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Processing and properties of bone-analogue biodegradable and bioinert polymeric composites

Rui A. Sousa[a,b], Rui L. Reis[a,*], António M. Cunha[a], Michael J. Bevis[b]

[a]Department of Polymer Engineering, University of Minho, Campus de Azurém, 4800-058 Guimarães, Portugal
[b]Wolfson Centre for Materials Processing, Brunel University, Uxbridge, Middlesex, UB8 3PH, UK

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Abstract

This paper summarizes the processing and properties of bone-analogue composites aimed to be used in temporary or permanent orthopaedic applications. The studied matrices were two biodegradable starch based blends (with ethylene-vinyl alcohol copolymer or with cellulose acetate) and three high density polyethylene (HDPE) grades. Composites of these materials with hydroxyapatite (HA—the main inorganic constituent of the human bone) were produced by extrusion compounding and subsequently injection moulded. A non-conventional injection moulding technique known as shear controlled orientation in injection moulding (SCORIM) was used deliberately to induce a strong anisotropic character to the processed composites. For the case of HDPE based composites, an alternative reinforcement system based on carbon fibres (C fibres) was also studied. For that, a special moulding technique that combines, in a single equipment, a compounding with an injection unit was used. Composites featuring a sandwich like structure were also produced by mono-sandwich injection moulding. These composites combine a HDPE/HA outer layer and HDPE/C fibre reinforced core. The aim is to produce composites with a mechanical behaviour matching that of human cortical bone and simultaneously a strong bioactive (bone-bonding) character. For all the cases, the mechanical performance of the produced composites was assessed and the structure developed investigated and related to the processing conditions. It was possible to produce, both biodegradable and bioinert matrix composites, with properties that might allow for their application in the orthopaedic field.

Keywords: A. Polymers; A. Short-fibre composites; B. Mechanical properties; E. Injection moulding

1. Introduction

1.1. Bone as a composite material

Bone can be regarded as a very complex composite material, composed by a polymer matrix (collagen fibrils) and an inorganic reinforcement phase (mainly hydroxyapatite crystals—HA) [1–3]. The composition, structure and arrangement of its constituent elements, at different scale levels, confer to bone unique mechanical properties such as a high stiffness and strength, associated to a strong anisotropy and an evident viscoelastic behaviour [3–9]. The mechanical properties of human bone strongly depend on the respective morphology and consequently on a large range of bone features such as type, location and personal patient characteristics [10–12]. In spite of this fact, indicative values of tensile modulus in the bone longitudinal direction are in the range of 7–25 GPa [10–12]. When developing, hard tissue substitute materials, the mechanical behaviour is a crucial aspect since the stiffness of the implant defines the amount of load carried by the healing/surrounding tissue [13,14]. It is known that bone remodelling is strongly dependent on an adequate loading of the bone that strictly relies on the implant's stiffness [13,14]. So, a bone-matching mechanical performance is essential to assure the proper load transfer and the adequate healing of the bone.

1.2. The bone-analogue concept

The temporary or permanent replacement of hard tissues in load bearing applications demands mechanically

* Corresponding author. Tel.: +351-253-604498; fax: +351-253-604492.
E-mail address: rgreis@dep.uminho.pt (R.L. Reis).

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strong biocompatible materials. The attainment of such bone-matching mechanical performance depends on the technological ability to mimic the bone anisotropic character. Polymer based composites can, in principle, combine adequately stiffness and strength together with a clear anisotropic and viscoelastic character. Bonfield et al. [15–29] introduced the bone-analogue concept, when proposed composites comprising a polymer ductile matrix (polyethylene—PE) and a ceramic stiff phase (hydroxyapatite—HA). The idea is to use a semi-crystalline material that can develop a considerable anisotropic character by means of adequate orientation techniques reinforced with a bone-like ceramic that simultaneously assures the mechanical reinforcement and the bioactive character of the implant [17,18,24]. Recently, the use of hydrostatic extrusion to process PE/HA composites has shown to be successful route for the production of composites with bone-matching mechanical performance [25–29]. Values of tensile modulus and tensile strength of 10.8 GPa and 79 MPa respectively have been reported [25–27]. Nevertheless, the geometry and dimensions of the processed composites are constrained by the limitations of the extrusion process itself. In fact, it does not allow for the production of very thick and geometrical complex parts.

1.3. Bioinert and biodegradable polymers

The use of implants in high load bearing applications is dependent on the development of a material with adequate mechanical performance that is clearly biocompatible. Polymers are a class of materials with great potential within this field. In theory, the chemical structure of the polymer matrix can be tailored in order to tune adequately its degradation behaviour, making it, under physiological conditions, bioinert or biodegradable over a defined time frame. Based on these two distinct behaviours, polymers used in medicine can be classified in two large groups: biodegradable and bioinert. Two good examples of biodegradable polymers employed in the orthopaedic area are the poly(lactic acid) (PLA) and the poly(glycolic) acid (PGA), used in pins, screws, bone fixation plates and more recently in tissue engineering scaffolds [30–36]. Biodegradable orthopaedic implants are aimed to present a balanced mix of mechanical performance and degradation behaviour and ideally, the products of their degradation should be readily absorbed under normal metabolic conditions. As the degradation occurs, the loss, at a controlled rate, of its stiffness and strength occurs, which enables a progressive transfer of stress to the healing tissue. This degradation process ultimately ends with the total resorption of the polymer [37]. Conversely to biodegradable polymers, bioinert polymers are meant to be chemically and physically unchanged during its application time. An example of a polymer used with such aim is the ultra-high molecular weight polyethylene (UHMWPE) employed in acetabular cups and several kinds of joints [38–42].

1.4. Starch based polymers as alternative biodegradable systems

It is already unquestionable the role of biodegradable polymers as biomaterials [30–33,35,43–49]. The current gold standards of biodegradable systems, in terms of clinical application, are PLA, PGA and their copolymers. Concerning the mechanical performance, PGA typically exhibits values of tensile modulus and strength of 6.5–7.0 GPa and 57–100 MPa respectively [35,47,50,51]. In terms of degradation behaviour, the respective weight loss is complete in a period between 60 to 80 days [35,47,49,50]. The inducement of anisotropy by means of self-reinforcing (SR) techniques, such as sintering self-reinforcing and fibrillation self-reinforcing, has further enhanced the stiffness reported for this system. Values of tensile modulus up to 13 GPa have been obtained for hot drawn SR-PGA [31,35,47,50,51]. In spite of the good mechanical performance exhibited by these systems, some studies indicated that PLA/PGA implants can generate inflammatory responses due to the leaching of low molecular weight components and acidic products which constitutes a major drawback for these systems [52–56].

In several studies, Reis et al. [57–62] proposed alternative biodegradable systems to be used in temporary medical applications. These systems are blends of starch with ethylene-vinyl alcohol copolymer (SEVA), cellulose acetate (SCA) and polycrapolactone (SPCL) [57–62]. They were proposed for a large range of applications such as temporary hard tissue replacement, bone fracture fixation, drug delivery devices or tissue engineering scaffolds [57–64]. These blends can be processed as any ordinary thermoplastic by conventional melt based processing techniques, namely extrusion and injection moulding. Depending on their chemical constitution (ethylene-vinyl alcohol copolymer, cellulose acetate or polycrapolactone), these starch based blends can present different mechanical behaviours ranging from an almost rubbery like material (SPCL) to a stiff one (SEVA and SCA). This range of mechanical performance makes these blends potentially suitable to the substitution of soft or hard tissues. Attempts to enhance the mechanical performance of these systems in order to allow for their use as hard tissue substitutes have partially relied on the respective reinforcement with fillers such as HA [60,65–67] and bioactive glasses [68–79] that are also aimed to provide a bioactive character to the composite.

1.5. Non-conventional processing of bone-analogue composites

The development of synthetic bone-analogues for high load bearing applications with a mechanical

biocompatible behaviour is dependent on the capacity of inducing a high anisotropic degree. Unfortunately, conventional melt processing techniques are not able to induce levels of orientation enough to fulfil such ambition. As previously referred, the use of hydrostatic extrusion with PE/HA composites [25–29] allowed for the attainment of bone-matching properties, even though such approach presented limitations in terms of geometry and dimensions of the final processed composites. In the case of injection moulding, the structure development of the polymer is determined by the shear stress conditions and the solidification rate profile along the part thickness under pressurized conditions. As a result of this specific thermo-mechanical environment, semicrystalline polymers, when conventionally injection moulded, show a clear laminated morphology comprising an orientated skin layer (close to the mould wall) and a more or less isotropic core [70–72]. The control of the structure development of the core is limited, since the melt cools down in almost quiescent conditions and under mild cooling rates. Such scenario constituted the driving force for the development of shear controlled orientation in injection moulding (SCORIM) by Allan and Bevis [73–75]. In this case, the melt is continuously displaced inside the mould during the solidification course, which causes the application of a macroscopic shear stress field to the material at the melt/solid interface. The application of this processing technique has proved to be a valid approach for the inducement of a strong anisotropic character in both starch based blends and high density polyethylene as well as in their respective composites with HA [60,76–78].

