Types of Synthetic Materials in Bone Grafts

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To decide which material is most appropriate for a given procedure, it is necessary not only to have a good understanding of the biological function (osteogenesis, osteoinduction, and osteoconduction) of each material but also to consider the patient condition, as this is an essential criterion for the incorporation of any bone graft. Bone grafts are evolving and undergoing innumerable changes and there has long been talk of synthetic bone grafts and bone substitutes to the detriment of autologous, allogeneic, or even xenogeneic grafts.

bone defects bone reconstruction bone graft

1. Types of Synthetic Materials

To decide which material is most appropriate for a given procedure, it is necessary not only to have a good understanding of the biological function (osteogenesis, osteoinduction, and osteoconduction) of each material but also to consider the patient condition, as this is an essential criterion for the incorporation of any bone graft. Bone grafts are evolving and undergoing innumerable changes and there has long been talk of synthetic bone grafts and bone substitutes to the detriment of autologous, allogeneic, or even xenogeneic grafts [1][2][3].

Bioactive cements are considered good alternative bone substitutes, due to their moldability, self-hardening, and osteoconductivity. However, although these biomaterials are already widely used, they still need to improve their mechanical properties [4]. Regarding synthetic bone grafts, scaffolds give mechanical support and serve as a substrate where osteoblastic or osteoprogenitor cells can adhere, proliferate, and differentiate for the formation of new bone. They can also be used as carriers for other materials, with the addition of growth factors or drugs, or mixed with other types of bone grafts to increase or improve bone formation [5][6][7][8]. The most studied biomaterials among synthetic bone grafts are cements based on calcium phosphate, calcium phosphate ceramics, calcium sulphate, bioactive glasses, and polymers [1][2][9][10][11][12][13][14][15].

2. Calcium Phosphate Cements

Calcium-phosphate-based materials have been used since the 1980s in the fields of dentistry and orthopaedics and are currently commercially available in a wide variety of compositions [16]. Calcium phosphate cements (CPCs) have several advantages, including being bioactive, allowing for large-scale manufacturing, easy handling, and injectability to adapt to irregularly shaped bone defects, in addition to not having the inherent risks of autogenous and allogeneic grafts, such as donor site morbidity and risk of infection. Furthermore, their biocompatibility and proximity to bone composition make CPCs good candidates for use in bone regeneration [17][18].

Among CPCs, there are two main groups: those of brushite that have a shorter hardening time and those of apatite that have a longer hardening time. Apatite is formed from tetracalcium phosphate (TTCP) or α-TCP, while brushite is a by-product of β-TCP or monocalcium phosphate monohydrate (MCPM). The difference between these two by-products derives from the fact that cements that form brushite absorb more water in their mixing and hardening reaction, while apatite absorbs little or no water. Brushite-based CPCs react and harden much faster than apatite CPCs; therefore, to satisfy the necessary clinical requirements of cement application during surgery, the setting time of CPCs materials based on brushite must be increased, while the setting time of apatite-based CPCs should be reduced [18]. Through absorbing more water, the cements that turn into brushite have less resistance to tension, compression, and shear [19][20].

3. Calcium Phosphate Ceramics

Ceramic materials based on calcium phosphate (CP) can be found in the form of granules or blocks with none or different porosities [21][22][23] and include HA, tricalcium phosphate (α-TCP and β-TCP), biphasic calcium phosphate (BCP), and amorphous calcium phosphate (ACP), among others [1][2][24].

3.1. Hydroxyapatite

Hydroxyapatite's ($Ca_{10}(PO_4)_6(OH)_2$) (HA's) composition has a great similarity with the mineral part of the bone and, for this reason, it has been widely documented for its ability to promote bone growth through its osteoconductive mechanism without causing local or systemic toxicity, inflammation, or undesirable immune reactions [23][24][25]. All these advantages make this material very useful in the area of bone repair in dentistry, such as in the treatment of periodontal defects, alveolar crest augmentation, and maxillary sinus elevation [25][26][27][28].

HA nanoparticles, with particle size smaller than 100 nm in at least one direction, have greater surface activity and an ultrafine structure, very similar to the mineral found in hard tissues, which stimulates their use in the area of bone regeneration. In addition to chemical similarities with the mineral phase of bone, they also have excellent biological properties [29][30][31].

Another advantage of this material, shown in several studies, would be its affinity with certain osteogenic and anti-resorptive molecules, which can be used to create reservoirs for growth factors, antibiotics, or medication to inhibit osteoclasts [5][32].

3.2. Tricalcium Phosphate

Beta-tricalcium phosphate (β-TCP) is sintered at a temperature lower than ~1125 °C and has the advantage of thermodynamic stability in a biological environment and being more resorbable than HA at room temperature.

Alpha-tricalcium phosphate has been gaining great attention in the area of biomaterials as a raw material, due to its properties such as injectability and biodegradation. This material remains stable when, after the sintering process, it is cooled to room temperature [33]. Despite having similar chemical composition, α and β TCP have considerable differences in their structure, density, and solubility, which determine their biological characteristics and specific clinical applications. Since α-TCP is more soluble and reactive than β-TCP, its ultrafine powder is the mostly used in the preparation of cements for bone repair, to improve the moldability and injectability of the cement [33].

