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博士論文

Electric Charge Dependence of Controlled Dye-Release Behavior in Glass Ionomer Cement Containing Nano-Porous Silica Particles

（ナノ多孔質シリカ含有グラスアイオノマーセメントにおける電荷依存性の色素放出挙動）

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Electric Charge Dependence of Controlled Dye-Release Behavior in Glass Ionomer Cement Containing Nano-Porous Silica Particles

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We investigated in controlled dye-release behavior of nanosized silica particles containing nanocavities (Nanoporous silica, NPS). To determine this, NPS were mixed with glass ionomer cement (GIC), which is a medical material used as a matrix. The dye-release behavior was observed using a UV-visible spectrometer. After cationic dye was charged into GIC pellet containing NPS, the pellet could gradually release cationic dye for up to two weeks. To understand the dependence of electric charge on the dye-release behavior, three types of dyes with different charge were also investigated. Dyes having a neutral or negative electric charge were quickly released from the pellet within a couple of days. These results suggest that the nanocavities present in NPS can selectively bind cationic dyes and allow for their gradual release. This result reveals the excellent sustained dye-release property of NPS.

Keywords: Nanoporous Silica, Glass Ionomer Cement, Ion Release Ability.

1. INTRODUCTION

Because nanotechnology[1–3] markedly developed in recent years, nanomaterials[4–6] have been paid much attention from many researchers in academic and industrial fields. In particular, inorganic nanoparticles have attracted interest because of their unique size-dependent properties. By virtue of this size effect, nanomaterials are expected to exhibit superior optical, electrical, and physical properties and chemical reactivities. For the development of controlled release material, several types of materials have been investigated. For example, poly(lactic acid) and poly(glycolic acid) have been investigated because of their biodegradation properties.[7–9] Rosca et al. determined that the mechanism of solvent elimination from emulsion droplets and its influence on the particle morphology, encapsulation, and release behavior.[10] Virus-like encapsulation materials have also been investigated. Niikura et al. reported that virus-like particles (VLPs) coupled with cyclodextrins as hydrophobic pockets through disulfide bonds inside the VLPs, where hydrophobic drugs can be incorporated. The VLPs with removable cyclodextrins afford highly promising carriers of hydrophobic drugs without chemical modification of drugs.[11] Nano porous materials have also been investigated. Wu et al. investigated mesoporous titanium oxide and its application for the delivery of the potential anticancer drug vinorelbine bitartrate under physiological conditions.[12] Seker et al. demonstrated that nanoporous gold is a promising novel material that benefits from compatibility with microfabrication, electrical conductivity, and well-established gold-thiol conjugate chemistry.[13] In this study, we focused on nanosized silica particles with nano porous cavity structures. Although the particles have many nano-cavities, they were expected to remain some molecules and ions. Nanoporous silica (NPS) is frequently used owing to its desirable structural properties, such as controllable pore size, large surface area, and reactive surfaces.[14–17] Silica is widely used as a filler in dental materials and its biological safety is relatively recognized. In a previous study, we reported that cationically charging NPS resulted in a slow release of water-soluble dye, which could be recharged by NPS. However, we did not evaluated the anionically

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charged and uncharged molecular sustained-release properties of NPS. In this study, we added nano-silica into glass ionomer cements (GIC), which is a type of dental cement having a sustained-release property of fluorine. Fluorine ions prevent teeth from developing caries via fluoroapatite formation, remineralization and anti-enzymatic action. This is one of the reasons why GIC is a widely used adhesive in dentistry. However, dental caries cannot be entirely prevented using GIC. Dental caries can occur around the GIC filling or at the adhesive interface using GIC. By increasing the amount of released fluoride ions or adding enhanced sustained-release properties to the cement, this problem could be resolved. In addition, the development of novel multi-functional dental cement is required. Then, we focused on nano porous materials as the substance charging ions or molecules. The purpose of this study was to prepare GIC containing NPS (GIC-NPS) and, to compare the difference of its sustained-release property with different charge properties. In this study, water-soluble dyes were used to visually evaluate the sustained-release properties of differently charged NPS.

