**Introduction**

It is legitimate to ask questions about the harmfulness of the components released from dental biomaterials like composite resins, adhesives and pit and fissure sealants. Recent studies show that monomers and co-monomers are released in solvents like water, ethanol or methanol, especially when submitting properly polymerized restorative biomaterials to stresses simulating chewing, in an effort to get closer to the clinical situation. All biomaterials do not behave in a similar manner and release different components, both in nature and in quantity. One of the co-monomers most commonly released by the composite resins, however, is TEGDMA, a co-monomer used to decrease the viscosity of the monomer forming the backbone of the composites: the Bisphenol A-diglycidylether methacrylate (Bis-GMA) (1).

A special concern appeared recently: the release of Bisphenol A (BPA) from various synthetic materials, such as polycarbonates used for example for baby bottles or for lining the preserve cans (2). The question of release of BPA from dental biomaterials is a very old one, since the first papers on that subject have been published already in 1998 (3).

The aim of this paper is to evaluate the risk arising from the elution of the co-monomer TEGDMA present in most of the composite resins, and also of Bisphenol-A, a molecule not present in composite resins, adhesives and sealants, but which could possibly be released in some very particular conditions.

**TEGDMA**

Tri-ethylene-glycol-dimethacrylate (TEGDMA) (molecular weight MW 286) is a long molecule terminated by two functional methacrylate groups, just as with Bis-GMA, the backbone molecule of composites. The part of the molecule between the two methacrylate groups, however, is linear, as compared to Bis-GMA (MW 512), and therefore has not the high viscosity specific of the Bis-GMA. It is why TEGDMA is used as a dilutant for the Bis-GMA, improving the handling of the composite resin both during fabrication (improvement of the coating of the filler particles) and when used by the dentist. The proportions of Bis-GMA and TEGDMA vary considerably among the products; the most elaborate table about the composition of the resin matrix (4) does not give, however, the proportions of the components.

**Bisphenol A (BPA)**

BPA does not exist as such in composites, adhesives or sealants, but it is used in the synthesis of the main backbone molecule of the composite resins: the bisphenol A-diglycidyl methacrylate (Bis-GMA), or in monomers like bisphenol A-diglycidylether (BADGE), or bisphenol A-dimethacrylate (Bis-DMA), used in some adhesives and sealants.

**TEGDMA and BPA in dental biomaterials**

TEGDMA is a linear co-monomer which terminates with two functional methacrylate groups identical to those terminating Bis-GMA. During polymerization, acrylic bonds are created with Bis-GMA as well as with other molecules of TEGDMA, and also with the mineral filler particles, by means of a coupling agent grafted on these filler particles and having also a terminal functional methacrylate group. A tridimensional network is thus formed, characterized by a high mechanical and chemical resistance; the acrylic bonds thus formed are highly stable in the oral environment. The polymerization of the monomers and co-monomers is never complete. The conversion rate (proportion of polymerized molecules compared to the initial amount un-polymerized molecules) is estimated between 30 and 80 %, depending on the resins. There is therefore always free monomers and co-monomers in a composite resins, which could possibly be eluted. It is highly unlikely that TEGDMA can be produced by degradation of the polymerized matrix. The eluted TEGDMA comes therefore from un-polymerized...
molecules. It has been demonstrated (5, 6) that the amount of eluted TEGDMA decreases when a composite is subjected to a longer light irradiation, that is when polymerization increases and content of free TEGDMA decreases.

Concerning BPA, this component is never introduced intentionally in the composition of a composite resin, an adhesive or a sealant. It has been found, however, as impurity in bisphenol A-diglycidylether (BADGE) and bisphenol A-dimethacrylate (Bis-DMA) from some producers of base chemicals (7), these two components being used to prepare some sealants.

**Release of TEGDMA and BPA from dental biomaterials**

Since the study by Geurtsen in 1998 (3), several other papers on the same domain have been published. Among those, the paper by Moharamzadeh (8), including also an ormoecer, shows that neither Bis-GMA nor UDMA (urethane-dimethacrylate, the main component in some composite resins) have been detected. In the more recent work by Polydorou (6), already cited, also including an ormoecer, Bis-GMA has been detected in amounts superior to TEGDMA in Filtek Supreme XT and Ceram X, which contradicts the previous papers.

