

Protein Tyrosine Phosphatases...(continued)

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New Product Highlights

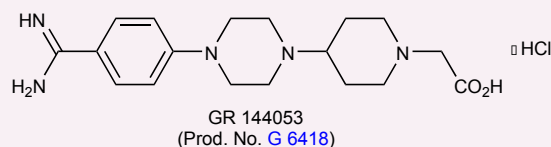
GR 144053: Non-peptide antagonist of the platelet glycoprotein IIb/IIIa (GP IIb/IIIa) fibrinogen receptor

Following vascular injury, platelets become activated and adhere to damaged blood vessel walls and exposed sub-endothelial connective tissues thereby forming the initial platelet plug. Platelets play a central role in thrombus formation and are known to participate in many life-threatening thrombotic disorders such as acute myocardial infarction, stroke and pulmonary embolism. One platelet receptor involved in this activation is glycoprotein Ib/IX (GP Ib/IX) together with its ligand von Willebrand factor (vWF). Activation causes the exposure of phospholipids (PL) and the membrane glycoprotein IIb/IIIa (GP IIb/IIIa) on the platelet surface, providing a platform upon which the members of the coagulation cascade can assemble.

GR 144053 (Prod. No. **G 6418**) is a potent and selective, non-peptide antagonist at the glycoprotein IIb/IIIa (GP IIb/IIIa) fibrinogen receptor [1,2]. It acts as a mimetic of the peptide RGD-sequence, a potent inhibitor of GPIIb/IIIa. Binding of GR 144053 to GPIIb/IIIa competitively blocks the binding of its normal ligand, **fibrinogen** (Prod. No. **F 4883**), and alters the signaling properties of the GPIIb/IIIa heterodimer. It attenuates platelet aggregation, activation and degranulation both *in vivo* and *in vitro* and inhibits ADP-induced platelet aggregation with an IC₅₀ value of 17.7 nM [2].

GR 144053 also suppresses the activation of platelets by **aurintricarboxylic acid** (ATA, Prod. No. **A 0885**) [2]. The molecular mechanism of ATA action has not been completely elucidated. One possible mechanism is through its binding to GP Ib, thereby blocking binding of vWF. This observation suggests additional activities for GR 144053 that are not mediated by the GP IIb-IIIa receptor [2].

GR 144053 is a useful tool for studying the mechanisms of platelet activation and degranulation events. Currently, anti-thrombotic therapy includes anti-platelet, anti-coagulant, pro-thrombolytic or pro-fibrinolytic agents. GR 144053 may be potentially useful in achieving anti-thrombosis effects while maintaining the integrity of the vascular system.



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