Polymeric Coatings for Dental Care

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Abstract
The performance demands of dental care products reflect the importance of healthy teeth over the entire span of human life. One approach towards the prevention of dental hypersensitivity, tooth demineralisation and dental caries involves the use of polymeric dental coatings that block dentinal tubules (a key mechanistic strategy in the treatment of dentine hypersensitivity), provide a barrier to the acid-mediated demineralisation of enamel, and also inhibit the bacterial colonisation of teeth. This paper presents the physicochemical principles that govern the molecular design of such polymeric-coating treatments.

Keywords: Coatings, Polymers, Dental, Enamel, Bacterial adhesion, Dental erosion.

Introduction

Dental caries is considered to be the most common form of chronic disease among children, accounting for the majority of hospitalisations for those of primary school age.(1) In adults, untreated tooth decay is seen in ca. 30% of people aged 35 – 44 and in ca. 20% of people over 65.(2) The pioneering bacterial colonisers are primarily Streptococci, representing 47 – 85% of the cultivable cells from rinses following tooth brushing.(3,4) The attachment of the pioneer species is followed by colonisation with increasing proportions of Actinomyces, and the consequential progression of plaque to a mature bacterial community that contains high levels of Gram-negative anaerobic filamentous organisms(5) that are embedded within a biofilm. It is the acidic bacterial metabolites of plaque that are responsible for the onset of dental caries: the localised chemical dissolution of dental hard tissues by acidic by-products from metabolic events taking place within the biofilm.(6) Once plaque is established, the continuous production of acid metabolites distorts the acid/base equilibrium of the demineralisation/remineralisation process, which, owing to the presence of water amongst the hydroxyapatite (HA) microcrystals, is not limited to the tooth surface.(7) Electron acceptor H^+ ions diffuse into the bulk of the tooth effecting the dissolution of Ca^{2+} and phosphate ions into the aqueous phase, which, if this process is undisrupted, results in the formation of cavities.(8) The principal aetiological species in tooth caries is S. mutans:(9) in addition to its capability to grow and survive in low pH environments, this organism produces highly erosive lactic acid on metabolising dietary carbohydrates and also converts dietary sugars to glucan polymers that contribute to the formation of the plaque biofilm.(9)

Bacterial adhesion: physicochemical considerations

Bacteria adhere readily to surfaces for survival and propagation. Generally, this brings about the formation of an adherent layer (biofilm, dental pellicle) composed of bacteria embedded in an organic matrix. The biofilm matrix is primarily a glycoprotein (the exopolymer), which is generated by the bacteria and may contain matter that is derived from the environment. Usually, bacterial adhesion is promoted by the formation of a conditioning layer. Once colonisation has been achieved, the formation and subsequent growth of the bacterial biofilm are largely independent of the substrate. A sequence of four phases is involved: (i) transport of bacteria to the surface; (ii) reversible attachment of bacteria to that surface – van der Waals interactions overcome repulsive electrostatic forces; (iii) development of specific interactions involving chemical bonding develop between the bacterium and the substrate, and (iv) colonisation of the surface and formation of a bacterial biofilm.

The initial adhesion of microorganisms to a surface is influenced by long-range and short-range forces. The nature of interactions may be considered to be governed by the same rules as those that dictate the aqueous stability of colloidal particles;(10) even though bacteria are far from ideal particles, having neither simple geometry nor a simple uniform molecular composition.(11)

Prerequisite to the bacterial colonisation of dental surfaces is the adherence of a colonising organism onto the target surface.(12) Dependent upon the interaction of the aqueous medium with the surface addressed by colonising bacteria, one of two physico-chemical approaches may be employed to describe the mechanism of initial attachment. The interaction between hydrophilic surfaces and bacteria are best explained by the thermodynamic approach, whereas the DLVO theory-based approach is more readily applied to lipophilic surfaces.(13,14) It is axiomatic to both approaches that surface properties that minimise the initial adsorption processes would also make the

substrate unattractive for the direct attachment of colonising organisms.

Dental erosion

In addition to the mechanical tooth-wear processes (attrition, tooth-to-tooth wear, and abrasion wear from externally applied particles or objects),[15] dental surfaces are routinely challenged by erosive tooth wear (dental erosion; the loss of dental hard tissue through chemical etching by acids or chelating agents of non-bacterial origin).[16] Apart from the extrinsic causes of tooth demineralisation that are commonly associated with the consumption of acidic beverages,[16] intrinsic demineralisation – resulting from the effects of gastric acid reaching the teeth as a result of vomiting, gastro-oesophageal reflux, rumination, or from impaired remineralisation mechanisms due to insufficient saliva production or from calcium deficiency – is also common.[16]

Dependent upon its pK_a, acid within the aqueous environment of the mouth dissociates to produce H^+ ions which attack the tooth mineral[17] and dissolve it by interacting with the CO_3^{2-} and PO_4^{3-} groups of HA (Eq. 1)[17] which in turn leads to surface etching.

$$Ca_{10-x}\,Na_x\,(PO_4)_{6-y}\,(CO_3)_z\,(OH)_{2-u}\,F_m + 3H^+ \rightarrow (10-x)Ca^{2+} + xNa^+ + (6-y)(HPO_4^{2-}) + z(HCO_3^-) + H_2O + mF^- \quad \text{(Eq. 1)}$$

Many of the hydroxy organic acids that are abundant in fruit and vegetable products (mainly citric acid and malic acid) are capable of attacking teeth.[18] Beverages can also contain citric acid: respective concentrations in drink juices, orange and lemon juice are ca. 0.3, 1 and 6%.[19] Lactic acid, commonly formed as a result of the natural fermentation of dairy, meat and some pickled products, is also capable of attacking teeth.

There is a strong body of evidence to suggest that the excessive consumption of acidic foods and drinks pose a risk to dental hard tissues.[20] In 2007, the worldwide annual consumption of soft drinks reached 552 billion L, the equivalent of just under 83 L person^{-1} y^{-1}. By 2009, average consumption in the US had reached 212 L person^{-1} y^{-1}.[20] While the minimisation of the amount of sugar in soft drinks to reduce the formation of plaque-bacteria-derived organic acids is now a commercial reality,[21] the projected significant reduction in the erosive potential of soft drinks consequent to a possible increase in the typical pH from ca. 3.3 to ca. 4.0,[22] is impeded by associated compromises in the taste and microbial stability of the product.[23] An alternative strategy that has received considerable interest involves the enrichment of acidic drinks with Ca^{2+},[24] which functions by chelating a proportion of the available citric acid. For example, adding Ca^{2+} (0.0198 g/100 mL) to citric acid (0.24 g/100 mL) at pH 3.8 has been shown to reduce enamel dissolution by 50%.[25] Kolahi et al. have suggested that tooth friendly soft drinks may be formulated by incorporating fluoride at a concentration of ca. 1 – 1.2 ppm.[26] Another approach towards the reduction of the erosive potential of soft drinks involves the use of matrix metalloproteinase (MMP) inhibitors,[27] as exemplified by the work of Barbosa et al.[28] and Kato et al.[29] who investigated the supplementation of soft drinks with natural MMP inhibitors from green tea extracts.

The demineralisation and remineralisation of enamel

Each time teeth are exposed to plaque or food acids, the natural demineralisation-remineralisation equilibrium that is integral to the health of the entire tooth becomes distorted. The effects of demineralisation may be manifested as: surface softening (removal of minerals is limited to a depth of 1 – 10 µm), caused by short-term exposure to acid in food and beverages at pH 2 – 4; subsurface demineralisation (depth of lesions in the range 20 – 1000 µm), induced by dental plaque acids maintaining a long-term pH of 4.5 – 6.5; surface etching (irreversible tissue loss), caused by prolonged exposure to strong acid.[30]

Natural remineralisation is a carbonic acid-mediated equilibrium process that occurs as HA crystal growth through the deposition of calcium and phosphorus compounds at the surface of teeth.[31] The transport of these minerals is driven by the gradient of decreasing concentration that exists between the biofilm/saliva and the aqueous phase of dental HA.[32] The presence of plaque or food acids, distorts the equilibrium in favour of demineralisation, but the process is normally reversible if adequate recovery time is allowed between acid challenges.[32] The mechanism of remineralisation is influenced by the degree of demineralisation. In the case of surface softening, enamel remineralisation has been suggested to involve a seeded growth of HA-like material in which an amorphous calcium phosphate (ACP) phase loses water to form crystalline HA (ACP → octacalcium phosphate, OCP → HA) .[33] Lesion remineralisation is believed to proceed via the direct deposition of HA onto the growing crystal. The presence of F^-, even at the 1 ppm level, has a twofold effect upon the remineralisation process: it increases the deposition rate by a factor of 2 – 3, and results in the simultaneous formation of fluorohydroxyapatite (FHAP), which is a material less susceptible to demineralisation than biological HA.[30,34]

The effect of saliva on enamel demineralisation and remineralisation

The importance of saliva in dental health is signified by the simple observation that the relative susceptibility of teeth to erosive agents is dependent upon their position within the oral cavity: dental erosion is most commonly observed on the palatal surfaces of the upper teeth, which are poorly bathed in saliva, while

erosion is less common on lingual surfaces of the lower teeth, which are constantly bathed in saliva.[35,36]

Stimulation of salivary flow aids the re-deposition of calcium and phosphorus onto demineralised surfaces and increases the buffering capacity of the saliva. Magalhães et al.,[37] who reviewed preventative measures for patients with increased risk for erosion, have documented that saliva stimulated by the use of sugar-free chewing gum promotes remineralisation, and that the consumption of certain PO_4^{3-}- and Ca^{2+}-rich foods (milk or cheese) are beneficial since these bestow salivary proteins (statherin) with the high concentrations of Ca^{2+} and PO_4^{3-} that are essential to the remineralisation process.[37]

The salivary pellicle is integral to the natural tooth-protection mechanism, as demonstrated from comparative surface-microhardness measurements on pellicle-coated and pellicle-free enamel specimens that had been exposed to erosive acid.[38] As expected, the protective effect of the pellicle layer against the erosive influence of organic acids is reported to be controlled by the duration of the acid treatment and by the concentration of the erosive agent.[39] An inverse relationship has also been reported between the thickness of the acquired pellicle and the degree of erosion.[37] An investigation on the origins of the protective effect of the in situ pellicle on dentin erosion has led to the suggestion that the pellicle functions mainly as an ion-permeable network, rather than as a protective barrier.[40]

Studies on the remineralisation of carious lesions have shown that early stage enamel surface demineralisation is reversible, but no conclusive evidence has been presented as yet regarding the dominant mechanisms governing the remineralisation of softened enamel and that of dental lesions.[41] An in vitro study examined the time element of the artificial saliva-induced remineralisation process of citric acid-softened enamel: within the time limits imposed by the experimental protocol, remineralisation is reported to have affected the partial re-hardening of enamel, but to have failed to restore the original surface structure.[41] The composition of the remineralisation medium is important, however, as is exemplified by the work of Lippert et al.[42] who demonstrated the significance of trace elements, such as Zn and Sr, in promoting remineralisation.

Dentin hypersensitivity

Dentin hypersensitivity (DH) is characterised by short sharp pain arising from exposed dentin in response to stimuli (typically thermal, evaporative, tactile, osmotic or chemical) that cannot be ascribed to any other dental defect or disease.[43] DH can occur on all tooth surfaces but is predominantly localised at the cervical part of the buccal surface,[44] normally as a result of the exposure of dentinal tubules subsequent to loss of enamel or due to gingival recession.[45] Discomfort from tooth hypersensitivity is common, with a considerable proportion of the adult population experiencing it at some point in their lifetime.[46] The pain associated with DH is mediated by dental nerve terminals that respond to the displacement of the liquid content of dentinal tubules:[47] a pain provoking stimulus applied to dentin increases the flow of dentinal tubular fluid, activating the nerves situated at the inner ends of the tubules or at the outer layers of the pulp.[43] The permeation of substances across dentin may occur by diffusion or by convection. The driving force for diffusion is a concentration gradient (chemical potential energy) whereas that for convective transport is movement of bulk fluid, which in turn is induced by differences in hydraulic pressure.[48] SEM imaging has shown that sensitive teeth have ca. 8 times as many open tubules at the surface as non-sensitive teeth and that those tubules are larger, as a result of the progressive loss of dentin.[49] On the basis of the hydrodynamic theory, approaches that involve a decrease in tubular diameter represent the most widely used strategy for the management of tooth sensitivity.

