Chapter 9
Emerging Polymers in Dentistry

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Abstract Polymers represent the foundation of modern restorative Dentistry. The majority of dental procedures currently utilized in clinical dentistry depend on the close interaction of polymeric materials with dental tissues. In fact, the dental matrix itself is largely constituted of natural polymers, such as collagen fibrils, that constitute the organic matrix of dentin, cementum and bone. In this chapter, several direct restorative materials will be described in light of their polymeric composition and dental application. Particular emphasis will be given to emerging restorative materials, such as new classes of dental adhesives and composite resins. Additionally, we discuss emerging classes of dental polymers, which have been recently utilized to infiltrate demineralized enamel and to assist remineralization of collagen fibrils in carious dentin.

Keywords Resin composite · Dental adhesion · Bonding · Caries · Dentin · Dental polymer

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Abbreviations

PDL	Periodontal ligament
ECM	Extracellular matrix
Bis-GMA	2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane
HEMA	Hydroxyethyl methacrylate
TEGDMA	Triethyleneglycol-dimethacrylate
10-MDP	10-methacryloyloxydecyl dihydrogen phosphate monomer
4-MET	4-methacryloxyethyl trimellitic acid
Phenyl-P	2-methacryloxyethyl phenyl hydrogen phosphate
PPD	1-phenyl-1,2-propanedione
Lucerin-TPO	2,4,6-trimethylbenzoyl-diphenylphosphine oxide
BAPO	Bisacylphosphine oxide
DPIHP	Diphenyliodonium hexafluorophosphate
MDPB	12-methacryloyloxydodecylpyridinium bromide
BAC	Benzalkonium chloride
CHX	Chlorhexidine
MMPs	Matrix metalloproteinases
PGs	Proteoglycans
GAG	Glycosaminoglycan
EDC/NHS	1-ethyl-3-[3-dimethylaminopropyl] carbodiimide hydrochloride/ n-hydroxysuccinimide
OPACs	Oligomeric proanthocyanidins
PPRF	Prepolymerized resin fillers
QAS	Quaternary ammonium compounds
TCD	Tricyclodecane
SDR	Stress decreasing resin
MMA	Methyl methacrylate
PMMA	Poly(methyl methacrylate)
PILP	Polymer induced liquid precursor
PASP	Poly-L aspartic acid
PGLU	Poly-L-glutamic acid
PVPA	Polyvynilphosphonic acid
PAA	Polyacrylic acid
ACP	Amorphous calcium phosphate

Introduction

Dentistry encompasses a breadth of clinical activities that can range from complex surgical oral maxilofacial reconstructions, preventive treatments against pathological conditions, restorative procedures for treating tooth decay, among a long list of procedures that make up the field of dental sciences. The application of different

types of polymers in these procedures is vast, and it can be said that polymers have paved the way for important transitions in clinical dentistry [1].

Like any biological tissue, the tooth complex is essentially constituted of a complex combination of biopolymers [1]. These structures—which include enamel (the outer layer covering the tooth crown), dentin (the tissue immediately underneath the enamel), pulp (the sensory unit and vascular component of the tooth), cementum (the structure covering the root of the tooth), periodontal ligament (PDL-the soft tissue anchoring the root of the tooth), and alveolar bone (the site of anchorage for the tooth in the oral cavity) [2]—present a wide range of biopolymeric building blocks, in the sense that they are composed of proteins with repeating monomeric units having carbon as a structural backbone forming well-defined organic matrices [3].

Biopolymers are present in dental tissues in the form of polynucleotides, 13 or more nucleotide monomers covalently bonded in a chain (i.e. RNA and DNA), which contribute to the genetic make up regulating the functions of odontobalsts and stem cells in the dental pulp [4]. Similarly, polypeptides, which are short polymers of amino acids, form the basic building blocks of the extracellular matrix (ECM) in dentin, alveolar bone, cementum, PDL and pulp in the form of collagen fibrils [1] and elastin (in the pulp and PDL/bone vasculature) [5]. Another example of biopolymers present in the tooth are the polysaccharides that also compose the ECM. These structures are carbohydrate molecules composed of long chains of monosaccharide units bound by glycosidic bonds that are present in dental tissues mostly in the form of proteoglycans and glycosaminoglycans [1, 6].

Given that the structural building blocks of the tooth are essentially composed of polymeric constituents, it is no surprise that the progress of dentistry and dental biomaterials would seek to approximate the polymeric composition of the natural tooth [7]. Interestingly, however, it was not until the mid 1900s that polymeric materials emerged as an alternative material for dental applications [8].

The origins of dental sciences date back to approximately 500 year before Christ, when reports suggest that Hippocrates and Aristotle studied patterns of tooth eruption, dental extractions techniques and methods for stabilization of loose teeth using metallic wires [8]. Ever since the description of these procedures by antique societies, metals have formed the basis for the majority of dental treatments. Thus, it may be argued that, for a long time, metals formed the basis for clinical dentistry. The ability of polymers to provide excellent aesthetic quality, easy manipulation, tunable physical properties, amongst other advantages, has arguably allowed the greatest transition in dental sciences. In 1949, Hagger developed the first type of polymeric restorative system in an attempt to bond acrylic resin to dentin [9]. This, followed by a wide range of studies on dental polymers, particularly the ones pioneered by Buonocore et al. in 1955, which represented the greatest shift in dental materials development and applications to date. Ever since it was demonstrated that polymeric dental materials had sufficient biocompatibility for direct restorations, the focus of dental materials development shifted from metals to polymers, a trend that has remained virtually untouched since the mid 1900s.

Nowadays, polymers are largely used for restorative applications as a treatment for decayed teeth, as materials for prosthetic applications in the fabrication of partial and complete dentures, in different laboratorial methods for molding and modeling, and more recently for controlled remineralization of teeth and tissue engineering, amongst other applications. In this chapter, we will discuss the applications of polymers in the wide field of clinical dentistry, with particular emphasis in restorative procedures and emerging 'smart' polymeric materials with potential dental applications.

Polymers in Dental Adhesion

Composition and Classification of Dental Adhesives

Adhesion of restorative dental biomaterials to tooth substrates is primarily based on micromechanical interlocking of resin monomers to the components of the hard tissue. In addition to micromechanical retention, chemical bonding can be achieved via functional monomers, which are able to chemically and mechanically bond to the tooth [10, 11]. While commonly classified as generations by industry, the most appropriate way to classify the current adhesive systems is by the dentin surface treatment and application techniques. The application techniques recommended by manufacturers is greatly influenced by the composition of the adhesive polymer [12]. A summary of the current adhesive systems is shown in Table 9.1.

Table 9.1 Contemporary dental adhesive systems and their composition

Clinical steps	Etching	Primer	Resin
Etch-and-rinse (3-steps)	Phosphoric acid (30–35 %)	HEMA, organic solvent (ethanol/acetone/water), proprietary monomers	Hydrophilic and hydrophobic monomers (HEMA, TEGDMA, Bis-GMA, UDMA), initiators
Etch and rinse (2-step)	Phosphoric acid (30–35 %)	Hydrophilic and Hydrophobic monomers (HEMA, TEGDMA, Bis-GMA, UDMA, proprietary monomers), organic solvent (ethanol/acetone/water), fillers, initiators	
Self-etching (2-step)	Functional and hydrophillic acidic monomers (Phenyl-P, 4-MET, 10-MDP, MDPB and HEMA), initiator, solvents and water		Functional, hydrophilic and hydrophobic monomers (Bis-GMA, TEGDMA), initiator
Self etching (1-step)	Functional, hydrophilic acidic and hydrophobic monomers (4 META, Phenyl-P, 10-MDP, HEMA, Bis-GMA, UDMA), initiators, solvents and water		
Universal	Optional Phosphoric acid (30–35 %)	Functional, hydrophilic and hydrophobic monomers(10-MDP, HEMA, Bis-GMA, TEGDMA), proprietary monomers, solvent, initiator	

The basic components of a dental bonding system include a primer, the adhesive resin, an organic solvent and polymerization initiators. Primers contain *hydrophilic* blends of resin monomers/co-monomers. Adhesive resins contain blends of *hydrophobic* monomers/co-monomers. Solvents are added to the systems to enhance resin infiltration into the tissue, whereas photoinitiators are commonly used for convenient operator-controlled photopolymerization of the adhesive. Other ingredients such as fluoride, glutaraldehyde, antimicrobials are also commonly added to the mixture in an attempt to further protect or strengthen the adhesive interface.