This paper has two objectives. The first one is to summarize in a integrated manner the processing and properties of starch based bone-analogue composites with special emphasis to the structure development during SCORIM of both the unreinforced and the HA reinforced formulations. The second objective is to describe additionally the SCORIM processing of HDPE and HDPE/HA composites. However, for the HDPE system, an alternative reinforcement strategy, based on the use of carbon fibres (C fibres) is also presented. As a consequence of the specific line of research followed for this case, the use two non-conventional moulding techniques is described. These are the compounding injection moulding (CIM) and the mono-sandwich injection moulding techniques. For HDPE, the current research aim is to produce a bi-composite moulding combining a bioactive HDPE/HA outer layer and a very stiff HDPE/C fibres core with adequate surface properties and mechanical performance. For both systems (starch based blends and HDPE), the main research purpose is to develop bone-analogue composites featuring adequate surface bioactivity and a bone-matching mechanical performance during the respective time in service. So, the structure arisen during processing for both systems is investigated and the respective relationship with the mechanical performance studied, in order to establish valid structure/properties relationships that enable for the development of composites that might be used in load bearing applications.

2. Materials and methods

2.1. Materials

The polymeric materials studied in this work were:

(1) Two biodegradable thermoplastic blends of corn starch (50±2% by weight—wt.) with ethylene vinyl alcohol copolymer (60/40 mol/mol) designated as SEVA-C and of starch (50±2% wt.) with cellulose acetate designated as SCA, both produced by Novamont SpA (Italy).
(2) Three high density polyethylene (HDPE) grades, namely two high molecular weight HDPE grades with references HD8621 and GM 9255F produced respectively by DSM research (The Netherlands) and Elenac GmbH (Germany), and finally a HDPE, with the reference A6016, produced by Vestolen GmbH (Germany).

Composites of these materials have been produced using two types of reinforcements: a bone-like ceramic powder, hydroxyapatite (HA), and short carbon fibres (C fibres). The HA powder used had an average particle size of 10.1 μm and was supplied by Plasma Biotal Ltd (UK). HA was used with two aims: i) assure the bioactive behaviour of the composite (that defines its bone-bonding ability) and ii) mechanically reinforce the polymer matrix. C fibres were used exclusively as a mechanical reinforcement and were studied exclusively with HDPE matrices. Short fibre reinforced HDPE composites were produced using a C fibre type HTA, with 6 mm of length and a length/diameter ratio of 860, from Tenax Fibers, GmbH & Co. (Germany).

2.2. Twin screw extrusion (TSE) compounding

All the composites produced (except when other mentioned) were compounded by twin screw extrusion (TSE) using a Leistritz AG-LSM 36/25D modular co-rotating twin screw extruder. Compounds of SEVA-C with 10, 30 and 50% wt. of HA were produced using a temperature profile between of 140 (feeding zone) and 170 °C (die zone) and an output rate of 3.2 kg/h.

Composites of HDPE with 25 and 50% wt. HA were compounded using a temperature profile between 160 and 190 °C and output rates respectively of 2.94 and 3.40 kg/h. The composite formulation for 50% wt. HA included 0.5% wt. (relative to the HA fraction) of a zirconate coupling agent (NZ12, Kenrich Petrochemicals, Inc.,

USA). In a previous study, the use of titanate and zirconate additives was found to improve considerably the filler dispersion in HDPE/HA composites [79]. Similar study by Vaz et al. [80] demonstrated that these coupling agents (that exhibit a non-toxic behaviour) are successful in the improvement of the degree of interfacial interaction in starch based composites filled with HA.

For both composite systems, the cooling of the extrudate was performed in air, being the subsequent pelletizing assured by a rotating knife.

Short fibres reinforced composites of HDPE, using 25% wt. C fibres, were also compounded in the TSE equipment, using a temperature profile between 160 and 210 °C. Separate polymer and fibre feeding ports were used, in order to avoid the fibre breakage that would eventually occur during the simultaneous conveying of the solid pellets and the C fibres before the melting of the polymer phase. The extrudate was chopped manually in 60 mm long segments for subsequent injection moulding.

2.3. Shear controlled orientation in injection moulding (SCORIM)

The materials were moulded using a Demag D-150 NCIII-K (Germany) moulding machine equipped with a SCORIM generation I device. SCORIM bases its principle of operation on the application of a macroscopic shear stress field to the moving melt/solid interface during the course of solidification during injection moulding. The solidification of the material in an extended state, as imposed by the shear stress applied, results in an increase of the anisotropy degree of the polymer with advantageous mechanical consequences. A schematic diagram of a SCORIM generation I head is presented in Fig. 1. In this version of SCORIM, the device is attached to the injection barrel. The SCORIM pistons are hydraulically actuated after filling of the mould cavity during the holding pressure stage, using three possible modes of operation. In mode A, both pistons actuate out-of-phase causing the melt inside the mould to be continuously sheared. Conversely, in mode B, both pistons actuate in-phase, which causes the successive compression and decompression of the molten material inside the mould. Finally, in mode C, both pistons are held down together causing the packing of the material inside the mould. These operation modes can be combined sequentially in several stages during injection moulding, which enables the possibility of creating an almost infinite number of processing programmes. The relevant processing parameters of SCORIM include the holding pressure, the frequency of piston movements, the piston pressures and the duration of shear application [76,77].

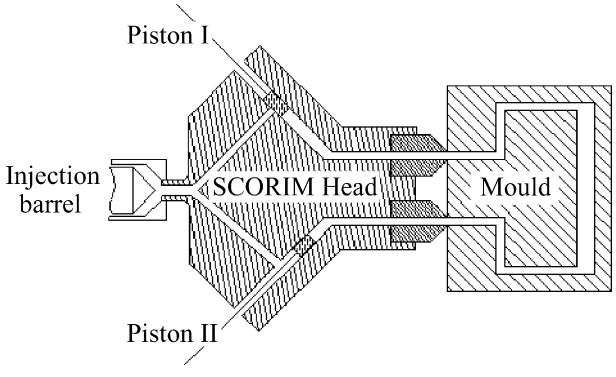

Fig. 1. Schematic diagram of a SCORIM generation I device.

In the present work, the cavity pressure profiles (CPP) during moulding were monitored, by piezo-electric transducer measurements, in order to evaluate the influence of different processing conditions applied in moulding. Fig. 2 presents a typical CPP gained for a HDPE grade during SCORIM together with the schematic diagram of the moulding geometry employed. The specimens moulded were axisymmetric tensile test bars (5 mm of diameter). In the schematic diagram, the arrow indicates the point of the pressure transducer measurements. It is possible to distinguish three sequential stages (1, 2 and 3) during the CPP. In stages 1 and 2, the cavity pressure oscillation results from the mode A operation (out-of-phase) of the hydraulic pistons. The use of a lower level of piston pressures in stage 2 is clearly visible by the decrease in intensity of the peaks. Stage 3 consisted in the application of a packing stage, mode C operation.

The optimisation of the processing parameters (following a maximum stiffness and strength criteria) is essential to assure the best mechanical behaviour of the moulded part. For starch based blends, the optimum processing conditions should additionally avoid any thermo-mechanical degradation that can eventually occur for these thermo-sensitive blends. The optimisation of the processing parameters in SCORIM for both SEVA-C and HDPE was based on the combined use of design of experiments (DOE) and analysis of variance (ANOVA) [77,78]. The importance of each processing parameter on the variation of mechanical performance observed was quantified and an optimum processing window was defined for each case. The SCORIM operating conditions employed for SEVA-C/HA and HDPE/HA composites were defined based on the results of these preliminary optimisation studies for the respective matrices.

