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ABSTRACT

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ANTIMICROBIAL POTENTIAL OF DENTURE BASE MATERIALS MODIFIED WITH METAL-BASED NANOPARTICLES

Introduction. Removable dentures remain a popular type of dental prosthetics and provide significant improvements in oral care and quality of life for edentulous patients. Acrylic resins, especially polymethyl methacrylate, are known materials for the removable dentures, but do not exclude complications of microbial origin in users, which requires their improvement. The aim of the work is to review the current scientific literature on the use of metal/metal oxide nanoparticles (NPs) to impart the antimicrobial properties to acrylic denture base materials

Methods. The search for literature was carried out in the PubMed/Medline database. After applying the inclusion and exclusion criteria, 76 documents were selected for final consideration.

Results. It was shown that the oral microbiome has certain features in persons with dentures. The denture surfaces are easily colonized by bacteria and fungi, which form a biofilm and become potential pathogens. To prevent this, prosthetic materials are modified with metal/metal oxide NPs. The NP ability to inhibit microorganisms depends on the surface charge, size, shape and coating of NPs, their concentration, nature of the medium, the phase of microorganism development, features of the microbial cell wall, and biofilm formation. Silver NPs are widely used for modification of denture materials. They have a wide range of antibacterial action and antifungal properties, anti-adhesive and antibiofilm activity. The development of surfaces resistant to microbial colonization can also be carried out by incorporating NPs of zinc oxide, titanium dioxide, zirconium dioxide, and copper oxide NPs into the acrylic resin.

Conclusions. Therefore, metal/metal oxide NPs can improve the antimicrobial properties of denture base materials, however, clinical

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“translation” of nanoengineered dentures requires a standardized technology for introducing NPs into/on dentures, achieving local long-term NPs release, and ensuring safety for humans.

Keywords: nanoparticle, metal, metal oxide, antibacterial effect, antifungal effect, denture, acrylic resin, polymethylmethacrylate.

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АНТИМІКРОБНИЙ ПОТЕНЦІАЛ МАТЕРІАЛІВ ДЛЯ БАЗИСУ ЗУБНИХ ПРОТЕЗІВ, МОДИФІКОВАНИХ НАНОЧАСТИНКАМИ НА ОСНОВІ МЕТАЛІВ

Вступ. Знімні протези залишаються популярним видом стоматологічного протезування та забезпечують значне покращення догляду за ротовою порожниною та якості життя пацієнтів з відсутністю зубів. Акрилові смоли, особливо поліметилметакрилат, є відомими матеріалами для знімних зубних протезів, але не виключають ускладнень мікробного походження у користувачів, що вимагає їх удосконалення. Метою роботи є огляд сучасної наукової літератури щодо використання метал/металоксидних наночастинок (НЧ) для надання антимікробних властивостей акриловим матеріалам для базису зубних протезів.

Методи. Пошук літератури проводився в базі даних PubMed/Medline. Після застосування критеріїв включення та виключення для остаточного розгляду було відібрано 76 документів.

Результати. Було показано, що мікробіом ротової порожнини має певні особливості у людей із зубними протезами. Поверхні зубних протезів легко колонізуються бактеріями та грибами, які утворюють біоплівку та стають потенційними патогенами. Щоб запобігти цьому, протезні матеріали модифікують НЧ металів та оксидів металів. Здатність НЧ пригнічувати мікроорганізми залежить від поверхневого заряду, розміру, форми та покриття НЧ, їх концентрації, природи середовища, фази розвитку мікроорганізмів, особливостей клітинної стінки мікробів та формування біоплівки. НЧ срібла широко використовуються для модифікації матеріалів зубних протезів. Вони мають широкий спектр антибактеріальної та протигрибкової дії, антиадгезивну та антибіоплівкову активність. Розробка поверхонь, стійких до мікробної колонізації, також може бути здійснена шляхом включення в акрилову пластмасу НЧ оксиду цинку, діоксиду титану, діоксиду цирконію та наночастинок оксиду міді.

Висновки. Отже, метал/металоксидні НЧ можуть покращити антимікробні властивості базисних матеріалів зубних протезів, проте клінічна «трансляція» наноінженерних зубних протезів вимагає стандартизованої технології введення НЧ у зубні протези, досягнення локального довготривалого вивільнення НЧ та забезпечення безпеки для людини.

Ключові слова: наночастинки, метал, оксид металу, антибактеріальний ефект, протигрибковий ефект, зубний протез, акрилова смола, поліметилметакрилат.

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ABBREVIATIONS

Ag – Argentum, silver
CTAB – cetyltrimethylammonium bromide
Cu – Cuprum, copper
CuO – copper oxide
NP – nanoparticle
PMMA – polymethylmethacrylate
Ti – Titanium, titania
TiO_2 – Titanium dioxide
Zn – Zinc
ZnO – Zinc oxide
Zr – Zirconium, zirconia
ZrO_2 – Zirconium dioxide

INTRODUCTION

Our time is characterized by the intensive development of nanotechnology and the wide spread of nanomaterials. They are defined as materials that have at least one dimension in the range from 1 to 100 nm and that acquire unique properties useful in materials science, biology and medicine [1]. The use of nanomaterials and nanotechnologies for the diagnosis, treatment and prevention of dental diseases is the focus of nanodentistry, which is implemented in orthodontics, preventive dentistry, prosthetics, restorative dentistry, periodontology, dental surgeries, tooth restoration technologies, and other branches of dentistry [2].

