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Comparative Analysis Of Different Bone Graft Materials

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Abstract

When a tooth is lost, permanent bone resorption occurs, resulting in insufficient bone mass for a successful implant. To overcome this obstacle, bone grafting becomes necessary, a procedure required in 25% of dental implant patients. Recent developments have centered on enhancing manufacturing techniques and material optimization to ensure the longevity of dental implants. This article provides a comprehensive overview of various oral surgical procedures utilizing both natural and synthetic replacements, accompanied by a detailed analysis of their effective[1]ness. Classification schemas are outlined, categorizing commercially available items based on their unique physical characteristics, with particular emphasis on biocompatibility considerations.

Despite considerable progress, current methods still exhibit limitations that necessitate further innovative solutions. Potential avenues for research and development, including tissue engineering and growth-factor-based cell replacements, are proposed as viable approaches to augment outcomes beyond the constraints of conventional techniques. This discourse draws upon accumulated insights from dental offices worldwide, contributing to a well-informed perspective on future advancements within the industry.

Keywords: *replacing tooth loss; dental implant; bone defects; bone reconstruction; bone graft; bone tissue engineering; natural and synthetic bone substitutes.*

Introduction

The transplantation of living tissue capable of promoting bone healing into a bony defect, alone or in combination with other materials, is known as bone grafting [1,2]. Natural or synthetic substances that contain only mineralized bone matrix without viable cells and achieve the same purpose are called bone substitutes [3]. For centuries, medical professionals have used these techniques in dentistry to repair various defects caused by trauma or disease. However, despite their popularity and advantages over autografts and allografts currently used globally for this

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procedure, there are still drawbacks associated with current methods, such as cost, effectiveness, and low angiogenic potential. Exploring modern technologies for novel implants is essential due to the rising demand from an aging global population. Moreover, considering that up to 50% of all dental implantation procedures currently rely on underutilized surgical methods, costing an estimated average of $664 million per year (as of 2018), further research is needed to explore modern tools. These tools should aim to improve patient comfort by reducing morbidity levels and ensuring immunological acceptance [4]. In conclusion, there is a need for more research given the limited safety data backing innovative complementary plans discussed here. Monitoring the increasing global demand annually rather than biennially, and planning resource allocation efficiently while swiftly developing next-level return on investment strategies, is crucial.

In this literature review, we examine the current options for dental bone grafts and substitute materials available in commercial markets. We address these limitations while considering how synthetic bone substitutes have emerged as promising alternatives in recent decades. Our objective is to illustrate the gap between existing products and an ideal future material choice for bone substitution, identifying research areas that hold promise for creating novel substances with better biological and mechanical attributes. Readers will gain insight into contemporary offerings in dentistry's bone-grafting field, including relative efficacies and shortcomings, and identify potential avenues of study for enhancing properties within new replacement solutions on the horizon—a comprehensive update discussing progress made thus far.

Characteristics of an Ideal Bone Grafting Material

The primary objective of bone grafts is to provide mechanical support and activate osteoregeneration to replace the missing or damaged bone tissue [5]. The four essential biological characteristics for achieving successful performance are osseointegration, osteogenesis, osteoconduction, and osteoinduction [6]. Osseointegration refers to the capacity of a grafting substance to adhere to the surface of the underlying bones without interference from fibrous tissues. Osteogenesis involves generating new bone by utilizing either existing progenitor cells or newly introduced cells into the grafted material. Meanwhile, scaffolding formed via bioactivity on which medical experts let host cells develop through this technique known as Osteocoundaction enabling migration (Figure 1) among vessels along with other significant elements like host progenitor cell as well Osteoblasts development arises because Tissue indicated proteins mainly depend upon growth factors that contributed significantly such Fibroblast Growth Factors (FGFs), Platelet-derived growth factors(PDGF's), transformations within transforming-growth-factors-β impel stem-cell conversion towards forming functional bones exploiting these fundamental qualities aid timely regeneration parallelly fusion between different areas[16-18]. Nevertheless

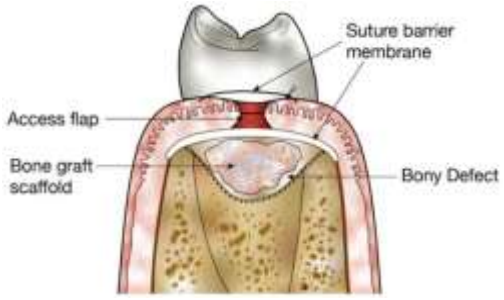


Figure 1 shows the utilization of structural scaffolds for remedying bone defects. To restore the alveolar bone void, a bone graft scaffold was inserted following surgical access flap generation.

Various properties, besides biocompatibility, bioresorbability, sterility, structural integrity, and porosity for vascular ingrowth, among others, affect the success rate of bone grafts. It is important to consider a combination of these factors to promote adequate host tissue tolerance over time and increase the chances of successful osteoregeneration processes [8]. Cost effectiveness, plasticity, and compressive strength are also significant determinants for their use [8].

Research has revealed that most of the bone graft and substitute materials currently available only fulfill one aspect - osteoconductivity–by providing a structural foundation for regeneration to take place. Nevertheless, all existing non-autograft-derived options still pose problems related to graft vs. host reactions, which require attention in ongoing efforts towards creating improved bone substitutes over time.

Classification of Dental Bone Graft and Substitute Materials

Bone grafts and substitute materials used in dentistry are classified based on tissue source or material group. There are five categories of dental bone substitutes (Figure 2). This article explores the diverse options currently used to fill bony voids or reconstruct periodontal and alveolar bone defects.

Figure 2 illustrates the classification of bone grafts and substitute materials used in dentistry. This figure also depicts the associated subcategories.

According to this definition, materials of natural origin refer to those obtained from living sources without any alteration. These materials can be categorized into four groups: autografts, allografts (including demineralized bone matrix), xenografts and phytogenic substances [9]. Research has shown that approximately 90 percent of all global bone grafting procedures incorporate naturally sourced alternative materials or substance [10]. Table one presents the essential features of commercially available substitutes and natural dental-related products made from bones.

The characteristics of readily available natural bone grafts and replacement materials are listed in Table 1.

