BOR DERGİSİ
JOURNAL OF BORON
Journal homepage: www.journal.boren.gov.tr

Boron-substituted bioceramics: A review

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ARTICLE INFO

Artlice history:
Received 8 February 2016
Received in revised form 27 February 2016
Accepted 27 February 2016
Available online 24 March 2016

Keywords:
Boron,
Ion-Substitution,
Hydroxyapatite,
Calcium Phosphate,
Bioglass

ABSTRACT

Biomaterials can be designed by imitating and taking inspiration from the forms and compositions of natural tissues. The inorganic component of the hard tissues; bone, dentin and enamel, is hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) containing various trace elements that are important in biochemical reactions of bone metabolism. Boron is considered as an essential element for human physiology and it has many biologic effects especially on hard tissues. As it is in the natural hard tissues, substitution of boron into the structure of hydroxyapatite or other bioceramics, such as calcium phosphates and bioglasses, could enhance angiogenesis and osteogenesis of the damaged tissue. This review covers briefly the recent and very recent works on preparing numerous bioceramic, bioglass and glass-ceramic systems containing boron.

1. Introduction

The definition of the term biomaterial is “a substance that has been engineered to take a form which, alone or as part of a complex system, is used to direct, by control of interactions with components of living systems, the course of any therapeutic or diagnostic procedure, in human or veterinary medicine” [1]. Biomaterials can be divided into different groups according to their structural, chemical, and biological characteristics. They are classified as ceramics, glasses, metals, polymers and composites likewise to the general material classification. In addition, biopolymers, self-assembled systems, nanoparticles, carbon nanotubes and quantum dots are also the parts of the biomaterial family.

Bioceramics are the group of biomaterials that are used for the repair and reconstruction of diseased or damaged parts of the musculoskeletal system. They can be bioinert (alumina, zirconia), resorbable (tricalcium phosphate (TCP)), bioactive (hydroxyapatite (HA), bioactive glasses, and glass-ceramics), or porous for tissue ingrowth (HA-coated metals, alumina) [2]. Bioactive ceramics are capable of direct bonding to living tissues without causing the formation of a fibrous tissue layer at the interface. In contrast, bioinert ceramics are biologically inactive and have no ability to bond to the surrounding living tissue; therefore they are mostly encapsulated by a fibrous tissue with variable thickness. Consequently, bioactive bioceramics are more suitable when new bone tissue growth and mechanical support are needed. Resorbable bioceramics are preferred for filling in gaps to be replaced by normal bone.

The composition and features of various bioceramics are given in Table 1. Calcium phosphate (CaP) family, especially HA, is the main member of bioceramics that can be used for repair of bone defects, e.g. for joint or tissue replacement, applied as coatings for metal implants to improve biocompatibility of the surface, and function as a resorbable temporary framework. They can also find use in drug delivery systems.

The most widely used CaP compounds in medical area are HA and TCP. All CaPs have different characteristics. For example, monocalcium phosphate monohydrate (MCPM) is the most acidic and the most soluble at almost all pH values, dicalcium phosphate (DCP) is the most stable at low pH, tetracalcium phos-

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phate (TetCP) is the most soluble below a pH of 5 and the most basic, and HA is the most stable in aqueous solutions and the most biocompatible one in the CaP family [5].

The history of the use of CaPs in healthcare starts in 20th century. TCP was first applied *in vivo* by Albee and Morrison in 1920 [6]. It was in 1952 that Ray et al. [7] implanted HA in rats and guinea pigs to compare synthetic HA with fresh autogenous and frozen bone in filling various skeletal defects. HA has been used as a bioactive and biocompatible coating material on metallic implants since the publication of first clinical results by Furlong and Osborn in 1991 [8]. Calcium phosphate cement (CPC), which sets to HA when moistened, was first formulated by Brown and Chow [9] in 1985 and this water setting cement was a new form of CaPs for the treatment of bone defects especially in craniofacial and maxillofacial areas.

