

An Overview on the Characterization and Investigation of Polymerized Bio-Ceramics for Bone Regenerative Applications

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Abstract

Many osseous faults resulting from fracture offer inherent capacity of the body to overhaul and activate the bone grafts for recovery process. In the early development, nonautologous bone grafts made of Titanium and stainless steel were suitable because of their mechanical strength, corrosion resistance, biocompatibility and durability. Biodegradable polymers belonging to the family of polymers and bioceramics also, play a major role in orthopaedics. The polymers, poly glycolic acid, poly lactic acid, hyaluronic acid, chitosan and poly vinyl alcohol were degraded by hydrolysis, enzymatic mechanism that provides related mechanical and physical properties. The degradation characteristics were subjected to various parameters including their molecular structure, crystallinity and co-polymer ratio. Bioceramic materials, calcium phosphate, Beta tri-calcium phosphate (β -TCP), calcium sulphate, hydroxyapatite, tetra calcium phosphate and β calcium phosphate improves mechanical strength, biocompatibility, wound healing process, proliferation rate and bonding strength to bone tissue which depends on the features of size of pore, shape of pore, porosity, inter-connectivity and surface area. These biomaterials were rapidly attaining identification in the domain of tissue engineering for scaffolds, extra-cellular matrix components and bone replacement for osteoporosis that can be tailored for specific patients. This review mainly focuses on the investigation and characterization of polymerised bioceramics for the bone regenerative applications.

Keywords: Polymers, bioceramics, biodegradable, biocompatibility, scaffold techniques, bone regeneration

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INTRODUCTION

The orthopaedic biodegradable implants have many factors such that the material could be degradable within the given time. So that scaffold acts as a short-term hold up but it develops new form of tissues to replace defects. Other architectural scaffold attributes were, shape of pore, cell seeding and pore wall morphology, mass transport, growth migration and novel tissue development in 3-dimensions [1, 2]. This process can be expanded to mass production. The material must have appropriate mechanical strength to resist loads which are taken into defects at healing process. Bone tissue keeps stability between the generation of fresh bone in the form of collagen fibres and calcium phosphate. Bone has the composition such that 69% weight of calcium phosphate, 21% weight of collagen, 9% weight of H₂O and 1% weight of other components. There are different

types of cells formed in tissues – like osteocytes, osteoclasts, and osteoblasts with induced cell proliferation and cell migration – to repair tissues [3, 4]. Scaffolds are generally useful for internal fixation devices like screws, rods, pins, plates, and suture; whereas the bone fracture occurred due to low bone mass density, sports injury or osteoporosis. Stiffness and great mechanical strength were most significant in the model of biodegradable devices for orthopaedic applications in which more loads would be considered, after implanting the devices.

Material possess good mechanical characteristics, till newly grown tissues, material behaviour exists in several mechanisms like hydrolysis and enzymatic degradation. The requirement of biodegradable materials were non inflammatory, immunogenic, chemically inert and should meet biocompatibility. Bone substitutes should possess inter-connected porosity, biodegradability, bioactivity, osteo-conductivity and osteo-inductivity [5]. In present years, evolution takes place in the domain of resorbable and osteo-conductive materials. Bone grafting techniques – like allograft, autograft and ceramic growth factor – has been frequently practised for reconstruction of bone defects. Autologous bone grafts show the sign of gold standard, but donor site morbidity, pain and visceral injuries were notably, more expensive. Auto grafts and Allografts have severe disadvantages. Calcium phosphate ceramics are widely used to reconstruct and repair the diseased, damaged and missing of worn-out parts of human musculo-skeletal system like bone. Most studied CaPs comprised of Biphasic Calcium Phosphate, Beta Tri-calcium Phosphate (β -TCP), and HAp. The overhauling rate of body tissues through CAP bioceramic implants are extremely important in the entire process [6, 7].

