DENTAL MATERIALS 30 (2014) e362–e370

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.intl.elsevierhealth.com/journals/dema

Development of calcium phosphate/sulfate biphasic cement for vital pulp therapy

Kai-Chun Chang[a,1], *Chia-Chieh Chang*[a], *Wei-Tang Chen*[b], *Chung-King Hsu*[b], *Feng-Huei Lin*[c], *Chun-Pin Lin*[a,d,*]

[a] *Graduate Institute of Clinical Dentistry, School of Dentistry, National Taiwan University, No. 1, Chang-De St., Jhong-Jheng District, Taipei City 100, Taiwan, ROC*

[b] *Institute of Materials Science and Engineering, National Taipei University of Technology, No. 1, Sec. 3 Chung-Hsiao E. Rd., Da-an District, Taipei City 106, Taiwan, ROC*

[c] *Institute of Biomedical Engineering, National Taiwan University, No. 1, Sec. 1, Ren-Ai Rd., Jhong-Jheng District, Taipei City 100, Taiwan, ROC*

[d] *National Taiwan University Hospital, National Taiwan University, No. 1, Chang-De St., Taipei City 100, Taiwan, ROC*

ARTICLE INFO

Article history:
Received 19 April 2014
Received in revised form
28 July 2014
Accepted 8 August 2014

Keywords:
Calcium phosphate cement (CPC)
α-Calcium sulfate hemihydrate (CSH)
Biphasic cement
Vital pulp therapy (VPT)
Mechanical property
Cytotoxicity

ABSTRACT

Objectives. Bioactive calcium phosphate cement (CPC) has been used widely to repair bone defects because of its excellent biocompatibility and bioactivity. However, the poor handling properties, low initial mechanical strength, and long setting time of CPC limit its application in vital pulp therapy (VPT). The aim of this study was to synthesize biphasic calcium phosphate/sulfate cements and evaluate the feasibility of applying these cements in VPT.

Methods. The physical, chemical, and mechanical properties of CPC were improved by mixing the cement with various amounts of α-calcium sulfate hemihydrate (CSH). The hydration products and crystalline phases of the materials were characterized using scanning electron microscopy and X-ray diffraction analysis. In addition, the physical properties, such as the setting time, compressive strength, viscosity, and pH were determined. Water-soluble tetrazolium salt-1 and lactase dehydrogenase were used to evaluate cell viability and cytotoxicity.

Results. The developed CPC (CPC/CSH cement), which contains 50 wt% CSH cement, exhibited no obvious temperature increase or pH change during setting when it was used as a paste. The initial setting time of the CPC/CSH biphasic cement was substantially shorter than that of CPC, and the initial mechanical strength was 23.7 ± 5.6 MPa. The CPC/CSH cement exhibited higher viscosity than CPC and, thus, featured acceptable handling

* *Corresponding author at*: National Taiwan University Hospital, National Taiwan University, No. 1, Chang-De St., Taipei City 100, Taiwan, ROC. Tel.: +886 2 3123456x62148; fax: +886 2 3831346.
E-mail addresses: d96422005@ntu.edu.tw (K.-C. Chang), pinlin@ntu.edu.tw (C.-P. Lin).
[1] Tel.: +886 2 3123456x81456; fax: +886 2 23940049.

http://dx.doi.org/10.1016/j.dental.2014.08.368

properties. X-ray diffraction analysis revealed that the relative peak intensity for hydroxyapatite increased, and the intensity for calcium sulfate dehydrate decreased as the amount of CPC was increased. The cell viability and cytotoxicity test results indicated that the CPC/CSH cement did not harm dental pulp cells.

Significance. The developed CPC/CSH biphasic cement exhibits substantial potential for application in VPT.

1. Introduction

Vital pulp therapy (VPT), including direct and indirect pulp capping and partial pulpotomy, in which material is placed directly over exposed pulp tissue, can be administered to maintain the vitality of exposed pulp and to promote pulp healing and generate reparative dentin [1]. A study suggested using numerous materials in VPT [2]. Calcium hydroxide has been considered the standard direct pulp capping material for several decades [3]. However, calcium hydroxide is highly soluble and is subject to dissolution over time [4]. In addition, calcium hydroxide has no inherent adhesive qualities and provides poor sealing; thus, it cannot prevent long-term microleakage [5,6]. Mineral trioxide aggregate (MTA) has recently been used as a VPT material. MTA has exhibited excellent biocompatibility, sealing ability, antibacterial properties, mechanical strength, and radiopacity, and can induce the release of bioactive dentin matrix proteins [7,8]. In addition, MTA promotes the formation of a dentin bridge barrier and causes little or no inflammation at the pulp exposure site [9]. However, the long setting time (approximately 165 min), sandy consistency, and low viscosity limit the application of MTA in VPT [2,10,11].

