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Effect of Binder on Bio-ceramic Mechanical Properties and Surface Roughness when Milling

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Abstract

Under pressing during milling, the study focuses on the impact of binders on the surface roughness of bioceramics, specifically hydroxyapatite (HAp). The main goal is to find the ideal binder percentage in HAp bioceramics to attain the required surface roughness. The application of polyvinyl alcohol (PVA) and polyethene glycol (PEG) as binders at different concentrations is investigated in this work. The process comprises prepping the HAp samples, combining them with binders, compressing and sintering them, and then milling them under carefully monitored conditions. Next, the machined parts' surface roughness is measured. The goal of the research is to optimise the binder composition of bioceramic implants in order to improve their mechanical properties and surface integrity. By shedding light on the processing variables that affect the functionality and calibre of bioceramic implants, this study advances the field of biomaterials..

1. Introduction

Numerous materials and circumstances are involved in bone regeneration, and interactions between substrates and environmental factors result in a balance between osteoclasts and osteoblasts. Biomaterials have been the subject of much clinical research on bone regeneration. It involves numerous biological processes and is clinically complex. Both in vitro and in vivo research have been done on a wide range of topics, including the interaction between osteoclasts and osteoblasts, osteogenic differentiation, the stimulation effects of bone, cell growth, signalling pathways, and bone growth factors.

Calcium phosphate exhibits osteoconductive and, in certain situations, osteoinductive properties, and it has found widespread application in bone regeneration applications. To promote bone regeneration, the activation of osteoblasts and osteoclasts is regulated by releasing calcium and phosphorus ions. The regulation of calcium phosphate's surface characteristics and porosity impacts the growth and adhesion of cells and proteins and the formation of bone minerals. Different calcium phosphate types, such as HAP and TCP, have different properties that affect bioactivity [1]. These variations can be used in different applications due to differences in ion release, solubility, stability, and mechanical strength. Different calcium phosphates have been combined or mixed with other materials to highlight their advantages and complement their drawbacks to take advantage of these properties.

Calcium Phosphate has specific bioactive properties and is effective in promoting bone regeneration. It has been used for bone regeneration in various forms, including scaffolding, cement, and coating [2]. Furthermore, several studies have been actively conducted to enhance the effectiveness of calcium phosphate when combined with different healing agents. Calcium phosphate can improve the clinical treatment strategy for bone defects and diseases by providing an overview of the substance's characteristics and future research directions.

In a machining operation, milling is done by cutters revolving to remove material from the workpiece in the direction of the angle with the tool axis. Applying the milling process may conduct various operations and functions and produce high-precision items ranging in size from small to huge [3]. Existing milling processes and mechanical properties of porous HAp have certain drawbacks, which lead to increased machining cost and time. The surface properties of machined HAp play an important role in the quality of implants, which demands good surface integrity. With scale grains, the mechanical properties of HAp ceramic are improved significantly, and there is a potential for this material to act alone as implants in specific applications

The bio-ceramic biocompatibility, such as HAp, depends on the combination percentage of binder, which will enable HAp to have porous structures, be bioresorbable and have stronger bonding to the bone. A binder is any material or substance that holds other materials together to form a cohesive whole mechanically and chemically, as well as adhesion or cohesion. Clarifying the interaction between HAp and percentage binder will have some effect on the milling operation and surface roughness.

Surface roughness is crucial in determining the functionality and quality of machined components in precision machining. Pursuing optimal surface finishes has prompted scientists and technicians to investigate novel techniques that can augment the milling procedure [4]. The selection of binders adds a complex layer to the machining process because binders are components of composite materials, their properties can greatly affect the end-milled product's surface quality and structural integrity. Moreover, the relationship between binders and surface roughness is further complicated by using cold isostatic pressure, a method well-known for its capacity to densify and homogenise powders. Comprehending the complex interactions among these factors is essential for enhancing milling procedures and attaining targeted surface finishes in diverse industrial uses. To provide a thorough overview of studies that examine the effects of binders and pressure on surface roughness during milling, this literature review attempts to synthesise the body of knowledge already available on the topic. We aim to identify patterns, gaps, and areas ready for more investigation by carefully examining the methodologies, findings, and trends in the literature. In the end, this synthesis will further the development of machining methods by offering knowledge that can guide the creation of more accurate and efficient milling procedures.

2. Biomaterials

Biomaterials are now vital to medicine because they aid in patients' recovery from diseases and injuries and enable them to regain function. Synthetic or natural biomaterials are used in medical applications to replace, enhance, or maintain biological functions or damaged tissue. Biomaterials were first used in history when the ancient Egyptians used animal sinew sutures. The fields of medicine, biology, physics, chemistry, and, more recently, materials science and tissue engineering have all impacted the current understanding of biomaterials. The field has grown significantly over the last ten years due to advancements in tissue engineering, regenerative medicine, and other areas. Any material, including glass, ceramics, metals, plastic, and even living cells and tissue, can create a biomaterial. They can be reengineered into moulded or machined parts, coatings, fibres, films, foams, and textiles for biomedical products and devices [5]. Among them are implants in the teeth, hip replacements, heart valves, and contact lenses. They frequently leave the body gradually after serving a purpose because they are biodegradable and, in some cases, bio-absorbable as new. The fields of medicine, biology, physics, chemistry, and, more recently, materials science and tissue engineering have all impacted the current understanding of biomaterials. Over the last ten years, significant growth has been seen in the field due to developments in tissue engineering, regenerative medicine, and other fields.

