

Trends in restorative composites research: what is in the future?

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Abstract: Clinical trials have identified secondary caries and bulk fracture as the main causes for composite restoration failure. As a measure to avoid frequent reinterventions for restoration replacement, composites with some sort of defense mechanism against biofilm formation and demineralization, as well as materials with lower susceptibility to crack propagation are necessary. Also, the restorative procedure with composites are very time-consuming and technically demanding, particularly concerning the application of the adhesive system. Therefore, together with bulk-fill composites, self-adhesive restorative composites could reduce operator error and chairside time. This literature review describes the current stage of development of remineralizing, antibacterial and self-healing composites. Also, an overview of the research on fiber-reinforced composites and self-adhesive composites, both introduced for clinical use in recent years, is presented.

Keywords: Composite Resins; Calcium Phosphates; Anti-Bacterial Agents; Adhesives

Introduction

As resin composites approach a half century of clinical use, it is possible to identify their “developmental cycles” motivated by deficiencies observed in the clinic. In the first two decades (1980’s and 1990’s), the focus was on filler systems that would allow for materials with superior mechanical properties, wear resistance and good polishing, resulting in the development of microhybrid composites.¹ From the mid-1990’s to mid-2000’s, efforts were directed towards reducing polymerization shrinkage as a strategy to reduce post-operative sensitivity, cuspal deflection, and interfacial gap formation.² In this decade, bulk-fill composites are becoming increasingly popular due to the clinical appeal of reducing the time necessary to insert the composite into the cavity preparation.³

While the use of restorative resin composites becomes more and more ubiquitous and indication boundaries are extended, their service time is usually abbreviated by the development of new caries lesions at the tooth-restoration interface (“secondary caries”) or by fracture of the material.^{4,5} Such occurrences are not necessarily related to a material deficiency. The skill level of the professional and the patient’s awareness regarding good dietary and oral hygiene habits seem to be determinative for restoration success.^{6,7} Still, the accumulated clinical experience suggests

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that improvements in composite fracture toughness (*i.e.*, resistance to crack propagation), as well as the incorporation of protective mechanisms to reduce the risk of caries development are necessary to increase the restoration's longevity.

The aim of this review is to present to the reader some of the technologies recently made available for clinical use and to describe some of the current research efforts that, if translated to the clinical practice, may allow for composite restorations with extended service life. The topics discussed can be divided into three main strategy groups: 1) simplification of the restorative procedure (self-adhesive composites); 2) strategies to reduce the risk of composite bulk fracture (fiber-reinforced and self-healing composites); 3) defense mechanisms against new caries lesions at the tooth-restoration interface (remineralizing and antibacterial agents).

Strategy 1: Self-adhesive restorative composites

Self-adhesive restorative composites (SACs) were introduced in the dental market in 2009 and, currently, there are three examples available for clinical use (Table 1). These low-viscosity materials are indicated for small class I cavities and non-carious cervical lesions.⁸ Unfortunately, reports of *in vitro* evaluations of these materials are scarce and clinical studies are almost non-existent.

A key difference between SACs and self-adhesive resin cements (SARCs) is that SACs do not undergo acid-base neutralization reactions nor contain fluoride-releasing glass fillers.¹⁰ In fact, SACs are more

akin to self-etch adhesive systems due to the presence of acidic monomers such as glycerol phosphate dimethacrylates (GPDM), carboxylic methacrylates (for example, 4-MET) or phosphate ethyl methacrylates (BMEP). These monomers vary in acidity from mild (for example, GPDM with a pH = 1.9) to ultra-mild (4-MET, pH=3-4)¹¹ and are responsible for partially etching the tooth substrate and penetrating through the smear layer, forming a submicron-thick hybrid layer.¹² Hydroxyethyl methacrylate (HEMA) is added to increase the wettability of the material on the dentin surface.¹³

Similar to self-adhesive resin cements, though, is the fact that SAC interaction with dentin is limited by the extent of decalcification produced by the acidic monomers. Furthermore, their relatively high viscosity as the result of filler incorporation makes wetting of the bonding substrate even more difficult,^{12,14,15} limiting the diffusion of monomers into the collagen fibers network.¹⁶ Notwithstanding, some chemical interaction with calcium from hydroxyapatite has been verified, suggesting that the retention relies not only on micro-mechanical interlocking.^{17,18}

Overall, studies agree that SACs exhibit lower bond strength values to dental tissues than conventional restorative systems (Table 2),^{12,19,20,21,22,23,24} with a few exceptions where composites were tested on radicular dentin^{25,26} Several studies suggest that pre-etching enamel and dentin with phosphoric acid significantly increases bond strength, as phosphoric acid removes the smear layer and enhances surface area.^{8,9,19,27,28,29} Using a self-etch adhesive prior to the application of Vertise Flow significantly increased

Table 1. Composition of commercially available self-adhesive composites.

