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Polycarprolactone-Based Polyurethane Composite For Functional Orthopedic Implants

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POLYCAPROLACTONE-BASED POLYURETHANE COMPOSITE FOR FUNCTIONAL ORTHOPEDIC IMPLANTS

ABSTRACT

Composite materials containing polycaprolactone based polyurethane and tricalcium phosphate were created and tested. These materials are intended for use as mechanical bone implants, requiring them to be biocompatible, biodegradable, osteoconductive, rigid, and melt processable. Commercial and synthesized polyurethane were used in tests. Commercial polyurethanes were compounded with calcium phosphate up to 50wt% in melt processing. Synthesized polyurethanes were compounded with calcium phosphate up to 50wt% in melt processing and up to 5% in synthesis. Dynamic mechanical analysis revealed storage modulus and loss modulus of all materials increased with increased calcium phosphate content. The Tg of commercial polyurethane was determined to be approximately -22°C and synthesized polyurethane approximately 30°C. Tensile testing revealed the Young's modulus of all materials increased with increased calcium phosphate content. DSC revealed expected polycaprolactone thermal transitions as well as a cold crystallization transition in synthesized polyurethanes.

INTRODUCTION

Advanced implant materials for orthopedic surgery are in use and development. The importance of medical applications allows for the selection of high value materials. These materials are chosen to improve surgical outcomes and decrease recovery time. A common orthopedic implant group is bone fixation implants. These implants are designed to attach important functional materials and tissues to bones in specific places. Examples of bone fixation implants are suture anchors and tenodesis screws. Suture anchors are used in applications such as rotator cuff repair in which a detached rotator cuff muscle is fixed to the bone while it heals. Tenodesis screws are used in applications such as ACL repair in which a tenodesis screw fixes a detached ACL in a bone cavity while the tendon heals.

Bone fixation implants may be made from permanent or biodegradable materials. Common permanent materials are titanium and polyether ether ketone. Common biodegradable materials are polyethylene glycol, polyglycolic acid, and polylactic acid. Permanent implants are designed to either remain in the body or be removed. Biodegradable implants are designed to degrade over a period of time as the body regenerates the displaced tissue. The benefit of biodegradable implants is that they transfer stresses to the healing tissue, do not require removal surgery, and are less likely to cause osteoporosis like

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rigid metal implants.[1] Reducing the incidence of revision surgery dramatically reduces recovery time and number of required surgeries. Osteoconductive materials such as calcium phosphate may be mixed with the degradable material to improve bone regrowth. Calcium phosphate is very similar in structure to hydroxyapatite, the primary mineral making up bone structure. Biodegradable materials also offer a platform for drug delivery research.[2] Hydrolytic degradation of polymers such as polyglycolic acid causes the release of an acidic byproduct.[3] Reducing the release of byproducts with potential to cause reactions would improve repair quality.

Polyurethanes are a common class of materials used in biodegradable implants. The versatile nature of the carbamate linkage allows for the tailoring of important material characteristics. Their elastic and foamable nature makes them popular in many implant applications including endoprostheses, cardiac valves, and regenerative membranes.[4] Rigid biodegradable polyurethane materials are largely unexplored. Rigid polyurethanes are found in many nonmedical applications including insulation, wood substitutes, furniture, etc.[5] Polyurethanes are formed from a polyol "soft-segment" and a multifunctional isocyanate "hard segment". The mechanical properties of the material may be chosen by the size and nature of these segments. Rigidity may be imparted by increasing the relative size of disocyanate "hard-segments" or cross-linking. Additionally, chain extenders, cross-linking agents, and fillers may be added to the material. It is desirable to develop polyurethane that is biocompatible, biodegradable, melt processable, and mechanically suitable for use in a bone fixation implant.

It is proposed that polycaprolactone based polyurethane be developed as a functional implant material. The material will be made from polycaprolactonediol (Figure 1), methylene diphenyl diisocyanate (Figure 2), butanediol chain extender (Figure 3), and tricalcium phosphate filler. Polycaprolactone is known for its biocompatible and biodegradable nature as an implant material. Methylene diphenyl diisocyanate is a rigid multifunctional isocyanate that is used in existing biodegradable implant materials.[6,7] Toxicity exhibited in methylene diphenyl diisocyanate is considered as tradeoff for the rigid properties that it imparts.[8] Short polycaprolactone chains with an average Mn of approximately 530 will be used in the polyol in order to decrease the effect of the "soft segment". The molecular weight of the material will be increased using butanediol chain extender. Increasing rigidity through cross-linking is not suitable because it is prohibitive of melt processing. Increasing rigidity through large aromatic "hard segments" is not suitable because of their lack of biocompatibility, especially in a biodegradable application. Tricalcium phosphate will be used as a filler to improve the mechanical characteristics and osteoconductivity material. Filler mixing will be tested both during synthesis and melt processing. Polyurethane synthesized with no calcium phosphate is designated "0wt% synthesized polyurethane". Polyurethane synthesized with 5wt% calcium phosphate is designated "5wt% synthesized polyurethane". A commercially available polymer synthesized from polycaprolactone, methylene diphenyl diisocyanate, butanediol, and dipropylene glycol (Figure 4) will be used as a comparison and in the testing of processing and com-

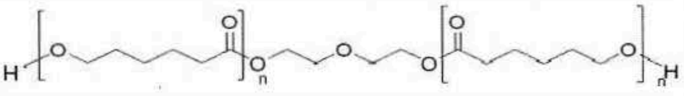

Figure 1: Polycaprolactonediol[9]

