APAC, A DUAL ANTIPLATELET AND ANTICOAGULANT ATTENUATES COLLAGEN-INDUCED PLATELET AGGREGATION AND FIBRIN ELASTICITY IN BLOOD

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INTRODUCTION
APAC2, a semisynthetic mimic of heparin proteoglycans2-4 is a conjugate of unfractionated heparin chains (UFH) and albumin
• APAC inhibits both collagen-induced platelet aggregation in platelet-rich plasma (Fig 1A) and procoagulant activity in vitro and in vivo1
• In two baboon models of arterial thrombosis, collagen-coated shunt (S. Hanson, USA) and 30-90% stenosis model of injured femoral artery (J. Roodt, SA), APAC reduces platelet thrombus formation maintaining vessel patency
• APAC-[14C]retains at site in rat femoral anastomosis model 48 -120h
• APAC alleviates ischemic reperfusion injury in acute kidney injury

RESULTS
• Control (PBS) max aggregation (n=9): 90 ± 8 % and AUC 48 ± 8 %
• APAC (1-100 μg/mL) dose-dependently prolonged lag time, reduced slope and AUC reaching plateau at 30 μg/mL, 85 ± 12 %
• UFH (100 μg/mL) was without any effect

APAC inhibits B) collagen (CIPA)- and C) ristocetin-induced platelet aggregation unlike UFH in blood

METHODS
• Blood perfusion over collagen (coating with 200 μg/mL) at arterial shear rate of 90 dyn/cm² for 4 min
• Platelets stained with Mepacrine (10 μM)
• Von Willebrand factor (VWF) immunostained with polyclonal rabbit anti-human VWF (cat no AD082, Dako)
• Inverted epifluorescence microscope Zeiss Axiovert 200 with Axiacam camera, and analyzed with ImageJ

RESULTS
APAC inhibits A) CIPA unlike UFH in PRP

APAC broadly attenuates blood coagulation measured with ROTEM while UFH acts mainly in INTEM

APAC reduces platelet deposition under arterial shear rate on collagen surface in whole blood

CONCLUSIONS: APAC
✓ inhibits collagen- and ristocetin-induced platelet aggregation both in blood and PRP, unlike UFH
✓ reduces platelet deposition on collagen surface at high shear rate with subsequent decrease of VWF binding
✓ is a stronger and broader anticoagulant in ROTEM than UFH
✓ carries dual anti-platelet and anticoagulant functions