

Evaluating the Biocompatibility of Maxillofacial Silicone Enhanced by Hexagonal Boron Nitride Particles

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Abstract

This study aims to evaluate the biocompatibility of a novel filler material intended to improve the longevity of polymer systems used in prosthetics in respect of cytotoxicity and skin irritation. RTV50F silicone elastomer incorporated with various percentages of hexagonal boron nitride (H-BN) (0.1, 0.3, 0.5, 0.7, and 1 wt%) have been tested. Silicone without H-BN was utilized as the control for comparison. The *in vitro* cytotoxicity test includes specimens (n=18) with 10 mm in diameter and 2 mm in thickness applied directly to the normal human fibroblast cell line (NHF) and incubated for 72 hours, then 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was used to determine the cell viability. The skin irritation test was conducted *in vivo*, in which specimens (n=12) with 25 mm × 25 mm dimensions were applied on the back of 5 different rabbits for 4 hours, then the skin response was evaluated after 24, 48, and 72 hours. The acquired *in vitro* data were statically analyzed using one-way ANOVA and post-hoc Tukey's tests with GraphPad Prism 8, where *P*-value < 0.05 was considered statistically significant. The H-BN powder and silicone specimens were studied via field emission scanning electron microscopy (FE-SEM). The results revealed a negligible effect of maxillofacial silicone on cell viability after 72 hours of incubation, only one group (1wt%) showed a significant difference compared to the control group but the toxicity percentage didn't exceed 30% of cell viability and there was no skin irritation during the *in vivo* test.

Keywords

Biocompatibility, Field Emission Scanning Electron Microscopy, Hexagonal Boron Nitride, Maxillofacial Silicone, MTT Assay

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1. INTRODUCTION

Maxillofacial prostheses are used on individuals who have malformations in the maxillofacial region caused by disease, trauma, or hereditary problems. Maxillofacial prostheses are made from many types of polymers. Silicone elastomers, on the other hand, are the most often utilized polymers in maxillofacial prosthodontics due to their favorable characteristics (Sahu et al., 2020). Because the maxillofacial defects cause substantial psychological and social issues in these individuals, the prosthesis has to be as realistic and aesthetically pleasant as possible, its visual and tactile qualities are crucial. Because the mechanical and physical properties of silicone prostheses degrade quickly over time, and because such prostheses are particularly difficult to repair, they should be changed frequently (Abraham et al., 2018). Improved mechanical and physical properties of silicone elastomers have been the main focus of current research by incorporating different fillers into the silicones such as nanoparticles (NPs) and microparticles, the special characteristics of these additions such as their huge surface area, high surface energy, and polarity or strong chemical

reactivity, may be related to the improvements of the physio-mechanical properties of reinforced polymers. These features enable the interaction between the particles and the polymer chains, resulting in a three-dimensional composite with special properties (Wang et al., 2014). Some of these fillers have a mild toxicity impact and can be used to enhance the antibacterial properties of the silicone (Ibrahim and Abdul-Ameer, 2021).

Boron nitride is a synthetic ceramic-based thermally conductive material made up of one molecule each of boron and nitrogen (Su et al., 2019). Additionally, it exists in four main different crystalline forms: cubic boron nitride (C-BN), hexagonal boron nitride (H-BN), wurtzite boron nitride (W-BN), and rhombohedral boron nitride (R-BN) depending on pressure and temperature. They exhibit various physio-mechanical and chemical properties depending on their crystalline forms (Xu et al., 2018).

The H-BN is the most chemically and thermally stable form among other crystalline forms of boron nitride (Su et al., 2019). Sometimes referred to as "white graphite" because it has the same structural properties as graphite (Fang et al., 2016).

