Comparative In Vitro Efficacy of Different Platelet Glycoprotein IIb/IIIa Antagonists on Platelet-Mediated Clot Strength Induced by Tissue Factor With Use of Thromboelastography

Differentiation Among Glycoprotein IIb/IIIa Antagonists

Shaker A. Mousa, Sandeep Khurana, Mark S. Forsythe

Abstract—In the present study, the in vitro efficacy of different platelet glycoprotein IIb/IIIa (GPIIb/IIIa) antagonists on platelet-fibrin-mediated clot strength under shear was compared with the antiaggregatory efficacy by using tissue factor (TF) thromboelastography (TEG). The ability of platelets to augment the elastic properties of blood clots under shear conditions was measured by computerized TEG under conditions of maximal platelet activation accelerated by recombinant TF. Under these conditions, platelets significantly enhance clot strength 8-fold (relative to platelet-free fibrin clots). This effect was inhibited to a different extent by various platelet GPIIb/IIIa receptor antagonists; this inhibition appears to be dependent on the transmission of platelet contractile force to fibrin via the GPIIb/IIIa receptors. The GPIIb/IIIa antagonists with high binding affinity for resting and activated platelets and slow platelet dissociation rates (class I) but not those with fast platelet dissociation rates (class II) demonstrated potent and comparable inhibition of platelet aggregation and TF-TEG clot strength. Platelet GPIIb/IIIa antagonists of class I, such as XV459 (free-acid form of roxifiban), DMP802, XV454, and c7E3, demonstrated comparable inhibitory dose responses of TF-TEG clot strength and platelet aggregation, with an IC50 of 50 to 70 nmol/L. In contrast, platelet GPIIb/IIIa antagonists from class II, with comparable antiaggregatory efficacy, such as DMP728, YZ202 (free-acid form of orbofiban), YZ211 (free-acid form of sibrafiban), YZ751, and other antagonists, have a much lower efficacy in altering the strength of TF-mediated clot formation (IC50 > 1.0 μmol/L). These data suggest differential efficacy among different GPIIb/IIIa antagonists in inhibiting platelet-fibrin clot retraction despite of equivalent antiaggregatory potency. (Arterioscler Thromb Vasc Biol. 2000;20:1162-1167.)

Key Words: platelet glycoprotein IIb/IIIa antagonists ■ binding kinetics ■ integrins ■ tissue factor ■ thromboelastography

Intravascular thrombosis is one of the most frequent pathological events and a major cause of morbidity and mortality in western civilization. Critical steps in the development of acute coronary syndromes are the disruption, rupture, or erosion of atherosclerotic plaque and the exposure of surface tissue factor (TF) with the formation of either partially or completely occlusive thrombus under shear.1–3 Factors that stimulate thrombosis include vascular damage, stimulation of platelets, and activation of the coagulation cascade. Platelet adhesion to exposed subendothelial surfaces of injured vessels, with subsequent activation, and the resulting platelet-rich clot formation have been shown to be associated with various pathological conditions, including cardiovascular and cerebrovascular thromboembolic disorders, such as unstable angina, myocardial infarction, transient ischemic attack, stroke, and atherosclerosis.3,4 Platelet-fibrinogen interaction is a key step in the pathogenesis of coronary artery thrombosis.1,4 The clinical benefit of aspirin and the more dramatic antithrombotic effect of intravenous antagonists of the platelet surface glycoprotein IIb/IIIa (GPIIb/IIIa) receptor underscore the importance of platelet involvement in acute coronary ischemia.5–8 Platelet GPIIb/IIIa blockade with c7E3 (ReoPro) reduces myocardial infarction and death associated with unstable angina and percutaneous transluminal coronary angioplasty.8 Such therapy, however, may be associated with a risk of hemorrhagic complications. There is considerable person-to-person variability in the number of GPIIb/IIIa receptors and their ligand binding functions; in patients with coronary artery disease, enhanced platelet GPIIb/IIIa receptor expression may be a marker for increased thrombotic risk. Furthermore, variable inhibition of GPIIb/IIIa function, which is partly due to
differences in platelet count, may occur after the administration of weight-adjusted c7E3. Although conventional light transmittance platelet aggregometry has been used to measure the degree of ex vivo platelet aggregation inhibition in early clinical studies and dose-finding studies, its routine clinical use for dosing in individual patients has not been feasible.9