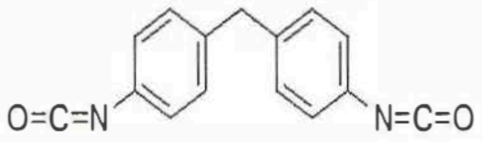

Figure 2: Methylene diphenyl diisocyanate[10]

Figure 3: Butanediol[11]

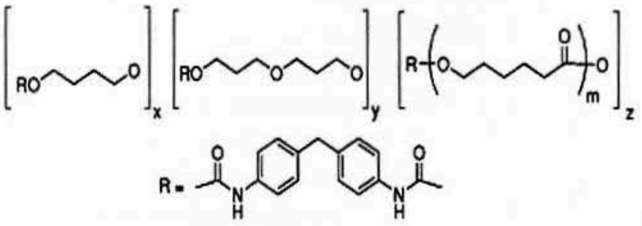

Figure 4: Chemicals contained in commercial polyurethane comparison[12]

Material	Compounding	Calcium Phosphate (wt%)	T_g (°C)	25°C Storage (MPa)	37°C Storage (MPa)	25°C Loss (MPa)	37°C Loss (MPa)
Commercial	None	0	-14.28	31.97	27.42	4.20	2.57
	Melt	0	-23.79	36.68	25.05	3.72	2.10
		5	-18.23	52.77	44.74	6.67	4.59
		10	-21.43	69.01	52.14	8.32	4.87
		20	-27.40	76.44	64.62	8.47	5.59
		30	-25.81	98.42	94.84	14.00	9.09
		40	-22.48	115.00	97.80	12.01	8.45
		50	-22.12	99.76	74.36	10.66	6.71
Synthesized	Melt	0	42.92	1391.00	199.80	163.50	180.90
		5	30.96	289.90	63.02	170.60	39.03
		50	30.76	499.60	174.00	211.30	73.83
	Synthesis	5	30.70	1078.00	55.22	404.90	83.53

Table 1: DMA results for commercial and synthesized polyurethanes

pounding. This comparison material is designated "commercial polyurethane.

RESULTS AND DISCUSSION

Dynamic Mechanical Analysis

Dynamic mechanical analysis was performed on commercial, 0wt% synthesized, and 5wt% synthesized polyurethanes. General DMA results may be found in Table 1. Commercial and 0wt% synthesized polyurethanes were tested with calcium phosphate filler content up to 50wt% through melt compounding. All samples underwent tensional strain cycling over a temperature range from -70°C to at least 50°C. All storage modulus, loss modulus, and tan δ data may be found in Appendix 8.1.

The Tg was determined as the peak maximum of tan δ. The Tg of commercial polyurethane is approximately -22°C and synthesized polyurethanes is approximately 30°C. This difference in Tg indicates that synthesized polyurethane may have a greater molecular weight than commercial polyurethane. The commercial polyurethane is also expected to have a lower Tg due to its di(propyleneglycol) component. Di(propyleneglycol) reduces the Tg of materials because it is acts as a plasticizer.[13] All materials exhibited a Tg below normal body temperature of 37°C.
No discernable change in Tg of commercial polyurethanes was observed over the range of calcium phosphate wt%. Variability in Tg between samples is attributed to differences in thermal history through melt pressing and extruding. It is notable that the Tg of 0wt% synthesized polyurethane is much higher than other synthesized polyurethane measurements. This difference may be due to an anomaly in thermal history for the sample. Compounding with calcium phosphate may reduce the polymer molecular weight by degrading the polymer chains, thereby decreasing the Tg.

The storage modulus and loss modulus of commercial polyurethane with up to 50wt% calcium phosphate were compared from -70°C to 50°C (Figure 5, Figure 6). The storage modulus and loss modulus are both seen to increase with increased calcium phosphate filler. The lower and upper storage moduli at -70°C the storage moduli are respectively approximately 2700MPa for 0wt% and approximately 4600MPa for 50wt%. The lower and upper peak loss moduli are respectively approximately 250MPa for 0wt% and approximately 410MPa for 50wt%. This increase in storage modulus and loss modulus indicates that calcium phosphate filler has a reinforcing effect on the material. The storage modulus and loss modulus were recorded at ambient room temperature of 25°C and normal human body temperature of 37°C (Figure 7, Figure 8). The storage modulus and loss modulus are both seen to increase with increased calcium phosphate filler at both temperatures.

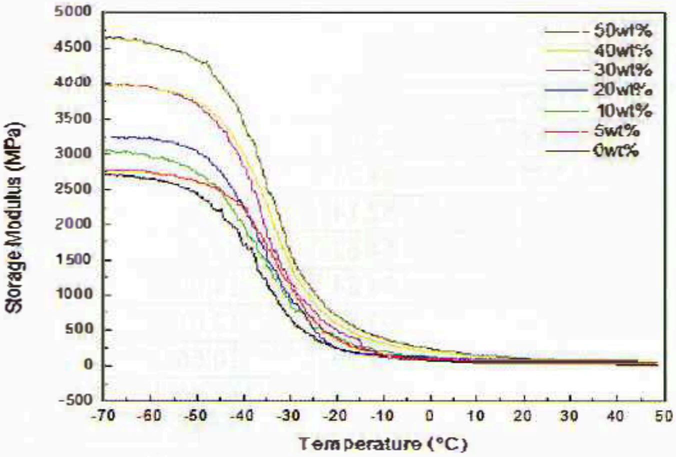

Figure 5: Storage modulus of commercial polyurethane composite with calcium phosphate

