

# DEGRADATION PROCESS OF TMC-BASED POLYMERS BY MASS SPECTROMETRY

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## Abstract

*This paper presents results of degradation process investigations of resorbable poly(lactide-trimethylene carbonate). Materials used in this work were synthesized by the ring opening polymerization. Polymerization was carried out in bulk using  $Zr(acac)_4$  as initiator. The resulting copolymers were characterized by high resolution NMR spectroscopy. Then the copolymers were allowed to degrade in  $H_2O$  for 53 weeks. These conditions allowed to analyze the degradation products of poly(lactide-trimethylene carbonate) and to determine the structure of oligomers using multi-stage mass spectrometry technique (ESI-MS<sup>n</sup>). ESI-MS analysis revealed the presence of two kinds of oligomers.*

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## Introduction

Poly(trimethylene carbonate) (PTMC) is an amorphous elastomer which exhibits good mechanical properties: high flexibility and high tensile strength [1]. Such elastic biodegradable material is required in the production of medical implants and porous scaffolds [2]. It was observed that in phosphate buffer saline at pH=7 and at a temperature of 37°C, PTMC degrades very slowly. However, *in vivo* degradation occurs rapidly by surface erosion [1].

High molecular weight statistical copolymers of TMC and DLLA were synthesized using  $Sn(oct)_2$  as an initiator, characterized and compared with the corresponding homopolymers PTMC and PDLLA [3]. The obtained results showed that the thermal and mechanical properties of the polymers strongly depend on the composition. All materials were hydrophobic. The properties of the TMC and DLLA copolymers suggested their suitability as materials for resorbable biomedical devices. The highly elastic PTMC and copolymers with high TMC content seemed more suitable for application as coatings or drug delivery systems [3].

PTMC and TMC-based copolymers were also successfully synthesized by ring opening polymerization with the use of low toxic metals: iron, zinc, zirconium [1-2]. Degradation of LLA/TMC copolymers prepared with  $Zr(acac)_4$  initiator was examined by Hua et al. [1]. By varying the chemical composition, chain microstructure and morphology various degradation behaviors and degradation rates were obtained.

Low-molecular weight poly( $\epsilon$ -caprolactone-co-1,3-trimethylene carbonate) and poly(1,3-trimethylene carbonate) were examined as potential vehicles for the delivery of water-soluble agents such as vitamin B12. The rate of release was the fastest for the amorphous oligomers and dependent on their viscosity [4].

## Materials and Methods

Copolymers of lactide and trimethylene carbonate were obtained by ring opening polymerization using  $Zr(acac)_4$  as initiators. Temperatures of reaction were 110°C and 180°C. The molar ratio of comonomers/initiator was 1000:1. Polymerization was carried out in bulk. The copolymers were compression moulded. Square specimens with approximately 0.5 mm thick were then cut from the material. The resulting form of copolymers was submitted to degradation in water at 37°C for 53 weeks. The resulting copolymers were characterized by <sup>1</sup>H NMR. NMR spectra were recorded with a Bruker Avance II spectrometer operating at 600 MHz, using  $CDCl_3$  as a solvent. Chemical shifts ( $\delta$ ) were given in ppm using tetramethylsilane (TMS) as an internal reference. The spectra were obtained with 32 scans, 11  $\mu$ s pulse width and 3.74 s acquisition time for <sup>1</sup>H NMR.

The structure of degradation products was determined with aid of multistage mass spectrometry technique (ESI-MS<sup>n</sup>). Degradation medium was withdrawn at established periods of time, then samples were freeze-dried and dissolved in methanol/chloroform (1/1 v/v) solution and such solutions were introduced to the ESI source by continuous infusion by means of the instrument syringe pump at a rate of 3 mL/min. The ESI source was operated at 4.5 kV, with the capillary heater at 200°C, and sheath gas pressure 40 psi. For ESI-MS<sup>n</sup> experiments mass-selected monoisotopic molecular parent ions were isolated in the trap and collisionally activated with 40% ejection RF-amplitude at standard He pressure. The experiments were performed in both positive- and negative-ion mode.

## Results and Discussion

Copolymers samples PLATMC (50/50) with various chain microstructure were obtained changing the temperature of polymerization: 110°C (PLATMC110) and 180°C (PLATMC180).

The co-monomeric units content were estimated using high resolution NMR spectroscopy [1].