2. MATERIALS AND METHODS

2.1. Preparation of Nanoporous Silica Particles

Cetyltrimethylammonium bromide, tetraethoxysilane, rhodamine B (RhB), rose bengal (RB), and fluorescein (FL) were purchased from Sigma Inc. (St. Louis, MO, USA). NPS was synthesized in accordance with the protocol set by Tagaya.[17] Briefly, 1.37 mmol of cetyltrimethylammonium bromide were added into 120 mL of distilled water and then 1.75 mL of 2 M NaOH solution was added to this solution. The mixture was stired for 30 min at 80 °C. Then, 12.4 mmol of tetraethoxysilane was added and stirred for 2 h at 80 °C. The resulting suspension was filtered, washed and dried. The obtained particles were calcinated at 550 °C for 4 h to remove cetyltrimethylammonium bromide. The obtained white particles were observed using a scanning electron microscope (SEM: S-4800, HITACHI, Tokyo, Japan) and a transmission electron microscope (TEM: JEM-2010, JEOL, Tokyo, Japan). They were also characterized using powder X-ray diffraction (XRD: RINT-2000/PC, Rigaku, Tokyo, Japan). Silica particles were purchased from High-purity Chemicals (Tokyo, Japan) as silica nanoparticles without nano-cavities. Hereafter, it is denoted as SiO_2.

2.2. Preparation of GIC-NPS and Molding Test Pellet

Fuji I (GC, Tokyo, Japan) was used for GIC. The obtained NPS was added to the powdered part of GIC at 5 wt% concentration. The test pellets were prepared by mixing the GIC powder containing NPS and the liquid part of GIC, as specified by the manufacturer. The size of GIC-containing NPS pellets (GIC-NPS) was set to 1 mm in thickness and 10 mm in diameter.

2.3. Evaluation of Sustained Dye-Release Property

RhB was selected as a cationic water-soluble dye, RB was selected as an anionic water-soluble dye, and FL was selected as an uncharged water-soluble dye. For charge, the GIC-NPS were immersed into the aqueous dye solutions of 1 wt% concentration for 24 h at 37 °C. After removal from the dye solutions, they were rinsed with distilled water. Then the obtained charged GIC-NPS containing dye was immersed into 5 mL of distilled water at 37 °C for 24 h. After 24 hours, GIC-NPSs were removed from the solution and re-immersed into fresh distilled water. This procedure was repeated for 13 days. The absorption spectra of the supernatant were measured using a UV-visible spectrophotometer (V-650, Jasco, Tokyo, Japan) to evaluate the amount of dye released each day. After the dye-release, the GIC-NPS was immersed into dye solution again then the dye-release behaviour was determined with same procedure.

GIC containing SiO_2 instead of NPS and the raw GIC without NPS (hereafter, referred to as GIC-SiO_2, and GIC only, respectively) were also investigated their dye-release properties.

3. RESULTS AND DISCUSSION

3.1. Nano Porous Silica (NPS) Particles and Dental Cement Containing NPS Particles

Figure 1 shows a typical SEM image of NPS particles. The obtained NPS particle was spherical in shape with a diameter of approximately 0.3 μm. Figure 2 shows their TEM images. The NPS particles had numerous cavities that were approximately 2.5 nm in diameter. The XRD measurements demonstrated peaks at (100), (110), (200), and (220) reflecting a hexagonal structure (Fig. 3). This suggests that highly ordered arrangements are preserved.

