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Acceleration Healing and Osseo-Integration Processes of CpTi Implant by Coating Teeth with Collagen-Polycaprolactone Fiber Scaffold

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ABSTRACT

Objective: *This study aimed to enhance osseointegration and healing by combining electrospinning techniques with collagen and polycaprolactone (PCL) as a coating for commercial pure titanium (CpTi) implants.* ***Methods:*** *In vitro experiments utilized glacial acetic acid as a solvent system to create collagen/PCL coatings with varying PCL concentrations (10%, 15%, 20% w/v). Morphological and physical characterizations were conducted using scanning electron microscopy (SEM), atomic force microscopy (AFM), and wettability tests. In vivo studies involved implanting collagen/PCL-coated CpTi cylinders into the femoral bone of New Zealand rabbits, followed by histological analysis at 2 and 6 weeks.* ***Results:*** *SEM revealed that scaffolds with higher PCL concentrations exhibited finer nanofiber structures (average diameter: 232 nm) and enhanced hydrophilicity and roughness. Histological analysis demonstrated significant osteogenic activity and basal bone formation, with well-formed bone plates observed at 6 weeks for implants coated with 20% collagen and 20% PCL.* ***Novelty:*** *The study highlights the potential of electrospun collagen/PCL coatings to create optimal surface properties for dental implants, achieving improved tissue integration and healing outcomes. This innovative approach demonstrates the versatility of electrospinning for fabricating fibrous scaffolds that can incorporate therapeutic agents, offering transformative implications for regenerative medicine and implantology.*

INTRODUCTION

Titanium is one of the most widely used dental implant materials due to its fabulous physical properties, outstanding osteo-conductivity, and passive corrosion resistance layer yet some goals of implant surface modifications to increase clinical performance in areas with poor bone quality or quantity are recommended[1]. Further, to accelerate bone healing for new prosthetic loading protocols, and stimulate bone growth for implant placement in areas with insufficient residual alveolar ridge are sustained[2]. Earlier studies to enhance the biological impact of titanium via modification of both surface topography and chemistry represented a classic example of a natural polymer was collagen[3][4]. Collagen is characterized, as an excellent biocompatibility, low antigenicity, low inflammatory and cytotoxic responses meanwhile its use in biomedical applications, has expand quickly; especially in the field of bioengineering[5][6]. In extracellular matrix (ECMs), collagen type-I is the main fibrillary structural component, which exist almost everywhere in the body's tissue, with the exception of cartilaginous tissues, where collagen type-II is predominate[7]. Both types-I and II collagens and the natural polymers were frequently utilized in cartilage tissue engineering because they

provide biological signals that help chondrocytes connect with the scaffold and provide the developing tissue enough room needed[8]. The latter has been considered cellular enzymes recognizing collagen[9]. The majority of investigations had focused on using collagen type-I scaffolds as cell carriers for Mesenchymal Stem Cells (MSCs) or chondrocytes. At full-thickness defects in rabbit articular cartilage, allograft chondrocytes were implanted within collagen type-I gels within 24 weeks following transplantation, the defects were filled with hyaline cartilage as opposed to those lacking seeded gels, which were filled with fibrocartilage[10]. In 2009, an in vivo study conducted by Tillman and co-workers referred to collagen in a scaffold form revealed a considerable stability by sustaining high biomechanical strength over time[11]. Collagen used as a coating material for titanium and alloys had promoted surface biological properties by increasing the proliferative capacity of osteoblasts[12]. The effects of collagen coating on tissue vascularization, inflammatory response, macrophage activity, and osteoclast activity have already been investigated[13] meanwhile, biochemical alteration of titanium (Ti) surfaces by collagen could also accelerate wound healing in animal models[14]. A most recent study claimed that collagen coating promotes cell adhesion, differentiation, and mineralization of the extracellular matrix[15], while other studies claimed stimulatory effect[16][17]. Recently, the biodegradable synthetic semi-crystalline polymers PCL have become more popular in a range of surgical applications and is biocompatibility, versatility, processability, and its suitability for various biomedical applications have cemented its position as a valuable polymer[18][19]. Its ability to blend with other polymers also enhances its adaptability and allows for the creation of custom materials tailored to specific medical needs[20]. Accordingly, this polymer has recently been approved by the United States Food and Drug Administration (FDA) for use in human medical devices which emphasizes an in vivo applicability and that their non-toxicity factor has also been evaluated[21].

Electrospinning technique, frequently used to make scaffolds for tissue engineering, is a common nano-technique used to fabricate scaffolds of aligned polymeric nanofibers (NFs) with diameters varying between 3 to >5 μm [22-24]. A thin polymer solution is stretched during solidification by electrostatic forces where the resultant scaffold becomes an effective way for manufacturing micro and nanofibers for tissue engineering since the fibers closely mirror the dimensions and composition of the natural extracellular matrix [25-28]. Similarly, use of solvents and aqueous-based solutions helps in the assimilation of biological substances e.g. collagen and elastin combinations are only one of the many uses for electrospinning of collagen[29]. Scaffolds has already been constructed of polycaprolactone and collagen for the creation of vascular tissue[22] and fibrinogen fibers that allow for natural collagen deposition during cell growth[30]. The success of human tissue adopting the scaffolds in the future may depend on the inclusion of chemicals i.e. antibiotics, to polymer-collagen blends because there are many therapeutic uses for scaffolds that require for monitoring bacterial growth. For instance, maintaining optimal levels of an antibacterial antibiotic during medicine administration

is one standard for monitoring intra-abdominal infection[31]. Some extra application in bone therapy may also be possible to explore via some modifications of the application techniques. Our research aims to examine the electrospinning coating method for coating CpTi with collagen using PCL as a binder and to assess the osseo-integration reaction to the electrospun fibrous scaffold.

