

02

(033 332) WK 06

ANTI-ANGINAL DRUGS

2015 • JANUARY						
M	T	W	T	F	S	S
1	2	3	4			
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	

Angina Pectoris:

- Severe pain in chest. Radiates 1cm precordium to left shoulder & down the arm.
- Major symptom of ischemic Heart disease.
- ∵ of imbalance of O₂ demand & supply.

Types:-

Exertional & Stable

① classic Angina ~~so~~② Variant ~~so~~ — Prinzmetal's / Vasospastic

③ Unstable Angina.

- Anti-anginal drugs decreases the demand of the O₂ to heart & or O₂ supply to myocardium or reduce load (heart rate, contractility) of heart
- These drugs release NO, which ↑ cGMP & causes Venodilation.

①

NITRATES - They cause redistribution of coronary blood flow to the ischemic area & reduce myocardial O₂ demand.

- Don't increase total coronary flow of blood

- In classic angina: reduce preload & cardiac output.
- Reduces peripheral resistance during myocardial contractions.

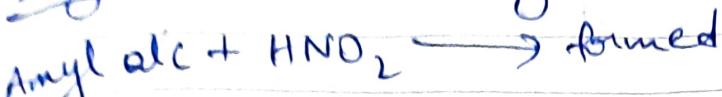
MARCH • 2015
M 1 W 2 T 3 F 4 S 5 S 6
7 8 9 10 11 12 13 14 15
16 17 18 19 20 21 22
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WK 06 (034 331)

03

- Have Oxidⁿ state of N₂ is +3
- React with thiol groups to form unstable S-nitrosothiols which rapidly decompose to give NO.

② Amyl nitrite: (Isopropyl nitrite)



- Oral &

In cyanide poisoning 0.25 min (onset)

Inhalation

1 min (Duration)

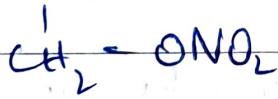
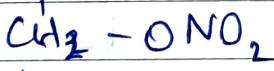
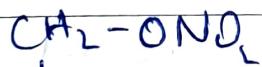
③ Nitroglycerin: 2 min (O) 30 min (D)

Prepared by mixⁿ of glycerin & HNO₃ & H₂SO₄.

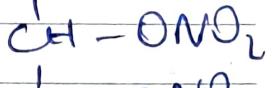
Workers in its mfg are prone to headaches & it has radiating action.

Producers coronary collateral circulation & it is only drug which prevents exp myocardial infarction by coronary occlusion.

- Instability due to volatilization of Na.



15 min (O)
180 min (D)



④ Diluted Erythritol tetranitrate

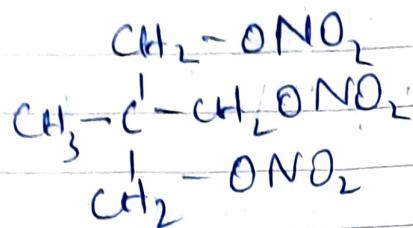
- for acute attacks of Angina pectoris & to ↓ BP in arterial hypertension.
- ↓ cardiac preload, ↓ of B.P on arterial sides in stressful conditions. Prevents angina attack
- Sustained release forms. for long action

WEDNESDAY • FEBRUARY • 2015

04

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(d) Pentaerythritol Tetranitrate



(longer duration)

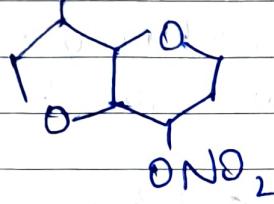
(e) Dil. Isosorbide Dinitrate

3 min (onset)
60 min (duration)

- Sublingual / chewable.
- Treatment & prophylaxis of angina attacks.

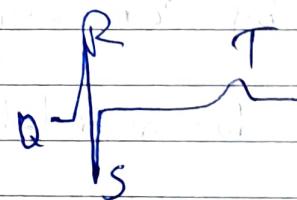
(m) \rightarrow Isosorbide-5-mononitrate

by denitration ONO_2 (higher $t_{1/2}$)



(g) Ca^{2+} Channel Blockers:

(h) Ca^{2+} CHANNEL BLOCKER



In Ventricular cells - there are 5 phases of stimulation of cardiac cells.

Phase 0! When cardiac cell reaches its threshold, ion channels are opened and Na^+ enters the cell through Na^+ channels resp for fast Na^+ current.

Phase 1! K^+ comes out as transient K^+ ch open

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MARCH • 2015						
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05

Phase 2: Current is caused by slow activ of L-type of Ca^{+2} ion ch Ca^{+2} into the cell (plateau phase)

K^{+} moves out of cell via delayed rectified K^{+} channels.