Activated platelets exert contractile force; when allowed to interact with polymerizing fibrin, tensile strength is significantly increased.10–12 This physical property of activated platelets and fibrin can be measured by computerized thromboelastography (TEG).10,13 In a recent report, the active form of roxifiban, XV459, demonstrated antiplatelet efficacy and specificity to the platelet GPIIb/IIIa receptors; antiaggregatory efficacy depends on the degree of receptor occupancy, the type of agonist used, and its concentration.14 TEG has great advantages over other techniques in measuring clot strength in whole blood (WB) under shear. However, its value in relation to the prediction of clinical outcome still remains to be determined in clinical trials.

The present study was undertaken to characterize the efficacy of comparable antiaggregatory platelet GPIIb/IIIa antagonists with different platelet GPIIb/IIIa binding kinetics on platelet-fibrin clot retraction by use of TF-TEG. Those GPIIb/IIIa antagonists can be classified on the basis of their platelet binding kinetics into 2 classes. Class I includes GPIIb/IIIa antagonists with relatively high and comparable binding equilibrium affinity for resting and activated platelets and slow platelet dissociation rates. In contrast, class II GPIIb/IIIa antagonists include compounds with relatively lower affinity for resting platelets and fast platelet dissociation rates. Examples of class I include roxifiban (XV459), DMP802, XV454 (nonpeptide), and c7E3 (monoclonal antibody), and class II includes DMP728 (cyclic peptide), orbofiban (YZ202), YZ211 (sibrafiban), and YZ751 (nonpeptide).

Methods

Thromboelastography

TEG has been used in various hospital settings since its development by Hartert15 in 1948. The principle of TEG is based on the measurement of the physical viscoelastic characteristics of blood clots. Clot formation was monitored at 37°C in an oscillating plastic cylindrical cuvette (“cup”) and a coaxially suspended stationary piston (“pin”) with a 1-mm clearance between the surfaces by use of a computerized Thrombelastograph (TEG model 3000, Haemoscope). The cup oscillates 4°45 (1/12 radian) in either direction every 4.5 seconds, with a 1-second mid-cycle stationary period, resulting in a frequency of 0.1 Hz and a maximal shear rate of 0.1 per second. The pin is suspended by a torsion wire that acts as a torque transducer. With clot formation, fibrin fibrils physiologically link the cup to the pin, and the rotation of the cup, as affected by the viscoelasticity of the clot (transmitted to the pin), is displayed online by using an IBM-compatible personal computer and customized software (Haemoscope Corp). The torque experienced by the pin (relative to the oscillation of the cup) is plotted as a function of time (Figure 1).

TEG assesses coagulation by measuring various parameters, such as the time latency for the initiation of the clot (R), the time to initiation of a fixed clot firmness (K) of ~20 mm amplitude, the kinetics of clot development as measured by the angle (α), and the MA of the clot.

The following parameters were measured from the TEG tracing (Figure 1): (1) The reaction time (gelation time) represents the latent period before the establishment of a 3D fibrin gel network (with measurable rigidity of ~2-mm amplitude). (2) MA (in millimeters) is the peak rigidity manifested by the clot. (3) Shear elastic modulus or clot strength (G, in dynes per square centimeter) is defined as $G=(5000A)/(100−A)$.

Blood clot firmness is an important parameter for in vivo thrombosis and hemostasis because the clot must stand the shear stress at the site of vascular injury. TEG can assess the efficacy of different pharmacological interventions on various factors (coagulation activation, thrombin generation, fibrin formation, platelet activation, platelet-fibrin interaction, and fibrin polymerization) involved in clot formation and retraction. The effect of TF (25 ng) on the different clot parameters measured by computerized TEG in human WB is shown in Table 1.

Blood Sampling

Blood was drawn from consenting volunteers under a protocol approved by the Human Investigations Committee of William Beaumont Hospital. By use of the 2-syringe method, samples were drawn through a 21-gauge butterfly needle, and the initial 3 mL blood was discarded. WB was collected into siliconized Vacutainer tubes (Becton Dickinson) containing 3.8% trisodium citrate such that a ratio of citrate WB of 1:9 (vol/vol) was maintained. TEG was performed within 3 hours of blood collection.

