

Adverse reactions to denture resin materials

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Abstract. – Irrespective of the new generation of dental materials, acrylates still have a wide indication field. Although they are classified as biomaterials, acrylates can have both local and systemic side effects. The individual components of the acrylic materials may leave the dental restorations and diffuse into saliva. The aim of this study was to point out the potentially toxic components of acrylic dental materials, as well as their possible adverse effects on oral tissues and the organism in general. The paper was based on the assumption that the appropriate selection of the type of acrylic material and the proper method of their preparation reduce their adverse effects to a minimum, which was proven using literature data.

Key Words:

Denture resin, Adverse, Reactions.

Introduction

The long-term use of acrylic materials in dentistry is the proof of their satisfactory biological, physical and mechanical properties. However, in time it has been shown that the acrylic polymers announced in the first half of the twentieth century are not the ideal building material. Although not perfect, they considerably meet the requirements of everyday dental practice due to relatively good biocompatibility, their chemical inertness, fair mechanical properties, dimensional stability, the possibility of coloring and transparency, simple processing, the possibility of repairing as well as their low price^{1,2}.

As construction materials in dental medicine, acrylate polymers have various fields of application. They are used for making bases of full and partial dentures, their relining and repairs as well as preparation for obturator prosthesis and maxillofacial defects, faces prosthesis, splints, removable orthodontic appliances and dental space

holders, artificial teeth, veneers and temporary crowns and bridges^{3,4}. Soft acrylic materials are used in the preparation, conditioning, and treatment of damaged and inflamed tissue. Special types of acrylates are used as a part of the structure of materials for the permanent binding of fixed dentures (resin cement, glass ionomer resin modified cement). As supporting materials acrylates have found the application in making individual trays, certain dental restorations models, bite planes and occlusal templates^{1,2}.

Acrylics, depending on their indication field, may differ by type and method of preparation. The classification of acrylic polymers in dentistry is shown in Table I.

Dental acrylates are most often composed of poly (methyl methacrylate) (PMMA) generated by addition polymerization of methyl methacrylate (MMA), although there are variations which are primarily related to the type of monomer (butyl methacrylate-butyl, ethyl methacrylate-EMA and urethane dimethacrylate (UDMA)) and crosslinking agents (Table II).

The aim of this work was to point out potentially toxic components of acrylic dental materials as well as the possible adverse effects of acrylates on oral tissues and the organism in general, which was proven using available literature data.

The study was based on the assumption that the appropriate selection of the type and method of preparation of acrylate materials can reduce their side effects to a minimum.

Acrylates as Biomaterials

Acrylates are classified as biomaterials due to their morphological and functional role as substituents in the oral cavity⁵. Acrylate biomaterials are used to replace and compensate for the lost or damaged tissues, and perform a particular function in the oral cavity⁶. While being in contact with oral structures, acrylates lead to a number

Table I. Classification of dental base polymers.

Denture base polymers type	Description
1	Heat cured polymers (powder and liquid form)
1 ^a	Heat cured polymers (plastic cake form)
2	Self-cured-auto-polymerized polymers
3	Thermoplastic type resins
4	Light activated type resins
5	Microwave cured type resins

Table II. Composition of acrylic denture base materials.

Component	Constituents
Powder	
Polymer	Poly (methylmethacrylate) (PMMA)
Initiator	Benzoyl peroxide
Pigments	Salts of cadmium or iron or organic dyes
Liquid	
Monomer	Methyl methacrylate (MMA)
Cross-linking agent	Ethylene glycol dimethacrylate (EGDM)
Inhibitor	Hydroquinone
Activator	N,N'-dimethyl-p-toluidine

of complex interactions, which are collectively referred to as biological tissue response⁷. Therefore, biocompatibility is considered to be an essential feature of dental materials; so it is very important for the success of dental therapy and also the patient's health.

Biocompatibility is a material characteristic of being accepted in a specific living environment without adverse or unwanted side effects. The absence of harmful effects of materials implies a harmony with the biological functions of living tissues. Since there is no dental material that is fully biologically inert, we cannot talk about absolute, but a certain degree of biocompatibility. As applied material and host tissue change over time, biocompatibility should be seen as a dynamic process. Any change in tissues (inflammation, thermal, chemical and mechanical damage) reduces the degree of biocompatibility of the applied material⁸.

