ANTI- ANGINAL DRUGS

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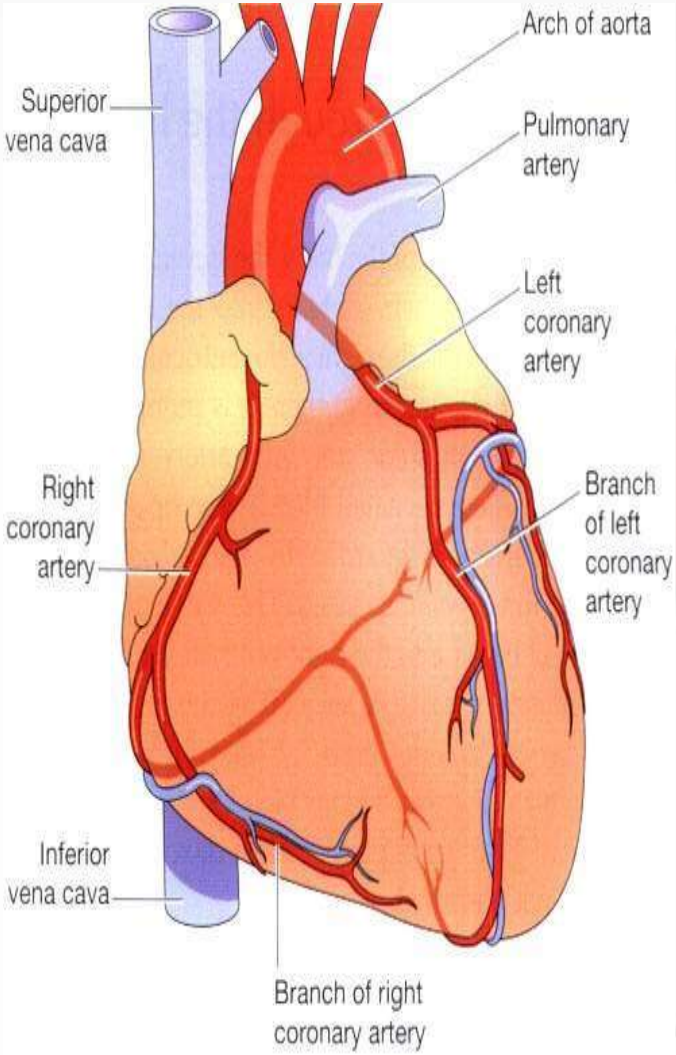

- Anti anginal drugs
  - Angina pectoris
  - Types
  - Classification
  - Nitrates
  - Calcium channel blockers
  - β blockers

CONTENT

ANTI-ANGINAL DRUGS

- Antianginal drugs may relieve attacks of acute myocardial ischemia by increasing myocardial oxygen supply or by decreasing myocardial oxygen demand
- Three groups of pharmacological agents have been shown to be effective in reducing the frequency, severity, or both of primary or secondary angina.
- These agents include the nitrates, adrenoceptor antagonists, and calcium entry blockers.
- To understand the beneficial actions of these agents, it is important to be familiar with the major factors regulating the balance between myocardial oxygen supply and demand.

ANTIANGINAL DRUGS

ORGANIC NITRATES

- *Isosorbide dinitrate*
- *Isosorbide mononitrate*
- *Nitroglycerin*

β-BLOCKERS

- *Acebutolol*
- *Atenolol*
- *Metoprolol*
- *Propranolol*

Ca^{2+} CHANNEL BLOCKERS

- *Amlodipine*
- *Diltiazem*
- *Felodipine*
- *Nicardipine*
- *Nifedipine*
- *Verapamil*

