# PROCESSING BIOCOMPATIBLE POLYMER BLENDS VIA DENSE GAS TECHNOLOGY

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## Abstract

Dense gas technology (DGT) employs fluids at or near their critical point and exploits their liquid-like density and gas-like mass transfer properties to provide a more controlled and efficient method of processing polymers. Conventional methods of processing polymers have limitations such as high viscosity, low diffusivity and use of toxic and hazardous chemicals. In this work, the feasibility of using DGT for the production of biocompatible polymer blends has been investigated.

In the field of biomedical engineering the use of polymer blends is highly desired for their unique properties. Polymer blends possess unique properties which are intermediate to the components. Dense gas technology provides a green and often non-laborious method of creating these blends without the additional stages of purification and extraction. A polymer blend of a physically strong biocompatible polymer and a biodegradable polymer can offer distinctive advantages for prosthetic applications compared to the use of one single polymer. In this work bisphenol A polycarbonate (BPAPC) was used as a model polymer with strong mechanical properties and polycaprolactone (PCL) was selected as the biodegradable component.

A dense gas such as $CO_2$ is a suitable reaction medium for the polymerization of BPAPC. The synthesis of BPAPC is conducted in DG as a polycondensation reaction between BPA and diphenyl carbonate (DPC). Sodium hydroxide (NaOH) is used as the catalyst. The BPAPC synthesis generates phenol as the by-product. Phenol is highly soluble in DG; and can easily be extracted by the supercritical fluid (SCF) thus driving the synthesis of BPAPC to higher MW. In this work, operating pressures (100-200 bar), temperatures (120-150°C), and time (6-12 hours) have been varied to optimize the synthesis of BPAPC via DGT. Molecular weight analysis was carried out using Gel Permeation Chromatography (GPC) and matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF).

The blending of BPAPC with PCL was a two-step process. The first step employed DGT to synthesize the BPAPC using $CO_2$ as the reaction medium. In the second step, the BPAPC was ground into particles then embedded into PCL. Once embedded in the PCL, BPAPC was polymerized further. The BPAPC/PCL blends were characterized using thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC).

## Background

Polycarbonates are very versatile, and have been used for a variety of industrial, commercial, and medical applications. Bisphenol-A polycarbonates are aromatic PCs, which have stronger mechanical properties than aliphatic PCs. Aromatic PCs exhibit strong mechanical properties, heat resistance and unique optical clarity. The conventional synthesis of BPAPC involves the use of phosgene ($COCl_2$), an environmentally hazardous substance. Considerable research has been done on employing DG to implement alternative BPAPC polymerization routes. The formation of BPAPC occurs by transesterification, as shown in

Figure 1 and is a type of polycondensation reaction with phenol as its by product.Carbon dioxide ($CO_2$) has been used as a reaction medium in heterogeneous polymerizations such as DG melt-phase polymerization, Solid State Polymerization (SSP) and dispersion polymerization.[2-4] In all cases $CO_2$ is used to extract the by-product which is highly soluble in the DG, thus driving the synthesis towards the formation of high MW PC. Dense gas melt-phase polymerization employs melt transesterification as its reaction mechanism. In SSP, $CO_2$ acts also as a plasticizer, whilst in dispersion polymerization it is the dispersing medium. [3] [4]