Biocompatibility of dental materials is most commonly observed through their potential local or systemic toxicity. The material is considered biocompatible if it does not cause irritation or allergy, nor does it have any mutagenic or car-

cinogenic properties. A negative reaction to its presence may be a result of other harmful factors, such as the accumulation of the infectious substrate on the material⁹. Therefore, the material toxicity should be seen as just one aspect of their biocompatibility.

To safely use a material in the professional field, it must have a standard label mark regulating its quality-standards of the European Union's target, International Organization for Standardization (ISO). Dental materials and instruments are certified by the ISO-TR 7405.

Potentially Toxic Substances in Acrylates

Acrylics are not completely safe materials because their polymerization chain reaction is never absolute. Potential causes of their harmfulness are unpolymerized components and by-products of the polymerization reaction¹⁰. The individual components of acrylic materials have the ability of leaching dentures and diffusing into saliva, thus influencing oral tissues and the organism in general^{5,11-13}. The components which are released from the acrylic resin material by electrolysis or hydrolysis processes are absorbed into the oral mucosa, gastrointestinal tract, skin, and respiratory system. The absorption mechanism depends on the nature and chemical properties of the released elements. Adverse effects of acrylate components on tissues are less often caused by their toxicity but, more frequently, by their immunological functioning^{15,16}.

Residual monomers represent a certain amount of monomer which was not bound during the polymerization process. Incomplete polymerization of acrylates reduces the physical-mechanical, and biological qualities of dental restorations. It has been proven that the unbound MMA is an allergen and tissue irritant¹⁸⁻²². A certain amount of residual MMA was found in dentures that had been worn for seventeen²³ to even thirty years²⁴. By hydrolyzing MMA, methacrylic acid is formed with its proven cytotoxicity^{25,26}. Gawkröd-

ger et al²⁷ stated EGDM as the strongest allergen in the acrylic material. The potentially toxic effect is associated with the BuMA, the EMA and UDMA, and also with the co-monomer crosslinker (ethylene glycol dimethacrylate – EGDM)^{28,29}. To overcome problems with allergies related to conventional acrylates, new hypoallergenic acrylic materials were introduced, where MMA was replaced with diurethane dimethacrylate, polyurethane, polyethylene terephthalate, and polybutylene terephthalate, but they did not prove to be definitely safe²⁵. Also, the hypoallergenic features of light-polymerized acrylates were disproven by the sensitivity of individual patients to UDMA and bisphenol-glycidyl methacrylate (Bis-GMA)³⁰.

Over time, the residual monomer leaves the acrylic compensation and diffuses into saliva dissolving in it. The amount of free monomer is proportional to its overall residue in the matrix of resin, although a certain amount of the unbound monomer remains trapped in the polymer structure, never diffusing to the external environment³¹.

It is difficult to predict the individual tolerance level of residual monomers for each person. Polymerization at high temperatures, close to the T_g values of PMMA (glass transition temperature = 115°C), results in a more compact structure of the material, and consequently a smaller amount of residual monomer^{31,32}. Given that the polymerization of the cold polymerized material is carried out at room temperature and without pressure, and its structure is more porous, the quantity of residual monomer is higher in comparison to the heat-polymerized acrylate^{33,34}. In this regard, microwave and light curing provide satisfactory results, but their use in making dentures is complicated and very expensive. Therefore, their use, especially in the US market, comes down to denture repairs and rebase, by which low-quality cold polymerized acrylates are phased out of use.

To remain within the tolerance limits, the amount of residual MMA should be in the range of 1 to 3%³⁵. According to the standard (ISO 1567:1999)³⁶ the maximum allowed amount of residual MMA for hot polymerized acrylate is 2.2%, and for the cold polymerized is 4.5%.

In order to reduce the amount of residual monomer in the acrylate polymerization additional compensation is recommended (hot or microwave post-polymerization), as well as immersion into aqueous solutions in a water bath for 1-7 days before applying the prosthesis to the patient. Subsequently binding of monomer or its release into an

aqueous solution reduces the amount of residual monomer for up to 25%³⁷⁻³⁹.

Formaldehyde in acrylic polymer appears as a side effect of the oxidation of the methacrylic group or the degradation of the oxido-methacrylic copolymer. The amount of the generated formaldehyde depends on the MMA concentration and polymerization completeness. The reduction can be achieved by removing from the surface, less polymerized acrylic material. According to Oysaed et al⁴⁰, the largest amount of formaldehyde is left in the structure of cold polymerized acrylates.

