Anticoagulant properties of coated Fe-Pd ferromagnetic shape memory ribbons

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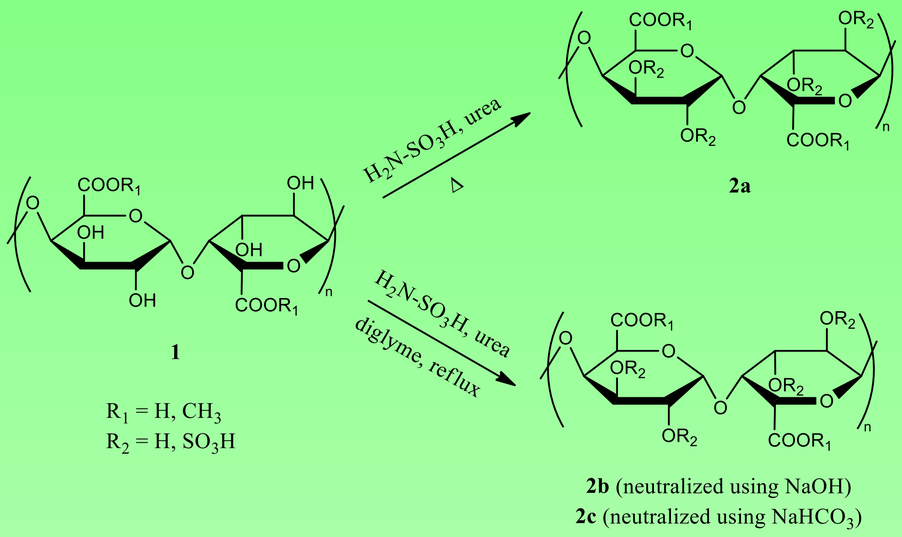
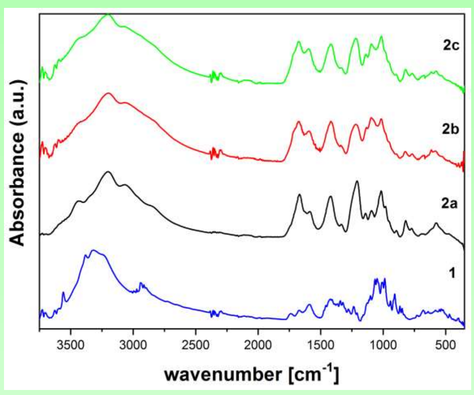
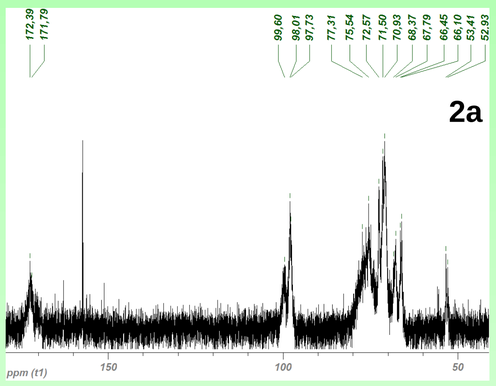
Motivation: Ferromagnetic shape memory alloys are interesting new materials for the manufacture of stents. Their shape-changing ability allows them to be used as a self-expanding device based on temperature or magnetic field, without the need of additionally introduced mechanical force like in balloon angioplasty. Iron-palladium alloys in particular can be used to manufacture temporary stents due to their optimum rate of degradation. In order to avoid blood clotting upon introduction of the stent, they are often coated with anticoagulants. In this study, sulfated pectin, a heparin mimetic, was synthesized in different ways and used as coating on multiple iron-palladium alloys. Static and dynamic PT and APTT of the prepared materials were compared to samples uncoated or coated with polyethylene glycol. Sulfated pectin was characterized by NMR and FTIR, and the coated alloys by SEM and EDX.

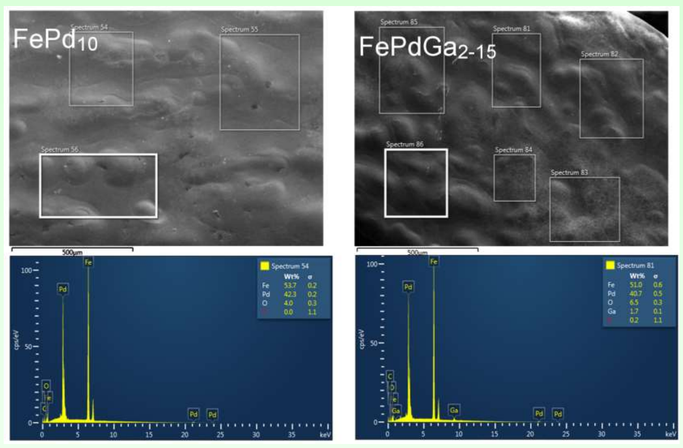


Synthesis: Three samples of sulfated pectin were synthesized using sulfamic acid as a mild and stable reagent under different reaction conditions.[1,2] This is the first time sulfated pectin has been prepared in these ways.





FTIR shows the successful incorporation of sulfate groups into pectin in all cases. It also shows differences in the degree of sulfation, which was also confirmed by photometric analysis of sulfate content. Comparison of ^{13}C-NMR spectra with literature data[3] also confirmed that sulfated pectin was obtained.



