Dentin as bone graft substitution

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Abstract

Nowadays, bone grafting is required increasingly in oral surgery works, particularly in implant dentistry. The ideal bone substitutes should have comparable compositions and characteristics with bone being replaced, no immunological response, and osteopromotive property. The article summarized the physico-chemical compositions and biological properties of dentin as bone graft substitution. Briefly, dentin shares similarity with bone as they both are composed of calcium phosphate based mineral, collagen, and growth factor proteins, which enhance new bone formation as the osteoinductibility. Microstructural characteristics of dentin represent dense collagen fibers as networks suggesting the osteoconductibility. In vitro and in vivo studies, as well as, clinical applications showed consistent results in biocompatibility and osteopromotive properties of dentin used as bone graft substitutes. From the literatures, dentin has the potential to be used as a bone substitute and should be further developed to obtain optimal preparation process and to apply for clinical uses as a new cost-effective bone graft materials.

Keywords: *Bone graft substitution, dentine, material*

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Bone and bone graft properties

Bone is the rigid tissues that constitute part of the skeleton of human body. It supports the body and stores mineral that needed for the metabolic functions. Bones are composed of an organic matrix which is strengthened by deposits of calcium phosphate crystals. The organic matrix is composed of type I collagen (approximately 95%) and of proteoglycans and numerous non-collagenous proteins (5%).[1]

Bone grafting is a procedure to prepare or repair insufficient bony sites to become acceptable bone support for dental prostheses particularly for dental implant. Bone graft substitutes can be classified into four majorities based on donor or origin of materials: autografts, allografts, xenografts, and synthetic materials. Osteogenesis, osteoinduction and osteoconduction are the required properties for bone regeneration and repairing process. To date, autogenous graft, which has all three osteopromotive properties, is considered as the gold standard for bone grafting.

Similarity between bone and tooth
Morphology and microstructure

Both bone and tooth are hard tissue in the body. During developmental period, alveolar bone as well as dental tissues including enamel, dentin, cementum, pulp, and periodontal ligament are also derived from the neural crest cells. (Figure 1)

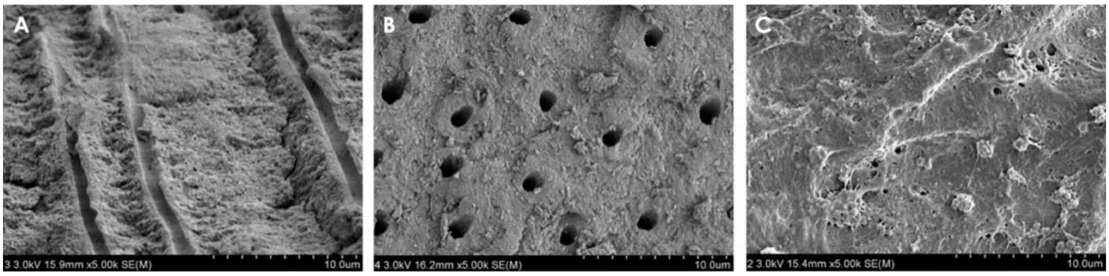

Figure 1 The SEM views of A, crown of the tooth (x5000); B, root of the tooth (x5000); C, cortical bone (x5000) (From Kim YK, et al., 2014)[5]

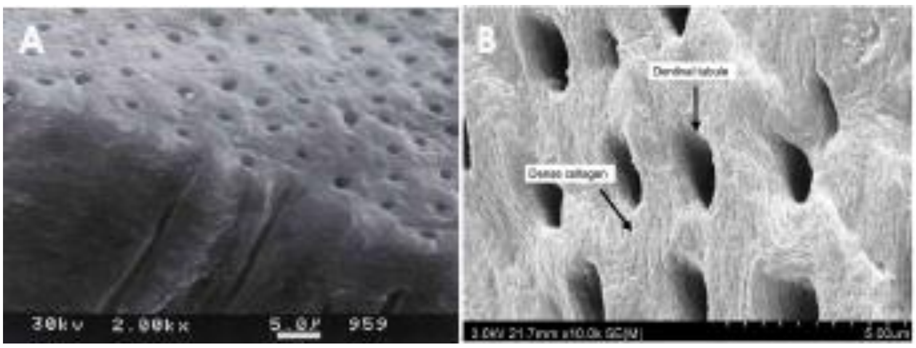

Figure 2 The SEM view of A, mineralized dentin (x1000) showing tubules, peritubular zone, and intertubular matrix (From Marshall GW, 1993)[2]; B, demineralized dentin surface (x10,000) (From Kim YK, et al., 2009)[6]

While bone is constructed by multiple Harversian's systems, dentin built up as a complex hydrated composite of 4 elements: 1) oriented tubular 2) a high mineralized peritubular zone embedded in an intertubular matrix 3) type I collagen with embedded apatite crystals, and 4) dentinal fluid (Figure 2A).[2] When dentin is demineralized (Figure 2), the dentinal tubule would become wider and expose dense collagen fibers as network and channel for releasing essential growth factors.[3,4]

