The biocompatibility of resin-modified glass-ionomer cements for dentistry

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\textbf{A B S T R A C T}

Objectives. The biological effects of resin-modified glass-ionomer cements as used in clinical dentistry are described, and the literature reviewed on this topic.

Methods. Information on resin-modified glass-ionomers and on 2-hydroxyethyl methacrylate (HEMA), the most damaging substance released by these materials, has been collected from over 50 published papers. These were mainly identified through Scopus.

Results. HEMA is known to be released from these materials and has a variety of damaging biological properties, ranging from pulpal inflammation to allergic contact dermatitis. These are therefore potential hazards from resin-modified glass-ionomers. However, clinical results with these materials that have been reported to date are generally positive.

Conclusions/significance. Resin-modified glass-ionomers cannot be considered biocompatible to nearly the same extent as conventional glass-ionomers. Care needs to be taken with regard to their use in dentistry and, in particular, dental personnel may be at risk from adverse effects such as contact dermatitis and other immunological responses.

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1. Introduction

Resin-modified glass-ionomers are dental restorative materials of the glass-ionomer family. This means that they contain basic ion-leachable glass powder and a water-soluble polymeric acid such as poly(acrylic acid). In addition, they contain organic monomers, typically 2-hydroxyethyl methacrylate, HEMA, and an associated initiator system \cite{1}. Initiators are generally photo-sensitive, so that most resin-modified glass-ionomer formulations are light-cured, using a conventional dental curing lamp that emits light at a wavelength centered on 470 nm.

In addition to HEMA, some brands of resin-modified glass-ionomer are modified by the inclusion of branches grafted onto the parent poly(acrylic acid) \cite{2}. These branches end in vinyl groups, and these are capable of copolymerizing with HEMA once initiation has occurred. This means that these particular resin-modified glass-ionomer develop organic crosslinks as they cure.

Though the details of their composition vary, resin-modified glass-ionomers are generally able to form strong bonds to both enamel and dentin \cite{3} and also to release fluoride \cite{3,4}. Other ions are also released, namely Na, Ca, Sr, Al, P and Si \cite{5}. These ions are the same as those released by conventional glass-ionomers, though levels of phosphorus released by resin-modified glass-ionomers have been found to be much lower than those found for conventional glass-ionomers \cite{5}.
The presence of HEMA alters the acid-base reaction in resin-modified materials [6]. It becomes slower and would, in principle, lead to the formation of a significantly weaker material (see Table 1). In practice, the polymerization of HEMA contributes significantly to the strength of the set material, so that resin-modified glass-ionomers have about the same strength as conventional glass-ionomers.

Resin-modified glass-ionomers have been developed for a number of specific applications in clinical dentistry. Originally formulated as liner/base materials [7], modern resin-modified glass-ionomers can be used as restorative materials in their own right, for core build-up and for luting [8]. Clinical reports for specific uses, such as Class V restorations, have shown them to be reliable materials that give good results in terms of both aesthetics and durability [9]. They have found particular use in pediatric dentistry [10,11], where their success has been such that at least one authority has recommended that they be used instead of amalgam in all repairs to children’s teeth [12].

Biocompatibility is an important feature of any material designed for use within the body. The term is defined as "the ability to perform with an appropriate host response in a particular application" [13]. This definition is one of bio-functionality [14] and is not a single property but a collection of processes that occur from the interaction of the tissues with the artificial material [8]. Given this, it is clearly meaningless to describe a material as biocompatible without referring to the specific context in which the material is to be used. For the purposes of this review article, we are concerned with the application of resin-modified glass-ionomers in dentistry, which means that we are concerned with the interaction with the tooth surface and possible influences on the pulp. We also cover aspects of the interaction of resin-modified glass-ionomers and their components with dental personnel, specifically involving skin contact and inhalation.

The biocompatibility of conventional glass-ionomers was reviewed many years ago [15], and the general conclusions of that review remain valid. Specifically, for application in clinical dentistry, conventional glass-ionomers show good biocompatibility because they have the following properties:

(i) low setting exotherm [16];
(ii) rapid neutralization [17];
(iii) release of generally benign ions from the set cement.

