

EFFECT OF TiO₂ DECORATED CELLULOSIC MATERIALS ADDITION ON PHYSICAL AND BIOLOGICAL PROPERTIES OF A DENTAL ADHESIVE COMPOSITE

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The purpose of this study was to prepare cellulose fibers decorated with titanium dioxide, and then incorporate them into the formulation of dental adhesive composites. The influence of this filler on the mechanical, chemical, and biological characteristics of the composites was examined. Different proportions of the filler were mixed with the monomers and then the prepared materials were analyzed through chemical, mechanical, and microscopic characterization. Biocompatibility tests were performed using fibroblast cell lines. Mechanical characterization included the hardness test, the biaxial flexural strength (BFS) test, and the shear bond strength test (SBT). The fillers were found biocompatible, as suggested by the Alamar blue assay, while the mechanical properties of the composites increased with higher filler content. The experimental composite presented good physical and biological properties, and thus, it can be used as a dental adhesive material.

Keywords: cellulose, titanium dioxide, filler, adhesive composite, strength

INTRODUCTION

The evolution of dental adhesive materials has led to remarkable improvements in adhesive and restorative dentistry.¹ These materials adhere either micromechanically or chemically to the tooth structure and do not need any mechanical retentive feature, including grooves, dovetails, sharp internal angles, and undercuts. As these features are not required in modern adhesive materials, a sound tooth structure is conserved.² Besides this, the incidence of secondary caries due to microleakage may be either diminished or eliminated by use of these advanced adhesive materials and systems.³ After the introduction of the acid etching technique by Buonocore, in 1955, this method did not get any success until the synthesis of bis-GMA by Bowen. This invention led to the concept of adhesive materials in restorative dentistry.⁴ This concept got popularity due to the high demand of esthetic restorations. Therefore, the advancement resulted in different types and generations of adhesive materials. Still, researchers have been continuously working to improve these materials with new concepts, to introduce new variations in the technique, chemistry, and mechanism of the adhesives and their effectiveness.¹

With the use of a good adhesive, the restoration lasts for a longer time. Adhesion to dentin is complex. Due to the application of the adhesive, collagen fibrils are exposed, leading to the activation of metal proteinases and cysteine cathepsins, which gradually destroy the collagen fibrils. So, it is difficult to achieve a stable bond with dentin.⁵ Nowadays, various methods are used to stabilize the bonding of adhesive materials with dentin, including the addition of collagen cross-linking agents, antioxidants, protease inhibitors, and strengthening the resin matrix with fillers and/or remineralizing agents. Moreover,

modification of the bonding procedure, and laser treatment of the substrate prior to bonding are also done in order to achieve a stable bond.³

The matrix of dental adhesives can be reinforced with nanoparticles and fillers to strengthen the interaction between the resin and dentin.⁶ Nanoparticles of titanium dioxide, copper, silver, zirconia, and zinc oxide have been incorporated into the resin matrix of dental adhesives to increase their strength.⁷ Microcrystalline cellulose is a natural polymer that consists of many monosaccharide units connected by β -(1 $\rightarrow$ 4)-glycosidic bonds.⁸ It is a polymeric material obtained from plants or microorganisms.⁹ It has numerous applications in food products, in medical and pharmaceutical fields, paper and board industries, due to its low cost, easy availability, low density, and outstanding mechanical properties.¹⁰ It has tensile strength of approximately 500 MPa, with nearly similar values to those of aluminum, and stiffness of about 140–220 GPa.¹¹ In dentistry, it has been utilized in surgical dressings, the regeneration of pulp and periodontal tissues, as well as for intraoral wounds. Although cellulose has excellent properties, it does not possess antimicrobial activity, which is of high importance in dentistry.¹²

Titanium dioxide (TiO₂) is a fine, white powder, in which oxygen is bound to titanium through a double covalent bond. It is used in cosmetics, paper, sunscreen, and toothpaste, due to its shape and surface chemistry, as well as due to its resistance to corrosion caused by the formation of the oxide layer.¹³ It is widely used considering its easy availability, good biocompatibility, and antimicrobial potential. Furthermore, it is economical and has good mechanical properties, such as high strength and wear resistance. It has been used in dentistry as a coating for dental implants, and as filler in dental resins due to its antimicrobial properties.¹⁴

Therefore, in this study, novel filler particles were synthesized by decorating cellulose fibers with titanium dioxide, to combine the known antibacterial activity of TiO₂ with the mechanical properties of cellulose fibers. The prepared fillers were added into the formulation of dental adhesives in various concentrations and their effect on the mechanical and biological properties of composite adhesives were examined.

