Effect of Ethyl Ester L-Lysine Triisocyanate addition to produce reactive PLA/PCL bio-polyester blends for biomedical applications

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Abstract

We report in this paper the effects of Ethyl Ester L-Lysine Triisocyanate (LTI) on the physical-mechanical properties of Poly(lactide)/Poly(ε-caprolactone) (PLA/PCL) polyesters blends. The PLA/PCL ratios considered were 20/80, 50/50 and 80/20 (wt/wt %) and LTI was added in amounts of 0.0-0.5-1.0 phr. PLA and PCL reacted with LTI during processing in a Brabender twin screw internal mixer to produce block copolymers in-situ. The resulting blends have been characterized by torque measurements, uniaxial tensile tests, Differential Scanning Calorimeter, contact angle measurements with a Phosphate Buffered Saline (PBS) solution, ATR analysis and morphological SEM observations. Experimental results highlighted how LTI enhanced interaction and dispersion of the two components, resulting into a synergic effect in mechanical properties. Mechanical and physical properties can be tailored by changing the blend composition. The most noticeable trend was an increase in ductility of the mixed polymers. Besides, LTI decreased blend's wet ability in PBS and lowered the starting of crystalline phase formation for both polymers, confirming an interaction among them. These reactive blends could find use as biomedical materials, e.g. absorbable suture threads or scaffolds for cellular growth.

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1. INTRODUCTION:

Many types of bio-polyesters have been widely used in the last years, for the growing quest of sustainable materials and for various biological applications, in which they demonstrate to be very useful. One example is their use as absorbable sutures threads or scaffolds for cellular growth of various geometries [1-3].

Among this class of thermoplastic polymers, Poly (lactide) (PLA) and Poly (ε- caprolactone) (PCL) are two of the most used polymers, well known for their bio-compatibility, bio-degradability, and environmental sustainability (especially for PLA which can be obtained from renewable resources).

PLA, when not quenched, is a brittle polymer at room temperature, due to its glass transition being about 60°C, and the situation worsen with time due to physical aging, but it shows high tensile strength if compared to other similar polyesters [4].

PCL, instead, has longer portions of CH_2 units between the ester linkages, resulting in a more flexible structure and a lower glass transition temperature (about -60°C). This results in a rubber-like thermoplastic material with one of the highest ductility of its class [3,4].

The complementary characteristics of the two polyesters have given rise to a plethora of studies to obtain blends of PLA and PCL that could take advantage of their best properties. For applications, it would be highly desirable to obtain high yield stress and maximum stress in tensile conditions, moderate Young's modulus and high ductility [5,6].

However, the main problem to overcome is the very poor miscibility of PLA and PCL in the molten state, due to the high interfacial energy between the two macromolecules, that results into a "coalescence effect" and a very low dispersed morphology [1,2].

It has been proved that the dispersion is also strictly related on the processing method, and some physical blends with good dispersion of the PCL phase in the PLA matrix were obtained by injection molding [7].

Another possible mean to achieve good blends is the use of compatibilizers, such as "triblock" or "diblock" copolymers of the two polyesters, but this may require rather costly synthesis to achieve the right balance of the blocks for a given blend. [1,8].

A further method with a lower overall cost and high effectiveness is the "reactive mixing". It consists in adding specific chemical agents, which can generate new chemical species during the thermo-mechanical processing of the materials. The chemical agents added to the blends can

react with both polymers, creating 'in-situ' block copolymers that can act as phase-compatibilizer, sensibly lowering the interfacial energy between the two polymeric components and favoring their blending [3].

Other authors had already employed essential amino-acids derivates such as Ethyl Ester L-Lysine Triisocyanate (LTI) as reactive agents, to bring compatibilization between the two aliphatic polyesters. All of these studies demonstrate how, even at low amounts of LTI, the toughness of the blends, can be sensibly increased [4,9-10]. They have used different LTI amounts, generally 0,15-0,3-0,5 phr, but also higher amounts, such as 1 phr, and 2 phr, which, to our knowledge, is the maximum amount of this reactive agent used till now. The aim of their studies was the toughening of PLA and the improvement of both impact and bending strength, for generic applications.

The biocompatibility of lactide-caprolactone structures obtained by reaction with LTI has been confirmed by other studies on the characterization and synthesis of co-polyester-urethane networks for medical purpose and application [**11-13**]. In order to have an optimal performance of these materials, it's very important that also their degradation products are nontoxic and biocompatible. Robson et al. [**14**] have observed that the ultimate degradation products of bioabsorbable PLA-urethane based composites (such as L-lysine and lactic acid) are nontoxic. Schreader at al. [**15**] highlighted the wide range of *in-vivo* applications of polyurethane based polymers (for scaffolds, hard tissue replacement, and biocompatible bone adhesive); both the *in-vitro* and *in-vivo* tests gave good results in terms of normal cells growth and immunological response. Zhang et al. [**16**] have suggested as well that a lysine diisocyanate based polymer is biodegradable and biocompatible, so that it can have biomedical applications.

Lactide-caprolactone structures could be employed in orthopedics field. One of the most common and most relevant problem in orthopedics is represented by infections, and consequent bio-film formation on the part, which can contribute to severe septic phenomena. A material showing proper mechanical characteristics, but able to biodegrade, could then be used as bone-implant and drug-delivery system (for instance an appropriate antibiotic delivery) without these issues.

Furthermore, to have an appropriate alternative to metals that is able to biodegrade, could avoid further surgeries targeted to remove the implant, which in some cases can be a source of concern for the patient. For those reasons a blend of bio-polyesters with proper mechanical

characteristics and long term dissolving feature, could prove very useful for this application. Improved mechanical properties in terms of strength and of stiffness, can be obtained by cross-linking with a polyfunctional compatibilizing agent, such as the LTI, and/or with a filler composed by nanoparticles like hydroxyapatite. A grade of entirely laevogyrate Poly(lactide) (PLLA) could also be used since its elastic modulus value is in the range of 4GPa [17].

The change in mechanical properties of polymer blends and polymer composites is commonly analyzed by bulk analyses, such as static tensile mechanical tests. However, it can be also detected by local surface measurements techniques, such as the nanoindentation one [18]. For example Pillin at al. [19] highlighted that nanoindentation can be more accurate to detect changes in mechanical properties than macroscopical tests because during the degradation of PLA, low molecular weight chains diffuse toward interfaces and are preferentially located at the surfaces probed by this technique.

In the literature however, at present there is a lack of a deep physical and mechanical characterization of these reactive blends as a function of their composition. Generally, mechanical investigation on bio-polymers, pure or in blend, is very important in order to know key mechanical characteristics such as yield strength, modulus, toughness, and fracture properties [9, 20-21]. For these reason, we undertook a systematic study of the PLA/PCL blends, pure and with different amounts of LTI added, in various compositions. We have studied torque values on the mixer screws during mixing, mechanical tensile properties, thermal behavior, and wet ability in a fluid simulating the animal tissues conditions (Phosphate Buffered Saline Solution or PBS). The change in chemical structure has been followed by FT-IR and the dispersion of the two polymeric phases has been observed by SEM microscopy. Our aim was to control the microstructure of these reactive blends, and hence the macroscopic features of these materials, by setting and tailoring their composition. The results obtained can give a better understanding of the physic-mechanical properties of these blends and help for their correct *application in the biomedical field.*

2 - MATERIALS AND METHODS

2.1 Materials

PLA/PCL, i.e. blends and PLA/PCL/LTI reactive blends (obtained by adding the reactive compatibilizing agent in various amounts), were produced from:

-Poly(lactide) – code: PLA (solid pellets, BioFlex- 6510 supplied by FKUR($\overline{M}_n$ = 197000 Da);

-Poly (ε-caprolactone)-PCL (solid pellets, purchased from Sigma-Aldrich (IT) $\overline{M}_n$ = 80000 Da);

-Ethyl Ester L-Lysine Triisocyanate- LTI (Liquid, optical purity 80, purchased from Infine Chemicals ltd).

