

Cardiovascular Agents

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CARDIOVASCULAR AGENTS

Globally:

- Cardiovascular disease (CVD) is common in the general population, affecting the majority of adults past the age of 60 years.
- In 2012, CVD was estimated to result in 17.3 million deaths worldwide on an annual basis

Europe:

- CVD is the leading cause of death, accounting for over 8 million deaths each year (49 % of all deaths). 1 in 6 men and 1 in 7 women in the EU die from **CHD**

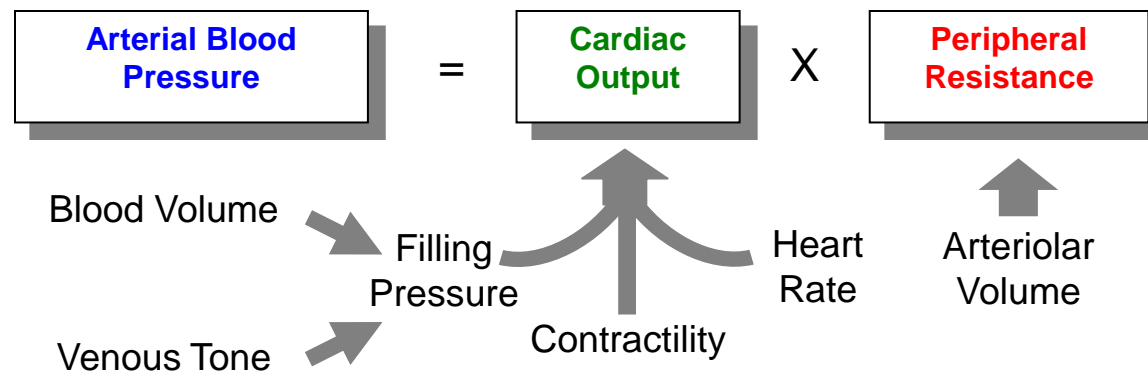
US:

- 1 in 5 suffer from some form of heart disease (60,800,000)
- Almost one out of every 2.5 deaths results from CVD.
- About every 29 seconds an American will suffer a coronary event, and about every minute someone will die from one.
- The cost of cardiovascular disease in 2001 is estimated at \$298.2 billion -
- Someone in the US suffers a stroke every 53 seconds; someone dies every 3.3 minutes from stroke.

ANTIHYPERTENSIVE DRUGS

Hypertension

- Systolic BP 140 mm Hg or higher
- Diastolic BP 90 mm Hg or higher
- 95 % of all cases are Primary (essential) Hypertension, the rest is either renal or due to endocrine abnormalities



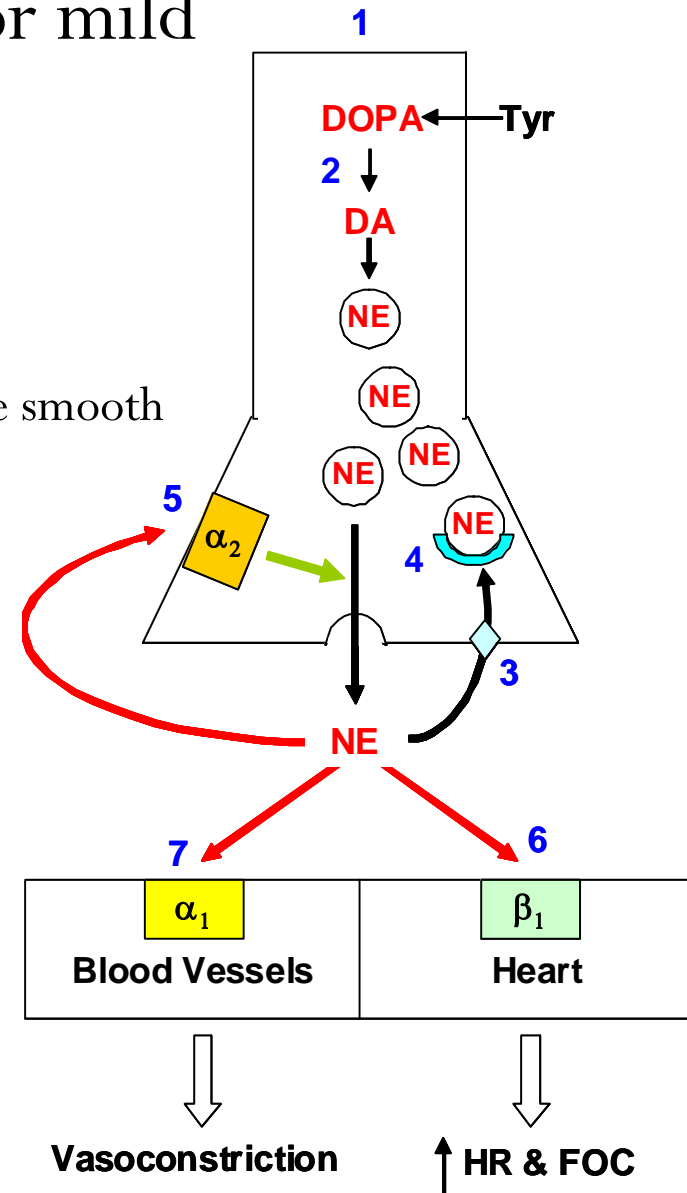
- Classes of Antihypertensive Drugs
 - i. Diuretics.
 - ii. Sympatholytics.
 - iii. Renin Angiotenin System (RAS) inhibitors.
 - iv. Vasodilators