The free residual monomer and formaldehyde molecules can be associated with proteins in the patient's mouth forming large molecules responsible for oral tissue allergic reactions⁴¹. They are most commonly manifested as type I hypersensitivity reactions (anaphylaxis) or type IV (contact stomatitis, dermatitis and, upon repeated contact with the allergen).

Benzoyl peroxide is added to the acrylate material in powder, in very low concentrations from 0.2 to 1.28%⁴². Research has shown that the total amount of the activator is not consumed in the polymerization procedure, so it is released from the polymerized acrylate to the oral cavity⁴³.

Its cytotoxicity was also demonstrated *in vitro*, in multiple cell lines⁴⁴. The toxicity of benzoyl peroxide is associated with the free radicals formation and also with the intracellular antioxidants wear, and the peroxidation of cell lipids⁴²⁻⁴⁴. Some studies^{47,48} have suggested the carcinogenic effect of benzoyl peroxide. If there is a proven allergy to benzoyl peroxide, Boeckler et al⁴⁹ recommend heat polymerization period for a few hours.

Koda et al⁵⁰ have described the release of *methacrylic and benzoic acid* from acrylates into artificial saliva. The mentioned acids originate from the MMA and benzoyl peroxide. Mikai et al⁵¹ have found a certain amount of *methyl benzoate* to be a product of the reaction of the monomer and the activator, in acrylic dentures that had been worn for more than fifteen years.

The toxicity of phthalates, which are added to the soft acrylic materials as plasticizers, has also been proven^{52,53}. *In vitro* and *in vivo* testing have shown that acrylates used for conditioning of the oral tissue, release a large amount of phthalate esters⁵⁴.

Dix et al⁵⁵ have pointed to the cytotoxicity of N,N dimethyl-p-toluidine that is used as an activator.

Hydroquinone is used as an acrylic materials stabilizer, a polymerization inhibitor, and an an-

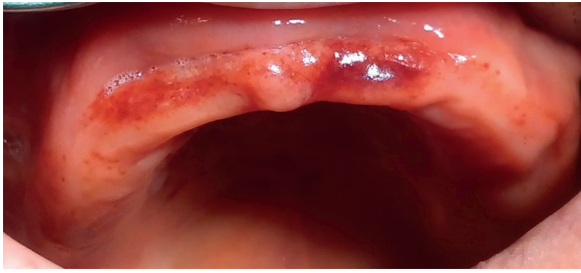


Figure 1. Stomatitis protetica caused by wearing prosthetics upper denture.

tioxidant. Its release from the dental restorations into the oral environment as well as its tissue toxicity has been demonstrated, also under *in vitro* and *in vivo* conditions⁵⁶⁻⁶⁰.

Inorganic compounds, such as cobalt, nickel, and beryllium, can also be the cause of allergic reactions to acrylates. The acid environment in the mouth leads to the erosion of acrylic dentures and the release of ions of cadmium under experimental conditions, whereby the level of metals release increases with temperature rise⁶¹.

The Clinical Aspect of Adverse Reactions to Acrylates

Although the resin materials are considered to be biologically acceptable, there is an evidence of their individual components' harmful effects on the organism, both at local and system levels.

Side effects associated with acrylic materials are, in the majority of cases, of local nature and are manifested as cheilitis and stomatitis, annealing and burning mouth, painful sensations of different intensity and candidiasis (Figure 1)⁶²⁻⁶⁷. The allergic reaction to the presence of acrylates compensation can also occur in the form of extensive allergic reactions such as erythema multiforme⁶⁷. Ergun et al⁶⁸ have proven the potential toxicity of temporary acrylic dental restorations. In clinical practice, contact stomatitis in children caused by wearing removable orthodontic appliances has been described⁶⁹.

The described changes are more common in patients whose mucous membranes of the oral cavity are already infected, inflamed and damaged by various drugs or vomiting⁷⁰. Certain regions of the oral cavity are particularly susceptible to irritation by acrylate compensations⁷¹. Areas with a subgingival epithelium represent places that are less sensitive to the effects of harmful acrylate components⁷².

The largest number of irritations in the mouth is of an acute character, and the symptoms disappear

quickly after removing the cause⁷³. Chronic prosthetic stomatitis is much rare and occurs mainly in elderly patients in the form of fibrous hyperplasia⁷⁴. Chronic acrylate irritation can seldom lead to the development of oral cavity cancer⁷⁵.

Systemic reactions to dental acrylic restorations in patients are rare and they are manifested in the form of respiratory and gastrointestinal dysfunctions as well as generalized dermatological allergic reactions, usually urticaria⁷⁶⁻⁷⁸. Nevertheless, the fact that users of orthodontic appliances and dentures with time ingest different amounts of potentially toxic substances requires constant attention.

