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Addition of bioactive glass to glass ionomer cements: Effect on the physico-chemical properties and biocompatibility

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ABSTRACT

Objectives. Glass ionomer cements (GICs) are a subject of research because of their inferior mechanical properties, despite their advantages such as fluoride release and direct bonding to bone and teeth. Recent research aims to improve the bioactivity of the GICs and thereby improve mechanical properties on the long term. In this study, two types of bioactive glasses (BAG) (45S5F and CF9) are combined with GICs to evaluate the physico-chemical properties and biocompatibility of the BAG-GIC combinations. The effect of the addition of Al^{3+} to the BAG composition and the use of smaller BAG particles on the BAG-GIC properties was also investigated.

Materials and methods. Conventional aluminosilicate glass (ASG) and (modified) BAG were synthesized by the melt method. BAG-GIC were investigated on setting time, compressive strength and bioactivity. Surface changes were evaluated by Fourier transform infrared (FT-IR), scanning electron microscopy (SEM), EDS and PO_4^{3-} -and Ca^{2+} uptake in SBF. Biocompatibility of selected BAG-GICs was determined by a direct toxicity assay.

Results. The addition of BAG improves the bioactivity of the GIC, which can be observed by the formation of an apatite (Ap) layer, especially in CF9-containing GICs. More BAG leads to more bioactivity but decreases strength. The addition of Al^{3+} to the BAG composition improves strength, but decreases bioactivity. BAGs with smaller particle sizes have no effect on bioactivity and decrease strength. The formation of an Ap layer seems beneficial to the biocompatibility of the BAG-GICs.

Significance. Bioactive GICs may have several advantages over conventional GICs, such as remineralization of demineralized tissue, adhesion and proliferation of bone- and dental cells, allowing integration in surrounding tissue. CF9 BAG-GIC combinations containing maximum 10 mol% Al^{3+} are most promising, when added in $\leq$20 wt% to a GIC.

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1. Introduction

Glass ionomer cements (GICs) were invented in the early 70's by Wilson and Kent [1]. They are formed by an acid-base reaction between a polyalkenoic acid and a basic aluminosilicate glass (ASG) [1]. The polyalkenoic acid is usually a polyacrylic acid, polyitaconic acid, polymaleic acid or a copolymer of the previous ones [2]. The ASG contains Ca^{2+}, Al^{3+} and Si^{4+} as essential components, linked to each other by bridging oxygens. Other ions, such as F^- and PO_4^{3-} are usually added to the glass composition. Fluoride increases the compressive strength and decreases the setting time of the cement. This effect is ascribed to the formation of Al–F–Ca(n), F–Ca(n) and possibly Si–F–Ca(n) species, which increase the reactivity of the glass, so that less bonds have to be hydrolyzed during setting [3–5]. PO_4^{3-} groups in the glass increase the working and setting time but decrease the compressive strength. These PO_4^{3-} groups, released during hydrolysis in the setting reaction, compete with the polyalkenoate groups of the PAA for the binding of cations [6]. Water or an aqueous solution of tartaric acid is an essential component in the formation of a GIC to initiate the acid-base reaction [1]. When polyalkenoic acid, ASG and water are mixed, a paste is formed in which the protons of the polyalkenoic acid degrade the ASG. The bonds in the glass-network are hydrolyzed and Ca^{2+}, Al^{3+}, F^- and PO_4^{3-} are released. In a second reaction step, the released Ca^{2+} and Al^{3+} bind with the polyalkenoate groups, which form the strong matrix. A silica gel layer is formed around the remaining glass particles, which impedes further degradation [7,8].

GICs were initially pushed forward as a revolutionary white dental filling material to replace the less esthetic and more toxic amalgam fillings in restorative dentistry [9,10]. Also in ENT surgery, GICs are more and more used, for example as otological implants [11]. GICs have a lot of advantages such as direct bonding with teeth by the interaction of the natural apatite (Ap) with the carboxylate-groups of the PAA. Moreover, they have good biocompatibility properties, they release and take up fluoride and thus an antibacterial action and enhance remineralization of fluorapatite (FAp). In contrast to composites, their shrinkage upon setting is negligible [12–17]. But despite their major benefits in comparison to other commonly used restorative materials, their mechanical properties are since the development of this product still subject of improvement [15,18].

