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Investigation into property and bioactivity polymeric bone cement

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ABSTRACT Polymeric bone cement is a bone repair material, which is able to give immediate augmentation of bone defects and accelerates normal bone healing through appropriate biodegradation rate. The aim of the present study was to develop polymeric bone cement and to investigate the bioactivity using Scanning Electron Microscope (SEM) and X-ray Diffraction technique (XRD). The bioactivity of the bone cement produced was tested under simulated body fluid (SBF) solution. In the present study, polymeric bone cement was developed from poly (vinyl pyrrolidone) (PVP), unsaturated polyester poly (propylene fumigate), benzyl peroxide (BP) and hydroxyapatite (HA) by hand mixing. Benzyl peroxide initiated the cementing process while PVP accelerates to achieve cross linked between polyester chains. SEM observation of the cement after soaking in SBF showed the formation of new plate like apatite crystals in the structure. Therefore, the developed bone cement has a potential as a repair material especially for cancellous bone.

(Polymeric bone cement, Biodegradation rate, Bone cement, Cross-linking, Hydroxypatite)

INTRODUCTION

A wide variety of implant materials have been used to repair, restore and augment defect skeletal bone. This includes autologous bone, synthetic polymers and inert metals. These implant materials would promote significant effect that can include patient pain, risk of infection during operations, lack of biocompatibility, cost and the risk that the inserted hardware can further damage the bone.

In the early 1980's, researches were focusing on the use of HA to augment skeletal defects and for the use as coating material on prosthetic implants. Sintered HA is a biomaterial that has attracted much interest as a substitute for injured bone and teeth as results of the principal inorganic constituent of these hard tissues. This sintered preformed HA prosthetic material has several disadvantages which include difficulty in physical shaping and installing during surgery, having insufficient strength to support heavy loads and less absorbable by the host by slow biodegradation rate of less than 1% per year.

It would be useful to provide a material that could be used as bone cement that is non-toxic and biocompatible with the surrounding tissue. The material developed could be provided in physical form that could be injected or applied to the site of action in a manner that would permit minimum invasive surgery and would allow the cement to intimately contact the parts to be joint. It would be beneficial if such material could cure quickly, developed a high compressive strength upon curing and biodegradable.

Biodegradable bone developed in this study is a cement system consists of ceramic and polymeric materials, proposed to be used in bone surgery, either for repairing of bone defects or for bone augmentations. It provides immediate structural support and accelerates normal bone healing, remodeling process, exhibit bone formation and resorption characteristics [1]. They do not require removal through secondary surgery due to its ability to deteriorate in the body via natural pathways and progressive loss of degradable implant material will lead to regeneration of healing tissues. Biodegradable ceramics and polymers are two major compounds that can be found in formulations of this bone cement, which are designed to degrade gradually with time be replaced with natural tissues [2].

PPF is unsaturated polyester that can be cross-linked through the fumarate double bond in situ [3] and hydrolyzed at the ester linkage. This characteristic makes PPF as a good candidate for developing biodegradable and mouldable implants. It is first being used in acrylic bone cement in order to enhance the biodegradability of this bone cement. The role of cross-linking agent is taken by PVP [4]. The objective of this study is to develop biocompatible and biodegradable surgical cement that can be utilized for repairing living bone. Apart from that, HA and PPF were synthesized in our laboratory.

MATERIALS AND METHOD

The soluble polymeric solution used is PPF that is synthesized by direct esterification method [5]. 3.0 moles of fumaric acid (348 grams) and 3.3 moles of propylene glycol (251 grams) were placed in triple-necked 1000 cc flask with overhead mechanical stirrer, thermometer and Barret trap beneath a condenser. The reaction was initiated by heating at 145°C with continuous stirring. After 2 hours, water began to collect in the Barret trap. The mixture was heated for 5 hours by which time about 40 ml of water had been collected. The temperature was then increased to 180°C in order to release off the propylene glycol. The mixture was cooled at room temperature to prevent further polymerization. In order to remove the excess fumaric acid precipitate, 85 parts by weight of the mixture were diluted with 15 parts by weight PVP monomer, placed on rotary stirring rack for 12 hours at 37°C to ensure thorough mixing and centrifuged at 6000 RPM for 30 minutes. The PPF polymer was formed at the upper layer of the mixture.

