



MASTEROPPGAVE
**Adverse Reactions to Dental Resin
Based Materials**

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Summary

Introduction

Dentists give dental treatment with resin-based materials to patients every day, and these materials are known to contain several substances that may cause unwanted reactions in human. Possible reactions in a shorter time limit are contact allergy and toxic contact dermatitis. Some plastic materials are also known to release substances which may have an estrogenic effect.

Aims

The aim of this master thesis was to explore by a literature research the risk for the patient getting adverse reactions when treated with resin-based materials.

Materials and Methods

Relevant studies were acquired through a search in PubMed for adverse reactions and resin-based materials. Three relevant articles were found.

Results and Discussion

Dental resin-based materials used for restoring of lost tooth substance contain reactive substances (e.g. methacrylates, initiators etc.). Precautions should be taken in all patients to decrease the leakage and direct exposure of these substances. This should be considered when the patient has a known allergy. Dentures and orthodontic baseplates may contain Phtalates and Bisphenol A, known as xenoestrogens. The amount of released substances is, however, considered to be low and therefore adverse effects in patients may be rare. The dentist should be aware of that, and know what to tell the patient when a concern about this comes up. Still, the awareness and knowledge of adverse effects toward those materials are limited and more clinical studies are needed.

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Introduction

This master thesis seeks to explore the possible hazards dental patients are exposed to when receiving treatment with resin-based materials. Dentists work with polymer resin-based materials every day. Composite filling materials, bonding, resin based glassionomer cements and polymers for prosthodontic and orthodontic applications come into this category. Materials mentioned in this paper are summarized in table 1. All of these materials contain highly reactive substances in advance of polymerization. Handling and polymerization of these substances are partly done inside the oral cavity of the patients.

Polymer Resin-Based Materials mentioned in this paper

Direct Restorative Materials	Filling material that is placed and formed in one session. Hereby referred to as composites.
Pit and Fissure Sealants	Flowable composite material of low viscosity. Mainly used for preventive measures on children and adolescents
Resin-reinforced Glassionomer Cements	A direct filling material widely used in the primary dentition.
Bonding	Adhesive between tooth substance and the composite/ luting cement. Low viscosity and high wettability.
Luting Cements	Materials for adhering ceramic crowns, onlays and veneers to tooth substance.
Denture Lining Materials	Rebasing materials for acrylic base of full and partial dentures
Orthodontic Appliances	Removable plastic devices used as retention, space-keepers, tipping of teeth etc.

Table 1 Overview on the resin-based materials mentioned in this text [1, 2]

From 01.01.2008 amalgam has been totally prohibited in Norway, leaving composite and glassionomers as main alternative when direct restoring of lost tooth substance. There has been extensive research done on biological

reactions to amalgam, but reactions to other materials that substitute amalgam have not been examined to the same extent. For both patients and personnel, adequate information on possible hazards on amalgam replacing materials seems not sufficient [3]. Handling of polymer resin based materials is more demanding compared to phosphate cements and amalgam. Resin-based materials are far more sensitive to water contamination, and to get a sufficient polymerization depending on the operator and in part the circumstances. This will be discussed later in this paper. Before the dental composites entered the market, early methacrylic resins and silicate cements were used as an esthetic alternative to amalgam for anterior fillings. As the physical advantages of composites have improved during second half of the last decade, it has become the material of choice. As amalgam has lost its popularity, composites have taken over. Etching technique enables the use of composite materials in a variety of treatments. Sealants are used in caries preventing manners and orthodontics brackets can be bonded [4]. Cements that are used as adhesive for porcelain onlays and crowns do also to a great extent contain resins.

Chemical characteristics of dental resin-based materials

For understanding of the biological effects of polymer resin based materials, it is crucial to have knowledge of the chemical background. A dental resin-based material, is a mixture of different substances (e.g. monomers, initiators, fillers etc.). Composite consists of filler particles (e.g. silica, barium glasses etc.) embedded in a resin matrix of hydrocarbon polymers. During the curing process, polymerization, monomers are linked to each other forming long chains of polymers, cross-linked in a three- dimensional network.

