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Polymer nanocomposites for bone tissue substitutes

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Abstract

Following the quest for new composite biomaterials for bone tissue engineering, this work presents the processing of new nanocomposite made of polycaprolactone matrix and wollastonite particles. Wollastonite nanopowder was obtained by thermal treatment of polymethyloxosilane resin mixed with silica and calcium hydroxide. Bioactive character of the ceramic nanopowder was verified in simulated body fluid (SBF). The apatite formation on wollastonite grain surface after immersion in SBF was observed. Basic mechanical properties of the samples containing various amount of ceramic nanoparticles have been examined. It was shown that the presence of small amount of wollastonite nanoparticles (0.5–1.0 wt%) improves significantly the Young's modulus, tensile strength, and work-of-fracture of polymer matrix composite. Increased content of ceramic nanoadditive (>2%) in nanocomposites resulted in degradation of their mechanical characteristics.

Keywords: A. Precursors: organic; B. Nanocomposites; D. Apatite; E. Biomedical applications

1. Introduction

Ageing societies and significant increase in number of sport injuries lead to growing medical and scientific interest in new venues for bone repair technology. The bone tissue is the second most frequently transplanted human tissue and the demand is growing in medical market for new materials for reconstitution of bone defects. These new materials should replace defective tissue and allow for its regeneration and reconstruction during the therapy period. Currently used methods of broken and defective bone treatment apply metal and polymer orthopedic implants, unfortunately showing many deficiencies; metal materials are stiffer than natural bones and after serving the purpose they have to be removed from the body during second surgery. On the other hand the polymer materials are characterized by loss of mechanical strength within the period of application [1,2].

The use of strongly porous and biodegradable materials in biomedical applications, in particular for bone tissue regeneration, meets growing interest in recent years. Such biomaterials constitute a temporary scaffold replacing the missing bone tissue and they should be biocompatible, osteoinductive, osteoconductive, porous as well as mechanically compatible with the bone tissue. Additionally, these porous structures should be made of biodegradable materials subjected to self-decay after playing a role of a scaffold for a specific period of time. Currently designed scaffold materials fulfill only part of these requirements, therefore the search for better materials continues [1–5]. One of the proposed solutions may be to manufacture biomaterials in the form of nanocomposites. Nanocomposite, porous scaffolds in various geometrical forms offer a good potential for tissue-engineered implants [6–8].

Nanocomposites made of resorbable polymers and ceramic nanoparticles may become good alternative materials for scaffolds for growing bone tissue cells, in view of their superior mechanical and bioactive properties compared to conventional materials. It is already known that such materials containing nano-sized surface components show very good osteointegration and stimulate the osteoblasts, thus enhancing their adhesion [9–11]. Polymers or other materials as well as polymer nanocomposites may enhance the deposition of calcium phosphate, forming apatite layer on the surface of the implant, also improving

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protein adsorption, therefore improving the adhesion of osteoblasts [12–16].

Bone tissue itself is a typical nanocomposite in view of both its structure and composition, as it is based on collagen, containing hydroxyapatite nanocrystals. Since the discovery of this nanocomposite structure of the bone tissue, the design of bone implants and scaffolds have concentrated on this specific group of materials.

Polymer nanocomposites containing hydroxyapatite (HAp) constitute a particularly large and interesting group, including among others: collagen/HAp, PLA/collagen/HAp, alginates/collagen/HAp, chitozan/Hap, gelatine/HAp, PCL/HAp, PLA/HAp [14–18]. Bone implant scaffolds made of these materials contain pores of the size allowing the osteoblasts to penetrate inside the implant. During the next stage, the in-growth of blood vessels and neurons occurs inside the defect filled by the implant. After fulfilling the role of a scaffold, the polymer resorbable matrix undergoes a self-decay process, and the implant is replaced by patient's own new bone tissue.