The structure of the degradation products of PLATMC was determined by multistage mass spectrometry technique (ESI-MS<sup>n</sup>). It was possible to detect distinguishable signals since 41<sup>st</sup> week of degradation (FIG. 1).

Signals detected in ESI-MS spectra were associated with appropriate structure of oligomers. ESI-MS analysis revealed two kinds of oligomers (FIG. 2). Structures I and II possess carbonate unit:  $-O-(CH_2)_3-O-C(O)-$  and lactidyl unit:  $-O-CH(CH_3)-C(O)-$ . Structure I corresponds to oligomers with carboxyl-end of the chain as well as hydroxyl-end of the chain and is abbreviated as TL. Structure II corresponds to oligomers (in majority) with two carboxyl-ends of the chain and is abbreviated as T'L'. Second mode spectra of selected signals confirm these conclusions. One of them is presented in FIG. 3.

It is possible to identify a series of oligomers detected in ESI-MS spectra of PLATMC (FIG. 4).

In the case of PLATMC110, the observed series of oligomers are identified as following:

T'L'2÷T'3L'2, T'L'3÷T'3L'3 (41<sup>st</sup> week of degradation)

T'L'2÷T'5L'2, T'L'3÷T'5L'3, T2L÷T4L (53<sup>rd</sup> week of degradation)

In the case of PLATMC180, the observed series of oligomers are identified as following:

T'L'2÷T'3L'2, TL2÷T3L2, T'L'3÷T'3L'3, TL3÷T5L3, T2L÷T3L (41<sup>st</sup> week of degradation)

T'L'2÷T'6L'2, T2L÷T3L (53<sup>rd</sup> week of degradation)

It is clearly seen that oligomers detected in 41<sup>st</sup> week of degradation are short and consist of several units. Longer oligomers are detected in 53<sup>rd</sup> week of degradation.

