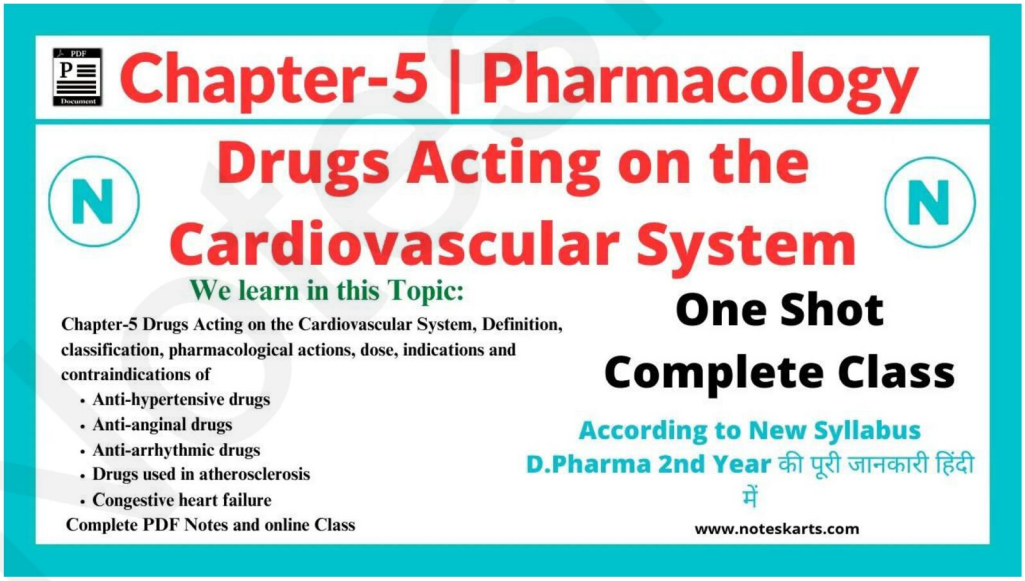
Chapter-5
Pharmacology & Toxicology

D.Pharma 2nd Year Notes

Chapter- 5

Drugs Acting on the Cardiovascular System Definition, classification, pharmacological actions, dose, indications and contraindications of

1. **Anti-hypertensive drugs**
2. **Anti-anginal drugs**
3. **Anti-arrhythmic drugs**
4. **Drugs used in atherosclerosis and Congestive heart failure**



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1. Anti-hypertensive drugs

- These are those drugs which are used to in the treatment of Hypertension.

Hypertension

- Hypertension is define as either a sustained systolic Blood Pressure (BP) of greater then 140 mmHg or sustained diastolic BP of greater than 40mmHg.

Or

- It is a condition of elevated blood pressure in our body (High Blood Pressure).

$$\text{Normal} = \frac{120}{80} = \frac{\text{Systolic}}{\text{Diastolic}}$$

Stage of Hypertension:

Hypertension	Systolic	Diastolic
Stage-I	140-159	90-99
Stage-II	160-179	100-109
Severe	>180	>110

Hypertension Can Cause

- Heart Failure
- Brain Stroke
- Kidney Failure
- Vision loss
- Sexual dysfunction

Risk Factor

- NA+ Intake ↑
- Smoking ↑
- Stress ↑
- Obesity ↑

Anti-hypertensive drugs

- These are those drugs which are used to in the treatment of Hypertension.

Or

- The antihypertensive of the 1960-70s were methyldopa, B blockers, thiazide and high ceiling diuretics and clonidine.
- The status of ß blockers and diuretics was consolidated in the 1970s and selective α, blocker prazosin broke new grounds.
- The antihypertensive introduced in the 1980-90s were angiotensin II converting enzyme (ACE) inhibitors and calcium channel blockers.
- Angiotensin receptor blockers (losartan, etc.) were added soon after, and the direct renin inhibitor aliskiren is the latest drug.

Classification Anti-hypertensive drugs:

1. **Diuretics**
    - Furosemide
    - Thiazides
    - Eplerenone, etc.
2. **ACE Inhibitors**
    - Captopril
    - Lisinopril
    - Quinapril, etc.
3. **Beta Adrenergic blocker**
    - Atenolol
    - Metoprolol
    - Propranolol, etc.
4. **Calcium Channel Blockers**
    - Verapamil
    - Diltiazem
    - Nifedipine
    - Felodipine, etc

Diuretics:

Mechanism of Action of diuretics is based upon decreasing blood volume which ultimately leads to decrease blood pressure.

Thiazide diuretics:

- Thiazide diuretics are mainly used to treat high blood pressure (hypertension). They are occasionally also used for heart failure.
- When used to treat heart failure they are often combined with another type of medicine called a loop diuretic.