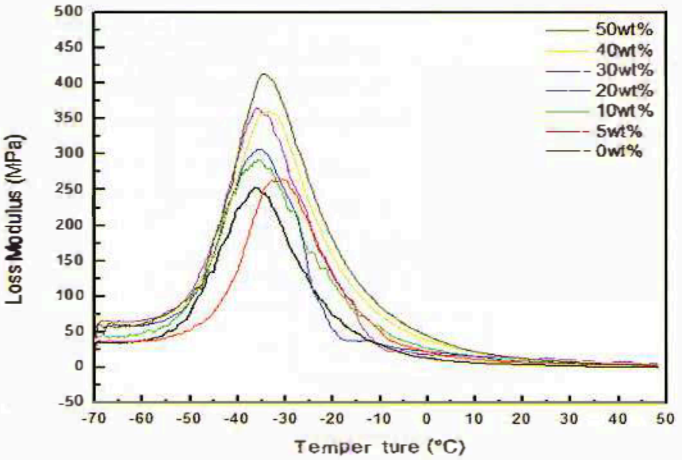

Figure 6: Loss modulus of commercial polyurethane composite with calcium phosphate

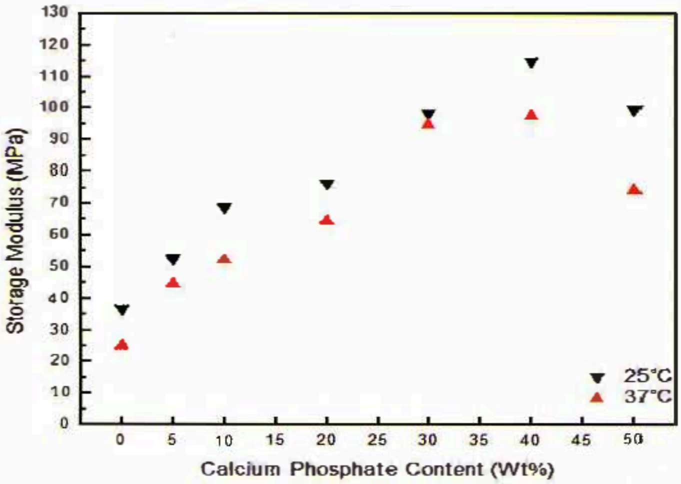

Figure 7: Storage modulus of commercial polyurethane composite with calcium phosphate at 25°C and 37°C

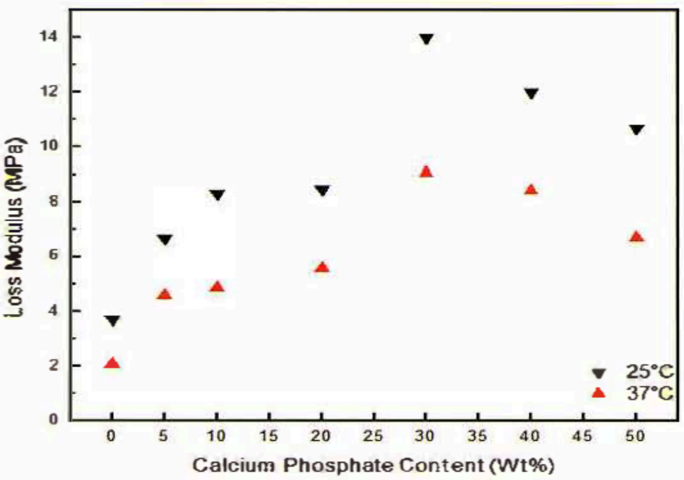

Figure 8: Loss modulus of commercial polyurethane composite with calcium phosphate at 25°C and 37°C

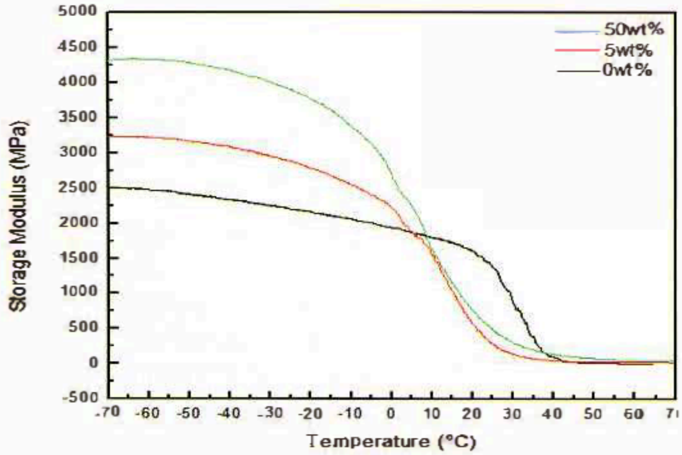

Figure 9: Storage modulus of 0wt% synthesized polyurethane composite with calcium phosphate

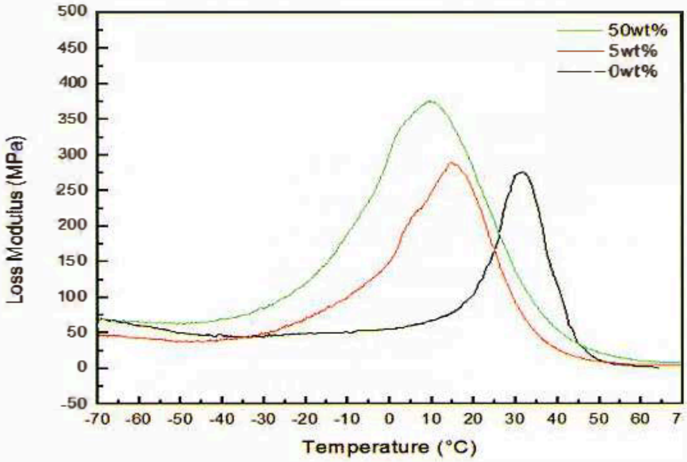

Figure 10: Loss modulus of 0wt% synthesized polyurethane composite with calcium phosphate