RESEARCH METHOD

A primary polymer of pure type-I collagen (bovine tendon powder, type-I collagen) from Sigma SKU (molecular weight 2,500–4,000 g/mol.), PCL (C6H10O2)n (molecular weight 45,000 gm.mol-1 density 1.146 gm/mL at 25 °C) Sigma-Aldrich, were used. The scaffold was created using an electrospinning system (Nano NC, ESB200, Southern Korea). The setup of electrospinning device (Fig-1C) consists of three main parts i.e. a conductive collector, flow rate, and a high-voltage power source. The electrospinning processes method produces nanofibers[32]. At a certain voltage, the repulsive forces overcome the surface tension of the polymeric solution, causing a jet to emerge from the Taylor cone. The jet moves between the needle tip of the syringe and the collector, dividing into a vast number of filaments, which then undergo solvent evaporation along with the distance. [33][34].

1. Method

a). Specimen design for in vitro: Investigation of surface modification was conducted on a substrate of CpTi (15 mm/diameter and 2 mm/thickness), prepared with a wire cutting machine a round bar (dk7,735 China). The specimen was then mechanically polished with grinding and polishing to create a mirror-like surface. The "conventional" method of machine polishing uses abrasive grit sizes 240, 320, 400, and 600, grit.

b). Preparation of Collagen/PCL scaffolds: A pure collagen solution was prepared by dissolving 20% W/V of collagen in 98% concentrated glacial acetic, acid stirred with a magnetic bar for an hour at room temperature. The PCL pellet was also dissolved in the acetic acid 98% solvent system, where the solution was prepared at three different concentration levels (10%, 15%, and 20% W/V) and stirred by a magnetic stirrer for 3 hours at room temperature[11]. Both polymer solutions were mixed and the mixture of collagen and PCL prepared at rate 1:1 V/V was stirred with a magnetic bar for 2 hours to create a homogeneous solution. Therefore, the first group (G1) had 20% collagen mixed with 10% PCL 1:1; G2 was formed from 20% collagen mixed 1:1 V/V with 15% of PCL and the third group (G3) was 20% of both collagen and PCL mixed in 1:1 rate. The prepared solutions were collected using a 10 mL syringe with a voltage of 15 Kv a needle tip diameter of 0.7 mm, and a distance between electrodes of 15cm. electrospinning performed at flow rate of 1 mL/hour (Fig. 1.A). A DC power supply with voltage (Fig. 1.D) regulation created the electrically charged collagen and PCL jet[26]. The electro-spun collagen fibers and PCL scaffold sheet were left to dry at room temperature[35] followed by characterization of coat layer.

c). Characterization of electrospinning scaffold: The field emission scanning electron microscope. (FESEM) examination at a 15 KV accelerating voltage was used to evaluate fiber diameter and porosity inside the fibers scaffold while the specimens were first coated in gold using sputtering, followed by scaffold analysis utilizing Image-J software and SEM characterization[36]. Then, the wettability test conducted to determine the contact angle indicates hydrophilicity of the surface. Analysis for the surface morphology and roughness was carried out using Atomic force microscopy (AFM) 2D and 3D imaging with particle size distribution and finally, examination, was done using AFM to provide high-resolution three-dimensional (3D) topographic data, making it an excellent tool for topographic investigation of relatively flat surfaces [37].

2. In vivo study: A CpTi implant was prepared in a 3mm diameter and 8mm length, meanwhile, while the electrospinning coating performed for two groups e.g. control group non-coated CpTi; another was chosen upon in vitro analysis to selected better morphological and physical properties i.e. a 20% collagen: 20% PCL was used for histological analysis. White, healthy male 10-12-month-old New Zealand rabbits weighing 2.2-2.5 Kg were employed as test subjects meanwhile the rabbits were, priory, submerged in an anti-parasite agent to avoid any external skin infections.

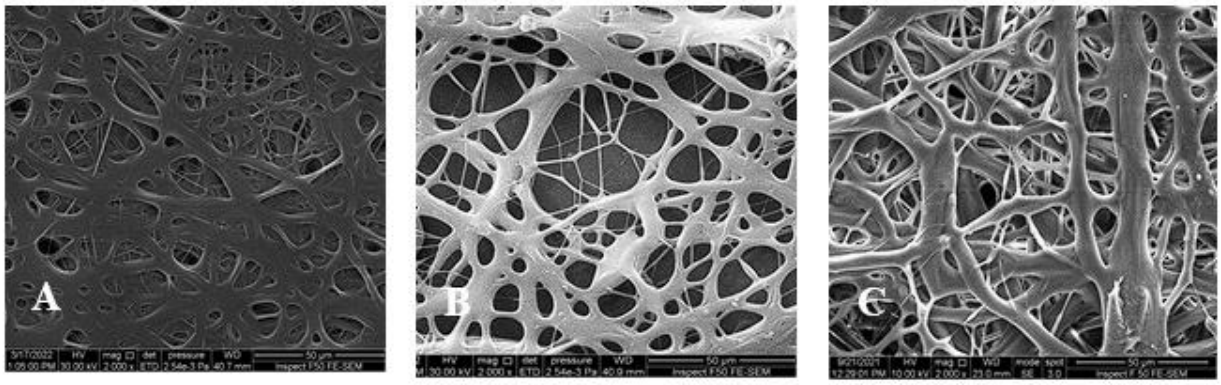
(Fig. 1): (A). In vitro specimen polishing instrument; (B). Polymer solution preparation; (C). Atom syringe pump to control flow rate and (D). High voltage DC to control high power supply.

