

CURRENT TRENDS IN PREVENTION OF DENTURE STOMATITIS: DENTURE BASE MATERIALS WITH ANTIMICROBIAL EFFECT

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ABSTRACT

The occurrence of oral infections could be a prerequisite for the development of systematic diseases which predefines their prophylaxis as a priority. Among the most frequent oral cavity diseases in complete denture wearers is denture stomatitis. The elaboration of removable dentures made of materials that have antimicrobial effects is a possible way to prevent this disease. The present review researches the data in dental literature about the various types of modified denture materials, their antimicrobial properties, advantages, and disadvantages. Additionally, we have discussed the issues remaining unclear in view of their clinical application. To this end, e-search was performed in four databases: PubMed, Web of Science, Google Scholar, and Scopus. Within the range of this research, we could conclude that via the inclusion of various modifying agents significant number of denture materials with proven antimicrobial properties have been invented. The established positive effects of suppressing the development of pathogens that cause denture stomatitis is a prerequisite for these materials to be included as a component in contemporary strategies for disease prevention. In order to be successfully integrated into routine dental practice, we need additional clinical research to clarify the antimicrobial effectiveness of different materials in real conditions of the oral cavity and after taking into consideration the impact of the accompanying general and local factors.

Key words: Denture materials, Antimicrobial effect, Denture stomatitis, Denture stomatitis prevention.

Introduction

The health of the oral cavity is an essential factor related to nutrition, general health status, and life quality of the patients treated with complete dentures. The oral microflora includes great versatility of microorganisms that in healthy individuals do not manifest pathogenicity and do not cause diseases. We could find over 700 different bacteria and fungi whereas the prevailing representatives are the ones of Firmicutes, Actinobacteria, Proteobacteria, Fusobacteria, Bacteroidetes Spirochaetes, and Candida species [1-3].

Some prerequisites could provoke the occurrence of pathogenicity of microorganisms that normally inhabit the oral cavity, especially in complete denture wearers. The risk of development of oral mucous diseases in patients who use removable dentures varies from 36.7% to 65% [4, 5]. The oral microbiome of patients with complete dentures contains representatives of fewer microorganism species compared to the ones in patients with available dentition [6]. This supports the proliferation of commensals such as *C. albicans* and the prevalence of Candida species could be increased significantly [7]. The biofilm formed under the denture promotes the retention of microorganisms along their surface thus forming a depot that causes the development and sustain of infection [8]. The most frequent manifestation of this trend is the development of denture stomatitis [9].

The denture stomatitis etiology and its clinical symptoms have been already researched in detail. The development of denture stomatitis could be provoked by various microorganisms such as bacteria of the species *Staphylococcus* sp., *Streptococcus* sp., *Fusobacterium* sp., and *Bacteroides* sp. but the main pathogen is *Candida albicans* - in more than 1/2 of the patients (cases) [10]. There is agreement of opinion that denture stomatitis results from violated balance between representatives of oral microflora [9, 11].

The organism has natural defense mechanisms against the development of denture stomatitis that include antimicrobial factors in the saliva, innate adaptive cellular immune mechanisms, and mechanical barrier against the penetration of microorganisms, provided by the healthy epithelial surface of mucous membrane. However, the natural immune response of the organism is not always sufficient for the prevention of denture stomatitis [12].

A complex of local factors has a direct impact on the development of denture stomatitis. Some of them are related to oral cavity conditions such as saliva quantity Ph level and oral mucosa integrity [9]. Other are denture-related factors such as surface characteristics of denture base material, [13] period of using of complete dentures (age of the dentures) [14, 15], and hygiene maintenance of the dentures [16, 17].

The surface characteristics of the denture material could be considered an important local factor that impacts the occurrence of denture stomatitis. Denture materials with high surface roughness and hydrophobicity can be prerequisites for easy adhesion of microorganisms [18]. In order to reduce the opportunity for fixation and colonization of microorganisms, the denture base material should be hydrophilic, smooth, and with minimum porosity [13].

