Biocompatibility of dental resin composites

Rahmi Khairani AULIA

Department of Dental Materials, Faculty of Dentistry, Andalas University, Padang, Sumatera Barat, Indonesia

Corresponding Author Email: rahmi.khairani@dent.unand.ac.id

Received; January 5, 2022, Revised; February 15, 2022, Accepted; April 26, 2022

ABSTRACT Dental resin composites have become the first choice among the filling materials due to their aesthetic potential to suit a variety of therapeutic indications and can conserve the tooth structure. However, there are concerns that this material may be toxic because of the possibility of releasing components after restoration. Bisphenol-A (BPA) is a primary material for dental resins that is a precursor for BisGMA as a natural resin, and degradation of dental resins can leach BPA to the oral cavity. Despite the possibility of a leachable substance, many studies concluded that the release of BPA from dental resin composites might not be absorbed systemically. They leached less than the toxic level that may cause adverse effects.

KEYWORDS: BisGMA, BPA, resin composites,

INTRODUCTION

A dental material ideally should be harmless to all oral tissues, gingiva, mucosa, pulp, and bone when placed in the oral cavity. It should not be poisonous, leachable, or diffusible materials that can be ingested into the circulatory system that can cause systemic reactions, such as teratogenic or carcinogenic reactions. Despite a long time of excellent clinical performance, using amalgam as a tooth filling material remains controversial. The most common reasons people leave amalgam restoration are environmental pollution and possible hazardous health effects due to the release of mercury. In recent decades, dental resin composites have been considered an alternative to amalgam because of their aesthetic and toxicological considerations. It has been assumed that this material has excellent mechanical properties with good aesthetic quality. Furthermore, dental resin composites are easy to handle and can bond with the enamel surface.

Dental resin composites are synthesized of four major components: an organic matrix, usually methacrylate-based monomers, inorganic filler particles (commonly glass, quartz, or ceramic oxides), coupling agents between the filler and the matrix such as silanes, and an initiator/inhibitor polymerization system. The most common dental resins for the resin matrix are (meth)acrylates. The most common resin system in dental resin composites consists of a primary resin, usually bisphenol A glycidyl methacrylate (BisGMA), and triethylene glycol dimethacrylate (TEGDMA), which is included to compensate for the high viscosity of the primary resin.

Even though dental resin composites are growing in popularity, there are concerns that this material may be toxic because of the possibility of releasing components after being placed in the oral cavity. It has been found that several elements are leached out from each dental resin composites into the oral environment due to degradation and corrosion. This situation possibly will cause adverse local and systemic effects. Based on the concern above, this paper will discuss different substances that may release from dental resin composites and the possible side effect caused by leachable substances from the material.

DISCUSSION

This study used Mendeley as a reference manager. The data were collected from data source searches using PubMed, Google Scholar, and Science Direct. Articles were selected based on keywords: dental resin composites, the biocompatibility of resin composites, substance release of resin composites,
degradation of resin composites, and the effect of release substance of resin composites from 2012-2022. The paper was written in English, and the discussion focused on the biocompatibility of dental resin composites. From the data search, 30 articles and systematic reviews were collected.

Substance Release from Dental Resin Composites

Dental resin composites are subject to significant biological breakdown in the oral cavity due to condensation-type bonds within the resin. Such bonds, including esters, urethanes, and amides, are found primarily in di-vinyl monomers and are prone to chemical hydrolysis, catalyzed by acids, bases, or enzymes. Therefore, after placement of the restoration, dental resin composite materials may release unpolymerized monomers, additives, and filler components in the oral environment. In the first hours after initial polymerization, unbound monomers or additives are eluted by solvents or polymer degradation. The release is due to imperfect photopolymerization, thermal, mechanical, or chemical factors. After the polymerization process, approximately 15-50 percent of the methacrylic groups remain unreacted. An important factor affecting residual monomer leaching is the nature and the size of the monomers in the resin materials. Smaller molecules are expected to leach more and more rapidly than larger, bulkier molecules. Therefore, presumably, TEGDMA would strain better than BisGMA. However, in some cases, BisGMA might leach higher amounts than TEGDMA due to double bond conversion of BisGMA is lower than TEGDMA.

Bisphenol-A (BPA) is a primary material for dental resins that is a precursor for BisGMA and Bis-DMA. Although BPA is relatively stable, in the laboratory, the carbonate linkages can be hydrolyzed at high temperatures, resulting in the release of BPA. On the other hand, the degradation of dental resins can leach BPA, and this reverse process is accelerated with heat, mechanical wear, and bacterial or salivary enzymatic action.

