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The effect of plasma surface modification on biodegradation rate and biocompatibility of a poly(butylene succinate)-based copolymer

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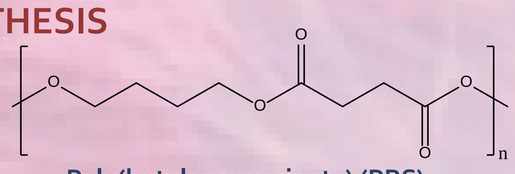
INTRODUCTION

The use of biodegradable polymers in regenerative medicine has attracted considerable attention in recent years. This is mainly because, thanks to their hydrolysis in the human body, the need of surgery to remove the implant can be avoided. Of course, to be employed as biomaterials, these polymers need to show excellent biocompatibility and the degradation products must be nontoxic to the organism.[1] Moreover, their biodegradation rate has to satisfy the requirements according to the intended function.
Among other classes, aliphatic polyesters (APs), have been widely used as they combine proven biodegradability with good biocompatibility and promising mechanical properties.[2]
Poly(butylene succinate) (PBS) represent one of the most interesting Aps: it is commercially available, it can be easily processed into various forms and structures and it possesses mechanical properties resembling those of PE and PP.[3] Unfortunately, the hydrophobicity and low surface energy of PBS lead to inefficient cell attachment, spreading and proliferation.[4]
As a result, surface modification is usually necessary to improve their biocompatibility. Besides other techniques, plasma treatment is a very convenient strategy for the production of functional groups: it can be efficiently use to incorporate functional groups on the polymer surface without affecting its bulk characteristics. In addition, as being a solvent-free technique, the use of hazardous solvents is evaded.[4]
With the aim of improving PBS wettability and mechanical properties, a novel PBS-based copolymer containing thioether linkages P(BS85TDGS15) is here presented. P(BS85TDGS15) and PBS have been synthesized by melt polycondensation and their solid-state properties have been evaluated. Both polymers have been then subjected to plasma surface treatment and its effect on their biodegradation rate and biocompatibility has been considered. Finally, studies performed with H9c2 cells demonstrate that PBS and P(BS85TDGS15) films are not cytotoxic and support cell proliferation, both before and after plasma treatment.

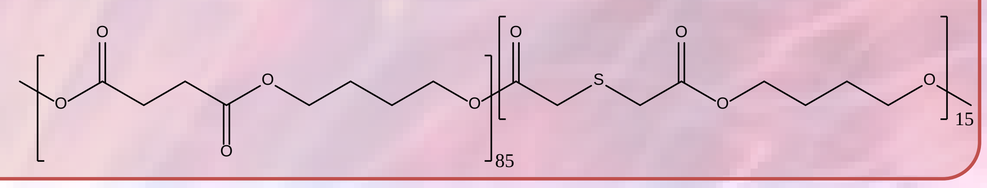
SYNTHESIS



Poly(butylene succinate) (PBS)

Two step melt polycondensation
- I step: 180°C, N_2 flow, 100 rpm, 2 hours
- II step: 230°C, 0,0655 mbar, 100 rpm, 4 hours

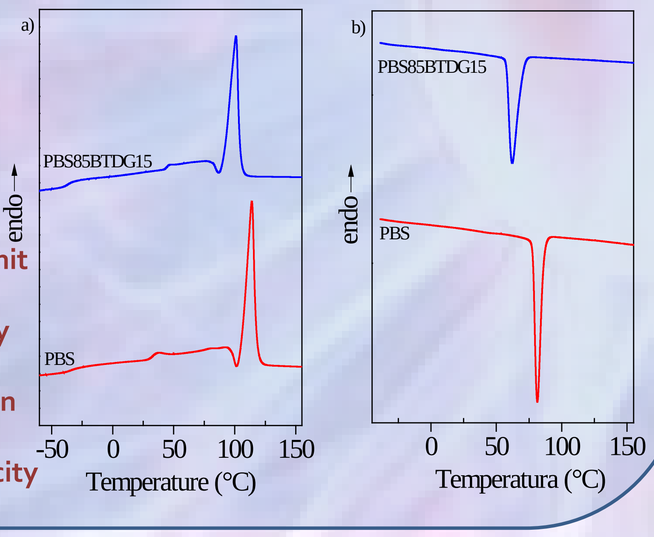
Poly(butylene succinate/thiodiglycolate) (P(BS85BTDG15))



