Novel Bioactive Zinc Phosphate Dental Cement with Low Irritation and Enhanced Microhardness

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Wide range of cements used in dentistry for cementation of dental restorations to tooth structure. The properties of dental cements should be carefully considered during their selection for achievement of long-term clinical performance of cemented dental restorations. Conventional zinc phosphate cement and other types of dental cements except polycarboxylate and glass-ionomer depend on their retention to tooth structure upon mechanical bonding. Bioactive glasses have shown a talented result in minerals regeneration. Therefore, the aim of this article is to create bioactivate zinc phosphate dental cement by incorporation of nano-sized bioglass. A total of 20 specimens; 10 specimens per type of cement were prepared. The control group was made by mixing the conventional zinc phosphate dental cement. The other group was made by addition of 5 wt% nano-sized bioactive glass powders (45S5) to the conventional zinc phosphate dental cement. The fresh mix packed into cylindrical Teflon molds and then stored in deionized water for 7 days. The pH variations were measured immediately after immersion and after 7 days storage using pH meter. Calcium and phosphorus ion release were measured using inductively coupled plasma optical emission spectroscopy. It also evaluated the surface microhardness of the experimental cements using digital Vickers hardness tester. Regarding pH changes mean values, the bioglass contained zinc phosphate cement group showed significantly higher mean pH values than control group. As regards the bioglass contained zinc phosphate cement group; there was a significant increase in mean pH values after setting as well as after 7 days storage. While in control group, there was a significant decrease in mean pH values after setting followed by a significant increase in mean pH values after 7 days storage. Regarding calcium and phosphorus ions release mean values, the bioglass contained zinc phosphate cement group showed significantly higher mean values than the other control group. Regarding surface microhardness, the bioglass contained zinc phosphate cement group showed significantly higher mean surface microhardness values than control group. In conclusion, bioactivation of conventional zinc phosphate cement by addition of nano-sized bioglass filler leads to calcium and phosphorus ions release which may be beneficial for chemical bonding to tooth structure with enhanced surface microhardness and minimal irritating effect. [DOI: 10.1380/ejssnt.2018.431]

Keywords: Zinc phosphate; Dental cement; Bioactive glass; Ions release

I. INTRODUCTION

Many types of dental cements are available now in market, each with its own merits, though, the main dental cements in current use are zinc phosphate, polycarboxylate, glass-ionomer and resin composite [1]. Zinc phosphate cement is the oldest widely used dental cements; it is commonly used as permanent luting cement for metallic restorations, base materials and provisional restoration [2]. Its high compressive strength, its ability to create a thin film mix, its slight setting shrinkage and its suitable working time are of great impact to clinical use. However its low initial pH, may cause pulpal irritation immediately at the first hours after their application due to rapid drop in pH which increased gradually by time, especially when used under thin layer of remaining protective dentin layer [2, 3].

Conventional zinc phosphate cement, as well as all other types of dental cements except polycarboxylate and glass-ionomer depends in their retention mechanism to tooth structure upon micro-mechanical bonding [3]. A careful selection of the dental cement should be done for each application to fit their specific demands. Since no only one type of cement could perform adequately under all circumstances, thus the need for continuous development of dental cement. Zinc phosphate dental cemented restorations had a minimum risk of failure compared to other cements such as glass ionomer or resin-modified glass ionomer [4]. Recently, bioactive materials have been introduced in many fields of dentistry to take advantage of their ability to precipitate calcium phosphate in their environment [5].

Bioactive glasses are group of surface-active ceramics, in which minerals can bind to strongly. The basic constituents of bioactive glasses are sodium dioxide, calcium oxide, phosphorus and silica. By changing all of these constituents, different forms of bioactive glasses can be achieved. The original bioglass 45S5 composition is soda-lime-phosphosilicate (Na2O-CaO-P2O5-SiO2) glass. Within all bioceramics, 45S5 Bioglass has the highest bioactivity index (Class A) which display an actively interaction with tissues by promoting repair and regeneration besides bonding to tissue. Bioactive glasses studies have shown a promising result in minerals bone regeneration [6]. The mechanism of the high bioactivity of bioglass could be described as the follows; leaching out of ions from the glass to form carbonated calcium deficient hydroxyl apatite, which binds to the collagen of the tissue. Moreover the leached ions regulate genes that encode growth factors and stimulate the secretion of bone matrix
The term bioactive material appears first by Hench et al. to describe the interfacial bond developed between the calcium silico-phosphate glass (bioactive glass) and host tissue, due to the unique surface reactivity of bioactive glasses [8]. Nowadays there are a new paradigm in bioactivity concept, it expand to comprise the ability of a bioactive material to contribute calcium and phosphate ions to help rebuild demineralized dental tissues [7, 9]. Previous investigations have suggested that incorporation of bioactive glass into conventional and resin-modified glass ionomer enhance mineral formation [10, 11].