EXPERIMENTAL

Synthesis of TiO₂ decorated cellulosic fillers

All the materials used in this experiment were of analytical grade and were obtained from Sigma Aldrich. The cellulose fibers were dispersed in distilled water, under magnetic stirring at 400 rpm, while TiO₂ was dispersed in water through ultrasonication. The TiO₂ suspension was then added dropwise to the cellulose suspension, followed by stirring for three hours to ensure the complete adsorption/decoration of TiO₂ on the surface of cellulose fibers. After stirring, the sample was centrifuged at 12000 rpm to obtain the precipitate that was dried in an oven for 24 hours to achieve the desired fillers in various ratios.

Synthesis of experimental adhesives

For the synthesis of experimental dental adhesives, initially, bisphenol A-glycidyl methacrylate (*bis*-GMA) and triethylene glycol dimethacrylate (TEGDMA) were mixed in the ratio of 60:40 wt/wt, respectively. After mixing the monomers, photo-initiator Camphorquinone (CQ) and activator dimethyl amino ethyl methacrylate (DMAEM) were added (0.5 wt% each) and the mixture was stirred for 30 min in the dark, at room temperature, to prevent immature polymerization. This was done in order to have a homogenous solution. Then, the TiO₂ decorated cellulosic filler was added in increments and stirred for 2 hours. A total of five groups of experimental composites were synthesized containing different proportions of cellulose/titanium dioxide filler, as given in Table 1.

Characterization of fillers

To analyze the functional groups, a Fourier transform infrared spectrophotometer (IR Tracer-100, Shimadzu Corporation, Japan) was used. About 256 scans were performed with the resolution of 8 cm⁻¹ over the region of 4000–400 cm⁻¹.¹⁵ Using electron microscopy (Model: L1600300, England), the surface morphology of the fillers was examined. After gold sputtering for 90 s at 10 mA current, images were captured at various magnifications and 15 kV of accelerated voltage was applied. Energy dispersive spectroscopy (EDS) was used to carry out the elemental analyses.¹⁶

Using an X-ray diffractometer (JDX-3532, JEOL, Japan), the X-ray diffraction (XRD) patterns of each group of samples were obtained with monochromatic Cu-K _{α} radiations (λ = 1.54 Å). Scans were taken in the 2 θ range of $\approx$ 20–

80°, with a step size of 0.02° every 1 second.¹⁷ Thermal gravimetric analysis (TGA) (E112245, MET Company, USA) was performed to examine the thermal behavior of the cellulose/titanium dioxide dental filler between 50 and 800 °C. One sample of each group was heated by N₂ gas at a rate of 10 °C per minute.¹⁸

Table 1
Composition of experimental composites

Groups	Resin monomers (wt%)	Cellulose/titanium dioxide ratio (wt%)
1	<i>bis</i> -GMA = 60%	0% cellulose, 5% titanium dioxide
2	TEGDMA = 40%	1% cellulose, 4% titanium dioxide
3	DMAEM = 0.5%	2% cellulose, 3% titanium dioxide
4	CQ = 0.5%	3% cellulose, 2% titanium dioxide
5		4% cellulose, 1% titanium dioxide

Biocompatibility of fillers

A fibroblast cell line NIH/3T3 was grown in a medium consisting of DMAEM supplemented with 100 g/mL of Penicillin/streptomycin (Sigma Aldrich, Life Sciences, USA) and 10 percent fetal bovine serum (Sigma Aldrich, Life Sciences, USA). In the Corning Biosystem T75 culture flask, NIH/3T3 cells were proliferated. The cells were then propagated and cultivated to 90% confluence in a moistened incubator at 37 °C with 5% CO₂ and media were changed after every two days. The cells were then removed using trypsin–EDTA (Sigma Aldrich, USA).