Pharmacological Action:

- Their action is to make the kidneys pass out more fluid.
- They do this by interfering with the transport of salt and water across certain cells in the kidneys.
- Thiazide diuretics tend to have only a weak action on the kidneys so you don't notice a great increase in urine if you take these (compared with loop diuretics).
- They also have the effect of widening (dilating) blood vessels. A combination of these two effects reduces the blood pressure.

Dose

- Tablet
- 15 mg
- 25 mg
- 50 mg

Indications

- Thiazide diuretics are mainly used to treat high blood pressure (hypertension)

Contraindications

- Blood sugar level
- Increase in the level of uric acid
- Upset stomach.
- Dizziness on standing

ACE Inhibitors:

These drugs block the enzyme ACE (Angiotensin Converting Enzyme) which convert Angiotensin-I to Angiotensin-II (Vasoconstrictor).

Examples of ACE inhibitors include:

- Benazepril (Lotensin) (20 to 40 mg per day)
- Captopril (Table:-12.5 mg, 25 mg, 50 mg, 100 mg)
- Enalapril (Vasotec)
- Fosinopril
- Lisinopril (Prinivil, Zestril)
- Moexipril
- Perindopril
- Quinapril (Accupril)
- Ramipril (Altace)
- Trandolapril

Pharmacological Actions:

ACE Inhibitors decrease angiotensin-II & Increase bradykinin levels vasodilators of both arteries and veins occurs as a results of decreasing vasoconstriction (Due to decreasing in Angiotensin-II) & enhanced vasodilation (from ↑ bradykinin levels).

Indication:

- Migraines
- High blood pressure (hypertension)
- Coronary artery disease
- Heart failure
- Diabetes
- Certain chronic kidney diseases
- Heart attacks

Contraindication

- Dry cough
- Increased potassium levels in the blood (hyperkalemia)
- Fatigue
- Dizziness from blood pressure going too low
- Headaches
- Loss of taste

2. Anti-anginal drugs

- These are those that prevent or terminate attacks of angina pectoris.
- Antianginal drugs are used to treat angina pectoris, a symptom of ischemic heart disease that causes chest pain.
- They work by reducing the heart's oxygen demand, either by dilating coronary blood vessels to increase blood flow to the heart, or by reducing the heart's workload.

Angina Pectoris:

- It is a pain syndrome due to induction of an adverse oxygen supply/ demand situation in a portion of the myocardium.
- Metabolites that accumulate due to myocardial ischaemia elicit the pain.
- It is also known as ischemic chest pain.

Cause:

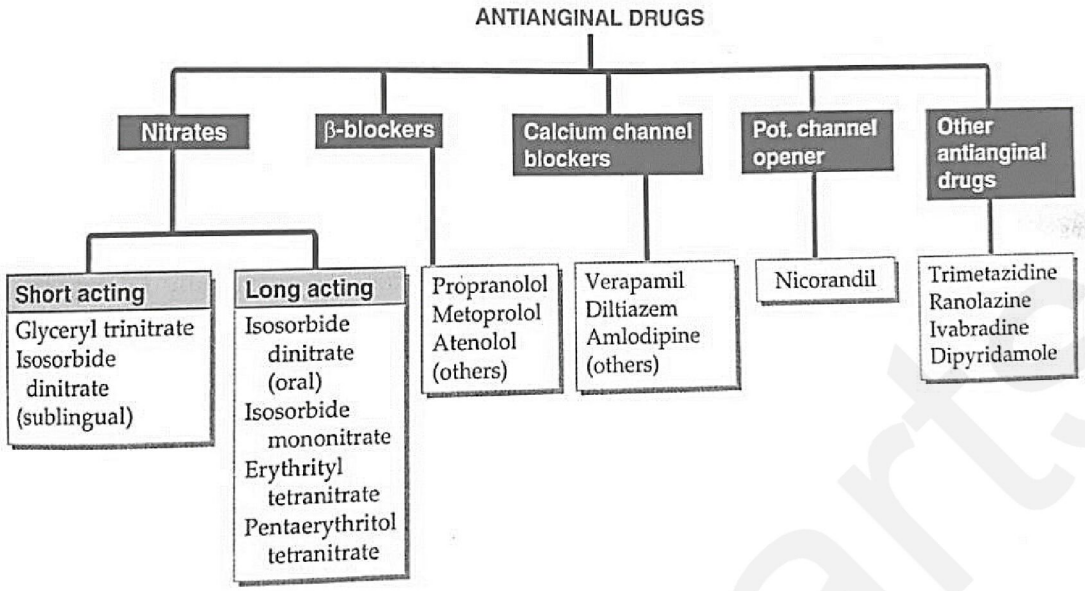
- Less O2 supply in heart.
- Less O2 demand in heart.
- Less blood supply in heart