MOLECULAR & THERMAL CHARACTERIZATION

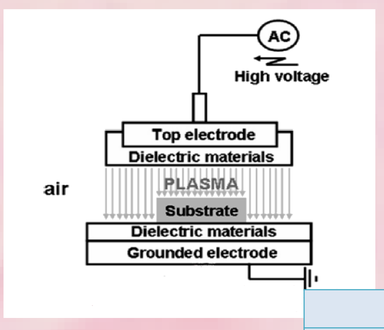
					I SCAN				
Polymers	M_n	PDI	T_{id} (°C)	T_{max} (°C)	T_g (°C)	ΔC_p (J/g °C)	T_m (°C)	ΔH_m (J/g)	T_{cc} (°C)
PBS	60165	2.1	382	408	-36	0.074	114	49	81
P(BS85BTDG15)	41200	2.3	354	391	-37	0.058	101	44	62

Polymers	WCA (°)
PBS	90 ± 0.6
P(BS85BTDG15)	88± 0.6



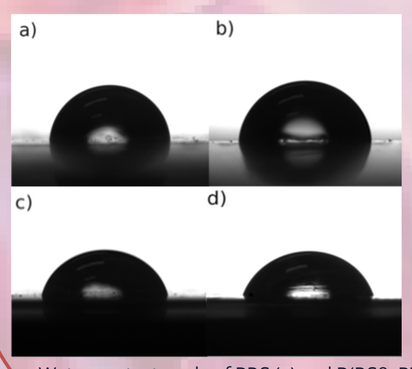
The introduction of BTDG co-unit causes:
- a decrement of thermal stability
- a decrease of the T_m and ΔH_m
- a slowing down of crystallization process
- a slight increment of hydrophilicity

PLASMA OPERATING CONDITIONS & CHARACTERIZATION



Low-energy pulsed (without termic energy):
- gas: air
- exposition time: 30 s
- duty cycle: 50%
- energy: 100 J

					I SCAN			
Treated polymers	M_n	PDI	T_{id} (°C)	T_{max} (°C)	T_g (°C)	ΔC_p (J/g °C)	T_m (°C)	ΔH_m (J/g)
PBS_p	60000	2.1	399	411	-35	0.047	114	56
P(BS85BTDG15)_p	33000	2.3	349	379	-37	0.117	101	55