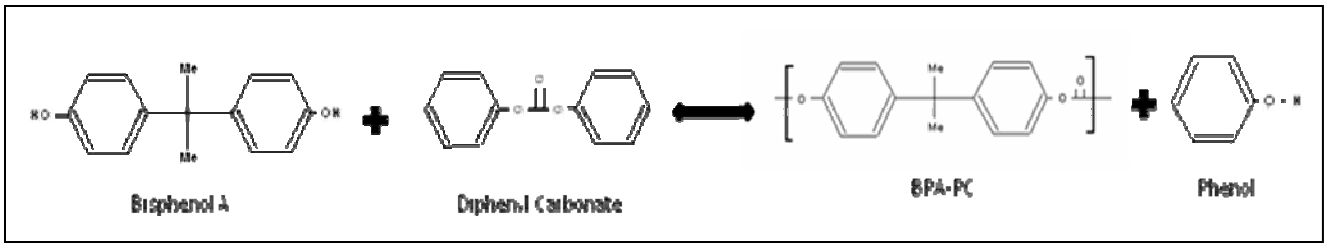


**Figure 1 - Polycondensation of Bisphenol A and Diphenyl Carbonate (Me=Methyl group)**

Polycaprolactone (PCL) is a well-known biodegradable polymer widely used in the biomedical field. It is most commonly used for tissue engineering applications because of its favourable and prolonged rate of degradation *in vivo*.[5] Dense gas processing of PCL has also been studied and the foaming of PCL with DGT has proven to create unique micro and nano-architecture. [6, 7]

Blends of two polymers, when one is biodegradable such as PCL, are referred to as bioblends. Bioblends are gaining wide interest in the biomedical field for drug delivery devices, implantable/non-implantable formulations and also in the agricultural field for materials/packaging applications.[8] The DGT is unique tool which can be used to create a bioblend of BPAPC/PCL by first synthesizing BPAPC, then blending it with PCL. Dense gas provides a polymer synthesis and processing method without the use of toxic solvents.

## Experiment Section

**BPAPC prepolymer synthesis.** Bisphenol A (99% purity), DPC (99% purity) and Sodium Hydroxide (99% purity) were used as received from Aldrich. Sodium Hydroxide (NaOH)) was used as the catalyst in a 1:10 mole ratio with both monomers. Bisphenol A and DPC were ground together in equivalent molar ratios, and then placed in a 5ml high pressure reactor with the catalyst. The reactor content was magnetically stirred and placed in a temperature controlled oil bath. Pressure and temperature were monitored by a *Druck DPI 260* pressure transducer and *WiseStir™ MSH-20D* temperature sensor respectively.

**Table 1 - Polymerization Procedure**

| **Parameter** | **Step 1: Prepolymer Synthesis** | | | **Step 2: Solid State Polymerization of BPAPC/PCL Blend*** |
|---|---|---|---|---|
| Stage | PS1 | PS2 | PS3 | SSP |
| Time (hrs) | *2* | *2* | *2* | *12* |
| Temperature (°C) | *120* | *120* | *150* | *120* |
| Pressure (bar) | *1* | *200* | *200* | *200* |
| Gas Phase | $N_2$ | $CO_2$ | | $CO_2$ |

*BPAPC prepolymer was ground and mixed with grounded PCL

The polymerization procedure is reported in Table 1. A gradual temperature and pressure transition occurred between the three stages: PS1, PS2 and PS3. The system was isolated throughout stage PS1 with 1 bar $N_2$ atmosphere. During stages PS2 and PS3 the $CO_2$ flow-rate was maintained between 0.3 and 0.5 ml/min using a metering valve. The stirring was maintained at 200 rev/min. The polymerization procedure and parameters in Table 1 were adapted from Gross *et al*. who optimized it for SSP of PC particles. [2, 3, 9] At the end of stage PS3, the BPAPC samples were analyzed by THF GPC for MW, MALDI-TOF for structure confirmation, thermogravimetric analysis (TGA) for pyrolysis profile, and DSC for heat flow characteristics. [1, 10]

**Polymerization of Blend.** The BPAPC prepolymer was ground into smaller particles using a mortar and pestle, then placed in a 5ml high pressure stirred vessel. Polycaprolactone from Sigma Aldrich (MW=14000g/mol) was also ground using a mortar and pestle, and then loaded into the same vessel. Varying mass ratios of BPAPC prepolymer and PCL were processed. Specifically BPAPC: PCL mixtures with mass ratios of 4:1, 3:1 and 2:1 were processed (Table 2). The BPAPC/PCL processed samples were analyzed using GPC, TGA and DSC.

