Poly(2-oxazoline) based tissue tape

Development of a General Adhesive Tissue Tape

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Introduction

A number of innovative materials are available to repair and support tissue, but none of them is able to replace sutures.[1] We are developing a general adhesive tissue tape (GATT) based on poly(2-oxazolines) (POX) containing NHS esters in the side chain as biocompatible scaffold.[2] The NHS functionalised polymer will be crosslinked by POX containing amines or other functional amines. In this way a crosslinked polymer film will be formed. The material properties are tunable by e.g. controlling NHS content and NHS : amine ratio.

The NHS functional polymer will be prepared via a hydrolysis route: poly(2-ethyl-2-oxazoline) can be partially hydrolysed (figure 1 & 2).[3] The resulting copolymer of PEtOx and poly(ethylene imine) (PEI) is functionalised with a protected carboxylic acid linker, which is subsequently modified with an NHS moiety (figure 3) or an amine (figure 4).
The adhesion and cohesion of the crosslinked films was tested on bovine peritoneum (figure 5).

Synthesis

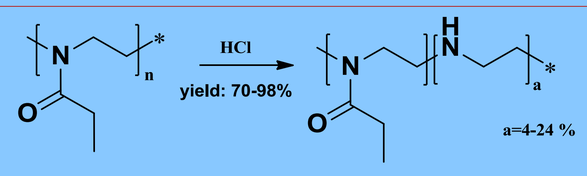

Figure 1: Partial acidic hydrolysis of Aquazol (PEtOx, Mn 50000)

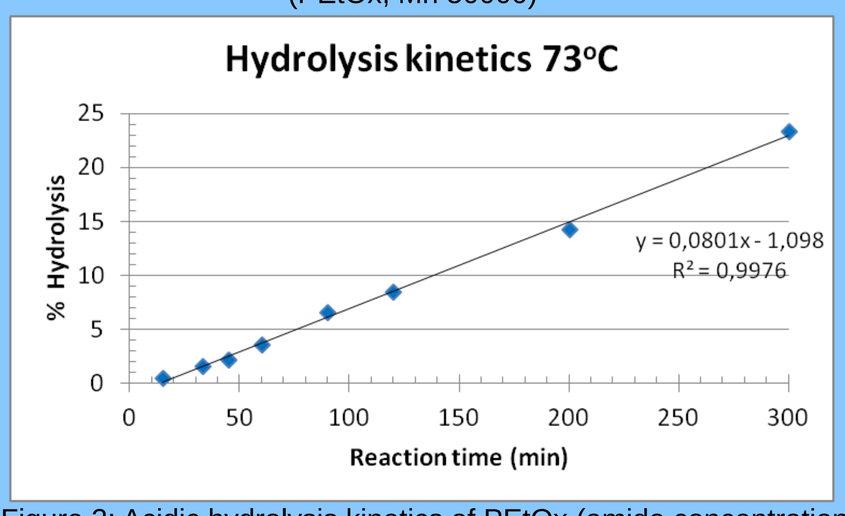

Figure 2: Acidic hydrolysis kinetics of PEtOx (amide concentration 0.48 M)