Staining

Tooth colour, which varies from tooth to tooth, is determined by the combined effects of intrinsic colour (light absorption properties of enamel and dentin) and the presence of any extrinsic stains (adsorption of chromogens onto the pellicle coated tooth surface). In general, mandibular anterior teeth appear more lightly coloured than maxillary anterior teeth. Also, lateral incisors and canines appear more lightly coloured than maxillary central incisors. Teeth become discoloured with age: as dental pulp shrinks, it becomes darker and adopts a more yellow colouration. In addition, with increasing age, dentin becomes less permeable and harder, promoting the deposition of ions that permeate the layer of enamel.[50]

Extrinsic staining has been linked to smoking, tooth-brushing technique, consumption of coloured foods (red wine, tea), the use of cationic medications (the most well-known being chlorhexidine, CHX) and the deposition of certain metal ions such as those of Sn or Fe. Many individuals are dissatisfied with their tooth colour,[51] making whitening toothpastes the fastest growing sector of the oral hygiene market.[52] Many whitening dentrifices help to reduce staining by the use of abrasives within the product (for the mechanical removal of the pellicle and dental stains), while others contain chemical constituents that reduce staining either via the inhibition of their deposition or by stain-removal. Chemicals that have been evaluated for their potential to either lighten or desorb existing stains include surfactants, enzymes, Ca^{2+} chelating builders and calcium phosphate adsorbants.[53] Tooth staining may be evaluated using visual inspection, stain guides, colourimetry, spectrophotometry and by the computer-facilitated analysis of digital images.

Strategies for preventing the build-up of dental plaque

The most commonly used method for disrupting plaque maturation (regular mechanical disruption by tooth brushing) is insufficient to achieve complete removal of plaque, especially in interdental and crevicular areas where complementary professional mouth cleaning is often needed.[54] Mechanical brushing may also be complemented by antimicrobial agents. It has been demonstrated that a 99% reduction in bacterial counts is required before a 6 h delay in the onset of plaque formation can be achieved.[55] In addition to having acceptable taste and possessing good oral substantivity, antibacterial agents must be non-toxic and must exhibit a broad spectrum of antibacterial activity, such that the oral ecology is not disturbed.[55]

Alternative approaches to chemical treatment with antimicrobial agents include the use of quorum-sensing inhibitors or the deployment of biocompatible polymers as barriers to plaque build-up by creating a non-permanent tooth shield. Central to the performance demands of such coatings are the capability of the polymer to form a continuous film, and the in vivo substantivity of that film.

Adsorbed antimicrobial agents

Amongst the several classes of antimicrobials that have been identified (Fig. 1),[57] the poly-cationic biocides have been used extensively in mouth rinses, lozenges, sprays and gels.[57] Of particular interest in dental care is cetylpyridinium chloride (CPC), which readily adsorbs onto enamel[58] and also diffuses through the exopolysaccharide (EPS) component of the salivary pellicle to exert its antibacterial action by destroying the cytoplasmic membrane.[59] Effective oral formulations of CPC include nanoemulsions,[60] resins,[61] and orthodontic adhesives.[62] The dental-care benefit of CPC was also confirmed by Moran et al. whose investigations into the activity of benzalkonium chloride (BAC; 0.1% and 0.05%) concluded that this material was not as effective an antiplaque agent as CPC or CHX.[57] However, BAC has been suggested to be a useful antimicrobial for incorporation into orthodontic resins.[63]

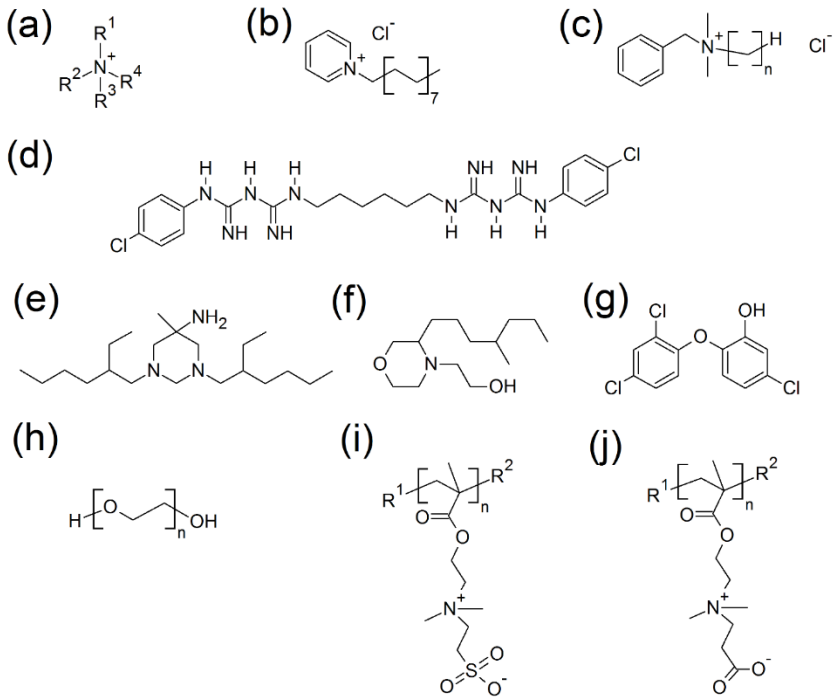

Fig. 1: (a) General structure of quaternary ammonium compounds, (b) cetylpyridinium chloride (CPC), (c) benzalkonium chloride (BAC; n = 7, 9, 11, 13, 15 or 17), (d) CHX, (e) hexetidine (HEX), (f) delmopinol, (g) triclosan (TC), (h) PEG, (i) poly(sulphobetaine), (j) poly(carboxybetaine).[56]

CHX, a surfactant bis (biguanide), is a cationic antimicrobial that has been successfully used in dentistry for over 50 years owing to its proven effectiveness in inhibiting the development of plaque, and hence caries and gingivitis.[64,65] The pharmaceutical industry recognises CHX as the gold standard against which anti-plaque agents may be measured.[66] CHX functions by binding to negatively charged regions in the membrane of microorganisms, often phospholipids of the inner membrane, inducing to exposed microbes loss of osmotic flow, leakage of intracellular components and coagulation of the

proteins in the cytoplasm.[67,68] The clinical efficacy and long-term bactericidal effects of CHX are further enhanced by good oral substantivity that stems from an affinity for adsorption onto HA.[69] in a fashion that does not block the active sites of the agent.[67] The usefulness of CHX extents from mouth rinses to gels, controlled release formulations,[70] varnishes,[64] and coatings (Fig. 2).[71] The dental-care benefits of CHX are however counterbalanced by the undesirable effects of tooth staining, formation of calculus[72] and bitter taste. In an effort to suppress these effects, Menegon et al. prepared a hydrophilic tetra-cation salt of CHX palmitate, which when formulated with poly(vinyl pyrrolidone) was claimed not to exhibit the undesirable side effects of CHX.[73] In a separate effort, Solis et al. employed patients with chronic periodontitis to demonstrate the improved clinical efficiency of CHX mouthwash with an incorporated anti-discoloration system (composed of ascorbic acid, and sodium metabisulphite).[74]

The broad spectrum antiseptic pyrimidine[75] derivative hexetidine (HEX),[76] which exhibits a lower tendency to cause tooth staining than CHX is also of value in the formulation of dental-care products.[75,77] The efficacy of HEX is amenable to amplification by metal ions, as is exemplified by the synergistic effect against Streptococcus mutans observed in the presence of Zn^{2+} .[78]

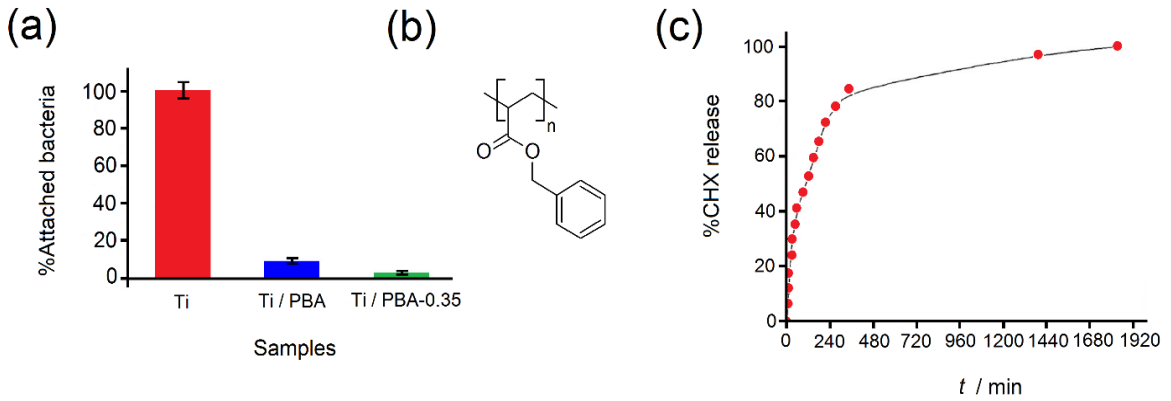

Fig. 2: (a) %Bacterial adhesion (mean ± sem) to Ti (control, 100%), Ti / poly(benzyl acrylate) PBA and Ti / PBA-0.35 after immersion in phosphate-buffered-saline (PBS) for 48 h and then in the culture medium for 2 days; (b) structure of PBA; (c) %CHX release from the Ti / PBA-0.35 coating in PBS (37 °C). Adapted from [71] and used with permission.

Delmopinol, an aminoalcohol, is another molecule that combines significant substantivity with antiplaque properties.[79] Its mechanism of action involves the inhibition of pellicle formation[80] and the consequent reduction in the number of bacteria in the pellicle and plaque matrix.[81] Since delmopinol is not as powerful a stain chromogen as CHX, Addy et al. proposed the use of its mouthwash formulations as an adjunct measure for the prevention of plaque and gingivitis.[81]

An active that is free of known side effects is triclosan (5-chloro-2-(2,4-dichlorophenoxy)phenol; TC; Fig. 1),[82] a chlorinated diphenyl ether that exhibits a broad spectrum of activity against Gram-positive bacteria, including Streptococcus mutans. The primary limitations of TC are its low aqueous solubility (< 10 μg mL^{-1})[8] and its limited affinity for plaque or oral tissues, with the implication that its oral concentration is not readily sustainable at levels sufficient to effect the treatment of dental caries.[83] Of significance in the development of improved oral formulations of TC has been the patented (1990) discovery that poly(vinyl methylether-co-maleic acid) – a dual-function polymer in which the carboxyl group acts as a tooth-anchoring moiety and the methoxyether groups provides a solubilising matrix for triclosan – increases the retention of TC in the oral cavity. Kockisch et al. demonstrated the controlled-release behaviour of TC-loaded chitosan microspheres,[84] while Loftsson et al. utilised a cyclodextran matrix for the same purpose.[85] Fe et al. developed a mineral-binding micellar drug delivery system of alendronate and pluronics that is reported to not only inhibit biofilm formation but also reduce the viability of preformed biofilms.[9] Another alternative dosage form for the improved delivery of TC has utilised fast-dissolving films of hydroxypropyl-β-cyclodextrin and poloxamer.[86] It is now widely accepted that the twice-a-day use of TC copolymer toothpastes can give clinically significant improvements in plaque control and gingivitis and may slow the progression of periodontal disease.[87]