This last point was examined in some detail. As already stated, conventional glass-ionomers are known to release Na, Al, Si, P and F under neutral conditions, and to also release Ca under acidic conditions [18,19]. Apart from aluminum, these ions are acceptable in the body and useful for a variety of physiological processes, some of which are associated with remineralisation of the tooth surface. Aluminum is of more concern since it has the potential to be toxic towards the central nervous system, the skeleton and the haematopoietic system [20]. However, total amounts of aluminum released from glass-ionomer cements are low [18] and this, coupled with the low bio-availability of aluminum taken into the gastro-intestinal tract, suggests that this is not an important problem. There have certainly been no reported adverse effects of these materials, and they are generally considered to be highly biocompatible when used in clinical dentistry.

### Table 1 – Effect of HEMA on the properties of a glass-ionomer cement [6]

<table>
<thead>
<tr>
<th></th>
<th>Setting time (min)</th>
<th>Compressive strength (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glass-ionomer (alone)</td>
<td>9.1</td>
<td>230</td>
</tr>
<tr>
<td>Glass-ionomer (with HEMA)</td>
<td>19.1</td>
<td>147</td>
</tr>
</tbody>
</table>

2. The reported biocompatibility of resin-modified glass-ionomers

The biocompatibility of resin-modified glass-ionomers has been considered in terms of their cytotoxicity towards pulp cells in an MTT assay [21]. These studies have shown that the concentration of inorganic ions, namely Sr$^{2+}$, Al$^{3+}$ and F$^-$ are too low to have any cytotoxic effect [21]. However, unpolymerized HEMA is released. Using FTIR, HEMA has been identified in the eluate from the resin-modified glass-ionomer Vitremer. Surprisingly triethylene glycol dimethacrylate, TEGDMA, was also found [21]. Following treatment with ethanol, which also elutes these monomers, the cytotoxicity was found to be substantially reduced [21].

HEMA release occurs mainly in the first 24h after polymerization, and HEMA is undoubtedly the substance that compromises the biocompatibility of resin-modified glass-ionomers [22]. HEMA has the potential to be systemically distributed from its location in the mouth and to be the source of adverse effects in patients. Dental personnel, too, are at risk, as manual contact with unprotected skin can lead to allergic reactions, ranging from the relatively mild (i.e. contact dermatitis) to the severe. Since HEMA is volatile, they are also at risk from inhalation of HEMA vapor.

In another study, the resin-modified glass-ionomer Vitremer was compared with calcium hydroxide as a pulp-capping material [23]. Buccal class V cavities were prepared in sound human premolars, the pulps exposed then covered with the pulp-capping materials. The cavities were then filled with an appropriately bonded composite resin [23]. Teeth were later extracted at time intervals of up to 300 days, and examined histologically. Vitremer was found to cause a moderate to intense inflammatory response in the pulp, together with the formation of a large necrotic zone [23]. Over time, the teeth pulp-capped with calcium hydroxide showed pulp repair and the formation of an intact bridging layer of dentin around the site of the pulp exposure. Teeth with pulps capped with Vitremer not only failed to match this type of positive biological effect, but they showed a persistent inflammatory response as a result of substances leached from the Vitremer. The authors did not identify the cause of this adverse reaction, but it is consistent with the substantial amounts of HEMA monomer known to be released by resin-modified glass-ionomers. The overall conclusion from this study is that Vitremer should not be used clinically for direct pulp capping [23].

More recent studies have confirmed this lack of biocompatibility. Using several brands of resin-modified glass-ionomer, experiments were carried out using cultures of MDPC-23 cells,
Table 2 – Properties of HEMA (from www.osha.gov)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>130.14</td>
</tr>
<tr>
<td>Melting point</td>
<td>−12 °C</td>
</tr>
<tr>
<td>Boiling point</td>
<td>205 °C</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>1.072–1.076</td>
</tr>
<tr>
<td>Flash point</td>
<td>107 °C</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Oral rat LD50: 1600 mg/kg</td>
</tr>
</tbody>
</table>

and also implating samples subcutaneously into rats [24]. As before, the cell culture used MTT assay as a means of determining cell viability. All resin-modified cements showed significant cytotoxicity, with cytotoxicity being greater after 48 and 72 h exposure than after 24 h, which suggests that HEMA release continues well beyond the 24 h recorded in earlier experiments [24]. In rats, all materials tested showed an inflammatory response at 7 days that varied from moderate to intense. By 90 days, however, substantial healing had occurred in almost all cases [24].

Resin-modified glass-ionomer has been shown to be cytotoxic in experiments using an immortalised odontoblast cell line [25], with cytotoxicity varying between brands. It was, though, minimized in all cases when appropriate lengths of cure time were used for cement specimens.

