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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. The use of caffeine to stay awake and alert is a long-standing habit. Coffee, which is the richest caffeine source, is used daily by most of the general population worldwide.
Moreover, it appears that coffee has health benefits due to the content of caffeine, cafestol, kahweol, chlorogenic acid and micronutrient (potassium, magnesium, niacin and vitamin E).

Targeting multiple platelet activation pathways is a promising strategy to develop effective anti-platelet therapy. In our recent project (2016-2019), we put forward a concept and verified it experimentally that the use of two types of drugs together (blockers of P2Y12 receptor for ADP activators of adenosine receptors) is a promising strategy.

The aim of this study is to verify the role of caffeine in affecting the efficacy of antiplatelet drugs.
Our assumption is that 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.

This poster presents the results of a pilot study to evaluate the effects of caffeine and its main metabolite, paraxanthine, on platelet aggregation.

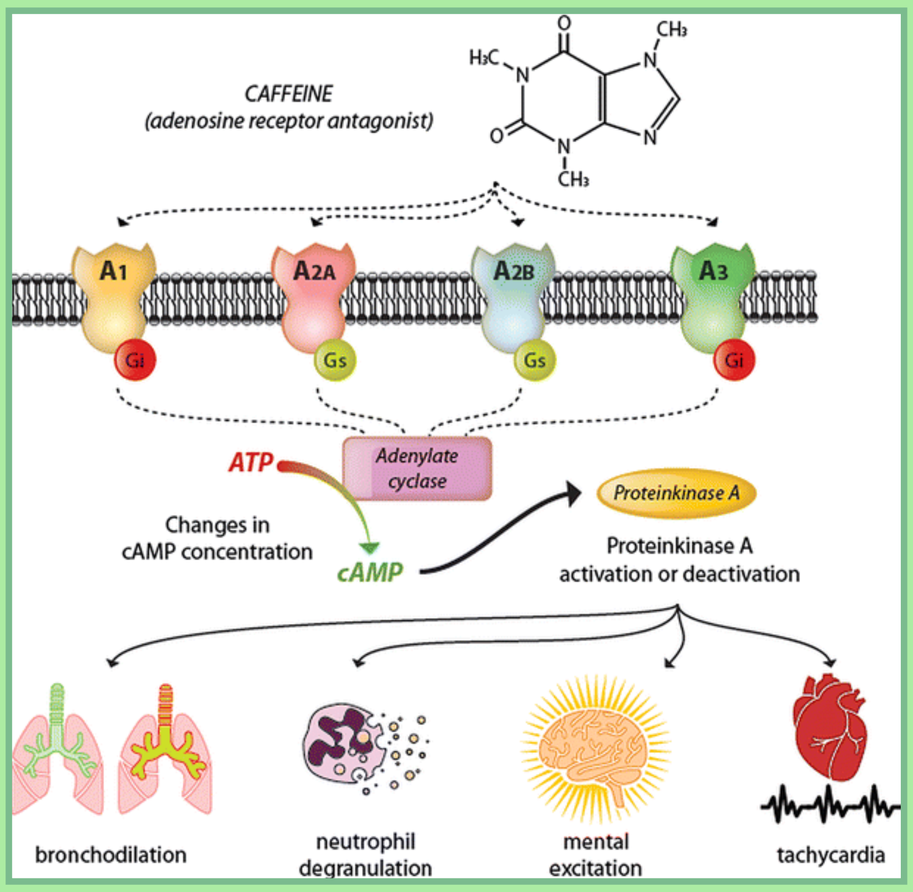

Figure 1: Scheme on the caffeine effects imposed by interaction with different adenosine receptors.
Source: Zulli A et al. Caffeine and cardiovascular diseases: critical review of current research. European Journal of Nutrition. 2016 Jun;55(4):1331-1343.

MATERIALS AND METHODS

We developed and used food frequency questionnaire to assess the amount of caffeine consumed by the donors. We determined a rate of platelet aggregation using an impedance technique (Multiplate aggregometer, Roche).

The study included 10 adults, 5 men and 5 women, at the age between 25 and 49.

The whole blood was collected from each of the participants and then incubated with two differents concentrations of caffeine (”low” level - 25 µM and „high” level - 100 µM) and two different concentrations of paraxanthine (”low” level - 10 µM and „high” level - 40 µM), as well as adenosine agonists (0.2 µM HE-NECA, 1.2 µM regadenoson and 23 µM PSB0777).

Incubation with caffeine and paraxanthine lasted 10 minutes, with adenosine agonists - 3 minutes. The blood was incubated at 37 degrees C.