The prevailing part of complete dentures is made of poly methyl-methacrylate (PMMA) with heat-activated polymerization. The natural porosity of this material could become the reason for the facilitated fixation of microorganisms and the development of denture stomatitis, especially in the presence of other predisposing conditions, for example, poor hygiene. Nevertheless, PMMA has relatively high final hardness and retains fewer microorganisms in comparison, for example with the so-called elastic denture base materials [19]. Some of the elastic materials have significant porosity. That results in the formation of a greater biofilm quantity that contains versatile microflora [20]. One of the contemporary strategies for preventing denture stomatitis is the creation of modified denture base materials with antimicrobial characteristics via which to overcome these negative effects.

The objective of this review was to research the data available in dental literature about modified denture base materials with antimicrobial properties, as well as outline the issues remaining unclear in relation to their application for the prevention of denture stomatitis.

Materials and Methods

E-search was performed in four databases: PubMed, Web of Science, Google Scholar, and Scopus. The keywords used were “denture base materials,” “modified denture materials,” “denture stomatitis,” “biofilm formation,” “antimicrobial effect,” and “antifungal agents”.

It was performed screening of the extracted articles based on the inclusion and exclusion criteria as follows:

Inclusion criteria

1. In vivo and in vitro studies
2. Research with a focus on modified denture-base materials
3. English language of publication
4. Articles published between 2018 and 2023

Exclusion criteria

1. Research with a focus on other types of modified dental materials
2. Publications other than the English language
3. Articles published out of the period 2018-2023

We tried to find the answers to the following purposeful questions:

- What modified denture base materials with antimicrobial effects have been researched in the last 5 years?
- What are the advantages and disadvantages of the modified denture base materials?
- What are the issues that remain unclear about their application for the prevention of denture stomatitis?

Literature review

The features such as hydrophobicity, final hardness, roughness, and elasticity are among the factors that impact the adhesion of microorganisms [13].

The modification of materials aims at the alteration of their superficial characteristics via the transfer from hydrophobicity to hydrophilicity and the improvement of their mechanical properties. The main ways to improve materials' qualities are adding various modifying agents to the denture acrylic resin or the creation of a coating for the denture base with antibacterial properties [21-24].

Denture base materials incorporated with nanoparticles from various ingredients

In recent years, numerous researches on the effect of adding nanoparticles from various ingredients to denture acrylic resin that demonstrated significant improvement in their surface qualities [21-42]. These kinds of materials show much lower adhesion levels of the main causer – *C. albicans*. It is believed that this effect is due to the improved smoothness of their surface, which does not allow the thick fixation of microorganisms and facilitates their elimination with hygiene procedures. These properties of the modified materials predefine the opportunity to be used in preventing denture stomatitis.

One of the ways to improve the PMMA properties is by adding nanoparticles of Titanium Dioxide (TiO₂) [21]. The changes in mechanical properties are about increased micro-hardness, elasticity module, and stability of the chemical compounds. The improved mechanical properties ensure the opportunity for easy and very good polishing. The denture base materials with added TiO₂ demonstrate good antibacterial activity against Gram-negative and Gram-positive bacteria, for example, *E. faecalis*, *P. aeruginosa*, and fungi, including *Candida albicans* [21].

Another way to modulate the properties of denture resins is to use fillers that contain silver nanoparticles. The silver nanoparticles have broad-spectrum antibacterial activity [43]. It is proven that even in low concentrations they suppress the growth of *Streptococcus mutans*, *Staphylococcus aureus*, *Candida sp.*, and other microorganisms [22]. Takamiya *et al.* [25] found out that silver nanoparticles addition at 0.05 and 0.5% into acrylic resin monomer exhibit antimicrobial effects against *C. albicans* biofilm and may be considered biocompatible. The antibacterial effect of silver nanoparticles is due to their adhesion to the sulfhydryl groups of proteins within the membrane of bacterial cells. Thus, they violate the integrity

of the cellular membrane then silver nanoparticles damage the intracellular DNA [26, 27].

Various ways to enrich PMMA with silver nanoparticles have been elaborated. Bacali *et al.* [28] refer to PMMA graphene silver nanoparticles (G-AgNp) composite, synthesized via radio-frequency catalytic chemical vapor deposition (RF-CCVD) method.

Sun *et al.* [29] synthesize a solution of silver nanoparticles that they mix with acrylic acid and methyl methacrylate monomer to create a new denture material type (NS/PMMA).