The release of chemical substances from commercial composite resins is not limited to TEGDMA. As shown by Durner et al. (9), up to 64 different chemical moieties have been detected by gas chromatography coupled to mass spectrometry from two composites, one compomer and two ormoceers – with no traces of BPA. Among these 64 chemical substances, base monomers, co-monomers, photo-initiators, co-initiators, photo-stabilizers, inhibitors and degradation products have been found.

The very low amounts of the released components require the use of very powerful analytical techniques if one wants to precisely quantify the released substances. Very recently, two papers have been published mentioning the use of gas chromatography coupled to mass spectrometry (GC/MS): the work of Michelsen (10) is aimed more specifically at the release of TEGDMA and HEMA (hydroxyethyl-methacrylate) in the saliva from two composites (Tetric Evo Ceram and Filtek Z 250). HEMA has been released by the two composites. The work of Seiss (11) looks at the release of TEGDMA, BHT (butylated hydroxytoluene, an inhibitor) and DMABEE (4-N,N dimethylanisobenzoic acid ethyl ester, a co-inhibitor) from 7 composites. The highest amounts of TEGDMA and BHT have been released by the composite Venus, DMABEE has been found in larger quantities with Filtek Supreme XT and Artemis, while the composite e.l.s. “extra low shrinkage” has released no TEGDMA, no DMABEE and only a very low amount of BHT.

About the release fo BPA, the work of Schmalz et al. (7) shows how Bis-GMA remarkably resists to the attack of both solvents and enzymes; it degrades into bisphenol A-diglycidylether and methacrylic acid, but never into BPA. However, Bis-DMA degrades in liberating BPA and methacrylic acid, and this at very high conversion rates: 99.8 % at pH 11, 82.5 % after 24 hours of contact with porcine esterase, and still 81.4 % after 24 hours in saliva.

More recently, a paper by Pulgar (12) has mentioned the release, from various polymerized composites, of Bis-GMA and BADGE (from the composites Brilliant, Charisma, Pekalux, Polofil, Tetric, Filtek Z200 and from the sealant Delton) and of BPA (from the composites Brilliant, Charisma, Pekalux, Polofil, Silux, Tetric, Filtek Z100, and from the sealant Delton). Some Bis-DMA has been found mainly in the sealant Delton. The highest amounts of BPA have been observed after an immersion of 24 hours in water at pH 7.

According to Polydorou (6), BPA has been found in eluates of un-polymerized Filtek Supreme XT and Ceram X and in eluates from the immersion of polymerized Ceram X, which contradicts the results of the preceding papers.

In a recent paper, Koin (13) shows that the most sensitive part of the molecule Bis-GMA is the ester bond of the terminal methacrylic group. In some circumstances, a hydrolysis may happen at the level of this bond, with release of methacrylic acid, but leaving untouched the ether bond between the central group of the bisphenol A and its two terminal glycidyl groups. There is therefore no release of BPA.
From the above, one can conclude that the residual co-monomer TEGDMA is released more easily and more frequently from polymerized composites than BPA. The main reason for this behavior comes from the fact that BPA is not present as such in the composite resins or sealants. The possible presence of BPA in eluates results from the degradation of one of the main monomers present in some sealants, that is the Bis-DMA.

Toxicology of TEGDMA and BPA

The release of the free co-monomer TEGDMA from polymerized composite resins has been clearly demonstrated in many research works. One should think now about the risk which this component may have on the organism, that is its toxicity.

In a presentation during the recent congress of the European division of IADR in Munich in 2009, Reichl (14) has shown first that TEGDMA tends to degrade into triethyleneglycol and methacrylic acid, and second that the various methacrylate-related diseases tend clearly to increase in frequency. Thus, the dental professions regroup 45 % of all allergies due to methacylates, the dental personal is more sensitive (5 % of cases in Scandinavia, values 2007) than the dentists (4 %) and than the patients themselves (2.3 %).

Various studies have been devoted to the stability of TEGDMA and to its action on different types of cells. Seiss (15) shows that TEGDMA and HEMA can degrade under the effect of enzymes such as the esterase, with the risk of forming lipophilic intermediary products, which can therefore accumulate in adipose tissues. Geurtsen (16) has published a very thorough review of the chemical and biological interactions of TEGDMA. He concluded already in 2001 that this substance is able to interact with various cell structures and represents therefore a high toxicity. Later, the work of Emmler (17) on the toxicity of TEGDMA on pulmonary cells, this of Gregson (18) on human pulp and gingival fibroblasts, and this of Imazato (19) on osteoblast-type cells, have all confirmed the cytotoxicity of TEGDMA. The various origins of these three studies (Germany, United States of America, and Japan) and their very recent date of publication (2008-2009), point to the significance and actuality of this problem.