Treatment of Angina Pectoris

NBC

Nitrates

Beta Blocker

Calcium Channel Blocker

Vien

Heart

Artery

Venodilator
-- preload

-- Cardiac work

Arteriodilator
-- afterload

\+

Coronary dilatation

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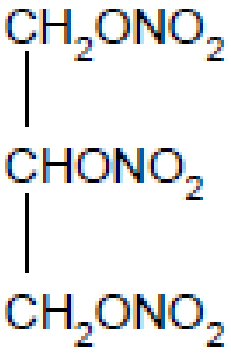
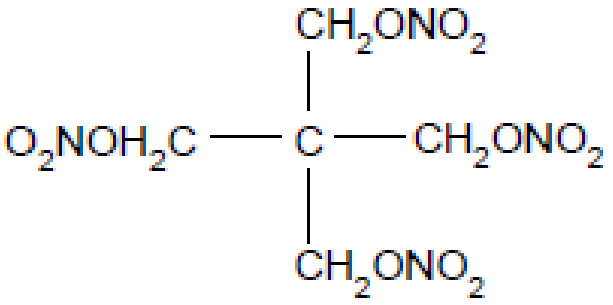
NITRATES

Classification of nitrates:

1. Rapidly acting nitrates
   * used to terminate acute attack of angina
   * e.g.- Nitroglycerin and Amyl nitrate
   * usually administered sublingually
2. Long acting nitrates
   * used to prevent an attack of angina
   *e.g. – tetra nitrate, Iso sorbide di nitrate, Penta erythrytol tetra nitrate
   * administered orally or topically



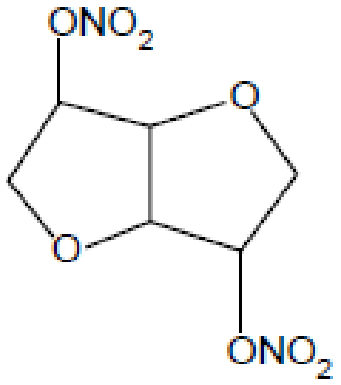
Nitroglycerine



Pentaerythritol tetranitrate

$(CH_3)_2CHCH_2CH_2O{\cdot}NO$

Amyl nitrite



Isosorbide dinitrate

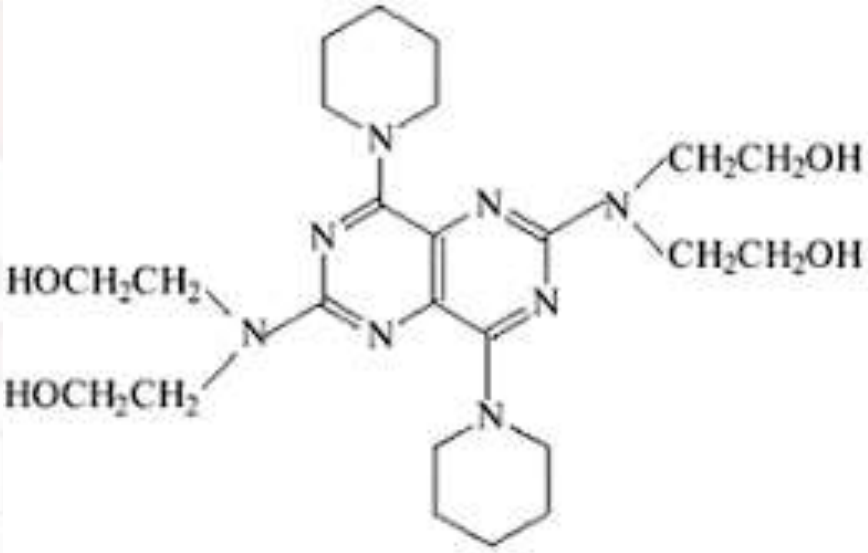
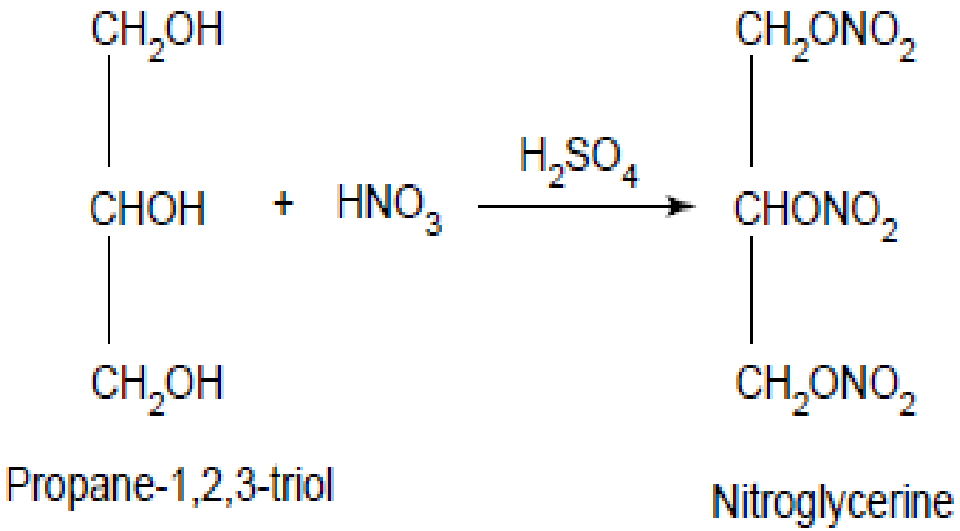


