

Poly(*N*-vinylcaprolactam) nanocomposites containing nanocrystalline cellulose: a green approach to thermoresponsive hydrogels

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Abstract In this work, we report on the synthesis and characterization of thermoresponsive poly(*N*-vinylcaprolactam), PNVCL, nanocomposite hydrogels containing nanocrystalline cellulose (CNC) by the use of frontal polymerization technique, which is a convenient, easy and low energy-consuming method of macromolecular synthesis. CNC was obtained by acid hydrolysis of commercial microcrystalline cellulose and dispersed in dimethylsulfoxide. The dispersion was characterized by TEM analysis and mixed with suitable amounts of *N*-vinylcaprolactam for the synthesis of PNVCL nanocomposite hydrogels having a CNC concentration ranging between 0.20 and 2.0 wt%. The nanocomposite hydrogels were analyzed by SEM and their swelling and rheological features were investigated. It was found that CNC decreases the swelling ratio even at small

concentration. The rheological properties of the hydrogels indicated that CNC strongly influenced the viscoelastic modulus, even at concentrations as low as 0.1 wt%: both G' and G'' , and the viscosity increase with CNC content, indicating that the nanocellulose has a great potential to reinforce PNVCL polymer hydrogels.

Keywords Nanocellulose · Stimuli responsive hydrogel · Frontal polymerization · Nanocomposite systems · Hydrogels

Introduction

Hydrogels are polymeric materials, chemically or physically crosslinked, characterized by a three-dimensional and elastic network capable to swell or deswell when immersed in aqueous solutions. In particular, chemically crosslinked hydrogels are prepared either through water-soluble polymer crosslinking or by converting hydrophobic into hydrophilic polymers, which in turn are then crosslinked to form a network. This structure allows hydrogels swelling or deswelling by retaining or expelling a large quantity of water in the network without dissolving. Conversely, physical crosslinking is due to non-covalent interactions and often is the result of hydrogen bonding, hydrophobic or ionic interactions.

Lately, a particular class of polymer hydrogels has gained more interest in the scientific community: the

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so called *smart* or *stimuli*-responsive hydrogels, which are able to change their size and shape in response of an external stimulus, such as temperature, pH, ionic force, pressure, electric and magnetic field. The change in solubility or the degree of swelling are due to a fine balance among competing interactions such as electrostatic forces and hydrophobic dehydration.

As a matter of fact, enthalpic and entropic contributions shift the minimum of the free energy and cause the volume phase transition.

Moreover, some systems have been developed to combine two or more *stimuli*-responsive mechanisms into one polymer system. For instance, temperature-sensitive polymers may also respond to pH changes (Tengfei et al. 2011). Recently, dual *stimuli*-responsive or ternary *stimuli*-responsive polymer hydrogel microspheres were prepared and applied in various fields, especially in controlled release drug delivery systems (Garbern et al. 2010).

Because of these peculiar features, *stimuli* responsive hydrogels are being developed for uses in pharmaceutical and biological fields such as for contact lenses (Liu et al. 2009), reconstruction of cartilages (Peppas and Langer 1994), artificial tendons and organs (Vernon et al. 2000), and drug delivery systems (Bayer and Peppas 2008). Furthermore, they have also found application in medicine for making chemical valves (Osada and Hasebe 1985), immobilization of enzymes and cells (Ruel-Gariépy and Leroux 2004), and in bulk engineering for microfluidic devices (Barker et al. 2000), motors/actuators (Hoffmann et al. 1999), and sensors (Sorber et al. 2008).

Specifically, thermoresponsive polymer hydrogels are systems which undergo a volume phase transition at a certain temperature, thus resulting in an abrupt change in the solvation state. Hydrogels exhibiting a lower critical solution temperature (LCST) become insoluble upon heating, while those having an upper critical solution temperature (UCST), become soluble upon heating.