The adhesion mechanism is tissue-dependent; in general bonds with greater clinical durability are achieved on enamel surfaces when compared to dentin. The surface treatment, adhesive chemistry, application protocol and different forms of enamel and dentin are also determinant factors in the adhesion process. The main mechanism of bonding to sound enamel is the formation of resin microtags following infiltration of resin monomers into a superficially decalcified microstructured prismatic layer. In dentin, resin tags can also be formed and it is estimated that 60–80 % of the bond strength to dentin is provided by the formation of the hybrid layer, which is the impregnation of the collagen network with the adhesive resin (further details below). The complexity in composition and structure of dentin is a major obstacle for proper interfacial sealing and high bond strength overtime. A proof to the importance of the hybrid layer was poor success rate of earlier dental adhesive systems that did not bond to dentin. Due to the importance of dentin to the extended service-life of a restoration, novel materials have been developed based on high affinity for the dentin structure components. The process of hybrid layer formation is described below.

The Process of Hybrid Layer Formation

In order to properly bond to dentin, resin monomers must interact with the dentin matrix. The term hybrid layer is used to describe the physical interaction between the resin and the demineralized dentin. Adhesion in dentin is mainly obtained by micromechanical inter-locking of cured resins and the exposed dentin collagen network. Earlier adhesive systems provided the foundation for the development of a hybrid layer in dentin. These systems called “etch-and-rinse” remove smear layer—a surface layer composed of organic and inorganic debris resulting from the drilling process—smear plugs and superficially decalcify the dentin with a separate application step of acidic etchant—generally phosphoric acid. Microscopically, a clean surface with the exposed collagen fibrils is apparent and ready for the priming step with hydrophilic-based monomers and subsequent coating with hydrophobic blends of resin monomers. Following resin polymerization, the infiltrated resin will be anchored onto the exposed dentin matrix. This complex process takes place very quickly, usually between 30–90 s.

The primer is constituted of a blend of organic solvents and hydrophilic monomers to enable proper resin infiltration. Following the priming step, a more hydrophobic adhesive layer is applied acting as a barrier for the outward water movement from the dentin tubules, also providing the necessary hydrophobicity to chemically bond the adhesive material with the resin composite, which will make up the bulk of the dental restoration. Because of the presence of water and organic components, the technique is highly sensitive. The surface of dentin must remain hydrated prior to the application of the primer to avoid collapse of the collagen exposed during decalcification. The technique was developed in the early 90s and is called *wet bonding technique*. Overwetting and overdrying the dentin will result in a significant decrease in the bond strength. The later generation of etch-and-rinse system simplified the technique by applying the primer/adhesive at the same time (Table 9.1).

Self-etching systems also have the ability to form hybrid layers however in a limited manner and non-uniform fashion. A thinner hybrid layer is also observed when functional acidic monomers are used to demineralize and simultaneously infiltrate the dentin matrix. The functional monomers in the adhesive blends are ionized in water and etch the dentin surface while penetrating within the collagen framework [12]. The adhesive system is further polymerized in both techniques, resulting in mechanical interlocking with the dentin matrix. Hydrophilic monomers are preferable for penetrating within the dentin matrix after demineralization. However the excess water may result in separation of the hydrophilic and hydrophobic components of the adhesive system, decreasing the mechanical properties of the resin-dentin interface [13]. Good penetration of the adhesive system enveloping the exposed collagen fibrils is important for the success of the hybridization process.

Adhesive Interface Degradation

The hybrid layer is believed to be essential for maintaining the integrity of the resin-dentin bonded interface. The complete replacement of mineral by resin monomers during infiltration is unlikely even with the use of low viscosity hydrophilic monomers and organic solvents [12]. The infiltration of adhesive into demineralized dentin is influenced by the diffusion ability of the resin monomers plus organic solvents within the dentin matrix. Complete enveloping of the dentin matrix is likely not to occur by passive infiltration of the resin monomers due to the size of the molecules and the available spaces within the collagen molecules [1, 14]. The incomplete resin infiltration affects the stability of the interface by establishing pathways for fluid penetration accelerating hydrolytic and enzymatic degradations.

In addition to the hybrid layer, critical components of the adhesive interface are the underlying dentin and the adhesive layer itself (Fig. 9.1). The biomechanical properties of these 3 components are distinct and their integrity overtime also

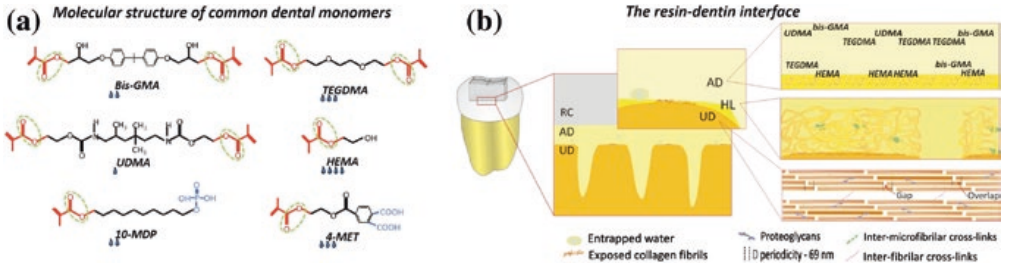

Fig. 9.1 **a** Typical monomer molecules used in dental adhesive systems. **b** Schematic of the resin dentin interface

plays an important role in the service-life of dental restorations. Hydrolytic and enzymatic degradation mechanisms are believed to be major players in the degradation of the interface components. The processes can be accelerated by the chemical, mechanical stresses in the oral environment. Some of the well-established mechanisms of interfacial degradation are described below in detail.

Degradation of Resin at the Interface

The hydrolysis of monomers and breakdown of polymeric chains of methacrylate-based resins are associated with adhesive degradation. After polymerization the adhesive resins absorb water by diffusion through poorly polymerized chains and hydrophilic domains [15–17]. The distance between polymers tends to increase, allowing water to stay entrapped between the polymeric networks, decreasing the mechanical properties of the polymer [16, 18]. The decrease in the modulus of elasticity of the polymer, will allow for polymer chain movement, facilitating the swelling of unreacted monomers [19]. Water can break the ester bonds in methacrylate monomers. In addition to hydrolysis, degradation of 2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (Bis-GMA), by salivary and bacterial esterases has been reported [20, 21]. Hydrophilic monomers are used as priming agents to facilitate the diffusion of resin into the collagen rich layer in dentin. However, hydrophilic monomers such as HEMA (Hydroxyethyl Methacrylate) and diluent monomers with ethylene glycol group (i.e. TEGDMA—triethyleneglycol-dimethacrylate) greatly increase the water sorption of adhesives [22].

The clinical technique can also affect the performance of dental adhesive systems. Significant reduction in the degree of conversion and mechanical properties of adhesive systems was observed when solvents were not properly evaporated [23–26]. The application of simplified-step adhesive systems to an excessively wet dentin surface may lead to phase separation and a hydrophobic-poor and hydrophilic-rich zone may be formed, lowering the stability of the adhesive interface [13]. Acidic monomers remain active when poorly polymerized resulting in continuous etching of the underlying dentin [27].

Degradation of Dentin Matrix at the Interface

Dentin matrix is mainly composed of type I collagen fibrils, non-collagenous proteins and enzymes [1, 28]. Proteolysis of collagen and non-collagenous components are associated with loss of anchorage to the dentin reducing the bond strength and increasing permeability at the resin-dentin interface. At the adhesive interface, the organic dentin matrix can either be left exposed by incomplete resin infiltration or become exposed following degradation of adhesive components. The exposed collagen is vulnerable to hydrolytic and proteolytic degradation. Collagen degradation at the interface has been linked to host-derived enzymes that are commonly latent in fully mineralized dentin [29, 30]. More specifically, the degradation process takes place by activation of host-derived matrix metalloproteinases (MMPs) and cysteine cathepsins [31]. The MMPs are zinc and calcium-dependent proteolytic enzymes capable of degrading the organic network. Collagenolytic (MMP-1, -8 and -13) and gelatinolytic (MMP-2) enzymes, can cleave the collagen triple-helical molecule in ¼ and ¾ fragments. The denatured fragments can be further degraded by gelatinases and other non-specific tissue proteinases.

