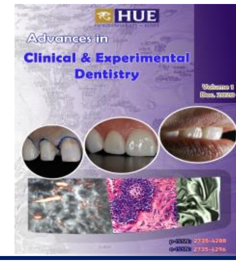
Advances in Clinical and Experimental Dentistry



The state-of-the-art validity of using methacryloyloxy-ethyl compounds in dentistry

Veronica Pavlov[1] and Mira Ibrahim[2]

Abstract

Background Methacryloyloxyethyl compounds, including 2-Methacryloyloxyethyl phosphorylcholine (MPC), is now used in dentistry given their biological compatibility and anti-bacterial properties.

Objective This overview highlights the recent advances methacryloyloxyethyl derivatives have brought into dentistry.

Results PC is a biocompatible and hydrophilic biomedical polymer, which is ventured into operative dentistry, orthodontics and endodontics. Its use is always enhanced with another chemical derivative or nanoparticles.

Advances in Knowledge The effect of incorporation of a protein repellent agent into soft lining material on biofilm formation has not been reported. Therefore, this study investigated the reported findings regarding the influence of adding MPC in different ratios to the powder of soft denture liner to benefit from its excellent ability to repel protein adsorption and prevent bacterial adhesion. Adhesive dentistry has improved resin composite with MPC and dimethylaminohexadecyl methacrylate for enhancing the inhibitory effect on secondary caries.

Keywords

MPC; resin; adhesive dentistry; biomaterial

1. School of Dentistry, Charles University, Prague, 2. Department of Biomaterials, Faculty of Dentistry, Horus University in Egypt. **DOI**: 10.21608/ACED.2021.107459.1007

Introduction

MPC and other methacryloyloxyethyl compounds are biocompatible and hydrophilic biomedical polymers, which are ventured into medicine and dentistry as an excellent biomedical polymer[1,2]. MPC has been shown to have an excellent ability to repel protein adsorption and prevent bacterial adhesion. It also showed adhesions properties that made it an excellent candidate for drug delivery [3–5]and nanosciences [6] . The phosphorylcholine group generates several unique properties arising from its dipolar ion structure, consisting of a phosphate anion and a trimethylammonium cation [7]. The effect of incorporation of a protein repellent agent into soft lining material on biofilm formation has not been studied. Therefore, this study underpins the previously reported findings to support the state of art potential and applications of using methacryloyloxyethyl compounds in dentistry. Regarding the protein-repellent mechanism, abundant-free water, but no bound water, is reported in the hydrated MPC polymer[8]. Protein adsorption increased with the presence of bound water[9]. On the other hand, a large amount of free water around the phosphorylcholine group is considered to detach proteins and repel protein adsorption. Since it was ushered to dental biomaterials, combinations with other methacryloyloxyethyl groups.

Successful bacterial or fungal adherence on a dental surface is an important step in forming biofilms. In this regard, the saliva or serum pellicles, such as mucins, fibrinogen and complements, during the colonization process and subsequent multilayer biofilm formation plays a vital role by binding to blastospores and germ tubes possibly modifying the process. Accordingly, there is a great need to develop a novel resin that can repel proteins. Such resin can repel proteins and hence inhibit bacteria attachment and it can further enhance the antibacterial potency of resin restorations by having a protein-repellent capacity[10–13]. Biofilm colony forming unit is the standard method used for evaluating biofilm formation in oral microbiology[11,14,15] . The primary adhesion of bacteria was aimed at by using polymers, which usually inhibit the initial adhesion of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The authors concluded that the mechanical property of the thin-film is one of the influential factors determining bacterial adhesion. These findings would be of significance in designing antibacterial materials[16].

Therefore, the research articles have used this method as the golden standard. With the enhanced biological compatibility of the methacryloyloxyethyl compounds, this study underpins the medical literature and classify the different uses in dentistry.

Method

We collated a corpus of all published articles that reported the use of any of the derivatives of methacryloyloxyethyl in dentistry. Running python codes and corpus analysis, we retrieved the concordance of each experimental and clinical items to collect the data and annotate it. The sued medical subject headings included "MPC", "methacryloyloxyethyl," "anti-bacterial", adhesive dentistry, biofilm, resin, and synonyms. Wildcards were used to augment the various spellings and morphological word forms. Therefore, this article provides the advances in ushering methacryloyloxyethyl compounds.