3.2. Colour Differences of Supernatant

Figure 4 shows photo images of each supernatant in which GIC plates were immersed for different immersion time periods. When GIC-NPS with RhB was immersed into

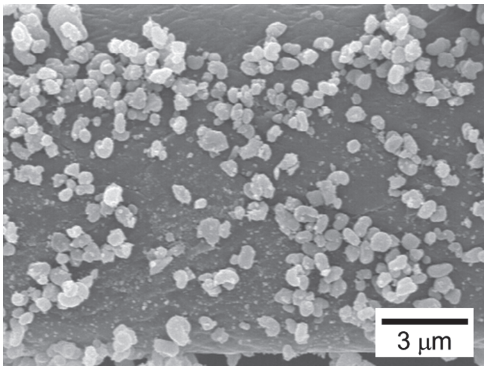

Figure 1. A typical SEM image of nano porous silica particles.

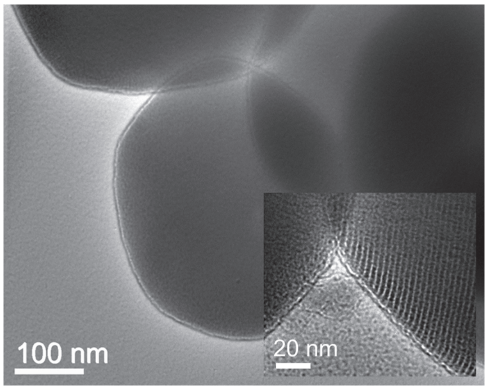

Figure 2. A typical TEM image of nano porous silica particles.

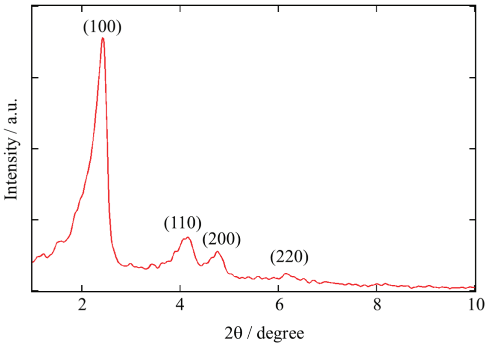

Figure 3. Powder X-ray diffraction pattern of NPS.

water, the supernatant exhibited a clear red color up to seven days (Fig. 4 (left)). The color of the supernatant gradually became fainter with longer immersion time. In contrast, the supernatant from GIC only exhibited red color for only one day. In the case of pellets immersed in RB, the supernatant of GIC-NPS exhibited red color for only a day, and the supernatant from GIC only remained transparent even after a day of immersion (Fig. 4 (middle)). Figure 4 (right) shows emission images of supernatant in which GIC plates were immersed into FL solution. FL is a typical fluorescent dye, which fluoresces under ultraviolet light. The supernatant of both GIC-NPS and GIC only were green for a day. However, the emission from the supernatant from GIC-NPS was stronger than that from GIC only.

3.3. Absorption Spectra of the Supernatant

Figure 5 shows the absorption spectra of their supernatant depending on the immersion period (two, four, and seven days). The supernatants of FL, RB and RhB had sharp absorption spectra with their peaks appearing at 489, 549 and 554 nm, respectively. In the case of immersion into RhB, the absorption spectra of the supernatant from GIC-NPS gradually decreased depending on the immersion time. In contrast, the supernatant from GIC only revealed a markedly weak absorption spectrum even two days following immersion. The spectrum almost disappeared four days following immersion. With the other dyes, their absorption rapidly decreased between two days and four days following immersion, this was also the case for GIC-NPS. During all immersion periods, the absorption from GIC-NPS was higher than that of GIC only at day two.

