SYNTHESIS AND CHARACTERIZATION OF COMPOSITE POLY (1.8 OCTANEDIOL CO-CITRATE) (POC) / NANO-HYDROXYAPATITE AS CANDIDATE BIODEGRADABLE BONE SCREW

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ABSTRACT The high number of bone fractures, around 300-400 cases per month, are treated with orthopedic surgery method using internal fixation by *bone screw* which is aimed at accelerating patients' mobilization. There is a necessity to invent biomaterial which possesses two main characteristics: biocompatible and biofunctional, as well as having an important element of biodegradable without conducting *reoperation.* A research focused on the various composition of nano-hydroxyapatite (HA) derived from extracted snapper fish scales on Poly (*1,8-octanediol-Co-Citrate* (POC) as *Biodegradable Bone screw*. This research is purported to synthesize Poly (*1,8-Octanediol-co-Citrate* (POC) and characterize the influence of HA compositions against mechanical properties and compatibility of POC-HA composite that enable it to be used as *Biodegradable Bone screw* material. The condensation polymerization method is applied in synthesizing POC to produce POC *pre-polymer* by the formation of an ester bond group C=O *stretch* at 1731 cm^{-1} through a test of functional groups (FTIR). POC *pre-polymer* is composited with nano-HA compositions of 62%, 65%, 68% and 71% and followed by *post-polymerization* treatment. POC-HA composites formed were tested on hardness and biodegradability. The results obtained indicate that the composition of HA nanoparticles influences the mechanical properties and biocompatibility of the material. Best results were from 62% HA composition in which the hardness value was of 885.57 MPa, close to that of bone hardness which is 150-664 MPa. Results also showed that the rate of biodegradation reached 3.42% (4 weeks) which is in accordance to fracture bone grafting period of 21 months. Based on the characteristics result indicated in this study, the composite of *Poly (1,8-Octanediol-co-Citrate)* (POC)-Nano Hydroxyapatite is a potential candidate for biodegradable bone screw material.

INTRODUCTION

Injury is one of major public health problems worldwide. More than two-thirds of bone fractures reportedly happens in developing countries such as Indonesia [1]. Some reasons causing fracture incidents are the rapid development of transportation in terms of a number of users, the number of vehicles, the number of public transportations users and the speed. One significant side effect is traffic accident which may cause a fracture or fractures. Fracture is defined as a discontinuity of bone, either totally or partially (in part). Most fractures occur due to the failure of bone to sustain bending, twisting and pulling pressures [2].One of the medical treatments carried out on fractures is orthopaedic surgery method.

Data obtained from dr. Soetomo Hospital in Surabaya showed that the number of orthopedic surgery cases ranges around 300-400 cases per month [3]. It is a common phenomenon that nearly 80% of patients are in their productive age, and most of them (63%) underwent surgery using

internal fixation with bone screw intended to exceed the recovery so that the patients are soon able to move and work again [4].

Bone screw is a special screw for bone as a method of handling fracture [1]. The implant technique of bone fracture fixation using bone screw is considered simpler and taking a shorter time. In Rahayu [5] study there was a simple innovation on fixation of bone fractures using *screw* which is made of a mixture of titanium and *stainless steel* on the cortical bone. Further, Respati [6] research concluded that *stainless steel* is a good material for bone screw for its mechanical property, but are less suitable for the body tissues. Stainless steel is not immune to the *body fluid* since it may experience localized corrosion. Therefore, we need composite materials which are not only good for mechanical property but also biocompatible for the body tissues, such as polymer.

Research on developing polymer-based composites as biomaterials for prosthetic biomaterial excels along with the advanced of biomaterial technology. The biomaterial for implants is expected to possess biocompatibility properties. One of the polymers suitable as a biomaterial in the medical field is polyethylene. Many studies have reported that biomaterials derived from *Poly (1.8 Octanediol-co-Citrate)* (POC) are biocompatible, non-toxic and economical [7]. POC has a great potent to form a composite material such as biodegradable bone screw in terms of improvement of the mechanical properties. In fact, Qiu [8] tried to make POC composites with micro hydroxyapatite scaled for bone screw.

Hydroxyapatite (HA) is a ceramic material, a member of the mineral apatite group with a chemical formula $Ca_{10}(PO_4)_6(OH)_2$, which is biocompatible and bioactive due to its bone-like mineral content both chemically and physically [6]. This advantage indicated that HA material has a great potential as a base material for the prosthesis. Nano sized hydroxyapatite is very beneficial, especially when it is functioned as *filler* in the polymer since it can stimulate bone growth and bone formation as well as increase the strength [9].