To ensure that the animals were parasite-free, intravenous intramuscular injection was administered, and oxy-tetracycline intramuscular injection was used as an antibiotic to cover the infection[38]. The surgical operation was performed gently, by sterile surgical technique while all instruments and towels were autoclaved at 134oC and 15

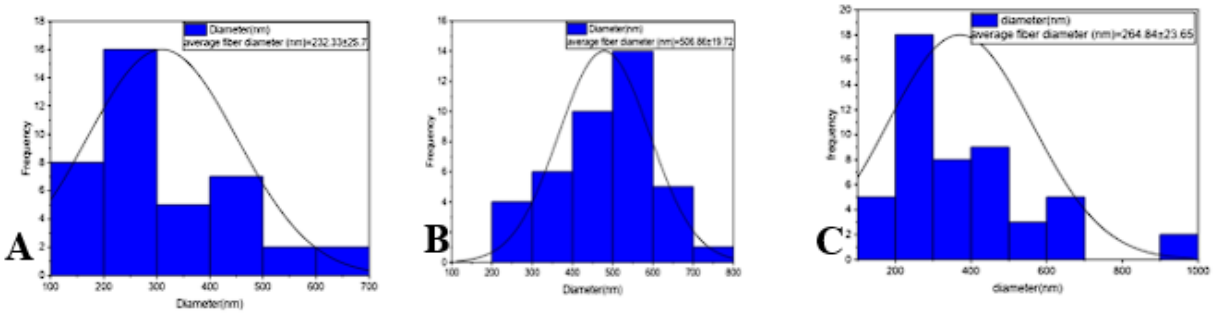
bars for 90 minutes [39]. Due to the organic nature of coating samples; the sterilization was carried out under UV radiation for 24 hours [40]. The two groups of implants were subjected to in vivo investigation i.e. the uncoated CpTi (G1) was used as a control group while the G2 was coated with a scaffold of 20% collagen and 20% PCL. The study involved the evaluation of implants at two distinct time intervals, namely 2 weeks and 6 weeks post-implantation, in animal subjects. The animals were then humanely sacrificed to retrieve the implant sites. To assess the bone response to the implants, histological specimens were meticulously prepared from extracted bone blocks at these intervals. Subsequently, a series of well-defined laboratory procedures were executed to prepare slides for examination under a light microscope[41]. This comprehensive histological analysis allowed for the in-depth examination of tissue and bone interactions with the implanted material over time, to shed light on the biocompatibility and long-term effects of the implants within the biological system [42].

RESULTS AND DISCUSSION

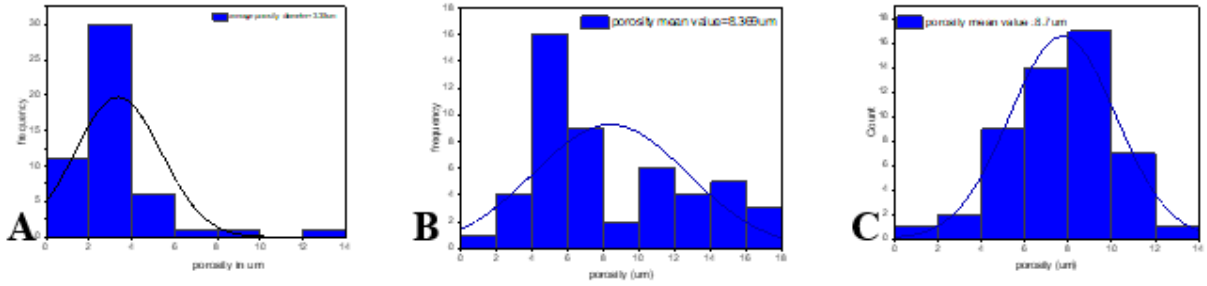
3.1. FESEM analysis: Both, the software of Image-J and origin were used to analyse the scaffold by scanning elctron microscope (SEM) in (Fig-2). The porosity diamter had ranged as the widest porosity size in G3 of 20% PCL reached to almost 8.7µm (Fig. 3) and the smallest pores size found in group-1 10% PCL (G1) was 3.4 µm (Fig. 4).



(Figs. 2): (A). Illustrates a scaffold made of 20% collagen and 10% PCL prepared with the lest average fiber diameters 232nm; (B). A scaffold made of 20% collagen and 15% PCL, with increase in an average fiber diameter of 506.86nm and (C). the scaffold, of 20% collagen and 20% PCL was made in between an average fiber diameters of 264nm.



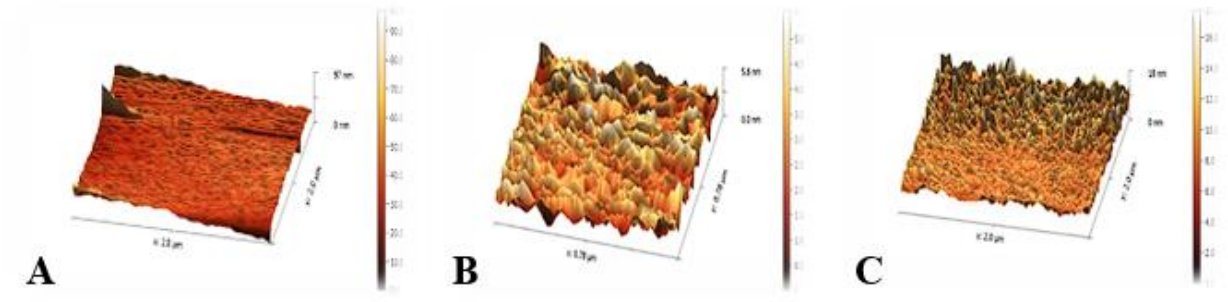
(Figs. 3): Mean fiber diameters and standard deviation (±sd) via Image-J and origin software of 20% collagen scaffold: (A). 10% PCL; (B). 15% PCL; and (C). 20% PCL.