The formulation for this study includes a composition of 68 wt% HA, PPF 23 wt % and 6 wt% PVP while initiator was prepared using 0.7 wt% benzyol peroxide and 2.8 wt% PVP. The mixture started to heat up and hardened. 10 ml of distilled water was added if the mixture was too dry and hard to blend. Mixing was done thoroughly and by using the flat end of the spatula, the cement was packed carefully into the mould and the bottom part was left opened to allow the cement to pack into it. The bottom of the mould need to be checked periodically to make sure that the cement was fully packed. It took practiced to properly packed the mould. After the cement samples were dried for about 15 minutes, the moulds were opened. This procedure had to be done with extra care to avoid cracks. The cement was then left for 24 hours before testing.

RESULTS AND DISCUSSION

During applications, the cement sets quickly within 15 minutes and setting temperature was 37°C. Reliability, reproducibility and workability were the salient properties but sticky, low viscosity and porous structure were the drawbacks. During mixing, samples exhibit exothermic reaction, due to the cross-linking action of PPF. This phenomenon supports the obsevation of temperature increased during mixing of the bone cement. However, even though heat is released on curing process, the temperature was still acceptable in physiological environment. The bone cement paste was able to cure in body temperature or at slightly higher temperature.

The bone cement represents a highly biocompatible tissue substitute precursor or synthetic implant material for skeletal reconstruction. The setting time for the bone cement is important to give enough time for surgeon to inject the bone cement before it is cured. Theoretically, setting time is a function of cross-linking action and the workability of the bone cement is related to wet ability of the mixing. A wet cement mixing would give a high viscous paste and a dry cement mixing would give a low viscous paste and is difficult to handle.

When 10 ml of water was added into the formulation, the workability of the slurry paste was ideal and it could be easily poured into the mould with good injectable properties. Workability of the bone cement was also determined by the PPF content in the mixture. When PPF was added, the bone cement became sticky; this is because of the nature of PPF, which is a very sticky liquid. Cement with low powder to PPF ratio yields a very dry mixture and took more time to set. More cross-linking took place when the amount of PPF was increased with the same amount of cross-linking agent and an initiator with constant setting time. These will result of an increase in mechanical

properties of the bone cement. Overall, the surface of the bone cement after setting process was covered with pores. These pores are beneficial for bone ingrowths even though it is the source of mechanical failure. The main reason of the pore formation is due to the mixing technique. Hand mixing will introduce air pores into the cement, which can grow a few millimeters.

Figure 1 shows the XRD spectrum of bone cement, which is typical of all samples. From the broad peaks in the spectrum with close 2θ angles and d spacing it shows all samples are of low crystallinity. The strongest peak of the samples falls at 2θ = 32° and inter planar spacing around 2.77 A. This illustrates the similarity of spectrum with the JCPDS No. 9-432, indicating that the major compound in the bone cement produced were unsintered HA.

