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A mini-review on different polymerization protocols for resin-based dental composites

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Abstract. Biocompatibility is one of the major prerequisites for safe clinical application of materials. Dental resin composites may release their components into oral environment, which can lead to adverse reactions. Several studies have identified that many organic components of composites resin, such as bisphenol-A-glycidyl-methacrylate (Bis-GMA), triethylene glycol dimethacrylate (TEGDMA), urethane dimethacrylate (UDMA) and 2-hydroxyethyl methacrylate (HEMA) show a cytotoxic profile. Cytotoxicity is mainly sustained by free monomers released after polymerization process. Direct restorations are polymerized at body temperature by visible light emitting lamps, but the conversion from monomer to polymer after light-curing is never complete. To improve the degree of conversion of resin-based composites, additional curing protocols performed at increased temperatures, such as heat-curing, can be employed. Polymerization reaction plays a key role in the conversion of the free monomers into polymers and resin-based composites with high degree of conversion might show higher biocompatibility. The aim of this mini-review is to report current knowledge about the cytotoxicity of different composite resins, cured in two different ways. Further studies are necessary to better understand the relationship between the cytotoxicity and the degree of polymerization of resin-based composites.

Keywords: composite, cytotoxic, polymerization.

INTRODUCTION

In restorative dentistry decayed tooth tissues and dental defects can be replaced by direct and indirect dental composite. Direct composite restorations are light-cured at body temperature, while indirect restorations can be subjected to supplementary heat-curing cycles. Resin composites are widely used in restorative dentistry, although their safety in terms of biocompatibility is not yet completely understood (Yang et al. 2018).

Biocompatibility, which is defined as the ability of a material to induce an appropriate biological response following a specific application, is con-

sidered a key property for any material used in contact with human tissues. In the oral cavity, biocompatibility depends on the host, the material and the function performed. The polymerization process and the intra-oral degradation are considered two main factors able to influence the free-monomer release from a polymeric matrix (Goldberg 2008). Biocompatibility and degree of monomer conversion seem to be correlated as the cytotoxic effect is directly affected by the monomers released by uncured resin in the composite (Inoue et al. 1988). Intra-oral degradation is defined as a chemical degradation caused by hydrolysis or enzyme catalysis and by the interactions between the composite resins and the human saliva-derived esterases and pseudocholinesterases (Goldberg 2008). Polymeric weight loss occurs as a result of water and solvents entering and eroding the polymer, while free monomers spread as a result of the expansion of the polymer network (Goldberg 2008). These monomers showed a cytotoxic effect *in vitro* for dental pulp and gingival cells (Goldberg 2008). Some ions as Cu^{2+}, Al^{3+}, and Fe^{2+} could be also implicated in the production of reactive oxygen species (ROS) (Goldberg 2008). The purpose of this mini-review is to report current knowledge about the cytotoxicity of resin-based dental composites subjected to two different polymerization protocols: light-curing and heat-curing.

COMPOSITE RESINS

Resin composites are composed by polymer matrix, filler, silane coupling agents and chemicals that catalyse or inhibit the curing reaction. Biocompatibility of the composite resins can be affected by the organic matrix components as bisphenol-A-glycidyl-methacrylate (Bis-GMA), triethylene glycol dimethacrylate (TEGDMA), urethane dimethacrylate (UDMA), and 2-hydroxyethyl methacrylate (HEMA) (Yang et al. 2018; Goldberg 2008). Bis-GMA is the mainly used monomer in dental resins, due to its mechanical properties and relatively low curing shrinkage (Gajewski et al. 2012). Salivary hydrolysis may promote the release of small amounts of Bisphenol A (BPA) in Bis-GMA based materials (Kingman et al. 2012) (Fig. 1). BPA estrogenic potential effects can affect the human health (Söderholm and Mariotti 1999). After composite placement in oral cavity, short-term increases in BPA levels were observed (Kingman et al. 2012). Promising results have been obtained by Bis-GMA-free composites, but to appreciate stability of these materials over time, further research is needed (Pérez-Mondragón et al. 2020). Moreover, according to the literature, the combined action of many monomers
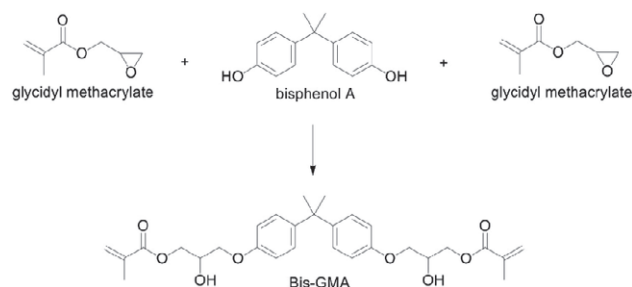

Figure 1. Chemical structure of Bis-GMA. The original figure has been published in: "Šimková M, Tichý A, Dušková M, Bradna P. Dental composites - a low-dose source of bisphenol A? Physiological research. 2020;69(Suppl 2):S295-s304."

included inside a commercial composite formulation may produce different cytotoxic and genotoxic effects compared to their single action (Wisniewska-Jarosinska et al. 2011), suggesting that biocompatibility of complex materials should not be assessed based on the effect of single specific components (De Angelis et al. 2021). The *in vitro* elution of resin-based dental composites seems to be influenced by organic and water-based solvents, molecular mass, volume and surface area of the composite restoration (De Angelis et al. 2022). Also, the type of inorganic filler should be considered. The inorganic filler content positively enhances mechanical properties of current resin-based composites (Ferracane 2011), but a potential cytotoxic risk related to modern nanoscale fillers has been pointed out with concern by some authors (Nel et al. 2006).

