

TXA, Fibrin Structure & Fibrinolysis

A mechanistic study explaining why timing and clot environment shape tranexamic acid efficacy

1 Timing changes the effect

Prophylactic model



When TXA was incorporated into the clot before tPA exposure, its antifibrinolytic effect could be lost. At physiological plasminogen (2.5 μM), lysis became **paradoxically faster**.

Therapeutic / active bleeding model



When clotting and fibrinolysis occurred simultaneously in the presence of TXA, lysis time was **consistently prolonged** across plasminogen concentrations.



Context matters more than dose alone.

2 TXA remodels fibrin architecture

Without TXA



Thinner fibers

With TXA (64 μM)



Thicker fibers



- TXA thickened fibrin fibers, even at low concentrations (16 μM).



- At 64 μM , the top-quartile fiber diameter more than doubled (~108.5 nm to ~228.3 nm).



- These structural changes likely alter how the clot responds to plasmin-mediated degradation.



Visualized by scanning electron microscopy (SEM)

TXA increases fiber thickness and alters fibrin network architecture.

3 Mechanistic insight from the assays



- The paradoxical acceleration in the prophylactic-style model was **not** caused by enhanced plasminogen activation.



- TXA **inhibited** plasmin generation at the clot surface across plasminogen concentrations.



- In ClotPro-style viscoelastic testing, TXA increased both **lysis time** and **maximal clot firmness**.

Key assay signals



Longer lysis time



Greater maximal clot firmness



Consistent antifibrinolytic effect in intrinsic assays



Net TXA effect = timing + plasminogen availability + clot microenvironment



Clinician takeaway

- ✓ Do not assume TXA has the same effect in every bleeding or prophylactic setting.
- ✓ The most consistent benefit aligns with early treatment of active bleeding / hyperfibrinolysis.
- ✓ Dynamic clot-based testing may help interpret antifibrinolytic response and fibrinolysis status.



Ideas for further research



Validate these mechanisms in whole blood and patient-derived samples.



Identify clinical settings or plasminogen states linked to reduced or paradoxical TXA response.



Test whether viscoelastic-test-guided TXA strategies improve outcomes.



Mechanistic in vitro study. Useful for hypothesis generation and clinical interpretation; not a stand-alone treatment protocol.