Changing the composition of the ASG affects the mechanical properties of the GIC. Within certain limits, an increase of Al^{3+} or F^- content can improve strength, while PO_4^{3-} decreases the mechanical properties [6,8,19–23]. Also the type, amount and molar mass of the PAA and the powder/liquid (P/L) ratio used to form the cement have an influence on the mechanical properties [2,7,21]. Within the limits of workable cements, the highest P/L ratio leads to the best outcomes. As such, high viscosity GICs, with high concentrations of PAA and high molar mass, are now mostly used [24,25]. Another way to increase packing density of a GIC is by adding nanoparticles to the ASG fraction. Nanoparticles have a higher specific surface area, and therefore release more ions within the same amount of added water, and thus react faster. Although nanoparticles indeed increase initial compressive strength, no improvement in strength can be seen on the long term [18].

Nowadays, research groups are focusing on the bioactivation of GICs aiming to improve the long term mechanical properties [17,26,27]. There are several definitions for bioactivity: first, it can be defined as the property of a material to bond with living tissue without the formation of a fibrous layer *in vivo* [28]. Since GIC can bind chemically with enamel, dentin and bone by the interaction of the polyalkenoic acid component of GIC with the apatite component of these tissues, GIC can be considered bioactive. According to a second definition, a material is considered bioactive when it is able to form a layer of material inherent to the body, for example apatite, and in this way integrate with the body [28–30]. According to this second definition, GICs are not yet bioactive. This last type of bioactivity can easily be monitored *in vitro* using a simulated body fluid (SBF) [17,26,31]. Some researchers are critical about this method, as both false positive and false negative results can occur. So after positive results in SBF, *in vitro* cell tests and *in vivo* experiments should be conducted to validate the results [32]. It is shown that the formation of a crystalline HAp layer is delayed in *in vitro* or *in vivo* conditions where proteins are able to co-adsorb on the surface of the cement [33]. Cells can only adhere to a bioactive material, if the material can be resorbed in the body, apatite can be redeposited and proteins and growth factors can adhere to the remineralized material. But the adhesion of these proteins thus hamper further Ap growth. However, if apatite is formed *in vitro*, it is also believed to interact with living dental tissue *in vivo* as long as no toxic constituents are released [31]. The amount of toxicity of course depends on the volume and the flow of surrounding tissue fluid in which ions are leached.

If GICs would have the potential to be bioactive, the possible applications of GICs would become much broader. Apatite will be able to integrate within dentin structures and may enhance the bonding with the implant by mechanical interlocking next to the chemical bonding and thus improve the (mechanical) properties of the material in the long term. Moreover, proteins and cells could be attracted and tissue regeneration could be accelerated significantly. The remineralization potential of bioactive GICs may also be of interest in ART as in this minimal invasive technique GIC may be placed in a cavity, still containing remnants of demineralized dentin. Also in shallow preparations, the remineralizing potential may be beneficial to improve the retention of the material [34,35]

Bioactive glass (BAG) was developed in 1969 by Hench [29,30]. Until then, implants were merely bioinert and evoked an undesirable fibrous encapsulation of the material. While this new material formed a stable bond or interface with tissues by the formation of an Ap layer [30]. The first commercial bioactive glass consisted of 46.1 mol% SiO_2, 24.4 mol% Na_2O, 26.9 mol% CaO and 2.6 mol% P_2O_5 and was called 45S5 or Bioglass® [29,30]. When this glass is incubated in aqueous conditions, an Ap layer is formed on the surface of these glasses. In a first phase, due to hydrolysis, rapid cation exchange of Na^+ and/or Ca^{2+} with H^+ from the solution occurs. Phosphate is also leached from the glass. This creates silanol groups (Si–OH) on the glass surface. The pH of the solution increases and a silica-rich (cation-depleted) region forms near the glass surface. Soluble silica is lost in the form of $Si(OH)_4$