Concerning the BPA, there is today a controversy on its influence on health, particularly at the endocrine level, and on the development of diseases like diabetes, and cardiac and liver diseases, as mentioned by Tillet (20). It is pointed out that 93 % of Americans aged over 6 years have residues of BPA in their urine. This BPA tends to accumulate in adipose tissues and has certainly a non-food origin. Dental restorative materials like composite resins and sealants are mentioned as a possible source of BPA, among others. Already in 1999, Arenholt-Bindslev et al. (21) have shown that the sealant Delton (containing Bis-DMA) released BPA in saliva at the time of application of the sealant, and that the BPA from this origin had an effect on the oestrogen activity of the human saliva.

This problem of the presence of BPA in the human body is considered very seriously, especially in the USA where the National Toxicology Program (NTP) and its Center for the Evaluation of Risks to Human Reproduction (CERHR) (22) have attributed to the BPA problem the level "some concern", corresponding to the intermediary value on a scale of 5 levels. The expressed concern relates to the influence of the actual levels of exposure of human fetuses, of infants, and of children to BPA on possible changes in the development of their prostate and brains and on a decrease of the sexual differences. This highly official group has initiated this year a search of information at the scientific level to know the present level of research on the effects of BPA on human health. For this reason, it is asked to consider in the research works a better understanding of the exposure sources to BPA in humans, a comparison of the metabolism of BPA in rodents, primates and humans to see how it varies with time, and to develop studies on the pharmacokinetics of BPA and on the toxicology of development. As it can be seen, the problem is far from being understood and solved.

Evaluation of the risk

Regarding TEGDMA, it is clearly established that the majority of dental composites release TEGDMA, in vitro and in vivo, and that this compound is toxic. The risk for human health is therefore important: allergies, cytotoxicity. How to avoid this? A recent study (23) offers to replace TEGDMA in composite
formula by very reactive mono-acrylates to obtain resins with the same mechanical properties. There is already a composite resin without TEGDMA and without HEMA: that is the resin “e.l.s. Extra Low Shrinkage” by Saremco (24), available since several years and whose clinical behavior has already been favorably evaluated clinically. Several studies, among them (25), show clearly that this resin does not release TEGDMA or HEMA, when compared to most of the composite resins of today. A good way to eliminate the risk associated with the release of TEGDMA is therefore to use composites made without TEGDMA and HEMA.

About BPA, the mention “some concern” recently attributed to the problem of BPA in the body (see above) should place this compound in a quite difficult position. The recent statement by the American Dental Association (ADA) (26) puts this question seriously in perspective. After having mentioned that products containing Bis-DMA could release small amounts of BPA through degradation of the Bis-DMA molecule by salivary enzymes, it says precisely: “Based on current research the Association agrees with the authoritative government agencies that the low-level of BPA exposure that may result from dental sealants and composites poses no known health threat”. Moreover, ADA cites, in the same document, a statement of the U.S. Department of Health and Human Services (HHS) saying: “Dental sealant exposure to bisphenol A occurs primarily with use of dental sealants [containing] bisphenol A dimethacrylate. This exposure is considered an acute and infrequent event with little relevance to estimating general population exposures.”

Thus, if BPA becomes a public health problem, it is more because of the multiple possibilities of exposure in everyday life (particularly through applications using polycarbonates) than through the very limited use of dental sealants, among which only a few contain Bis-DMA potentially susceptible to degrade into BPA.

**Conclusion**

TEGDMA and BPA present potential risks for human health. The probability of release of TEGDMA from composite resins is high, and the risk of allergies and cytotoxicity has been recognized. The best way of protection is to use composites without TEGDMA. Concerning BPA, even if it presents potentially much more serious threat for health, particularly by affecting the endocrine equilibrium, its probability of availability from dental restorative materials is much lower; it is limited to dental sealants only, whose use is less frequent than that of dental composite resins. Here again, the best protection is to simply avoid using sealants containing Bis-DMA.

**References :**

5) Fadini L, Brambilla R, Cagetti MG, Gagliani M : G It Cons 2006 Suppl vol IV n. 1, January-March
24) Résine composite dentaire els Extra Low Shrinkage, Saremco Dental AG, Rohnacker, 9445 Rebstein, Suisse. www.saremco.ch.

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