3.3. Calcium Sulphate

Calcium sulphate hemihydrate ($CaSO_4 \cdot 1/2H_2O$), also known as plaster of Paris, has been used since the mid-1920s as a bone filler. The dissolution properties of this material have been used in the study and development of carrier materials for molecules that improve bone quantity or quality or as a carrier for drugs such as antibiotics [24].

3.4. Bioactive Glasses

Bioactive glasses (BGs) are a group of synthetic materials based on silica, calcium, and disodium oxide. As calcium and silicate ions are progressively released from the material, they interact with surrounding cells and thus have properties that allow it to bind to bone [34]. They have unique properties when compared to other ceramics such as HA and TCP, namely, the formation of an amorphous layer on their surface where proteins, collagen, fibrin, and growth factors connect. This surface contributes to the bone reconstruction process, as it is chemically and structurally equivalent to the bone mineralization phase [34]. Depending on their chemical composition, BGs differ in their bioactivity and resorption. In vivo, this material showed good osteoconductivity and appears to promote new bone growth on its surface, demonstrating a balance between intramedullary bone formation and material resorption [10][35]. Some studies demonstrate little or no inflammatory reaction, foreign body reaction, or fibrous encapsulation of the material when bioactive glasses are used [34][36]. Due to their osteoconductive properties, composition, and in vitro and in vivo results, BGs have been a group of constant study for use as a bone substitute [34][36].

3.5. Polymers

Studies involving polymers are based on the search for materials that can support and maintain space for the period necessary for the formation of new bone and, after this period, can be degraded and eliminated by the host organism [37]. The most studied materials currently are polymers based on glycolic acid and lactic acid, also known as PLGA and PLA, respectively. These polymers can be easily degraded by the organism, but the lack of mechanical resistance, as well as their low osteoconductivity, make this material unsuitable to be used alone as a scaffold [38]. Its degradability is a great advantage and, therefore, this material has been incorporated into CPC- or BG-based materials, with the aim of improving the handling of these materials as well as injectability [18][37]. These polymers have also been used to improve the osteogenic properties of other materials, in addition to being extensively studied as carriers of molecules, such as growth factors or drugs [39].

In **Table 1** examples of trademarks, composition, and mechanisms of action described by manufacturers of synthetic materials used as bone grafts.

Table 1. Trademarks, composition, and mechanisms of action described by manufacturers.

Trademarks	Composition	Mechanisms of Action Described by Manufacturers	Reference
BonePlast®	Calcium Sulphate with/without HA granules	Osteoconductive; Resorbable	[40]
Conduit™	100% β-TCP	Osteoconductive; Resorbable	[41]
OpteMx™	HA/TCP biphasic	Osteoconductive; Resorbable; Osteogenic and osteoinductive when mixed with medullary bone	[5]
Integra Mozaik™	80% β-TCP, 20% collagen type I	Osteoconductive; Resorbable	[42]
MasterGraft™	Biphasic Calcium Phosphate (15% HA, 85% β-TCP)	Osteoconductive; Resorbable	[43]
NovaBone®	Bioactive silicate	Osteoconductive; Resorbable	[44]
Vitoss®	100% β-TCP/80% β-TCP + 20% collagen/70% β-TCP, 20% collagen, 10% bioactive glass	Osteoconductive; Resorbable; Osteogenic and osteoconductive when mixed with medullary bone	[45]
Calceon® 6	Calcium sulphate	Osteoconductive; Resorbable	[41]
Norian® SRS®	Calcium Phosphate	Osteoconductive; Resorbable	[46]
MIIG X3	Calcium sulphate	Osteoconductive; Resorbable	[47]
Osteoset®	Calcium sulphate	Osteoconductive; Resorbable	[48]
Pro Dense™	75% calcium sulphate, 25% calcium phosphate	Osteoconductive; Resorbable	[49]
Pro-STIM™	50% calcium sulphate, 10% calcium phosphate, 40% demineralized bovine bone	Osteoconductive; Resorbable; osteoinductive	[50]
CopiOS® Bone	Biphasic calcium phosphate and collagen type 1	Osteoconductive; Resorbable; Osteogenic and limited osteoinductive when mixed with medullary bone	[51]
Cerasorb®	100% β-TCP	Resorbable	[52]
Straumann Bone Ceramic®	Biphasic calcium phosphate (60% HA/40 β-TCP)	Osteoconductive; Able toinduce vascularization and osteoblast migration	[45]
EasyGraft™ crystal	Biphasic calcium phosphate (60% HA/40 β-TCP)	Resorbable; Osteoregenerative	[53]
EasyGraft™ classic	Pure β-TCP phase (>99%)	Resorbable; Osteoregenerative	[54]

Trademarks	Composition	Mechanisms of Action Described by Manufacturers	Reference
ENGIpore®	Synthetic HA	Osteoconductive	[55]
Apaceram®	Synthetic HA	Osteoconductive	[56]
Ostim®	Pure HA phase	Osteoconductive; Resorbable	[57]
Ceros® TCP	100% β-TCP	Osteoconductive; Resorbable	[58]
Calciresorb®	96% β-TCP, 4% HA	Osteoconductive; Resorbable	[59]
Fisiograft®	HA and polyethylene glycol (PEG)	Partially resorbable	[60]

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