Monomers

Monomers are small molecules that during a polymerization reaction are able to form long polymeric chains. Monomers used in dentistry can be mono-, di- or multi-functional due to the number of reactive methacrylic groups. The backbone of the molecules varies greatly and can be of aromatic or aliphatic origin. The monomers used in polymer resin based materials are a blend of aromatic and/or aliphatic dimethacrylates. Monomers with

a low molecular weight are added to increase the degree of conversion, as well as to lower the viscosity of the material [1].

Polymerization reaction

The Polymerization is an addition reaction where the monomers are joined together to long and stable chains – “polymers”. The reaction is started when the initiator is cleaved into two radicals. Activation is either done by exposure to light, or by chemical activation (a two component system where two different substances are mixed). If light is used as an activator, the energy of the source is highly important. The activator gives energy to an initiator (for example Camferoquinone), that splits into free radicals (Figure 1). Those are activating the monomers which will be linked together creating a three-dimensional network of chains by continuous splitting of double bonds and addition of more monomers to the free electron end (Figure 2).

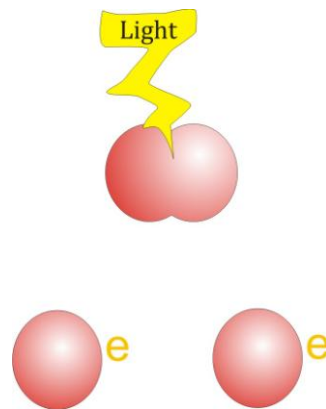


Figure 1 The initiator (e.g. Chamferquinone) is here activated with light as the energy source.

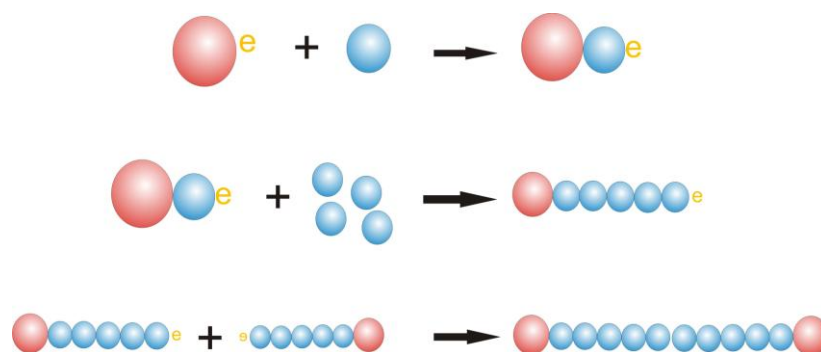


Figure 2. The initiator (red) is after activation reactive, with a free electron. Monomers (blue) are successively added to the chain. The final polymer chain is finished when two growing chains couple up.

The degree of conversion is the percentage of consumed carbon double bonds at the end of the methacrylate group. Important factors for the degree of conversion are for light curing materials curing time, distance to the light source and light intensity [5]. For chemical cured materials the ratio of activators vs. initiators are crucial. The polymerization ends by coupling of two growing chains together in creating a covalent bond. Termination of the process also occurs when there are not sufficiently monomers left to react, and/or the distance between the reacting molecules becomes too long. Due to different factors (e.g. the chemical structure of the methacrylates, the mobility etc), there will always be remaining monomers and free radicals left after polymerization [1].

At the surface, these free electrons at the end of the methacrylate group will be inhibited by oxygen molecules and making the newly polymerized filling reactive. When putting on another layer of composite, this will enhance bonding between the layers but can be considered as hazardous when in contact with unprotected skin or mucosa [1, 6].