The polyesters were dried at 50°C overnight before processing; LTI was used as received.

The Phosphate Buffered Saline solution (PBS, purchased from Sigma-Aldrich) was obtained by dissolving a tablet composed by phosphate salts in 200 mL of distilled water.

2.2 Blends and sample preparation

Materials were first mixed in an internal mixer, the Brabender Plasticorder PL200 at 180 °C, 25 rpm for 15 minutes; the reactive blends were obtained by adding LTI 5 minutes after the mixing started in the Brabender, following the conditions described by Tuba et al. [**9**]. Those processing parameters represent the less demanding but still effective conditions described in the literature to obtain PLA-based reactive blends, since its well-known sensitivity to thermo-mechanical degradation.

All solid blends were compression molded at 180°C and 100 bars for 10 minutes by a hot press inside a stainless steel mold of 12cmx 12cm dimensions, 1 mm thickness (Campana s.r.l.), with teflon releasing films (126 microns thickness) supplied by P.A.T.I. srl, and then cooled by a water cooling system. The tensile test samples were obtained by a Ray-Ran cutter in conformity with ASTM D-638 standard for sample shapes.

Blends of various composition of polyesters (wt. %) and various amounts of LTI in phr (per hundred resin, 0.0 phr or un-compatibilized, 0.5 phr and 1.0 phr) were produced and the components identified by a code containing "A" for PLA , "C" for PCL , and "T" for LTI . Each letter is followed by a number, which indicates the percentage of the polymer and the LTI phr amount. A100 and C100 samples are pure PLA and pure PCL; they have been processed in the

Brabender mixer in the same conditions of the blends. All the blends produced and studied are listed and codified in Table 1.

Table I – Blends code

Code	PLA (wt.%)	PCL (wt.%)	LTI (phr)	Torque at 15 minutes (N*m)
A100	100 (pure)	0	-	9.02
C100	0	100 (pure)	-	6.54
A80C20	80	20	0	7.56
A80C20T05	80	20	0,5	12.79
A80C20T1	80	20	1	20.94
A50C50	50	50	0	7.44
A50C50T05	50	50	0,5	10.44
A50C50T1	50	50	1	14.18
A20C80	20	80	0	6.74
A20C80T05	20	80	0,5	8.94
A20C80T1	20	80	1	10.26

2.3 Characterization and testing

Torque measurement during mixing is an index of the changing viscosity of the blends in the molten state; it was read and recorded by the Torque transducer of the Brabender Plasticorder PL2000, interfaced with the PC Brabender software. It provided torque values expressed in N*m every 30 s, for all the 15 min duration of the mixing process.

Uniaxial tensile tests were conducted by Lloyd LR10K universal testing machine, following the standard ASTM D638-10 with type V specimens and crosshead speed of testing of 10 mm/min. This was found to be the ideal speed of testing for all the blends made, considering the great difference in ductility between the two pure polyesters. The mechanical parameters investigated were: Young modulus (E, MPa), stress at yielding (σ_y, MPa) stress at break (σ_b, MPa) and maximum stress (σ_{max}, MPa), elongation at yielding (ε_y, %) and at break (ε_b, %), and the work at break (W_b, J).

Wet ability measurements were obtained using the "Sessile drop method" using a prototype of the "Polymer laboratory" at University of Messina. Drops of 5μLof the Phosphate buffered saline (PBS) solution prepared in advance of the testing were deposited on the sample surface. Each drop image was measured by means of the software Image J [22].

FT-IR and ATR spectroscopic analyses were conducted using a Shimadzu FT-IR, on films of about 50 microns in thickness. 64 scans from 600 to 4000 cm^{-1} were acquired with a resolution of 4 cm^{-1}.

Thermal analyses were conducted by means of Differential Scanning Calorimetry using a TA Instruments DSC Q100, from room temperature to 200°C, with a heating rate of 10 °C/min and water cooling. The crystalline degree of PCL, χ, was calculated using the following equation:

$$\chi = \frac{\Delta H_m}{\varphi \cdot \Delta H_0} \qquad (1)$$

where ΔH_m [J/g] is melting enthalpy, φ is the weight fraction of the studied material and ΔH_o [J/g] is the theoretical enthalpy of fusion of a polymer crystal of infinite extension [9].

Initial crystalline fraction of PLA, χ_i, was calculated using the following equation:

$$\chi_i = \frac{\Delta H_m - \Delta H_{cc}}{\varphi \cdot \Delta H_0} \quad (2)$$

where ΔH_{cc} [J/g] is the "cold-crystallization" enthalpy of PLA,. Cold crystallization is due to the well-known phenomenon of PLA re-organization in more ordered regions induced by the thermal heating of DSC test [9]. For this reason equation 3 has been used to calculate the crystalline degree of the cold crystallized PLA (χ_{cc}):

$$\chi_{cc} = \frac{\Delta H_{cc}}{\varphi \cdot \Delta H_0} \qquad (3)$$

Finally, Scanning Electron Microscopy (SEM) images were obtained using a FEI Quanta FEG 450 microscope operating with an accelerating voltage of 5 kV in low vacuum mode and placing the samples on aluminum holders by means of a graphitic adhesive.

3 - RESULTS AND DISCUSSION

3.1- Torque measurements during the blend mixing

Torque values during mixing are strictly related to the melt viscosity of thermoplastic materials; a change in these values during time suggests modifications in the structure of the polymers, for instance in the molecular weight or, generally, in the macromolecular structure.

In **figure 1,a** torque value *vs* mixing time of all the un-compatibilized blends is shown. Torque values are low and constant for "rich in PCL" blends (C100, A20C80 and A50C50), around 6-7 N·m); in pure PLA sample(A100) it became the highest one (9.02 N·m) with a rapid decrease during time. A similar but less rapid behavior is shown in the "rich in PLA" blend (A80C20). So, two different trends are evident, due to the higher thermo-mechanical degradation resistance of PCL with respect to PLA. Thus PLA confirmed to be susceptible to thermo-mechanical degradation, most likely due to degradation in its molecular weight with time. In **figure 1,b** torque values of the A50C50 blend before and after the addition of different amount of compatibilizer (LTI) are plotted. In this case, the presence of compatibilizer induces a great increment of all torque values (as indicated by the arrow in the graph) that increases with the addition of higher amounts of LTI, suggesting the formation of high molecular weight compounds in the blend. In **table I** are listed the torque values after 15 minutes of processing for all the investigated blends. Experimental data indicate that the changes are proportional to the LTI amount. Similarly, the other blends (A20C80 and A80C20) show a progressive increase in torque values with increasing the LTI amount (see **table I**). The graphs, not shown for brevity, confirms again the formation of a higher-molecular weight component in all the blends.

3.2- Mechanical features of the blends

Table II lists the mechanical parameter values of pure materials. Pure PCL (C100) has a great ductility, with elongation at break values (ε_b) of about 1400%. Instead ε_b decreased of ~15 % in pure PLA (A100), which has higher stiffness than PCL (~ 8156 MPa and ~150 MPa, respectively).

