composite materials and predicting the mechanical behavior can be obtained by combining the empirical tests and the mathematical models [35].

Munker et al. [41] provided a general investigation on the effect of different sterilization methods on the mechanical properties of personal medical devices based on the PMMA. PMMA methyl methacrylate materials were sterilized with different methods, and ethylene oxide, hydrogen peroxide gas plasma, autoclavation and y-radiation, mechanical properties with bending strength test, bending modulus, fracture toughness and the impact strength were determined. The autoclave equipment is not suitable for sterilization of PMMA materials. It seems that hydrogen peroxide gas plasma, ethylene oxide and y-radiation are the appropriate techniques for sterilizing the PMMA-based medical devices. Radiation-Y can even increase the effective bending power in a wet environment [41]. The results of the experiments regarding increasing the elastic modulus of PMMA and the two-phase CaP common bone cement, the results of the experiments showed that the addition of bioceramic BCP to this bone cement increases its elastic modulus by more than three times, and the two-phase CaPcan be an appropriate substance to improve the properties of PMMA due to biocompatibility, bioactivity, and the ability to increase the elastic modulus [38].

Preparation of polymethyl methacrylate bone cement

PMMA is prepared in two single-array and multi-array methods: Prepare a solution of MMA, toluene, lithium fluorovinyl, and methanol for the single-array method. Dry the inflated solid substance and dissolve it in acetone, and after that pass it through a filter.

Obtain a solution of fluorine, tetrahydrofuran, some freshly prepared butyl lithium, methyl methacrylate, methanol, ether and benzene for the multi-array method, and then centrifuge the solution and precipitate it again in the ether. Then, sift the polyester and wash it with methanol. The polymethyl methacrylate will then be obtained [44].

Conclusion for bone recovery and repair using polymethyl methacrylate bone cement

1) PMMA bone cement creates an isothermic reaction during the polymerization process that damages the bone tissue at the time of orthopedic surgery [32].

2) The semi-static mechanical properties (bending strength and compression strength) were not affected in this type of cement by the sterilization process with ethylene oxide or gamma radiation on bonacryl bone cement, although gamma radiation changes the molecular weight of

PMMA [33].

3) Autoclave systems are not suitable for PMMA materials sterilization. It seems that hydrogen peroxide gas plasma, ethylene oxide and y-radiation are appropriate techniques for sterilizing PMMA-based medical devices. Radiation-Y can even increase the effective bending power in a wet environment [71-78].

4) The bone cement extracted from PMMA cannot create an adhesive chemical bond to prepare a stable cement interface. Bioactive bone cement can indicate bone graft ability, but its clinical application is limited, since bone absorption is observed after the implantation. Porous PMMA increases the growth of bone by adding carboxymethyl cellulose (CMC) microparticles, alginate and gelatin. Formation of apatite layer and bone implantation in the bone graft is obtained with a higher level of bond strength to use for bone cement [34].

5) Polymerization reactions in analytical thermal properties such as setting time, maximum temperature and enthalpy of PMMA/Ca^{+2} bone cement polymerization does not change the structure of the forces that are important for improving the biocompatibility. Also, it is used since this material has appropriate biological stability and mechanical properties. In the case of enthalpy polymerization, the obtained values are ten times lower than the MMA base monomers and the resulting fluctuation is between 1 and 8 kJ/mol. Making acrylic bone cement is a complex process because the contact between the liquid and solid states leads to the onset of several physical and chemical events that occur simultaneously [42].

The effective suggestion of previous researchers on polymethyl methacrylate bone cement.

1) Hydrogen peroxide gas plasma, ethane oxide and y-radiation can be appropriate substances for sterilization of the PMMA-based medical equipment [41].

2) Adequate research and development are required to exploit the MWCNT in PMMA bone cement. In particular, a detailed study of the biocompatibility of MWTCN composite cement is required [42].

3) PMMA/BCD composite bone cement can be an appropriate candidate for biomedical activities [38].