Material Type	**Product Name**	**Material Source**	**Forms Available**	**Clinical Applications**	**Advantages**	**Limitations**	**Type of Study and Outcome**	**Reference**
Cortical Allograft	MinerOss CorticalTM	Mineralized cortical allograft	Fresh, frozen, freeze-dried	Alveolar ridge augmentation	Osteoconduction Osseointegration	Risk of disease transmission	Clinical trial	[**12**]
			Whole bone segments, block, pieces	Periodontal osseous defects	Avoids donor site morbidity	Immunogenicity	Bone formation 6 months following sinus augmentation procedures.	
				Sinus augmentation			Average of 3.5 mm horizontal ridge width gain, 4 months following placement of FDBA	
Cancellous Allograft	MinerOss CancellousTM	Mineralized cancellous allograft	Fresh, frozen, freeze-dried	Cleft repair	Osteoconduction	Same as cortical allograft		
			Chips, wedges, pegs, powder		Osteoinduction			
					Osseointegration			
					Avoids donor site			

					morbidity			
Demineralised Bone Matrix	Dynagraft D PuttyTM	Human DBM	Putty, moldable pastes, blocks, particulates, powder	Bony void filler	Osteoinduction	Poor mechanical strengths	Clinical trial	[**12**]
	OptefoRmTM			Periodontal osseous defects	Osteoconduction	Osteoinductive potential can be affected by tissue processing and host responses	50–60% resolution of periodontal intrabony defects	
	Grafton DBMTM			Sinus augmentation	Ease of handling		Remineralization and new bone formation following sinus augmentation with DBM	
					Low immunogenicity			
					Avoids donor site morbidity			
Deproteinised bovine bone	BioOssTM	Bovine	Block, granules, particulates	Sinus augmentation	Good osteoconduction	Brittle	Clinical Trial	[**13**]

	Osteo GrafTM			Socket/ridge preservation	Similar structures and biomechanical properties to human bone	Lacks fracture toughness	New bone formation, intermingled with BioOssTM particles 6-7 months following graft placement	
	CeraboneTM			Horizontal and vertical augmentation	Low immunogenicity		14/14 implants placed in patients with insufficient alveolar ridge width in the maxillary lateral incisor region successfully osseo integrated and were functionally stable	
				Peri-implant defects				
Algae-based	AlgiporeTM	Red algae	Granules	Alveolar bony defect filler	Osteoconduction	Lack of studies investigating use in humans	Clinical trial	[**12**]

				Preservation of ridge height	Good resorbability		Ninety-five percent implant survival rate in atrophic maxilla grafted with Algipore 14 years following graft placement	
					Large surface area for protein adhesion		New bone formation around and within the pores of implanted AlgiporeTM particles, 7 months following graft placement	
					Low immunogenicity			
					Resorbability			
Coral-based	ProOsteonTM	Marine coral	Block, Granules	Sinus augmentation	Osteoconduction	Brittleness	Clinical trial	[12]
	BioCoralTM			Periodontal osseous defects	Good compressive strength	Poor resorption	Decrease in periodontal probing depths and gingival recession 5 years following grafting with BioCoral	-

	InterPoreTM			Restoration of alveolar ridges	Improved cell adhesion	Low tensile strength	Bone formation within, and along the walls of the pores of grafted Interpore 200TM, starting 3 months and continuing beyond 6 months following graft placement in periodontal osseous defects of three recipients	-
					Low immunogenicity			-

Autografts

Autografts are commonly used sources of cortical and cancellous bone obtained from intraoral or extraoral sites within the same individual. Suitable grafting sites include the mandibular symphysis, mandibular ramus, external oblique ridge, iliac crest, proximal ulna, and distal radius [2]. Autografts from the ramus of the mandible can result in minor complications downstream compared with other intraoral sources, and there is an increased risk of inferior alveolar nerve damage during extraction. Ramus-harvested bone should be utilized for augmentations no greater than four teeth wide with a thickness of less than 4 mm [14]. There are no issues with histocompatibility or immunogenicity associated with autograft use, making it one of the safest biological choices available. Nonetheless, utilizing these does tends to carry downsides such as requiring additional surgical visits, which may increase costs resulting in donor site injury scarring, raising significant risks, such as bleeding infection inflammation and pain limiting usage on smaller defects only. Hence when confronted by larger craniofacial deficits Autographs might not prove at all practical thus unable to recommend its application [15]

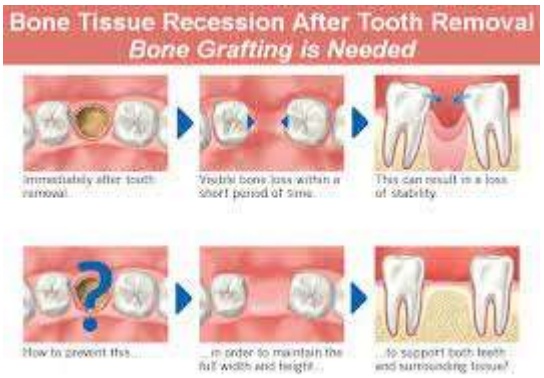
Autografts using cancellous bone are commonly used because of their osteoblast and progenitor cell contents, which possess enormous potential for promoting bone growth. Large trabecular surfaces within cancellous bones create an environment that facilitates revascularization and incorporation into the recipient site, leading to effective healing through osteoinduction. Conversely, cortical grafts lack these same components but provide structural integrity as well as promote bone healing via a process called osteoconduction; however, they integrate slower

than cancellous grafts, which have limited revascularization capabilities relative to other augmentation procedures. To optimize performance in regard to both remodeling existing tissue while enhancing quantities thereof so maximal implants may be appropriately placed without resulting compromise, practitioners will use combinations containing copies from BOTH source material types equally balanced upon recommendation given by various doctoral studies across the years, indicating that if performing additional work interventions, one can only achieve success rates adjacent or equaling those testimony-agreeing autogenous blocks produce comparable systemic (stem cells) enhancements, yielding increased predictability when conducting complicated posterior mandibular edentulous reconstructions [16]. Despite the development of alternative materials since the onset of medical intervention practices many decades ago, it remains clear why traditional gold-standard techniques were adopted widely. Such field experts adhere staunchly today: not just because satisfactory outcomes underlined inherent biological properties supporting this theory far beyond simple manufacturing alone suffices even here at present.

Allogenic Grafts

Allograft materials are the primary alternative to autografts and can be obtained from compatible living donors or cadaveric bone sources. These materials are available in three forms: fresh, frozen, or freeze-dried. Although fresh and frozen allografts have superior osteoinductive properties, they pose a higher risk of host immunogenic response and disease transmission but also have limited shelf life, which limits their use (Table 1). Freeze-drying allows for increased shelf life with decreased immunogenicity, but results in reduced structural strength and osseointegration potential along with lower levels of osteoinductivity [17].

In recent years, the use of allograft materials has become a more popular option [36] due of their ability to address many concerns associated with autografting procedures, especially in cases of larger bony defects. However, limitations still exist when it comes to the potential risk of transmitting infectious diseases, such as HIV and Hepatitis B and C. In fact, research indicates that approximately 8% of osteoarthritic femoral heads removed during hip arthroplasty are affected by unknown illnesses [18]. These risks can often be mitigated through various tissue-processing methods, including sterilization techniques such as mechanical debridement, gamma irradiation, and ultrasonic washing [19]. Recently, there have been successful uses where an allograft is paired with xenografted tissues, specifically for bone regeneration (see Figure 3).



