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Antiplatelet activity of some flavonoids

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Background: quercetin, rutin, naringin and naringenin are flavonoids found in the mesocarp of the fruits of different species of the genus Citrus (Rutaceae). The first two stand present an important phebotonic activity, while naringin and naringenin present in grapefruit are known by their interactions with other drugs, such as some antihistamines, whose association can lead to arrhythmias, a risk that is not present with quercetin and rutine.

Aims: It has been demonstrated that quercetin and rutin, and other polyphenols may exhibit antiplatelet effects "in vitro". In this study we have compared the antiplatelet activity of several polyphenols.

Methods: The study was performed using a flow cytometry technique in whole blood from healthy individuals (n = 20). Venous blood was collected from the antecubital vein into sodium citrate (3.8% wt/vol) tubes. Blood samples were analyzed by imaging and classical flow cytometry after density gradient separation. Acquisition and analysis were performed using a four fluorescences cytometer (Fac Dickinson) and the Summit analysis software (FlowJo-Treestar). For each subject, a two-dimensional dot-plot was constructed in three regions in which the platelets are distributed depending on the state of aggregation of the same. Two antibodies were used to identified platelets: a monoclonal antibody anti-GPIIIa (CD61) and polyclonal antibody IgG-FITC.

Drugs (quercetin, rutin, naringin and naringenin) were dissolved in DMSO at a final concentration of 2 mM and added to the corresponding blood tubes and incubated 30 min at 18-20°C. Calcium ionophore (A23187) was used at the final concentration of 25 mM dissolved in DMSO.

Results: All flavonoids tested increased platelet aggregation in the presence of the ionophore as compared to the control in the absence of the proaggregant. At the concentration of 2 mM the inhibition was $66.1 \pm 8.2\%$ for quercetin, 48.3 ± 11.8 for naringenin and $88,9 \pm 8.0$ for naringina ($p < 0,05$). However, rutin did not exhibit platelet antiaggregant properties.

Conclusion: Quercetin, but not quercetin-3-O-rutinoside (rutin), naringin (a flavanone glycoside) and naringenin (the main flavanone in grapefruit) inhibit human platelet aggregation but there was no correlation between the results obtained with the heterosides and the genins.