Poly(*N*-isopropylacrylamide), PNIPAAm, is the most studied thermoresponsive hydrogel, with an LCST located at ca. 32 °C, which makes it particularly interesting for application in drug delivery systems (Ramkissoon-Ganorkar et al. 1999). However, pNIPAAm is characterized by some disadvantages related to its non-biodegradability and the production of small toxic amide compounds in strong acid conditions. Therefore, many studies have been carried out to search alternative systems. Among these, poly(*N*-

vinylcaprolactam), PNVCL, is a promising candidate; this is a non-ionic biodegradable water-soluble, non-adhesive polymer belonging to the group of poly(*N*-vinylamide) macromolecular compounds (Imaz and Forcada 2008). Moreover, PNVCL is non-toxic and stable against hydrolysis (Kirsh 1998). Furthermore, PNVCL is characterized by an LCST of 34 °C, which is even closer to the physiological one than that of pNIPAAm itself.

All these properties make it an interesting candidate for biomedical and pharmaceutical applications (Liang et al. 2012).

However, because of the random nature of the crosslinking reactions produced by a large number of organic crosslinker polymer hydrogels exhibit poor mechanical properties, which strongly limit their use in structural applications. For such a reason, different nanofillers, such as silicates (Loizou et al. 2005), ceramics (Liang et al. 2000), metals (Cohen Stuart 2008), magnetic particles (Liu et al. 2008) and graphene (Alzari et al. 2011; Sanna et al. 2012a, b) have been introduced into the hydrogel matrices thus obtaining the corresponding nanocomposites.

In recent years, thanks to an increasing interest toward environmental issues, the use of natural fibers as fillers in polymer nanocomposites has gained much attention (John and Thomas 2008).

Among natural fibers, nanocrystalline cellulose represents an appropriate filler for hydrogels because of its good mechanical properties and renewability. In fact, it is characterized by high aspect ratio, high bending strength (10 GPa), high Young's modulus (150 GPa), large surface area, low density, low extension to break, biodegradability and biocompatibility (Zhang et al. 2010; Lin et al. 2011).

Cellulose nanocrystals, CNC, also known as whiskers, are the main building blocks of wood cellulose. They are constituted of rodlike cellulose crystals, having a width of 5–70 nm and a length included between 100 nm and several micrometers. The morphology and dimensions of CNC are strongly influenced by the cellulose source: cotton and wood yield to a distribution of highly crystalline nanorods (width: 5–10 nm, length: 100–300 nm) (Dong et al. 1996), whereas tunicin (Favier et al. 1995), bacteria (Grunert and Winter 2002) and algae (Klemm et al. 2011) produce crystals with larger polydispersity and dimension (width: 5–60 nm, length: 100 nm to several micrometers).

CNC are produced by the removal of amorphous sections of a purified cellulose source (cotton, tunicin, cellulose fiber from lignocellulosic materials) by acid hydrolysis, often followed by ultrasonic treatment, which disperses the nanocrystals in a homogeneous stable suspension. The structure and features of CNC suspension are strongly affected by hydrolysis temperature and time, the type of mineral acid used and its concentration, and the intensity of the ultrasonic bath (Klemm et al. 2011).

However, there are some problems related to the use of nanocrystals of cellulose, such as its low degradation temperature (located around 230 °C), which limits composite processing at temperature below 200 °C, and the insolubility of CNC in non-aqueous media. In fact, CNC show low dispersibility in aqueous medium and in organic solvents with high dielectric constants, such as dimethylsulfoxide, DMSO, and diethylene glycol, but tend to aggregate in highly hydrophobic solutions (Klemm et al. 2011).

To overcome these problems, CNC were submitted to several surface modifications as well as silylation (Roman and Winter 2006), acylation (Grunert and Winter 2002), carboxylation (Habibi et al. 2006) or esterification (Braun and Dorgan 2009). Specifically, for the obtainment of nanocomposites based on hydrophobic polymers, CNC were dispersed in an appropriate solvent in order to process and prepare the corresponding nanocomposite polymers. On this respect different nanocomposite polymers containing CNC were prepared, such as pNIPAAm (Ruitao et al. 2012), poly(acrylamide) (Yang et al. 2013), polypyrrole (Nystrom et al. 2010), poly(lactid acid) (Fortunati et al. 2012a, b), polyurethanes (Cao et al. 2007), poly(vinyl alcohol) (Cho and Park 2011), poly(ϵ -caprolactone) (Goffin et al. 2011), poly(styrene-co-hexyl acrylate) (Mabrouk et al. 2011), poly(vinyl chloride) (Chazeau et al. 1999), polypropylene (Ljungberg et al. 2005) and waterborne epoxies (Matos Ruiz et al. 2001).