The coupling of antimicrobials to biopassive polymers has also been considered (Fig. 3).[88,89] A comparative study of antibacterial films of poly(methylmethacrylate-co-methacrylic acid) and poly(methylmethacrylate-co-trimethylaminoethylmethacrylate chloride) found that both types of material are promising antifouling surface treatments, in that the negatively charged polymer

delays the onset of biofilm formation while the positively charged macromolecule acts by inhibiting bacterial proliferation.[90]

Despite their inherent anti-bacterial properties, the value of Ag coatings in effecting a reduction of bacterial adhesion has been the subject of some debate.[91] Nonetheless, the addition of microparticulate Ag to resin composite material has been shown to increase resistance to bacterial colonisation and to produce bactericidal effects[92] while complexes of Ag and perfluorodecanethiolate have been shown to exhibit antifouling and antibacterial properties.[93]

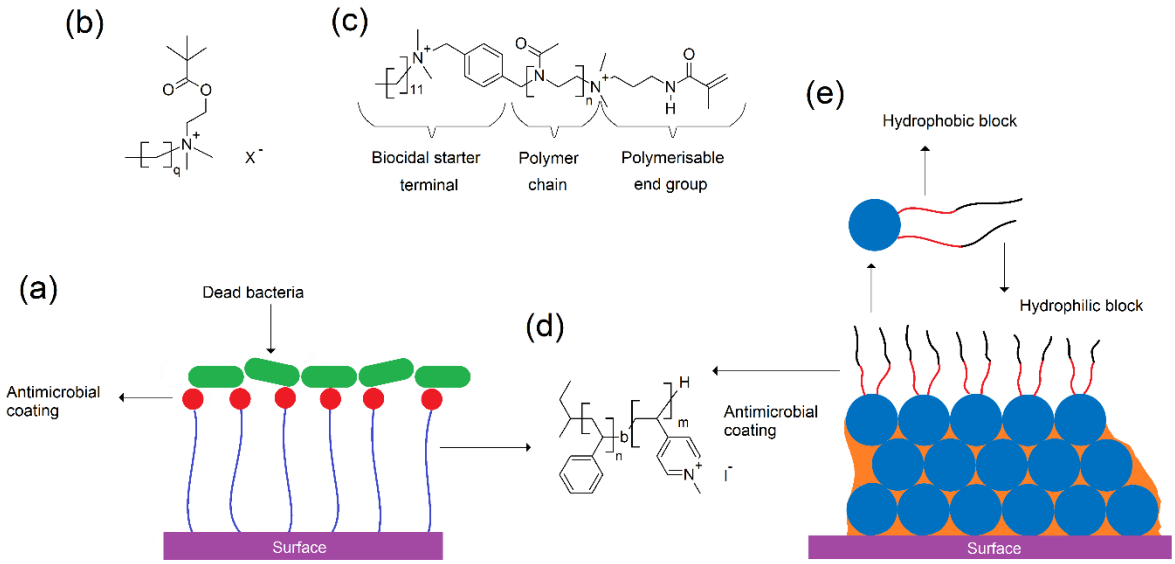

Fig. 3: Schemes illustrating the immobilisation of antimicrobial coatings to actively kill any bacteria that adhere to the surface: (a) with pertinent examples highlighted from the literature; (b) antimicrobial polymer based on quaternary ammonium compound; (c) structure of synthesised antimicrobial poly(2-methyl-2-oxazoline) (PMOX) with acrylate polymerisable end group and N,N-dimethyldodecylammonium (DDA); (d and e) preparation of contact-active antimicrobial coating from an aqueous polymer suspension of hydrophobic poly(styrene) block (PS) and hydrophilic block of antimicrobial polymer poly(4-vinyl-N-methylpyridinium iodide) (P4VMP); (e) polymeric particles obtained using PS/P4VMP as the emulsifier shown via blue circles. Adapted from [88] and used with permission.

Natural Extracts

Driven by consumer demand, and in view of the issues of increasing microbial resistance to conventional antibiotics, many researchers have attempted evaluations of natural products, as is exemplified by studies on honey derived from the flowers of the Manuka tree (Leptospermum scoparium**,** New Zealand). Badet and Quero[94] and independently Nassar[95] have suggested oral-health benefits of such products by demonstrating that Manuka honey is capable of inhibiting the formation of a biofilm of S. mutans. Nayak et al., following their comparative study of CHX, xylitol chewing gums and Manuka honey, concluded that this honey is an effective inhibitor of plaque formation.[96] More viable alternatives to conventional antimicrobials are provided by chitosan and essential oils.[97] Tea-tree oil has received considerable attention for its broad spectrum antibacterial activity[98] and because of its documented growth-inhibiting effects on cariogenic bacteria and its anti-adherence effects on S. mutans.[99] Essential oil mouth rinses[100] have been claimed to offer oral-care benefits that are similar to those of CHX[98] or CPC[101] with no alteration of basic salivary parameters.[102] Chitosan, a product derived from the deacetylation of chitin, has been shown to exhibit antimicrobial properties against oral bacteria and to be capable of altering the physico-chemical properties of the pellicle.[103] Water-soluble (reduced) chitosan has been shown to have a potent effect against S. mutans and to exhibit plaque-reducing action.[104] These findings have underpinned the development of a chitosan-containing polyherbal toothpaste.[105]

Quorum sensing inhibitors

The use of quorum-sensing inhibitors is an evolving concept that may prove of value in inhibiting the formation of oral biofilm.[106] Since the discovery that quorum sensing in S. mutans biofilm growth is primarily regulated by the competence stimulating

peptide (CSP) and the ComD/ComE two-component signal transduction system, attempts have been made to develop therapeutic or preventative agents against dental caries.[107] Early work suggested that the use of CSP at high concentrations is capable of effecting growth arrest and eventual cell death in S. mutans,[107] but considerable research developments are needed before this approach can be considered for clinical applications.

Inhibiting bacterial adhesion onto tooth surfaces: the non-toxic approaches

The initial adhesion of bacteria to a surface is influenced by both the chemistry of the addressed surface and the aqueous environment surrounding that surface. In the oral environment, the colonisation of dental surfaces is influenced by the interplay of factors that include the chemistry, charge and roughness of the tooth surface, and also by the nature of the acquired pellicle, which is in turn is at least in part influenced by the dietary intake and habits of the individual. Towards the inhibition of bacterial adhesion to surfaces, three non-toxic coating approaches have been evolved: (1) the hydrophilic approach, (2) low-surface-energy approach, and the (3) mobile-polymeric-surface approach.[108]

Hydrophilic approach

The most widely employed strategy towards preventing the attachment of bacteria (B) and proteins from an aqueous environment (W) onto a surface (S) involves the pre-adsorption of a hydrophilic macromolecular chain. The approach is underpinned by consideration of the free energy of adhesion (Eq. 2):

$$\Delta G_{ads} = -(\gamma_{SB} - \gamma_{SW} - \gamma_{BW}) \quad \text{(Eq. 2)}$$

where γ = interfacial free energy between substrate (S), bacteria (B) and water/media (W). For an unprotected surface, bacteria would become strongly attached (Eq. 3),

$$\gamma_{SB} > \gamma_{SW} + \gamma_{BW} \quad \text{(Eq. 3)}$$

and the adsorption of proteins would also be favourable. The protective layer, an ultra-thin coating of a polymeric amphiphile, presents a hydrated surface to the liquid phase, so that the adsorption of proteins and other molecules involves the displacement of adsorbed water. Although this would give an increase in entropy, the enthalpy requirement for the desorption of strongly-bound water molecules is much more significant at the physiological temperature and the process is unfavourable $\Delta G_{ads} > 0$ (or much less favourable, $\Delta G_{ads} < 0$, but small). A kinetic barrier may also be introduced, inhibiting the adsorption process even if it is thermodynamically favourable. Similarly, the attachment of bacteria to the surface is not favoured because it would be accompanied by a decrease in the value of ΔG_{ads}, as S-W and B-W interfaces are replaced by S-B interfaces. Thus, bacterial and other biofouling may be avoided by preparing a formulation from which a polymeric amphiphile can become available for adsorption onto enamel in a manner that allows: (a) the less hydrophilic–component of the surfactant to anchor to the surface and (b) the more hydrophilic component to extend into the aqueous phase.

Poly (ethylene glycol)s (PEGs) and their congeners are the materials of choice for such applications. These polymers offer a high degree of hydration (> 80% w/w) and a water interfacial energy of < 5 mJ m^{-2}.[109] The immobilisation of these polymers onto the surface may be achieved either through physisorption or via the controlled covalent coupling of appropriately functionalised derivatives to anchoring surface groups .[109,110] The free energy change associated with binding/adsorption involves both enthalpic and entropic contributions, but, for PEGs in aqueous media at physiologically relevant temperatures (37 °C), the competing, entropic term becomes of little significance (the enthalpic term dominates up to ca. 85 °C.[111]

The simplest method for the attachment of hydrophilic/amphiphilic polymers to a surface is by encouraging adsorption through the adjustment of the hydrophilic/hydrophobic balance of a (co) polymer according to the nature of the addressed surface. Since it is prerequisite to dental applications that the adsorbed polymer be substantive, the fouling-resistant polymer may be mixed with a second, priming, polymeric component that facilitates anchoring at the tooth surface by virtue of its compatibility with both the non-hydrophilic segments of the functional polymer and the tooth surface. Although several methods are available for the chemical grafting of hydrophilic polymers onto surfaces, the value of the approach to dental care has yet to be assessed.

Since the grafting density[112] and chain length of PEGs[113,114] are critically important in determining the efficiency of a coating at preventing protein and bacterial adhesion, the so called polymer brushes (polymers that adhered to a target solid surface), are the subject of considerable research.[112,115] Olsson et al. have shown that poly(alkylene oxide) derivatives inhibit the binding of S.mutans to non-pelicilised hydroxyl apatite.[116] This study, and also independent work by Saldarriaga Fernandez et al.[117] established that, owing to the favourable association of salivary mucins with PEG chains, the presence of saliva renders PEG coatings less effective at inhibiting bacterial colonisation. Shimotoyodome et al. found that mouthwash formulations of methacryloxydecyl phosphate-PEG and pyrophosphate are capable of preventing dental biofilm formation.[118] Consequently, alternative bioinert polymers including polysaccharides, non-ionic, zwitterionic and peptidomimetic compounds are being investigated.[111,119] Among the zwitterionic polymers,[120] sulphobetaines[121] have been found to be effective anti-adherent coatings to biofouling. Polymer brushes synthesised from carboxybetaine polymers are expected to be effective low-fouling surface modifiers

in different biological environments in inhibiting protein adsorption.[120] Poly(sulphobetaine) and poly(carboxybetaine) have been found reported to reduce the formation of biofilms from both Gram-positive and Gram-negative bacteria (Fig. 4).[122,123]

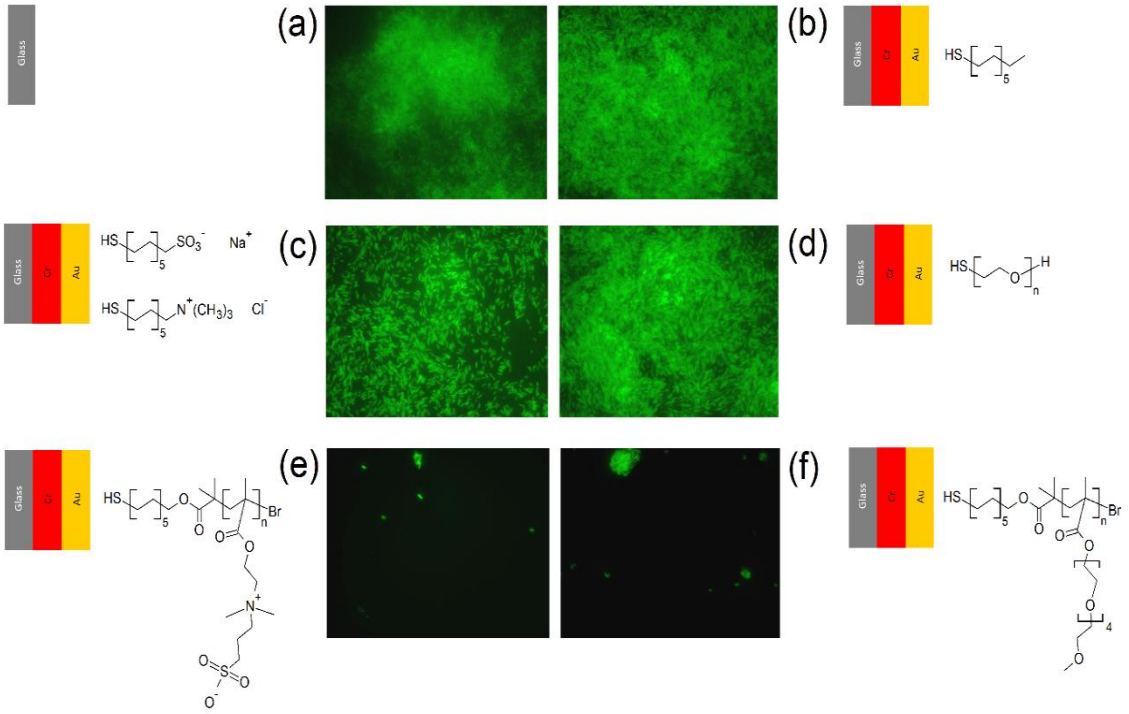

Fig. 4: Self-assembled monolayer thiol structures / polymers on Au coated glass (via a Cr adhesion layer) and resultant representative fluorescence microscopy images showing Pseudomonas aeruginosa attachment after 24 h exposure. Adapted from [122] and used with permission.