Biodegradation of resin-based materials

Biodegradation is a transformation in a substance's chemical, physical and mechanical properties due to its environmental conditions. A material's molecular chemistry as well as its environment determines the level of biodegradation [7]. The ecology of the oral cavity constitutes a demanding environment for resin-based materials. The materials are constantly exposed to water and saliva components like enzymes that have impact on the degradation of the materials [2]. All organic ingredients of the resin matrix can be extracted from the polymerized material by a solvent like ethanol, and can also occur in an aqueous environment, however more slowly and not to the same degree [8, 9]. In the oral cavity, water from the saliva infiltrates the three-dimensional network of polymers by electrolysis and hydrolysis, causing a swelling of the network with increasing distance between the chains [2, 10]. This facilitates diffusion of free residual monomers and additives (e.g. initiators, stabilizers inhibitors etc.) from the polymer network into the oral cavity [2, 11]. From polymerized composite, released Triethyleneglycol- dimethacrylate (TEGDMA) can be found, but also other substances such as Bisphenol- A- glycidyl- dimethacrylate (Bis-GMA), urethane- dimethylacrylate (UDMA), ethyleneglycol dimethacrylate (EGDMA) and formaldehyde, have been detected, to a lesser amount [10, 12, 13]. It is evident that there is a greater degradation in cases with unpolymerized oxygen-inhibited outer surface of the material [9].

Biodegradation of resin based materials due to microorganisms in the oral cavity may occur, but are not sufficiently investigated [2]. Mechanical stress from biting and chewing can lead to fatigue and micro-cracks in the material, this might also add to the amount of released substances. Varying temperature, pH and chemicals from the diet are also expected to have an impact on biodegradation of dental materials [2, 14].

An in vitro study from Brazil simulated the leakage from polymerized dental materials in a pH cycling environment corresponding to a cariogenic environment. This study proved that leakage of by-products in a high-acid environment is higher than for a neutral solution. This suggests that leakage will be of a larger problem for

patients with high caries risk, because of the more acid environment [15]. Due to this, an improvement of oral hygiene, could lead to less leakage of byproducts.

Leakage from these materials can be seen for a long time after polymerization [10]. Concerning the material's mechanical properties, the result of the biodegradation are reduced surface hardness and wear and fatigue resistance [2].

In summary, the oral environment requires a great degree of inertness of the materials applied.

Biocompatibility

The Williams Dictionary of biomaterials defines biocompatibility as *"The ability of a material to perform with an appropriate host response in a specific application"* [16]. A material is biocompatible when it does not interfere, neither toxic, injurious nor immunological, with living tissue. An important aspect of biocompatibility of a resin-based dental material is the material's degree of monomer- polymer conversion. A material with a low degree of conversion, will have more unreacted double bonds, and will therefore have a greater ability to cause a reaction in living tissue [1]. Biocompatibility is also dependent on the material being appropriately polymerized; this is encouraged scientifically and by clinical knowledge. Easy handling of the material will increase the biocompatibility as a thorough polymerization will be easier to achieve for the operators [17].

Adverse Reactions

Despite being exposed to potential allergens and toxic substances, the oral mucosa seldom shows inflammatory and allergic reactions. In addition, wounds and lesions heal faster in the oral cavity compared to skin. This is proved to be due to diminished inflammatory response in the oral mucosa. It is therefore strong reasons to believe that the immune system of the oral cavity helps to diminish the degree of reactions to materials [18, 19].

Adverse reactions to dental materials are unwanted reactions, either subjective or objective. An adverse reaction can be of allergic, toxic or psychological origin. An unwanted biological reaction can further be local (e.g. contact dermatitis) or general (systemic, for example a hormone-effect).

Contact dermatitis

Contact dermatitis can, on a cellular level, be divided in mostly two categories: Allergic or toxic (irritative).

Allergic Contact Dermatitis is of allergic type IV origin, while an irritative contact dermatitis is a non-immunological reaction with direct cell damage followed by an inflammatory reaction [20]. Clinically it can be impossible to distinguish the different types of reactions without a deeper anamnesis or allergy test [21].

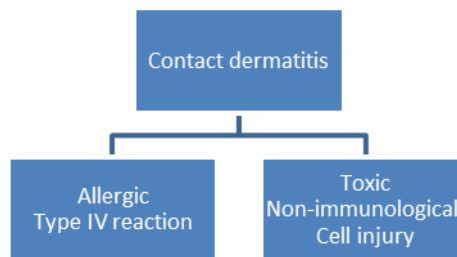


Figure 3 Contact dermatitis can be of either toxic or allergic origin

Allergy

Allergy to dental resin-based materials is due to a reaction to some of the substances in the resin matrix (e.g. monomers, inhibitors, stabilizers). To develop an allergy the person has to be sensitized to the specific allergen at an earlier occasion. Some monomers with allergic potential are described in table 2. These methacrylic monomers often cross-react, this indicates that a patient who have been sensitized to one monomer, will likely

react to one or more of the others [22]. Allergic reactions to dental resin-based materials are normally type IV hypersensitivity reactions meanwhile type I are extremely rare [17], and will not be dealt with in this paper.