Nitrates:

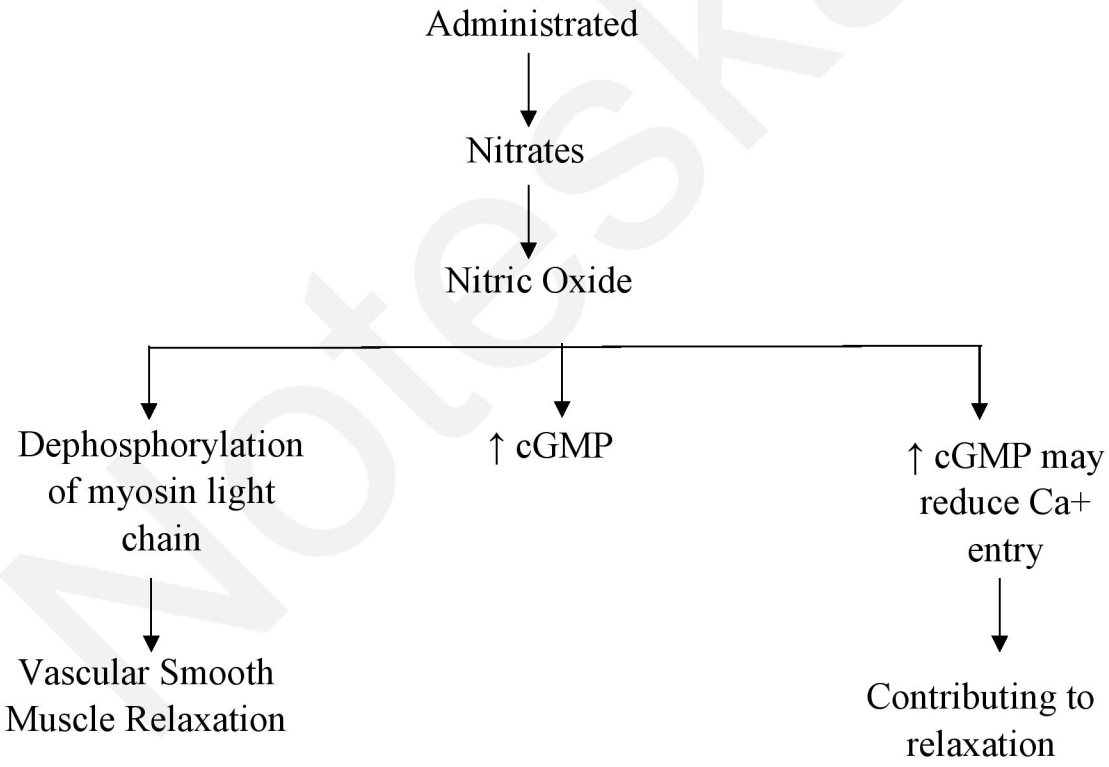
Reason:

- Coronary artery disease (CAO)
- Vasospasm of coronary arteries.
- All organic nitrates share the same action differ only in time Course.
- The major action is direct nonspecific smooth muscle relaxation, particularly vascular smooth muscle.

Classification of Anti-anginal drugs:



Pharmacological Action:



Dose:

Drugs	Dose
GTN (Nitroglycerine)	• 0.5 mg sublingual • 0.4—0.8 mg s.l. spray • 5-15 mg SR oral • One patch for 14—16 hr per day • 5—20 pg/min i.v.
Isosorbide dinitrate	• 5 mg sublingual • 10—20 mg oral • 10—40 mg SR oral
Erythrityl-tetranitrate	• 15—60 mg oral

Indications:

- Angina pectoris
- Congestive heart failure
- Stroke (damage to brain tissue caused by obstruction to the blood flow)

Contraindications:

- Headache
- Dizziness
- Nausea
- Lightheadedness
- Restlessness
- Stomach discomfort
- Hypotension (low blood pressure)

Beta Blockers

- The β-blockers decrease the oxygen demand of the myocardium by blocking β1, resulting in decreasing heart rate, contractility, cardiac output and blood pressure.
- These agents reduce the oxygen demand during exerting and at rest. They can reduces both the frequency & severity of angina attacks.

Propranolol:

- Propranolol is a non-selective beta-blocker medication used to treat various cardiovascular conditions, including angina pectoris (chest pain).

