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WERASAK SUTIPORNPALANGKUL : STUDIES OF BLOOD-BORNE FACTOR(S) AFFECTING PLATELET FUNCTION IN THALASSEMIA. THESIS ADVISORS : UDOM CHANTHARAKSRI, Ph.D., YUPIN SANVARINDA, Ph.D., SUPEENUN UNCHERN, Ph.D. 153 P. ISBN 974-663-274-4

This study focuses on searching for oxidized phospholipids that mediate platelet dysfunction in β-thalassemia/Hb E patients. Evidence on the role of oxidatively modified phospholipids in the pathophysiological basis of cardiovascular-related diseases; i.e., in the genesis of atherosclerosis and thrombosis has been accumulating. The effect of oxidative stress in β-thalassemia/Hb E on the pathogenesis of platelet dysfunction has also been implicated.

By using three paramagnetic labeled compounds (5-, 12-, and 16-spin labeled stearic acids, SLS), oxidized phospholipids which have structural modification can be detected. Significantly higher levels of erythrocyte membrane fluidity were revealed with 12-, 16-SLS as probes in splenectomized patients when compared with nonsplenectomized and normal controls. In addition, the membrane fluidity was negatively correlated with various oxidative markers (TBARs, Iron indices). It became obvious that oxidative modified phospholipids were formed. This suggestion was strongly supported by the finding that vitamin E, a chain-breaking antioxidant can reduce membrane fluidity after daily supplementation for one month.

In recent years increasing evidence suggests that these oxidized lipids are resided in LDL and are key factors in the pathogenesis of thrombosis. Thalassemic LDLs were investigated to determine whether they can induce platelet activation. The shape-change parameter of the plasma-free human platelets was monitored following exposure of the platelet preparation to LDL, oxidized LDL, thalassemic LDL, or different fractions of lipid extract of the corresponding LDLs. In agreement with the previous finding, oxidized LDL, but not the native LDL, showed the platelet activating activity on the shape-change parameter. Although, thalassemic LDLs have no effect on the platelets. The LDLs from splenectomized thalassemia patients were more sensitive to the copper in generating platelet-activating activity in LDL molecules (less copper was needed) than that of nonsplenectomized and normal volunteers. Specifically phosphatidyl serine (PS) was found as the active compound in oxidized LDL that activates the platelets. These results suggest that bioactive phospholipids (PS) generated during the oxidative modification of LDL were likely the active components of oxidized LDL responsible in modifying the functionality of platelet in thalassemia.