The reason why HA is widely used in dental and orthopedic areas today is that it is biocompatible, bioactive and osteoconductive since it naturally constitutes the inorganic composition of human hard tissues in carbonated form. Compared to TCP, HA is a more stable phase under the physiological conditions, has a lower solubility and accordingly a slower resorption [10]. Since it forms the mineralized extracellular component of bone, it provides the necessary strength and rigidity. Without HA phase, bone would be mainly composed of collagen and exhibit high ductility and elasticity but very low brittleness and stiffness. The mineral phase of bone also is a storage site of metals in the blood that circulates to the skeleton. In other words, it is a metal reservoir which acts as the repository of body burdens [11].

HA is one of the group of minerals with most common chemical formula of $Ca_5(PO_4)_3(F,OH,Cl)$ which are

Table 1. Compositions and features of various bioceramics [3,4]

	Name	Ca/P	Formula	Feature/Application/Shape
Ca/P Family	MCPA monocalcium phosphate anhydrous	0.50	$Ca(HPO_4)_2$	Soluble in water
	MCPM monocalcium phosphate monohydrate	0.50	$Ca(HPO_4)_2•H_2O$	Soluble in water; cement powder
	DCPD dicalcium phosphate dehydrate	1.00	$CaHPO_4•2H_2O$	Cement powder
	DCPA dicalcium phosphate anhydrous	1.00	$CaHPO_4$	Cement powder
	OCP octacalcium phosphate	1.33	$Ca_8H_2(PO_4)_6•5H_2O$	Transient intermediate phase; reaction product in cement setting; powder
	ACP amorphous calcium phosphate	1.50	—	Amorphous; transient intermediate phase; powder
	β-TCP tricalcium phosphate	1.50	$Ca_3(PO_4)_2$	Resorbable; sintered body (dense and porous), powder
	α-TCP tricalcium phosphate	1.50	$Ca_3(PO_4)_2$	Cement powder
	Calcium deficient HA	1.50–1.67		Low or moderately crystalline; decomposes above approx. 700°C; low crystalline material is resorbable
	HA hydroxyapatite	1.67	$Ca_5(PO_4)_3OH$	Low to highly crystalline; sintered body (dense or porous), powder,coating,composite,fiber; low crystalline material is resorbable; highly crystalline material is nonresorbable and osteoconductive
	TeCP tetracalcium phosphate	2.00	$Ca_4(PO_4)_2O$	Cement powder
Others	Y-TZP yttria-stabilized tetragonal zirconia		Y_2O_3-ZrO_2	Sintered body (dense)
	Aluminum oxide (alumina)		Al_2O_3	Sintered body (dense)
	Titanium oxide (titania)		TiO_2	Sintered body (dense)
	Silicon nitride		Si_3N_4	Sintered body (dense)
	Silicon carbide		SiC	Sintered body (dense)
	Carbon		C	Fiber
	Bioactive glasses system		SiO_2-P_2O_5-Na_2O-CaO	Bulk
			SiO_2-P_2O_5-Na_2O-K_2O-CaO-MgO	Bulk
			SiO_2-P_2O_5-CaO-Al_2O_3	Bulk
	Bioactive glass-ceramics system		SiO_2-P_2O_5-CaO-MgO Apatite-Wollastonite (A-W)	Bulk
			SiO_2-P_2O_5-Na_2O-K_2O-CaO-MgO (Ceravital)	Fiber

called apatites [12]. More generally, the term apatite includes a large class of minerals and synthetic compounds represented by $M_{10}(AO_4)_6X_2$. M is most often an alkaline earth ion, the tetrahedral group is generally (PO_4) and X is usually a hydroxide, halide, oxide or sulfide ion [13].

The channel site in the HA structure is occupied by OH^-, but when the other substituting ions F^- or Cl^- fully occupies this site the apatite becomes fluorapatite and chlorapatite, respectively. Apatite is more prone to accept chemical substitutions compared to most other minerals. Ion substitutions affect the structure of apatites and change their mineral properties, such as solubility, hardness, brittleness, strain, thermal stability, and optical properties [14].