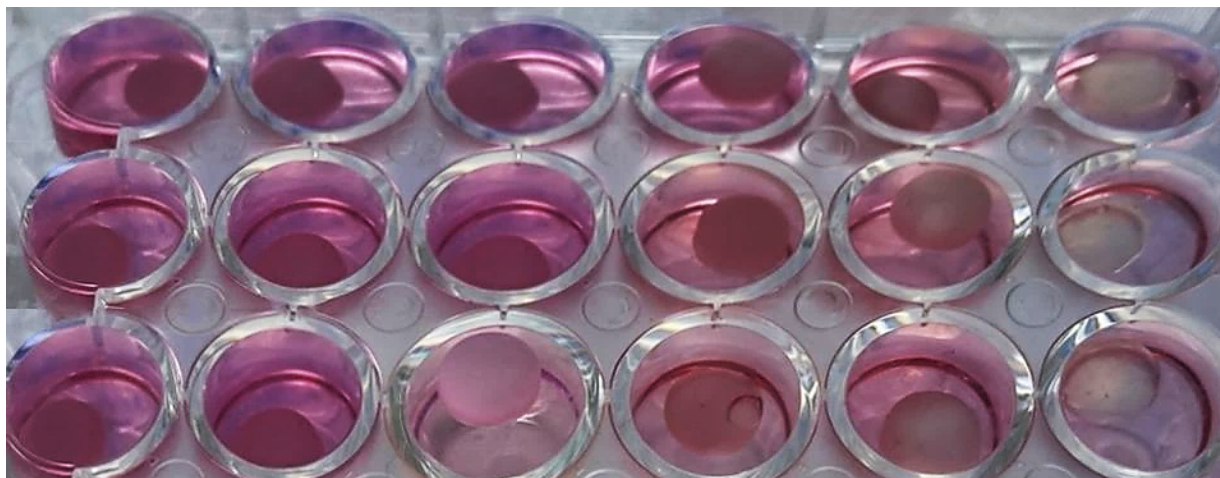


Figure 1. Cytotoxicity Test

Compared to carbon materials, H–BN has superior resistance to corrosion and wear, and its potential applications and research will grow in the coming years (Ouahad et al., 2022). Excellent thermal stability, oxidation resistance, and thermal conductivity characterize H–BN, which remains stable below 3000 °C. Its excellent chemical stability prevents it from reacting at room temperature with alkali, acid, or water (Sheng et al., 2022). Due to its unique properties, H–BN has a variety of medical applications.

The H–BN's lamellar structure is especially interesting from a tribological standpoint. The B–N link in each layer is long and the boron and nitrogen atoms are arranged in opposite directions. The trigonal orbital hybridization (sp^2) which involves the mixing of one 's' orbital and two 'p' orbitals between the atoms of nitrogen and boron creates a strong triple covalent bond between them. There is no boron–nitrogen bonding between the layers, and large interplanar distances separate the H–BN's neighboring layers, which causes only mild interactions between their atoms in the form of physical forces with an energy value of around 16.7 kJ/mol (Wang et al., 2017).

Understanding the cytotoxicity risk of H–BN is a critical prerequisite for its safe and sustainable use. The toxicity of the material is based on cell/tissue type and anatomical site, particle clearance, and repair mechanisms (Domanico et al., 2022). Kivanç et al. (2018) showed that H–BN demonstrates strong antibiofilm efficacy that stopped the biofilm of *Candida albicans*, *Staphylococcus pasteur*, and *Streptococcus mutans* from development at a amount of 0.1 - 0.4 mg/mL. Domanico et al. (2022) showed that H–BN is cytotoxic at high doses in primary mouse tracheal epithelial cells (200 g/mL), cytotoxic at moderate doses in immortalized human alveolar epithelial cells (40 and 80 g/mL), and cytotoxic at low doses in human corneal epithelial cells (4, 10, 20, and 40 g/mL). Kar et al. (2021) reported that 1.6 and 3.2 mg/kg H–BN NPs treatment could cause severe complications in the heart, kidney, liver, spleen,

and pancreas of laboratory rats (wistar albino) and that the H–BN NPs may be appropriate for biomedical applications where low doses between 0.05 and 0.8 mg/kg are not toxic.

According to the Food and Drug Administration (2023) and ISO 10993-1 (2018), the maxillofacial silicone is considered a surface medical device with long-term contact duration. Because it was modified with a novel filler material so that it required to pass many tests to be declared biocompatible and suitable for use on human.

This study is the first to uncover the biocompatibility of H–BN incorporated with maxillofacial silicone with respect to cytotoxicity and skin irritation. However, the remaining tests are still unverified and required to be completed prior to being used on humans.

2. EXPERIMENTAL SECTION

2.1 Materials

The specimens were made of VST-50F maxillofacial silicone elastomer (Factor II Inc. USA) and incorporated with H–BN (Hongwu International Group Ltd. China, 99.8%, 45-200 nm) using a vacuum mixer. The H–BN was incorporated in various weight percentages (0.1, 0.3, 0.5, 0.7, and 1 wt%). The normal human fibroblast (NHF) cell line was obtained from stock-frozen cell lines (Celprogen, USA) and was cultured in minimum essential medium (MEM) (Capricorn Scientific, Germany) supplemented with 10% (v/v) fetal bovine serum (FBS) (Capricorn Scientific, Germany), 100 IU penicillin, and 100 µg streptomycin incubated in laminar air flow cabinets (Esco, Korea) at 37 °C for 24 hours for attachment and monitored by an inverted microscope (Meiji-Techno, Japan). Exponentially growing cells were used for experiments (Salman et al., 2022).