The images in Figure 3 depict the pre- and postoperative steps taken to address an edentulous patient's dental issues using a guided bone tissue regeneration implant.

Various forms of allografts are readily available and exhibit good histocompatibility. Custom shapes can also be produced to match the recipient site requirements. However, both cancellous

autografts and allografts exhibit weak mechanical strength with limited healing capabilities because of the tissue processing techniques that reduce osteoinductive abilities. Cancellous allografts may lead to an inflammatory response in hosts, resulting in fibrous tissue formation hindering bone reformation, whereas cortical allografts aid scaffolds for initial recovery after inflammation [7,12]. Allograft materials have been used extensively, but recent findings concerning high failure rates over long periods coupled with regulatory restrictions have resulted from a shift towards synthetic grafting materials over them [3], even though they have amply filled periodontal defects and replenished lost ridge height or severe atrophy, allowing adequate implant placement (Table 1) [20].

Demineralized bone matrix (DBM) is a form of allograft derivative that undergoes acid treatment to remove its mineral mesh. This process uncovers the underlying inner bone matrix rich in growth factors, including TGF-β and FGF, which can stimulate mesenchymal stem cells' differentiation into osteoblasts. Its osteoinductive capacity surpasses that of cancellous or cortical allografts owing to the high concentration of growth factors. However, DBM preparation techniques impact their potential; lactic acid and acetic acid nitric treatment decrease it from being highly dependent upon tissue processing methods such as alcohol and adversely affect their stimulating properties negatively. After demineralization, the trabecular frameworks for vascular ingrowth facilitate progenitor cell infiltration, leading to new establishment sites that provide an optimized surface for regeneration following implantation. Freeze-dried forms have provided alternative options, such as block particulate powders and other preparations containing glycine glycerol salmon-hyaluronate collagen hydroxyapatite tricalcium phosphate, common materials composed of varying combinations depending on the needs desired by practitioners for optimal efficiency handling adaptability [21]. However not all sources appreciated because some origins susceptible easily destroyed sterilizing agents consisting significantly immunological response possibility. Despite these limitations, researchers arise exploring avenues, improving designs, and overcoming existing disadvantages about synthetic origin plant-based compounds. Moreover, demonstrating significant progress and representing newfound hope innovative medical procedures which ultimately enhances patients dental health and well-being. This positively impacts professionals working across disciplines relying tools to produce maximum benefit for the sake of the patient's comfort. Restoring quality life which is lost due to disease trauma time constraints finances among limiting obstacles faced substrates formed conventionally are limited therapeutic interventions ushering era change marked scientific breakthrough derived surprising findings discordant thereby raising fresh questions namely ethical concerns morality surrounding source fabrication rendering necessary urgent comprehensive dialogue pertaining complex issues raised expects inform regulate drive policy formulation governing production use contribute continued evolution restoration medicine benefiting individuals humanity whole advancing societal welfare achieving commonly held aspirational aspirations promoting human development wellbeing [22].

Collagen-based materials, such as extracellular bone matrix, can be found in the market. These materials promote optimal conditions for new bone formation by facilitating mineral deposition, vascularization, and growth factor adhesion. However, because of its low structural integrity and potential risk of adverse immune reactions, it is not commonly used alone as a graft substitute. When combined with BMPs or hydroxyapatite carriers, it has been shown to enhance osseointegration [23].
Xenografts were characterized as described in Section 3.1.3.

As previously discussed, while autografts and allografts are successful in bone grafting practice, they have limitations. Therefore, natural bone substitutes have been developed to improve osteogenic potential by creating a favorable environment for bone growth. One of these substitutes is a xenograft material derived from a species that is genetically unrelated to the host. In dentistry, deproteinized bovine bones, such as BioOssTM, are commonly used as they provide excellent mechanical support and stimulate bone healing through osteoconduction. BioOssTM has proven to be more stable than other alternatives with low immunogenicity levels, making it an ideal candidate for procedures such as maxillary sinus lifting and implantation because of its superior stability (Table 1). Studies show that after six months of applying both Autogenous Graft Bone and BioOsSTM together at Maxillary Sinus Defect Sites, similar new bone formation occurs, with higher retention demonstrated by the BioOsSTM. Comparative analysis between autograft osseous tissue and the new bone formation from BioOsSTM suggests that its efficacy closely matches or even exceeds that of autogenous grafted bones. A further study conducted over five years, also concluded that predictable simultaneous placement was possible following one-stage maxillary sinus augmentation procedures utilizing bovine-bone grafts [24, 25]. Clinically, Bio-Oss® must be used according to good quality protocols for successful dental implant surgeries. [24].

Additional bovine bone-based products, such as OsteoGrafTM and CeraboneTM (Table 1), can also be found on the market. These are subjected to high-temperature treatment, which removes all organic constituents and minimizes the immunogenicity levels of the resulting materials. Similar to BioOssTM properties, these items demonstrate structural and biochemical characteristics comparable to those observed in human bones, thereby acting effectively as osteoconductive grafting agents [12].

Chitosan, a naturally occurring polymer derived from the exoskeletons of crustaceans and composed of glucosamine and N-acetylglucosamine, is currently being researched as a potential xenograft material. This promising option can stimulate bone regeneration by providing structural support for osteoblastic activity in various in vitro conditions. Although chitosan has poor mechanical properties on its own, it can be combined with other materials, such as gelatin, calcium phosphates, or bioglass, to enhance its efficacy. For instance, combining chitosan with hydroxyapatite (HA) produces an improved scaffold that promotes cell attachment and vascularization, while reducing degradability. Moreover, chitosan-based substitute materials possess low immunogenicity along with fibrous encapsulation capability, which means they have great applicative versatility beyond autograph usage in dental procedures such as GBR membrane coating implant surfaces guided tissue etc., suggesting them as gold-standard substitutes. Recent studies showed successful application of this substrate within alveolar periodontal restoration resulting in even greater height recovery than through traditional grafting methods which prove further benefit for these versatile biomaterials.[26]

Silk, obtained from the silkworm Bombyx mori, is a natural biopolymer composed of fibroin and sericin proteins. After removing sericin through degumming, silk fibroin (SF) can be used as a bone scaffold in the form of sponges, fibers, films, and hydrogels. SF offers excellent degradability, tissue integration, and permeability to oxygen and water, making it highly compatible with biological processes. Recent studies show that despite its poor mechanical properties for GBR use cases, SF has been found to be effective due to favorable biological traits that enable membrane-like formation when extracted into mat form. In 2016, trials were conducted wherein patients who received this treatment following extraction of impacted molars displayed significant gain in new bones measuring approximately 4 mm just six months post-grafting [12]. The versatile nature along exhibit good tensile strength once tested under

duress make them excellent for several types medical implants beyond tooth extractions alveolar deficiencies or cyst/tumor areas clearance so suitable implant placement may take place Myriad clinical investigations indicate their remarkable usefulness impacting different crucial life aspects positively where osseointegration matters greatly. Although there are limitations linked towards using xenograft substitutes live cell conservation Process, resorption rates among other factors require resolving before total adoption. Optimism could not thrive withstanding prospects that look hopeful concerning these materials.

