Comparison of the binding character of triflavin and on resting and activated aIIbb3 integrin in human platelets by electron microscopy.

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Abstract

Triflavin, an Arg-Gly-Asp (RGD)-containing disintegrin purified from venom peptide, inhibited platelet aggregation by interfering with the interaction of fibrinogen with aIIbb3 integrin. Using an immunostaining technique and electron microscopy, we investigated and compared the distribution of triflavin binding in both resting and activated platelets. Triflavin uniformly and strongly stained the plasma membrane and the open canalicular system (OCS), whereas a lesser extent of staining was seen on a-granules in both resting and activated platelets. Furthermore, resting unfixed platelets were incubated with triflavin for 10 min at 4°, and then rewarmed at 30° for 0, 10, and 30 min to advance internalization. At 0 min, platelets showed an extensive rim-staining pattern of bound triflavin on the surface membrane, which was then gradually internalized into the cytoplasmic OCS with prolonging of incubation times. However, triflavin bound fewer to a-granules than to the OCS within the 0–30-min period of internalization in both resting and activated platelets. Furthermore, triflavin did not influence physiologic endocytosis in resting platelets. Comparing the 3D structures of triflavin and another disintegrin, echistatin, we found that the spatial differences between the RGD motif and the C-termini of structures of disintegrins may mediate functional differences of binding activity toward aIIbb3 integrin in resting platelets. These data indicate that (1) triflavin binds effectively to aIIbb3 on the platelet membrane and cytoplasmic OCS, but a relative lesser extent to a-granules in both resting and activated platelets; (2) triflavin is internalized in resting platelets independent of cellular activation; and (3) spatial differences between the RGD motif and the C-termini of disintegrins may play an important role in mediating disintegrin binding to aIIbb3 in resting platelets.