Among the world's leading causes of mortality are infectious diseases caused by bacteria. In 2019, drug-resistant bacterial infections claimed the lives of 4.95 million people despite the use of numerous antibiotic treatment approaches. The yearly death toll will rise to 10 million by 2050. Bacterial heterogeneity in the infection microenvironment, including drug-resistant bacteria, biofilms, persister cells, intracellular bacteria, and small colony variants, could contribute to the rising mortality rate. Furthermore, biomaterials with direct antimicrobial activity are inadequate for the long-term treatment of chronic bacterial infections due to the immune microenvironment's complexity at different infection stages. The inability of the biomaterials to alter the immune cells' active antimicrobial activity may be partially to blame for the rising death rate [6].

2.1 Bio-Ceramic

Both organic and inorganic materials can be found in bone. Water makes up about 8–10% of bone, the inorganic phase accounts for 60%, and the remaining portion comprises organic materials. The organic portion of bone comprises cells (about 2%) and various non-collagenous proteins in addition to collagen type I. This component is crucial to the bones' function and significantly impacts their biochemical and mechanical characteristics. Three polypeptide chains make up the structure of type I collagen. The structure leads to the formation of a nearly 300 nm-long, stiff layer of molecules. A collagen fibril is formed by the arrangement of individual molecules next to one another. These fibrils then group together to form a collection of collagen fibres.

The mineralised framework of bone comprises collagen fibres and calcium salts. Magnesium phosphate, calcium carbonate, and calcium hydroxyapatite are the minerals. As illustrated in Fig. 1, there are two types of bone: cortical and trabecular, each having a unique structure. Bone can regenerate itself quite well. Most fractures heal quickly with straightforward internal or external fixation. The extent of the damage can determine how much the bone can heal itself, even with this superior quality. As a result, small damage can be healed, but large defects, like segment bone defects (SBD), are difficult to heal. Scaffolds are a porous material that offers a structural and mechanical foundation for cell proliferation in tissue engineering (TE) [7]. The interconnected structure of scaffolds allows oxygen and nutrition to migrate from the scaffolds' surface to the inner part [8]. In addition, the porous architecture provides more surface area for the cells and scaffold interaction [7].

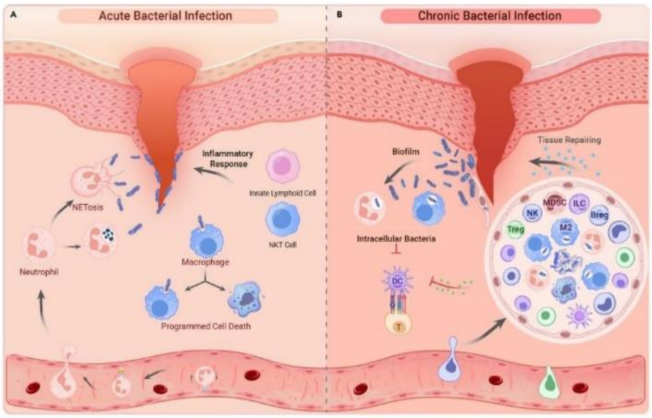


Fig.1 *Illustration shows changes in the immune microenvironment during the acute and chronic phases of bacterial infection [6]*

2.2 Hydroxyapatite (HAp)

Hydroxyapatite (HAp) is a member of the crystallographic family of apatites, whose general formula is $Me_{10}(XO_4)_6(Y)$ 2 P.N Lim. Its chemical formula is $Ca_{10}(PO_4)_6(OH)_2$. Isomersophous inorganic compounds sharing the same hexagonal structure make up this family. XO4 is a trivalent anionic group (PO_4^{3-}, VO_4^{3-}, or AsO_4^{3-}), Me usually denotes a bivalent cation (such as Ca^{2+}, Mg^{2+}, or Zn^{2+}), and Y can be either an anion or a monovalent ionic group (such as OH^-, Cl^-, or F^-). High biocompatibility, non-toxicity, bioactivity, bio-resorbability, and osteoinductivity, osteoconductivity, and osteointegration are just a few benefits of using hydroxyapatite, a natural ceramic material. The polyethene glycol (b) and hydroxyapatite (a) structures are shown in Fig. 2.

(a) **(b)**

Fig. 2 *Structures of (a) hydroxyapatite and (b)polyethylene glycol (PEG) [9]*

Due to its high mechanical strength, hydroxyapatite has several possible uses in biomedical engineering, including drug delivery, orthopaedics, dentistry, filling in bone defects, and bone cement [10]. Hydroxyapatite demonstrates a strong chemical resemblance to natural bone and biocompatibility. However, the low mechanical integrity of pure Hydroxyapatite is a drawback that needs to be appropriately addressed to meet the demands of the biological application [10]. For bioactivity and relative mechanical reliability, the perfect implant is essential. Research has focused on creating Hydroxyapatite bio-ceramics through various processing techniques to do this. Because there are many natural biowastes and low-cost methods for preparing industrially useful ceramic materials, it is noteworthy that producing Hydroxyapatite materials from natural sources offers the chance to reduce waste pollution and is also economical, friendly and environmentally sustainable [11]. It has been demonstrated that creating Hydroxyapatite powder from biogenic sources and producing ceramic compacts at a competitive price can be done and affordably using the conventional sintering technique [12]. Hydroxyapatite has been produced using a few of these procedures. The structures and materials used in these designs have well-established mechanical and physical characteristics. However, little is known about the structure-property relationships, interactions, and mechanistic complexity required for robust material design and process optimization.