Complete loss of teeth and defects in the dentition is a global phenomenon. Edentulism occurs as a result of dental caries, periodontal disease, trauma and oral cancer, and the number of edentulous patients continues to grow due to the increasing proportion of elderly people in the population [3].

Removable dentures remain a popular type of dental prosthetics and provide significant improvements in oral care and quality of life for patients [4]. For the fabrication of removable dentures, such types of materials as metal alloys, ceramics and plastics are used, which are constantly being improved, in particular based on nanotechnology [5]. Acrylic resins, especially polymethyl methacrylate (PMMA), are one of the most widely used materials for the complete and partial removable dentures [6]. Due to their optimal mechanical and physicochemical properties and ease of processing, dentures have been manufactured for decades from thermosetting PMMA and repaired using cold-setting PMMA [7]. Dentures made of PMMA have a rough inner surface, and this roughness, combined with other factors (e.g., poor hygiene, xerostomia, or HIV infection), often contributes to the occurrence of microbial complications in denture wearers [8].

The surface roughness and porosity create conditions for easy colonization of the denture base by microorganisms, including *Candida albicans, Streptococcus mutans, Staphylococcus aureus*, and other microorganisms. The formation of biofilm on the surface of acrylic dentures can lead to a number of oral diseases, such as denture stomatitis, erythema, chronic mucositis, periodontitis and caries, as well as systemic diseases of the bronchopulmonary and digestive systems [9]. Denture stomatitis caused by *C. albicans* is one of the most common clinical problems for wearers of complete removable dentures [10].

The biomechanical and, especially, antimicrobial properties of acrylic prosthetic plastics can be improved by using nanomaterials as fillers or coatings because NPs of metals and their oxides are able to modify the physicochemical characteristics of materials into which they are incorporated as well as to inhibit the growth of microorganisms and their biofilm formation [11, 12, 13]. This became an occasion to analyze the modern literature data on the use of antimicrobial metal/metal oxide nanoparticles (NPs) in prosthodontics, in particular in modification of polymeric materials for prosthetics of dentition defects.

The aim of the work is to review the current scientific literature on the use of metal/metal oxide NPs to impart the antimicrobial properties to acrylic base materials used in dentures.

MATERIALS AND METHODS

A search for literature sources was conducted in the electronic database PubMed/Medline. To identify articles, the controlled vocabulary Medical Subject Headings (MeSH) was used. Terms “nanoparticle”, “metal”, “metal oxide”, “antimicrobial”, “denture”, “base material”, “acrylic resin”, “polymethyl methacrylate”, as well as these words combinations, including with clarification of the nature of metal: silver (Ag), titanium (Ti), zinc (Zn), zirconium (Zr), copper (Cu), served as the search queries. The inclusion criteria were: publication in English, availability of the article full text, *in vivo* and *in vitro* studies, original articles and reviews, year of publication 2015–2025. The exclusion criteria were: case from practice, conference report; short comment, letter to the editor, clinical trials, no relation to dentures, polymeric base material, or antimicrobial NPs. The antimicrobial effect was considered to be the inhibition of bacterial and fungal growth, prevention of microorganism adhesion or biofilm formation, as well as the nanocomposite potential for the treatment of denture stomatitis. The research methods were bibliographic and analytical. A total of 98 publications were found, from which, after systematization and exclusion of duplicate results, 76 documents were selected for the final consideration.

RESULTS AND DISCUSSION

Features of the oral microbiome during denture use. Commensal microorganisms of the oral cavity perform important functions and contribute to the health of the host. However, the oral microbiota also plays an important role in the pathogenesis and development of oral and systemic diseases. The oral cavity is home to many microorganisms, including those that form biofilms, a complex community of bacteria or fungi that protects pathogens from drugs and host defense mechanisms [14].

The quantitative characteristics of the microbiome in denture wearers vary significantly and the level of oral dysbiosis varies depending on the type of denture [15]. The oral microbiome may be characterized by a higher prevalence of some microorganisms than others in subjects with removable or fixed dentures, depending on the oral health status, the prosthetic materials, and any pathological conditions caused by inadequate denture fabrication or poor oral hygiene [16]. Denture surfaces are easily colonized by bacteria and fungi (e.g., *C. albicans, S. aureus, S. mutans*), which can become potential pathogens and contribute to the biofilm formation [17]. To prevent this complication, modification of prosthetic materials with NPs with antimicrobial properties can be used [18, 19].

