



BASIC RESEARCH:

Evaluation of Cellular Response to 3D-Printed Scaffolds Based on Polyhedral Geometries: Icosahedron, Dodecahedron, and Truncated Icosahedron

Evaluación de la respuesta celular a andamios 3D con geometrías basadas en poliedros: icosaedro, dodecaedro e icosaedro truncado

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ABSTRACT: Tissue engineering has increasingly focused on developing scaffolds capable of providing structural support while promoting cell adhesion and distribution on the scaffold surface, thereby supporting tissue regeneration. In this study, polyhedral-based scaffolds with dodecahedron, icosahedron, and truncated icosahedron geometries were designed and fabricated from polylactic acid (PLA) using fused deposition modeling (FDM) 3D printing. The morphology and pore size of the scaffolds were characterized using optical microscopy, and their mechanical behavior was evaluated through uniaxial compression tests in flat and vertical orientations. Human gingival fibroblasts (HGF) were cultured on the scaffolds to evaluate cell proliferation using WST-1 assays after 1, 3, and 7 days, as well as cell morphology and distribution by scanning electron microscopy (SEM) and fluorescence microscopy after 24 h. Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test ($p < 0.05$). The results demonstrated that the scaffold geometry and loading orientation significantly influenced the mechanical behavior of the printed structures. The vertically oriented icosahedron scaffold exhibited the highest compressive strength (378.45 ± 0.09 MPa), whereas the truncated icosahedron exhibited the highest elastic modulus (147.07 ± 2.13 MPa). HGF proliferation remained comparable to that of the tissue culture plate control over the evaluated time periods. SEM

and fluorescence microscopy revealed cell adhesion and distribution on all scaffold surfaces, although differences in cell organization were observed depending on the scaffold geometry. The results indicate that polyhedral architectures influence both the mechanical properties and cellular response of 3D-printed PLA scaffolds.

KEYWORDS: Tissue engineering; Scaffolds; Mechanical properties; 3D-printing; Polyhedron; Cellular response.

RESUMEN: La ingeniería tisular se ha enfocado en el desarrollo de andamios capaces de proporcionar soporte estructural, favorecer la adhesión celular y la distribución de células en su superficie, y promover la regeneración tisular. En este estudio, se diseñaron y fabricaron andamios basados en geometrías poliédricas de dodecaedro, icosaedro e icosaedro truncado utilizando ácido poliláctico (PLA) mediante impresión 3D por deposición fundida (FDM). La morfología y el tamaño de poro de los andamios fueron caracterizados mediante microscopía óptica, mientras que su comportamiento mecánico fue evaluado mediante ensayos de compresión uniaxial en orientaciones planas y verticales. Fibroblastos gingivales humanos (HGF) fueron cultivados sobre los andamios para evaluar la proliferación celular mediante ensayos WST-1 a 1, 3 y 7 días, así como la morfología y distribución celular mediante microscopía electrónica de barrido (SEM) y microscopía de fluorescencia después de 24 h. El análisis estadístico se realizó mediante un análisis de varianza (ANOVA) de una vía, seguido de la prueba post hoc de Tukey ($p < 0.05$). Los resultados demostraron que la geometría y la orientación de carga influyeron significativamente en el comportamiento mecánico de las estructuras impresas. El andamio de icosaedro en orientación vertical presentó la mayor resistencia a la compresión (378.45 ± 0.09 MPa), mientras que el icosaedro truncado mostró el mayor módulo elástico (147.07 ± 2.13 MPa). La proliferación de HGF se mantuvo comparable a la del control en placa de cultivo durante los periodos evaluados. Las imágenes por SEM y microscopía de fluorescencia mostraron adhesión y distribución celular sobre todas las superficies de los andamios, aunque se observaron diferencias en la organización celular dependiendo de la geometría del andamio. Los resultados indican que las arquitecturas poliédricas influyen tanto en las propiedades mecánicas como en la respuesta celular de los andamios de PLA impresos en 3D.