Pharmacological Actions:

- Propranolol works by blocking beta-adrenergic receptors in the heart. This reduces the effects of hormones like adrenaline, which normally increase heart rate and force of contraction.
- By blocking these receptors, propranolol allows the heart to beat slower and with less force, decreasing its workload and oxygen demand.

Dose: Propranolol dosage varies depending on the specific condition being treated. For angina, it typically starts at 40mg twice daily and can be adjusted by a doctor.

Indications:

- Angina pectoris: Propranolol reduces angina episodes by lowering heart rate and oxygen demand.
- Hypertension: Propranolol relaxes blood vessels and lowers heart rate, leading to decreased blood pressure.

Contraindications:

- Slow heart rate (bradycardia): Propranolol can further slow the heart, which can be dangerous in people with already slow heart rates.
- Heart block: Propranolol can worsen heart block, a condition where electrical signals travel too slowly through the heart.
- Severe heart failure: Propranolol can worsen heart failure by further reducing the heart's pumping ability.
- Asthma: Propranolol can worsen asthma symptoms.

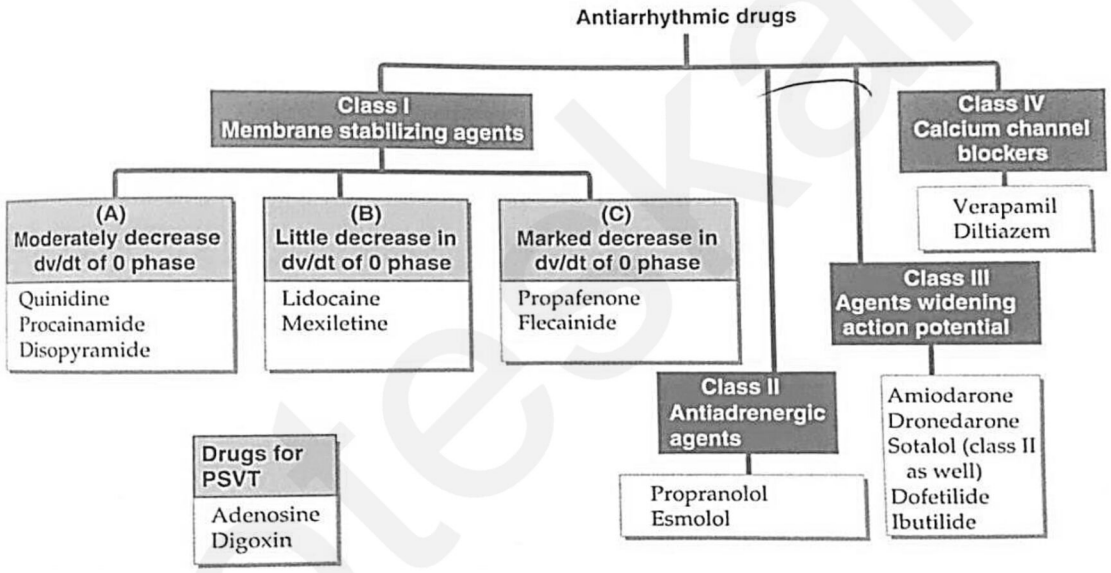
3. Anti-arrhythmic drugs

- These are drugs used to prevent or treat irregularities of cardiac rhythm.

Arrhythmias

- Arrhythmias are the most important cause of sudden cardiac death. However, only few arrhythmias need to be treated with antiarrhythmic drugs.
- Abnormal automaticity or impaired conduction or both underlie cardiac arrhythmias. The generation and propagation of cardiac impulse.

Classification of Anti-arrhythmic drugs:



Quinidine

- It is the dextro isomer of the antimalarial alkaloid quinine found in cinchona bark.
- Quinidine is used to treat certain types of irregular heartbeats. Quinidine is in a class of medications called antiarrhythmic medications.

Pharmacological Action of Quinidine:

- Quinidine blocks the rapid sodium channel (INa), decreasing the phase zero of rapid depolarization of the action potential.

- Quinidine also reduces repolarizing K+ currents (IKr, IKs), the inward rectifier potassium current (IK1), and the transient outward potassium current Ito, as well as the L-type calcium current ICa and the late INa inward current.
- The reduction of these currents leads to the prolongation of the action potential duration

Dose:

- Form: oral immediate-release tablet (200 mg and 300 mg)

Indications:

- irregular heartbeats
- Cardiac arrhythmias (paroxysmal supraventricular tachycardia, ventricular tachycardia pre- dysrhythmias)
- Treatment of severe malaria

Contraindications:

- Hypersensitivity.
- Thrombocytopenic purpura, quinidine or quinine-assoc.
- Myasthenia gravis, Intraventricular conduction defects, Complete AV block w/ junctional rhythm, Complete AV block w/idioventricular rhythm, congenital long QT syndrome, uncorrected Electrolyte abnormalities.