i. DIURETICS:

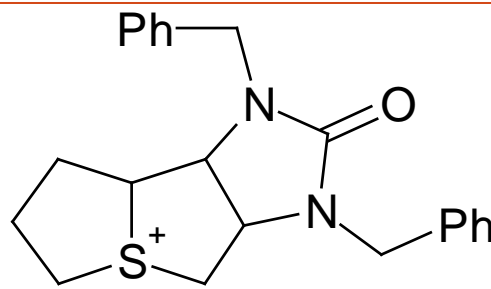
- First line single drug treatment for mild hypertension.
- Decrease BP by two mechanisms
 - Decrease Blood Volume so decrease COP.
 - Decrease PVR by decreasing sodium content of the smooth muscles so decrease **contractility**.

ii. SYMPATHOLYTIC:

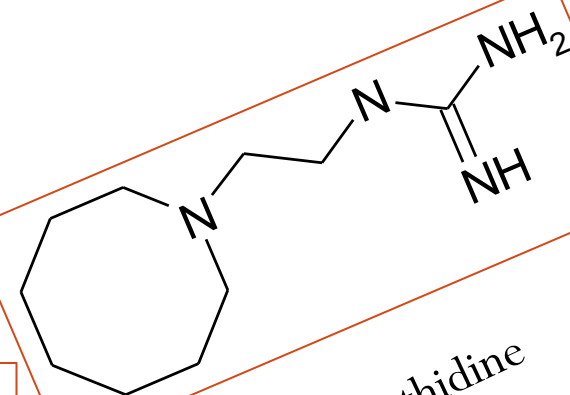
- a) Ganglionic Blockers
- b) Agents depleting NE Stores
- c) Centrally Acting Drugs
- d) Adrenergic Receptor Blockers