2.2 Methods

The H–BN powder and the silicone specimens were examined using a field emission-scanning electron microscope (FE-SEM) (Quanta FEG 200, FEI, Netherland). It was used to investigate

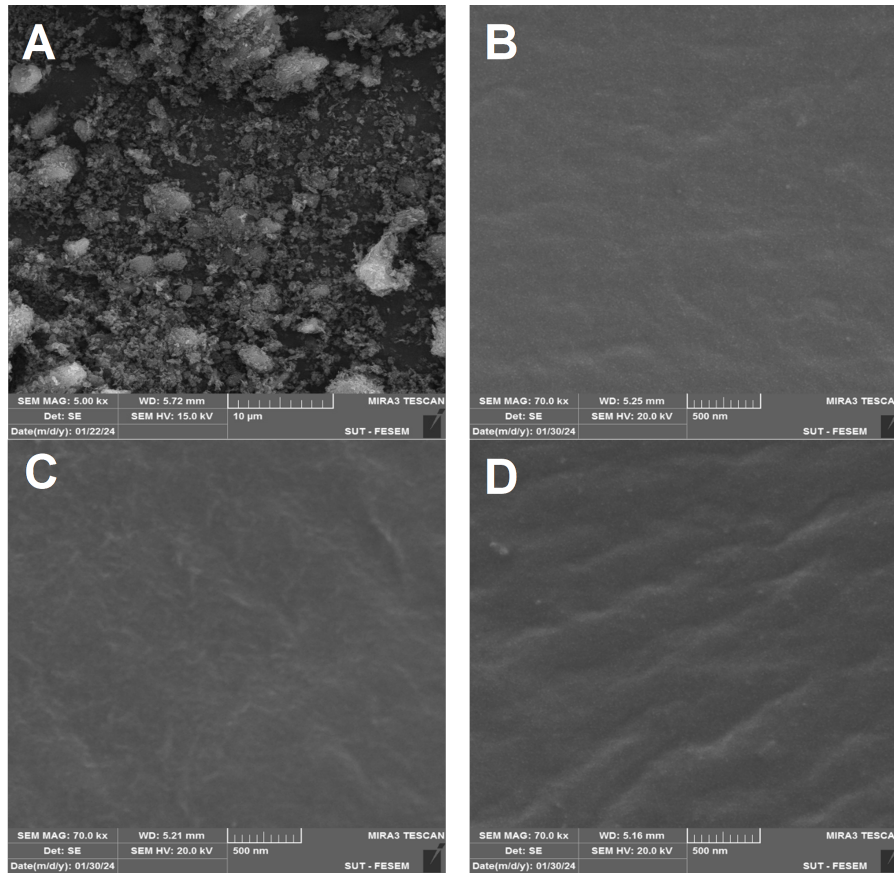


Figure 2. FE-SEM Images: A. Hexagonal Boron Nitride Powder; B. Maxillofacial Elastomer Alone; C. Maxillofacial Elastomer with 0.5 wt% Hexagonal Boron Nitride; D. Maxillofacial Elastomer with 1 wt% Hexagonal Boron Nitride

