Physical and Biocompatibility Characterization of Ca-Si-P-ZnComposite Loaded Pmma Scaffolds for Future Biomedical Application

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**Abstract:** Bone Tissue engineering and regenerative medicine have emerged as promising fields in the development of therapies for bone repair.One key component in these approaches is the utilization of biocompatible scaffolds that provide structural support, guide tissue regeneration, and facilitate the delivery of bioactive agents. The use of bioactive glass in bone regeneration offers a promising approach to accelerate and enhance the healing process of bone defects. The Ca-Si-P-Zn system is one such bioactive composite that combines the beneficial properties of calcium (Ca), silicon (Si), and zinc (Zn). PMMA has been widely employed in biomedical engineering due to its favorable properties, including biocompatibility, mechanical strength, and ease of fabrication. However, incorporating bioactive materials into PMMA scaffolds can further enhance their functionality and tissue regenerative capabilities.Transparent bio glass solution was prepared by SOL GEL METHODPMMA was employed as the material for the polymer matrix and was purchased from Alfa Aesar in India. It has a molecular weight of 550000 and a density of 1.18 g cm3.3.6g of PMMA and 0.3g of bioglass were added to 20 ml of acetone.Stir it constantly until it dissolves entirely to create a uniform solution free of Clumps. A glass plate was loaded with the mixture and heated at 65 degrees.The heat treatment was essential since the dissolubility of PMMA in these solvent mixture at room temperature is very low The EDAX test provided valuable information about the elemental composition of a material, including both major and trace elements. EDAX analysis helps to confirm the presence and distribution of specific elements within the scaffolds, such as calcium (Ca), silicon (Si), zinc (Zn).FTIR confirmed the chemical elemental composition of PMMA bioglass. A lower contact angle indicates higher hydrophilicity, which is desirable for promoting cell attachment and spreading on the scaffold surface. The 3D profile and surface hardness of the scaffold was analyzed by the AFM ( Atomic force microscopy ) which indicated that PMMA bioglass surface roughness is 4.135 nm. Biocompatibility of the scaffold was identified by zebrafish study and hemocompatibility test.In conclusion, the research on the physical and biocompatibility characterization of Ca-Si-P-Zn composite loaded PMMA scaffolds furnished that the addition of the PMMA can enhance the mechanical properties of the scaffolds, making them more suitable for load-bearing applications and providing structural support during tissue regeneration. It has provided valuable insights into the potential of these scaffolds in tissue engineering and regenerative medicine, particularly in dental applications, for future biomedical application.

**Keywords**: PMMA scaffolds , Ca-Si-P-Zn composite , bone tissue regeneration , SOL GEL method.

# INTRODUCTION

The phrase "tissue engineering" first appeared in print in 1987 [(Lanza et al., 2000)](https://paperpile.com/c/52ksJi/6RTm). It is the multidisciplinary approach to improve or replace biological tissues. It is a field which combines engineering, biology, and materials science with bone tissue engineering. The goal of the Bone Tissue Engineering workshop was to 1. demonstrate the current state of translational techniques to bone regeneration. comprehend the physical and chemical elements that impact biological responses to biomaterials, as well as how to construct biomaterial interfaces that drive cell function. [(Ajay et al., 2023; Chokkattu et al., 2023; Padarthi et al., 2023)](https://paperpile.com/c/52ksJi/D8oxZ+ahLY0+X4AFI) Contrast several methodologies for bone tissue creation that involve biologic augmentation of scaffolds with osteogenic genes, proteins, or cells [(Sanz-Herrera, 2020)](https://paperpile.com/c/52ksJi/mWUq).The obtained basic material for bone replacements is classified into three types based on its biological origin: biological materials, organic biomaterials, and alloplastic grafts. Autologous graft or autograft, homologous or allogeneic graft, and heterologous or xenogeneic graft are all possible biological materials [(Shanmugam et al., 2013)](https://paperpile.com/c/52ksJi/Cz7G). The autologous bone graft is taken from another portion of the graft recipient's body. Allografts or homologous/allogenic bone transplants are received from a different individual of the same species as the donor. The heterologous bone grafts, also known as xenografts, are harvested from a species other than the graft recipient [(Zizzari et al., 2016)](https://paperpile.com/c/52ksJi/qeqA). Decellularization of various tissues such as skin, tendon, and cartilage is the most common method for obtaining organic biomaterials.[(Dharman et al., 2023; S. Sindhu et al., 2023; Sreenivasagan et al., 2023)](https://paperpile.com/c/52ksJi/OhQf0+PWOy8+t1rhD) Despite this method's potential and bright future, no successful decellularization of hard tissues such as bone has been documented to yet. This is while a massive global market is expected to await the discovery of a suitable material to be utilized as a bone graft or matrices for bone regeneration [(Sladkova et al., 2019)](https://paperpile.com/c/52ksJi/IWgw).Scaffolds are critical in bone tissue engineering. Their goal is to emulate the structure and function of natural bone extracellular matrix (ECM), which can create a three-dimensional (3D) environment to promote adhesion, proliferation, and differentiation while also having suitable physical qualities for bone regeneration [(Sladkova et al., 2019; Soleymani & Naghib, 2023)](https://paperpile.com/c/52ksJi/IWgw+CruC). A good scaffold should be biodegradable, biocompatible, bioactive, osteoconductive, and osteoinductive. The biomaterials (biomedical materials), which are basic components of scaffolds, play an important role in bone tissue engineering[(Dorozhkin, 2012)](https://paperpile.com/c/52ksJi/9NwV). Researchers have investigated a range of biocompatible materials, with ceramics and polymers standing out among all other biocompatible materials for scaffold production [(Dorozhkin, 2012; Lanza et al., 2000)](https://paperpile.com/c/52ksJi/9NwV+6RTm).Calcium is one of the ions that make up the bone matrix. Calcium ions promote bone development and maturation via calcification. Furthermore, calcium ions influence bone repair via cellular signaling.[(Ramakrishnan et al., 2023; Shenoy & Maiti, 2023; J. S. Sindhu et al., 2023)](https://paperpile.com/c/52ksJi/b74q2+Qtg6O+ODlsT) Calcium stimulates mature bone cells via nitric oxide production and induces bone growth precursor cells for bone tissue repair [(Foreman et al., 2005)](https://paperpile.com/c/52ksJi/5vkg). Additionally, calcium ions control how osteoclasts develop and perform their resorptive duties [(Kuroda et al., 2008)](https://paperpile.com/c/52ksJi/IDja). As a trace element, silicon has received little attention [(Sathya et al., 2024)](https://paperpile.com/c/52ksJi/zW4J). Its influence on the formation of bone and connective tissue has typically been limited to a minor one. By enhancing bone regeneration and raising bone mineral density, silicon plays a crucial part in bone biology [(Renaud et al., 2023)](https://paperpile.com/c/52ksJi/fRyH).A crucial trace element called zinc (Zn), which makes up around 30% of the body's total supply, is typically present in skeletal tissue. Zn is essential for the growth, development, mineralization, and upkeep of strong bones [(Neščáková et al., 2019)](https://paperpile.com/c/52ksJi/lmxh). Additionally, Zn shortage in humans can cause conditions including dwarfism, osteoporosis, and delayed bone development because it is a mediator of bone development and growth.[(Ajay et al., 2023; Chokkattu et al., 2023; Padarthi et al., 2023)](https://paperpile.com/c/52ksJi/D8oxZ+ahLY0+X4AFI) As the release of Zn2+ may boost the osteogenic differentiation of cells for faster bone regeneration, Zn incorporation is anticipated to improve the osteogenic ability of synthetic polymer materials [(Luo et al., 2014)](https://paperpile.com/c/52ksJi/M95h).A crucial mineral that is crucial for bone growth and overall skeletal health is phosphorus. Along with calcium, it is one of the essential components of hydroxyapatite, the mineral phase of bone tissue[(Thiripelu et al., 2024)](https://paperpile.com/c/52ksJi/FYTo). Numerous biological processes, such as bone mineralization, energy metabolism, and cellular communication, involve phosphorus. Phosphorus has a variety of functions in relation to bone regeneration, including preserving bone integrity and assisting in the healing of fractures and bony deformities. Due to some of its distinctive qualities, polymers are frequently used in tissue engineering. PMMA was chosen by the U.S. Food and Drug Administration among a variety of biocompatible polymers [(Shimko & Nauman, 2007)](https://paperpile.com/c/52ksJi/LbLZ). PMMA finds itself in high demand as a preferred choice for bone augmentation and substitution, primarily due to its remarkable biocompatiThe efficacy of these composite-loaded PMMA scaffolds in biological applications hinges significantly upon their harmonious integration with living systems. Assessments of cytotoxicity, the inflammatory response, and cellular vitality are vital to decipher how effectively the scaffold interfaces with host cells [(Viishaal Srikanth Srivatsa & Manogaran, 2024)](https://paperpile.com/c/52ksJi/yDHh). Furthermore, the scaffold's sustained performance over time and the potential release of any consequential byproducts that might influence the recuperative process are elucidated through its biodegradability. Our research endeavors to shed light on the intricate interplay between Ca-Si-P-Zn composite-loaded PMMA scaffolds and the dynamic biological milieu, thereby laying the groundwork for their application in cutting-edge regenerative methodologies. [(Kasabwala et al., 2021; Rajeshkumar & Lakshmi, 2021; Varghese et al., 2023)](https://paperpile.com/c/52ksJi/3VM10+1Jdf5+NeQso)The primary goal of this research is to develop new techniques and materials for the regeneration or restoration of damaged or missing bone tissue. This emerging field holds great potential for the treatment of bone abnormalities, fractures, and illnesses by offering an alternative to conventional bone transplants and prosthetic implants. This study's objective is to meticulously scrutinize Ca-Si-P-Zn composite-enriched PMMA scaffolds, placing a special emphasis on their inherent physical attributes and biocompatibility, with the ultimate aim of discerning their suitability for impending breakthroughs in the realm of biomedical applications.