Material	Manufacturer	Composition
Fusio Liquid Dentin*	Pentron Clinical, Orange, CA, USA	Resin: aliphatic diurethane dimethacrylate (UEDMA), triethylene glycol dimethacrylate (TEGDMA), hydroxyethyl methacrylate (HEMA), trimellitic acid methacrylate (4-MET), catalyst Fillers: SiO ₂ (65 wt%), silanated barium glass, NaF
Vertise Flow*	Kerr, Orange, CA, USA	Resin: glycerolphosphoric acid dimethacrylate (GPDMA), HEMA, bisphenol glycidil dimethacrylate (Bis-GMA), catalysts Fillers: pre-polymerized filler, silanated barium glass, nano-sized colloidal SiO ₂ , YF ₃ (70 wt%)
Embrace Wetbond**	Pulpdent, Watertown, MA, USA	Resin: aliphatic diurethane dimethacrylate (UEDMA), bis-methacryloyloxy ethyl phosphate (BMEP), trimethylol propane trimethacrylate (TMPTMA), HEMA, water, catalysts Fillers: SiO ₂ , NaF (37 wt%)

*from Reference 9; **manufacturer information.

Table 2. Bond strength studies.

Reference	Bonding substrate	Testing method	Self-adhesive composite	Control group	Outcome
Giachetti et al. (2012) ²⁵	radicular dentin	Push-out	Vertise flow	etch-and-rinse adhesive + resin cement	SAC: 21.6–23.2 MPa Control: 20.4–24.7 MPa
Mobarak and Seyam (2013) ²⁶	radicular dentin	Push-out	Vertise flow	etch-and-rinse adhesive + resin cement or dual cure self-etch resin cement	SAC: 18.0–19.1 MPa Control: 11.3–14.4 MPa
Vichi et al. (2013) ¹²	enamel/dentin	Shear	Vertise flow	self-etch adhesive + flowable composite	Enamel: SAC: 2.6 ± 2.6 MPa; Control: 5.0–12.1 MPa Dentin: SAC: 3.4 ± 1.6 MPa; Control: 5.8–12.2 MPa
Poitevin et al. (2013) ¹⁹	enamel/dentin	Micro-tensile	Vertise flow Fusio liquid dentin	self-etch adhesive + flowable composite	SAC (enamel): Vertise flow: 11.0 ± 4.2 MPa Vertise flow with previous etching: 23.1 ± 7.1 MPa Fusio liquid dentin: 13.0 ± 4.3 MPa Control (enamel): 28.0 ± 9.8 MPa SAC (dentin): Vertise flow: 1.8 ± 2.7 MPa Vertise flow with previous etching: 18.7 ± 11.0 MPa Fusio liquid dentin: 17.7 ± 8.6 MPa Control (dentin): 7.9–44.8 MPa
Goracci et al. (2013) ⁹	enamel	Shear	Vertise flow	etch-and-rinse or self-etch adhesive + orthodontic cement	SAC: Vertise flow: 3.0 ± 1.2 MPa Vertise flow with previous etching: 6.6 ± 1.1 MPa Control: 9.0–11.7 MPa
Fu et al. (2013) ²⁴	dentin	Micro-tensile	Vertise flow Fusio liquid dentin	self-etch primer adhesive system + resin composite	SAC: Vertise flow: 13.0 ± 9.9 MPa Fusio Liquid Dentin: 25.2 ± 6.1 MPa Control: 79 ± 16.1 MPa SAC (primary dentin): Vertise flow: 4.1 ± 2.3 MPa Vertise flow with previous self-etch adhesive: 8.7 ± 1.7 MPa
Tuloglu et al. (2014) ²¹	primary and permanent dentin	Shear	Vertise flow	self-etch adhesive + flowable composite	Control (primary dentin): 15.6 ± 2.6 MPa SAC (permanent dentin): Vertise flow: 19.3 ± 2.3 MPa Vertise flow with previous self-etch adhesive: 25.6 ± 3.0 MPa Control (permanent dentin): 35.7 ± 2.9 MPa
Makishi et al. (2015) ²²	dentin	Shear	Vertise flow Fusio liquid dentin	etch-and-rinse adhesive + resin composite	SAC: Vertise flow: 13.9 ± 3.6 MPa Fusio liquid dentin: 11.3 ± 3.2 MPa Control: 27.3 ± 6.1 MPa
Sachdeva et al. (2016) ²³	primary dentin	Shear	Vertise flow Fusio liquid dentin	conventional flowable composite	SAC: Vertise flow: 12.0 ± 3.1 MPa Fusio liquid dentin: 14.2 ± 4.1 MPa Control: 21.1 ± 3.8 MPa