a. Ganaglionic Blockers

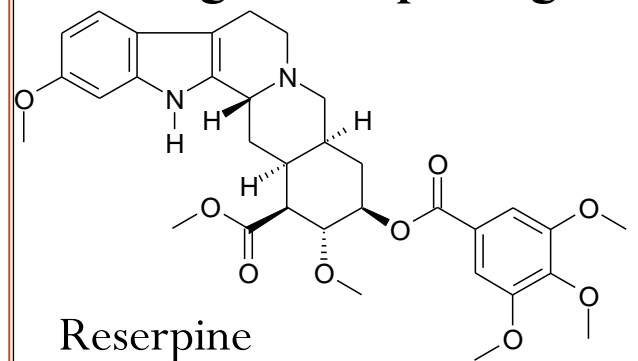


Trimethaphan

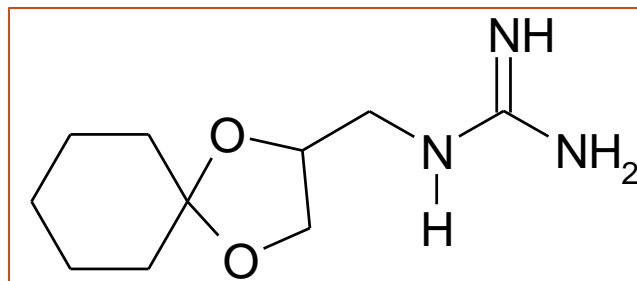


Guanethidine

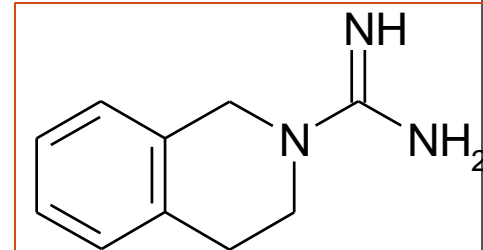
b. Agents Depleting NE Stores



Reserpine

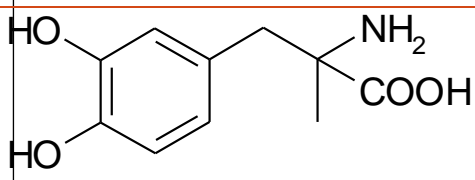


Guanadrel

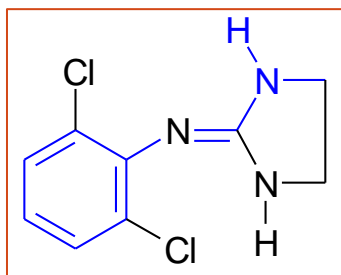


Debrisoquin

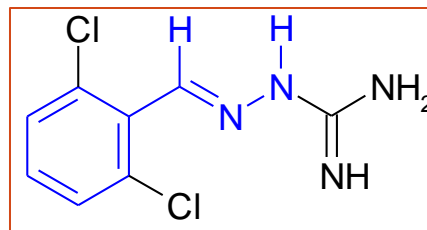
c. Centrally Acting Drugs:



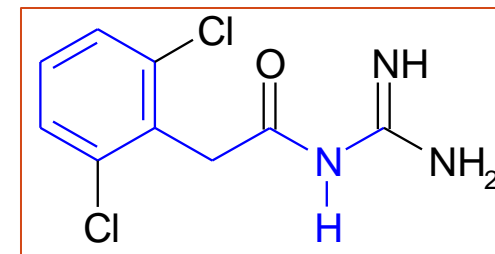
α -methyl dopa



Clonidine

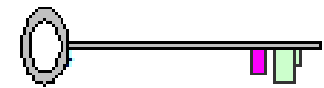
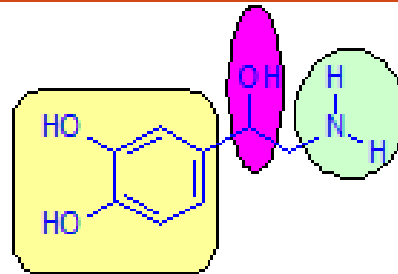