Figure 1. Structure of dipyridamole (DIP).

Synthesis of Nitroglycerine

Synthesis



ORGANIC NITRATES

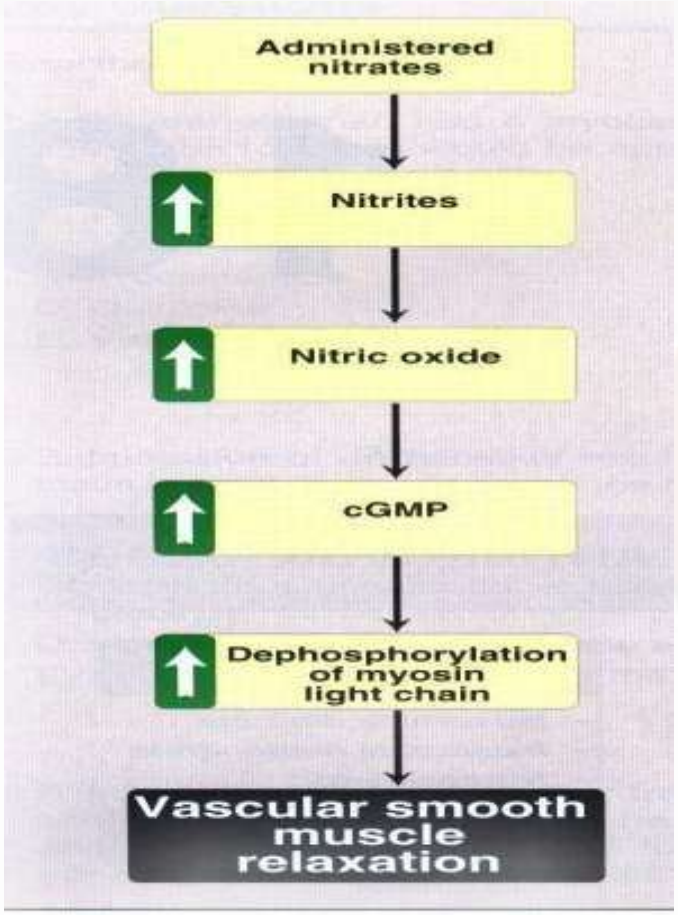
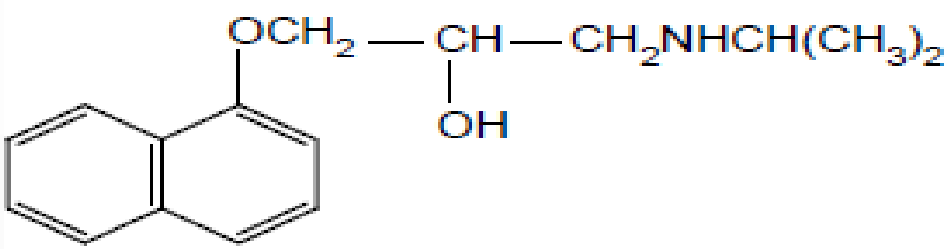