Results and Discussion

MPC seems to be the key derivative of methacryloyloxyethyl that is used in dentistry. The primary medical domains include oncology, pharmacology and dentistry (Figure 1). The use of this resin is mainly attributed to its diverse superior physical properties (Figure 2). The two figures show clustering of relevant terminologies with the same color while the distance between each term encodes the frequency of their co-occurrences. Because the code generates the automatic clustering using deep static word embeddings.

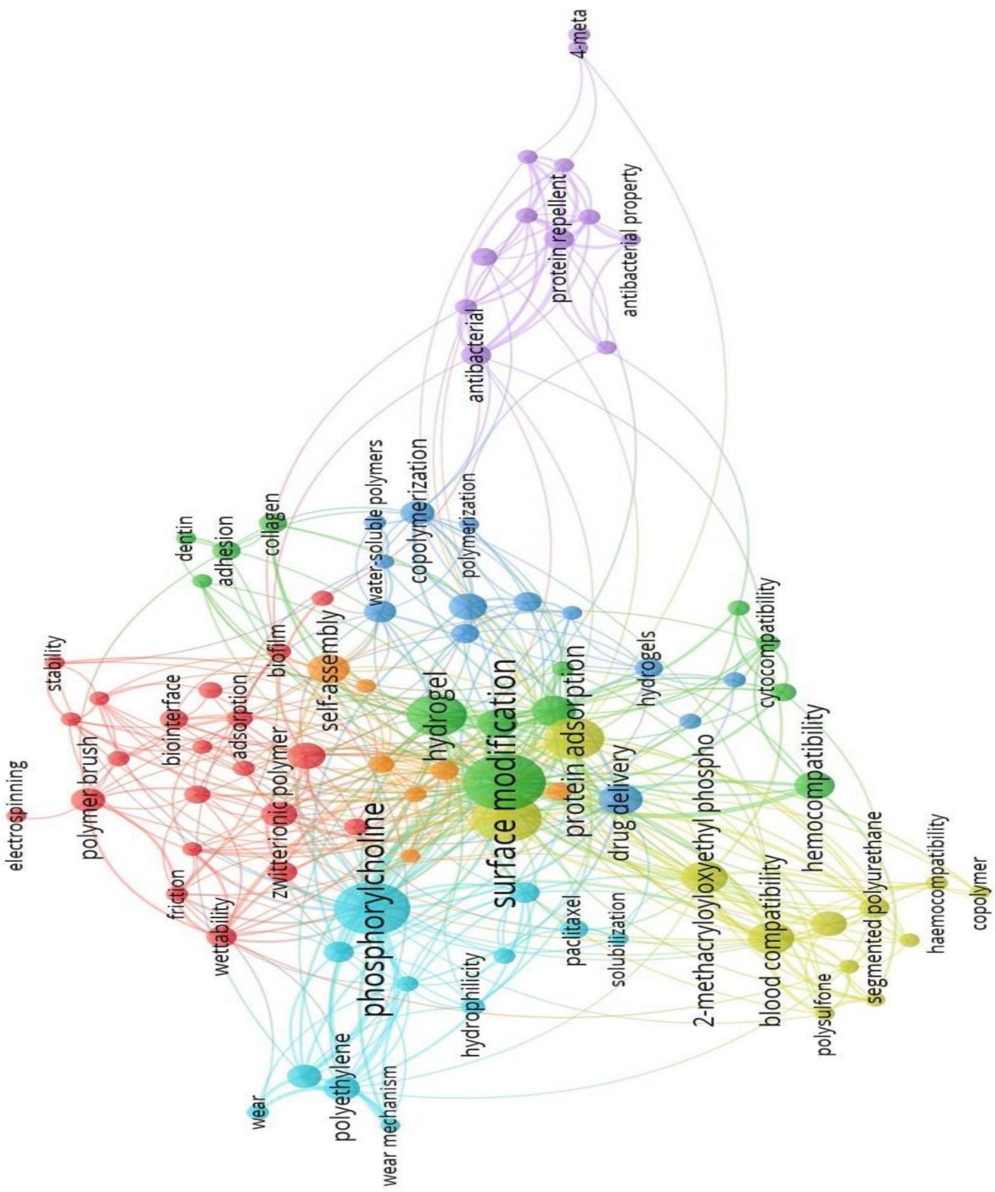


Figure 1. network analysis for all MPC-based research activities in bioscience. The turquoise color the hydrophilic physical properties and miscibility. The purple color denotes the biological properties the resin demonstrates. The red color represents the processing of the resin to enhance its properties.