Type IV hypersensitivity reaction or delayed- type hypersensitivity reaction, occurs 1-3 days after exposure to the specific antigen. The reaction is mainly localized to the area in direct contact to the antigen. The lipid- soluble molecules diffuse cell- membranes, and conjugates to proteins, and in this manner complete antigens are made. The antigen-presenting Cells of Langerhans binds to the allergen-protein complex, and a cellular response takes place with T lymphocytes. The amount of antigen required for a type IV reaction is about 100- 1000 times greater than that required for a type I reaction [11, 20].

Genotoxicity

Toxicity refers to chemical breakdown of biological tissue. Genotoxicity is the ability of a material to break down or mutate DNA. A genotoxic material is considered carcinogen because of its abilities to change DNA expression [23].

Estrogenic effect

It is well known that some chemical substances can bind to estrogen receptors and cause a similar effect as this sex-hormone. Such a substance is called a xenoestrogen. Disturbances in this endocrine system can lead to alterations in puberty onset and damages to the fetus [7]. Bisphenol-A that has been found in some pit- and fissure sealants is well known to be a xenoestrogen [24]. This will be discussed later in this paper.

Clinical signs of adverse reactions

Possible clinical intra-oral findings after reactions to resin-based materials are swelling, sores or necrosis of the oral mucosa [25]. Burning mouth syndrome has also been observed [25, 26]. Extra-orally there has been found sores, swelling, rash and itching. In addition to the local reactions, general symptoms have also been reported, such as headache, anxiety, difficulties in concentrating, vertigo, fatigue and pain from muscles and joints [25].

Burning mouth syndrome (BMS) has been suggested to be a possible adverse reaction to dental polymers, a study [26] failed to find a significant association. Anyhow the study states that reactions to dental polymeric materials should be taken into consideration when evaluating BMS patients.

With all these adverse reactions, is it really safe for the patients to receive dental treatment with reactive polymers?

Hypothesis

Adverse reactions to dental resin-based materials in patients are a known phenomenon. Still, it may be a condition that is not always considered in everyday dental practice. The hypothesis of the present study was that adverse reactions occurs towards resin based materials to such extent that the awareness of those conditions should be more focused on in general dental practice.

Aims

The aims of the present study were to investigate the probability of occurrence of adverse reactions to resin based materials in dental practice, and to seek for actions that can be done to diminish this problem. An attempt to make an overview on some of the substances causing such reactions has also been made.

Materials and methods

Search in Pub Med and equal databases for patient reactions were performed. Key words used were resin-based materials AND adverse reactions. This search gave 28 articles. After excluding articles not concerning dental patients, articles written before 1990 and articles on endodontic materials, nine articles were identified. From this sample, six articles were review articles and three articles were cohort studies. In addition, similar searches were also done from "Tidende". The annual reports from "Bivirkningsgruppen" were also included in this paper.

For substances capable of causing adverse reactions used in resin-based polymer materials for dental use, relevant literature was searched for using PubMed.