In addition, anions, such as AsO_4^{3-}, SO_4^{2-}, CO_3^{2-}, SiO_4^{4-} can replace PO_4^{3-}, and many cations, such as K^+, Na^+, Mn^{2+}, Ni^{2+}, Cu^{2+}, Co^{2+}, Zn^{2+}, Sr^{2+}, Ba^{2+}, Pb^{2+}, Cd^{2+}, Y^{3+}, and trivalent ions of rare-earth elements can substitute for Ca^{2+} (usually in trace concentrations) [14]. Therefore, it is possible to design and develop advanced HA biomaterials for certain specific applications with the use of the ability to exchange various ions in this structure [15].

Boron is one of the dopant elements that attract the attention of biomaterial scientists due to its natural functions in human hard tissues. This paper aims to review the recent studies on substitution of boron into the structure of bioceramics with a main focus on calcium phosphates. From the studies in the literature, it can be said that current research on boron doping into the structure of bioceramics has shown some promises of enhancing the service characteristics of these biomaterials.

2. Boron and hard tissues

Boron (B, atomic number 5) is the first element in Group IIIA and the only nonmetal in the family. It exhibits the bonding and structural characteristics of both metals and nonmetals. In nature, boron does not occur in its elemental form [16]. It reacts with oxygen to form boric acid (H_3BO_3). Boron occurs naturally in the form of borates, such as borax, which are the salts or esters of boric acid and they are the compounds that contain or supply boric oxide (B_2O_3).

The Babylonians were believed to use borax for working gold over 4000 years ago and Egyptians were thought to use for mummifying, medicinal and other metallurgic applications. However, the first use of tinkar (i.e., $Na_2B_4O_7.10H_2O$, the mineral borax) dates back to the 8th century around Mecca and Medina, and it was brought there (and to China) by Arab traders. The use of borax by European goldsmiths dates to about the 12th century. [17]. The element boron was first isolated by Joseph Louis Gay-Lussac, Louis Jacques Thênard, and Humphry Davy separately in 1808 [18]. Currently, boron is largely produced in Turkey and the USA, and is used in a wide range of products, including glass, detergents, fire retardants, fibers to reinforce plane fuselages and body armor, and superhard materials [19].

The history of boron in biological systems is relatively recent and starts with its acceptance as an essential nutrient for plants. Boron was considered as necessary to complete the life cycle of plants after the reports by Warington in 1923 and Sommer and Lipman in 1926. It is now known as a constant constituent of foods of plant origin due to its structural role in plant cell walls [20]. Boron is also accepted as an essential trace element to human health, mainly for wound healing functions and bone health [21].

Boron has many biological effects, such as (1) actions on reproduction and embryogenesis, (2) improvement of wound healing and response to injury or infection, (3) modifications of calcium and bone metabolisms (4) beneficial effects on central nervous function, (5) effects on the presence or function of vitamin D and hormones, including thyroid hormone, insulin, estrogen and progesterone [20, 22]. It is known to interact with calcium, vitamin D and magnesium, all of which play a role in bone metabolism [23]. At the molecular level, it was reported that boron enhances RNA transcription in the isolated placental nuclei and stimulates mRNA translation, especially those encoding growth factors involved in angiogenesis and wound repair [22].

The accumulation of boron in bone is significantly greater than those found in blood or soft tissues and the concentrations depend on the intake [24, 25]. Boron level in human bone tissue of one individual is 0.90 ppm [25]. Although no estimated average requirement or adequate intake levels have been determined for boron, based on animal data, the tolerable upper intake level is set for an adult at 20 mg/day [26]. In a study where the subjects were instructed to take daily either a 3 mg/day boron supplement or a placebo, it was shown that even this amount of dietary boron intake can cause a slight increase in bone mineral density [27].