Table II- Mechanical parameters of pure materials

Code	E [MPa]	ε_y [%]	σ_y [MPa]	σ_{max} [MPa]	ε_b [%]	σ_b [MPa]	W_b [J]
PLA	640	9,05	28,09	28,09	35,42	20,62	0,30
Stand. dev.	± 63	± 0,9	± 2,13	± 2,13	± 3,1	± 1,83	± 0,03
A100	816	6,07	22,36	22,36	14,89	15,23	0,08
Stand. dev.	± 76	± 0,5	± 1,74	± 1,74	± 1,2	± 0,89	± 0,008
PCL	155	19,5	10,94	42,36	1518	-	-
Stand. dev.	± 12	± 1,9	± 0,9	± 2,76	± 155	-	-
C100	154	19,46	14,00	43,00	1405	39,82	10,81
Stand. dev.	± 14	± 1,4	± 0,59	± 1,04	± 46,37	± 1,19	± 1,03

Table II lists the mechanical tensile parameters of PLA and PCL (not processed) and processed in the Brabender Plasticorder (A100 and C100).PLA is susceptible to thermo-mechanical degradation, since it becomes even more brittle after processing. This is suggested by the increase in stiffness (from ~640 MPa to ~816 MPa), the decrease in deformability (from ~35% to ~15%) , in strength (from 20 MPa to 15 MPa) and in yielding (from 28 MPa to 22 MPa). Instead PCL retained its features after its processing confirming its high thermo-mechanical degradation resistance.

In **figure 2** the stress/strain curves of pure materials and of un-compatibilized blends are plotted in order to observe their difference in tensile behavior. In particular blends rich in PCL (as the A20C80 blend), exhibit a great ductility, with elongation at break values of ~850 %. Instead elongation at break decreases up to values of ~12% in PLA rich blend (as the A80C20 blend). Young modulus is much higher in PLA-rich blend than in PCL one (~380 MPa and ~150 MPa, respectively),as expected. The A50C50 blend has got intermediate properties.

In **table III**, the mechanical parameters of each blend before and after the addition of 0.5 and 1.0 phr of LTI are reported. The presence of 1 phr of LTI greatly improves all the properties of the three polyester blends, as suggested by the percentage variation of mechanical parameters (indicated in the table by the symbol: $\delta_{Pure-T1}$), calculated as difference between each parameter value of pure samples subtracted to the same parameter value of T1 blends.

These changes occur in all the blends but are particularly evident in the blend A50C50, where the mechanical features of the un-compatibilized blend where, as expected, the worse in the series due to the immiscibility of the PCL and PLA (see data in **table III**).

In particular, the A50C50T1 blend exhibits significant enhancements in yield stress (of 145%), deformation at yield (of 438%), elongation at break (of 6254%),and work of fracture (of 28500 %).

It should be also considered that, as LTI can react randomly with both PCL and PLA, the probability to form a block copolymer having at least one PCL and one PLA (the best to actually act as a compatibilizer) is higher in the A50C50 blend, compared to the blends with higher content of PCL or PLA.

The observed improvements are due to the enhanced dispersion of one polymeric phase in the other one. This is well visible in **figure 3** where SEM micrographs of A50C50 without and with LTI compatibilizer are shown. **Figure 3a** shows big particles, circular in shape and about 12 microns wide; suggesting a polymeric phase separated from the other one due to the poor miscibility.

Table III - Mechanical properties of the blends

Code	E [MPa]	ε_y [%]	σ_y [MPa]	σ_{max} [MPa]	ε_b [%]	σ_b [MPa]	W_b [J]
A80C20	386 ± 48	$5,0 \pm 0,9$	$12,7 \pm 1,1$	$18,07 \pm 0,7$	$13 \pm 0,9$	$16,9 \pm 1,2$	$0,05 \pm 0,01$
A80C20T05	467 ± 103	$8,3 \pm 1,3$	$24,1 \pm 0,8$	$26,27 \pm 1,4$	285 ± 60	$25,1 \pm 3,2$	$2,65 \pm 0,6$
A80C20T1	506 ± 39	$8,6 \pm 0,7$	$25,2 \pm 0,7$	$34,07 \pm 1,2$	360 ± 22	$33,9 \pm 1,2$	$3,33 \pm 0,2$
$\delta_{Pure-T1}$ [%]	**31**	**72**	**98**	**88**	**2729**	**100**	**6560**
A50C50	334 ± 36	$3,9 \pm 0,7$	$7,2 \pm 0,6$	$10 \pm 0,9$	$10 \pm 2,0$	$9,6 \pm 0,6$	$0,02 \pm 0,01$
A50C50T05	264 ± 47	$27,1 \pm 8,15$	$13,2 \pm 1,1$	$21,8 \pm 2,8$	446 ± 81	$21,6 \pm 2,8$	$3,05 \pm 0,9$
A50C50T1	370 ± 51	$21,1 \pm 5,57$	$17,6 \pm 1,2$	$39,02 \pm 2,1$	646 ± 39	$38,8 \pm 2,1$	$5,72 \pm 0,4$
$\delta_{Pure-T1}$ [%]	**11**	**439**	**145**	**290**	**6255**	**306**	**28500**
A20C80	159 ± 23	$20,4 \pm 4,92$	$11,4 \pm 0,6$	$21,76 \pm 1,0$	851 ± 46	$21,35 \pm 1,2$	$4,98 \pm 0,4$
A20C80T05	179 ± 41	$20,4 \pm 2,65$	$12,7 \pm 0,7$	$35,88 \pm 3,5$	1052 ± 94	$35,53 \pm 3,5$	$9,12 \pm 1,5$
A20C80T1	211 ± 56	$16,7 \pm 1,97$	$16,4 \pm 0,4$	$51,97 \pm 2,0$	1090 ± 47	$51,75 \pm 2,1$	$10,01 \pm 0,9$
$\delta_{Pure-T1}$ [%]	**33**	**-18**	**43**	**139**	**28**	**142**	**101**

The presence of 0.5 phr (**figure 3b**) and 1.0 phr (**figure 3c**) of LTI progressively reduces the particles dimension that become of ~ 3 μm and 1 μm, respectively. The high dispersion is well visible in **figure 3c** that appears quite homogeneous; this time is also visible a stress preferential direction imposed by the spinning force generated inside the mixing chamber.

This stress preferential direction is not visible in the first micrograph (**figure 3a**) and just outlined in the intermediate picture (**figure 3b**). It is interesting to note that this stress is completely lost after the molding step for the un-compatibilized blend, while it is retained in the presence of LTI.

The blend rich in PCL (A20C80) improves in strength after addition of 1.0 phr of LTI: the σ_{max} value grows of ~139% and σ_b value grows of ~142%. Then, the blend rich in PLA (A80C20) improves in ductility after 1.0 phr of LTI addition: the σ_y value grows of ~98% , ε_b grows of ~2730% and W_b of ~6500 %.

This suggest that the main improvement brought by the presence of LTI in the blends, is mostly on ductility, for those blends that were originally brittle, and in mechanical strength for those blends which were originally ductile but weaker. The synergic effect observed between the very different properties of PLA and PCL confirms that a good dispersion and compatibility are reached.

The stress strain curves, reported in **Fig. 4,** show the considerable improvements in ductility of the three blends after the addition of 1phr of reactive agent, as indicated by the arrows.

The un-compatibilized blends are represented by a continuous line while the 1 phr compatibilized ones are represented by a dashed line of the same color. The formation of the co-polyester-urethanes acts as compatibilizer and emulsifying agent, lowering the interfacial tension between the two polyesters (PCL and PLA).