Allergic hypersensitivity to acrylic polymers is a result of the exposure to allergens originating from the material and the patients' altered response to the recurring contact with the material^{78,79}. The consequences of the immune response are the released inflammatory mediators leading to different clinical manifestations, the most common being diffuse erythema, hyperplasia of mucous membranes and irradiating pains^{79,80}. According to the research by Marks et al⁸² and Wetter et al⁸³ immunological response to MMA was observed in 1% of the tested population. On the other hand, hypersensitivity to acrylates was discovered in 17% of the dental prostheses users⁸⁴. Local contact reactions of the skin to BuMA, UDMA and a variety of crosslinkers (EGDM, triethylene glycol dimethacrylate, 2-hydroxy ethyl methacrylate, etc.) were described clinically⁸⁵.

Allergic reactions to acrylates are also encountered with the dental staff, especially the dental technicians⁸⁶⁻⁸⁹. The first changes in the hands of dental technicians were described during the forties of the last century, shortly after the presence of the acrylates on the market⁸⁹. The literature data⁹⁰ suggest that, at present, even 20 to 40% of dental technicians have the immune reaction to acrylates. In recent years, the rise in the number of patients has been recorded^{91,92}. The reactions to acrylates can be severe, and can cause work disability or endanger the life of the person who is in constant contact with the material, so in such cases, it is necessary to change the person's workplace^{93,94}.

Allergies to acrylates are in most cases manifested in the form of contact dermatitis or hand eczema^{94,95}. Allergic contact dermatitis is considered to be the most common occupational disease of dental staff (Figure 2). The resulting changes are localized on the distal phalanges and palmar surfaces of the fingertips. Symptoms that occur are dryness, cracking, and peeling of the skin, itching, irritation, and swelling^{86,96-98}. The

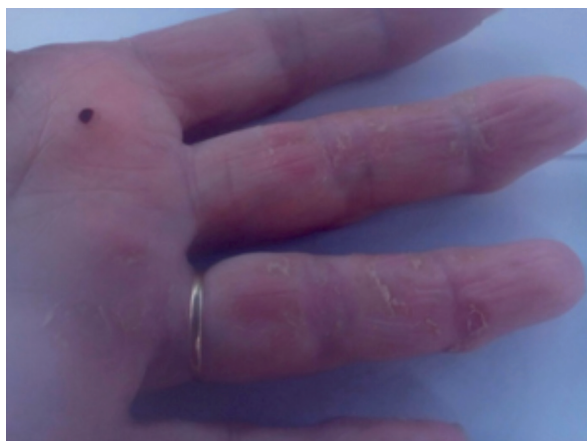


Figure 2. Eczematous changes in the hands of a dental technician.

greater predisposition for hand skin changes can contribute to mechanical friction, work with plaster, constant changes in temperature and the soaking of hands. Nail diseases are rarer⁹⁹. Contact dermatitis sometimes occurs on the face or eyes of the dental staff⁹⁹. The disease weakens at weekends and during holidays.

Occupational exposure to a two-component acrylic polymer system is associated with asthma, drowsiness, headache, nausea, anorexia and gastric motor activity reduction. Apart from that, it can lead to neurological disorders, paresthesia, and neuropathy^{91,100}.

It is very important that dental staff should adopt standard procedures for handling various substances and objects. They should avoid direct contact with the unpolymerized mass (no-touch technique) in processing acrylates. Protective gloves do not always provide adequate protection when processing acrylics. On the other hand, dental technicians deliberately avoid the use of protective latex gloves because the precision of their work is reduced⁵⁶. Hand hygiene is an essential factor in the protection against contact dermatitis. Because of the possibility of inhalation of particles and acrylate monomers, protective masks are required to be worn during the preparation and processing of acrylates, as well as adequate ventilation of the dental laboratories^{88,101}.

Conclusions

Despite the fact that acrylics are not ideal materials and that their integration in the orofacial system cannot be without any consequences, they are widely used and have an enviable list

of possible indications. The abundance of different acrylates on the dental industry market and eighty years of experience enable a much easier selection of materials for a particular clinical situation. A complete polymerization and better biological properties of heat-polymerized acrylates give them an advantage over the cold polymerized materials. Everyday work on improving the properties of dental resin materials contributes to a better quality.

Conflict of interest

The authors declare no conflicts of interest.

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