Proteoglycans (PGs), which represent about 3 % (w/v) of the organic composition of dentin, are organic structures strongly bound to collagen which play important roles on the structure and biomechanics of the matrix. The most prevalent PGs in dentin, decorin and biglycan, contain either one (decorin) or two (byglycan) glycosaminoglycan (GAG) chains attached to a core protein. In mature dentin, negatively charged GAGs provide tissue hydration and organization by interconnecting adjacent fibrils. Selective removal of GAGs and PGs results in decreased mechanical properties of mineralized dentin and also significantly affects the resin-dentin bond strength. Decrease in the resin-dentin bond strength of PGs-depleted dentin matrix has been reported following a re-wetting restorative technique [32]. Resin infiltration is compromised due to the inability of PGs- and GAGs- depleted dentin matrix to re-expand following surface desiccation. Reports have also shown that under hydrated condition, enzymatic removal of PGs may result in better diffusion of monomers into the dentin tubules [33], as PGs control diffusion through the matrix and water displacement. The function of PGs on mature dentin deserves more attention.

Emerging Concepts and Future Prospects for Polymers in Dental Adhesion

It is estimated that resin composite restorations have a service life of 6–7 years, which is far less than half of the service life of dental amalgam. The main reason for replacement of direct adhesive resin composite restorations is secondary caries. Therefore failures at the interface has, to a great extent, inspired development of novel strategies to reduce degradation of the resin-tooth interface. Limitations within the material and intrinsic properties of the dentin have

sparked a need to acknowledge the biology nature of the tissue as well as new directions in the resin chemistry that has been used in dental adhesive systems for the past 40 years. Some of the emerging and future concepts are detailed in the two sub-items below.

Material Perspective

Poor degree of conversion of dental resin monomers, elution of un-polymerized monomers and degradation of polymeric chains by enzymatic and hydrolytic challenges, have all been associated with the low stability of the resin at the bonded interface. Novel approaches have focused on improving the adhesion to the dental tissue as well as increasing stability of the resin and resin-dentin interface.

Resin monomers promoting chemical bond to enamel and dentin have been added to many contemporary adhesive systems in an attempt to achieve high bond strength via chemical bonding to the inorganic component of the tissue [34]. Specifically, formation of ionic bonds between 10-methacryloyloxydecyl dihydrogen phosphate monomer (10-MDP) and tissue hydroxyapatite crystals resulting in stable Ca-MDP salts [11]. Other functional monomers are also capable of chemical interaction with the tooth inorganic content. The functional monomers 4-methacryloxyethyl trimellitic acid (4-MET) and 2-methacryloxyethyl phenyl hydrogen phosphate (Phenyl-P) can also interact with hydroxyapatite crystal; however a more stable reaction is observed for Ca-MDP resulting salts [10, 11].

Aiming at establishing a polymeric chain that is less susceptible to degradation, a new class of monomers has been proposed. Silorane-based materials have an oxirane ring-opening mechanism of polymerization which is proposed to reduce polymerization shrinkage. In addition, siloxane molecules are more hydrophobic than methacrylate monomers, which may improve silorane resins` resistance to hydrolysis. However, the mechanical performance of silorane resins are not as predictable as compared to methacrylate resins [35], which may limits its application to areas of non-critical stresses. The substitution of TEGDMA by thiol-ene systems has been studied. Thiol-enes alone may not attain as good mechanical properties as methacrylate resins, but in association, the mechanical properties were equivalent. The methacrylate-thiol-ene resin systems showed increased methacrylate functional group conversion and decreased volumetric shrinkage [36, 37] and are promising alternative dental restorative materials.

Additional improvements on the degree of conversion of the adhesive systems were observed with new and less hydrophobic initiators of polymerization. Camphorquinone and aromatic amines are the most commonly used photoinitiator systems for light-activated dental resins, but they can be excessively hydrophobic making it difficult to activate the more hydrophilic monomers at the adhesive systems. The addition of alternative initiators such as 1-phenyl-1,2-propanedione (PPD), 2,4,6-trimethylbenzoyl-diphenylphosphine oxide (Lucerin-TPO) and bisacylphosphine oxide (BAPO) improve resin polymerization within hydrophilic domains and reduce susceptibility to inactivation by

acidic adhesive monomer in self-etching systems. The use of diphenyliodonium hexafluorophosphate (DPIHP) in Bis-GMA and HEMA based experimental adhesives accelerates the resin polymerization and improve the mechanical properties [38].

Biological approaches to reduce degradation of the organic matrix resulted on the investigation of functional monomers to inhibit collagenolytic enzymes. An example is the incorporation of 12-methacryloyloxydodecylpyridinium bromide (MDPB), a polymerizable quaternary ammonium methacrylate [39], into self-etching resin adhesive blends. As for total-etch adhesive systems, an enzyme inhibitory effect can be achieved by adding a quaternary ammonium group, the benzalkonium chloride (BAC), to the etching solution. Studies using experimental materials showed possible incorporating MMP inhibitors in the methacrylate resin composition, aiming to a slow and continuous release of the inhibitors within the adhesive interface.

Tissue Perspective

As a major component of the bonded interface, the dental tissue components have a dramatic effect of the stability of resin-tooth interface. While there is still much to learn about the composition and role of organic components in different forms of dentin and enamel, there is a consensus that the stability of the dentin matrix remains key to the long-term strength and permeability of the interface.

The application of enzyme inhibitors to prevent dentin matrix degradation has been extensively investigated and few materials are already available to allow dental practitioners to rinse the surface with agents such as chlorhexidine (CHX). CHX is a potent antimicrobial agent and it can inhibit MMP-2, -9 and -8 by binding to the enzyme's active sites. Similarly, it interacts with cysteine cathepsins, likely by interacting with the S2 subsites [40, 41]. It has been suggested that low concentrations of CHX (0.05–0.2 %) can inhibit the collagenolytic activity of dentin matrix, however the relative low substantivity of priming solutions may limit the long-term protective effect. Among other synthetic MMP inhibitors are the modified tetracycline. Special attention has been given to Galardin, a hydroxamate-based bisphosphonate, which inhibits MMPs by chelating its zinc active sites [31, 42]. This potential effect against MMP-1, -2, -3, -8 and -9 may reduce the bond strength loss overtime when compared to CHX. Because the inhibitory effect is mainly due to competitive binding of the inhibitory solutions with specific sites, the effectiveness is concentration dependent.

Remineralization of unprotected collagen at the dentin-resin interface has been proposed to preserve the adhesive bond strengths overtime. The biomimetic remineralization strategy is based on the use of polyanionic molecules such as polycarboxylic and polyphosphonic acids, which will be explained with greater detail below. The molecules mimic the mineral nucleation and growth control functions of endogenous non-collagenous proteins bound to collagen. In vitro intra-fibrillar

and extra-fibrillar mineralization has been reported at the adhesive interfaces in presence of Portland cement (tricalcium silicate, dicalcium silicate, tricalcium aluminate, and a tetra-calcium aluminoferrite) mineralized using the biomimetic mineralization approach.

Another innovative approach is the biomodification of dentin matrix by multifunctional agents that increase the biomechanical properties and reduce the biodegradation rates of the dentin matrix [43]. Enhanced mechanical properties of biomodified dentin matrices are a result of the presence of non-enzymatic collagen cross-links induced by synthetic and nature-derived agents. These agents are also potent enzyme inhibitors and greatly decrease biodegradation of dentin in presence of host-derived enzymes as well as bacterial collagenase. Plant-derived oligomeric proanthocyanidins (OPACs), in particular, strongly interact with dentin collagen and also non-collagenous components such as PGs and endogenous proteases. Glutaraldehyde is another effective synthetic agent for collagen crosslinking, however due to its toxicity its clinical use is limited. 1-ethyl-3-[3-dimethylaminopropyl] carbodiimide hydrochloride associated with n-hydroxysuccinimide (EDC/NHS) has received much attention as a synthetic option with lower toxicity when compared to glutaraldehyde. Priming dentin with EDC/NHS shows increased long-term stability of the resin-bonded interfaces [44]. Riboflavin [45] has also been studied for this purpose, but the use of UV light may limit its use in clinical setting. Strategies to incorporate most of these agents into the restorative systems are ongoing.