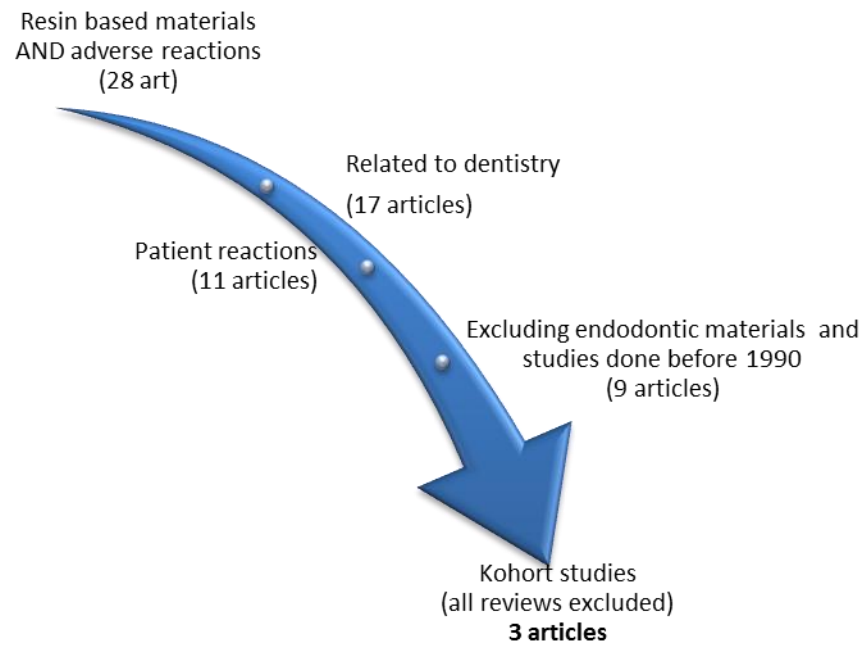


Figure 4. Search strategy in PubMed

Results and discussion

In the variety of articles found in the Pub Med search, only three were cohort studies. One study aimed to get an overview of the patients with possible reaction to resin-based material, referred to a National register of side-effects to dental materials in Sweden [25]. The two other studies were overviews on patients referred to “The Dental Biomaterials Adverse Reaction Unit” in Norway [27, 28]. The Swedish study was the only one considering just resin-based materials, whereas the Norwegian studies were focused mainly on amalgam. No Randomized Control Trials were found. Review articles were to a great extent based on case reports. In-vitro studies were found on several substances.

Prevalence

From the literature available, the prevalence of adverse reactions to resin-based materials cannot be estimated.

No Randomized control trials have been found, and most of the research is based on case reports.

Both in Norway and in Sweden attempts have been made to make dentists aware of adverse reactions and report any adverse reactions to dental biomaterials. In Norway “The Dental Biomaterials Adverse Reaction Unit” (BVG) was established in 1992 by the Norwegian Directorate of Health. One of the main tasks of BVG is the registration of adverse reactions to dental biomaterials, which is based on a voluntary reporting system. Dentists, dental hygienists and physicians are encouraged to report adverse reactions among patients [27]. In 1996, the Swedish National Board of Health and Welfare established a similar register on the possible side-effects to dental materials [25]. From the studies found in the literature search, two were from BVG and one was derived from the patient cases collected in the Swedish register.

BVG reported in 2009 an increase in reports with dental polymer resin-based materials as the suspected reason for the adverse reaction. From the unit’s start in 1993 to 2006, 28 of in total 630 reports were on plastic materials and cements [29]. From 1993 to 2009 the numbers had increased to 86 reports out of 1013 [30]. In 2008 the Unit reported an increase in reports due to resin-based materials, for the first time the amount of reactions had reached the level of reactions to amalgam (43% of the reports were on composites and cements). In 2009 one third of the reports received at BVG were on composites and cements [31]. In the Swedish study it was stated that 36 patients had a probable reaction to a resin-based material of in total 618 patients referred [25]. From those figures, it can be estimated that between 4-9% of all reactions to dental biomaterials were caused by resin-based materials over the last decades, and the numbers are increasing. A period prevalence based on the literature is however, not able to account for. Unfortunately, the reports don’t give adequate information on which materials that are involved.

Due to the fact that the Scandinavian systems are based on voluntary reporting, there are strong reasons to believe that there is an extensive under reporting. Based on studies on the attitudes of reporting adverse drug reactions among General Practitioners, only a few reports are made [32, 33]. Most likely this applies also to reporting on adverse reactions to dental biomaterials.

From the BVG studies it was stated that more than half of the reactions occurred within a week [31]. In the Swedish study as much as 30 out of 36 reactions occurred during or within 24 hours after treatment, and half of the reactions disappeared within a week. This may indicate that it is the leakage from the filling material during or straight after filling therapy that causes most of these reactions [25]

Most of the reactions in that study were concluded to most probably be non-allergic [25]. More women than men reported reactions [25, 31].