2.4. Compounding injection moulding (CIM)

In order to assess the reinforcement efficiency of C Fibres, composites of HDPE with 25% wt. C fibres were compounded and moulded into dumb-bell tensile test specimens with rectangular cross section (4×9 mm^2) in a single processing stage, using a compounding injection moulding (CIM). This device combines a co-rotating

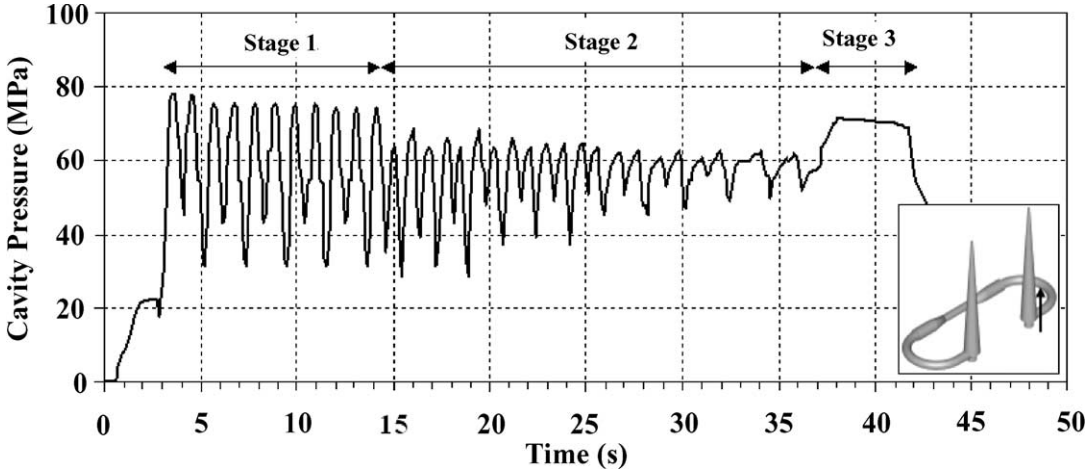

Fig. 2. Typical cavity pressure profile (CPP) during SCORIM used to process the moulding geometry presented. The CPP shows distinguishably the three consecutive SCORIM stages employed during moulding: Stage 1—mode A (out of phase oscillation of the pistons); Stage 2—mode A and Stage 3—mode C (both pistons are held down simultaneously).

twin-screw extruder with an injection moulding unit machine, from Dassett Processing Engineering Ltd (UK), was used. Fig. 3 presents the schematic diagram of the CIM equipment. The main advantages of compounding injection moulding for the processing of thermoplastic based composites as compared to the traditional approach (based on separated compounding and injection mouldings stages) are the single heat history, the reduction of molecular degradation (for the case of thermo-sensible materials), the superior maintenance of fibre morphology and the reduction of fibre damage due to the elimination of extra handling granulation step. In order to minimise fibre breakage during the compounding step, the feeding of the C fibres was performed using a separate port after melting of the HDPE pellets.

2.5. Mono-sandwich injection moulding

Bi-composite mouldings of composites of HDPE with 50% wt. of HA and 20% wt. C fibres were also moulded in a two-component injection moulding K-85 Ferromatik-Milacron (Germany) machine using the mono-sandwich technique. The mouldings produced were dumb-bell tensile test bars with rectangular cross section (4×10 mm^2) and impact test bars with rectangular cross section (9×13 mm^2) comprising a HDPE/HA outer layer and a HDPE/C fibres core.

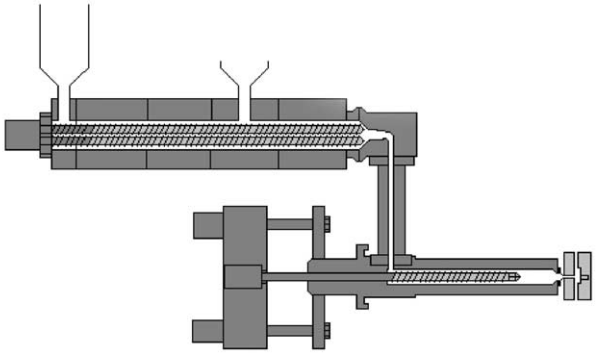

Fig. 3. Schematic diagram of the compounding injection moulding equipment combining a twin screw extruder with an injection moulding unit.

2.6. Tensile testing

The tensile mechanical performance of the processed matrices and the respective composites was assessed on an Instron 4505 universal testing machine fitted with an Instron 2630 resistive extensometer with 10 mm of gauge length. The tensile test bars were tested in order to determine the tangent modulus (E_t), the ultimate tensile strength (UTS) and the strain at break (ε_f). The tests were performed in a controlled environment (23 °C and 55% RH) with a cross-head speed of 5 mm/min (8.3×10^{-5} m/s) until 1.5% strain, to determine accurately the modulus, and then increased to 50 mm/min (8.3×10^{-4} m/s) until rupture.

2.7. Impact testing

Impact tests were conducted in a instrumented falling weight impact machine Rosand Type 5. The tests were performed at a test speed of 3 m/s, according to a charpy flexural scheme, using a support with 32 mm anvil span and 25 kg impact mass. For each test the force at peak (F_p), the peak energy (U_p) and the failure energy (U_f) were determined.

2.8. Microhardness

Microhardness experiments were carried out in order to investigate the mechanical performance variation

along the part thickness in selected injection moulded samples. The measurements were made at room temperature along the cross section thickness, in a Leica VMHT30A equipment, using a load of 0.3 kgf and a dwell time of 5 s.

2.9. Wide angle X-ray diffraction (WAXD) and X-ray diffraction (Debye) patterns

The structure developed during processing was studied by X-ray diffraction and patterns using Cu K_α radiation. The patterns were used to assess the preferred orientation of the mouldings. The Debye patterns were obtained at 1.5 mm from the edge of the mouldings. An aperture of 100 μm diameter was used to define the position and cross section of the incident X-ray beam. The diffraction data was obtained at a scanning rate of 0.02° 2θ/s and over a Brag angle range of $0^\circ < 2\theta < 50^\circ$. The samples were cut parallel to the flow direction with a thickness of 1 mm.

2.10. Optical light microscopy

The morphology of the mouldings was observed by optical microscopy. The respective samples for were obtained by cutting several cross section regions of the tensile and impact test specimens, followed by the respective immersion in an epoxy resin. After the resin cure, the immersed zones were: i) carefully polished in order to obtain a surface quality suitable for observation by both optical reflectance and stereo light microscopy; or ii) cut using a stainless steel blade in 15 mm thick slices to be observed by polarized light microscopy (PLM).

2.11. Scanning electron microscopy (SEM)

Scanning electron microscopy was used for fractographic analysis and was carried out on selected sets on a Leica Cambridge equipment. All the surfaces were mounted on a copper stub and coated with Au/Pd alloy prior to examination.

3. Results and discussion

3.1. Structure development of starch based blends during injection moulding

Temporary implant materials are aimed to be completely or at least fully resorbed at the end of their intended lifetime. So, in this case the bulk properties (namely cytotoxicity, biocompatibility, bioactivity) of the material are more relevant than for the case of bioinert materials, since during the degradation of the material and subsequent osteointegration, the inner regions of the implant will be progressively exposed to the organic fluids. The strategy followed for the enhancement of the mechanical performance should not compromise these bulk properties requirements. So, the development of structure anisotropy by means of orientation techniques, should avoid any thermomechanical degradation of the material that may alter its cytotoxicity and biocompatibility due to the leaching of low-molecular weight components. Furthermore, the use of bioactive reinforcements should not only assure adequate surface properties (bioactivity of the implant), but also promote the progressive tissue ingrowth upon the degradation of the matrix.

The use of SCORIM for the processing of SEVA-C results in the enhancement in both the stiffness and the strength as compared to conventional injection moulding. In fact, the typical values of tangent modulus (E_t) and ultimate tensile strength (UTS) for this blend when conventionally injection moulded are 2.2 GPa and 41 MPa respectively. The application of SCORIM (under optimised conditions) results in an enhancement in stiffness up to 31% and in strength up to 19%. The combined use of design of experiments (DOE) with analysis of variance (ANOVA) allowed for the identification of the relevant processing parameters concerning the mechanical performance variation of injection moulded parts [76]. The stiffness of SCORIM mouldings was found to be very dependent on parameters such as holding and pistons pressures during shear application, which define the cavity pressure level of the molten material inside the mould. Furthermore, the frequency of pistons oscillation and the time of shear application were also found to be relevant parameters concerning stiffness variation. Nevertheless, the influence of these parameters was observed to be very dependent on both the range of variation of the processing parameters and mould design. Stiffness of SEVA-C seems to be favoured by high holding and pistons pressures, long durations of shear application and intermediate frequencies of piston oscillation [76].