An ideal material for VPT features high biocompatibility, nontoxicity to pulp tissue, antibacterial properties, acceptable sealing ability, relative stability in the oral cavity, adequate mechanical strength, a short setting time, and excellent handling properties [2]. Although numerous materials have been developed, none of them have fulfilled these clinical demands.

Although MTA have been widely used for root canal therapy, its inconvenient handling properties due to prolong self-hardening time evoke the needs of other material to be developed. Calcium phosphate cement (CPC) has been widely used as a bone substitute in orthopedics, reconstructive surgery and dentistry since it can stimulate osteogenesis [12,13]. Final product of CPC after setting is hydroxyapatite (HAp), which is the primary mineral component in dentin and facilitates earlier formation of the dentin bridge barrier after it is placed on the exposure site [14]. Furthermore, CPC exhibits high biocompatibility and a self-hardening characteristic; thus, it owns potential properties in develop as an endodontic filling material [15,16] or sealer and to treat periodontal bone defects [17–19]. So far, some properties, such as initial mechanical weakness, and long setting time (over 60 mins), which can cause a severe inflammatory response, limit its application in vital pulp therapy (VPT) [20–22]. The aim of this study was to synthesize biphasic calcium phosphate/sulfate cements and evaluate the feasibility of applying these cements in VPT. We would like to develop a new CPC which own a promising applications in dentistry not only its biocompatibility, a mineralizing ability equivalent to that of MTA [23–25] but also its good handling property.

Since CPC has now been widely used in orthopedics and dentistry for decades, usually sets rapidly [26,27], in order to shorten the setting time and improve the handling properties of CPC, we try to mix CPC with various weight ratios of α-calcium sulfate hemihydrate (CSH; $CaSO_4{\cdot}1/2H_2O$). The major components of CPC been used in this study were tetracalcium phosphate (TTCP, $Ca_4(PO_4)_2O$) and dicalcium phosphate anhydrous (DCPA, $CaHPO_4$). These materials can be solidified through an in situ reaction with water to form HAp [28]. After the biphasic calcium phosphate/sulfate cement is mixed with water, it becomes a paste before it sets completely; thus, it features favorable handling properties.

In this study, we determined that varying the weight ratios of CSH in biphasic calcium phosphate/sulfate cements significantly affected the physical and mechanical properties of the cement, and an in vitro study was conducted using human dental pulp cells (HDPCs) as a cell source to evaluate the cell viability and cytotoxicity of the developed biphasic cements.

2. Materials and methods

2.1. *Preparation of calcium phosphate/sulphate cements*

All reagents used in this study were purchased from Sigma–Aldrich Co. (St. Louis, MO, USA). TTCP ($Ca_4[PO_4]_2O$) powder was prepared through a solid-state reaction in which 1 mol of calcium pyrophosphate ($Ca_2P_2O_7$, 401552) and 2 mol of calcium carbonate ($CaCO_3$, C6763) were heated to 1400 °C for 3 h. The product was quenched to room temperature, ground in a mortar, and sieved to obtain TTCP powder, which was mixed with a DCPA ($CaHPO_4$, C7263) powder in a molar concentration equal to that of the CPC.

Five cements were prepared by mixing CPC and CSH ($CaSO_4{\cdot}1/2H_2O$, 12090) at weight ratios of 0%, 25%, 50%, 75%, and 100% (CPC, 3CPC/CSH, CPC/CSH, CPC/3CSH, and CSH). Deionized (DI) water was added to obtain CPC-CSH biphasic cement. The liquid-to-powder ratio (L/P) for all cements was 0.35 mL/g. The mixture was turned into paste, placed into a stainless steel mold with a diameter of 12 mm and a height of 6 mm, and dried in air for 10 min. The specimens were removed from the mold and stored in a sealed container with