Characterisation of 2-arachidonylglycerol-induced platelet aggregation in rat whole blood

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The endocannabinoid, 2-AG, is released from activated platelets and can modulate aggregation in man (Maccarrone *et al.*, 2001). This study aimed to characterise the effects of 2-AG, and its interactions with other agonists, on platelet aggregation in rat whole blood. Male Sprague Dawley rats (300-500g) were anaesthetized with isoflurane and the carotid artery cannulated to allow blood withdrawal. Whole blood aggregometry was used to study the effects of 2-AG, ADP and the interactions among 2-AG, ADP and 5-HT (n=6-7). Data are expressed as mean ± SEM and compared with an unpaired Student's t-test or a repeated measure 2-way ANOVA (*P<0.05). 2-AG caused slowly developing aggregation that peaked at 10 min in contrast to the response to ADP which peaked at 2 min. Maximal responses to 2-AG 75, 150 and 300 μM were 9.8±3.4, 13.2±0.9 and 14.0±0.7Ω. Aggregation induced by 150 μM 2-AG was reduced to 2.0±1.7*Ω by 1 μM AM251 (CB_1 antagonist) and to 0.6±0.5*Ω by 1 μM AM630 (CB_2 antagonist). In further experiments, the TP antagonist ICI 192,605 markedly reduced aggregation induced by 150 μM 2-AG from 9.3±2.4 to -0.5±0.1*Ω. 5-HT did not cause platelet aggregation but it potentiated the response to 75 μM 2-AG at 5 min from 5.1±2.8 to 12.4±0.7*Ω. 2-AG prolonged and enhanced the aggregatory response to ADP and this effect was attenuated by ICI 192,605. This study demonstrated that the endocannabinoid, 2-AG, caused platelet aggregation in rat whole blood and interacted with other agonists to modulate aggregation through several mechanisms.

Maccarrone *et al.*, (2001) Eur J Biochem. 268, 819-825.