Polymers in Restorative Composites Resins

First introduced over 50 years ago, polymer-based dental materials revolutionized restorative Dentistry primarily due to their outstanding esthetic and adhesive properties. These characteristics have allowed for substantially improved preservation of healthy tooth structures, prevention of postoperative sensitivity, reduction of microleakage, among other advantages compared to dental amalgams.

Over the years, resin based restorative materials have been the focus of a great deal of research, being drastically improved by manufactures, particularly with respect to aesthetic quality and mechanical behavior. Despite great improvements, failure and replacement of dental composite restorations continue to have great impact on clinical outcomes [46]. For instance, restorative composites still present a number of drawbacks, like wear, lack of a consistent degree of conversion, fracture and secondary caries [47, 48].

There have been several attempts to improve clinical performance of composite restorative materials by incorporating novel multifunctional monomers, developing different polymerization strategies or modifying filler components of the formulation. The following sections will explore some of the recent developments in restorative polymer composites.

Composition and Classification of Composite Resins

Composites used in Dentistry were developed in 1962 by combining dimethacrylates (epoxy resin and methacrylic acid) with silanized quartz powder [49]. Modern restorative composites are comprised of synthetic monomers, typically dimethacrylates, reinforcing fillers, typically made from radiopaque glass, quartz or silica, chemicals which promote or modify the polymerization reaction, and silane coupling agents which bond the reinforcing fillers to the polymer matrix [26].

The resin matrix of commercial dental composites has bis-GMA (bisphenol-A-glycidyldimethacrylate) as its predominant base monomer. Due to its high viscosity, bis-GMA is mixed with other dimethacrylates, such as TEGDMA, UDMA or other monomers of lower molecular weight [26, 50] to reduce viscosity. The monomers are heavily reinforced with filler particles, which add dimensional stability, improve wear and strength of the material, also reducing polymerization shrinkage [51].

A number of classification systems have been proposed to describe restorative composites. These materials may be distinguished by their consistency, and classified as flowable, conventional and packable [26]; but the most used classification system is based upon filler particle size. As restorative composites have evolved, the size of filler particles and their size distribution have been changed in an attempt to achieve the best possible mechanical properties while maintaining esthetics.

Initial formulations of dental composites (also known as *macrofill*) had average particle-sizes ranging from 10 to 50 μm. Clinically they were very resistant, but difficult to polish, also retaining poor surface smoothness overtime. *Microfill* composites generally present a wide range of size-distribution of silica particles (40–400 nm). At this size, filler loading represents a challenge for manufacturing composites with higher filler content due to agglomeration of the small particles in the matrix. These characteristics render microfilled composites highly polishable, but generally weak due to their relatively lower filler content and particle size.

One of most recent innovations in composite resins has been the development of *nanofil* composites, containing nanoscale particles ranging from 1 to 100 nm with a more homogenous size distribution. The increased filler content results in a lower amount of resin, which may significantly reduce polymerization shrinkage and improve the physical performance of nanocomposites [52]. Further details on the advantages of nanocomposites are presented in Sect. "Nanocomposites".

The majority of resin composites in clinical use today are categorized in the general term of *hybrid or micro-hybrid composites* [41]. This broad category includes traditional hybrids, midifill, and minifill composites. The "hybrid" denomination implies a resin composite containing submicron inorganic filler particles and fine (over one micron) particles. Traditional hybrid resins consisted of a combination of 10–50 μm filler particles with amorphous spherical silica reinforcing particles of 40 nm. Midifill composites contain average particle sizes slightly greater than 1 μm, but also containing 40 nm-sized fumed silica microfillers. Minifill (also referred as mycrohybrid) materials present refinements in particle size, which generated restorative composites with sub-micron particles averaging from 0.4 to 1 μm.

Most manufacturers have modified the formulation of their mycrohybrids to include more nanoparticles, and have named this category as nanohybrids [26]. The combination of various sizes of filler particles corresponds to an improvement in physical properties as well as acceptable levels of polishability [53].

Emerging Classes of Composite Resins

Anti-caries and Ion-Releasing Polymers

Due to the high frequency of recurrent caries after restorative treatments, much attention has been given to the therapeutic effects manifested by direct restorative materials. Restorative composites have demonstrated to accumulate more biofilm over time, when compared to enamel and other restorative materials, thus favoring the development of recurrent caries around these restorations [54]. Therefore, in an attempt to control or even prevent secondary caries, alternative clinical methods for caries prevention have been proposed including the search for new restorative materials with antibacterial activity.

Great emphasis has been given to the development of fluoride releasing materials, however, the direct antibacterial effect of dental materials is another important property as the inactivation of bacteria is a direct way to eradicate the cause of dental caries. Many attempts for developing dentin-bonding systems and restorative materials presenting antibacterial activity have been performed [55–62].

In the pursuit of developing composites with antibacterial activity, alterations to the resin matrix and filler components have been performed. Alterations of resin matrix constituents have included two relevant methods: firstly, the addition of soluble and immobilized antimicrobial agents in the resin matrix; secondly, the alteration of the filler components by addition of silver. Similarly, the immobilization of an antibacterial agent in a prepolymerized resin filler (PPRF) utilizing an antibacterial monomer has been previously reported [63].

Polymers with Soluble Antimicrobial Agents

The antibacterial effects of the restorative composites are relevant primarily in inhibiting plaque accumulation on the surfaces of the restorative material and tooth structures surrounding the restoration. Soluble antimicrobial agents added to the resin matrix, when exposed to a wet environment, have a tendency to be released from the restorative material, thus preventing plaque accumulation. Commonly, large amounts of these agents are released within a few days, followed by a dramatic decrease in concentration.

Chlorexidine has been the most frequently antibacterial agent incorporated into the resin matrix, and has demonstrated a strong antibacterial activity due to the release of antibacterial agents [64]. However, while a strong effect against bacteria

has been obtained, the antibacterial activity drastically decreases over time, since large amounts of the agent are leached out within a few days [65]. Furthermore, it has been reported that the addition of chlorhexidine gluconate at a concentration of as low as 1 % resulted in significant a reduction of tensile and compressive strengths of restorative composite resins strengths [35].

Soluble fluoride agents have also been used to modify the resin matrix and obtain antibacterial properties in resin composites. Fluoride levels leached from composites are mostly much lower compared to levels released from conventional or resin-modified glass-ionomers [66]. Fluoride releasing resin composites might contribute to the decrease in cariogenic composition of dental biofilms if an appropriate amount of fluoride is released in the early stages of biofilm formation [67], yet challenges in developing composites with a sustained fluoride release remain.

Polymers with Immobilized Antimicrobial Agents

The immobilization of antibacterial components in the resin matrix has been another attempt to modify resin components to render restorative materials caries-resistant. This approach is used to obtain antibacterial composites that do not release any antibacterial component. Rather, the immobilized agent acts as a contact inhibitor against bacteria attaching the material surface [32].

To that end, quaternary ammonium dimethacrylate monomers, such as 12-methacryloyloxydodecylpyridinium bromide (MDPB), were copolymerized with resins to yield antibacterial activity. MDPB was developed by combining a quaternary ammonium—which presents a wide spectrum of antibacterial activity—and a methacryloyl group, incorporated into the composite matrix. This agent copolymerizes with other monomers in the composite and thus, the antibacterial component is covalently linked to the polymeric network [32]. The immobilized agent does not leach out of the composite but functions as a contact inhibitor against bacteria attaching to the surface, therefore its effect is not able to reach the tooth structures surrounding the restoration [68]. In summary, the effects of the MDPB-containing composites are not so intensive as the materials that release antibacterial agents. Its effect is mainly bacteriostatic, as the agent cannot penetrate through the cell wall or membrane unlike free antibacterial agents described above [32].