Substances which may cause adverse reactions

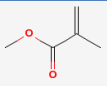
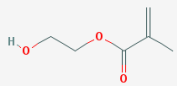
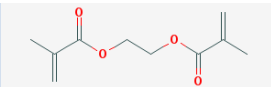
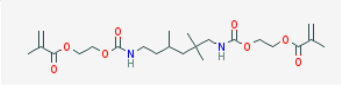
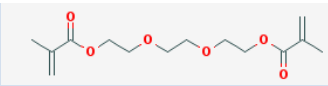
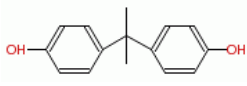
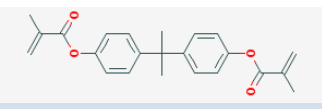
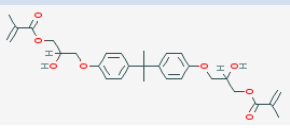
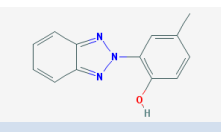
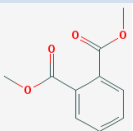
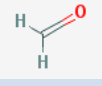
Compound	Use	Molecular structure	Possible adverse effect
MMA Methyl Methacrylate	Acrylate monomer, common in orthodontic baseplates and dentures		Allergy Toxic
HEMA 2-Hydroxy-ethyl-metakrylat	Common in bonding materials and resin-enforced glassionomer cements		Allergy
EGDMA Ethylene glycol dimethacrylate	Common monomer in composite and bonding		Allergy Cytotoxic
UDMA Urethane dimethacrylate	Monomer used in composites		Allergy Genotoxicity
TEGDMA Triethyleneglycol Dimethacrylate	Common monomer in composites and fissure sealants.		Allergy Genotoxicity
Bisphenol A	Present as a pollution in some materials		Xenoestrogen
Bis-DMA	Monomer used in some fissure sealants and composites		Xenoestrogen
Bis-GMA	Common monomer in composite fillings and fissure sealants		Allergy Genotoxicity
Tinuvin-P	UV- light absorber		Allergy
Phtalate	Softener in dentures and denture lining materials	 This picture: Dimethyl Phtalate	Xenoestrogen
Formaldehyde	“waste product” from polymerization		Genotoxicity Allergy

Table 2 Possible harmful substances in dental resin-based materials. Genotoxic: Either mutagen or carcinogen effect. Allergy: Components that is known to cause allergic/hypersensitivity reactions in humans [1, 9]. Molecular structures from PubChem Web [34]

Table 2 is a summary of substances found in the literature, capable of causing adverse reactions.

MMA, HEMA, EGDMA, UDMA

HEMA and EGDMA are both common monomers in resin based materials. They are cross-linking and diluents agents controlling viscosity and thereby the degree of conversion [8]. HEMA is also a common monomer in resin-reinforced glassionomer cements.

MMA, UDMA and HEMA are proved to leak from orthodontic base plate materials [35]. MMA has a high initial release, which decreased after 24 hours. UDMA did not show the same decrease after initial stage, and may therefore be present in the oral cavity at higher amounts for longer periods [35]. EGDMA is a water- soluble monomer common in composite and bonding materials as a crosslinking agent. It is shown to be both an allergen and cytotoxic [9].

TEGDMA (triethyleneglycol-dimethacrylate)

Diluents such as TEGDMA are added to a majority of polymer resin based dental materials. The purposes are to reduce the viscosity of the material, and make it possible to incorporate more filler particles. That makes the material stronger and easier to handle. TEGDMA has a flexible backbone, and in this way it facilitates molecular interaction and increases the degree of conversion, it will also act as a crosslinker, increasing the amount of crosslinkage in the material. TEGDMA is the most important diluents used today [4].

TEGDMA in resin based materials seems to be of considerable biological significance. It has been identified as the main leaking monomer [10]. The same study also proved TEGDMA as an early leaking monomer [10]. Due to its low molecular weight, relatively high hydrophilicity and detergent activity on liposomes, TEGDMA manage to penetrate cell membranes. It conjugates to intracellular proteins, and can therefore induce an allergic reaction [36]. Compared with other resin monomers and additives TEGDMA shows a major cytotoxic potency, and it has a great potential to degenerate DNA [36].

