[PB2-1] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Effects of the Angiotensin II AT1 receptor antagonist SK-1080 on isolated rat hearts and on platelet aggregation and coagulation in human blood.

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SK-1080 is one of the newly developed orally active nonpeptide Ang II AT1-receptor antagonist that selectively act at AT1 receptor with high affinity.
The cardiac effect on ischemia/reperfusion injury of SK-1080 was compared with those of losartan, a prototype of this class, in isolated rat hearts. Isolated perfused rat heart was pretreated with drug for 10min and then subjected to global ischemia for 30min followed by reperfusion with- or without drug for 30min.
The possible additive effect of SK-1080 on the platelet aggregation and coagulation in human blood was also studied. We investigated whether SK-1080 effects the platelet aggregation induced by ADP, a platelet agonist partially dependent on thromboxaneA2 .
The clotting times in the prothrombin time(PT) and activated partial thromboplastin time(APTT) were also examined in vitro as coagulation screening test.
SK-1080 improved reperfusion function(LVDP, left ventricular developed pressure; double product, LVDP×heart rate/1000) in a dose-related manner, whereas ADP-induced platelet aggregation was less inhibited than those by losartan.

[PB2-2] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Down-regulation of genes by Peroxisome Proliferator

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Peroxisome proliferators (PPs) induce hepatocyte proliferation, thus increasing the liver weight. Long-term treatment of PPs induced the hyperplastic state of liver and eventually developed to liver tumor in rodents. In this study, we first examined expression pattern of down-regulated genes in rat liver by treatment of PPs (clofibrate, di(2-ethylhexyl)phthalate, di(2-ethylhexyl)adipate, or wy14643, perchloroethylene) using differential display-reverse transcription polymerase chain reaction (DDRT-PCR). We examined the expression of down-regulated cDNA fragments by reverse northern blot. Only 12 fragments of the 82 cDNA were confirmed as down-regulated genes in reverse northern blot. According to the result of the DNA sequencing study, 3 of the 12 cDNA fragments showed 100% homolgy to reported proteins such as transferrin, apolipoprotein A1(Apo A1), or α-1-inhibitor III(α1IIII). α1IIII is known to one of acute phase proteins of which the plasma concentration is changed during the acute phase response to tissue injury and to acute and chronic inflammation. However down-regulation of α1IIII mRNA by PPs has not been reported previously. Apo A1 has been reported to have embryogenesis promoting effects. Transferrin has also been reported to be regulated by hepatocyte nuclear factor-4 and decreased by competitive action of peroxisome proliferator-activated receptor. Subsequently it is likely that PPs used in this study may affect the embryogenesis through the transcriptional reduction of three proteins, transferrin, α1IIII, or Apo A1.