In order to improve the antibacterial activity of these systems, the addition of antibacterial monomers in prepolymerized resin fillers (PPRF) have also been reported. Using this method, the PPRF can be highly cured and washed before they are loaded into the composite, thus ensuring greater immobilization of the antibacterial components than when the antibacterial agent is added to the monomer phase. In an attempt to increase the concentration of MDPB in resin composites, the antibacterial monomer was utilized as a PPRF. The incorporation of MDPB to the composite as a PPRF, for instance, has been shown to allow for an increase of MDPB concentration in the order of 10 times, thus promoting more reliable inhibitory effects on plaque accumulation [69]. An experimental

composite prepared by the addition of PPRF-MDPB to a commercially available composite demonstrated to inhibit the progression of artificially induced secondary root caries lesions regardless of adhesive system [70]. The satisfactory results found with MDPB led to the incorporation of quaternary ammonium compounds (QAS) into restorative composites. In recent years, many attempts to incorporate QAS into polymer based restorative materials have been performed, demonstrating good results in antibacterial activity [13, 19, 71, 72]. Therefore, it may be expected that future composites will present relevant antibacterial properties and that this will be a subject of intensive research in future years.

Antimicrobial Fillers

Similar to the modifications described above, alterations to the filler components have been conducted in order to achieve antibacterial composites. Numerous studies have evaluated composites modified by silver-functionalized filler particles. For dental composites, in particular, the use of silver-zeolite, silver-apatite, and silver-supported zirconium phosphate has been reported [46]. Silver-zeolite and silver-apatite show antibacterial effects which are dependent upon the slow release of silver ions, and these effects are expected to last for longer periods of time when compared to materials with embedded antibacterial components. Composites containing silver nanoparticles have demonstrated inhibited biofilm formation and reduction of biofilm viability [73]. However, poor color stability is a common problem for these types of restorative composites.

Low-Shrinkage Composite Resins

Ring-Opening Monomers

One of the main drawbacks in dental composites remains the high polymerization shrinkage of these materials. It is well recognized that the polymerization stresses resulting from polymerization shrinkage of composite restorations can lead to numerous adverse clinical effects, including de-bonding, post-operative sensitivity, marginal discrepancies, among other clinically relevant issues [26]. The extent of shrinkage is generally influenced by the volume of resin, its composition, and the degree of conversion of the cured monomers [41]. Current commercial dental composites have a volumetric shrinkage ranging from 1.6 to 8 vol % [74]. Therefore, the development of non- or minimal-shrinkage dental composites has been the focus of extensive research. Investigators have made several attempts to reduce shrinkage by introducing monomer molecules that present different polymerization strategies to more common linear chain lengthening, such ring-opening monomers like spiro-orthocarbonates [75], epoxy-base resins like the siloranes [76], as well as high-molecular-weight monomers like dimer acid-based dimethacrylates [77], tricyclodecane (TCD) urethane and

organically-modified ceramics (ormocers) [78, 79]. Low shrinkage oxiranes, for instance, are cyclic ethers that polymerize through a cationic ring-opening mechanism, in contrast to the free radical polymerization of methacrylates [54, 80]. Oxirane based-resins have shown many advantageous properties, such as improved depth of cure, lower polymerization shrinkage, higher strength, as well as comparable hardness and acceptable glass transition temperature when compared with conventional bis-GMA-based dental composites [81]. However, residual monomers released from oxirane-based composites after polymerization have shown relevant toxicity [82].

With the similar objective of introducing ring-opening monomers into restorative composites, Weinmann et al. [54] described the synthesis of a new monomer system, a 'silorane' which is an epoxy functionalized cyclic siloxane whose name is derived from the combination of its chemical building blocks *silo*xanes and oxi*ranes*. Siloranes were found to be stable and insoluble in biological fluids [24], while showing a much lower mutagenic potential than those of related oxiranes [83]. Silorane's network is generated by the cationic ring-opening polymerization of the cycloaliphatic oxirane moieties. In these systems, polymerization starts with an acidic cation that opens the oxirane ring and generates a new acidic center, a carbocation [16]. After the addition to an oxirane monomer, the epoxy ring is opened to form a chain or, in the case of two- or more multifunctional monomers, a network. The opening of the oxirane rings during the polymerisation process compensates to some degree for the polymerisation shrinkage [61].

The oxirane rings are responsible for the physical properties and the low shrinkage, while the hydrophobic properties of the material are related to the siloxanes [61]. As a consequence, exogenous discolouration and water absorption are reduced. All these reported advantageous characteristics serve to enhance the potential of silorane monomers to be used successfully in dental composite materials. Weinmann et al. [54] observed a low shrinkage rate (<1 %) and seven times more light stability for the silorane in comparison with resin-based methacrylates. The clinical application of siloranes is limited to the posterior teeth because only a few low translucent colours are available. Additionally, due to its hydrophobic properties, a special adhesive system must be used for silorane restorations.

Stress Decreasing Resin (SDR) Technology

Slowing down the polymerization rate is another mechanism that has been utilized to compensate for stresses generated upon polymerization in resin-based composites. These mechanisms increase the material flow capacity, lower stress build-up and thus promote improved interfacial integrity [84]. A recently introduced flowable resin-based composite material, intended to be used as a liner in occlusal and posterior proximal restorations, differs from conventional resin by incorporating a Stress Decreasing Resin (SDR) technology. This material provides an approximate 20 % reduction in volumetric shrinkage and almost an 80 % reduction in polymerization stress compared to a traditional resin system due to the addition of a urethane

dimethacrylate structure. This is due in part to the larger size of the SDR resin compared to conventional resin systems (molecular weight of 849 g/mol for SDR resin compared to 513 g/mol for Bis-GMA). The SDR Technology comprises the unique combination of such a large molecular structure with a chemical moiety called a Polymerization Modulator, chemically embedded in the center of the polymerizable resin backbone of the SDR resin monomer [85].

Emerging Classes of Low-Shrinkage Composites

Silsesquioxane (SSQ), an organosilicon compound forming a cage structure, have been studied and present great potential for low-shrinkage nanocomposites. The hardness and modulus of nanocomposites with different percentages of SSQ have been shown to decrease when increased amounts of SSQ monomers were added. Authors have interpreted that the incorporation of SSQ monomers helps to reduce both rigidity and polymerization shrinkage [86]. Therefore, in the correct formulation, SSQ materials have great potential to be used as low-shrinkage composites.

Lee and Rhee [87] developed a bioactive poly(methyl methacrylate)/SiO_2-CaO nanocomposite using either dimethyl-diethoxysilane (DMDES) or tetraethoxysilane (TEOS), which could create 2 and 4 siloxane linkages, respectively, after a sol-gel reaction. According to the authors, this nanocomposite can be applied as filler materials for bone cement as well as dental composite resin, because of its good bioactivity and improved mechanical properties. Chen et al. [88] also developed a low-shrinkage, high-strength nanocomposite by using a 4-epoxycyclohexylmethyl-(3, 4-epoxy) cyclohexane carboxylate (ERL4221) matrix with 55 % of 70- to 100-nm nanosilica fillers through ring-opening polymerization. The nanocomposite was shown to exhibit low polymerization shrinkage strain and a low thermal expansion coefficient comparable with that of the methacrylate-based composites. Other type of resin matrix includes photocurable epoxy-polyols, which were shown to have significant advantages over dimethacrylates, including lower polymer shrinkage, no oxygen inhibition layer, higher strength, and equivalent hardness, as well as acceptable glass transition temperatures [89].

Nanocomposites

Nanotechnology or nanoscience is the field that studies the manipulation of structures on the atomic and molecular scales, and where the dimensions of the resulting supra-atomic and supramolecular structures fall under 100 nm. The National Nanotechnology Initiative defines nanotechnology as the creation of functional materials with characteristic dimensions in the range of 0.1–100 nm. When inorganic phases in an organic/inorganic composite become nanosized, they are called nanocomposites.