2.3 Binder

Binders are materials that strengthen green ceramic bodies mechanically to withstand production processes and fire without breaking. Binder additions to bodies are frequently necessary, and certain production processes would not be possible without them. For example, adding organic binders to the pressing process of powders allows for a forming method that is not dependent on plasticity. Traditional ceramics use many binders, including synthetic materials like polyacrylates or polyvinyl alcohol and natural materials like cellulose or clays. There are several characteristics that a normal body binder must have, such as leaving a minimal amount of ash after firing, not being abrasive, its dispersion must be easy, not being toxic, etc.

2.3.1 Polyvinyl Alcohol

Typically, it is a binder for glazes before screen printing (where the surface to be painted is sprayed with a water solution containing polyvinyl alcohol). It is a potent surfactant whose ability to wet particles is related to its binding power (low molecular weight products have low viscosities and no effect on the viscosity of glazes or body slides). Because it doesn't ferment, it is stable. Typically, providers suggest polyvinyl alcohol in water solutions.

2.3.2 Polyethylene Glycols

Polyethylene glycols having low molecular weights are viscous liquids often used as plasticizers or lubricants. Those with high molecular weights are waxy solids used as binders and plasticizers in pressing. They are water-soluble and often used as basic mediums for the preparation of printing colours.

Belonging to the polyether family, polyethene glycol (PEG) is a linear polymer of ethylene oxide with a terminal hydroxyl group. PEG is a well-known, neutral, water-soluble, non-ionic biocompatible polymer. In addition, it is hydrophilic, biodegradable, non-toxic, and flexible. PEG is also frequently utilized because of its advantageous qualities in various industries, including biomedical applications. Because the polymer aggregates the nanoparticles, hydroxyapatite can be mixed with biopolymers like Polyethylene Glycol (PEG). PEG and hydroxyapatite combined can enhance the material's mechanical characteristics and biocompatibility, making it beneficial for various biomedical applications.

2.4 Surface Roughness

Surface quality, called surface integrity, is the material's outermost layer's morphology. To create the finished product, any material—including biomaterials—must undergo a manufacturing process, including sandblasting, acid etching, electrical discharge machining, anodic oxidation, and other steps. Surface roughness is the most used quantification parameter to define surface morphology, and it is crucial to quantify surface morphology.

Surface roughness is crucial to give filopodia attachment guidance cues. The cell's initial attachment is aided by the filopodia's extension into the pores [13]. Roughness on the nanoscale also affects proteins' ability to bind to surfaces, such as fibronectin, which helps cells attach to proteins via integrins [14].

Surface roughness affects osseointegration, cell attachment, and cell morphology. Therefore, looking into whether the ideal surface roughness exists makes sense. This can be used to predict cell behaviour and biocompatibility more accurately. Hatamleh and colleagues demonstrated the significance of achieving the ideal level of roughness on implant surfaces [15].

In this study, the impact of surface quality on material biocompatibility has been reviewed. The surface quality characteristics include porosity, surface chemistry, surface roughness, surface features, and crystallinity. There are procedures to alter the surface quality by applying coatings and removing surface materials to prepare the surface for a particular application. Depending on the type of cell, the surface quality affects biocompatibility differently.

3. Methodology

The methodology chapter introduces the systematic approach taken to complete the research. This includes sample testing and the fabrication process, thoroughly explaining how the research was conducted. The chapter uses flowcharts to depict the overall and experimental processes visually. Fig. 3 shows research flow charts for this study:

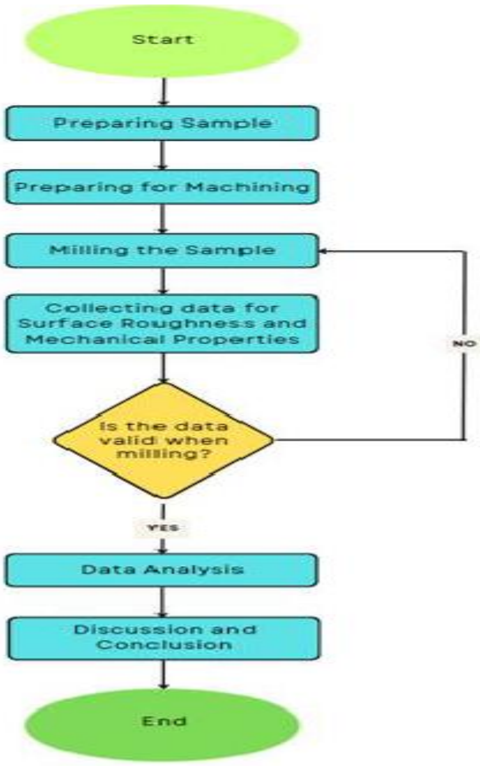


Fig. 3 *Experimental Flowchart*

4. Result and Discussion

Two test categories have been completed. The first is a powder characterisation test, a preliminary test for hydroxyapatite powder. The test that is conducted following machining is the second one. The following tests were performed to characterise the hydroxyapatite powder: X-ray diffraction, scanning electron microscopy, modulus of rupture (MOR), surface roughness, density, porosity, and tests conducted after sintering shrinkage. All of the data were analysed for a discussion and conclusion.