Taking into account the above considerations, we focused this work on the synthesis of nanocomposite polymer hydrogels containing CNC by using frontal polymerization (FP).

FP is an alternative technique of macromolecular synthesis that exploits the exothermicity of the reaction itself for the rapid conversion of monomer into polymer. The heat released during the reaction generates a polymerization front able to self sustain and propagate along the reactor. If compared with the traditional polymerization methods, FP generally

exhibits many advantages that make it a green technique of macromolecular synthesis. Indeed, it is characterized by shorter reaction times, lower energy consumption. Moreover, the protocols used are very simple and easily applicable even without special apparatuses and generally without involving the use of solvents.

Initially proposed by Chechilo and Enikolopyan (1975), FP was further studied by Pojman et al. (1995), Scognamillo et al. (2010a, b, c), Jimenez and Pojman (2007), Pojman et al. (1997), Mariani et al. (2001), Chen et al. (2006, 2008), Li et al. (2009, 2012), Cui et al. (2006), and by our group (Fiori et al. 2002; Frulloni et al. 2005; Mariani et al. 2003, 2004, 2007a, b; 2008a, b; Scognamillo et al. 2010a, b, c; Illescas et al. 2011; Illescas et al. 2012a, b; Fiori et al. 2003; Gavini et al. 2009; Brunetti et al. 2004; Vicini et al. 2005). Namely, stimuli-responsive hydrogels of poly(*N,N*-dimethylacrylamide) (Caria et al. 2009), poly(acrylamide-co-3-sulfopropyl acrylate) (Scognamillo et al. 2010a, b, c), poly(*N*-isopropylacrylamide-co-3-sulfopropyl acrylate) (Scognamillo et al. 2011), p(NIPAAm-co-NVCL) (Alzari et al. 2010), and poly(2-hydroxyethylacrylate-co-acrylic acid) (Sanna et al. 2012a) were successfully obtained.

Recently, we have proposed FP for the obtainment of polymer nanocomposites based on poly(tetraethylene-glycoldiacrylate) containing graphene (Alzari et al. 2010); moreover, some stimuli-responsive polymer hydrogels based on PNIPAAm, or PNVCL, and containing graphene have been successfully prepared by FP, as well (Alzari et al. 2011; Sanna et al. 2012b).

The objective of this study was to prepare and characterize “green” thermoresponsive hydrogels of PNVCL with improved mechanical properties by using biocompatible materials such as nanocrystalline cellulose, as filler, and the FP technique.

The influence of CNC on the swelling behavior, morphology, rheological features of the obtained hydrogels was investigated.

Experimental

Materials

N-vinylcaprolactam (NVCL, FW = 139.2 g/mol; d = 1.029 g/ml), *N,N*-methylene-bis-acrylamide (BIS, FW = 154.17 g/mol), DMSO (FW = 78.13 g/mol;

$d = 1.101 \text{ g/ml}$) and microcrystalline cellulose (MCC, dimensions of 10–15 mm) were purchased from Sigma Aldrich and used as received. Trihexyltetradecylphosphonium persulfate (TETDPPS, FW = 1115) was prepared following the method reported in our previous study (Mariani et al. 2008a, b).

Synthesis of CNC dispersion

CNC suspension was prepared from microcrystalline cellulose (MCC, dimensions 10–15 μm , supplied by Sigma Aldrich, Milan, Italy) by acid hydrolysis following the recipe used by Cranston and Gray (Cranston and Gray 2006). Hydrolysis was carried out with 64 wt% sulphuric acid at 45 °C for 30 min with vigorous stirring. After removing the acid, dialysis and ultrasonic treatment were performed. The resultant cellulose nanocrystal aqueous suspension was approximately 0.5 wt% while the hydrolysis yield was about 20 %.

Synthesis of PNVCL nanocomposite hydrogels

The nanocomposite polymer hydrogels were synthesized by varying the amount of CNC from 0.20 to 2.0 wt% (referred to the amount of NVCL monomer), and keeping constant the amount of crosslinker (BIS) and initiator (TETDPPS) to 2.5 and 0.5 mol% (referred to NVCL), respectively.

