INVESTIGATING THE HUMAN IN VITRO METABOLISM OF DENTAL MONOMERS USING HLM AND LC-QTOF-MS

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Background: Dental resin systems have been used for several decades and have gained a higher market share after the Minamata convention and the encouragement of the World Health Organization (WHO) for a global phase-down of dental amalgam. Many (meth)acrylic monomers are an important part of the dental resin system, and are either based on BPA or lack the BPA core. The degree of conversion/polymerization during restoration is in general between 50-70 %. This may allow leaching from unreacted monomers to the oral cavity where they can be taken up through the pulp or gastrointestinal tract after ingestion with subsequent hepatic metabolism.

Methods: This study identified the in vitro Phase I and Phase II metabolism of the dental resin monomers BisGMA, UDMA, BisPMA and TCD-DI-HEA, using human liver microsomes (HLM) and human liver cytosols (HLCYT). The samples were analyzed by liquid chromatography hypenated to a high resolution mass spectrometer to identify biotransformation products with high confidence during suspect screening data analysis.

Results: During Phase I incubation with HLM, the (meth)acrylic acid moiety in the monomers was rapidly cleaved with subsequent oxidative and hydroxylation pathways. For BisPMA, an O-dealkylation pathway occurred resulting in the formation of BPA. The carbamates moieties present in TCD-DI-HEA and UDMA were resistant to biotransformation reactions. Phase II biotransformation products were observed only for BisPMA and included conjugation reactions with sulphate and glucuronic acid.

Short discussion/conclusions: In total 4, 3, 12 and 3 biotransformation products were identified in this study for BisGMA, UDMA, BisPMA, and TCD-DI-HEA, respectively. Several identified biotransformation products are potential biomarkers for biomonitoring studies to assess the exposure to monomers after dental restorations. Possible human health effects of these biotransformation products remain unclear due to limited data availability.