Antimicrobial metal/metal oxide nanoparticles. Nanomaterials are increasingly being used to target microorganisms as an alternative to antibiotics. Examples include the use of NPs in antibacterial coatings for implantable devices and medical materials to prevent infection and promote wound healing, in antibiotic delivery systems, in sensors for detecting microorganisms, and in antibacterial vaccines to combat infections [20]. Scientific articles show that many NPs of metal and their oxides, including silver and its oxide (Ag_2O), titanium and titanium dioxide (TiO_2), zinc oxide (ZnO), copper and copper oxide (CuO), zirconium dioxide (ZrO_2), exhibit antimicrobial properties [21, 22].

Nanoparticles that have intrinsic antimicrobial activity kill microorganisms by producing large amounts of reactive oxygen and nitrogen species [23]. At the same time, they simultaneously affect many life processes and metabolic pathways of microorganisms; which makes it impossible to develop so many genetic mutations that would cause resistance to NPs [24]. There are several factors that affect the ability of nanomaterials to inhibit or kill microbial cells. These include the surface charge, size, shape and coating of NPs, concentration of the nanomaterial, dispersion and contact with the microbial cell, the presence of active oxygen, the release of antimicrobial ions, components of the environment and pH, the phase of development of the microorganism, the formation of biofilms and the features of the microbial cell wall [25, 26] (**Fig. 1**).

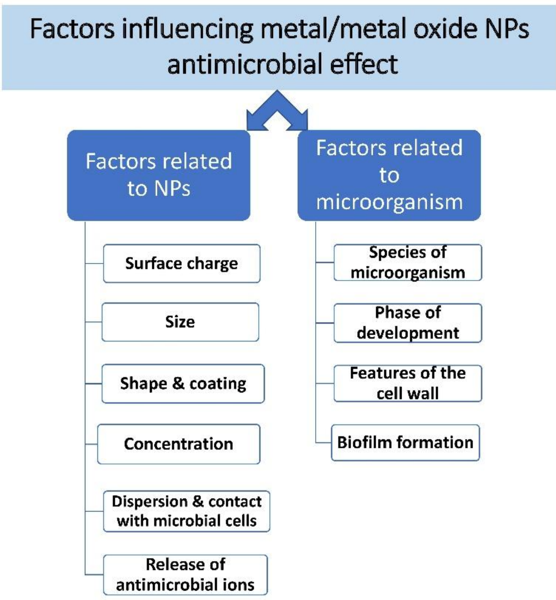

Figure 1 *– Antimicrobial effect relating factors of nanomaterial. The antimicrobial effect of nanoparticles (NPs) depends on their surface charge, size, shape, coating, concentration, dispersion, and release of antimicrobial ions as well as on nature of microorganism, phase of its development, biofilm formation, and cell wall features*

At the same time, most metal/metal oxide NPs are not toxic to humans at effective concentrations used to destroy bacterial or fungal cells, which creates conditions for their full-scale use [21]. This means that antimicrobial NPs are a promising strategy for the treatment and prevention of oral infections and can be applied in various fields of dentistry, including prosthodontics [27].

Silver nanoparticles and antimicrobial properties of denture base materials. Various nanofillers have been incorporated into prosthetic materials to enhance antimicrobial activity. The addition of metal NPs and their oxides, such as Ag [28, 29], ZnO [30], TiO_2 [31, 32] and ZrO_2 [33] has yielded a significant antimicrobial effect. They displayed direct influence on microorganisms and act indirectly due to changes of porosity, roughness, and hydrophilicity of denture material (**Fig. 2**).

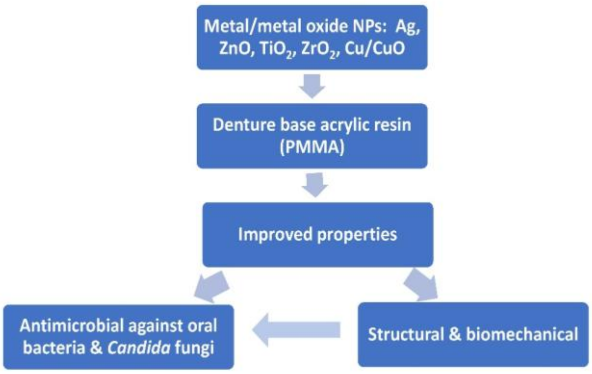

***Figure 2** – Metal/metal oxide nanoparticles in modification of denture base material. The nanoparticles (NPs) of silver (Ag), zinc oxide (ZnO), titanium dioxide (TiO_2), zirconium dioxide (ZrO_2), copper and copper oxide (Cu/CuO) are used for the modification of denture base materials, especially polymethyl methacrylate (PMMA) and impart direct antimicrobial effect to the resin. They also can change structural features of the resin (e.g., porosity, roughness) that improves antimicrobial effect indirectly*

Silver nanoparticles are most widely used for the modification of denture base materials [34]. They are synthesized by chemical and physical methods, as well as obtained by "green synthesis" [35] and introduced into the prosthetic material, which is most often an acrylic resin [36, 37, 38].

It is well known that nanosilver has a broad spectrum of antibacterial activity [39]. This is achieved by releasing silver ions that directly interact with proteins and at the same time enhance the generation of reactive oxygen species, resulting in impaired permeability of the bacterial cell wall, damage to DNA and enzyme systems [40].