Nanomaterial has become gorgeous because of their unique properties that completely differ than conventional bulk materials [12]. Nanotechnology offers new dental materials with enhanced properties. Currently, there is a trend for the development of nano-sized dental materials that have a bioactive function, in addition to their inherent properties [13]. Bioglass has been used in orthopedics and dentistry in many applications such as bone repair, implants coating and as a scaffolds for bone repair [6, 7]. Bioglass have a proven excellent ability for apatite formation. Therefore, recent investigations have considered bioglass as one of the most suggested materials for remineralization of hard dental tissues [7]. Therefore, the aim of this study is to bioactivate the conventional zinc phosphate dental cement by incorporation of nano-sized bioglass. The null hypothesis was that the incorporation of nano-sized bioglass into conventional zinc phosphate cement has no significant effect on the pH, calcium and phosphorus ions release and surface microhardness compared to conventional zinc phosphate cement.

### II. EXPERIMENTAL

#### A. Materials

A total of 20 specimens: 10 specimens per type of cement were prepared. The control group was prepared by mixing the conventional zinc phosphate dental cement. The intervention group was prepared by incorporating bioactive glass powders into the conventional zinc phosphate cement powders. Conventional zinc phosphate cement (Adhesor, Pentron, Spofa Dental, Czech Republic) was used in this study. Materials used in the current study are listed in Table I. Materials used in the current study are listed in Table I.

#### B. Methods

The novel cement was prepared by adding 5 wt% nano-sized bioactive glass powders (45S5 bioactive glass with an average crystal seizing 28 nm prepared by sol gel method [14], The lab of Inorganic Chemistry at Suez Canal University, Egypt) to 2.3 g conventional zinc phosphate cement powder, then the powders were mixed on a cooled glass slab to 0.5 mL cement liquid with a metal spatula. Following mixing, fresh pastes were packed into cylindrical Teflon mold (6 mm diameter and 12 mm height). The specimens removed from the mold and immersed in 8 cm$^3$ deionized water which was used as a storage solution [15], then stored in an incubator (CBM 2431/V, Italy) at 37°C for 7 days [15-17].

1. **pH changes**

The pH of the storage solution was measured immediately after specimens’ immersion using pH-meter (Jenway 3510 bench pH-meter, UK). After 7 days of storage, the changes in the pH of storage solution were measured again. The baseline pH value for deionized water was measured.

2. **Calcium and phosphorus ions release**

After 7 days incubation, calcium and phosphorus ions of the previous storage solution were measured in mg/L to determine the concentrations of ions using inductively coupled plasma optical emission spectroscopy (ICP-OES) (Ultima 2 ICP, Horiba, USA).

3. **Surface microhardness**

The specimens were then blotted dry and subjected to surface microhardness measurements using Digital Vickers hardness tester (NEXUS 400TM, INNOVATEST, model no. 4503, Netherland). The indentations were made within 20 s from the loading 200 g at 40× magnification for all specimens. Three measurements were made for each sample.

#### C. Statistical analysis

Sample size calculation was done using alpha ($\alpha$) level of 0.05 (5%) and beta ($\beta$) level of...
TABLE II. The mean, standard deviation (SD) values and results of repeated measures ANOVA test for comparison between pH changes of the different interactions.

| Time         | Intervention | Control | P-value (between groups) |
|--------------|--------------|---------|--------------------------|
|              | Mean    | SD     | Mean    | SD     | (between groups) |
| Base line    | 5.60C   | 0      | 5.60B   | 0      | NC**             |
| After setting| 5.67B   | 0.05   | 5.43C   | 0.05   | < 0.001*         |
| 7 days       | 6.61A   | 0.11   | 6.36A   | 0.08   | < 0.001*         |
| P-value (between times) | < 0.001* |         | < 0.001* |

* Significant at \( P \leq 0.05 \).
** Not computed because the variable is constant. Different superscripts in the same column are statistically significantly different.