CNC dispersions were prepared by dissolving the appropriate amount in 3 ml of DMSO, and sonicating it in an ultrasonic bath for 5 min. Then, CNC dispersions in DMSO and liquid NVCL were introduced in a common glass test tube (i.d. = 1.5 cm, length = 16 cm) and sonicated for 1 min. After that, BIS and TETDPPS were added, and the solution was sonicated again for 30 s to remove any bubbles present in it. A thermocouple junction was located at about 1 cm from the bottom of the tube and connected to a digital temperature recorder (Delta Ohm 9416). Front started by heating the external wall of the tube in correspondence of the upper surface of the monomer mixture, until the formation of the front became evident. Front velocity, V_f , was determined by measuring front positions as a function of time. Front temperature, T_{max} , was obtained by using a K-type thermocouple connected to the above digital thermometer (sampling rate: 1 Hz). For all samples, T_{max} ($\pm 10 \text{ }^\circ\text{C}$) and V_f ($\pm 0.05 \text{ cm min}^{-1}$) were measured.

After polymerization, all samples were washed in water for several days to remove DMSO and allow them to swell.

Characterization methods

Swelling experiments

The swelling behavior of the CNC-PNVCL nanocomposite hydrogels was measured in water from 3 to 50 °C, using a thermostatic bath. Three different heat rates were used: 3 °C/day (from 3 to 9 °C), 1 °C/day (from 26 to 36 °C) and 5 °C/day (from 36 to 51 °C). The swelling ratio (SR %) for each sample was calculated by applying the Eq. (1):

$$SR\% = \frac{M_s - M_D}{M_s} \cdot 100 \quad (1)$$

where M_S and M_D are the hydrogel masses in the swollen and in the dry state, respectively. All measurements were performed in triplicate.

Rheological analyses

Rheological tests were performed in a rotational rheometer ARES, with parallel plate geometry (ϕ 8 mm). Dynamic measurements have been performed in order to analyze the viscoelastic properties of the materials and the influence of CNC. Preliminary strain sweep tests to determine the linear viscoelastic region were done. Frequency sweep measurements at room temperature (25 °C) with a strain of 2 % in the frequency range of 0.03–100 rad/s were performed.

A special tool was used in order to maintain the sample immersed in water during the test thus avoiding any change in mechanical response due to sample drying.

FESEM and TEM analyses

The surface morphology was assessed by scanning electron microscopy (FESEM, Supra 25 Zeiss, Germany). Before the analysis, samples were lyophilized, fractured in liquid nitrogen, and the fractured surface was coated with gold.

The nanocrystals in water and DMSO suspensions were examined by transmission electron microscopy (TEM, JEOL JEM-1010), using an accelerating voltage of 100 kV. One drop of each sample was directly

placed in the electron microscopic grid and dry at room temperature.

Results and discussion

Figure 1 shows TEM analysis of pristine cellulose nanocrystals in aqueous suspension obtained after the acid hydrolysis, and the freeze-dried CNC re-dispersed in DMSO for the PNVCL nanocomposite hydrogel production. The hydrolysis process allowed obtaining well individualized CNC (Fig. 1a) that showed the typical acicular structure and the dimensions ranging from 100 to 200 nm in length and 5–10 nm in width, as previously reported Fortunati et al. (2012a, b).

Prior to the PNVCL nanocomposite hydrogel production process, the CNC suspension was freeze-dried, and then re-dispersed in DMSO. During the freeze-drying process, CNC tended to agglomerate and form strong hydrogen bonds as water sublimates. Results obtained for crystal shape and size after the re-dispersion in DMSO (Fig. 1b) highlighted that no particular morphological modifications occurred and CNC maintained its original acicular structure. The dispersion and self-ordering properties of cellulose nanocrystals are restricted to aqueous suspensions and the high tendency to agglomeration of these materials in non polar solvents is usually due to their electrostatic character. However their dispersion in some specific organic solvents with high dielectric constant, such as DMSO or ethylene glycol, was previously proved. (Turbak et al. 1983)

FP was used to prepare nanocomposite polymer hydrogels of PNVCL containing different amounts of CNC, which are included between 0.20 and 2.0 wt% referred to the monomer. As can be seen from Table 1, the frontal polymerization temperature increases of 12 °C introducing CNC in the polymer matrix, and remains constant around 117–120 °C when the CNC amount is further increased. At variance, front velocity is not significantly affected by the CNC content (0.30–0.33 cm/min). This behavior is in agreement with the V_f trend observed in our previous work about nanocomposite polymer hydrogels of PNIPAAm containing graphene as nanofiller (Alzari et al. 2011).