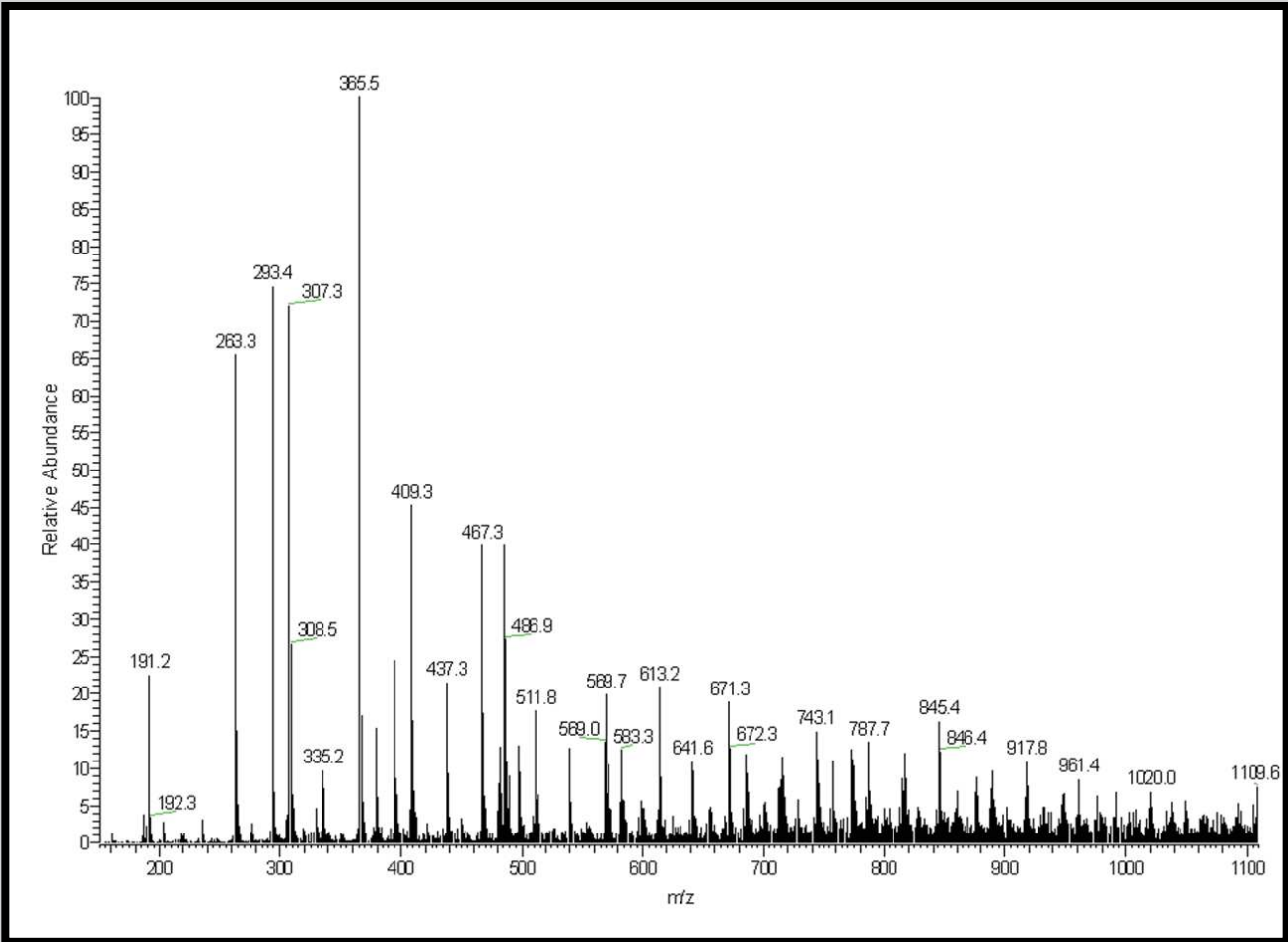


FIG. 1. ESI-MS spectrum of PLATMC180.

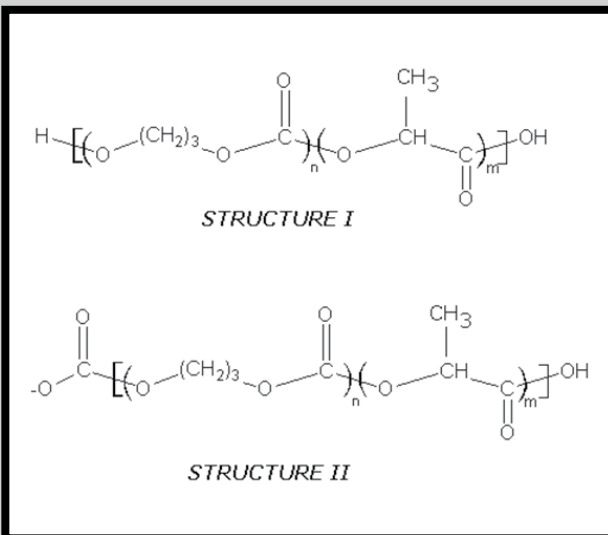


FIG. 2. Structures of oligomers detected in ESI-MS spectra.

## Conclusions

Copolymers of lactide and trimethylene carbonate were allowed to degrade in  $H_2O$  for 53 weeks. These conditions allowed to analyze the degradation products and to determine the structure of oligomers using multistage mass spectrometry technique (ESI-MS<sup>n</sup>). ESI-MS analysis revealed two kinds of oligomers:

- oligomers with carbonyl-end of the chain as well as hydroxyl-end of the chain and
- oligomers (in majority) with two carbonyl-ends of the chain.

It is possible to identify a series of oligomers detected in ESI-MS spectra of PLATMC. It is clearly seen that oligomers observed in 41<sup>st</sup> week of degradation are short and consist of several units. Longer oligomers are observed in 53<sup>rd</sup> week of degradation.

