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The Effect of Adding Magnesium Oxide Nanoparticles to The Cold Cured Acrylic Resin on Candida albicans Adhesion

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Abstract

Aims: This study aims to assess the impact of the addition of MgO nanoparticles (NPs) with size of 50nm at different concentrations,which are 1.25%,2.5% and 5% on adherence of Candida albicans to cold- cured acrylic resin. **Materials and Methods**: Twenty-four specimens with the dimensions of (10mm ×10mm×2mm) length, width, and thickness respectively were made and divided into four groups, 6 specimens for each group; controlled (without the addition of MgO NPs), group of 1.25% MgO NPs, group of 2.5% MgO NPs and group of 5% MgO NPs; were subjected to adherence test. The statistical analysis was done by using SPSS program including descriptive statistics, ANOVA, and the Duncan´s test at $p \leq 0.05$. **Results**: Results showed that, the maximum reduction in Candida albicans adherence obtained at a concentration of 5% followed by 2.5% then 1.25%; while the control group showed that the highest number of Candida albicans colonies adhered to cold-cured acrylic. **Conclusions**: The MgO NPs influenced the adherence of Candida albicans to cold-cured acrylic resin, there is a significant reduction in the number of Candida albicans attached to cold-cured acrylic modified with MgO nanoparticles at different concentrations;and this reduction increases with increasing the concentration of MgO nanoparticles.

الخلاصة

الأهداف: تهدف هذه الدراسة إلى تقييم تأثير إضافة جزيئات اكسيد المغنيسيوم النانوية بحجم ٥٠ نانومتر بتراكيز مختلفة ، والتي تبلغ ١,٢٥٪ ، ٢,٥٪ ، و ٥٪ على التصاق المبيضات البيضاء براتنج الأكريليك المعالج بالبرودة. **المواد وطرائق العمل**: تم عمل أربع وعشرين عينة بأبعاد (١٠ مم × ١٠ مم × ٢ مم) طول وعرض وسمك على التوالي وقسمت إلى أربع مجموعات ، ٦ عينات لكل مجموعة; التحكم (بدون إضافة جزيئات اكسيد المغنيسيوم النانوية) ،مجموعة ١,٢٥٪ من جزيئات اكسيد المغنيسيوم النانوية،مجوعة ٢,٥٪ جزيئات اكسيد المغنيسيوم النانوية ومجموعة ٥٪ جزيئات اكسيد المغنيسيوم النانوية ؛ خضعوا لاختبار الالتصاق. تم إجراء التحليل الإحصائي باستخدام برنامج SPSS بما في ذلك الإحصاء الوصفي ، انوفا ، واختباردنكن عند $p \geq$ ٠,٠٥. **النتائج**: أظهرت النتائج أقصى انخفاض في نسبة التصاق المبيضات البيضاء بتركيز ٥٪ يليه ٢,٥٪ ثم ١,٢٥٪ ، بينما أظهرت مجموعة التحكم أعلى عدد من المبيضات البيضاء الملتصقة بالأكريليك. **الاستنتاجات**: اثرت جزيئات اكسيد المغنيسيوم النانوية على التصاق المبيضات البيضاء براتنج الأكريليك المعالج بالبرودة ، وهناك انخفاض كبير في عدد المبيضات البيضاء المرتبطة بالأكريليك المعالج بالبرودة المعدل باستخدام جزيئات اكسيد المغنيسيوم النانوية بتراكيز مختلفة ؛ ويزداد هذا الانخفاض مع زيادة تركيز الجزيئات النانوية.

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INTRODUCTION

Polymethyl methacrylate (PMMA) acrylic resin is the most widely used material for the construction of removable dentures; and intraoral maxillofacial prostheses.Despite its desirable merits, PMMA denture base resin is vulnerable to the accumulation of microorganisms in the oral environment[1]. Several factors like roughness, porosity of surface, constant denture wearing, and bad denture hygiene may contribute to adhesion of microorganisms and biofilm accumulation on the surfaces of acrylic resins [2,3]; lead to inflammation in the adjacent mucosa and causes denture stomatitis [4].

Denture stomatitis is a disease related to *Candida albicans*, many researches mentioned that up to two-thirds or more of persons who wear removable dentures may have denture stomatitis [5] .*Candida albicans* is a polymorphic microorganism and can reversibly change its shape between yeast and hyphal growth forms[6].

The surface roughness of cold-cured acrylic material is higher than hot-cured acrylic material[7,8].A study has been made to test Candida adhesion on heat-cured, cold-cured, microwaved-cured, and light-cured materials,the study has found that the cold-cured materials are very susceptible to *C. albicans* adhesion[9].