Wollastonite is another bioactive and biocompatible material, which may become an interesting alternative to hydroxyapatite, in particular due to its high capacity for apatite formation on its surface after incubation in simulated body fluid (SBF) liquid (better than in other bioactive materials) as well as due to its ability of integration with the bone [19–22]. Wollastonite may be prepared by controlled pyrolysis of silicon organic precursors with active fillers [23–28].

The aim of this work was to obtain a new nanocomposite material: the resorbable polymer (PCL/wollastonite ceramic) designated for medical use in the field of regeneration of bone tissue. The poly-(ε-caprolactone), known as PCL, is a biodegradable polymer of aliphatic polyester group. It is a non-toxic product, having good ability to mix and good mechanical compatibility with many other polymers. This biocompatible polymer has been widely used in tissue engineering. Nanocomposite polycaprolactone/wollastonite samples were prepared with varying content of ceramic nanoparticles and their mechanical and surface properties were determined in view of possible medical applications as bone implant materials.

2. Materials and methods

Poly-(ε-caprolactone) purchased from Sigma–Aldrich (molecular mass, Mn 80,000; melting temp. 60 °C; polydispersion, w/Mn <2; the degree of crystallinity determined by DSC, 42.2%) was used in this work as a matrix raw-material for this nanocomposite. Wollastonite nanopowder was used as a modifier of PCL. It was obtained at the Dept. of Biomaterials, Univ. of Science and Technology, Poland, based on polymethyloxosilane resin Lukosil 901 (Lucebni Zavody, Kolin, Czech Republic) as a precursor. Silica (SiO_2) and calcium hydroxide $Ca(OH)_2$ were applied as inorganic additives. The resin was thermally cross-linked, milled and then mixed with inorganic additives using the weight ratio 65:35 ($10SiO_2$, $25Ca(OH)_2$). The pellets were formed from powder mixture by uniaxial pressing and the prepared material was subjected to pyrolysis in neutral atmosphere at the temp. of 1000 °C during 24 h, with heating rate of 0.7 °C/min. Wollastonite ceramic made in this way contained silica oxycarbide (about 10 wt%), being formed during the pyrolysis of the resin.

For characterization of in vitro bioactivity, the wollastonite ceramic samples in form of plates were soaked in SBF for 7 days. The simulated body fluid, with ion concentration nearly equal to that of human blood plasma suitable for apatite nucleation, was prepared according to the method proposed by Kokubo et al. [3,29]. After 7 days the ceramic surface was examined using a scanning electron microscope equipped with the EDS analyzer [NOVA 200 NANOSEM].

Thus obtained ceramic product was then milled in an attritor grinder for 12 h. Wollastonite powder morphology was determined in the scanning electron microscope. In order to define the average grain size and the grain size distribution, the Nanosizer-ZS Malvern Instruments was used, having the ability to measure the size of particles in the range from 0.6 nm to 6 μm.

The polymer matrix nanocomposite samples were prepared in the form of foils of 0.2 mm thick. Dichloromethane was applied as a solvent of PCL matrix material, to which wollastonite powder was added and then the suspensions were homogenized with use of an ultrasonic homogenizer, making the suspension uniform and breaking down powder soft agglomerates [20–22]. Five series of nanocomposite samples were prepared, containing the following amounts of modifying filler (by volume): 0.5%, 1%, 2%, 4% and 6%. One sample without wollastonite content was prepared as the reference material.

The first step in sample preparation was the dispersion of wollastonite nanopowder in dichloromethane, stirring the suspension using an ultrasonic homogenizer. In the next step the wollastonite suspension was mixed with 10% solution of PCL in dichloromethane, also using the ultrasonic homogenizer. Uniform suspension was poured onto Petri dishes to allow the evaporation of dichloromethane. Drying was carried out in two stages: first 24 h in atmospheric pressure, then the next 48 h at room temperature in a vacuum drier.