A boron-deficient diet (0 vs 3 mg/kg) leads to decreased weight gain, femur strength, and femur concentrations of the minerals associated with the organic matrix: copper, iron and magnesium in rats. In addition, the vertebral microarchitecture was also altered by boron supplementation, in such a way that trabecular thickness of boron-supplemented rats was found to be greater than that of boron-deficient rats [28]. Another study on the effect of boron on the concentrations of mineral elements associated with the bone organic matrix noted that the amount of zinc and potassium in tibia was increased by boron supplementation [29].

One study reports the altered periodontal alveolar bone modeling and remodeling due to an inhibition of bone formation in mice that were treated with a boron-deficient diet (0.07 vs 3 mg/kg diet for nine weeks) [30]. Another study revealed that boron supplementation (50 mg/kg body weight B in 96 h) resulted in significantly increased bone mineral density, maximum breaking force of femur and compression strength of tibia in rabbits fed with a high energy diet [31]. Boron intake (3 mg/kg daily for 40 days) was reported to have a positive effect on bone regeneration of the midpalatal suture in response to expansion in rabbits [32]. Boron supplementation in long-term diet as 5 mg sodium borate/kg was noted to increase the serum osteocalcin concentrations in gilts which can be assumed as a measure of increased osteoblast activity or bone remodeling [33].

In addition, *in vitro* cell studies showed that boron is a dose-dependent regulator on the osteoblastic cells. Hakki et al. [34] performed cell viability tests on pre-osteoblastic cells (MC3T3-E1) with different concentrations of boron in the cell culture media. It was shown that addition of boron at a concentration of 1000 ng/ml or above decreased cell survival rate in short time period (at 24 h), while there was no statistically significant difference in different boron concentrations when compared to untreated control group in long term. They also observed remarkable regulation in favor of osteoblastic function for collagen type I, osteopontin, bone sialoprotein, osteocalcin and Runx2 mRNA expressions in B-treated groups. The levels of bone morphogenic proteins (BMPs) were increased at 0.1, 1, 10 and 100 ng/ml B concentrations. Similarly, the proliferation and osteogenic differentiation of MC3T3-E1 cells was shown to be affected by the release of boron from a chitosan scaffold with boric acid-doped chitosan nanoparticles (diameter of approx. 175 nm) by Gümüşderelioğlu et al. [35]. The alkaline phosphatase (ALP) activity, which is the early stage marker of osteogenic differentiation, was shown to increase on scaffolds containing boron encapsulated nanoparticles.

3. Boron-substituted calcium phosphates

Based on the knowledge that boron has many physiological effects beneficial to bone growth and maintenance, it has been applied as a dopant element in CaPs. Anions, such as borate, may replace negatively charged PO_4^{3-} groups and/or OH^- sites in the HA lattice and this affects physicochemical, biological, functional, and surface features of HA and in turn its performance as a biomaterial. The electrostatic interactions and chemical bonding between the biomaterial and body proteins and solubility of substituted apatite would also be affected.

B-substituted HA particles were synthesized by the wet chemical processing method and a subsequent thermal treatment was applied at the temperature ranging from 700-1200°C by Hayakawa et al. [36]. Nuclear magnetic resonance (NMR) studies showed that no B atom was incorporated into HA lattice structure by this method without heat-treatment. When a heat-treatment above 900°C was applied to the particles, a chemical reaction took place resulting in the formation of B-substituted HA particles accompanied by the formation of β-TCP phase which transforms to α-TCP at 1200°C. The Ca/P ratio of 0.4 wt% B containing HA was 1.60 before and after being heat-treated, which means B-substituted HA was calcium-deficient compared with stoichiometric HA (Ca/P=1.67).

Barheine et al. [37] also used NMR to investigate the structural model of borate containing CaP prepared by a high-temperature solid state reaction sintering process. The material consisted of HA and a disordered borate containing CaP phase. The crystalline HA did not accommodate the borate groups and all borate units were located in CaP. The various BO_3^{3-} units were shown to be randomly distributed in the phosphate network of CaP phase.

