JOURNAL OF MATERIALS SCIENCE: MATERIALS IN MEDICINE 7 (1996) 551–557

Surface modification of hydroxyapatite to introduce interfacial bonding with polyactive™ 70/30 in a biodegradable composite

Q. LIU, J. R. DE WIJN, D. BAKKER[‡], C. A. VAN BLITTERSWIJK
Biomaterials Research Group, Leiden University, and IBME Research School,
Prof. Bronkhorstlaan 10, 3723 MB Bilthoven
[‡]HC Implants bv, Leiden, The Netherlands

A method was developed to improve the interfacial bonding between hydroxyapatite and a biodegradable copolymer Polyactive™ 70/30. Hydroxyapatite was first surface modified by the polyelectrolytes polyacrylic acid or poly(ethylene-co-maleic acid) in aqueous solutions. Subsequently the surface-modified hydroxyapatite was used as filler in composites with Polyactive™ 70/30. The strength, elongation at break and elastic modulus of the composite in aqueous environment were significantly improved by this method. Based on these experimental results, it is believed that the interface improvement is due to hydrogen bonding and/or dipole interactions formed between polyelectrolyte molecules and polyethylene glycol segments in the polymer matrix. Due to the introduction of interfacial bonding by using such method, a new biodegradable bone-bonding composite can be made.

---

1. Introduction

In recent years, several kinds of polymer–hydroxyapatite composites have been developed as bone substitute materials [1–3]. The purpose of making such composites is to reinforce the polymer and improve the bone bonding properties of the material, since it has been found that adding hydroxyapatite (HA) into a polymer matrix may turn an initially non-bioactive polymer into a bone bonding composite, and might simultaneously improve the mechanical properties [1–3], especially the elastic modulus and hardness.

In making HA/polymer composites, the lack of interfacial bonding between HA and the polymer matrix still remains an issue of concern [3, 4]. The interfacial bonding between inorganic and organic phase plays an important role in determining the ultimate mechanical properties of the composites. A strong interfacial bonding between the two phases usually is necessary for the composites to achieve good mechanical properties. For example, bone, a natural biocomposite, is mainly composed of inorganic bone mineral (hydroxyapatite-like material), organic matrix of type I collagen and non-collagenous proteins [5]. Bone mineral is not directly bound to collagen, but bound to collagen by these non-collagenous proteins [6]. These interfacial bonding forces are mainly ionic bonds, hydrogen bonds and hydrophobic interactions [5]. They give bone unique composite behaviour.

The polymer, Polyactive™, used in this study is a block copolymer from polyethylene glycol (PEG) and poly(butylene terephthalate) (PBT). When the weight ratio of PEG/PBT is 55/45 or higher (the molecular weight of PEG is 1000 Dalton), it is a biodegradable polymer and calcifies postoperatively, thereby inducing bond bonding [7, 8]. Polyactive™ has already been used in making composites with HA. Such composites showed promising results in guided tissue regeneration applications [9]. However, due to the larger amount of PEG present in the structure of Polyactive™ 70/30, it is a rubber like polymer with low elastic modulus. In an effort to strengthen the polymer, we chose HA as filler to make HA/polymer composites.

Since, in contrast to bone material and its collagen matrix, there are no strong bonding forces between HA and Polyactive™, it is necessary to introduce some kind of interaction between the two phases by surface modification of HA. Such an approach mimics the role of non-collagenous protein in bone.

In this study, a method was developed to improve the interface between HA and Polyactive™ by using water-soluble polyelectrolytes such as polyacrylic acid (PAA) and poly(ethylene-co-maleic acid) (EMA). This was based on the principle that polyacrylic acid and the copolymer of maleic acid have the ability to both form complexes with PEG [10], and be firmly adsorbed onto the surface of HA [11, 12].