3. HEMA release

The key component that is known to be released from resin-modified glass-ionomers is HEMA, the properties of which are shown in Table 2. High-performance liquid chromatography (HPLC) has been used to quantify this [26,27], in each case using water as the extraction medium.

Palmer et al. determined the factors that influence HEMA release from resin-modified glass-ionomers [26]. They determined levels of HEMA eluted from four different brands of material that had been subjected to varying lengths of cure and maturation. Disc-shaped specimens were prepared and cured with a dental curing lamp for (i) the manufacturer’s recommended time, (ii) half the recommended time (undercured) or (iii) 1.5 × the recommended time (overcured). An additional set of specimens were allowed to set in the dark. For these, there was no polymerization of HEMA, and setting was entirely due to the acid-base reaction of polymeric acid with the glass. As a result, these specimens contained by far the greatest amount of free HEMA monomer [26]. Light-cured specimens were allowed to undergo further maturation for varying time periods, before exposure to water.

All materials were found to release HEMA into the storage solutions. Materials behaved differently with regard to the effect of cure time, but in all cases, post-cure maturation time made little or no difference to the amount of HEMA released. As far as the time of cure was concerned, two brands (light-cured Viremer and Virebond) showed no difference when either under- or overcured. By contrast, one material (Fuji Lining LC) showed a significantly greater HEMA release when undercured, though no difference when overcured; and one material (Fuji II LC) showed a significantly lower HEMA release when overcured. There was no associated increase in HEMA release when this particular material was undercured.

Overall, though, Palmer et al. demonstrated clearly that degree of light cure is an important factor in controlling HEMA release [26], a finding confirmed in other studies [25,27]. The fact that there were variable results with respect to the recommended cure time is an indication that, generally speaking, manufacturers have optimised formulations in terms of cure times. It is clear, too, that in practical use, manufacturers’ recommended cure times should be followed in order to minimise HEMA release.

HEMA released from resin-modified glass-ionomers is able to diffuse through dentin, and this affects the pulp [28]. This has been studied in considerable detail by Hamid and Hum [28,29]. In one series of experiments, the effect of caries on the diffusion process was studied [28]. This involved the use of extracted human molars with different degrees of caries, which were obtained from consenting donors. Teeth were divided into three groups, namely mild, moderate and severe in terms of caries severity. HEMA was supplied in a bonding resin, and diffusion of HEMA through the tooth into a surrounding water medium was determined using HPLC. These experiments showed two things: first, dentin under all conditions of caries severity, including caries-free, allowed HEMA to diffuse through. Second, severely carious teeth showed a markedly higher rate of diffusion than teeth with either mild or moderate caries.

In a related study, Hamid and Hume determined the effect of dentin thickness on HEMA diffusion [29]. They used 40 extracted third molars with dentin thicknesses in the ranges 3.4–3.6, 2.4–2.6, 1.4–1.6 and 0.4–0.6 mm, respectively. Again, HEMA was provided by a dentin bonding agent, this time placed beneath a conventional composite resin restoration. HEMA was found to diffuse through to the pulp chamber in all cases. Decreasing thickness of dentin markedly increased the rate of diffusion of HEMA towards the pulp. It also increased the total amount of HEMA that crossed the dentin to the pulp. These results demonstrate that dentin is a poor barrier to HEMA and that thin layers of caries-affected dentin will allow HEMA to pass fairly readily to the pulp.

Although these studies of HEMA diffusion used dentin-bonding agents, the results are relevant to resin-modified glass-ionomers. Like bonding agents, resin-modified glass-ionomers are placed directly onto the dentin under conditions of clinical use. Like bonding agents, they release HEMA in significant amounts, and when used in teeth, this HEMA is clearly able to diffuse to the pulp. Having done so, various adverse biological effects may occur.

4. Effect of HEMA on the pulp

Surprisingly, the reported effects of resin-modified cements on the pulp are minimal [30,31]. For example, studies on the pulps of monkeys have been reported as showing little or no difference in response to that of zinc oxide-eugenol or calcium hydroxide cements [31]. Resin-modified glass-ionomer was placed over 36 exposed and 24 non-exposed pulps in teeth of healthy adult monkeys, and compared with calcium hydroxide (exposed pulps) or zinc oxide-eugenol (non-exposed pulps). Tissues were collected within three time periods, namely 6–7 days, 21–27 days and 90–97 days. After...
being demineralised, teeth were sectioned and stained before being examined by light microscopy. Non-exposed pulps showed almost no effects, whereas in eight of the 36 exposed pulps in the 6–7 day time period there were varying degrees of inflammatory response. However, after 21 and 97 days, over 80% of the pulps restored with resin-modified glass-ionomer showed dentin bridge formation [31]. The overall conclusion was that resin-modified glass-ionomers showed acceptable biological behavior for this application and were biocompatible towards both exposed and non-exposed pulps. Similar results had been found several years earlier with experimental formulations of resin-modified glass-ionomer [32].