It is long established that sugars and other bacteria-fermentable dietary carbohydrates are erosive-acid-generating substrates that play a major role in the aetiology of dental caries.[124] Sugar substitutes have been widely investigated for their effect in limiting the dietary sources of caries hazards.[125] Xylitol, a five-carbon sugar alcohol that has a similar taste to sucrose, represents one of the most extensively studied sugar substitutes[8] since the majority of plaque bacteria are incapable of fermenting xylitol into cariogenic acid products[126] xylitol is converted by oral bacteria to the glycolysis inhibitor xylitol 5-phosphate.[2] It has been claimed that xylitol chewing gum augments the buffering effect of saliva by increasing salivary flow,[2] and also reduces the counts of S. mutans in plaque and saliva.[127]

Long-range forces of adhesion: the DLVO theory

The DLVO theory of colloid stability may be used to describe the combination of the long-range forces that are responsible for the adhesion of microorganisms to the tooth surface.[13,14] Accordingly, the stability of the adsorbed state is determined by the sum of the potential energies that are associated respectively with the attractive van der Waals forces and the repulsive electrostatic forces (electrical double layer) that operate as a microorganism approaches the surface due to Brownian motion.

The electrostatic repulsion potential V_R between a plane surface and a sphere at separation x, due to relatively thin electrical double layers, is of the form (Eq. 4)[128]

$$V_R = P \ln(1 + e^{-qx}) \quad \text{(Eq. 4)}$$

where the constant P contains the zeta potential and the particle radius, and q is the inverse of the double-layer thickness. For this system, the attractive van der Waals interactions become relatively long-range (Eq. 5):

$$V_A = -\frac{S}{x} \quad \text{(Eq. 5)}$$

where the constant S contains the polarizabilities of the surface atoms of the interacting bodies. The individual potentials, the total potential V (Eq. 6):

$$V = V_R + V_A \quad \text{(Eq. 6)}$$

and the corresponding force of attraction F (Eq. 7):

$$F = \frac{S}{x^2} - \frac{Pqe^{-qx}}{1+e^{-qx}} \quad \text{(Eq. 7)}$$

are shown as a function of x in Fig. 5. The attractive van der Waals interactions begin to pull the bacterium towards the surface at nanoscale distances that are determined by the bacterial species, the nature of the surface and the aqueous medium. Since under most

physiological conditions, bacterial surfaces carry a net negative charge and most natural surfaces are also negatively charged, significant electrostatic repulsion occurs at somewhat shorter distances. This gives rise to a potential minimum (point 'B' in Fig. 5) at a separation of a few nanometres, which corresponds to a weakly adsorbed state (cf. the flocculated state of a colloid). In this state, the bacterium is readily displaced from the surface. A closer approach involves overcoming an energy barrier ('A' in Fig. 5) leading to an extremely low 'primary' potential minimum, not shown, at ca. 1 nm from the surface. The large force of adhesion at the primary minimum renders the adsorption irreversible.

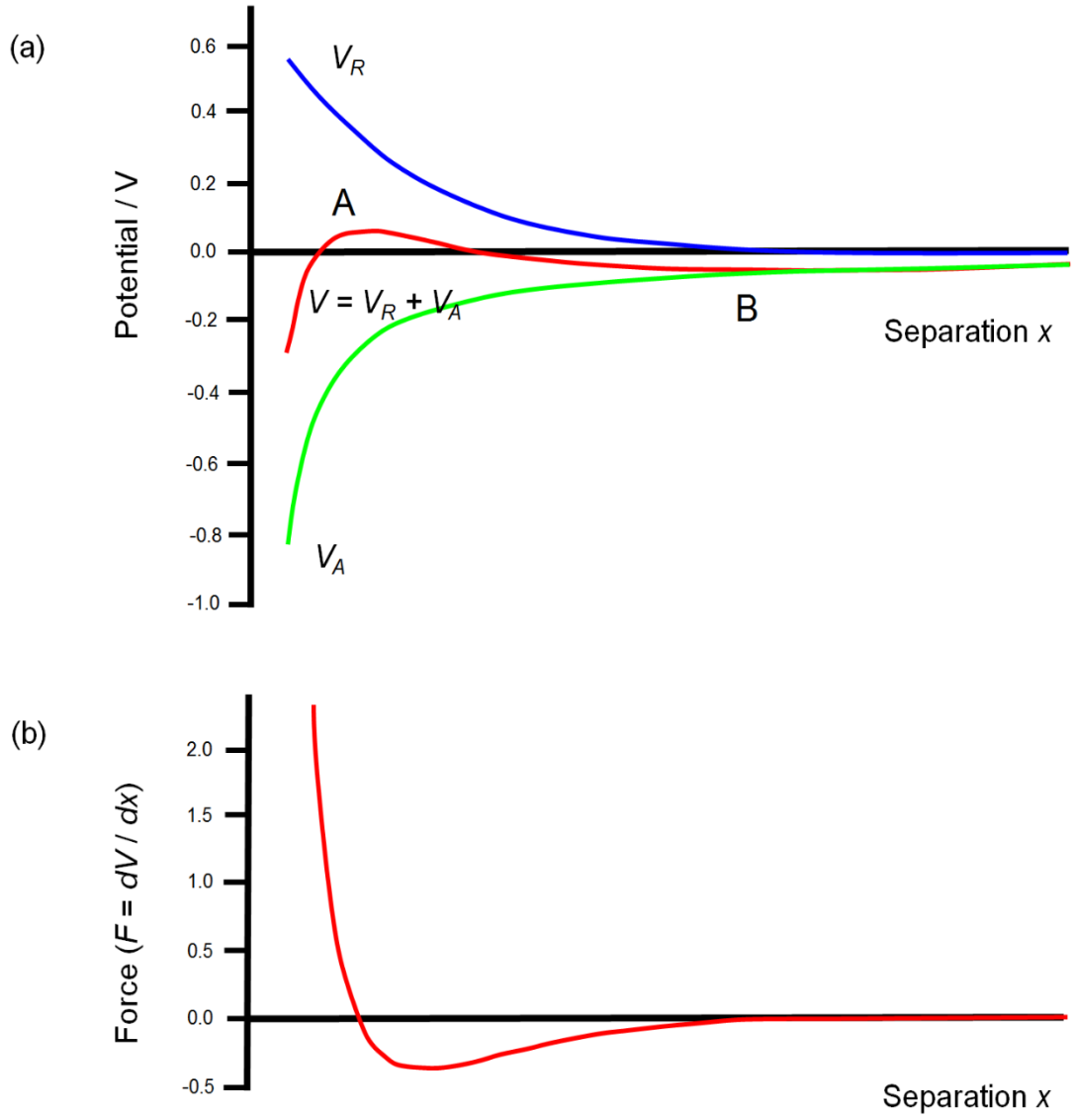

Fig. 5: Illustration of the (a) potential energy V and (b) force of attraction F between a bacterium and a plane surface as functions of separation x, as described using DLVO theory, drawn using equations (Eq. 4 – 7) with P = 1, q = 5 and S = 0.05.[56]

The strength of the repulsive interactions is determined by the density of the negative charges on the interacting surfaces and by the ionic strength of the medium.[129,130] If electrostatic repulsions are large and the energy barrier is high then the secondary minimum may not occur, and/or the formation of the strongly adsorbed state may be slow. If, however, electrostatic repulsions are reduced (electrolytic neutralisation of surface charges) then the potential barrier will be lowered and the strongly adsorbed state will be formed rapidly and irreversibly.[129]

Consistent with the observation that plaque accumulation starts at pits and grooves, studies designed to examine the relative contributions of surface roughness and surface energy with respect to susceptibility to bacterial colonisation have concluded that above a threshold value of approximately the same size as that of the bacterial colonisers[131] accumulation of plaque is encouraged irrespective of the energy of the surface.[132,133]

Low-surface-energy polymers

Interest in the low-surface-energy approach dates back to the early 1980s following the observation that gorgonian corals, which have low energy surfaces, are not susceptible to colonisation by marine microorganisms.[134] It is now established that the main molecular-design requirement for low surface energy polymer coatings is a flexible linear backbone onto which are attached pendant chains exhibiting low intermolecular interactions (aliphatic hydrocarbon or preferably perfluorocarbon; Table 1).[135,136]

Table 1: Surface free energies (20 °C) of films prepared from common polymers.[56]

Polymer	Surface free energy / mJ m^{-2}
Polyamide-6,6; nylon	47
Poly(ethylene glycol); PEG	43
Poly(styrene)	41
Poly(ethene)	34
Poly(trifluoroethene)	24
Poly(dimethylsiloxane); Silicone	21
Poly(tetrafluoroethene); Teflon	18
Poly(1H,1H,2H,2H-perfluorododecyl (meth)acrylate)	6

Weerkamp et al. demonstrated that lowering the surface free energy to below 60 mJ m^{-2} could retard plaque accumulation on smooth surfaces by inhibiting bacterial adhesion.[131] Tsibouklis et al. demonstrated that two classes of low surface energy polymers, namely poly(methylpropenoxyfluoroalkyl siloxane)s and poly(perfluoro (meth)acrylate)s, possessed good resistance against a range of bacterial and yeast colonisers.[134]

The same group has shown that films of poly(perfluoro (meth)acrylate)s that had been deposited onto human enamel from aqueous emulsions hold considerable promise as substantive dental barriers.[137] Zhao et al. also found the surface energy of coatings to have a significant influence on bacterial adhesion and calculated the optimum surface energy components of substrates for minimising adhesion to E. coli, Staphylococci epidermidis and Streptococci adhesion in water (Fig. 6).[91]

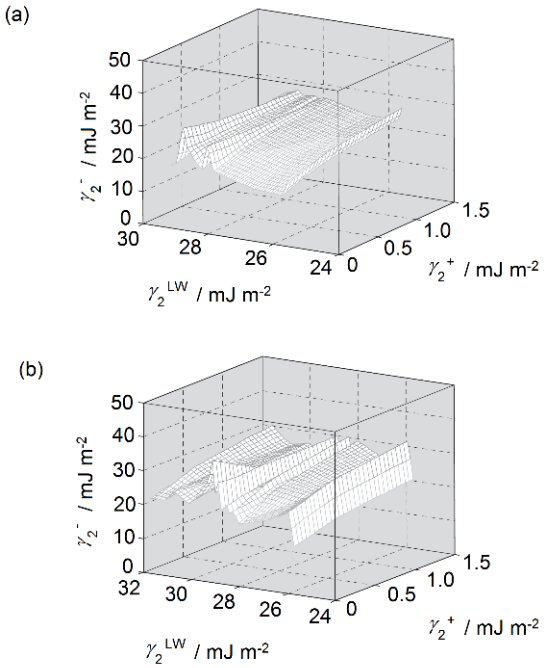

Fig. 6: Optimum surface free energy components of substrates for minimising (a) E. coli and (b) Staphylococci epidermidis adhesion in water. Adapted from [91] and used with permission.