4.1 Mechanical Properties Test

4.1.1 Shrinkage Test

An investigation into the behaviour of hydroxyapatite has been carried out using a shrinkage test. It is possible to improve the mechanical characteristics and bioactivity behaviour by carrying out shrinkage tests. The HAp sample is preheated for 24 hours at 56 degrees Celsius to remove the binder, and then it is sintered at 1200 degrees Celsius for 120 minutes. The length of the HAp sample is measured before and after sintering to perform the shrinkage test. Vernier callipers measure the HAp sample (+- 0.005mm). Equation 1, given below, can be used to calculate the percentage of shrinkage.

$$Percentage\ Shrinkage = \frac{wet\ length@weight\ before - weight\ after}{wet\ length\ @weight\ before} \times 100\% \quad (1)$$

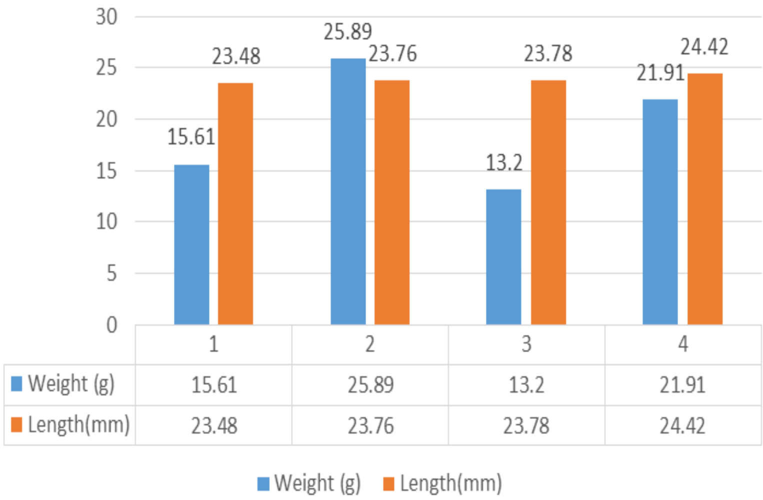


Fig. 4 *Graph Percentage of Weight and Length Shrinkage*

The shrinkage test was indicated using two ways: by the difference in length and weight of the HAp sample. Due to shrinkage after sintering, it is done between the green and sintered bodies. From the graph shown in Fig. 4, sample 4 has the highest percentage of weight shrinkage compared to other HAp samples, which is 24.42%. Other than that, sample 4 has the second highest percentage of length shrinkage, 21.91%, while the highest percentage of length shrinkage is sample 2. The difference in the percentage of shrinkage is due to the amount of water and binder in the HAp sample. This is due to the vaporisation of water and binder when sintering at 1200, in which the particles will closely pack and decrease towards the end of the process. By observing the shrinkage behaviour of the HAp sample after sintering, the expected outcome size of the HAp can be expected.

4.1.2 Modulus of Rupture (MOR)

The yield strength of the HAp sample can be determined using the maximum stress and strain that was achieved. Thus, the yield strength of the HAp sample is ascertained using Equation 2.

$$Yield\ strength = \frac{\max strength}{1 + Max\ strain} \quad (2)$$

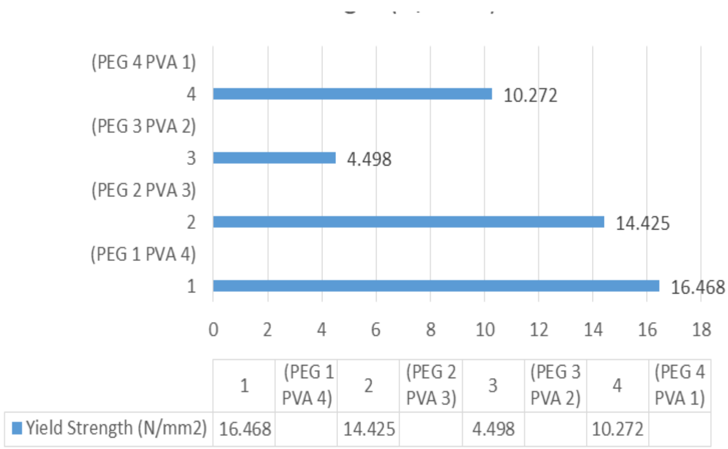


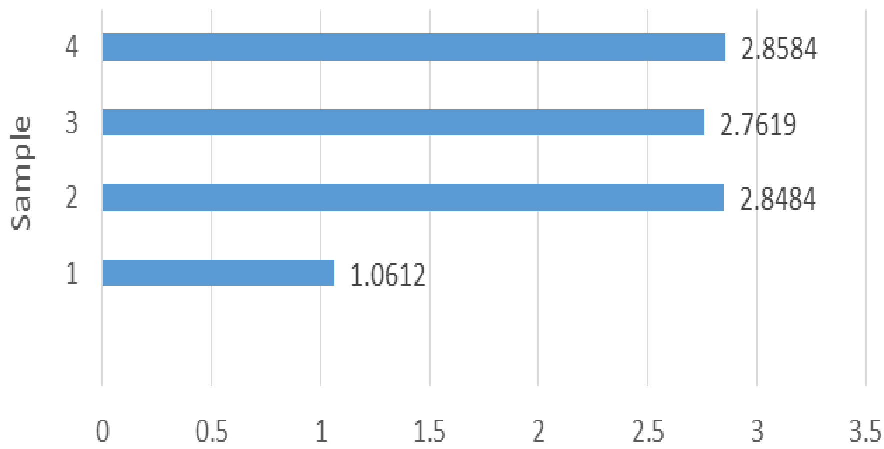
Fig. 5 *Yield strength Graph*

Sample 1 has the highest yield strength, 16.468 N/mm², according to the graph in Figure 4.2, while sample 2 has the second-highest yield strength, 14.425 N/mm2. Regarding samples 3 and 4, the yield strength values obtained fall within the range of 4.498 N/mm² to 10.272 N/mm². These values indicate the load that can be applied before it deforms plastically. Depending on the application, human bone can have acceptable yield strengths ranging from 5.7 to 356 N/mm² [16]. Any application that calls for a stronger and more resilient material can benefit from a higher yield strength, which typically indicates a higher ability of the HAp sample to resist deformation under applied stress. Additionally, greater HAp yield strength supports tissue integrity and failure resistance. Regarding HAp, additional significant variables must be considered, particularly its biocompatibility and bioactivity.