## Acknowledgements

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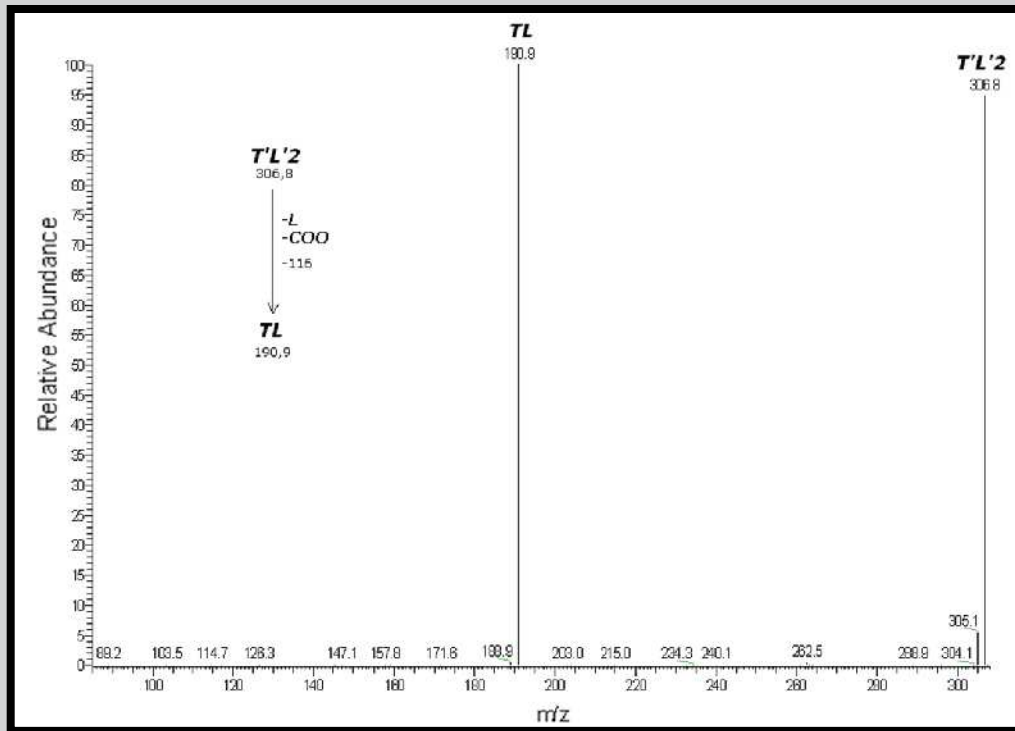


FIG. 3. Fragmentation of selected signal from ESI-MS<sup>n</sup> spectrum of PLATMC180.

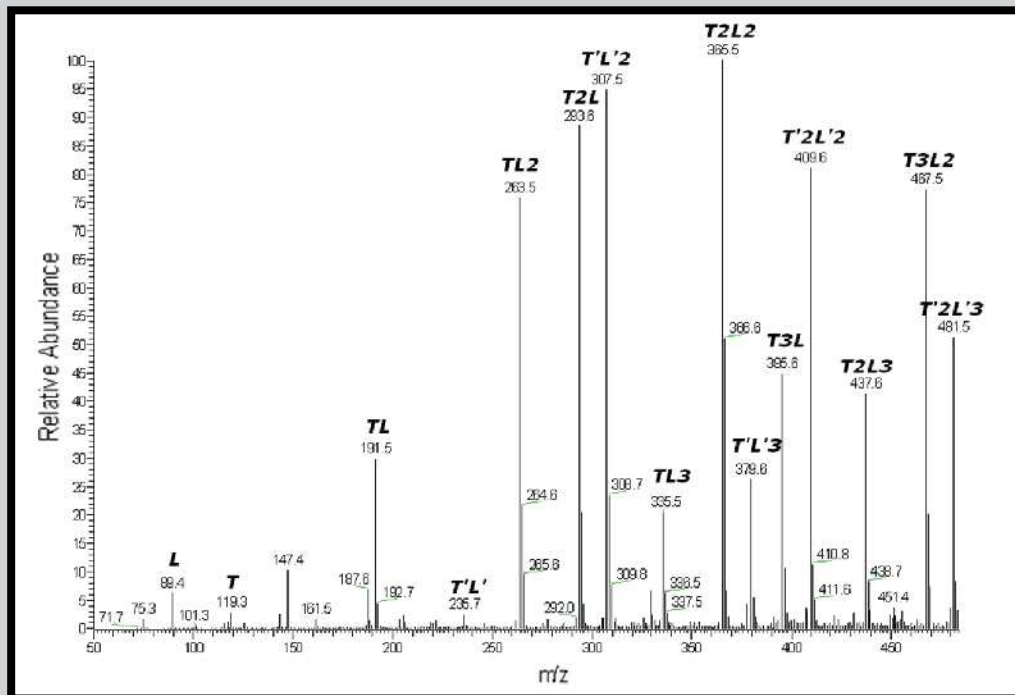


FIG. 4. ESI-MS spectrum of PLATMC180 (in spectral expansion in the mass range  $m/z$  50–500). Assignment of the signals to appropriate oligomer structure.

## References

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