# MATERIALS AND METHODS

## COMPOSITE PREPARATION BY SOL-GEL METHOD

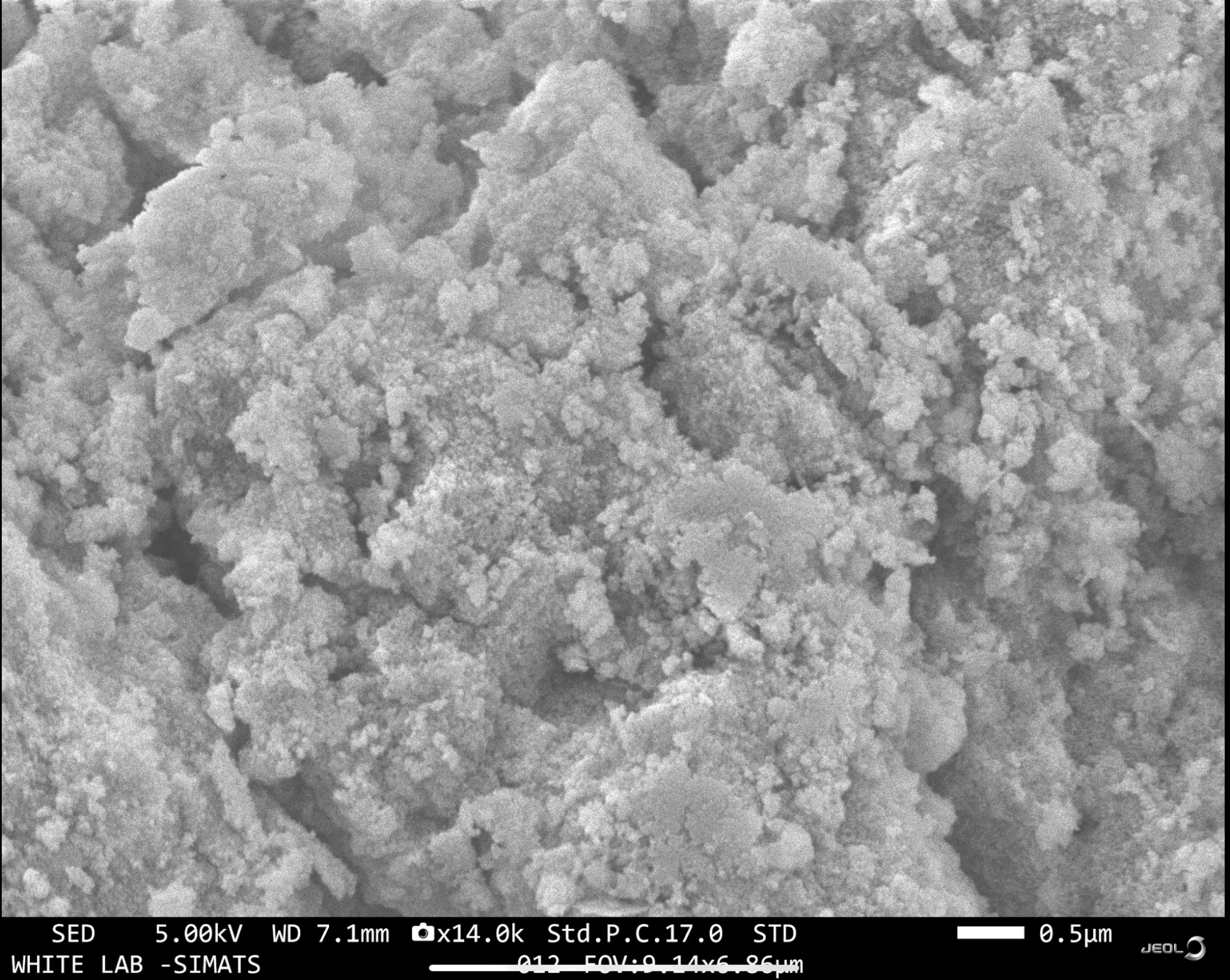
The manufacturing of Ca-Si-P-Zn composite materials uses the advanced Sol-Gel process. Utilizing the chemical conversion of sols (dispersed colloidal solutions) into gels (continuous three-dimensional networks), this ground-breaking method allows for exact control over the structure and composition of the composite materials that are produced. This technique has special potential when applied to Ca-Si-P-Zn composites because it makes it possible for these essential components to be evenly distributed and integrated at the molecular level.Precursor chemicals including calcium (Ca), silicon (Si), phosphorous (P), and zinc (Zn) are carefully mixed together to create the correct composite composition. Then, these precursors are dissolved in an appropriate solvent to create a sol that is distinguished by its colloidal condition. Controlled hydrolysis and polycondensation reactions cause the sol to gradually change into a gel, producing a strong three-dimensional network that contains the Ca, Si, P, and Zn components.

The versatility of the Sol-Gel process makes it a potential path for applications including controlled drug administration, tissue engineering, and bone regeneration by enabling the synthesis of Ca-Si-P-Zn composites with tailored characteristics. This ground-breaking method not only guarantees complete composition control, but also provides the opportunity to precisely adjust the physical and chemical properties of these composites to satisfy the stringent requirements of new biomedical technology.