Equally important, Ag NPs have antifungal properties, inhibiting the development of opportunistic pathogenic yeasts of the genus *Candida*, in particular *C. albicans*, which often colonize acrylic denture bases, causing denture stomatitis affected about 70% of denture wearers [29]. It is reported that the strength of the nanosilver effect was evaluated against different *Candida* species with a result: *Candida glabrata* susceptibility > *Candida tropicalis* susceptibility > *C. albicans* susceptibility [41].

Silver nanoparticles combined with polymers or as coatings on the surface of biomaterials demonstrate not only exceptional antimicrobial properties against oral microorganisms, but also an antibiofilm effect [27]. It has been reported that Ag NPs not only reduced the bioactivity and biomass of *C. albicans* biofilm, but also demonstrated anti-adhesive activity, reduced biofilm thickness and live/dead cell ratio when incorporated into the base resin at high concentrations (5%) [29].

The potential biocidal activity of nanosilver-modified acrylates is influenced by several factors: NP size, solubility, shape, surface area, and surface charge, which determine pharmacological activity and toxicity. Smaller NPs are believed to be more effective and release more silver ions to achieve optimal antimicrobial and antibiofilm effects. In particular, spherical Ag NPs with a size of 5 nm and 10 nm, incorporated into acrylic resin at concentrations of 0.05% and 0.5%, were effective in reducing the growth of *C. albicans* biofilms without reducing the flexural strength [42]. Nanocomposites Ag-PMMA resemble a solid solution with the weak interactions between the polymer matrix and NPs and can release biologically active silver [43]. The results of the latter study showed antimicrobial activity of both cold and thermally cured PMMA with 10% Ag NPs against *C. albicans* and *S. aureus*. In the case of modification of denture base resins with the lower concentrations of biocidal NPs, their diffusion into the substrate and subsequent inhibition of the microorganism growth did not occur, however, the authors noted that there was no microbial growth on the contact surfaces of the test samples, which confirmed their activity and suggested that when in contact with the mucous membrane their antimicrobial effect would be manifested even at lower concentrations of NPs in the material [43]. Along with studies where a sufficiently high concentration of nanosilver was used to modify the base acrylic resin, there are works in which the optimal antifungal effect was achieved at a much lower concentration (0.2%) of Ag NPs in heat-cured PMMA [44]. In another study, it was shown that PMMA to which the monomer methylmethacrylate was added with 1 μg/mL Ag NPs exhibited significantly less attachment of *C. albicans* cells compared to pure PMMA [41].

The effect of nystatin-coated Ag NPs was compared with the effect of nystatin alone in PMMA and it was found that these composites (10% w/w) inhibited the growth of *C. albicans* better than composites with the same concentration of nystatin [45]. In addition, Ag/nystatin nanocomposites showed a significant antibacterial activity against *S. mutans* and had no toxic effect on NIH 3T3 cells.

While exhibiting excellent antimicrobial properties, Ag NPs incorporated into the acrylic base resin as fillers could slightly modify its physical characteristics. In a systematic review, Galant et al. compared the mechanical properties of PMMA/Ag NP composites with pure PMMA, taking into account the average particle size and concentration [46]. They showed that the flexural strength increased only for NP sizes between 30-70 nm, the impact strength remained higher at sizes less than 80 nm and increased at 15-25 nm. The tensile strength was optimal at 55 nm. The flexural strength decreased with increasing the NPs wt%, the impact strength increased in the range up to 4.0 wt%, and the maximum tensile strength – at 0.5-2.0 wt%. This allowed the authors to suggest that the optimal mechanical properties of PMMA/Ag NPs are within the range of the average NP size of 15-70 nm and the concentration of 0.5-4.0 wt% [46].

In *in vitro* experiments, the nanosilver antimicrobial effect depends on many conditions, so there are works that note the absence of a positive result from the inclusion of Ag NPs in base resin specimens. Mukai et al. reported that Ag NPs showed activity against *C. albicans* on polypropylene surfaces, but not in thermo-polymerized PMMA resin, and did not exhibit antibacterial activity against *S. mutans* on any of these substrates [47]. It has also been shown that Ag NPs can impair the mechanical properties (flexural strength) of acrylic base resins, especially when the concentration increases to 5% [48].

Other metal/metal oxide nanoparticles in antimicrobial modification of denture base materials. Zinc oxide NPs are biocompatible, biosafe and non-toxic with significant biocidal properties against a wide range of Gram-positive and Gram-negative bacteria, including *Aeromonas hydrophila, Bacillus subtillis, Escherichia coli, Enterococcus faecalis, Streptococcus pyogenes, Salmonella typhimurium, Klebsiella pneumonia, S. aureus, Listeria monocytogenes*, and *Pseudomonas aeruginosa* [49]. Mirhosseini et al. noted that the antimicrobial activity of ZnO NPs increased with decreasing particle size, and *C. albicans, E. faecalis*, and *S. mutans* had a higher susceptibility to changes in ZnO size than other oral microorganisms [50]. Determination of the antibacterial activity of ZnO NPs of different sizes against *S. sobrinus* and *S. mutans* showed that these NPs with a size of 21 nm exhibited stronger inhibition of both bacteria compared to ZnO NPs with a size of 52 nm [51].