De Matteis *et al.* [22] established that in modifying PMMA with citrate-capped silver nanoparticles in the concentration of 3.5 wt%, the surface of the biofilm that contains *Candida* decreases from 90% to 6%.

Pai *et al.* [30] evaluate the changes in flexural strength of PMMA resins modified by the addition of silver nanoparticles and titanium dioxide nanoparticles, separately, and by the combination of both. Each reinforced group is divided based on concentrations - 0.5%, 1%, 2%, and 3%. The mean flexural strengths showed a gradual decrease and visible color changes on increasing the concentrations of nanoparticles.

Irrespective of the way of incorporating silver nanoparticles in PAMMA, all the research proves that this type of material has a lack of toxicity and a significant antibacterial effect [22, 29, 31]. However, disadvantages can be considered the reduction of flexural strength of denture base resins and color changes [30, 31].

The most recent research examines the effect of including a two-component nanocomposite that contains Boron Nitride and Silver Nanocomposite inside the denture base material. It was found significant improvement in the mechanical properties – compressive strength increased by 53.5%, and flexural strength – by 56.7% compared to material without additives. The modified material with 1.4 wt.% Boron Nitride/Silver Nanocomposite has an antibacterial activity of 92.1% higher compared to non-modified one [32].

Another kind of nanoparticle most commonly used for modification of PMMA is zinc oxide (ZnONP), ranging in size from 10 to 100 nm [33]. The inclusion of Zn-oxide nanoparticles in PMMA increases its hydrophilic nature thus reducing the potential of microbial adhesion [34].

It also studied the modification of PMMA via the inclusion of Nano graphene oxide (nGO) in the polymer powder. It was established that increased flexural strength and surface hardness as well as the significant long-term effect of preventing microorganism's adhesion to the denture surface [35].

We have analyzed the effect of the incorporation of nanoparticles of Zirconium Oxide in the denture base material and established a significant and continuous antifungal effect. This modification improves the tensile strength of the material but deteriorates the surface roughness and its transparency [36]. Gad *et al.* [37] examine the properties of PMMA denture base material reinforced with a mixture of Zirconium oxide nanoparticles and glass fibers. This material displays very good biocompatibility and high aesthetics as the applied modification does not change the color of PMMA.

A single study assesses the influence of artificial aging on the antifungal activity of zirconium dioxide nanoparticles (ZrO₂NPs) incorporated into denture base material [38]. Authors report that the addition of ZrO₂NPs to denture base material provides a long-term antifungal effect as the most appropriate concentration is 1% [38]. However, other research does not establish the effect of reduction of *C. albicans* that is good enough when using PMMA modified with Zirconium Oxide- nanoparticles [23].

A topic of great interest and detailed research in recent years was the opportunity for modifying the properties of denture resins, with the addition of nanodiamonds. Compared to some metal or metal oxide nanoparticles used for fillers, nanocarbons are chemically more stable, bio-compatible, and do not manifest cytotoxicity [39]. Nanodiamonds have proven antibacterial activity. It is supposed that this is related to the presence of oxygen-containing groups along their surface that interact with components of the bacterial cells. It was also established to improve of mechanical properties of PMMA which is about decreasing surface roughness and improving polishing capacity [39]. Fouda *et al.* [40] found out that the addition of small quantities of nanodiamonds between 0.5 and 1% to PMMA significantly decreases the adhesion of *C. albicans*.

Another researched modification is PMMA denture base resin incorporated with SiO₂ nanoparticles. The addition of a low concentration of nano-SiO₂ reduced *C. albicans* adhesion to the denture surface and has positive effects on hardness. The main disadvantages are that surface roughness and translucency adversely decreased at high concentrations [41]. Additionally, it was prepared special preparations that contain micro nanoparticles, could be used for the creation of silicon coating of dentures' surface. They provide a layer that possesses a super hydrophilic nature and self-cleansing effect [24].

Correa *et al.* [42] propose heat-cured Polymethyl methacrylate acrylic with the addition of copper nanoparticles (nCu) for producing dentures with antimicrobial properties. They report that dentures made of this material retained their mechanical and aesthetic properties as well as inhibiting the growth of *Candida* species on both the denture surface and patient palate.