In figure 5 the photographs of the dog-bone samples before and after a tensile test, are reported. In particular we can notice the difference in color of the PCL sample (C100) that's whiter than the PLA one (A100). The A50C50 blends became progressively darker (brown color) with increasing amount of LTI. The picture of the same samples before the tensile test highlights the considerable elongation at break of the PCL sample (C100) and the improved ductility of the A50C50 blend compatibilized with 1.0 phr of LTI, according to the results shown in the graph of figure 4.

In this research, the selected grades of investigated poly(lactide) and the poly(caprolactone) are chosen to have moderate stiffness, more suitable for suture applications. It is known that the remodeling process during wound healing at the suture sites is helped by a moderate strain field on the part [13]. For this reason, a PLLA grade with an Elastic Modulus in the order of GPa could be too rigid for sutures applications [17].

The graphs shown in **Figure 6** compare some of the properties of un-compatibilized and compatibilized blends, as a function of the PCL content. The values change with the composition of the blends. The reactive mixing that occurs after LTI adding, progressively improves all the mechanical properties such as the work at fracture (**fig.6a**), maximum stress **(fig.6b)**, stress at yielding **(fig.6c)** and Young modulus **(fig.6d)**, as indicated by the arrows in each graph.

The results shown suggest that this method can be used not just for improving PLA ductility or PCL strength, but mostly widely to obtain materials within a large range of properties deriving from both the polyesters, simply by changing the blend composition.

For example, if we consider applications in the biomedical field, for soft tissues, we would require materials which show low stiffness, and high ductility. For this purpose, the formulation could be composed by higher PCL content and lower LTI amount. This formulation can grant a moderate stress field on the tissue, maintaining an appreciable tensile strength, so that these materials could be successfully employed as internal surgery sutures **[13,23]**.

If instead higher stiffness and yield strength materials are needed, for instance in orthopedic applications like bone implants in forms of scaffolds for cellular growth, blends with high PLA and LTI content would be the most suitable materials [**24**].

3.3 Thermal properties

Thermal analysis results are shown in **figure 7a,b** and given in details in **tables IV and V**.

Table IV indicates melting temperature (T_m) and enthalpy (ΔH_m) of PCL, cold crystallization temperature (T_{cc}) and enthalpy (ΔH_{cc}) of PLA, in all the studied blends. The PLA fraction shows two phase transitions which are associated to cold crystallization (at about 104-113°C) and melting. The latter is composed by two components: one due to the initial crystalline order of PLA (at ~153°C-157°C) and the second due to cold crystallized component induced during

calorimetric test heating (at about 145°C-149°C). The correspondent peaks are indicated in the graphs reported in **figure 7a.**

Table IV- Calorimetric DSC parameters of all the studied blends

CODE	PCL		PLA				
	Tm	ΔHm	Tcc	ΔHcc	Tm		ΔHm
	°C	J/g	°C	J/g	°C		J/g
A80C20	62,25	15,51	104,16	12,32	147,73	155,94	13,41
A80C20T05	62,39	17,27	107,72	12,17	148,38	156,28	13,78
A80C20T1	59,45	11,31	113,73	12,92	149,75	153,51	13,65
A50C50	64,02	39,68	103,61	7,24	146,65	155,74	9,45
A50C50T05	62,83	35,57	111,05	6,21	148,31	154,37	8,35
A50C50T1	62,08	32,43	113,05	7,11	148,88	157,14	8,33
A20C80	64,54	56,11	105,85	3,53	145,97	154,12	3,55
A20C80T05	63,63	54,19	107,44	0,89	147,01	153,99	3,37
A20C80T1	60,92	48,67	111,79	0,61	146,6	156,7	2,88

Calorimetric data highlight as the LTI presence changes the melting temperatures of both PCL and PLA. In particular, T_m value of PCL in all the blends decreases with increasing the LTI content (from about 62°C to 59°C, from about 64°C to 62°C and from about 64°C to 60°C in the A80C20, A50C50 and A20C80 blend, respectively). Also the correspondent ΔH_m decreases from ~ 15 to 11.3 J/g, from ~ 39 to ~ 32 J/g and from ~ 56 to ~ 48 J/g.

Table V– Crystalline degree of PLA and PCL in all the studied blends

Blend code	χ_{iPLA} (%)	χcc_{PLA} (%)	χ_{PCL} (%)
A80C20	1,01	11,41	54,42
A80C20T05	1,49	11,27	60,6
A80C20T1	0,68	11,96	39,68
A50C50	3,28	10,72	55,69
A50C50T05	3,17	9,2	49,92
A50C50T1	1,81	10,53	45,52
A20C80	0,08	13,08	49,22
A20C80T05	9,2	3,29	47,54
A20C80T1	8,4	2,26	42,69

Similarly, the two melting peaks of PLA change in all the blends with increasing the LTI content. For example in the A80C20 blend, the melting peaks at ~147°C and ~156°C, became ~149°C and ~153°C in the A80C20T1 blend. Or similarly, in the A20C80 blend, the peaks are initially at ~145°C and ~154°C and became ~146°C and ~157°C in the A20C80T1. Enthalpy values generally decreases (for example from 9.45 to 8.33 J/g, in the A50C50 blend, and from 3.55 to 2.88 in the A20C80 blend) while it's constant in the A80C20 blend, around 13 J/g. Due to the presence of two peaks for two different contributes, it's difficult to clearly interpret the peaks' trend of PLA melting. They also changes in shapes, as visible in the expansion of **figure 7**, suggesting a re-organization inside the material.

In the presence of LTI, the cold crystallized component for PLA decreases in enthalpy, while the melting peak increases in temperature. For example, ΔH_{cc} and T_{cc} of A20C80 blend are about 3,5J/g, and 105°C respectively and about 0,6 J/g and 111°C in the of A20C80T1 blend.

Calorimetric experimental data have confirmed that PCL has an higher crystalline order than PLA in all the studied blends, as shown in table V. In fact, the crystalline degree of PCL is generally within the range of ~42% (min) - 60 % (max) while the initial PLA crystalline degree is within the range of ~ 0.08% (min) -9.2% (max). PLA crystalline degree improved after its cold crystallization up to ~ 2.26% (min) -13.08% (max) .

These experimental results highlight an overall change in the polymeric blend structure induced by LTI presence, due to a macromolecular re-organization. This further confirm the idea that LTI creates grafted and/or cross linked structures which are reasonably more amorphous or disordered than the pure blends. In order to investigate and explain all effects induced by LTI on the crystallinity of both PLA and PCL, further investigations will be performed in blends with LTI content higher than 1 phr.

3.4 Wet-ability

Wet ability tests indicate the kind of interactions between a solid substrate and a liquid substance: the lower is the contact angle between the two, the more is their interaction. This lowers the interfacial tension and lets an absorption of liquid in the polymeric material.

For highly biodegradable materials, an higher interaction between fluid and material substrate suggests an higher degradation rate due to hydrolytic reactions, changing the material's physical

properties. Generally, the contact angle values depend on various factors like the crystalline degree of the polymer substrate, the viscosity of the liquid, the surface features on the interface, and the ambient conditions for this kind of testing; their contribution can establish liquid diffusion inside the solid material, and so its degradation rate

The graph in **Figure 8** shows how the increasing amount of PCL in the PLA/PCL blends brings an increase in contact angle regardless of the LTI amount. This is clearly related to the lower hydrophilic behavior of PCL (with respect to the PLA) due to its higher crystallinity, and to its lower amount of hydrophilic groups (the hydroxyl ones at the end of the chains and ester bonds in the macromolecules). Furthermore, in the same picture, it can be noticed how the compatibilized blends (T0.5 and T1), exhibit an increased contact angle compared to the corresponding un-compatibilized ones (T0). This can be related to the new co-polyester-urethane networks, which should have a more hydrophobic behavior due to a change in structural composition that lowers the interaction between the liquid and the substrate.

