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RESEARCH ARTICLE

Biomaterial Composites

Synthesis and characterization of biocomposite of bovine bone-based hydroxyapatite-poly(lactic acid)-maleic anhydride

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Abstract: Human bone is a composite material of hydroxyapatite (HA) and collagen. HA ($Ca_{10}(PO_4)_6(OH)_2$) is a biomaterial with the calcium to phosphorus ratio being similar to the natural bone composition. In this study, composite materials were prepared by using poly(lactic acid) (PLA) as a polymer matrix, maleic anhydride (MAH) as a compatibilizer, and natural HA extracted from cow bone (BHA) as a suitable mechanical support filler with positive surface properties. Composites with varying HA (10-30 wt. %), PLA, and with or without MAH (0.5–8 wt. %) were prepared by a thermal decomposition method at 900 °C. In comparison to commercial HA (CHA), the effect of the PLA and MAH contribution on morphological, thermal, and mechanical properties of BHA were analyzed by X-ray diffraction (XRD), Fourier transform infrared (FTIR) spectroscopy, thermogravimetric analysis (TGA), scanning electron microscopy (SEM) and tensile strength measurements. As per the results, the HA30/PLA/4MAH composite with 30 wt. % HA, 66 wt. % PLA and 4 wt. % MAH offer the maximum mean tensile strength of 307.71 MPa. The overall results confirm the contribution of MAH compatibilizer in HA/PLA/MAH composite materials for bone tissue engineering from a mechanical point of view.

Keywords: Biocomposite, biomaterials, bone tissue engineering, compatibilizer, hydroxyapatite, poly(lactic acid), maleic anhydride.

INTRODUCTION

Biomaterials are substances that can be engineered to replace a part or a function of the body in a safe, reliable, economical, and physiologically acceptable way. Biomaterials are used in prostheses, scaffolds, hydrogels with cells, and growth factors to treat bone loss due to fracture, osteoporosis, osteoarthritis, and neoplasms (Ramesh *et al*., 2018). The implant material should be biodegradable, biocompatible, non-toxic, non-mutagenic, and non-immunogenic, with suitable mechanical support and positive surface properties, such as facilitating adhesion, proliferation, and differentiation of cells (Asghari *et al*., 2017). Human bone is a composite material of 70% HA, a high modulus filler, in a collagen matrix (Liao *et al*., 2013). HA ($Ca_{10}(PO_4)_6(OH)_2$) is considered an implant material possessing biocompatibility, good corrosion resistance, bioactivity, high osteoconductivity, nontoxicity, and displaying non-inflammatory and non-immunogenic behaviour, due to its calcium to phosphorus ratio being similar to the natural bone composition. It also has some drawbacks, such as brittleness, low fracture strength, low mechanical reliability, lack of resilience, debris formation, and relatively difficult fabrication. To overcome these drawbacks, biocomposites are designed to achieve a combination of the best properties of two or more materials to fulfill various mechanical and biological needs. In this case, polymer matrix composites are commonly considered due to similarity in composition and structure of natural tissue, good biocompatibility, moulding capabilities into desirable shapes and sizes, and controllability over mechanical properties and degradation characteristics (Liao *et al*.,

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2013; 2014). Petrochemical-based polymers such as polyetheretherketone (PEEK), polysulphone (PSU), and polypropylene (PP) have been reported as good candidates for matrices (Wang *et al*., 2001; Converse *et al*., 2007; Liao *et al*., 2013; 2014; Stubinger *et al*., 2016) However, biodegradable polymers such as polylactic acid (PLA), polyglycolic acid (PGA), polycaprolactone (PCL), and polyhydroxyalkanoates (PHAs) are more reliable in reducing inflammatory reactions, nontoxic, biodegradable, absorbable and can easily change into different 3D matrix structures (Fabbri *et al*., 2010; Gao *et al*., 2016; Lu *et al*., 2019). PLA is a biodegradable, bioadsorbable, thermoplastic aliphatic polyester, that can be derived from renewable resources (Wang *et al*., 2001; Converse *et al*., 2007; Liao *et al*., 2013; 2014; Stubinger *et al*., 2016; Asghari *et al*., 2017; Lu *et al*., 2019). PLA/HA biocomposite materials are designed both as scaffold materials and as carriers to supply drugs and other proteins to the host. However, the HA percentage in the PLA/HA biocomposites and the temperature influence in the mechanical properties of the composite (Sun *et al*., 2011; Ramesh *et al*., 2018). Tazibt *et al.* (2023) have shown the effect of hydroxyapatite (HA) on the morphology and properties of composites based on poly(lactic acid) (PLA) at various filler content ratios (5, 10, and 15 wt.%) using the solvent casting method, followed by thermo-compression. The properties of PLA can be enhanced by blending, copolymerization, cross-linking, and grafting methods (Meng *et al*., 2023).