(Figs-4): The mean porosity diameter (um) and slandered deviation measured by image-j and origin soft ware of 20% collagen scaffold: (A). 10% PCL; (B).15% PCL; and (C). 20% PCL, respectively.

3.2. Atomic Force Microscope (AFM) analyses:

Using the atomic force microscope the three distinct types of scaffolds made from three different PCL concentrations with 20% collagen revealed the scaffold surface roughness had increased proportionally with PCL content (Figures, 5A-C).

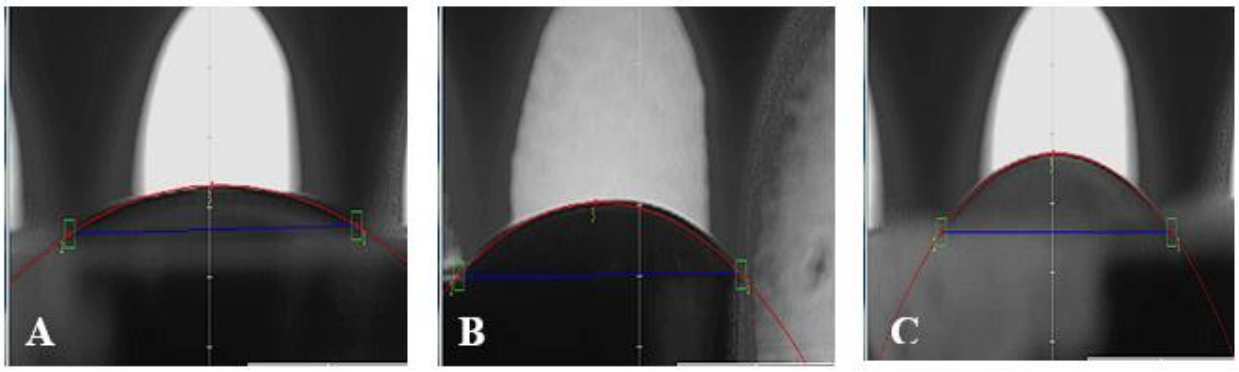


(Fig. 5): Atomic force microscope result (AFM) for 20% collagen with; (A). 10%; (B). 15% and (C). 20%. In A, an AFM test revealed 10% PCL, and the surface roughness is 0.069 µm; in B. The second specimen of 15% PCL, the surface roughness is 0.93 µm, and in C for 20% PCL is 0.24 µm.

3.3. Wettability test

The average contact angle for the first scaffold group (G1) of 20% collagen and 10% PCL was 12.75 (Fig-6A), 20.44 for the second scaffold group (G2) of 20% collagen and 15% PCL (Fig-6B), and 25.75 for the scaffold 20% collagen and 20% PCL (G3)(Fig-6C). The Bonferroni test showed a highly significant difference in contact angle measured between

scaffolds with 15% PCL and 20% PCL. The mean difference of -13 indicates (Table-2) that the scaffold with 20% PCL is significantly less hydrophilic than the one with 15% PCL.



(Fig-6): The wettability test contact angle in 20% collagen with; (A). 10% PCL; (B). 15%PCL and (C). 20%PCL. Note

(Table-1): The arithmetic means and SD of the contact angle analyzed using equal

Groups	Arithmetic means &SD	Differences
G1 (10%PCL) n=10	12.7±1.34	$p \leq 0.001$
G2 (15%PCL) n=10	20.4±1.35	$p \leq 0.001$
G3 (20%PCL) n=10	25.7±0.67	$p \leq 0.001$

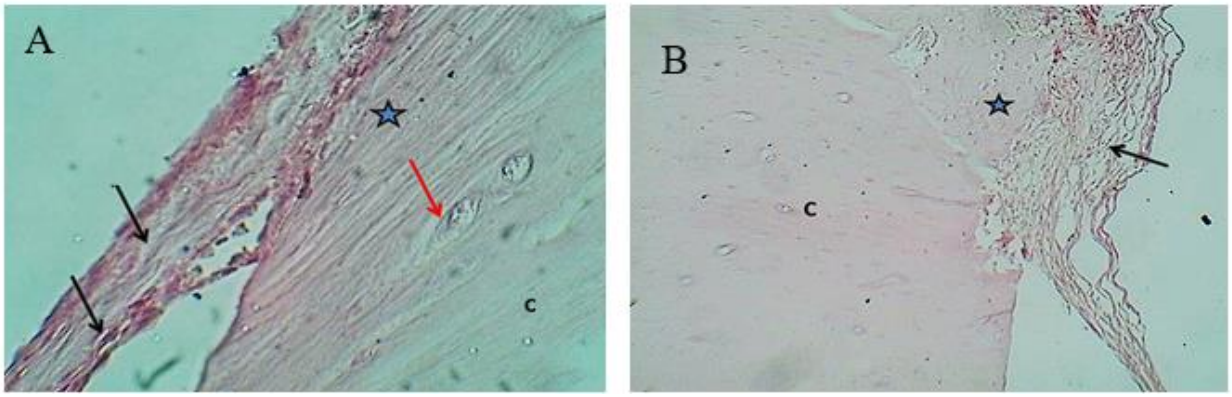
(Table-2): The Bonferroni test for comparison between the means of each two-tested group of contact angle measurement (*): Significant differences.