**Table 2 - Experiment Identification**

| Experiment Label | Mass Ratio Description |
|---|---|
| BPAPC-PS | 10mg BPA:10mg DPC: 1mg NaOH |
| BPAPC80/PCL20 | 4mg BPAPC : 1mg PCL |
| BPAPC75/PCL25 | 3mg BPAPC : 1mg PCL |
| BPAPC67/PCL33 | 2mg BPAPC : 1mg PCL |
| PCL | PCL only |
| PCL-NaOH | 25mg PCL : 1mg NaOH |

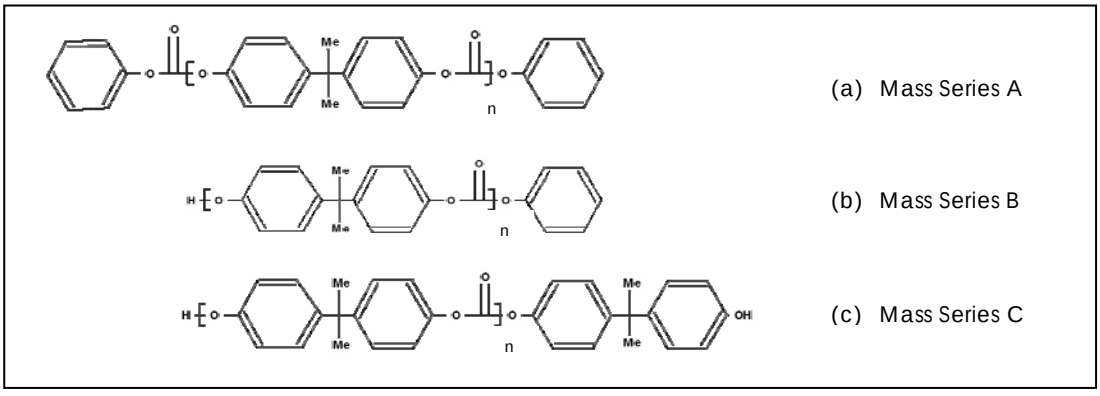


**Figure 2 - BPAPC Molecular Structure modified from Puglisi et al [1].**

**Analysis Techniques.** Gel permeation chromatograms were obtained using a *Shimadzu* GPC with tetrahydrofuran (THF) as the mobile phase. The GPC was calibrated using polystyrene (PS) standards. The MALDI-TOF spectra were obtained using a matrix solution of THF/Hydroxyphenylazo-benzoic acid (HABA), as reported by Puglisi *et al*.[1] Spectra were acquired on the *Voyager-DE™STR* and the *Voyager-DE™* in reflectron mode and linear mode. The peaks from the spectra were matched with BPAPC structures seen in Figure 2.[1] A *TA Instruments™ Hi-Res Modulated TGA 2950 Thermogravimetric Analyzer* was used with an air flow, and a gradient of 20°C/min up to 1000°C. A *TA™ Instruments DSC 2010 Differential Scanning Calorimeter* was used with $N_2$ gas flow, and a gradient of 20°C/min from -50°C up to 250°C.

## Results and Discussion

The MALDI-TOF spectra for the BPAPC-PS samples matched the BPAPC molecular structures from Figure 2, and consistently maintained equal spacing of 254g/mol (mass of BPAPC repeat unit). The existence of each of the mass series (A, B, and C), and no other unidentified peaks was a strong indication of successful synthesis of BPAPC. After exposing samples PCL-PS and PCL-NaOH-PS to the prepolymer synthesis conditions they had similar $M_w$, $M_n$ and PDI values (as seen in Table 3) to the neat PCL indicating that the polymer was relatively stable under the experimental conditions. During SSP, $CO_2$ facilitated the removal of phenol and lowered the glass transition temperature ($T_g$) of BPAPC allowing the polymer chains to be more mobile. The BPAPC prepolymer particles were embedded into PCL and allowed to polymerize further.

