10th World Congress on

Medicinal Chemistry and Drug Design

June 14-15, 2018 | Barcelona, Spain

Lyso-DGTS lipid isolated from microalgae enhances PON1 activities *in vitro* and *in vivo*, increases PON1 penetration into macrophages and decreases cellular lipid accumulation

Soliman Khatib^{1, 2} ¹MIGAL–Galilee Research Institute, Israel ²Tel-Hai College, Israel

igh-density lipoprotein (HDL) plays an important role in preventing atherosclerosis. The antioxidant effect of HDL is mostly associated with paraoxonase 1 (PON1) activity. Increasing PON1 activity using nutrients might improve HDL function and quality and thus, decrease atherosclerotic risk. We previously isolated and identified a novel active compound, Lyso-DGTS (C20:5, 0) from Nannochloropsis sp. ethanol extract. In the present study, its effect on PON1 activities was examined and the mechanism by which the compound affects PON1 activity was explored. Lyso-DGTS elevated recombinant PON1 (rePON1) lactonase and esterase activities in a dose- and time-responsive manner, and further stabilized and preserved rePON1 lactonase activity. Incubation of lyso-DGTS with human serum for 4 h at 37°C also increased PON1 lactonase activity in a dose-responsive manner. Using tryptophan-fluorescence-quenching assay, lyso-DGTS was found to interact with rePON1 spontaneously with negative free energy G=-22.87 KJ/mol at 25°C). Thermodynamic parameters and molecular modeling calculations showed that the main interaction of lyso-DGTS with the enzyme is through a hydrogen bond with supporting van der Waals interactions. Furthermore, lyso-DGTS significantly increased rePON1 influx into macrophages and prevented lipid accumulation in macrophages stimulated with oxidized low-density lipid dose-dependently. In-vivo supplementation of lyso-DGTS to the circulation of mice fed a high-fat diet via osmotic mini-pumps implanted subcutaneously significantly increased serum PON1 lactonase activity and decreased serum glucose concentrations to the level of mice fed a normal diet. Our findings suggest a beneficial effect of lyso-DGTS on increasing PON1 activity and thus, improving HDL quality and atherosclerotic risk factors.

solimankh@migal.org.il