Bis- GMA

Bis- GMA is used because of its properties during polymerization. It is a rigid monomer, as the link between the two aromatic rings is not flexible. This is believed to increase cross-linkage of polymeric chains. Adding bis-GMA to a polymer resin-based material will reduce shrinkage. Bis-GMA makes the material highly viscous, therefore use of diluters as TEGDMA is necessary [1, 4]. Bis-GMA has not been shown to hydrolyze into BPA [4]. The release of Bis-GMA seems to be slow from composites probably due to its size [14].

Bisphenol A

Bisphenol- A (BPA) is an industrial chemical resin compounded of two phenol functional groups, used in the production of plastic materials to make polycarbonate plastic and epoxy resins. Products containing BPA are used daily worldwide. Examples are bottles, bottle tops, food storage containers, glue, painting, sports- and medical equipment [24, 37].

Although pure BPA is not used in dental resin-based materials, several of the most common monomers are derivatives from BPA, and the monomer mixture may be contaminated by pure BPA [24, 38]. It is proved that bis-DMA, a BPA derivate, can hydrolyze into BPA in contact with salivary esterase's. Although, the amount of BPA found are probably more due to impurities of BPA in dental resins than degradation [10, 24].

Studies, both in vivo and in vitro, have evaluated the content of BPA, Bis- GMA and Bis-DMA in saliva after restoration with dental sealants and composites [10, 24]. The results have varied, probably because of differences in methods used. Several studies revealed leaching of BPA and bis- DMA after a short period of time, but no leaching of bis-GMA [24]. Time of possible salivary detection varied from 1- 3 hours after filling therapy, with the highest exposure immediate after placement, according to the in vivo studies. None of these studies measured salivary content of BPA and BPA derivates between 3 and 24 hours [24].

Little toxicological examination of BPA has been accomplished. Furthermore, examinations carried out have been conducted in experimental studies. In cause of different toxic kinetics between species, it is questionable to transfer the results of these studies direct to humans [24].

BPA was as early as in the 1930s recognized for its estrogenic effects. In vivo and in vitro studies have confirmed this, but few studies have examined the estrogenic effects of BPA derivatives [24]. Because of its character to imitate natural estradiol, and its weak affinity to estrogenic receptors, BPA and bis-DMA might be involved in the etiology of reproduction- and developmental disturbances and malignity [24, 39]. Studies have shown that BPA probably are thousand fold less potent than natural estrogen [1].

According to the US Environmental Protection Agency (EPA) acceptable daily BPA exposure is set to be <50 µg/kg body weight. Studies with BPA in animals has shown adverse effects, such as disturbances in the onset of puberty and changes in prostate and urinary tract. Compared to the exposure to BPA from the daily environment, the amounts leaked from dental materials are considered small. It is commonly known today that the probable leakage of BPA from composite fillings and fissure sealants is far below the amounts needed to cause a harmful effect [4, 24, 39].

Phthalat

Phthalates are a common description of a group of different chemicals, which are different in both chemical and physiological characters. They are used as softeners in the plastic industry, primary in the production of polyvinylchloride, PVC. Phthalates are also found in cosmetic, clothes, toys and medical equipment. In dentistry, phthalates are mainly used as plasticizers in denture soft-lining materials, dentures to a minor extent and in some orthodontic appliances [40, 41].

As the phthalates are not chemically bound to the polymeric matrix, but is situated between the polymers, it has a great potential to leach or migrate out into the surrounding atmosphere [40]. When used in prosthetic or orthodontic appliances, the patients will be exposed to these substances directly through the mucosa and saliva

[39]. Some phthalates are known to have estrogenic effect, and such have the ability to interfere with reproduction and create damage to the fetus. The main concern of phtalates is the potency of causing endocrine disruptions, mainly adverse effects on reproduction and development. No phthalates has been shown to be mutagen or genotoxic [40].