PALABRAS CLAVE: Ingeniería de tejidos; Andamios; Propiedades mecánicas; Impresión 3D; Poliedros; Respuesta celular.

INTRODUCTION

Tissue regeneration remains a major challenge in regenerative medicine, particularly when defects exceed the natural healing capacity of the body, thereby limiting the restoration of tissue structure and function (1). Conventional therapeutic approaches, such as autografts and allografts, have several limitations, including donor-site morbidity, limited availability, and the risk of immune rejection or disease transmission (2-4). In this context, tissue engineering (TE) has emerged

as an alternative strategy, focusing on the development of biomaterial-based scaffolds capable of providing structural support while promoting cell adhesion, proliferation, migration, and tissue formation (5,6).

Recent advances in additive manufacturing technologies have offered alternative scaffold fabrication methods for tissue engineering (TE) applications. Techniques such as fused deposition modeling (FDM), selective laser sintering (SLS), and digital light processing (DLP) enable the fabrication

of scaffolds with controlled architectures, porosity, and pore interconnectivity, thereby enabling the production of structures with reproducible macro- and microarchitectures (7-10). Compared with conventional fabrication methods such as salt leaching, phase separation, and electrospinning, additive manufacturing offers greater control over scaffold geometry and internal organization, facilitating the design of structures with complex architectures (9-13).

Scaffold geometry is an important parameter because it directly influences the mechanical behavior and biological performance of the construct (14). Parameters such as pore size, pore interconnectivity, surface topography, and structural organization can modulate nutrient diffusion, cell migration, mechanical stress distribution, and tissue colonization (15-19). Studies have demonstrated that scaffold architecture can influence cell adhesion, morphology, proliferation, and extracellular matrix organization by providing specific topographical and mechanical cues (17,20,21). In addition, the mechanical behavior of scaffolds is dependent on the spatial distribution of the structural elements and their ability to redistribute applied loads uniformly throughout the structure (22,23).

Most scaffold designs reported for TE applications are based on conventional geometries, such as cubic or cylindrical lattices. However, emerging polyhedral-based architectures, including dodecahedron, icosahedron, and truncated icosahedron geometries, have attracted attention for their high symmetry, interconnected pore distributions, and structural organization (16,24-28). Previous studies have suggested that polyhedral geometries may offer advantageous mechanical properties and stress distributions compared with traditional lattice structures, potentially influencing scaffold stability and cellular organization (29,30). Furthermore, geometries with interconnected porous networks may facilitate cell coloni-

zation along the scaffold architecture, providing more continuous pathways for cell migration and nutrient transport (18,31). Nevertheless, despite these potential advantages, the biological response to polyhedral scaffold architectures remains unclear, particularly in oral and craniofacial tissue engineering applications.

Evaluating scaffold biocompatibility helps determine whether the fabricated structures can support cell survival and colonization without inducing adverse cellular responses (32,33). Human gingival fibroblasts (HGF) are widely used as an *in vitro* model in oral tissue engineering because they are representative of oral connective tissues and are important for soft tissue repair and extracellular matrix remodeling (34-36). Moreover, fibroblasts are highly responsive to changes in surface topography and scaffold architecture, making them useful for evaluating early cell colonization (17,20,21).

Therefore, this study aimed to design and fabricate 3D-printed polylactic acid (PLA) scaffolds based on dodecahedron, icosahedron, and truncated icosahedron geometries using FDM technology and to evaluate the influence of these polyhedral architectures on the mechanical behavior and HGF cellular response. The morphology, pore size, compressive properties, cell proliferation, and cell distribution on the scaffold surfaces were analyzed to determine the influence of scaffold geometry on the performance of the printed structures for potential oral and craniofacial tissue engineering applications.

MATERIALS AND METHODS

DESIGN OF POLYHEDRON-BASED SCAFFOLDS

The scaffolds were designed using Autodesk Fusion software based on an unfolded dodecahedron, an unfolded icosahedron, and a truncated icosahedron to obtain computational models

(Figure 1). The scaffold sizes were as follows: $15 \times 15 \times 3$ mm for the dodecahedron, $15 \times 10 \times 3$ mm for the icosahedron, and 8 mm in diameter for the truncated icosahedron.