3.4. Time Profile of the Absorbance of the Released Dye from GIC-NPS

Figure 6 shows the time profile of the absorbance of the released dyes (FL, RhB and RB) from GIC-NPS. These data were normalized to the absorbance of released dye at the second day. Though the amount of released RhB gradually decreased during the immersion period, the dye release from GIC-NPS lasted for more than 10 days. The concentration of RhB in the supernatant at one and two weeks was estimated at 10 and 3 μmol/L, respectively. On the contrary, the amount of released FL and RB by GIC-NPS greatly decreased from day two to day three. The absorbance of released FL and RB reached the lower detection limit within a week of immersion. As described above, cationic dye were remained in GIC-NPS and were gradually released from them over at least two weeks. In contrast, dyes with anionic or neutral charge were rapidly released at an early period. Though it is known that the surface of silica has a negative charge,[18] only the cationic dyes were captured on the surface with

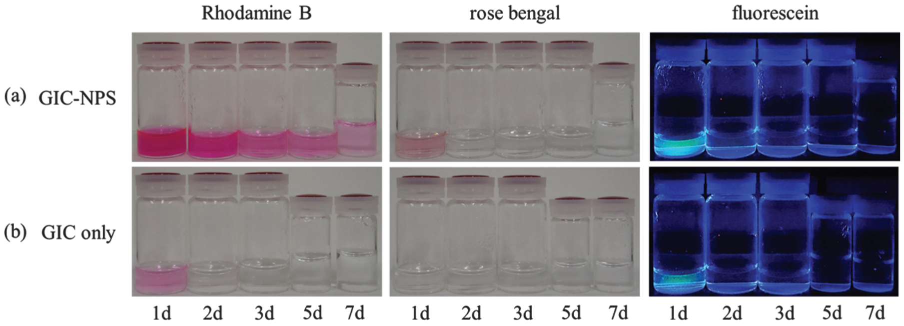

Figure 4. Photo image of released dye supernatants: (a) GIC-NPS (b) GIC only.

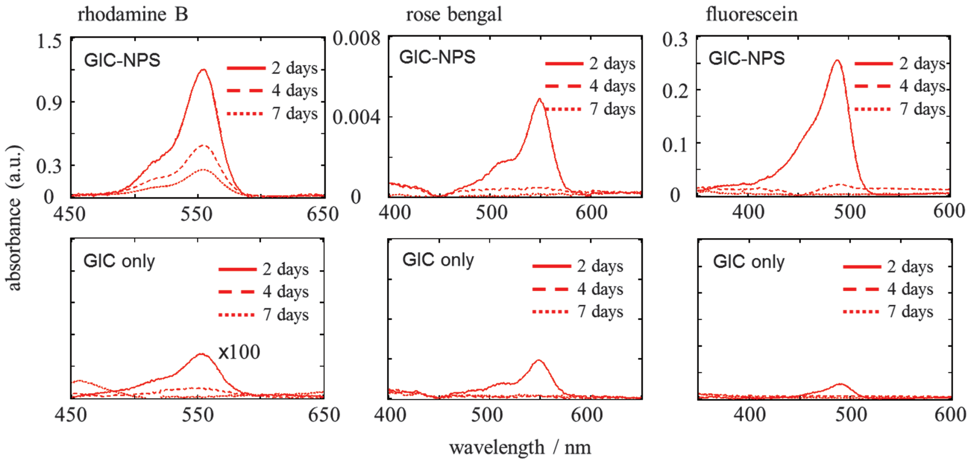

Figure 5. Absorption spectra of released dye solution from GIC-NPS (top) and GIC only (bottom): (left) rhodamine B, (middle) rose bengal, (right) fluorescein.