Glass ionomer bone cements

Glass ionomers are suitable for dental repair. Glass ionomer cement consists of calcium, alumina-silicate glass powder, and acrylic acid homopolymer or copolymer aqueous solution [45]. The structure, properties, and clinical applications of this cement show that this cement is set by one acid-base reaction within 2-3 minutes and forms a strong, acceptable strength with an acceptable appearance. This cement has certain unique properties that make them appropriate as repair and adhesive materials, for filling, tooth cover, adhesion regeneration, adhesion to tooth structure and base metals, anticoagulant properties due to releasing fluoride, thermal compatibility with the tooth enamel and biocompatibility [45, 79-91]. These materials release fluoride and are bioactive substances [46]. This cement is widely used as a dental material due to its ease of use, low thermal expansion coefficient, good biocompatibility with bone tissue as well as a good bonding with tooth surface and metals [48].

Effective parameters for improving the mechanical properties of glass ionomer bone cement

Several researchers have examined GIC cements by adding different materials such as sea shell for analyzing bone scaffold, bioactive nano-silica combined with dental cement, nano-field materials (NCR) and resin-modified glass ionomers (RMGI). Mechanical tests of glass ionomer bone cement for bone recovery and repair According to Xia Gua [49], the antibacterial ionomer glass has been developed non-absorbing nitrate (ammonium quarantine salt) (PQAS). The compressive strength of CS and stability of S. mutants are used to recover the antibacterial agents. The samples were placed in distilled water at 37°C before the experiments [49].

Some of the tests on GIC cement are such as CS compression strength and stability of S. mutants to restore antibacterial function [49], using SEM to investigate the structure of scaffold [50], XRD examination on cement glass ionomer to verify the electrical conductivity as well as dielectric and thermal properties [51], using XRD to detect the phase of prepared powder of the type of bioactive silica, spectrometry test to investigate the dispersed energy and using of TEM electron microscope to view the bioactive silica [52], agar diffusion test to measure the antibacterial activity of dental cements grown in Streptococcus mutants [53], *in vitro* test and Dunnet T-tests and Tamhan T2 [55], cytotoxicity test with Trypan blue exclusion test for the genetic toxicity and toxicity of certain

commercial orthodontic glass ionomers [55]. Cell metabolism is also evaluated using the methyl tetrazolium test [56]. Biological glass nanoparticles were evaluated by the synthesized sol-gel with a size of less than 80 nanometers. XRD, XRF, SEM, and TEM characterization tests were used for the fuzzy studies, confirmation of the presence of oxides in the final composition, size, and the particle shapes, respectively [48]. Tukey and Anova tests were also used to compare the residues made by two types of cements at different time intervals.

Application of glass ionomer bone cement for bone recovery and repair

Glass ionomer bone cement is used for the bone repair, gingival defect and dental items. Various researches are done on the glass ionomer bone cement for bone recovery and repair, which include:

The combination of bioactive nano-silica with dental cement improves its biological performance, which may be useful in overcoming the marginal cracks of commercial cement. FT-IR indicates that the prepared silica has a substance-dependent bioactivity, preparation method and dispersion environment. The TEM images illustrate the presence of bioactive silica in nanomaterials. The surface of prepared sample specimens and their compounds are uniformly coated with proper precipitants composed of calcium phosphate phases, after one-week immersion in the SBF solution. The bioactivity composition of the nanoscale with glass ionomers (GIC) increases its biological properties, which leads to preventing the formation of marginal cavities.