In Qiu study [8], the use of POC as orthopaedic implants is based on its proven compatibility (e.g, appropriate proliferation and differentiation tests). POC also possesses elastic properties. Therefore, this polymer is composited with hydroxyapatite under the expectation to improve the mechanical properties and osteointegration. However, research showed [8] that the higher weight percentage of HA with a micron-scale particle size above 70%, the composite fails to make perfect form and the mechanical properties are degrading.

That phenomenon triggers this research on a composite of *Poly (1.8 Octanediol-co-Citrate)* (POC) and various compositions of nano-hydroxyapatite as a candidate for *biodegradable bone screw* in order to produce a material that is biocompatible, strong and capable of reactivating osteoblast growth. POC is chosen due to its flexible degradation period. Osteoblasts can grow fast so that the expected material should not be permanent and must be degradable. If the material is permanent, then a surgery is required after the osteoblast regeneration process is complete in order to retrieve the residue of the polymer. Hydroxyapatite is used as filler and purported to improve the mechanical properties and compatibility of the good cells in the *bone screw* application and stimulate the growth of osteoblasts.

This study aims to demonstrate the synthesis of *biodegradable bone screw* composite with various compositions of nano-hydroxyapatite on *Poly (1.8 Octanediol-co- Citrate)* (POC) and get an overview of the results of the characterization of the *biodegradable bone screw* through functional groups test, hardness test, and biodegradation test. *Biodegradable Bone screw* as the result of POC-HA composite is expected to be able to act as a screw on bone fractures in which the biodegradation period is corresponding to the process of bone grafting and biocompatible in nature.

RESEARCH METHOD

Equipment and materials

The equipment used in this study includes Analytical Balance (Mettler Toledo), *Fourier Transform Infrared Spectrometry* (FT-IR) Tensor 27, Bruker, Shimadzu Micro hardness tester type M, Shimadzu Corporation Kyoto-Japan, thermometer, pH-meter, Teflon dishes, magnetic stirrer, hot plate, and a Gallenkamp Vacuum Oven. The materials used are *1,8-Octanediol* (98%) from

Sigma-Aldrich (St. Louis, MO, USA), citric acid (99.5%) [Mw: 210.14] from SAP hydroxyapatite (HA) [Mw: 502.32, assay> 90%; particle size <100nm of PAIR-BATAN, Ethanol for analysis (99.99%), Simulated Body Fluid (SBF) at pH 7.4 in 37°C liquid, Buffer solution in pH 7 from Research Center for Chemistry, Indonesian Institute of Sciences.

Polymer synthesis *poly (1,8 Octanediol-co-Citrate)* (POC)

Synthesis of the POC pre-polymer have been previously described [8]. 0.05 mol of 1.8 *Octanediol* and 0.05 mol of citric acid were added to a 100 ml three-neck round-bottom flas fitted with an inlet and outlet adapter and exposed to a constant flow of nitrogen gas. The mixture was melted under vigorous stirring at a temperature of 160°-165° C. Following melting, the mixture was polymerized at 140 ° C for 1 (one) hour to create the pre-polymer-POC [8].

Composite Synthesis POC / HA

POC pre-polymer was mixed with a various percentage of nano-particle-hydroxyapatite of 62%, 65%, 68% and 71% to obtain a composite. Once formed, the composite was molded into an 80°C heated Teflon dish. POC-HA mixture was stirred until a homogenous viscous paste was formed, which usually takes ± 1 hour depending on the amount of HA mass in the mixture. Then, the composite mixture was put in a Teflon mold dish as needed for mechanics test sampling. POC-HA composite in the mold was given *post-polymerization* treatment at 80°C for 3 days, followed by 120°C under vacuum pressure for 24 hours [8].

Test of Functional Groups with *Fourier Transform Infrared Spectroscopy* (FTIR)

Characterization of compound functional groups composites was analyzed using *Fourier Transform Infrared Spectroscopy* (FTIR). The POC pre-polymer samples are in a form homogenous viscous paste. The samples were then placed in the path of FTIR infrared beam for approximately 1 (one) minute. The characterization is conducted by analyzing spectra of composite POC-HA on the IR spectrum.