(I)	(J)	Mean Difference (I-J)	Differences
10%PCL	15%PCL	7.70	$p \leq 0.001$
	20%PCL	-5.30*	$p \leq 0.001$
15%	20%PCL	-13.0*	$p \leq 0.001$

3.4. Histological examination:

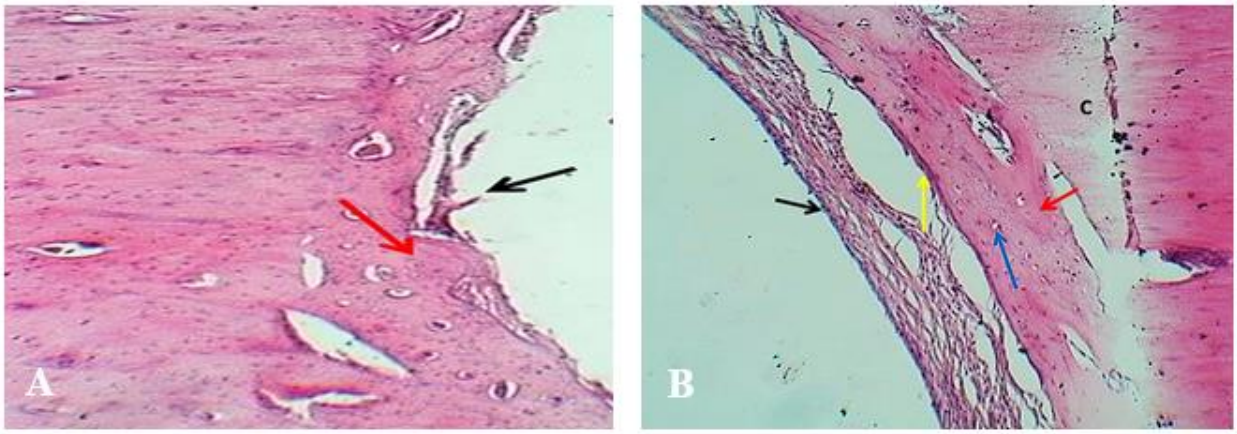
Both morphological and physical properties of a group of collagen and PCL with 20% were selected for histological examination to investigate the histological feature alteration of bone implant at two weeks post-implantation.

3.4.1. At 14 days post-operative: Microscopic examination of implant specimens of the non-coated CpTi and 20% of both collagen/PCL coated implant group revealed an almost normal appearance of the cortical bone. The rim of wall revealed formation of thin layer of fibrous osteogenic tissue in both groups, enriched with osteoblast that covered a newly deposited calcified matter composed of mature osteocytes trabeculae surrounded by osteoblast and basal bone around implant bed (Fig. 7).



(Fig-7): Sections of bone 2-week post implantation with osteogenic fibrous layer (black arrow), and almost a normal cortical bone (c); A. non-coated control group 20% collagen 20% PCL (H&E; x100).

3.4.2. Histological feature of bone implant 6 week post-implantation: Microscopic evaluation of implant specimens for the non-coated CpTi group and 20% collagen (G1) and PCL coated demonstrations were compared. The non-coated implant showed almost normal cortical bone, with development of thin layer of fibrous osteogenic tissue. A thin inner circumferential bone layer, composed of numerous osteoblasts, and numerous mature osteocytes had also developed while in collagen coated implant a thick layer of trabecular bone was developed, composed of osteogenic tissue within bone space and marked cracked cortical bone (Fig-8).



(Fig. 8): Sections of bone at 6 weeks implantation is compared with a non-coated control group 20% coated of collagen PCL (H&E; x100).

Discussion:

To enhance bone-healing efficiency, different combination of scaffolds prepared and various both in vitro and in vivo tests were used to assess the morphological, physical properties and histological responses. The intrinsic properties of polymer solution include type, structure of the polymer, as chain or molecular weight, viscosity or concentration, elasticity, electrical conductivity, polarity, surface tension of the solvent,

influence the morphology and diameter of fibers in the electrospinning process[43]. Other Processing parameters involves applied voltage, injection rate, and the collector distance that can also affect the properties of the fibers[44]. The molecular weight of the polymer, particularly, has a significant effect on rheological and electrical properties i.e. viscosity, surface tension, conductivity and dielectric strength [43]. In the present research the PCL used as binder polymer with molecular weight 4500gm/mol, that is higher than of collagen. Therefore, by increasing the concentration of PCL with polymer solution the viscosity increased, which has an important role in electrospinning procedure. Our results of SEM confirmed a positive correlation between an increase in viscosity and clarification of the fibers as prominent and less diameter. This result is in concomitant with a most recent work where the beaded electro-spun fibers had elongated as the concentration increases with a decrease in the diameter of porous than the fibroblast cell size, illustrating possibility of scaffolds type to prevent cells from getting through its fibers with a uniform and defect-free fibers at higher concentrations [45]. This might be attributed to high degree of chain overlap and the formation of entanglement coupling [46]. In a most recent research an increase in viscosity between three distinct concentrations caused decrease in fiber diameter followed by gradual [47]. An excellent nanofiber (NF) morphology has been experimentally obtained, may, ironically provide a range of ideal polymer concentration, subject to processing circumstances being adopted.

Atomic Force Microscope (AFM) can provide topographical analysis and high-resolution via three-dimensional (3D) topographic data for both micro- and Nano-scale structures. Surface roughness is also found to be essential to the osseo-integration and bone healing processes [48]. Our results showed that in first group (G1) the scaffold of 10% PCL content exhibited the lowest surface roughness that is substantiated by the SEM images of the first scaffold, where the fibers are characterized by smaller diameter, appeared less well-formed and devoid of prominent textural features. However, in G2 (15% PCL content), the scaffold displayed a higher degree of surface roughness. This rougher texture is attributed to increased fiber diameter and a larger pore size, as confirmed by SEM analysis. In G3 the surface, by SEM, the roughness trended to proportionally incline with fiber diameter i.e. the fiber diameter decreased by decrease in the scaffold's surface roughness. The latter, evidently, is attributed to the fact that a scaffold's surface roughness is intricately influenced by multiple factors i.e. viscosity, fiber diameter, and pore size. Furthermore, the degree of surface roughness plays a pivotal role in determining its suitability for promoting tissue integration [49].

