Research on Surface Modified Polysulfone as Potential Membrane for Simultaneous Hemodialysis and LDL Removal

李 晶（10929023）[1], 黄小军[1,*], Jörg Vienken[3], Thomas Groth[2], 徐志康[1]

[1] *MOE Key Laboratory of Macromolecular Synthesis and Functionalization (Ministry of Education), Department of Polymer Science and Engineering, Zhejiang University, Hangzhou 310027, China* [2] *Biomedical Materials Group, Dept. Pharmaceutics and Biopharmaceutics, Institute of Pharmacy, Martin Luther University Halle-Wittenberg, Halle (Saale) 06120, Germany* [3] *Fresenius Medical Care Deutschland GmbH, BioSciences Dept., Bad Homburg 61352, Germany.*

Introduction

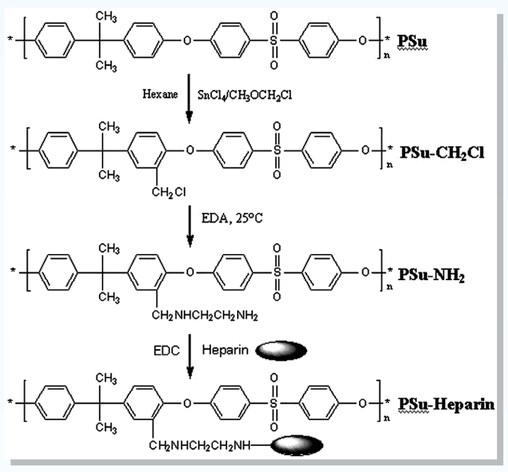
Symptoms and causes of chronic kidney disease (CKD), which always results in irreversible kidney damage requiring dialysis or kidney transplantation. The risk of dying from arteriosclerosis related diseases is higher in these individuals than the risk of dying from the causes related to end-stage renal disease (ESRD). Clinically, the abnormal and elevated level of **low-density lipoprotein (LDL)** in human blood has been regarded as one of the major causative elements for the progression of atherosclerosis. In order to treat patients with LDL-induced coronary heart disease (predominantly those patients with homozygous and severe heterozygous familial hypercholesterolemia), apheresis technologies for the lowering of LDL concentration in blood have been developed and gained broad clinical acceptance in recent years. Therefore, much attention has been attracted to develop more economical and effective adsorbents for LDL apheresis.

In our previous work, heparin was covalently immobilized onto **polysulfone (PSf)** dense films via various promoted methods. A PSf film with immobilized **heparin (PSf-Hep)** considerably enhanced the selective adsorption of LDL from protein mixtures. Moreover, adsorbed LDL could be easily desorbed with NaCl or urea solutions. Excellent blood compatibility of modified membrane was estimated from platelet adhesion, thrombin time, partial thrombin time and kallikrein activity, indicating potential as an LDL absorber for applications in **hemodialysis with simultaneous LDL removal**.

Inspired by the structure of heparin molecules, a "**multiple-interaction model**", where the saccharide components participate in the LDL adsorption process at biomaterial surfaces, was proposed. This proposed "multiple-interaction model" differs from earlier views in this field, and may allow for a better understanding of the interaction between LDL and LDL-receptor, the relationship between diabetes and hyperlipidemia, or the design of more efficient and low cost LDL adsorbers in the future.

Preliminary Research

Covalent heparinization of PSf via Chemical activation method [1]



Previous Work by Ph.D. Xiao-jun Huang [1]

√ **Covalent-immobilized**
chemically activated with amino groups, followed by heparinization

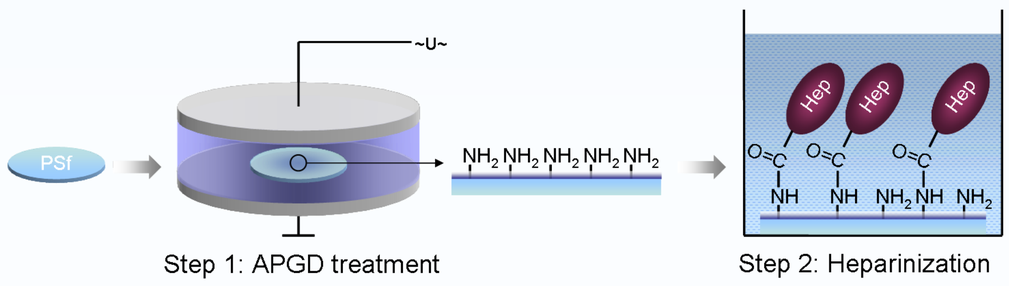
√ **LDL-affinity**
specific recognition and great absorbability to LDL from protein mixtures

× **Involving Toxic**
chemical activation process includes the use of tin(IV) chloride ($SnCl_4$) and chlorodimethyl ether

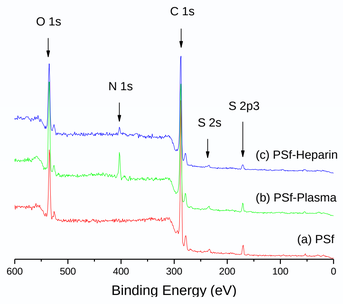
× **Time-consuming**

Potential Membrane for Simultaneous Hemodialysis and LDL Removal

Covalent heparinization of PSf : A simple and versatile method [2]



Scheme for heparinization of PSf membranes using **atmospheric pressure glow discharge** (APGD)