**Table 3 - MW of select experiments (PS=Prepolymer Synthesis, SSP= Solid State Polymerization)**

| Experiment (Material-Exposure Condition) | $M_n$ (g/mol) | $M_w$ (g/mol) | PDI |
|---|---|---|---|
| BPAPC-PS | 3400 | 3900 | 1.147 |
| BPAPC-PS-SSP | 6600 | 7800 | 1.182 |
| PCL-PS | 7300 | 12400 | 1.699 |
| PCL-NaOH-PS | 7600 | 12600 | 1.658 |
| PCL (unreacted) | 7400 | 11500 | 1.558 |

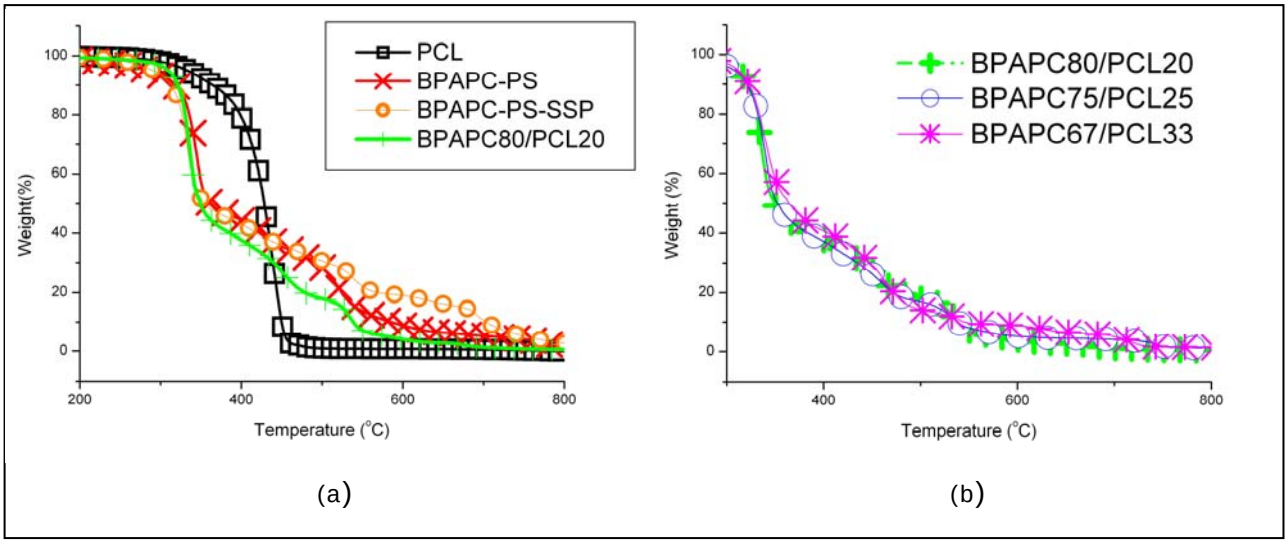


**Figure 3 - Thermal Degradation profiles from TGA.**
**(a) TGA data of PCL, BPAPC-PS, BPAPC-PS-SSP and BPAPC80/PCL20**
**(b) TGA data for BPAPC/PCL blends**

The thermal degradation profiles in Figure 3 provide information relating to the entanglement of the polymers in the blend and their temperature decomposition transition profiles. The thermal degradation profiles of the BPAPC/PCL blends (Figure 3(b)) had similar decomposition transitions as samples BPAPC-PS and BPAPC-PS-SSP (Figure 3(a)). The initial degradation of the BPAPC/PCL blends (approximately 250°C) was much earlier than neat PCL.