The cells were counted using a hemacytometer and a microscope on the day of seeding. The compatibility between NIH/3T3 cells and cellulose and titanium-cellulose particles was evaluated by seeding 50,000 cells on each specimen in 24-well plates. Before seeding, the samples were cleaned with 70% ethanol for 24 hours, followed by three 15-minute intervals of washing with 1x phosphate buffered saline. Then, 1 mg of the powder sample was added to 1 mL of DMAEM medium. As a control, cells were cultivated on tissue culture plastic plates, without specimens, for comparison with cells cultured in the presence of liquid specimens. There were three samples in each sample group.

The fluorescent plate reader measurements of the Alamar Blue assay were performed after 3 days to test the biocompatibility between the powder samples and the cells. Due to the presence of a redox indicator formed when the substrate is taken up by the cells, Alamar blue transforms from an oxidized (blue) form to a reduced (red) form based on the metabolic activity of the cells. The 0.5 mL of cells were added to 1 mL of Alamar Blue solution and incubated at 37 °C for 3 to 4 hours. The absorbance was recorded at 570 nm with the help of a fluorescence plate reader. A total of three samples were included in each test group.¹⁹

Mechanical testing of experimental adhesive composites

The mechanical properties of the prepared adhesive materials with the incorporation of the developed fillers and without, *i.e.*, biaxial flexural strength (BFS), Vickers hardness and shear bond (SBT), were evaluated according to ISO 6872:2008, ASTM E384-11e and ISO 29022:2013, respectively. The samples were immersed into a simulated body fluid at 37 °C for seven days before mechanical testing. For measuring each mechanical property, 5 samples were taken from each group.

Biaxial flexural strength (BFS)

The BFS of the experimental adhesive composites was determined by the piston-on-ring technique. The electrodynamic fatigue testing system, having a load cell of 1.5 kN, was used. Disc-shaped specimens, having 10 mm diameter and 4 mm thickness, were placed in the center of the ring with a diameter of 8 mm. The load was exerted *via* a flat punch (1 mm diameter) in the middle of the sample at a crosshead speed of 0.5 mm/min.²⁰ Fracture load (N) was noted for each sample and BFS was calculated through the following equation:

$$\sigma_{BI} = \frac{-0.2387P(X-Y)}{b^2} \quad (1)$$

where σ_{BI} is BFS in MPa, P = fracture load (N), b = specimen disk thickness at fracture origin (mm). X and Y were determined as follows:

$$X = (1 + \nu) \ln(r_2/r_3)^2 + [(1 + \nu)/2](r_2/r_3)^2 \quad (2)$$

$$Y = (1 + \nu)[1 + \ln(r_1/r_3)^2] + (1 - \nu)(r_2/r_3)^2 \quad (3)$$

where ν represents Poisson's ratio and it is expected to be 0.25 for composites, r_1 represents the radius of the support circle (mm), r_2 represents the radius area under the applied load (mm), and r_3 – the radius of specimen (mm).²¹

Shear bond strength (SBT)

For measuring the shear bond strength of the prepared adhesive materials, bovine (cow) teeth were used.²² Before application of the dental adhesive, the dentin of the teeth was exposed, and they were acid etched for 30 seconds with 37% phosphoric acid, followed by washing and drying. After complete drying, dental composite adhesive was applied to the etched dentin, as a filling with dimensions of 3 mm diameter and 6 mm height. This dimension was achieved with the help of a plastic tube chamfered at 45° to minimise its contact area. The SBT was determined using a Universal Testing Machine (model: M500-100KN, Testometric Company, United Kingdom), with a “flat-edge shear fixture” jig having 1.5 kN load cell and a cross-head speed of 0.5 mm/min. The load at break was measured and the bond strength τ was determined using the equation below, in which F is the load, and A is the bonded area:²³

$$\tau = \frac{F}{A} \quad (4)$$

Vickers hardness test

For determining the hardness of experimental composites, disc-shaped specimens (8 mm × 4 mm) were made and a total of three indentations were made on each sample, using a hardness tester (HVS-1000, China).²⁴ Vickers hardness was measured by applying 0.98 N force for 15 seconds, with a diamond indenter, and calculated using the following formula:²⁵

$$HV = 1.854 F / d_o \quad (5)$$

where HV – Vickers hardness number, F – indentation load, and d_o – indentation diagonal.