Most bio-fillers such as HA do not easily disperse in thermoplastic polymers because of strong intermolecular hydrogen bonding between biofillers and agglomerate during the compounding process with the polymer matrix. Therefore, the improvement of interfacial adhesion between bio-fillers and polymer matrix is very important for the application of composites. Currently, different methods have been studied to improve the interfacial adhesion of composites by modifying the biofiller surface (Prabhu *et al*., 2016; Moja *et al*., 2020; Tariq *et al*., 2021), for example, the construction of a stereo-complexation between poly(d-lactide) grafted hydroxyapatite and poly(l-lactide) via selective laser sintering (SLS) (Shuai *et al*., 2022) and the application of silane coupling agents to enhance the interfacial features between bioceramic and biopolymer composite (Shuai *et al*., 2020). In comparison to the above-discussed crosslinkers, maleic anhydride (MAH) is a low toxic, chemically active compound with a low potential to polymerize itself under free radical grafting conditions (Zhang *et al*.; 2004; Nainar *et al*., 2012; Sumathra *et al*., 2020). This study focuses on the development of a cost-effective, biocomposite material using natural hydroxyapatite (HA) which is extracted from waste cow bone by a thermal decomposition method, and a biodegradable polymer (PLA). The enhancement of interfacial coupling in hydroxyapatite and polylactic acid was achieved by incorporating maleic anhydride (MAH) as a compatibilizer toward a bioactive composite (HA/PLA/MAH) with enhanced interfacial bonding. The effect of MAH compatibilizer content on the formation, morphology, and physical properties of hydroxyapatite-poly(lactic acid)-maleic anhydride composites are further studied. Finally, the characteristics of the composites with and without compatibilizer (MAH) are compared.

METHODS AND MATERIALS

Preparation of hydroxyapatite composites

A fresh cow bone sample was cleaned by boiling in water for 4 hours, followed by drying in an oven at 180 ℃ for 1 hour. The cleaned and dried bones were then ground to a fine powder (<450 μm) using an agate mortar and pestle. The ground bone particles were treated with sodium hydroxide solution for 1 hour. Then the bone sample was neutralized with distilled water, dried in an oven at 180 ℃ for 4 hours, and sintered in a furnace at 900 ℃ for 3 hours. The resulting bone sample was crushed in a ball mill for 1 hour at 800 rpm to produce bone powder and sieved to obtain the particle sizes below 125 μm. The powdered sample was oven-dried at 120 ℃ for 1 hour to prepare composites.

Table 1: Preparation of HA/PLA composite without compatibilizer

Sample ID	BHA wt.%	PLA wt.%
HA10/PLA	10	90
HA20/PLA	20	80
HA30/PLA	30	70

To prepare composites according to Table 1 compositions, PLA pellets were melted in a stainless-steel container on a hot plate at 200 ℃. After the melting, BHA powder was slowly added to the melted polymer while continuously stirring using a mechanical stirrer for 1 hour. Thereafter, the mixture was poured into the created wooden mould which was prepared for the tensile test.

Table 2: Preparation of HA/PLA/MAH composite

Sample ID	BHA wt.%	PLA wt.%	MAH wt.%
HA30/PLA/0.5MAH	30	69.5	0.5
HA30/PLA/1MAH		69.0	1.0
HA30/PLA/2MAH		68.0	2.0
HA30/PLA/4MAH		66.0	4.0
HA30/PLA/8MAH		62.0	8.0

To prepare composites according to Table 2 compositions, PLA pellets were melted in a stainless-steel container on a hot plate at 200 °C. After the melting, MAH powder was slowly added to the melted polymer while continuously stirring followed by BHA addition to the PLA/MAH mixture while continuously stirring for 1 hour. Thereafter, the mixture was poured into the created wooden mould for the tensile test.