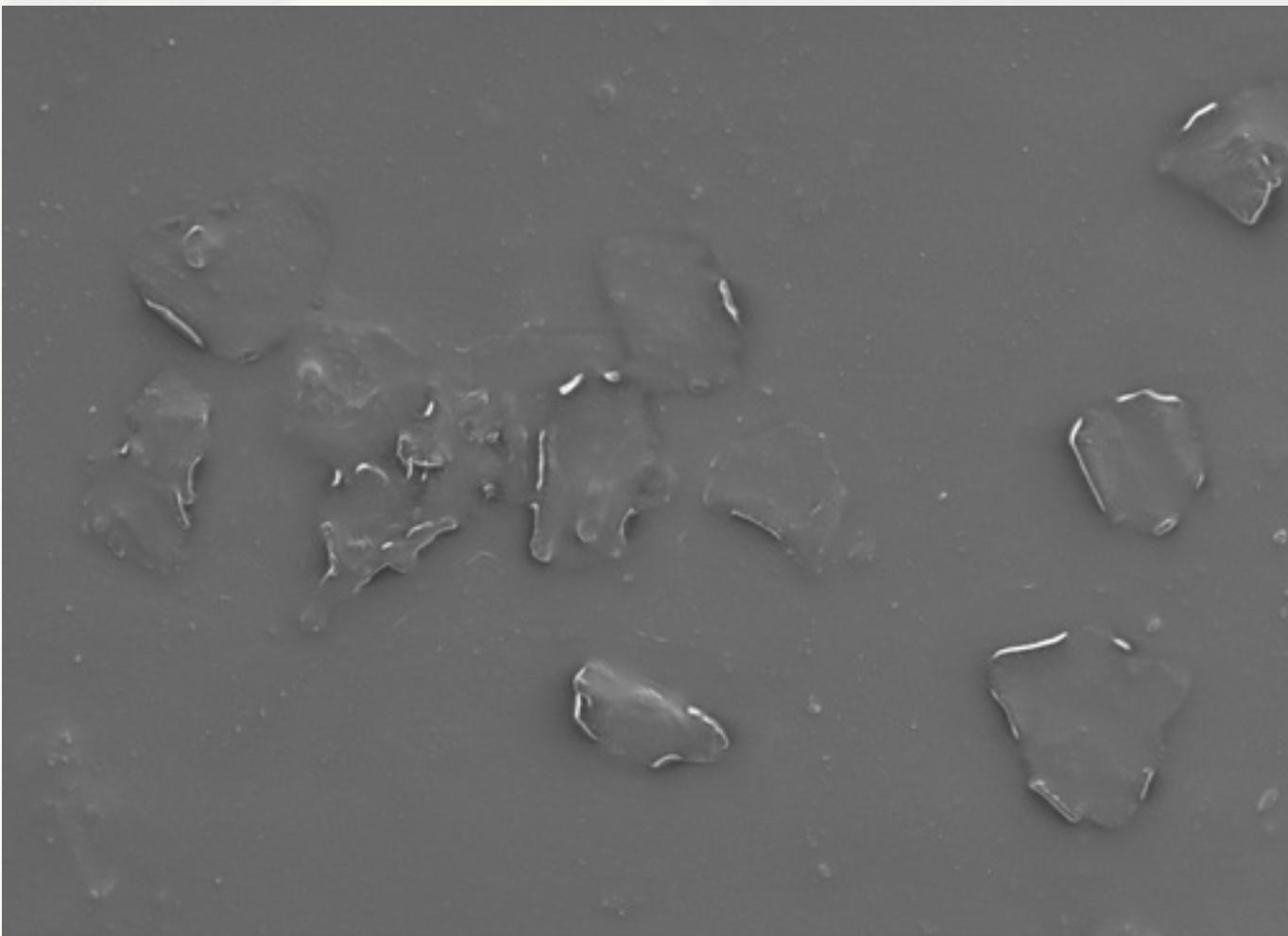
## INCORPORATION INTO PMMA

At the heart of this pioneering endeavor lies polymethyl methacrylate (PMMA), a versatile polymer matrix, procured from the esteemed Alfa Aesar in India. This remarkable PMMA boasts a substantial molecular weight of 550,000, rendering it an architectural cornerstone for the ensuing material symphony. With a density standing at 1.18 g/cm³, it provides the composition with both structural integrity and lyrical transparency(Nikalje et al., 2024).3.6 grams of PMMA and 0.3 grams of bioglass were delicately mixed together and sent adrift in the comforting embrace of 20 milliliters of acetone as the elemental overture began(Chehelgerdi et al., 2023). The performance arts started with a sophisticated choreography of constant stirring that was painstakingly performed until the elements harmony, constructing a tapestry of a smoothly uniform solution free of the discordant clumps that might have interfered with the material crescendo. Then, in a 65-degree dance, this melodious mixture, like a symphonist's masterpiece, was gracefully serenaded onto a clean glass plate where it was waiting to undergo alchemical transformation. As PMMA's solubility in the selected solvent blend proved hesitant at room temperature, requiring this temperature ballet to unlock the composition's full potential, this heat infusion, like to the crescendo of a symphony, was intrinsic. A translucent bio glass solution emerges through this symphony of scientific artistry, set to reshape the future of biomaterials and regenerative technology.