2. Materials and methods

Polyacrylic acid ($M_w = 5000$, 50% water solution) and poly(ethylene-co-maleic anhydride) were obtained from Aldrich. Poly(ethylene-co-maleic acid) was then obtained by dissolving poly(ethylene-co-maleic anhydride) in distilled water (Fig. 1). Hydroxyapatite was synthesized and sintered in our

0957–4530 © *1996 Chapman & Hall*

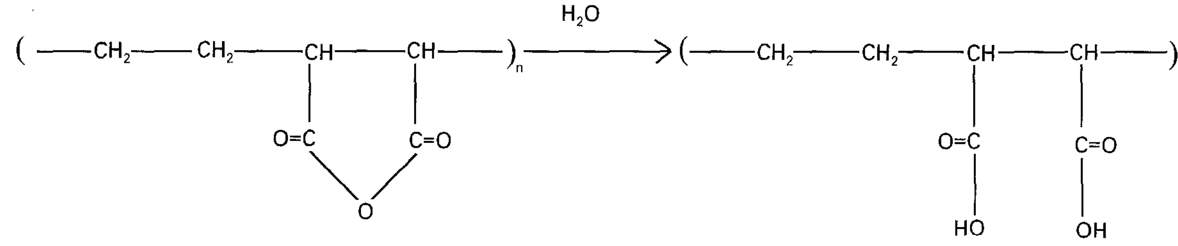

Figure 1 Preparation of EMa

laboratory. It was milled and sieved to powder with a particle size less than 45 μm. Polyactive™ 70/30 was obtained from HC Implants bv, the Netherlands. The molecular weight was about 1×10^5.

2.1. Coating of HA particles

PAA and EMa solutions were prepared and used for coating purposes. The pH of the PAA and EMa solutions was adjusted to pH 7 by using 10% NaOH solution, and the final concentrations of PAA and EMa were 2.5% and 1.5%, respectively.

HA particles were put into the PAA or EMa solution, and the suspension was stirred for 20 h at room temperature. The particles were then separated by centrifuging. After the particles were re-suspended and washed three times in distilled water, the particles were first exposed to 110 °C overnight and then dried in a vacuum oven at 80 °C for at least 72 h. Control HA particles underwent the same procedure but with NaCl solution (pH = 7, 1.8% concentration, the same molar concentration as NaOH in PAA solution) instead of PAA or EMa.

2.2. Characterization of HA particles

The surface area of HA particles was analysed using BET methods (Quantachrome Nova 1200 Adsorption Analyzer). N_2 was used as adsorption gas.

The size and size distribution of HA particles were measured both by scanning electron microscopy (SEM) (Phillips 525) and by Coulter particle counter before and after surface modification of the HA particles.

In order to measure the surface property changes of HA particles modification by PAA or EMa, a semi-quantitative sedimentation method was used: 0.5 g particles were put into a test tube of a diameter 1.4 cm containing 10 ml distilled water. After shaking, the time needed for the supernant to become clear was recorded.

The amount of surface adsorbed EMa and PAA was quantitatively measured by using a total organic carbon analyser (TOC). An amount of 0.54 g of coated HA particles was first dissolved in 100 ml hydrochloride acid solution of pH 1, then 10 ml of such solution was used for analysing the carbon content.

2.3. Preparation of composites

Surface modified and control HA particles were premixed with Polyactive™ 70/30 granules at 25% weight percentage and then blended twice at 150 °C using a single screw extruder (Colin 15 × 25). The granulated materials were hot pressed into 2 mm thick 50 × 50 cm sheets at a temperature of 190 °C and 20 ton pressure. Standard dumb-bell specimens were cut from the sheet using an ISO R37 type 1 die, and were then used for mechanical and other testing. All the specimens were kept at room temperature for 4 days before mechanical testing was performed.

2.4. Mechanical testing

In order to evaluate the effectiveness of the surface treatment of HA, we determined the tensile strength, elongation at break and the elastic modulus of composites both in dry and wet state (after swelling in distilled water). The wet state testing was carried out after the specimens had been immersed in distilled water for 24 h. The specimens were then taken out of the distilled water and kept wet during the testing process. A Hounsfield HN200 testing machine was used. The crosshead speed was 50 mm/min and the gauge length was 25 mm. In order to determine the elastic modulus, an Instron extensometer was used to measure the specimen extension. Ten specimens were used for each testing.

2.5. Swelling degree of the composites

Rectangular specimens of size 2 × 6 × 20 mm were used for swelling tests in distilled water at room temperature. For each composite, two specimens were used.

At certain time intervals, the specimens were taken out and the water at the surface was quickly removed with tissue paper. The swelling degree at different time intervals was calculated according to the following equation

$$Sw = \frac{W_t - W_0}{W_0} \times 100\%$$

where Sw stands for swelling degree and W_t is the weight of the sample at time t, W_0 is the weight of sample in dry state at the beginning of testing.