The relevance of nanotechnology in Dentistry, as exemplified by the widespread use of nanoparticles in dental composites, is not new [90]. Colloidal silica

particles of a diameter of approximately 40 nm have been in use in dental microfilled and hybrid composites for more than 10 years [91]. Currently, dental nanocomposites are composed of a blend of nanofillers distributed in a dispersed form or as clusters. Nanomers are monodispersed, non-agglomerated, and non-aggregated silica particles of 20 and 75 nm in diameter. Nanocluster fillers are loosely bound agglomerates of nanosized particles that maintain the morphology and properties of individual particles [16].

Nanofillers are usually invisible and offer many advantages to dental composites, such as optical property improvement [92], increase of the overall filler content to as high as 90–95 % of the composite by weight, and reduction of polymerization shrinkage due to a lower amount of the monomeric phase [16].

Nanofillers and nanoclusters enhance the long-term mechanical stability and polishing properties of micro-filled composites [38]. The mechanical stability is achieved in hybrid composites primarily due to larger filler particles in form of "nanoclusters". Wear in composite resins have typically been linked to an increase in surface roughness resulting from removal of resin while filler particle become more exposed to the surface of the restoration, or when filler particles are lost due to abrasion. Contrarily, in nanocomposites, nanoclusters are broken down into individual nanoparticles, and since these particles are smaller than the wavelengths of visible light, roughness is not significantly increased. It has been shown that surface polish of nanocomposites is also preserved for longer periods of time in composites with filler particles of less than 0.4 μm [38].

Although nanocomposites have been marketed as materials presenting superior mechanical performance, in some cases the wear and fatigue properties of composites containing nanoparticles were similar or worse than microfilled composites [4]. Additional studies, nevertheless, report that dental nanocomposites present high translucency, high polish and polish retention similar to those of microfilled composites, while maintaining physical properties and wear resistance equivalent to those of several hybrid composites [5].

Polymers for Denture Base Materials

For a long time, denture base systems relied completely on the use of metallic materials. The first non-metallic denture base material, Vulcanite, was introduced in the 1850s, and served as a denture base system for almost 100 years, when it was then replaced by poly(methyl methacrylate) (PMMA). Although PMMA was first developed in 1931 [93], the first commercially available product was not manufactured until 1935. PMMA for denture base resins is usually marketed as pre-polymerized beads of 35–200 μm in diameter, and cured via emulsion polymerization, whereby the methyl methacrylate (MMA) monomer, supplied as a liquid, is mixed with powder forming a dough upon initiation of curing, which will proceed via addition polymerization; as reinforcements, small proportions of other alkyl methacrylates (ethyl or butyl) may be added to copolymerize with MMA. Other modifications to

increase solubility and improve viscosity may be performed by adding small quantities (<5 %) of ethyl acrylate, whereas the most frequently used initiator is benzoyl peroxide (0.5–1.5 %). As the pure MMA is clear, addition of pigments to obtain the various tissue-like shades is also often preformed. Pigments are compounds such as mercuric sulfide, ferric oxide or carbon black. Similarly, opacifiers like zinc or titanium oxides as well as titanium dioxide are typically added to enhance pigmentation and improve aesthetics of denture base materials. Moreover, dyed nylon or acrylic fibers simulating blood vessels underlying the mucosa are commonly added to denture base polymer materials. Monomer liquid also contains a small quantity of cross-linking agent such as ethylene glycoldimethacrylate (EGDMA) [94], which is essential to improve hardness and wear resistance.

In addition to meeting the aesthetic requirements for denture base materials, the simple processing technique and relatively low cost of PMMA have been attributed to its widespread use in dentistry [95]. Oral tissues show good tolerance to PMMA. Also PMMA-based acrylic resins present good color stability, excellent polishing ability, and good marginal adaptation. Yet, the major drawbacks of this group of resins include exothermic polymerization, high polymerization shrinkage, low strength and wear resistance, and potential soft tissue irritation associated with excess free monomer [96].

PMMA was not the only type of polymer to be employed as a denture base material. Other synthetic polymers have also been introduced, including bakelite (phenol-formaldehyde) cellulose nitrate, nylon, epoxy resins, vinyl polymers (polyvinyl chloride and polyvinyl acetate) and polystyrene. Polycarbonates infiltrated with glass filler particles have also been used as denture based materials and, due to their filler content, have shown nine times higher impact properties than PMMA. Yet these materials have the disadvantage of more difficult molding than acrylics, since injection molding is required [97, 98].

Although PMMA satisfies the majority of mechanical, biocompatibility and surface criteria along with reasonable cost and ease of fabrication [99], it still presents relative low impact and flexural strengths, thus leading to high incidence of fractures. Further, the relatively rough surface of PMMA surfaces after fabrication encourage microorganism's adhesion to the denture surfaces adjacent to abutment teeth, with a potential negative impact on oral health and hygiene [100].

Recent improvements to the physical and mechanical properties of the polymeric denture base materials have been obtained by incorporating nanoparticles. For instance, it has been reported that the addition of nanometer ZrO_2 particles improves hardness and flexural strength of denture base PMMA resins [101]. Similarly, embedding carbon nanotubes (CNT), which are well known for having superior mechanical properties, has been attempted as an alternative to reinforce denture base acrylic resins. Two recent studies concluded that a remarkable reduction in polymerization shrinkage [102] and improvement in flexural strength [103] can be obtained. However, the interfacial bonding between carbon nanotubes and the resin matrix has been reported to be weak, as well as a additional factor contributing to crack propagation within the polymer structure. More recently, a new class of glass filler microparticles (ultrafine GM35429) (1.5 μm) modified with 2 % F ion

and coated with silane has been incorporated into PMMA for denture base applications. This recent study has shown that the fluoride containing microparticles functioned as a fluoride reservoir with relatively controlled F released over time, while improving mechanical properties and inhibiting microbial adhesion [104].

Polymers for Treatment of Dental Caries

Despite extensive progress in the prevention of tooth decay, caries disease continues to be a major challenge in the dental field [1]. In the US alone, dental treatments are responsible for over $100 billion of the total financial burden associated with the health care system in the country [105]. Therefore, new methods for prevention and treatment of caries in enamel and dentin have long been the focus of great attention in caries research. Although polymers have been used to restore decayed teeth since the late 1940s [8], new strategies have emerged recently, both for preventive treatments and to remineralize decalcified dental structures affected by caries.

Caries Infiltration with Low-Viscosity Polymers

Dental caries starts as small lesions on the surface of dental enamel. These lesions initiate and grow due to the acidic microenvironment that is created in the presence of bacteria colonizing the surface of the tooth. The bacteria-derived acids, combined with enzymes, progress to decalcify the highly organized hydroxyapatite crystallites that constitute about 96 % of enamel, and eventually reach the undelaying dentin [106]. Given the non-homogenous pattern of decalcification and constant variations in pH in the mouth, the appearance of these early enamel lesions is opaque, with loss of luster and whitish or yellowish in color—hence their name "white spot lesions" [107]. Microstructurally, early enamel lesions present a thin surface layer of mineral, while the subsurface lesion is much more porous [108, 109] and acts as diffusion pathways for organic acids and minerals.

Commonly, treatments of enamel white spot lesions have either been preventive (noninvasive), with a combination of fluoride-based remineralization [110] and readaptation of the patient's diet, or restorative (invasive), where the lesion is drilled and treated with the polymeric restorative materials and strategies described in sections "Polymers in Dental Adhesion" and "Polymers in restorative composites resins". Recently, monomers that are commonly utilized for adhesive restorative treatments, or combinations thereof, were modified to enable impregnation of white spot lesions with photocrosslinkable materials of low viscosity (Fig. 9.3) [111]. The rational behind this strategy stems from the idea that the infiltrant occludes the lesion porosity and blocks further diffusion pathways for cariogenic acids [111]. Moreover, polymeric resins are much more resistant to acid degradation than enamel apatite is resistant to acidic dissolution, hence further cavitation is prevented after infiltration and photopolymerization (Fig. 9.2).