LITERATURE SURVEY

Calcium Phosphate with Polymers

Porous calcium phosphate composite bioceramics were investigated with organic/inorganic hybrid pellets using extrusion-spheronization method. In general, ceramic bead sphere techniques are, drip casting, water-in-oil emulsion and extrusion-spheronization. Among these, extrusion-spheronization is used for the great production beads, narrow size dispensation and good sphericity. The phosphate-based glass liquid offers great microstructure, improved compression properties with larger pore size. It provides promised mechanical properties and immense pores, inside which are favourable for the new formation of bone. Hyaluronic acid in addition with multi-channel, Biphasic calcium phosphate injectable granules are used to stimulate the new formation of bone. Engineered bone under study, make expected bone development capacity with acceptable candidates [8, 9].

Table 1 demonstrates about the molar ratio, different type of compounds with their chemical formulae, solubility and pH stability range in the aqueous solution.

The recent study deals with resorbable and osteo-conductive biomaterials. Most of the studies mentioned about the dispersion of HAp in the human body for getting most favourable results, after implantation [10, 11]. Process of rate of dissolving of β -TCP ceramic is rapid for bone attachment to attain optimal resorbability of material studies, concentrated in BCP ceramics-controlled HAp and TCP. The particle properties as well as the porosity, affect the rate of dissolution that influence the interaction of material with tissue. Furthermore, the mechanism of dissolution control requires additional investigation. This investigation exhibited about resorbability, decrease with the rise in HAp where bimodal porous ceramics displayed more resorbability. Synthesized technique – like acid-base titration from aqueous solution – is used for HAp and TCP bioceramic powder. Some of the researchers proved that HAp ceramics were effectively used for bio-active and non-biodegradable bone substitute materials. As a result, β -TCP was improved as a bio-degradable substitute for the bone source. HAp-TCP composite precursors and powders may serve initial matrix bio-implant material with different levels of pore size and different areas of new bone generation with body fluids because of the complete resorption of TCP phase [12–15].

Table 1. Calcium ortho-phosphates and their main behaviours [8].

Ca/P molar ratio	Compounds and their abbreviations	Chemical formulae	Solubility at 25°C, $-\log K_s$	solubility at 25°C, g/L	pH stability range in aqueous solution at 25°C
0.5	Mono-calcium phosphate mono-hydrate	$\text{Ca}(\text{H}_2\text{PO}_4)2\text{H}_2\text{O}$	1.16	–19	0.0–2.1
0.5	Mono-calcium phosphate anhydrous	$\text{Ca}(\text{H}_2\text{PO}_4)_2$	1.15	–18	[c]
1.0	Di-calcium phosphate di-hydrate, mineral brushite	$\text{CaHPO}_42\text{H}_2\text{O}$	6.60	–0.078	2.0–6.0
1.0	Di-calcium phosphate anhydrous	CaHPO_4	6.91	–0.058	[c]
1.33	Octa calcium phosphate	$\text{Ca}_8 \cdot (\text{HPO}_4)_2(\text{PO}_4)_4 \cdot 5\text{H}_2\text{O}$	95.6	–0.0091	5.5–7.0
1.55	α -Tri-calcium phosphate (α -TCP)	$\alpha\text{-Ca}_3 \cdot (\text{PO}_4)_2$	26.5	–0.0035	[a]
1.55	β -Tri-calcium phosphate	$\beta\text{-Ca}_3 \cdot (\text{PO}_4)_2$	29.9	–0.0005	[a]
1.2–2.2	Amorphous calcium phosphates	$\text{Ca}_x\text{H}_y(\text{PO}_4)_z \cdot n\text{H}_2\text{O}$, $n = 3 - 4.5$; 15%–20% H_2O	[b]	[b]	–5–12
1.5–1.67	Calcium deficient hydroxyapatite	$\text{Ca}_{10-x}(\text{HPO}_4)_x(\text{PO}_4)_{6-x}(\text{OH})_2$ $-x$ ($0 < x < 1$)	–86	–0.0096	6.6–9.6
1.67	Hydroxyapatite	$\text{Ca}_{10} \cdot (\text{PO}_4)_6(\text{OH})_2$	117.8	–0.0004	9.5–12.1
1.67	Fluorapatite	$\text{Ca}_{10} \cdot (\text{PO}_4)_6\text{F}_2$	119.0	–0.0003	7–12
1.67	Oxyapatite	$\text{Ca}_{10} \cdot (\text{PO}_4)_6\text{O}$	–68	–0.088	[a]
2.0	Tetra-calcium phosphate	$\text{Ca}_4 \cdot (\text{PO}_4)_2\text{O}$	39–44	–0.0006	[a]