Phytogenic Material

Phytogenic materials obtained from plant-based sources such as Gusuibu, coral-based bone substitutes, and marine algae serve as valuable substitutes for bones. Gusuibu is an ancient Chinese herbal medicine that has long been used to treat osteoarthritis and bone fracture in Chinese patients [8]. It is made from the dried rhizome of a species called Drynaria fortune. Its known properties include its ability to induce osteoblast activity while promoting alkaline phosphatase activity, thereby facilitating calcification processes (as explained in Table 1) [27]. Wong and Rabie conducted experiments highlighting how new-bone formation increased by 24% after integrating collagen-scaffolded Guisuibu compared to only using grafted Guisuibu; additionally, it was found that when given alongside absorbable collagen sponge growth factors like BMP also play a role in further increasing results up to about 90%. These findings demonstrate that integration with collagen scaffolding can make Gusuibus' ability similar, if not equivalent, to autograft material, affirming its potential for serving --with said carrier-- causing positive outcomes upon usage. When utilized in dentistry applications including orthodontic tooth movement may accelerate reduction effects due to promotion on remodeling of osseous tissues via altering Osteoclastic/Oesteoblastic activities specifically seen within cell cultures studies[28]

Bone substitutes made from coral typically contain calcium carbonate, which can be either used in its natural form or processed by heating with ammonium phosphate to create crystalline hydroxyapatite (HA) with minimal residual carbonate. HA is a naturally occurring polymer of calcium phosphate found in bone and other materials such as coral, known for promoting bone healing by acting as a structural support[29]. However, coralline HA may be brittle and highly resorbable when it occurs naturally; therefore, many applications involve using crystallized blocks or granules instead to provide structure like trabecular bone. Research indicates that incorporating coralline HA improves vascularization compared with non-coralline versions while surpassing freeze-dried allografts regarding cell attachment promotion. In clinical settings where defects exist within bones needing repair/healing assistance like dental implants' placement on the alveolus after reconstruction surgeries: surgeons use autograft material integration along WITH osteoinductive growth factors-like BMPs-which release over time once applied onto injured areas allowing new tissue K/growth needed [8]. Recent studies reveal numerous attempts aimed at enhancing mechanical properties of Corralinnes artificially via doping methods involving zirconia fluoride addition among others—Strontium ions incorporated Aid stimulation related resistance construction inhibition procedures conducted leading towards improved outcomes further backed up testing grounds including Alveolar Defect induced animal models VEGF coated Coralines proving effective against traditional alternatives Low immunogenicity good bonding capacity yet few adverse qualities-found/unique need more exploration before final application decisions are made accordingly predictably - concurring most experts who study this field globally agree based upon current existing results & trends indicating these Substitute could indeed become the future gold standard should we continue tests yielding promising satisfactory returns thus far!

Since 1988, AlgiPoreTM has been used clinically as a bone substitute made from naturally occurring HA derived from marine algae [8]. It possesses desirable qualities such as low immunogenicity, good resorbability overtime and a large surface area for protein adhesion (Table 1). Furthermore, it can function as both a carrier for GFs and MSCs. Although in vitro studies show promising results regarding the use of AlgiporeTM grafting on bones together with clinical trials that demonstrate its effectiveness to heal fractures; there have only been few investigations conducted on humans or modifications thereof [30]. Recent advancements include using AlgiPoreTM alongside β-TCP which claims to maintain volume support required while decreasing the rate of resorption times thus improving efficiency ratios. Ewers conducted an extensive study spanning fourteen years where he found high implant survival rates at around ninety-five percent following sinus-cavity procedures employing Algiporw TM in atrophic maxillae patients [31]. Due to excellent biocompatibility properties like compatibility with tissues due responsiveness/ assimilation into body fluids mimicking natural tissue environments without posing adverse immune responses gradual biological degradations triggered by metabolic processes driven by cell activity occur and also enhance bone bonding capacity.[91] Clinically effective uses involve combining this material primarily post-tooth extraction surgery leading ridge deformities prevention Figuratively representing space fillers along other ancillary materials(Table I)[32]).

Synthetic Bone Substitute Materials

To mitigate potential immunogenicity and morbidity risks at donor sites, artificial synthetic bone substitute materials have been developed to closely imitate the biological properties of natural bones. However, despite these efforts, currently available synthetic substitutes only possess osteointegrative and osteoconductive characteristics [10]. Examples of such materials include calcium phosphate ceramics like hydroxyapatite (HA), tricalcium phosphate (TCP) and bioglass; metals including nickel-titanium; polymethylmethacrylate (PMMA), polyglycolides and calcium phosphate cements [12]. Table 2 describes the features of synthetically made dental-grade bone replacement products that are commercially accessible.

Material Type	**Product Name**	**Forms Available**	**Indications**	**Advantages**	**Limitations**	**Type of Study and Outcome**	**Reference**
Hydroxyapatite	OstimTM	Blocks, wedges, and granules	Intraosseous defects	Osteoconduction	Donor site morbidity	Clinical trial	[**31**]

	EndobonTM		Furcation defects	Macroporous structure comparable to human bone	Low mechanical strengths	Significant bone regeneration in 2 and 3-wall intrabony periodontal defects 6 months following placement of OstimTM graft	
			Socket preservation	Biocompatibility	Delayed resorption rate	Decreased periodontal pocket depth, decreased clinical attachment loss, decreased intrabony defect depth, 6 months following placement of OstimTM graft	
			Horizontal or vertical augmentation in non-stress bearing areas	Excellent hydrophilicity for vessel uptake	Limited availability		
			Periodontal osseous defects				

Tricalcium phosphate ceramics	CerasorbTM	Blocks, cylinders, wedges, granules	Void filler for alveolar, periodontal, periapical, peri-implant and cystic defects	Osteoconduction	Poor mechanical properties, in particular compressive strength	In vivo (goat)	[**32**]
	OSferionTM			Ease of handling		Bone regeneration comparable to that of autografts in alveolar clefts, 6 months following placement of β-TCP	
	OrthograftTM			Radiopacity allowing monitoring of healing		Clinical trial	
				Good resorbability		Successful osseointegration and prominent bone formation along graft surface evident 28 days after placement of OSferionTM	