Hardness Test

The measurement of samples hardness level was conducted using test device *Micro-hardness Vickers*. The process of *Vickers* hardness testing method was first the composite POC / HA surface was polished to minimize the obstruction during the process of indentation, then it was pressed using a pyramid-shaped diamond indenter which base is square-shaped. The angle measurement between the interface pyramid surfaces is 136°. Sample testing of hardness *(Vickers Test)* received pressure on the surface using the force (F) which is of 0.5 KgF. Initial force time was 2-8 seconds and the test force was conducted for 10-15 seconds. Once the force was released, the diagonal length of the indentation was measured and the average was calculated arithmetically. d is the area of the trace test results.. The test results in the form of grooves can be examined under a microscope

Vickers hardness number is given by the equation:

$$VHN = 1854,4\frac{P}{d^2}$$

Description:
VHN: *Vickers Hardness Number* (HV)
P: applied weight (gF)
d: Diagonal average of the pyramid areas as the result of trace indenter (m)

Biodegradation Test

Sample composite POC-HA was shaped with a diameter of 10 mm x thickness of 5 mm in a corresponding variation of HA composition percentage of 62, 65, 68 and 71 wt%. The samples were placed into *Simulated Body Fluid* (SBF), pH 7.4 at 37° C for 4 weeks in a static condition. Within the composites POC-HA, only the POC is expected to degrade when incubated in SBF solution. SBF was changed as necessary to ensure that the pH did not decrease below 7. Before weight measurement, samples were extensively rinsed with deionized water and dried. Weight loss was calculated by comparing the initial weight (W_0) by weight measured at 1,2,3, and 4 weeks (W_t), shown in the following equation:

$$\text{Weight loss (\%)} = \frac{W_0 - W_t}{W_0} \text{ x } 100\%$$

RESULTS AND DISCUSSION

Polymer synthesis *Poly (1.8 Octanediol-co-Citrate)* was reacted from citric acid and 1.8 mol *Octanediol* at the same mol. The method used in the reacting of both materials is a condensation method with temperatures treatment up to 160ºC then lowered into 140ºC for 1 hour using a set of reflux equipment with a constant flow of nitrogen gas. Temperature treatment was intended to incur crosslink between essential materials of polymer mix which were citric acid and 1.8 *Octanediol* since the product data stated that the boiling point of citric acid is 153ºC and the boiling point of 1.8 *Octanediol* is 57-61ºC. The nature of citric acid is binding itself with other chemical chain. Pre polymer formed was composited with various amount of nano-hydroxyapatite (62, 65, 68, 71 wt.% HA) by the post-polymerization process at the temperature of 80ºC for 3 days followed by the temperature of 120° C for 1 (one) day under vacuum conditions. These compositions were tested because HA composition of 60-65 wt.% is similar to that found in bone and is expected to improve osteointegration. The composite result after post-polymerization is denser and harder because it contains hydroxyapatite bioceramics giving white, the dominant color of the composite, is formed. Post polymerization process is extremely advantageous in the formation of the samples and the surface textures proved to appear perfectly flat and smooth.

Post-polymerization process temperature and timing affect the mechanical properties of these composites. Longer process time and more optimum temperature will improve the materials mechanical properties [7].