Figure 18.2
Effects of nitrates and nitrites or
smooth muscle. cGMP = cyclic
guanosine 3', 5'-monophosphat

- Organic nitrates & nitrites are simple nitric & nitrous esters of glycerol.
- These agents cause a rapid decrease in myocardial oxygen demand leading to rapid resolution of symptoms.
- Nitrates are effective for all types of angina.
- Activation of guanylate cyclase increases cGMP activating a cGMP kinase leading to dephosphorylation of myosin light chains decreasing contractile force.

BETA- BLOCKERS

- β-Blockers decrease oxygen demands of the myocardium by lowering the heart rate and contractility (decrease CO) particularly the increased demand associated with exercise.
- They also reduce PVR by direct vasodilatations of both arterial & venous vessels reducing both pre- and after load.
- These effects are caused by blocking β_1 receptors, selective β_1 antagonists (atenolol, metoprolol) lose their selectivity at high doses and at least partially block β_2 receptors.



Propranolol

MECHANISM OFACTION

Decrease heart rate & Contractility

Increase duration of diastole

Increase coronary blood flow

oxy.consumption

Increase oxygen supply

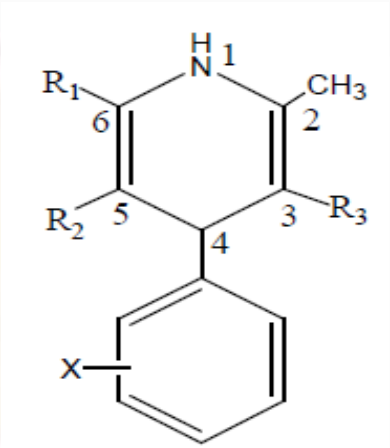
Decrease workload

Decrease

CALCIUM CHANNEL BLOCKERS

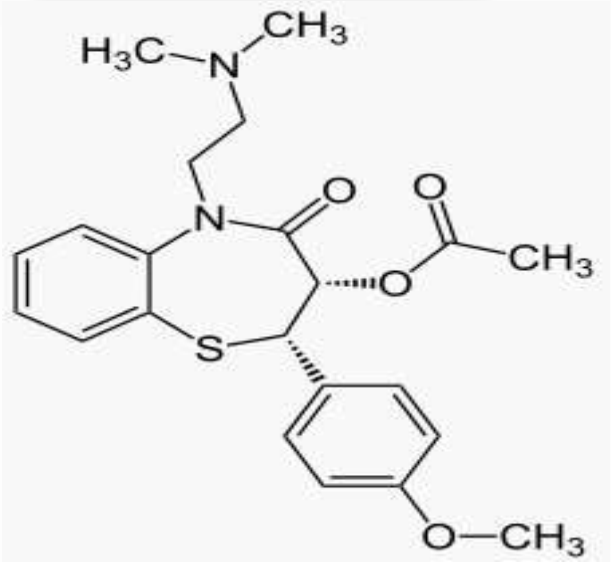
- Ca^{+2} channel blockers protect tissue by inhibiting the entrance of Ca^{+2} into cardiac and smooth muscle cells of the coronary and systemic arterial beds.
- All Ca^{+2} channel blockers produce some vasodilation (↓ PVR) and (-) inotropes.
- Some agents also show cardiac conduction particularly through the AV node thus serving to control cardiac rhythm.
- Some agents have more effect on cardiac muscle than others but all serve to lower blood pressure.
- CHF patients may suffer exacerbation of their failure as these are (-) inotropes.
- They are useful in Prinzmetal angina in conjunction with nitrates.