The antimicrobial effect of composite prosthodontic materials with ZnO NPs is based on their release into the medium. This was proven in the research where the release of ZnO NPs from nanocomposites with PMMA, as well as from a layer of ZnO NPs on pure PMMA were studied [52]. According to mentioned data, the release of ZnO from PMMA itself was 0.074 mg/L, and for individual nanocomposites at concentrations of 2.5%, 5% and 7.5% it was 2.281 mg/L, 2.143 mg/L and 3.512 mg/L, respectively; for the ZnO NP layer on PMMA – 4.878 mg/L. The released NPs did not have a negative influence on HeLa cells.

It is believed that the acidic lysosomal medium contributes to the degradation of ZnO NPs released from the material, which, in turn, leads to the transformation of the metal into ions that interrupt microbial cell reproduction. Other mechanisms of their antimicrobial action are a local change in the microenvironment near the microbes, the formation of reactive oxygen species, interaction with the -SH groups of enzymes, protein denaturation, and DNA damage [53].

The antifungal effect of ZnO NPs in PMMA against *C. albicans* has been described. Cierech et al. investigated the antifungal activity of both ZnO-PMMA nanocomposites and PMMA specimens coated with ZnO NPs. They found that such modification significantly improves the antifungal activity of the nanocomposite, which increases with increasing the NP concentration [54]

It is believed that the enhanced hydrophilicity and hardness contribute to the reduction of the microorganisms' growth on the ZnO- nanomodified denture base [55]. While exhibiting an antimicrobial effect, ZnO NPs do not violate the mechanical properties of the base material. In particular, the addition of ZnO NPs (1.4%) improved the PMMA flexural strength from 61.36 MPa in the control to 91.31 MPa [56]. Modification of PMMA with ZnO nanoparticles is esthetically acceptable at a mass concentration of 2.5% and 5%, but it did not reduce the changes in the specimens during their prolonged stay in distilled water or food liquids and made the color changes more noticeable at a higher content of NPs [57].

Titania NPs, along with nanosilver, are leaders in the modification of denture base materials in order to provide them with antimicrobial properties [58], and most often the size of these NPs was less than 30 nm [59]. These NPs have a wide spectrum of antimicrobial activity, including Gram-negative and Gram-positive bacteria and fungi. Titanium dioxide NPs improved the antimicrobial behavior of PMMA by significantly reducing the adhesion of *P. aeruginosa* and *E. faecalis* correlated with an increase in the NP concentration: the number of adhered microorganisms decreased by 38% with an increase in the NP concentration from 0 to 1% and by 50% with an increase in the NP concentration from 1 to 3% [31]. Incorporation of TiO_2 and silica NPs into PMMA showed significant antimicrobial activity against cariogenic bacteria and could kill microorganisms with prolonged exposure [60]. After atomic layer deposition of a titania nanofilm (30 nm) on PMMA, which demonstrated noticable wear resistance, significantly less attachment of *C. albicans* to such a surface was observed [61].

AlQahtani et al. described a novel technique for layering a denture base with TiO_2 NPs added to PMMA and investigated its effect on *C. albicans* adhesion, as well as on surface roughness, hardness, translucency, and flexural strength [62]. Examining a single-layer material (TiO_2 NPs/PMMA), a double-layer material (unmodified PMMA and a thin layer of TiO_2 NPs/PMMA), and a double-layer material with a dotted nanomaterial application at 1 and 2% NP concentrations, they showed that the addition of TiO_2 NPs reduced *C. albicans* adhesion with no significant difference between both concentrations in the same group before and after UV light activation, except for the 1% dotted layer. At the same time, NPs did not affect the surface roughness and hardness, but decreased transparency and flexural strength.

Both TiO_2 NPs and hybrid NPs, which, in addition to titanium oxide, included silver, had a positive effect on the antimicrobial properties of the base resin. In particular, their ability to reduce the number of colony-forming units in biofilms of *S. mutans* and *C. albicans* on the surface of plastic samples was demonstrated [32]. Liu et al. studied the photocatalytic antimicrobial effect of self-polymerized PMMA, modified with TiO_2 NPs or TiO_2/hydroxyapatite on *C. albicans in vitro*, and also evaluated its mechanical, optical, and cytotoxic properties [63]. They found that adding 1 wt% of such NPs gave the base resin optimal antimicrobial properties: the number of colonies in visible light was reduced by 86% and 94%, respectively, no germ tubes and mycelium were observed on the nanocomposite surface, and the fungal cells were disrupted. This occurred with improved mechanical properties and without significant changes in the cytotoxicity and optical properties of the PMMA doped with NPs.