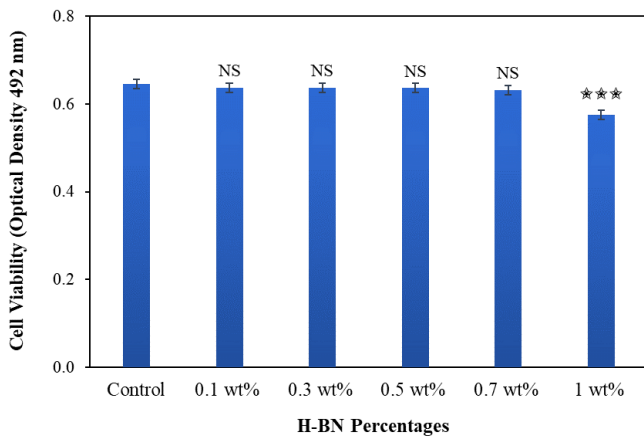


Figure 3. Cell Viability After 72 Hours

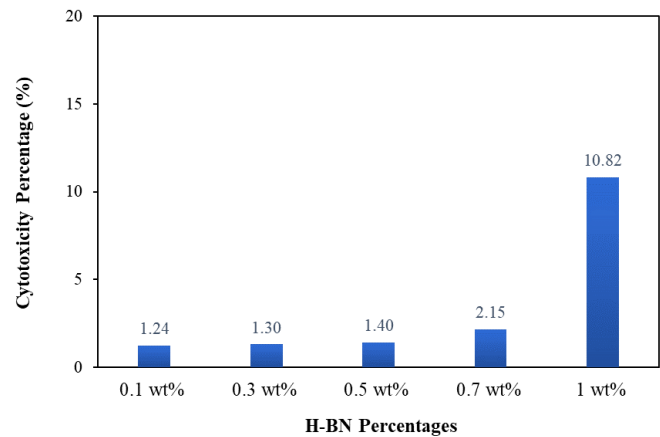


Figure 4. Cytotoxicity Percentage of Enhanced Maxillofacial Silicone

the H-BN particles and to compare the control group and experimental specimens by studying the topography of objects and showing the degree of H-BN dispersion within the silicon matrix. The FE-SEM operates by forcing the surface of the specimen with an electron beam focused by electromagnetic lenses. The reflected/interacted electrons form a picture of the

surface of the specimen and topography (Abd Mutalib et al., 2017).

Silicone elastomer is a type of polymeric material which means that it acts as an isolating form for the electrons of the FE-SEM beam causing the reflection of electrons just like the

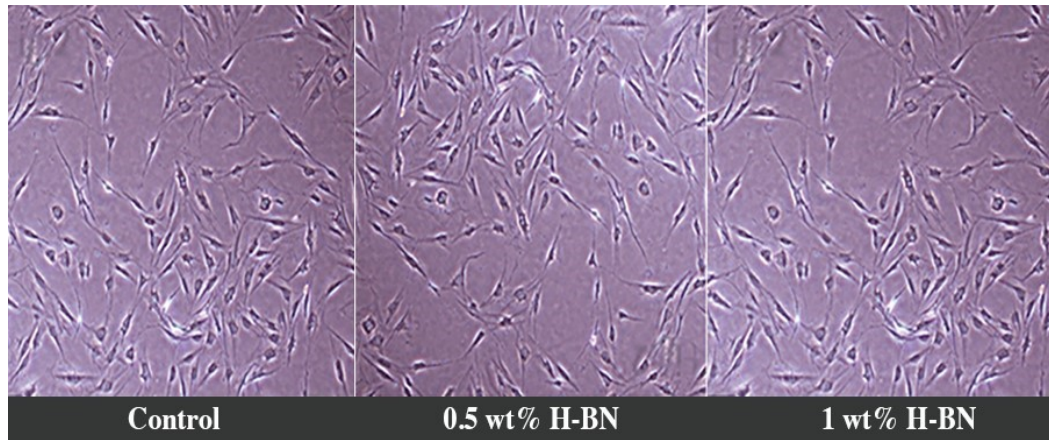


Figure 5. Microscopic Evaluation

Table 1. Scoring System for Skin Reaction

Reaction	Numerical Grading
Erythema and eschar formation	
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate erythema	3
Severe erythema (beet-redness) to eschar formation	4
Oedema formation	
No oedema	0
Very slight oedema (barely perceptible)	1
Well-defined oedema (edges of area well-defined by definite raising)	2
Moderate oedema (raised approximately 1 mm)	3
Severe oedema (raised more than 1 mm and extending beyond exposure area)	4
Maximal possible score for irritation	8

mirror. For this reason, the specimens are covered with a thin gold layer to allow the diffusion of electrons inside the specimen (Abd Mutalib et al., 2017).

Silicone without filler was utilized as the control for comparison. For the cytotoxicity test, disc specimens (n=18), measuring 10 mm in diameter and 2 mm in thickness were manufactured in accordance with Akay et al. (2016); Tukmachi et al. (2021), a direct contact test was carried out according to ISO 10993-5 (2009) together with a quantitative cytotoxicity assessment including counting the number of viable cells. For the skin irritation test, specimens with 25 mm × 25 mm dimensions (n=12) were used according to ISO 10993-23 (2021).