Platelet Contribution to Clot Strength

To assess the effect of TF on clot modification, peak clot strength was measured with and without the addition of TF (25 ng) in paired samples of WB and platelet-rich plasma (PRP). To document the contribution of activated platelets to the elastic modulus of fibrin

![Diagram of TEG and tracing showing the initiation and completion phases of platelet-fibrin clot initiated by TF (25 ng) under shear in human WB. TEG assesses coagulation by measuring various parameters, such as the time latency for the initiation of the clot (R), the time to initiation of a fixed clot firmness (K) of ~20 mm amplitude, the kinetics of clot development as measured by the angle (α), and the MA of the clot.](image)

**Figure 1.** Diagram of TEG and tracing showing the initiation and completion phases of platelet-fibrin clot initiated by TF (25 ng) under shear in human WB. TEG assesses coagulation by measuring various parameters, such as the time latency for the initiation of the clot (R), the time to initiation of a fixed clot firmness (K) of ~20 mm amplitude, the kinetics of clot development as measured by the angle (α), and the MA of the clot.

| Table 1. Effect of TF (25 ng) on Different TEG Parameters in Human WB |
|-------------------------|------------------|
| **TEG Parameters**      | **TF Effects**   |
| R, min                  | 14.8 ± 1.3       |
| K, min                  | 5.8 ± 1.0        |
| α                       | 45.0 ± 2.6       |
| MA, mm                  | 58.2 ± 1.7       |

Values are mean ± SEM (n = 22). R indicates time latency for initiation of clot; K, time to initiation of clot firmness of ~20-mm amplitude; and α, angle.

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clots, the effect of platelet number was measured by serially diluting PRP with platelet-poor plasma (PPP). The platelet count of each dilution was measured before performing TEG. TF-triggered TEG was performed with increasing concentrations (0, 0.625, 1.25, 2.5, 5, and 10 μmol/L) along with dimethyl sulfoxide added to the TEG cups such that the final dimethyl sulfoxide concentration in each TEG sample was 0.3% (vol/vol). The effect of GPIIb/IIIa blockade on clot strength was studied by adding increasing concentrations of c7E3 Fab (abciximab, Centocor), cyclic peptide, and peptidomimetic and nonpeptide GPIIb/IIIa antagonists (DuPont) to the TEG cup along with CaCl2 and TF. The TEG MA for MA for platelets was calculated by subtracting the MA from a PPP sample determined in 1 TEG well from the MA of WB run simultaneously in the second TEG well.

**Platelet Aggregation**

Agonist-induced platelet aggregation was measured as change in percent light transmission of PRP (platelet count 2 × 10^10 per μL). For studying the effect of GPIIb/IIIa antagonists on platelet aggregation, increasing concentrations were added to PRP for 5 minutes, after which 10 μmol/L TRAP (SFLLRN, Peninsula Labs) was added. The aggregation response was measured as the maximum response (t50) value and percent light transmission of PRP (platelet count 2 × 10^8 platelets). For the different radiolabeled GPIIb/IIIa antagonists to activated and nonactivated platelets, the resulting 3H-radioligand/PRP was carefully removed and centrifuged for 2 minutes (10,000 g) and counted with a liquid scintillation counter. Counts per minute recovered are compared with the control (t = 0) value and the wells and centrifuged for 2 minutes (10,000 g). The resulting MA for platelets was calculated by subtracting the MA from a PPP sample determined in 1 TEG well from the MA of WB run simultaneously in the second TEG well.

**GPIIb/IIIa Antagonist Binding Affinity to Activated and Resting Human Platelets**

This assay was used to determine the saturable binding of a compound to platelets by using PRP. Citrated WB (5 mL draw, Vacutainer tubes containing 3.2% sodium citrate) was collected from healthy, aspirin-free, human subjects and centrifuged for 10 minutes at 150g at 22°C with a Sorvall RT6000 Table Top Centrifuge (DuPont). PRP was removed and pooled, and platelets were counted with a Coulter T540 Hematology Analyzer. Saline (810 μL, 0.9% USP [Baxter], containing 1 mmol/L calcium chloride) and 40 μL of radiolabeled [3H]-XV459, [3H]-XV454, [3H]-DMP802, [3H]-DMP728, and [3H]-c7E3 at different concentrations were added to the assay tubes, followed by 50 μL of PRP (2 × 10^10 platelets per milliliter). Samples were incubated for 10 minutes at 22°C. For platelet activation, 100 μL of ADP (10 μmol/L final concentration) was added to all samples, followed by incubation for 10 minutes at 22°C (pH of 7.5). Platelets were harvested through Whatman 934AH GFB filters. Filters were washed quickly 3 times with 5 mL of ice-cold saline, removed, and placed into scintillation vials. Six milliliters of DuPont NEN formula 989 per vial was added. The vials were allowed to stand for 60 minutes, and then they were shaken and counted by a liquid scintillation counter. Equilibrium binding affinity for the different radiolabeled GPIIb/IIIa antagonists to activated and resting human platelets was calculated by using a Scatchard plot.