As reported in the Experimental, the swelling behavior of CNC-PNVCL hydrogels in water as a function of temperature was measured from 3 to 50 °C, using three different heating rates. As shown in Fig. 2, SR% decreases from 1,200 % for the neat polymer to 970 % for the nanocomposite containing the lowest amount of CNC (sample FP2). The introduction of nanocrystalline cellulose involves a strong increase of the hydrophobic character of the polymer, leading to its sharp contraction. Moreover, CNC can act as a physical crosslinker, giving rise to more junctions in the hydrogel network and thus increasing the crosslink density.

With the enhancement of the CNC amount, SR% decreases and reaches the minimum value of 870 % for the hydrogel containing 1.0 wt% of CNC (sample FP4). However, when CNC content is 2.0 wt% (sample FP5), SR% exhibits a slightly increase to 940 %. This behavior is probably due to the negative

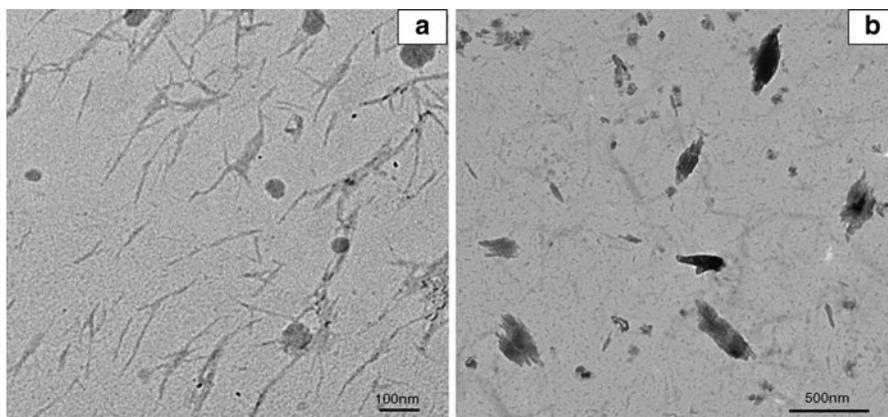


Fig. 1 TEM analysis of pristine cellulose nanocrystal suspensions in water (a) and CNC re-dispersed in DMSO by ultrasonic treatment (b)

Table 1 Composition of the polymer nanocomposites prepared in this study, and temperatures and velocities of the polymerization fronts

Sample	CNC Concentration (wt% referred to NVCL)	T_{max} (°C)	V_f (cm/min)
FP1	0	101	0.30
FP2	0.2	113	0.33
FP3	0.5	120	0.33
FP4	1.0	114	0.33
FP5	2.0	117	0.37

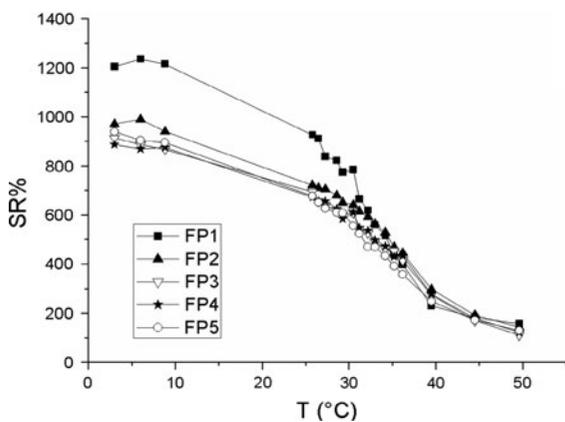


Fig. 2 SR% as a function of temperature for samples containing different CNC amounts (see Table 1 for compositions)

interference of cellulose nanocrystals in the crosslinking process within the polymer matrix (Sanna et al. 2012b). Moreover, the introduction of CNC in PNVCL hydrogels does not influence the LCST, located around 33–34 °C, a temperature that is very close to that of the human body.