The experimental specimens were sterilized in an autoclave for 15 minutes at 121°C to prevent bacterial contamination. NHF cells were seeded at a density of 10000 cells in a microplate and incubated with the silicone specimens at 37 °C for 72 hours then the silicone specimens were removed and cytotoxicity was investigated through the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay (Elab-

science, China). MTT dye solution of 28 μL of (2 mg/ml) was placed in each well with three hours of incubation. Viable cells convert the MTT into purple formazan (Figure 1), which can be solubilized, and its concentration is determined by measuring the absorbance at a specific wavelength using a spectrophotometer. The amount of formazan produced is directly proportional to the number of viable cells. The decrease in formazan production and thus a decrease in absorbance after treatment of the test compound indicates cytotoxicity. Then the medium containing the residual MTT was removed. A total of 100 μL of dimethyl sulfoxide was added to each well and incubated for 15 minutes to dissolve the insoluble purple formazan into a colored solution (Salman et al., 2022). The optical density was measured at 492 nm using a microplate reader (Thermo Fisher Scientific, USA) and microscopic evaluation was completed before the addition of MTT. The optical density data were analyzed using one-way ANOVA and post-hoc Tukey's tests with GraphPad Prism 8, where P-value < 0.05 was considered statistically significant.

Cytotoxicity percentage was calculated using Equation (1):

Table 2. Skin Irritation Test on Rabbits

Rabbit No.	Pretest Weight (kg)	Final Weight (kg)	Groups	Reaction	Interval (hours)		Score (left/right)	
					24	48	72	
1	2.06	2.09	Control	Erythema	0/0	0/0	0/0	
				Oedema	0/0	0/0	0/0	
			0.1 wt% H-BN	Erythema	0/0	0/0	0/0	
				Oedema	0/0	0/0	0/0	
2	2.11	2.13	Control	Erythema	0/0	0/0	0/0	
				Oedema	0/0	0/0	0/0	
			0.3 wt% H-BN	Erythema	0/0	0/0	0/0	
				Oedema	0/0	0/0	0/0	
3	2.16	2.20	Control	Erythema	0/0	0/0	0/0	
				Oedema	0/0	0/0	0/0	
			0.5 wt% H-BN	Erythema	0/0	0/0	0/0	
				Oedema	0/0	0/0	0/0	
4	2.11	2.15	Control	Erythema	0/0	0/0	0/0	
				Oedema	0/0	0/0	0/0	
			0.7 wt% H-BN	Erythema	0/0	0/0	0/0	
				Oedema	0/0	0/0	0/0	
5	2.13	2.18	Control	Erythema	0/0	0/0	0/0	
				Oedema	0/0	0/0	0/0	
			1 wt% H-BN	Erythema	0/0	0/0	0/0	
				Oedema	0/0	0/0	0/0	
Primary Irritation Index							0	

$$\text{Cytotoxicity Percentage} = \frac{(\text{OD Control} - \text{OD Specimen})}{\text{OD Control}} \times 100 \quad (1)$$

Where:

OD control is the mean optical density of the control wells.

OD specimen is the mean optical density of the experimental wells.

According to [ISO 10993-5 \(2009\)](#), the material is considered toxic when it causes a diminishing of cell viability of more than 30%.

The skin irritation test includes a total of 5 (3 females, 2 males) Blanc de bouscat rabbits, weighing (2-2.2 kg) and aged (10-12 months) were used in this study, the cage's area was more than 3500 cm² and the height was more than 45 cm according to the [European Union Council \(1986\)](#). The rabbits were kept in a room at a constant humidity (55 ± 10 %) and temperature of (15 - 21 °C) with 12 hours of light/dark cycle ([Brandstetter et al., 2015](#)). Skin irritation test was performed according to [ISO 10993-23 \(2021\)](#). This test was approved by the Ethics Committee at the University of Baghdad/College of Dentistry (reference no. 866). The fur was typically trimmed from the rabbits' backs within 24 hours, leaving about 10 to 15 cm on either side of the spine to allow appropriate applica-

tion and observation of all test locations. The specimens were applied directly to the skin, four specimens were used on each rabbit (2 from the control group, 2 from the single test group), and the specimens were moistened with distilled water to allow good contact with the skin, and then the application sites were covered by non-occlusive dressings (gauze patch) and then sealed with an occlusive bandage for a minimum of 4 hours. At the end of the contact time, the dressing was removed, and the rabbits' backs were washed with warm water. The scores of skin reaction for erythema and oedema were described according to the scoring system given in (Table 1) for each application site at each time interval. The appearance of each application site was observed at (1 ± 0.1), (24 ± 2), (48 ± 2), and (72 ± 2) hours following removal of the specimens. Only (24 ± 2), (48 ± 2), and (72 ± 2) hours observations were used for calculations. At the end of the observations, all erythema and oedema grades are totaled separately for each rabbit. The primary irritation score is determined by dividing the total of all values of the single group by six. The primary irritation index indicates the appropriate response category for the report.