Formaldehyde

Formaldehyde consists of an oxygen atom linked to carbon by a double bond (a carbonyl group) and two hydrogen atoms. Formaldehyde is a byproduct from polymerization [23]. Formaldehyde is shown to leach from some orthodontic base plate materials [35, 42]. It is evident that formaldehyde leaches from several composite resins in a long period after polymerization. In fillings with an oxygen-inhibited surface layer, the leakage seems to be more prominent since the inhibited methacrylic molecule will react with water from the saliva creating formaldehyde [9]. This substance is known to cause allergies as well as toxic/genotoxic reactions [23].

Tinuvin- P

Tinuvin P is an UV light absorber, and is added as a stabilizer to resin-based materials to prevent light disbanding processes such as discoloration. Leakage of Tinuvin- P from resin-based materials has been confirmed. It is also common in cosmetic products and has been shown to provoke contact allergy [8].

Material Safety Data Sheet

Material Safety Data Sheet (MSDS) are required for all chemical substances. It should contain information on hazardous substances as well as the composition of ingredients, handling and toxicological information. It is not obligatory to mention substances that is present in smaller concentrations (<1%). A study [3] shows that health risks are not sufficiently described in the MSDS for several dental materials. In that study only 26% of 219 substances had risk- and safety phrases. Other studies also confirms that the MSDS are far from complete [43]. This implies that a material can contain harmful substances even if it is not mentioned in the data sheet. This is also important to consider when choosing an appropriate material for an allergic patient.

Actions to prevent adverse reactions

Several studies [2, 8-10, 24, 44] have confirmed degradation and leakage of monomers such as TEGDMA, UEDMA, HEMA, Bis-GMA, and Bis-DMA from resin-based materials. Unpolymerized monomers are released into the oral cavity. As discussed previously in this paper, this may result in unwanted, adverse reactions in the patients [17, 21, 24, 25].

Correct handling of resin-based materials is crucial to achieve desirable result, such as minimizing post treatment complaints and unwanted reactions, as well as a long lasting restoration. Some adverse reactions may be prevented by material handling methods directed to reduce leakage and degradation and minimize direct exposure of unpolymerized material.

In treatment of patients with confirmed allergy to a specific substance, materials containing that substance should be avoided. A clinical challenge is that acrylic monomers do cross-react; this means that sensitizing induced by one monomer may extent to other monomers as well. The patients become multi- allergic and cannot be exposed to any monomers in resin based materials [22].

In treatment of patients with known hyper sensibility to dental materials, precautions should be taken. During therapy where handling of resin-based materials is required, the aim of the treatment should be to minimize unnecessary direct exposure of highly reactive, unpolymerized materials, as well as lower the possibility of monomer leakage during the first days after filling therapy. Use of rubber-dam will act as a barrier, and prevent monomers from bonding and composite to come in contact with the oral mucosa.

Some precautions to decrease direct exposure of unreacted monomers should be taken in every patient. When filling therapy is indicated, the dentist should avoid direct exposure of unpolymerized materials to the oral mucosa of the patient. Rubber-dam may act as a physical barrier to prevent contact. Resin-based bonding materials are low viscous, therefore attention should be directed to amount of bonding material applied, and use

of suction to reduce vapor. When use of a matrix system is required, this should be fitted tight around the tooth, to prevent cervical leakage and decrease the risk of oxygen inhibition.

Correct light curing results in decreased amount of unpolymerized reactive monomers in the composite filling or luting cements. The composite should be placed in several thin layers, to ensure polymerization in the deepest parts. Sufficient light curing also depends on light intensity, distance between the monomers and the light source, curing time and material [5]. The light intensity of the curing lamp should be at minimum 400 mW/cm² [5]. After curing of the last layer of composite, polishing is important to remove the oxygen- inhibited layer at the surface [24]. During therapy with some glassionomer composites, application of coating has been recommended from a Norwegian study to decrease leakage [44].

Prevent contact between monomers and the oral mucosa during bonding and filling	Rubber-dam	Physical barrier
	Adequate suction	Remove excess bonding material
	Tight matrix system	Physical barrier
Reducing the amount of free monomers in the filling	Light curing	Distance Intensity Curing time
	Polishing	Remove oxygen inhibited layer

Table 3 Summary of actions to reduce exposure to reactive monomers in patients

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