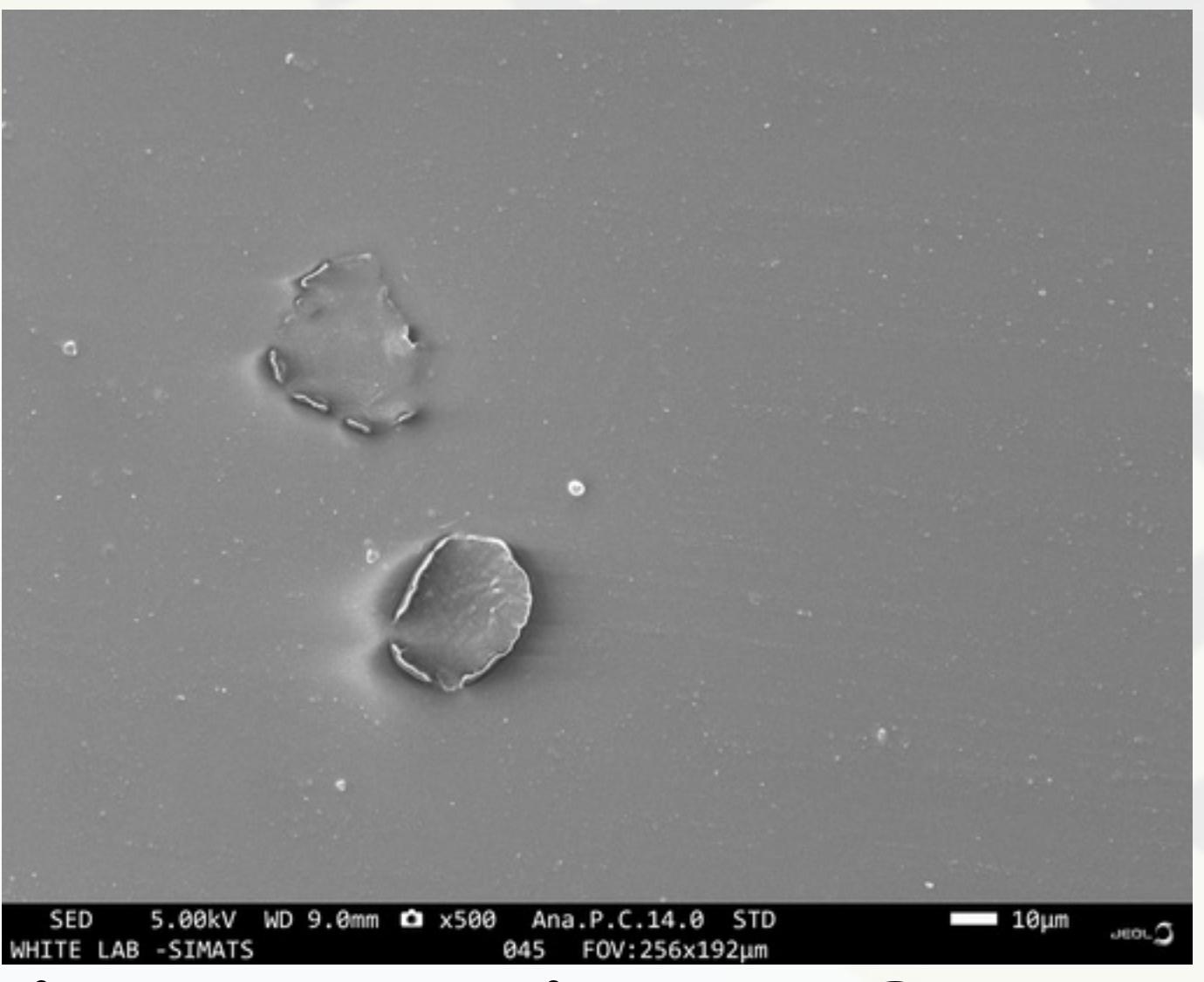
# RESULT



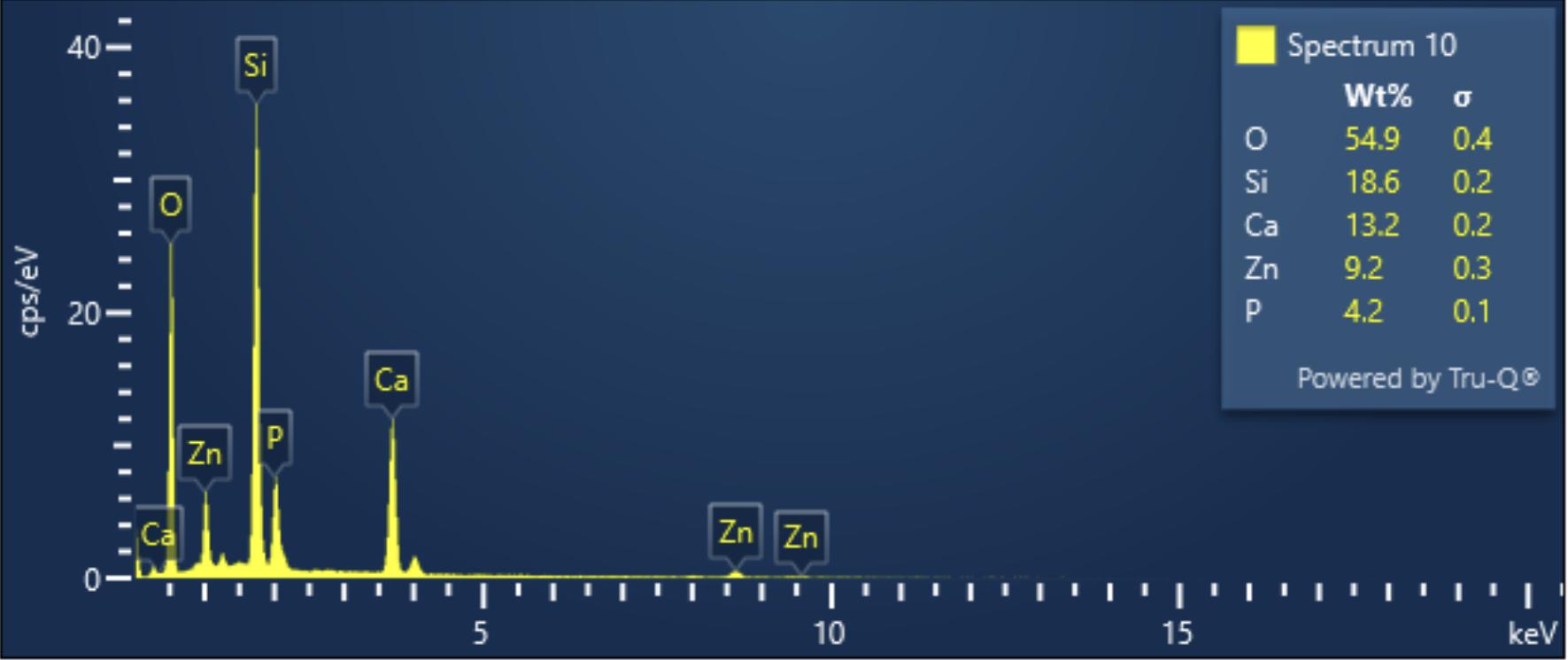
**FIG 1 :** SEM IMAGE OF BIO-GLASS



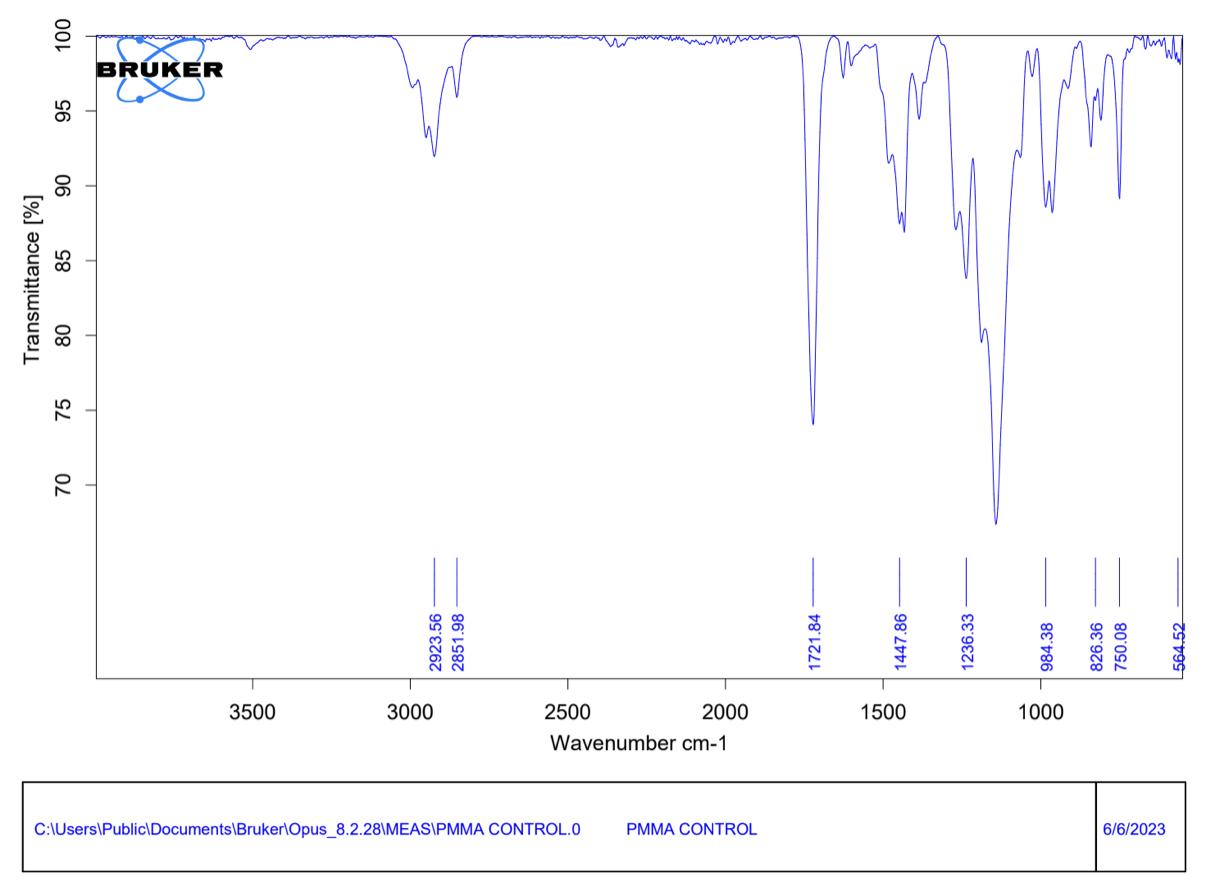
**FIG 2 :** SEM IMAGE OF PRISTINE PMMA



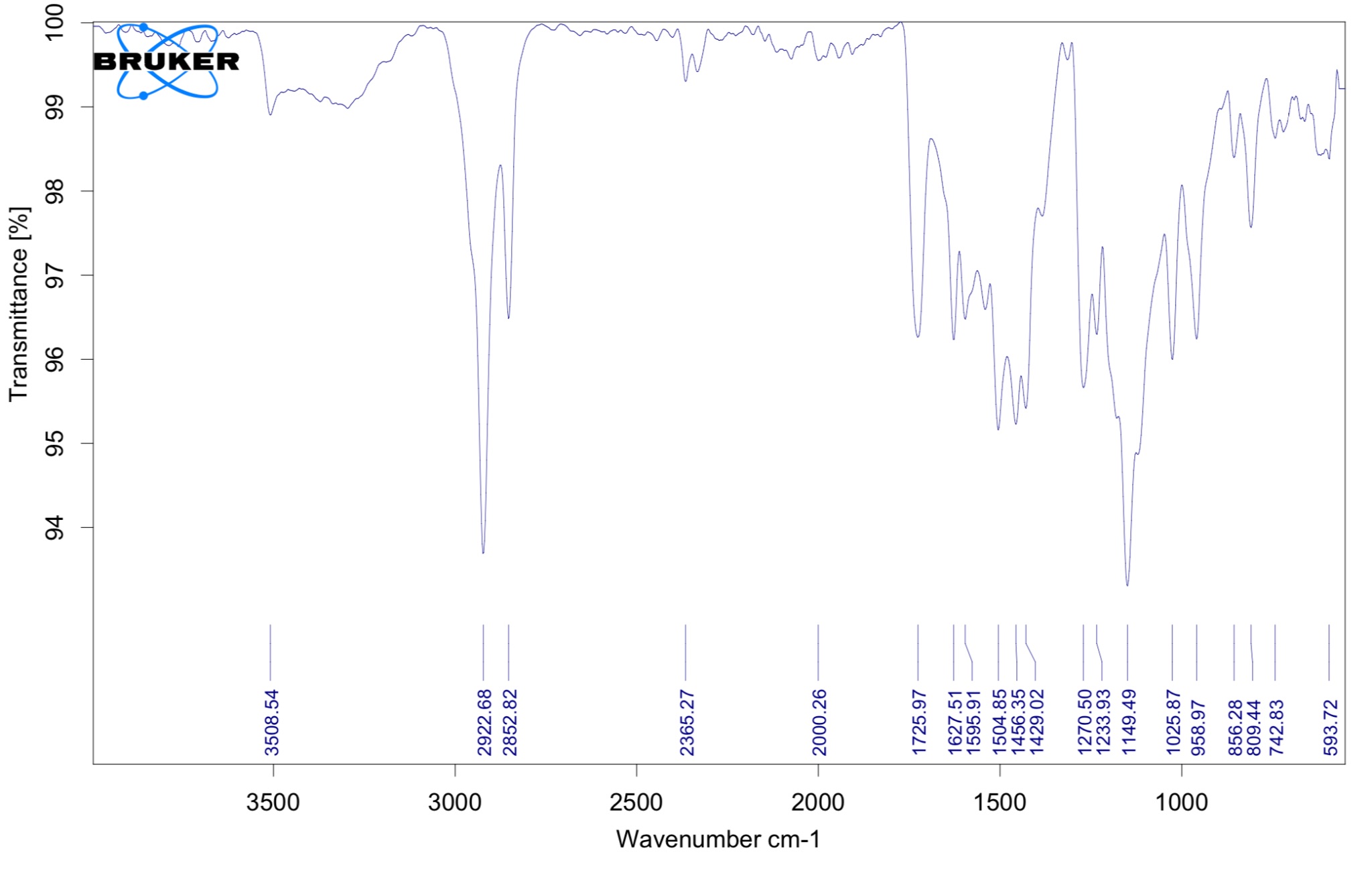