It was found that the bone attachment property of four calcium phosphate ceramics differ in both porosity and under non-weight bearing conditions. The failure loads of hydroxyapatite, tetra-calcium phosphate and β -calcium pyrophosphate increase with the time ($p < 0.55$). In TCP, failure load did not change, remained high and hence, failure load of TCP differs from the other four types. However, the mechanical strength is insufficient for load weight bearing [6]. PGA and β TCP are utilized for the bone tissue repair materials. The 1:1 and 1:3, weight ratios of PGA/ β TCP, three-dimensional porous composite scaffolds were produced by the particulate leaching and solvent casting techniques. The mineral density of fresh bone with PGA/ β TCP scaffolds shown greater value when compared with the HAP magnitude of ($p < 0.001$). Biodegradation provides the PGA/ β TCP scaffold, higher magnitude than the HAP and suited with osteo-genesis rates. PGA is one of the hydrophilic, biodegradable polymer among others. It shows optimal mechanical behaviours, biodegradation and non-toxicity as well as rapid rate of degradation [16, 17]. Further, PGA does not possess a favourable surface for cell proliferation and cell bond due to the lack of inflammatory reactions and cell-recognition signals. When it is blend with β -TCP, enhances the rate of biodegradation of scaffold and rate of growth of fresh bone tissues. The PGA scaffold behaves like a collagen matrix in the bone and also helps for osteo-genesis. Chitosan fibres were prepared by wet spinning of 2% of its aqueous acetic acid. Fibre behaviours are influenced through processing conditions of the composition of coagulation bath, drying situation and spin stretch ratio.

Acetylation fibre possesses improved thermal stability, tensile strength, wet and dry strength [16–18]. HAP, calcium sulphate hemihydrate and HyA laden collagenase (HAP/CS/HA-Col) were implemented as substitute of bone, till the process of bone regeneration. It was mechanically characterized and evaluated about the behaviour of biocompatibility. The mechanical strength of 6.69 MPa with remarkable biocompatibility was achieved for HAP/CS/HA-col composite material. Calcium sulphate hemihydrate is bio-compatible, bio-active and resorbable compound. In addition, CS offered easy way to obtain in paste form and fill the defects with uneven geometry which also improve the feasibility of operation [19, 20]. The compressive strength of 6.69 MPa for HAP/CS/HA-col is like natural trabecular bone, indicates about greater mechanical strength. It shows excellent cell viability

and favourable material for bone repair. Osteocytes in defected sites, treated with HAP/CS/HA-col composite would be examined as the possible substitute of bone for its regeneration in an economical manner [21]. Chitosan gel was very brittle to use in the cell culture which is cross-linked through GA to enhance the strength. Chitosan acts as a promising biopolymer for scaffold hepatocyte attachment that is superior to collagen surface of hepatocyte cultivation. Chitosan is a biodegradable natural polymer for improving wound healing to fabricate chitosan/tri-calcium phosphate sponges as well as scaffolds for bone generation through three-dimensional osteoblast culture. However, several intrinsic disadvantages were observed like weak integrity of structure, variable rate of degradation, insufficient penetration of tissue, and reaction of immune.

