Poster Board P3-003

0874 SULOCTIDIL DOES NOT INHIBIT VASCULAR PROSTACYCLIN ACTIVITY IN RATS.

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Suloctidil [1-(4-isopropyl-thiophenyl)-2-n-octylaminopropanol, Continental Pharma, Belgium] is a drug which inhibits platelet aggregation in human beings and possesses antiplatelet aggregation and antithrombotic properties in several animal models. In the present study, the acute effect of suloctidil on vascular prostacyclin activity was evaluated in rats. Male CD rats (250-300 g) were given the drug (200-400 mg/kg b.w.) orally 1 h before testing. Prostacyclin activity was measured as the platelet aggregation inhibitory potency of supernatant buffer following 4 min incubation with rings of either abdominal aorta or inferior vena cava. Treatment with suloctidil did not induce any significant modification of prostacyclin activity. In contrast, *in vivo* platelet aggregation induced by i.v. infusion of ADP (1 mg/kg) or collagen (2.6 mg/kg) was significantly ($p<0.001$) inhibited. It is suggested that suloctidil may interfere with platelet function without affecting the potential antithrombotic activity of the vascular wall.

P3-004

0875 EFFECT OF SULOCTIDIL ON PGI_2 PRODUCTION AND INHIBITION OF PLATELET AGGREGATION.

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Recent findings have suggested that the *in vivo* balance between the biosynthesis of proaggregating substances by blood platelets (e.g. thromboxane A_2, endoperoxides) and antiaggregating substances produced by the vessel wall (PGI_2) might be critical for thrombus formation. We therefore investigated the effect of suloctidil (S), indomethacin (I), acetylsalicylic acid (ASA) and tranylcypromine (T) on these parameters. Male Sprague-Dawley rats (200-300 g) fasted for 12 h were given a single i.v. dose (0.5 and 1 mg/kg) of S (glucuronate salt) or 200 mg/kg of the other compounds. Ten min after the injection, rats were killed and segments of the abdominal aorta and inferior vena cava were excised. PGI_2 production by these segments vascular tissue was assessed by platelet aggregation inhibitory activity. PGI_2 production was almost completely inhibited by ASA, I and T whereas S enhanced the production (or possibly the effect) of PGI_2-like activity. The effect of S was dose dependent and was statistically significant at 1 mg/kg. *In vitro* studies showed that 100 µM S potentiated the inhibitory effect of synthetic PGI_2 on platelet aggregation.

P3-005

0876 BAY i 7351, A NEW PLATELET INHIBITOR, AND ANTITHROMBOTIC COMPOUND

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4,4'-Dichloro-N,N'-bis [(1-methyl-4-piperidinyl)-methyl]-2,2'dithiobis-benzamide = BAY i 7351 was tested in animal models (rat and rabbit) of traumatically induced thrombosis. After prophylactic administration of small doses of BAY i 7351 (0.3 mg/kg p.o.) to rats the thrombus formation is inhibited ($p < 0.05$) both in the arterial and the venous system by 79% and 57%, respectively. Further on thrombi already formed (20 and 24 h old) are reduced in weight. The minimal effective doses of these thrombolytic effects in rats are 2 mg/kg p.o. in the carotid artery, and 6 mg/kg p.o. in the jugular vein, when administered in two single doses of 1 and 3 mg/kg. The compound is not an anticoagulant or a fibrinolytic drug. It is an inhibitor of platelet aggregation - induced with various aggregating agents including ADP -, in vitro with minimal effective concentrations in the range of 1-10 µg/ml as well as ex vivo (minimal effective dose: 3-10 mg/kg p.o., rat). Further investigations as to various platelet functions, influence on thromboxane and prostacyclin formation will be reported separately. BAY i 7351 is a compound with properties which are considered favourable for treatment of thromboembolic diseases.