4.1.3 Density

Because porosity and density can impact hydroxyapatite's mechanical characteristics and biological response in the human body, tests on these parameters were carried out. Every piece of information gleaned from the tests is documented. In order to determine the experimental density value. The density can be obtained using the formula in Equation 3 and plotted in Fig. 6.

$$\rho = \frac{dry\ weight}{(wet\ weight - weight\ in\ liquid)} \tag{3}$$



	1	2	3	4
Density (g/cm3)	1.0612	2.8484	2.7619	2.8584

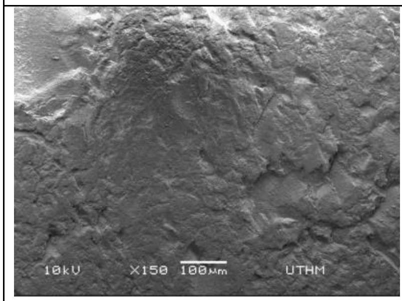
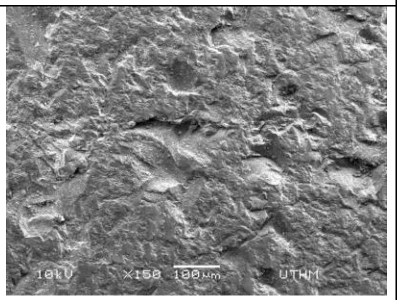
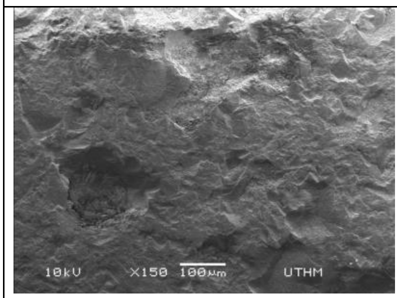
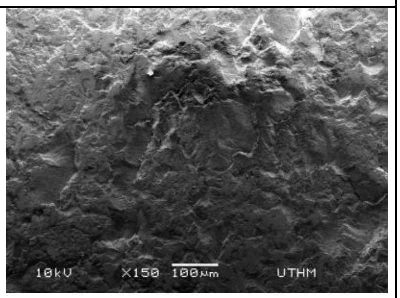
Fig. 6 *Graph Density of HAp samples*

Sample 1 has the lowest density on the graph, at 1.0612 g/cm³, and sample 3 is next, at 2.7619 g/cm³. Sample 2, which contains PEG 3 PVA 2, has the highest density of the other samples at 2.7619 g/cm³, and sample 4 has a 2.8584 g/cm3 density. The experiment's density data is then contrasted with the 3.16 g/cm³ theoretical density value of the HAp sample [17]. Sample 2 is thus found to have the density value closest to the theoretical density value. Porosity influences mechanical characteristics, biodegradability, HAp bioactivity, and density.

4.2 Powder Characterization Analysis

4.2.1 Scanning Electron Microscope

Table 1 *SEM micrograph analysis on the HAp sintered body*

PEG 1 PVA 4)	(PEG 2 PVA 3)
 Small size pores Small size depth Rough	 Medium size pores Small size depth Rough
(PEG 3 PVA 2)	(PEG 4 PVA 1)
 Medium size pores Medium size depth Rough	 Big size pores Big size depth Rough

4.2.2 X-ray Diffraction (XRD)

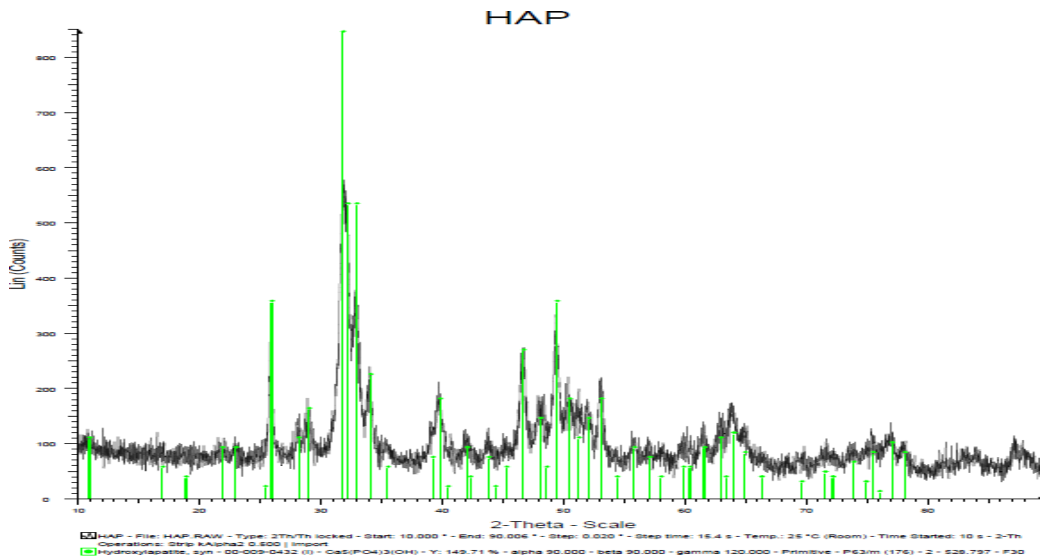


Fig. 7 *The analyses with the peak are marked with blue to show the HAp composition*