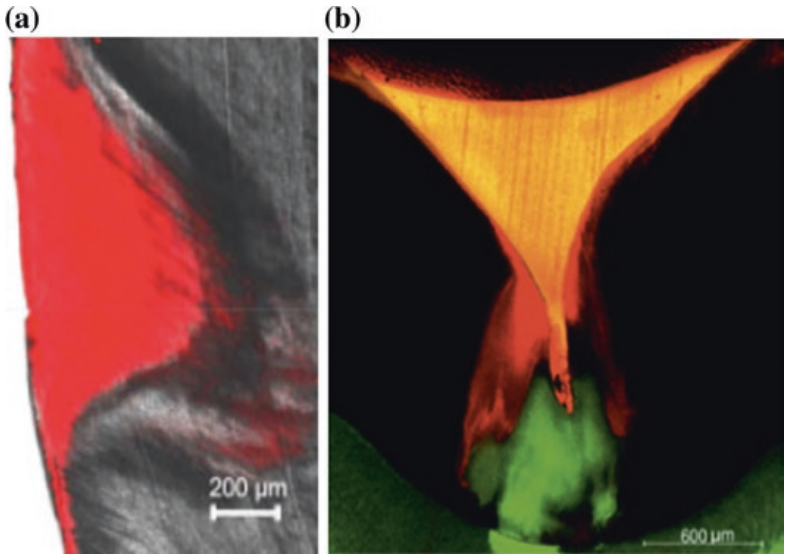

Fig. 9.2 **a** Confocal image of rhodamine-stained enamel proximal lesions treated with resin infiltrant (Icon; DMG). **b** Fissure caries lesions (*green*) infiltrated with resin (*red*) (color figure online). Reproduced with permission from [137] and [138]

Evidently, the ability of polymers to impregnate a porous substrate of intricate microstructural features, such as dental enamel, depends on a series of factors. It has been determined that such interaction may be better described by the Washburn equation [112], which accounts for the penetration of a liquid medium into a porous solid, where the porous solid is assumed to be bundle of open capillaries:

$$d^2 = (\gamma \cos\theta / 2\eta) rt \tag{9.1}$$

$$PC = \frac{\gamma \cos\theta}{2\eta} \tag{9.2}$$

in Eqs. (9.1) and (9.2), d is the distance moved by the liquid, θ the contact angle of the liquid to the substrate, γ the surface tension of the liquid, η is the dynamic viscosity of the liquid, t the penetration time and r is the capillary pore radius [112]. Therefore, from Eq. (9.2), it can be inferred that the penetration coefficient (PC) is heavily influenced by the dynamic viscosity of the liquid, η. Therefore, researchers identified that a combination of monomer molecules of sufficiently low molecular weight would facilitate diffusion into the affected tissues, while a blend of desirable properties after curing would be required for adequate reinforcement of the remainder of the tooth structure [111]. Early formulations of resins allowing for improved infiltration of caries enamel lesions were composed of a mixture of HEMA and ethanol [113–115]. However, mixtures of these components at various ratios showed imperfect hardening after photopolymerization. Formulation leading to the most desirable properties where then developed using blends of TEGDMA, HEMA and 20 % ethanol, which resulted in penetration coefficients of up to 475 cm/s [111].

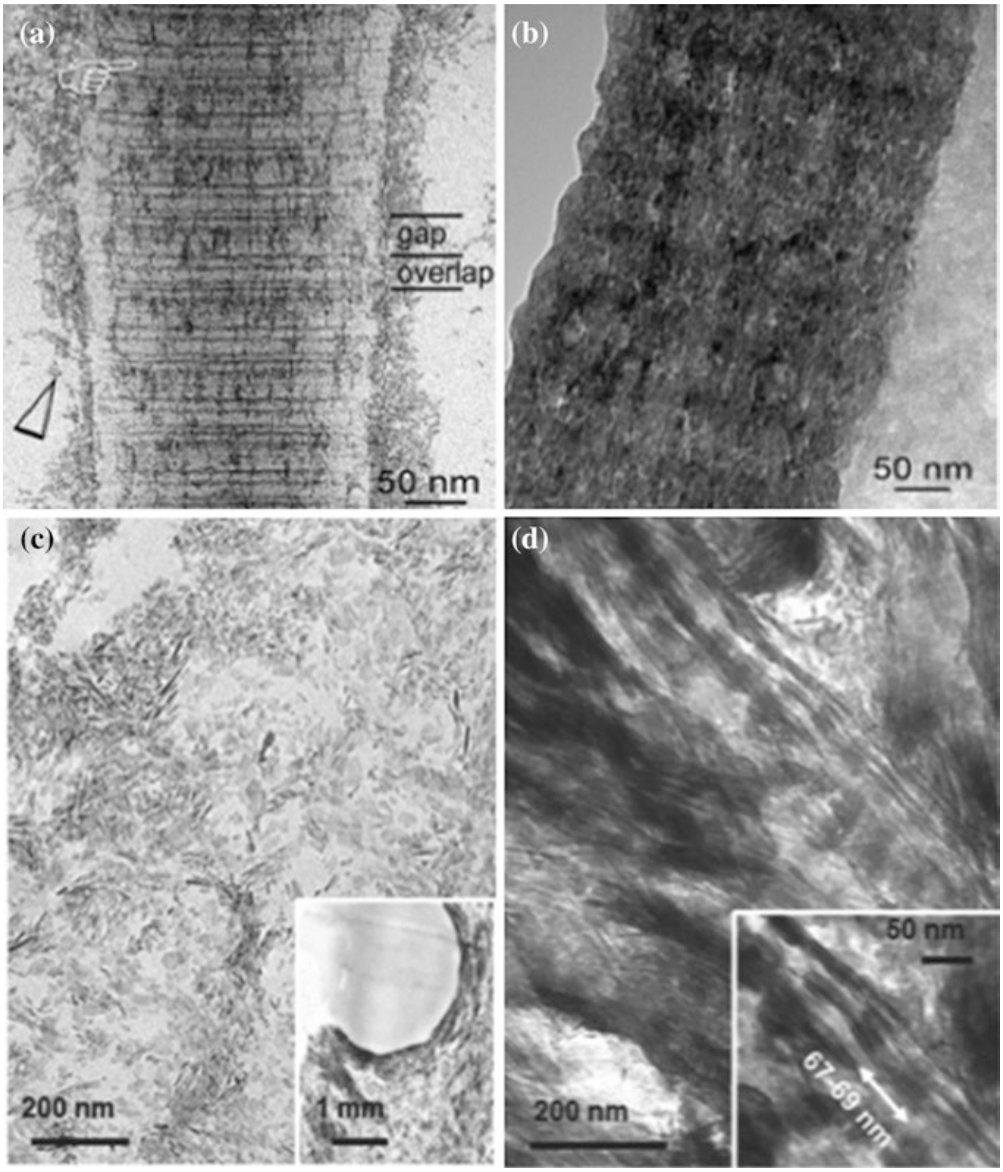

Fig. 9.3 TEM images of reconstituted collagen (**a**) and mineralized collagen using a dual biomimetic analog mineralization protocol (**b**). TEM images of dentin carious lesion (**c**) and lesions after 14 days of PILP-assisted remineralization (**d**). Reproduced with permission from [130] and [132]

Although desirable penetration coefficients could be attained by optimizing the ratios of TEGDMA, HEMA and ethanol, critical challenges associated with this method were not only restricted to minimizing viscosity (and contact angle) of the polymer. Modifying the microstructure of enamel lesions to facilitate impregnation with the resin was also a requirement [116–118]. It has been well known that subsurface lesions in carious enamel are much more porous than the so-called pseudo-intact surface layer, which forms by dissolution and re-precipitation of

mineral ions on the enamel surface. According to Eq. (9.1), the capillary pore radius will also have a significant effect on the ability of a viscous fluid to penetrate a porous solid via capillary action. To that end, researchers identified a need to acid-etch the pseudo-intact surface layer of enamel lesions and facilitate diffusion of the viscous fluids of the resins into the body of the lesion [117].

Phosphoric acid has traditionally been used as a conditioner of enamel and dentin for adhesive restorative treatments, as described in section "Polymers in Dental Adhesion". 37 % phosphoric acid has been shown to decalcify enamel and dentin in a desirable pattern, thus facilitating impregnation of adhesive monomers required for placement of composite resin restorations in the tissue matrix. Despite the known efficiency of 37 % phosphoric acid gels in acid-etching enamel and dentin, it has been shown that its effects in increasing the surface porosity of the pseudo-intact surface layer of enamel lesions was not sufficient [117]. To overcome this limitation, 15 % hydrochloric acid (generally for 2 min) has been tested and shown to remove about 30 μm of surface enamel, thus allowing for much improved penetration of viscous resins in white spot lesions [116].

