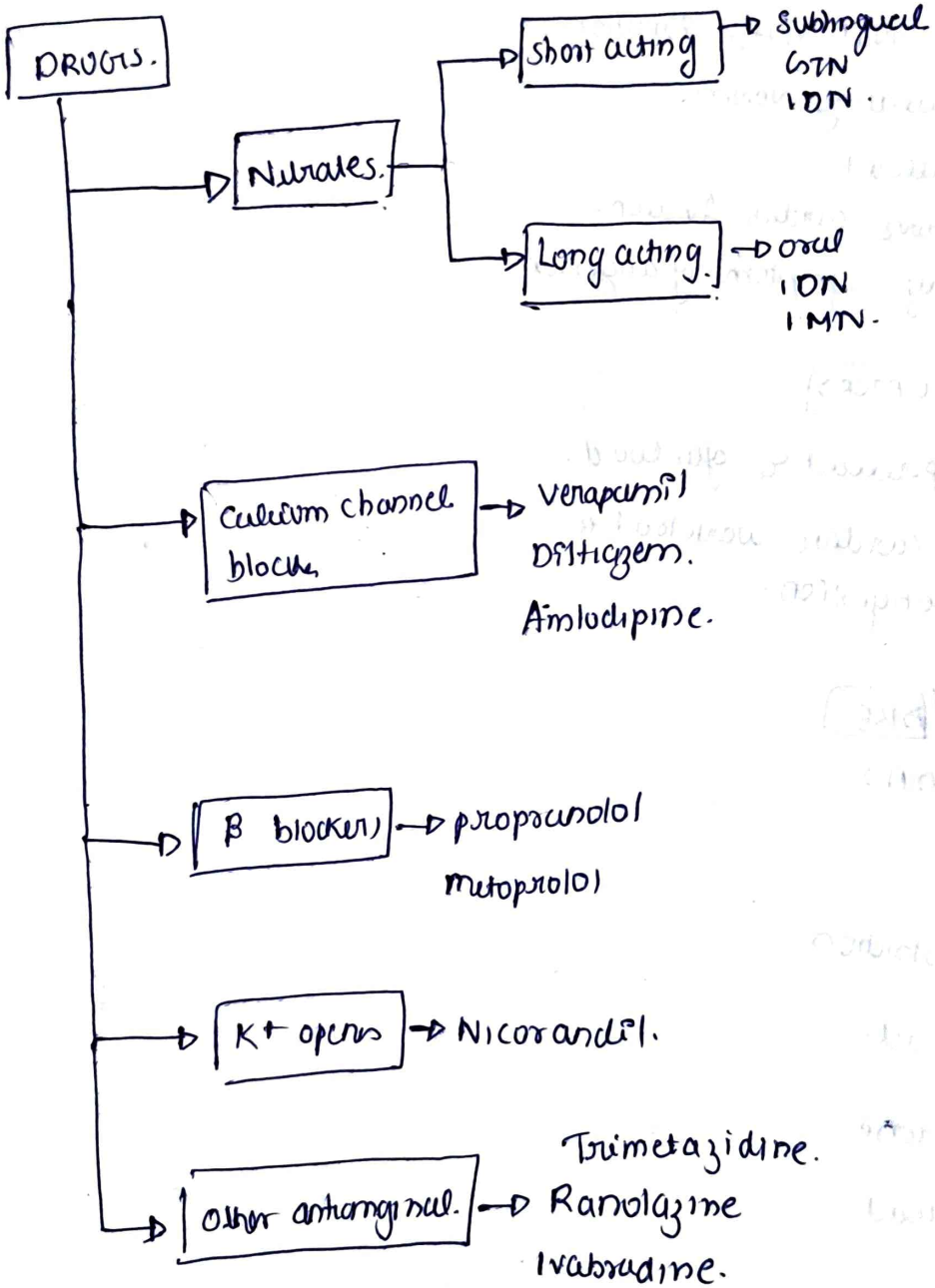

DRUGS.
Nitrates.
short acting
Sublingual
GTN
ISDN.
Long acting.
oral
ISDN
ISMN.
Calcium channel blocks
Verapamil
Diltiazem.
Amlodipine.
β blockers
propranolol
metoprolol
K+ opens
Nicorandil.
other antianginal.
Trimetazidine.
Ranolazine
Ivabradine.

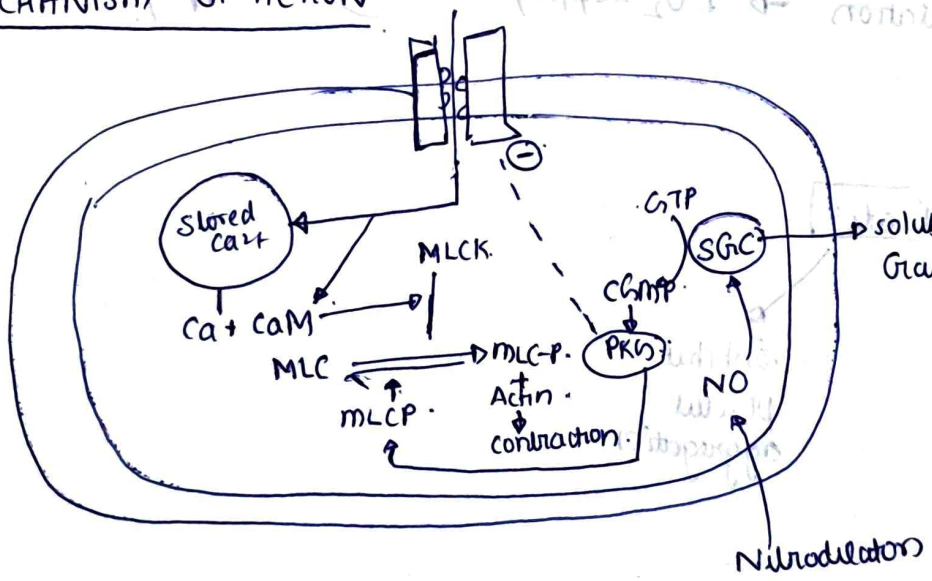
ANGINA

1. Classification ✓

Nitrates

- prodrug of Nitric oxide.