Our wettability tests had yielded crucial insights into how the composition of the scaffolds has influenced their hydrophilic or hydrophobic properties [24]. Hydrophilicity, the ability of a material to attract and interact with water, is of a paramount importance in the initial stages of the osseo-integration process, particularly for facilitating cell attachment and promoting the healing process [50]. In the present study the contact angle increased as the concentration of PCL increased due to the fact

that PCL is a hydrophobic material in nature, and any increase in the concentration of PCL caused the scaffold to be more hydrophobic [51].

Meantime, the present in vivo research, targeted assessment of comprehensive effects of scaffold variants by choosing collagen 20% with 20% PCL scaffolds for osseo-integration procedure. At 2 weeks post-implantation, the ossification development was almost the same as in 6 weeks post-implantation; yet with a thicker new bone formation was inspectable around G2 at 6 weeks post-implantation. The latter could be attributed as if collagen/PCL scaffold sustains a better impact by the long intervals [52]. Further to the biological role of collagen fibers, their influence on bone might be due to the improving titanium surface characteristics via increasing the surface roughness and presence of pores that attract osteogenic cells to boost cell adhesion. To further accelerate the bone regeneration, the collagen-based scaffolds can have their surfaces changed by adding bioactive materials which deems consistent with the capability of collagen-based hydrogel, to address the excessive collagen breakdown and swelling by combining collagen with other components. Depending on the type of substance, the breakdown period of collagen-based hydrogels can be postponed for many months. Meanwhile the hydrogels may be directly loaded with bioactive substances, that could then be released at right concentrations to boost local bone repair[53]. The present research endeavors undoubtedly to contribute to the benefits implied the application of electrospinning techniques in medical implants and tissue engineering. Further investigation to explore the full potential and advancing healthcare outcomes of our technique deems so important to achieve an utmost and a comprehensive outcome in this field.

CONCLUSION

Fundamental Finding: This study demonstrated that electrospun scaffolds combining 20% collagen and 20% polycaprolactone (PCL) effectively enhanced osseointegration and tissue healing when used as coatings for commercial pure titanium (CpTi) implants. The scaffolds exhibited optimal surface roughness, porosity, and hydrophilic properties, facilitating significant osteogenic activity and basal bone formation in vivo. **Implication:** The findings underscore the potential of electrospinning technology as a versatile tool for fabricating biomimetic coatings that improve implant performance, with applications extending to dental and orthopedic implantology. Moreover, the incorporation of therapeutic agents into the scaffolds could further enhance regenerative outcomes. **Limitation:** The study's in vivo analysis was limited to a single animal model and focused on short-term effects, restricting the generalizability of the findings to clinical settings. Additionally, challenges associated with the scalability and reproducibility of the electrospinning process remain. **Further Research:** Future studies should explore the long-term biocompatibility and mechanical stability of these coatings in diverse physiological environments, assess their performance in larger animal models, and investigate the integration of bioactive agents to enhance therapeutic efficacy.

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REFERENCES

[1] M. A. H. Al Najjar and S. S. Al- Adili, "Evaluation of crestal bone resorption around dental implants in flapped and flapless surgical techniques depending on Cone Beam CT Scan (Comparative Study)," J. baghdad colege Dent., vol. 11, no. 5, pp. 231–237, 2019.

[2] M. E. Hoque et al., "Titanium and titanium alloys in dentistry: current trends, recent developments, and future prospects," Heliyon, vol. 8, no. 11, p. e11300, 2022.

[3] Y. Shibata and Y. Tanimoto, "A review of improved fixation methods for dental implants. Part I: Surface optimization for rapid osseointegration," J. Prosthodont. Res., vol. 59, no. 1, pp. 20–33, 2015.

[4] T. L. Alzubaydi, S. S. Alameer, T. Ismaeel, A. Y. Alhijazi, and M. Geetha, "In vivo studies of the ceramic coated titanium alloy for enhanced osseointegration in dental applications," J. Mater. Sci. Mater. Med., vol. 20, no. SUPPL. 1, pp. 35–42, 2009.

[5] S. A. Sell, M. J. McClure, K. Garg, P. S. Wolfe, and G. L. Bowlin, "Electrospinning of collagen/biopolymers for regenerative medicine and cardiovascular tissue engineering," Adv. Drug Deliv. Rev., vol. 61, no. 12, pp. 1007–1019, 2009.

[6] J. K. Kular, S. Basu, and R. I. Sharma, "The extracellular matrix : Structure , composition , age-related differences , tools for analysis and applications for tissue engineering," vol. 2016, 2014.

[7] V. Pankova, K. Thway, R. L. Jones, and P. H. Huang, "The Extracellular Matrix in Soft Tissue Sarcomas : Pathobiology and Cellular Signalling," vol. 9, no. December, pp. 1–17, 2021.

[8] L. O. Farhan, E. M. Taha, and A. M. Farhan, "A Case control study to determine Macrophage migration inhibitor, and N-telopeptides of type I bone collagen Levels in the sera of osteoporosis patients," Baghdad Sci. J., vol. 19, no. 4, pp. 848–854, 2022.

[9] R. Naomi, P. M. Ridzuan, and H. Bahari, "Current Insights into Collagen Type I," Polym. MDPI, pp. 1–19, 2021.

