Title of the Thesis: The Role of nitric oxide in the aspirin induced thrombolysis in vitro and the purification of aspirin activated nitric oxide synthase from human blood platelet.

ABSTRACT

Background: Aspirin, a well-known inhibitor of platelet aggregation is extensively used for the prevention / treatment of coronary artery disease. The beneficial and antithrombotic effects of the compound are related to the inhibition of platelet cyclooxygenase. It is currently believed that aspirin has no effect on the formed thrombus which results in coronary artery disease. Methods & Results: It was found that the exposure of platelets to 4.0 μM aspirin either in vitro or in vivo resulted in fibrinolysis of the formed "thrombus" produced by the recalcification of platelet-rich plasma due to the production of NO in these cells by the compound. The lysis of clot in the presence of aspirin was found to be related to the fibrinolysis with simultaneous appearance of fibrin degradation products due to the generation of serine proteinase activity by NO in the assay mixture. The aspirin activated nitric oxide synthase that catalyzed the synthesis of NO in platelets was solubilized by Triton X-100 treatment and purified to homogeneity by chromatography on DEAE cellulose and Sephadex G-50 columns. The enzyme was found to be a single chain polypeptide with Mr 19 kDa. Investigation was carried out to determine fibrinolytic effect of in vivo exposure of platelets to aspirin in normal volunteers on the fibrinolysis of the clotted platelet-rich plasma in vitro. The thrombolytic effect of aspirin in situ was also carried out by injecting aspirin solution in the mice with ADP induced formed thrombi in the coronary artery. The treatment of human plasminogen with NO was found to directly activate the zymogen to plasmin without the formation of cyclic GMP in the assay mixture. Conclusion: Coronary artery disease has been established to be the consequence of the formation of thrombus at the site of atherosclerotic plaque rupture or fissuring in the coronary vessel wall. We investigated here that compared to other fibrinolytic agent, aspirin could be a very useful thrombolytic agent. A new way of application with the neutralized aspirin solution injection, through the stimulation of nitric oxide.