The X-ray Diffraction (XRD) analysis was done to obtain the highest peak of and it was confirmed that all the samples have the same formation of Nanocrystallite of X. From the analysis (Fig. 7), it is shown that the HAp powder with different ratio of binder has a hexagonal crystal structure with space group P63/m (No.176) and lattice parameters a = b = 9.41890 Å, z =1 and c = 6.88270 Å. Other than that, it is found that the HAp sample has a molecular weight of 1004.64 g/mol, and the volume detected is 528.80. The phase analyses were recorded in the angular range 2θ θ = 10 - 90 to obtain the peak pattern of HAp, and it was done using JCPDS card 00-055-0592. The result is that all samples have the same nanocrystalline Ca10(PO4)6(OH)2 formation. From the pattern obtained, it is observed that the HAp powder peak pattern has started to rise at 11o, and the highest peak obtained is at 33^{o}. Thus, it can be said that the difference in the amount ratio of binder affects the percentage of hydroxyapatite in the sample.

4.3 Surface Roughness

A surface roughness tester was used after a ball nose end mill cutter was used to machine the HAp sample. The testing aimed to identify the different binder compositions that result in rougher surface roughness. For the machining process, a single cutting parameter was chosen, which is the depth of cut (0.1 mm), feed rate (0.040 mm/rev), and cutting speed (27 m/s).

Fig. 8 displays a graph plotted to observe the surface roughness of the HAp, and Table 2 presents tabulation data for the HAp sample surface roughness following machining. A ball nose end mill is used to machine the HAp sample. According to the plotted graph, sample 3 had the highest surface roughness (5.35 um), while sample 4 had the lowest surface roughness (2.047 um). The range of other HAp samples is between 0.8 and 0.9 um. Previous studies have indicated that a higher value for the roughness of the HAp surface is advantageous for tissue integration because it promotes better cell attachment, proliferation, and protein absorption. As indicated in Fig. 9, all testing data are documented and compared with porosity.

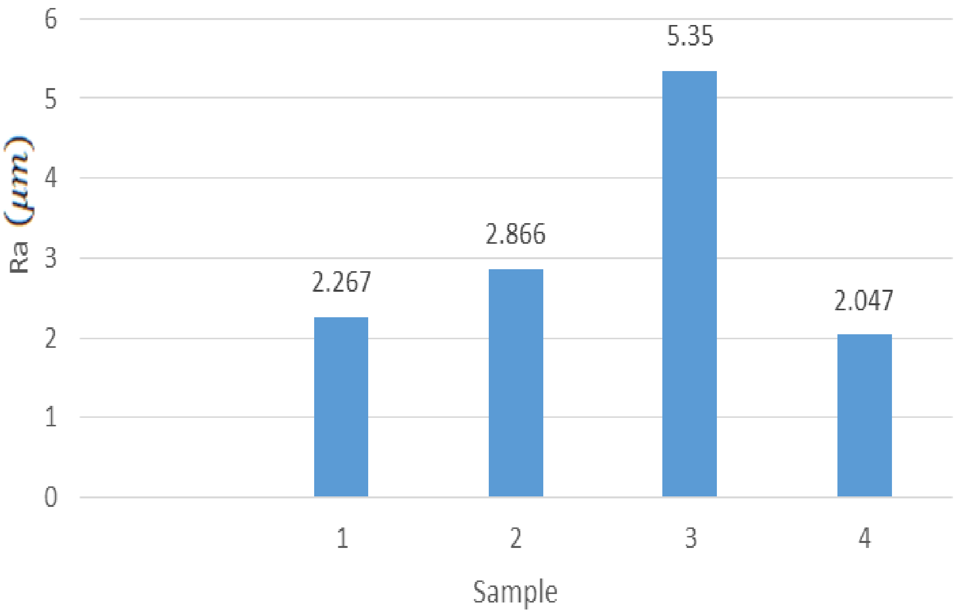
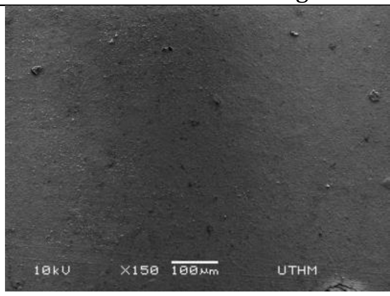
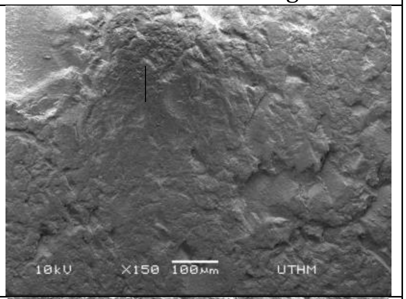
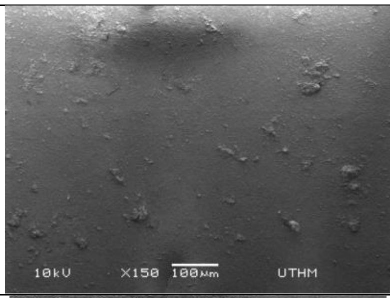
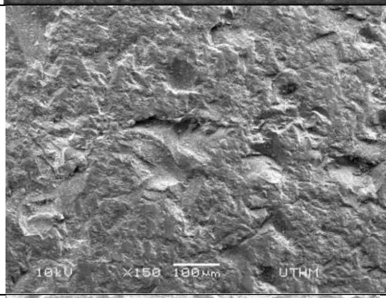
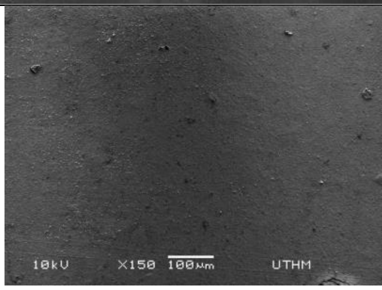
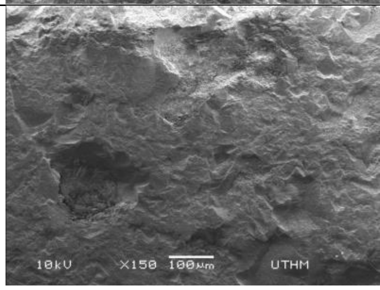
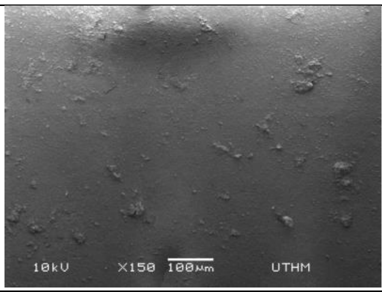
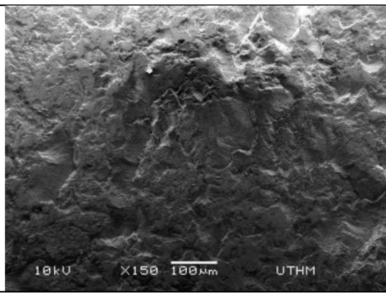