3. RESULTS AND DISCUSSION

The FE-SEM images (Figure 2) showed that the H-BN particles were well-dispersed inside the VST-50F silicon matrix. The process of agglomeration is controlled by thermodynamics.





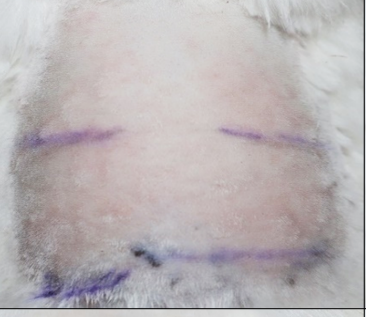
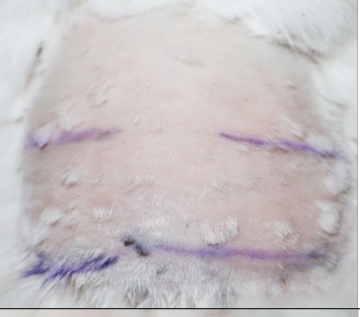









Groups	24 hours	48 hours	72 hours
0.1 wt%			
0.3 wt%			
0.5 wt%			
0.7 wt%			
1 wt%			

Figure 6. Skin Irritation Test on Rabbits, the Control Sites are the Top Right and the Bottom Left

Depending on the interaction, ensembles are made up of either weakly agglomerated (repelling) or strongly agglomerated (attracting) particles (Vollath, 2020). In this study, some agglomerations occurred within the silicone specimens as H-BN loading increased.

MTT assay which is used for *in vitro* cytotoxicity test indicates a negligible effect of maxillofacial silicone enhanced by H-BN on cell viability, which indicates no toxic effect (Figures 3 and 4).

The microscopic evaluation showed that there were no morphological changes in the NHF cells after 72 hours of incubation with the modified silicone (Figure 5).

The skin irritation test showed that all rabbits were fine, and no unusual symptoms were detected during the study. The skin's reaction on the testing side was not greater than that of the control side with the help of the inter-reliability test. As a result, it was determined that the primary irritation index was zero (Table 2), and the test's reaction was classified as negligible. The observations are shown in Figure 6.

Three categories of *in vitro* tests exist; the extract test, the direct contact test, and the indirect contact test. Because of the possibility of variations in the extraction properties between the intact and sliced surfaces, elastomer materials should be evaluated in their complete form whenever possible (ISO 10993-5, 2009). Several procedures, including the agar overlay test, Millipore filter test, dye exclusion assay, and MTT assay, can be used to verify the cytotoxic of biomaterials *in vitro* (Hussein and Mohsin, 2019; Sjögren et al., 2000). Since both the quantity of cells and their metabolic state are shown in the test findings, the MTT method is recognized as a reliable indicator of biomaterials' cytotoxicity. Simple, quick, repeatable, and radioisotope-free are the benefits of this assay (Ozdemir et al., 2009).

Although that the previous studies used extract test *in vitro* to evaluate the toxicity of the H-BN. In that test, the H-BN particles were freshly suspended in culture media and sonicated at room temperature to prevent agglomeration before being exposed to the cell line (Domanico et al., 2022; Kivanç et al., 2018).

In this study, H-BN particles were integrated into the silicone, and the direct contact test was done, in which the silicone specimens were directly placed in the cell culture medium to determine the toxicity. The cytotoxicity percentage of the silicone specimens up to 1 wt% H-BN didn't surpass 30%, indicating their safety. Disturbances in cell proliferation and genes and proteins involved in DNA replication were the main causes of cytotoxicity. Additionally, oxidative stress was produced by H-BN, amplifying their cytotoxic effects (Mao et al., 2023). Oxidative stress leads to increased ROS levels inside cells which damage DNA, lipids, and proteins (Schieber and Chandel, 2014).

The unsaturated boron atoms near the outer edge of the H-BN promote the generation of oxidative stress (Xie et al., 2021). The larger amount of the H-BN particles' surface would indicate the presence of more unsaturated boron atoms,

and since these atoms are highly reactive, they would create more ROS and compensate for the rising toxicity as particle diameters decrease (Merlo et al., 2018). Since the H-BN particles were effectively distributed throughout the silicon matrix, the toxicity of the unsaturated boron atoms has decreased to a suitable degree by preventing them from coming into contact with the cells. This aligns with previous research, which demonstrated no interaction between the filler material and the silicone (AbdulKareem and Hamad, 2019). The silicone elastomers are in touch with the skin for a duration longer than the study's findings suggest. Longer-term research in clinical circumstances may differ from those found in cell culture assays and *in vivo*. Thus, one drawback of this research is the use of a single cell line for cytotoxicity assessment.