RESULTS AND DISCUSSION

Fourier-transform infrared spectroscopy (FTIR)

The FTIR spectra of the dental filler formulations (neat titanium dioxide and with the addition of various cellulose amounts) were recorded between 4000-400 cm^{-1} and are shown in Figure 1. In Figure 1, as well as in further figures and tables, the sample groups were named according to the content of cellulose in their formulation. The peaks of various functional groups present in the materials can be identified. The broad peak corresponding to -OH stretching in cellulose can be observed in the range of 3000-3700 cm^{-1} . The C-H bending and stretching vibration due to -CH₂ -C6 bonding appears at 1430-2900 cm^{-1} . C-O-C bending was observed at 1010 cm^{-1} . The peak related to TiO₂ was observed at 2124 cm^{-1} in all the fillers. The methane groups (C-H) and hydroxyl groups (O-H) in cellulose were observed in the axial position and equatorial position, respectively, similarly to the findings by Kim *et al.*²⁶ The peak related to TiO₂ was observed at 2124 cm^{-1} in all the fillers, which is in accordance with the study reported by L. Khalid.²⁷

X-ray diffraction analysis (XRD)

XRD provides information about the crystallinity of a material. The XRD patterns of the experimental dental fillers are shown in Figure 2. Through X-ray diffraction, data were collected at 10-70 degrees in the 2-theta range. All the fillers showed characteristic peaks at 25, 37, 47, 55 and 63, which are related to TiO₂. However, the fillers containing 3 and 4% cellulose showed a characteristic broad peak of cellulose at a 2theta value of 22.5, while the fillers with 1-2% cellulose did not show any such peak.

Zhao *et al.* used XRD to examine hydrogen bonding in different phases of cellulose.²⁸ In cross-section, the cellulose chains have the shape of flat ribbons due to crystalline packing.²⁹ Hydroxyl groups are present on the thin edges, while C-H groups are present on the flat sides of the ribbons. Therefore, the edges are hydrophilic, while the flat sides are hydrophobic.³⁰ Intense peaks in XRD show crystalline cellulose.³¹ The fillers with a high concentration of cellulose showed a broad peak at a 22.4 theta value. While other peaks related to TiO₂ are presented at different theta values, as specified above.³² Hence, the XRD analysis confirmed the presence of both cellulose and TiO₂ in the prepared fillers.