This result suggests that the degradation rate will be lower and consequently the mechanical properties will be maintained for longer time during the use of the blend in a biological medium.

The polyesters studied in this work are well known to be susceptible to hydrolytic and/or enzymatic bio absorption and their physical properties trends are coherent with the molecular weight changes during use. It is possible then to make easy drug delivery systems with good drug absorption kinetics [24-29] which can also be studied by software modeling and further description [30].

3.5 FTIR-ATR spectroscopy

Harada et al. [3], highlighted as this kind of reactive mixing brings to the formation of high molecular weight, grafted and/or cross linked, co-polyester-urethanes (see the reaction scheme of **figure 9**).

This is confirmed by the results above discussed, since it was found that the increase in the torque values, and hence in viscosity, is strictly related to the amount of LTI added, as it can be

seen in the graph of **figure 1b** and **table I** . Besides, the same data are also in agreement with the calorimetric data which suggest the formation of new structures with more amorphous (or less ordered) composition.

In order to better investigate about new structure composition, FTIR-ATR spectroscopy have been performed and discussed in the following. **Figure 10** shows the change in FTIR-ATR spectra due to the LTI addition to the A50C50 blend. The stretching of carbonyl peak, around 1722 cm^{-1} .

In the A50C50 blend, is shifted to 1720 cm^{-1} after the addition of 0,5 phr of LTI and to 1712 cm^{-1} after the addition of 1.0 phr. This confirms that new structures containing carbonyls (probably the carbamate groups -NH(CO)O-) are formed during the reactive mixing inside the mixer chamber. Carbamate groups originates from the reaction of –OH functional groups of polyesters and N=C=O functional groups of LTI.

It was expected, in particular for the highest amount of LTI, to find the characteristic peak of N=C=O at about 2270 cm^{-1}, as this amount was considered to be in excess of the available OH groups. Its absence is however desirable as unreacted isocyanate groups are highly reactive and potentially toxic.

4. Conclusions

In this paper, we have reported a study on the effect of LTI as compatibilizing agent for PLA/PCL blends. Physical and mechanical features have been studied and compared before and after LTI addition in two different amounts (0.5 and 1.0 phr). The results highlight a synergicistic effect in the blends, thanks to the improved compatibility between the two polymeric phases. Compatibility increases by increasing the LTI amount In particular, the improvement in maximum deformation and breakage work evidenced a grown in ductility, while the improvement in yield stress and ultimate tensile strength highlighted an improvement in mechanical strength of the blends.

The ratio of PLA and PCL content in the compatibilized blends, results in materials with different properties that can be useful for different applications where specific strength, ductility and degradation rates are desired.

Due to the specific mechanical and physical features shown in this paper, our materials could be employed in the biomedical field as bio resorbable suture threads. Their high ductility, in fact,

is important to allow the formation of knots with good mechanical resistance. In addition, knots must have a stiffness that can support the sealing of tissues without compromising their integrity

Torque, calorimetric and FTIR analyses all suggest the in-situ formation of a block-copolymer that acts as a compatibilizer.

Studies are in progress to check the blends stability during the application time, and to verify, their applicability in the specific as absorbable suture threads or scaffolds for cellular growth. In fact, further steps forward in applicative fields could be done by adding our reactive blends with other substances during their processing. For examples blends could be mixed with antibiotics or Vascular Endothelial Growth Factor (VEGF) with the aim to solve infections or to stimulate cellular growth. Alternatively, the use of ceramics or carbon nanofiller can give a further enhancement in stiffness and in mechanical strength for bone implants application.

