Sol-gel derived fluoride-doped bioactive glass powders: Structural and long-term fluoride release/pH analysis

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ABSTRACT

The study aimed to compare the fluoride release behavior of newly synthesized bioactive glass powders and its effect on the pH. The bioactive glass (BG) and three groups of fluoride-doped (2.5, 5 and 7.5 mol%) bioactive glasses (F-BG) powders were synthesized by a base-catalyzed sol-gel method. The prepared samples were heat-treated and were characterized by Fourier Transform Infrared Spectroscopy, X-ray Diffraction, Scanning Electron Microscopy, and Brunauer–Emmett–Teller (BET) surface area analyzer. The prepared heat-treated F-BG samples were amorphous in nature, except F-BAG with 2.5 mol% fluoride which was glass-ceramic with few characteristic peaks of fluorapatite and teracalcium phosphate phases. High surface area of these prepared powders were observed, however, it was decreased with the increase in fluoride contents and particle size. A 6 month long fluoride release behavior was studied periodically in deionized water using an Ion Selective Electrode. Fluoride release was maximum with F-BG (7.5% mol.%), however, the insignificant difference was observed among samples. Initially, high pH value was exhibited by all samples, where highest pH was observed with BG and least with F-BAG (5 mol%). The resulting F-BG (5% mol.%) has potential to be used in dentifrices, restorative materials and for other dental applications.

1. Introduction

Currently, there is an emerging trend of developing "smart" ion-releasing bioactive dental restorative materials with therapeutic effects to re-mineralize the demineralized dentin [1, 2]. Bioceramics such as amorphous calcium phosphate (CaP), hydroxyapatite (HA) and bioactive glass (BG) initially explored in the field of biomedical materials as synthetic bone grafting materials [3, 4]. Later they were found to be beneficial in cases of hypersensitive dentin [3, 5–7] and as a reinforcing agent in dental restorative materials [8–10] to minimize the incidence of secondary decay. Among these, BG has gained special attention not only in research but it is also under focus in clinical dentistry. Since fluoride is popular in dentistry for controlling tooth decay due to its anti-bacterial and re-mineralizing nature. It was believed that marrying the two into one may synergize the re-mineralizing and anti-microbial effects in fluoride-containing bioactive glasses (F-BGs) [11–13].

It is established that upon exposure to physiological fluids, ion exchange processes start at the interface between the surface of BG particles and the surrounding fluid resulting in the development of silica gel layer on the exterior of BG particles [14–16]. BG exhibits greater alkalinity (pH ≥ 9) in aqueous media, which can prove hazardous to the oral soft tissues [14]. To decrease alkalinity of the BG, various attempts were made to modify its composition. One such successful attempt was the addition of fluoride, which displayed buffering action to some extent by fluoride release in physiological solutions [17, 18]. The fluoride release of up to 20 ppm exhibits direct bactericidal action, however, with aging, the amount drops, therefore the direct bactericidal effect of fluoride is irrelevant clinically [19]. Enamel remineralization is directly proportional to the amount of fluoride ions release from restorative materials, thus, a composite releasing 200–300 μg/cm^2 fluoride over a 1-month period would completely inhibit recurrent caries [20].

Prof. Hench in 1969 first developed "Bioglass®" by a melt-quench route which displayed greater loss of CaF by reaction with humidity [21, 22]. Later sol-gel systems were utilized extensively to produce BGs with less crystallinity, greater porosity and surface area with improved bioactivity [12, 22–24]. F-BGs form less soluble crystalline fluorapatite, therefore, is of greater interest in dentistry. By increasing the CaF

content, improved network connectivity in BGs has been observed as fluorine is coordinated with calcium ions which may lower their chemical reactivity [12].

Previously, F-BGs were synthesized by a melt-quench derived method and reported seven day fluoride release in acetate-buffered MEM. It was found that low fluoride content bioactive glass formed fluorapatite well at low pH (i.e. < 6) [25]. In another week-long study, F-BG showed a linear proportionality between fluoride release and fluoride concentrations [18]. It is reported in fourteen days study that low fluoride content (i.e. 0.97 and 4.17 mol%) melt-derived BGs showed increased fluoride release upon aging, whereas, higher fluoride content BG showed less pronounced pH rise [21]. Still much work is needed to explore the potentials of fluoride-containing BGs specifically for the prolonged period of time.

The aim of the study was to measure and compare the amount of fluoride release from the experimental F-BG powders synthesized by co-precipitation method (i.e. sol-gel) and to evaluate the effect of various concentrations on pH for six months. The hypothesis was that the fluoride release rate of the experimental powders decreases upon aging; however, the pH of the conditioning bath remained constant and exhibit no relation to the amount of fluoride release.

2. Materials and methods

2.1. Materials

The analytical grade chemicals used in the synthesis of F-BGs included tetraethylorthosilicate [TEOS, $(Si(OC_2H_5)_4)$, Merck], calcium hydroxide [$Ca(OH)_2$, Acros Organics], ammonium hydroxide (NH_4OH, Merck), diammonium hydrogen phosphate [$(NH_4)_2HPO_4$, Sigma Aldrich], nitric acid (HNO_3, Analar), ethanol (99.08%, Analar) and sodium fluoride (NaF, Sigma Aldrich).