2.6. Fracture surface study

The fracture part of the mechanical testing specimens after mechanical testing was cut off from the specimen using a sharp knife. The fracture surface was first observed by light microscope and then by a Phillips scanning electron microscope. All samples for SEM observation were sputter coated with gold.

3. Results

3.1. Characterization of HA particles

The surface area of HA particles as measured by BET method was 1.75 m^2/g.

SEM study showed PAA and EMa modification caused virtually no change in particle size and surface morphology of particles. Particle sizes in scanning electron microscopy were measured between 1 and 50 μm, the larger particles were of a porous structure (Fig. 2).

The particle size distribution patterns of the HA particles were nearly the same before and after surface modification by PAA or EMa (Fig. 3) as measured by Coulter particle counter.

The change in surface properties of HA particles after being modified by EMa or PAA can be seen from the sedimentation time changes of HA particles. Surface modification significantly increased the sedimentation time of particles, EMa and PAA having different effects on the sedimentation time of HA particles (Table I) : the PAA coating had a more distinct effect on the sedimentation time of the particles. More PAA was adsorbed on HA as compared to EMa (Table I).

3.2. Swelling behaviour of composites

Fig. 4 shows the swelling degree versus time curve of the composites. After 24 h of swelling in water at room temperature, the swelling gradually reached equilibrium. It can be seen that the swelling degree of PAA-HA and EMa-HA composites is somewhat lower than that of HA composites.

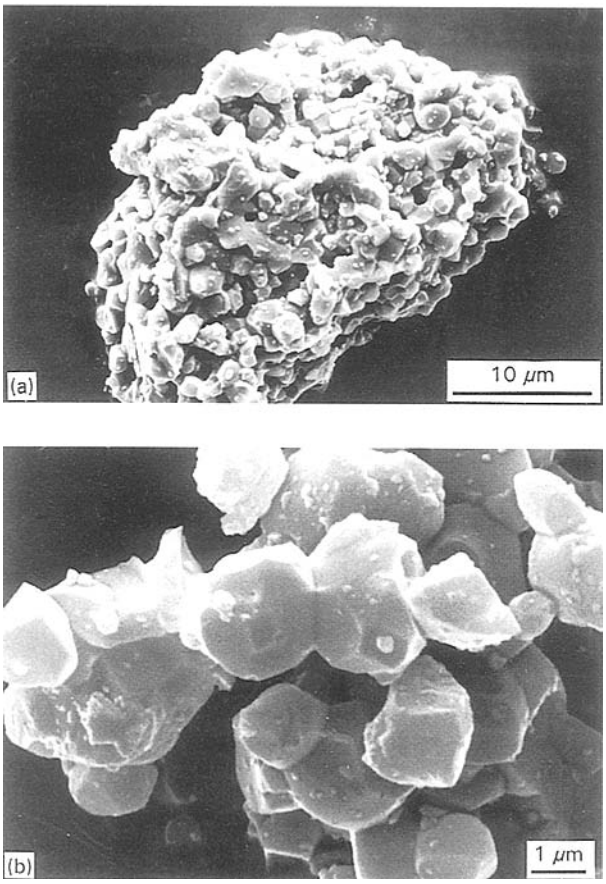

Figure 2 SEM pictures of HA particles. (a) The porous structure of HA particles. (b) HA surface-modified by PAA. Note that the typical rhombic crystals of HA can be seen.