**Dissociation Rates**

Citrated WB (5 mL draw, Vacutainer tubes, containing 3.2% sodium citrate) was collected from healthy, aspirin-free, human subjects. Blood samples were divided to be used as WB or to be centrifuged for 10 minutes (150g). The resulting PRP was removed, and platelet counts were determined to normalize the radioiodinated platelets. Designated individual tubes of WB were treated for 60 minutes, with or without activation (ADP, 100 μmol/L), with 0.04 μmol/L of [3H]-XV459. To help ensure sample viability during this period, the blood was maintained on a rocker. After this 60-minute incubation period, the tubes were centrifuged for 10 minutes (150g). The resulting [3H]-radioiodinated PRP was carefully removed and centrifuged with a liquid scintillation counter. Counts per minute recovered are compared with the control (t = 0) value and percent light transmission of PRP (platelet count 2 × 10^10 platelets). For the different radiolabeled GPIIb/IIIa antagonists to activated and nonactivated platelets, the resulting 3H-radioligand/PRP was carefully removed and centrifuged for 10 minutes (150g). The resulting 3H-radioiodinated PRP was carefully removed and centrifuged for an additional 10 minutes (=250g). The resulting PPP was removed, and the platelet pellet was resuspended (∼1.6 × 10^7/mL) in fresh PPP. This suspension (500 μL) was transferred to wells of a 24-well plate (blocked with 5% BSA). To initiate dissociation, 100 μmol/L nonradioiodinated ligand was added to the wells. At designated time points (0, 2, 15, 30, 60, 90, and 120 minutes), the [3H]- or [125I]-bound (CPM) GPIIb/IIIa antagonist to PRP was removed from the wells and centrifuged for 2 minutes (10,000g). The resulting platelet pellet was counted with a liquid scintillation counter. Counts per minute recovered are compared with the control (t = 0) value and

<p>| Table 2. Platelet Binding Kinetics of Various GPIIb/IIIa Antagonists to Activated vs Resting Human Platelets |
|--------------------------------------------------------|------------------|------------------|
| <strong>GPIIb/IIIa</strong>  | <strong>Dissociation,† min</strong> | <strong>Mean Kd, nmol/L</strong> |</p>
<table>
<thead>
<tr>
<th>Antagonists</th>
<th>Resting</th>
<th>Activated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roxifiban</td>
<td>7</td>
<td>3.87</td>
</tr>
<tr>
<td>DMP802</td>
<td>32</td>
<td>0.50</td>
</tr>
<tr>
<td>XV454</td>
<td>120</td>
<td>0.65</td>
</tr>
<tr>
<td>c7E3</td>
<td>40</td>
<td>9.50</td>
</tr>
<tr>
<td>DMP728</td>
<td>0.20</td>
<td>36.00</td>
</tr>
<tr>
<td>Orbofiban</td>
<td>0.20</td>
<td>663</td>
</tr>
<tr>
<td>Sibrafiban</td>
<td>0.20</td>
<td>16</td>
</tr>
</tbody>
</table>

Values are mean for n = 4 to 5. XV459 is the free-acid form of DMP754 orroxifiban. YZ202 is the free-acid form of orbofiban, and YZ211 is the free-acid form of sibrafiban. In this in vitro study, the free-acid forms of the different prodrug GPIIb/IIIa antagonists were used. †t1/2 for dissociation from resting human platelets.

**Statistical Analysis**

Data are expressed as mean ± SEM. Data were analyzed by either paired or group analysis with use of Student t test or ANOVA when applicable. Differences were considered significant at P < 0.05.