Fig. 4 plots the variation of stiffness (in terms of the tangent modulus—E_t) as a function of both the holding

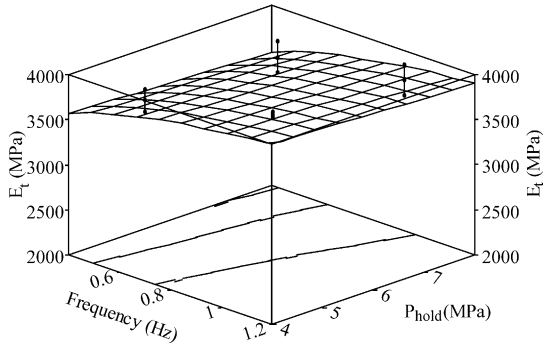

Fig. 4. Variation of tangent modulus (E_t) for SCA as a function of the holding pressure (P_{hold}) and frequency of pistons oscillation.

pressure and the frequency of piston movements for SCA mouldings. For the processing window analysed, both the processing parameters presented a positive influence on stiffness. Although SCA is a very low crystallinity blend, its mechanical performance is sensitive to the thermo-mechanical environment generated during the moulding cycle. Nevertheless, the optimisation of the thermo-mechanical environment of the starch based blends, for physical property enhancement, should consider the thermo-sensible character of these materials that are prone to processing induced degradation. Such susceptibility to degradation is further enhanced with the inclusion of particulate fillers such as hydroxyapatite (HA) that cause a sharp reduction of the processing window of the blend.

The enhancement of stiffness and strength with the application of shear is a direct consequence of the inducement of an anisotropic structure during injection moulding. Fig. 5 presents the scanning electron microscopy (SEM) photographs of the typical tensile failure surfaces of unreinforced SEVA-C processed by conventional injection moulding (Fig. 4 a) and SCORIM using low (2.6 MPa) and high (3.9 MPa) levels of holding pressure (Figs. 4b and c respectively). Conventionally injection moulded SEVA-C presents a planar brittle fracture surface. On the contrary, both SCORIM fracture surfaces present a highly orientated pattern of the failure surfaces, evidencing a skin/core morphology as a result of the molecular alignment caused by the applied shear field. The more defined skin/core morphology in Fig. 5c results exclusively from the higher level of holding pressure used in this case.

The observed morphological development is associated with a simultaneous increase in the anisotropic character of the blend as suggested by the X-ray diffraction patterns also shown in Figs. 5a and c. The Debye rings observed in the X-ray pattern for conventional moulding (Fig. 5a) give rise, with SCORIM application, to discontinuous arcs (Fig. 5b) which results from the development of structural anisotropy. Wide angle X-ray diffraction (WAXD) spectra gained for SCORIM specimens showed also an improvement in the crystalline peak intensity as compared to conventional moulding samples which is an indication of a simultaneous increase in SEVA-C crystallinity.

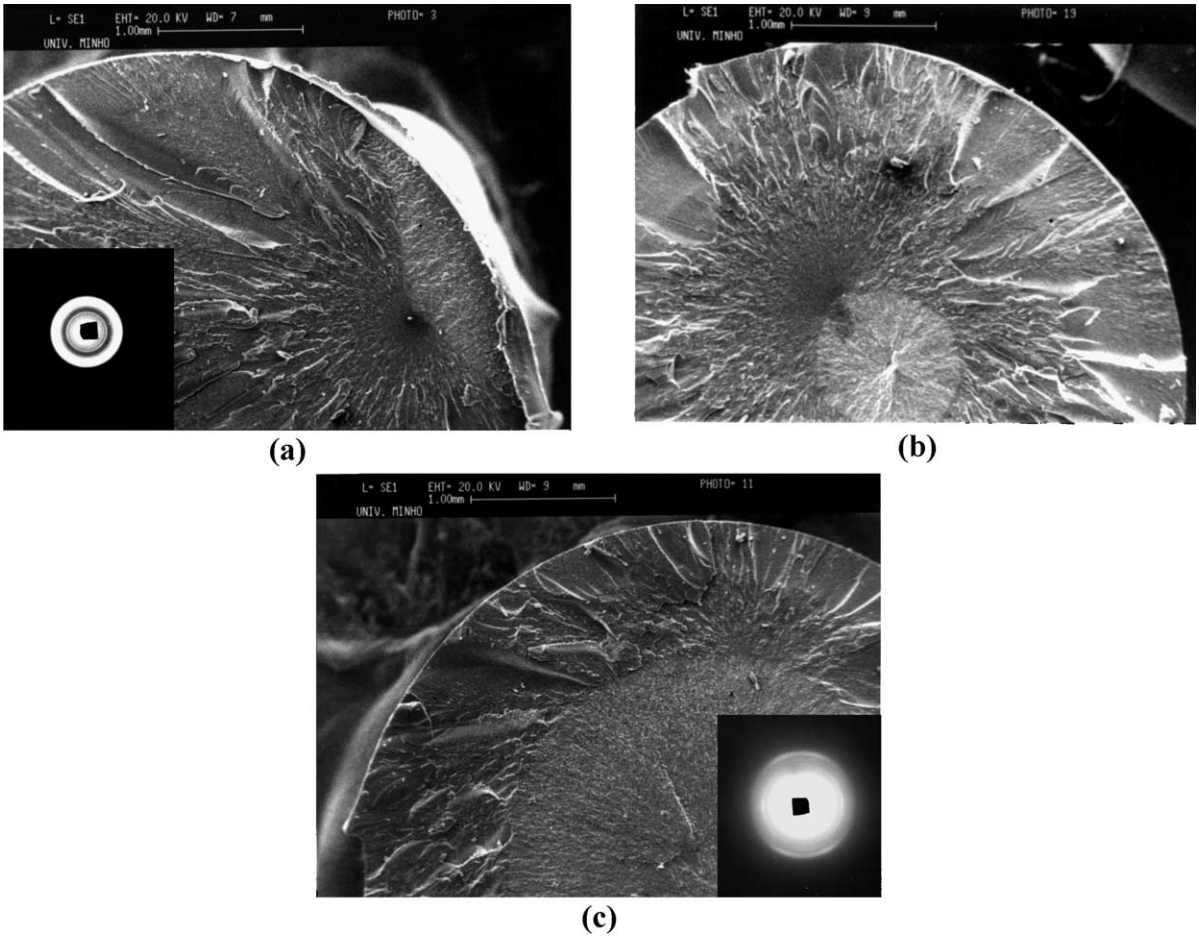

Fig. 5. Scanning electron microscopy (SEM) photographs of the tensile failure surfaces and the respective Debye patterns of SEVA-C produced by (a) conventional injection moulding (CM), (b) SCORIM—low holding pressure and (c) SCORIM—high holding pressure.

3.2. Mechanical performance of starch based composites

The inducement of a anisotropic character in injection moulded parts, through proper control of the structure development, combined with an adequate reinforcement strategy is a route for the development of implants with higher load bearing capacity. This is in fact, a similar strategy as that proposed by Bonfield et al for HDPE based bone-analogue composites [15–29]. Fig. 6 presents the variation of E_t as a result of hydroxyapatite (HA) reinforcement for both conventional and SCORIM processed SEVA-C/HA composites. HA particles are mainly used to assure a bioactive behaviour of the implant, i.e. the capacity of inducing, under physiological conditions, the growth of a calcium/phosphate (Ca/P) layer at the implant surface that favours the respective in-situ osteointegration and avoids fibrous encapsulation. Besides this purpose, HA particles are employed with a mechanical reinforcement objective in order to assure high stiffness values. For conventionally injection moulded SEVA-C/HA composites, it is possible to produce mouldings (with a rectangular cross section of 8 mm^2) with E_t up to 6.5 GPa for a HA amount of 50% wt. The use of SCORIM further extends the stiffness range of SEVA-C/HA composites. For 50% wt. HA, it is possible to produce composite moulded parts with a thicker cross sections (circular cross section with 20 mm^2) and superior stiffness values—E_t of 7 GPa, in the bounds of the values reported for human cortical bone [10–12].

For the case of SCA, the processing strategy, based on the combination of SCORIM, under optimised conditions, with HA reinforcement, allowed for the production of a composite, based in a biodegradable matrix, with a value of stiffness (E_t) of 8.6 GPa.

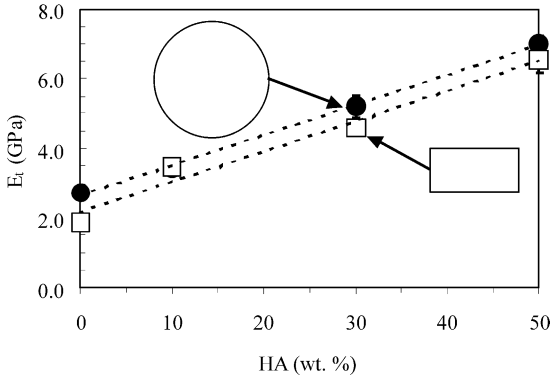

Fig. 6. Variation of the modulus of SEVA-C/HA composites as a function of the HA weight percentage for conventional injection moulding—rectangular cross section with 8 mm^2 (□) and SCORIM—circular cross section with 20 mm^2 (●).