Factors Causing Degradation of Resin Composites

The initial release of free monomers may occur during the monomer-polymer conversion, and the long-term release of leachable substances is generated by erosion and degradation over time. Two dominant factors influence the biodegradation of resin composites restoration:

1. Chemistry of the resin composites

A very commonly used monomer for the polymeric matrix is Bis-GMA, which was first introduced in the late '50s by Bowen. Bis-GMA contains hydrophobic aromatic rings in the backbone that provide the resin with low chain mobility and less deformation upon mechanical loading relative to linear non-aromatic monomers. Diluent monomers are used with Bis-GMA to enhance resin mobility for ease of handling and operation. TEGDMA is the most broadly utilized as a diluent in current resin restorations. However, with increasing TEGDMA content, the overall resin composite experiences a more significant volumetric shrinkage upon polymerization, which results in the potential for a more significant marginal gap upon curing and significantly increases water sorption due to the trimethylene oxide spacers in TEGDMA.

The elution of unreacted components from dental composites is influenced by several factors, including the solubility and the molecular weight of the monomers used, the degree of conversion, and the degree of crosslinking of the polymer network, the surface treatment of the filler particles and the nature of the solvent. The curing protocol and the density of crosslinking of the polymer network produced affect the number of leachable components from composite resin networks. Therefore, the elution of elements and the degree of cytotoxicity of resin composites depends on the mode of the polymerization process, such as the type of curing unit, total energy density, power density, irradiation time, and method of healing.

2. Biological factors

Water, as the primary component of saliva, can easily penetrate the polymer network allowing the diffusion of unbound or uncured monomers and additives from the material network. Polymers may be degraded in aqueous solutions through two primary mechanisms: hydrolysis and enzymatic reaction. Hydrolytic degradation and water uptake render the material more prone to mechanical wear during chewing due to the surface undergoing softening. For enzymatic response, many studies have confirmed that saliva contains enzymes capable of degrading resin composites via cleavage of the susceptible condensation linkages. Esterases are the most extensively studied class of enzymes against resin composites.

Degradation of resin composite materials can also be induced by fatigue caused by relatively weak repetitive loads such as ordinary chewing force. A continuous application of mechanical and environmental loads leads to progressive
degradation and crack initiation and growth, resulting in catastrophic failure of the resins. This process is further assisted by pre-existing voids introduced during material processing and residual stresses.\textsuperscript{19}

An in vitro study has shown that bacteria can colonize on surfaces of composite resin and that the surface roughness of the material increased after incubation with bacteria suggesting some surface degradation. This surface degradation is likely a result of acids produced by the bacteria.\textsuperscript{33}

Ferracane has concluded some essential factors for the release of unbound substances from polymerized dental composites: (1) The monomer-polymer conversion controls the number of leachable components; (2) The composition and solubility parameters of the solvent influence the kinetics and mechanism of elution processes; and (3) Size and chemical characteristics of the leachable substances determine the diffusion through the polymer network.\textsuperscript{34,35}

**Effect of Release Substance**

Released dental material components after resin placement can enter the body by two different routes, via the saliva and gastrointestinal tract. It is also possible for the release substances to pass in via the dentin and pulp if the resin is placed in the dentin.\textsuperscript{36} Eluted monomers may contribute to the cytotoxicity of composite resins. Studies reported that leachable substances from composite resin materials were cytotoxic to fibroblasts, and macrophages and cytotoxic aqueous resin eluates frequently contain high amounts of TEGDMA.\textsuperscript{37,38}

The release of TEGDMA has also been shown to stimulate caries-associated microorganism growth and to alter the growth and lipid metabolism of oral epithelial cells.\textsuperscript{39}

The most common substance identified by the researchers is Bisphenol A, which is known to disrupt endocrine function by mimicking estrogen.\textsuperscript{40-42} Animal studies showed increased uterine weight, premature vaginal opening, and increased differentiation and proliferation of mammalian epithelial cells in BPA-exposed female rats.\textsuperscript{43} These adverse side effects of BPA resulted in the concern of BPA release from resin composites. The US Environmental Protection Agency (EPA) reference range for acceptable daily BPA exposure is set at <50 µg/kg body weight per day. Nevertheless, low-dose BPA rates of 10 µg/kg body weight per day are related to changes in behavior and development of the prostate and urinary tract and early puberty.\textsuperscript{44}

BPA release can also affect macrophage activity. Macrophages play an essential role in the host’s immune response to inflammatory, infectious, and reparative processes. At the pulp and periapical tissue, macrophages, with phagocytosis and antigen presentation, have a central function in pulp inflammation and the repair of chronic apical periodontitis. Therefore, BPA release may cause the risks of pulpal and periapical toxicity, depending on their ability to diffuse through the dentin and accumulate in the pulp or to leak through the apical foramen to periapical tissues.\textsuperscript{41,45,46}