**Results**

**Platelet GPIIb/IIIa Binding Kinetics**

Table 2 shows the binding affinity to activated versus resting platelets. XV459 binds with high affinity to resting and activated human platelets with Kd values of 2.52 ± 0.98 and 0.80 ± 0.16 nmol/L, respectively. DMP802 and XV454 demonstrated high affinity to either activated or resting human platelets with Kd of 0.2 to 0.50 nmol/L. Similarly, the chimeric 7E3 demonstrated a comparable affinity for resting and activated human platelets with Kd values of 9.1 ± 0.5 and 9.5 ± 0.6 nmol/L, respectively (Table 2). In contrast, DMP728 binds with high affinity to activated human platelets with a Kd of 0.32 and to resting human platelets with a Kd of 36.0 nmol/L (Table 2). DMP728, YZ751, YZ211 (sibrafiban), and YZ202 (orbofiban) from class II showed relatively faster dissociation rates (half-time of 3 to 10 seconds) from resting human platelets.

**Effect of TF on Strength of WB Clot**

To study the interaction of platelets with the fibrin network induced by TF, clot strength was measured with and without maximal TF (25 ng) activation in WB. TF activation reduced the time latency for the initiation of the clot and triggered acceleration of clotting in the presence of PRP but did not augment the clot strength (in dynes per square centimeter) in the presence of PPP (Figure 2). Both roxifiban and c7E3 blocked platelet-mediated TF augmentation of clot strength (Figure 2). The TEG MA for platelets was calculated by subtracting the MA from a PPP sample determined in 1 TEG well from the MA of WB run simultaneously in the second TEG well. The addition of abciximab or roxifiban at 100 nmol/L each resulted in maximal inhibition of platelet aggregation, platelet contractile force, and platelet MA. Platelet
contractile force and MA were significantly more responsive than was WB MA to the effect of abciximab and roxifiban, along with its reversal with the addition of fresh PRP.

The effect of TF (25 ng) on the dynamics of clot formation in human WB assessed by use of TEG is shown in Figure 3 (top tracing), and the effect of c7E3 (abciximab) on TF (25 ng)–induced clot formation in human WB assessed by use of TEG is shown in Figure 3 (middle tracing). Additionally, a comparable efficacy for c7E3 (class I) in inhibiting platelet aggregation induced by TRAP and clot formation induced by TF is shown in Figure 3 (bottom).

A representative tracing of the effect of class I versus class II platelet GPIIb/IIIa antagonists on clot retraction mediated by TF-TEG is shown (Figure 4).

**Effect of Different GPIIb/IIIa Receptor Antagonists on TF-TEG Clot Strength Compared With Turbidometric Platelet Aggregation**

Increasing concentrations of GPIIb/IIIa antagonists impaired the rate of increase in shear elastic modulus force (developed without prolonging the time latency for the initiation of the clot by TF-activated WB clots) to a different degree depending on binding kinetics of the GPIIb/IIIa antagonist. The degree of platelet inhibition by c7E3, roxifiban, DMP802, and XV454 was similar whether measured by TF-TEG or TRAP-induced aggregation (Table 3). In contrast, DMP728, orbofiban (YZ202), YZ211 (sibrafiban), and YZ751, which are lower affinity antagonists for resting platelets with relatively faster platelet dissociation rates (3 to 10 seconds), demonstrated lower affinity in altering clot structure compared with their potent antiaggregatory efficacy. LM609 (a monoclonal antibody) and XT199, small molecule nonpeptide antagonists for α,β, integrin, were without any effect on either platelet aggregation or TF-TEG–mediated clot strength (Table 3). Thus, under the conditions of our TEG assay, c7E3, DMP802, roxifiban (XV459), and XV454 blocked the contribution of platelets to the physical properties of the fibrin clot (Figure 5).

**Discussion**

TEG has been used to monitor hemostatic disorders in cardiovascular surgery.16–18 TEG has been used in cardiopulmonary surgery to predict bleeding and monitor the effectiveness of blood transfusions.19 TEG was recently modified and computerized to provide a greater level of precision.13 In the present study, the utility of TEG in determining the efficacy of different platelet GPIIb/IIIa antagonists was assessed. The final step in platelet aggregate formation is mediated exclusively by the GPIIb/IIIa receptor. Various large-scale phase III clinical trials have illustrated the usefulness of ReoPro in the treatment of coronary interventions.20–22 Additionally, other selective GPIIb/IIIa antagonists, including integrin, tirofiban (Aggrastat), and lamifiban, are in advanced stages of clinical development and are aimed primarily for intravenous use in the treatment and prevention of acute ischemic heart diseases.23–25 The Integrin to Minimize Platelet Aggregation and Coronary Thrombosis-II (IMPACT II) and Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrin Therapy (PURSUIT) trials with integrin and the Randomized Efficacy
TABLE 3. Antiplatelet Effects of β₃ Antagonists in Inhibiting Platelet Aggregation and TF-Mediated Clot Strength

