

## Effect of NQ304, an Antithrombotic Agent, on the Arachidonic Acid Metabolism in Rabbit Platelet Aggregation

Dong-Ju Son, Young-Hyun Park, Yong-Ri Jin\*, Yeo-Pyo Yun\*

College of Natural Sciences, Soonchunhyang University, Asan, Korea

\* College of Pharmacy, Chungbuk National University, Cheongju, Korea

In the previous study, we have reported that 2-chloro-3-(4-hexylphenyl)-amino-1,4-naphthoquinone (NQ304), a vitamin K derivative, had potent inhibitory effects on human platelet aggregation *in vitro* and *ex vivo*, and on animal pulmonary thrombosis. In the present study, the effect of NQ304, an antithrombotic agent, on platelet aggregation and arachidonic acid (AA) metabolism was investigated using by rabbit washed platelets. Measurements of AA liberation and generation of thromboxane B<sub>2</sub> (TXB<sub>2</sub>) and prostaglandin D<sub>2</sub> (PGD<sub>2</sub>), through cyclooxygenase pathway, or 12-hydroxyeicosatetraenoic acid (12-HETE), through lipoxygenase pathway, from [<sup>3</sup>H]AA were evaluated by radio-chromatographic analysis with washed rabbit platelets *in vitro*. Collagen-, AA, or U46619-stimulated platelet aggregation were inhibited dose-dependently by NQ304. The IC<sub>50</sub> values of NQ304 on collagen-, AA- and U46619-induced rabbit platelet aggregation were calculated to be 3.9, 1.2 and 4.3 μM, respectively. Furthermore, NQ304 potently suppressed the AA liberation from [<sup>3</sup>H]AA-labeled rabbit platelets exposed to collagen, indicating that it may affect phospholipase A<sub>2</sub> (PLA<sub>2</sub>) activation on collagen-induced AA liberation from membrane phospholipids. However, NQ304 didn't suppress the TXB<sub>2</sub> generation induced by addition of [<sup>3</sup>H]AA in intact rabbit platelets, whereas PGD<sub>2</sub> and 12-HETE generation were enhanced by NQ304.

These results suggest that NQ304 may affect PLA<sub>2</sub> activation and which stimulate PGD<sub>2</sub> or 12-HETE generation from AA, thus eliciting the inhibition of platelet aggregation.