INTRODUCTION
Platelet Multidrug resistance Protein 4 plays a modulating role on platelet function. Platelet function and thrombus formation are impaired in MRP4 knockout mice models, and, among aspirin treated patients, high on aspirin residual platelet reactivity (HARPR) positively correlates with MRP4 levels.

OBJECTIVES
Assess the impact of cilostazol-induced inhibition of MRP4 mediated transport and assess aspirin-induced antiplatelet effects and rates of HARPR in humans.

METHODS
Platelet aggregation (PA) evaluated as percent of aggregation observed after 4 min stimulation (%PA) in response to collagen (threshold concentration).
ATP release (luciferin–luciferase assay) was measured to evaluate platelet secretion.
VASP Phosphorylation to study cAMP dependent cilostazol effects.
Populations: healthy volunteers (HV); patients under chronic aspirin treatment (N=122).

RESULTS
Collagen induced PA and secretion were inhibited when platelets were activated 10" after cilostazol addition (Figure 1).
VASP phosphorylation was absent at this time, indicating that such inhibition is not cAMP-cGMP correlated (Figure 2).
The effect of Cilostazol on PA is dependent on MRP4 inhibition, similar reduction was obtained using an MRP4 selective inhibitor, Ceefourin1 (Figure 3).
In aspirin treated platelets Collagen induced PA and secretion were inhibited by cilostazol (Figure 4).
Cilostazol treatment reduces collagen induced PA in patients with HARPR (Figure 5).

CONCLUSIONS
This study supports the role of MRP4 on platelet function which exerts its effects through cAMP independent mechanisms.
Inhibition of MRP4 by cilostazol enhances aspirin-induced antiplatelet effects.
Inhibition of MRP4 reduces HARPR, in patients under chronic aspirin treatment.