the dentin bond strength and reduced microleakage scores, when compared with the application of the SAC alone.²¹ Obviously, adding an extra step to the restorative procedure with self-adhesive composites defeats the purpose of simplifying the procedure. Interestingly, despite their low bond strength, Vertise Flow showed better marginal sealing ability in comparison with self-adhesive and etch-and-rinse adhesive systems possibly due to hygroscopic expansion and a relatively low polymerization stress development at the bonded interface.^{12,14,23} Another evidence of the limited adhesion of these materials to tooth structure was the retention rate of only 33% displayed by Fusio liquid dentin in non-cariou cervical lesions after a six-month clinical evaluation, in comparison to the 100% retention of a conventional restorative composite.³⁰

The physical properties of SACs have not been thoroughly evaluated. In one study, Vertise Flow showed flexural strength similar to conventional (*i.e.*, non-self-adhesive) flowable composites.³¹ After toothbrushing abrasion, Vertise flow had a rougher surface compared to that resulting from the application of Fusio liquid dentin and a conventional restorative composite.³² Results can be related to the type of organic matrix, since urethane-based composites have a better wear resistance than Bis-GMA-based composites, other factors being equal.³³ SACs also showed a much poorer performance in terms of gloss retention than a conventional control.³² Self-adhesive composites are more hydrophilic than conventional composites due to the presence of acidic monomers and HEMA. In fact, Vertise Flow showed much higher hygroscopic expansion³⁴ and higher water sorption³⁵ when compared with conventional composites after 150 days in water. A drawback indeed, since SACs hydrophilicity may facilitate network plasticization, enhance biofilm formation and increase degradation.^{28,34}

The idea of bonding the composite directly to the tooth structure is enticing. However, based on the limited amount of information available, it seems that self-adhesive restorative composites are still at their inception and more research is necessary to solve the limitations found with the current materials.

Strategy 2A: Fiber-reinforced composites

Current restorative composites present fracture toughness (K_{Ic}) values varying between 0.9 to 1.8 MPa.m^{0.5},¹ which seems insufficient to avoid clinical failures by bulk fracture.^{4,5} The incorporation of small fractions of short, random glass fibers as part of the filler system is one of the strategies currently in use to create tougher composites.

The use of glass fibers as reinforcement in dental composites is not new. The use of randomly-oriented low aspect ratio (AR: length-to-diameter ratio) glass fibers as reinforcing phase in composites was published in 1989³⁶ and in the 1990s composites containing low AR fibers (20–120 µm in length, 6 µm in diameter) associated with filler particles appeared in the market (Restolux, Lee Pharmaceutical, South El Monte, CA, USA, and ALERT, Pentron, Orange, CA, USA). In fact, studies showed higher K_{Ic} values for ALERT compared to other packable and regular consistency materials, but no difference in flexural strength was observed.^{37,38}

Recently, a bulk-fill composite containing high AR E-glass fibers (1–2 mm in length, 17 µm in diameter) was released (EverX Posterior, GC Europe, formerly known as Xenius Base). Its total mass filler fraction is 74.2 wt% (53.6 vol%), with 8.6 wt% (7.2 vol%) of glass fibers.³⁹ Its resin matrix is constituted by BisGMA, TEGDMA and PMMA (polymethyl methacrylate), forming a semi-interpenetrating polymer network (semi-IPN).⁴⁰ As fibers impair polishing, it is indicated as a substructure material and a final layer of particulate composite is mandatory. Overall, its fracture strength does not seem to differ from those of particle-only composites.^{20,41} Fatigue strength of teeth restored with this material also did not differ from that of a conventional composite.⁴² The only report on the material's K_{Ic} showed a significantly higher value, compared to other commercial composites.⁴³

