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Mesoporous silica fillers and resin composition effect on dental composites cytocompatibility

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ABSTRACT

Objective. Many new dental composites containing mesoporous silica fillers have been developed to improve rheological properties and enhance the resin–filler interface. To investigate the correlation between the cytocompatibility of several dental composites and their composition; two aspects have been considered: presence of bisphenol A (BPA)-glycidyl methacrylate (Bis-GMA) or triethyleneglycol-dimethacrylate (TEGDMA) among the resin monomers and presence of porous particles among the filler blends.

Methods. Five commercial composites with different resin matrices and mineral fillers were compared to four experimental composites designed without any BPA-based monomers or TEGDMA. Porous fillers, with or without silanation, were added in some of the experimental composites. Two reference resin matrices were also selected. Cytocompatibility with cultured primary human gingival fibroblasts was assessed by confocal laser scanning microscopy with time-lapse imaging. Fourier transform infrared spectroscopy was used to control monomer conversion rate.

Results. Conversion rates of the experimental composites ranged from 57% to 71%, a comparable ratio for dental composites. Experimental samples were better tolerated than tested commercial samples not containing TEGDMA and significantly better than those containing TEGDMA. Experimental composites with porous fillers exhibited good cytocompatibility, especially when surfaces were silanated.

Significance. Cytotoxicity was associated with resin amount and especially resin nature. Composites containing porous fillers might behave as if the resin trapped into pores has no effect on toxicity. The cytotoxicity of composites with and without BPA derivatives was mainly attributed to the release of residual TEGDMA rather than the BPA derivatives.

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1. Introduction

Dental composites are the first choice for dental restoration for most practitioners because they are easy to manipulate and have superior esthetics. The search is continuous for dental composites with an ideal combination of good mechanical and biological properties. Many scientific papers report the development of new dental composites to improve their longevity, wear resistance and particularly cytocompatibility.

However, composites have cytotoxic effects that can occur early after their placement because of the release of free monomers during the monomer–polymer conversion and later because of the release of leachable substances generated by erosion and degradation over time [1,2]. Among these substances, bisphenol A (BPA) has garnered particular attention because of its detrimental effects on reproductive hormones [3–5]. BPA can be found in most dental composites as a degradation product. The stiffest monomers available, BPA-glycidyl methacrylate (Bis-GMA) and ethoxylated BPA-methacrylate (Bis-EMA), can leach BPA and other smaller chemical compounds. BPA has been reported to induce oxidative stress mediated cytotoxicity in various cell types. Recently, BPA was shown to induce hBMSCs cytotoxicity in a time and a dose-dependent manner [6,7]. Therefore, removing this kind of monomer from the resin formula may decrease the estrogenic potential and also the cytotoxicity to oral cells [8]. In addition, cytotoxicity can depend on a complex combination of factors: low conversion rate (CR) [9–11], low monomer molecular weight, chemical structure [12,13], and filler functionalization [14]. Hence, curing and a suitable light intensity is recommended to maximize monomer cross-linking and decrease cytotoxicity [15]. Consequently, the resin rate reduction and the selection of monomers may be the most important factors in avoiding toxicity of oral cells in contact with restorations. Conventional inorganic fillers may also affect cytocompatibility, but their effect seems negligible as compared with the resin matrix [16].

Porous fillers were first introduced by Bowen and Reed to improve bonding between filler particles and the resin matrix [17]. Some authors used porous particles with organized porosity: Luo et al. synthetized experimental SiO_2 gels to improve the wear resistance of composites [18] and found no difference in wear with and without porous particle silanation. Mechanical anchoring provided by pores can replace chemical bonding by silanation. Praveen et al. obtained enhanced wear resistance with mesoporous fillers and claimed that interconnected pores may provide an additional benefit [14]. However, because mesoporous fillers are too weak to provide good mechanical properties, the authors mixed dense particles and mesoporous fillers in a second study [19]. Recently, Zhang et al. used Santa Barbara amorphous 15 (SBA-15) mesoporous particles impregnated with chlorhexidine inside dental composites to release this antibacterial agent around the restoration [20] and achieved an antibacterial effect for 3 days. Carpenter et al. leached nitric oxide for 23 days in a similar study [21,22]. Other authors used porous particles without a controlled pore diameter: fumed silica was used in several dental composites as a thixotropic agent. Atai et al. used sintered nanoparticles to obtain porous clusters of 31 μm in diameter and achieved a filler rate of 70% wt with a rough surface for mechanical interlocking and homogenous filler dispersion. The authors obtained good polishability, good flexural strength and enhanced toughness [23]. Hence, porous fillers may enhance mechanical properties. However, their extended surface area could lead to cytotoxicity.

The cytotoxicity of dental composites and their components has been widely evaluated with cell culture systems [11,24,25] assessing cell proliferation and cell viability [26]. To our knowledge, the cytocompatibility of dental composite with porous fillers has not been assessed. The absence of toxicity to cells is the main criteria of such materials, according to ISO 10993 and ISO 7405 recommendations [27,28]. Here, we aimed to compare the cytocompatibility of commercial and experimental dental composites for a better understanding of factors affecting cytotoxicity. We used 3D time-lapse confocal laser scanning microscopy (CLSM) combined with LIVE/DEAD staining for analysis. The monomer CR is known to affect monomer leaching and composite toxicity [9,10]. So we used Fourier transform infra-red (FTIR) spectroscopy to evaluate the CR. Our main objectives were to investigate the effect of resin amount with identical resin matrix on composite toxicity and the possible effect of mesoporous fillers. We also aimed to investigate whether BPA-free resin improved the cytocompatibility. For this, we mixed mesoporous fillers with or without functionalization in an original BPA-free resin.

2. Materials and methods

2.1. Preparation and selection of dental composites

2.1.1. Mesoporous fillers

Mesoporous fillers were synthetized as described by Zhao et al. [29] to obtain a pore morphology called SBA-15. Porosity forms cylindrical channels of diameter about 7 nm locally organized with an hexagonal symmetry. SBA-15 structure can be obtained in super acidic conditions and in presence of a non-ionic surfactant; channels are issued from the self-assembly of block copolymers (Pluronic P123; Cas-No. 9003-11-6) with silica precursors (Tetraethoxysilane; Cas-No. 78-10-4). After particles synthesis, a surface functionalization was performed. Three types of mesoporous fillers were used in this study: SBA-x, SBA-M and SBA-V, for unfunctionalized SBA-15 particles, SBA-15 particles silanated with [3-(methacryloyloxy)propyl]trimethoxysilane (Cas-No. 2530-85-0) and SBA-15 particles silanated with vinyltrimethoxysilane (Cas-No. 2768-02-7), respectively.

2.1.2. Preparation of experimental composites

Experimental composites were prepared by mixing different fillers with an identical BPA-free resin (Septodont, Saint Maur-des-Fossés, France) by using a planetary mixer (SpeedMixer DAC150FVZ-K, Landrum, SC, USA). This resin was based on UDMA like monomers and thus was BPA-free; the monomer used to reduce the viscosity was HDDMA and hence was TEGDMA-free. Blended fillers were progressively added into the resin matrix to obtain a composite with a consistency close to that of a commercial composite. The consistency was calibrated with a viscosity bench: a fixed quantity of compos-