Mechanical properties of nanocomposites were examined using the universal testing machine ZWICK 1435 equipped with testXpert V8.1 program. Samples in form of strips with the thickness of 0.2 mm (measured with the accuracy of 0.01 mm) were cut out from the composite foil with dimensions 0.5 cm × 7 cm. Each strip for the tensile test was mounted in the metallic grips covered with rubber designed for testing polymeric materials. The same grip span of 4 cm was used for each sample and they were all subjected to uniaxial tensile force at the constant crosshead speed of 2 mm/min. Longitudinal rupture strains of the samples were obtained from the traverse displacement in tensile loading. Series of five samples for each type of the examined material were tested and the values of tensile strength, Young's modulus, work-of-break and maximum strain-to-break were determined as means ±standard deviations (S.D.). The statistical significance between two sets of data was calculated using Student's *t*-test. Data were taken to be significant, when a *P*-value of 0.05 or less was obtained.

3. Results and discussion

3.1. Wollastonite ceramics

Fig. 1 shows the SEM micrographs of wollastonite grains before and after immersion in SBF fluid. The apatite formation on the surface of this material is visible. Additionally, the EDS analysis confirmed the presence of peaks related to the presence of phosphate, and also showed clear signals indicating the presence of silicon and calcium elements.

The results of examination of grain size distribution of the processed wollastonite powder are shown in Fig. 2, and its morphology can be observed in Fig. 3. Wollastonite powder has the grains in nanometric range, as most of its grains are smaller than 150 nm, with a maximum of the grain distribution at 100 nm. However, larger grain fractions are also visible.

As it can be seen from the micrograph (Fig. 3), the analyzed wollastonite powder is made of regular, spheroidal grains of uniform size, with certain tendency to form small soft agglomerates. These agglomerates were disintegrating during the process of nanocomposite preparation. Due to nanometric size and spheroidal form of powder grains, this material may be easily combined with resorbable polymeric matrices and transformed into polymer/ceramic nanocomposite. The polymer matrices of such composites, during slow degradation in biological environment, may become bioactive sources of ceramic particles.

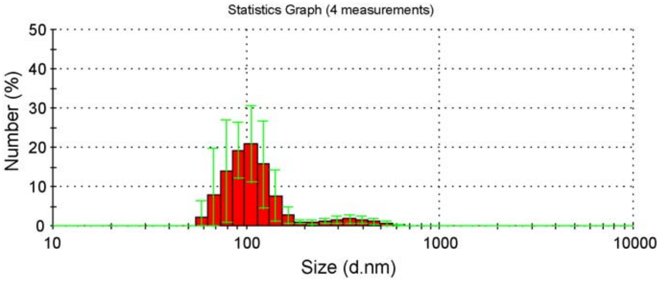

Fig. 2. The grain size distribution of wollastonite powder.

3.2. The mechanical properties of nanocomposite PCL/wollastonite ceramics

The results of mechanical properties examination (Young's modulus, tensile strength, maximum strain and the work-of-break) are shown in Figs. 4 and 5, representing the average values and their standard deviations calculated from five samples. The Young's moduli of the samples were determined from the slopes of the stress–strain curves in their initial, linear range. This linear stress–strain range in the initial relationship of tensile test was observed for all types of samples examined in

