490f Tocopherols and Cehcs Modulate Platelet Thrombus Formation

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Platelets play a major role in atherosclerotic plaque formation leading to thrombosis or cardiovascular disorders. Many studies have reported that tocopherols possess anti aggregating properties along with anti oxidant properties when incorporated into the diet. The main goal of this project is to study the direct effect of tocopherols and their metabolites, carboxy ethyl hydroxyl chromans (CEHCs), on initial stages of platelet adhesion and aggregation and to investigate the underlying signaling mechanism.

Methods: We studied the effect □ – tocopherol , □ – tocopherol ,□ – CEHC and □ – CEHC on platelet adhesion and aggregation on collagen Type III surface at a shear rates of $100s^{-1}$ and $1000s^{-1}$ using whole blood in a parallel plate flow chamber. The effect of these drugs on platelet – platelet interactions was studied in a platelet aggregometer using convulxin as agonist. Activation of platelets by thrombin was studied in a flow cytometer by measuring platelet P-selectin expression.

Results: We saw that there was a significant decrease in platelet aggregation in the presence of □ – tocopherol (50 μM) compared to control, but not □ – tocopherol (50 μM). □ - CEHC (5μM) and □ – CEHC (5μM) have greater effect in reducing platelet aggregation than tocopherols at 1000 s^{-1}. However, there was no effect of these drugs at 100 s^{-1}. In the presence of L-NAME (L-Nitro arginine methyl ester), a potent inhibitor of nitric oxide production, there was less inhibition of platelet aggregation suggesting a role for eNOS (endothelial nitric oxide synthase). There was a dose dependent effect of □ - tocopherol and CEHCs in inhibiting platelet aggregation.

Conclusions: □ – tocopherol, also known as vitamin E, did not have any effect on reducing the platelet aggregation where as □ – tocopherol and other metabolites of tocopherols significantly inhibit platelet aggregation. Flow chamber studies indicate that □ – tocopherol and CEHCs partially effect platelet aggregation by eNOS pathway, but complete signaling mechanism needs to be investigated.