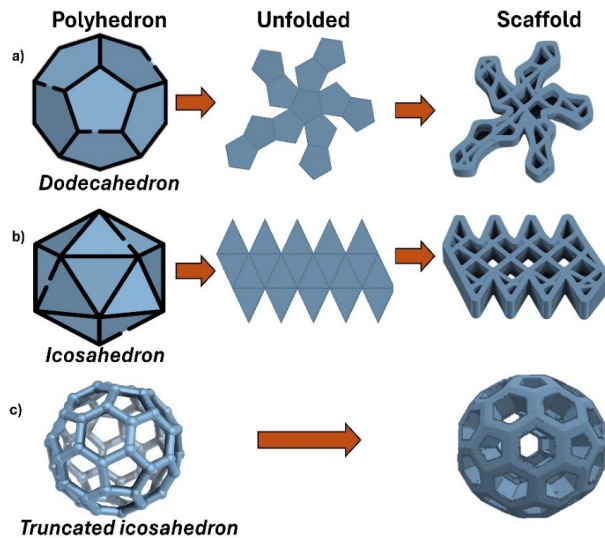


Figure 1. Reference polyhedra, their unfolded shape, and the designed scaffold. a) Dodecahedron. b) Icosahedron. c) Truncated icosahedron.

3D PRINTING OF THE DODECAHEDRON, ICOSAHEDRON, AND TRUNCATED ICOSAHEDRON SCAFFOLDS

The generated files described in the previous section were processed using the slicing software, Orcaslicer 2.3.1. The established printing parameters were as follows: layer height of 0.2 mm, speed of 200 mm/s, rectilinear infill with a density of 20%, and no top or bottom covers for the dodecahedron and icosahedron to preserve their open architecture and porosity. For the truncated icosahedron, the same values for the layer height, printing speed, infill density, and type were set without modifying the presence of the top and bottom covers to maintain structural stability during the printing process. The models were printed using a PLA filament (white, 1.75 mm diameter, Creality), employing the Fused Deposition Modeling (FDM)

additive manufacturing technique with a Creality 3D printer (model K1C) and a 0.4 mm diameter print nozzle. The PLA filament was heated to 200°C and deposited on the print bed at 50°C to promote model adhesion. Twenty scaffolds were fabricated for each geometry.

MORPHOLOGICAL CHARACTERIZATION

The scaffolds were examined using an inverted optical microscope (RoHS brand, model XIB-100) at 10x and 40x magnifications to observe their structure and determine pore size.

COMPRESSIVE STRENGTH TEST

The mechanical properties of the printed scaffolds were evaluated using uniaxial compression tests in a Shimadzu universal testing machine (model AGS-X; Kyoto, Japan) equipped with a 10 kN load cell. The tests were performed at a strain rate of 5 mm/min until structural failure. Three samples of each scaffold were tested; the dodecahedron and icosahedron were evaluated in two orientations, flat and vertical (Figure 2.a and Figure 2.b), and the truncated icosahedron was evaluated in a single orientation (Figure 2.c).

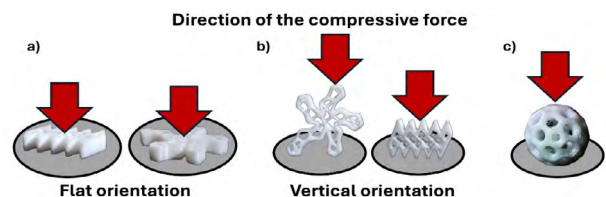


Figure 2. Compression test. a) Flat orientation of the scaffolds for evaluating the compressive strength in the largest areas of the dodecahedron and icosahedron scaffolds. b) Vertical orientation of the scaffolds for evaluating the compressive strength in the smallest area of the dodecahedron and icosahedron scaffolds. c) Area of force application in the truncated icosahedron scaffold.