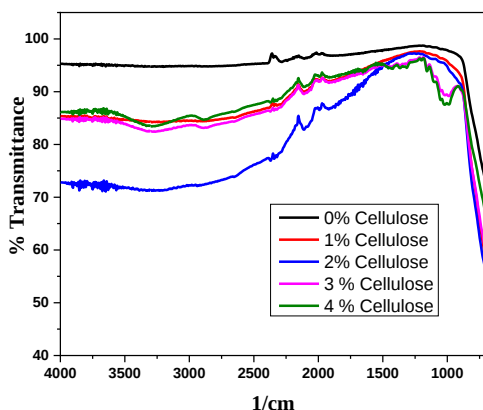


Figure 1: FTIR spectra of TiO₂/cellulose dental fillers

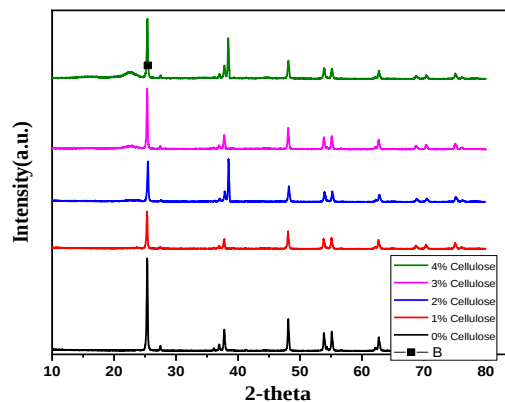


Figure 2: X-ray diffraction patterns of TiO₂/cellulose fillers

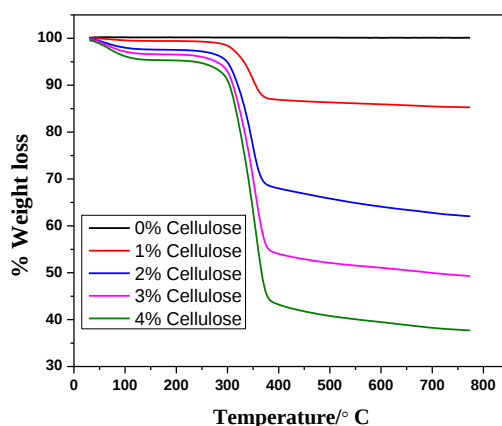


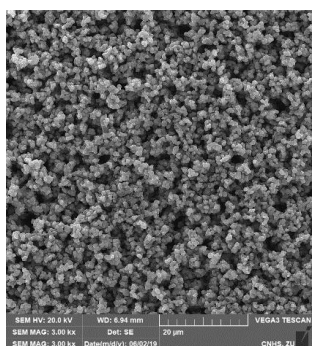
Figure 3: Thermogravimetric curves of TiO₂/cellulose dental fillers

Thermogravimetric analysis (TGA)

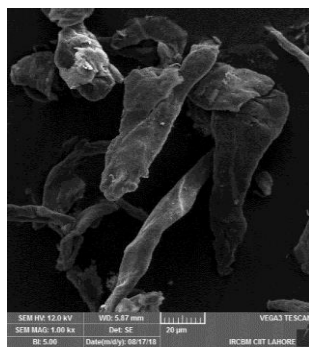
The thermal degradation profiles of the TiO₂/cellulose dental filler materials are shown in Figure 3. The filler containing 0% cellulose and 5% titanium dioxide exhibited no degradation until 800 °C, as TiO₂ is thermally stable up to this temperature. However, the fillers containing cellulose in the range of 1-4% showed two thermal degradation stages, the first in the range of 100-150 °C and the second – between 300-400 °C. These weight losses are related to the evaporation of adsorbed water and the degradation of pyranose structure of cellulose-based glucose, respectively. Beside this, the depth of the degradation curve increased as the cellulose content was increased. Moreover, as the concentration of cellulose decreased (4-0%) and titanium dioxide increased (1-5%), an increment in the residual content at 780 °C was observed, which confirms the content of titanium dioxide in the fillers. The thermal degradation curve showed the presence of both cellulose and TiO₂ in the prepared fillers. The maximum decomposition temperature of cellulose was observed at 338 °C, however, the addition of TiO₂ caused an increase in the decomposition temperature. These results are in accordance with previous findings reported by Yeng.³³

Scanning electron microscopy (SEM) and energy dispersive X-ray analysis (EDX)

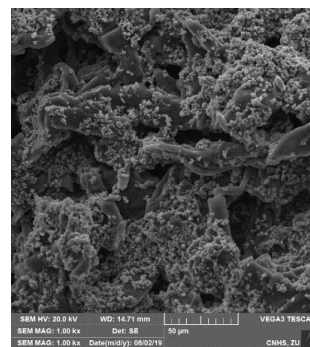
The SEM results for TiO₂, cellulose and TiO₂ decorated cellulose are given in Figure 4 (A to F). Figure 4 (A) shows nanoparticles of TiO₂, which are spherical in shape and are in the form of clusters. Figure 4 (B) corresponds to pure microcrystalline cellulose and shows its irregularly shaped clear surface. Figure 4 (C to F) shows the surface of TiO₂ decorated cellulose. As can be clearly seen from the images, when the concentration of TiO₂ was increased, more particles and irregularities appeared on the surface of cellulose.