3.3. Structure development of HDPE during injection moulding

The use of SCORIM to mould high crystallinity materials such as polyethylene has profound consequences in terms of the structure and properties exhibited after processing [77]. Fig. 7 presents the WAXD spectra for conventional and SCORIM mouldings together with the respective Debye patterns gained at 1.5 mm from the mould wall. The higher crystallinity of the SCORIM processed samples is evident as seen by the increase in intensity of the (110) and (200) reflections. Furthermore, the X-ray diffraction pattern acquired for SCORIM shows clear signs of c-axis orientation parallel to the main direction of flow (MDF), which is a sign of the development of a strong anisotropic character. The increase in crystallinity observed following SCORIM application has been also observed by differential scanning calorimetry (DSC) measurements [77]. The heating scans of SCORIM processed HDPE specimens revealed the existence of an additional melting peak endotherm at higher temperatures (not observed for conventional moulding) that is an indication of a shear induced morphology designated as shish-kebab [77]. The shish-kebab consists of a central group of highly orientated fibrils (shish) from which thick lamella crystals have grown (kebabs) during crystallization process. The combination of the high anisotropy of these row nucleated structures with the interlocking of the respective kebabs with adjacent ones explains the mechanical performance enhancement observed in SCORIM moulded HDPE. This strong

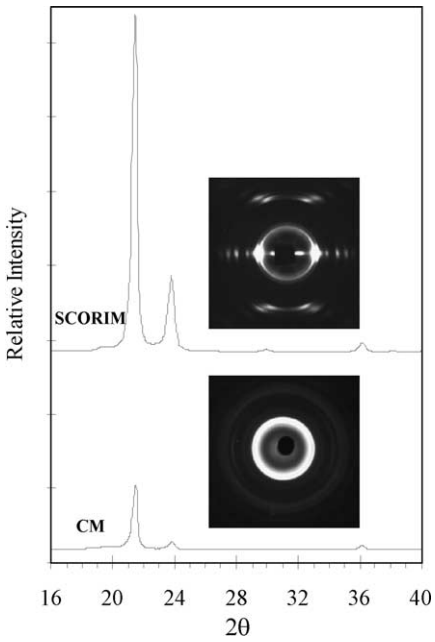

Fig. 7. Wide angle X-ray diffraction (WAXD) spectra and the respective Debye patterns gained for samples produced by conventional injection moulding (CM) and SCORIM.

anisotropic character results in improvements of stiffness up to 400% as compared to conventional injection moulding. Values of E_t and UTS respectively of 7.2 GPa and 155 MPa were attained following a suitable optimisation of the SCORIM process [77].

3.4. Morphology and properties of HDPE/HA composites

It is also possible to confer a similar anisotropic mechanical character to HDPE/HA composites through the application of SCORIM [78,79]. However, the incorporation of a filler with a limited reinforcing capacity (such as particulate HA) results in limited stiffness improvements relative to unreinforced HDPE. A maximum value of E_t of 7.4 GPa has been reported for a HA amount of 30% wt. Further increase in the filler weight amount leads to a stiffness decrease. The smaller improvement of stiffness observed in HDPE with HA reinforcement as compared with a lower crystallinity material such as SEVA-C, results from the much higher dependence of the structure development on the thermo-mechanical environment for the former matrix. The substitution of a high crystallinity phase, such as polyethylene with a self-reinforcement capability under suitable thermo-mechanical conditions, by a low aspect ratio reinforcement, such as HA particles, leads to limited stiffness improvements.

Fig. 8 presents the variation of microhardness along the cross section diameter for conventionally injection moulded and SCORIM processed HDPE/HA composites together with the respective polarized light microscopy (PLM) photographs of the cross sections. Conventional mouldings are composed by a thin skin layer and a large core region (see the PLM photograph for conventional moulding). The anisotropic skin corresponds to a rapidly cooled zone on which the shear induced orientation was frozen in. Conversely, the almost isotropic core corresponds to a slowly cooled region crystallized under a reduced shear stress environment. This skin/core morphology gives rise to an almost flat microhardness profile variation along the part diameter. SCORIM processed HDPE/HA composites exhibit a clear layered morphology (see the PLM photograph for SCORIM). The application of a controlled macroscopic shear stress field during the solidification of the material induces the development of concentric layers with a shear induced crystallized structure. The microhardness measurements in SCORIM samples shows the existence of a M-pattern hardness profile in which it is possible to distinguish three regions: a low crystalline skin (in the vicinity of the frozen layer), a highly crystalline transition layer (associated with a clear laminated morphology) and a less crystalline core (central zone of the cross section). The hardness reaches its maximum in the transition layer, being, as expected, minimum at the core region. The hardness evolution across the part thickness reveals the materials morphology heterogeneity, as a result of the local thermo-mechanical environment imposed.

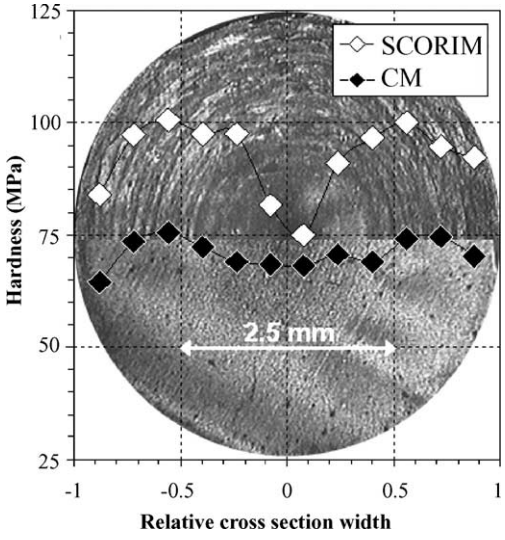

Fig. 8. Microhardness variation along the cross section diameter and the respective polarized light microscopy (PLM) photographs for HDPE/HA composite mouldings produced by conventional injection moulding (CM) ◆ and SCORIM ◇.

3.5. Alternative strategies for the development of biomedical HDPE matrix composites

As it was previously shown, the mechanical reinforcement of HDPE accomplished with HA powders is very limited. Such limitation arises from both the reduced aspect ratio of the particles and the poor interfacial interaction between HA and the polyolefin matrix [79]. The selective replacement of the HA particles in the bulk of moulded parts, where its use is not needed or advantageous, by a very stiff filler, such as short fibres, is a possible approach for the development of mechanically biocompatible composites. In order to follow such aim, the processing and properties of carbon fibres (C fibres) reinforced composite mouldings have been assessed. Within this line of research, a compounding injection moulding machine that combines a co-rotating twin-screw extruder with an injection moulding unit machine has been used. This preliminary investigation, reported in greater detail in reference 81, has shown that values of E_t up to 10 GPa were obtained for a fibre weight amount of about 20% wt. Nevertheless, the range of stiffness obtained with such reinforcement strategy is still limited by a pronounced variation of the C fibres orientation along the part thickness. Fig. 9 presents the variation of the C fibres orientation in terms of the second order tensors a_{11}, a_{22} and a_{33} along half thickness of a tensile test bar (rectangular cross section of 4×9 mm^2). A high level of orientation of the fibres in the MDF is associated with values of a_{11} close

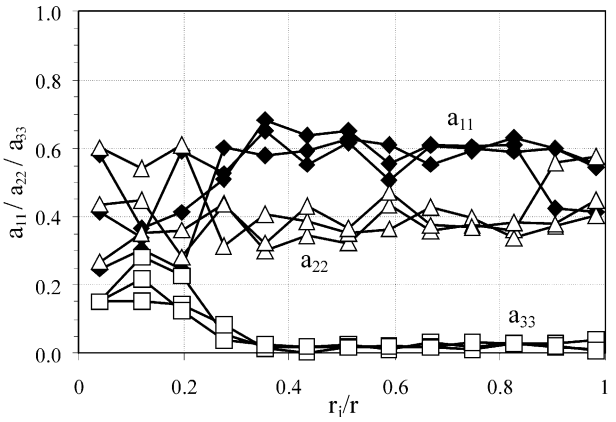

Fig. 9. Fibre orientation along the half thickness (r_i/r) of the tensile test bar for HDPE/C fibre composites produced by compounding injection moulding (CIM)—r_i/r of 1 corresponds to the mould wall and r_i/r of 0 corresponds to the moulding core.

to 1. Based on the values of the second order tensors, it is possible to distinguish two distinct zones along the part thickness: i) a shell zone close to the mould wall where fibres are predominantly aligned parallel to MDF (high a_{11}) and a ii) a core zone where fibre orientation is mainly perpendicular to the MDF (high a_{22}). This shell/core morphology is disclosed upon fracture of the mouldings as it can be seen in the SEM photographs of both the shell and core regions in a HDPE/C fibres composite after tensile testing, presented in Fig. 10. The relative dimensions of the shell and core regions and final fibre length were found to be dependent on the rheological behaviour and moulding conditions used during processing [81]. Very high viscosity HDPE grades are associated with a thin skin, large core dimensions and low average fibre length.