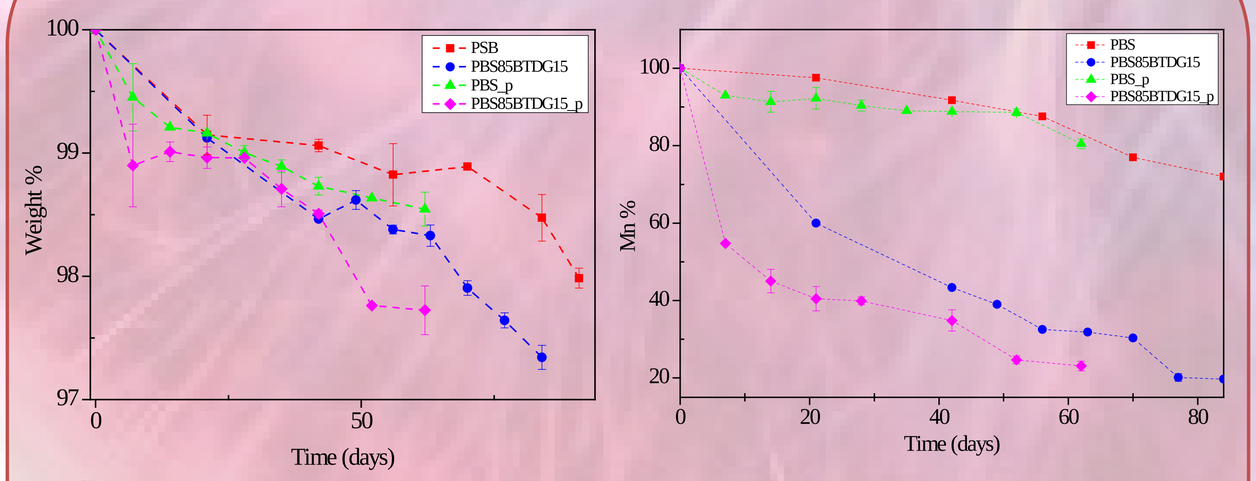


Water contact angle of PBS (a) and P(BS85BTDG15) (b) before plasma treatment and PBS (c) and P(BS85BTDG15) (d) after plasma treatment

Treated polymers	WCA (°)
PBS_p	79 ± 1.6
P(BS85BTDG15)_p	74± 2.3

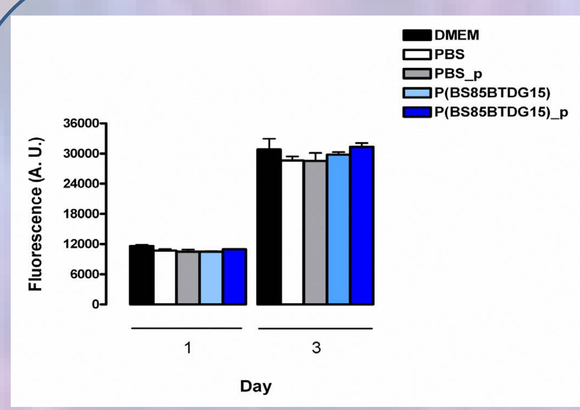
The plasma treatment causes:
- a slight decrement of P(BS85BTDG15) molecular weight
- a significant increment of hydrophilicity of both polymers

HYDROLYTIC DEGRADATION



- Both polymers are biodegradable, the copolymer degrading significantly faster than PBS, due to its higher hydrophilicity and lower crystallinity degree
- After plasma treatment, both polymers degrade faster than the corresponding non treated ones

INDIRECT CYTOTOXICITY TEST



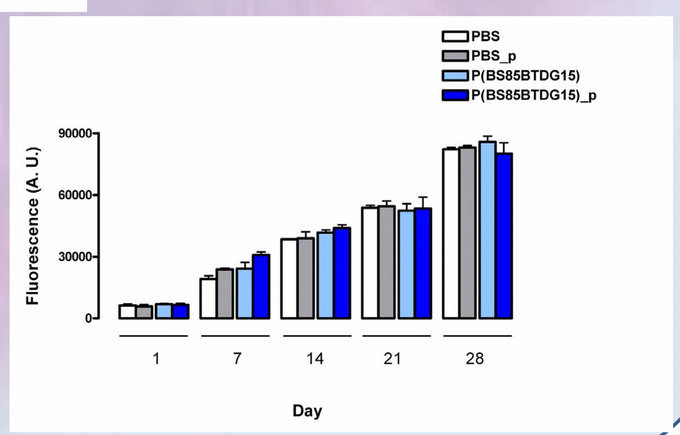
Cytotoxic degradation products are no release in the culture medium for both tested polymers before and after plasma treatment.

Cardiomyoblast H9c2 cell line

DIRECT CYTOTOXICITY TEST

Tests with H9c2 cell line show for both tested polymers:
- increase in cell adhesion over time
- increase in cell proliferation over time

No significant effect of plasma treatment was observed on material biocompatibility.



CONCLUSIONS

✓ Copolymerization revealed a winning strategy to improve PBS biodegradability, acting on hydrophilicity and crystallinity degree.

✓ Plasma treatment effectively contribute to further accelerate biodegrdation process, keeping a good biocompatibility.

[1] A.W. Lloyd, *Med Device Technol* **2002**, *13*, 18; [2] V. Tserki, P. Matzinos, E. Pavlidou et al., *Polym Degrad Stab* **2006**, *91*, 367; [3] I. Vroman, L. Tighzert, Materials **2009**, *2*, 307; [4] R. Morent, N. De Geyter, T. Desmet et al., *Plasma Process Polym* **2011**, *8*, 171.

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