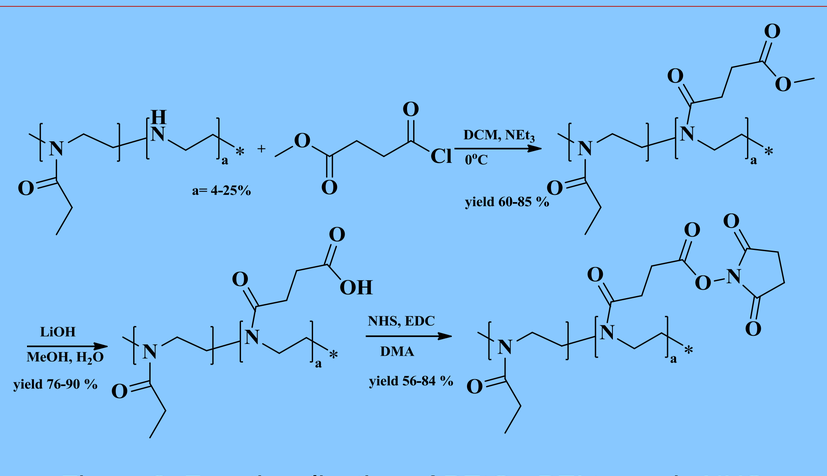

Figure 3: Functionalisation of PEtOx-PEI towards NHS functionalised POx

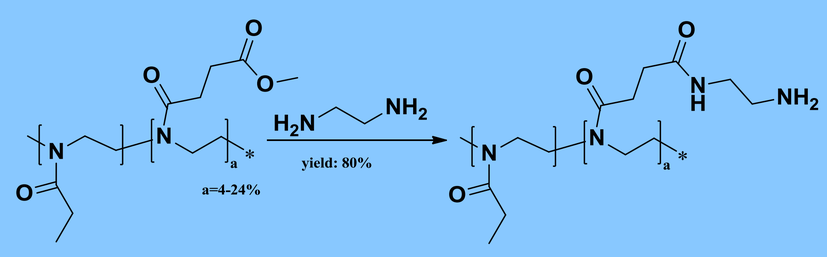

Figure 4: Synthesis of amine functionalised POX

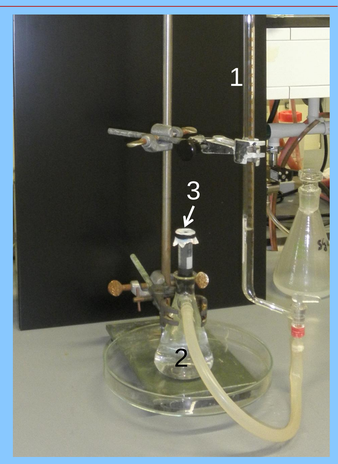

Figure 5: adhesion test set up
1. Water column
2. Erlenmeyer
3. Bovine peritoneum with 3 mm incision

Adhesion test:
- Film is placed on top of peritoneum
- Water level is increased until failure

Results

Efficiency of couplings:
- POX-PEI 24% → POX-NHS 23%: 96%
- POX-PEI 12% → POX-NHS 11.9%: 99%

Table 1: Crosslink test results

Ratio		POX-NHS	Amine	
NHS	NH_2	%	Type	Crosslink time
1.1	1	4.4	Trilysine	< 60 seconds
1.1	1	4,4	POX-NH_2 12%	< 20 seconds
2	1	23	POX-NH_2 6%	15 seconds

Table 2: Adhesion test results of POX films

Ratio		POX-NHS	Amine	Height water	Failure	Cohesion
NHS	NH_2	%	crosslinker	column (cm)	by	
-	-	-	PEtOx	4	Adhesion	Film dissolves very fast
1	0	4,4	-	5	Cohesion	Film dissolves very fast
5	1	4,4	Trilysine	15	Adhesion	The cohesion of the swollen film is not very good
1	1	4,4	Trilysine	5	Adhesion	Film swells, but the material is quite strong
5	1	4,4	POX-NH_2 12%	31,5	Cohesion	Very good, the swollen film bent with the same curvature as the peritoneum
2	1	23	POX-NH_2 6%	-	Adhesion	Good, material is very tough, when the film swells it folds
5	1	23	POX-NH_2 6%	22,5	Cohesion	Good, but it contains gas bubbles

Conclusion

Poly(2-ethyl-2-oxazoline)s can be partially hydrolyzed and functionalized to obtain NHS side-chain activated POX. These polymers can be crosslinked with amines to obtain a film which can adhere to tissue. The strength of the films is influenced by the crosslink density, amount of functional groups and type of crosslinker used. This will be studied in more detail as basics for a general adhesive tissue tape.

References

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