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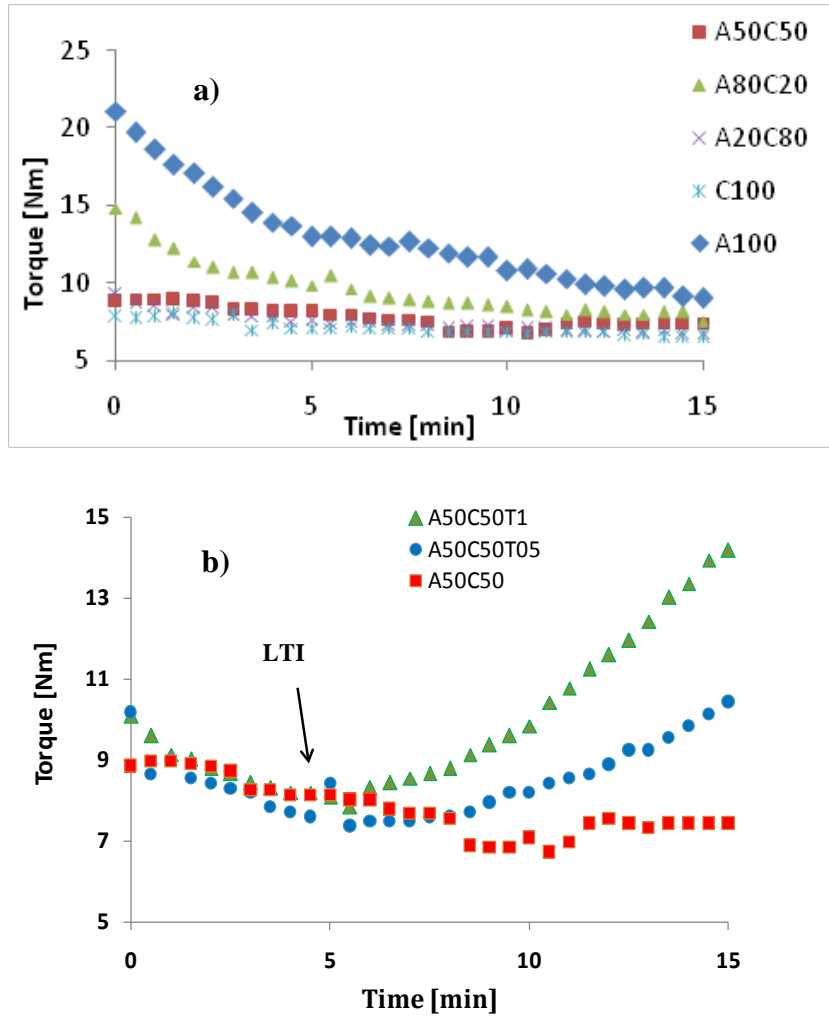
Figure 1- Torque trends during mixing time of pure polymers and blends (a); of A50C50 blend before and after the addition of different amounts of LTI compatibilizer (b).
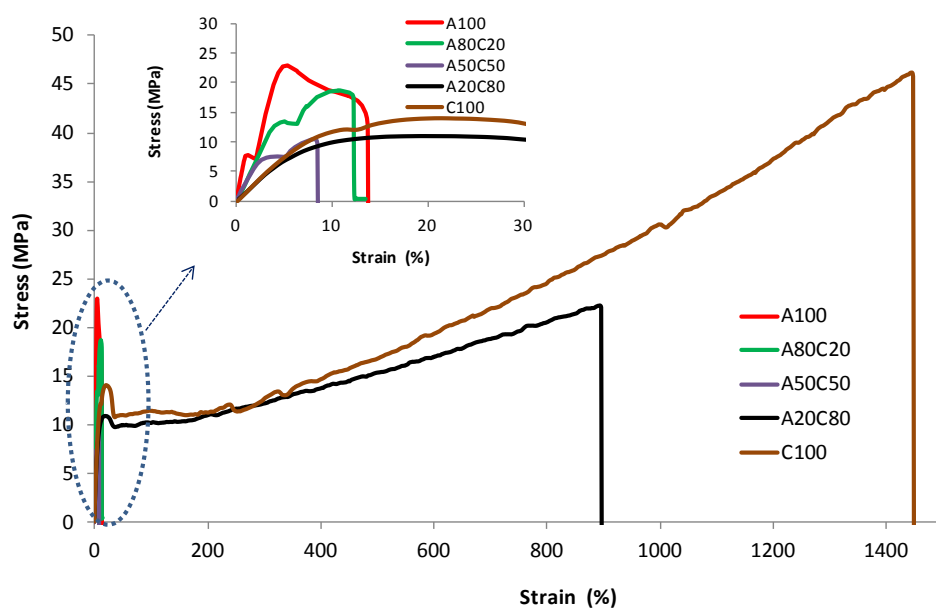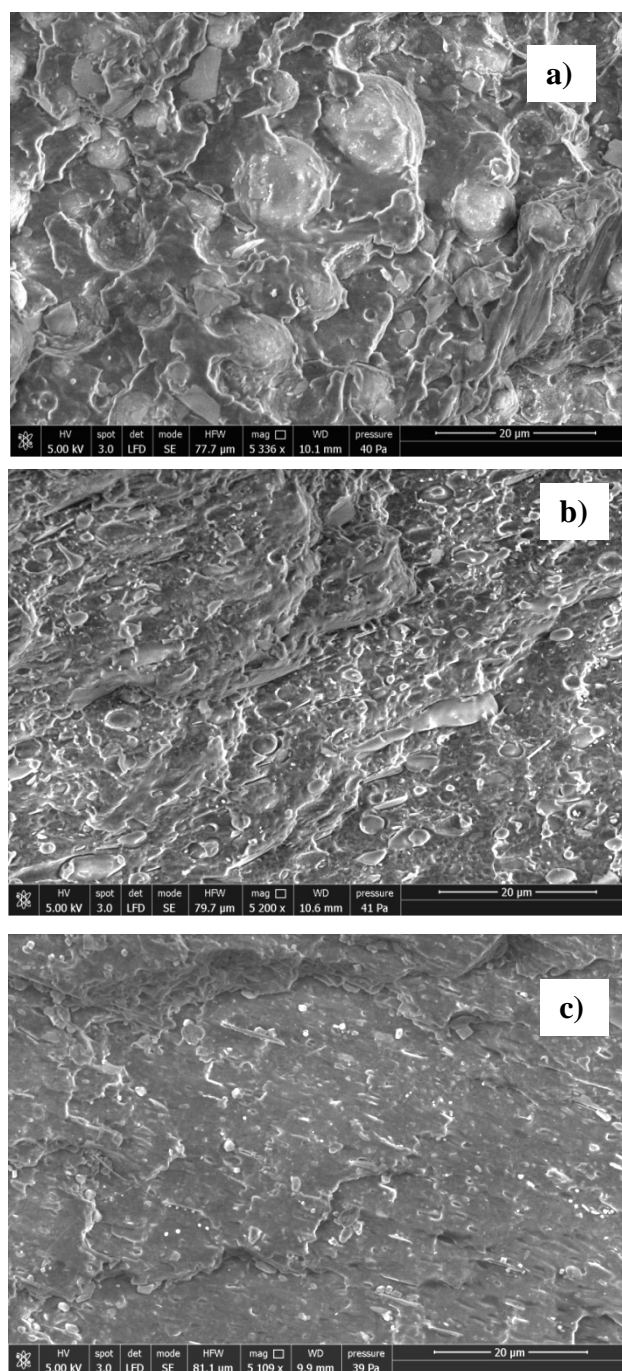
Figure 2 – Stress Strain curves for pure materials and un-compatibilized blends

Figure 3 –SEM micrographs of A50C50 blend un-compatibilized (a), and compatibilized with 0.5 phr (b) and 1 phr(c)
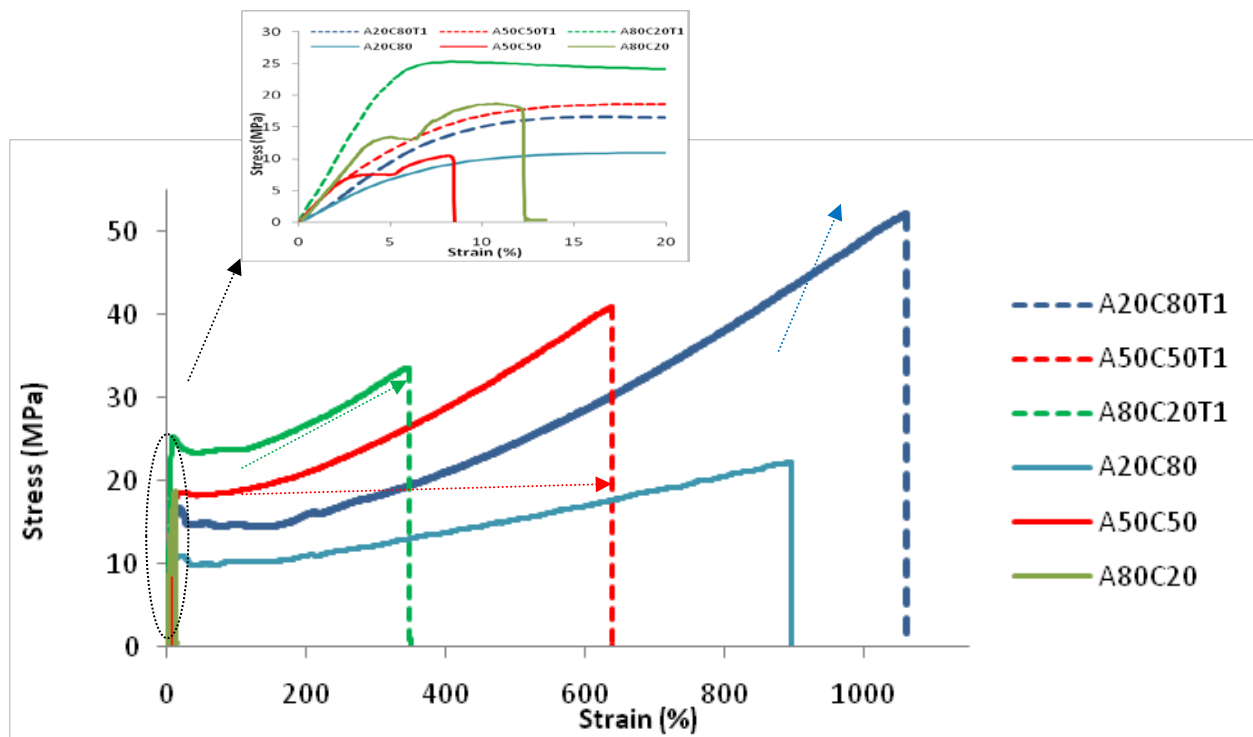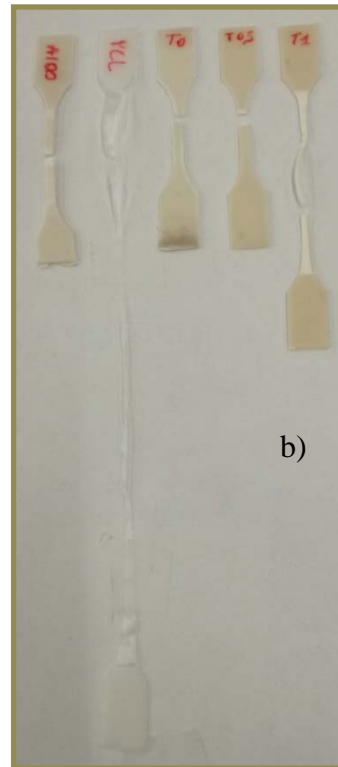
Figure 4 – Stress Strain curves for pure and compatibilized blends