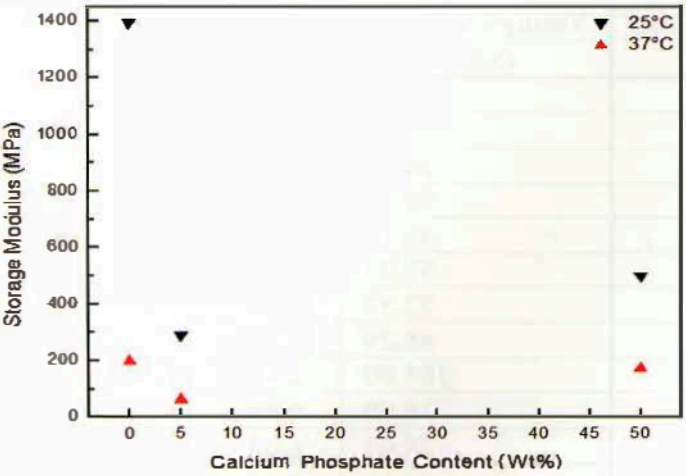

Figure 11: Storage modulus of 0wt% synthesized polyurethane composite with calcium phosphate at 25°C and 37°C

The storage modulus and loss modulus are both seen to increase with increased calcium phosphate filler. The lower and upper storage moduli at -70°C the storage moduli are respectively approximately 2500MPa for 0wt% and approximately 4400MPa for 50wt%. The lower and upper peak loss moduli are respectively approximately 280MPa for 0wt% and approximately 380MPa for 50wt%. The storage modulus and loss modulus were recorded at ambient room temperature of 25°C and normal human body temperature of 37°C (Figure 11, Figure 12). No definite trend is observed in this data due to the small number of sample measurements and the close proximity to the material Tg.

The storage modulus of commercial, 0wt% synthesized, and 5wt% synthesized polyurethanes were compared from -70°C to 70°C (Figure 13). Commercial and 0wt% synthesized polyurethanes were melt compounded to 5wt% calcium phosphate. Both synthesized composites have a larger storage modulus than the commercial composite at temperatures less than approximately 40°C. This difference is primarily due to the Tg of the commercial polyurethane is approximately -22°C while the Tg of the synthesized polyurethanes is approximately 30°C. The commercial composite has a larger storage modulus than either synthesized composites at temperatures greater than approximately 40°C. At this temperature all materials have exceeded their Tg rendering their amorphous phase mobile.

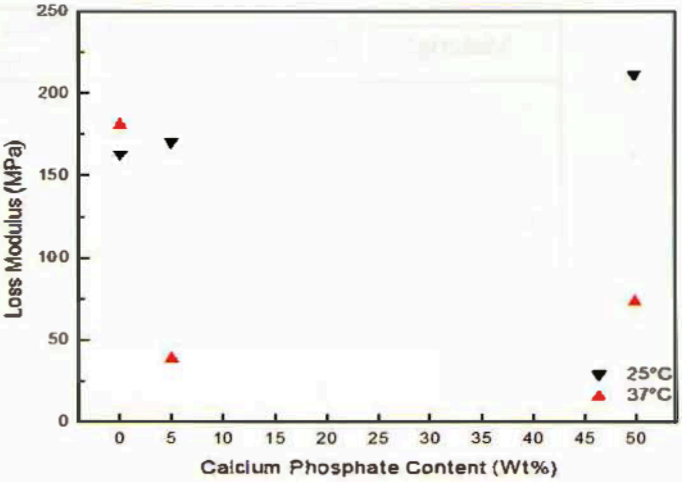

Figure 12: Loss modulus of 0wt% synthesized polyurethane composite with calcium phosphate at 25°C and 37°C

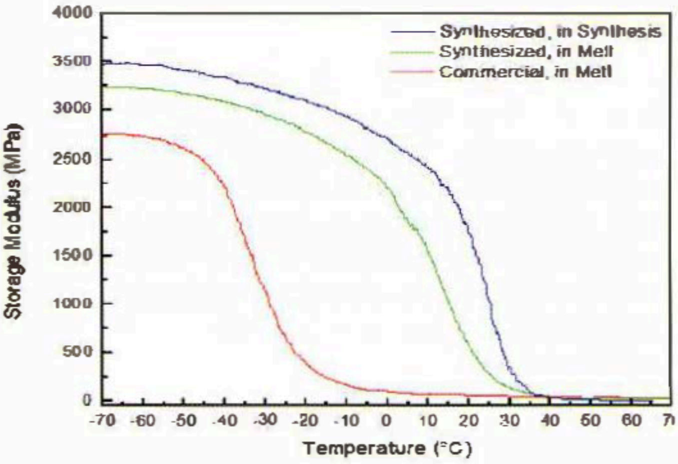

Figure 13: Storage modulus of commercial, 0wt% synthesized, and 5wt% synthesized polyurethane composites with 5wt% calcium phosphate

Tensile Analysis

Tensile testing was performed on commercial, 0wt% synthesized, and 5wt% synthesized polyurethanes. General tensile testing results may be found in Table 2. All testing was performed at 25°C. Commercial, 0wt% synthesized polyurethanes were tested with calcium phosphate filler content up to 50wt% through melt compounding. Young's modulus and yield data were obtained for all samples. Yield stress and strain were calculated at the onset strain of the relaxation transition. Testing device strain limit was reached prior to sample failure in all measure-

Material	Compounding	Calcium Phosphate	Young's Modulus	Yield	
		(wt%)	(MPa)	(%)	(MPa)
Commercial	None	0	26.24	18.17	3.734
	Melt	0	26.49	14.74	2.841
		5	30.45	12.55	3.060
		10	40.96	12.32	4.143
		20	36.11	13.27	3.832
		30	57.03	9.45	4.125
		40	52.57	11.72	4.549
		50	48.29	11.58	4.301
Synthesized	Melt	0	384.60	2.96	9.104
		5	38.60	9.89	3.387
		50	78.65	6.02	4.335
	Synthesis	5	43.41	14.14	4.569

Table 2: Tensile testing results for commercial and synthesized polyurethane

ments unless otherwise stated. All stress-strain data may be found in Appendix 8.2.