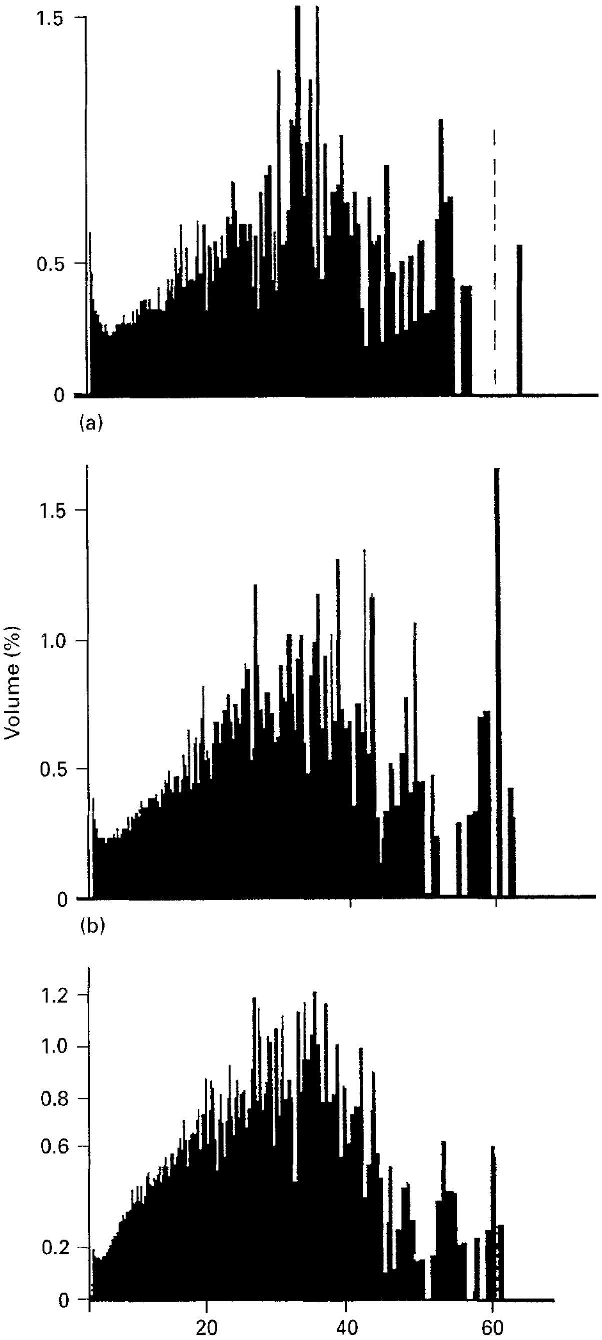

Figure 3 Particle size distribution of surface-modified and unmodified HA particles: (a) HA particles; (b) EMa-modified HA particles; (c) PAA-modified HA particles.

TABLE I Characteristics of surface-modified HA particles

	Particle		
Characteristic	HA	EMa-HA	PAA-HA
Sedimentation time	50 min	3 h	20 h
Adsorption (mg C/g)	As control	0.57	2.29

3.3. Tensile strength

The tensile strengths of the composites, both in dry and wet state, are given in Fig. 5. In the dry state, there are no significant differences between the strengths of HA, EMa-HA and PAA-HA composites. The general level of strengths of composites was lower than that of Polyactive^{TM} 70/30. All strengths decreased after the specimens had been immersed in water. In the wet state, however, the strength of composites with surface-modified HA particles was higher than that of control HA composites, whereas the strength of PAA-HA composite was higher than that of EMa-HA composite and comparable to the strength of pure Polyactive^{TM} 70/30 in the wet state.

3.4. Elastic modulus

Fig. 6 gives the elastic modulus of the composites. In the dry state, all the composites had much higher elastic moduli than pure polymer. In the wet state, although the elastic moduli were decreased for all materials, all composites still had higher elastic moduli than pure Polyactive^{TM}. However, the control HA composite had lower elastic moduli than EMa-HA and PAA-HA composites. EMa-HA and PAA-HA composites had nearly the same elastic modulus in the wet state.

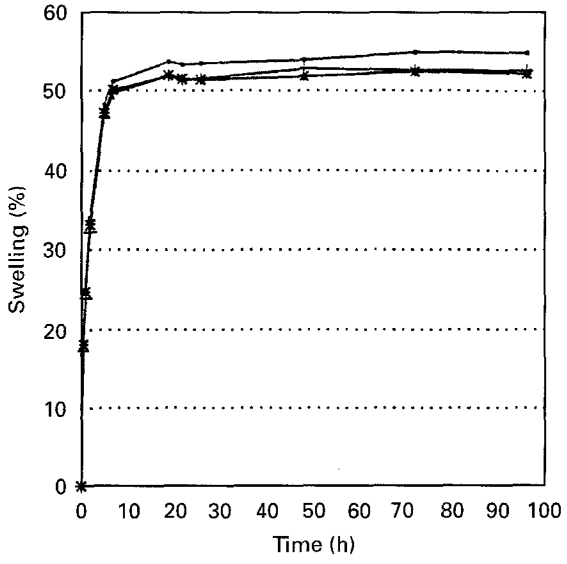

Figure 4 Swelling degree of the composites: —●— HA; —+— EMa-HA; —×— PAA-HA.