The experimental data on compressive stress (MPa) and strain (%) were continuously recorded for each test to generate the corresponding curves

and obtain the parameters of elastic modulus (E), maximum compressive strength (σ_{max}), strain at failure (ϵ_f), and absorbed energy.

BIOCOMPATIBILITY ASSAYS

To evaluate the influence of 3D scaffolds with different geometries on cell proliferation and colonization, human gingival fibroblasts (HGF, ATCC PCS-201-018) were used. The HGF were cultivated in Dubelcco's Modified Eagle Medium (Biowest, Nuaille, Francia) supplemented with 10% of fetal bovine serum (FBS, Gibco, Waltham, MA, USA), 1% of antibiotic solution (penicillin 100 UI/ml and streptomycin 100 μ g/ml), and L-glutamine. The cell culture was maintained at 37°C in a humidified atmosphere containing 5% CO₂ and 95% air. The 3D scaffolds were previously placed into a 48-well cell culture plate and sterilized for 30 minutes with UV light (3 samples per group).

The proliferation of HGF cells was assessed using the WST-1 kit (Roche Diagnostics GmbH, Mannheim, Germany) after 1, 3, and 7 days. For this purpose, HGF cells were seeded onto 3D scaffolds at a density of 2×10^4 per sample. On the specified days, the cell culture media were replaced with fresh media containing the WST-1 reagent at a 1:10 ratio, and the cultures were incubated for 4 h. After the incubation period, the medium was removed and placed in 96-well plates for absorbance measurement at 450 nm using a spectrophotometer (PKL PPC 145 Microplate reader, Paramedical, SA, Italy). This assay is based on the reduction of tetrazolium salt to soluble formazan by viable cells; the measured absorbance is directly related to cell viability. The experiments were conducted in triplicate.

To evaluate the behavior of HGF on the 3D scaffolds with different geometries after 24 h,

scanning electron microscopy (SEM) and fluorescent microscopy were used. After 24 h of cell culture, the samples were washed with phosphate-buffered saline (PBS) to remove non-adherent cells. For SEM microscopy, the samples were fixed with 2% glutaraldehyde, dehydrated with increasing concentrations of alcohol (25-100%), and air-dried. For observation by field-emission scanning electron microscopy (FESEM; JEOL, JSM-7800F, Tokyo, Japan), the samples were previously coated with gold. For fluorescent microscopy, PKH67 Green fluorescent cell linker (PKH67, Sigma-Aldrich, MO, USA) was used. Briefly, before cell seeding, the cells were washed, resuspended in Diluent C, and incubated with the dye solution for 5 min according to the manufacturer's instructions. Once stained, the cells were seeded onto the 3D scaffolds at a density of 4×10^4 per sample. After 24 h, the samples were washed and fixed with PBS and 2% glutaraldehyde. Before imaging, samples were washed with MilliQ water and observed with a fluorescence LED microscope (Amscope, Irvine, CA, USA).

STATISTICAL ANALYSIS

The results are presented as mean $\pm$ standard deviation (SD). A one-way analysis of variance (ANOVA) followed by Tukey's post hoc test to identify statistical differences ($p < 0.05$) between groups in compressive strength and biocompatibility tests. The statistical analysis was performed using GraphPad Prism 8 software.

RESULTS

The scaffolds were printed exactly as designed, with respect to size and pore size. Microscopic observations revealed the different polymer layers that formed the scaffolds, as well as the square pores in the dodecahedron and icosahedron.

dron scaffolds and the pentagonal and hexagonal pores in the truncated icosahedron scaffold (Figure 3).