The stress-strain relationship of commercial polyurethane with up to 50wt% calcium phosphate was compared (Figure 14). The stress-strain relationship is seen to significantly increase with increased calcium phosphate filler. There is an increase in stress-strain between 0wt% and 30wt% calcium phosphate content. There is no discernable change in the stress-strain relationship between 30wt% and 50wt% calcium phosphate content. Young's modulus and yield stress increased with increased calcium phosphate content (Figure 15, Figure 16). Yield strain decreased with increased calcium phosphate content (Figure 17). The modulus after yield of 50wt% commercial polyurethane is significantly lower than that of other commercial composites.

The stress-strain relationship of 0wt% synthesized polyurethane with up to 50wt% calcium phosphate was compared (Figure 18). Polyurethane processed without any calcium phosphate filler exhibited a visibly unique stress-strain relationship. This relationship is characterized by a larger Young's modulus of 384.6MPa and lower yield strain of 2.96% than any other samples tested. There is also evidence of necking after yielding. This unique stress-strain relationship is due to the material being well below its Tg. The Tg of this sample was 42.92°C as reported in DMA, which is significantly greater than that of any other sample. The stress-strain of 50wt% calcium phosphate content is seen to be greater than that of 5wt% calcium phosphate content. Young's modulus, yield

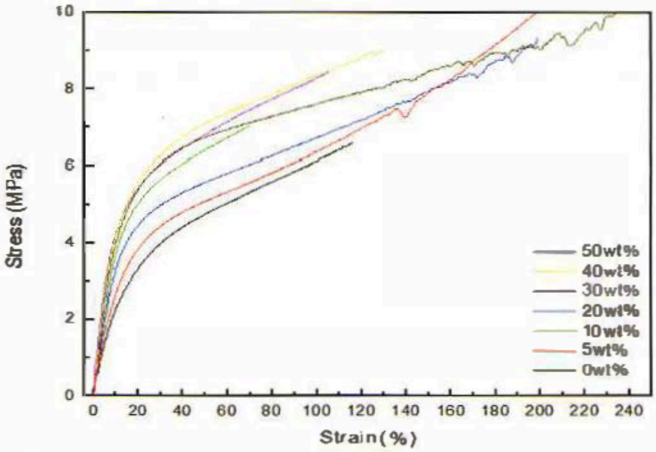

Figure 14: Stress-strain relationship of commercial polyurethane composite with calcium phosphate

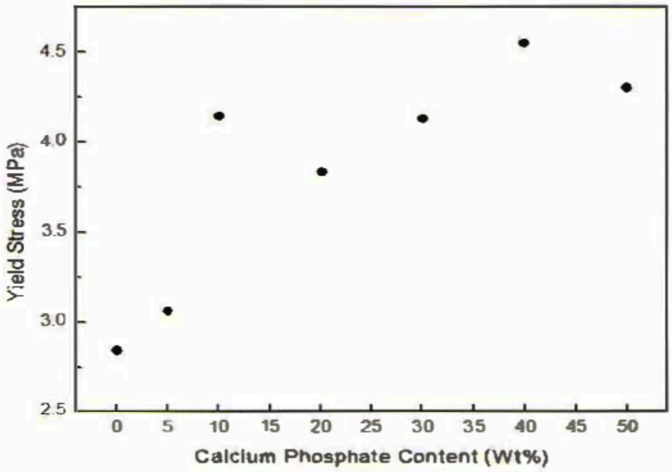

Figure 15: Yield stress of commercial polyurethane composite with calcium phosphate

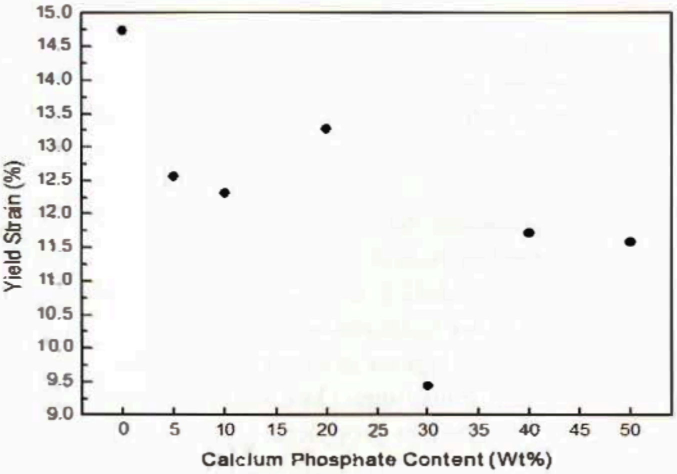

Figure 16: Yield strain of commercial polyurethane composite with calcium phosphate