Fig. 8 *Graph of surface roughness after machining*

Table 2 *Surface Roughness SEM micrograph of HAp sintered body*

Sample	Before Machining	After Machining
1 (PEG 1 PVA 4)		
2 (PEG 2 PVA 3)		
3 (PEG 3 PVA 2)		
4 (PEG 4 PVA 1)		

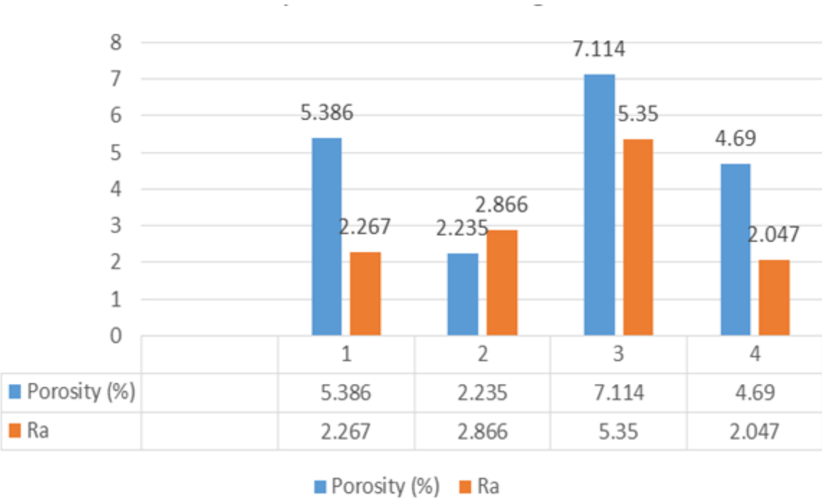


Fig. 9 *Graph relationship between porosity and surface roughness*

5. Conclusion

This study concluded the effects of binders on bio-ceramic surface roughness when milling. The objectives of this study were achieved by mixing, compressing, sintering, machining, and testing various mechanical characteristics to determine the best percentage binder that could produce the required surface roughness when milling the bio-ceramic machined part. Two different binders, Polyvinyl Alcohol (PVA) and Polyethylene Glycol (PEG) were utilised in this study. Both binders have affected the mechanical and machining properties of HAp samples. This conclusion can be drawn from the data collected from the various experiments performed on the sample. The machinability of the Hydroxyapatite bio-ceramic samples is high. Still, the effects of the binders can only be determined through tests such as shrinkage, modulus of rupture, density and porosity, Vickers hardness tests, and surface roughness tests.

In the surface roughness test, we determined that the binders affect the machining and surface roughness. The surface roughness and hardness tests yielded different results based on the mixture proportion. The porosity and density measurement also recorded a range of data indicating numerous. The sample (PEG 4 PVA 1) has a high potential for machining because it has the suitable porosity and density and gives the lowest surface roughness, 0.988 (μm), of any mixture tested. This mixture's surface roughness is also averagely smooth. The Vickers hardness test on this sample indicates that this mixture of materials is too firm and soft for the machine. The observed modulus of rupture indicates that (PEG 1 PVA 4) bio-ceramics have more significant yield strengths and are, therefore, more likely to be suitable for applications requiring sturdier and more resilient materials. To exhaustively evaluate the bio-ceramics suitability, it is necessary to consider additional factors, such as biocompatibility, bioactivity, and application-specific requirements. Finally, it was determined that the binders PEG and PVA effectively affected the bioceramic machining on various factors, as demonstrated by all the tests conducted on sintered hydroxyapatite ceramics. All of the objectives that had been outlined were accomplished.