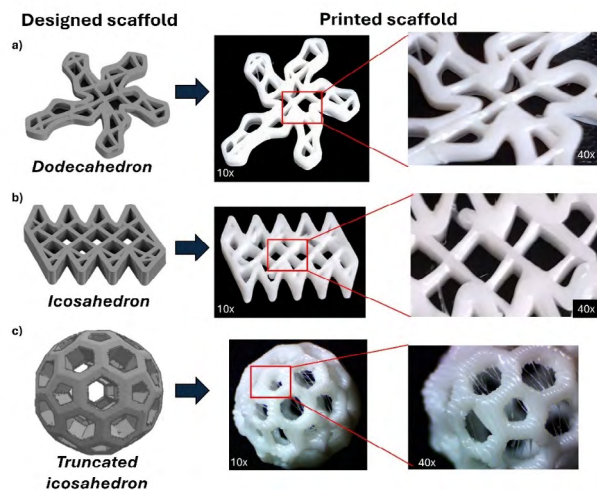


Figure 3. Comparison between the designed and printed scaffolds and their observations under an optical microscope at different magnifications (10x and 40x). a) Dodecahedron. b) Icosahedron. c) Truncated icosahedron.

Conversely, the pore size was larger for the dodecahedron and icosahedron scaffolds, whereas the truncated icosahedron exhibited two different pore sizes depending on whether they were pentagonal or hexagonal, with the former being smaller (Table 1).

Table 1. Pore size of scaffolds.

Scaffold	Pore size (mm $\pm$ SD)
Dodecahedron	1.64 $\pm$ 0.42
Icosahedron	1.66 $\pm$ 0.42
Truncated icosahedron (pentagonal pore)	0.85 $\pm$ 0.21
Truncated icosahedron (hexagonal pore)	1.43 $\pm$ 0.08

The results of the compressive strength tests on the three scaffolds with different geometries are presented in Table 2. The truncated icosahedron scaffold exhibited the highest modulus of elasticity (147.07 $\pm$ 2.13 MPa), whereas the flat dodecahedron showed the lowest elastic modulus (2.00 $\pm$ 0.01 MPa), with statistically significant differences

between the groups. The icosahedron scaffold evaluated in the vertical orientation presented the highest compressive strength (σ_{max} = 378.45 $\pm$ 0.09 MPa), which was statistically significant compared to all other analyzed configurations. The icosahedron and dodecahedron scaffolds evaluated in the flat orientation showed the greatest deformation at failure, 112.13 $\pm$ 6.14% and 117.88 $\pm$ 14.53%, respectively, with statistically significant differences between the groups. The icosahedron scaffold evaluated in both orientations absorbed the most energy, followed by the dodecahedron scaffold, with statistically significant differences between groups.

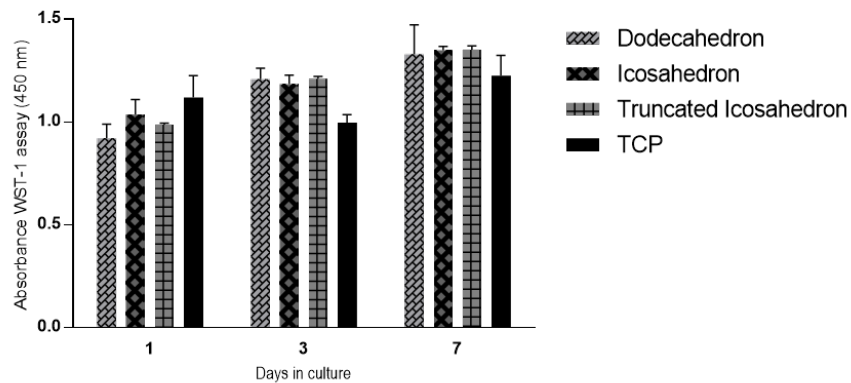
The proliferation of HGF seeded directly onto the different 3D scaffolds was evaluated using WST-1. Over the days, an increase in HGF proliferation was observed in all groups, comparable to the culture plate (TCP), without showing significant differences (Figure 4).