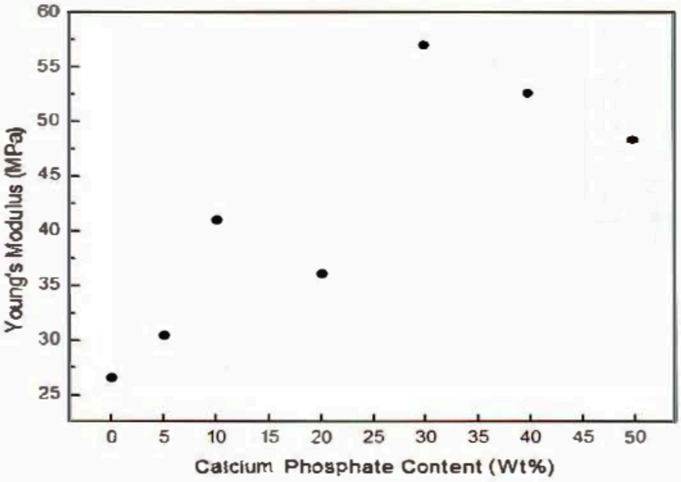

Figure 17: Young's modulus of commercial polyurethane composite with calcium phosphate

stress, and yield strain data are not adequate to determine trends (Figure 19, Figure 20, Figure 21). More intermediate samples are necessary to determine a definite trend in stress-strain due to calcium composite content. It is notable that the 50wt% compounded polyurethane was the only sample to fail prior to completion of testing. This failure indicates that greater calcium phosphate filler content makes the material more brittle.

The stress-strain relationship of commercial, 0wt% synthesized, and 5wt% synthesized polyurethane was compared (Figure 22). Commercial and 0wt% synthesized polyurethanes were melt compounded to 5wt% calcium phosphate. Both synthesized composites have a greater stress-strain than the commercial polyurethane composite. This difference is partly due to the Tg of the commercial polyurethane being approximately -22°C and the Tg of the synthesized polyurethanes being approximately 30°C as reported in DMA.

Differential Scanning Calorimetry

Differential Scanning Calorimetry was performed on commercial, 0wt% synthesized, and 5wt% synthesized polyurethanes. All samples were heated to 250°C, cooled to

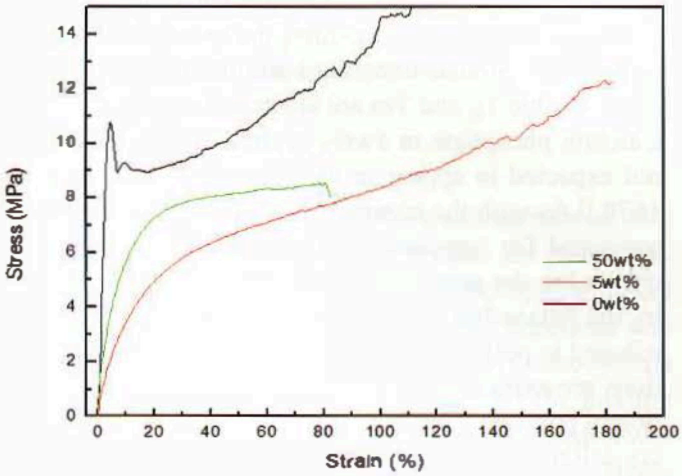

Figure 18: Stress-strain relationship of 0wt% synthesized polyurethane composite with calcium phosphate

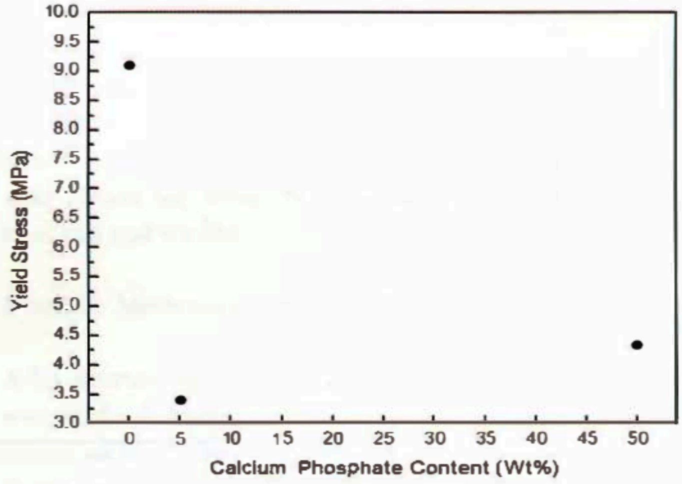

Figure 19: Yield stress of 0wt% synthesized polyurethane composite with calcium phosphate

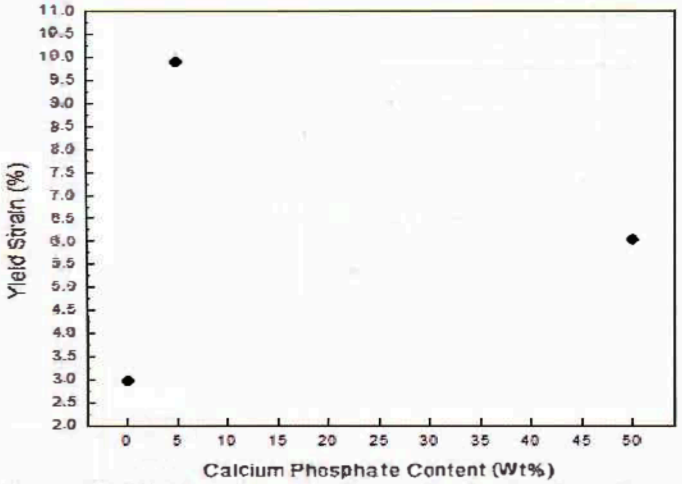

Figure 20: Yield strain of 0wt% synthesized polyurethane composite with calcium phosphate