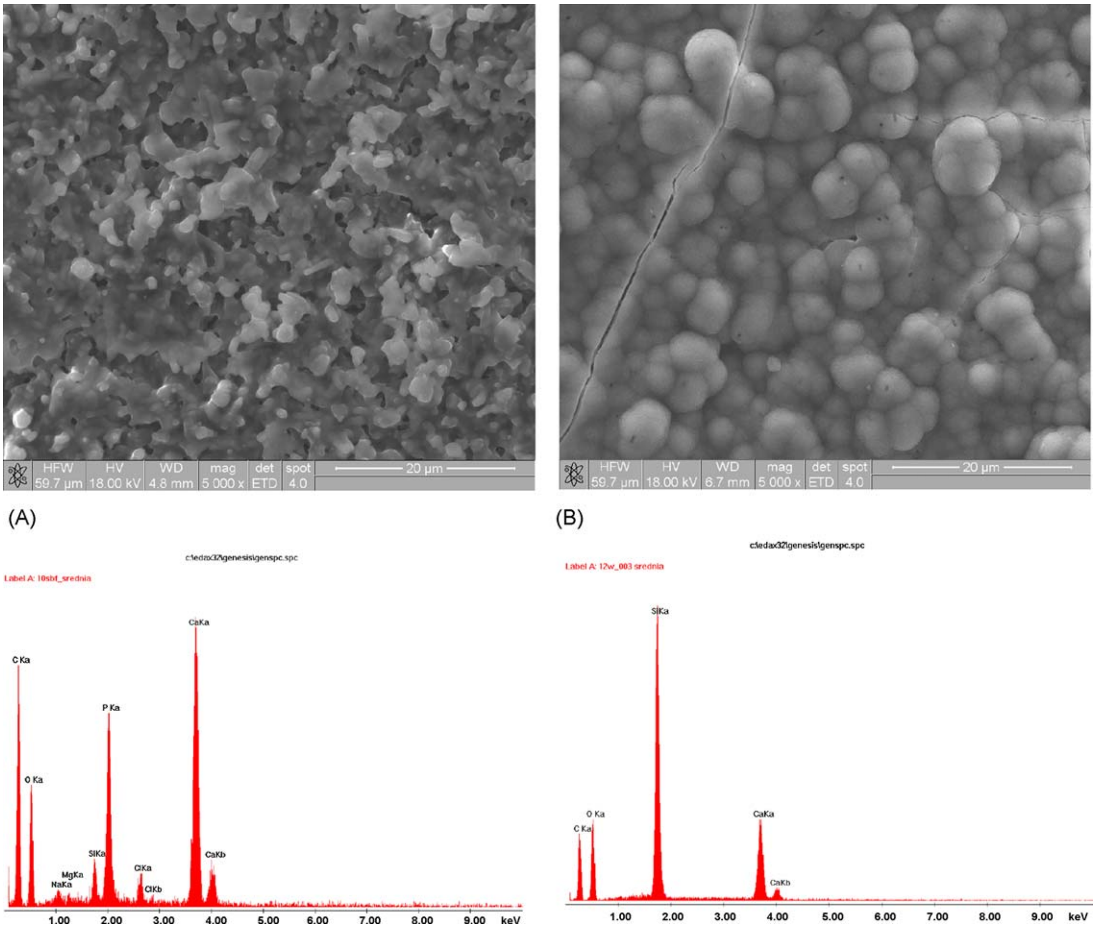

Fig. 1. SEM micrographs and EDS spectra of wollastonite ceramic sample obtained from polysiloxane containing active fillers (A), and this sample after soaking in SBF fluid for 7 days (B).

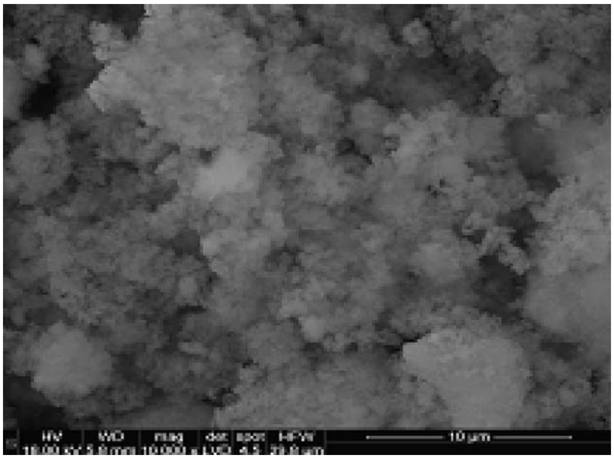

Fig. 3. SEM micrographs of wollastonite powder (NOVA NANO SEM, FEJ EUR. Company).

tensile test (Figs. 6 and 7). The evaluation of mechanical properties of PCL/wollastonite nanocomposite shows that small additions of wollastonite significantly affect these properties, increasing tensile strength, maximum strain-to-break, Young's modulus and work-of-break. It is noticeable that the highest values of all enumerated parameters were obtained at the lowest contents of wollastonite nanopowder, i.e., 0.5 and 1 wt%, where the average values of tensile strength and rupture strain increased almost twice. However, with increasing content of wollastonite nanopowder (>2%), the values of these parameters systematically decreased. Fig. 4A confirms that low contents of wollastonite nanoparticles effectively increase the tensile strength, whereas high nanoparticle contents in the samples cause their embrittlement, decreasing their strain to failure.