Dihydropyridine derivative

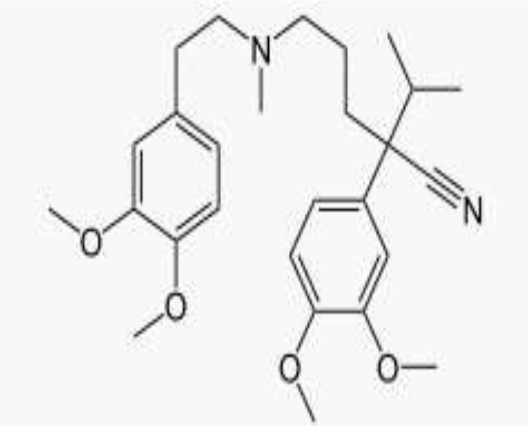


Compounds	R_1	R_2	R_3	X
Amlodipine	**$CH_2OH_2CH_2NH_2$**	**$CO_2CH_2CH_3$**	**CO_2CH_3**	**2-Cl**
2-Felodipine	**CH_3**	**$CO_2CH_2CH_3$**	**CO_2CH_3**	**2,3-Cl_2**
Nicardipine	**CH_3**	**$CO_2(CH_2)_2$-NH(Me)CH_2-Ph**	**CO_2CH_3**	**3-NO_2**
Nifedipine	**CH_3**	**$CO_2CH_2CH_3$**	**CO_2CH_3**	**2-NO_2**
Nimodipine	**CH_3**	**CO_2CH_2 CH_2OCH_3**	**$CO_2CH(CH_3)_2$**	**3-NO_2**
Nisoldipine	**CH**	**$CO_2CH_2CH(CH_3)_2$**	**CO_2CH_3**	**2-NO_2**

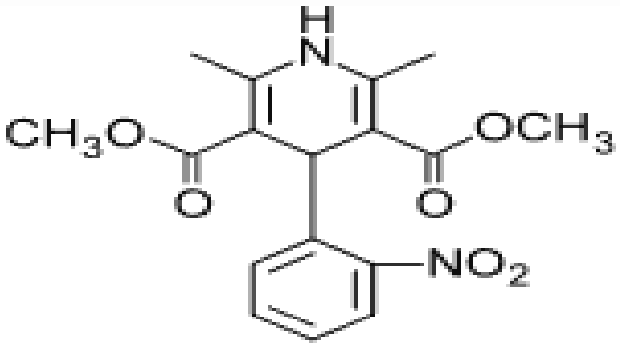
Diltiazem



Verapamil



Nifedipine



AGENTS

Nifedipine:

- This Ca+2 channel blocker works mainly on the arteriolar vasculature decreasing after load it has minimal effect of conduction or HR.
- It is metabolized in the liver and excreted in both the urine & the feces.
- It causes flushing, headache, hypotension and peripheral edema.
- It also has some slowing effect on the GI musculature resulting in constipation.
- A reflex tachycardia associated with the vasodilatation may elicit myocardial ischemia in tenuous patients, as such it is generally avoided in non-hypertensive coronary artery disease.

VERAPAMIL

- The agents has its main effect on cardiac conduction decreasing HR and thereby O2 demand.
- It also has much more (-) inotropic effect than other Ca+2 channel blockers
- It is a weak vasodilator.
- Because of its focused myocardial effects it is not used as an antianginal unless there is a tachyarrhythmia. It is metabolized in the liver.
- It interferes with digoxin levels causing elevated plasma levels; caution and monitoring of drug levels are necessary wit concomitant use.

DILTIAZEM

- This agent function similarly to Verapamil however it is more effective against Prinzmetal angina.
- It has less effect on HR.
- It has similar metabolism and side effects as Verapamil.

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