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THE ROLES OF ATP AND CALCIUM IN MORPHOLOGY CHANGES AND CYTOTOXICITY INDUCED BY BENZOQUINONE IN PLATELETS

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To understand mechanism of benzoquinone-induced cytotoxicity, the roles of ATP and calcium in platelet toxicity and morphology changes was investigated. Using scanning electron microscopy, morphological changes to platelets following 1,4-benzoquinone exposure consisted of membrane blebbing at 5 min which was significantly different from shape changes (pseudopod formation) observed in response to physiological agonists. Benzoquinone-induced platelet membrane bleb formation was associated with rapid depletion of intracellular ATP and independent of presence of extracellular calcium. Benzoquinone-induced platelet lysis (LDH leakage) observed between 20-30 mins was dependent on extracellular calcium and associated with increased cytosolic calcium. Benzoquinone-induced cytotoxicity was inhibited by calmodulin antagonists, suggesting that calmodulin could play a major role in 1,4-benzoquinone toxicity via protease activation. These results suggested that the progression of events for quinone-induced cytotoxicity in platelets to be as follows: quinones deplete intracellular ATP; formation of blebs occurs; calcium homeostasis is disrupted, resulting activation of calmodulin-dependent proteases; irreversible cytotoxicity occurs.