				Low immunogenicity			
Biphasic calcium phosphate ceramics	MASTERGRAFTTM	Moldable putty, granules	Void filler for alveolar, periodontal, and cystic defects	Osteoconduction	Compressive strength remains lower than that of cortical bone	Clinical trial	[**22**]
			Preservation of sockets	Osteoinduction		New bone formation with histological observation of osteogenic activity surrounding MASTERGRAFT granules, 4-5 months following graft placement	
			Ridge augmentation	Resorbability		New bone formation and minimal ridge width reduction observed in post-extraction alveolar ridges of fifteen patients	

			Maxillary sinus lifting	Comparatively greater mechanical strengths than either TCP or HA alone			
			Periapical surgery				
Bioglasses	PerioglasTM	Particulates	Periodontal defects	Osteoconduction	Brittle	Clinical trial	[**22**]
	BiogranTM		Furcation defects	Biocompatibility	Low mechanical strength	88.6% success rates of implants placed in sites grafted with bioactive glasses, 29 months following bioglass material	

			Socket preservation	Antimicrobial activity	Poor fracture resistance	Decreases in periodontal pocketing depth, clinical attachment loss, gingival recession, depth of bony defect observed, 9 months after placement of PerioglasTM either alone, or in combination with a non-resorbable membrane GoreTexTM or bioresorbable membrane Resolut AdaptTM	
			Cystic defects	Porous structure			
			Fenestration and dehiscence defects	Completely resorbable			
Calcium phosphate cements	NorianTM	Injectable paste, moldable putty	Bony defect filler	Osteoconduction	Low speed of cell adhesion	Clinical Trial	[**31**]

	ChronOS injectTM		Reconstruction of bony fractures	Self-setting ability	Brittle	Complete bone regeneration in alveolar ridge defects, 6 months following placement of CPC material	
	HydrosetTM		Implantology	Mouldability	Concerns relating to extrusion of material to adjacent tissues	Case Report	
	BoneSourceTM			Biocompatibility		Complete replacement by newly formed bone of NorianTM graft placed in a large 3-wall mandibular defect, one year following graft placement	
Calcium sulfates	OsteoSetTM	Diverse sizes pellets	Void filler for surgical defects and furcation defects	Osteoconduction	Rapid resorption which is faster than that of human bone	Clinical trial	[**19**]

			Preservation of sockets and alveolar bone heights	Low cost	Relatively considerable risk of infection and inflammation	When used in combination with FDBA, resulted in the reduction of periodontal probing depths, gains in clinical attachment, defect fill and resolution, 12 months following placement of calcium sulfate graft material	
				Readily available		Double-blind randomized trial 42% of bony defect filled with new bone, 6 weeks after placement of OsteoSetTM graft. No statistically significant additional bone formation observed during a 3–6-month period.	

				High moulda bility			
				Biocom patibilit y			
				Short setting time			
Polym ers	Bioplant HTR Synthetic BoneTM	Particu lates, granule s, ready to use in syringe	Ridge augme ntation and preser vation	Osteoc onducti ve	Concern s relating to acidic degradat ion products	Clinical trial	[**18**]
			Furcat ion defect s	Biocom patible		Reduction in periodontal probing depths, clinical attachment gain and significant resolution of defects in alveolar crest bone, 6 months following placement of Bioplant HTR Synthetic BoneTM	

				Customizable forms		Decreased periodontal probing depths, mean horizontal and vertical furcation probing attachment levels, six years after placement of Bioplant HTR Synthetic BoneTM	
				Low immunogenicity			
				Porous structure			
				Radiopaque			
Metals	OSS BuilderTM	Mesh/membrane available in lateral and papilla design forms	Lateral forms — horizontal or vertical bone augmentation	Osteoconduction, acts as a membrane barrier for GBR	Need for a second surgical visit	Clinical trial	[**21**]

			Papilla forms — restoring papilla height for aesthetics	Good mechanical strength	Possibility of soft tissue dehiscence and exposure of the membrane	Significant bone formation in alveolar ridge, 4 months following placement of autograft with titanium mesh	
				Good biocompatibility		Case Report	
				Corrosion resistance		Increase in alveolar crestal bone width and height observed, 5 months after placement of autograft mixed with equine-derived xenograft and a titanium mesh	
				Porous structure enhancing cell adhesion			
Composites	NanoBone TM	Putty, granulate, block, ready to use "QD"	Bone void filler	Osteoconduction	Lack of studies investigating use of Nano BoneTM in humans	In vivo (mouse)	[**22**]

	(nanocrystalline HA/silicon dioxide)		Socket preservation	Osteoinduction		New trabecular bone formation, followed by resorption of graft material, 8 months following placement of NanoBoneTM In vivo (dog)	
				Resorbability		A significantly greater amount of new bone formed in extraction sockets observed at 45 and 90 days after placement of NanoBoneTM with PRF than NanoBoneTM alone or in the control group	
				Moldability			
				Good cell adhesion			
	Fortoss VitalTM	Paste	Alveolar bone augmentation	Osteoconduction	Contact with blood will delay setting time of the paste	Clinical trial	[**25**]

	(β-TCP/calcium sulphate)		Implant rehabilitation	Osteoinduction		Formation of new viable bone, 12 weeks after placement of Fortoss VitalTM	
			Socket preservation	Fully resorbable		Reduction in periodontal pocketing depth, clinical attachment loss, but increases in gingival recession observed 2 years after placement of Fortoss VitalTM	
				Moldability			
				Porous structure			
				Good cell adhesion			
	SmartBone TM	Blocks, microchips, plate, granules, wedge, cylinder, rod	Periodontal osseous defects	Similar morphology to human bone	Comes in individual use only packages	Clinical trial	

	(DBM/polymer/collagen)		Socket preservation	Rapid blood cell adhesion and proliferation due to high hydrophilicity		Formation of new bone, and increases in alveolar bone dimension, 4 months following placement of SmartBoneTM	
			Alveolar ridge augmentation	Improved volumetric stability		Successful osseointegration and new bone formation observed surrounded by vascular connective tissue, 4 months following placement of SmartBoneTM graft.	
			Sinus augmentation	High load resistance for large bony defects			

Hydroxyapatite (HA)

HA, a bone grafting material with a chemical composition like the inorganic component of natural bone, lacks trace elements like Na+, Mg2+, K+ and Sr+. This absence affects biomechanical reactions. It also has no microporous structure unlike bovine-derived HA. Synthetic HA takes time to resorb as it has high Ca/P ratio and crystallinity. Furthermore, its low mechanical strength restricts its use at high load-bearing sites (Table 2). Studies reveal that synthetic HA, alone or combined with polymer, are inadequate for preserving alveolar ridge heights during placement of end osseous implants or sinus lifting management [117]. Thus

dentistry limits the application of this material mainly to implant coating, external fixator pins and areas requiring low loading stress (Table 2) [8]

Advancements in HA-based bone substitute materials have focused on creating nano-sized particles of HA, which possess superior biomechanical properties that more closely resemble the composition of natural bone. The development of these nanomaterials aims to achieve a closer resemblance to the extracellular matrix of bones and enable faster response to external stimuli while enhancing delivery and controlled release of bioactive molecules like growth factors for enhanced osteo-regenerative properties [33]. Nanocrystalline HA outperforms conventional forms by displaying improved biological performance and dissolution rates [120]. Its larger surface area-to-volume ratio boosts adhesion, proliferation, differentiation capabilities among osteogenic progenitor cells; enhances sinter ability resulting in dense structures with better fracture toughness plus other mechanical characteristics improving their overall suitability [116-122]. Despite considerable progress across all domains when compared with traditional forms' limited evidence is available yet regarding its widespread adoption [116, 118].