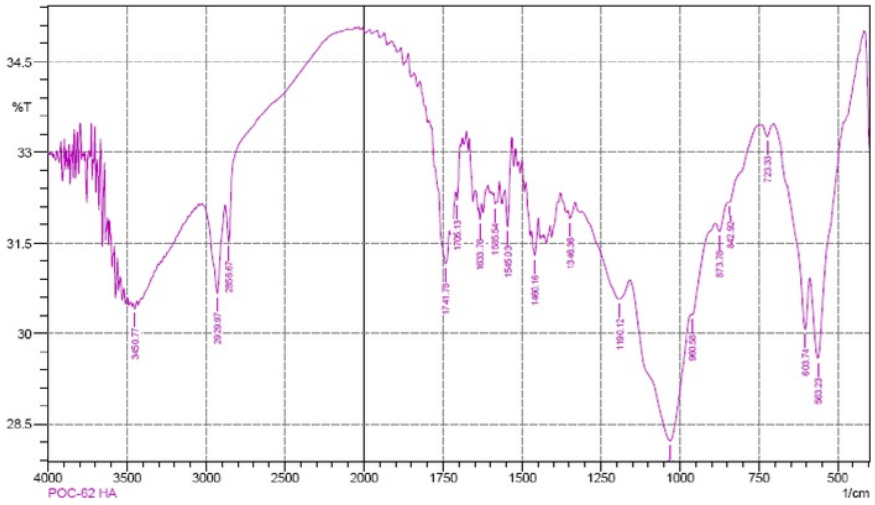

Figure 1. Spectrum IR composite POC-HA

The absorption spectrum triggered the appearance of functional groups uniqueness of each hydroxyapatite and polymer POC. At wave number 1545 cm^{-1} - 1346 cm^{-1} there was an indication of functional group CO_3 of hydroxyapatite and at wave number 1030 cm^{-1} - 563 cm^{-1} there was functional group PO_4^{3-}. The groups that appeared in this analysis was in accordance to Moradi research [10] which states that the functional group at wave number 592 cm^{-1} 601 cm^{-1} 962 cm^{-1} 1030 cm^{-1} and 1089 cm^{-1} are a phosphate group of hydroxyapatite biomaterials. While the peaks of a typical spectrum of the polymer *Poly (1,8 Octanediol-co-Citrate)*(POC) also showed ester group at wave number 1741 cm^{-1} [11]. Based on the analysis of functional groups in the spectrum IR composites POC-HA it showed the absence of the newly formed group. This is because composites formed between polymer POC, in this case as the matrix and hydroxyapatite as *filler,* create no chemical bonding, but only physical bound [10].

Table 1 Absorption Ribbon Functional Groups on FTIR spectrum Composites POC- HA

The wave numbers (cm^{-1})	Group Functions	Molecule
3450	OH-	POC
2929	$-CH_3$ (methyl group)	POC
2856	CH	POC
1741	C=O stretch (ester)	POC
1633-1705	C=O stretch (carboxylic acid)	POC
1585	CC stretch (aromatic)	POC
1545	CO_3^{2-}	Hydroxyapatite
1460	CO_3^{2-}	Hydroxyapatite
1346	CO_3^{2-}	Hydroxyapatite
1190	CH wag ($-CH_2$ X) (alkyl halide)	POC
1030	PO_4^{3-}	Hydroxyapatite
960	PO_4^{3-}	Hydroxyapatite
873	HPO_4^{2-}	Hydroxyapatite
842	OH	POC
723	$P_2O_7^{4-}$	Hydroxyapatite
603	PO_4^{3-}	Hydroxyapatite
563	PO_4^{3-}	Hydroxyapatite

Hardness testing using *Vickers microhardness* carried out to determine the resistance of material to the press deformation (indentation). This testing is executed especially on the materials intersect between two components and moving one against another. The testing process is done by pressing a sample of 0.5 KgF (4.903325 N) by a pyramid-shaped indenter.

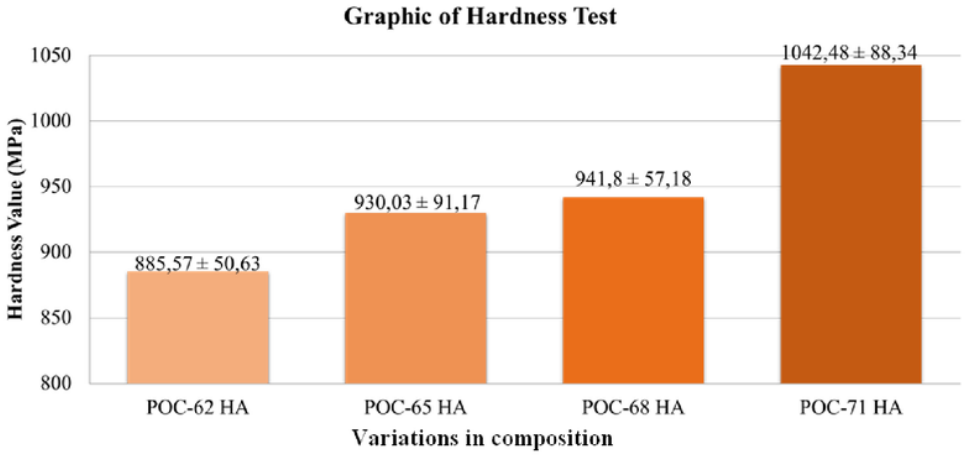

Figure 2. Graphics on influence of HA composition to Composite POC-HA

Data on hardness test results showed that the highest hardness value was found on the sample composite POC-71HA with a hardness value of 1042.28 MPa. It was different from sample composite POC-HA by varying hydroxyapatite compositions respectively, 62% wt, 65% wt and 68% wt which gained increasing hardness values of 885.57 MPa, 930.03 MPa and 941.8 MPa. Based on the hardness value of each sample, there was an increase in hardness along with an increase of HA nanoparticles composition in the composite. This is because bio-composite POC-HA possesses a higher percentage of hydroxyapatite composition compared to polymer POC. The hydroxyapatite has a hardness of 4.86 GPa [12].