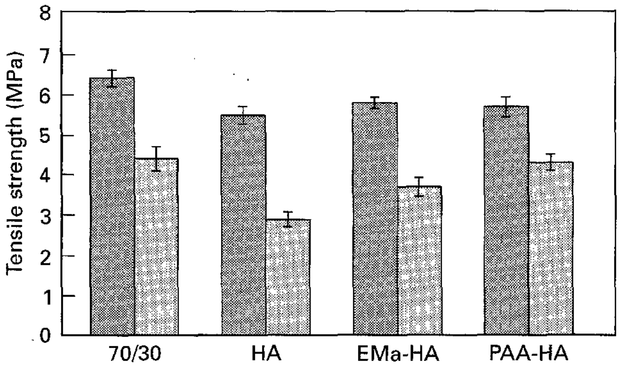

Figure 5 Tensile strengths of composite: ▩ dry; ▨ wet.

3.5. Elongation at break

Incorporation of filler into the polymer significantly decreased the elongation at break, both in the dry and wet state. However, composites with surface-modified HA particles had a higher elongation at break both in the dry and in wet state as compared to control HA composites (Fig. 7). It is also clear that the PAA-HA composite had a higher elongation at break than EMa-HA. The general level of elongation at break was lower after the specimens had been immersed in water.

3.6. Fracture surface study

By using scanning electron microscopy, it could be seen that voids existed between the control HA particle and polymer matrix after the samples were broken (Fig. 8). Sometimes mechanical interlocks were observed between the larger HA particles and polymer matrix due to the infiltration of polymer into the pores of HA. For EMa and PAA surface-modified HA particles, better contact and more mechanical interlocks with the polymer matrix were observed.

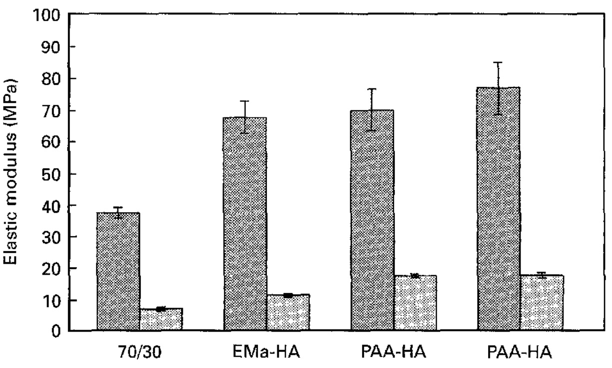

Figure 6 Elastic modulus of composites in dry (▩) and wet (▨) state.

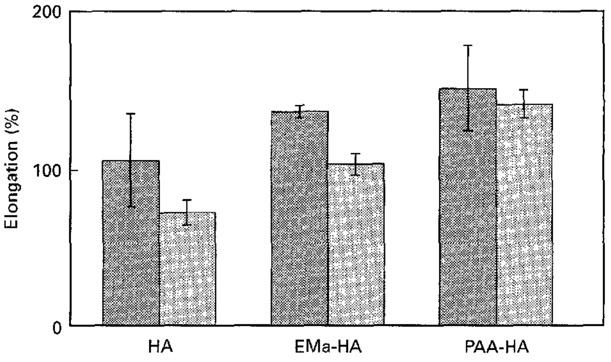

Figure 7 Elongation at break of composites in dry (▩) and wet (▨) state (the elongation at break of Polyactive^{TM} 70/30 are 432 ± 83% in dry state and 219 ± 35% in wet state).