The interaction of fibroblasts with the surfaces of the printed models demonstrates cell colonization across the different structural architectures evaluated (Figure 5). On the surface of the dodecahedron scaffold, the fibroblasts are observed distributed in small cell aggregates (Figure 5.a). Moreover, in fluorescence images, the cells exhibit irregular morphology and cytoplasmic extensions, suggesting initial contact with the material, preferentially on the angles of the porous structures (Figure 5.a'-Figure.a''). The surface of the icosahedron model exhibits a higher cell density and larger clusters of adhered fibroblasts (Figure 5.b). These cells display an elongated morphology, consistent with adhesion and anchorage along the surface of the scaffold (Figure 5.b'-Figure.b''). The surface of the truncated icosahedron scaffold exhibits a more homogeneous cell distribution (Figure 5.c). On fluorescent images, it was possible to observe the cell colonization along the scaffold architecture (Figure 5.c'-Figure 5.c'').

Table 2. Parameters obtained from the compressive strength test.

Scaffold/orientation	E (MPa)	σ_{max} (MPa)	ϵ_f (%)	Absorbed energy (MJ/m ³)
Dodecahedron				
Flat ⁽⁺⁾	2.00 ± 0.01	44.04 ± 0.01	117.88 ± 14.53	17.80 ± 0.03
Vertical ⁽⁻⁾	51.00 ± 0.02 ⁽⁺⁾	234.98 ± 0.05 ⁽⁺⁾	93.59 ± 3.05 ⁽⁺⁾	20.50 ± 0.29
Icosahedron				
Flat ^(/)	1.10 ± 0.09 ⁽⁻⁾	81.09 ± 0.03 ^(+,-)	112.13 ± 6.14 ⁽⁻⁾	32.25 ± 0.22 ^(+,-)
Vertical ^(x)	87.67 ± 1.50 ^(+,-/)	378.45 ± 0.09 ^(+,-/)	65.64 ± 1.96 ^(+,-/)	33.22 ± 0.56 ^(+,-)
Truncated icosahedron ^(&)	147.07 ± 2.13 ^(+,-,/x)	34.31 ± 5.98 ^(+,-,/x)	24.51 ± 4.39 ^(+,-,/x)	2.35 ± 4.60 ^(+,-,/x)

Elastic modulus (E), maximum compressive strength (σ_{max}), and strain at failure (ϵ_f). Statistically significant differences ($p \leq 0.05$) between the flat dodecahedron (+), vertical dodecahedron (-), flat icosahedron (/), vertical icosahedron (x), and truncated icosahedron (&).

**Figure 4.** HGF viability seeded onto 3D printed dodecahedron, icosahedron, and truncated icosahedron after 1, 3, and 7 days of cell culture.

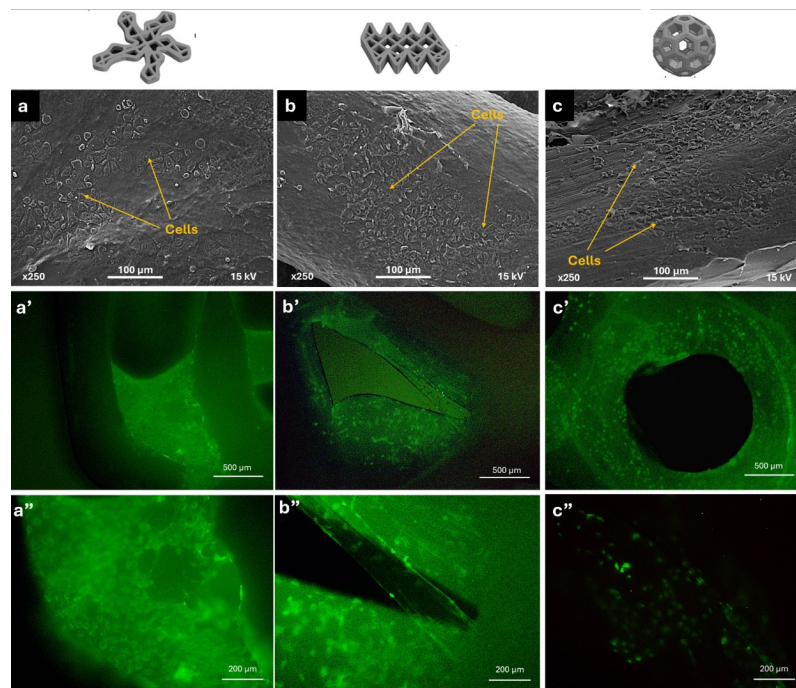


Figure 5. SEM images of HGF seeded on the 3D-printed dodecahedron (a), icosahedron (b), and truncated icosahedron (c) scaffolds; and corresponding fluorescent images (a', a''), (b', b''), and (c', c'').

