Nano-roughness Modification Of 3D Printed Poly (Lactic Acid) Polymer Via Alkaline Wet Etching Towards Biomedical Applications

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The developments of nano-roughness surface textures are important to implement enhanced osseointegration, cell adhesion, and proliferation in polymers for biomedical applications such as tissue engineering scaffolds and orthopaedic implants. The hydrophilicity of the polymeric implants is a crucial factor for cell adhesion, which can be improved via adapting the roughness of the surface. This study explores the surface modification of poly (lactic acid) (PLA) polymer through an alkaline wet etching process, varying alkaline concentration and etching time under both room temperature and elevated conditions. The main objective is to refine the PLA surface through wet etching, altering its properties for potential use in biomedical contexts. The assessment of surface roughness is conducted through scanning electron microscopy (SEM), atomic force microscopy (AFM), and fourier-transform infrared spectroscopy (FTIR). These techniques offer a comprehensive analysis of surface topography, nanoscale roughness, and potential chemical changes resulting from the wet etching process. The nano-roughness of treated 3D printed PLA was increased by 1.4 times compared to the control 3D printed PLA. The research contributes to the broader field of biomaterial engineering, laying the groundwork for subsequent investigations that will focus on applying the derived conclusions to enhance PLA's biocompatibility and functionality in tissue engineering and orthopaedic applications.

Keywords: Surface modification; Nanostructures; Tissue engineering; Biocompatible; Biodegradable

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1. Introduction

PLA is a biocompatible, biodegradable polymer which is made from renewable resources such as corn starch or sugarcane [1]. It is commonly used in many biomedical applications including bone tissue engineering, drug delivery, implant fixation devices (screws, pins, and wires), stents, and sutures [2–7]. Despite PLA's low mechanical strength, it has several advantages such as high biocompatibility, osteoblast stimulation, 3D printability, and non-toxic degradation, making it a viable solution for biomedical applications [4, 8, 9]. Among them, 3D printability is a crucial aspect in biomedical implants due to its inherent advantage of customization, and fabrication of complex structures in patientspecific implants. Moreover, having a rougher surface or nanoporous surface can increase the surface area of the implant and make more attachment sites for the cells to adhere [10–12]. This can enhance cell spreading and proliferation. Deng et al. have studied the effect of surface roughness and hydrophilicity of carbon fiber-reinforced polyetheretherketone (CFRPEEK)-nanohydroxyapatite ternary composites polymer compared to pure PEEK on cellular response of osteoblast cells via in vitro and in vivo studies [13]. Results revealed that the composite with optimal roughness can enhance the biocompatibility in vitro and osseointegration in vivo. Interestingly, Majhy et al. enhanced the roughness of polydimethylsiloxane (PDMS) substrate by making a coating using carbon soot particles [12]. This resulted in increased surface energy due to increased roughness which led to enhancement in cell growth and proliferation. From these studies, it is evident that surface roughness plays a vital role in such biomedical applications. Overall, in orthopedic and dental implant applications, surface roughness promotes osseointegration which is the direct structural and functional connection between living bone and the surface of a load-bearing implant [13–15]. This results in better stability and long-term success of the implant [14, 15].

Different surface modification methods have been conducted in metals and polymers such as turning, blasting, acid etching, alkaline etching, anodizing, electropolishing, plasma spraying, composites, coatings and biochemical etching [12–14, 16–18]. Moreover, mechano-bactericidal polymeric surfaces also consist of nano-scale roughness due to the nanofeatures present for bacteria lysing activities [4, 19–22]. Fabrication methods like reactive ion etching, colloidal lithography, electron beam lithography, nanoimprinting lithography, laser-based lithography, and anodic aluminum oxide templating are precise nanostructure fabrication methods for polymers [4, 19]. However, the development of nano-rough surfaces using a facile and costeffective method is still an unmet need.