Many clinical implementations that require the use of cold-cured acrylic resin material in dental practice, support the value of exploring the antifungal effects of nanoparticles in the resins[10] .Metal can be converted into nanomaterials (NMs), ranging from 1 to 100 nm. Nanoparticles (NPs) have strong, targeted, and expanded antimicrobial activity at smaller dosages due to smaller dimensions than bacteria; and large surface area/volume ratio, metallic nanomaterials show strong antimicrobial interaction with bacteria and biofilms [11] .

Among many inorganic metal oxides, magnesium oxide nanoparticles (MgO NPs) have antibacterial effect with the benefits of being nontoxic and relatively easy to get. MgO NPs have been approved as safe materials by the United States Food and Drug Administration (21CFR184.1431) [12].

MATERIALS AND METHODS

Approval of study was from the Scientific Research Committee / Department of Prosthodontics / College of Dentistry (UoM.Dent / DM. L.43/21) Total number of specimens were twenty four, six specimens for each group which was controlled (without the addition of MgO NPs) , 1.25% MgO NPs ,2.5% MgO NPs and 5% MgO NPs. This study was done at the college of dentistry in university of Mosul.

Specimens´ preparation:

Specimens of cold-cured acrylic with dimensions of 10 mm × 10 mm × 2 mm (length,width,thickness) were

fabricated by investing plastic sheet [13] with previous dimensions into the dental stone using flask,then specified proportion of MgO nanoparticles (1.25% , 2.5%, and 5% US Research Nanomaterials, Inc., USA) mixed with monomer and placed in ultasonic device to ensure good distribution of nanoparticles, then powder was mixed with (momomer/ nano MgO) suspension until reached the dough stage; then packed into the prepared stone molds, the two pieces of the flask were sealed tightly together and then put under the hydraulic press at 2,000 N for 15 min[14,15]. After setting, the specimens were retrieved from the molds, finished, polished (except the intaglio surface); then underwent to the microbiological test .

Microbiogical test:

- ***Candida albicans* suspension preparation:**

Candida albicans local strain (previously obtained from a patient with denture stomatitis) was identified and confirmed using standard microbiological methods [16]. Pure *C. albicans* stock was cultured on Sabouraud dextrose agar (ACUMEDIA, UK) and incubated at 37 °C for 48 hours,after that 0.5 McFarland standard suspension containing 1.5× 10^8 CFU/ml was prepared and used for adherence test.

- **Adherence test:**

Adherence test was performed according to Gad *et al*.[10] and Naji *et al*. [17] with slight modification(Normal saline was used instead of broth to prepare Candida suspension).In order to perform adherence test, all prepared acrylic specimens were placed in separated sterile containers and 10 ml of freshly prepared *C. albicans* 1.5× 10^8 CFU/ml (0.5 McFarland standard) in sterile normal saline (S-NS) (0.9% NaCl) was added to each container and incubated at 37 °C for 24 hour. After that, acrylic specimens were transferred into new sterile test tubes and washed with 3 ml S-NS for three times to remove *C. albicans* cells that not adhere properly. All the acrylic specimens were exposed to the evaluation process to calculate the colony forming units (CFU) of the adhered cells. Briefly, under aseptic conditions, all the acrylic samples were placed in sterile test tubes contain 1 ml of S-NS and vortexed for 3 min to allow the adhered cells to detached from the acrylic .After that, 10-fold serial dilutions (1/10) and (1/100) was performed by taking 100 µl of S-NS containing detached *C. albicans* and added to 900 µl S-NS and mixed well by short vortexing.The diluted tubes were subjected to direct culture by spreading 100 µl of each dilution directly on Muller-Hinton agar (Neogen, UK) plate with 3 replicates using sterile glass-spreader. All the cultured plates were incubated at 37 °C for 24 hour. Visible Candida colonies as shown in Figure(1), were counted and CFU/ml was calculated

by multiplying number of colonies by dilution factor.

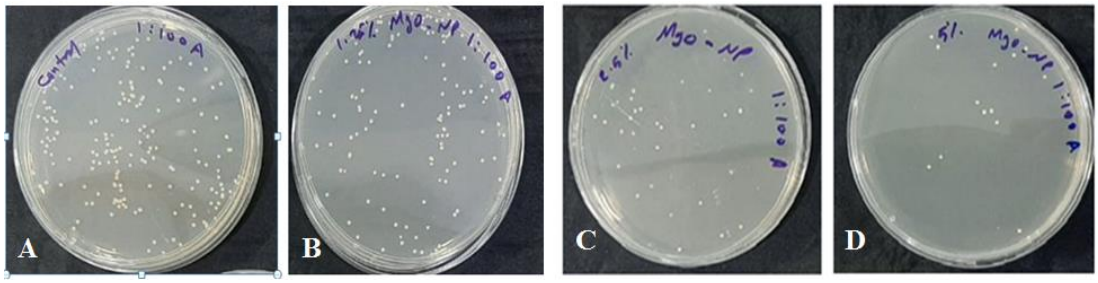


Figure (1): *Candida albicans* colonies appear on agar media at different concentration of MgO nanoparticles added to cold-cured acrylic resin (A) Control (B) 1.25% (C) 2.5% (D) 5%.

