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Antiplatelet characteristics of Z4A5, a novel selective platelet glycoprotein IIb/IIIa inhibitor, under long-term infusion

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Glycoprotein IIb/IIIa inhibitors are important in the treatment of acute coronary syndromes (ACS) and percutaneous coronary interventions due to their effects on the final common pathway of platelet aggregation. Z4A5 is a new hexapeptide IIb/IIIa inhibitor with antiplatelet and antithrombotic effects. This study was performed to assess the stability of the antiplatelet effects and characteristics of Z4A5 with long-term infusion. Light-transmission aggregometry was used to measure platelet aggregation to assess the antiplatelet efficacy of Z4A5 *in vitro* and *ex vivo*. The activity of Z4A5 against platelet aggregation and template bleeding time were evaluated after 8-hour intravenous infusions in Beagle dogs following a 3×3 Latin square design. The recovery of platelet function after suppression by Z4A5 was compared with the recovery following eptifibatide and tirofiban administration 4h after termination. Z4A5 completely inhibited Adenosine diphosphate (ADP)-induced *in vitro* platelet aggregation with an IC50 of 265.8±22.9 nM. It also markedly and stably prevented ADP-induced *ex vivo* platelet aggregation and prolonged the bleeding time throughout the 8-hour infusion. Platelet function suppressed by long-term infusion of Z4A5 recovered significantly faster than after eptifibatide infusion. Consistent with the faster platelet function recovery, the template bleeding time returned to baseline sooner after Z4A5 infusion. Z4A5 can be more readily controlled by physicians to monitor platelet function and is safer for clinical use because it decreases the risk of post-dose bleeding in ACS patients compared with two other GP IIb/IIIa inhibitors.

Biography

Xiao-Lian Shi has completed her Ph.D. at the age of 34 years from Sun Yat-sen University and postdoctoral studies from University of Pittsburgh School of Medicine. She has published more than 10 papers in reputed journals and is the Winner of 11th CNPHARS-Servier Young Investigator Awards in Pharmacology in 2007.

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