Research showed [13] that the hardness value of human bone (cortical and cancellous) ranges between 150-664 MPa. In the POC-62HA sample, the hardness value is higher but closer to the hardness of human bone. This is supported by the increase in *interface* hardness and beneficial in improving internal fixation of bone as the skeletal system [14].

Biodegradation testing conducted as a simulation of biodegradation process when candidates *biodegradable bone screw* is inserted in the body. Based on observations, there was a physical change marked by the dissolution of sample material due to interaction with the environment, in this case, a solution of *Simulated Body Fluid* (SBF). The composition of SBF solution is simulated as the synovial fluid that acts as a source of nutrients for the cartilage of joints and plasma transudate. Soaking in SBF solution is a proof of the material bioactivity [15].

It was also observed that the dissolution process of the material was indirect. The material gradually degraded starting from the surface of the sample material. The graphic illustrates the influence of hydroxyapatite composition addition on several samples against the rate of bio-degradation shown in Figure 3 below.

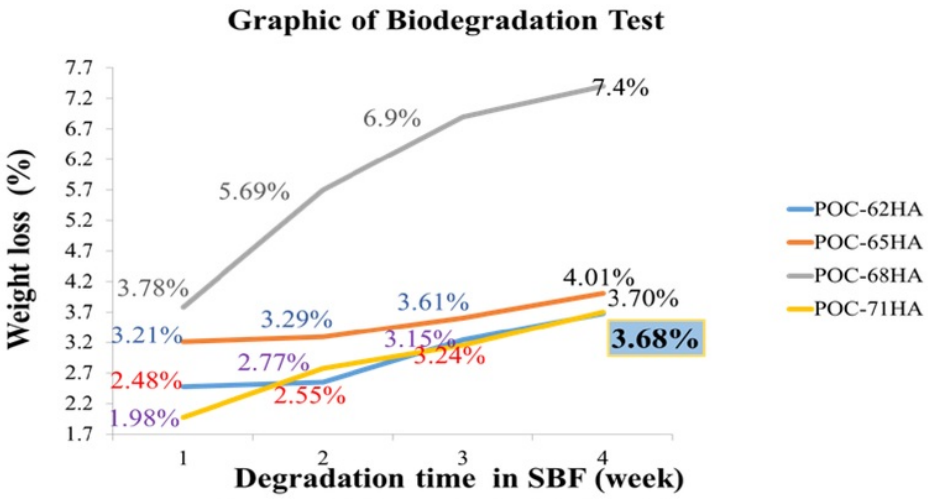

Figure 3 Weight Lost During Biodegradation Test

Biodegradation process was carried out by means of samples incubated in *Simulated Body Fluid* at pH 7.4 and room temperature (±30°) for 4 weeks [8]. The percentage rate of bio-degradation of hydroxyapatite composition variations of 62%, 65%, 68% and 71% respectively by 3.68%; 4.01%; 7.4% and 3.7% is obtained. These values refer to [8] study that within a period of 0-5 weeks the percentage of weight reduction reached 8%.

Then, the calculation of the period of total bio-degradation-composite POC-HA was conducted until the percentage comparison reached 100%. The result was shown in Table 2.

Table 2. Time Required for 100% Degrading Composite

Samples	Weight reduction for 4 weeks (%)	Period Weight reduction 100% (week)
POC-62HA	3.677758	108.761914
POC-65HA	4.009623	99.7600024
POC-68HA	7.398411	54.0656636
POC-71HA	3.236483	108.066342

Based on data analysis, it was learned that the best result was on a sample composite POC-62HA. This sample possessed a stable rate of biodegradation and was supported by the results of total degradation calculation on sample POC-62HA in which biodegradation time total was over 109 weeks (27 months). This total degradation time is in accordance with the maximum period of bone grafting process according to Apley's systems that require time period of 3 months - 21 months [16].

CONCLUSION

1. Hydroxyapatite variations influence the mechanical characteristics of *poly (1,8-octanediol-co-citrate)* (POC). The Higher percentage of hydroxyapatite composition added increases the value of hardness strength produced. However, there are other factors that contribute to the high value of mechanical properties, i.e., the interaction between the polymer matrix POC and *filler* hydroxyapatite. Based on the analysis result, the best composition was on sample POC-62HA

which hardness value was of 885.57 MPa, close to human bone hardness range from 150-664 MPa.

2. The addition of hydroxyapatite composition also increases the rate of bio-degradation. The result on sample POC-62HA showed a maximum rate of bio-degradation, 27 months, which was longer compared to the bone fracture healing time that required a period of 3 to 21 months.

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