[57]. Giacomelli et al. [50] considered the possibility of changing the properties of the glass ionomer by adding the sea shell to make the materials in the ossification scaffold. They transformed the white and black sea shells into a homogeneous and fine powder. To analyze them, they sent sea shell samples for the EDX and XRD analysis. The bases of sea shells were mixed with various concentrations (1.5, 10%) with glass ionomer cement, and the samples without the sea shells were used as the control group. The pH values among the experimental solutions with different concentrations (1.5, 10%) did not have significant differences. The analysis with the SEM showed that the specimens containing sea shells consisted of bone scaffolds. The structure of the materials can be changed by adding sea shell powder to the glass ionomer cement to be used as a substance for the formation of bone scaffolds [50]. Babu et al. [51] examined the electrical conductivity as well as the dielectric and thermal properties of glass ionomer cements. If the room temperature is 300K, GIC for the teeth should have free moving charges similar to the F ions. The samples lost their free moving charges at 80°C. XRD examination of these materials also showed that GICs had several non-elastic materials. The GIC material is as a prepared sample that has a high dielectric constant in low frequencies. The highest temperature was reported at 100°C, which lost H2O for an ointment and the secondary reaction was set. The investigation of the DC properties showed that the reaction time had a direct relationship with the dielectric resistance and the dielectric constant, which was increased by increasing the setting time [51]. Zayed et al. [53] performed a study on the antibacterial properties of dental cement in the streptococcus mutants network. They produced 10 discs of three types of bioactive substances and used the agar release test for measuring the antibacterial activity by measuring the areas around the discs. After observing the results of the test, it was found that there was a significant difference between the bio dentin groups with the largest inhibiting area and subsequently the modified resin as the glass ionomer. While bio dentin exhibits the most potent antibacterial properties, the bioactive glass ionomer and the calcium hydroxide cement are also effective as standard products for the pulp production in preventing the growth [53].

Tüzüner et al. [54] study to investigate the effect of the abnormal GIC bacteria on the surface hardness by using microfuge IX. Cetrimide (CT), CPC, and a chlorhexidine (CHX) were added to the powder and benzalkonium chloride (BC) to Fuji IX liquid at different concentrations of 1% and 2%. VHN measurements were recorded at 1, 7, 15, 30, 60, and 90 days after storage in distilled water at 37°C for the control group, and the one-way analysis was performed on each sample [54].Ghanbarzadeh et al. [58] researched comparing the storage of residues made with two types of glass cement at different time intervals. In their experiment, 60 teeth were extracted from the upper jaw and were prepared using the step-by-step method and filled them with gutta-percha filler. The pastes were made using a conventional method by Duralay resin and superfast alloy. They divided the teeth randomly into 6 groups, three of them which were cemented

using Aria mix cement and three other groups using glass Ionomer cement. The tension test was performed in each of the two groups at 20 minutes, 1 hour and 24 hours after the cementation. The obtained results of the experiment were evaluated using Anava and Tukey methods. It was found that the value of the storage of the paste with GC Fuji material or Aria mix cement was not significantly different [58].El-Anwar et al. [60] used the 3D techniques for analyzing the finite element methods (FEM) for investigating the effects in using 2 types of cement with three different thicknesses on the compressed surface and placing them inside the bone around the pro-molar implantation. They studied two cement materials (zinc phosphate and glass ionomer) with three dimensions of the cement layer phosphate scale with various size and dimension (20, 40, 60 microns) [59]. Isler et al. [60] considers NCCL an ideal treatment method for gingival recession. They express the aim of their studies to be the evaluation of the gingival recession treatment related to cartilage lesions with the advanced coronary flap (non-carious cervical lesions "NCCL") [60].