RESULTS

SYMBOLS EXPLANATION:

KL - caffeine low (low concentration)
KH - caffeine high (high concentration)
PL - paraxantine low (low concentration)
PH - paraxantine high (high concentration)
H - HE-NECA
P - PSB0777
R - REGADENOSON

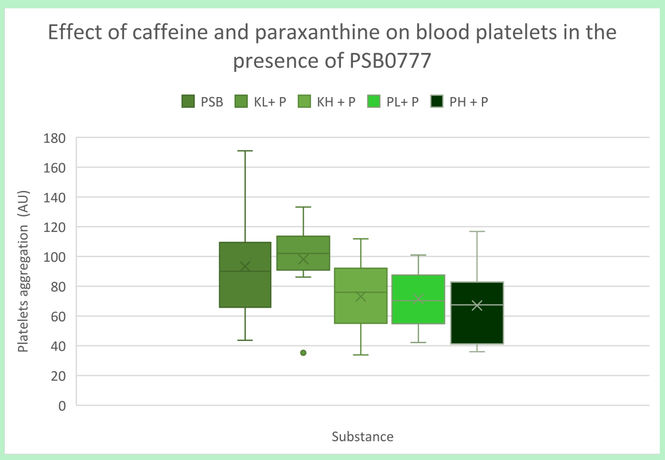

Figure 2: Comparison of platelet aggregation in samples containing PSB0777 and caffeine in low and high concentration (KL and KH, as well as paraxanthine in low and high concentration (PL and PH).

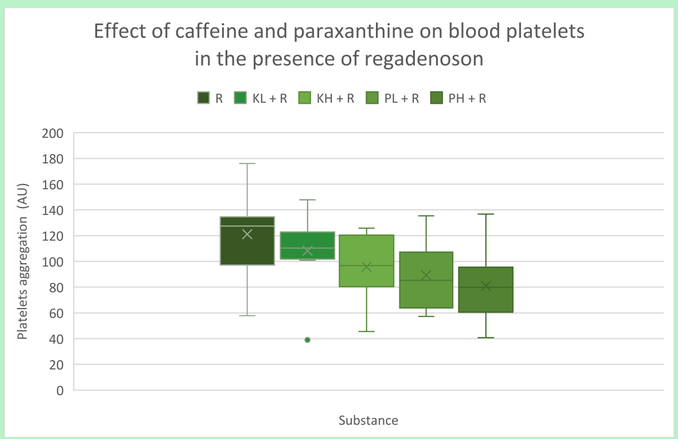

Figure 3: Comparison of platelet aggregation in samples containing regadenoson and caffeine in low and high concentration (KL and KH, as well as paraxanthine in low and high concentration (PL and PH).

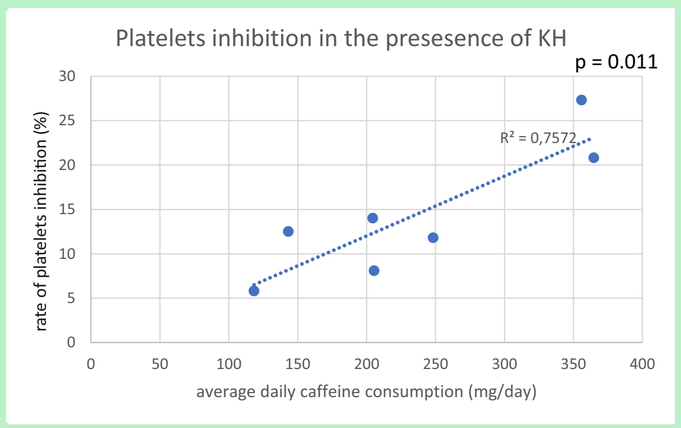

Figure 4: Correlation between platelets inhibition in the presence of caffeine in high concentration and average daily caffeine consumption among donors.

CONCLUSIONS

Our preliminary studies have proven that significant effects of regadenoson and PSB0777 on platelets incubated with caffeine and paraxanthine in different concentrations can be observed. As we initially assumed, incubation with the mentioned adenosine agonists deepened the inhibitory effect of caffeine and its main metabolite on platelet activity.

At the same time, a significant correlation ($R^2 = 0.7572$) between the amount of caffeine consumed by the donors and the degree of platelet inhibition was noted. In the other configurations, this correlation was no longer so apparent.

Nevertheless, due to the small study group (10 subjects), it would be necessary to continue the study in order to obtain more reliable results.