On the other hand, borate groups, such as BO_3^{3-} and BO_2^-, were shown to partially substitute both PO_4^{3-} and OH^- sites in HA [38]. A borohydroxyapatite (BHA) with nominal stoichiometry $Ca_{10}[(PO_4)_{6-x}(BO_3)_x][(BO_3)_y(BO_2)_z(OH)_{2-3y-z}]$ was proposed by Ternane et al. [38]. When P/B ratio = 7.22, borate groups are introduced the apatitic lattice. This suggested that borate group can enter into the HA lattice with an amount dependent manner. This substitution leads to a decrease in lattice parameter *a* (when x=0, *a*=9.4180*Å* and x=1, a=9.3760*Å*) and increase lattice parameter *c* (when x=0, *c*=6.8840Å and x=1, c=6.9122*Å*). It was also shown that when the amount of boron is increased to a concentration over P/B ratio = 7.22, this yields secondary phases as $Ca_3(BO_3)_2$ and CaO. Similarly, Barheine et al. [39] prepared BHA by a high-temperature solid-state reaction processing method. They also reported that the lattice parameter *a* decreased, while the lattice parameter *c* and unit cell volume increased with the increasing B content. The length of *a*-axis was reported as 9.406Å in HA and 9.389Å in phase pure BHA (analyzed P/B ratio=6.10). The length of *c*-axis was 6.882Å in HA and 6.927Å in phase pure BHA.

In another study of Ternane et al. [13], the assignments for infrared (IR) and Raman spectra of a pure oxyboroapatite were provided. Table 2 summarizes the bands in the IR and Raman spectra of oxyboroapatites. The previously reported assignments for the BHA were also for both triangular BO_3 groups and linear BO_2 groups. The bands at 1304, 1253, 1208 and 784, 771, 755 cm^{-1} were attributed to the antisymmetric stretching v_3 and the symmetric bending v_2 modes of the BO_3^{3-} groups. The weak peaks at 2002 cm^{-1} and 1932 cm^{-1} were at-

tributed to the antisymmetric stretching v_3 mode of the BO_2^- groups, respectively [38]. However, Güler et al. [41] did not detect BO_2 substitution in the IR analyses of BHA which was synthesized by the solid-state reaction of colemanite as a primary reactant for both Ca and B source. The amount of B was found as 0.195 mol by using a spectrometric method. Therefore, they concluded that since only BO_3 group replaced partially with the PO_4 groups, the assigned chemical formula could be as $Ca_{10}[(PO_4)_{5.80}(BO_3)_{0.20}](OH)_2$.

Table 2. Infrared and Raman band wave numbers and assignments for oxyboroapatite [13,40].

Assignment	IR (cm^{-1})	Raman (cm^{-1})
$v_3(BO_2^-)$	2002, 1932	
$v_3(BO_3^{3-})$	1304, 1250-1252, 1208	
$v_3(PO_4^{3-})$	1090, 1050, 1044	1076, 1049, 1030
$v_1(PO_4^{3-})$	962	962
$v_1(BO_3^{3-})$		912
$v_2(BO_3^{3-})$	784, 772, 755	
$v_4(PO_4^{3-})$	671, 602, 570	608, 593, 581
$v_2(PO_4^{3-})$	472	448,431

Not only the structure, but the morphology, optical properties and dielectric properties of the BHA are also dependent on the amount of B-doped into the lattice. The change in size, UV shielding properties and dielectric constant with the amount of dopant element in BHA, which was produced by using sol-gel method, were studied by AlHammad [42]. It was stated that absorbance and reflectance of BHA increased gradually while the dielectric constant decreased with increasing boron concentration.