More complex relation is related to the Young's modulus determined from the slope of initial linear part of stress–strain curves; an increase of this parameter is from 20% to 40% in comparison to the pure polymer and is observed for all nanocomposite samples (Fig. 5B). The differences between the nanocomposite samples are not, however, statistically significant ($P < 0.05$). For example, the Young's modulus of the samples containing 0.5% and 6% ceramic nanopowder is 347 and 358 MPa, respectively.

Modification of polycaprolactone's mechanical properties by the presence of wollastonite nanophase is most pronounced when the stress–strain curves are analyzed. The examples of

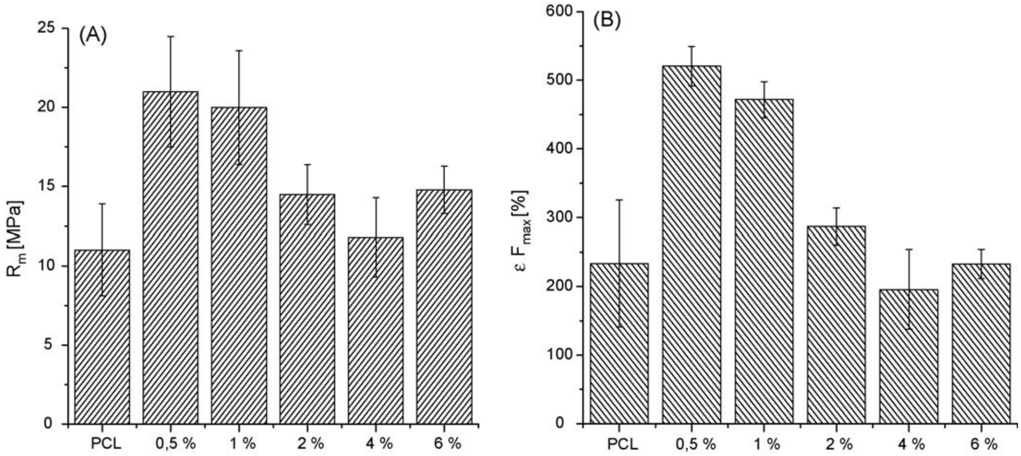

Fig. 4. The values of tensile strength (A), and the values of maximum strain at fracture (B) of pure polymer (PCL) and nanocomposites with different amount of wollastonite ceramic particles.

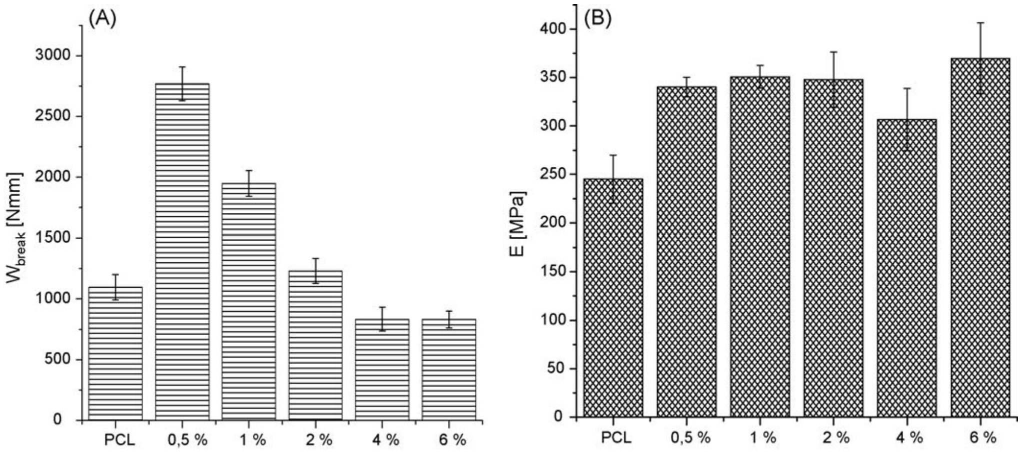

Fig. 5. The values of work-of-break (A), and Young modulus (B) for pure polymer and nanocomposite samples with different content of wollastonite ceramic nanoparticles.

