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**CAROLINE KARDEBY** received her Bachelor of Science degrees in Medical Science and Biomedical Laboratory Science from Uppsala University, in collaboration with Mid Sweden University, in 2011. She continued her studies at Örebro University where she was awarded her Master of Science degree in Medicine 2013. During her master studies Caroline took a special interest in platelet and their role in haemostasis. In 2014, Caroline started her doctoral studies at the

Haemostasis is a complex and tightly regulated process which is essential for survival. Platelets are paramount in maintaining haemostasis and protecting us from bleeding. If the haemostatic balance is disrupted, bleeding or thrombosis may occur. Thus, inflammatory processes of the vessel wall, like atherosclerosis, can lead to severe consequences like myocardial infarction and stroke. Inhibition of platelets and coagulation are common treatments to prevent unwanted blood clot formation. There is a great need for increased knowledge on the mechanisms of thrombosis and characterisation of new substances with possible therapeutic potential.

This thesis uses unique synthetic drugs to study platelet signalling and endothelial responses. The thesis describes the effect of two synthetic molecules; Synthetic sulfated glycopolymers that mimic the chemical properties of sulfated polysaccharides from seaweed, and a synthetic purine analogue with a nitrate ester motif.

It was found synthetic glycopolymers and natural polysaccharides cause human platelet aggregation via the Platelet endothelial aggregation receptor 1 (PEAR1), while mouse platelet aggregation is mainly dependent on C-type lectin-like receptor 2. Aggregation is supported by Glycoprotein Ib $\alpha$  in both species. In addition, the glycopolymers and polysaccharides trigger a proinflammatory response in cultured human endothelial cells. In contrast to the glycopolymers, the synthetic purine analogue with a nitrate ester motif reduces platelet functions by inhibiting Rho-associated protein kinase.

This thesis describes unique synthetic drugs that can be used for further studies of the mechanisms underlying the biological processes of thrombosis and inflammation. The synthetic glycopolymers can be used to further elucidate the physiological role of PEAR1, a potential future therapeutic target.

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Doctoral Dissertation

## Studies of platelet signalling and endothelial cell responses using unique synthetic drugs

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*Medical Science with a Specialisation in Biomedicine*

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