The strategy followed for the development of HDPE matrix load bearing implants with complex geometry, specific tailored chemical properties and controlled mechanical behaviour is based on the production of a sandwich moulding featuring two composite systems. Efforts have been made to develop sandwich mouldings comprising a HDPE/HA composite outer layer and a HDPE/C fibres composite core. The HDPE/HA outer layer is intended to assure specific surface properties (namely bioactivity), and the HDPE/C fibres core aims to guarantee the mechanical performance of the part within a desired range of stiffness. Tensile test bars (rectangular cross section of 4×10 mm^2) moulded with a sandwich-like morphology exhibited 5.6 GPa of E_t and 35.5 MPa of UTS [82]. The low strength of the sandwich mouldings as compared to HDPE/C fibres composites (UTS in the range of 67–73 MPa] can be partially attributed to the existence of a thick and heavily filled skin. In terms of impact performance, sandwich mouldings (rectangular cross section of 9×13 mm^2) exhibited a similar impact behaviour to HDPE/C fibres composite mouldings. Nevertheless, the values of energy absorbed during the crack initiation (U_p) and propagation stages (U_f) for the bi-composite materials were still below those obtained for single HDPE/C fibres composites.

Fig. 11 presents the evolution of the average outer layer thickness along the flow length for the impact test bars. An increase of the HDPE/HA composite layer thickness occurs, as it would be expected from the advancement of the progressively cooler melt front during the filling stage. The HDPE/C fibres composite core evidences two distinct zones: a shell region, where the C fibres are mainly parallel to the main direction of flow (MDF); and a central region where the C fibres are predominantly perpendicular to MDF. The shell region of the HDPE/C fibres core is located in the vicinity of the HDPE/HA outer layer and is the main responsible for the stiffness exhibited by the these mouldings.

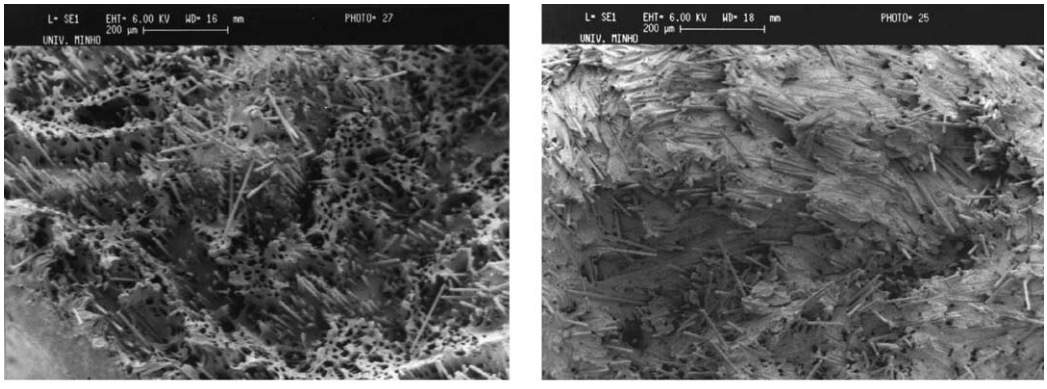

Fig. 10. Scanning electron microscopy (SEM) photographs of HDPE/C fibre composites produced by compounding injection moulding (CIM): (a) shell zone and (b) core region.

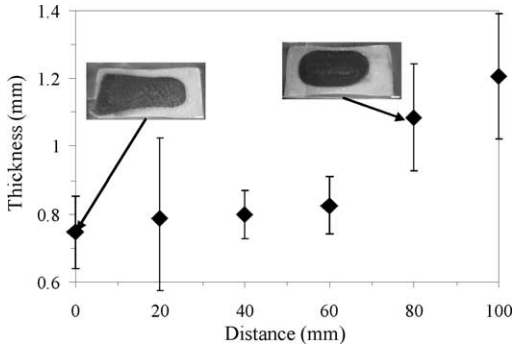

Fig. 11. Variation of the outer layer thickness along the flow path for HDPE/HA/C fibre composites (0 mm corresponds to the gate point).

4. Concluding remarks

It was possible to develop bone-analogue composites based on the HA reinforcement of blends of starch and high density polyethylene with a mechanical performance that may allow for their application in the orthopaedic field. For both cases, SCORIM was successfully employed to induce a strong anisotropic character in the processed composites and enhance their respective mechanical performance. The reinforcement of HDPE with C fibres was studied as an alternative to particulate HA. Two moulding techniques were employed to process this composite system: i) compounding injection moulding and ii) mono-sandwich injection moulding. Using this latter moulding technique it was possible to produce composites featuring a sandwich like structure that combine a HDPE/HA outer layer and a HDPE/C fibre reinforced core. As a consequence of the research strategy adopted, several conclusions were attained regarding the mechanical performance and structure development of the several composite systems investigated.

4.1. Mechanical performance of starch based composites

Table 1 summarizes the reference mechanical properties (quasi-static tensile tests) in terms of tangent modulus (E_t), the ultimate tensile strength (UTS) and the strain at break (ε_f) for SEVA-C, SCA and their composites with HA processed by conventional injection moulding and SCORIM. For these cases, it was possible to produce, by injection moulding, bone-analogue composites combining a biodegradable character with a mechanical performance comparable to human cortical bone. The observed increase of mechanical anisotropy reported in this study for these blends and composites, as compared to the conventional injection moulding, is justified by the development of an orientated morphology.

Table 1
The reference mechanical properties in terms of tangent modulus (E_t), the ultimate tensile strength (UTS) and the strain at break (ε_f) for SEVA-C, SCA and their composites filled with HA processed by conventional injection moulding and SCORIM (different moulding geometries apply)

	HA wt. (%)	Conventional			SCORIM		
		E_t (GPa)	UTS (MPa)	ε_f(%)	E_t (GPa)	UTS (MPa)	ε_f(%)
SEVA-C	0	1.8–3.1	40–48	12–30	2.2–3.0	41–49	7–48
SEVA-C/HA	30	4.5–5.2	36–40	1–2	4.5–7.2	40–43	1–2
SCA	0	2.0–3.2	35–70	3–5	4.0–5.8	55–99	5–9
SCA/HA	30	4.9	60	4.1	8.6	65	3.1

4.2. Mechanical performance of HDPE based composites

Table 2 summarizes the tensile test properties of HDPE based composites. The larger improvement of mechanical performance achieved with SCORIM for unreinforced HDPE, as compared to starch based blends, results from both the superior crystallinity and the much higher dependence of the structure development on the thermo-mechanical environment during processing for the former polymer matrix. The high values of tensile strength (25–100 MPa) that are presented for conventional injection moulding, are achievable through the use of very small cross section mouldings (diameter of 1.5 mm), where the relative thick skin determines most of the mechanical behaviour of the mouldings. The strong anisotropic character of SCORIM processed HDPE results from the crystallization under shear of row-nucleated structures that act as reinforcement agents.

4.3. HA and C fibre reinforcement of starch blends and HDPE

For both type of polymer matrices investigated, the combined use of HA fillers with the SCORIM application enables the production of bone-matching (mechanical performance) composites. Nevertheless, the

Table 2
The reference mechanical properties in terms of the tangent modulus (E_t), the ultimate tensile strength (UTS) and the strain at break (ε_f) for HDPE/HA, HDPE/C fibres and HDPE/HA and HDPE/C fibres sandwich composites

	Filler wt. (%)	Conventional			SCORIM		
		E_t (GPa)	UTS (MPa)	ε_f(%)	E_t (GPa)	UTS (MPa)	ε_f(%)
HDPE	0	1.2–1.5	25–100	13–17	3.0–7.1	55–155	12–21
HDPE/HA	25–50	1.6–4.0	35–39	6–35	5.9–7.5	74–91	19–31
CIM							
HDPE/C fibres	20	8.5–10.1	6872	7–9	–	–	–
Sandwich moulding							
HDPE/HA	50				–	–	–
HDPE/C fibres	25	5.6	35	3			

particulate nature of the HA powder (low aspect ratio) act as a severe constrain to the enhancement of stiffness for both cases. The use of alternative reinforcement like C fibres for HDPE, proved to be a valid approach for extending the respective stiffness range. However, the HDPE/C fibres mouldings exhibit a shell/core morphology with very distinct orientation patterns at both these regions, which constrains the mechanical performance exhibited.