Wet etching is an economical option in terms of the low complexity of the process and the raw materials used. Wet etching uses acidic or basic solutions [23, 24]. In most of the studies, a mask is used to etch the surface selectively to get a homogeneous roughness or micro-nanofeatures [25, 26]. Also, it can be performed in elevated temperatures beyond room temperature and uses other supporting processes like ultrasonication to control the etching [23]. To investigate the impact of alkaline concentration, etching time, and temperature on the alterations in surface roughness of PLA surfaces, 3D-printed PLA substrates were employed. To facilitate this exploration, a wet etching process was implemented in an alkaline environment. We used different concentrations of sodium hydroxide (NaOH) solution as the wet etching medium. Concentration and reaction time are critical parameters in the wet etching process. According to the study of Vaid et al, PLA undergoes a hydrolysis process in an alkaline medium [27]. They examined the hydrolytic degradation of PLA in high pH conditions and the impact on physical and mechanical properties. Moreover, another group of researchers studied the effects of aqueous NaOH treatment on 3D printed PLA scaffolds [24]. They concluded that alkaline treatment induced surface changes, initially roughening and later smoothing before dissolution. Further, this study concluded erosion rates and morphologies are controllable without compromising bulk mechanical properties. Another group of researchers studied the effect of crystallinity and the density changes in PLA/Date palm wood green composites via NaOH and potassium hydroxide (KOH) treatment to assess it for thermal insulations [28]. This study also revealed that the treatment enhanced the crystallinity while producing lighter composites. These nanostructured PLA surfaces have been coated with nano-hydroxyapatite after alkaline (ammonia) treatment for 6 hours [29]. The results showed that cell adhesion was improved after the treatment.

Besides alkaline solutions, solvents and acids are extensively used to modify the surfaces of PLA [30, 31]. Abdulkareem et al., modified the PLA surface using food additives such as ascorbic acid (ASA) and fumaric acid (FA) through plasma-initiated grafting reactions. The modified PLA exhibited improved adhesion to aluminum foil in laminate structures, with peel resistance increasing by 74% (ASA) and 184% (FA) compared to untreated PLA [30]. Moreover, Karthikeyan et al. used a process called the dip-dip-dry (DDD) surface modification. This was a solvent induced surface modification method that used acetone and deionized (DI) water to treat PLA. initially, this was established for amorphous 3D-printed PLA, and was optimized for enhancing the wettability of commercially available PLA [31]. A preheat treatment in ethylene glycol reduced surface crystallinity, facilitating microstructure formation with acetone/water. The shift from hydrophilic to superhydrophobic was linked to increased surface roughness, confirmed by SEM micrographs.

Despite several studies on alkaline, solvent, and acid treatment for PLA, the effects of roughness, concentration, etching time, and temperature have not been thoroughly investigated. These factors not only alter the roughness but also lead to the formation of nano-porous structures. Surface modification of 3D printed PLA using alkaline wet etching was examined, and the results were subsequently statistically analyzed. This analysis aimed to identify the relationships between parameters, laying the groundwork for the potential modification of PLA surfaces for biomedical applications.

2. Methodology

2.1. Experimental setup

Relevant PLA substrates were 3D printed using Lulz bot mini 2 fused deposition modeling (FDM) 3D printer with 0.25 mm layer thickness. The sample size was 10 mm × 8 mm × 1 mm (L x W x H). Moreover, for the comparison of the control sample, surface molded flat PLA substrates were purchased from Alfa Chemistry, USA. Samples were cleaned via a three step cleaning process. They were sequentially cleaned with 99.7% (V/V) ethanol, miliiQ (18.2 M Ω .cm at 22.5°C via Millipore Q-pod milliQ water system) water, and N₂(g).NaOH (99%, $M_W = 40$ g mol⁻¹, Sigma-Aldrich) solutions with different concentrations, such as 0.25 M (*moldm*⁻³), 0.5M, 0.75M, and 1 M were used for 3 D printed PLA. During the preparation of NaOH solutions, NaOH pellets were added to milliQ DI water and sonicated to mix it properly in a water bath sonicator for 5 minutes.

2.2. Alkaline wet etching at room temperature conditions

3D printed PLA substrates were added to the prepared solution with 4 replicates with 3 repeats, kept at room temperature (22.5°C), and taken out after 2 hours and 24 hours as shown in Table 1 and Fig. 1. Samples were properly cleaned before and after the wet etching via the 3-step cleaning method. After the cleaning process, the samples were dehydrated by keeping them inside the dehydrating oven (fan dehydration) for 3 hours at 40 °C to remove trapped ethanol and moisture.



Fig. 1. Experimental setup of 2-hour and 24-hour wet etching.