Fabricated chitosan/TCP sponge 3-dimensional porous structure of 100 μm is brittle when dehydrates and still, it is soft, malleable and marginally expandable with tissue culture medium, after wetting. It is very difficult to predict the characteristics of chitosan and also it seems to be poorly soluble except in the acidic medium. Porous β -tri-calcium phosphate/chitosan scaffolds are fabricated by freeze drying technique. The composite scaffold displayed greater rate of proliferation when compared with the pure chitosan scaffold. It provides a good condition for the ingrowth of Human periodontal ligament cells (HPLCs) and also better cyto-compatibility than pure chitosan [22–25]. The protein exhibits about alkaline phosphate and osteopontin, reflecting the generation of hard tissue that was enhanced in the composite scaffold. The formation of Chitosan in porous scaffolds, regulated the microstructure in geometry of tissues. Bulk scaffolds are formed in a specific shape by using suitable molds [10–14]. Chitosan, also known as polysaccharide is a suitable chemical for enzymatic modification. The altered chitosan possessing covalently linked imidazole groups of 700000 average molecular weight, 0.28 degree of substitution and 0.08 degree of acetylation were utilized to stimulate the generation of bone. Imidazole group into chitosan is an osteo-inductive biopolymer, activating biological functions and the formation of bone. IMIC appears to be very effective in the healing of bone when compared with the chitosan [26, 27]. Composition of micro-crystalline chitosan-calcium phosphate/ β -TCP with complex shape was achieved from the function of two or several materials like bioactivity and biodegradability. It is a well-shaped 3-dimension structure that can be utilized in the future medical applications to produce scaffolds and as implants in the regenerative medicine. The effect of bioactivity on the generation of apatite layer is still under investigation. It gives most superior mechanical properties for bone.

Chitosan exhibits physio-chemical and biological behaviours like low toxicity and allergenicity, biocompatibility, biodegradability, and bioactivity. Gelatin/montmorillonite – chitosan Nano composite scaffolds were fabricated through freeze drying technique and intercalation procedure. Gel/MMT-CS scaffold are provided with favourable mechanical behaviours and controllable rate of degradation. However, this kind of scaffold is not great enough for engineering of hard tissues. The water content declines when the chitosan ratio rises and the water adsorption content reduced while improving the quantity of MMT. The degradation procedure involves hydrolyzation of Gelatin and degradation of enzymes. The future depends on biocompatibility and biodegradation of Gel/MMT-CS Nano composite scaffolds [28, 29]. Novel and injectable calcium phosphate/chitosan composites were mouldable due to its consistent paste behaviour even, after mixing. They developed four cement groups with different % of citric acid. The compressive strength of the specimen improved with the rise in concentration of citric acid. The material was found to be bioactive through SBF solution test. The material – like chitosan/calcium phosphate – are easily available, cheaper than HAP and polymethyl methacrylate. Now a days, the popularity of minimally invasive techniques are partially increasing and one of the major thrusts in orthopaedic is that it has been developed into injectable system which can mould to shape of the bone cavity. It can be moulded into any desired shape.

Calcium phosphate bioceramics with inter-connected pore structure are fabricated through foaming of HAP and poly methyl phenyl melts in the temperature, ranging from 250°C to 310°C. PCS provide good accommodation to fill the empty spaces by eco-friendly cell formation and bone tissue development. This work achieved porous ceramic spheres of β TCP, HAP, and BCP with rough type of

surfaces and varying sizes without using solutions. So, this technique improved continuous movement of particles mechanically, rolling in a cylindrical vessel for longer periods. Physical forces associated in the procedure – like attraction of particles, gravity, centrifugal forces, and shocks – make ceramic rounds, as the appearance of golf ball on its surface. Snow balling technique to fabricate PCS is a mechanical process with low cost and eco-friendly, without additives, net shape and use of hazardous chemicals. Bone generation in porous calcium carbonate and porous HAP with the shape of discs were implanted. Hydroxyapatite ceramics are biocompatible, osteo-conductive and osteo-philic with bone, directly attaching to the HAP surface. The ability of calcium phosphate to generate bone when compared with well-known bio-active calcium phosphate ceramic, like Hap, is still a question mark. However, the generation of bone does not occur in CC, before the process of degradation, extensively. Although the exact mechanism of bone formation of CC and HAP is not clear [30, 31]. Bone can be regenerated by the two rhBMPs, BMP-2 and BMP-7. Histology exposed that the fresh bone was fabricated through osteo-conduction rather than osteo-induction. Bone quality is measured by the bio-mechanical strength, thickness of bone and degree of mineralization.