These results are surprising in the light of the studies, mentioned previously, which show that HEMA is able to diffuse through dentin to the pulp [28,29]. When this happens, there is considerable damage to the pulp, for example, pulpal inflammation [33–36]. This has been demonstrated as being due to the effect of chemicals, not to bacterial contamination. It has also been suggested that such pulpal damage may lead to immune-mediated responses of varying degrees of severity in a sensitized individual [33,37]. Overall, it can be concluded that, although the effects of HEMA release from resin-modified glass-ionomer on the pulp may be short-lived, they are significant. They may also lead to effects of greater biological importance in susceptible or sensitized individuals.

5. Effect of HEMA on cells

Several studies have considered the effect of HEMA on cells of various types, and the general conclusion is that it is cytotoxic and a health hazard. For example, Yoshih [38] demonstrated that HEMA was cytotoxic and suggested that the hydroxyl group especially enhanced the cytotoxicity compared with other monomers leached from dental restorative materials. The fully formulated resin-modified glass-ionomer Vitrebond was shown to have severe cytotoxic effects on 3T3 fibroblast cells [39]. Unlike most workers, however, the authors of this study concluded that the monomer TEGDMA, rather than HEMA, was responsible for the observed cytotoxic reactions. In view of the numerous studies which show that HEMA is the most abundant (often the only) monomer released from these materials, this seems unlikely, but whatever the origin of the effect, the fact remains that this material was still shown to have significant cytotoxicity in vitro.

HEMA itself undoubtedly causes damage to biological systems. In one study, it was shown that exposure of human THP-1 monocyte macrophages to only 0.75 mmol dm$^{-2}$ inhibited proliferation by almost 50% after a week [39]. Other significant changes were observed in the cells. For example, total protein in the cell increased by up to 80% and mitochondrial activity decreased by 60–80%. Overall, this study demonstrated clearly that extremely small amounts of HEMA are capable of causing major disruption to functioning cells, inhibiting proliferation and a range of other important biological activities [39].

In the fully functioning tooth, pulp fibroblast cells differentiate into odontoblasts, and thus contribute to the tooth development [40]. Monomers, including HEMA at low concentrations, may affect this development. At levels well below a toxic concentration, HEMA has been shown to inhibit the expression of collagen 1, osteonectin and dentin sialoprotein, and thus to reduce the formation of mineral nodules within the tooth [40].

Finally, HEMA has been shown to elicit an immunological response in vivo [41]. It is able to bind to endogenous proteins, which leads to the possibility of auto-antibody production in vivo. This kind of structural modification to the body’s proteins may lead to adverse immunological responses, and this may explain phenomena such as allergic reactions including contact dermatitis in dental personnel [42]. The detailed mechanism by which HEMA induces its adverse biological effects is beginning to be understood as a result of experimental studies of this topic, though there is still a long way to go before the mechanisms are fully elucidated [43]. In particular, the effects of HEMA on cell death have yet to be fully characterized.

Recently, however, it has been shown that HEMA is able to promote apoptotic death in cells [43,44]. For example, one study considered both healthy individuals and patients with established hypersensitivity towards HEMA. Experiments showed that HEMA induced apoptotic death in Peripheral Blood Mononuclear Cells (PBMCs) obtained from both healthy and sensitized patients. It also demonstrated HEMA-induced apoptosis in murine RAW cells, with the effect being related to dose. The induction of cell death occurred with lower levels of HEMA in PBMCs obtained from sensitized individuals than from healthy ones [43]. This led the authors to conclude that the decreased susceptibility of lymphocytes to HEMA-induced death might be important in generation and continuation of hypersensitivity in affected individuals [43].

Another study [44] considered a variety of dental monomers (glycerol dimethacrylate, TEGDMA and HEMA), testing them against rat alveolar macrophages and the J744A1 macrophage cell line. Of these monomers, HEMA caused the highest level of apoptosis, though it was not the most cytotoxic of the monomers. Apoptosis is known to cause less inflammatory response in tissues than a necrotic process, but nonetheless it is an adverse biological response. It should be taken into account when evaluating the biocompatibility of dental materials [44].