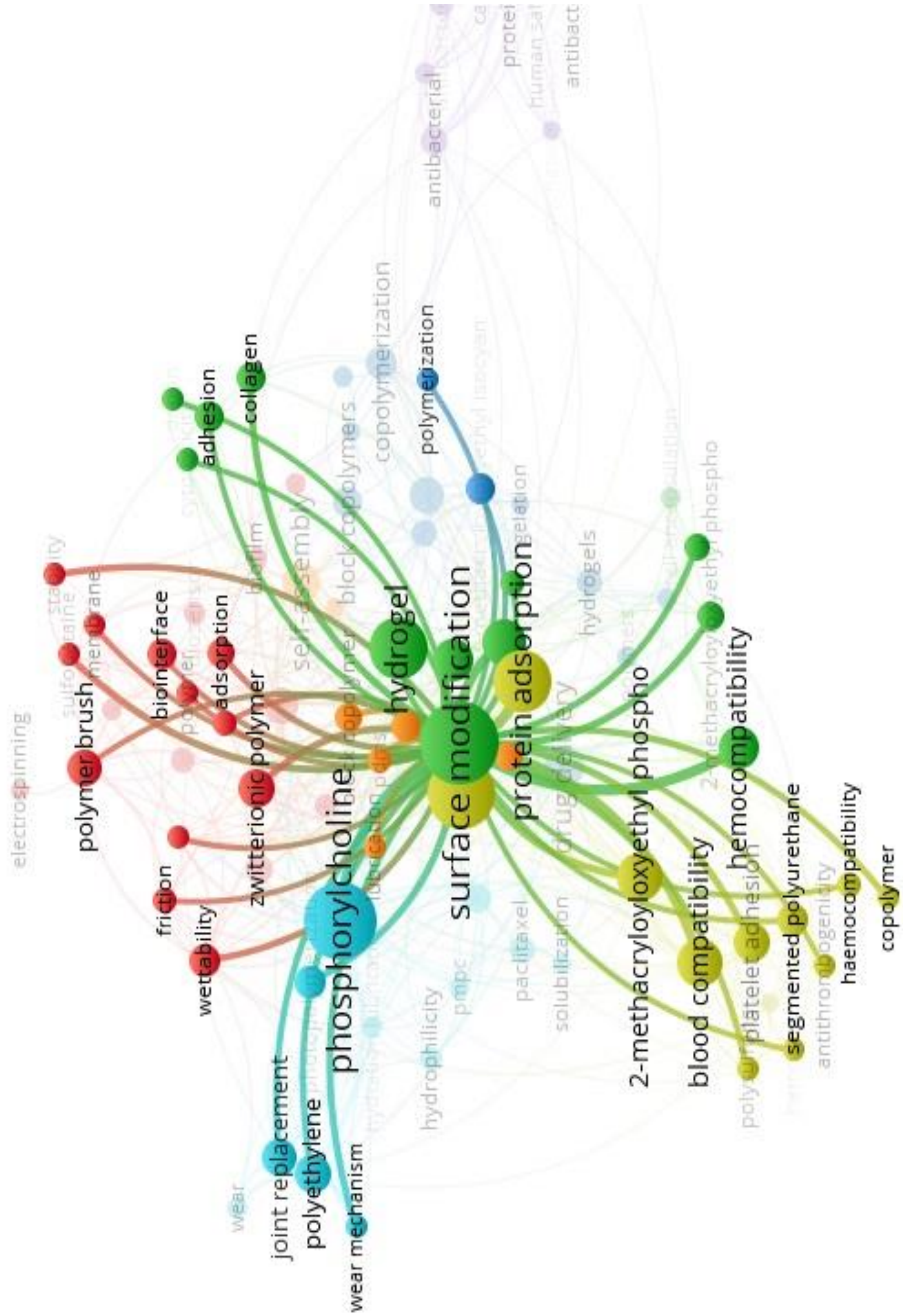


Figure 2. Network analysis for MPC physical properties.