4. CONCLUSIONS

It may be assumed that the H-BN added to the silicone elastomer used in the manufacture of maxillofacial prosthesis is harmless up to 1 wt%. However, the remaining biocompatibility tests are required to be finished before being used on humans.

5. ACKNOWLEDGMENT

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REFERENCES

- Abd Mutalib, M., M. A. Rahman, M. H. D. Othman, A. F. Ismail, and J. Jaafar (2017). Chapter 9 - Scanning Electron Microscopy (SEM) and Energy-Dispersive X-Ray (EDX) Spectroscopy. In N. Hilal, A. F. Ismail, T. Matsuura, and D. Oatley-Radcliffe, editors, *Membrane Characterization*. Elsevier, pages 161–179
- AbdulKareem, A. A. and T. I. Hamad (2019). The Effects of Nano Alumina On Mechanical Properties of Room Temperature Vulcanized Maxillofacial Silicone (Pilot Study). *Journal of Baghdad College of Dentistry*, **31**(4); 1–8
- Abraham, H. M., P. Dhamini, J. M. Philip, C. J. Venkatakrishnan, and C. R. Chandran (2018). A Review of Materials Used in Maxillofacial Prosthesis - Part 1. *Dental Implants Today*, **10**; 1067–1070
- Akay, C., P. Cevik, D. Karakis, and H. Sevim Akan (2016). In Vitro Cytotoxicity of Maxillofacial Silicone Elastomers: Effect of Nano-Particles. *Journal of Prosthodontics*, **27**; 190–198
- Brandstetter, H., W. Eichelkraut, A. Haemisch, G. Hilken, R. Kluge, R. Post, M. Scheer, and R. Tolba (2015). *Specialist Information Planning and Organization of Laboratory Animal Housing Units and Laboratories*. GV-SOLAS
- Domanico, M., A. Fukuto, L. M. Tran, J. M. Bustamante, P. C. Edwards, K. E. Pinkerton, S. M. Thomas, and L. S. Van Winkle (2022). Cytotoxicity of 2D Engineered Nano-