In order to understand the effect of fibers on composite properties, it is important to look at the variables involved in fiber reinforcement using systematic experimental designs. Two important parameters related to composite reinforcement using random, short fibers are the fiber AR and volume fraction. An effective stress transfer from the matrix to the fiber requires fibers with a minimum length

“critical length”), estimated from the fiber strength and diameter (therefore, related to fiber AR) and on the interfacial bond strength between the fiber and the matrix.⁴⁴ For example, the addition of 20 vol% high AR fibers (AR=68) to a commercial flowable composite (filler fraction: 43.6 vol%) had a positive effect on flexural strength compared to low AR fibers (AR=5.2).⁴⁵

The replacement of up to 7.5 vol% of particles by fibers (AR = 140) did not increase the flexural strength of experimental composites containing 60 vol% of fillers. Though randomly oriented fibers are supposed to result in a material with isotropic behavior, it is possible that the insertion of the composite into the mold during specimen preparation results in some fiber orientation perpendicular to load application, which reduces reinforcement efficiency.⁴⁶

On the other hand, studies agree that fiber-containing commercial composites present higher K_{Ic} than particle-only composites.^{37,38,39,43,47} In fact, the replacement of 5 vol% of glass particles by fibers in a composite with 60 vol% of fillers resulted in a two-fold increase in K_{Ic} (from 1.25 to 2.6 MPa.m^{1/2}).⁴⁶ The presence of fibers increases “crack bridging”, *i.e.*, when a crack propagates through the material, fibers pull the crack faces together and, as a result, more energy is necessary for the crack to propagate further.⁴⁸

Besides increasing K_{Ic} , fibers may also interfere with composite polymerization shrinkage. Composites containing continuous, oriented fibers present anisotropic behavior in terms of shrinkage, with lower values being registered in the direction of the fibers in comparison to the perpendicular direction.^{43,49} On the other hand, composites containing short random fibers are expected to show isotropic behavior. However, depending on the specimen configuration and testing method, fiber-containing composites may show lower shrinkage than particle-only composites. For example, Xenius base showed 43–51% lower post-gel shrinkage in comparison to composites with higher filler fractions when tested by the strain gage method.⁴³ Also using the strain gage method, an inverse relationship between fiber content and post-gel shrinkage was observed when 2.5 vol% to 7.5 vol% of the filler particles were replaced by 1.4 mm glass fibers in a 60 vol% filler experimental composite, with shrinkage reductions reaching 70%

at the highest fiber content.⁴⁶ Strain gages record mostly the shrinkage taking place adjacently to the sensor grid and during specimen preparation, some degree of fiber orientation may result from pressing the composite against it. Consequently, the material does not behave as totally isotropic. When using the mercury dilatometer, a composite containing 6 vol% of fibers and 54 vol% particles showed a much subtler reduction in total shrinkage (11%) in comparison to the 60 vol% particle-only composite. As polymerization stress development is the result of complex interactions between composite elastic modulus, shrinkage and testing system compliance, such difference in shrinkage was not enough to reduce stress magnitude.⁴⁶ Other studies showed that EverX Posterior developed either similar or higher polymerization stress and gap formation *in vitro* compared to other bulk-fill materials.^{3,50}

Strategy 2B: Self-healing composites

Failure mechanism in polymers can be described as the result of damage accumulation, where microcracks propagate due to thermal or mechanical stress concentration at the crack tip.⁵¹ Therefore, bringing crack extension to a halt by sealing the crack faces (“crack healing”) may increase composite life-span. The development of self-healing polymers was a major breakthrough in polymer chemistry. According to Huyang et al.⁵² “self-healing mechanisms are biomimetic models of autonomic repair systems in living tissues that efficiently handle damage, for example, the healing of a broken bone”. The “proof of concept” for this approach was published by Dry.⁵³ In a series of experiments, she used hollow glass fibers filled with either a two-part epoxy system or a cyanoacrylate adhesive embedded in epoxy specimens to demonstrate the material’s self-healing ability. Besides recovering part of the initial strength after fracture, the self-repair system was shown to arrest microcracks and prevent crack reopening.