Four samples of FePd FSMA were prepared by melt spinning, pure FePd alloy and alloys doped with Ga and Mn. SEM showed the typical columnar structure, and EDX proved the composition to be the expected Fe, Pd as well as dopings of Ga and Mn

Results

➔Sulfated pectins 2 were prepared via a new, milder method using sulfamic acid

➔PdFe based FSMA ribbons (also doped with Ga and Mn)were prepared by melt-spinning

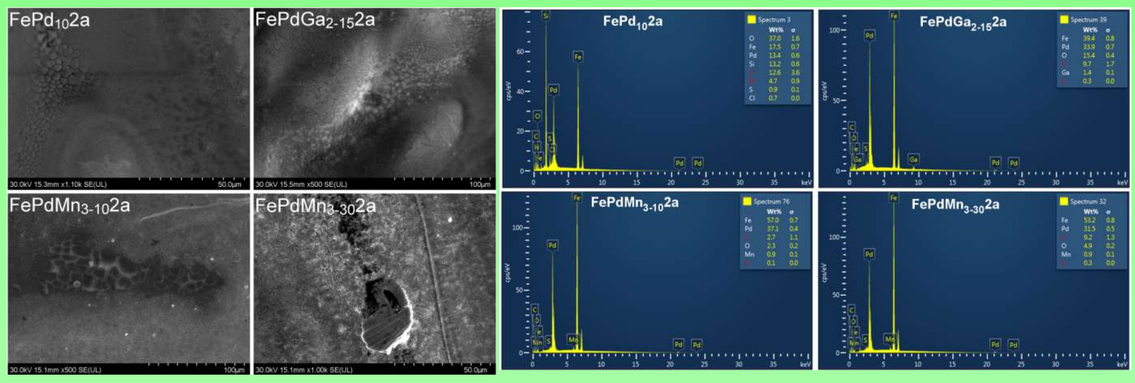
➔The FSMA ribbons were coated for the first time with anticoagulative polymers

➔APTT and PT tests demonstrate an anticoagulant activity of the new materials

➔The prepared coated ribbons thus show good potential to be used for temporary cardiovascular stents

[1] J.A. Sirvio, J. Ukkola, H. Liimatainen, *Cellulose*, **2019**, *26*, 2303-2316.
[2] V. Levdansky, A.S. Kondracenko, A. Levdansky, B. Kuznetsov, L. Djakovitch, C. Pinel, *J. Sib. Fed. Univ. Chem.*, **2014**, *7*, 162-169.
[3] Y. Roman, H.P.D. Barddal, M. Iacomini, G.L. Sassaki, T.R. Cipriani, *Carbohydr. Polym.*, **2017**, *174*, 731-739

Coating: The FSMA ribbons were then covered with both PEG as well as all three sulfated pectins by dip-coating. EDX proved that the coating was successful by showing higher carbon content and (in case of the sulfated pectins) also sulfur content.



Representative APTT (activated partial thromoboplastin time) and PT prothrombin time) values are shown below: while the influence of PEG and pectin coatings on either are negligible, coating with sulfated pectins 2 gives in each case an increased APTT, which means a significant anticoagulative effect. Since the PT values remained almost unchanged the anticoagulative effect of sulfated pectin is likely mainly for the intrinsic pathway. Also, the different sulfated pectins show a slight change in APTT overall, with the anticoagulative effect increasing in the order **2a** < **2b** < **2c**.

Entry	Sample	PT/INR [s] -static-	APTT [s] -static-	PT/INR [s] -dynamic-	APTT [s] -dynamic-
1	Normal	10,5 / 0.9	34	11,2 / 1.0	34
2	Positive control	11,4 / 0.9	32,7	11,4 / 0.9	32,7
3	$FePd_{10}$	11,2 / 0.9	33,2	13,2 / 1.1	38.2
4	$FePd_{10}$PEG	10,7/ 0.9	38,5	10,7 / 0.9	37,3
5	$FePd_{10}$**1**	11,7/1.0	30,2	11,7 / 0.9	37,3
6	$FePd_{10}$**2a**	12,5/1.0	44,5	12,6/1.1	46,2
7	$FePdGa_{2\text{-}15}$**2a**	14,3/1.0	44,7	10,3 / 0.9	47,3
8	$FePdMn_{3\text{-}10}$**2a**	11,5 / 1.0	40,9	12,1 / 1.1	44,2
9	$FePdMn_{3\text{-}30}$**2a**	13,6 / 1.0	43,3	11,9 / 1.0	45,1
10	$FePd_{10}$**2b**	11,9 / 0.9	52,6	11,6 / 0.9	54,9
11	$FePdGa_{2\text{-}15}$**2b**	12,7 / 1.0	50,6	12,5 / 1.0	57,3
12	$FePdMn_{3\text{-}10}$**2b**	12,5 / 1.0	47,5	13,1 / 1.0	50,5
13	$FePdMn_{3\text{-}30}$**2b**	12,4 / 1.0	49,3	11,9 / 0.9	51,2
14	$FePd_{10}$**2c**	11,5 / 0.9	61,5	11,4 / 0.9	65,4
15	$FePdGa_{2\text{-}15}$**2c**	14,3 / 1.0	64,5	12,7 / 1.0	65,3
16	$FePdMn_{3\text{-}10}$**2c**	12,4 / 1.0	49,7	12,5 / 1.0	51,8
17	$FePdMn_{3\text{-}30}$**2c**	13,1 / 1.0	52,4	12,3 / 1.0	55,4

Conclusions

Sulfated pectin materials were synthesized via new methods, using the milder reagent sulfamic acid, with sulfate contents of 1.44-2.44 mmol/g as proven by FTIR and ^{13}C-NMR. Several Fe/Pd based FSMA were prepared via melt-spinning, and have then been coated with potential anticoagulants for the first time. The successful coating was proven by EDX. Their anticoagulant activity was then investigated, and it was found that all sulfated pectins increase APTT both in static as well as in dynamic experiments above normal values. These results further demonstrate the usefulness of FSMA for biomedical applications, especially for temporary cardiovascular stents.

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