Figure 5 –Image of a dog bone sample of A100, C100, A50C50, A50C50T0.5, A50C50T1.0 before (a) and after (b) a tensile test.
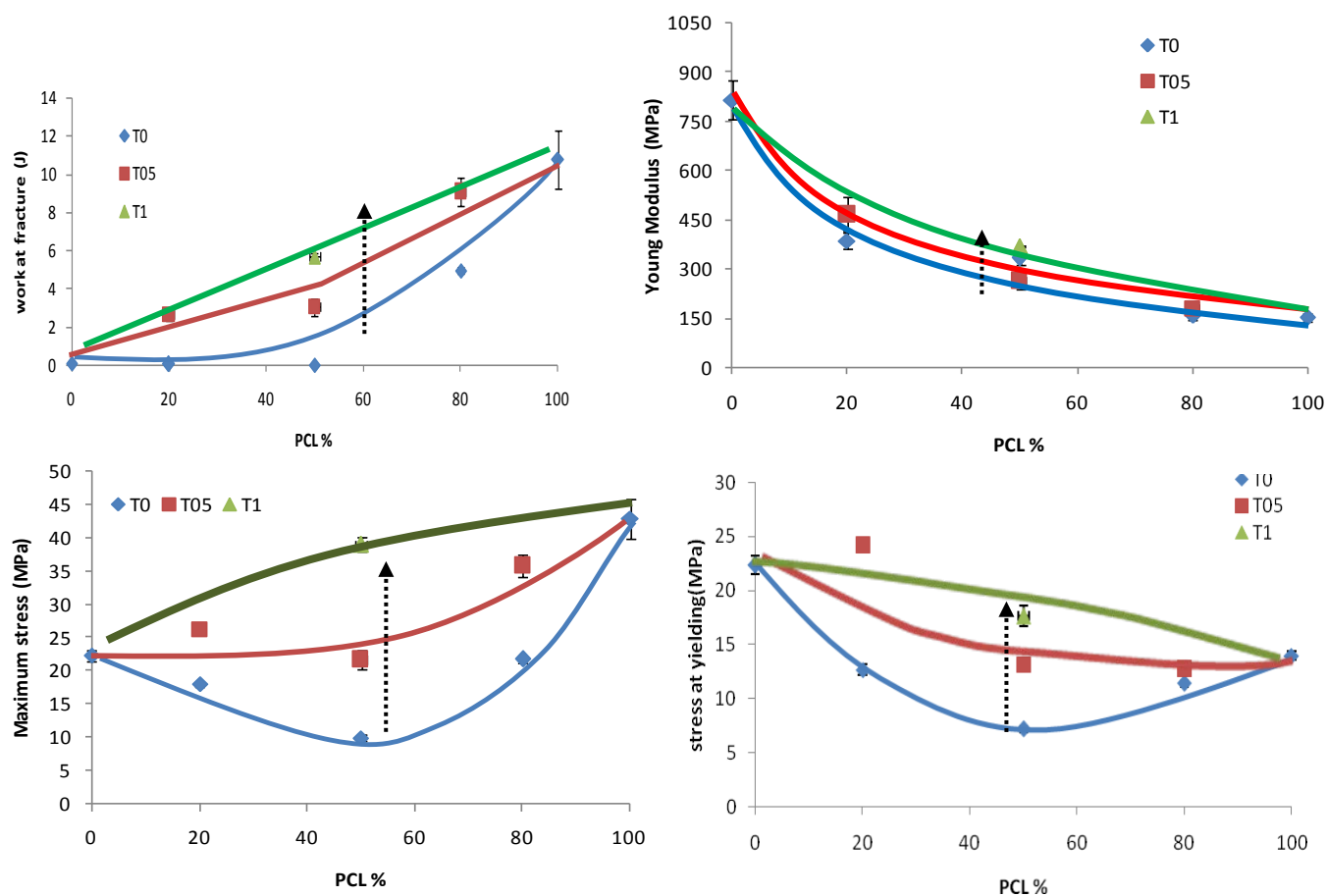
Figure 6-Work at fracture (a),Young Modulus (b), maximum stress (c) and stress at yielding (d) for all the blends (pure,T0.5 and T1) as a function of the PCL content.
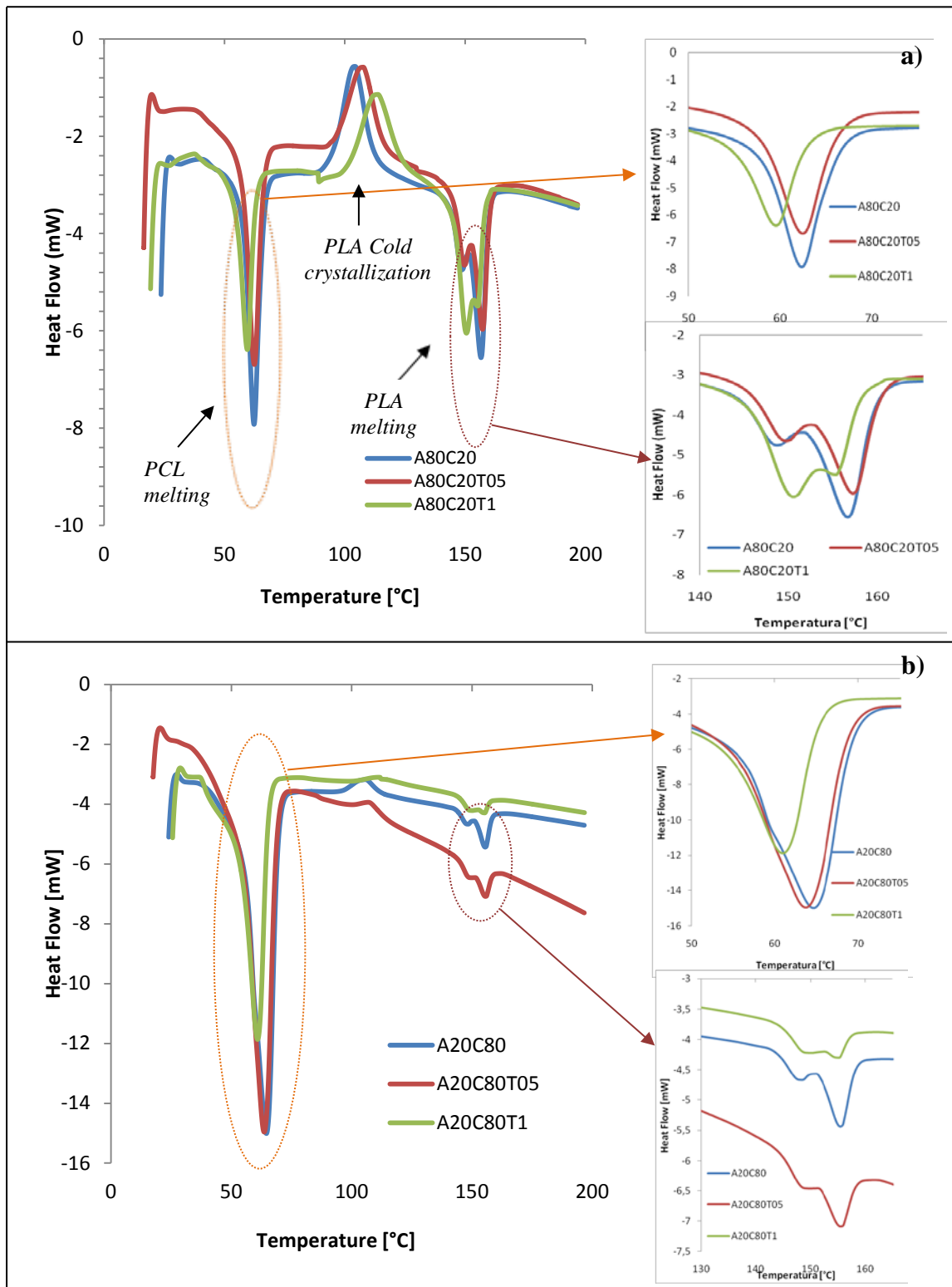