It has been shown that micronuclei develop in cells affected by HEMA [45]. This indicates that, at the molecular level, HEMA causes damage to the chromosomes and breaks the DNA strands. This damage to the DNA delays important steps in the mammalian cell cycle. There is increased oxidative stress due to the effect of HEMA on levels of production of glutathione. This is a naturally occurring radical scavenger and its role is to protect cell structures from damage by reactive oxygen species. By depleting the availability of glutathione, HEMA causes an elevation in local levels of reactive oxygen species, and these are then able to activate biochemical pathways leading to apoptosis. Experiments in which known radical scavengers, such as N-acetylcysteine, ascorbate or vitamin E were added to cell cultures have shown that the cytotoxic effects of HEMA can be suppressed [45]. This confirms the role of HEMA in perturbing the levels of reactive oxygen species in the cells.

By altering the biochemical mechanisms regulating the cell cycle and cell death, HEMA may be able to alter the functions
of various cells in the mouth at levels below those that cause acute cytotoxicity [45]. Processes which are likely to be affected include homeostasis, dentinogenesis and tissue repair. Work is continuing on this important topic.

### 6. Dermatological effects of HEMA

Exposure of individuals to HEMA can lead to adverse biological responses of various kinds, including contact dermatitis [46,47] (see Table 3). In one study, the source of HEMA was an acrylic structural adhesive designed for industrial use that was found to contain 24.6% HEMA [46]. A patient who used this adhesive became sensitized to the HEMA, and developed dermatitis on the hands that spread to the lower arms, chest, neck and face. The condition was sufficiently serious that the patient could not continue in her workplace because of the severity of the recurring symptoms when she attempted to do so [46].

An evaluation of cases of contact dermatitis presenting to a clinic showed that HEMA was one of the most common contact allergens [48]. This is partly due to its widespread applications, both industrial and dental. However, a significant proportion (approximately 45%) of the patients turned out to be connected with dentistry, working as either dentists or dental technicians [48]. It was noted that prospective dentists and dental technicians are exposed to acrylic monomers early in their training, and that sensitization can occur before the allergenic nature of these substances is fully appreciated [48].

Another interesting source of acrylic monomers, including HEMA, is from nail care cosmetics, including artificial nails [47]. Beauticians specializing in nail care are at particular risk of developing allergic contact dermatitis from these products [47]. Dorsal regions of hands and fingers are most commonly affected, but cases have been reported of distant sites, such as the face and neck, being affected. It has also been found that cross-reactions can occur, with structurally similar acrylic monomers being capable of triggering allergic reactions [47].

Contact dermatitis has been demonstrated using HEMA-based solutions applied to the skins of guinea pigs and humans [49]. Skin to which solutions of HEMA at concentrations as low as 0.2% had been applied developed redness and itchiness, and showed clear evidence that delayed allergic reactions had occurred at all HEMA concentrations.

Adverse reactions have also been reported following a single exposure [50] and even during patch testing [51]. In the reported single exposure case, a 50-year-old man developed contact dermatitis at the site of an electrosurgical grounding plate 2 weeks after orthopedic surgery. Patch testing demonstrated positive reactions to both hydroxylethyl acrylate and methacrylate (HEMA), both of which were components of the plate. The patient reported having no previous contact with acrylate-containing materials, so that the authors concluded that it was probable that the primary sensitization had occurred as the result of a single contact [51].

Patch testing itself has been shown to lead to sensitization in at least one individual [52]. The person concerned was a 45-year-old orthodontist who was being tested for reaction to acrylates and methacrylates. HEMA was among the substances tested, and though methacrylates are generally considered to be less powerful sensitizers than acrylates, this occurrence shows that methacrylates, including HEMA, are able to sensitize at the relatively low concentrations used in patch testing.

### 7. Effects on dental personnel

Dental personnel (dentists and dental nurses) using resin-modified glass-ionomers are exposed to HEMA and may be affected by this. HEMA is volatile and may be inhaled, a hazard for which face-masks do not provide protection. The eyes may also be exposed to this monomer vapor. Latex gloves are inadequate as protection for the skin, because they have been found to be permeable to HEMA and other monomers [53]. By contrast, gloves made of other materials, for example nitrile rubber, have been found to provide good protection against the passage of HEMA [53], and are therefore recommended for use when handling resin-modified glass-ionomers.