In their comparative study of a hydrophylic and a hydrophobic material, Lassen et al. found that PEG-co-poly(ethylene imine) was more susceptible to colonisation by S. mutans than a hydrophobic surface of plasma-polymerised hexamethyldisiloxane.[138]

Mobile surface polymers

Typified by thick films of silicone-oil-fortified silicones, another strategy for preventing cell adhesion involves the use of materials that present a highly mobile surface. The near zero barrier to rotation of the siloxane (-SiO-) backbone[139] and the inherent low surface energy of the material renders it a useful antifoulant.[140-142] Although films of these materials have found extensive uses in marine-antifouling applications, their performance within the oral environment may be limited by their thickness.

Strategies to reduce dental erosion

Fluorides

Dependent upon the level of F^- in drinking water, healthy sub-surface enamel contains F^- at ca. 20 – 100 ppm while the outer few µm of enamel may reach levels in the range 1000 – 2000 ppm.[143] The most convenient access to fluoridated medicaments is through the over-the-counter availability of dentifrices and rinses. The levels of F^- contained in these are dictated by the anti-caries monographs of regulatory agencies. In the absence of a specific anti-erosion monograph, and given the concerns for fluorosis

associated with the use of higher levels of F^- in children, technologies that augment the anti-erosion efficacy of medicaments containing F^- at current concentrations (900–1500 mg kg^{-1} for dentifrices and 90–450 mg kg^{-1} for mouth rinses) are of particular interest for future development. The high efficacy of F^- in inhibiting the development of caries owes its origins to the capability of this ion to substitute for -OH groups in HA, $Ca_{10}(PO_4)_6(OH)_2$. This results in the formation of partially or fully fluoridated apatitic phases, $Ca_{10}(PO_4)_6F_x(OH)_{2-x}$, whose resistance to acid-mediated dissolution is much greater than that of the precursor non-fluoridated apatite.[144] Remineralisation of early caries lesions is also promoted by F^- through mineral uptake encouragement at the less soluble fluoridated apatitic phase.

The substitution (full or partial) of the OH^- lattice position by F^- improves the resistance of the enamel to demineralisation; this is reflected by a reduction in the critical demineralisation pH of FHAP (dissolves at pH 4.5) as compared to HA (pH 5.5).[145,146] F^- makes apatite crystals less soluble in acid by two mechanisms. In FHAP, F^- ions form strong hydrogen bonds with neighbouring OH^- ions, making FHAP crystals more resistant to dissolution than either HA or fluorapatite;[147] this occurs in competition with other ion impurities (those of Mg, Na, Se, CO_3^{2-}, acid phosphate), which are known to increase the solubility of HA crystals [144]. Also, F^- incorporation increases the packing density and quality of the crystalline lattice;[148] FHAP crystals have fewer imperfections than HA crystals – due to the slightly smaller size of F^- (1.32 Å) relative to that of OH^- (1.68 Å) – with the implication that fluorapatite and FHAP crystals are less accessible to the solubilising medium than HA crystals. However, the presence of carious lesions on shark enamel (which consists of solid fluorapatite)[149] highlights the need for further investigations into the mode of action of fluoride.

In addition to the tooth-strengthening effects of F^-, there has been the suggestion that the same agent may offer a subtle antimicrobial benefit.[150] Kamotsay et al. suggested that high concentrations of NaF slow down the multiplication of cariogenic oral bacteria and fungi.[151] Clinch, in his review of the effects of F^- on oral bacteria, states that 'although in vitro studies suggest that F^- may have anti-microbial effects, the in vivo evidence using F^- concentrations commonly used in toothpastes (500 – 1500 ppm; with subsequent mouth-rinsing with water) fails to demonstrate any clinically significant antagonistic effect on the bacteria involved in cariogenic activity'. In fact, no available research has shown that F^- at 1 ppm in water significantly alters plaque metabolism or plaque growth (bactericidal effects).[152]

The efficacy of F^- has been related to concentration and pH, while the formation of a CaF_2 reservoir may also be of significance.[37] While the erosion and caries prevention properties of compounds such as NaF, amine fluoride (AmF), stannous fluoride (SF) and acidulated phosphate fluoride (APF) are well documented, tetrafluorides have been highlighted as agents worthy of further investigation. In their study of polyvalent metals, McCann et al.[153] identified TiF_4 as a candidate compound for clinical and epidemiological studies: TiF_4 is thought to synergise the effect of F^- through the formation of a surface layer with increased mechanical strength.[154] Complementary work by Hove et al.[155] and others[156-160] further support the notion of an acid-resistant surface layer. The potential benefits of formulations for the controlled release of F^- may also be worthy of investigation.[8]

Casein

Of considerable interest in the prevention of tooth erosion is casein, a phosphoprotein found in bovine milk. Casein phosphopeptides (CPP; -Ser (P)-Ser (P)-Ser (P)-Glu-Glu),[161] that may be formed from the tryptic digestion of casein, solubilise minerals, especially those of Ca^{2+}, by forming amorphous phosphate nanocluster complexes (CPP-ACP),[162] that prevent its growth to the critical size necessary for nucleation, phase transformation and precipitation.[163,164] Rose et al.[165] showed CPP-ACP to bind well to dental plaque, which they suggested provides a large Ca^{2+} reservoir that assists remineralisation and also acts as a barrier to demineralisation. There is evidence that CPP-ACP inhibits demineralisation by sports drinks,[166] soft drinks,[167] and confections.[168] Synergistic interactions with co-formulated F^- [169,170] have been shown to augment these effects further. Stable and highly soluble CPP-ACP has been trademarked as Recaldent™.[8] Several paste formulations are available, such as Tooth Mousse™ (GC International Tokyo, Japan), Topacal C-5 (NSI Dental, Hornsby, Australia) and MI Paste Plus (GC International) .[164]

Strategies for treating dentin hypersensitivity

In addition to the zero tolerance towards adverse effects, the performance demands of modern hypersensitivity treatments are determined by the requirement for a rapid onset of action.[171] The treatment of DH is now integral to many dentifrices, though the incorporation of technologies designed to prevent the induction of pain either through the inactivation of nerve responses or by the prevention of the movement of liquid within dental tubules.[172]

Potassium ions

Potassium ions (in the form of citrates, NO_3^-, oxalates and Cl^-) are known to inhibit DH by inactivating nerve responses though the sustained depolarisation of the nerve-fibre membrane.[173-175] KNO_3, which has FDA approval, has found wide use[176] even though its mechanism of action is not fully

understood. Apart from the desensitising effect of K^+,[177] it has been suggested that complementary oxidising effects and the blocking of tubules by crystallisation may be of significance.[171,178]

Oxalates

Oxalates were first proposed as agents for the treatment of DH in the late 1970s, by which time numerous studies had suggested their effectiveness at inhibiting hydraulitic conductance by the blocking of dentinal fluid flow as a result of the soluble potassium oxalate converting to insoluble calcium oxalate within the tubules.[179-181] More recent work, however, appears to suggest than monohydrogen monopotassium oxalate is the only efficacious potassium oxalate for the treatment of DH.[182-185]

Fluorides

Stannous fluoride (SF) has been shown to be effective not only in the prevention of dental caries,[187] but also in the reduction of DH.[187-189] This agent acts by effecting a decrease in dentinal permeability through the precipitation of CaF_2 crystals in the tubules.[190] However, SF has been associated with extrinsic staining. Attempts to address this issue through re-formulation[191] have seen SF being used in conjunction with KNO_3[192] and sodium hexametaphosphate.[193,194] A dentifrice containing SF and NaF has shown to generate in situ, during tooth brushing, an SF complex that does not cause staining.[191,195] It has been claimed that the formulation offers a multitude of oral-care benefits, namely: anti-caries potential, plaque reduction, hypersensitivity inhibition, extrinsic stain prevention, and improved breath malodour.[196]

Calcium phosphate precipitation

The in vitro capacity of calcium phosphate precipitation to effect dental-tubule occlusion appears to owe its origins to the pH sensitivity of the aqueous solubility of calcium phosphate: experiments have shown that a two-step procedure, in which dentin is saturated with disodium phosphate (5%) and then treated with $CaCl_2$ (10%), induces the deposition of calcium phosphate in the tubules and on the dentin surface.[197] The synergistic effect of NaF has also been investigated, with the conclusion that its presence leads to more apatitic precipitation formation.[198]

Bioactive glasses

Rationalised by the principle that silica can act as a nucleation site for precipitation of calcium and phosphorus, dental-tubule occlusion through the use of bioactive glasses has also received some attention as is exemplified by published work on biosilicates[199,200] and the FDA approval of the NovaMin anti-hypersensitivity treatment.[201] The active ingredient of NovaMin is calcium sodium phosphosilicate (CSPS), which on exposure to aqueous media liberates Ca^{2+} and phosphorus ions that re-form into hydroxy-carbonate apatite.[201] In vitro experiments by Burwell et al.[202] have shown that the formed mineralised layer of hydroxy-carbonate apatite is mechanically strong and resistant to acid challenges.

Further materials and techniques

Studies have shown that a technology that affects the sealing of dentin tubules with an acid resistant plug that contains arginine, $CaCO_3$ and phosphate is effective at relieving DH.[203,204] This finding has led to the design of a dentifrice, Pro-Argin™ and its whitening variant, which are claimed to offer instant relief to DH-induced pain .[203,205] The performance of arginine-containing pastes has been the subject of a comparative study involving Sr formulations. Both strontium acetate and $SrCl_2$ have been shown to form mineralised deposits within dentinal tubules and on the surface of exposed dentin, with the acetate salt exhibiting clinically proven effectiveness.[206,207] Other approaches towards increased dental-tubule occlusion have included NaF treatment in conjunction with iontophoresis,[208,209] or with erbium-doped yttrium aluminium garnet ($Er:Y_3Al_5O_{12}$; Er:YAG),[210] or neodymium-doped YAG (Nd:YAG)[211] laser irradiation.

State of the art and future direction

Despite significant advances in anti-hypersensitivity, remineralisation and tooth-whitening technologies, the long-standing challenge of plaque control remains central to improved dental care. Linked to this is the increasing prevalence of dental erosion, particularly amongst the young. A possible alternative to the use of antimicrobials to control plaque is to employ non-toxic, anti-adhesion polymers that form a thin protective coating onto the tooth surface. Complicated by the rapid formation of the salivary pellicle, the major challenge is to design the delivery system (toothpaste or mouth rinse) such that the polymer is deposited as a thin but substantive coating on the tooth surface. A key issue with conventional occlusive technologies that use inorganic salts, such as amorphous calcium phosphate, is the susceptibility of the precipitated mineral to acid attack, which impacts upon substantivity. The blocking of the tubule lumen by calcium oxalate or silica gives a longer-lasting benefit, but the use of polymer thin films provides an opportunity not only to treat existing DH, but also to help prevent its occurrence by laying down a shield that protects against acid erosion and the action of tooth chromogens. Aqueous nanoparticulate suspensions of the 2:1 copolymer of 1H,1H,2H,2H-perfluorodecyl acrylate and 2-hydroxyethyl acrylate have been shown to form into substantive dental coatings that offer significant resistance to staining, to bacterial colonisation and to demineralisation, and also to inhibit the dentinal fluid flow that provides the pain stimulus of dental hypersensitivity (Fig. 7).[212,213] The

prohibitive production cost for this material has provided the impetus for current research activities on, amongst other readily accessible materials, aqueous latexes of the poly(alkyl methacrylate)s. While the potential utility of one such material, poly(butyl methacrylate), to be deposited as a substantive tooth coating[215] that offers protection against dental staining, dentinal hypersensitivity and acid demineralisation[216,217] has been shown, its plaque-inhibition properties remain to be tested.

