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Letter to Editor

The Underestimated Toxicological Burden of Residual Monomers Released from Polished and Aged Dental Composite Restorations

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Dear Editor,

Resin-based composites have emerged as an obvious replacement for amalgam, because of their highly esthetic properties, mercury-free nature, simple cavity preparation requirements, and successful adhesive bonding, for current restorative dentistry [1]. This phase-down of dental amalgam has also been further accelerated by the global Minamata Convention, and now composite resins make up the vast majority of the direct posterior restorations being performed in the world. In this context of the widespread clinical application, an increasingly large amount of biocompatibility data has emerged suggesting a potential for systemic effects with chronic low-level exposure to residual monomers and degradation products. We do this through Oral Sphere to highlight this overlooked, but clinically relevant problem, and provide an emphasis on recent evidence published in the last 5 years [2].

Resin composites used today use a mostly dimethacrylate matrix of components, such as dimethacrylate monomers, Bisphenol A-glycidyl methacrylate (Bis-GMA), urethane dimethacrylate (UDMA), triethylene glycol dimethacrylate (TEGDMA), 2-hydroxyethyl methacrylate (HEMA) and ethoxylated bisphenol-A dimethacrylate (Bis-EMA). Even under manufacturer-recommended light-curing protocols, the inherent incompleteness of photopolymerisation of these systems ensures that a degree of conversion of 50–75% is usually reported in recent in-vitro studies [3]. The unreacted residual fraction (25–50% of the initial monomer content) is still available to be eluted into the oral environment, and the kinetics of elution depend on the saliva exposure, mechanical stresses, thermal cycling and the chemical aggressiveness of the food environment [4].

Since 2021, many quantitative high-performance liquid chromatography and tandem liquid chromatography–mass spectrometry studies have been published that repeatedly show clinically significant elution. By HPLC of patient saliva, Tkáčiková and Sabo found that Bis-GMA, TEGDMA, UDMA and Bis-EMA can be identified in vivo during the initial 24 hours after composite placement, but that the elution profiles remained above background levels after the first 24 hours and were only partially reduced by light-curing for prolonged periods [5]. The values reported for the salivary concentrations of HEMA, TEGDMA and Bis-GMA are by no means insignificant: HEMA has been measured up to 45.0 μg/mL in aqueous extraction media, TEGDMA up to 18.7 μg/mL and Bis-GMA up to 5.2 μg/mL - all values suitable within the range of salivary concentrations that have been shown to be cytotoxic and genotoxic in human pulp fibroblasts and odontoblast-like cells [6].

In a 260 day study, Tichy et al. (2021) [7] demonstrated that Bis-GMA based composites leach detectable amounts of Bisphenol A (BPA) into artificial saliva for many months following placement, and that significantly greater amounts are leached from conventional Bis-GMA based composites than from “BPA free” alternatives, and that BPA leaching is much greater from alcohol-based extraction media which simulate dietary alcohol exposures.

Lopes-Rocha et al. (2024) [8] also carried out a systemic review of the literature that substantiated the quantification of BPA in saliva, urine and blood, including measuring low levels of BPA using LC–MS/MS, which is the most sensitive method to measure BPA even at trace levels. Importantly, this monomer elution does not occur at one point, when the index restoration is placed but there is evidence that mechanical procedures like in-office bleaching can re-mobilise residues of monomers even from aged restorations, thus increasing the systemic exposure load long after the index restoration.

HEMA and TEGDMA are genotoxic at sub-millimolar concentrations and are responsible for the formation of micronuclei and cell-cycle arrest, which can be rescued by antioxidants, showing that oxidative stress is a critical mediator of genotoxicity [9]. The upregulation of pro-inflammatory cytokines such as IL-1β, IL-6 and TNF-α, has been reported in pulp tissue exposed to leached monomers, which suggests a mechanism for the post-restorative pulpal hypersensitivity that has, to date, been attributed, somewhat reductively, to thermal conduction alone by clinicians. In addition to the pulp–dentine interface, beyond the degradation products of Bis-GMA, BPA released from the hydrolysis and esterase activity of Bis-GMA is now known to be a well characterised endocrine-disrupting chemical with several documented effects on neurological, reproductive and metabolic systems, as recently reviewed [10] for effects on neurodevelopment, cognition, and behavior at exposures previously thought to be safe. The Tolerable Daily Intake for BPA was re-evaluated to 0.2 ng/kg body weight/day for BPA exposure by composite materials in 2023, which has been lowered by 20,000-fold from the previous value, and is well within the range of regulatory concern, especially for pregnant patients, children and patients with multiple, recently placed restorations [11].

Also, the recent understanding that the BPA released from dental composites is not only a contamination of the starting monomer, but can also be formed in vivo as a result of enzymatic and chemical degradation of Bis-GMA and Bis-EMA is noteworthy. This contradicts the traditional view that mature, well-polymerised restorations are "biologically inert". It also elaborates the concept of why there is an increase in salivary BPA weeks to months after the placement, because the restoration is exposed to mechanical, thermal and microbial challenges within the oral cavity [12].

All of the above shows that the composite resin is not a completely harmless biomaterial, and that its use needs to be reconsidered. Clinicians are encouraged to maximize both the degree of conversion and the irradiance (IR) (at least 1000 mW/cm^2) while strictly following recommended exposure times by the manufacturer, careful positioning of the curing tip in direct apposition to the restoration and incremental layering. It is important to understand that post-cure finishing and polishing should be considered as biological, rather than cosmetic processes because the most unreacted monomer is found in the oxygen inhibited surface layer. Manufacturers should be encouraged and, in some cases, mandated to provide the elution profile of their products under a standardised set of conditions and to speed up the development of BPA-free and TEGDMA-reduced products with validated biocompatibility data. Regulatory agencies need, in turn, to give high priority to organ-specific, comprehensive toxicological profiling of dimethacrylate monomers and degradation products, especially of paediatric, immunocompromised, and pregnant patients who are most susceptible to chronic low dose exposure.

Thus, the dental profession has an ethical and scientific responsibility to recognize and act on these risks. The esthetic, conservative and functional properties of resin composites are undeniable, but this

must be coupled with a thorough and evidence-based approach to patient safety. Such a balance requires open science, well-informed clinical decision making, conservative use of materials, and a culture of strong pharmacovigilance for dental biomaterials. The profession as a whole must do this, or the silent danger that lurks in our restorations can become a loud one in the future.

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ABBREVIATIONS USED IN THE STUDY

a) Bis-GMA: Bisphenol A-glycidyl methacrylate
b) UDMA: Urethane dimethacrylate
c) TEGDMA: Triethylene glycol dimethacrylate
d) HEMA: 2-Hydroxyethyl methacrylate
e) BPA: Bisphenol A

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