The structural and mechanical changes of the biphasic mixture of B-doped HA (BHA) and β-TCP of varying BHA/β-TCP ratios after sintering at variable temperatures of 1000, 1100 or 1200 °C for 2 h has previously been studied [43]. The amount of β-TCP in the needle-like nano-size biphasic mixture was reported to increase with the increasing amount of boron in the precipitation stage or increasing the sintering temperature. B-doping was shown to increase the decomposition of HA into β-TCP. However, as the boron content increases, the sinterability, density and microhardness of the B-doped mixture decreased.

As stated before, the substitution of borate groups occurs on PO_4 and OH sites, predominately the first. Therefore, it is also possible to co-dope the ions of other elements together with B, especially cations which can be replaced with Ca^{2+}, into the HA lattice without creating a competition between boron and other dopant element. The cations, such as Eu^{3+} [44] and Ce^{3+} [45], were previously doped into BHA separately to change the luminescent properties of BHA.

From the bioengineering point of view, concepts such as biocompatibility and bioactivity, are equal or more important than the structure and physico-chemical properties of a material, thus they need to be deeply investigated. Çiftçi et al. [46] examined the adhesion, proliferation and differentiation of B-substituted nano HA with human bone marrow derived mesenchymal stem cells (MSCs). They reported that the adhesion and proliferation rates of MSCs were higher than controls while adipogenic and osteogenic differentiation potential remained unchanged.

In addition to using B as a dopant element into HA or various other CaP-based systems, it is also possible to design composites that include both bioceramics and boron compounds. There are recent studies on B-containing composites. Ali et al. [47] used boron nitride nanotubes (BNNTs) as a reinforcement additive for HA and β-TCP. Atila et al. [48] prepared composites consisting of nano-sized hexagonal boron nitride (hBN) and HA. They reported that implantation of these composites to rats resulted in statistically increased serum B levels experimental groups compared to healthy group.

4. Other boron-substituted bioceramics

In addition to the use of B as a dopant or component in the composites consisting of the CaPs, it also finds use in other bioceramics, especially glasses. Concerning the borophosphate compounds, glasses were investigated more widely. The physico-chemical properties of calcium borophosphate glasses, with the composition of $(1\text{-}x)Ca(PO_3)_2\text{–}x(B_2O_3)$ where x=B/B+P ≤6, are previously studied [49]. The presence of BO_4 was observed to increase the glass transition and crystallization temperatures, density and microhardness, while it decreased the solubility in water and the cut-off wavelength in the UV region.

A more complex system with other substitutions was proposed as $(50\text{-}x)P_2O_5\text{–}20CaO\text{–}20SrO\text{–}10Na_2O\text{–}x$ B_2O_3 with x = 0, 1.25, 2.5, 3.75 and 5 mol% B_2O_3 [50]. An increase in B_2O_3 led to an increase in the density, the refractive index and glass transition temperature and a decrease in the molar volume. Small amounts of B_2O_3 reduced the glass dissolution rate but the presence of B_2O_3 only slightly affected the dissolution rate of the glass at high concentrations.

HA and borophosphate glasses were previously combined to form a ternary system with the formula of $(1\text{-}X)((NaPO_3(x/(1\text{-}x))Na_2B_4O_7))XCa_5(PO_4)_3OH$ where x is the molar fraction of $Na_2B_4O_7$ in the binary system and X is molar amount of HA [51]. The changes in physical and chemical properties were investigated in terms of addition of HA rather than considering boron as the main effector. When HA-free system was compared with the ternary system, HA was considered to improve most of the physical and chemical properties of the boron containing glass system, such as microhardness and water resistance.

Another glassy state borophosphate was prepared with selenium (Se) in different %mol SeO_2 amounts to form $xSeO_2(100-x)(48P_2O_5–50CaO–2B_2O_3)$ system [52]. The Se ions replaced dominantly with the B units. The electronic density of the bonding state of the B, P and O atoms was shown to be modified by SeO_2 content. Copper (Cu) is another element which is studied in combination with B-containing bioceramics. In order to take the advantage of the angiogenic characteristic of Cu, B-containing bioactive glass-based scaffolds [53] and borosilicate glasses [54] were enriched with Cu.