2.3. Alkaline wet etching at elevated temperature conditions

A set of experiments was conducted to modify the PLA surface inside a hydrothermal vessel (Fig. 2(b)) at elevated temperature conditions. NaOH was used as the alkaline medium. The hydrothermal vessel contains a polytetrafluoroethylene (PTFE) container with 100 ml volume which prevents the alkaline medium from reacting with the container. The low-temperature alkaline wet etching process was conducted at 70 °C, hence there was no pressure buildup inside the vessel due to no evaporation of the alkaline solution at this temperature. The same three step cleaning procedure was used before and after wet etching. Cleaned samples were arranged in a PTFE holder as depicted in Fig. 2(a). Since the etching temperature exceeded the glass transition temperature (GTT) of PLA, this PTFE holder was used to avoid contact between samples. Also, the holder contained grooves that can accommodate the samples to be placed at an angle of 45° to allow the sample to react with NaOH effectively. Holders with fixed 3D printed PLA substrates were added to the prepared NaOH solution with different concentrations and etching times as depicted in Table 2. Each experiment consisted of 4 replicates and was repeated 3 times. Samples were properly cleaned via the three step cleaning method after the wet etching process. Except for experiment WE/70/1M/2h+24h, all the samples were immediately taken out from the hydrothermal vessel and cleaned via the three step cleaning process. Then the samples were dehydrated by keeping them inside the dehydrating oven (fan dehydration) for 3 hours at 40 °C.





2.4. Surface characterization

Surfaces were characterized using Tescan Mira 3 SEM to identify surface topography after the modification. Samples were coated using platinum material with a 6nm layer. The bottom side of the sample was coated with carbon paint and attached to the SEM stub for proper fixation and

Experiment Code	NaOH Concentration	Etching Time		
Experiment Code	(moldm $^{-3}$)	(hours)		
WE/RT/0.25M/2 h	0.25	2		
WE/RT/0.5M/2 h	0.5	2		
WE/RT/0.75M/2 h	0.75	2		
WE/RT/1M/2h	1	2		
WE/RT/0.25M/24 h	0.25	24		
WE/RT/0.5M/24 h	0.5	24		
WE/RT/0.75M/24 h	0.75	24		
WE/RT/1M/24 h	1	24		
Table abbreviations: Wet etching-WE; Room temperature-RT				

Table 1. Comparison of time performance and performance with different superpixel methods

Table 2. List of elevated temperature alkaline wet etching experiments.

		Primary		
	NaOH	Etching Time at	Secondary Etching	
Experiment Code	Concentration	Elevated	Time at Room	
1.	(moldm $^{-3}$)	Temperature of	Temperature of 22.5 ∘C	
	, ,	70°C (hours)	1	
WE/70/0.75M/1 h	0.75	1	0	
WE/70/0.75M/2 h	0.75	2	0	
WE/70/1M/2 h	1	2	0	
WE/70/1M/2 h + 24 h	1	2	24	
Table abbreviations: Wet atching WE				

Table abbreviations: Wet etching-WE



Fig. 3. (a). 3D printed PLA substrate; (b). Molded flat PLA substrate; (c-e). SEM micrographs of 3D printed PLA at scale: 5μ m; (f). SEM micrographs of molded flat PLA at scale: 10μ m

increased conductivity of the sample for better visibility in SEM. A lower beam energy and intensity with beam deceleration mode was used due to the non-conductivity and porosity of the sample. Moreover, due to the availability of hydrocarbons from trapped ethanol on the surface, images drifted during the imaging. Hence samples were properly dehydrated inside the dehydration oven for 3 hours at 40 °C. Moreover, samples were cleaned using Evactron plasma cleaner for 2 minutes at 250 mTorr pressure and 15W of plasma power to remove impurities contaminated during the processing. Bruker atomic force microscopy (AFM) was used to characterize the surface deviation of the wet-etched PLA substrates. Scanasyst air mode with tapping mode was used. A 5µm scan size and 512 histogram bins were used for 3 repeated samples. Due to the high deviation of surface in 3D printing, 1st order plane fit and flatten option was used to make the surface fit to the horizontal plane for assessing the roughness results. To assess the surface chemistry of the modified surface, Nicolet FT-IR was used with VariGATR germanium surface.

2.5. Statistical data analysis

The statistical analyses of roughness was performed using One-way ANOVA of the general linear model at the 95% confidence interval with Minitab software (Version 21.1), and the pairwise mean comparison was done with the Tukey method at the same confidence interval. Not significant (NS): P>0.05, significant: $P \le 0.05$.

3. Results and discussion

Initially, the 3D printed samples were imaged through SEM to get an understanding of the surface topography compared to the flat PLA substrate. The 3D printed samples contained large pores and deviations of the surface due to layer-by-layer deposition of material in 3D printing.