**FIG 3 :** SEM IMAGE OF PMMA BIOGLASS



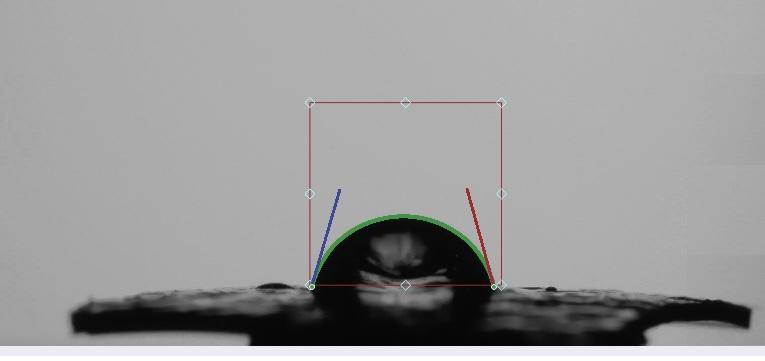
**FIG 4:** EDAX OF BIO-GLASS



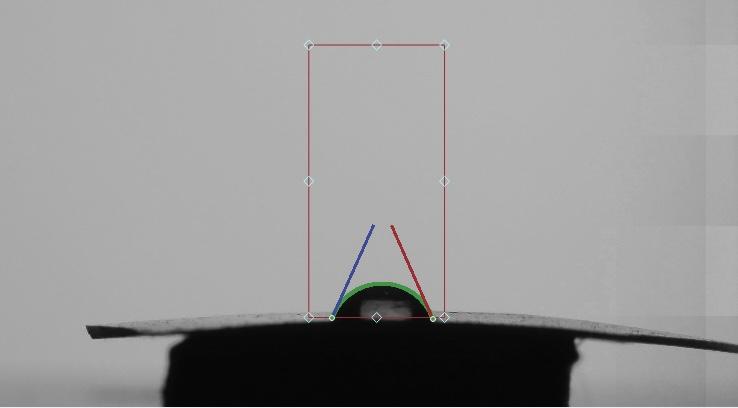
**FIG 5:** FTIR Ca-Si-P-Zn .



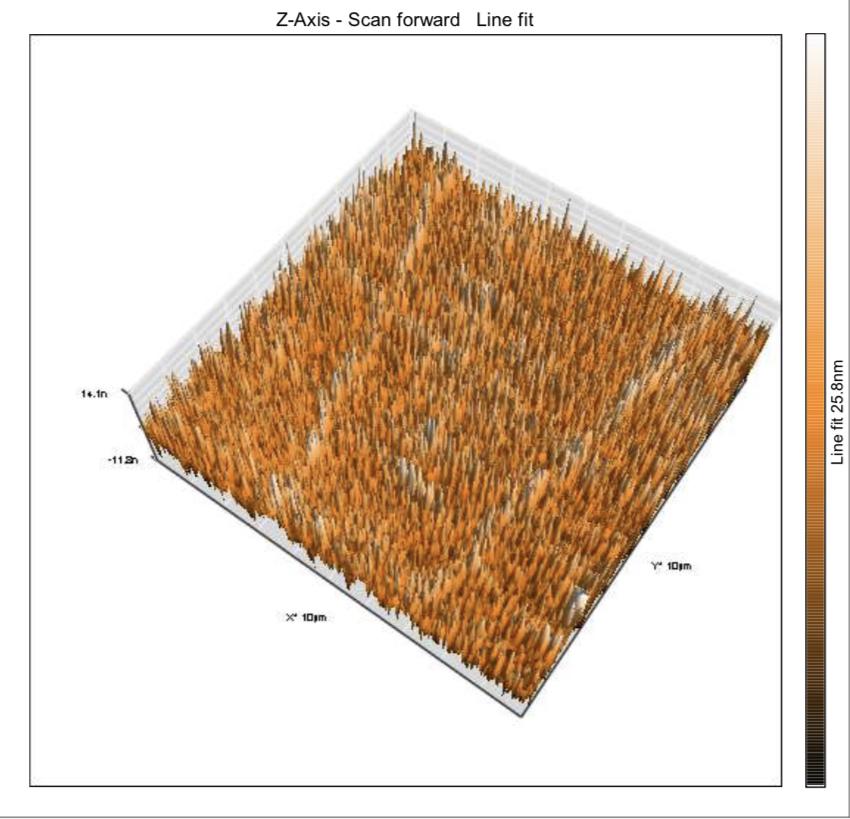
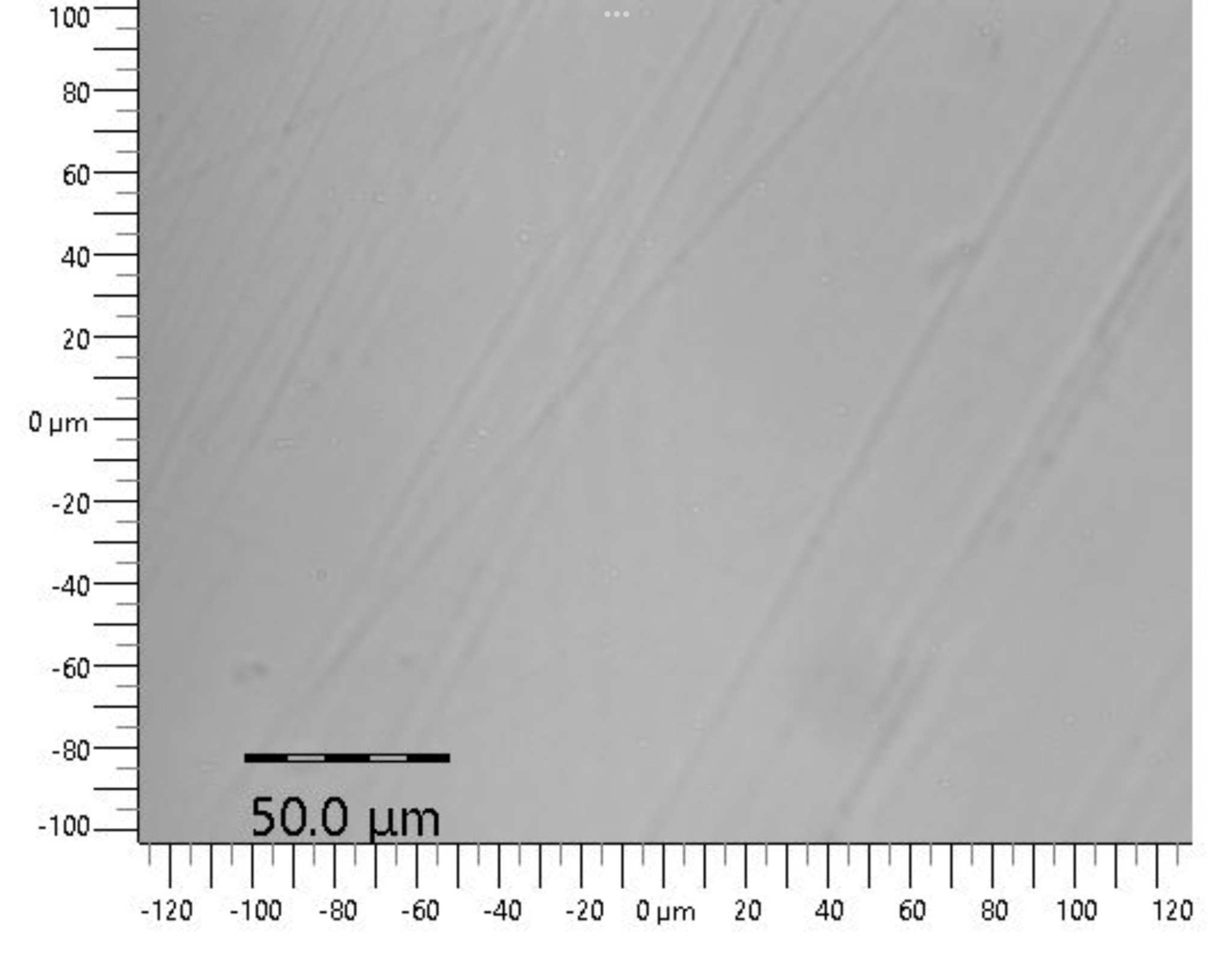
**FIG 6 :** FTIR PMMA / BIOGLASS