The changes in the physical and chemical characteristics of bioglasses by the addition of certain ions influence the *in vitro* and *in vivo* properties. Haro Durand et al. [55] investigated the *in vitro* angiogenic effects of the ionic dissolution products (IDPs) from 2 wt% B_2O_3 doped 45S5 bioglass (BG) system (SiO_2–CaO–Na_2O–P_2O_5). It was reported that the IDPs from B-doped BG stimulated the proliferation and migration of human umbilical vein endothelial cell (HUVEC). In addition, *in vitro* HUVEC tubule formation and secretion of interleukin 6 (IL6) and the basic fibroblast growth factor (bFGF) was enhanced. It was noted that the controlled and localized release of boron ions from BGs could stimulate angiogenesis and osteogenesis. A more recent study [56] showed that the ionic dissolution products released from the B-doped BGs stimulate angiogenesis also *in vivo*.

Unlike 45S5 glasses, the borate and phosphate glasses dissolve uniformly and borate glass reacts much faster than the 45S5 silicate glasses, when they are soaked in a phosphate rich solution to form HA [57]. A borophosphate glass with the mol% composition as $25Na_2O–25CaO–5P_2O_3–45B_2O_5$ started to form HA in four days in this solution. It was faster when compared to the osteoconductive $NaCaPO_4$ (rhenanite) crystal phase [58]. In another study, B-containing bioglass-based scaffold coated with degradable poly($_{D,L}$-lactic acid) were tested in simulated body fluid (SBF). The test showed that a HA layer was deposited on uncoated and coated scaffolds again on four days of immersion [59]. The degradation rate is another important factor together with the rate at which the bioactive glass converts to HA. It is also related with rate at which the degradation products are released. As an example, the amount of B released from a borate-based bioactive glass scaffold into a phosphate solution was reported to increase rapidly during the first 24 h, reaching a value equal to ~20% of the boron content of the starting material after an immersion time of 360 h [60]. This rate is important in the early cellular response to the high concentration of degradation products.

A new calciumsilicate borate ($Ca_{11}(SiO_4)_4(BO_3)_2$) ceramic was recently prepared by using a conventional solid-state reaction [61]. As stated before, CaO–SiO_2 based glass materials are already known to exhibit bioactivity. Similar to above mentioned studies, when BO_3 groups were added into the lattice, a greater *in vitro* HA-forming ability was obtained in SBF. This is attributable to the released BO^{3-} ions which could improve the supersaturation of the SBF and enhance the nucleation of HA.

The scaffolding materials for bone tissue engineering should be osteoconductive. Mesoporous bioactive glass serves a greater surface area and allows osteoblast adhesion, proliferation, and differentiation due to its structure. By using a boron-containing mesoporous bioactive glass scaffold as a dexamethasone drug-delivery system, Wu et al. [62] obtained a controllable release of boron ions. The scaffold significantly improved the proliferation of primary osteoblasts and expression of bone-relative genes Collagen I and Runx2.

5. Concluding remarks

This paper aimed to provide a brief overview about the biological approach to the use of boron element. The data reviewed here provides evidence of the increasing interest with recent advances in substitution of boron into the structure of ceramic, glassy or combined biomaterial systems due to its close relationship with the hard tissues. These boron containing materials can be used in any application like their un-doped forms, such as bone substitutions, implant coatings or components, dental materials and drug delivery vehicles. However, the physicochemical properties, e.g. structure, composition, dissolution rate, density, crystallinity, hardness, strength etc., would be changed depending on the amount of boron and this in turn affect the biological response especially biocompatibility and bioactivity of the resulting material. It is also possible to combine the known angiogenetic and osteogenetic properties of boron with the various properties of functional ions of other elements, such as anti-bacterial and anti-cancer and/or growth factors and drugs.

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