<table>
<thead>
<tr>
<th>β₃ Antagonists</th>
<th>PRP Aggregation</th>
<th>TF-TEG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class I</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roxifiban</td>
<td>0.063±0.010</td>
<td>0.07±0.015</td>
</tr>
<tr>
<td>DMP802</td>
<td>0.044±0.008</td>
<td>0.05±0.004</td>
</tr>
<tr>
<td>XV454</td>
<td>0.038±0.007</td>
<td>0.05±0.006</td>
</tr>
<tr>
<td>c7E3</td>
<td>0.062±0.012</td>
<td>0.068±0.002</td>
</tr>
<tr>
<td><strong>Class II</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMP728</td>
<td>0.049±0.010</td>
<td>&gt;1.0</td>
</tr>
<tr>
<td>Orbofiban</td>
<td>0.200±0.010</td>
<td>&gt;1.0</td>
</tr>
<tr>
<td>YY751</td>
<td>0.170±0.030</td>
<td>&gt;1.0</td>
</tr>
<tr>
<td>Sibrafiban</td>
<td>0.110±0.050</td>
<td>0.74</td>
</tr>
<tr>
<td>αβ₃ antagonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LM609</td>
<td>&gt;1.0</td>
<td>&gt;1.0</td>
</tr>
<tr>
<td>XT199</td>
<td>&gt;1.0</td>
<td>&gt;1.0</td>
</tr>
</tbody>
</table>

Values are mean±SEM. Platelet aggregation (light transmittance) was performed by using PRP and TRAP (10 μmol/L). Clot strength was mediated by TF and measured by TEG. XV459 is the free-acid form of DMP754 or roxifiban, YZ202 is the free-acid form of orbofiban, and YZ211 is the free-acid form of sibrafiban. In this in vitro study, the free-acid forms of the different prodrug GPIIb/IIIa antagonists were used.

Study of Tirofiban for Outcomes and Restenosis (RESTORE) trial with tirofiban (Aggrastat) as well as other trials have demonstrated significant clinical benefits in acute ischemic syndromes. Clinical studies with orally active GPIIb/IIIa antagonists, including xemilofiban, orbofiban (YZ202), lotrafiban, and lefradafiban, have demonstrated oral antiplatelet activity in humans when administered 2 to 3 times per day.26 –30 Roxifiban and lefradafiban, have demonstrated oral antiplatelet activity in clinical studies with orally active GPIIb/IIIa antagonists, including roxifiban (class I, a) vs orbofiban (class II, b) in inhibiting TF (25 ng)–mediated clot formation under shear with use of TEG.

Table 3 shows the antiplatelet effects of β₃ antagonists in inhibiting platelet aggregation and TF-mediated clot strength. The table compares the IC₅₀ values (μmol/L) for various β₃ antagonists in PRP aggregation and TF-TEG clot strength. The data indicate that different β₃ antagonists exhibit varying degrees of efficacy in inhibiting platelet aggregation and clot strength.

In conclusion, a comparable inhibitory dose response for GPIIb/IIIa (class I) antagonists with high affinity for resting platelets and relatively slow dissociation rates (c7E3, XV459, XV454, DMP802, and others) in inhibiting clot strength (TF-TEG) and TRAP-induced platelet aggregation has been demonstrated. In contrast, GPIIb/IIIa (class II) antagonists demonstrate different efficacy in inhibiting platelet aggregation and clot strength under shear conditions.
with relatively lower affinity for resting human platelets along with relatively fast platelet dissociation rates from human platelets, such as DMP728, Y2202, YZ751, and others, have a much lower efficacy in inhibiting clot strength under shear, which might explain their potential differences in attaining different levels of clinical benefits.

References


4. Davies MJ, Thomas AC. Platelet-fibrin clot under shear, which might explain their potential differences in attaining different levels of clinical benefits.

References


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