Guanabenz

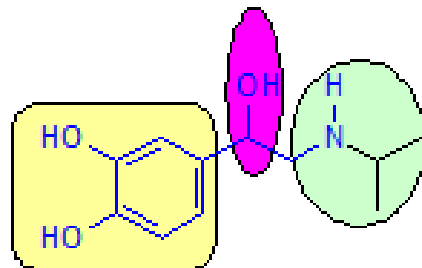


Guanfacine

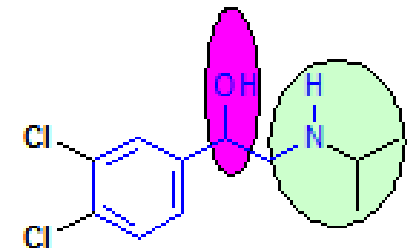
d. Adrenergic receptor blockers



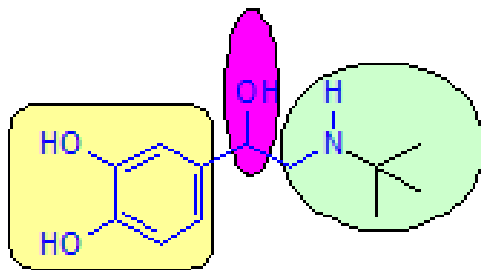
β-Selective Blockers



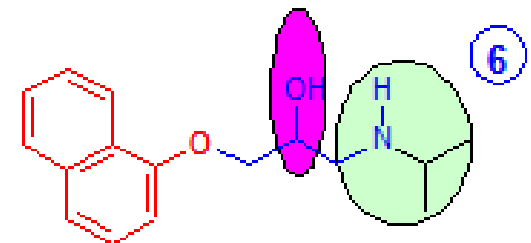
Isoproterenol, *Isoprenaline*®



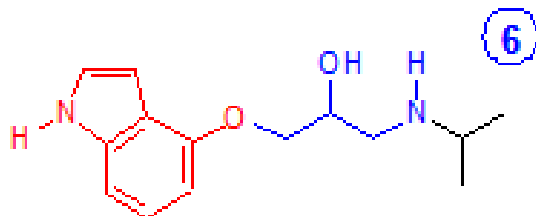
Dichloroisoproterenol, *DCI*



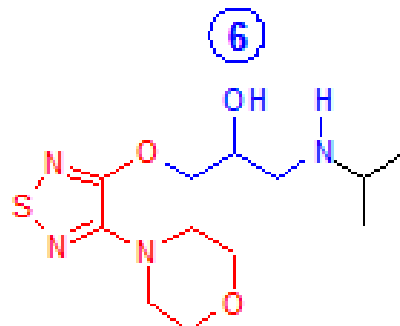
Colterol



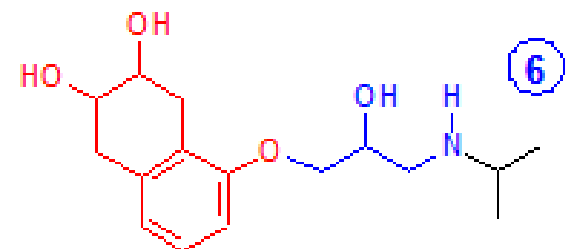