Fig. 4. Surface topography via SEM and AFM (*) micrographs. (a). 3D printed PLA (scale: 5μ m; (b-i) Room temperature wet etching (scale: (b-e) 5μ m, (f-i) 2μ m); (j-m). Elevated temperature wet etching (scale: 5μ m) (AFM Z-axis is expanded to visualization (aspect ratio = 0.4)).

The SEM images of the same sample shown in Fig. 3(c-e) confirmed this. However, the molded flat PLA substrates showed an almost flat surface through SEM as depicted in Fig. 3(b, f). Hence, to study the roughness and heights through AFM, set of flat (less deviation) 5 μ m x 5 μ m areas were used.

The reaction time was used as 2 hours to avoid major degradation of the PLA substrates. As per Vaid et al., complete degradation of PLA occurs in 3M NaOH concentration over 48 hours [27]. Therefore, this study employed a low concentration to avoid excessive degradation and distortions in samples. As per the SEM images depicted in Fig. 4, compared to the control sample (Fig. 4(a1)), hydrolyzed substrates have shown a change in surface topography without demonstrating homogenous nanofeatures except in 0.5M concentration (Fig. 4(c1-3)). However, nanofeature height is low compared to other samples etched in room temperature. Under elevated temperatures, the surface height exhibited minimal changes compared to the experiments conducted at room temperature, particularly in comparison to WE/RT/0.75M/2h and WE/RT/1M/2h with WE/70/0.75M/2h and WE/70/1M/2h, as evidenced by SEM images. This interpretation was further supported by the average roughness (Ra) data (Fig. 5). The graph indicates comparable results, as these experiments share the common letters A and B, attributing to a high standard deviation (SD) of roughness. Notably, the experiment WE/70/1M/2h+24h displayed elevated roughness and porosity compared to other experiments (Fig. 4(m1) and Fig. 5).

Despite the SEM image of the WE/70/1M/2h+24h experiment showing a distinct topographical difference among elevated temperature surface modifications, as shown in Fig. 5, the Ra remained consistent. However, porosity, as observed in the SEM images, was exclusive to the WE/70/1M/2h+24h experiment. This occurrence may be attributed to the additional 24 hours of etching, leading to further cleavage of the PLA. When comparing the elevated temperature experiments with the control sample, all samples exhibited a notable increase in Ra, except for the WE/70/1M/2h experiment. The WE/RT/0.5M/24h experiment displayed the highest mean Ra, revealing some nanofeatures visible in the SEM micrograph (Fig. 4(g1)), akin to the same experiment conducted with a 2-hour etching time. However, the roughness was significantly lower than in the 24-hour etching experiment. Despite the significant changes in roughness observed through SEM in the WE/RT/0.5M/2h experiment compared to the control sample; the mean Ra values presented in the graph

(Fig. 5) indicated that the roughness is nearly identical in both cases. The WE/RT/0.75M/24h and WE/RT/1M/24h experiments exhibited nearly identical topography in SEM micrographs, and the corresponding Ra values displayed the lowest mean among all experiments, even lower than the control sample. However, due to the high standard deviation in the control sample Ra, roughness is considered comparable.

Moreover, the Ra values of elevated temperature experiments are significantly higher compared to these two experiments. The reason for this can be due to the shifting of PLA substrate from solid state to rubbery state at 70 °C due to exceeding the GTT of PLA which is at 60-65 °C [4]. Moreover, the etching rate is accelerated at higher temperatures. Also, the observed low SD in elevated temperature experiments compared to RT experiments could be due to the decrease in surface irregularities and deviations when PLA becomes rubbery via surpassing its GTT. In summary, it can be inferred that Ra values increase with longer etching times and higher temperatures. Additionally, both room temperature and elevated temperature wet etching result in a porous structure in PLA.



Fig. 5. Roughness values obtained from AFM micrographs for both room temperature and elevated temperature wet etching. Average roughness is denoted in Ra. Bars that do not share a letter are significantly different (95% confidence interval).

The FTIR spectrum revealed the presence of the O-H functional group within the wavenumber range of 2950-3750 cm⁻¹ (Fig. 7(a)). This broad absorbance peak indicates the stretching vibrations of the O – H functional group in response to infrared energy, suggesting the presence of moisture, alcohol, and acid in the samples [32]. In contrast, the control sample exhibited this peak with lower intensity. According to the literature, the hydroxyl (O-H) functional group resulting from acids typically falls within the range of $2500 - 3300 \text{ cm}^{-1}$, while O – H (alcohol) is expected in a narrower wavenumber range ($3230 - 3550 \text{ cm}^{-1}$). The broad peak observed in the IR spectra after wet etching suggests an increased presence of both O-H (acids) and O-H (alcohol), likely due to the formation of lactic acid through hydrolysis and the cleaning process with ethanol.