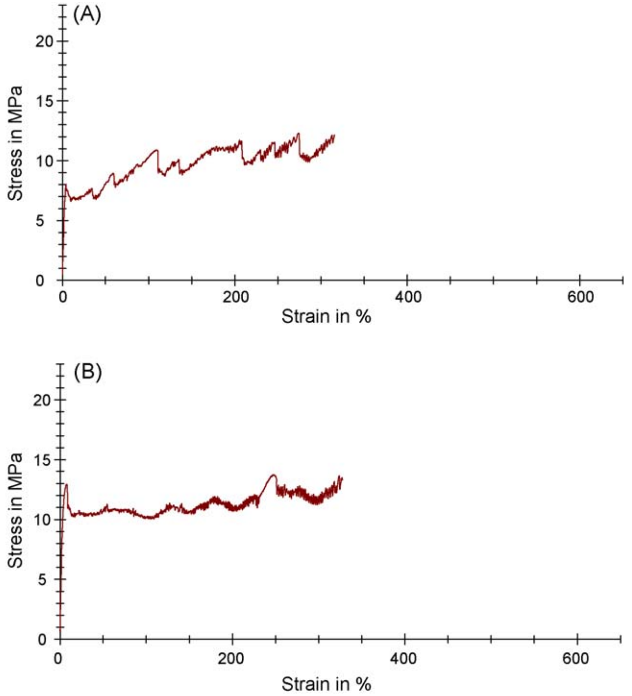

Fig. 6. The stress–strain curve for samples: (A) unmodified PCL and (B) modified with 6% $CaSiO_3$.

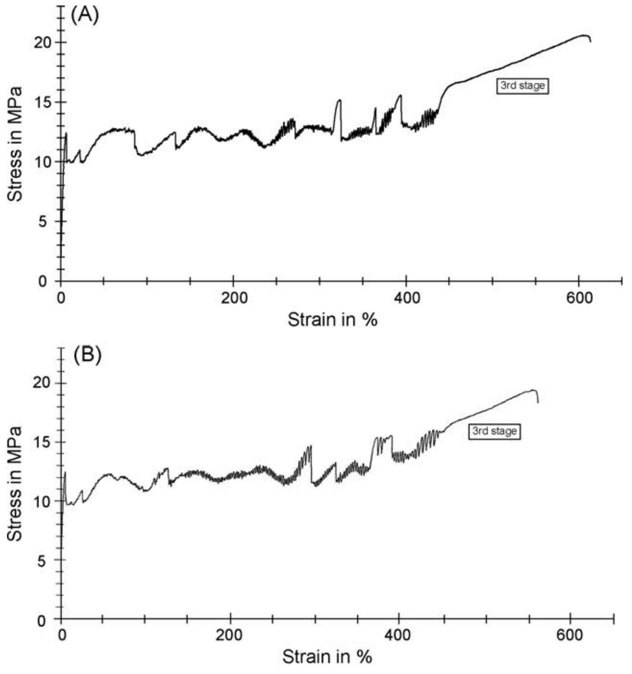

Fig. 7. The stress–strain curve for samples: (A) PCL + 0.5% $CaSiO_3$ and (B) PCL + 1% $CaSiO_3$.