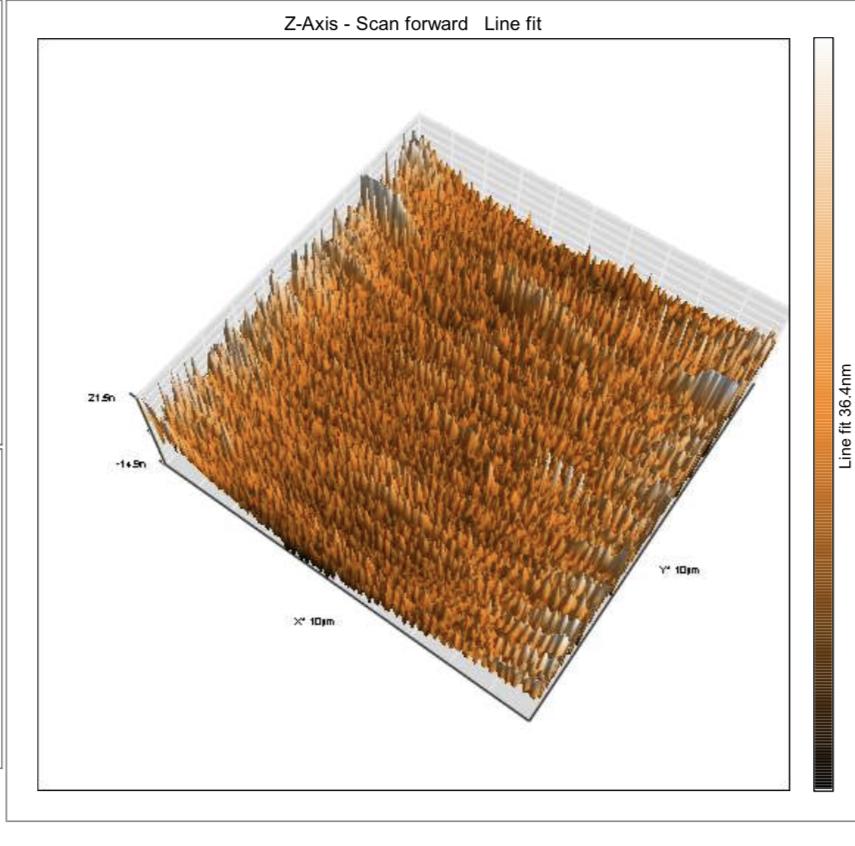
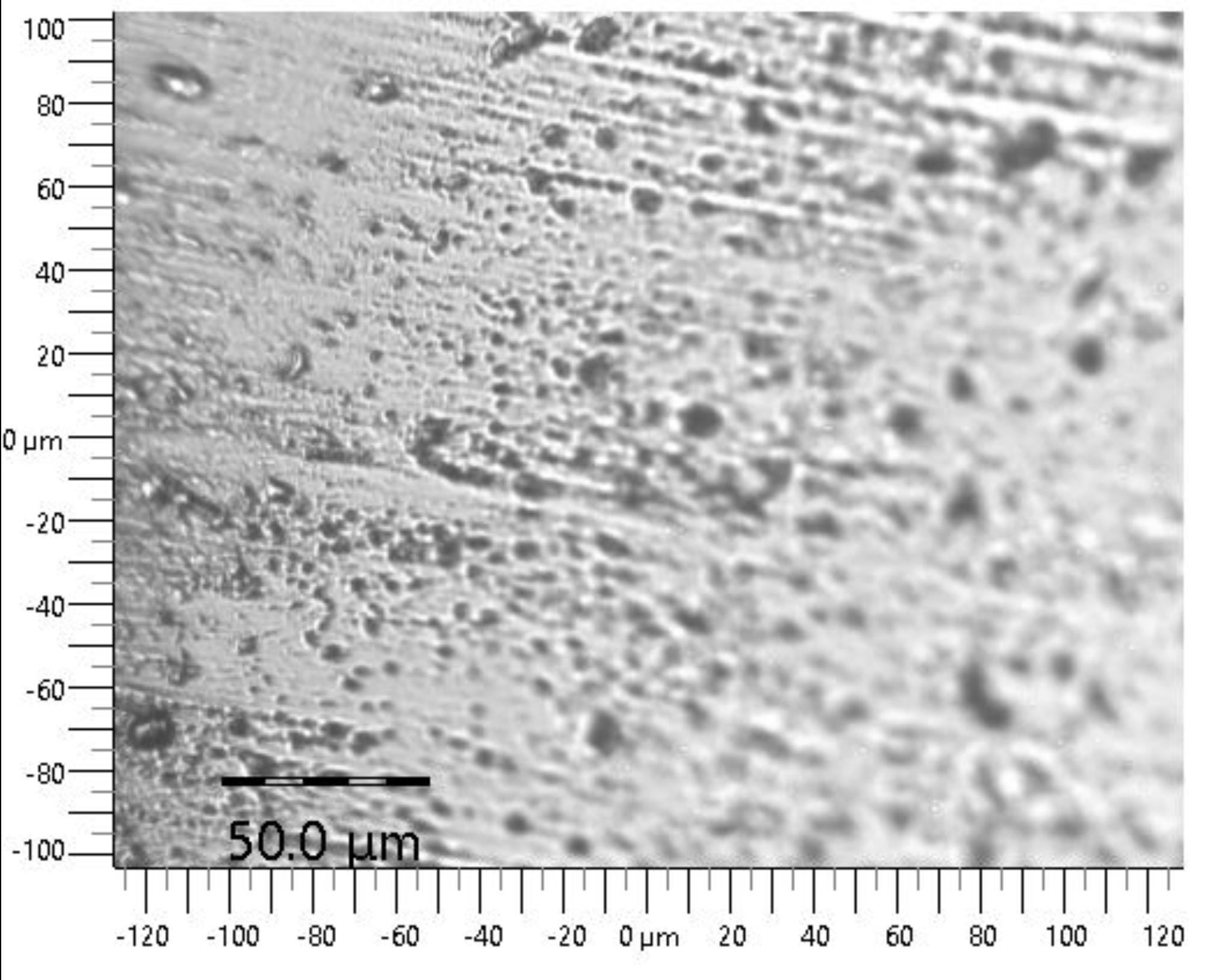
**FIG 7 :** CONTACT ANGLE - PRISTINE PMMA - 74.16 degree