**Studies Related to Substance Release of Dental Resin Composites**

Many studies have observed the effect of substances released from dental resin composites. The release of a sense from resin composites can be assessed by using gas chromatography/mass spectroscopy (GC/MS), ultraviolet (UV), infrared radiation (IR), and high-performance liquid chromatography (HPLC).\textsuperscript{47}

Reichl et al. observed the distribution and excretion of BisGMA in Guinea Pigs.\textsuperscript{48} The groups of guinea pigs were injected with BisGMA solution then the feces and urine were collected. Based on this experiment, although the dosage of BisGMA adjusted for body weight was more than 20 times greater in this experiment than that experienced by humans, the highest levels of BisGMA were found in tissue samples obtained from guinea pigs were lower than the known toxic level of BisGMA. It is therefore doubtful that any systemic consequences will occur from the release of BisGMA from restorative materials.

Oertengren et al. identified monomers released from resin composites in an aqueous environment.\textsuperscript{49} They tested several resin composites products by storing the samples in 37 °C distilled water 37 °C for four h, 24 h, and 7, 60, and 180 days. The HPLC analysis of eluted components revealed that TEGDMA was the main monomer released, and no detectable quantities of bisphenol-A were observed in this test.

Pongprueksa et al. investigated monomer elution concerning the conversion degree for different composites.\textsuperscript{50} In this study, they determined the degree of conversion using micro-Raman spectroscopy. They assessed the monomer release by liquid chromatography/mass spectroscopy based on different placement techniques: an incremental layer and a bulk-filling technique. They found that the release of BisGMA and TEGDMA was initially very high but rapidly dropped in the second week. The total monomer release was significantly lower for the incremental...
layer technique than for the bulk-filling procedure. Therefore, the reduced degree of conversion at 4-mm depth resulted in a higher monomer elution when the composite was applied following a bulk-fill application method.

However, Alshali et al. found a different result based on their analysis of long-term monomer elution from bulk-fill and conventional resin composites. They concluded that despite the high rise in resin thickness, the elution of monomers from bulk-fill resin composites was equal to that of traditional composites. Monomer elution highly depends on the base monomer’s hydrophobicity and the resin matrixes’ final network features.

Gul et al. identified the amount of monomer released from two nanohybrid composite resins upon which two different bleaching processes were applied (office-type bleaching and home-type bleaching). The study found that the amounts of monomer released from the two nanohybrid composite resins decreased over time. However, bleaching did not affect the number of released monomers from resins; the monomers released were well below toxic doses.

Chung et al. investigated the relationship between the number of sealants and composite filling surfaces and BPA concentration in urine among children aged 8-9. Children were chosen as the sample because they are more susceptible than adults to possible adverse effects of the same levels of external BPA exposure. In this study, they found no significant increases in BPA concentration shown in the study population using resin composites as a sealant and restoration. It suggests that BPA released from a dental cement or repair might not be absorbed, detected, or metabolized.

In this study, saliva and urine were collected before and after placing the lingually bonded retainer for 1 day, 1 week, and 1 month to evaluate the levels of BPA exposure. This research resulted in the amount of BPA leaching from resin composite used for bonding orthodontic lingual retainers being low and far below the reference doses for daily uptake. The level of BPA in immediately collected saliva was the highest among other collection times but still in low-dose effect. The BPA level in urine in this study did not appear to have any relevance to the placement of the lingually bonded retainer. It is also possible that the amount of BPA leaching decreased rapidly and did not affect the 1-day-after urine BPA level.

Kingsman et al. stated in an in vitro study that there was no detection of BPA or BPA derivatives over observation periods as long as 10 days after sealant or restoration placement. BPA exposure after resin composites placement was most likely an acute event. Presumably, the unpolymerized monomer was fully absorbed into saliva at a certain point after treatment, raising no chance of chronic low-dose BPA.

CONCLUSION

Degradation of resin composites may cause the release of substance unpolymerized monomers, additives, and filler components in the oral environment after placement. TEGDMA would leach better than BisGMA because of the monomers' nature and size. However, in some cases, BisGMA might filter higher amounts than TEGDMA due to double bond conversion of BisGMA being lower than TEGDMA. Bisphenol A determined to be the most concerned leachable substance because of its activity to disrupt endocrine function by mimicking estrogen, which could lead to changes in behavior and prostate and urinary tract development.

Despite the possibility of leachable substance from resin composites restoration and sealant, many studies concluded that the release of BPA from dental resin composites might not be absorbed systemically. They leached less than toxic levels that may cause adverse effects.

The uncured layer of the resin appears to be the primary source of the immediately released monomer. Therefore, reducing the uncured layer is the key to lowering the monomer release. The incremental layer of composite resin placement should be considered as a placement technique of resin composite to increase the degree of conversion.

REFERENCES