The surface properties of denture base material are also depending on the elaboration technology. The new trends include the modification of denture base materials designed for the elaboration of complete dentures through digital technologies. The PMMA-based polymers for CAD/CAM technology were polymerized in advance and have increased final hardness and lowered porosity, thus supporting the prevention of microorganisms' retention, and the occurrence of denture stomatitis, correspondingly [44]. Composites for the elaboration of denture base via additive 3-D printing technology have been enriched with the addition of nanoparticles from Nano-silver loaded zirconium phosphate (6SNP3). In these materials, were established improvements of mechanical properties and significant antibacterial activity, especially towards *Escherichia coli* sp. [45].

Khattar *et al.* [46] research the antibiofilm activity and surface roughness of a 3D-printed denture base resin modified with different concentrations of zirconium dioxide nanoparticles - 0.5 wt%, 1 wt%, 3 wt%, and 5 wt%). The addition of ZrO₂ nanoparticles in low concentrations (0.5%) significantly reduced *C. albicans* adhesion and proliferation whereas did not affect the surface roughness of the 3D-printed resins.

Aati *et al.* [47] developed a novel 3D printed denture base resin material modified with mesoporous silica nanocarrier loaded with silver (Ag/MSN) in order to enhance mechanical and antimicrobial properties. Various proportions of Ag/MSN (0.0-2.0 wt%) were incorporated in Acrylate resin-based material. The addition of Ag/MSN in a concentration lower than 1% improved significantly surface hardness but the surface roughness significantly increased when the concentration of Ag/MSN was ≥ 1.0 wt%. The modified 3D-printed resin-based material showed enhanced antimicrobial properties against *C. albicans*, as the inhibition proficiency is correlated with the proportion of the filler.

We could summarize that adding nanoparticles improves in general the mechanical properties of PMMA and its antibacterial properties. Nevertheless, the shortcoming of these methods is that sometimes higher nanoparticle concentrations cause material color changes. To overcome this issue is suggested elaboration of two-layered dentures, whereas only the internal layer could be modified. This way we would be using the effect against the adhesion of microorganisms while keeping the denture's aesthetical appearance [40].

Denture base materials modified with different inorganic and natural ingredients

The search for optimal methods to modify denture base materials, to ensure reliable prevention of denture stomatitis is still a current topic of scientific research. In recent years, in addition to nanoparticles, we have studied a wide spectrum of other ingredients and materials that individually or in combination could be used to this end. For example, we have analyzed the opportunity to get material with high

antimicrobial properties by adding inorganic ingredients. One researched variant for modification of denture base material is the inclusion of N-dimethylaminoethyl methacrylate (DMAEMA) [48]. This type of denture resin manifests an antimicrobial effect on *S. aureus* (Gram-positive), *E. coli* (Gram-negative), and *C. albicans*. However, the authors [48] report that modification with this agent, especially if it is done in higher concentrations could result in the deterioration of color and mechanical features, while increasing the surface roughness and decrease of its flexural strength.

Investigation of the effect of zinc-dimethacrylate (ZDMA) modification of PMMA on its mechanical and antibacterial properties shows that ZDMA mass fractions up to 5 wt% enhanced the mechanical properties and have antibacterial effect versus *Streptococcus mutans* [49].

Gad *et al.* [50] evaluate the effect of the addition of different concentrations of Thymoquinone (TQ) on the mechanical properties of PMMA denture base material. They found that the addition of Thymoquinone significantly decreased flexural strength and elastic modulus at high concentrations of over 1%, but did not affect the surface properties of PMMA denture base material at low concentrations (0.5%-1% TQ) and could be incorporated into it as an antifungal agent.

Da Silva Barboza *et al.* [51] modify conventional polymethylmethacrylate through the addition of zirconium methacrylate, tin methacrylate, and di-n-butylidimethacrylate-tin to the liquid of a PMMA resin. It was established that the incorporation of di-n-butylidimethacrylate-tin significantly increased the hardness of the modified material. It displayed lower roughness and higher antifungal activity against *C. albicans* than the conventional material. Khader *et al.* [52] also confirm that the addition of a modified monomer to PMMA promoted the best antimicrobial activity and cytocompatibility, while the mechanical properties and color stability remained unchanged.