BMP in favourable 3D pattern requires further investigation. TCP ceramic incites low grade inflammatory reaction, macrophages and giant cells, slowly replaced by fibrous tissue. Implants of TCP/BMP induce new bone formation and deposits larger than comparable implants of BMP alone. The TCP ceramics (Ca/p = 1.50), α TCP and β TCP in different phase compositions were implanted. There was critically, different response of tissues among α -TCP and β -TCP ceramics. The greater cell populations are found inside the pores of β TCP when compared with α TCP. The bone tissue was observed in β TCP but no generation of bone was observed in α -TCP implants, during the study. β TCP possess greater rate of resorption than the hydroxyapatite ceramics and the system of osteo-conduction of calcium phosphate was not clearly explained. But in general, chemical composition, geometry, macro pores and micro pores were the important factors for osteo-conduction [32, 33]. The Scaffolds are composed of PLGA polymer with 20% W/W β tri-calcium phosphate (β -TCP), prepared by solid free form fabrication technique with engineered macroscopic channels. The development of controlled pore size and regulated porosity gradient are mandatory for the ingrowth of fresh bone. The Scaffold casting fabrication methods are user sensitive and will not go for inter-connected porosity, throughout the scaffold. BAE method has better performance, increases load bearing capacity and better mechanical properties during crush testing. BAE tubes are optimal material system for the fabrication of future stents, leading to greater radial stiffness. The influence of blended gelatin with cellulose in the existence of MMT are studied. The cross-linked biocomposites with GA of N, N-Methylene-bisacrylamide are prepared. The 3D biomimetic porous scaffold was built successfully which exploits the cell matrix interpolation. It contains 12 to 16% MMT cross linked by 0.5% to 5% of GA, seems to be two most active and efficient biodegradable scaffolds.

MMT improved cyto-compatibility between the osteoblast and biocomposite. It indicates good biocompatibility of the scaffold, as a novel potential candidate of biohybrid material for engineering of tissues [34, 36]. Another study of natural bones of cuttlefish has been positively altered into porous BCP scaffolds with the range of compositions of HAP and β TCP. BCP scaffold was regulated through changing the concentration of phosphoric acid solution. It gets, porosity > 90% with the continuous micro porous channel having smallest cross-sectional openings of 400 μm x 100 μm size. The capacity of tailored composition of scaffolds permitted remarkable micro structural and mechanical behaviours which supported the efficient osteo-integration and osteo-induction. The resultant phase composition of HAP and β TCP of cuttlefish natural bone to porous BCP scaffolds were tested to evaluate their potential for biomedical applications. The use of osteo-inductive biomaterials in the domain of bone morphogenetic research of proteins were explored. Osteo-inductive proteins with proper carrier materials attain novel composition and function as slow delivery system for the expression of maximum activity of BMP. It was reported that a woman at the age of 20, after orthodontic treatment of genioplasty and contour augmentation with BMA/HAP, as the substitute of bone. Osteo-inductive biomaterials must fulfil the various requirements associated with the mechanical, chemical and biological behaviours [37–39]. Physio-chemical composition is significant for better understanding of its biological and

mechanical behaviours. Micro porosity left the particles of powder and are not completely joined, after sintering. Macro porosity refers about the larger size of pore that allow ingrowth of bone when the diameter is greater than 100 μm . Ca/p ratio is important factor for governing biodegradation and it was reported that CPC with Ca/p ratios of either 10:6 or 3:2 are biocompatible.