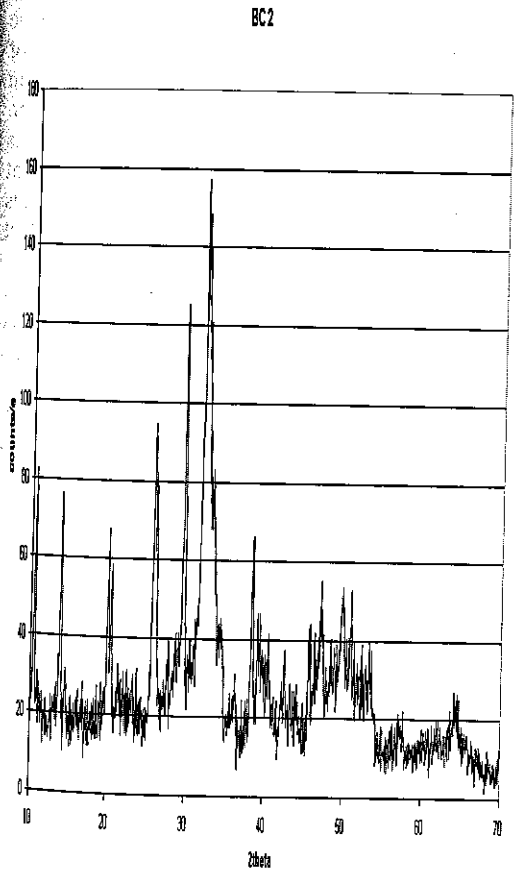


Figure 1. XRD spectrum of bone cement.

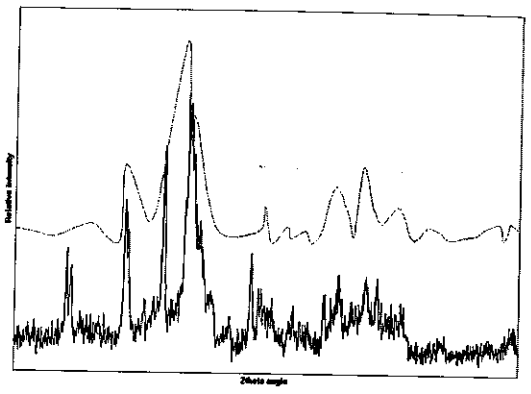


Figure 2. Comparison between XRD spectrums of natural bone (top) with bone cement (bottom).

Figure 2 indicated the similarity in the XRD spectrum of the bone cement produced (bottom) with natural bone (top) in the non-crystalline apatite nature and the chemical properties of both spectra. It is important for the bone cement to contain elements such as magnesium, sodium, potassium, fluorine, and chlorine and carbonate ions. The apatite mineral in bone is closely associated with the collagen fibers and is made up of plate like nanocrystals [6]. Crystalline forms of bone cement are osteogenesis in nature but its resorption rate has been reported relatively slow compared to the rate of new bone formation [7]. On the other hand, bone cement with non-crystalline compound is more efficient in controlling the resorption rate in order to match the new bone ingrowths process.

During the mixing process of cement slurry, HA acts as filler, which was cross-linked in between the PPF. This results in the appearance of HA peaks which are characteristic of the bone cement. After the mixing process a slight change appears in the peak orientation. This is probably due to the addition of water or addition of free radical catalyst (benzyol peroxide) and cross-linking agent (polyvinyl pyrrolidon). During the mixing process not all PPF react in the composition, some PPF remain due to extrinsic factor (mixing, temperature or human error). Portion of HA spectral appears in Fig 2 because HA fail to react in the cross-linking process during curing time whereby HA is trapped between the cross linking network of PPF. Many factors can contribute to this failure; among them is low curing temperature, which inhibit the formation of cross-linking network. The non-homogenous mixing during slurry preparation is

also a possible reason as to why benzyol peroxide does not fully react with PPF. This will yield a low mechanical strength of the bone cement produced. This explains that the strength of the bone cement is proportional to cross-linking effect during mixing time. Therefore, when the numbers of cross-linking drop, the mechanical properties of the bone cement will be reduced.

The compression test results for the bone cement produced are depicted in Table 1.

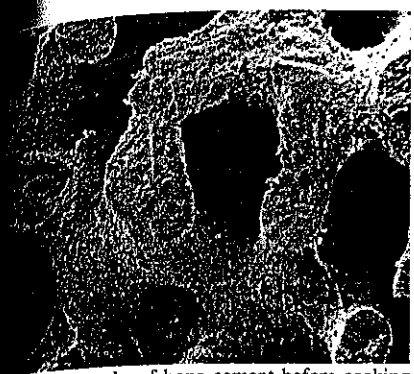
Table 1: Mechanical properties of bone cement.