Tricalcium Phosphate Ceramics (β-TCP)

There are two forms of TCP: α-TCP and β-TCP [68,123]. For many years, the latter has been widely used as a bone substitute due to its faster biodegradation and absorption. It also possesses desirable properties such as ease of handling, radiopacity for monitoring healing progress, good osteoconductivity thanks to microporosity promoting fibrovascular ingrowth and osteogenic cell adhesion. Furthermore, β-TCP is characterized by low immunogenicity risk compared with bovine bone grafts (Table 2) [36]. Nonetheless, its poor mechanical strength under compression caused by the interconnected porous structure makes it unsuitable as a full replacement material in bony defects despite being ideal as filler at morphological sites. Beta-TCP can be found often used to repair marginal periodontal or periapical defects or partially resorbable fillers in alveolar bony defects (Table 2) [37]. Research conducted by Nakajima et al. also discovered that regenerative abilities were similar when comparing Beta-TPC freeze-dried bones but because of limitations on mechanical changes wider usage remains limited.[3]

Biphasic Calcium Phosphate Ceramics (HA and β-TCP Ceramics)

In recent decades, efforts have been made to create a material that could harness the resorbability of β-TCP and the osteoconductive potential of HA. This resulted in biphasic calcium phosphate (CP) ceramics, which typically combine both materials. By using these ceramics instead of just HA or β-TCP alone, bone regeneration rates can be improved, and greater mechanical properties achieved [3, 37, 38]. Furthermore, by adjusting the ratio between HA and β-TCP it is possible to control their levels of resorption and osteoconductivity [128]. While biphasic CP ceramics boast stronger compressive strength than pure & beta; --TCP-based materials still fall short when compared with cortical bone [3, 37] (Table2). San bone has helped show promising outcomes within its use as a bone substitute in periapical surgery with complete healing over a two-year period [38], suggesting further clinical applications for this technology's osteoinductive abilities might prove fruitful.

Bioactive Glass

Bioactive glasses (BAG) are a type of synthetic silicate-based ceramic. They consist of silicate molecules linked with other minerals such as calcium (Ca), sodium oxide (Na2O), hydrogen

(H), and phosphorus (P) [3, 11]. Initially, their composition was primarily silicon dioxide (SiO_2), sodium oxide (Na_2O), calcium oxide (CaO), and phosphorus pentoxide (P_2O_5). However, it has been modified to improve stability by adding potassium oxide (K_2O), magnesium oxide (MgO), and boric acid (B_2O_3). When implanted, exposure to body fluids causes the accumulation of silicon ions from the bioactive glass. These silicon ions leach out into the surrounding tissues' fluids, which subsequently stimulates the formation of a hydroxyapatite layer on the surface of the glass. This layer promotes the adherence of osteogenic progenitor cells, essential for bone formation. Bioactive glasses are desirable due to their optimal features, including osteoconductivity (the ability to promote bone growth onto its surface), good biocompatibility (compatibility with living tissue), and a porous structure that stimulates blood vessel growth (vascularization) [38, 35]. Recent research has explored ways to improve Bioactive Glass properties by incorporating various ions. For instance, zinc-doped varieties can reduce microbial buildup associated with periodontal disease due to their inherent antimicrobial properties. Additionally, silver-doped glasses exhibit controlled release capabilities of silver ions, which can be effective against microbes known to destroy tissue surrounding dental implants, such as Porphyromonas gingivalis (P.g.) and Prevotella intermedia (P.i.).

Although Bioglass (BAG) has been valuable in dentistry for certain applications, such as managing periodontal osseous defects and preserving alveolar bone following tooth extractions in orthodontic patients or augmenting the unilateral cleft alveolar bone, its low mechanical strength and poor fracture resistance limit it to low-stress environments unless used with other grafting materials. This information is summarized in Table 2 [133,137], alongside successful examples of BAG usage.

Calcium Phosphate Cements (CPCs)

Typically consisting of an aqueous component and a powder containing sintered Calcium Phosphate (CP) material, such as α-TCP and HA, Calcium Phosphate Cements (CPCs) are two or three-component systems. Once mixed to form a workable paste that hardens in situ at room temperature into HA nanocrystals through self-setting ability, these cements possess numerous benefits including replicating the structure of bone while being biocompatible with high osteoconductive properties readily available for several types of bony defects [3,11]. However, CPC tends to lack sufficient microporous structures restricting both cell adhesion speed and fluid exchange which thereby reduces restorability potential; there is also a risk that incomplete setting reactions lead to adverse inflammatory reactions highlighting its weaknesses [15]. Researchers have recently sought out ways to address these limitations by exploring advanced strategies, such as pre-fabricated 3D-printed Calcium Phosphate Cement (CPC) scaffolds, rather than relying solely on injectables with viscous binders (e.g., chitosan, gelatin, and hyaluronic acid). Optimization of particle sizes and shaping techniques, regulation of CP powder inter-particle interactions, and the addition of ions may help prolong material degradation. Furthermore, using growth factors, stem cell infusion, and other modifications may provide better results in improving bioactivity and boosting osteo-inductivity, which are invariably desired within clinical dentistry scopes, including dental implantology and reconstructive works. Moreover, filling up any bony fractures should be approached differently, avoiding load-bearing sites and focusing on non-load-bearing ones, to prevent possible extrusions that could cause muscle damage.