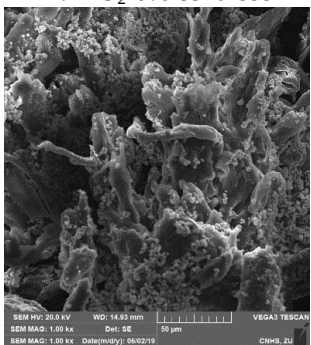
A: TiO₂-0% cellulose



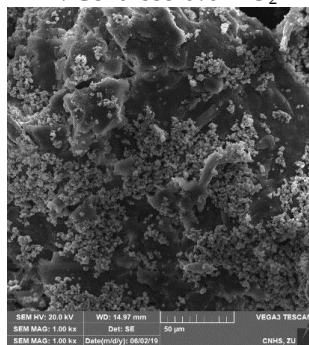
B: Cellulose-0% TiO₂



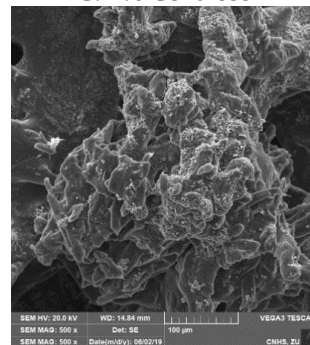
C: 4% Cellulose



D: 3% Cellulose

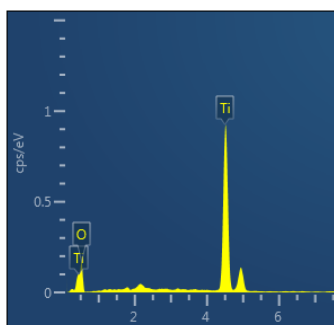


E: 2% Cellulose

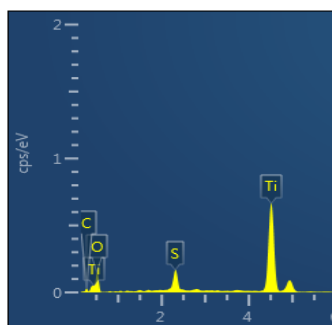


F: 1% Cellulose

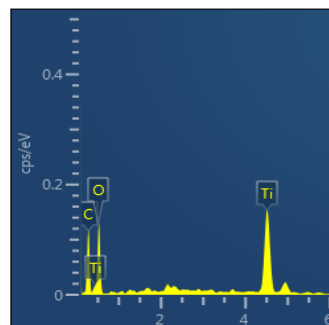
Figure 4: SEM images of TiO₂/cellulose dental fillers



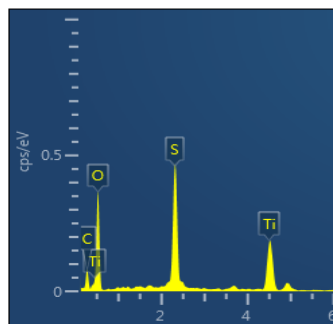
0% Cellulose



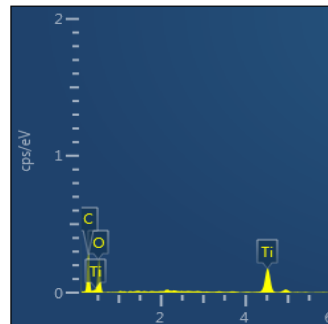
1% Cellulose



2% Cellulose



3% Cellulose



4% Cellulose

Figure 5: EDX spectra of experimental TiO₂/cellulose dental fillers

Table 2
Percentage of Ti, O₂ and C in sample groups

Groups	Ti	O ₂	C
0% Cellulose	51.41	40.59	
1% Cellulose	47.67	42.58	5.05
2% Cellulose	24.06	55.74	12.98
3% Cellulose	12.66	54.90	18.81
4% Cellulose	15.61	50.73	33.66

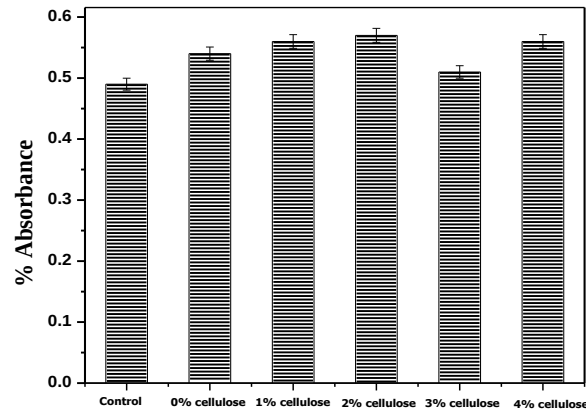


Figure 6: Percent absorbance of experimental groups of dental fillers

The SEM images shown in Figure 4 were confirmed by EDX analysis. Figure 5 shows high levels of titanium in the filler consisting of only TiO₂ (0% cellulose). The level of titanium reduced, while the level of carbon rose in the dental filler formulations containing 0 to 4% cellulose, as given in Table 2.