Nommeots-Nomm et al. [61] states that a synthetic biomaterial significantly increased the implication of the bone morphology, and only bioactive glass lasted between them. Bioactive glasses provide a new method for investigating about the materials that have the potential application for bone regeneration. Regarding their ability in promoting the cells, proliferation and differentiation, they are mostly considered for their applications. However, a 3-D structure with interconnected and open pores is desirable to promote bone recovery and repair. However, many silica networks have been degraded by the bioactive glass composites and lead to crystallization. The common point of all the scaffold processing techniques requires medium to high-temperature deposition stage. Curing the bioactive glasses often cause the crystallization action; the relationship between crystallization and bioactivity of the bioactive glasses is of great importance. Regardless of the glass composite, the partial to complete crystallization led to a significant change in the rate of ion release and analysis of their mechanism. The dissolution of various crystallization phases depends on the original glass. Crystallization of the bioactive glass was very useful for the controlling aspects [61]. Shebl et al. [62] aimed to evaluate the shear bond strength of the new generation of glass for the tooth enamel with regards to an ionomer (glass carbomer), i.e. the resin-modified glass (nano-ketac), as a type of common storage after several days. They divided the crowns of 36 newly extracted permanent molars into two parts. The buccal or convex angles were gradually divided using abrasive surface of silicon carbide with cold water of 200, 400, 600 g to obtain the surfaces of a flat enamel [62]. Mabrouk et al. [52] prepared four types of bioactive nano-silica by different methods, and used GIC to improve the commercial issues related to dental matters. The powder, prepared by the XRD was organized to detect the formed phase. Bioactive powder samples were prepared and the cement mixes were used in the simulated body fluid (SBF). The change in morphology and composition levels after soaking in the SBF was determined after a week at 37°C. Carbonates apatite were observed on the silica surface by using spectroscopy as well as the SEM. The combination of bioactive nano-silica with the dental cement improves their bioactive performance, which may be useful for overcoming the marginal gaps that is one of the disadvantages of commercial cement. The surfaces of prepared sample specimens and their compounds after one week of immersion in the SBF solution are uniformly coated with proper precipitants of CaP phases. The bioactive compound of the nanoscale with GIC increases its biological properties, which leads to the prevention of marginal cavities [52]. Wilder et al. [63] evaluated the relationship between the composite resin and the teeth surfaces for tooth repair based on cavities with dental drills and laser radiation. After the dental repair process, the micro-settlement test was performed using the blue methylene. Using the general linear methods, there was no significant difference in the rate of micro-settlement between the common groups of drilling and laser ($P<0.1\%$) in the resin and the restored teeth by glass ionomer. These samples significantly showed a permeation of painting color. There was no significant relationship between the fluorescence and micro-settlement using the repairing materials ($P<0.05$). It is vital to note that using the laser as a substitute for a dental drill can be important [63]. Alatawi et al. [47] investigated the glass cement was an important material for tooth repair for filling approaches. The purpose of their study was to improve the mechanical, morphological, antibacterial, and fluoride properties by addition of the released materials of the glass ionomer cement by combining different percentages of the nano-

HA powder. The result of their study indicates that addition of nano HA increased the release of GIC ions into fluoride, and also enhanced the compressive strength and antibacterial effect against streptococcus mutants, and the fourth bacterial region reaches to about 6.8 mm when 8 wt% HA is used. This indicates that the addition of HA nanoparticles to the GIC to produce the GIC-HA hybrid, which can be used as suitable materials to improve fluoride ion release [47]. Shebl et al. [64] analyzed that releasing fluoride is an important feature for the glass ionomer cement. The number of fluoride ions released from the ionomer glass cement is very important the concentrations of fluoride ions released in the ionomer cements were indirectly evaluated by the optional fluoride WTW and the electrodes F500 along with the reference electrode R503/D. The correlation is high between the fluoride ion concentration and the cytotoxic response of the NIH3T3 mouse fibroblast cell after 8 hours, which is highly positive for GICs. The correlation coefficient between the concentration of fluoride ion released by the tested ionomer glass cement and the cytotoxic response of UMR-106 osteoblasts and NIH3T3 rat fibroblast cells is relatively high [64].