Propranolol, *Indral*®



Pindolol, *Visken*®

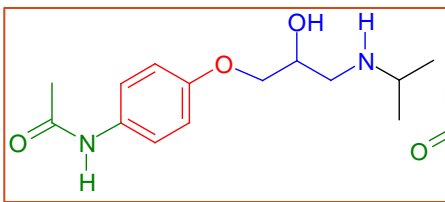


Timolol, *Timoptic*®

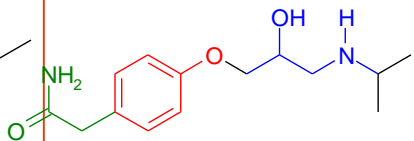


Nadolol, *Corgard*®

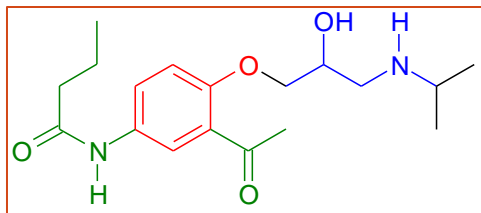
β 1-Selective Blockers



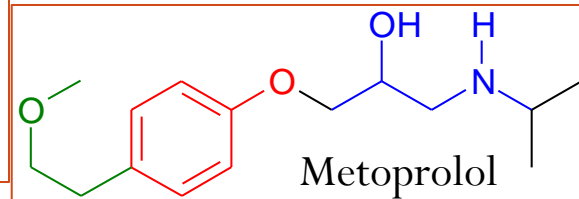
Practolol



Atenolol

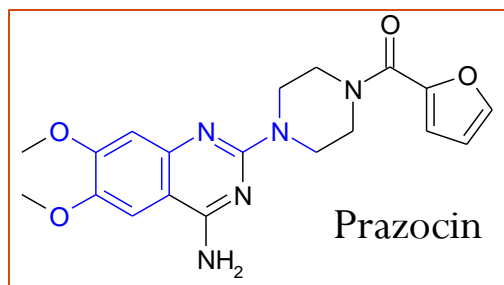


Acebutolol

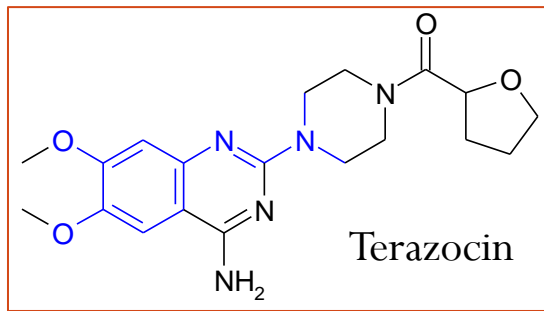


Metoprolol