In the oral cavity, a pellicle coat is formed by the adsorption of salivary proteins onto the teeth and material surfaces. Salivary pellicle film affords the essential receptors which allow the adherence of bacteria. Consequently, salivary proteins adsorption is a prerequisite for attachment of bacteria and the formation of biofilm. Therefore, the inhibition of nonspecific adsorption of proteins at the surface of dental restorative materials is the desired goal for antibacterial approaches. Many strategies for imparting high resistance to protein adsorption have been investigated[17]. Dental Plaque is the accumulation of biofilms that comprise a great number of microorganisms (MO) and their metabolites. For dental plaque microcosm biofilm evaluation, bacterial strains that have been identified in denture biofilms were tested. Most commensal oral Streptococcus species have antigen I/II, a cell wall-anchored protein receptor that induces binding to specific partner MO including *C Albicans*, the fungus primarily attributed to denture-associated infections. As adhesion of bacteria is a requisite for fungal biofilm development, a logical strategy for inhibition of denture plaque accumulation is by prevention streptococcal biofilm formation[15].

In resin-based dentistry and endodontics, most of research articles aimed to develop a bioactive endodontic sealer through MPC, dimethylaminohexadecyl methacrylate (DMAHDM) and nanoparticles of amorphous calcium phosphate (NACP) and to assess the inhibition of early-stage and mature multispecies endodontic biofilm, bond strength to root canal dentin, and calcium and phosphate release[18,19]. Previous attempts aimed at producing nanoparticle-doped adhesive as a carrier to deliver medicaments to the pulp and improve adhesive penetration into dentinal tubules[10]. PMMA resin containing MPC and quaternary DMAHDM were used to improve the mechanical properties, protein-repellency and antibacterial sealers. Moreover, PMMA–based dental resin's ability to inhibit bacterial plaque formation, and improve durability against water soaking and chemical exposure were investigated[20].

In cariology and operative dentistry, the main trends included developing a protein-repellent dental composite by incorporating MPC and investigating for effects of MPC mass fraction on protein adsorption, bacteria attachment, biofilm growth, and mechanical properties[12,15]. Adding MPC to a resin composite containing nanoparticles of amorphous calcium phosphate, calcium and phosphate for enhancing the mechanical properties of restoration materials were explored. The development of antibacterial (protein-repellent) dental resin composites is the staggering hope to fight dental caries. Adding DHMAI to MPC has been experimented[21]. Introducing rechargeable composite with nanoparticles of amorphous calcium phosphate was also attempted. Composite containing MPC and DMAHDM greatly reduced biofilm growth and lactic acid production, without compromising mechanical properties of the composite[15,22].

Other studies evaluated the synergetic effect between surface pre-reacted glass ionomer filler and 2-MPC[8,23], for inhibiting multi-species biofilm formation, while maintaining or even improving the original beneficial features of SPRG-filled resin-based glass ionomer [20] and composite [21].

Several methods for the amount of plaque accumulation's measurement have been reported. Between them, the colony-forming unit (CFU) counts method assigned in this study is commonly used for measuring the area of plaque surface. This method is now digitised to minimise subjectivity, and make it retrievable. Moreover, it is a biofilm quantification assay able to measure the 3D thickness of biofilms adhered to the denture surface[9].

Colony-forming units (CFU), and microcosm biofilm model assessed bacterial engorgement and its metabolic activity. Protein adsorption onto the PMMA resin was measured using a micro bicinchoninic acid. Mechanical properties, like hardness/durability, were measured in three-point flexure.