Another examined method for improving the antimicrobial properties of denture resins is adding various percentages of Phytoncide (1.25%, 2.5%, 3.75%, and 5%) to the monomer liquid. It registered a significant reduction of *Candida albicans* quantity and biofilm thickness underneath the dentures [53].

We have analyzed the effect of adding food preservatives to PMMA – sodium metabisulfite (0.5 % w/w) and potassium sorbate (1.0% w/w). It was found that they improve the antimicrobial properties of the material, without manifesting cytotoxicity [54].

It also examined the opportunity for processing denture resins with probiotics, to analyse their antibacterial effect. *Lactobacillus rhamnosus* sp. and *Lactobacillus casei* sp.

manifest antifungal activity against representatives of Blastocoonidia and *C. albicans* sp. and suppress the development of colonies onto the denture base [55].

Another approach is adding various natural ingredients to the denture resins with antifungal effects such as Chitosan, Neem Powder, and Henna [56, 57]. Clinical research confirms the antimicrobial effect of cytosine against *Candida albicans* [58, 59].

Hamid *et al.* [60] modified heat-polymerized polymethyl methacrylate denture base material through the addition of *Azadirachta indica* (AI) powder in different concentrations (0.5, 1, 1.5, 2, and 2.5 wt%). The surface roughness of the material did not significantly change, whereas hardness decreased at 2.5% AI concentration. Flexural strength and translucency were significantly decreased at all levels of concentration.

Venante *et al.* [61] investigate the opportunity for inhibition of the growth of *C. albicans* biofilm by coating the conventional heat polymerized and pre-polymerized poly methyl methacrylate with Fibrin Biopolymer incorporated with antimicrobial agents – digluconate chlorhexidine or *Punica granatum* alcoholic extract. According to the authors, this is a reliable method for controlling the formation of denture biofilm.

Another proposed modification of the surface of denture base material is coating with cinnamon-laden nanofibers. It was established that the deposition of 20 wt.% cinnamon-laden nanofibers onto PMMA surfaces led to a significant reduction of the adhesion and proliferation of *C. albicans*. However, concentrations over 20 wt.% can have a toxic effect on epithelial cells, and Cinnamon-laden nanofibers at 40 wt.% lead to increased cell death [62].

It could be concluded that the effect of adding natural ingredients depends on their quantity, whereas the higher concentrations could unfavorably impact some material properties, for example, increasing the surface roughness, cytotoxicity, or changing its color [57, 63, 64].

The modification of PMMA via the incorporation of some antimicrobial medicines is proposed rather as a method of treatment for denture stomatitis than for its prevention. Modifying a denture reline material with antimicrobials such as Nystatin or Chlorhexidine diacetate at minimum inhibitory concentrations provided a therapeutic option for denture stomatitis [65, 66]. The best effect was found when using chlorhexidine [67, 68]. This strategy is especially useful in the presence of some accompanying factors, for example in the case of immune-deficient conditions brought by general diseases.

The most recent research has also surveyed the modification of denture base material with the addition of protein repellent agent (2-methacryloyloxyethyl phosphorylcholine-

MPC), which is added individually or in combination with dimethylaminohexadecyl methacrylate [69, 70]. The addition of these biomaterials has a significant antifungal effect without changing the surface roughness of the material yet it decreases flexural strength.

Results and Discussion

One of the most frequent diseases of the oral cavity in elderly people who use removable dentures is denture stomatitis. Bearing in mind the global trends of patients with complete denture growth and the relatively high frequency of denture stomatitis, the establishment of an effective approach towards the prevention of the disease is a priority of great social significance [4].

The analysis of dental literature demonstrates that there is great versatility of innovative modified denture base materials with antimicrobial properties. When it comes to the prevention of denture stomatitis, the doctor of dental medicine should make an informed decision concerning the denture base materials which depends on knowing its mechanical characteristics and clinical behavior in detail.

Research of significant amounts is directed towards the improvement of the mechanical and antimicrobial properties of denture base material with the assistance of various modifying agents [24-42, 44, 45]. However, there is still no uniform opinion on the materials with the highest effectiveness in preventing denture stomatitis.