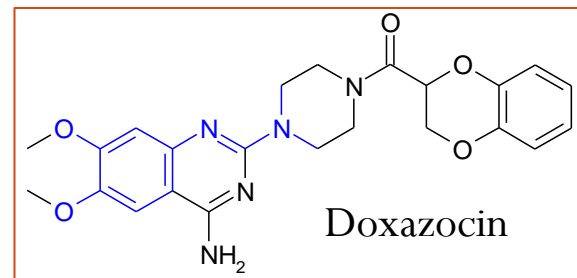
α 1-Selective Blockers



Prazocin

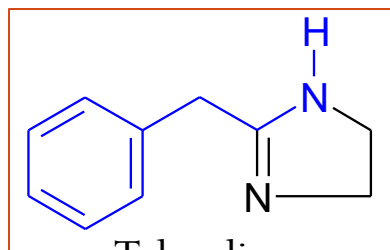


Terazosin

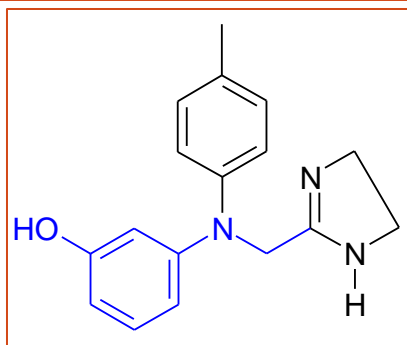


Doxazosin

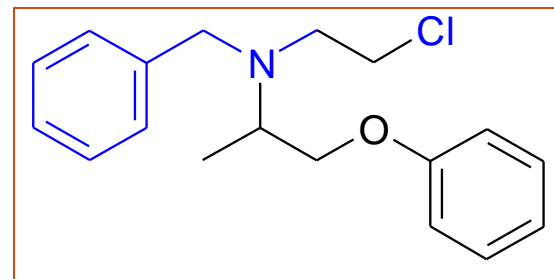
Nonselective α -Blockers



Tolazoline

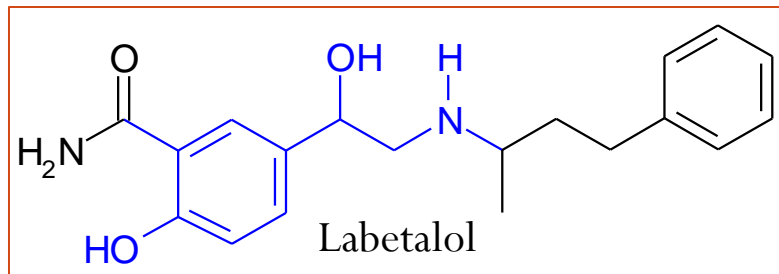


Phentolamine



Phenoxybenzamine

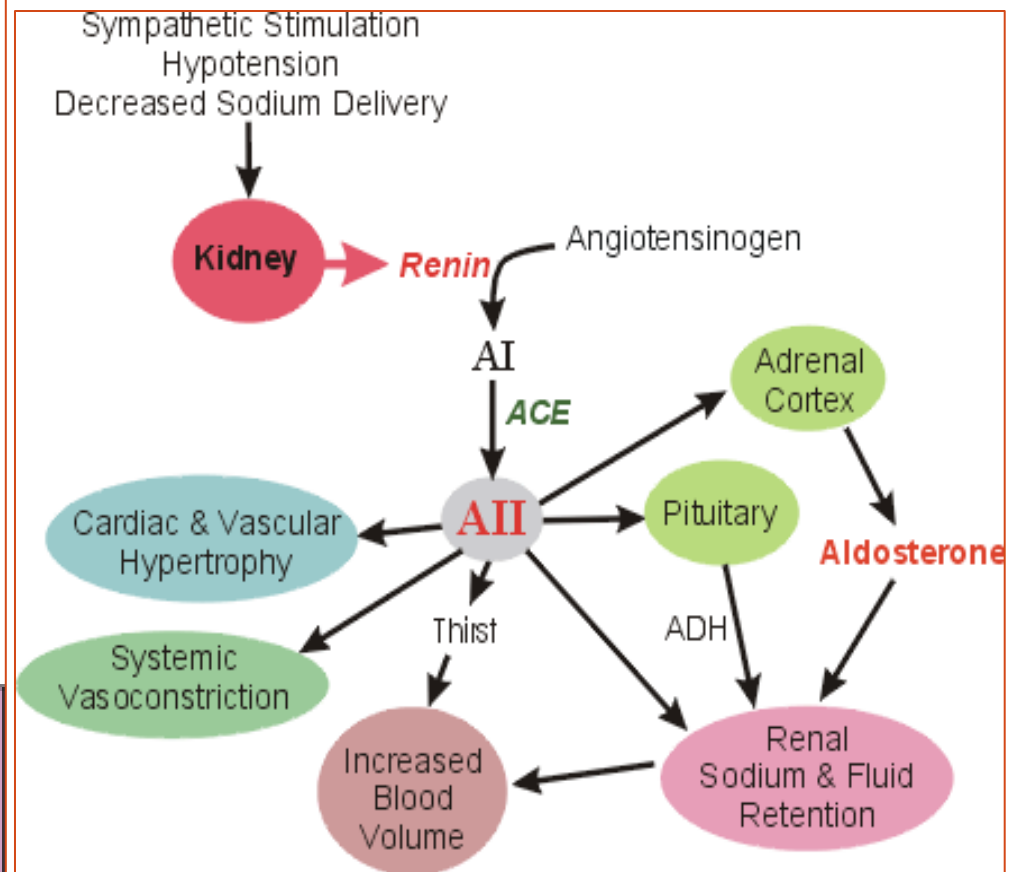
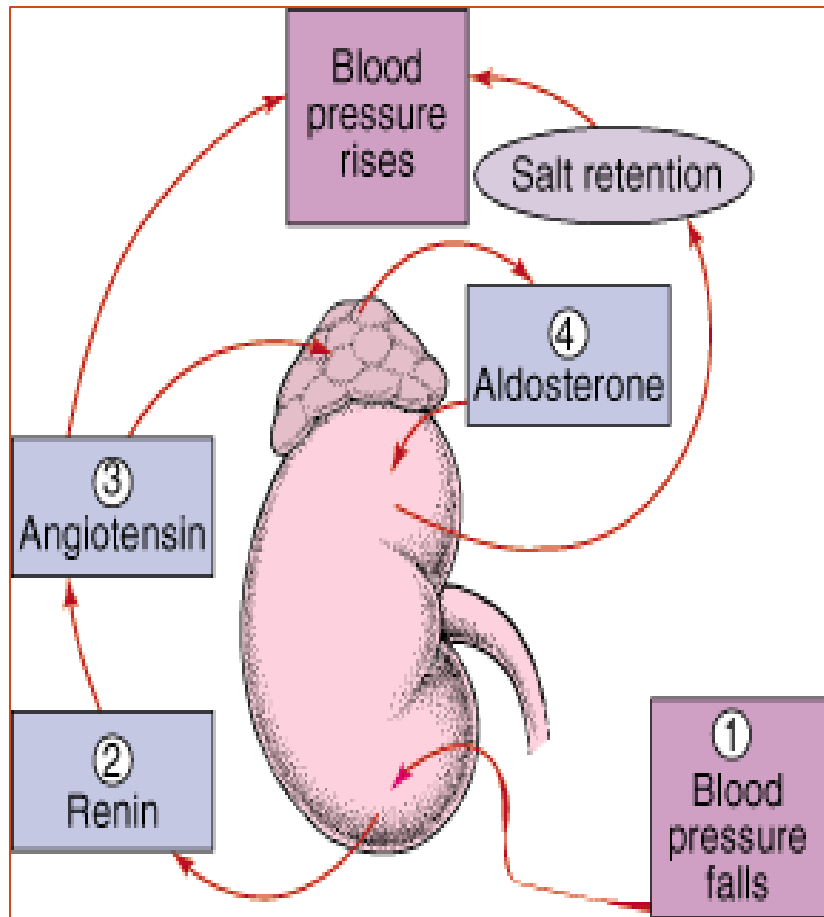
α / β -Blockers