The morphological characterization of the obtained nanocomposite polymer hydrogels were carried out by FESEM analysis. Unfortunately, by this technique it was not possible to detect the presence of nanocrystalline cellulose. In Fig. 3, FESEM images of the neat polymer (sample FP1, Fig. 3a₁, a₂) and of the corresponding nanocomposite containing 0.2 (sample FP2, Fig. 3b₁, b₂) and 0.5 wt% (sample FP3, Fig. 3c₁, c₂) of cellulose nanocrystals, respectively, are reported. It can be seen that all the samples analyzed show the porous structures typical of hydrogel systems (Alzari et al. 2009; Sanna et al. 2012a, b).

The results of rheological analysis in terms of storage (G') and loss (G'') moduli are reported in Fig. 4. As can be observed, G' is always higher than G'' for pristine PNVCL and all nanocomposites in the whole frequency range, thus indicating that the material response is prevalently elastic.

As expected, nanocomposites have higher moduli than pure PNVCL, which increase with the CNC concentration. The effect on G' is more pronounced and this is due to the mechanical behaviour of CNC, which is characterized by high stiffness and therefore

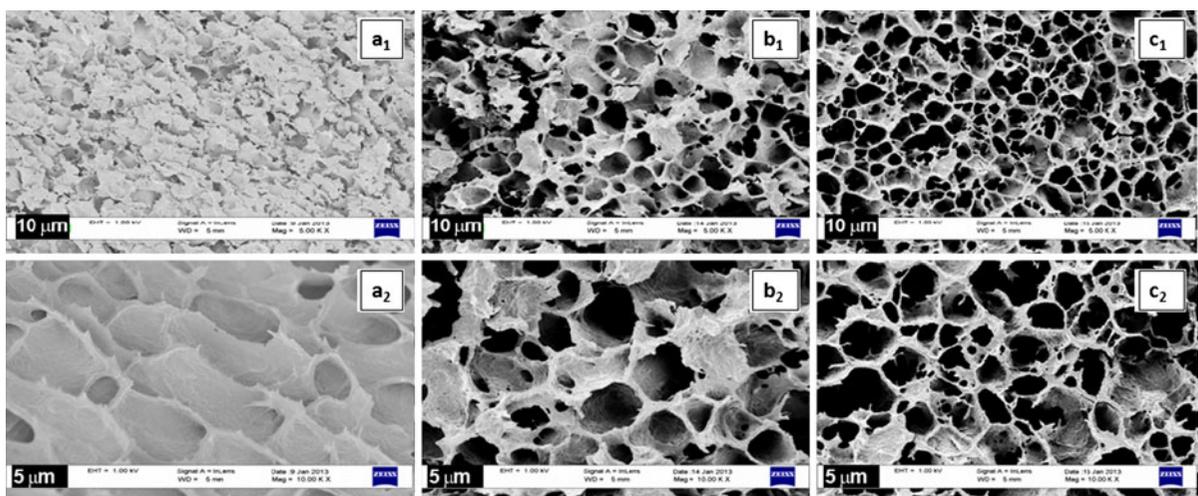


Fig. 3 FESEM micrographs of: PNVCL (a₁ ×5,000, a₂ ×10,000, sample FP1), b PNVCL-0.2 wt% CNC (b₁ ×5,000, b₂ ×10,000, sample FP2), and c PNVCL-0.5 wt% CNC (c₁ ×5,000, c₂ ×10,000, sample FP3)

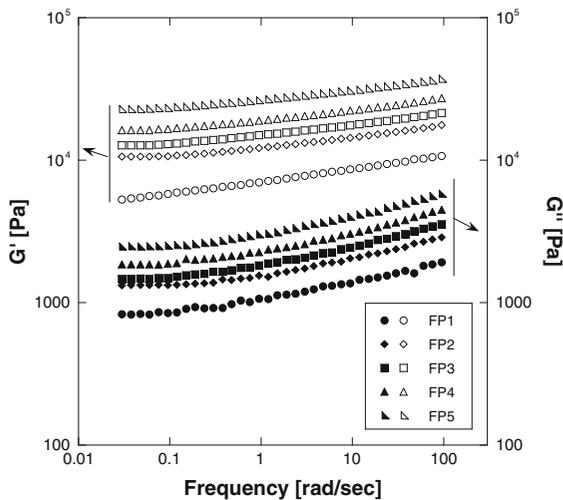


Fig. 4 Storage (G') and loss (G'') moduli behavior as functions of frequency

low viscous response (Fortunati et al. 2012a, b). The increase in G' confirms that cellulose nanocrystals act as reinforcement of PNVCL hydrogels improving their stiffness.