Characterization techniques

Commercial hydroxyapatite (CHA), prepared HA from cow bone (BHA), and selected HA/PLA and HA/PLA/MAH composites were characterized using fourier transform infrared spectroscopy (Alpha Platinum AKR, FTIR), X-ray diffractometry (Rigaku-Ultima 1V X-Ray diffractometer1, XRD), scanning electron microscopy (LEO-1420P, SEM), and thermogravimetric analysis (SDT Q600, TGA with N_2 environment); the tensile was tested on a JTM-S1000 universal tensile testing machine using a load cell of 98.5 kN.

RESULTS AND DISCUSSION

Bovine bones were first boiled in hot water, and then immersed in a sodium hydroxide solution to remove collagen, fat, and organic substances. Deproteinized white-coloured cow bone pieces (Figure 1A) were ball-milled to make HA powder (BHA) (Figure 1B). The bones were washed with distilled water, dried, and sintered at 900 °C for 3 h to transform to fully crystallized hydroxyapatite. To form composites, BHA was mixed with PLA polymer and moulded into cylindrical shapes using a trial bone plate (Figure 1C) with and without MAH compatibilizer (Figure 2 and 3) to test tensile strength. The highest HA weight percentage containing HA30/PLA composition was selected to continue the study which is more compatible with human bone composition (HA : organic : water = 70:25:5; Rakmae *et al*., 2011).

Figure 1: Hydroxyapatite A) Raw bone pieces; B) Bone hydroxyapatite; C) Trial bone plate

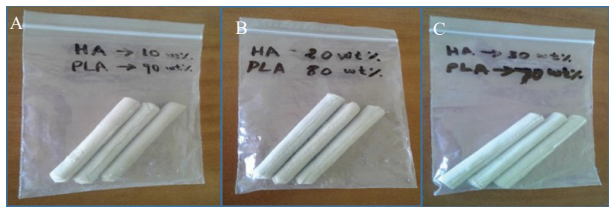

Figure 2: HA/PLA Biocomposites A) HA10/PLA; B) HA20/PLA; C) HA30/PLA

Figure 3: HA/PLA/MAH Biocomposites A) HA30/PLA/0.5MAH; B) HA30/PLA/1MAH; C) HA30/PLA/2MAH; D) HA30/PLA/4MAH; E) HA30/PLA/8MAH

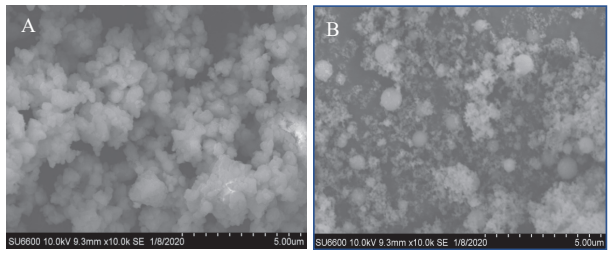

Figure 4: SEM images of HA powder A) BHA, B) CHA

SEM Analysis

According to the SEM images of BHA (Figure 4A) and CHA (Figure 4B), HA particles have an irregular sphere shape and mostly consist of agglomerated big particles with a size of ~1-5 μm, due to the strong intermolecular bonding of HA particles to each other. Agglomeration of HA powder particles will reduce the important surface properties, correlation, and performance of the composites. In the SEM images of the HA30/PLA/4MAH composite (Figure 5), HA was detected on the polymer matrix in a closely packed form, and dark holes were observed in the surface matrix as in Figure 5A and 5B. The appearance of micropores in samples as dark holes would improve surface topographical features for the osteoconductivity of bioceramics and proper porosity is a desirable factor for cell growth through the channels of the scaffold (Chan *et al*., 2012; Baier *et al*., 2019; Mishchenko *et al*., 2023). Normally HA biofiller does not easily disperse in biodegradable polymers such as PLA because of strong intermolecular hydrogen bonding between HA particles, and they agglomerate during the compounding process with the polymer matrix. However, less pullout of HA powder and less agglomeration of HA powder were observed in the PLA polymer matrix (Figure 5C and 5D). The results indicated that modifying the HA surface with MAH compatibilizer would result in better interfacial adhesion between the HA powder and PLA matrix and would enhance the dispersion properties of the composite (Rakmae *et al*., 2011; Hapuhinna *et al*., 2017; 2018).