typical deformation curves for unmodified PCL samples and the samples with varying content of ceramic nanopowder are collected in Figs. 6 and 7. Fig. 6 illustrates the stress–strain curves for (A) unmodified PCL and (B) nonocomposite with 6% wollastonite content. Both curves are similar in shape, namely after the force is being applied, the sample material is initially elongated in an elastic (linear) way, followed by plastic deformation up to failure. The second stage of elongation for pure polymer and composite samples corresponds to the transformation of amorphous phases of the polymer. PCL is a thermoplastic resin consisting of the amorphous and crystalline components. The degree of crystallinity for pure PCL used in this study is 42.2%. The amorphous phase of the sample during the stretching is reorienting up to break. For wollastonite-modified PCL (6%) the slight increase in strength and Young's modulus can be observed as compared to pure matrix sample. On the other hand, the curves obtained for nanocomposites containing 0.5% and 1% wollastonite, show that the initial linear elastic strain range typical for unmodified polycaprolactone, is followed in these materials by significant higher range of plastic deformation (Fig. 7), which is quite different from the behaviour of pure polymer as well as of nanocomposite with 6% of wollastonite. Following this plastic deformation range the samples again start to behave in purely elastic manner (marked in Fig. 7 as '3rd stage') with further increasing tensile load. Such a linear deformation preceding sample failure is neither observed for pure polymer material nor for nanocomposite with higher content (>2%) of wollastonite. This distinct enhancement of tensile strength and strain properties for nanocomposites modified with small amount of ceramic nanofiller suggests that there is some interaction between nanoparticles and polymer matrix indicating that the ceramic filler contributes to the overall elastic properties of the composite samples. Similar behaviour has already been reported in case of other ceramic nanofillers (montmorillonite, $CaCO_3$) used for modification of polymer matrices [30,31]. It is also known, that the dispersion of nanoparticles and their interaction with polymer matrix may play a crucial role in resulting mechanical properties of the nanocomposite [32]. The results of the present study suggest that at low level of wollastonite content introduced into polymer matrix the grains of nanopowder may be relatively well dispersed. The enhancement of the modulus of nanocomposites at such low ceramic concentration cannot be attributed to the introduction of higher modulus ceramic filler. Since the slope of obtained stress–strain curves increases in the initial linear range (related to Young's modulus increase) it could indicate that nanoparticles may create a weak linkage between the polymer chains, acting similarly to well-known cross-linking bonds in polymer matrices, making the nanocomposite stiffer [31]. Upon further loading, the applied stress leads to debonding of the nanoparticle–polymer weak interface and the nanocomposite displays high plastic deformation followed by typical straightening of polymer chains (3rd phase). It is likely that during this phase of tensile loading the nanoparticles facilitate reorientation of polymer chains leading to improvement of the resulting mechanical properties. However, at higher content of nanofiller (>2%) the good dispersion of individual wollastonite particles during composite fabrication is more difficult, since these nanoparticles were not functionalized before introducing them into polymer solution. It is likely that during the composite preparation the process of secondary aggregation of nanoparticles took place. As a result, the reduction of deformability of these samples is observed: the stress–strain curve of the nanocomposite containing 6% ceramic powder does not exhibit the third phase of elongation and it's shape is very similar to that of pure polymer (Fig. 6A). Moreover, the value of work-of-fracture for the composite samples containing 6 wt% of nanoparticles was only one-third of the value measured for samples having the lowest nanopowder content.

4. Conclusions

1. The new polycaprolactone/wollastonite nanocomposite with varying content of modifying nanoparticles has been obtained in this work. It was shown that the best mechanical properties can be obtained when the range of content of reinforcing modifier remains between 0.5 and 1 wt%.
2. Intensive nucleation of calcium phosphate on the surface of wollastonite ceramic is responsible for bioactive properties of this material.
3. The bioactive wollastonite ceramics in form of nanofiller has specific properties, allowing for its application as reinforcement in polymer matrices.
4. Wollastonite may modify PCL matrix at the molecular level, bringing about unique mechanical properties of the composite.
5. The study demonstrated that the mechanical properties of the composite samples may be controllable via proper formulation of composite composition.
6. The PCL/nanowollastonite composite may constitute a suitable candidate material for porous substrate constructs and further investigations are needed, particularly regarding its biocompatibility, in view of possible application in regenerative medicine and bone tissue engineering.

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