Inhibitory effects of lycopene on in vitro platelet activation and in vivo prevention of thrombus formation

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摘要

Abstract

Lycopene is a natural carotenoid antioxidant that is present in tomatoes and tomato products. The pharmacologic function of lycopene in platelets is not yet understood. Therefore, in this study we sought to systematically examine the effects of lycopene in the prevention of platelet aggregation and thrombus formation. We found that lycopene concentration-dependently (2 - 12 μmol/L) inhibited platelet aggregation in human platelets stimulated by agonists. Lycopene (6 and 12 μmol/L) inhibited phosphoinositide breakdown in platelets labeled with tritiated inositol, intracellular Ca+2 mobilization in Fura-2 AM - loaded platelets, and thromboxane B2 formation stimulated by collagen. In addition, lycopene (6 and 12 μmol/L) significantly increased the formations of cyclic GMP and nitrate but not cyclic AMP in human platelets. Rapid phosphorylation of a protein of 47,000 Da (P47), a marker of protein kinase C activation, was triggered by PDBu (60 nmol/L). This phosphorylation was markedly inhibited by lycopene (12 μmol/L) in phosphorus-32 - labeled platelets. In an in vivo study, thrombus formation was induced by irradiation of mesenteric venules in mice pretreated with fluorescein sodium. Lycopene (5, 10, and 20 mg/kg) significantly prolonged the latency period for the induction of platelet-plug formation in mesenteric venules. These results indicate that the antiplatelet activity of lycopene may involve the following pathways: (1) Lycopene may inhibit the activation of phospholipase C, followed by inhibition of phosphoinositide breakdown and thromboxane B2 formation, thereby leading to inhibition of intracellular Ca+2 mobilization. (2) Lycopene also activated the formations of cyclic GMP/nitrate in human platelets, resulting in the inhibition of platelet aggregation. The results may imply that tomato-based foods are especially beneficial in the prevention of platelet aggregation and thrombosis.