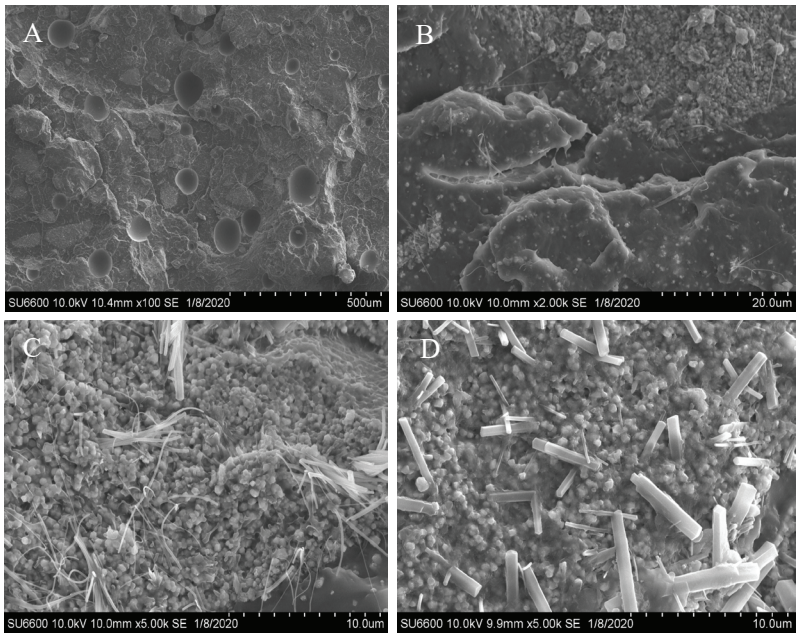

Figure 5: SEM images of HA30/PLA/4MAH biocomposite

XRD Analysis

The XRD peak positions of BHA (Figure 6B) and CHA (Figure 6C), are overlapped with characteristic peaks related to the crystallographic planes of HA at (002), (210), (211), (112), (300), (202), (310), (222), (213), and (004). Phase analysis according to the standard JCPDS 00-009-0432 revealed that all major peaks of HA present in both BHA and CHA powders are in good agreement with hexagonal HA in reference material (Mondal *et al*., 2014). Data further shows the purity of the prepared HA from cow bone waste and the crystallinity behaviour of BHA during the sintering process. It indicated that the sintering temperature influences the phase stability, densification behaviour, and hardness of HA ceramics. BHA shows sharp peaks in the XRD pattern due to the higher degree of crystallinity of planes after the sintering process at 900 °C (Figure 6B). The absence of other peaks corresponding to impurities indicates that a pure phase of HA has been synthesized during the procedure (Ferri *et al*., 2017; Hapuhinna *et al*., 2017).