RESULTS

The statistical analysis :Descripitive statistic,test of normality,Inference statistic(ANOVA and Duncan´s test) were done by using spss program version(19).In the test of normality,the results of shapero test were not significant with normal distribution at ($P \geq 0.05$),so we can use parametric tests.

Descriptive statistics(mean and standard deviation of four groups of adherence test which included (Control,1.25% MgO NPs, 2.5% MgO NPs and 5%MgO NPs) were presented in table(1),it showed that mean of the control group had highest numbers of *Candida albicans* adhered to pure acrylic (cold-cured acrylic without MgO NPs additive), while the means of other three groups which contained MgO nanoparticles of 1.25% ,2.5% and 5% showed a reduction in numbers of *Candida albicans* colonies adhered to acrylic specimens with the highest reduction in a group with 5% concentration followed by 2.5% then 1.25%,which indicated that as concentration increased the anticandidal effect of MgO nanoparticles also increased.

Table(1): Descriptive statistics of adherence test.

Groups	Mean	Std. Deviation
Control	194.00	1.414
1.25% MgO NPs	116.16	1.169
2.5% MgO NPs	30.00	1.414
5% MgO NPs	13.16	2.316

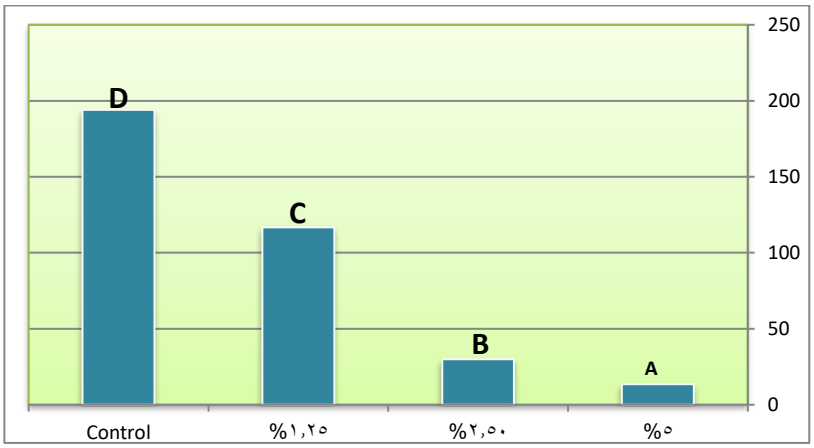
Note: Means multiplied by 10^4 which is the dilution factor.

Analysis of variance (ANOVA) was presented in table(2),it showed that there was a significant difference between all groups at $P \leq 0.05$.

Table (2): Analysis of variance (ANOVA) of adherence test.

	Sum of Squares	df	Mean Square	F	Sig.
Between Group	125957.667	3	41985.889	15646.91	.000
Within Groups	53.667	20	2.683		
Total	126011.333	23			

Duncan´s multilpe analysis range test was shown in figure(2) indicated that all groups modified with MgO NPs showed a significant reduction in numbers of colonies attached to cold-cured acrylic resin in comparison to control group,also a significant difference was found between all modified groups(1.25%,2.5% and 5%) of MgO nanoparticles.



Figure(2):A graph representing Duncan´s multiple analysis range test of adherence test.

***Different letters mean significant difference at $P \leq 0.05$.

DISCUSION

Cold-cured acrylic resin has been used in the construction of interim removable prostheses, orthodontic appliances, repairing fractured denture bases, relining of a denture ,maxillofacial prosthesis in addition to its use in crown and bridgework as a temporary coverage for prepared tooth [18] . The widespread use of cold-cured acrylic resin in prosthetics is related to its ease of use at room temperature, less time, and less equipments need [19], but it has some drawbacks like adherence of microbes and low mechanical properties.

Fungal attachment to rough surfaces is greater than on smooth surfaces.The roughness of the surface directly affects the initial surface attachment of microbes, formation of biofilms, and aggregation of Candida species. Materials with coarsest surfaces show greater numbers of yeast.These large numbers of yeast are caused by the surface irregularities that act as a store for microbes[20] .