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Conflict of Interest

The authors declare no conflict of interest regarding the paper's publication.

References

[1] Jeong, J., Kim, J. H., Shim, J. H., Hwang, N. S., & Heo, C. Y. (2019). Bioactive calcium phosphate materials and applications in bone regeneration. Biomaterials research, 23(1), 4. https://doi.org/10.1186/s40824-018-0149-3

[2] Hou, X., Zhang, L., Zhou, Z., Luo, X., Wang, T., Zhao, X., ... & Zheng, L. (2022). Calcium phosphate-based biomaterials for bone repair. Journal of functional biomaterials, 13(4), 187. https://doi.org/10.3390/jfb13040187

[3] ANON (2024) CNC Milling: Definition, Processes, Applications, https://www.rapiddirect.com/blog/what-is-cnc-milling/

[4] Hassan, M. S., & Amin, A. M. (2022). Optimisation of Surface Roughness in The CNC Milling Process. Research Progress in Mechanical and Manufacturing Engineering, 3(1), 267-277. https://penerbit.uthm.edu.my/periodicals/index.php/rpmme/article/view/3839

[5] Agrawal, R., Kumar, A., Mohammed, M. K., & Singh, S. (2023). Biomaterial types, properties, medical applications, and other factors: a recent review. Journal of Zhejiang University-SCIENCE A, 24(11), 1027-1042. https://doi.org/10.1631/jzus.A2200403

[6] Zhang, S., Yang, H., Wang, M., Mantovani, D., Yang, K., Witte, F., & Qu, X. (2023). Immunomodulatory biomaterials against bacterial infections: Progress, challenges, and future perspectives. The Innovation. https://doi.org/10.1016/j.xinn.2023.100503

[7] Jodati, H., Yılmaz, B., & Evis, Z. (2020). A review of bioceramic porous scaffolds for hard tissue applications: Effects of structural features. Ceramics International, 46(10), 15725-15739. https://doi.org/10.1016/j.ceramint.2020.03.192

[8] Lin RS, S. Romanazzo, I. Roohani, 3D printing of bioceramic scaffolds – barriers to the clinical translation: from promise to reality, and future perspectives, Materials 12 (17) (2019) 2660

[9] Bouazzi, D., Chérif, I., Mehri, A., Touati, H., Caccamo, M. T., Magazù, S., & Badraoui, B. (2023). A joint experimental and theoretical study on Structural, Vibrational and morphological properties of newly synthesized nanocomposites involving Hydroxyapatite-alt-Polyethylene Glycol (HAP/PEG). Journal of Molecular Liquids, 390, 123192. https://doi.org/10.1016/j.molliq.2023.123192

[10] Osuchukwu, O. A., Salihi, A., Abdullahi, I., Abdulkareem, B., Salami, K. A., Etinosa, P. O., ... & Obada, D. O. (2024). A pedagogical approach for the development and optimization of a novel mix of biowastes-derived hydroxyapatite using the Box-Behnken experimental design. Heliyon, 10(1). https://doi.org/10.1007/s42452-021-04795-y.

[11] Farombi, A. G., Amuda, O. S., Alade, A. O., Okoya, A. A., & Adebisi, S. A. (2018). Central composite design for optimization of preparation conditions and characterization of hydroxyapatite produced from catfish bones. Beni-Suef University journal of basic and applied sciences, 7(4), 474-480. https://doi.org/10.1016/j.bjbas.2018.04.005.

[12] Luneeva, O. L., & Zakirova, V. G. (2017). Integration of mathematical and natural-science knowledge in school students' project-based activity. EURASIA Journal of Mathematics, Science and Technology Education, 13(7), 2821-2840. https://doi.org/10.12973/eurasia.2017.00720a.

[13] Zhu, X., Chen, J., Scheideler, L., Altebaeumer, T., Geis-Gerstorfer, J., & Kern, D. (2004). Cellular reactions of osteoblasts to micron-and submicron-scale porous structures of titanium surfaces. Cells Tissues Organs, 178(1), 13-22. https://doi.org/10.1159/000081089

[14] Gongadze, E., Kabaso, D., Bauer, S., Slivnik, T., Schmuki, P., van Rienen, U., & Iglič, A. (2011). Adhesion of osteoblasts to a nanorough titanium implant surface. International journal of nanomedicine, 1801-1816. https://doi.org/10.2147/IJN.S21755

[15] Hatamleh, M. M., Wu, X., Alnazzawi, A., Watson, J., & Watts, D. (2018). Surface characteristics and biocompatibility of cranioplasty titanium implants following different surface treatments. Dental Materials, 34(4), 676-683. https://doi.org/10.1016/j.dental.2018.01.016

[16] Morgan, E. F., Unnikrisnan, G. U., & Hussein, A. I. (2018). Bone mechanical properties in healthy and diseased states. Annual review of biomedical engineering, 20(1), 119-143. https://doi.org/10.1146/annurev-bioeng-062117-121139

[17] Swain, M. V. (2009). Unstable cracking (chipping) of veneering porcelain on all-ceramic dental crowns and fixed partial dentures. Acta biomaterialia, 5(5), 1668-1677. https://doi.org/10.1016/j.actbio.2008.11.002