the electric interaction then caused a gradual dye-release behavior. When SiO_2 particles without nanoporous were added to GIC instead of NPS, the samples exhibited a different RhB release behaviour than that of GIC-NPS (Fig. 6). The absorbance at 554 nm greatly decreased with increasing immersion period in distilled water. This behaviour was similar to that of the GIC-NPS-RB or FL. In fact, the release behavior of GIC which contains SiO_2 nanoparticls without nanocavities was similar to that of GIC only (Fig. 6). These results suggest that the nanostructure of nanocavities also perfomed to enhance their dye-release properties. In fact, Losic et al. demonstrated dye-release properties of titania nanotubes (TNT) could be developed with nanostructure formation.[19] When the TNT was generated internal structure based on oscillatory voltage apply, obtained TNT had periodically modulated nanostructure and the dye-loading and dye-release properties were enhanced. These results suggest that the nanocavities in NPS can specifically capture cationic ions and gradually release them. Iler mentioned that hydroxyl groups bound to the surface of SiO_2 gave the surface a neat negatively charge.[18] Shibata et al. demonstrated that presence of hydroxyl group on the silica microsphere surface enhanced the interaction with silver ions.[20] Sivan et al. determined the combined effects of cation size and charge (valency) on the interaction between silica surfaces using an AFM measurement.[21] Martinelli et al. investigated the interaction between room temperature ionic liquid (RTIL) and surface of nanoporous silica.[22] Based on solid state NMR measurement, they determined that cation moiety of RTIL bound to hydroxyl group of SiO_2 surface. Therefore, the capture and release behavior of cationic dye can also be due to electric interaction. Unlike biodegradable polymers and vesicle-type capsules, this method can re-charge the released materials (Fig. 7). Because controlled release materials based on biodegradable polymers or vesicle-type capsules performed by their structural destroy, they were unable to re-chargeable usage. These results also suggest that GIC-NPS can be used for the manufacture of controlled release of cationic materials such as proteins, antibodies, growth factors and those used in drugs, and perfume.

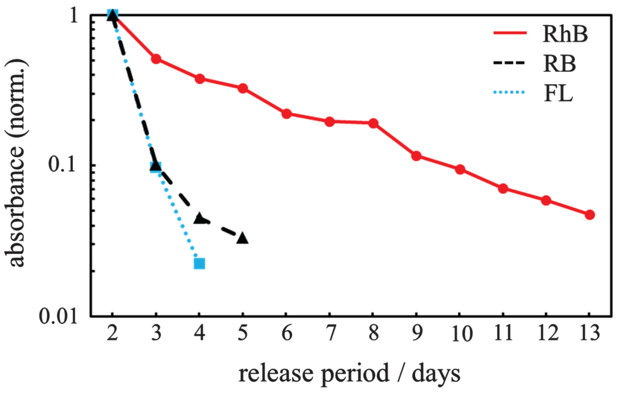

Figure 6. Time-profiles of dye-release behavior based on their absorbance.

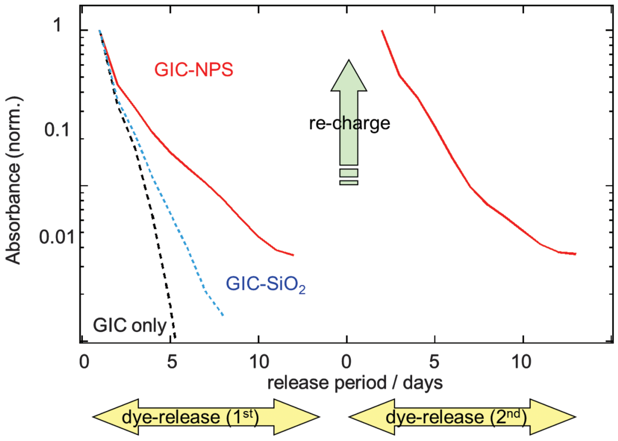

Figure 7. Time-profiles of dye-release behavior on re-charge procedure.

4. CONCLUSION

In this study, we investigated the controlled dye-release behavior of nanosized NPS. After cationic dye was added to the GIC-NPS pellet, the pellet could gradually release the cationic dye for up to two weeks. In contrast, dyes with a neutral or negative electronic charge were rapidly released from the pellet within a couple of days. In addition, the sample containing nano-silica without nanocavities also released dyes rapidly even if they had a cationic property. These results suggest that nanocavities of NPS can selectively bind cationic dyes and gradually release them. This suggests that NPS particles have an excellent sustained controlled release property for cationic materials, which could be highly applicable in the manufacture of cosmetics, drug and perfume.

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