Calcium Sulfates

Heated gypsum in powder form is known as calcium sulfates, which can eventually transform into a crystalline structure called alpha hemihydrate. When rehydrated, this powdered hemihydrate can become a moldable paste that hardens on its own and takes the shape of bony defects both big and small. For years, calcium sulfate has been widely used for bone regeneration due to its osteoconductive properties; recent studies suggest it also possesses osteoinductive traits by releasing molecules that contribute to bone healing. Calcium sulfate holds numerous benefits: cost efficiency, high availability with short setting times plus biocompatibility support. Nevertheless, quick resorption periods pose considerable limitations since the rate exceeds new bone formation; consequently, rendering significant loss regarding mechanical abilities at defect sites. In addition, it increases infection risk whereby other products like antibiotics are added before use. Calcium sulfates were traditionally challenging when applied under dental applications because saliva or bleeding interfered routinely. However, biphasic formulas containing 33% hydroxyapatite improved hardened ability even amid bodily fluids leading through more advancements such as surgical defenses, maintaining alveolar ridge height, furcation defense including being utilized as void filler (Table2)

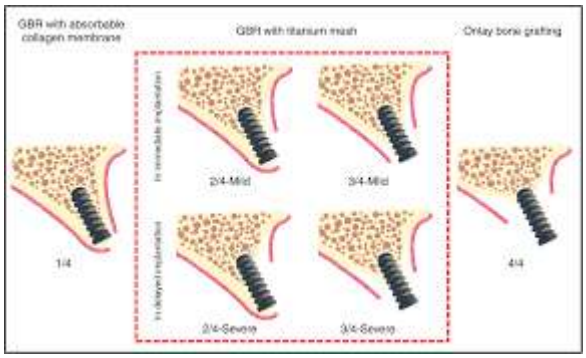
Polymers

There are two types of synthetic polymers, degradable and non-degradable. The aliphatic polyesters that fall under the former category are commonly used in bone regeneration such as polylactic acid, polyglycolic acid, and polyp-caprolactone along with their copolymers and derivatives [12,17]. They offer benefits like customized shapes/forms, low immunogenicity levels while being controllably resorbable yet maintaining porosity and favorable physiochemical structures [12]. Nevertheless, concerns regarding the release of acidic degradation products resulting in changing pH at a local level leading to osteoconductivity issues or weak cell adhesion capacity persistence which restricts usage within dental fields (Table 2) [15]. Studies based on polymer substitute materials have been conducted using animals showing varying results from no adverse complications arising for most cases to reactions prone towards inflammation occurring occasionally [17]. It has been suggested by experts adding HA or TCP material onto polymer-based scaffolds may improve regenerative potential hence improving overall function for skeletal use[12], A recently published study found coats made from silk fibroin loaded with VEGF can attain enhanced angiogenic properties allowing controlled delivery/release furthering increased osseointegration into grafted sites achieved bioactive molecules helping areas where they come up short.[12],160 Another publication concluded three-dimensionally printed biopolymer built out PLA having pore diameters around two-hundred micro-millimeter resulted in raised cellular differentiation rates facilitated additional authorized graft incorporation points compared to prior studies done before this period,[33] HTR Synthetic BoneTM serves an example illustrating commercially available versions containing PMMA/polyhydroxy ethyl methacrylate/calcium hydroxide content successfully administrated therapy capable managing/fighting off any serious-periodontal intrabony-furcation defects depending upon severity degree - Table 2 [29].

Metals

Recently, research has uncovered the key role that metallic ion like magnesium (Mg), strontium (Sr), zinc (Zn) and silicon (Si) play in maintaining bone health and promoting osteogenesis [11]. In dentistry, nickel-titanium materials have been investigated for their ability to regenerate bones due to favorable properties such as good biocompatibility, mechanical strength,

corrosion resistance and elastic modulus. Studies indicate that a nickel-titanium membrane with pore sizes between 50-125 µm effectively promotes vascularization which leads to successful bone healing by providing a physical barrier against epithelial cells/fibroblasts whilst selectively allowing migration of osteogenic progenitor cells towards the site where new bone forms [32]. The primary function of nickel-titanium membranes is serving as structural scaffolding support wherein cell adhesion occurs prior to proliferation then differentiation thus leading into new formation of healthy tissues more particularly on newly formed or regenerated desirable bones, but disadvantages include requirement for additional surgical procedures plus risks arising from soft tissue exposure/dehiscence. In time past years however Titanium based membranes were used in many clinical settings ranging from reconstructing alveolar bony sites; stabilizing autograft splints placed at affected areas; supplementing other grafts/tractions related medical practices along being employed simultaneously as Barrier Membranes during GBR treatments using Table 2's comparative synopsis shown below regarding the various titanium uses covering dental care: .[31]



Recently, Liu et al. have devised a bone substitute made from pure magnesium (99.9%) and a Mg-30wt% Sr alloy in a high-purity graphite crucible produced under mixed gas conditions. By merging the biocompatibility, degradability and exceptional mechanical characteristics of both substances, this composite material was created [33]. The researchers demonstrated that when compared to standard commercial bone grafts like HA calcium sulfates or TCP materials; their innovative Mg-based product had increased tensile strength and compressive properties as well as more effective antibacterial activity promoting improved biocompatibility for potential use in weight-bearing areas within the body [31].

Composite Bone Substitute Materials

The objective of composite bone substitutes is to enhance the mechanical characteristics by combining varied materials, like bioglass and polymers while simultaneously leveraging their osteoconductive properties. These products are frequently incorporated with bone marrow or utilized as carriers for BMPs to augment both osteoinductive and osteoconductive traits [12]. To capitalize on various benefitting materials, composite bone substitutes often incorporate two or more substances [15].

A novel composite bone substitute called NanoBoneTM combines 76% w/w nanocrystalline HA with 24% w/w silicon dioxide [17]. The included silicon dioxide component induces the adhesion of autologous proteins on the surface and aids in bone remodeling. Despite its high porosity, this material maintains great fracture toughness and mechanical strength while exhibiting a swift mechanism for integrating into host tissue. Research has documented newly developed trabecular bones in animal models followed by complete resorption nine months

after regeneration was completed [31]. In human subjects, studies have shown that using NanoBoneTM can preserve alveolar bone height for extraction sites as well as stimulate faster mandibular cyst excision recovery when paired with platelet-rich fibrin (Table2) [32]

Fortoss VitalTM is a commonly utilized resorbable composite bone replacement product in dentistry. It consists of calcium sulfate and β-TCP, which creates an adaptable paste that sets itself in place for high compatibility with defect sites. This material acts as an osteoconductive scaffold possessing negative surface charges to attract positively charged BMPs and interstitial fluid, promoting migration by osteoblasts leading to improved regeneration of bones. Upon setting the mixture forms a barrier membrane preventing unwanted cells from infiltrating while retaining osteogenic cell population required for mediating further bone regrowth (Figure 4). Fortoss VitalTM has been highly effective when applied during procedures such as alveolar augmentation surgery or post-implant rehabilitation treatments where significant improvements were observed through dental practices (Table2) [33]. Composite substitutes are becoming increasingly popular options over autograft materials due to their excellent performance clinically.