Berger *et al.* [7] and Al-Irhayim *et al.*[21] have mentioned in their studies that the surface roughness of cold‑cured acrylic resin is more than heat‑cured acrylic resin, so the microbial adherence will increase as the surface roughness has increased.

The adhesion of Candida is connected to the presence of micropores of the denture surface[22] , and if such a situation occurs, Candida species can readily proliferate.

These disadvantages of self polymerization may be illustrated by the chemical initiator that minimize the conversion degree during polymerization process;and disorganize the surface structure[9,23,24].

Conventional antifungal medicaments have antifungal activity by preventing cells or killing fungal cells,in both issues the development of resistance to drugs is inevitable[25]. Therefore, it is crucial to detect new strategies to develop new antifungal drugs [26,27].

Metal-based nanomaterials are the most common inorganic nanomaterials and provide a good and promising alternative against the resistance of microbes to conventional antibiotics, not only because they adopt modes of action that are completely unlike those for conventional antibiotics,but they also aim at different biological molecules that impede the evolution of resistant strains[28] .

Among many metal nanomaterials,MgO NPS have gotten much attention due to their low price and uncomplicated antifungal conditions and is a safe antifungal agent[29,30]. Because of their biocompatibility and degraded by-products, they are getting much interest for medical applications [31] .

It has been mentioned that MgO nanoparticles have a high antimicrobial

effect against bacteria (Gram-positive , Gram-negative and spores) [32, 33] .

The antimicrobial merits are proved by many studies like a study conducted byNoori and Kareem.[34] have concluded that a glass ionomer cement modified with MgO nanoparticles show a good antimicrobial and antibiofilm effects against both *Streptococcus mutans* and *Streptococcus sobrinus* so MgO NPs considered a promising material in dental applications.

Monzavi *et al*.[35] have studied the antimicrobial effects of MgO nanoparticles as an irrigant solution for root canals against *Enterococcus fecalis*.Their study stated that MgO nanoparticles have a significant efficiency in the elimination of *E. Faecalis* .

Our study is directed toward investigating the MgO nanoparticles impact on adherence of *C. albicans* to acrylic. It is performed using cold-cured acrylic resin as a repairing material and for removable prosthesis construction and as relining.

This study has proved that, the MgO nanoparticles have an antimicrobial effect against *Candida albicans* at all concentration which are (1.25%,2.5% and 5%) and this effect is increased as the concentration of MgO nanoparticles has increased and this agrees with Jin and He [36]who has stated that higher MgO NPs concentrations lead to higher inactivation of bacteria.

These effects may be attributed to the antimicrobial property of MgO nanoparticles or due to their effect in enhancing surface characteristics of acrylic resin.

Electrostatic interaction is one of mechanisms for antimicrobial effects of MgO nanoparticles, the microorganisms have surface with negative charge, hence nanoparticle with contrary charge will be attracted to microorganisms and lead to disfigurement of cell wall , causing more damage due to leakage of microbial cell contents [37]. Phosphomannosylation which is a modified protein that presents in cell wall of some types of yeast microorganisms, including *Candida albicans*, this modified protein give a negative charge to the cell wall, which is beneficial for the interactions with phagocytic cells of the immunity and cationic antimicrobial agents[38]. Stoimenov *et al*.[39] mentions that MgO nanoparticles has a positive charge, which leads to potent interaction with negatively charged microbes.Another cause for antimicrobial effects of MgO nanoparticles is that the generation of reactive oxygen species (ROS)[40],which can destroy and inactivate fundamental biomolecules, including DNA, proteins, and lipids ,as the concentration of nanoparticles increase the amount of ROS species also increases which may explained the reason for increasing antimicrobial effects of nano as the concentration of it increased.[41].

The reduction in *Candida albicans* adhesion may also attributed to increasing in surface hydrophilicity of acrylic by incorporating MgO NPs into acrylic.Zhao *et al*. [42] have stated that MgO NPs are improving the hydrophilicity of the polylactic acid (PLA) modified matrix. Hydrophobic interaction is one of the factors which influences the attachement of *Candida albicans* to acrylic prosthesis , because poly methylmethacrylate has a hydrophobic properties,so many studies are directed toward improving hydrophilicity of PMMA surface by making some modification like a study performed by Azuma *et al*.[43],who modified acrylic denture surface by coating with silica nanoparticles.Their study have shown a decrease in *Candida albicans* adherence due to increase hydrophilicity of the surface.

CONCLUSION

The MgO nanoparticles affected *Candida albicans* adhesion.It showed that there is a significant reduction in the number of *Candida albicans* cells attached to cold-cured acrylic modified with it;and this reduction was increased as the concentration of MgO nanoparticles has increased.

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