![Line chart representing changes over time in the mean pH values within each group after 7 days immersion in deionized water.](image)

0.2 (20%), i.e., power = 80%, performed using IBM® SPSS® SamplePower® Release 3.0.1 for Windows (SPSS Inc., IBM Corporation; USA), \( n = 10 \) specimens/group in each test. Numerical data were explored for normality by checking the distribution of data and using tests of normality (Kolmogorov-Smirnov and Shapiro-Wilk tests). All data showed normal (parametric) distribution. Data were presented as mean and standard deviation (SD) values.

Repeated measures Analysis of Variance (ANOVA) was used to study the effect of group, time and their interaction on mean pH. Bonferroni’s post-hoc test was used for pair-wise comparisons when ANOVA test is significant. Student’s t-test was used to compare between calcium and phosphorus ions release in the two groups as well as to compare between surface microhardness of the two groups. The significance level was set at \( P \leq 0.05 \). All statistical analysis was performed with IBM® SPSS® Statistics Version 20 for Windows (SPSS Inc., IBM Corporation; USA).

III. RESULTS AND DISCUSSION

The pH values of dental cement are an essential physical feature, which is associated with pulp response [10]. Dental pulp is subjected to variation in the extracellular pH under different environments [18]. The low initial pH of some dental cement may lead pulp insult with subsequent post-cementation teeth sensitivity and thus limitation of their use [19]. The increase in calcium and phosphorus ions release and microhardness suggest enhancement of mechanical and chemical properties of the dental cements by improvement in mineral precipitation [20].

The percentage of 5 wt% nano-sized bioactive glass filler loading represent the maximum filler loading that leads to workable coherent non-friable mass by the trial. Calcium and phosphorus ion release reflect the primary step of apatite deposition which is considered as the preliminary signal for bioactivity [4, 21].

A. pH changes

Regarding pH changes values of the deionized water alone were approximately 5.6 (the baseline). Repeated measures ANOVA results showed that group, time and the interaction between the three variables had a significant effect as shown in Table II and Fig. 1. At base line (deionized water alone); pH was constant in the two groups so no comparison was performed. After setting as well as after 7 days storage, the intervention group showed significantly higher mean pH values than control group. Moreover, the intervention group showed a significant increase in mean pH values after setting as well as after 7 days storage. While in control group, there was a significant decrease in mean pH values immediately after setting followed by a significant increase in mean pH after 7 days storage. This may be contributed to the addition of bioglass increased calcium and phosphorus ion release; this could be due to the bioglass composition which comprise calcium and phosphorus with alkaline properties [11] which may counteract the acidic nature of the unreacted phosphoric acid component of the zinc phosphate cement. In addition, the calcium and phosphorus ions concentration increased by time up 7 days which might be due to the more dissolution of bioglass by effect of time [11]. While the initial significant decrease in mean pH values in control group may be attributed to the acidity of the unreacted phosphoric acid component of the zinc phosphate cement [22]. The significant increase in pH values in control group by time may be due to rapid reaction of phosphoric acid with zinc oxide powder during setting [23]. The changes in pH measurement in this study were in agreement with observations of Cerruti et al. in which the presence of glass 45S5 particles leads to rapid increase in pH took place in the solution immediately [24].
FIG. 2. Bar chart representing the mean calcium and phosphorus ion release concentration values after 7 days of specimen immersion in deionized water.

FIG. 3. Bar chart representing the mean Vickers microhardness values of the groups.

B. Calcium and phosphorus ions release

Calcium and phosphorus ions release was measured after 7 days of samples immersion in deionized water as the calcium and phosphorus ion release rate from the bioglass became stable over 7 days [25]. Moreover, the in vitro bioactivity and remineralization could be observed after 7 days [26]. Regarding calcium and phosphorus ions release, the intervention group showed significantly higher mean calcium and phosphorus ions release values than control group as shown in Table III and Fig. 2. This may be contributed to release of calcium and phosphorus ions from bioactive glass [20].