Research in dental composites self-repair systems derives from the approach introduced by White et al.⁵⁴ They synthesized dicyclopentadiene (DCPD) -filled microcapsules (50–200 μm) with a urea-formaldehyde (UF) shell and dispersed them in an epoxy matrix. When the crack front reached a microcapsule, its shell was

ruptured and DCPD was released within the crack plane by capillarity. Polymerization of the healing agent was triggered by contact with a transition metal catalyst (Grubbs' catalyst) incorporated in the matrix. A healing efficiency of 60% was reported in notched specimens containing 10 wt% of microcapsules and 2.5 wt% of catalyst, monotonically loaded to failure in mode I (*i.e.*, perpendicular to the precrack) and re-tested after being allowed to heal for 48 hours. In a subsequent development, they tested microcapsules filled with an epoxy-solvent mixture.⁵⁵ In this case, healing occurs by swelling of the set epoxy and transport of the residual amine to the crack plane. The additional epoxy released from the microcapsule increases the chance of crack healing by crosslinking. After a first healing event with a 100% efficiency (*i.e.*, full recovery of the initial K_{Ic}), a maximum of five healing events were verified, with decreasing efficiency due to the depletion of healing agent, as well as the available amine.

Fatigue loading represents a more clinically relevant scenario for testing polymer self-repair than static conditions. It has been verified that under cyclic loading healing efficiency is related to crack growth rate (defined by stress amplitude and frequency), the polymerization rate of the healing agent and the occurrence of rest periods. For example, in an epoxy resin containing 20 wt% of DCPD-filled UF microcapsules, if stress intensity is such that crack extension occurs at a similar rate of that of healing agent curing, the fatigue life extension ranged from 89% to 213%.⁵⁶

The first attempt to formulate a self-healing dental composite used the DCPD-filled UF microcapsules developed by White et al.⁵⁴ Specimens made of a BisGMA/UDMA/TEGDMA resin containing 55 wt% of silanated silica, 5 wt% microcapsules (average size: 50 μm) and 2 wt% of Grubbs' catalyst were tested for K_{Ic} and re-tested after a 7-day healing period at room temperature, with average healing efficiency of 57%.⁵⁷ It should be noted that the presence of the capsules within the resin may provide some benefit in terms of mechanical properties, regardless of the self-healing effect. For example, polyurethane (PU) nanocapsules (~500 nm) containing TEGDMA were synthesized and loaded into a commercial two-step, single-bottle adhesive system. Crack healing was not

expected, as no extra initiators were incorporated. Still, a significantly higher bond strength to dentin was verified for the material containing 9 wt% of nanocapsules, possibly due to a toughening effect provided by the flexible PU shells.⁵⁸

Concerns about the biological safety of DCPD⁵⁹ prompted the research of different self-repair systems for dental composites, also based on microencapsulated healing agents. Reports on the use of poly(urea formaldehyde) microcapsules (average diameter: 70 μm) filled with TEGDMA and a tertiary amine (N,N-dihydroxyethyl-p-toluidine, DHEPT) as activator in experimental composites were recently published.^{60,61,62} This self-repair system uses benzoyl peroxide (BPO) added to the resin matrix as initiator to polymerize the healing liquid. In the first study,⁶² these microcapsules were added to a BisGMA-TEGDMA resin. For microcapsule mass fractions up to 15%, no adverse effects were observed in flexural properties while K_{Ic} increased by 40% at the maximum microcapsule loading. Healing efficiency showed a plateau starting at 10% of microcapsules, of approximately 65%. In a follow-up study, experimental composites containing 35% of reinforcing fillers, 20 wt% of ACP nanoparticles (to foster remineralization), 3.75 wt% of an antibacterial agent (dimethylaminohexadecyl methacrylate, DMAHDM), 0.5 wt% of BPO and different mass fractions of TEGDMA-DHEPT microcapsules were tested. The initial K_{Ic} was not affected by the presence of microcapsules up to 7.5 wt%. Twenty-four hours after repositioning the fragments in the mold, specimens were re-tested and healing efficiency was found to be linearly related to microcapsule content, ranging from 25% (2.5 wt% of microcapsules) to 81% (10 wt%).⁶¹ Healing efficiency of composites with 75% of TEGDMA-DHEPT microcapsules was not affected by prolonged water storage of the specimen prior to initial K_{Ic} test (up to six months), or when healing took place in water.⁶⁰

