Baicalein induction of hydroxyl radical formation via 12-lipoxygenase in human platelets: an ESR study

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摘要

Abstract

The pro-oxidant activities of baicalein, morin, myricetin, quercetin, and rutin were examined in various cell-containing systems including human platelets, rat vascular smooth muscle cells, human umbilical vein endothelial cells (HUVECs), human THP-1 cells, and fibroblast cells. Electron spin resonance (ESR) results showed that only baicalein generated hydroxyl radicals in a resting human platelet suspension, whereas the other flavonoids showed no effects on any of the resting cell systems. A low concentration of arachidonic acid (AA) increased the intensity of hydroxyl radicals, but a high concentration inhibited it. Collagen and thrombin, platelet aggregatory agents that can cause the release of AA by platelets, enhanced baicalein-induced hydroxyl radical formation, whereas ADP and U44619 showed no significant effects. Quinacrine and 5,8,11,14-eicosatetraenoic trifluoromethyl ketone, both PLA2 inhibitors, significantly attenuated baicalein-induced hydroxyl radical formation. These results suggest that baicalein-induced hydroxyl radical formation is associated with AA metabolite enzymes in human platelets. The formation of hydroxyl radicals was significantly inhibited by lipoxygenase inhibitors including nordihydroguaiaretic acid, (-)-epicatechin, (-)-epicatechin gallate, and hinokitiol, but was not affected by desferroxamine or the heme protein inhibitors KCN and NaN3. On the other hand, semiquinone free radicals were generated when baicalein was incubated with horseradish peroxidase/H2O2 or platelets/AA. The semiquinone radicals formed in the platelets/AA system could be extensively inhibited by desferroxamine, diethylenetriaminepentaacetic acid, KCN, and NaN3, indicating that prostaglandin H synthase (PGHS)-peroxidase may be involved. The results of this study led to the proposal that baicalein induces hydroxyl radical formation via 12-lipoxygenase and induces semiquinone radical formation via PGHS-peroxidase in human platelets.