POLYMERIZATION

The extent of polymerization is defined as the degree of conversion of monomers into polymers. Direct composite restorations are light-cured at body temperature, while indirect restorations are subjected to further curing cycles. During polymerization reaction, an amount of monomeric methacrylate groups ranging between 15% and 50% may remain unreacted (Ferracane 1994). Unbounded monomers may be released to external environment by an incomplete polymerization and possibly cause irritation, inflammation, and allergic reactions of oral mucosa (Goldberg 2008). As a result of the incomplete polymerization reaction, the residues of free methacrylate monomers may promote the production of prostaglandin E2 (PGE2), cyclooxygenase 2 (COX2), and the increase of interleukin-1β (IL-1β), IL-6, and nitric oxide (NO), triggering a proinflammatory response (Kuan et al. 2013). The curing time, the intensity and the distance of the light-curing
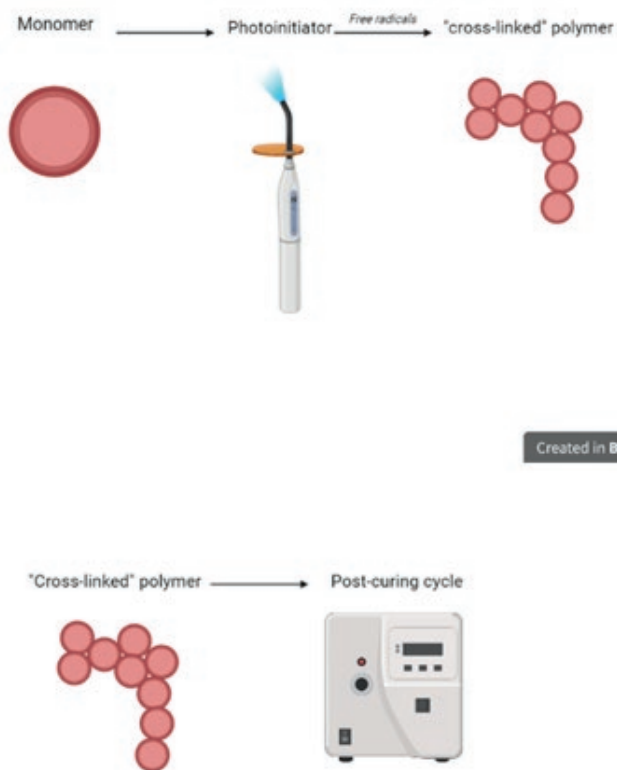
Figure 2. Light-curing and heat-curing process. The figure has been created in biorender.com.

Table 1. Factors affecting the polymerization. The table has been published in: "Hervás-García A, Martínez-Lozano MA, Cabanes-Vila J, Barjau-Escribano A, Fos-Galve P. Composite resins. A review of the materials and clinical indications. Medicina oral, patologia oral y cirugia bucal. 2006;11(2):E215-20."

Factor	Clinical repercussions
Curing time	It depends on: resin shade, light intensity, box deep, resin thickness, curing through tooth structure, composite filling.
Shade of resin	Darker composite shades cure more slowly and less deeply than lighter shades (60 seconds at a maximum depth of 0.5 mm).
Temperature	Composite at room temperature cure more completely and rapidly.
Thickness of resin	Optimum thickness in 1-2 mm.
Type of filler	Microfine composites are more difficult to cure than heavily loaded composites.
Distance between light and resin	Optimum distance < 1 mm, with the light positioned 90 degrees from the composite surface.
Light source quality	Wavelength between 400 to 500 nm. A power density about 600 mW/cm^2 is required to ensure that 400 mW/cm^2 reaches the first increment of composite in a posterior box.
Polymerization shrinkage	Depends on the amount of organic phase.

lamp from the specimens are factors affecting the monomer conversion (Leloup et al. 2002), which inadequate conversion may jeopardise the mechanical properties of dental-based resin composites (Ferracane 1994). Additional heat-curing cycles, providing light at increased temperatures ranging between 50 and 170 °C, can be performed to increase the degree of monomer conversion of composite resins, reducing the amount of unreacted material at the composite surface, simultaneously improving the material mechanical properties (Magne et al. 2015) (Fig. 2). Higher amounts of eluted monomers are correlated to a lower extent of monomer to polymer conversion (Miletic and Santini 2008). According to Caughman and coll. (Caughman et al. 1991), the percentage of increased monomer conversion should be proportional to a decreased cellular toxicity. However, to our knowledge, no previous study was able to demonstrate a difference in cytotoxicity between heat- and light-cured composites. Moreover, according to Säilynoja and coll. (Säilynoja et al. 2004), cytotoxicity would not be affected by heat-curing process due to the slow release of molecules from the matrix, although UTMA-based materials were considered in their study (Table 1).

Similar results were obtained by Vallittu and coll (Vallittu and Ekstrand 1999). Thus, the correlation between degree of conversion and cytotoxicity of resin composites seems to need further investigations.

CONCLUSIONS

In conclusion, from a clinical point of view, resin-based dental composites should demonstrate the lowest possible citoxicity, preserving their mechanical properties and clinical performance after the polymerization process. The present mini-review evidenced the importance of polymerization reaction for the release of residual monomers. However, the correlation between the cytotoxicity of dental resins composite and the degree of monomer conversion or the composite chemical formulation seems still to be better understood.

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