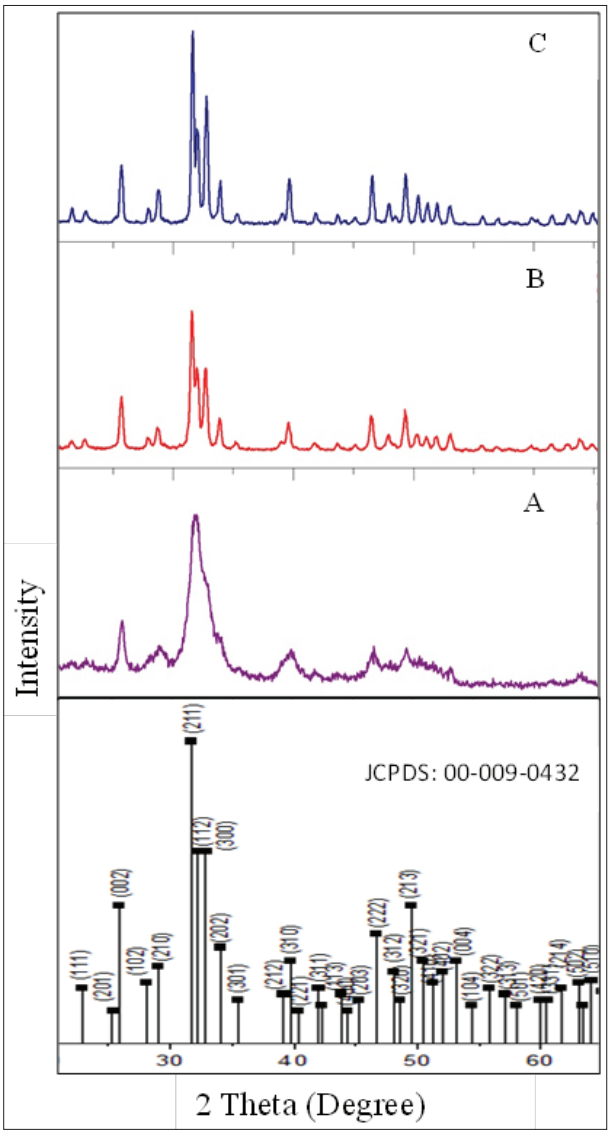

Figure 6: XRD patterns of A) Raw bone HA, B) Sintered bone HA and C) Commercial HA samples.

FTIR Analysis

The representative FTIR spectrum in Figure 7, confirms the presence of phosphate groups (PO_4^{3-}) for all raw bone HA, BHA, and CHA. FTIR peaks at 475, 560 – 601, 640, 963, 1023, and 1090 cm^{-1} were assigned to different vibration modes of phosphate groups. The peaks at 475 cm^{-1} correspond to V_4 of PO_4^{3-} modes, 560 - 601 cm^{-1} relate to V_4 of the bending modes of P-O bonds, 640 cm^{-1} and 963 cm^{-1} to V_1, and the stretching vibrations of PO_4^{3-} of V_3 appear at 1023 and 1090 cm^{-1}. It confirms the presence of the HA phase in BHA (Hapuhinna *et al*., 2017; 2018). The characteristic peak for OH^-/hydroxyapatite appeared nearly at 3572 cm^{-1} in CHA and BHA. Stretching and bending vibrations of OH groups in HA powder were observed at 631 and 3542 cm^{-1} (Rakmae *et al*., 2011; Ferri *et al*., 2017; Hapuhinna *et al*., 2017). The characteristic band of the vibrational mode of structural OH can be seen at 631 cm^{-1}. The stretching vibration band of OH (3542 cm^{-1}) was invisible for raw bone HA due to absorbed water. The peaks at frequencies of ~875 cm^{-1} and ~1450 cm^{-1} resulted from a small amount of carbonate absorbed as CO_2 from the atmosphere during the synthesis process. It is common for biological apatite to allow substitution of other ions, such as carbonate, fluoride, and chloride substitution of either OH^- or PO_4^{3-} groups. Raw bone HA powder shows the presence of amide groups (1660 cm^{-1}, 1547 cm^{-1}, 1244 cm^{-1}) due to collagen and other organic compounds present in the bone (Paschalis *et al*., 2011; Rana *et al*., 2017). However, after the heat treatment at 900 °C, BHA becomes more compatible with CHA (Hapuhinna *et al*., 2017; 2018).

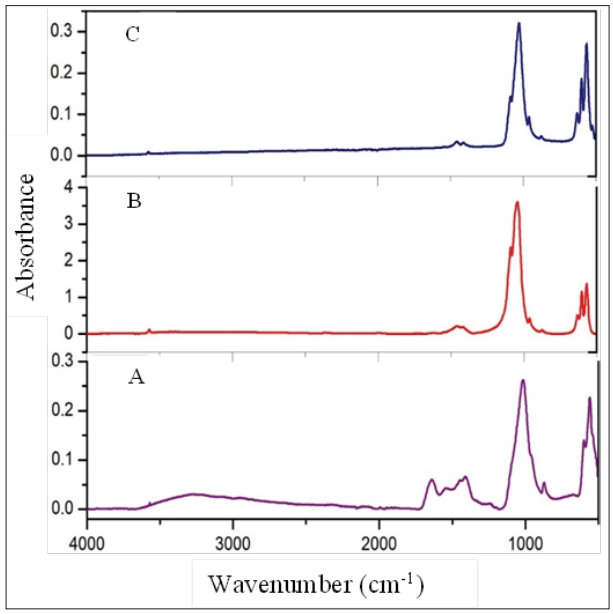

Figure 7: FTIR results of A) Raw bone HA, B) Sintered bone HA and C) Commercial hydroxyapatite samples