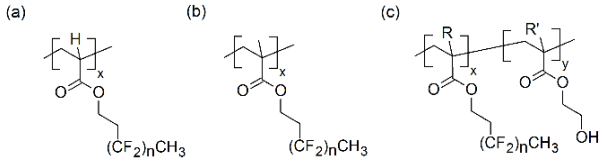

Fig. 7: Low-surface-energy polymers: (a) 1H,1H,2H,2H-perfluoroalkyl acrylates, (b) 1H,1H,2H,2H-perfluoroalkyl methacrylates and (c) 1H,1H,2H,2H-perfluoroalkylacrylate (methacrylate)-co-2-hydroxyethyl acrylate (methacrylate); n = 2, 3, 7; R, R′ = H / CH_3. Adapted from [212] and used with permission.

Dedication

We dedicate this work to Dr Thomas G. Nevell who sadly passed away shortly after the completion of the project from which this review originated.

References

1. S. K. Templeton: Rotten teeth put 26,000 children in hospital, Sunday Times, 13th July 2014, UK. http://www.thesundaytimes.co.uk/sto/news/uk_news/Health/Sugar/article1433860.ece
2. H. Nadimi, H. Wesamaa, S. J. Janket, P. Bollu and J. H. Meurman: Br. Dent. J., 2011, **211**, (7), E15.
3. P. E. Kolenbrander and J. London: J. Bacteriol., 1993, **175**, (11), 3247–3252.
4. H. F. Jenkinson and R. J. Lamont: Crit. Rev. Oral Biol. Med., 1997, **8**, (2), 175–200.
5. B. Rosan and R. J. Lamont: Microbes Infect., 2000, **2**, (13), 1599–1607.
6. E. A. M. Kidd: Essentials of Dental Caries: The Disease and its Management, 3rd Ed., 2005, Oxford University Press, Oxford, UK.
7. J. D. B. Featherstone: Aust. Dent. J., 2008, **53**, (3), 286–291.
8. F. Chen and D. Wang: Expert. Opin. Ther. Pat., 2010, **20**, 5, 681–694.
9. C. Fu, R. Kelly, L. Xin–Ming, R. Richard, B. Kenneth and W. Dong: Pharm. Res., 2010, **27**, (11), 2356–2364.
10. K. Hori and S. Matsumoto: Biochem. Eng. J., 2010, **48**, (3), 424–434.
11. S. Bayoudh, A. Othmane, F. Bettaieb, A. Bakhrouf, H. B. Ouada and L. Ponsonnet: Mater. Sci. Eng. C, 2006, **26**, (2–3), 300–305.
12. C. J. Whittaker, C. M. Klier and P. E. Kolenbrander: Annu. Rev. Microbiol., 1996, **50**, (1), 513–552.
13. B. Derjaguin and L. Landau: Acta Physico. Chemica URSS, 1941, **14**, 633.
14. E. J. W. Verwey and J. Th. G. Overbeek: Stability of Colloids, 1948, Elsevier, Amsterdam.
15. F. Khan and W.G. Young: Toothwear The ABC of the Worn Dentination, 2011, **231**, John Wiley & Sons, New York.
16. B. T. Amaechi and S. M. Higham: J. Dent., 2005, **33**, (3), 243–252.
17. A. Lussi: Dental Erosion, from diagnosis to therapy, 2006, **219**, Karger, London.
18. Y. H. Al-Dlaigan, L. Shaw and A. Smith: Br. Dent. J., 2001, **190**, (3), 145–149.
19. N. X. West, J. A. Hughes and M. Addy: J. Oral Rehab., 2000, **27**, (10), 875–880.
20. A. Lussi, B. Megert, R. P. Shellis and X. Wang: Br. J. Nutrition, 2012, **107**, 252–262.
21. J. F. Tahmassebi, M. S. Duggal, G. Malik-Kotru and M. E. J. Curzon: J. Dent., 2006, **34**, 2–11.
22. M. E. Barbour, D. M. Parker, G. C. Allen, K. D. Jandt: Eur. J. Oral Sci., 2003, **111**, 258–262.
23. N. X. West, J. A. Hughes and M. Addy: J. Oral Rehab., 2002, **29**, (2), 167–174.
24. A. C. Magalhaes, S. M. Moraes, D. Rios, A. Wiegand and M. A. R. Buzalaf: Oral Health Preventive Dent., 2010, **8**, (1), 41–45.
25. J. A. Hughes, N. X. West, D. M. Parker, M. H. van den Braak and M. Addy: J. Dent., 2000, **28**, 147–152.
26. J. Kolahi, M. Fazilati and M. Kadivar: Med. Hypotheses, 2009, **73**, (4), 524–525.
27. M. T. Kato, A. L. Leite, A. R. Hannas and M. A. R. Buzalaf: J. Dent. Res., 2010, **89**, (5), 468–472.
28. C. S. Barbosa, M. T. Kato and M. A. R. Buzalaf: Aust. Dent. J., 2011, **56**, (3), 317–321.
29. M. T. Kato, A. C. Magalhaes, D. Rios, A. R. Hannas, T. Attin and M. A. R. Buzalaf: J. Appl. Oral Sci., 2009, **17**, (6), 560–564.
30. J. Arends and J. M. ten Cate: J. Cryst. Growth, 1981, **53**, 135–147.
31. H. Ehrlich, P. G. Koutsoukos, K. D. Demadis and O. S. Pokrovsky: Micron, 2008, **39**, (8), 1062–1091.
32. F. García-Godoy and M. J. Hicks: J. Am. Dental Assoc., 2008, **139**, (Suppl. S), 25S–34S.
33. J. P. Barone and G. H. Nancollas: J. Colloid Interface Sci., 1977, **62**, (3), 421–431.
34. R. Z. LeGeros: J. Clin. Dent., 1999, **10**, (2), 65–73.
35. B. T. Amaechi and S. M. Higham: Arch. Oral Biol., 2001, **46**, (8), 697–703.
36. D. W. Bartlett and B. G. N. Smith: Definition, classification and clinical assessment of attrition, erosion and abrasion of enamel and dentine. In: M. Addy, G. Embery, W. M. Edgar and R. Orchardson (Eds.), Tooth Wear and Sensitivity – Clinical Advances in Restorative Dentistry, 1st Ed., 2000, Martin Dunitz, London, pp. 87–93.
37. A. C. Magalhães, A. Wiegand, D. Rios, H. M. Honório and M. A. R. Buzalaf: J. Appl. Oral Sci., 2009, **17**, 75–86.
38. M. Hannig and M. Balz: Caries Res., 2001, **35**, (2), 142–148.
39. Y. Nekrashevych, M. Hannig and L. Stosser: Oral Health Prevent. Dent., 2004, **2**, (1), 5–11.
40. C. Hannig, K. Becker, N. Häusler, W. Hoth-Hannig, T. Attin and M. Hannig: Arch. Oral Biol., 2007, **52**, (5), 444–449.
41. M. Eisenburger, M. Addy, J. A. Hughes and R. P. Shellis: Caries Res., 2001, **35**, (3), 211–215.
42. F. Lippert, D. M. Parker and K. D. Jandt: J. Colloid Interface Sci., 2004, **280**, (2), 442–448.
43. R. Orchardson and D. G. Gillam: J. Am. Dent. Assoc., 2006, **137**, (7), 990–998.