Biocompatibility

In biocompatibility testing, cell proliferation was examined using Alamar blue and cell absorbance was measured, compared with the control. The absorbance is directly proportional to cell viability. The biocompatibility results obtained for the prepared filler materials are presented in Figure 6. According to the data, the samples containing 0% cellulose and 5% titanium dioxide had a percent absorbance of 0.56 ± 0.02 , while those having 1% cellulose and 4% titanium dioxide had a percent absorbance of 0.55 ± 0.01 . The experimental group of fillers composed of 2% cellulose and 3% titanium dioxide recorded the highest absorbance of 0.57 ± 0.02 , while the lowest – of 0.49 ± 0.01 – was recorded for the filler formulation comprising 3% cellulose and 2% titanium dioxide. Finally, the samples with 4% cellulose and 1% titanium dioxide showed a percent absorbance of 0.55 ± 0.01 .

As may be noted, the cell proliferation slightly increased for the filler composed of 2% cellulose and 3% titanium dioxide, compared to the control, closely followed by the experimental groups containing 1% and 3% cellulose. A high absorbance rate indicates high cell proliferation. Overall, the materials were biocompatible and no as obvious decreases in cell concentration were remarked.

Mechanical properties

The mechanical properties, including biaxial flexural strength, shear bond strength and Vickers's hardness, of the dental adhesive composites (with the incorporation of the fillers) were examined and the results are given in Table 3 – the sample groups of the composite materials were named according to the content of cellulose within the fillers. The evaluation of mechanical properties is critical for dental application of adhesive materials, considering that posterior teeth are under massive occlusal forces during mastication.³⁴ The adhesive materials are subjected to multiple forces in the oral cavity, such as tensile, compressive, shear stress, and a combination of all these make flexural strength.³⁵ The measurement of

biaxial flexural strength is therefore a critical indicator for the long-term use of materials like resin-based sealants as they are brittle in nature. The shear stress in the oral cavity directly affects the bond between the tooth structure and the adhesive materials.³⁶ As dental adhesives are attached to the tooth structure either micromechanically or chemically, any stress on the interface will lead to the formation of a gap between them, consequently, causing microleakage, adhesive failure or secondary caries. Therefore, a strong bond between the tooth structure and the adhesive material is crucial.³⁷ The measurement of hardness of a material provides a way to determine the opposition to localized plastic deformation.³⁸ This has importance in dentistry as surface behavior is linked to stress and scratches, consequently relating resistance to long-term clinical efficacy.³⁹

All the mechanical properties were found to increase when the concentration of cellulose was increased. This can be explained by the fact that cellulose fibers reinforce the dental composites and are the chief-load bearing component in the formulation when added as a filler.⁴⁰ As the polymeric matrix is organic in nature and titanium dioxide particles are inorganic, a coupling agent is required to achieve a better interface between them. In the case of cellulose, the increase in the mechanical properties may also be attributed to the formation of chemical bonding between the carbonyl group present in the resin matrix and the hydroxyl group present in the cellulose. Thus, more bonds were formed when the mass concentration of cellulose was increased, consequently the stresses were distributed evenly, so more energy was required to break the bond.⁴¹ The results obtained in this study are better than those reported by Sabir *et al.*, who added cellulose nanocrystals and silica particles as reinforcing agents to dental adhesives.⁴²

Table 3
Mechanical properties (biaxial flexural strength, shear bond strength and Vickers hardness)
of dental adhesive composites

Experimental groups	Biaxial flexural strength (MPa) $\pm$ SD	Shear bond strength (MPa) $\pm$ SD	Vickers hardness VHN $\pm$ SD
0% Cellulose	45.52 $\pm$ 2.63	34.52 $\pm$ 0.63	25.62 $\pm$ 0.63
1% Cellulose	48.91 $\pm$ 2.48	31.91 $\pm$ 0.48	26.24 $\pm$ 0.63
2% Cellulose	59.81 $\pm$ 3.63	34.52 $\pm$ 0.63	31.25 $\pm$ 1.25
3% Cellulose	69.29 $\pm$ 4.63	38.29 $\pm$ 0.63	31.25 $\pm$ 1.25
4% Cellulose	83.23 $\pm$ 5.63	40.17 $\pm$ 0.63	31.87 $\pm$ 1.25

CONCLUSION

In this study, experimental dental adhesive composites were synthesized and a filler based on cellulose and titanium dioxide, in different weight ratios, was incorporated into their formulation. The effect of the filler on the physical and biological properties of the composites was investigated. All the mechanical properties significantly improved with higher cellulose content in the filler. Also, the materials were found biocompatible, with values within clinical ranges, which recommends such an adhesive material for clinical application.

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