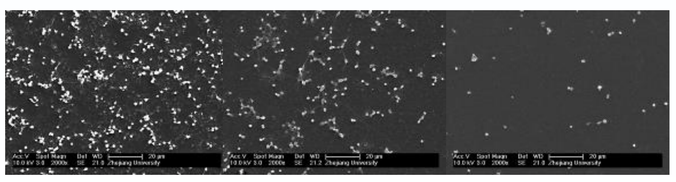


XPS confirmed successful **heparinization** of PSf

Simple

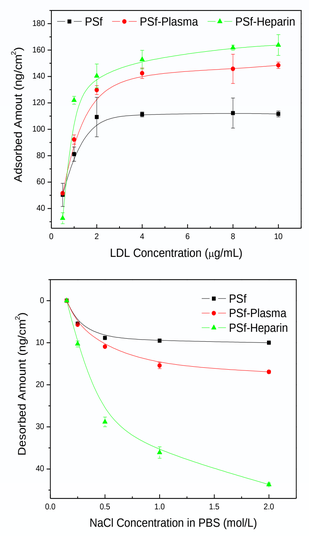
Convenient

Economical



Platelet adhesion on PSf (left), PSf-NH_2 (middle) and PSf-Hep (right) membranes visualized by SEM.

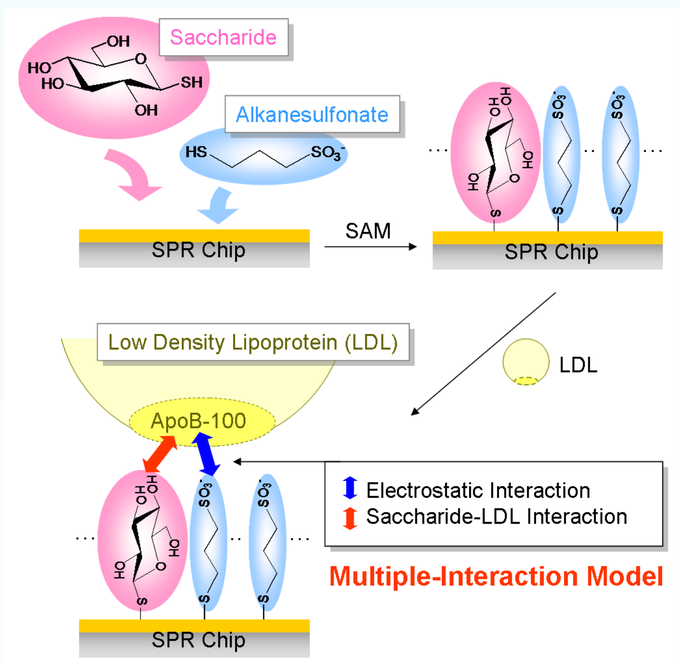
The potential for application of this **easily fabricated biomaterial** in LDL apheresis



Adsorption (up) and **desorption** (down) of LDL from single protein solution

Typical Research

New strategies for LDL affinity materials [3]

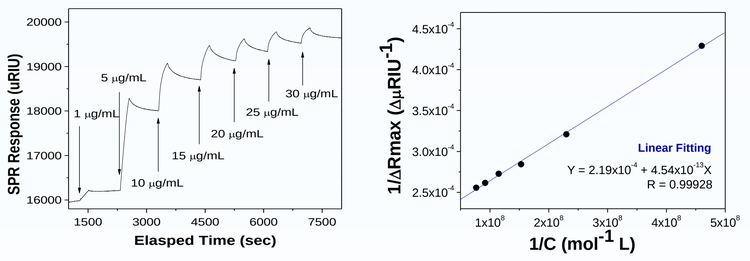


A model study of interactions between LDL protein and mixed SAM surface

✓ **New interaction**
between ligand and LDL besides electrostatic binding

✓ **New expression**
of possibility on LDLR in vitro

✓ **New strategies**
for LDL affinity materials in biomedical



The apparent affinity constant K_A for LDL of the sample (5-2) was 4.82×10^8 M^{-1}.

Left: Typical SPR adsorption sensorgram for sample (5-2)
Right: 1/*Req* vs 1/*C* plot for SPR measurement of sample (5-2)

LDL adsorption amounts of SPR chips with different surface ratios of glucosyl to sulfonic groups. On the x-axis, the input ratios of SAM solutions are presented in brackets, and the XPS detected ratios of surface composition given below.

Enhancing adsorption capability of LDL

Grant

The National Natural Science Foundation of China (Grant no. 21274126)
National "Twelfth Five-Year" Plan for Science & Technology Support of China (No. 2012BAI08B01)
Zhejiang Provincial Innovative Research Team (Grant no. 2009R50004)
The Open Foundation of Key Laboratory of Advanced Textile Materials and Manufacturing Technology (No. 2012001)

References:

[1] Huang, X. J.; Guduru, D.; Xu, Z. K.; Vienken, J.; Groth, T. *Acta Biomater* **2010**, *6*, 1099.
[2] **Li, J**.; Huang, X. J.; Ji, J.; Lan, P.; Vienken, J.; Groth, T.; Xu, Z. K. *Macromol Biosci* **2011**, *11*, 1218
[3] Bio-inspired Multiple-Interaction Model Revealed in Adsorption of Low-density Lipoprotein (LDL) to Surface Containing Saccharide and Alkanesulfonate, *submitted*

Contact:

Tel: 0571-87952605 **E-mail:** candysmile@zju.edu.cn