Tranexamic acid (TXA) summary
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Introduction
Tranexamic acid (TXA) is a drug that reversibly inhibits fibrinolysis and was introduced five decades ago. It was initially predominantly used in the obstetric setting in the management of postpartum haemorrhage (PPH), but currently the indications for TXA have increased. In Mzantsi Afrika, TXA is commonly known as Cyklokapron, which is the brand name. TXA is mentioned in emergency courses like Advanced Trauma Life Support (ATLS), Battlefield Advanced Trauma Life Support (BATLS), and International Truman Life Support (ITLS). TXA is approved by the South African Health Products Regulatory Authority (SAHPRA). TXA is also recommended by the South African Medicines Formulary (SAMF) and the Standard Treatment Guidelines and Essential Medicines List of South Africa.

Figure 1: A visual imagery of tranexamic acid.

Drug class [1, 2]
Tranexamic acid (TXA) is an **anti-fibrinolytic** amino acid derivative and it is a synthetic analogue of the amino acid **lysine**. Another drug in this class which is similar to TXA is **aminocaproic acid** which is 10-times less potent than TXA.

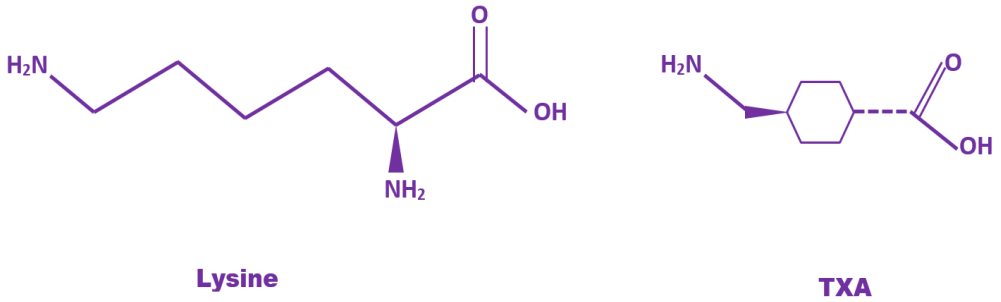

Figure 2: The biochemical structures of the amino acid lysine and TXA.

Mechanism of action [3, 4]
TXA competitively inhibits fibrinolysis. In the fibrinolysis pathway, TXA inhibits the conversion of plasminogen to plasmin, which results in plasmin being prevented from binding to fibrin. The ultimate mechanism of TXA results in the promotion of platelet aggregation.

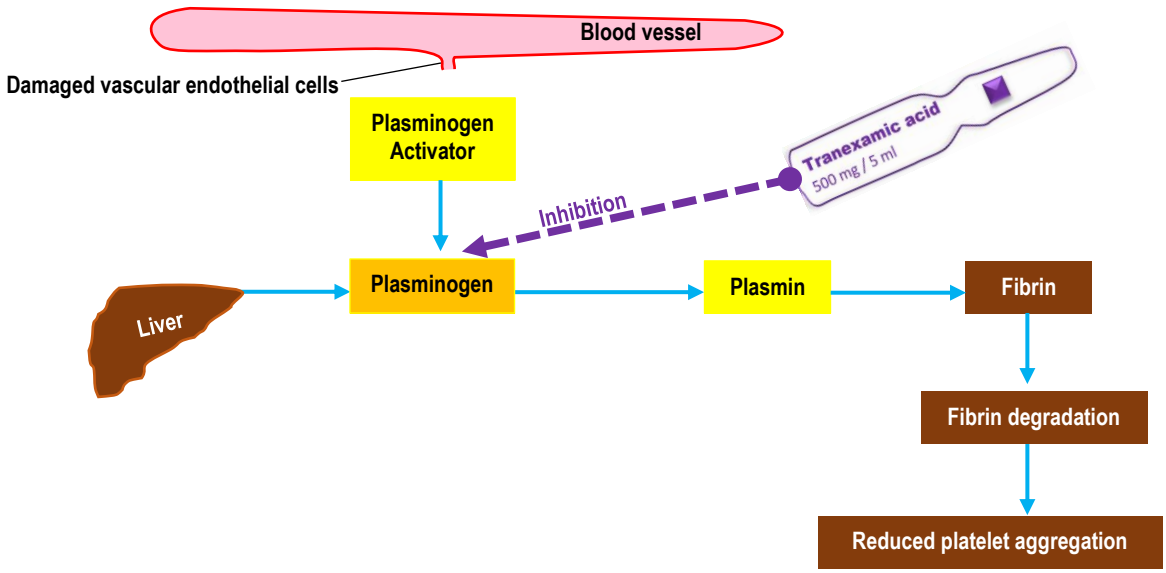

Diagram 1: Inhibition of plasminogen activation by TXA.

Side effects [5,6]

- Nauseas, vomiting and diarrhoea
- Colour vision disturbances
- Light-headedness
- Hypotension
- Hypersensitivity
- Seizures

Indications [7]

There are numerous opinions with regards to the use of TXA in Mzantsi Afrika. There is a differentiation between on-label use and off-label use of TXA. It is advised that the clinician follow the local guidelines with regards to the use of TXA.

