

## **Abstract**

The potential of root canal dressing containing S-PRG fillers for apical  
periodontitis treatment evaluated *in vivo* and *in vitro*

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## Abstract

**[Objective]** Recently, the surface reaction-type pre-reacted glass-ionomer fillers (S-PRG) has gained popularity in dentistry. The S-PRG fillers have been formulated to exert therapeutic action in various clinical conditions, such as coating of root surfaces, oral rinsing, and direct pulp-capping. It is suggested that multiple ions, Al, B, F, Na, Si, and Sr, released from S-PRG fillers are correlated to the beneficial bioactive properties of S-PRG-containing materials in clinical applications like antibacterial activity, acid buffer capacity, and mineral induction properties. Previous studies have suggested that S-PRG-based material is possible to be used as an endodontic sealer or a single-visit root repair material in non-vital teeth. Moreover, the evidence in previous studies has shown that ions released from S-PRG fillers can be eluted through the root canal structure in the human tooth and have the potential to enhance the tissue repair by stimulating human gingival fibroblast cell line HGF-1 migration.

Based on the previous description of S-PRG-containing materials, we aimed to evaluate the efficacy of a prototype root canal dressing containing S-PRG fillers on repairing rat periapical lesions. Calcium hydroxide ( $\text{Ca(OH)}_2$ ), regarded as an ideal intracanal medication, was applied as a comparison in the healing process. Besides, a vitro study on MC3T3-E1 mouse osteoblastic cells would also be performed to evaluate the influence of aqueous eluates obtained from S-PRG in osteogenesis, which may indicate partly mechanism of S-PRG root dressing (S-PRG-containing ion releasing aqueous pastes) treatment involving the periapical tissue repair process.

**[Materials and Methods]** *In vivo*, the pulp chamber of the maxillary first molars in 39 male Wistar rats at 16 weeks was opened to induce periapical lesions. After 28 days, the mesial canal of each tooth was prepared, only irrigated with 2.5% sodium hypochlorite (NaOCl) (negative controls, irrigation) or followed by the respective dressing filling (positive controls, irrigation +  $\text{Ca(OH)}_2$ ; test group, irrigation + S-PRG), and sealed with composite resin for 3 days or 7 days (6/gp). 3 rats with healthy molars were used as blank controls. The periapical repair was evaluated radiographically, histologically and immunohistochemically after treatment. *In vitro*, MC3T3-E1 cells were exposed to medium with or without different dilution ratios of S-PRG eluates. The proliferation of MC3T3-E1 cells was measured using the CCK-8 assay. Cell differentiation and mineralization were analyzed by alkaline phosphatase activity assay and alizarin red S staining. Data were analyzed by variance (ANOVA) with Tukey's HSD and  $P < 0.05$  was judged to be statistically significant.

**[Results]** *In vivo*, S-PRG and Ca(OH)<sub>2</sub> increased periapical gray value and inhibited the osteoclast activity at 3 days and 7 days; the significant difference in radiographic result was observed at 3 days compared with the negative controls. The reparative tissue was observed in the periapical resorbed necrotic area after S-PRG and Ca(OH)<sub>2</sub> treatment for 3 days and 7 days by histological observation. The number of macrophages was significantly decreased at 3 days in S-PRG specimens, but not in Ca(OH)<sub>2</sub> specimens, when compared with the negative controls; no statistical significance was observed for intergroup comparison at 7 days. *In vitro*, MC3T3-E1 cells proliferation was promoted by 10<sup>3</sup>, 10<sup>4</sup>, and 10<sup>5</sup>-fold-diluted S-PRG eluates when compared with control cells. The ALP activity level of cells was significantly increased cultured in the growth medium containing 10<sup>5</sup>, 10<sup>6</sup>, and 10<sup>7</sup>-fold-diluted S-PRG eluates at 21 days; ALP activity of cells was enhanced in the differentiation medium supplemented with 10<sup>6</sup> and 10<sup>7</sup>-fold-diluted S-PRG eluates. The maximum level of ALP activity and mineralization was reached at the dilution ratio of S-PRG eluates at 10<sup>7</sup>.

**[Discussion]** The rat model for evaluating the effect of intracanal medication involved in apical periodontitis has been well-established. The new prototype of S-PRG dressing, consisting of S-PRG fillers and distilled water, was used for endodontic treatment in our rat periapical lesions and its aqueous eluates were used in culture on MC3T3-E1 osteoblastic cells. As stated previously, S-PRG cement can eliminate 99% of *P. gingivalis*, exert an antibacterial on *Propionibacterium acnes* and *Actinomyces israelii*, and a fungicidal effect on *Candida albicans*. It is suggested that Al, B, F, Na, and Sr released from S-PRG were correlated to the disinfection process, consequently, initiating the periapical repair. Previous studies supported the actions of Sr, F, Al, Si, Na, and B in regulating bone metabolism and/or enhancing wound healing. Moreover, the combinations of F-Al and F-Sr are suggested to exert an additive effect on the bone generation process. In our present study *in vitro* demonstrated that 6 ions in S-PRG eluates stimulated the osteoblastic differentiation and mineral nodule formation at a low concentration, and the tissue healing in periapical lesions was obtained after S-PRG dressing treatment *in vivo*, suggesting ions released from S-PRG dressing is possibly responsible for the biological effects on experimental rat periapical lesions.

**[Conclusion]** S-PRG-containing ion releasing aqueous pastes was comparable with Ca(OH)<sub>2</sub> in promoting periapical healing *in vivo*. Moreover, aqueous eluates from S-PRG fillers promoted the osteogenesis of MC3T3-E1 cells *in vitro*. S-PRG pastes has the potential to be used as an alternative intracanal dressing in teeth with apical periodontitis.