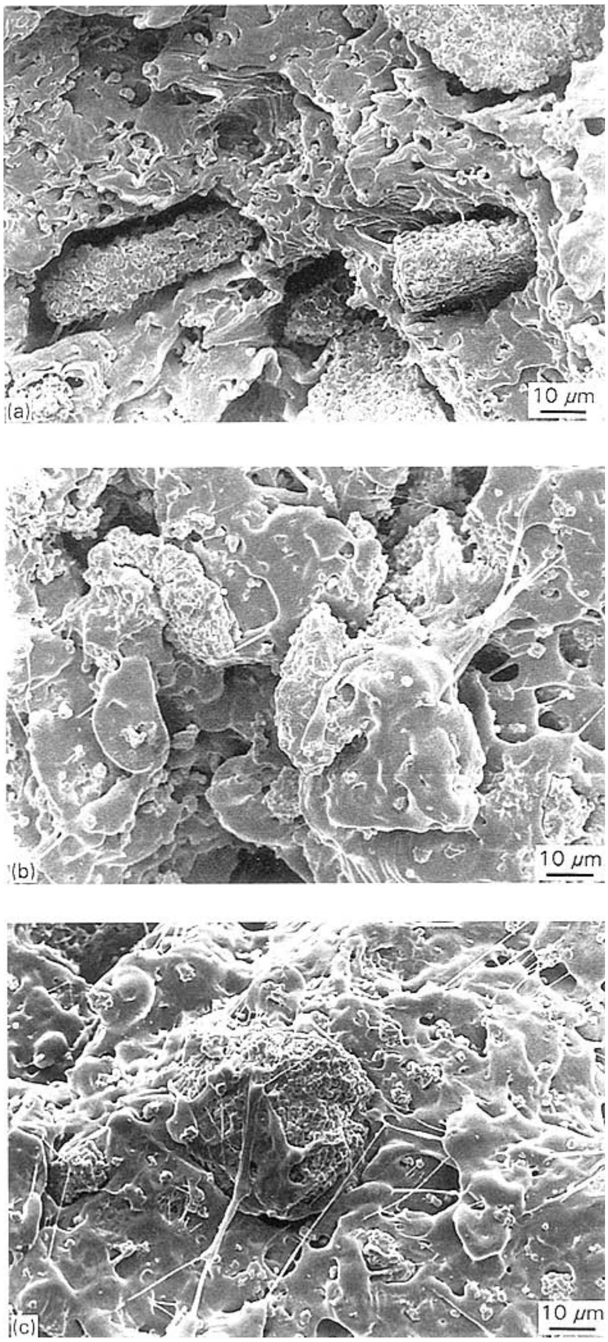

Figure 8 SEM pictures of fracture surfaces of composites: (a) HA composite; (b) EMa-HA composite; (c) PAA-HA composite. Note the voids between HA particles and polymer matrix in (a) and the better contact remaining in (b) and (c).

4. Discussion

One of the reasons why Polyactive™ 70/30 is used as bone filler is its bone bonding ability. The bone bonding ability is closely related to the calcium ion complexing ability of PEG segments [7, 8]. Therefore, any strengthening of the polymer should not interfere with the calcium ion complexing ability of the PEG segments. Crosslinking of polymer, which is usually an effective way of strengthening the polymer, is not applicable in this case. Therefore, an ideal way to strengthen the polymer is to make composites by using fibres or fillers.

However, due to the high swelling ability of Polyactive™ in water, the interfacial problem may be critical since the composite is intended to be used *in vivo*. Lack of interfacial bonding between HA and polymer matrix may cause loose contact between HA particles and polymer matrix and therefore result in early failure (disintegration) of implants. It can be seen that the mechanical strength, elongation at break and elastic modulus of HA composites decreased drastically after being immersed in water for 24 h. Hence it is necessary to modify the surface of HA to introduce interfacial interaction between HA and polymer matrix and to maintain the necessary strength and structure integrity of the composites.

4.1. Surface modification of HA particles

It is well documented that PAA and EMa can be firmly adsorbed to the surface of HA [11, 12]. In this study, the amount of adsorption was not very high (Table I) due to the relatively larger size particles used in our study. After the surface modification of HA, no obvious surface morphological changes were observed. The surface properties of HA particles were significantly changed after surface modification. One of the major changes is their sedimentation rate in distilled water. The surface-modified HA particles can suspend very well in water and thus have longer sedimentation times. We also noticed that the sedimentation time for PAA-HA was much longer than that of EMa-HA particles. This difference may come from the lower adsorption amount of EMa on the surface (Table I).

4.2. Mechanical properties of composites

Although the total amount of surface adsorption of PAA or EMa is low due to the small surface area of HA particles in our study, we can see the effect of surface modification on the mechanical properties of composites. The increase in the elongation at break for EMa-HA and PAA-HA composites as compared to HA composites in the dry state is the evidence of interfacial improvement. In addition, the introduction of interfacial interaction had a more distinct effect on the mechanical properties of the investigated composites in the wet state.