Composition

Dentin, a part of tooth, is almost similar in chemical component with bone. Mature dentin components are by weight 70% mineralized inorganic material, 20% organic material, and 10% water, whereas those of the alveolar bone are 60%, 25%, and 15% respectively.[7]

Physicochemical properties

The major component of the inorganic
compartment contains 4 types of the calcium phosphate including hydroxyapatite (HA), beta-tricalcium phosphate (beta-TCP), amorphous calcium phosphate (ACP), and octacalcium phosphate (OCP).[8] The presenting of inorganic part is responsible to thephysicochemical and strength of the tissues. The Ca/P molar ratio was studied to determine the phase of calcium phosphate apatites in tooth or dentin,[9] whereas the X-ray diffraction (XRD) analysis was used to evaluate crystallinity degree. The Scanning Electron Microscopic studies were performed to examine the surface characteristics of the processed dentin as well. As shown in Table 1, the studies regarding physicochemical properties of dentin prepared as a bone substitute were summarized. Similarity in the physicochemical properties suggested that dentin could be a promising scaffold material in bone substitution.

Osteo-inductive property

The bone formation potential or osteo-inductivity of the dentin was also observed in several studies. Generally, during osseous tissue repair, growth and differentiation factors not only may be produced by the local cells but also can be released from the mineralized matrix. Then, the released growth factors by resorption process of osteoclasts exert their functions on local cells.[14] Type I collagen constitutes approximately 90% of the dentin organic matrix, while the remaining as non-collagenous proteins include small amount of growth factors such as endogenous bone morphogenetic protein(BMP), phosphoproteins, osteocalcin, proteoglycans, dentin sialo-phosphoprotein. Therefore, dentin after the decalcification could be defined as a composite matrix of type I collagen and growth factors.[15]

Bone morphogenetic protein (BMP), extracted from bone and dentin, plays an important role in bone formation. As the osteoinduction requires signaling and activation by growth factors, to date, at least 20 members of the Bone morphogenticprotein (BMP) family have been identified. BMP-2 and BMP-7 provide the most promising results for the enhancement of bone repair.[13,14] They are the only signaling molecules which can induce de novo bone formation at orthotopic and heterotopic sites and their osteoinductive potency makes them clinically valuable as alternatives to bone graft.[16]

Sialophosphoprotein plays a primary role in the formation and growth of hydroxyapatite (HA) crystals in an extracellular matrix of hard tissue such as bone and teeth. Mineralization inducing peptides (MIPs) within Dentin sialophosphoprotein (DSPP) were reported to support the human bone marrow stromal cell (hBMSC) differentiation into osteoblastic cells as well as HA nucleation activity.[17]

In vivo study and clinical application

Several animal studies demonstrated the potential of dentin in different preparation forms used as bone grafts substitutes as summarized in Table 2. The results were consistent in yielding or promoting new bone formation. Furthermore,

Table 1 Previous physicochemicalstudies of dentin as bone graft substitute.[2-4,8-13]

Methods	Determined characteristics	Results
Scanning electron microscopy (SEM)	Surface topography	Demineralized autogenous tooth[3,4,8-10] • Many dentinal tubuleswith diameters of the dentinal holes approximately 1-2 µm. • Dense collagen matrix, exposed in the vicinity of the dentinal tubules, observed as a network for diffusing nutrient after grafting. • Relatively similar density, roughness, and homogeneity of autogenoustooth to those of autogenous cortical bones.[10] • Dentinal tubules were exposed thoroughly and loosening fiber bundles of intertubular and peritubular dentins, provided channels for releasing proteins and factors from the dentin matrix.[3,4]
Energy dispersive spectroscopy (EDS)	C/P ratio (phase separation)	Demineralized autogenous tooth[9] • The total tooth were the range of 1.24-1.46. - Tricalcium phosphate (TCP) and octa- calcium phosphate (OCP) • Crown portion was 1.75. - Hydroxyapatite (HA) • Root portion was 1.32. - Amorphous calcium phosphate (ACP)

X-ray diffraction (XRD)	Crystallinity	Demineralized autogenous tooth[8-10] • The level of HA crystallization in AutoBT and the amount of HA differed greatly depending on the tooth area; higher value in crown than in root portion.[8,9] • Autogenous tooth dentin, allogeneic bone, and autogenous cortical bone suggesting similar low crystalline HA structures[10] and possibly other calcium phosphate minerals.[8,9]

Table 2 In vitro and in vivo studies of dentin as bone substitution.[13,15,18-24]