In adhesive dentistry, introducing an ion-rechargeable and protein-repellent resin-based adhesive is always aimed to decrease carious disease occurrence and increase the restoration longevity. The polymerization kinetics of amine-functionalized dental adhesive cured with MPC has improved the MPC-based dental materials. Additionally, Ag is more toxic than many other metals against a broad spectrum of sessile bacteria and fungi which colonize on the plastic surface. In medical and life-care polymers silver has been broadly used because of their antimicrobial action. Modification of soft linings by AgNPs can be an improvement in that respect. Additionally, few reports confirm the effectiveness of AgNPs in their use for dentistry. Surface roughness was assessed using atomic force microscopy. X-ray photoelectron spectroscopy, polarized light microscopy, confocal microscopy, and optical coherence tomography were used to assess the internal structure[25]. In prosthodontics, the same returns useful with merging nanostructured silver vanadate (AgVO3) and antimicrobial activity, adhesion of a soft denture liner among other mechanical properties. [11,17,26].

Orthodonotia is always challenged by the de facto enamel demineralization as an inevitable side effects of bonding brackets for the due therapeutic orthodontic course. Developing a triple merited resin that is able to permit Ca and P ion recharge, repel protein-repellent and inhibit bacterial growth is aimed by integrating different proportions and concentrations of DMAHDM and MPC resins. Eventually, some success was attained with introducing the "RMGI + MPC + DMAHDM + NACP" cement, which minimized the depth of carious lesion and improved enamel hardness under biofilm acid attacks[8,27].

When bacteria adhere to the surfaces of internal prosthodontic devices, especially the S. epidermidis, they proliferate and aggregate producing a biofilm in which a thin layer of polysaccharides capsulates and protects the pathogenic bacteria from phagocytosis and immunological responses, as well as antibacterial agents commonly applied for therapeutic purposes. Hence, the formation of biofilms on the surface of devices establishes refractory infections, i.e., device-associated infections.

Given the universal surface grafting of MPC to achieve an antifouling property on various biomedically relevant substrates to prevent nosocomial infections caused by bacterial biofilms on dental devices (Figure 3). This simple and universal antifouling coating process can be applied to diverse commercially available materials, such as actual tubular catheter or implants[17].

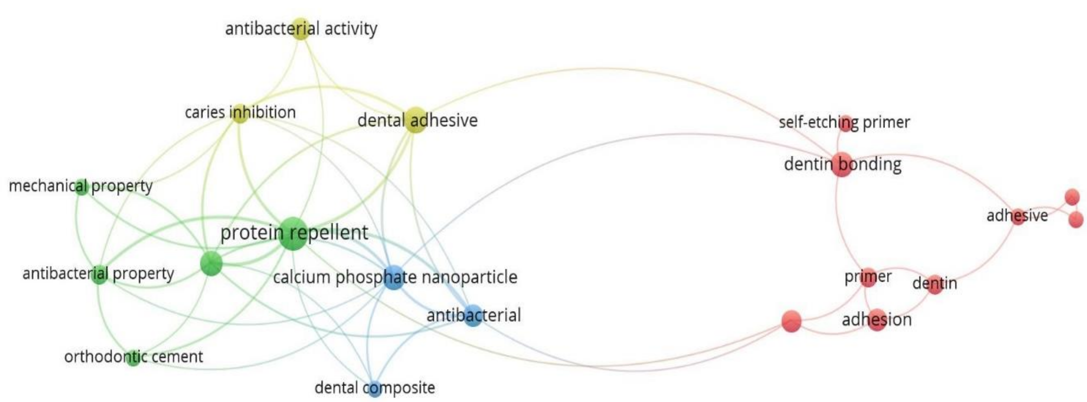


Figure 3. Methacryloyloxyethyl derivatives in dentistry.

Conclusion

Adhesive dentistry has improved resin composite with MPC and DMAHDM for reducing biofilm activity and is promising to inhibit secondary caries. Methacryloyloxyethyl compounds have various successful applications in resin composites, glass ionomer, denture bases and soft liners, orthodontic adhesives, cements. The efficacy of biofilm repellency or antibacterial activity in MPC and DMAHDM are superior to those materials that do not include these resins. We recommend examining the many merits that using methacryloyloxyethyl compounds may enhance in all dental subdomains.

Notes: None

Acknowledgements: None

Funding resources: None

Conflict of interest: The authors declare that there is no conflict of interest.