- materials in Pulmonary and Corneal Epithelium. *NanoImpact*, **26**; 100404
- European Union Council (1986). Council Directive 86/609/EEC of 24 November 1986 on the Approximation of Laws, Regulations and Administrative Provisions of the Member States Regarding the Protection of Animals Used for Experimental and Other Scientific Purposes. *Official Journal of the European Communities*, **358**; 1–28
- Fang, H., S.-L. Bai, and C. P. Wong (2016). "White Graphene" – Hexagonal Boron Nitride Based Polymeric Composites and Their Application in Thermal Management. *Composite Communications*, **2**; 19–24
- Food and Drug Administration (2023). Use of International Standard ISO 10993-1, "Biological Evaluation of Medical Devices - Part 1: Evaluation and Testing within a Risk Management Process
- Hussein, R. A. and A. J. Mohsin (2019). Trypan Blue Exclusion Assay Verifies In Vitro Cytotoxicity of New Cis-Platinum (II) Complex in Human Cells. *Baghdad Science Journal*, **16**(3); 555–561
- Ibrahim, H. and F. Abdul-Ameer (2021). Influence of Kappa-Carrageenan Powder Addition on Staphylococcus Epidermidis Adhesion on the Room Temperature Vulcanized Maxillofacial Silicone. *Pakistan Journal of Medical and Health Sciences*, **15**; 359–362
- ISO 10993-1 (2018). Evaluation and Testing within a Risk Management Process
- ISO 10993-23 (2021). Biological Evaluation of Medical Devices-Tests for Irritation.
- ISO 10993-5 (2009). Biological Evaluation of Medical Devices - Tests for In Vitro Cytotoxicity
- Kar, F., C. Hacıoğlu, Y. Göncü, . Söğüt, H. Şentürk, D. Burukoğlu Dönmez, G. Kanbak, and N. Ay (2021). In Vivo Assessment of the Effect of Hexagonal Boron Nitride Nanoparticles on Biochemical, Histopathological, Oxidant and Antioxidant Status. *Journal of Cluster Science*, **32**(2); 517–529
- Kıvanç, M., B. Barutca, A. T. Koparal, Y. Göncü, S. H. Bostancı, and N. Ay (2018). Effects of Hexagonal Boron Nitride Nanoparticles on Antimicrobial and Antibiofilm Activities, Cell Viability. *Materials Science and Engineering C*, **91**; 115–124
- Mao, Y., Q. Guo, X. Geng, H. Zeng, S. Liu, X. Yin, and Z. Yang (2023). Hexagonal Boron Nitride Nanodots Inhibit Cell Proliferation of HUVECs and the Underlying Mechanism. *Colloids and Interface Science Communications*, **56**; 100738
- Merlo, A., V. R. S. S. Mokkapatil, S. Pandit, and I. Mijakovic (2018). Boron Nitride Nanomaterials: Biocompatibility and Bio-Applications. *Biomaterials Science*, **6**(9); 2298–2311
- Ouahad, O., H. A. Merad, T. Hidouri, I. S. Yahia, and H. Y. Zahran (2022). Probing the Physical Properties of Boron Nitride with Randomly Distributed Vacancies: A Promising Semiconductor for Optoelectronics. *Solid State Communications*, **348**; 114744
- Ozdemir, K. G., H. Yilmaz, and S. Yilmaz (2009). In Vitro Evaluation of Cytotoxicity of Soft Lining Materials on L929 Cells by MTT Assay. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, **90**(1); 82–86
- Sahu, N., A. S. Vathare, R. V. C. Tiwari, S. Kumar, S. Meshram, and H. D. Tiwari (2020). Aesthetic Management in Maxillofacial Prosthesis - A Review. *Saudi Journal of Medicine*, **5**(2); 90–94
- Salman, M. I., A. M. Al-Shammari, and M. A. Emran (2022). 3-Dimensional Coculture of Breast Cancer Cell Lines with Adipose Tissue-Derived Stem Cells Reveals the Efficiency of Oncolytic Newcastle Disease Virus Infection via Labeling Technology. *Frontiers in Molecular Biosciences*, **9**; 754100
- Schieber, M. and N. S. Chandel (2014). ROS Function in Redox Signaling and Oxidative Stress. *Current Biology*, **24**(10); R453–R462
- Sheng, M., R. Yang, H. Gong, Y. Zhang, X. Lin, and J. Jing (2022). Enhanced Thermal Conductivity and Stability of Boron Nitride/Phenyl Silicone Rubber Composites via Surface Modification and Grain Alignment. *Journal of Materials Science*, **57**(10); 5805–5824
- Sjögren, G., G. Sletten, and J. E. Dahl (2000). Cytotoxicity of Dental Alloys, Metals, and Ceramics Assessed by Millipore Filter, Agar Overlay, and MTT Tests. *Journal of Prosthetic Dentistry*, **84**(2); 229–236
- Su, C., Z. Yin, Q. B. Yan, Z. Wang, H. Lin, L. Sun, W. Xu, T. Yamada, X. Ji, N. Zettsu, K. Teshima, J. H. Warner, M. Dincă, J. Hu, M. Dong, G. Su, J. Kong, and J. Li (2019). Waterproof Molecular Monolayers Stabilize 2D Materials. *Proceedings of the National Academy of Sciences of the United States of America*, **116**(42); 20844–20849
- Tukmachi, M., I. N. Safi, and M. Ali (2021). Evaluation of Mechanical Properties and Cytotoxicity of Maxillofacial Silicone Material after Incorporation of Zirconia Nanopowder. *Materials Today: Proceedings*, **42**; 3061–3066
- Vollath, D. (2020). Agglomerates of Nanoparticles. *Beilstein Journal of Nanotechnology*, **11**; 854–857
- Wang, J., F. Ma, and M. Sun (2017). Graphene, Hexagonal Boron Nitride, and Their Heterostructures: Properties and Applications. *RSC Advances*, **7**(27); 16801–16822
- Wang, L., Q. Liu, D. Jing, S. Zhou, and L. Shao (2014). Biomechanical Properties of Nano-TiO₂ Addition to a Medical Silicone Elastomer: The Effect of Artificial Ageing. *Journal of Dentistry*, **42**(4); 475–483
- Xie, X., Z. Hou, G. Duan, S. Zhang, H. Zhou, Z. Yang, and R. Zhou (2021). Boron Nitride Nanosheets Elicit Significant Hemolytic Activity via Destruction of Red Blood Cell Membranes. *Colloids and Surfaces B: Biointerfaces*, **203**; 111765
- Xu, C., M. Miao, X. Jiang, and X. Wang (2018). Thermal Conductive Composites Reinforced via Advanced Boron Nitride Nanomaterials. *Composite Communications*, **10**; 103–109