Figure 7 – DSC spectra of pure and compatibilized A80C20 (a) and A20C80 blends (b) in the left with and expansion of two peaks in the right.
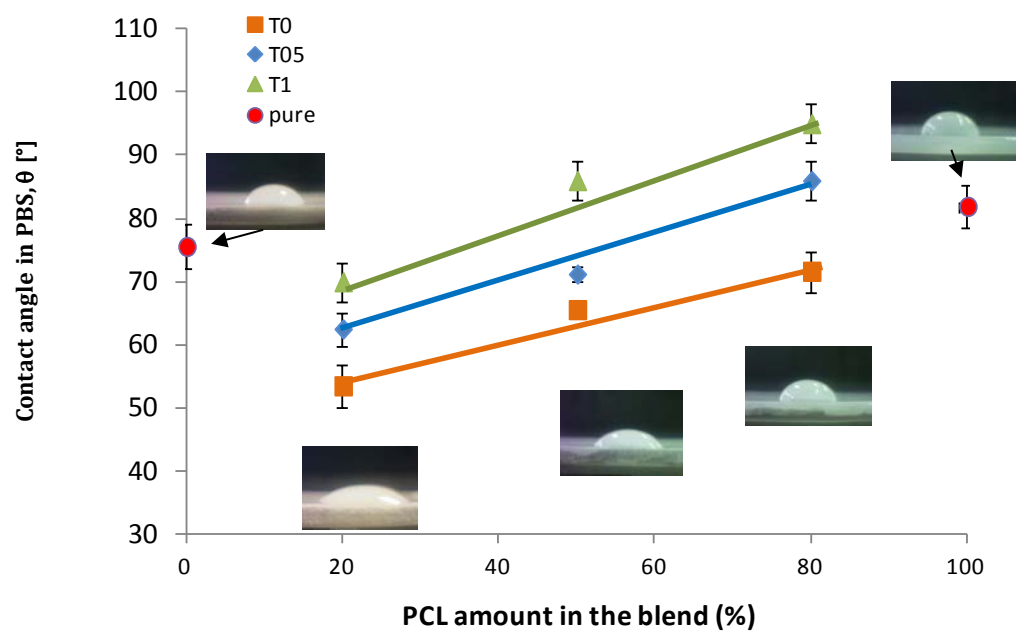
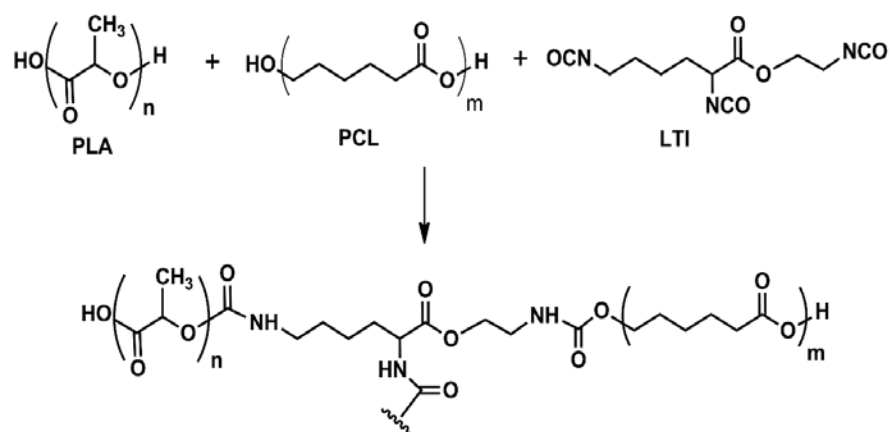*Figure 8 - Contact angle in PBS as a function of PCL amount and of the LTI amount*
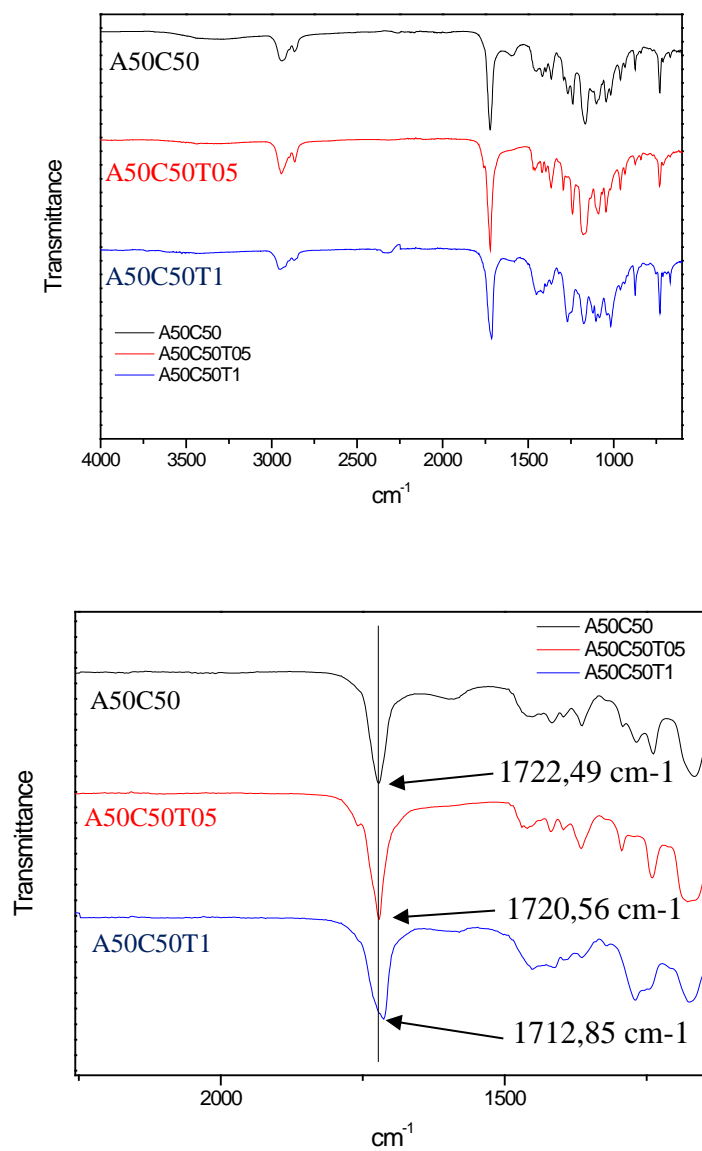
Figure 9 – Reaction Scheme for PLA - PCL – LTI

Figure 10- ATR Spectra of A50C50, A50C50T0.5 and A50C50T1