Porosity is essential but not as the complete requirement for biodegradation like lattice texture, imperfections of lattice, trace elements, pH value, and concentration of serum protein. Porous hydroxyapatite ceramics are fabricated through sintering bovine bone by physio-chemical methods. Most important properties of such ceramic based biomaterials were not only for filling bone defects but also investigated of their chemical composition with other inorganic elements like MgO, CaO, $\text{Ca}_3(\text{PO}_4)_2$, $\text{Ca}_4\text{O}(\text{PO}_4)_2$, and NaCaPO_4 . Sintered HAP is almost water insoluble; it gives enough size of pore and an inter-connected pore texture, needed for osteoblasts, cause pH changes, organic solvents permit to load and enhance the healing of bone [40–43]. β TCP/HAP bi-phase ceramic scaffolds are Synthesized from cancellous bone. Bovine bone soaked with P_2O_5 solution for different periods, reacted with HAP to construct β -TCP. By increasing soaking time, calcined bone progressively altered from HAP/TCP ratios. BCP bioceramics, recommended the additives with autogenous bone for orthopaedic applications. They are available in the form of blocks, particulates and customized models for precise applications. BCP ceramics also used as gut blissing abrasive to modify the implant subtract surfaces by using super-critical fluid method that possess some benefits such as drying without collapse. CO_2 is the most aesthetic fluid. Further, CO_2 is abundant, non-toxic, non-flammable, non-corrosive, cheap and available at great purity. polycaprolactone is a semi-crystalline aliphatic polyester which is widely used for the fabrication of bone scaffolds. It is noted that LPCL possess poor mechanical behaviour for the replacement of bone. HPCL produces micro tubular morphology due to high viscosity and so, blending with HPCL, LPCL provide improved mechanical and structural properties. Adding HAP nanoparticles to PCL, blends the reinforced mechanical behaviour but their drawbacks are the reduction of porosity and pore size [44–48].

Fabrication Methods of Biodegradable Scaffolds

- Solvent casting.
- Freeze drying.
- Particle leaching.
- Thermally induced space separation.
- Injection moulding.
- Extrusion.
- Foaming.
- Wet spinning and electro spinning methods.

Table 2 reveals about the various type of methods used to produce calcium phosphate powders.

Table 2. Methods to produce spherical CaP particles [48–50].

S. N	Types of reagents	Description
1	Solution based method	May be aqueous (precipitation, spray-drying). Non-aqueous (precipitation, flame-synthesis) or mixture (precipitation-emulsification).
2	Slurry based method	Like solution method because liquid already contains dispersed particles. That is primary particles dispersed in slurry, e.g., 1mm particles obtained by drip casting equal to (droplet extrusion) emulsification, hydro casting, low wax method and suspension plasma spraying method.
3	Paste method	Adjustment is difficulty of their rheological properties, (spray-granulation, sieve shaking).
4	Powders method	Among other reagents, powders are widely used like “plasma melting” also called combustion flame spraying and flame spheronization.

Methodology of Fabrication of Biodegradable Scaffolds

- Starting materials – solution, slurries, pastes and solids.
- Dispersion phases – gas, solution and solid.
- The dispersion tools – nozzles, propellers, sieves and molds.
- Consolidation method – drying, precipitation, gelling and freezing.

The porous, spherical HAp granule seems to be the better candidate for bone defect filling material that holds great promise in the orthopaedic applications. Forming, shaping of calcium phosphate (CaPO_4) and rapid prototyping science revolutionized physical designs to produce customized implants with great level of geometric complexity. A custom-made implant will reduce the time to perform the procedure of medical implantation and subsequently, reduces the risk to patient, exact fitting and directly applied to the damaged site rather than replacement. An organic binder – like PVA – assists to bind particles of powder altogether by ball milling procedure. Bioresorbable polymer materials are rapidly increasing for the choice of implantable orthopaedic fixation devices. Low energy electron beam irradiation towards surface, alter the poly hydroxy acid specimens, prepared through the incorporation of beta-tricalcium phosphate (β -TCP). Bulk degradation is determined as the long-term preservation of mechanical behaviours and in growth of tissues since, implants retain mass but no useful strength. To enhance the long-term mechanical behaviours and release additive profiles, surface degradation was triggered ahead of bulk degradation. Increasing additives – like anti-microbials and calcium fillers – are being combined with poly hydroxy acid implants for orthopaedic treatments. However, further investigation is required in this domain on bone healing procedure [49–52].

Table 3 illustrates about the crystalline ceramics, fabrication methods, size & shape of pores, % of porosity and their applications in bone regeneration.

Table 3. Porosities and pore sizes of crystalline ceramic scaffolds for bone regeneration.