- On label indications
    - Menorrhagia
    - Patients with coagulopathies who are going to be undergoing minor surgeries such as dental extractions.

- Off-label
    - Massive traumatic haemorrhage requiring massive transfusion.
    - Hereditary angioedema.
    - Hyphema.
    - CABG.
    - Postpartum haemorrhage (**PPH**).
    - Traumatic hyphema.
    - Total knee replacement.
    - Epistaxis in patients with Von Willebrand's Disease.

TRANEXAMIC ACID (TXA) INDICATIONS	
On-label	**Off-label**
• Menorrhagia • Dental extractions in haemophilia patients	• Hereditary angioedema • Traumatic hyphema • CABG • Massive Traumatic haemorrhage • Massive transfusion protocol • Postpartum haemorrhage (**PPH**) • Total knee replacement surgery • Epistaxis in Von Willebrand's Disease

Table 1: indications for Tranexamic acid.

Contraindications [8]

- A true hypersensitivity to TXA
- Upper urinary tract haemorrhage
- Subarachnoid bleeding
- Active intravascular clotting
- History of ischemic stroke, acute coronary syndrome (ACS), deep venous thrombosis (DVT) or pulmonary embolus in the preceding 6 months.
- Retinal vessel occlusion
- Epilepsy / seizures
- Vascular stent placement in the preceding 6 months.
- Combined oral contraceptives
- Liver impairment
- Renal impairment

Pharmacokinetics [9]

The oral bioavailability of TXA is not affected by food, and it is between 30% and 50%. The time taken to reach maximum concentration (T_{max}) is 2.5–3 hours. The elimination half-life (T½) post-intravenous administration is 2 hours. 95% of TXA is

excreted in the urine as an unchanged drug. After intravenous administration, 90% of the drug is eliminated within 24 hours. However, after oral administration, only 39% of the drug is eliminated within 24 hours.

Dosage [10]

Numerous dosing regimens for TXA have been documented by different protocols, and it is best advised that the clinician follow their local protocols.

- Menorrhagia: 1 – 1.5 g orally 3 – 4 times daily.
- Dental extractions: 25 mg/kg orally, 2 hours before procedure; 25 mg/kg 3 – 4 times daily for 7 days postoperatively.
- Hereditary angioedema: 1 – 1.5 g orally 2 – 3 times daily.
- Epistaxis in Von Willebrand's Disease: 1 g orally 4 times daily.
- Traumatic hyphema: 25 mg/kg orally 3 times daily for 7 days.
- CABG: 10-15 mg/kg IV over 20 minutes, then 1 mg/kg/hr continuous infusion for 6-10 hours.
- Total knee replacement: 10 -15 mg/kg IV over 30 min before inflation of tourniquet and 3 hr after first dose.
- PPH: 1 g slow IV over 10 minutes. Then repeat the dose after 30 minutes if there is ongoing vaginal bleeding.
- Massive transfusion: 1st dose: 1 g of TXA in 100 ml normal saline or ringers lactate and give over 10 minutes. 2nd dose 1 g TXA infused over 8 hours. Must be given within three hours from the onset of injury.

Important Studies on TXA

Numerous trials have changed how TXA is viewed and the table below lists some of these trials.

NAME OF STUDY	SUMMARY	IMPORTANT FINDINGS.
CRASH-2 2010	**A randomised controlled trial and economic evaluation of the effects of tranexamic acid on death, vascular occlusive events and transfusion requirement in bleeding trauma patients** Effects and cost-effectiveness of the early administration of a short course of TXA on death, vascular occlusive events and the receipt of blood transfusion in trauma patients. 1 g of TXA vs placebo given within 3 hours of trauma.	Early administration of TXA reduced the risk of death in bleeding trauma patients. Early administration of TXA in trauma patients is highly cost-effective. TXA administration after 3 hours of injury is ineffective.
MATTERS 2011	**Military Application of Tranexamic Acid in Trauma Emergency Resuscitation** To assess the effect of TXA administration on total blood product use, thromboembolic complications, and mortality.	Improved coagulopathy and survival. Most benefit noted in massive transfusion protocol (MTP) patients.
WOMAN TRIAL 2017	**World Maternal Anti-Fibrinolytic Trial** Randomised trial to assess the effects of TXA on death and surgical interventions in women with PPH. 1 g of TXA given to treat PPH	TXA reduces death due to bleeding in women with PPH with no adverse effects. TXA to be given as soon as possible after haemorrhage onset.
ATACAS 2018	Effects of TXA on cardiac surgery	Use of TXA was associated with a lower risk of bleeding post-operatively and was not associated with increased risk of death or thrombotic effects when compared to the administration of a placebo

Table 2: Examples of Trials on tranexamic acid.

Further reading

- Aminocaproic acid
- Dental extraction in haemophilia patients.
- Massive transfusion protocol.
- Management of postpartum haemorrhage.
- Role of TXA in cardiac surgery.
- CRASH-2 trial of 2010.
- MATTERS trial of 2012.
- Tissue plasminogen activator (t-PA) toxicity.

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