[10] V. Horbert et al., "In Vitro Analysis of Cartilage Regeneration Using a Collagen Type I Hydrogel (CaReS) in the Bovine Cartilage Punch Model," Cartilage, vol. 10, no. 3, pp. 346–363, 2019.

[11] B. W. Tillman, S. K. Yazdani, S. J. Lee, R. L. Geary, A. Atala, and J. J. Yoo, "The in vivo stability of electrospun polycaprolactone-collagen scaffolds in vascular reconstruction," Biomaterials, vol. 30, no. 4, pp. 583–588, 2009.

[12] M. Morra, "Biochemical modification of titanium surfaces: Peptides and ECM proteins," Eur. Cells Mater., vol. 12, pp. 1–15, 2006.

[13] S. Hauck et al., "Collagen/hyaluronan based hydrogels releasing sulfated hyaluronan improve dermal wound healing in diabetic mice via reducing inflammatory macrophage activity," Bioact. Mater., vol. 6, no. 12, pp. 4342–4359, 2021.

[14] S. M. Lupi, M. Torchia, and S. Rizzo, "Biochemical modification of titanium oral implants: Evidence from in vivo studies," Materials (Basel)., vol. 14, no. 11, 2021.

[15] A. J. Morwood, I. A. El-Karim, S. A. Clarke, and F. T. Lundy, "The Role of Extracellular Matrix (ECM) Adhesion Motifs in Functionalised Hydrogels," Molecules, vol. 28, no. 12, p. 4616, 2023.

[16] M. S. Carvalho and J. M. S. Cabral, "Bone Matrix Non-Collagenous Proteins in Tissue Engineering : Creating New Bone by Mimicking the Extracellular Matrix," pp. 1–33, 2021.

[17] C. Behrens, P. Kauffmann, N. von Hahn, U. Schirmer, K. Liefeith, and H. Schliephake, "Collagen-Based Osteogenic Nanocoating of Microrough Titanium Surfaces," Int. J. Mol. Sci., vol. 23, no. 14, 2022.

[18] M. Christen, "Polycaprolactone : How a Well-Known and Futuristic Polymer Has Become an Innovative Collagen-Stimulator in Esthetics," Clin. Cosmet. Investig. Dermatol., 2020.

[19] I. N. Safi et al., "Preparing polycaprolactone scaffolds using electrospinning technique for construction of artificial periodontal ligament tissue," J. Taibah Univ. Med. Sci., vol. 15, no. 5, pp. 363–373, 2020.

[20] B. Sowmya, A. B. Hemavathi, and P. K. Panda, "Poly (ε-caprolactone)-based electrospun nano-featured substrate for tissue engineering applications: a review," Prog. Biomater., vol. 10, no. 2, pp. 91–117, 2021.

[21] E. Margerrison, M. Argentieri, D. Kommala, and C. N. Schabowsky, "Polycaprolactone (PCL) Safety Profile Report Details Date of Submission ECRI Corporate Governance Project Manager," no. 540, 2021.

[22] L. Muthukrishnan, "An overview on electrospinning and its advancement toward hard and soft tissue engineering applications," Colloid Polym. Sci., pp. 875–901, 2022.

[23] T. H. Sabreen Waleed Ibrahim, "Electrospun Nano-Barium Titanate/Polycaprolactone Composite Coatings on Titanium and Ti 13Nb 13Zr Allo," Compos. Adv. Mater., pp. 1–3, 2023.

[24] A. A. Mohammed and T. I. Hamad, "Assessment of Anti-Bacterial Effect of Faujasite from Patients with Periimplantitis," J. Res. Med. Dent. Sci., vol. 9, no. 9, pp. 166–170, 2021.

[25] L. J. Del Valle, R. Camps, A. Díaz, L. Franco, A. Rodríguez-Galán, and J. Puiggalí, "Electrospinning of polylactide and polycaprolactone mixtures for preparation of materials with tunable drug release properties," J. Polym. Res., vol. 18, no. 6, pp. 1903–1917, 2011.

[26] S. A. Moosa, A. R. Jabur, and E. S. Al- Hassani, "Preparation and physical properties of Pcl-metoprolol tartrate electospun nanofibers as drug delivery system," Key Eng. Mater., vol. 886, pp. 183–188, 2021.

[27] A. R. Tan, J. L. Ifkovits, B. M. Baker, D. M. Brey, R. L. Mauck, and J. A. Burdick, "Electrospinning of photocrosslinked and degradable fibrous scaffolds," J. Biomed. Mater. Res. - Part A, vol. 87, no. 4, pp. 1034–1043, 2008.

[28] A. R. Jabur, E. S. Al-Hassani, A. M. Al-Shammari, M. A. Najim, A. A. Hassan, and A. A. Ahmed, "Evaluation of Stem Cells' Growth on Electrospun Polycaprolactone (PCL) Scaffolds Used for Soft Tissue Applications," Energy Procedia, vol. 119, no. September, pp. 61–71, 2017.

[29] A. Ross, M. A. Sauce-guevara, and E. I. Alarcon, "Peptide Biomaterials for Tissue Regeneration," vol. 10, no. August, pp. 1–16, 2022.

[30] M. Li, M. J. Mondrinos, X. Chen, M. R. Gandhi, F. K. Ko, and P. I. Lelkes, "Elastin Blends for Tissue Engineering Scaffolds," J. Biomed. Mater. Res. Part A, vol. 79, no. 4, pp. 963–73, 2006.

[31] A. Zielińska et al., "Scaffolds for drug delivery and tissue engineering: The role of genetics," J. Control. Release, vol. 359, pp. 207–223, 2023.