Crystalline ceramic	Fabrication technique	Shape	Pore size (μm)	Porosity (%)	Application	References
Hydroxyapatite	Sintering	Scaffolds with honeycomb pores	88–121 and 348	–	BMP-2 delivery and ectopic bone formation in rats	[53]
	Sintering	Scaffolds with honeycomb pores	98–198	–	BMP-2 delivery and ectopic bone formation in rats	[53]
	Sintering	Scaffolds	368, 443	38, 44	Mandible defects	[54]
	Sintering	Scaffolds	398, 780	60, 72	Goat bone marrow stromal cells ex vivo and ectopic bone formation in goats	[54]
	Sintering	Blocks	480	75	Ectopic bone formation in mice	[55]
	Sintering	Cylinders	410–600	78	Femoral Defects in rats	[55]
	Sintering	Blocks	100–200	–	BMP-2 delivery and ectopic bone formation in rats	[55]
	Sintering	Blocks	108–212, 212–300, 300–400, 400–500, and 500–600	–	Ectopic bone formation in rats	[56]
	Sintering	Particles	152	72	Ectopic bone formation in rats	[56]
	Sintering	Particles	236	70	Ectopic bone formation in rats	[57]
	Sintering	Rods	202, 400		Ectopic bone formation in dogs	[57]
Tri-calcium phosphate cement	Salt-leaching	pellets	0.3, 8.6	32, 64	-	[58]
Calcium meta-phosphate	Sintering	Blocks	200	–	Rat bone marrow stromal cells ex vivo and ectopic bone formation in mice	[59]
Hydroxyapatite / Tri-calcium Phosphate	Sintering	Blocks	102–148	38	Femoral defect in dogs	[60]

CONCLUSIONS

Most investigated calcium phosphates include the combination of HAp, β TCP and BCP. Calcium phosphate bioceramic implants in the rate of repair of body tissue is extremely important key of an optimal composition, like scaffold resorption, suitable for bone growth by keeping the mechanical strength. Poly glycolic acid is a better hydrophilic, biodegradable polymer when compared with the other polymer materials. It has proper mechanical behaviours, non-toxic and biodegradable but it seems to be poor surface for cell bond and cell growth. The future biosynthetic bone implant requirements were the improvement of mechanical performance, enhanced bioactivity, development of smart biomaterials and improved biomimetic composites. Still there are some requirements for better understanding of the biological system, like bonding among collagen and bone mineral, which remains unclear. Strategies implemented in the last four decades for this goal was unsuccessful. In future, novel formation of gene activating calcium phosphate-based scaffolds, tailored for unique patients and diseased status must be explored.

Data Availability

No new data were created or analysed in this study. Data sharing is not applicable to this article.

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Competing Interests

All authors declare that they have no conflicts of interest.

Author's Contribution

Dr. Ravikumar Kuppusamy – Conceptualization and full paper write up.

Dr. Arunnath A – Methodology.

Dr. Nirmal Kannan V – Project administration.

Dr. Rajadurai Narayanamurthy – Supervision.

Dr. Dinesh Kumar S – Analysis.

Abbreviations

Terms	Full Form
CAp	Calcium Phosphate
PLA	Poly Lactic Acid
PGA	Poly Glycolic Acid
PVC	Poly Vinyl Alcohol
β TCP	β Tri-Calcium Phosphate
BCP	Bi-phasic Calcium Phosphate
HAp	Hydroxyapatite
HyA	Hyaluronic acid
CS	Chitosan
HPLCs	Human Periodontal Ligament Cells
ACP	Alkaline Phosphate
OPN	Osteo-pontin
IMIC	Imidazole Group into Chitosan
Gel	Gelatin
MMT	Montmorillonite
SBF	Simulated Body Fluid
rhBMPs	Recombinant Human Bone Morphogenetic Proteins
PLGA	Poly Lactic-co-Glycolic Acid

SSF	Solid Free form Fabrications
GA	Glutaraldehyde
MBA	Methylene-bisacrylamide
BMP	Bone Morphogenetic Protein
PCL	Poly Capro Lactone

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