44. M. Addy: Dentine hypersensitivity: definition, prevalence, distribution and aetiology. In: M. Addy, G. Embery, W. M. Edgar and R. Orchardson (Eds.), Tooth Wear and Sensitivity – Clinical Advances in Restorative Dentistry, 1st Ed., 2000, Martin Dunitz, London, pp. 239–248.
45. M. Addy: Clin. Adv. Restorative Dent., 1989, **13**, 957–964.
46. P. A. Walters: J. Contemp. Dental Pract., 2005, **6**, (2), 107–117.
47. M. Brännström: J. Endodont., 1986, **12**, (10), 453–457.
48. D. H. Pashley: Dent. Clin. North Am., 1990, **34**, (3), 449–473.
49. E. G. Absi, M. Addy and D. Adams: J. Clin. Periodontol., 1987, **14**, (5), 280–284.
50. A. Joiner: J. Dent., 2004, **32**, 3–12.
51. A. Joiner: J. Dent., 2010, **38**, e17–e24.
52. S. Sheen, N. Banfield and M. Addy: J. Dent., 2002, **30**, (7–8), 365–369.
53. N. C. A. Claydon, J. Moran, M. L. Bosma, S. Shirodaria, M. Addy and R. Newcombe: J. Clin. Periodontol., 2004, **31**, (12), 1088–1091.
54. K. Takeyoshi: Int. Congr. Ser., 2005, **1284**, 140–149.
55. A. Gaffar, J. Afflitto and N. Nabi: Eur. J. Oral Sci., 1997, **105**, (5), 502–507.
56. S. J. Upson: 'Multifunctional coatings for oral care: structure-activity relationships', PhD Thesis, University of Portsmouth, Portsmouth, UK, 2012.
57. J. Moran, M. Addy, R. Jackson and R. G. Newcombe: J. Clin. Periodontol., 2000, **27**, (1), 37–40.
58. P. Bonesvoll and P. Gjermo: Arch. Oral Biol., 1978, **23**, (4), 289–294.
59. C. Sandt, J. Barbeau, M.-A. Gagnon and M. Lafleur: J. Antimicrobiol. Chemother., **60**, (6), 1281–1287.
60. K. Ramalingam, B. T. Amaechi, R. H. Ralph and V. A. Lee: Arch. Oral. Biol., 2012, **57**, (1), 15–22.
61. N. Namba, Y. Yoshida, N. Nagaoka, S. Takashima, K. Matsuura-Yoshimoto, H. Maeda, B. Van Meerbeek, K. Suzuki and S. Takashiba: Dent. Mater., 2009, **25**, (4), 424–430.
62. T. A. Al-Musallam, C. A. Evans, J. L. Drummond, C. Matasa and C. D. Wu: J. Orthod. Dentofacial Orthop., 2006, **129**, (2), 245–251.
63. V. Sehgal, V. S. Shetty, S. Mogra, G. Bhat, M. Eipe, S. Jacob and L. Prabu: Am. J. Orthod. Dentofacial Orthop., 2007, **131**, (4), 525–529.
64. J. Autio-Gold: Oper. Dent., 2008, **33**, (6), 710–716.
65. C. G. Emilson: J. Dent. Res., 1994, **73**, (3), 682–691.
66. G. J. Christopher: Periodontol. 2000, 1997, **15**, (1), 55–62.
67. C. A. de Souza, A. P. V. Colombo, R. M. Souto, C. M. Silva-Boghossian, J. M. Granjeiro, G. G. Alves, A. M. Rossi and M. H. M. Rocha-Leão: Colloids Surf. B Biointerfaces, 2011, **87**, (2), 310–318.
68. S. Sekino, P. Ramberg, N. Guzin Uzel, S. Socransky and J. Lindhe: J. Clin. Periodontol., 2004, **31**, (8), 609–614.
69. M. Cousido, T. I. Carmona, L. García-Caballero, J. Limeres, M. Álvarez and P. Diz: Clin. Oral Invest., 2010, **14**, (4), 397–402.
70. P. A. Heasman, L. Heasman, F. Stacey and G. I. McCracken: J. Clin. Periodontol., 2001, **28**, (1), 90–95.
71. M. C. Cortizo, T. G. Oberti, M. S. Cortizo, A. M. Cortizo and M. de Mele: J. Dent., 2012, **40**, (4), 329–337.
72. F. B. Zanatta, R. P. Antoniazzi and C. K. Rösing: J. Appl. Oral Sci., 2010, **18**, 515–521.
73. R. F. Menegon, L. Blau, N. S. Janzantti, A. C. Pizzolitto, M. A. Correa, M. Monteiro and M. C. Chung: J. Pharm. Sci., 2011, **100**, (8), 3130–3138.
74. C. Solis, A. Santos, J. Nart and D. Violant: J. Periodontol., 2011, **82**, (1), 80–85.
75. N. C. Sharma, H. J. Galustians, J. Qaqish, C. H. Charles, J. W. Vincent and J. A. McGuire: J. Clin. Periodontol., 2003, **30**, (7), 590–594.
76. F. Afennich, D. E. Slot, N. Hossainian and G. A. Van der Weijden: Int. J. Dent. Hygiene, 2011, **9**, (3), 182–190.
77. C. P. Ernst, K. Canbek, A. Dillenburger and B. Willershausen: Quintessence Int., 2005, **36**, (8), 641–652.
78. J. E. Moermann and H. R. Muehlemann: J. Dent. Res., 1983, **62**, (2), 135–137.
79. N. Claydon, L. Hunter, J. Moran, W. Wade, E. Kelty, R. Movert and M. Addy: J. Clin. Periodontol., 1996, **23**, (3), 220–228.
80. N. Vassilakos, T. Arnebrant and J. Rundegren: Caries Res., 1993, **27**, (3), 176–182.
81. M. Addy, J. Moran and R. G. Newcombe: J. Clin. Periodontol., 2007, **34**, (1), 58–65.
82. P. D. Marsh: J. Dent. Res., 1992, **71**, 1431–1438.
83. P. Kraivaphan, C. Amornchat, T. Laothumthut and T. Triratana: Southeast Asian J. Trop. Med. Public Health, 2009, **40**, (4), 840–848.
84. S. Kockisch, G. D. Rees, J. Tsibouklis and J. D. Smart: Eur. J. Pharm. Biopharm., 2005, **59**, (1), 207–216.
85. T. Loftsson, N. Leeves, B. Bjornsdottir, L. Duffy and M. Masson: J. Pharm. Sci., 1999, **88**, (12), 1254–1258.
86. A. Dinge and M. Nagarsenker: AAPS PharmSciTech, 2008, **9**, (2), 349–356.
87. A. Blinkhorn, P. M. Bartold, M. P. Cullinan, T. E. Madden, R. I. Marshall, S. L. Raphael and G. J. Seymour: Br. Dent. J., 2009, **207**, (3), 117–125.
88. M. Charnley, M. Textor and C. Acikgoz: React. Funct. Polym., 2011, **71**, (3), 329–334.
89. J. R. Smith and D. A. Lamprou: Trans. IMF, 2014, **92**, (1), 9–19.
90. B. Gottenbos, D. W. Grijpma, H. C. van der Mei, J. Feijen and H. J. Busscher: J. Antimicrobiol. Chemother., 2001, **48**, (1), 7–13.
91. Q. Zhao, C. Wang, Y. Liu and S. Wang: Int. J. Adh. Adhes., 2007, **27**, (2), 85–91.
92. R. Bürgers, A. Eidt, R. Frankenberger, M. Rosentritt, H. Schweikl, G. Handel and S. Hahnel: Arch. Oral Biol., 2009, **54**, (6), 595–601.
93. J.-S. Chung, B. G. Kim, S. Shim, S.-E. Kim, E.-H. Sohn, J. Yoon and J.-C. Lee: J Colloid Interface Sci., 2012, **366**, (1), 64–69.
94. C. Badet and F. Quero: Anaerobe, 2011, **17**, (1), 19–22.
95. H. M. Nassar, M. Li and R. L. Gregory: Appl. Environ. Microbiol., 2012, **78**, (2), 536–540.
96. P. A. Nayak, U. A. Nayak and R. Mythili: Contemp. Clin. Dent., 2010, **1**, (4), 214–217.
97. A. S. Pedro, E. Cabral-Albuquerque, D. Ferreira and B. Sarmento: Carbohyd. Polym., 2009, **76**, (4), 501–508.
98. R. P. Allaker and C. W. I. Douglas: Int. J. Antimicrob. Agents, 2009, **33**, (1), 8–13.
99. K. Takarada, R. Kimizuka, N. Takahashi, K. Honma, K. Okuda and T. Kato: Oral Microbiol. Immunol., 2004, **19**, (1), 61–64.
100. M. A. Botelho, R. A. dos Santos, J. G. Martins, C. O. Carvalho, M. C. Paz, C. Azenha, R. S. Ruela, D. B. Queiroz, W. S. Ruela, G. Marinho and F. I. Ruela: Phytother Res., 2009, **23**, (9), 1214–1219.
101. C. A. Charles, J. A. McGuire, N. C. Sharma and J. Qaqish: Pesqui Odontol. Bras, 2011, **25**, (4), 338–344.
102. S. C. Cortelli, J. R. Cortelli, M. Holzhausen, G. C. N. Franco, R. Z. Rebelo, A. S. Sonagere, C. d. S. Queiroz and F. O. Costa: J. Clin. Periodontol., 2009, **36**, (4), 333–342.

103. M. J. Verkaik, H. J. Busscher, D. Jager, A. M. Slomp, F. Abbas and H. C. van der Mei: J. Dent., 2011, **39**, (3), 218–224.
104. K. Bae, E. Jun, S. Lee, D. Paik and J. Kim: Clin. Oral. Invest., 2006, **10**, (2), 102–107.
105. M. C. Nitin and Y. V. Adhikrao: Indian J. Dent. Res., 2010, **21**, (3), 380–384.
106. V. Lazar: Anaerobe, 2011, **17**, (6), 280–285.
107. D. Senadheera and D. G. Cvitkovitch: Adv. Exp. Med. Biol., 2008, **631**, 178–188.
108. D. Cunliffe, C. A. Smart and C. Alexander: Polymer technologies for control of bacterial adhesion, Encyclopaedia of Food Microbiology, 1999, Academic Press, Massachusetts.
109. S. Krishnan, C. J. Weinman and C. K. Ober: J. Mater. Chem., 2008, **18**, (29), 3405–3413.
110. D. E. Owens and N. A. Peppas: Int. J. Pharm., 2006, **307**, (1), 93–102.
111. Y. Y. Luk, M. Kato and M. Mrksich: Langmuir, 2000, **16**, 9604–9608.
112. A. T. tenCate, S. Reinders, A. F., D. H. Turkenburg, A. Bruin, F. D'Souza, G. Donnelly, T., P. Willemsen, R., J. H. Maas and J. C. van Bommel: Prog. Org. Coat., 2009, **64**, (2–3), 221–224.
113. K. D. Park, Y. S. Kim, D. K. Han, Y. H. Kim, E. H. B. Lee, H. Suh and K. S. Choi: Biomaterials, 1998, **19**, (7–9), 851–859.
114. I. Szleifer: Biophys J., 1997, **72**, (2), 595–612.
115. M. R. Nejadnik, H. C. van der Mei, W. Norde and H. J. Busscher: Biomaterials, 2008, **29**, (30), 4117–4121.
116. J. Olsson, A. Carlen and K. Holmberg: J. Dent. Res., 1990, **69**, (9), 1586–1591.
117. I. C. S. Fernandez, H. C. van der Mei, M. J. Lochhead, D. W. Grainger and H. J. Busscher: Biomaterials, 2007, **28**, (28), 4105–4112.
118. A. Shimotoyodome, T. Koudate, H. Kobayashi, J. Nakamura, I. Tokimitsu, T. Hase, T. Inoue, T. Matsukubo and Y. Takaesu: Antimicrobiol. Agents Chemother., 2007, **51**, (10), 3634–3641.
119. N. B. Holland, Q. Yongxing, M. Ruegsegger and R. E. Marchant: Nature, 1998, **392**, 799–801.
120. L. Wu, J. Jasinski and S. Krishnan: J. Appl. Polym. Sci., 2012, **124**, (3), 2154–2170.
121. A. B. Lowe, M. Vamvakaki, M. A. Wassall, L. Wong, N. C. Billingham, S. P. Armes and A. W. Lloyd: J. Biomed. Mater. Res., 2000, **52**, (1), 88–94.
122. G. Cheng, Z. Zhang, S. F. Chen, J. D. Bryers and S. Y. Jiang: Biomaterials, 2007, **28**, (29), 4192–4199.
123. S. Y. Jiang and Z. Q. Cao: Adv. Mater., 2010, **22**, (9), 920–932.
124. B. E. Gustafsson, C.-E. Quensel, L. S. Lanke, C. Lundqvist, H. Grahnén, B. E. Bonow and B. Krasse: Acta. Odontol. Scand., 1953, **11**, (3–4), 232–364.
125. T. Matsukubo and I. Takazoe: Int. Dent. J., 2006, **56**, (3), 119–130.
126. L. Trahan: Int. Dent. J., 1995, **45**, (1 Suppl 1), 77–92.
127. S. Haresaku, T. Hanioka, A. Tsutsui, M. Yamamoto, T. Chou and Y. Gunjishima: Caries Res., 2007, **41**, (3), 198–203.
128. A. W. Adamson: Physical Chemistry of Surfaces, 1990, Wiley, New York.
129. M. M. Tunney, S. P. Gorman and S. Patrick: Rev. Med. Microbiol., 1996, **7**, (4), 195–205.
130. A. T. Poortinga, R. Bos, W. Norde and H. J. Busscher: Surf. Sci. Rep., 2002, **47**, (1), 1–32.
131. A. H. Weerkamp, M. Quirynen, M. Marechal, H. C. Van Der Mei, D. Van Steenberghe and H. J. Busscher: Microbial Ecology in Health and Disease, 1989, **2**, (1), 11–18.
132. M. Quirynen, M. Marechal, H. J. Busscher, A. H. Weerkamp, P. L. Darius and D. Vansteenberghe: J. Clin. Periodontol., 1990, **17**, (3), 138–144.
133. W. Teughels, N. Van Assche, I. Sliepen and M. Quirynen: Clin. Oral Implants Res., 2006, **17**, (S2), 68–81.
134. J. Tsibouklis, M. Stone, A. A. Thorpe, P. Graham, V. Peters, R. Heerlien, J. R. Smith, K. L. Green and T. G. Nevell: Biomaterials, 1999, **20**, (13), 1229–1235.
135. H. Kobayashi and M. J. Owen: Trends Polym. Sci., 1995, **3**, (10), 330–335.
136. M. J. Owen: Comments Inorg. Chem., 1988, **7**, (4), 195–213.
137. D. Churchley: 'Ultra-low surface energy coatings with inherent resistance to bacterial colonisation: A route to plaque and stain prevention in the oral cavity', PhD Thesis, University of Portsmouth, Portsmouth, UK, 2004.
138. B. Lassen, K. Holmberg, C. Brink, A. Carlen and J. Olsson: Colloid Polym. Sci., 1994, **272**, (9), 1143–1150.
139. M. J. Owen: Chemtech, 1981, **11**, (5), 288–292.
140. D. P. Edwards: 'Interfacial Behaviour and Resistance to Marine Fouling of Silicone Elastomers', PhD Thesis, University of Portsmouth, Portsmouth, UK, 1995.
141. T. G. Nevell, D. P. Edwards, A. J. Davis and R. A. Pullin: Biofouling, 1996, **10**, (1–3), 199–212.
142. J. D. Adkins, A. E. Mera, M. A. Roe-Short, G. T. Pawlikowski and R. F. Brady Jr: Prog. Org. Coat., 1996, **29**, (1–4), 1–5.
143. J. D. B. Featherstone: Commun. Dent. Oral Epidemiol., 1999, **27**, (1), 31–40.
144. J. Hicks, F. Garcia-Godoy and C. Flaitz: J. Clin. Pediatr. Dent., 2004, **28**, (2), 119–124.
145. J. M. ten Cate and J. D. Featherstone: Crit. Rev. Oral Biol. Med., 1991, **2**, (3), 283–296.
146. W. J. N. Collins, T. F. Walsh and K. H. Figures: A Handbook for Dental Hygienists, 4th Ed., 1999, Wright, Oxford.
147. Y. Chen and X. Miao: Biomaterials, 2005, **26**, (11), 1205–1210.
148. J. P. Simmer and A. G. Fincham: Crit. Rev. Oral Biol. Med., 1995, **6**, (2), 84–108.
149. B. Ögaard, G. Rölla, J. A. N. Ruben, T. Dijkman and J. Arends: Eur. J. Oral Sci., 1988, **96**, (3), 209–211.
150. R. E. Marquis: Can. J. Microbiol., 1995, **41**, (11), 955–964.
151. K. Kamotsay, A. Herczegh, F. Rozgonyi, I. Nasz, Z. Gintner and J. Banoczy: Acta Microbiol. Immunol. Hungar., 2002, **49**, (1), 47–58.
152. C. Clinch: Fluoride, 2010, **43**, (4), 205–214.
153. H. G. McCann: Arch. Oral Biol., 1969, **14**, (5), 521–531.
154. T. Büyükyilmaz, B. Ögaard and G. Rölla: Eur. J. Oral Sci., 1997, **105**, (5), 473–477.
155. L. Hove, B. Holme, B. Ögaard, T. Willumsen and A. B. Tveit: Caries Res., 2006, **40**, (5), 440–443.
156. A. C. Magalhaes, D. Rios, H. M. Honorio, A. C. B. Delbem and M. A. R. Buzalaf: J. Appl. Oral Sci., 2009, **17**, (1), 56–60.
157. A. Wiegand, W. Meier, E. Sutter, A. C. Magalhaes, K. Becker, M. Roos and T. Attin: Caries Res., 2008, **42**, (4), 247–254.
158. A. Wiegand, B. Hiestand, B. Sener, A. C. Magalhaes, M. Roos and T. Attin: Arch. Oral Biol., 2010, **55**, (3), 223–228.
159. A. C. Magalhaes, M. T. Kato, D. Rios, A. Wiegand, T. Attin and M. A. R. Buzalaf: Caries Res., 2008, **42**, (4), 269–274.