TGA Analysis

As shown in Figure 8, BHA and CHA samples were subjected to TGA analysis. The first significant weight loss of BHA occurs at nearly at 200 °C, corresponding to the dehydration of the sample. Thereafter, the TGA

curves of BHA and CHA samples showed weight reduction at a low rate close to 650 °C, due to the removal of bone structure collagen remains (Rakmae *et al*., 2011; Ferri *et al*., 2017; Hapuhinna *et al*., 2017). In addition, a fine TGA descending slope was observed in the temperature range 700 – 1000 °C, with weight loss corresponding to the decomposition of HPO_4^{2-} ($2\ HPO_4 \rightarrow P_2O_7^{4-} + H_2O$ and $P_2O_7^{4-} + 2\ OH^- \rightarrow 2PO_4^{2-} + H_2O$) and gaseous compound elimination. Weight loss patterns have shown relatively similar patterns above 500 °C due to composition similarities (Rakmae *et al*., 2011; Ferri *et al*., 2017; Hapuhinna *et al*., 2017).

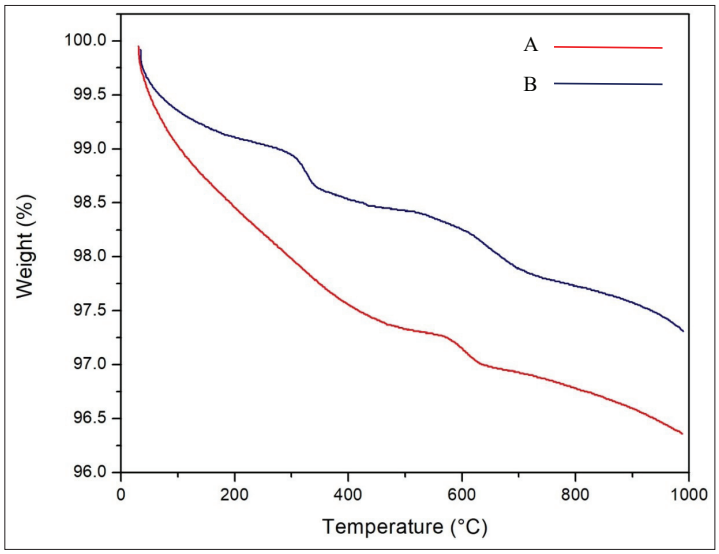

Figure 8: TGA analysis of A) Sintered bone HA and B) Commercial hydroxyapatite samples