Angelieri et al. [55] dealt with the analysis of the genetic toxicity and the toxicity of some commercial orthodontic glass ionomer cement in laboratory conditions in the rat fibroblast. Each of the solutions was prepared according to the instructions for 0, 2, 4, 8, 18, 32, 64 days' immersion in artificial saliva at 37°C temperature. The cytotoxicity test was performed using the trypan blue exclusion test. All samples of orthodontic cements were healthy after 2, 4, 8,18, 32, and 64 days exposed to the test and did not cause any cell deaths. No statistically significant difference was found between the groups ($p> 0.05$). Vidrion was able to produce genetic toxicity after 64 days of exposing to the eluates. Multi cure showed relative toxicity on day 32. The results showed that cement derived from the orthodontic glass ionomer from the combination of composite resin glass (multi cure) and compomer (ultra-band Lok) could cause genetic damage in the mammalian cells in the laboratory. The "Optband" of the obtained solutions were able to produce genetic damage after 64 days [55]. Salehi et al. [39] studied the toxicity of the cells in the ordinary modified glass ionomer cement, resin on UMR-106 osteoblastic cells, and NIH3T3 rat fibroblast cell culture. The samples were prepared and regulated for each empirical material [39]. Krishnan et al. [66] released a report about the bioglass, a new and eco-friendly innovation in biomaterials domain. The purpose of this report was to provide an overview of the various medical applications and miraculous materials that can create bonding between osteoporosis and bone surface. Their reports indicated that for the critical analysis, the Young's modulus of the bioglass is between 30 GPa and 50 GPa, which is almost close to the normal bone with a great advantage. Their obtained results showed that the bioglass is a diversified alternative that is available in various forms and can also be designed according to the patient requirements [66].

Preparation of glass ionomer bone cement

Producing the ceramic part of glass ionomers included the materials such as aluminum oxide (Al_2O_3), silicon oxide (SiO_2), strontium fluoride (SrF), aluminum phosphate ($AlPO_4$) and calcium fluoride (CaF_2). The glass ionomer cement component was made by a fusion method. Initially, the specified weight percentages of these oxides were prepared and then mixed to form the powder in a ball mill tool with alumina balls. Subsequently, the determined amount of the raw material was entered in the electric fusion furnace. In this study, an alumina vessel was used for melting of the raw materials. Molten glass was obtained by melting of the crystalline materials. The obtained glass was cooled at the ambient temperature and was subjected to crushing in a high energy ball mill with zirconium abrasion-resistant chamber. Also, other factors such as ball-to-powder (BPR) ratio, ball number and rotational speed was significantly important to effect the powders characterization results. The obtained powder from this stage was passed through a sieve to make a glass powder according to the American society testing materials (ASTM) standards. The resulting powder was a glass ionomer cement ceramic component. At the next step, a ceramic powder was mixed with a polymeric liquid (polyacrylic acid) and glass ionomer samples were prepared for further testing. The glass ionomer powder was primarily distributed on a cold slab for preparing the samples. Then, half of the powder was slowly added to the polymeric liquid (polyacrylic acid). After that, the second part of the glass powder was completely added to the mixture. The final mixture had a glossy and wet surface [48]. The phase and glass structure of the glass ionomer cement

ceramic component was analyzed by using XRD. XRF analysis was used to confirm the presence of oxides in the final composition of the glass ionomer powder according to the weight percentages. Also, the scanning electron microscope was used to study the size, morphology, shape and structure of the ceramic component and the glass ionomer cement composite. Finally, the compressive strength test was applied to measure and determine the compressive strength of composite samples.

1) Analysis of the DC properties showed that the reaction times for the dielectric constant and the dielectric resistance had a direct relation and dielectric constant and the dielectric resistance are increased by increasing the setting time [51].

2) The significant difference between the biodentin groups indicated the largest inhibiting area followed subsequently by the so-called resin-modified glass ionomer. While the bio dentin exhibits the most potent antibacterial properties, the bioactive glass ionomer and the bioactive calcium hydroxide are effective as the standard products for pulp production in preventing the growth, but the best and most effective (bioactive substances) are to prevent the growth of the S. mutants organism [53].

3) By increasing the thickness of the cement layer, the durability range, and crown setting can be guaranteed, since increasing the thickness of the cement layer reduces the maximum Von-Misses Stress and increases its deformation in the cement layer.

Regardless of the type of cement, a layer of thicker cement (60 μm) is preferred to reduce the cortical bone pressure by 6.5%, while the trabecular bone is not sensitive to the type of cement or its thickness. The type and thickness of the cement used in this study have the least effect [59].