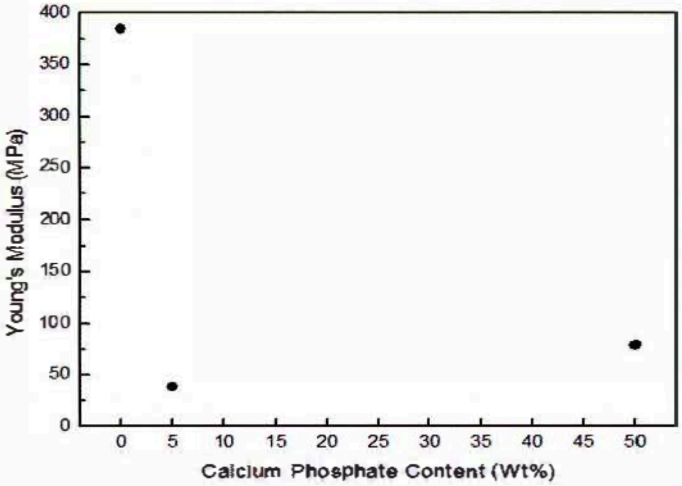

Figure 21: Young's modulus of 0wt% synthesized polyurethane composite with calcium phosphate

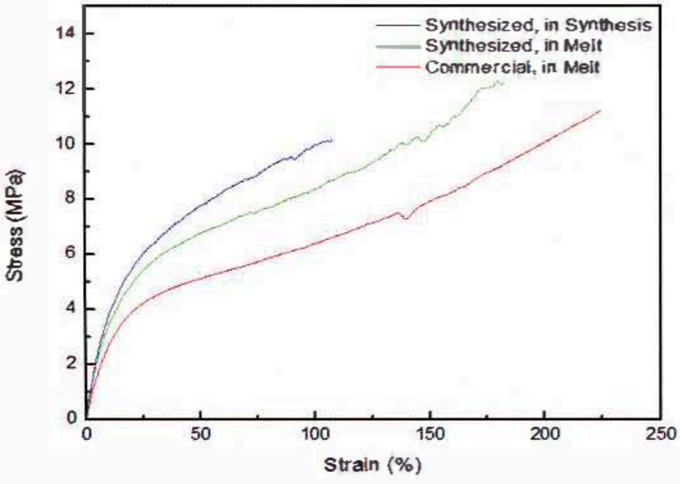

Figure 22: Stress-strain relationship of commercial, 0wt% synthesized, and 5wt% synthesized polyurethane composites with 5wt% calcium phosphate

-70°C, and then heated to 250°C. Data from the first cooling and second heating cycles was analyzed. All differential scanning calorimetry data may be found in Appendix 8.3.

Thermal transitions for 0wt% synthesized polyurethane were exhibited as Tc at 86.4°C (9.692J/g), Tm at -25.61°C (4.582J/g), Tg at 33.72°C (0.2725J/(g•°C)) during heating, and Tm at 163.64°C (5.381J/g). The predominant component, polycaprolactone is expected to exhibit the most visible thermal transitions. The shallow Tm at -25.61 is suspected to be due to propylene glycol segments. This Tm is similar to a general reported Tm of polypropylene glycol of -49.9°C.[14] The Tg and Tm at 163.64°C are attributed to polycaprolactone segments. The Tm is significantly greater than a general reported polycaprolactone Tm of 59-64°C.[15] This increase in Tm is expected due to the great increase in molecular weight created by the butanediol chain extender. The measured polycaprolactone crystallinity for the Tc is 7% and for at163.64°C Tm is 4%. The heat of fusion for polycaprolactone used was 139.5J/g.[16]

Thermal transitions for 0wt% synthesized polyurethane were exhibited as Tc at 52.02°C, Tg at 13.83°C (-0.2516J/(g•°C)) during cooling, Tg at 19.38°C (0.4629J/(g•°C)) during heating, Tcc at 64.26°C (5.969J/g), and Tm at 140.03°C (10.16J/g). Thermal transitions for 5wt% synthesized polyurethane were exhibited as Tc at 21.19°C, Tg at 5.04°C (-0.1277J/(g•°C)) during cooling, Tg at 18.47°C (0.1980J/(g•°C)) during heating, Tcc at 70.21°C (1.468J/g), and Tm at 131.13°C (2.371J/g). In both synthesized materials the predominant component, polycaprolactone is expected to exhibit the most visible thermal transitions. Similar transitions are observed in both samples. Visible Tg and Tm are attributed to polycaproctone. Calcium phosphate in 5wt% synthesized polyurethane is not expected to appear in the thermal cycle as its Tm is 1670.[17] As with the commercial polyurethane, the greater measured Tm compared to the general reported Tm is attributed to the great increase in molecular weight created by the butanediol chain extender. The Tc and Tcc are attributed to polycaprolactone. These crystallization transitions are expected due to the favorable crystalline formation of polycaprolactone. The measured polycaprolactone crystallinity in 0wt% synthesis for Tcc is 4% and for at Tm is 7%. The measured polycaprolactone crystallinity in 5wt% synthesis for Tcc is 1% and for at Tm is 2%. The heat of fusion for polycaprolactone used was 139.5J/g.[16] This degree of crystallinity is low as polycaprolactone has been reported as being as much as 59.1% crystalline.[18] The low percent crystallinity is due to the interaction of other polymer components with the polycaprolactone segments. The lower Tg of 5wt% synthesized polyurethane compared to 0wt% synthesized polyurethane is due to the presence of calcium phosphate hindering polycaprolactone crystallization. For both tests, the Tc occurring during cooling is approximated as a broad peak maximum. Percent Tc is not determined as its proximity to the cooling Tg prohibits isolation. This limitation reduces the significance in the noted temperatures for Tc of 0wt% and 5wt% synthesized polyurethanes.