A self-healing dental composite (or, more precisely, a compomer) based on glass ionomer cement chemistry was recently developed.⁵² Silanated silica microcapsules filled with an aqueous solution of polyacrylic acids (average diameter: 29 μm) were prepared and dispersed in an experimental composite containing a photocurable BisGMA/HEMA matrix and 70 wt% of strontium fluoroaluminasilicate glass

particles. The idea was to form a reparative glass ionomer cement in the crack when the healing liquid is released. Microcapsule silanization was used to improve the interfacial strength between the shell and the resin matrix to favor its rupture rather than interfacial debonding upon meeting with the crack front. Re-testing K_{1c} specimens after four days allowed a maximum healing efficiency of 25%, obtained with a microcapsules content of 10 wt%.

Strategy 3A: Remineralizing composites

Calcium orthophosphate (CaP) particles have been studied as ion-releasing fillers in resin-based composites for decades.^{63,64} Calcium and phosphate ions released from the composite would make the surrounding medium supersaturated, favoring their deposition on the enamel hydroxyapatite (HAP) crystals.⁶⁵ Several CaP phases have been tested as bioactive fillers in restorative composites, for example, amorphous calcium phosphate (ACP),^{66,67} dicalcium phosphate dihydrate (DCPD),⁶⁸ dicalcium phosphate anhydrous (DCPA)⁶⁹ and tetracalcium phosphate (TTCP).⁷⁰

The efficacy of CaP-containing composites in promoting mineral recovery of dental tissues were demonstrated in several studies. For example, a material containing 40 wt% of ACP in a BisGMA/TEGDMA/HEMA matrix was capable of recovering 71% of the enamel mineral content of non-cavitated bovine enamel lesions after four weeks under a static remineralization model and 38% after two weeks under pH cycling (dynamic model).⁶⁴ A resin cement containing 20 wt% of DCPA particles (1.1 μm), 60 wt% of TTCP particles (16 μm) and 1.5 % of sodium hexafluorosilicate in contact with demineralized human dentin promoted an increase in mineral in mineral content between 38% and 47% after 5-week immersion in saliva-like solution.⁷¹ A resin-based material containing 40 wt% of Zr-modified ACP (55 μm) dispersed in a BisGMA/TEGDMA/HEMA matrix led to a 14% mineral recovery in non-cavitated human enamel lesions after 30 days of pH cycling.⁷² The first study associating ACP nanoparticles (116 nm, 40 wt%) and reinforcing glass fillers (1.4 μm , 20 wt%) in a BisEMA/TEGDMA/HEMA matrix verified a 22% remineralization in pH cycling conditions similar to those used in the previous study.⁶³ It is interesting

to point out that these *in vitro* studies share the characteristic of formulating their experimental materials with fairly hydrophilic resin matrices, which facilitates fluid transit through the material, consequently increasing ion release. Also, notice that experimental models utilizing pH cycling result in lower mineral recovery in comparison to static remineralization models (*i.e.*, immersion in calcium solutions). The protective effect of CaP-containing composites against enamel demineralization was verified in an *in situ* study. Cavity preparations in human enamel fragments were restored with an experimental composite containing ACP (116 nm, 40 wt%) and glass fillers (1.4 μm , 20 wt%) in a less hydrophilic matrix (BisGMA/TEGDMA). After 14 days in the presence of biofilm, mineral loss was 59% lower in fragments restored with the ACP-containing composite in comparison to a control.⁷³

Composites containing CaP particles are considered “smart materials” because ion release increases in more acidic conditions due to an increase in particle erosion.⁷⁴ Also, in order to maximize ion release, particles with high surface area are preferable.⁷⁵ Ion release increases exponentially with particle volume fraction.⁷⁶ Finally, the hydrophilicity of the resin matrix must also be taken into account, as it interferes with the water access to the particles and, consequently, with ion release.⁷⁷ As it could be expected, ion release does not occur indefinitely and fine-tuning all the variables to come up with a material able to provide a long-lasting protection against demineralization is challenging. Recently, it was demonstrated that a composite containing 20 wt% ACP and 50 wt% silanated glass was capable of recharging after complete exhausting its ion release (after 70-days immersion at pH = 4) by immersion in calcium and phosphate solutions (one minute, 3x/day, for three days).⁷⁸