Growth Factor-Based Bone Substitutes (GFBSs)

Growth factors such as BMPs, PDGFs and IGFs have osteoinductive properties that promote bone regeneration in bony defects. In dentistry, PRGF, PRP and PRF are bioactivated materials used to accelerate bone healing in patients with BRONJ. However, recent studies suggest mixed results when using additional grafting material alongside PRP for infra bony defect treatment or sinus augmentation. BMP-2 and BMP-7 were the commonly approved USFDA growth factors until concerns emerged regarding life-threatening complications associated with InfuseTM use, leading to OsigraftTM production halting altogether[39]. GFBS products offer innovative bio substitutes like AugmentTM, which utilize recombinant rhPDGR-BB and other carriers to target specific areas for bone regeneration effectively along lines. However, one challenge is their lack of efficacy without structural support, alongside the need to satisfy therapeutic requirements within a limited time frame while retaining bioactivity. Strategies addressing these challenges include entrapping the substances within scaffolds and binding them covalently or naturally using nanoparticles or micro-particles. These methods act as reservoirs, prolonging controlled release over an extended period. These approaches have progressed beyond animal testing into potential human applications, primarily targeting bilateral augmentations of the maxillary sinuses and addressing ridge deficiencies. Hopefully, this approach will help avoid challenges arising from poor delivery techniques and exploit biological processes to enhance scar-free tissue repair over time.

The novel concept of Sticky Bone involves enriching a bone graft matrix with growth factors using autologous fibrin glue to stabilize it in bony defects, leading to faster regeneration and less loss of bone [21]. Advantages include easy shaping, structural stability, as well as selectivity for osteogenic progenitor through the prevention of soft tissue cell migration via the interconnections between fibrin strands. The rapid cell adhesion facilitated by this network also accelerates healing time [25]. When combined with Concentrated Growth Factor (CGF) or a titanium mesh membrane during grafting for an atrophic alveolar ridge case study over 4 months yielded favorable three-dimensional results compared to cases without its use.

Bone Substitutes with Infused Living Osteogenic Cells

MSCs, which are viable progenitor cells for bone formation and derived from bone marrow, can be utilized independently or alongside cytokines, GFs, scaffolding carriers (including DBM) to promote osteogenesis and new bone growth. MSCs possess multipotent qualities that enable them to differentiate into various forms of osteogenic cells capable of repairing large bony injuries in collaboration with a scaffold [24]. Demonstrations reveal bioengineered substitutes using MSC-enriched materials enhance extraction wound healing better than those built simply through non-MSC induced substances alone; moreover, presenting an augmented biomechanical performance thereby increasing successful dental implant placement rates [24]. Additionally direct administration speeds up the consistent reconstruction process [31].

Numerous preclinical studies within the dental industry have explored utilizing multipotent stem cells for periodontal regeneration. Cao et al. and Hu et al. both discovered that employing heterologous MSCs, derived from extracted third molars' dental pulp, in cell sheets or injections enhances regenerating alveolar bone heights by 52.7 mm and 32.4 mm respectively when implemented into experimental pig models [32]. The differing increase in results are due to 3D structure's ability in mimicking structural scaffolds physiological functions significantly better than other methods like cell injection [35]. Furthermore, Park et al.'s research demonstrated using MSCs obtained from a different source - heterologous periodontal ligament tissue instead of heterologous dental pulp - generated higher levels of regenerated bone during treatments applied to affected areas on an experimental dog model [34]. Clinically approved products available commercially include Bioseed-Oral BoneTM along with Ostergrens plant DENTTM; these currently use autogenous sources of modified sclerosing cholangitis (MSC) combined with appropriate scaffold materials [194], allowing sinus augmentation deeming it useful for placing implants even amongst severely atrophied maxilla regions providing predictable outcomes per FDA-approved procedures recommending their usage as indicated only under controlled circumstances changing guidelines according novel findings arising frequently over time [36].

Although products infused with stem cells have numerous advantages, there are still limitations that remain. These include low survival rates of stem cells after transplantation, the high expense and complexity of procedures, production challenges related to autogenous cells, the requirement for special storage conditions (e.g., below -80°C), lengthy wait times and processing periods as well as legal regulations. As a result of these obstacles, using bone substitutes infused with stem cells is presently not commonly utilized but rather restricted to specific indications [194].

Future of Bone Substitute Materials in Dentistry

Despite having established criteria defining the optimal bone grafting material decades ago, autografts remain unbeatable as they are the only ones that possess all four critical biological properties [68]. Nonetheless, their scarce availability and associated constraints have led to a transition towards alternative materials and innovative synthetic substitutes. Despite considerable efforts made in this area, currently available products still exhibit biomechanical insufficiencies [17].

Developing a porous structure that is both mechanically strong and capable of promoting optimal osseointegration and vascularization remains the biggest challenge in material development. Synthetic bone substitutes are limited to only being osteoconductive, resulting in

inadequate outer surface layer bone regeneration [68]. Therefore, it is essential to carefully consider biological factors such as resorbability, pore size and morphology during structural design when developing new materials [12]. A recent trend has been incorporating growth factors or MSCs with scaffolds for increased regenerative potential while inhibiting unwanted inflammatory responses from recipients. Moreover, time-release delivery systems have gained traction recently as a means of maintaining bioactivity within therapeutic windows [29]. Novel grafting materials should aim at integrating ideal biological parameters whilst also considering clinical evidence-based practices; cost-effectiveness should not be overlooked either so accessibility is ensured.

One significant obstacle that we must confront is the inadequate exploration of newer bone grafting materials' safety and effectiveness [31]. Most data on these advancements arise from case studies or animal experiments, thus making their reliability questionable. Standardized preclinical and clinical investigations need to be conducted with more comprehensive documentation before introducing products into the market to grasp each material's clinical feasibility and benefits. This will help us understand every component better for commercial availability purposes.

Conclusions

Dental procedures often require the use of bone graft and substitute materials to regenerate missing hard tissue structures. However, there is a growing need for more efficient options that go beyond just serving as structural frameworks for osteo-regenerative processes. Current non-autograft-derived materials also face potential issues related to graft versus host responses. Recent advancements in tissue engineering have led to innovations, such as ceramic and polymeric-based substitutes integrated with growth factors or living cells capable of inducing bone regeneration. These innovations offer better control over structure and surface properties while enhancing interaction with other materials and the physiological environment. Despite promising developments, cost remains an important factor when considering these new technologies compared to existing implants, which only offer osteoconductivity criteria without additional benefits from hybridization, such as utilizing growth factors or living cells induced by biomaterials within porous structured units similar to natural bones during healing. This aspect requires further studies as it is still under development. Mechanical stability degradation rates need to match those found naturally, thereby refining dental implant outcomes effectively. Overall, there is an increase in compliance compared to financially equivalent competitors, which have shown improvements, proving the worth of adapting the aforementioned emerging trends. These trends reflect advanced care via biomimicry technology applications progressing continually into clinical practice, providing superior results compared to those offered previously.

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