MECHANISM OF ACTION.



Nitrate
↓ mitochondrial aldehyde dehydrogenase.
NO
↓
activate soluble GC.
↓
↑ cGMP
↓
activates protein kinases G (PKG).

PK-G
↓ intracellular Ca^{2+}
① blocks L-type Ca^{2+} channel.
↓ Ca^{2+} influx.
② ↑ Ca^{2+} uptake into sarcoplasmic reticulum.
↓ Ca^{2+} - calmodulin complex.
↓ MLCK activation.

↑ myosin LCP.
• MLCP dephosphorylate myosin light chain.
↓
myosin cannot bind actin
↓
Relaxation.

Final effect.

↓

Smooth muscle relaxation (vasodilation)

↓

→ predominant VENODILATON : ↓ preload. ↓ demand

→ Arteriolar dilation (high dose) : ↓ afterload.

→ Coronary dilation → ↑ O_2 supply ↑ Supply.

From Jahanzeb

Nitrates

Smooth muscle relaxation (Vasodilation)

Inhibit platlet aggregation

Adverse effects.

due to vasodilation

- Orthostatic hypotension
- Throbbing headache.
- flushing
- tachycardia.
- methemoglobinemia.
- tolerance → monday disease.

USES

1. all types of angina.
   - acute attack
   - prophylaxis.
   - Unstable angina er.
2. acute MI
3. Hypertensive Emergency
4. Heart failure.
5. Biliary colic
6. Osophageal spasm.
7. cyanide poisoning

Calcium Channel Blockers — (drug classification) ✓

- Blocks L-type Ca^{2+} channel - voltage gated.

MOA

CCB

↓

Block L-type Ca^{2+} channels

↓

↓ Ca^{2+} entry into cardiac & vascular smooth muscles.

↓ ↓

- ↓ HR
- ↓ Contractility
- ↓ conduction velocity

↓ O_2 demand.

Vascular smooth muscle relaxation.

↓

(1) Vasodilation of coronary and peripheral arteries.

↓

↑ coronary blood flow.

→ ↓ afterload.

(2) relieves coronary spasms. esp in prinzmetal angina.

overall → ↓ O_2 demand

↑ O_2 supply in vasospastic angina.

USES (CVS)

(1) angina — prinzmetal* (first line). stable.

(2) CCF

(3) Hypertension.

(4) Arrhythmias.

(others)

- ✓ SAH
- ✓ preterm labours
- ✓ migraine prophylaxis
- ✓ Raynaud's

ADR

- Vasodilation → hypotension
  reflex tachycardia ★
  Headache
  flushing.
  ankle edema. (common).
- Hyperglycemia.
- Gingival hyperplasia – Nifedipine ★

D/I

- verapamil / diltiazem + β blockers – severe bradycardia
  AV block.
- Digoxin + verapamil → ↑ digoxin levels.

DHP → Nifedipine, Amlodipine → main → vascular smooth muscle

Non DHP → Verapamil, Diltiazem → main → Heart
↓HR, ↓contractility etc.

- Unstable angina : β blockers + nitrates + antiplatelets
- Stable angina : β blocker + nitrates
- variant : CCB, nitrates. β-blocker – C/I.
  prinzmetal

Stable angina (Exertional)

↓

O_2 demand > O_2 supply.

- First line: β blockers.
- add on : Nitrates.
- CCB ✓ but careful.
  { reflex tachycardia }
  Nifedipine ✗.

Variant / prinzmetal / vasospastic

- coronary artery spasm.

↓

↓ O_2 supply.

- First line : CCBs.
- Nitrates ✓.

C/I – β Blockers. – due to unopposed α1 vasoconstriction

↓

relieves spasm.

Unstable – subtotal occlusion → rupture plaque.

- antiplatelet
- anticoagulant
- Nitrates.
- β blockers.

Nifedipine

- DHP
- vasular ✓.

→ reflex tachycardia

→ gingival hyperplasia.

→ C/I in unstable angina.

Why **β blocker + Nitrates.**

Nitrates : ↓ preload & afterload

↓

↓ O_2 demand.

But

reflex tachycardia &

↑ contractility.

[Baroreceptors sense ↓ BP]

β blockers: ↓HR & contractility.

blocks reflex tachycardia.

But

↑ preload (LV filling).

Combination: ADR of each cancel out.

β- blockers in angina.

- Block β_1 receptors.

↓ HR

↓ contractility

↓ BP

↓ O_2 demand.

↑ diastolic filling time.

better coronary perfusion ✓

use

stable angina – 1st line.

CI

prinzmetal.

ADR

- Bradycardia
- AV block.
- Bronchospasm.

, mask hypoglycemia symptoms.