Authors/Year	**Dentine preparation forms**	**Results**
Gomez et al. 2002[19]	Demineralized dentin matrix (ADDM)	• ADDM slices showed osteoconductive properties. • Resorbed during the bone remodeling process. • Accelerated bone repair process
Moharamzadeh et al. 2008[18]	Non-demineralized dentin (Processed boiled dentin)	• Excellent biocompatibility in vitro • Stimulated formation of new bone, completely incorporated into the new bone in vivo
Yagihashi et al. 2009[20]	Demineralized dentin matrix (DDM)	• DDM acts as a scaffold for osteochondral regeneration • Yielding active new bone formation early in the postoperative period.
Murata et al. 2010[24]	Human demineralized dentin matrix (DDM) Human demineralized root dentin (DRD)	• Human recycled DDM and DRD might be effective materials as osteoinductive collagenous carriers of BMP-2 for bone engineering
Murata et al. 2012[15]	Human demineralized dentin matrix (DDM)	• Human DDM should be an effective carrier for delivering BMP-2 and superior scaffold for bone-forming cells.
Bormann et al. 2012[22]	Fresh perforated autogenous dentine slices	• Neovascularization response • Osteointegration with new bone
Atiya et al. 2012[23]	Liquid nitrogen- treated calcified autogenous dentin	• Accelerating bone regeneration in bone defects in a manner similar to that of autogenous bone grafts

Reis-Filho et al. 2012[21]		• Accelerates the bone healing, by stimulating bone deposition and neovascularization
de Oliveira et al. 2013[13]	Demineralized human dentin matrix (DHDM)	• DHDM acted as a scaffold for osteoblast differentiation • Actively yielding new bone formation

Table 3 Clinical studies and case report of using autogenous dentin as bone substitution.[8,25-29]

Authors/Year	Clinical uses	Results
Kim et al. 2010[8]	Implant placement	• Gradual resorption. • Replaced by new bone of excellent quality through osteoinduction and osteoconduct-ion.
Kim et al. 2011[27] (case report)	Combined with tooth auotransplantation	• Increased initial stability of the transplanted tooth • Reasonably considered for facilitating reattachment by the osteoinduction and osteoconduction properties of autogenous tooth-bone graft material
Jeong et al. 2011[25]	Maxillary sinus augmentation	• Gradual resorption • New bone formation through osteoconduc-tion and osteoinduction
Park et al. 2012[26]	Implant placement with simultaneous GB (with or without membrane)	• Significant bone gain in vertical bone defect sites regardless in use of membranes
Chang et al. 2014[29] (case report)	Guided Bone Regeneration(GBR) followed by implant placement and prosthetic restoration	• No significant marginal bone loss differences were noted radiographically at immediately after GBR, implant placement and prosthesis delivery

there are some case reports and clinical studies using autogenous dentin as bone grafting materials. Table 3 represents some clinical studies provided in these recent years. From the literatures mentioned above, dentin, apparently, has the potential to be used as a bone substitute in bone repair and regeneration despite the differences in preparation processes. Further researches including precise preparation methods and the clinical application should be performed in order to develop new biomaterial using in bone substitution.

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การใช้เนื้อฟันเป็นสารทดแทนกระดูก

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บทคัดย่อ

ปัจจุบันการปลูกถ่ายกระดูกเป็นสิ่งจำเป็นมากขึ้นในงานผ่าตัดในช่องปากโดยเฉพาะอย่างยิ่งในทางทันตกรรมรากเทียม สารทดแทนกระดูกที่เหมาะควรมีองค์ประกอบและลักษณะเทียบเคียงกับกระดูกที่ถูกแทนที่โดยไม่มีการตอบสนองทางภูมิคุ้มกันและมีการกระตุ้นการสร้างกระดูกบทความนี้ทำการสรุปองค์ประกอบทางกายภาพและสมบัติทางเคมีและชีวภาพของเนื้อฟันสำหรับใช้เป็นสารปลูกกระดูกทดแทน เนื้อฟันมีความคล้ายกับกระดูกโดยที่ทั้งสองจะประกอบด้วยแร่ธาตุแคลเซียมฟอสเฟต คอลลาเจนและสารประกอบโปรตีนซึ่งเป็นปัจจัยที่เพิ่มการสร้างกระดูกใหม่เป็น ลักษณะของเนื้อฟันทางจุลภาคแทนเส้นใยคอลลาเจนหนาแน่นเป็นโครงสร้างตาข่ายการศึกษาทั้งในห้องปฏิบัติการและในการศึกษาทางคลินิกแสดงให้เห็นผลที่สอดคล้องกันในกันในทางชีวภาพ จากการทบทวนวรรณกรรมพบว่าเนื้อฟันมีศักยภาพที่สามารถจะนำมาใช้แทนกระดูกและควรได้รับการพัฒนาต่อไป

คำสำคัญ: เนื้อฟัน, สารทดแทนกระดูก

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**ภาควิชาศัลยศาสตร์ช่องปากและแมกซิโลเฟเชียล คณะทันตแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์