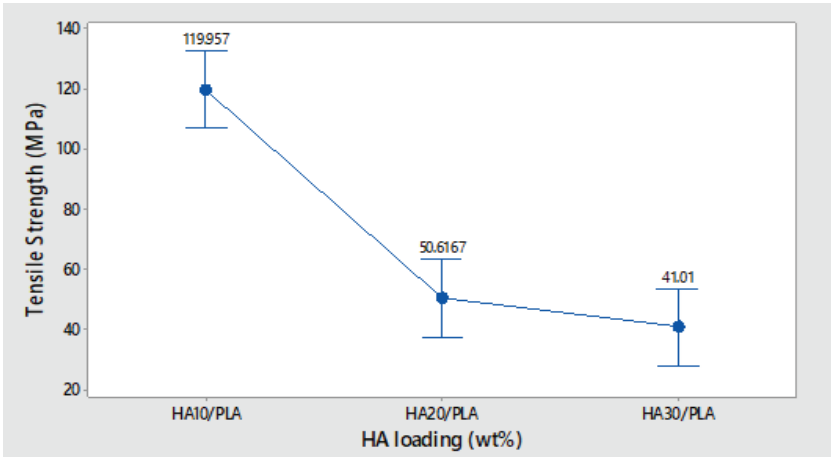

Figure 9: Plot of Tensile strength of HA/PLA composite without compatibilizer

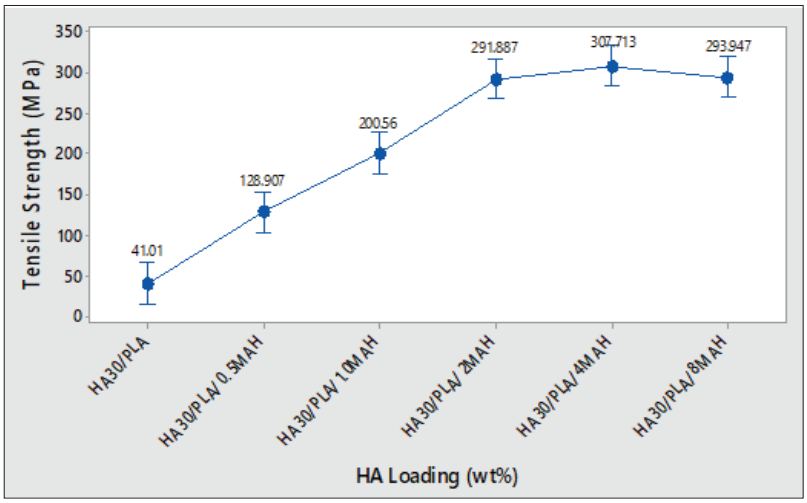

Figure 10: Plot of Tensile strength of HA/PLA composite with MAH compatibilizer

Tensile strength test

The mechanical properties of the HA/PLA without and with MAH are illustrated in Figures 9 and 10 respectively. According to Figure 9 plot, the evolution of tensile strength as a function of the wt. % of hydroxyapatite without compatibilizer, HA10/PLA shows the maximum mean tensile strength of 119.96 ± 8.01 MPa. The Tukey multiple comparison test was run at 95% confidence to get the highest strength. As seen in the results, the tensile strength of the HA/PLA composites decreased with increasing HA loading because of poor dispersion of the filler material in the polymer matrix, detachment of HA from the matrix, weak interfacial adhesion, and low compatibility between the hydrophilic HA and hydrophobic PLA (Kim *et al*., 2007; Gong *et al*., 2017). With HA loading, agglomeration of HA powder particles in the PLA matrix would reduce the surface contact area and create physical voids and defects in the composites which are eventually responsible for inefficient transferring of loading stress between PLA matrix and HA powder particles (Vainio *et al*., 1998: Hong *et al*., 2005). The tensile strength of a particulate HA/polymer composite depends on a uniform filler distribution and the effective interfacial adhesion in the polymer matrix (Rakmae *et al*., 2011; Ferri *et al*., 2017; Hapuhinna *et al*., 2017).

As shown in Figure 10, in comparison to the tensile strength of HA/PLA composites, HA/PLA composite material with MAH compatibilizer results in higher tensile strength (307.71 ± 1.91 MPa in HA30/PLA/4MAH composite) (Rakmae *et al*., 2011; Ferri *et al*., 2017). The tensile strength of the HA/PLA composite increases with increasing amount of compatibilizer up to 4 wt. % of MAH. The composite obtained from HA and PLA with MAH shows better mechanical properties due to the improvement of interfacial adhesion between HA and PLA and effective filler dispersion in the polymer matrix (Vainio *et al*., 1998; Hong *et al*., 2005). The anhydride groups present in MAH could enhance the dispersion of the filler material in the composite by making crosslinks between HA and PLA. Thereby, MAH compatibilizer would result in better interfacial adhesion between the HA powder and PLA matrix and would enhance the mechanical properties of the biocomposite (Rakmae *et al*., 2011; Ferri *et al*., 2017; Hapuhinna *et al*., 2017).

CONCLUSION

XRD and FTIR analysis reveals the similarity of commercial hydroxyapatite and hexagonal hydroxyapatite produced using cow bone waste by the thermal decomposition method at 900 ℃ as a cost-effective method. The hydroxyapatite (HA) and poly(lactic acid) (PLA) polymer matrix were prepared with and without maleic anhydride (MAH) compatibilizer and mechanical properties were assessed. The mechanical properties of HA/PLA composites with MAH compatibilizer were found to be improved in comparison to HA/PLA

composites. MAH incorporation has shown a significant increase in tensile strength due to the ease of dispersion of HA in PLA polymer matrix and enhanced interfacial adhesion between filler and matrix material. Hence, HA/PLA/MAH composite demonstrates the usefulness from a mechanical point of view for bone tissue engineering.

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