TABLE III. The mean, standard deviation (SD) values and results of Student’s t-test for comparison between calcium and phosphorus ions release in the two groups.

|          | Intervention | Control | P-value |
|----------|--------------|---------|---------|
| Calcium  | Mean: 4.35 SD: 0.27 | Mean: 2.02 SD: 0.06 | < 0.001* |
| Phosphorus| Mean: 11.35 SD: 0.66 | Mean: 1.59 SD: 0.09 | < 0.001* |

* Significant at $P \leq 0.05$.

FIG. 4. Representative image of indentation determination of Vickers microhardness test.

C. Surface microhardness

Regarding surface microhardness, the intervention group showed significantly higher means surface microhardness values than control group as shown in Table IV and Figs. 3 and 4. This may be due to the reinforcement effect of the incorporated nano-sized bioglass filler into cement and their close interaction and homogenous distribution within the zinc phosphates matrix [26–28].

Conventional micro-sized bioglass has a great ability to bond chemically with the surrounding tissues when they implanted within it due to their atomic structure, as it dissolves gradually in tissue fluids leading to calcium and phosphorus ions release which in turn promote the growth of a carbonated hydroxyapatite layer along the tooth restoration interface. This dissolution mechanism is enhanced by the presence of sodium and calcium [29]. Although recent studies incorporated nano-bioactive glass to some dental restorations which increased their bioactivity [30], no previous researches attempted to bio-activate the dental zinc phosphate cement.

The creation of novel bioactive dental cement is seen as a convenient way to develop tightly seals and strong chemical bonds between dental restorations and teeth to act as a “monoblock” which considered as a revolution in dental bonding field to avoid the possible leakage between teeth and dental restoration which may lead to recurrent caries and teeth hypersensitivity. Moreover, the decreased acidity of cement protects the teeth from the possible post-cementation teeth hypersensitivity [19, 29].

TABLE IV. The mean, standard deviation (SD) values and results of Student’s t-test for comparison between surface microhardness of the two groups.

|          | Intervention | Control | P-value |
|----------|--------------|---------|---------|
| Calcium  | Mean: 154.60 SD: 7.28 | Mean: 108.80 SD: 3.88 | < 0.001* |
| Phosphorus| Mean: 11.35 SD: 0.66 | Mean: 1.59 SD: 0.09 | < 0.001* |

* Significant at $P \leq 0.05$. 

434 J-Stage: https://www.jstage.jst.go.jp/browse/ejssnt/
The uniqueness of incorporated nano-bioglass fillers into conventional zinc phosphate cement to create bioactive dental cement may be come from the greater bioactivity of the nano-bioglass fillers than the conventional micro-sized, mainly due to their nano-size that leads to a higher surface area and thus more contacting surface between the material and the physiological fluid in tooth. Thus, higher dissolution and ions release rate and faster formation of apatite layer. In addition to their nanometric size allows easily adaptation and shaping of material into teeth [29].

The benefits of nanotechnology in the synthesis of bioglass affect positively their properties leading to improve-into teeth [15]. Higher dissolution and ions release rate and faster bioactivity of the nano-bioglass fillers than the conventional applications.

The null hypothesis of the present study was rejected, as this study showed that the incorporation of nano-sized bioglass particles into conventional zinc phosphate dental cement renders the bioactive properties.

IV. CONCLUSION

Bioactivation of conventional zinc phosphate cement by addition of nano-sized bioglass filler leads to calcium and phosphorus ions release which may be beneficial for chemical bonding to tooth structure with enhanced surface microhardness and minimal irritating effect.