4) Antibacterial compounds of CHX, CT, CPC, BC at 1% and 2% concentrations are effective on the surface hardness that can be measured. The obtained cement reduces the hardness and BC 1% and CHX 1% were identified as the most suitable compounds, while CT2% and CPC2% were almost negative [54].

5) The nano-structure glass ionomer (nGIC) shows better mechanical properties and bioactivity in the physiological environment of the body as compared to the micro-structure glass ionomer (μ GIC) [48].

6) Addition of nano HA increased the release of GIC ions in fluoride, compressive strength and antibacterial effect against Streptococcus mutants, and the fourth bacterial region is about 6.8 mm when HA8 wt% is used. This indicates that the addition of HA nanoparticles to the GIC to produce the GIC-HA hybrid, which can be used as the suitable materials to improve the fluoride ion release, better mechanical properties, and inhibition of remaining bacteria in the dentin [58].

1-1. The effective suggestion of previous researchers on glass ionomer bone cement

1) No adequate information is yet defined for the state of comparing the bioactivity of the cement [46].

2) The difference between the groups for analyzing the width depth (rcAl), the relative clinical dependence (rRH) or the keratinized tissue (kTw) thickness of the keratin tissue is not significant between any of them at any time, which requires more investigation [60].

3) The mechanisms of laser effects on the implant should undergo further studies [63].

4) GIC and MTA powder for improving the setting time and handling of MTA properties can reduce the ability to release calcium from the resulting mixture. However, GIC does not show a significant reduction in calcium emissions in the ratio of 2:1 to MTA and can be recommended for the above aim. However, the conclusion of this study requires more clinical verifications [65].

CONCLUSION

This study was aimed to investigate CaP-containing 5% Sr cement had a maximum compressive strength of 36 MPa. The cement mechanical resistance was 48 ± 2.3 MPa. When the ratio of liquid to solid bone cement was 0.6, and the compressive strength of bone cement decreased to 21 ± 2.5 MPa. Calcium phosphate cement better to use the biologically active ions, e.g. of magnesium, zinc, fluoride and strontium, to improve the mechanical properties and biological function. Gelatin can be used to integrate and expand the osteoblastic cells. Gelatin and soy can be used to increase the elasticity of cement paste. To reduce the stiffness of cement, we can use a cement with a low modulus or the brushite cement, which has a soft texture and is similar to trabecular bones in the body. Studies have indicated that the bone cement with the ionic composition (Sr-Mg-Zn) is an appropriate replacement for clinical, orthopedic and dental applications. Surgeons use bioceramics for the maxillofacial surgeries that require bone

grafting. According to the experimental results, foam with soybean extracts can contribute to bone formation and increase the mechanical performance. Calcium phosphate (CaP) bone cement is highly available and affordable for the injuries. Porous PMMA can be achieved with the addition of carboxymethylcellulose (CMC), alginate and gelatin microparticles to promote bone ingrowth. Adding of fibre as a reinforcing agent increases the hardness and strength of PMMA bone cement. Fatigue and reinforcement properties of PMMA are improved by carbon fibre, HA particles, titanium nanoparticle, zirconia nanoparticles, etc. Additives nanoparticle such as magnesium oxide, hydroxyapatite, chitosan, barium sulfate, silicate and substituted monomers can be used with PMMA beads and MMA monomers to reduce isometric temperatures. After adding sea shells powder to glass ionomer cement, researchers found that sea shells have altered the structure of the material and are effective in improving the formation of etching framework. Also, the addition of HA nanoparticles to the GIC to produce the GIC-HA hybrid, which can be used as suitable materials to improve fluoride ion release, mechanical properties, and inhibition of remaining bacteria in the dentin. Regarding the glass ionomers, the mechanisms of the laser effect that affects the transplant require more investigations.

CONFLICT OF INTEREST STATEMENT

All authors declare that no conflicts of interest exist for the publication of this manuscript.

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