Although high volume fractions of CaP particles may increase the composite remineralizing potential, their presence in the material may cause a significant reduction in some of its mechanical properties.^{68,70,79} For example, an experimental composite containing 40 vol% of reinforcing glass (0.5 μm) and 20 vol% of DCPD (8 μm) presented a 28% lower flexural strength in comparison with a control containing 60 vol% glass fillers. K_{1c} was initially improved with the replacement

of some of the glass fillers with DCPD. However, after 28 days of storage in water, a 35% reduction was observed in the DCPD-containing composite, while no significant change in occurred in the control.⁶⁸

The main cause of the negative effect of CaP particles on the mechanical properties is the lack of a strong chemical bonding between them and the resin matrix.^{70,80} To eliminate or at least reduce this limitation, functionalization of the CaP particles was attempted.^{81,82} The use of silane to functionalize DCPA particles caused a significant increase in composite fracture strength, compared to a control containing non-silanized DCPA; however, ion release was compromised due to the silane hydrophobic character, which hinders the access of water to the particles.⁷⁵ Good mechanical results were also obtained when HAP particles were treated with acrylic and methacrylic acids. Unfortunately, ion release was not tested.⁸² Recently, the synthesis of TEGDMA-functionalized DCPD particles was described.⁸³ TEGDMA is capable of bonding to Ca²⁺ via ion-dipole interactions with the oxygen atoms from the ethylene glycol groups. The incorporation of 20 vol% of these particles in a BisGMA/TEGDMA resin resulted in a 32% increase in flexural strength in comparison to the material containing non-functionalized particles.⁸⁴ A similar improvement was observed in a subsequent study where an experimental composite containing 40 vol% of barium glass (0.5 µm) and 20 vol% of TEGDMA-functionalized DCPD (19 µm) was compared to a similar formulation containing non-functionalized DCPD.⁸⁵

Composites containing CaP particles may undergo more severe degradation after prolonged water immersion than their conventional counterparts, possibly due to the higher water sorption allowed by the transit of fluids along CaP-matrix interfaces.⁸⁶ For example, composites containing DCPD particles showed up to 33% reduction in flexural strength after 28 days in water versus a 16% reduction for composites without DCPD.⁶⁸ But no difference in strength was observed after two years of immersion in water for composites containing 10–20 wt% of ACP nanoparticles (112 nm) and 65–50 wt% of barium glass (1.4 µm) and the control with 75 wt% of glass fillers.⁸⁷

Despite all the research activity involving CaP composites, it seems that the concept has not yet been embraced by dental materials manufacturers. The sole

exception is a restorative composite containing 38 wt% ACP, released in 2012 (Aegis V, Bosworth, Skokie, USA). Literature reports and manufacturer information are scarce. Its flexural strength is reduced, comparable to that of a microhybrid composite, which explains its indication only for restoring class V cavities. From the same manufacturer, ACP-containing sealant and orthodontic cement showed remineralizing potential similar to fluoride-containing materials *in vitro*.^{88,89}

Strategy 3B: Antibacterial composites

While adhesive systems containing antibacterial agents have been on the market for several years, restorative composites with antibacterial activity are still under development. Ideally, antibacterial composites must meet a critical set of requirements, including: 1) non-toxicity,⁹⁰ 2) antibacterial action against a broad spectrum of microorganisms⁹¹ and 3) maintain a long-lasting effect.^{92,93} Also, it is very important that incorporation of antibacterial agents does not compromise the mechanical and optical properties of the restorative material.^{93,94}

The association between quaternary ammonium (QAM) and methacrylate terminal groups results in an antibacterial monomer with low lexiviation (*i.e.*, leaching) levels.^{90,91,92,95} The first attempt of incorporating a copolymerizable antibacterial monomer in experimental composites was reported more than 20 years ago. When MDPB (12-methacryloyloxydodecylpyridinium bromide) was incorporated into a BisGMA/TEGDMA composite (filler fraction: 83 wt%) in 0.1 wt% and 0.2 wt% fractions, the growth of *S.mutans* on the composite surface was inhibited for up to 90 days, without significant effects on the composite flexural properties.⁹⁶ The proposed antibacterial mechanism for these monomers is that quaternary ammonium would damage the bacterial cell membrane, leading to cell death.⁹⁰