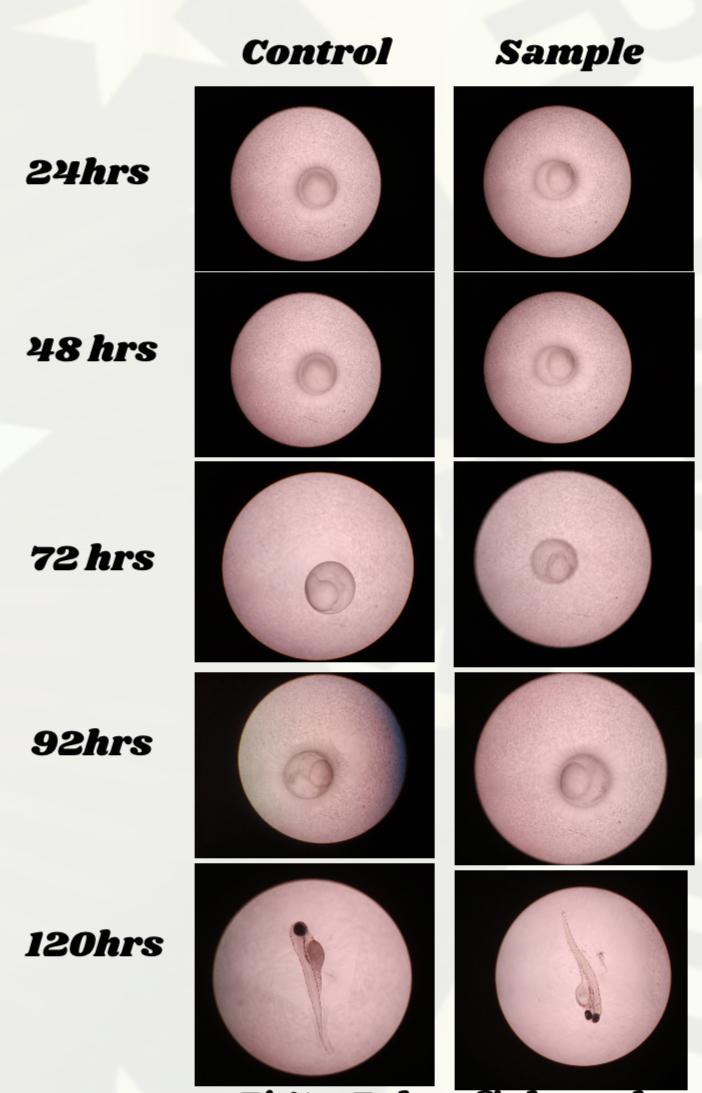
**FIG 8 :** CONTACT ANGLE - PMMA BIOGLASS - 65.0 degree



