Phycocyanobilin is a new binding partner of human alpha-2-macroglobulin that protects the protein against oxidative stress

Abstract

Under simulated physiological conditions, this study investigates the interaction between nutraceutical phycocyanobilin (PCB) and the universal anti-protease protein human alpha-2-macroglobulin (α_2M). Extensive molecular docking analyses on multiple α2M conformations, spectroscopic techniques, and α2M activity assays were utilized to examine the complex formation. The results revealed that for every protein conformation, two high energy binding sites exist: the first, conformationally independent, at the interface region between two monomer chains and the second, conformationally dependent, in the pocket composed of amino acids from four distinct domains (TED, RBD, CUB, and MG2) of the single protein chain. Spectrofluorimetric measurements indicated a moderate affinity between α_2M and PCB with a moderately high binding constant of 6.3 ×× 10^5 M^{-1} at 25 °C. The binding of PCB to α_2M resulted in minor changes in the secondary structure content of α_2M. Furthermore, PCB protected α_2M from oxidation and preserved its anti-protease activity in the oxidative environment. These findings suggest that PCB binding could indirectly impact the body’s response to oxidative stress by influencing α_2M's role in controlling enzyme activity during the inflammatory process.