With the development of new technologies, polymeric materials printed on a 3D printer are beginning to replace PMMA, and therefore studies of the antibiofilm activity of 3D-printed prosthetic materials with NPs are emerging. A new biocompatible nanocomposite material made of acrylic resin “NextDent denture 3D+” (ethoxylated bisphenol A dimethacrylate, 7,7,9-trimethyl-4,13,14,dioxo-3,14,diazahexadecane-1,16-diyl bismethacrylate, 2-hydroxyethyl methacrylate, silicon dioxide, diphenyl (2,4,6-trimethylbenzoyl) phosphine oxide, and titanium dioxide) and silane-coated TiO_2 NPs (10-30 nm) with antifungal properties has been proposed, which is suitable for 3D printing of denture bases [64]. The obtained material at a NP concentration of 0.1-0.5 wt% caused a significant decrease in the count of *Candida* cells attached to the surface of the specimens, while the content of 0.75 wt% did not show a significant difference compared to the control, which could be explained by the aggregation of NPs at their high concentrations. At the same time, another study noted that silanized TiO_2 NPs, as well as Ag and ZrO_2 NPs, at concentrations of 0.5-1.5% introduced into 3D-printed base resins inhibited the growth of *S. pyogenes*, *S. aureus* and *C. albicans* in the disk diffusion method, more actively with increasing their concentration [65].

Titanium dioxide NPs reduce the adhesion of microorganisms not only to PMMA, but also to other prosthetic materials, including ceramic glass and stainless steel [66]. If the data on their antibacterial and antifungal properties are unambiguous, the effect on the mechanical properties of the base resin may differ depending on the concentration of NPs, the technique of specimen preparation, and other experimental conditions. It is more often noted that TiO_2 NPs in the composition of the base plastic improved the mechanical characteristics. For example, it is described that the addition of 5 wt% of titania NPs to self-curing PMMA causes a significant increase in the flexural strength of the material and reduces water sorption compared to control PMMA [67].

Zirconia dioxide is another NPs that are of interest to prosthodontists. They have good biocompatibility and, unlike other metal oxide NPs, do not impair the aesthetics of dentures [68]. Gad et al. established the inhibitory effect of ZrO_2 NPs on the adhesion of *C. albicans* to cold-curing acrylic resin and to the repaired bases of hot-curing PMMA dentures, which was most effective at a concentration of 7.5 wt% NPs in the resin and explained this by the less porous and denser structure of such a material [33]. However, in another study the researches did not observe a statistically significant decrease in *Candida* adhesion to heat-cured PMMA specimens with ZrO_2 NPs (2.5–7.5%) after 48 hours of incubation in a yeast culture and at the same time recorded an increase in surface roughness [69].

The properties of the 3D-printing acrylic base resin modified with different concentrations of ZrO_2 NPs were studied. Cell proliferation assays showed a significant reduction in *C. albicans* for specimens with 0.5% of these NPs compared to PMMA and other concentrations of ZrO_2 NPs, without affecting surface roughness, which, according to the authors, may be useful for the treatment and prevention of denture stomatitis [70].

The development of surfaces resistant to microbial colonization, which is highly desirable for the improvement of prosthetic materials, can be achieved by incorporating CuO NPs into acrylic resin. These NPs, when introduced into thermocycled PMMA (2.5% and 7.5%), demonstrated antimicrobial activity against the standard yeast strain *C. dubliniensis*, and the oral bacteria *S. sobrinus*, *S. salivarius* and *S. sanguis* at both concentrations, and against *S. mutans* at a concentration of 7.5% [71]. At the same time, they were inferior to TiO_2 NPs in their effect on *C. albicans*.

Given the differences in the antimicrobial activity of NPs against different strains of microorganisms, it may be appropriate to combine different metals and/or their oxides in one nanomaterial, in particular chemically synthesized NPs of CuO, cetyltrimethylammonium bromide (CTAB), coated with CuO and ZnO (separately and in combination) in PMMA [72]. The effectiveness of these nanocomposites was evaluated against *S. aureus* and *E. coli*. The results revealed a species-specific response of bacteria to nanomaterials: CuO NPs (0.1% w/v) were more effective against *E. coli*, while CTAB NPs coated with CuO or ZnO were very effective against *S. aureus*, and the combination of NPs increased the effectiveness of the nanocomposites against both species of bacteria. Using the specimens with different concentrations of CuO NPs in the heat-polymerized PMMA, it was shown that they are cytotoxic only in high concentrations (50 and 500 μg/ml) and at the same time increase the flexural strength of this denture base resin [73].

To provide antimicrobial properties to dental prosthetic materials, copper NPs can be used in addition to copper oxide. There is a study in which thermoset PMMA with Cu nanoparticles was synthesized to fabricate dentures with antimicrobial properties and the ability to prevent denture stomatitis [74]. A Cu/PMMA nanocomposite with 0.045% nanocopper showed maximum antimicrobial activity against *C. albicans* and other oral microorganisms without significant cytotoxicity. Dentures made from this nanocomposite retained their mechanical and aesthetic properties, and also inhibited the growth of *Candida spp*. both on the denture surface and on the patient's prosthetic bed, which reduced the frequency and severity of denture stomatitis.

Core original articles integrating denture resin modification with metal/metal oxide NPs and its antimicrobial effect are summarized in the **Table 1**.