4. Drugs used in atherosclerosis and Congestive heart failure

Atherosclerosis

- Arteriosclerosis occurs when the blood vessels that carry oxygen and nutrients from the heart to the rest of the body (arteries) become thick and stiff sometimes restricting blood flow to the organs and tissues.
- Atherosclerosis is the buildup of fats, cholesterol and other substances in and on the artery walls. This buildup is called plaque.
- The plaque can cause arteries to narrow, blocking blood flow.
- The plaque can also burst, leading to a blood clot.

Symptoms

- Chest pain
- Weakness in your arms or legs
- High blood pressure or kidney failure

Drugs used in atherosclerosis

1. **Calcium channel blockers**— which block the calcium channels in myocardium and thereby, reduce the contractility of myocardium. Exphenylalkylamine, benzothiazepine, dihydropyridines.
2. **Vasodilators**— reduce the blood pressure by the vasodilation. Ex- sodium nitroprusside, hydralazine, minoxidil, fenoldopam, diazoxide.
3. **Diuretics**— diuretics cause diuresis and reduce the ECF volume and blood volume. Ex thiazide diuretics, loop diuretics, potassium-sparing diuretics, osmotic diuretics, and carbonic anhydrase inhibitors.
4. **Angiotensin converting enzyme inhibitors (ACE inhibitors)**— it reduce the blood pressure by blocking the formation of angiotensin.
5. **Angiotensin (AT1) receptor blocker—** Ex- losartan, telmisartan, melavinus, valsartan, eprosartan.
6. **Sympathetic inhibitors**—
    a) ***Alpha Beta adrenergic blockers***— arotinolol, labetalol, carvedilol, bucindolol.

b) ***Alpha adrenergic blockers***— Prazosin, doxazosin, naftopidil, phenoxybenzamine.

c) ***Beta adrenergic blockers***— Atenolol, metoprolol, timolol, oxprenolol, nipradilol.

d) ***Central sympatholytics***— methyldopa, reserpine, clonidine.

Congestive heart failure.

- Heart failure or congestive heart failure is an abnormal condition involving impaired cardiac pumping. In this condition heart is fail to pump the sufficient blood to our organs due to the less nutrients and oxygen supply to the myocardial destruction (less ability of cardiac muscle).

Types of heart failure—

- **Left-sided heart failure**— Most common form of heart failure. Fluid may back up in your lungs, causing shortness of breath.
- **Right-sided heart failure**— often occurs with left sided heart failure. Failure may back up into your abdomen, legs and feet, causing swelling.
- **Systolic heart failure**—the left ventricle cannot contract vigorously indicating a pumping problem.
- **Diastolic heart failure**—the left ventricle cannot relax or fill fully, indicating a filling problem.
  - Congestive heart defects may be diagnosed before birth, right after birth, during childhood or not until adulthood. It is possible to have a defect and no symptoms at all.

Clinical manifestations

- Tachycardia
- Oedema (swelling in ankles, legs and abdomen).
- Cachexia and muscle wasting.
- Crepitations or wheeze.
- Third heart sound
- Hepatomegaly.
- Pulses alterations

Drugs used in Congestive heart failure (Classification of Congestive heart failure Drugs)

1. **Calcium channel blockers**— which block the calcium channels in myocardium and thereby, reduce the contractility of myocardium. Exphenylalkylamine, benzothiazepine, dihydropyridines.
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Drugs & Dose in atherosclerosis and Congestive heart failure

Drugs	Dose
Sodium nitroprusside	25mg/mL (50mg/2mL vial)
Losartan	Tablet • 25mg • 50mg • 100mg

Verapamil	Tablet • 40 mg • 80 mg • 120 mg

Verapamil (Imp)

Indications:

- **Angina pectoris:** Verapamil helps manage chest pain (angina) by relaxing coronary arteries and reducing heart rate and workload.
- **Hypertension:** Verapamil can be used alone or combined with other medications to lower blood pressure.
- **Arrhythmias:** Verapamil is effective in treating certain types of irregular heartbeats, like paroxysmal supraventricular tachycardia (PSVT).

Contraindications:

- **Heart Failure:** Verapamil can worsen heart failure in some cases.
- **Slow Heart Rate (Bradycardia):** It can further slow an already slow heart rate.
- **Sick Sinus Syndrome:** This condition affects the heart's natural pacemaker, and verapamil can worsen it.
- **AV Block:** Verapamil can worsen atrioventricular block, a condition where electrical signals travel slowly between the heart's upper and lower chambers.