4.4. Selective HA and C fibre reinforcement of HDPE

The use of mono-sandwich injection moulding allowed for the production of bi-composite mouldings featuring a HDPE/HA outer layer, aimed to assure the bioactive behaviour of the implant, and a HDPE/C fibres composite core, which mostly determines the mechanical properties exhibited. At this stage of research, it was not possible yet to control adequately the structure development of both composites in final moulded part. The final aim is to apply controlled thermo-mechanical environment (by means of shear application) in order to manipulate the structure development of both the HDPE/HA outer layer and the HDPE/C fibres core and achieve the desired mechanical performance range.

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References

[1] Fawcett D. A textbook of histology. Philadelphia: W.B. Saunders Co; 1986.
[2] Weiner S, Wagner HD. The material bone: structure-mechanical function relations. Ann Rev Mater Sci 1998;28: 271–98.
[3] Martin RB, Burr DB. Structure, function and adaptation of compact bone. New York: Raven; 1989.
[4] Ravaglioli A, Krawjewski A, Celloti GC, Piancastelli A, Bachinni B, Montanari L, et al. Mineral evolution of bone. Biomaterials 1996;17:617–22.
[5] Evans GP, Behiri JC, Bonfield W, Currey JD. Microhardness and Young's modulus in cortical bone exhibiting a wide range of mineral volume fractions and in a bone analogue. J Mater Sci: Mater in Med 1990;1:38–43.
[6] Goldstein SA. The mechanical-properties of trabecular bone-dependence on anatomic location and function. J Biomech 1987; 20:1055–61.
[7] Carter DR, Hayes WC. Mechanical-properties and composition of cortical bone. Clin Orthop 1978;135:192–217.
[8] Ziv H, Wagner H, Weiner S. Microstructure-microhardness relations in parallel-fibered and lamellar bone. Bone Bone 1996;18: 417–28.
[9] Weiner S, Arad T, Sabanay I, Traub W. Rotated plywood structure of primary lamellar bone in the rat: Orientations of the collagen fibril arrays. Bone 1997;20:509–14.
[10] Bonfield W. In: Burny F, Pruers, R, editors. Monitoring of orthopaedic implants. Amsterdam: Elsevier Scienc;, 1993.
[11] Bonfield W. Advances in the fracture-mechanics of cortical bone. J Biomech 1987;20:1071–4.
[12] Keller TS, Mao Z, Spengler DM. Young's modulus, strength and tissue physical properties of human compact bone. J Orthop Res 1990;8:592–603.
[13] Otani T, Whiteside LA, White SE. Strain distribution in the proximal femur with flexible composite and metallic femoral components under axial and torsional loads. J Biomed Mater Res 1993;27:575–85.
[14] van der Sloten J, van der Perre G, Labey L, van Audekercke R, Helsen J. The development of a physiological hip prosthesis: the influence of design and materials. J Mater Sci: Mater in Med 1993;4:407–14.
[15] Bonfield W, Grynpas MD, Tully AE, Bowman J, Abram J. Hydroxyapatite reinforced polyethylene—a mechanically compatible implant. Biomaterials 1981;2:185–9.
[16] Bonfield W. Composites for bone replacement. J Biomed Eng 1988;10:522–6.
[17] Huang J, Di Silvio L, Wang M, Tanner KE, Bonfield W. In vitro mechanical and biological assessment of hydroxyapatite-reinforced polyethylene composite. J Mater Sci: Mater in Med 1997; 8:775–9.
[18] Huang J, Di Silvio L, Wang M, Rehman I, Ohtsuki IC, Bonfield W. Evaluation of in-vitro bioactivity and biocompatibility of bioglass reinforced polyethylene composite. J Mater Sci: Mater in Med 1997;8:809–13.
[19] Suwanprateeb J, Tanner KE, Turner S, Bonfield W. Influence of sterilization by gamma irradiation and of thermal annealing on creep of hydroxyapatite-reinforced polyethylene composites. J Biomed Mater Res 1998;39:16–22.
[20] Suwanprateeb J, Tanner KE, Turner S, Bonfield W. Influence on Ringer's solution on creep resistance of hydroxyapatite reinforced polyethylene composites. J Mater Sci: Mater in Med 1997; 8:469–72.
[21] Deb S, Wang M, Tanner KE, Bonfield W. Hydroxyapatite-polyethylene composites: effect of grafting and surface treatment of Hydroxyapatite. J Mater Sci: Mater in Med 1996;7:191–7.
[22] Wang M, Porter D, Bonfield W. Processing, characterisation, and evaluation of hydroxyapatite reinforced polyethylene composites. British Ceram Trans 1994;93:91–5.
[23] Guild FJ, Bonfield W. Predictive modelling of hydroxyapatite-polyethylene composite. Biomaterials 1993;14:985–93.
[24] Tanner KE, Downes RN, Bonfield W. Clinical applications of hydroxyapatite reinforced materials. British Ceram Trans 1994; 93:104–7.
[25] Wang M, Ladizesky NH, Tanner KE, Ward IM, Bonfield W. Hydrostatically extruded HAPEX™. J Mater Sci 2000;35:1023–30.
[26] Ladizesky NH, Ward IM, Bonfield W. Hydrostatic extrusion of polyethylene filled with hydroxyapatite. Polym Adv Tech 1997;8: 496–504.
[27] Ward IM, Bonfield W, Ladizesky NH. The development of load-bearing bone substitute materials. Polym Int 1997;43:333–7.
[28] Ladizesky NH, Ward IM, Bonfield W. Hydroxyapatite/high-performance polyethylene fiber composites for high load bearing bone replacement materials. J Appl Polym Sci 1997;65:1865–82.
[29] Ladizesky NH, Pirhonen EM, Appleyard DB, Ward IM, Bonfield W. Fibre reinforcement of ceramic/polymer composites for a