The table shows that heat-cured PMMA is the most popular material for such modification and NP concentration varies from 0.05 to 10%. Standard strains of *C. albicans* is used as microorganism test culture in majority researches and its adhesion to composite material is evaluated as living microbial cells count (colony-forming units) on the specimen surface. This choice reflects the role of candida in denture stomatitis and the importance of new nanocomposite materials in its prevention.

Thus, there are many metal/metal oxide NPs that can improve the antimicrobial properties of denture base materials for prosthodontics and thus ensure the prevention of infectious complications when using dentures, especially in the elderly or in denture wearers with compromised immunity. Dentures made of nanomodified materials have certain prospects, but important questions arise regarding overcoming the gap between experiment and practice. Clinical "translation" of dentures from nanoengineered materials is complicated by optimizing fabrication, achieving local long-term release of NPs, adapting *in vivo* models, and ensuring safety for humans. Most of the studies described in the literature are based on planar specimens of modified acrylic resin, which are far from the complex geometry of real dentures used in the clinic, so the development of a standardized technology for introducing or applying NPs specifically into/on dentures is relevant.

While nanoparticle-enhanced resins offer some hygiene benefits, it is important to understand that long-term safety is still being evaluated. There is a need to ensure that NPs do not "leach" out of the resin over time and cause adverse effects. Released metal NPs potentially can damage various systems, including respiratory, nervous, endocrine, immune, and reproductive systems and have carcinogenicity [75]. The mechanisms of their toxicity include oxidative stress, mitochondrial damage, inflammatory reaction, apoptosis, DNA damage, cell cycle, and epigenetic regulation. By understanding the mechanisms of metal-based NP toxicity, researchers have developed several strategies to mitigate their potential adverse impacts, especially to achieve the goal of clinical translation [76]. They are surface coating, surface chemistry modifications by altering charge density

Table 1 *– Modification of denture base resin with nanoparticles and resulting antimicrobial effect*

Denture base resin	**Metal/metal oxide NPs**	**NPs concentration**	**Microbial test culture**	**Antimicrobial effect**	**Reference**
PMMA	Ag/sulfa-diazine/ mesoporous silica	0.5-5%	*C. albicans, S. oralis*	↓ adhesion	[28]
PMMA	Ag	5%	*C. albicans*	↓ adhesion, ↓ thickness & live/died cells ratio in biofilm	[29]
PMMA h/c	Ag	0-0.5%	*C. albicans*	↓ adhesion	[37]
PMMA h/c	Ag/Aloe barbadensis miller, Ag/Morinda citrifolia, Ag/Boesen-bergia rotunda	0.05-0.1%	*C. albicans*	↓ adhesion	[38]
PMMA h/c	Ag	0.05-5 vol% into monomer	*C. albicans*	↓ biofilm formation	[42]
PMMA h/c, c/c	Ag	2-10%	*C. albicans, S. aureus*	↓ microbial growth at 10%	[43]
PMMA h/c	Ag	0.05-0.2%	*C. albicans*	↓ microbial growth, max at 0,2%	[44]
PMMA h/c	Ag/nystatin	0.1-10 wt%	*C. albicans, S. mutans*	↓ microbial growth, max at 10 wt%	[45]
PMMA h/c, PP	Ag	80 ppm (30 ml +100 g PMMA)	*C. albicans, S. mutans*	↓ colonization by fungi for PP, no effect for PMMA, no effect for bacteria	[47]
PMMA/ PVC	ZnO	2.5-10%	*S. aureus, S. pyogenes, B. subtilis, E. coli, S. typhi, P. aeruginosa*	↓ bacterial growth, ↓ biofilm formation by *S. aureus* & *S. typhi*	[13]
PMMA h/c	ZnO/ methacryl oxypropyl-trimethoxy-silane	1.25-5 wt%	*C. albicans*	↓ fungal cells on the surface	[30]
PMMA	ZnO	2.5-7.5%	*C. albicans*	↓ biofilm deposition	[54]
PMMA h/c	TiO_2	1-3 wt%	*E. faecalis, P. aeruginosa*	↓ adhesion	[31]
Selecta Plus	TiO_2, TiO_2/SiO_2	0.5-1%	*L. acidophilus, S. mutans*	↓ bacterial count, max 1% TiO_2/SiO_2 under UVA	[60]
PMMA h/c	TiO_2	Nanofilm	*C. albicans*	↓ adhesion	[61]
PMMA h/c	TiO_2	1-2.5% in the layer with NPs	*C. albicans*	↓ adhesion, no difference due to concentration & UV	[62]
PMMA s/p	TiO_2/hydroxy-apatite	1 wt%	*C. albicans*	↓ adhesion, cell rupture, no germ tubes & mycelium	[63]
NextDent denture 3D+	TiO_2/silane	0.1-0.75 wt.%	*C. albicans*	↓ adhesion, except 0.75 wt%	[64]
PMMA c/c	ZrO_2	2.5-7.5 wt%	*C. albicans*	↓ candida count, max at 7.5 wt%	[33]