Load Peak (N)	Stress Peak (MPa)	Strain Break (%)	Load Break (N)	Young's Modulus (MPa)
441.40	14.480	7.029	441.40	66.950

The average load and stress of the bone cement produced are 441.4 N and 14.48 MPa respectively before the sample break. The bone cement samples are able to bear high stress due to the change in strain dimension at 7.029 %. The mechanical properties and stiffness of the bone cement can be improved by increasing the PPF content during mixing. From the table, the Young's modulus for bone cement is 66.95 MPa. This is considered very low compared to the other bioactive material [8]. This characteristic may result from the wetting process. The wetting process occurs when 10 ml of water was added during mixing process. The wetting of the cement surface would reduce the mechanical properties of resultant samples. Another factor that can contribute to the reduced mechanical properties is from the porous nature of the sample. Increase in cross-linking between the unsaturated polymers can create a stronger internal structure of the bone cement. Pores formation was unavoidable during hand mixing technique. The results also show that the Young's modulus and compressive strength of the cement samples matched the cancellous bone [9]. Cancellous bone is the less load bearing part of the skeletal tissue and is less dense than the cortical bone. It is usually found at the end of long bone with honeycomb like internal structure. The compressive strength for cortical bone is about twenty times of cancellous bone. Overall, the samples produced are suitable for the use in cancellous bone but the characteristic strain at break need to be modified to match the natural bone.

Figure 3 shows the SEM micrographs of the bone cement microstructure before soaking in SBF solution. The porosity is clearly seen about 40% of the sample structure. The pore size observed were roughly 100 micron, interconnected and round in shape. This pore size is normally suitable for bone ingrowths. With these porous substrates, it is feasible to fabricate both aggregates for substituting damage skeletal osteo parts. The pores were also contributed to low mechanical strength of the cement produced but it is a strategic location for the concentration of stress before the structure fail. Figure 4 shows the SEM micrograph that illustrates the progressive development of the microstructure of the cement as it cured in contact with SBF solution in 21 days. New apatite nano crystallites can be seen grown all over the surfaces of the samples. It appears to be heterogeneously nucleated over the surfaces of the particles with some needlelike crystals in an interconnected open framework arrangement. The formation of new apatite nano crystallites can be due to dissolution of smaller cement particles and reprecipitated, filling in the gaps with semi porous material to form more compact form of HA.

Results of degradation test was measured against mass is shown in Figure 5. In this test, the bone cement sample is being soaked in 150 ml SBF solution. Rate of degradation process is mainly controlled by the amount of PPF used in the composition. Generally, for bone cement application the molecular weight of PPF is 600 to 3000. The degradation rate and cross-linking effect are also influenced by the differences in molecular weight of PPF. The results show that after 7 days soaking in SBF solution the mass indicated 20 % of weight loss. However, mass degradation after 21 days increased to 27 %. This indicated that degradation process is very fast at early implant but then slowly decreased as time is increased. The dissolution and reprecipitation processes caused the degradation of bone cement.



...micrographs of bone cement before soaking

...micrograph of bone cement after soaking in ...for 21 days.

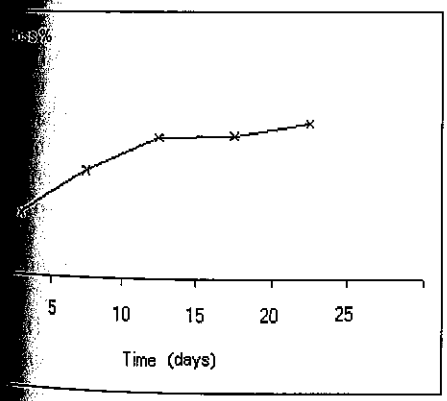


Figure 5. Weight loss versus time.

CONCLUSION

...RD and SEM results show that the ...ped bone cement is low crystalline apatite ...and chemical properties similar to natural ...he bone cement produced can undergo ...bio integration and promotes tissue ... The cement has complied with the specific criteria by achieving setting time within 25 minutes, setting at human body temperature and good workability. Mechanical characteristics were found to be in the range of cancellous bone properties. Hence, the developed bone cement has a potential as a bone repair material.

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