The most widely researched are the materials that were modified via the addition of various ingredients in the pattern of nanoparticles [25-34, 36, 38-42]. The conclusions about the antimicrobial effect of these materials are mainly based on the assessment of their impact on the main denture stomatitis causer – *Candida albicans*. The number of researches that analyze the effectiveness of modified denture base materials on bacterial causes or a broader range of pathogens is limited [21, 48, 49].

Based on the data available at present, we cannot explicitly make an answer to the question: Which modified materials would be most effective for preventing oral infections? It seems that the most promising potential is the materials modified via the incorporation of silver nanoparticles bearing in mind its direct impact on cells of the main denture stomatitis causer – *C. Albicans* [22, 26, 27]. Also, in most of the research was established that this kind of modification improves the mechanical properties of the material. Nevertheless, to prove this hypothesis, we need additional comparative research on the antimicrobial effectiveness of materials modified with other agents.

The main advantages inherent to modifications are the following: improvement of superficial qualities of materials – an increase of final hardness, a decrease of porosity which results in the reduction of microorganisms' adhesion onto

denture surface [58]. It was observed easier and more effective materials' polishing, facilitates the maintenance of higher hygienic denture status. However, the reported results about the mechanical properties of materials are not unambiguous [24, 39, 40]. Numerous researches established that some modifying agents could deteriorate certain mechanical properties. For example, the decrease in flexural strength could be the reason behind the unsatisfactory mechanical dentures' resistance against the masticatory forces. This can result in more frequent fractures of the dentures [30, 31].

Another disadvantage is the established influence on denture material's color by modifying agents such as silver nanoparticles, SiO₂ nanoparticles, etc. [30, 41]. The deterioration of color features of the denture base could hinder the achievement of a satisfactory aesthetical effect via denture treatment. Numerous researchers comment on the correlation of modifying agents' concentration on one hand with the effectiveness of antimicrobial effect and the other hand with the negative changes in some mechanical and optical properties of materials [30, 41, 60]. The increase of modifying agents' concentration ensures better protection against the development of denture stomatitis, yet simultaneously deteriorates some materials' qualities whereas the greatest impact is on the materials' color. In some research, damage to the epithelial cells in the case of high levels of natural ingredients used as modifying agents [62]. Because of these reasons, the authors suggest the application of modifying agents in minimum concentrations. However, there comes the question of whether the manifested antimicrobial effect of the materials created this way is sufficient for sustainable prevention of denture stomatitis. We need to undertake additional research to establish the optimal balance between the concentration of modifying agents, antimicrobial effectiveness, and biocompatibility of these materials. Additionally, it was not clarified whether the modified materials preserve their antibacterial effect throughout time. A single study assesses the influence of artificial aging on the antifungal activity of modified denture base material [38]. Also, there is no sufficient research work on the impact of various cleaning agents and the application of disinfection means of dentures on the antimicrobial properties of the modifying materials.

Most research was performed in laboratory circumstances that do not provide us with information about materials' behavior in real conditions inside the patient's mouth. The number of clinical trials is quite insufficient. It was not established whether the antimicrobial properties of materials are being influenced by factors such as variations of saliva Ph, and materials' contact with various medications, foods, and drinks consumed by the patient. Additionally, we have not clarified whether the established antimicrobial properties of modified materials would be sufficiently effective to prevent the occurrence of denture stomatitis in patients of complicated health status, for example suffering from

diabetes or immunodeficient conditions that have proneness towards the development of oral infections.

Conclusion

We have invented various modified denture base materials that manifest antimicrobial properties being the prerequisite to be included as an element of modern strategies for the prevention of denture stomatitis. To be successfully integrated into the routine dental practice, we need to clarify numerous issues about the behavior of modified materials in their clinical application. We have not clarified the sustainability of antimicrobial effect throughout time during the interaction with numerous factors related to the conditions inside the oral cavity, hygiene maintenance of the complete dentures, health status of the patient, and use of medications. In this light, we need additional clinical research, including comparative ones to clarify the antimicrobial effectiveness of different materials in real conditions and after taking into consideration the impact of the accompanying general and local factors.

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