[1] G. J. P. Fleming, R. M. Shelton, G. Landini, and P. M. Marquis, Dent. Mater. 17, 14 (2001).
[2] J. S. Sivakumar, B. N. Suresh Kumar, and P. V. Shyama, J. Pharm. Bioall. Sci. 5, 120 (2013).
[3] Y. Liu and H.-Y. Yu, Med. Hypotheses 73, 257 (2009).
[4] A. Durán, A. Conde, A. G. Coedo, T. Dorado, C. García, and S. Ceré, J. Mater. Chem. 14, 2282 (2004).
[5] A. R. Prabhakar, J. Paul M, and N. Basappa, Int. J. Clin. Pediatr. Dent. 3, 69 (2010).
[6] T. A. van Vught, J. A. P. Geurts, J. J. Arts, and N. C. Lindfors, in: Management of Periapical Joint Infections (PJs) (Elsevier, Woodhead Publishing, 2017) Chap. 3.
[7] D. Fernando, N. Attik, N. Pradelle-Plasse, P. Jackson, B. Grossgogeat, and P. Colon, Mater. Sci. Eng. C 76, 1369 (2017).
[8] L. L. Hench, J. Mater. Sci.: Mater. Med. 17, 967 (2006).
[9] T. M. Hamdy, EC Dent. Sci. 16, 52 (2017).
[10] E. Luczaj-Cepowicz, G. Marczuk-Kolada, M. Pawinska, M. Obidzinska, and A. Holownia, Folia Histochem. Cyto- biol. 55, 86 (2017).
[11] V. Krishnan and T. Lakshmi, J. Adv. Pharm. Technol. Res. 4, 78 (2013).
[12] M. El-Hofy, M. G. El-Roby, and M. Elkhatib, Adv. Nat. Sci.: Nanosci. Nanotechnol. 6, 035018 (2015).
[13] T. M. Hamdy, EC Dent. Sci. 15, 151 (2017).
[14] W. Xia and J. Chang, Mater. Lett. 61, 3251 (2007).
[15] S. de Fátima Carvalho Souza, D. N. de Souza, A. de Fátima V. Pereira, L. P. Barroso, and A. C. Bombana, J. Contemp. Dent. Pract. 16, 36 (2015).
[16] A. R. Prabhakar, J. Paul M, and N. Basappa, Int. J. Clin. Pediatr. Dent. 3, 69 (2010).
[17] B. Czarnecka, H. Limanowska-Shaw, and J. W. Nicholson, J. Mater. Sci.: Mater. Med. 14, 601 (2003).
[18] Y. Hirose, M. Yamaguchi, S. Kawabata, M. Murakami, M. Nakashima, M. Gotoh, and T. Yamamoto, J. Endod. 42, 735 (2016).
[19] M. Almuhaiza, J. Contemp. Dent. Pract. 17, 331 (2016).
[20] G. F. Dias, A. C. R. Chibinski, F. A. dos Santos, V. Hass, F. B. T. Alves, and D. S. Wambier, Rev. Odontol. UNESP 45, 33 (2016).
[21] A. Vladescu, D. M. Vranceanu, S. Kulesza, A. N. Ivanov, M. Bramowicz, A. S. Fedonnikov, M. Braic, I. A. Norkin, A. Koptyug, M. O. Kurtukova, M. Dinu, I. Pana, M. A. Surmeneva, R. A. Surmenev, and C. M. Cotrut, Sci. Rep. 7, 16819 (2017).
[22] K. Ladha and M. Verma, J. Indian Prosthodont. Soc. 10, 79 (2010).
[23] N. Hiraishi, Y. Kitasako, T. Nikaïd, R. M. Foxton, J. Tagami, and S. Nomura, Int. Endod. J. 36, 622 (2003).
[24] M. G. Cerruti, D. Greenspan, and K. Powers, Biomaterials 26, 4903 (2005).
[25] L. A. Adams, E. R. Essien, A. T. Adeolu, and M. L. Julius, J. Sci.: Adv. Mater. Devices 2, 476 (2017).
[26] L.-C. Gerhardt and A. R. Boccaccini, Materials 3, 3867 (2010).
[27] L. Liverani, J. Lacina, J. A. Roether, E. Boccari, M. S. Killian, P. Schmuki, D. W. Schubert, and A. R. Boccaccini, Bioact. Mater. 3, 55 (2018).
[28] S. Heid, F. R. Stoessel, T. T. Tauböck, W. J. Stark, M. Zehnder, and M. Tenner, BMJ. Biomed. Glasses 2, 29 (2016).
[29] C. Vichery and J.-M. Nedelec, Materials 9, 288 (2016).
[30] H. Yu, M. Zheng, R. Chen, and H. Cheng, Oral Health Dent. Manag. 13, 54 (2014).