Despite these evident hazards, to date there have been no reports in the literature of dental personnel showing symptoms of acrylate allergy associated specifically with the use of resin-modified glass-ionomers. However, such effects have been reported in workers in other industrial sectors, and in dental personnel exposed to HEMA from other sources, notably dentin bonding agents. It seems likely that there have been occurrences of allergic reactions but that these have not been reported. Whatever the truth of the matter, though, it is apparent from the literature that by adding HEMA to formulate resin-modified glass-ionomers, the biocompatibility of the original glass-ionomer cements has been compromised significantly. It is apparent, too, that greater care is needed in using these materials than conventional glass-ionomers.

### 8. Clinical handling of resin-modified glass-ionomers

In order to use resin-modified glass-ionomer cements safely, the following precautions are recommended. It should be noted that these do not apply to the use of conventional glass-ionomers. Suggested precautions are:

(i) Ensure that the work space is well ventilated;
(ii) avoid inhalation of HEMA vapor;
(iii) touch unset material only with instruments, never hands, even when wearing gloves;
(iv) avoid contact of resin-modified cement (set or unset) with the oral mucosa of the patient;

### Table 3 – Biological effects of HEMA

<table>
<thead>
<tr>
<th>Effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation, human pulp</td>
<td>[23,33–36]</td>
</tr>
<tr>
<td>Monkey pulp</td>
<td>[31]</td>
</tr>
<tr>
<td>Subcutaneously (rats)</td>
<td>[24]</td>
</tr>
<tr>
<td>Cytotoxicity</td>
<td>[38,39]</td>
</tr>
<tr>
<td>Immunological effects (mice)</td>
<td>[42]</td>
</tr>
<tr>
<td>Apoptosis</td>
<td>[43,44]</td>
</tr>
<tr>
<td>Damage to DNA</td>
<td>[45]</td>
</tr>
<tr>
<td>Contact dermatitis</td>
<td>[46–52]</td>
</tr>
</tbody>
</table>

Effect Reference

- Inflammation, human pulp: [23,33–36]
- Monkey pulp: [31]
- Subcutaneously (rats): [24]
- Cytotoxicity: [38,39]
- Immunological effects (mice): [42]
- Apoptosis: [43,44]
- Damage to DNA: [45]
- Contact dermatitis: [46–52]
(v) use with a liner to prevent diffusion of HEMA to the pulp;
(vi) build-up restorations in increments (optimum thickness
1 mm, maximum thickness 2 mm) to enable each incre-
ment to be properly through-cured, thereby reducing the
amount of HEMA available for release;
(vii) light-cure unused remnants of cement before disposal,
to reduce the possibility of exposure to volatile HEMA
vapor.

9. Conclusion

Resin-modified glass-ionomer cements are useful clinical
materials for repair of teeth affected by dental caries. They
can be formulated for use as either liners or full restoratives.
Their mechanical properties are acceptable for their applica-
tions, and they have the clinically useful properties of inherent
adhesion to the tooth surface and release of fluoride.

However, even when properly cured according to manu-
facturer's instructions, they are able to release the monomer
HEMA (2-hydroxethyl methacrylate). This can diffuse readily
through the dentin to the pulp, and once in the pulp, it can
lead to a variety of adverse biological effects, from persistent
inflammation to sensitization and potential allergic reactions
in the patient.

For dental personnel (dentists and dental nurses), there
are potential problems of long-term exposure to HEMA, a
substance that has been shown to be capable of producing sen-
sitization in an individual from a single contact, and at very
low concentrations. HEMA can penetrate latex gloves of the
type commonly used in clinical dentistry, and once through
can cause contact dermatitis of varying degrees of severity.
It is volatile, and its vapor can be readily inhaled, leading to
adverse reactions in the respiratory system.

The monomer HEMA, which is an essential component
of resin-modified glass-ionomers, and is released from these
materials under all cure conditions, has a variety of adverse
biological effects. These include cytotoxicity, inducing of
apoptosis, persistent inflammation, respiratory problems,
allergy and contact dermatitis. It is clear that such adverse
effects are possible and, indeed likely when resin-modified
glass-ionomers are used clinically. Surprisingly, though, to
date there have been few reports of adverse effects attributed
to resin-modified glass-ionomers.

The overall conclusions from this review are that the biocom-
patibility of resin-modified glass-ionomers in dentistry is
much less than that of conventional glass-ionomers and that
the inclusion of the monomer HEMA is responsible for this
lack of biocompatibility.

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