3736151 SCPM/D : MAJOR : PHARMACOLOGY; Ph.D. (PHARMACOLOGY)
KEY WORD : LIPID HYDROPEROXIDES / LIPID PEROXIDATION / THALASSEMIA / LIPOPROTEINS

NARUMON LAOHAREUNGPANYA : ROLE OF LIPID HYDROPEROXIDES ON THE OXIDATIVE MODIFICATION OF LIPOPROTEINS IN THALASSEMIA. THESIS ADVISORS :UDOM CHANTHRAKSRI, Ph.D., YUPIN SANVARINDA, Ph.D., SUPEENUN UNCHERN, Ph.D., KOVIT PATTANAPANYASAT, Ph.D. 108P. ISBN 974-662-753-8

Abnormal lipoproteinemia is commonly found in thalassemia. The biochemical compositions and markers of oxidatively modified lipoproteins were studied in 10 β/Hb E thalaassemic patients and compared with those of 12 healthy volunteers. Abnormal lipoproteins in thalassemia were found in the oxidized forms. All fractions of thalassemic lipoproteins had significantly lower levels of total cholesterol with correspondingly higher level of the total iron and TBARs (a lipid peroxidation marker) than those of lipoproteins separated from healthy volunteers.

Lipid hydroperoxides (LOOHs) and the Fenton related reaction were found to play important roles in the oxidative modification of thalassemic lipoproteins. The higher levels of LOOHs in thalassemic LDL and HDLs were presented as the LOOHs to total cholesterol ratios. The endogenous levels of LOOHs in thalassemic lipoproteins were associated with degrees of iron overload in the patients. Deferiprone (L1), an orally active iron chelator, was able to lower the endogenous levels of LOOHs in lipoproteins without affecting the levels of total cholesterol and TBARs.

The LOOHs were shown to have a direct effect on the oxidative modification of LDLs *in vitro*. They were demonstrated in this study that: 1) ebselen, a LOOHs scarvenging compound was able to lower the extent of both auto- and $FeSO_4$-induced oxidation of LDLs 2) the endogenous levels of LOOHs in LDLs correlated inversely ($r = -0.55$, $P < 0.01$) with the levels of vitamin E in plasma suggesting that LDL was oxidatively modified in the thalassemic circulation, and 3) the elevated levels of LOOHs in HDLs were associated with the lowering in protective ability of HDLs in the oxidative modification of LDLs. The lower peroxidase like activities of HDLs in thalassemia was indeed refecting a compromized protective ability of HDLs on the LDLs from the pressure of oxidative insult. It thus concluded that LOOHs were playing an important role in the oxidative modification of lipoproteins in thalassemia.