

Dihydro-alpha-lipoic acid binds and protects fibrinogen from oxidation and affects fibrin formation

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N. Gligorijević^I, V. Šukalović^{II}, A. Penezić^I, O. Nedić^I

^IInstitute for the Application of Nuclear Energy (INEP), University of Belgrade, Belgrade, Serbia, Belgrade, Serbia, ^{II}Institute of Chemistry, Technology and Metallurgy, University of Belgrade, Njegoševa 12, 11000 Belgrade, Serbia, Belgrade, Serbia

A reduced form of the alpha-lipoic acid, dihydro-alpha-lipoic acid (DHLA) is a potent, naturally occurring antioxidant that is found in higher amounts in plants like spinach, broccoli, potatoes, tomatoes, carrots, beets and rice. DHLA can be consumed as a food supplement as well, at doses up to 600 mg/day. DHLA has an inhibitory effect on coagulation as it can reduce concentrations of some coagulation factors. This study investigated a direct interaction between DHLA and fibrinogen, the main protein in coagulation and hemostasis. DHLA binds fibrinogen with a moderate straight. Calculated constant from spectrofluorimetric titration for DHLA/fibrinogen complex was 10^4 M^{-1} . Fibrinogen stability remains the same with only marginal structural changes in its secondary structure favouring more ordered molecular organisation upon DHLA binding, as determined by Fourier-transform infrared spectroscopy. Coagulation assay showed that fibrinogen with bound DHLA forms fibrin with thicker fibres, as measured by coagulation assay and is protected from oxidation to a certain extent. Docking analysis showed that DHLA may bind fibrinogen in its D regions, which are directly involved in the fibrin formation. Obtained results support beneficial effects of DHLA on fibrinogen and consequently on coagulation process, suggesting that DHLA supplementation may be indicated for persons with an increased risk of developing thrombotic complications, particularly those whose fibrin is characterised by increased oxidative modification and formation of thinner and less porous fibres. Although further investigation is needed, our results suggest that DHLA in complex with fibrinogen can be located at the site of injury where it may exert antioxidant effects.

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