[32] X. Gao, S. Han, R. Zhang, G. Liu, and J. Wu, "Progress in electrospun composite nanofibers: Composition, performance and applications for tissue engineering," J. Mater. Chem. B, vol. 7, no. 45, pp. 7075–7089, 2019.

[33] B. N. Blackstone, S. C. Gallentine, and H. M. Powell, "Review collagen-based electrospun materials for tissue engineering: A systematic review," Bioengineering, vol. 8, no. 3, pp. 1–16, 2021.

[34] H. A. Owida et al., "Recent Applications of Electrospun Nanofibrous Scaffold in Tissue Engineering," Appl. Bionics Biomech., vol. 2022, pp. 1–15, 2022.

[35] J. R. Dias, A. Sousa, A. Augusto, P. J. Bártolo, and P. L. Granja, "Electrospun Polycaprolactone (PCL) Degradation: An In Vitro and In Vivo Study," Polymers (Basel)., vol. 14, no. 16, pp. 1–15, 2022.

[36] N. Brodusch, H. Demers, and R. Gauvin, Field emission scanning electron microscopy: New perspectives for materials characterization. 2018.

[37] Z. Chen, J. Luo, I. Doudevski, S. Erten, and S. H. Kim, "Atomic Force Microscopy (AFM) Analysis of an Object Larger and Sharper than the AFM Tip," Microsc. Microanal., vol. 25, no. 5, pp. 1106–1111, 2019.

[38] B. Thomas, K. Bhat, and M. Mapara, "Rabbit as an animal model for experimental research," Dent. Res. J. (Isfahan)., vol. 9, no. 1, p. 111, 2012.

[39] B. Skiles, N. A. Johnston, G. K. Hendrix, and D. L. Hickman, "Effectiveness of the Glass Bead Sterilizer for Sterilizing Surgical Instruments," J. Am. Assoc. Lab. Anim. Sci., vol. 61, no. 3, pp. 252–255, 2022.

[40] F. A. and A. and M. AL-Askar, "Does Ultraviolet Radiation Exhibit Antimicrobial Effect against Oral Pathogens Attached on Various Dental Implant Surfaces ?," Dent. J., 2022.

[41] A. A. Bazzaz (2020). Poor nociceptive innervation of neck skin in 3 domestic ruminants. European Journal of Molecular & Clinical Medicine; 7(9): 111-117. ISSN 2515-8260.

[42] Z. S. Abdullah, M. S. Mahmood, F. M. A. Abdul-Ameer, and A. A. Fatalla, "Effect of commercially pure titanium implant coated with calcium carbonate and nanohydroxyapatite mixture on osseointegration," J. Med. Life, vol. 2023, no. 1, pp. 52–61, 2023.

[43] G. J. Colmenares-Roldán, Y. Quintero-Martínez, L. M. Agudelo-Gómez, L. F. Rodríguez- Vinasco, and L. M. Hoyos-Palacio, "Influence of the molecular weight of polymer, solvents and operational condition in the electrospinning of polycaprolactone," Rev. Fac. Ing., vol. 2017, no. 84, pp. 35–45, 2017.

[44] A. Al-Khateeb, E. S. Al-Hassani, and A. R. Jabur, "Metallic Implant Surface Activation through Electrospinning Coating of Nanocomposite Fiber for Bone Regeneration," Int. J. Biomater., vol. 2023, 2023.

[45] H. El-Hamshary, M. E. El-Naggar, A. El-Faham, M. A. Abu-Saied, M. K. Ahmed, and M. Al-Sahly, "Preparation and characterization of nanofibrous scaffolds of ag/vanadate hydroxyapatite encapsulated into polycaprolactone: Morphology, mechanical, and in vitro cells adhesion," Polymers (Basel)., vol. 13, no. 8, pp. 1–19, 2021.

[46] M. G. McKee, G. L. Wilkes, R. H. Colby, and T. E. Long, "Correlations of Solution Rheology with Electrospun Fiber Formation of Linear and Branched Polyesters," Macromolecules, vol. 37, no. 5, pp. 1760–1767, 2004.

[47] S. Akkoyun and N. Öktem, "Effect of viscoelasticity in polymer nanofiber electrospinning: Simulation using FENE-CR model," Eng. Sci. Technol. an Int. J., vol. 24, no. 3, pp. 620–630, 2021.

[48] J. Han et al., "Surface Roughness and Biocompatibility of Polycaprolactone Bone Scaffolds: An Energy-Density-Guided Parameter Optimization for Selective Laser Sintering," Front. Bioeng. Biotechnol., vol. 10, no. July, pp. 1–12, 2022.

[49] S. Kligman et al., "The impact of dental implant surface modifications on osseointegration and biofilm formation," J. Clin. Med., vol. 10, no. 8, 2021.

[50] L. Parisi et al., "Titanium dental implants hydrophilicity promotes preferential serum fibronectin over albumin competitive adsorption modulating early cell response," Mater. Sci. Eng. C, vol. 117, no. June, 2020.

[51] S. Moosa, A. Jabur, E. Al-Hassani, and A. Al-Shammari, "Evaluation of PCL Electrospun Scaffolds Concentration on Metformin Hydrochloride Release Ratio," Eng. Technol. J., vol. 40, no. 12, pp. 1–12, 2022.

[52] P. Melo et al., "Electrospun Collagen Scaffold Bio-Functionalized with Recombinant ICOS-Fc: An Advanced Approach to Promote Bone Remodelling," Polymers (Basel)., vol. 14, no. 18, 2022.

[53] Y. Li et al., "Collagen-based biomaterials for bone tissue engineering," Mater. Des., vol. 210, p. 110049, 2021.

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