Differential scanning calorimetry measurements are used to obtain qualitative and quantitative information about blend characteristics. In Figure 4 (a), neat PCL clearly exhibits a low melting transition temperature ($T_m$) of 60°C. The DSC profile for BPAPC-PS (Figure 4(a)) has a noticeable release of heat at 275°C, which is attributed to the onset of its pyrolysis. Figure 4(b) provides a comparative look at the DSC curves for the three BPAPC/PCL blends between -50°C to 250°C. BPAPC-PS has a small exothermic release near 50°C which is possibly due to the exothermic release of residue phenol from the sample. Phenol has a $T_m$ of 50°C. One of the characteristics of an intimate blend between two polymers is the disappearance of one of the components' melting temperatures from the DSC profile. As seen in Figure 4(b), the melting point of PCL was absent in the DSC profiles of the BPAPC/PCL polymer blends prepared by DGT. The plasticized PCL chains and BPAPC chains could easily interact and tangle when exposed to the DG SSP operating temperature of 120°C and pressure of 200bar.

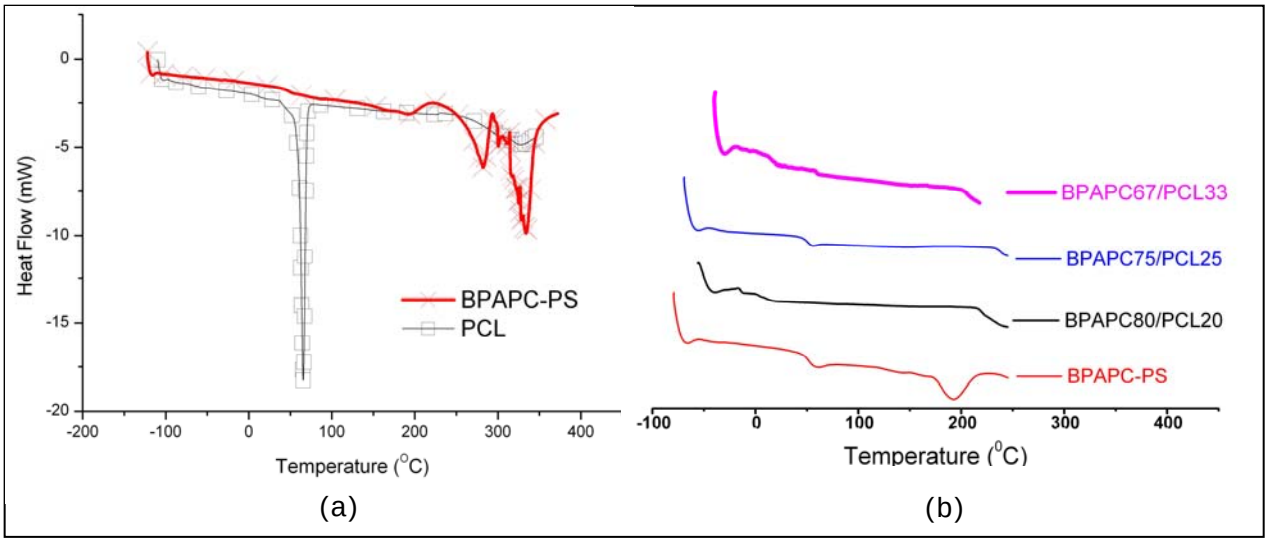


**Figure 4 - DSC curves: (a) BPAPC-PS and PCL**
**(b) BPAPC/PCL blends**

## Conclusion

Polymer blends of BPAPC/PCL have potential industrial and biomedical applications both *in vivo* and *in vitro.* The biodegradability of PCL has long been exploited to culture biological components. The applicability of PCL can be extended by enhancing its mechanical properties by creating a bioblend with a stronger polymer such as BPAPC. Using a DG such as $CO_2$ first as a polymerization medium to synthesize BPAPC, and secondly as a processing medium to create BPAPC/PCL blends, has proven to be successful in creating intimate bioblends with properties intermediate to both components. The lack of a distinctive $T_g$ or low $T_m$ on the BPAPC/PCL DSC curves support the intimate nature of the blend and proves the efficacy of the method presented in this work as a blending technique. To further prove the industrial and biomedical applicability of DG produced BPAPC/PCL blends mechanical tests must be completed.

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