# Pathophysiological and platelet anti-aggregatory effects of nitric oxide

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# Thesis Summary

## *Background*

The phenomenon of platelet hyper-aggregability, documented in several cardiovascular disease states, is a factor that predisposes subjects towards pathological thrombotic events. Moreover, decreased platelet responsiveness to exogenously donated nitric oxide, implying reduced sensitivity to both nitric oxide donors and to endogenous sources of nitric oxide, with the resultant failure to regulate platelet function, may also contribute to the pathological complications associated with coronary artery disease (CAD).

The series of studies described herein were designed to firstly examine the phenomenon of platelet hyper-aggregability and attenuated platelet responsiveness to donors of nitric oxide in a series of patient cohorts. The first series of experiments was also designed to examine what role superoxide plays within each phenomenon. In doing so a whole blood superoxide detection method was established. Following on from these initial investigations, a study was then undertaken to examine potential determinants of reduced platelet responsiveness to nitric oxide. Finally, the thesis examined the anti-aggregatory and vasomotor effects of acute and chronic nitrate pharmacotherapy in a cohort of subjects with mild to moderate stable angina pectoris (SAP). As the final investigation was performed in a randomized fashion, an examination of the effects of nitrate pharmacotherapy on the phenomenon of reduced platelet responsiveness to nitric oxide was performed, along with an examination of the phenomenon of nitrate tolerance development following chronic nitrate exposure. An examination of the incidence of possible platelet hyper-aggregability upon acute nitrate withdrawal, as a means of explaining the phenomenon of "rebound" ischaemia, was also performed.