QAMs were also incorporated within experimental composites associated with polyethyleneimine nanoparticles (140 nm). Due to their positive charge, these nanoparticles (QPEI) are attracted to the bacterial cell membrane. This charge imbalance increases cell permeability, ultimately leading to disruption of the cell membrane.⁹⁷ The incorporation of 1 wt% of these nanoparticles into commercial composites did not

reduce their initial flexural properties and inhibited the growth of *S mutans* and *A viscosus* for up to four weeks.⁹⁸

Another example of an antibacterial monomer with methacrylate functionality is dimethylaminohexadecyl methacrylate (DMAHDM). It has been tested in association with a protein-repellent biopolymer, 2-methacryloyloxyethyl phosphorylcholine (MPC), which reduces bacterial adsorption on the composite surface. Composites containing 70 wt% of glass fillers and 1.5 wt% of DMAHDM, associated with 3 wt% of MPC showed higher antibacterial activity against cariogenic and periopathogenic bacteria than either components alone. Flexural properties were not affected by the presence of either compound.⁹⁹ However, MPC is hydrophilic and its presence significantly increases composite water sorption, which may accelerate matrix degradation.⁹¹

Bioactive glass (BAG) particles were also investigated as antibacterial agents in dental composites. An experimental BisGMA/TEGDMA composite with 57 wt% of reinforcing glass and 15 wt% BAG particles (0.04–3 μm , SiO_2 , CaO and P_2O_5) were shown to reduce bacterial penetration into the tooth-restoration interface and tooth demineralization in comparison to a control. The possible hypothesis for bacterial inhibition is a local increase in pH and/or some of the ions directly affecting bacteria.¹⁰⁰ Silver-doped BAG particles (25 μm , SiO_2 -CaO- P_2O_5 - Al_2O_3 - Na_2O - K_2O - Ag_2O) incorporated into a commercial flowable composite at mass fractions of 5% and 15% resulted in significant reduction in *S mutans* activity. As pH remained stable throughout the study, antibacterial activity was ascribed to Ag^+ ion release from the material.¹⁰¹

Though composites containing silver compounds or metallic silver (Ag^0) nanoparticles have shown great efficacy against bacteria without compromising their mechanical properties,¹⁰² their presence even in small concentrations causes significant darkening of the composite.¹⁰³ Zinc oxide particles have a more tooth-like color and were shown to possess antibacterial activity probably due to the release of Zn^{2+} ions, which inhibit the metabolism of sugars and interfere with bacterial enzymatic activity by displacing Mg^{2+} ions.¹⁰⁴ Their efficacy, however, is much lower than that of silver, as 10 wt% of ZnO nanoparticles (40–100 nm) added to a commercial composite showed significant lower

Streptococci inhibition compared to 1 wt% of silver.¹⁰⁴ In another study, the incorporation of up to 5 wt% of ZnO nanoparticles (20 nm) to a commercial flowable composite significantly inhibited *S. mutans* growth in non-aged and 48-h aged specimens. However, specimens aged for one week and four weeks did not show any inhibitory effect.⁹⁴

Chlorhexidine (CHX) was also investigated as an antimicrobial agent in composites. Because CHX salts are not soluble in the resin matrix, they tend to form relatively large agglomerates, which negatively affects composite mechanical properties.¹⁰⁵ To overcome these problems, CHX was loaded into mesoporous silica nanoparticles (MSNs), with significant improvements in mechanical properties compared to materials containing directly added CHX. Furthermore, composites with MSNs sustained a lower surface roughness and allowed for a more controlled CHX release over time.⁹³

Final Remarks: Can All These Strategies Co-Exist?

Some of the above strategies may be mutually exclusive, because there are practical limits to intelligent addition of multiple chemicals - especially to a unitary (light cured) material formulation. Also, with self-adhesive materials there may be limited shelf life due to the incorporation of reactive chemicals. However the strategies 2A and 2B to produce stronger composites might be compatible by incorporation of both fibers and self-healing capsules into the resin matrix. Despite the great potential of bulk fill composites, it may be desirable to have separate base-layer composites with anti-microbial and/or remineralizing functionality. It seems inevitable that some kind of trade off will still be required between ease/simplicity of application and the number of material functions desired and achievable. It is important that some of these strategies be advanced from *in vitro* to *in situ* studies, and then to controlled clinical trials.

Meanwhile, with the present composite materials available, it is essential to deploy them optimally, particularly by optimal light curing. The consequences of failing to do so are serious for restoration longevity. But that is another story.

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