Phase 3: - Ca^{+2} ch closes but K^{+} delayed rectified ch remains open & return of threshold membrane potential -90 mV .

Phase 4: - Na^{+} & Ca^{+2} ch close
 K^{+} keep threshold memb at -90 mV

- The release of Ca^{+2} from sarcoplasmic reticulum in the cell is resp for the contractile process of cardiac muscle.

Phase 0 & 1 - QRS - Depolarization

Phase 2 - ST - Plateau wave

Phase 3 - T - Repolarization.

4 types of Ca^{+2} channels

L-type - Skeletal or smooth muscle

T-type - Pacemaker cells, Ca^{+2} entry, inactivated at more -ve potential (more fast than L-type)

N-type - Neurons

P-type - Purkinje fibres

FRIDAY • FEBRUARY • 2015

06

1037 3210 Wk OA

3 states of Ca^{+2} channels

M	T	W	T	F	S	S
5	6	7	1	2		
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Open

Ca^{+2} Bh blockers block

Resting

L-type ch.

Inactivated

causing the long lasting action if memb is depolarized

L-type ch in cardiac cell is activated by β -Adr stimulation through cAMP

dependent process

L-type ch is smooth muscle by G-protein coupled IP_3/DAG system

L-channel Blockers

① Phenylalkylamines

Verapamil (1st C)

Anipamil

Bepридil (2nd C) — has diarylamine ethel propylamine moiety.

② 1,4-Dihydropyridine: - Nifedipine (1st C)

Amlodipine

Felodipine

Isradipine

Nicardipine (2nd C)

(3) Benzothiazepine!

Diltiazem

WK 06 (03B-32)

07

Diltiazem & Verapamil have effect on cardiac & vascular tone.

- DHPYD - in producing vasodilation at periphery

Verapamil: \approx st to papaverine

- In angina, arrhythmias & ischemic myocardial syndrome & supraventricular arrhythmia.
- Acts on slow Ca^{+2} ch resulting in slowing of AV conduction & sinus rate.
- High affinity for inactivated state of Ca^{+2} ch.
- In hypertension, & hypertrophic obstructive cardiomyopathy.

S isomer $>$ R isomer

\downarrow
Has FP metabolism.

Side effects! - Constipation
Ankle edema.

SUNDAY 08

MONDAY • FEBRUARY • 2015

09
1040 1251 WK 07

Diltiazem:

- In variant Angina

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- Dilates peripheral arteries & also q myocardial O₂ supply by relieving coronary artery spasm & reducing O₂ demand (by decreasing heart rate & overload).

first pass metabolism m

Deacetyl diltiazem
& (O) & (N)

demethylated
& origin of phenolic metabolites.

Nifedipine:

- ~~No~~ Nitro group for antianginal effect.
- 3 & 5 - Carboxylic groups are present & protected by ester functionality.

- At 4th regd aromatic subs is an e- withdrawing group at o or p position.

- In classical angina - causes hyperglycemia vasospastic
- In hypertension -

- Amlodipine: for vascular smooth muscle than myocardial tissue & longer t_{1/2}
- Stable angina
- Hypertension As Besylate salt

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WK 07 (041-324)

10

Nimodipine - In subarachnoid hemorrhage
asso neurological deficits.

Nisoldipine; long acting Ca^{+2} ch blocker
& in hypertensive emergencies.

III β -BLOCKERS

- Reduce cardiac work load.
- Contraindicated in variant angina
- ↓ mortality in patients w/ coronary artery disease & with post myocardial infarction.

IV K^+ CHANNEL BLOCKERS

Nicorandil - causes coronary dilation by activating ATP sensitive K^+
- possesses NO releasing property.

V TRIMETAZIDINE - Utilizes Partial Fatty acid oxidation inhibitor. (p FOX)

- Also inhibits lipid peroxidation.
↓ in gen' of free radicals & protection of myocardium from harmful effects of ischemia
- Acts by Non-Hemodynamic mechanism.

WEDNESDAY • FEBRUARY • 2015

VI MISCELLANEOUS

(042 323) WK 07

M	T	W	TH	FR	SU
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→ Ivabradine

- Bradyarrhythmic agent
- ↓ heart rate without affecting conduction & contractility.
- Blocks hyperpolarization activated Na^+ ch. carries If funny current

Side effect :- visual disturbance

→ Fasudil:

- Selective RhoA / Rho kinase Inhibitor (ROCK)
- In Cardiac remodeling & Vasoconstriction.
- In angina & cerebral vasospasm.

It inhibition causes vasodilation