160. N. Schlueter, C. Ganss, U. Mueller and J. Klimek: Caries Res., 2007, **41**, (2), 141–145.
161. Y. Iijima, F. Cai, P. Shen, G. Walker, C. Reynolds and E. C. Reynolds: Caries Res., 2004, **38**, (6), 551–556.
162. W. R. Aimutis: J. Nutrition, 2004, **134**, (4), 989S–995S.
163. A. Azarpazhooh and H. Limeback: J. Am. Dental Assoc., 2008, **139**, (7), 915–924.
164. X. Wang, B. Megert, E. Hellwig, K. W. Neuhaus and A. Lussi: J. Dent., 2011, **39**, (2), 163–170.
165. R. K. Rose: Arch. Oral Biol., 2000, **45**, (7), 569–575.
166. L. Ramalingam, L. B. Messer and E. C. Reynolds: Pediatric Dent., 2005, **27**, (1), 61–67.
167. D. J. Manton, F. Cai, Y. Yuan, G. D. Walker, N. J. Cochrane, C. Reynolds, L. J. Brearley-Messer and E. C. Reynolds: Aust. Dent. J., 2010, **55**, (3), 275–279.
168. G. D. Walker, F. Cai, P. Shen, G. G. Adams, C. Reynolds and E. C. Reynolds: Caries Res., 2010, **44**, (1), 33–40.
169. N. Srinivasan, M. Kavitha and S. C. Loganathan: Arch. Oral Biol., 2010, **55**, (7), 541–544.
170. A. J. White, L. H. Gracia and M. E. Barbour: Caries Res., 2011, **45**, (1), 13–20.
171. P. M. Bartold: Aust. Dent. J., 2006, **51**, (3), 212–218.
172. R. Orchardson: Strategies for the management of dentine hypersensitivity. In: M. Addy, G. Embery, W. M. Edgar and R. Orchardson (Eds.), Tooth Wear and Sensitivity – Clinical Advances in Restorative Dentistry, 1st Ed., 2000, Martin Dunitz, London.
173. R. Docimo, L. Montesani, P. Maturo, M. Costacurta, M. Bartolino, W. Devizio, Y. P. Zhang and S. Dibart: Am. J. Dent., 2007, **20**, (4), 209–211.
174. S. Noparatkailas, S. Wanachantararak, N. Vongsavan and B. Matthews: Arch. Oral Biol., 2009, **54**, (1), 50–54.
175. K. Markowitz, G. Bilotto and S. Kim: Arch. Oral Biol., 1991, **36**, 1–7.
176. S. Babel: Int. J. Contemp. Dent., 2011, **2**, (5), 76–79.
177. K. Markowitz and S. Kim: Dent. Clin. North Am., 1990, **34**, (3), 491–501.
178. R. Pereira and V. K. Chava: J. Int. Acad. Periodontol., 2002, **4**, (2), 44–48.
179. J. D. Greenhill and D. H. Pashley: J. Dent. Res., 1981, **60**, (3), 686–698.
180. J. C. Pereira, A. D. Segala and D. G. Gillam: Dent. Mater., 2005, **21**, (2), 129–138.
181. F. L. Pillon, I. G. Romani and E. R. Schmidt: J. Periodontol., 2004, **75**, (11), 1461–1464.
182. J. Cunha-Cruz, J. R. Stout, L. J. Heaton and J. C. Wataha: J. Dent. Res., 2011, **90**, (3), 304–310.
183. S. Poulsen: Evidence-based Dentistry, 2011, **12**, (2), 47.
184. T. Suge, A. Kawasaki, K. Ishikawa, T. Matsuo and S. Ebisu: Dent. Mater. J., 2005, **24**, (4), 522–529.
185. R. Orchardson and D. G. Gillam: J. Orofacial Pain, 2000, **14**, (1), 9–19.
186. T. Willumsen, K. Solemdal, M. Wenaasen and B. Ogaard: Gerodontology, 2007, **24**, (4), 239–243.
187. T. He, J. L. Chang, R. Cheng, X. Li, L. Sun and A. R. Biesbrock: Am. J. Dent., 2011, **24**, (6), 336–340.
188. J. A. Aas, B. J. Paster, L. N. Stokes, I. Olsen and F. E. Dewhirst: J. Clin. Microbiol., 2005, **43**, (11), 5721–5732.
189. T. He, M. L. Barker, J. Qaqish and N. Sharma: J. Clin. Dent., 2011, **22**, (2), 46–50.
190. S. Miglani, V. Aggarwal and B. Ahuja: J. Clin. Dent., 2010, **13**, (4), 218–224.
191. L. X. Ni, T. He, A. Chang and L. Sun: Am. J. Dent., 2010, **23**, 17B–21B.
192. T. Schiff, Y. Bonta, H. M. Proskin, W. DeVizio, M. Petrone and A. R. Volpe: Am. J. Dent., 2000, **13**, (3), 111–115.
193. T. Schiff, L. Saletta, R. A. Baker, J. L. Winston and T. He: Comp. Continuing Ed. Dent., 2005, **26**, 35–40.
194. T. Schiff, T. He, L. Sagel and R. Baker: J. Contemp. Dent. Pract., 2006, **7**, (2), 1–8.
195. T. Day, J. Einwag, J. S. Hermann, T. He, M. K. Anastasia, M. Barker and Y. Zhang: J. Contemp. Dent. Pract., 2010, **11**, (1), E001–008.
196. T. He, M. Britt and A. R. Biesbrock: Am. J. Dent., 2010, **23**, 3B–10B.
197. Y. Imai and T. Akimoto: Dent. Mater., 1990, **9**, (2), 167–172.
198. A. Kowalczyk, B. Botulinski, M. Jaworska, A. Kierklo, M. Pawinska and E. Dabrowska: Adv. Med. Sci., 2006, **51**, (Suppl 1), 40–42.
199. C. Tirapelli, H. Panzeri, R. G. Soares, O. Peitl and E. D. Zanotto: Brazilian Oral Res., 2010, **24**, 381–387.
200. C. Tirapelli, H. Panzeri, E. H. G. Lara, R. G. Soares, O. Peitl and E. D. Zanotto: J. Oral Rehab., 2011, **38**, (4), 253–262.
201. J. S. Wefel: Adv. Dental Res., 2009, **21**, (1), 40–43.
202. A. Burwell, D. Jennings, D. Muscle and D. C. Greenspan: J. Clin. Dent., 2010, **21**, (3), 66–71.
203. D. Cummins: Am. J. Dent., 2010, **23**, 3A–13A.
204. S. A. Lavender, I. Petrou, R. Heu, M. A. Stranick, D. Cummins, L. Kilpatrick-Liverman, R. J. Sullivan and R. P. Santarpia: Am. J. Dent., 2010, **23**, 14A–19A.
205. R. Docimo, L. Montesani, P. Maturo, M. Costacurta, M. Bartolino, Y. P. Zhang, W. DeVizio, E. Delgado, D. Cummins, S. Dibart and L. R. Mateo: J. Clin. Dent., 2009, **20**, (4), 137–143.
206. A. Kobler, O. Kuss, H. G. Schaller and C. R. Gernhardt: Quintessence Int., 2008, **39**, (4), 321–325.
207. T. Layer and N. Hughes: J. Clin. Dent., 2010, **21**, (2), 56–58.
208. L. J. Chen, Q. F. Meng, Y. M. Chen, R. J. Smales and K. H. K. Yip: J. Dent., 2008, **36**, (9), 697–702.
209. P. Singal, R. Gupta and N. Pandit: J. Periodontol., 2005, **76**, (3), 351–357.
210. S. D. Ipci, G. Cakar, B. Kuru and S. Yilmaz: Photomed. Laser Surg., 2009, **27**, (1), 85–91.
211. W. H. Lan, H. C. Liu and C. P. Lin: J. Endodontics, 1999, **25**, (6), 424–426.
212. D. Churchley, G. D. Rees, E. Barbu, T. G. Nevell and J. Tsibouklis: Int. J. Pharm., 2008, **352**, (1–2), 44–49.
213. D. P. Churchley, E. Barbu, R. J. Ewen, Z. Shen, Y. Kim, M. A. McHugh, Z. Y. Zhang, T. G. Nevell, G. D. Rees and J. Tsibouklis: J. Biomed. Mater. Res. A, 2008, **84A**, (4), 994–1005.
214. E. Barbu, D. R. Churchley, T. G. Nevell, G. D. Rees and J. Tsibouklis: New comb fluoropolymers useful for e.g. combating dental erosion and tooth wear, and treating dentin hypersensitivity, Patent WO2007141330–A1, 2007.
215. B. Nielsen, T. Nevell, E. Barbu, G. Rees and J. Tsibouklis: J. Therm. Anal. Calorimetr., 2010, **102**, (1), 121–126.
216. B. V. Nielsen, T. G. Nevell, E. Barbu, J. R. Smith, G. D. Rees and J. Tsibouklis: Biomed. Mater., 2011, **6**, (1), 015003.
217. B. V. Nielsen, T. G. Nevell, E. Barbu, J. R. Smith, G. D. Rees and J. Tsibouklis: Polymers, 2011, **3**, (1), 314–329.

List of abbreviations

ACP	amorphous calcium phosphate
APF	acidulated phosphate fluoride
BAC	benzylalkonium chloride
CPC	cetylpyridinium chloride

CPP	casein phosphopeptides
CSP	competence stimulating peptide
CSPS	calcium sodium phosphosilicate
CHX	chlorhexidine
DDA	N,N-dimethyldodecylammonium
DH	dentin sensitivity
DLVO	Derjaguin and Landau, Verwey and Overbeek
EPS	exopolysaccharide
FDA	Food and Drug Administration
FHAP	fluorohydroxyapatite
HA	hydroxyapatite
HEX	hexetidine
MMP	matrix metalloproteinase
OCP	octacalcium phosphate
P4VMP	poly(4-vinyl-N-methylpyridinium iodide)
PBS	phosphate buffered saline
PEG	poly(ethylene glycol)
PMOX	poly(2-methyl-2-oxazoline)
PS	poly(styrene)
SEM	scanning electron microscopy
sem	standard error of mean
SF	stannous fluoride
TC	triclosan
YAG	yttrium aluminium garnet