References

[1] Thongthai P, Kitagawa H, Kitagawa R, Hirose N, Noree S, Iwasaki Y, et al. Development of novel surface coating composed of MDPB and MPC with dual functionality of antibacterial activity and protein repellency. J Biomed Mater Res - Part B Appl Biomater 2020;108. DOI: 10.1002/jbm.b.34661.

[2] Kimura M, Takai M, Ishihara K. Tissue-compatible and adhesive polyion complex hydrogels composed of amphiphilic phospholipid polymers. J Biomater Sci Polym Ed 2007;18:623–40. DOI: 10.1163/156856207780852541.

[3] Maeda T, Hagiwara K, Yoshida S, Hasebe T, Hotta A. Preparation and characterization of 2-methacryloyloxyethyl phosphorylcholine polymer nanofibers prepared via electrospinning for biomedical materials. J Appl Polym Sci 2014;131. DOI: 10.1002/app.40606.

[4] Defife KM, Yun JK, Azeez A, Stack S, Ishihara K, Nakabayashi N, et al. Adhesion and cytokine production by monocytes on poly(2-methacryloyloxyethyl phosphorylcholine-co-alkyl methacrylate)-coated polymers. J Biomed Mater Res 1995;29:431–9. DOI: 10.1002/jbm.820290403.

[5] Wada M, Jinno H, Ueda M, Ikeda T, Kitajima M, Konno T, et al. Efficacy of an MPC-BMA co-polymer as a nanotransporter for paclitaxel. Anticancer Res 2007;27:1431–5.

[6] Soletti L, Nieponice A, Hong Y, Ye SH, Stankus JJ, Wagner WR, et al. In vivo performance of a phospholipid-coated bioerodable elastomeric graft for small-diameter vascular applications. J Biomed Mater Res - Part A 2011;96 A:436–48. DOI: 10.1002/jbm.a.32997.

[7] Zhang N, Zhang K, Xie X, Dai Z, Zhao Z, Imazato S, et al. Nanostructured polymeric materials with protein-repellent and anti-caries properties for dental applications. Nanomaterials 2018;8. DOI: 10.3390/nano8060393.

[8] Zhang N, Zhang K, Melo MAS, Chen C, Fouad AF, Bai Y, et al. Novel protein-repellent and biofilm-repellent orthodontic cement containing 2-methacryloyloxyethyl phosphorylcholine. J Biomed Mater Res - Part B Appl Biomater 2016;104:949–59. DOI: 10.1002/jbm.b.33444.

[9] Kim D, Lee MJ, Kim JY, Lee D, Kwon JS, Choi SH. Incorporation of zwitterionic materials into light-curable fluoride varnish for biofilm inhibition and caries prevention. Sci Rep 2019;9. DOI: 10.1038/s41598-019-56131-5.

[10] Xie X, Wang L, Xing D, Zhang K, Weir MD, Liu H, et al. Novel dental adhesive with triple benefits of calcium phosphate recharge, protein-repellent and antibacterial functions. Dent Mater 2017;33:553–63. DOI: 10.1016/j.dental.2017.03.002.

[11] al-Qarni FD, Tay F, Weir MD, Melo MAS, Sun J, Oates TW, et al. Protein-repelling adhesive resin containing calcium phosphate nanoparticles with repeated ion-recharge and re-releases. J Dent 2018;78. DOI: 10.1016/j.jdent.2018.08.011.

[12] Al-Dulaijan YA, Weir MD, Melo MAS, Sun J, Oates TW, Zhang K, et al. Protein-repellent nanocomposite with rechargeable calcium and phosphate for long-term ion release. Dent Mater 2018;34. DOI: 10.1016/j.dental.2018.09.005.

[13] Melo MAS, Weir MD, Rodrigues LKA, Xu HHK. Novel calcium phosphate nanocomposite with caries-inhibition in a human in situ model. Dent. Mater., vol. 29, 2013, p. 231–40. DOI: 10.1016/j.dental.2012.10.010.

[14] Zhang N, Melo MAS, Bai Y, Xu HHK. Novel protein-repellent dental adhesive containing 2-methacryloyloxyethyl phosphorylcholine. J Dent 2014;42:1284–91. DOI: 10.1016/j.jdent.2014.07.016.