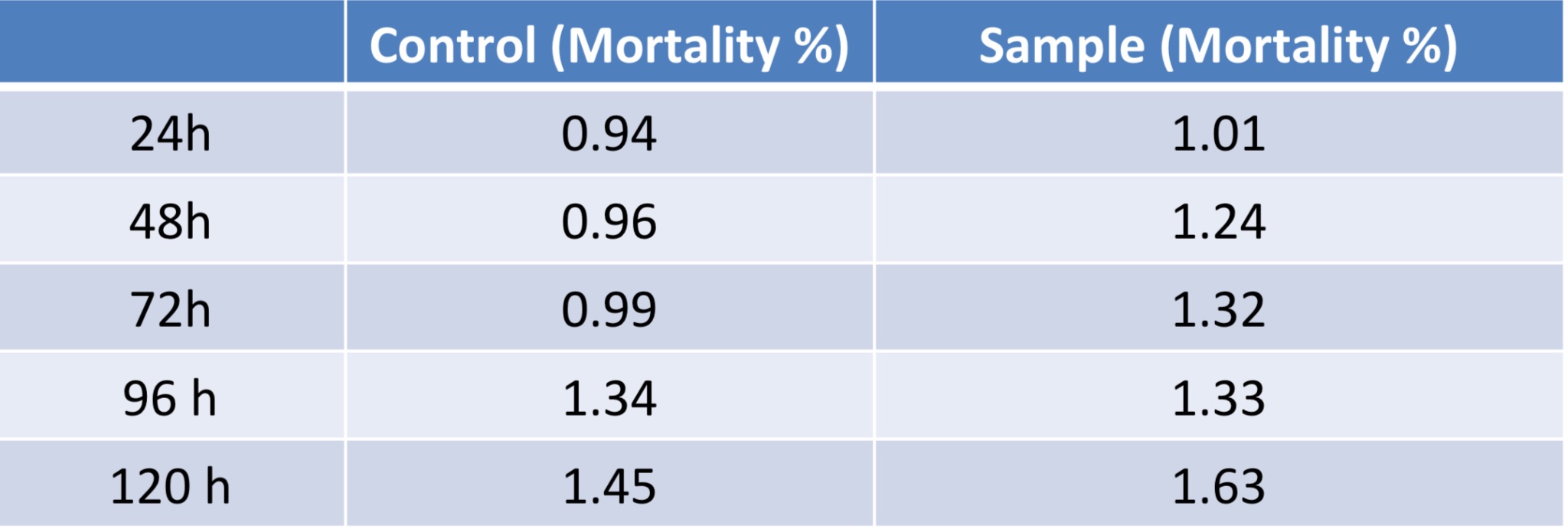
**FIG 9 :** AFM - PRISTINE PMMA



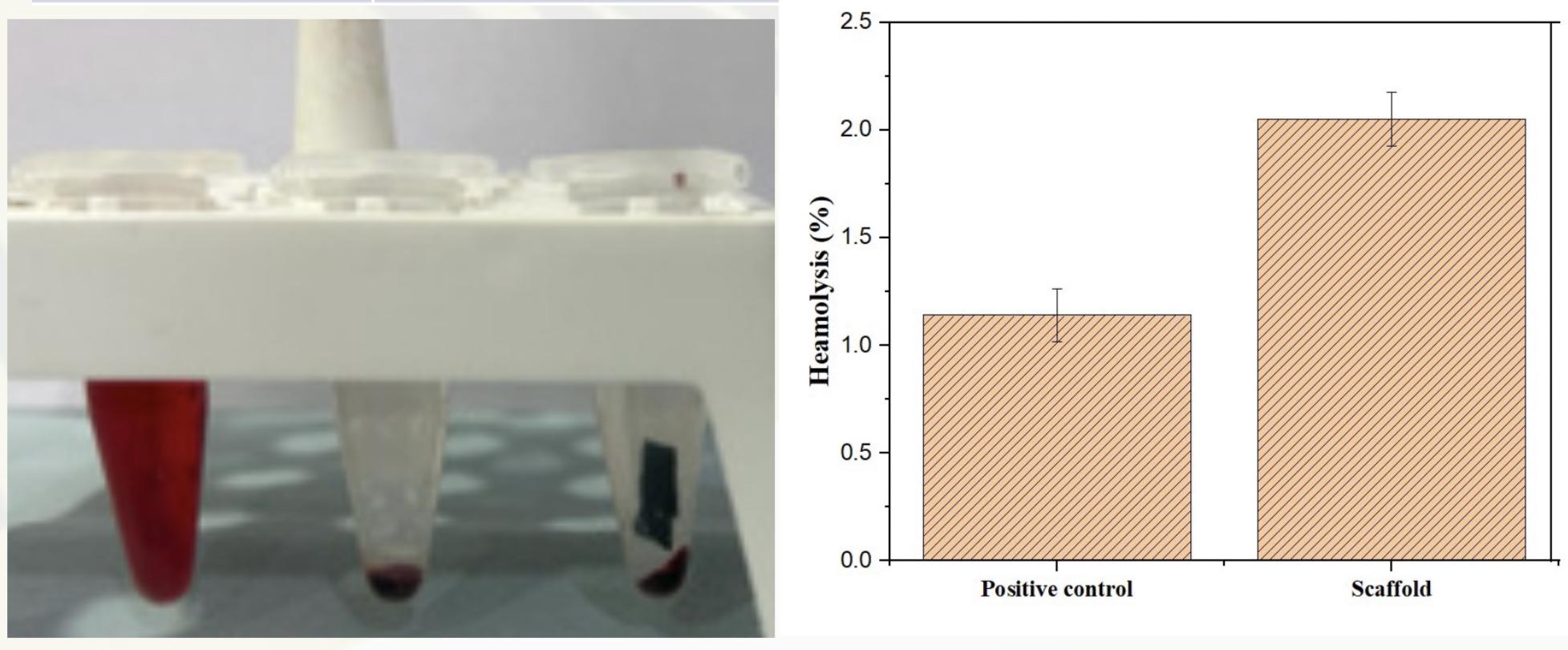
**FIG 10 :** AFM ANALYSIS



**FIG 11**: ZEBRAFISH STUDY



**Fig 12:** ZEBRA FISH MORTALITY RATE



**FIG 13:** HEMOCOMPATIBILITY TEST

Delving into the intricate world of physical characterization, a mesmerizing tapestry of scaffold morphology unfurled before our discerning gaze. The enchanting dance of electron dispersive X-ray analysis (EDAX) played a pivotal role in this symphony, bestowing upon us a treasure trove of elemental insights. In a harmonious convergence of major and trace elements, the analysis unveiled the intricate elemental composition of the scaffolds, a testament to the presence and judicious distribution of elemental virtuosos such as calcium (Ca), silicon (Si), and zinc (Zn) phosphorous (P) . This elemental exposé breathed life into our understanding of the scaffold's structural essence.The crescendo continued with the entrancing notes of Fourier-transform infrared spectroscopy (FTIR), an alchemical maestro that bestowed upon us the veritable chemical elemental composition of the PMMA bioglass composite. Here, we ventured into the realm of contact angles, where the hydrophilic nature of the PMMA bioglass revealed itself. Lower contact angles, akin to an eloquent sonata, resonated with higher hydrophilicity—a coveted attribute in the realm of cell attachment and proliferation on the scaffold's surface.The symphony ascended to a tactile crescendo with the application of Atomic Force Microscopy (AFM). This virtuoso painted a 3D portrait of the scaffold's surface profile and unveiled its surface hardness, a mere 4.135 nanometers of textured elegance. Meanwhile, in a parallel performance, the zebrafish and hemocompatibility tests took center stage, harmoniously concluding our exploration. These captivating biocompatibility evaluations wove a tale of safety and compatibility, setting the stage for the grand finale—the development and refinement of composite scaffolds endowed with not only enhanced functionality but also an innate affinity for harmonious interaction with biological systems.

# DISCUSSION

Genuine tissue regeneration stands apart as a distinct phenomenon when contrasted with the mechanism of biomaterial-facilitated tissue healing. Nevertheless, a well-constructed biologic scaffold, when implanted with precision, can lead to favorable tissue restructuring and remarkable therapeutic achievements. The efficacy of biologic scaffold-based therapies is contingent upon a constellation of variables that collectively steer the course of the wound healing response [(Londono & Badylak, 2015)](https://paperpile.com/c/52ksJi/2dyC). Essentially, the pivotal gauge of triumph for an implanted biomaterial endures as the host's dynamic reaction to the material's presence, transcending the traditional yardsticks historically rooted in the physical attributes of the biomaterial itself.[(G. & Ganapathy, 2022; Kumar & Ramesh, 2021)](https://paperpile.com/c/52ksJi/Uh2wT+FLhQa))In this current research , The EDAX investigation proved to be a useful method for determining the material's elemental composition, including both dominant and trace elements. We were able to confirm the presence and distribution patterns of particular elements within the scaffolds thanks to EDAX analysis, most notably calcium (Ca), silicon (Si), zinc (Zn) and phosphorus (P). In the meantime, FTIR entered the scene with the ability to verify the PMMA bioglass composite's chemical elemental makeup.[(*Evaluation Composite Restoration Posterior Teeth Proanthocyanidin Pretreatment Liner Using Fédération Dentaire Internationale Criteria: Split-Mouth Randomized Controlled Trial*, n.d.; Pranati et al., 2021; Sakthi, 2021)](https://paperpile.com/c/52ksJi/S4y29+O5mG9+JVudZ) Through the contact angle evaluation, the subtleties of surface features were revealed. A lower result indicated increased hydrophilicity, a prized property that encourages cellular attachment and widespread proliferation over the scaffold's surface. Atomic Force Microscopy (AFM) took the lead in a different area of our investigation, shedding light on the scaffold's three-dimensional profile and surface hardness and offering priceless insights into the PMMA bioglass surface. [(Ramakrishnan et al., 2023; Shenoy & Maiti, 2023; J. S. Sindhu et al., 2023)](https://paperpile.com/c/52ksJi/b74q2+Qtg6O+ODlsT)A hybrid scaffold, blending a matrix and polymer, imbued with enhanced biomechanical attributes, could prove highly beneficial across various facets of tissue engineering, notably in endeavors like the development of heart valve tissues [(Hong et al., 2008; Londono & Badylak, 2015)](https://paperpile.com/c/52ksJi/2dyC+MAnh). In reference to which, in this present research we incorporated our bioglass with PMMA polymer. Numerous medical disciplines quickly grabbed upon and adopted its biocompatibility, dependability, relative ease of manipulation, and low toxicity. PMMA has been utilized in (a) bone cements, (b) contact and intraocular lenses, (c) bone screw fixation, (d) filler for bone cavities and defects in the skull, and (e) stabilizing the vertebrae in patients with osteoporosis [(Frazer et al., 2005; Hong et al., 2008; Londono & Badylak, 2015)](https://paperpile.com/c/52ksJi/2dyC+MAnh+payu). This investigation on the physical and biocompatibility characterization of Ca-Si-P-Zn composite loaded PMMA scaffolds furnished that the addition of the PMMA can enhance the mechanical properties of the scaffolds, making them more suitable for load-bearing applications and providing structural support during tissue regeneration. Similarly research done by [(Vedhanayagam et al., 2020)](https://paperpile.com/c/52ksJi/9Jf1) incorporated PdO–TiO2⁠ with PMMA and the results conclude that, A material based on collagen-g-PMMA-PdO-TiO2 is the best scaffold for bone tissue engineering applications.[(Keerthana & Ramesh, 2021; Murugesan, 2021; Tiwari & Jain, 2021)](https://paperpile.com/c/52ksJi/1Dt1H+hQna8+vBhGa)[(Keerthana & Ramesh, 2021; Murugesan, 2021; Subramanian et al., 2021; Tiwari & Jain, 2021)](https://paperpile.com/c/52ksJi/1Dt1H+hQna8+vBhGa+JPAKM)Subsequent research endeavors can delve into the realm of composite composition optimization and the extensive evaluation of long-term performance. The exploration of synergistic interactions between bioactive factors and the composite of Ca-Si-P-Zn can unlock avenues for crafting scaffolds enriched with supplementary functionality. [(Dharman et al., 2023; S. Sindhu et al., 2023; Sreenivasagan et al., 2023)](https://paperpile.com/c/52ksJi/OhQf0+PWOy8+t1rhD) Drug releasing scaffolds can also be considered in reference to the previous study which stated that the drug-releasing scaffolds enable local administration of a sufficient dose of bioactive molecules for a predetermined amount of time while minimizing active agent release to non-targeted areas. This supports and promotes tissue regeneration, which typically takes a long time to complete [(Dorati et al., 2017)](https://paperpile.com/c/52ksJi/hTTN).These forthcoming strides hold immense potential for reshaping the landscape of dental tissue engineering and the broader domain of regenerative medicine, promising impactful advancements.

# CONCLUSION

In the pursuit of advancing biomaterials for biomedical applications, this research has unveiled a promising horizon through the comprehensive exploration of Ca-Si-P-Zn composite-loaded PMMA scaffolds. The amalgamation of these innovative scaffolds stands as a testament to their potential in transforming the landscape of regenerative medicine and tissue engineering.Through rigorous physical characterization, including EDAX and FTIR analysis, we have gained profound insights into the elemental composition and chemical characteristics of these composite scaffolds. Their favorable morphology, hydrophilic nature, and meticulous surface profiling, as revealed by contact angle assessments and AFM, underscore their suitability for biomedical applications. The information on the security and compatibility of these scaffolds inside biological systems has been greatly aided by the biocompatibility analyses, which include zebrafish studies and hemocompatibility testing.

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