DISCUSSION

In this study, three polyhedral architectures printed using FDM, namely dodecahedron, icosahedron, and truncated icosahedron, were evaluated to analyze how geometric topography influences the mechanical strength and cellular response of HGF. The geometric design of scaffolds is one of the factors that determines both the mechanical behavior and biological response in TE applications (22,23).

All printed scaffolds showed consistent dimensional accuracy and structural reproducibility, as observed by visual inspection and optical microscopy, maintaining the designed geometric features and pore distribution.

The scaffold dimensions were selected to maintain comparable overall sizes among the different geometries while preserving the charac-

teristic polyhedral architecture and interconnected pore structure of each design.

The results of the mechanical behavior showed that the icosahedron geometry in the vertical orientation exhibited the highest mechanical strength, reaching values of 378.45 ± 0.09 MPa, which was significantly higher than that of the other configurations evaluated. This behavior can be explained by the more uniform spatial distribution of the structural points of the icosahedron, which supports better redistribution of compressive loads throughout the three-dimensional structure (37).

Various studies have shown that geometries based on regular polyhedra provide a more uniform distribution of mechanical stresses than conventional cubic or cylindrical geometries (29,30), thereby improving mechanical properties. In particular, the high connectivity of the edges in the printed icosahedron may contribute to the creation of

more efficient load transmission routes, reducing concentrations of local stress and delaying structural failure (38).

In contrast, the dodecahedron scaffolds evaluated in the vertical orientation also exhibited high compressive strength (234.98 ± 0.05 MPa), although lower than that of the vertical icosahedron (378.45 ± 0.09 MPa). This suggests that although both architectures exhibit high structural connectivity, the angular distribution of the faces of the icosahedron allows for more efficient load transmission under compression than that of the dodecahedron (39).

Another relevant aspect of this study was the influence of scaffold orientation during compression testing. In both the dodecahedron and icosahedron, samples evaluated in the vertical orientation exhibited greater strength than those evaluated in the flat orientation. This behavior can be attributed to the inherent anisotropic nature of materials manufactured using FDM, where the mechanical strength largely depends on the orientation of the deposited layers. When the load is applied parallel to the direction of the layers, the structure can withstand greater stress due to the continuity of the extruded filament, whereas in the flat orientation, the load is distributed along the interfaces between layers, which are usually areas of lower mechanical cohesion (40,41). This phenomenon has been reported in FDM-printed structures, where the manufacturing orientation can significantly alter the elastic modulus and compressive strength of scaffolds (42).

In contrast to the maximum strength, the dodecahedron and icosahedron scaffolds evaluated in the flat orientation exhibited the greatest deformations before failure, indicating a higher capacity for plastic deformation before structural failure. This behavior can be associated with the progressive collapse mechanisms of the structu-

ral cells, which are characteristic of porous architectures (43). Similarly, the icosahedron scaffolds exhibited the highest energy absorption capacity, regardless of the evaluation orientation. This result suggests that the icosahedral architecture offers greater structural strength and a higher capacity to dissipate mechanical energy, a desirable property in scaffolds intended to withstand physiological loads or mechanical impacts in biomedical applications (44).