It is important to note that at low frequencies the viscoelastic properties of the nanocomposites deviate from the PNVCL behaviour; indeed, they have a pronounced solid-like behaviour with a clear tendency to reach a plateau for both G' and G'' . This is probably due to the CNC–CNC and PNVCL–CNC interactions that are responsible for the formation of an interconnected structure (Pötschke et al. 2002) that strongly affects the viscoelastic properties of the hydrogel matrix. In fact, cellulose nanocrystals are nanoparticles with high aspect ratio, this allows the formation of a network that induces the solid-like behaviour. On

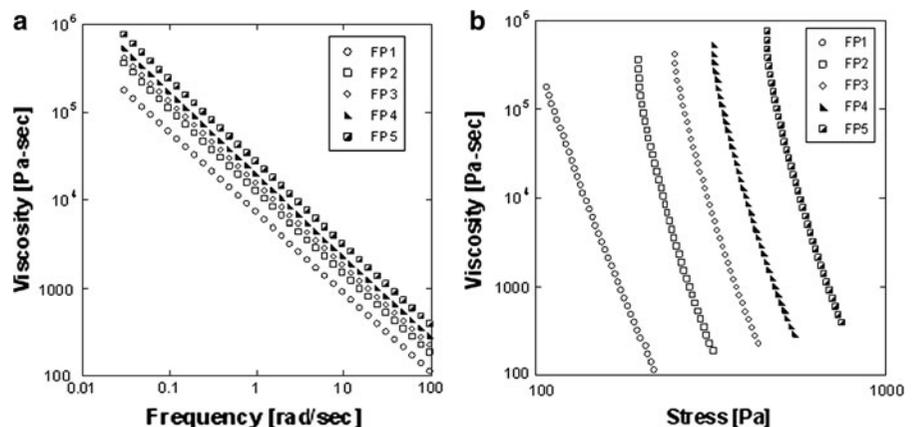
this respect, it should be reminded here that several authors observed the same behaviour in other systems reinforced with nanoparticles having high aspect ratio (Lin et al. 2005).

In Fig. 5, the complex viscosity curves are reported. The viscosity of CNC-filled formulations is higher than that of the pristine hydrogel and, as expected, increases with the cellulose nanocrystal concentration (Fig. 5a).

The analysis of the complex viscosity as a function of stress confirms that the CNC dispersed into the matrix generates an interconnected structure that strongly affects the viscoelastic response of the hydrogel hindering the mobility of the network of hydrogel chains. In fact, in Fig. 5b it is possible to observe that nanocomposites show a clear deviation from the matrix behaviour with an asymptotic tendency indicating the presence of a yield stress for these formulations. Several authors (Abbasi et al. 2009; Mobuchon et al. 2007; Rignot et al. 2005) previously observed the presence of yield stress in nanocomposite systems with an interconnected structure, suggesting that this kind of structure is present also in the analyzed systems.

This rheological behaviour also suggests that CNC are well dispersed into the hydrogel matrix; in fact, agglomerated systems with low aspect ratio have lower tendency to induce solid-like behaviour and yield stress, with the consequence that these phenomena became relevant only at high filler concentration. In the present case, solid-like behaviour and yield stress are observed also at very low concentration (0.20 wt%) and became more relevant when the CNC content increases, suggesting the presence of low filler

Fig. 5 Results of complex viscosity from frequency sweep tests: **a** viscosity versus frequency curves; **b** viscosity versus stress curves



agglomeration (Wagener and Reisinger 2003; Koo et al. 2003).

Conclusion

For the first time, FP was successfully exploited for the preparation of PNVCL hydrogels containing CNC. This very easy technique was chosen because is considered “greener” than most of the classical methods in that it is faster and requires only very low amounts of energy.

Moreover, CNC was easily prepared by microcellulose hydrolysis, and its formation was confirmed by TEM.

The resulting PNVCL nanocomposites were characterized by thermoresponsive behavior, showing an LCST located at ca. 33–34 °C, a value that is closer to the physiological one than that of PNIPAAm itself. However, if compared with this latter, PNVCL is a much safer and cheaper polymer and should be preferred especially in biomedical applications. The presence of CNC resulted in a significant increase of the mechanical properties even at very low CNC concentrations, as confirmed by rheological tests.

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