major load bearing bone substitute materials. Comp Sci Tech 1998;58:419–34.
[30] Ibnabddjalil M, Loh IH, Chu CC, Blumenthal N, Alexander H, Turner D. Effect of surface plasma treatment on the chemical, physical, morphological, and mechanical properties of totally absorbable bone internal fixation devices. J Biomed Mater Res 1994;28:289–95.
[31] Tormala P, Laiho J, Pohjonen T, Vasenius J, Rokkanen P. Ultra-high-strength absorbable self-reinforced polyglycolide (SR-PGA) composite rods for internal fixation of bone fracture: in vitro and in vivo studies. J Biomed Mater Res 1991; 25:1–22.
[32] Hutmacher DW. Scaffolds in tissue engineering bone and cartilage. Biomaterials 2000;21:2529–43.
[33] Bos RRM, Rozema FR, Boering G, Nijenhuis AJ, Pennings AJ, Verwij AB, et al. Degradation of and tissue reaction to biodegradable poly(L-lactide) for use as internal fixation of fractures. A study in rats. Biomaterials 1991;12:33–8.
[34] Claes LE, Ignatius AA, Rehm KE, Scholz C. New bioresorbable pin for the reduction of small bony fragments: design, mechanical properties and in vitro degradation. Biomaterials 1996;17:1621–6.
[35] Tormala P. Biodegradable self-reinforced composite materials: manufacturing structure and mechanical properties. Clinic Mater 1992;10:29–34.
[36] Litsky AS. Clinical reviews. J Appl Biomaterials 1993;4:109–11.
[37] Claes LE. Mechanical characterisation of biodegradable implants. Clinic Mater 1992;10:41–6.
[38] Wang A, Essner VK, Polineni VK, Stark C, Dumbleton JH. Lubrication and wear of ultrahigh molecular weight polyethylene in total joint replacements. Tribology Int 1998;31:17–33.
[39] Cornwall GB, Bryant JT, Hansson CM, Rudan J, Kennedy LA, Cooke TD. A quantitative technique for reporting surface degradation patterns of UHMWPE components of retrieved total knee replacements. J Appl Biomater 1995;6:9–18.
[40] Mckellop H, Shen F-W, Lu B, Campbell P, Salovey R. J Orthop Res 1999;17:157–67.
[41] Oonishi H, Takayama Y, Tsuji E. Improvement of polyethylene by irradiation in artificial joints. Radiat Phys Chem 1992;39:495–504.
[42] Parks JB, Lakes RS. Biomaterials an introduction. New York: Plenum Press; 1992.
[43] Bucholz RW, Henry S, Henley MB. Fixation with bioabsorbable screws for the treatment of fractures of the ankle. J Bone Joint Surg 1994;76:319–24.
[44] Verheyen CCPM, deWijn JR, Vanblitterswijk CA, Degroot K. Evaluation of hydroxylapatite- poly(L-lactide) composites—mechanical behavior. J Biomed Mat Res 1992;26:1277–96.
[45] Verheyen CCPM, de Wijn JR, van Blitterswijk CA, de Groot K, Rozing PM. Evaluation of hydroxylapatite/poly(L-lactide) composites: an animal study on push out strengths and interface histology. J Biomed Mater Res 1993;27:433–44.
[46] Shikinami Y, Okuno M. Bioresorbable devices made of forged composites of Hydroxyapatite (HA) particles and poly-L-lactide (PLLA): part I. Basic characteristics Biomaterials 1999;20:859–77.
[47] Stohelin A, Liedtke H. In: Skov H, editor. Medical plastics, vol. 9, Denmark: Hexagon Holding Aps; 1995.
[48] Koskikare K, Hirvensalo E, Pätiälä H, Rokkanen P, Pohjonen T, Törmälä P, et al. Intraosseous plating with absorbable self-reinforced poly-L-lactide plates in the fixation of distal femoral osteotomies on rabbits. J Biomed Mater Res 1996;30:417–21.
[49] Vainionpaa S, Rokkanen P, Tormala P. Surgical applications of biodegradable polymers in human tissues. Prog Polym Sci 1989; 14:679–716.
[50] Manninen MJ. Self-reinforced poly-L-lactide screws in the fixation of cortical bone osteotomies in rabbits. J Mater Sci Mater Med 1993;4:179–85.
[51] Tormala P. Ultra-high strength, self-reinforced absorbable polymeric composites for applications in different disciplines of surgery. Clinic Mater 1993;13:35–40.
[52] A. Sliedregt, Hydroxyapatite/polylactide composites for reconstructive surgery: an in vitro and in vivo biocompatibility study, PhD thesis, University of Leiden, The Netherlands, 1993.
[53] Helson JA, Jaecques SV, van Humbeeck J, Athanasiou KA, Niederauer, Agrawal CM. Sterilization, toxicity, biocompatibility and clinical applications of polylactic acid/polyglycolic acid copolymers. Biomaterials 1996;17:93–102.
[54] Agrawal CM, Athanasiou KA. Technique to control pH in vicinity of biodegrading PLA-PGA implants. J Biomed Mater Res 1997;38:105–14.
[55] Kobayashi H, Shiraki K, Ikada Y. Toxicity test of biodegradable polymers by implantation in rabbit cornea. J Biomed Mater Res 1992;26:1463–76.
[56] Ruedi M, Rahn BA, Illi OE. Interface reactions between biodegradable implants and avascular bone grafts or vascular host site in the porcine skull. J Mater Sci: Mater in Med 1995;6:181–5.
[57] Reis RL, Cunha AM. Characterisation of two biodegradable polymers of potential application within the biomaterials field. J Mater Sci: Mater Med 1995;6:786–92.
[58] Reis RL, Cunha AM, Bevis MJ. Mechanical behaviour of injection moulded starch based polymers. J Polym Adv Tech 1996;7: 784–90.
[59] Reis RL, Mendes SC, Cunha AM, Bevis MJ. Processing and in-vitro degradation of starch/EVOH thermoplastic blends. Polym Int 1997;43:347–53.
[60] Reis RL, Cunha AM, Allan PS, Bevis MJ. Structure development and control of injection moulded hydroxylapatite reinforced starch/EVOH composites. Adv Polym Tech 1997;16:263–77.
[61] Reis RL, Cunha AM, Bevis MJ. Shear controlled orientation injection molding of polymeric composites with enhanced properties. In: SPE Proceedings, 57th Annual Technical Conference, Atlanta, USA, 1998. p. 487–93.
[62] Malafaya PB, Elvira C, Gallardo A, Reis RL, San Román J. Processing of a new porous starch-based polymeric drug delivery system for arthritis and rheumatism treatment. In: Proceedings of the EPS 2000—European Physics Society, Guimarães, Portugal; 2000, p. 163–4.
[63] Mano JF, Vaz CM, Mendes SC, Reis RL, Cunha AM. Dynamical mechanical properties of hydroxylapatite reinforced and porous starch-based degradable biomaterials. J Mater Sci Mater Med 1999;12:857–62.
[64] Gomes ME, Ribeiro AS, Malafaya PB, Reis RL, Cunha AM. A new approach based on injection moulding to produce biodegradable starch based polymeric scaffolds. Biomaterials 2001;22: 883–9.
[65] Reis RL, Cunha AM, Bevis MJ. Using nonconventional processing routes to develop anisotropic and biodegradable composites of starch-based thermoplastics reinforced with bone-like ceramics. J App Med Polym 1998;2:49–53.
[66] Sousa RA, Mano JM, Reis RL, Cunha AM, Bevis MJ. Mechanical performance of starch based bioactive composite biomaterials molded with preferred orientation for potential medical applications. Polym Eng Sci 2002;42:1032–45.
[67] R. L. Reis, A. M. Cunha, Bevis MJ. Reinforced starch based blends: a new alternative for bioresorbable load-bearing implants. SPE In: Proceedings, 57th Annual Technical Conference, Atlanta, USA, 1998. p. 2733–9.
[68] Reis RL, Cunha AM, Lacerda SR, Fernandes MH, Correia RN. Reinforcement of polyethylene and starch based thermoplastics with hydroxylapatite and bioactive glasses. In: Kokubo T, Nakamura T, Miyaji F, editors. Bioceramics 9. Oxford: Elsevier Science; 1996. p. 435–8.
[69] Reis RL, Leonor IB, Rego MT, Cunha AM, Lacerda SR, Fernandes MH, Correia RN. Stiff and bioactive composites based on

starch, polyethylene and SiO-CaO·P_2O_5-MgO glasses and glass-ceramics. In: Legeros RZ, Legeros JP, editors. Bioceramics 11. Singapore: World Scientific; 1998. p. 169–72.
[70] Cunha AM, Pouzada AS, Crawford RJ. A study of the impact behaviour of injection moulded polypropylene using two different modes of testing. Plast Rubb Comp Proc Appl 1992;18:79–88.
[71] Fujiyama M. In: Karger-Kocsis J, editor. Polypropylene structure, blends and composites: structure and morphology, London: Chapman and Hall; 1995.
[72] Viana JC, Cunha AM, Billon N. The tensile behaviour of an injection-moulded propylene-ethylene copolymer: the effect of the local thermomechanical processing conditions. Int Polym 1997; 43:159–66.
[73] Allan PS, Bevis MJ. Multiple live-feed injection moulding. Plast Rubb Proc Appl 1987;7:3–10.
[74] Allan PS, Bevis MJ. Development and application of multiple live-feed injection moulding for the management of fibres in injection moulding parts. Comp Manufac 1990;2:79–84.
[75] Allan PS, Bevis MJ. Shear controlled orientation technology: a route to optimised polymer properties. Mater World 1994;2:7–9.
[76] Sousa RA, Kalay G, Reis RL, Cunha AM, Bevis MJ. Injection molding of a starch/EVOH blend aimed as an alternative biomaterial for temporary applications. J Appl Polym Sci 2000;77:1300–15.
[77] Kalay G, Sousa RA, Reis RL, Cunha AM, Bevis MJ. The enhancement of the mechanical properties of a high density polyethylene. J Appl Polym Sci 1999;73:2473–83.
[78] Reis RL, Cunha AM, Oliveira MJ, Campos AR, Bevis MJ. Relationships between processing and mechanical properties of injection moulded high molecular weight polyethylene/hydroxylapatite composites. Mat Res Innovat 2001;4:263–72.
[79] Sousa RA, Reis RL, Cunha AM, Bevis MJ. Interfacial interactions and structure development in injection molded HDPE/hydroxyapatite composites. In: SPE Proceedings, 61st Annual Technical Conference, Dallas, USA, 2001. p. 2550–4.
[80] Vaz CM, Reis RL, Cunha AM, Improvement of interfacial interactions in starch-EVOH/HA composites. In: Proceedings of the 2nd Esaform Conference. Guimarães, Portugal, 1999. p. 377–80.
[81] Sousa RA, Reis RL, Cunha AM, Bevis MJ, Non-conventional processing of short fibre reinforced composites. In: SPE Proceedings, 61st Annual Technical Conference, Dallas, USA, 2001. p. 804–08.
[82] Sousa RA, Reis RL, Cunha AM, Bevis MJ, Development and properties of Bi-composite mouldings. In: Conference Proceedings of the Polymer Processing Society, Seventeenth Annual Meeting PPS-17, Montreal, Canada, 2001. p. 296.