ANTI-PLATELET ACTIVITY OF ADENOSINE A2a RECEPTOR AGONISTS IN THE PRESENCE OF CAFFEINE AND ITS MAIN METABOLITES

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INTRODUCTION

Caffeine is the most frequently consumed behaviourally active substance in the world. Coffee, which is the richest caffeine source, is used daily by most of the general population worldwide.

Activation of blood platelets plays a crucial role in the initiation and development of arterial thrombotic diseases, which are the leading cause of morbidity and mortality in Western countries. An antiplatelet therapy is „a first choice" in the treatment of arterial thrombotic disorders. Targeting multiple platelet activation pathways is a promising strategy to develop effective anti-platelet therapy. However, according to our assumptions the use of A2A receptor agonists could play a significant role in anti-platelet combined therapy.

If so, extremely popular all over the world, habitual behaviour such as drinking coffee is likely to modulate such a therapy.

The aim of the current project is to verify the role of caffeine in affecting the efficacy of antiplatelet drugs. This poster presents the results of this year's research carried out to evaluate the effects of caffeine and its main metabolite, paraxanthine, on platelet function.

MATERIALS AND METHODS

We developed and used food frequency questionnaire to assess the amount of caffeine consumed by the donors.

We assessed the platelet function using two methods:
a) platelet aggregation (Multiplate aggregometer, Roche)
b) analysis of platelet activation markers using flow cytometry.

The study included 24 adults, 15 women and 9 men, at the age between 18 and 45.

Whole blood was incubated with caffeine (25 μM and 100 μM) and paraxanthine (10 μM and 40 μM), as well as adenosine agonists (0.2 μM HE-NECA, 1.2 μM regadenoson and 23 μM PSB0777).

RESULTS

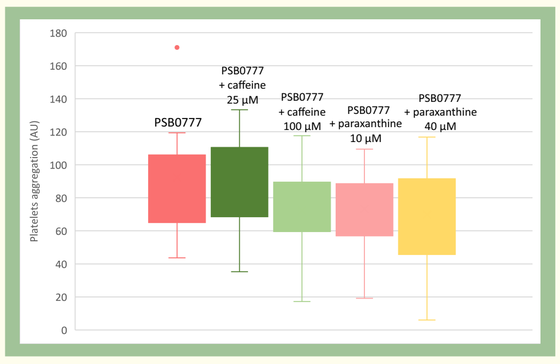

Figure 1. Inhibition of platelet aggregation by PSB0777 and by combinations of caffeine in low and high concentration (25 μM and 100 μM), as well as paraxanthine in low and high concentration (10 μM and 40 μM).

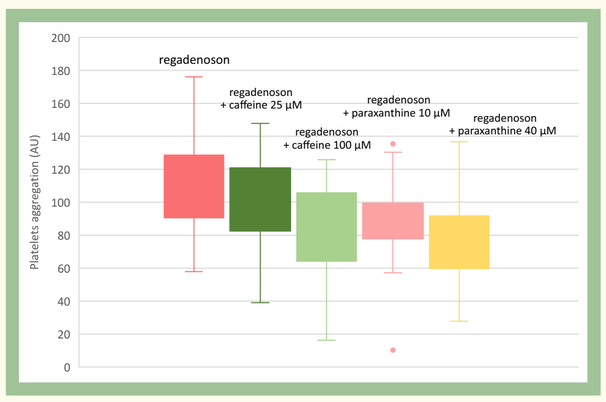

Figure 2. Inhibition of platelet aggregation by regadenoson and combinations of caffeine in low and high concentration (25 μM and 100 μM), as well as paraxanthine in low and high concentration (10 μM and 40 μM).

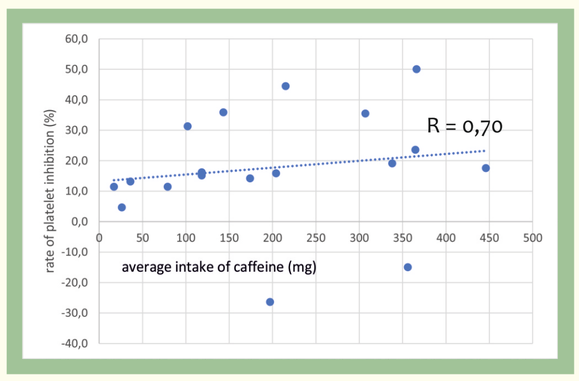

Figure 3. Correlation between platelets inhibition in the presence of caffeine in high concentration (100 μM) in vitro and average dietary intake of caffeine in the blood donors.

CONCLUSIONS

Our studies demonstrated the significant inhibitory effect of caffeine and paraxantine on platelet function.
Furthermore, adenosine agonists regadenoson and PSB0777 deepened the inhibitory effect of caffeine and its main metabolite on platelet activity.

Additionally, significant correlations were observed:

a) positive (R=0,70) between caffeine intake and degree of platelet activity inhibition when blood was incubated with caffeine 100 μM,

b) negative between caffeine intake and the degree of platelet activity inhibition when blood was incubated with paraxanthine 40 μM and HE-NECA (R=-0.59 for PAC-1 expression and R=-0.55 for P-selectin expression), as well as PSB0777 (R=-0.53 for PAC-1 and R=-0.57 for P-selectin).

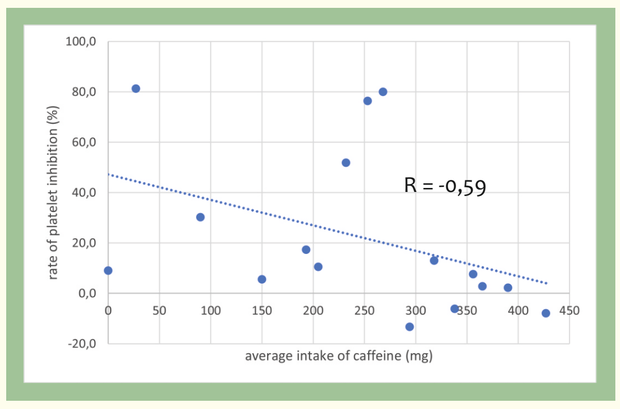

Figure 4. Correlation between platelets inhibition (PAC-1) in the presence of paraxanthine in high concentration (40 μM) and HE-NECA in vitro and average dietary intake of caffeine in the blood donors.

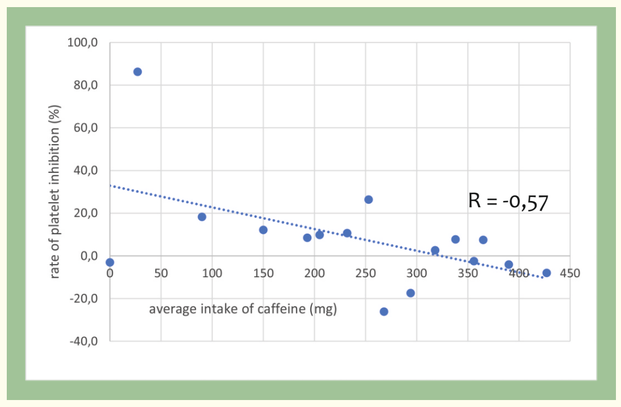

Figure 5. Correlation between platelets inhibition (P-selectin) in the presence of paraxanthine in high concentration (40 μM) and HE-NECA and average dietary intake of caffeine in the blood donors.