[15] Wang L, Xie X, Qi M, Weir MD, Reynolds MA, Li C, et al. Effects of single species versus multispecies periodontal biofilms on the antibacterial efficacy of a novel bioactive Class-V nanocomposite. Dent Mater 2019;35. DOI: 10.1016/j.dental.2019.02.030.

[16] Fujiwara N, Murakami K, Yoshida K, Sakurai S, Kudo Y, Ozaki K, et al. Suppressive effects of 2-methacryloyloxyethyl phosphorylcholine (MPC)-polymer on the adherence of Candida species and MRSA to acrylic denture resin. Heliyon 2020;6. DOI: 10.1016/j.heliyon.2020.e04211.

[17] Ishihara K, Kozaki Y, Inoue Y, Fukazawa K. Biomimetic phospholipid polymers for suppressing adsorption of saliva proteins on dental hydroxyapatite substrate. J Appl Polym Sci 2021;138. DOI: 10.1002/app.49812.

[18] Zhang N, Zhang K, Weir MD, Xu DJ, Reynolds MA, Bai Y, et al. Effects of water-aging for 6 months on the durability of a novel antimicrobial and protein-repellent dental bonding agent. Int J Oral Sci 2018;10. DOI: 10.1038/s41368-018-0019-9.

[19] Clarin A, Ho D, Soong J, Looi C, Ipe DS, Tadakamadla SK. The antibacterial and remineralizing effects of biomaterials combined with DMAHDM nanocomposite: A systematic review. Materials (Basel) 2021;14. DOI: 10.3390/ma14071688.

[20] Kwon JS, Kim JY, Mangal U, Seo JY, Lee MJ, Jin J, et al. Durable oral biofilm resistance of 3d-printed dental base polymers containing zwitterionic materials. Int J Mol Sci 2021;22:1–13. DOI: 10.3390/ijms22010417.

[21] Cherchali FZ, Mouzali M, Tommasino JB, Decoret D, Attik N, Aboulleil H, et al. Effectiveness of the DHMAI monomer in the development of an antibacterial dental composite. Dent Mater 2017;33:1381–91. DOI: 10.1016/j.dental.2017.09.004.

[22] Duarte de Oliveira FJ, Ferreira da Silva Filho PS, Fernandes Costa MJ, Rabelo Caldas MRG, Dutra Borges BC, Gadelha de Araújo DF. A comprehensive review of the antibacterial activity of dimethylaminohexadecyl methacrylate (DMAHDM) and its influence on mechanical properties of resin-based dental materials. Jpn Dent Sci Rev 2021;57:60–70. DOI: 10.1016/j.jdsr.2021.03.003.

[23] Lee MJ, Kwon JS, Kim JY, Ryu JH, Seo JY, Jang S, et al. Bioactive resin-based composite with surface pre-reacted glass-ionomer filler and zwitterionic material to prevent the formation of multi-species biofilm. Dent Mater 2019;35:1331–41. DOI: 10.1016/j.dental.2019.06.004.

[24] Yoshihara K, Nagaoka N, Maruo Y, Sano H, Yoshida Y, Van Meerbeek B. Bacterial adhesion not inhibited by ion-releasing bioactive glass filler. Dent Mater 2017;33:723–34. DOI: 10.1016/j.dental.2017.04.002.

[25] Liu C, Long L, Li Z, He B, Wang L, Wang J, et al. Hollow poly(MPC-g-PEG-b-PLA) graft copolymer microcapsule as a potential drug carrier. J Microencapsul 2012;29:242–9. DOI: 10.3109/02652048.2011.646328.

[26] Choi A, Yoo KH, Yoon SY, Park SB, Choi YK, Kim Y Il. Enhanced antimicrobial and remineralizing properties of self-adhesive orthodontic resin containing mesoporous bioactive glass and zwitterionic material. J Dent Sci 2021. DOI: 10.1016/j.jds.2021.09.029.

[27] Cao L, Wu J, Zhang Q, Baras B, Bhadila G, Li Y, et al. Novel protein-repellent and antibacterial resins and cements to inhibit lesions and protect teeth. Int J Polym Sci 2019;2019. DOI: 10.1155/2019/5602904.