Although solid evidence for the efficacy of polymer infiltrants in arresting tooth decay and preventing further demineralization [119–121], a few aspects remain to be answered. Resins composed of mixtures of hydrophobic monomers, as we detailed in section "Polymers in Dental Adhesion", have been extensively demonstrated to undergo hydrolytic degradation in the presence of oral fluids [122]. These conditions have been mostly restricted to dentin, which are not the most common applications of resin infiltrants. Nevertheless, not only these polymers are recommended for infiltration of dentin-affected caries (at early stages), but also marginal degradation due to hydrolyses from oral fluids have been extensively reported for restorative composite resins. It is unclear to which extent resin infiltrated caries will develop similar patterns of degradation over time. Similarly, newer chemistries that enable chemical retention of photolabile resins to hydroxyapatite, such as the 10-MDP molecule currently used in various dental bonding systems, may provide further improvements for the nano- and micro-scale interactions between enamel and polymer resins for infiltration of tooth decay.

Polymers for Assisted Remineralization of Carious Dentin

Although the requirements for caries prevention and diseases development have been well established from many years of research in the field of cariology, our perception of how tooth decay may be remineralized has expanded substantially in the last decade.

One of the primary aspects allowing for such rapid transition has been an improved understanding of the complexity of the mineral-matrix interactions occurring in mineralized tissues, particularly in dentin and bone. Early work has identified that in mineralized tissues, collagen fibrils are reinforced with mineral crystallites that are positioned both intrafibrillarly (inside the fibrils) and

extrafibrillarly (outside the fibrils) [123, 124]. This partitioning has been shown to have important implications for remineralization strategies [106]. For instance, it has been shown that the mineral concentration of dentine lacking intrafibrillar mineral (due to dentinogenesis imperfect type II) has little correlation to the tissue's mechanical properties, particularly its elastic modulus [125, 126]. These results led to the hypothesis that, although mineral concentration may be a sufficient endpoint for assessing remineralization of carious enamel, it may not have the same efficiency in evaluating treatment of carious dentin, where the specific interactions between the organic and inorganic components appear to have a greater influence than mineral content alone [106, 125].

Traditionally remineralization of tooth structures have relied on well established concepts of nucleation and crystal growth. Mineral ions interact with the tooth substrate and crystallization occurs at specific thermodynamic conditions that are appropriate for formation of an stable apatite phase in register with the preserved tooth structures. Using these approaches, researchers have been able to demonstrate that in carious dentin, the intrafibrillar mineral that is not fully dissolved upon acidic attack may function as nucleation sites for subsequent deposition of calcium and phosphate within the intrafibrillar compartments of collagen fibrils [127]. This, in turn, has been shown to lead to significant increases in the mechanical properties of partially demineralized dentin.

In nature, however, noncollagenous proteins such as osteopontin, bone sialoprotein, dentin matrix protein 1 (DMP1), dentin sialophosphoprotein (DSPP), and dentin phosphoprotein (DPP), have been associated with the mineralization of the tissue's collagen scaffold [128, 129], thus characterizing a protein-mediated mineralization mechanism that is rather different from the classic remineralization strategies traditionally used in dentistry. It is generally accepted that the carboxylate groups on the polyaspartic acid residues of highly anionic noncollagenous proteins renders these proteins important regulators of biominerlization [130, 131]. Therefore, it has been the focus of much research to develop strategies that enable mimicry of these biological functions using acidic polymers capable of inhibiting apatite nucleation while stabilizing calcium and phosphate ions in an amorphous phase. This conjecture forms the basis for the polymer-assisted mineralization of collagenous tissues that is the focus of contemporary approaches for remineralization of dentin [130]. We point out, as well, that similar polymer-based mineralization strategies have been extensively studied recently to prevent degradation of resin-dentin bonds.

Polymer Induced Liquid Precursor (PILP) System

A recent polymer-assisted biominerlization method that has shown great effectiveness in remineralizing carious dentin is based on a Polymer Induced Liquid Precursor (PILP) methodology (Fig. 9.3) [132, 133]. The PILP process is based on the action of minute amounts of acidic polypeptides which are added to a remineralization solution. The anionic polymer functions be sequestering

calcium ions, which then builds up a charge to sequester phosphate or carbonate, thus inducing liquid-liquid phase separation in the crystallizing medium [8, 10, 11] and hence facilitating formation of mineral inside collagen fibrils. Several anionic polymers have been studied as the process-directing agent and tested for their ability to sequester calcium and phosphate ions and form amorphous precursors that could infiltrate the intrafibrillar spaces in demineralized collagen [132–134]. Further studies have also compared poly-L aspartic acid (PASP), poly-L-glutamic acid (PGLU), polyvynilphosphonic acid (PVPA) and polyacrylic acid (PAA). PASP, in particular, represents the original polymeric combination in which a carboxylated group is attached to the amino acid backbone by one methylene group, thus mimicking one of the two most prevalent aminoacids in acidic noncollagenous proteins [131]. PGLU, PAA and PVPA are similar carboxylated molecules that have been tested due to their potential combinatorial effects with PASP in PILP strategies [134]. Results from these studies showed that, among the polymers investigated, PASP and the combination of PASP and PGLU/PASP formed stable mineralization solutions and resulted in effective intrafibrillar mineralization of collagen fibrils. A similar approach was later utilized to remineralize dentin specimens with simulated caries lesions [132].

In the polymer-assisted remineralization, calcium and phosphate ions are sequestered by biomimetic analogs of non-collagenous proteins. Similar to the function of the native proteins, these biomimetic analogs inhibit early crystallization of mineral forming pre-nucleation clusters, which eventually aggregate and form larger amorphous calcium phosphate (ACP) particles, which further stabilize to form apatite crystallites [131].

Dual Biomimetic Analog Strategy

Similar strategies have utilized a dual biomimetic analog strategy to facilitate mineralization of apatite depleted collagen matrices (Fig. 9.3). Contrary to the original PILP method, the dual mineralization strategy utilizes a polyphosphate-containing biomimetic analog which are allowed to bind to the collagen fibrils prior to immersion in a in a poly(anionic) acid-containing mineralization medium [135, 136]. In these systems, polyacrylic acid or polyaspartic acid have originally been used as the phosphoprotein analog for sequestering calcium ions released by a calcium silicate cement, or a supersaturated solutions of calcium and phosphate. Additional biomimetic analogue agents have included polyvinylphosphonic acid, sodium trimetaphosphate or sodium ascorbyl phosphate [130]. The objective of incorporating these analogs is to prevent fluidic amorphous calcium and phosphate particles from agglomerating into larger particles crystalized structures which would prevent the formation of a more stable apatite phase in the intrafibrillar spaces in collagen fibrils. Furthermore, the protein analogues are believed to function as an apatite nucleation inhibitor, preventing auto-transformation of the amorphous phase into apatite prior to their entry into the spaces.

Conclusion

In summary, in this chapter we review emerging concepts of polymeric materials applied to different areas of clinical dentistry. Tooth structures are inherently constituted of natural polymers, such as collagen and noncollagenous proteins. These so-called biopolymers, particularly in dentin, form the substrate onto which dimethacrylate adhesive resins are diffused into to bond restorative composites. Different approaches taking advantage of innovative polymer chemistry and manipulation methods of the natural polymers themselves have been presented as methods to prevent degradation of dentin bonding. Existing and emerging classes of composite resins were also described. Recent noteworthy composites include anti-caries materials with soluble or immobilized antimicrobial agents and antimicrobial fillers. Recent formulations of low-shrinkage composites also represent innovative types of polymers used in restorative dentistry. Ring-opening polymerization methods have been described as well as stress decreasing resins (SDR). Finally, emerging polymers used for denture base materials and prevention/treatment of tooth decay were touched upon. In summary, polymers represent one of major pillars of current restorative dentistry and will continue to evolve with the advent of newer technologies and polymer characterization tools. This review may provide guidance for future developments in the field of polymeric dentistry.

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