MATERIALS AND METHODS

Materials

Poly[4,4'-methylenebis(phenylisocyanate)-alt-1,4-butanediol/di(propyleneglycol)/polycaprolactone]
(Aldrich430218-250G, Batch#02609BC)

Polycaprolactonediol
(Aldrich189405-250G, Batch#04216DH)

4,4'-Methylenebis(phenylisocyanate), 98%
(Aldrich256439-500G, Batch#MKBC3781)

Butanediol, ReagentPlus®, ≥99%
(Aldrich240559-100G, 13323ED)

Calcium phosphate
(Aldrich21218-1KG, Lot#0001447745)

Synthesis

A 250ml 3-necked round bottom flask was assembled with a mechanical stirring mechanism, oil bath, stir plate, temperature controller, reflux condenser, and dropping funnel connected to an argon gas manifold. The apparatus was flushed with argon gas. Methylene diphenyl diisocyanate was added. Calcium phosphate was added. The mixture was stirred and heated to 60°C. Polycaprolactonediol was added slowly through the dropping funnel. The mixture was heated to 80°C and stirred for 4hr. Butandiol in was dimethyl sulfoxide added. The mixture was heated to 80°C and stirred for 2hr. The reaction mixture was poured in water and allowed to sit overnight.

Film Preparation

A Carver laboratory press Model C was used. The press was heated to 190°C. Polyurethane was placed between two sheets of Teflon and two steel plates. The sample and plates were inserted into the melt press which was then closed with minimal pressure. Upon returning to 190°C the press remained closed with minimal pressure for 1min then was compressed with 0.5-1Mton for 3min. The sample and plates were removed and cooled.

Composite Film Compounding

A Carver laboratory press Model C was used. The press was heated to 190°C. Polyurethane film and calcium phosphate were placed between two sheets of Teflon and two steel plates. The sample and plates were inserted into the melt press which was then closed with minimal pressure. Upon returning to 190°C the press remained closed with minimal pressure for 1min then was compressed with 0.5-1Mton for 3min. The sample and plates were removed and cooled. The pressing procedure was performed 3x.

Measured Film Preparation

A Carver laboratory press Model C was used. The press was heated to 190°C. Polyurethane and composite films were placed between two sheets of Teflon coated aluminum foil and two steel plates. The sample and plates were inserted into the melt press which was then closed with minimal pressure. Upon returning to 190°C the press remained closed with minimal pressure for 1min, compressed with 0.5-1Mton for 10sec 3x, and compressed with 5Mton for 10sec 3x. The sample and plates were removed and cooled.

Dynamic Mechanical Analysis

A TA Instruments DMA Q800 with tension clamp fixture was used. A rectangular film sample was inserted in the clamp. The Module was set to DMA Multi-Frequency - Strain and the ProcName was set to Temperature Ramp. The initial temperature was set to -70°C. The motor drive was turned on and the sample temperature was ramped

3°C/min to 70°C. The storage and loss modulus were measured over the temperature range.

Tensile Testing

A TA Instruments DMA Q800 with tension clamp fixture was used. A rectangular film sample was inserted in the clamp. The Module was set to DMA Strain Rate and the ProcName was set to Mark Stres-Strain. The temperature was equilibrated at 25°C. The motor drive was turned on and the sample strain was ramped 20%/min to 300%. The stress-strain relationship was measured of the strain range.

Differential Scanning Calorimetry

A TA Instruments DSC Q2000 was used. Sample was sealed in an aluminum pan. The Module was set to DSC Standard Cell RC and the ProcName was set to LC Modulated.

The initial temperature was set to -70°C. The temperature was ramped 10°C/min to 250°C. The temperature was ramped 10°C/min to -90°C. The temperature was ramped 10°C/min to 250°C. Heat flow was measured throughout the thermal cycle.

CONCLUSIONS

Polycaprolactone based polyurethane composites for use in functional orthopedic implants was proposed. Increased calcium phosphate filler content is shown to have a reinforcing effect on the material in dynamic mechanical analysis and tensile testing. Cold crystallization was observed in synthesized polyurethanes. This crystallization may be used to optimize material characteristics through semi-crystalline fractions. Synthesized polyurethanes were observed to have a higher Tg than commercial polyurethane. Increasing the Tg of the materials is of interest for rigid operation in the functional environment of 37°C.

Future work will focus on improving the mechanical and biodegradable material properties through composite, thermal, and chemical processes. Increasing the calcium phosphate content in commercial polyurethane composites may reveal a maximum loading composition. Trends in 0wt% synthesized polyurethane composites may be determined through sample measurements at more calcium phosphate compositions. Synthesized polyurethanes with increased calcium phosphate content in synthesis may determine improved material characteristics due to decreased thermal requirements compared to melt compounding. Tensile testing at 37°C is necessary to reveal mechanical properties of the materials in their intended functional environment. Tensile tests in which the sample is strained to failure in all cases are optimum. Infrared spectroscopy performed on commercial and synthesized polyurethanes may be used to determine information pertaining to difference in chemical structure. Dependence on thermal history of the materials should be analyzed and the melt processing procedures optimized for best material properties. The effect of hydrolytic degradation on the materials should be analyzed with simulated body fluid. The effect of degradation caused by atmospheric humidity should be analyzed. The cold crystallization of synthesized polyurethanes may be used to improve their material characteristics through increased crystalline content.

Go to case.edu/source/discussions for appendix.

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