Table 1 continued

Denture base resin	Metal/metal oxide NPs	NPs concentration	Microbial test culture	Antimicrobial effect	Reference
PMMA h/c	ZrO_2	2.5-7.5%	*C. albicans*	↓ attached candida count insignificantly	[69]
PMMA h/c, NextDent	ZrO_2	0.5- 5 wt%	*C. albicans*	↓ adhesion, ↓ candida count, max at 0.5 wt% in NextDent	[70]
PMMA h/c	TiO_2, CuO	2.5-7.5%	*C. albicans*, *C.dubliniensis*, *S. mutans*, *S. sobrinus*, *S. salivarius*, *S. sanguis*	↓ biofilm (*S. mutans* – CuO, *C. albicans* – 7.5% TiO_2)	[71].
PMMA	CuO, CTAB/CuO, CTAB/ZnO, CTAB/CuO/ ZnO	0.1% w/v	*S. aureus*, *E. coli*	↓ adhesion, CuO more active against Gr-, CTAB/CuO or ZnO against Gr+, CTAB/CuO/ ZnO against both strains	[72]
PMMA h/c	Cu	0.045%	*C. albicans*, *S. mutans*, *S. aureus*, *A. actinomyce-temcomitans*	Surface inhibitory capacity against fungi & bacteria, ↓ adhesion, no candida germ tubes & gyphal forms	[74]
PMMA	ZrO_2/silanized $AlBO_3$, +TiO_2, +Ag/TiO_2, +Ag/$Zr_3P_4O_{16}$, +tetrapod-like ZnO whiskers	2 wt% 3 wt% 3 wt% 3 wt% 3 wt%	*C. albicans* *S. mutans*	↓ adhesion, max for Ag/TiO_2 & Ag/$Zr_3P_4O_{16}$	[32]
3D-printed acrylic base resin	Silanized Ag ZrO_2 TiO_2	0.5-1.5%	*C. albicans* *S. pyogenes* *S. mutans*	↓ microbial cells count in biofilm, max at 1.5%	[65]

Footnotes: PMMA – polymethyl methacrylate; PP – polypropylene; h/c – heat-cured; c/c – cold-cured; s/p – self-polymerized; NP – nanoparticle; CTAB – cetyltrimethyl ammonium bromide; wt – weight; vol – volume; w/v – weight/volume; max – maximum; UV – ultraviolet; ↓ – inhibition or reduction

and hydrophobicity, and introducing to naturally derived cell membranes. Obviously, first three mentioned strategies can be used to reduce the potential toxicity of metal-based NPs in denture base materials.

Despite promising results, many studies are still *in vitro* and more well-designed clinical trials are needed to fully understand the long-term safety and efficacy of nanomaterials in patients. They should establish the action of the released bioactive nanoparticles or ions and achieve sustained release *in vivo* when the denture surface is in close contact with the oral mucosa and saliva. The effects of dentures modified with metal NPs and their oxides on the human microbiome, as well as the optimal nanoparticle size, loading doses, and biological safety of different nanoparticles in dentures, still need to be investigated.

CONCLUSIONS

Our results show that antimicrobial NPs of metals and their oxides have significant prospects for application in dental prostheses, in particular in acrylic base materials. It is expected that antimicrobial nanomaterials with high mechanical and aesthetic qualities will be developed and applied in the clinical practice of prosthodontics. Metal//metal oxide NPs have a pronounced antimicrobial effect, but their antibacterial and antifungal properties are influenced by concentration, type, shape and other physicochemical factors. The specific mechanisms of action and toxicity have not yet been fully elucidated, therefore further studies of nanomodified denture base materials are needed to determine them. It should also be noted that the presented literature analysis does not cover all aspects of the application of antimicrobial NPs in dental prosthetics, as it has limitations in terms of the search base, the period of the last decade and the inclusion of publications related only to metal/metal oxide NPs. It is obvious that further studies of the influence of metal/metal oxide nanoparticle-modified denture base materials on the oral microbiome *in vivo,* as well as optimization of their manufacturing processes, will facilitate their successful implementation in clinical practice to reduce infectious and inflammatory complications in individuals wearing dentures. It is necessary to assess benefits and risks of different materials, including traditional acrylic resins and newer options with added metal/metal oxide NPs based on the patient's individual needs. But even all problems relating to nanomaterials in dental prostheses will be solved successfully, such constructions will stay the mean of individualized therapy and only dentist can choose what is better in the given case: newest nanocomposite or traditional denture resin.

PROSPECTS FOR FUTURE RESEARCH

The analysis of modern scientific literature in the branch of dental implant nanoengineering, its advances and limitations will be the direction of our future research.

AUTHOR CONTRIBUTIONS

Liubov Lugova: Writing – Original draft;
Oksana Dobrovolska: Investigation, Visualization;
Oleksandr Dobrovolskyi: Investigation, Writing – Original draft;
Elena Vazhnichaya: Conceptualization, Project administration, Supervision;
Antonina Sydorenko: Methodology, Writing – Review and editing;
Nellia Bobrova; Investigation, Data curation.

All authors approved the manuscript for publication and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work will be appropriately investigated and resolved.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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