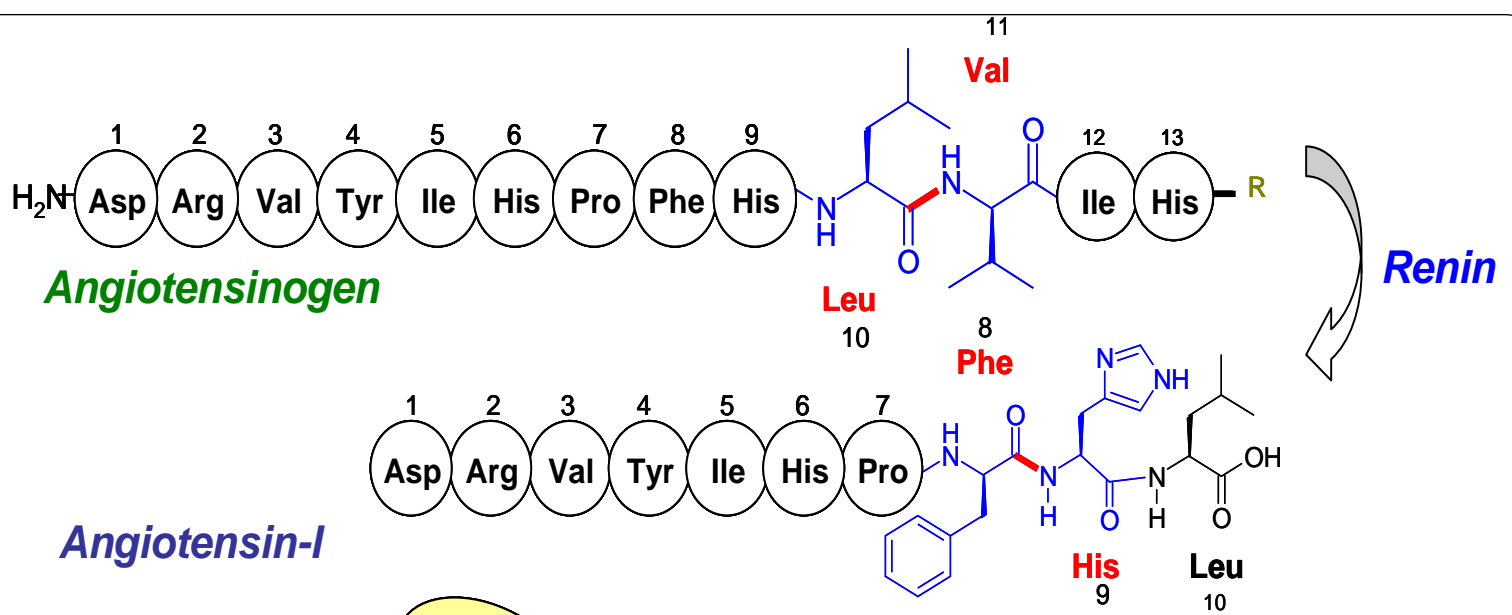


Labetalol

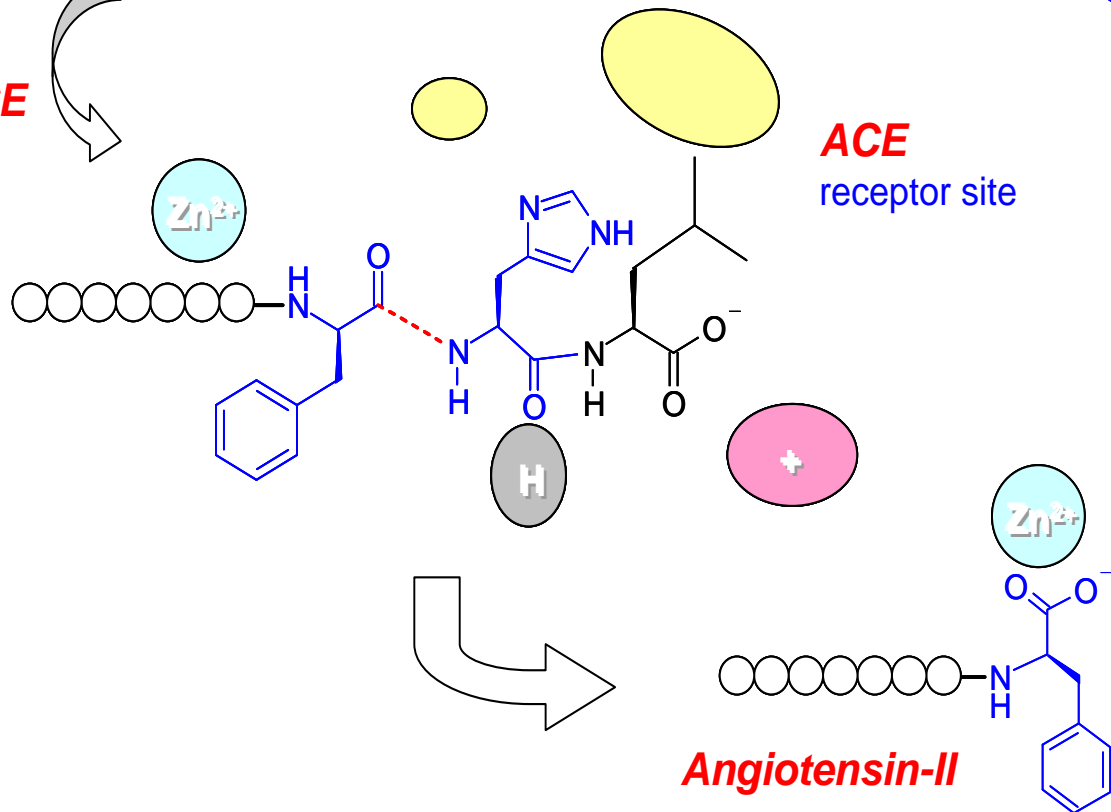
iii-RENIN ANGIOTENSIN SYSTEM INHIBITORS

- The renin-angiotensine system is a **hormonal system** that plays a central role in the control of sodium excretion and body fluid volume