2.2. Synthesis of bioactive glasses

Three different types of F-BG samples with compositions (mol.%) $46SiO_2$: $28.5-xCaO$: $23Na_2O$: $2.5\ P_2O_5$: $xNaF$ (where $x = 2.5/5/\ 7.5$) were synthesized using various concentrations (2.5, 5 and 7.5 mol%) of fluoride through co-precipitation method. Initially, TEOS (23.0 mmol) was dissolved in 24 mL ethanol and pH of the solution was adjusted up to 1–2 by using 1.0 N HNO_3. Then $Ca(OH)_2$ (14.0 mmol) and NaOH (11.5 mmol) solution were mixed in TEOS solution. Later $(NH_4)_2HPO_4$ (1.25 mmol) was dissolved in 400 mL deionized water and pH was maintained at 11 using ammonia solution. The mixture of TEOS, Ca $(OH)_2$, NaOH, and NaF were added dropwise into this solution raising the final volume up to 600 mL. The final solution was stirred for 48 h. The prepared solution was filtered and washed with deionized water to neutralize the product and dried at 75 °C for 24 h and calcined at 600 °C for 6 h at the heating rate of 2 °C min⁻¹. The mole percentage of all components for the synthesis of BG and F-BGs is given in Table 1. The prepared BG samples with 2.5, 5, and 7.5 mol% of fluoride were labeled as F-BG 2.5, F-BG 5, and F-BG 7.5 respectively.

Table 1
Mole percentages of bioactive glasses and fluoride substituted bioactive glass nanoparticles.

	Mole (%)				
	SiO_2	CaO	Na_2O	P_2O5	NaF
BG	46	28.5	23	2.5	Nil
F-BG 2.5	46	26	23	2.5	2.5
F-BG 5	46	23.5	23	2.5	5
F-BG 7.5	46	21	23	2.5	7.5

2.3. Characterizations

2.3.1. Fourier Transform Infrared Spectroscopy (FTIR)

Fourier Transform Infrared Spectroscopy (FTIR) was used to analyze the functional groups present in BG and F-BG and the observed structural changes using Thermo Nicolet 6700 USA having Attenuated Total Reflectance (ATR) mode. The spectral range was 4000–550 cm⁻¹ at the resolution of 8 cm⁻¹ with 256 number of scans.

2.3.2. X-ray diffraction (XRD)

X-ray diffractometer evaluated the crystalline phases of BG and F-BGs using PANalytical XPERT-PRO with Cu Kα radiation operated at 40 mA and 40 kV. An angle range of 2θ ≈ 10°–60° and a step size of 0.02° was used to investigate the sample.

2.3.3. Scanning Electron microscopy (SEM)

Surface morphology of F-BG was done using SEM (TESCAN Vega3 LMU). Prior to scan, the particles were sonicated for 15 min in ethanol solution to separates the nanoparticles. Samples were coated with gold for 90 s using a sputter coater (Quorum Technologies). To get SEM images of samples, an acceleration voltage of 20 kV with a beam intensity of 4 pA was used.

2.3.4. Brunauer–Emmett–Teller (BET) analysis

Brunauer–Emmett–Teller (BET) method was used to analyze the surface properties of three samples from each group using Micromeritics; New TriStar II Surface Area and Porosity system. Before analysis, degassing conditions at 150 °C with 10 °C min⁻¹ heating ramp was used for 3 h under nitrogen environment.

2.3.5. Fluoride release and pH analysis

For fluoride release analysis, 0.3 g of each sample (n = 7) was immersed in 10 mL deionized water and were allowed to condition in an incubator (Fisher Isotemp, Model 413D) set at 37 °C. During conditioning, elutes were extracted periodically i.e. 1, 3, 9, 16. 24, 40, 60, 90, 120, 150, and 180 days. For elute collection, the samples were centrifuged (Hettich EBA 20) at 6000 rpm for 10 min. The pH of elutes was measured with pH/Ion selective electrode (ISE) meter (Hanna HI3222 pH/ISE meter). For fluoride release analysis, 1 mL TISAB III agent was added to each 10 mL elute sample and the analysis was carried out by using pH/ISE meter and Fluoride electrode.

The mean and standard deviation values were calculated. The statistical analysis was done by One-way repeated measures ANOVA and Post Hoc Tukey's test using SPSS version 22.

3. Results

3.1. Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR spectra of non-calcined and calcined BG and F-BG sintered at 600 °C is given in Fig. 1(a–d). The broad band around 3600–3300 cm⁻¹ and the peak at 1645 cm⁻¹ showed the presence of molecular water in the form of intermolecular hydrogen bonded to hydroxyl (OH−) group in non-calcined samples. Stretching asymmetric peak of carbonate appeared at 1454 cm⁻¹ and the stretching absorption peak specific to Si−O−Si was observed at 1028 cm⁻¹ [26]. A symmetric stretching peak at 969 cm⁻¹ showed the presence of phosphate functional group. A peak at 871 cm⁻¹ was attributed to an asymmetric bending peak of carbonate [27]. After calcination, the broad –OH band (3600–3300 cm⁻¹) disappeared and intensity of carbonate peaks reduced. Whereas, the stretching peak of Si−O−Si became broader and overlapped the P−O peak and converted into a band, where P−O appeared as shoulder peak. The intensity and area of Si−O−Si spectral band were increased after calcination. The area of Si−O−Si spectral band before/after calcination of F-BG 2.5, F-BG 5, and F-BG 7.5 was 7.5/13.41, 15.6/20.04, and 21.02/25.3 respectively.