The biocompatibility of biomaterials is an important parameter in the field of TE to ensure a proper interaction with cells without interfering with the healing and regeneration processes (45). In this work, 3D PLA scaffolds with different geometries (i.e., dodecahedron, icosahedron, and truncated icosahedron) were placed in direct contact with HGF to evaluate cell proliferation and colonization along the scaffold architecture. The results showed that cell proliferation remained constant over time, confirming the biocompatibility of PLA and creating a suitable environment for cell growth (46-48). Furthermore, SEM and fluorescent images revealed fibroblast adhesion and colonization on all surfaces of the evaluated scaffolds, confirming the biocompatibility of the material. In the case of the dodecahedron scaffold, HGF formed small cell aggregates, mostly at the angles, with irregular morphology, indicating cell adhesion. The icosahedron geometry exhibited a more extensive cell distribution on the scaffold surface than the other evaluated geometries, which may be associated with differences in scaffold architecture and pore organization (17,20). The truncated icosahedron exhibited a more homogeneous distribution of cells, with fibroblasts displaying elongated morphology, and following the patterns of the scaffold. The elongated morphology of cells on the surfaces of 3D-printed scaffolds is characteristic of cells that have formed stable adhesions to the surface and are colonizing the topography of the material (20,21).

Several studies have demonstrated that the surface topography and porous architecture of scaffolds can modulate cell adhesion, migration, and organization, as cells are able to detect and respond to these structures (17,49). In this context, the polyhedral architectures evaluated in this study provide topographic cues for cell colonization and extracellular matrix deposition (31). The combination of high porosity, stress distribution, and cell colonization observed in these geometries could contribute to improving tissue integration and regeneration (18,19).

The evaluated scaffold geometries may have potential applications in oral, periodontal, and craniofacial tissue engineering, where scaffold architecture, porosity, and cell colonization are important for soft-tissue regeneration and tissue integration. The ability of the scaffolds to support HGF viability and distribution on their surfaces suggests that these polyhedral structures may serve as structural platforms for future studies focusing on oral connective tissue regeneration. However, additional *in vitro* and *in vivo* studies are required to evaluate further their regenerative potential and clinical applicability (17,20,31,36).

CONCLUSION

In this study, 3D-printed PLA scaffolds based on dodecahedron, icosahedron, and truncated icosahedron geometries were successfully fabricated using FDM to evaluate the influence of scaffold architecture on the mechanical behavior and cellular response. The results demonstrated that the scaffold geometry and loading orientation influenced the compressive properties of the printed structures. In particular, the vertically oriented icosahedron scaffold exhibited the highest compressive strength, whereas the truncated icosahedron exhibited the highest elastic modulus among the evaluated groups.

Biological evaluation demonstrated that all scaffold geometries maintained HGF viability throughout the evaluation period. In addition, SEM and fluorescence microscopy analyses showed cell colonization and distribution along the scaffold surfaces.

The findings of this study suggest that polyhedral scaffold architectures influence both the mechanical behavior and early cellular response of 3D-printed PLA scaffolds. Among the evaluated geometries, the icosahedron scaffold exhibited the highest compressive strength and a more homogeneous cell distribution on the scaffold surface. These structures have potential applications in oral, periodontal, and craniofacial tissue engineering.

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CONFLICT OF INTEREST: The authors declare that they have no conflict of interest.

DATA AVAILABILITY: All the data required to support the study's conclusions are included in this manuscript.

AUTHOR CONTRIBUTION STATEMENT: Conceptualization and design: I.C.-M., R.A.-Ch. and M.A.A.-P.; Literature review: I.C.-M., R.A.-Ch. and M.A.A.-P.; Methodology and validation: I.C.-M., R.A.-Ch. and J.S.-B.; Formal analysis: I.C.-M. and R.A.-Ch.; Investigation and data collection: I.C.-M., R.A.-Ch., J.S.-B. and J.A. A.-A.; Resources: J.S.-B., J.A. A.-A. and M.A.A.-P.; Data analysis and interpretation: I.C.-M., R.A.-Ch., J.S.-B., J.A. A.-A. and M.A.A.-P.; Writing-original draft preparation: I.C.-M., R.A.-Ch., J.S.-B. and M.A.A.-P.; Writing-review & editing: I.C.-M., R.A.-Ch. and M.A.A.-P.; Supervision: J.S.-B. and J.A. A.-A.; Project administration: J.S.-B. and M.A.A.-P.; Funding acquisition: J.S.-B. and M.A.A.-P.

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