During the hydrolytic degradation of PLA in alkaline conditions, hydroxyl ions (OH^-) attack the ester carbon. However, when a higher concentration of hydroxyl is present, the ether which is linked to the tetrahedral intermediate (CH_3CO^-) induces hydrolysis of the PLA chain by producing oligomers with alcohol and carboxylic acid end groups. This leads to chain scission and consequently, polymer degradation via producing polymer monomer like lactic acid and its salt sodium lactate as illustrated in Fig. 6 [24, 27, 33].



Fig. 6. PLA hydrolysis under alkaline solution.

All the curves were similar showing almost the same composition, but differences were observed in a few experiments. A low-intensity narrow peak, identified within the region of $2800 - 3000 \text{ cm}^{-1}$, can be attributed to the stretching of C - H in CH_3 functional groups [32, 34, 35]. The intensity of this peak was higher in the majority of the elevated temperature experiments compared to room temperature experiments. This can be due to the structural changes that occurred after etching at 70°C which leads to a change in bond length and angle. Additionally, in the fingerprint region ($< 2000 \text{ cm}^{-1}$), specific functional groups become crucial in describing the effects of surface modification. According to the literature, the peak observed between $1700 - 1800 \text{ cm}^{-1}$ is linked to the stretching vibrations of the C = O functional group [30, 36–38], likely originating from the carboxylic functional group in PLA. Notably, this peak was increased in elevated temperature etching conditions compared to the control sample, indi-



Fig. 7. IR spectra obtained from all wet etched 3D printed PLA samples.

cating higher absorbance intensities due to cleavage of PLA and increase in C = O functional group concentrations. Furthermore, a narrow low-intensity peak in the FTIR spectrum between $1300 - 1500 \text{ cm}^{-1}$ (peaks (d) and (e) in Fig. 7) was likely due to the bending of methyl (CH₃) groups, C-H groups, and O-H groups [32, 34, 38, 39]. Multiple peaks between 1000-1300 cm⁻¹ were attributed to the C-O stretching in the ester group of PLA and lactic acid [37, 38], following cleavage during the etching process.

In conclusion, the FTIR spectrum of the experiments showed similar peaks at specific wavenumbers, with no new peaks observed after etching. However, intensity changes were observed due to variations in different functional groups resulting from the hydrolysis of PLA.

4. Conclusion

This study focused on surface modification of 3D-printed PLA through alkaline wet etching at various concentrations, etching times, and temperatures. The results from all characterizations indicated that temperature played the most dominant role in changing the roughness, compared to other factors such as alkaline concentration and etching time. Under elevated temperature conditions, Ra increased significantly. Subjecting samples to elevated temperature wet etching followed by an additional 24-hour wet etching resulted in a rougher surface with a porous structure.

While the direct implications for enhanced osseointegration, cell adhesion, and proliferation due to the roughness of PLA after treatment were not investigated in this paper, the obtained conclusions lay the foundation for future endeavours aiming to leverage these outcomes for these biomedical applications. Moreover, this research lays the groundwork for understanding how polymer surfaces can be tailored for increased roughness. By conducting additional experiments and obtaining more measurements of porosity, it would be feasible to establish correlations between the treatments and the alterations in porosity. It is evident that as the sample becomes porous, the mechanical strength of PLA diminishes. Therefore, further investigation is warranted to bridge the gap to understand the relationship between roughness and mechanical strength. Additionally, numerous studies suggest that hydrophilic surfaces attract osteoblast cells and bacteria more effectively. A comprehensive study on surface wettability is needed, and these findings can be correlated with the use of these surfaces in biomedical applications, especially in bone scaffolds, to create scaffold surfaces with enhanced osseointegration, cell adhesion, and proliferation compared to 3D-printed scaffolds without surface treatments.

Furthermore, this study identified some nanofeatures in certain experiments. By systematically altering parameters, the surfaces could be modified to possess antibacterial properties. Given the cost-effectiveness and simplicity of this method, it stands as a potentially effective solution for a wide range of biomedical applications.

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