Generally speaking, water can decrease the mechanical properties in two ways. First, water can cause polymer swelling and thereby increase the cross-section area and thus decrease the strength and elastic modulus. Second, water can act as plasticizer to decrease the intermolecular chain interaction and thereby decrease the strength and elastic modulus of the polymer. So it is not surprising to find that mechanical properties for all composites decreased after the composites had been immersed in water for 24 h. However, the EMa-HA composite and PAA-HA composite still retained relatively good mechanical properties. In our experiments, in addition to the effect of the higher swelling ability of composites in water and the plasticization effect of water molecules, it is also considered that the worsening of mechanical properties was caused by deterioration of the interface between the inorganic and organic phases of the composites, as we can see from the changes in tensile strength (Fig. 5). We can see that the swelling degrees of all the composites are about 50%. That means swelling in water will cause about 30% increase in the cross-section area of the sample and hence, in principle, 30% decrease in strength (if we consider only the effect of swelling or the increase in cross-section area). But the decrease in strength was far more than 30% for HA composites and less than 30% for PAA-HA composites. Since the surface modification of the HA particles change the swelling degree of the composites only slightly, we believe that the improvement of mechanical properties is largely due to the interface improvement of the composites.

The amount of adsorption of EMa and PAA on HA seems to have some effect on the mechanical properties of the resulting composites. Since there was less EMa adsorbed on the surface of HA compared with the adsorption of PAA, so the thinner EMa coating on the HA has less effect on the mechanical properties of the resulting composites.

4.3. Fractography of composites

SEM studies of the fracture surface suggest that there indeed exist mechanical interactions between HA and polymer matrix. Due to the rough surface and porous structure of HA particles, the mechanical interlocks between HA (both surface modified and unmodified) particles and polymer matrix could be observed at the fracture surfaces. But for surface-modified HA particles, more such mechanical interlocks could be observed, some particles were even largely covered by polymer (Fig. 8).

4.4. The mechanism of interfacial interactions

The introduction of EMa and PAA onto the surface of HA improved the interface between HA and polymer matrix. It is considered that such improvement is caused by hydrogen bond formation and/or dipole interactions between the surface-coated polymer molecular chains and PEG segments of Polyactive^{TM}. Since EMa and PAA may form stable hydrogen bond complexes with PEG both in an aqueous mixed system and in a heated blending system (Fig. 9) [10, 13], the mechanical properties of the composites both in the dry and the wet state can be improved. Although the complex is easily formed in an aqueous mixed system at lower pH, at a slightly basic condition, complexation may also occur [13], but the interaction may contribute to a dipole interaction similar to ionic bonding. An indication of such complexation between the EMa or PAA and PEG segments is that the swelling degree of EMa-HA and PAA-HA composites is lower than HA composites. Hydrogen bond or ionic complexes formation may cause a slight decrease in swelling degree which is mainly from the hydrophilic properties of PEG segments.

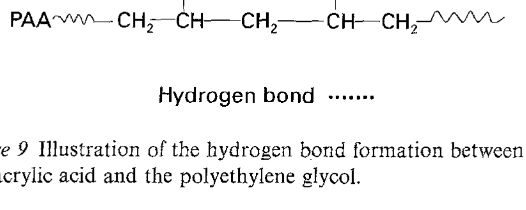

Figure 9 Illustration of the hydrogen bond formation between the polyacrylic acid and the polyethylene glycol.

4.5. Effect of the coating on the bioactivity of HA

HA is similar to bone mineral both in structure and composition. It is also considered to be a bioactive material with bone bonding ability. It is thought that the bone bonding process involves a process of HA dissolution followed by reprecipitation and formation of calcium phosphate microcrystals [14–16]. Therefore the solubility and dissolution rate of HA in a physiological environment are believed to have a close relation to the formation of bone-like apatite mineral both *in vitro* and *in vivo*. Although the EMa and PAA on the surface of HA may prevent the dissolution of the HA to some extent, both EMa and PAA are water-soluble polymers, and the attachment of such water-soluble molecules to the surface of HA may not change the hydrophilic characteristics of HA. Furthermore, it is thought that PAA has the ability to nucleate the formation of HA due to the carboxylic groups it has [17, 18]. This may be one of the advantages of using water-soluble polymers to modify the surface of HA.

5. Conclusion

By introducing water-soluble polymer, i.e. polyacrylic acid and poly(ethylene-co-maleic acid), onto the surface of HA, we significantly improved the interface of HA particles with polymer Polyactive^{TM}, thus allowing better load transfer throughout the material. As a result, the strength, elongation at break and elastic modulus of HA-Polyactive^{TM} 70/30 composites in the wet state can be significantly improved. By using 25% PAA-HA filler, a composite with a higher elastic modulus and tensile strength comparable to the polymer can be made.

Acknowledgement

The authors thank Sonja van de Meer, Henk Leenders and Pieter Koopmans for their technical help. The help of Mv. Toledo in measuring BET surface area and TOC results of HA particles is also acknowledged.

References

1. W. BONFIELD, in "Materials characteristics vs. in vivo behaviour", edited by P. Ducheyne and J. E. Lemons (New York Academy of Science, New York, 1988) p. 137.

2. K. E. TANNER, C. DOYLE and W. BONFIELD, in "Clinical implant materials; advances in biomaterials", Vol. 9 (Elsevier Science, Amsterdam, 1990) p. 149.
3. C. C. P. M. VERHEYEN, J. R. DE WIJN, C. A. VAN BLITTERSWIJK, P. M. ROZING and K. DE GROOT, in "Bone-bonding biomaterials", edited by P. Ducheyne, T. Kokubo and C. A. van Blitterswijk (Reed Healthcare Communications, Leiderdorp, Netherlands, 1992) p. 153
4. M. WANG, D. PORTER and W. BONFIELD, *Brit. Ceram. Trans.* **93** (1994) 91.
5. W. R. WALSH, M. OHNA and N. GUZELSU, *J. Mater. Sci. Mater. Med.* **5** (1994) 72.
6. E. M. RAIF and M. F. HARMAND, *Biomaterials* **14** (1993) 978.
7. D. BAKKER, J. J. GROTE, C. M. F. VROUENRAETS, S. C. HESSELING, J. R. DE WIJN, C. A. VAN BLITTERSWIJK, in "Clinical implant materials", edited by G. Heimke, U. Stoltese and A. J. L. Lee (Elsevier Science, Amsterdam, 1990) p. 99.
8. C. A. VAN BLITTERSWIJK, D. BAKKER, H. LENDERS, J. V. D. BRINK, S. C. HESSELING, P. BOVELL, A. M. RADDER, R. J. SAKKER, M. L. GALLARD, P. H. HEINZE, G. J. BEUMER, in "Bone-bonding biomaterials", edited by P. Ducheyne, T. Kokubo and C. A. van Blitterswijk (Reed Healthcare Communications, Leiderdorp, Netherlands, 1992) p. 153.
9. J. A. JANSEN, J. E. DE RUIJTER, P. T. M. JANSEN and Y. G. C. J. PQUAY, *Biomaterials* **16** (1995) 819.
10. K. L. SMITH, A. E. WINSLOW and D. E. PETERSON, *Ind. Eng. Chem.* **51** (1959) 1361.
11. J. C. SKINNER, H. J. PROSSER, R. P. SCOTT and A. D. WILSON, *Biomaterials* **7** (1986) 438.
12. J. ELLIS, A. M. JACSON, R. P. SCOTT and A. D. WILSON, *ibid.* **11** (1990) 379.
13. F. E. BAILEY and J. V. KOLESKE, in "Poly(etheylene oxide)", (Academic Press, New York, 1976) Chapter 5.
14. R. Z. LEGROS, *Clin. Mater.* **114** (1993) 65.
15. R. Z. LEGROS, G. DACULSI, I. ORLY, M. GREGOIRE, M. HEUGHEBAERT, M. GINESTE and R. KIJKOWSKA, in "Bone-bonding biomaterials", edited by P. Ducheyne, T. Kokubo and C. A. van Blitterswijk (Reed Healthcare Communications, Leiderdorp, Netherlands, 1992) p. 201.
16. C. A. VAN BLITTERSWIJK, Y. P. BOVELL, J. FLACH, H. LEENDER, I. V. D. BRINK, J. DE BRUIJN, in "Hydroxyapatite coated hip and knee arthroplasty", edited by J. A. Epinette and R. G. T. Geesink (Expansion Scientifique Francaise, Paris, 1995) p. 33.
17. S. I. STUPP and G. W. CIEGLER, *J. Biomed. Mater. Res.* **26** (1992) 169.
18. O. N. TRETINNIKOV, K. KATO and Y. IKADA, *ibid.* **28** (1994) 1365.

Received 18 December 1995
and accepted 15 March 1996