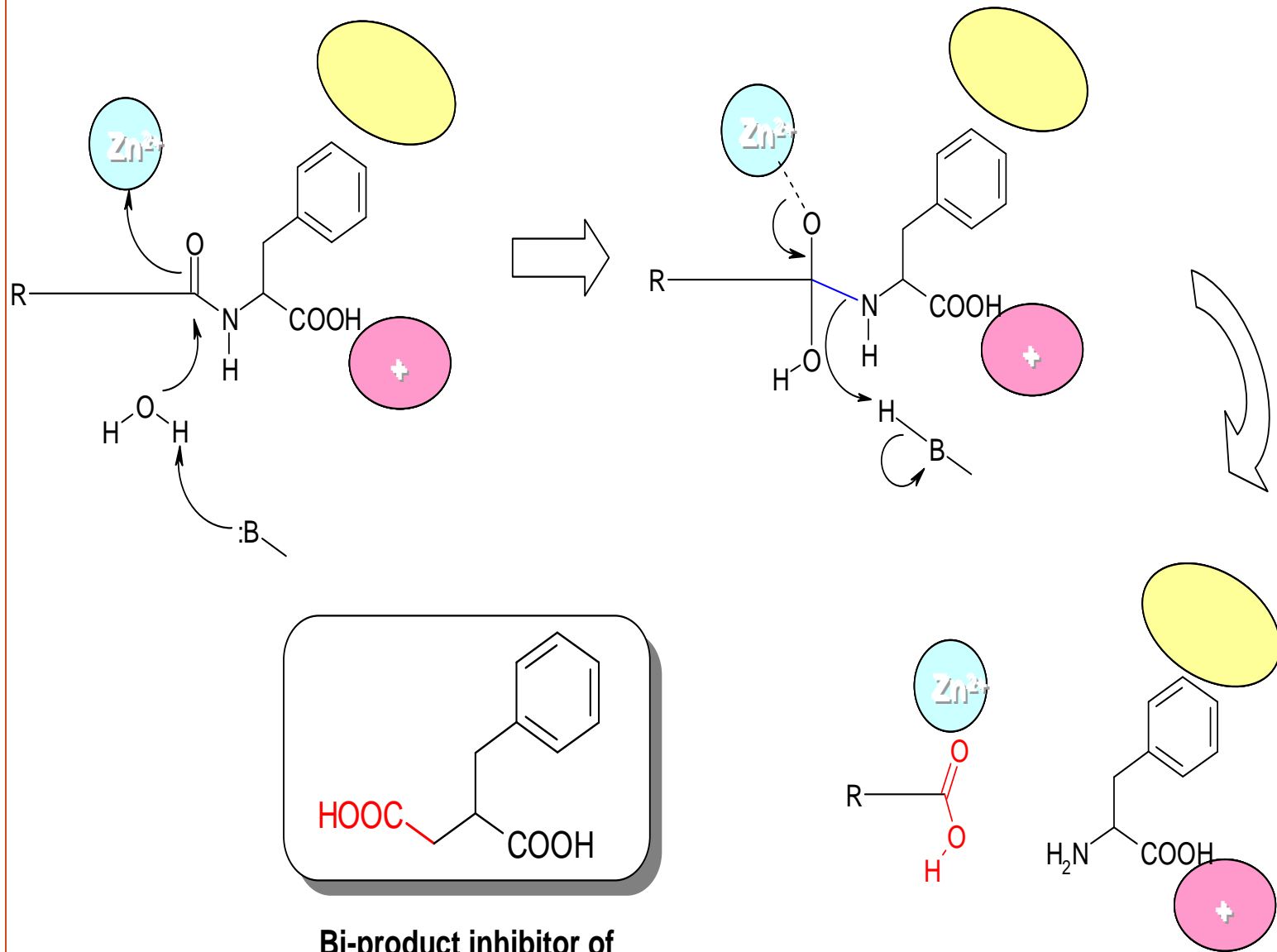


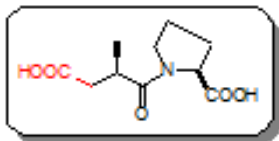
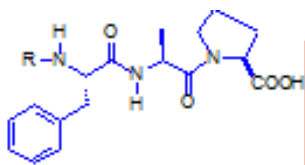


ACE

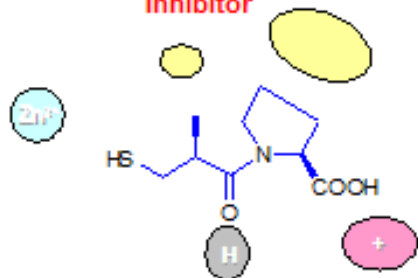


Mechanism Of **Carboxypeptidase** Enzyme



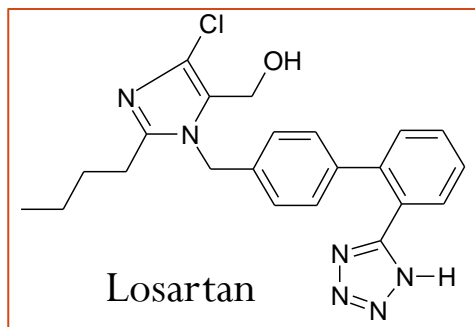


First Nonpeptide ACE Inhibitor

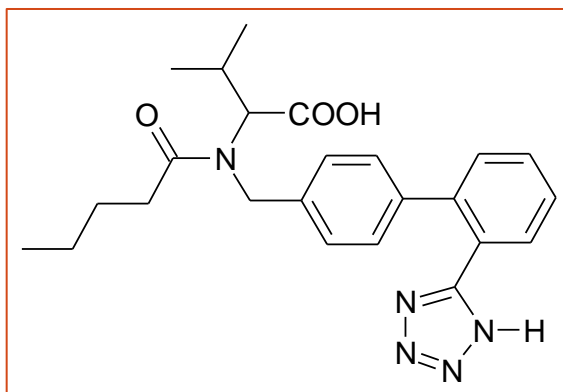


Captopril, Capoten®

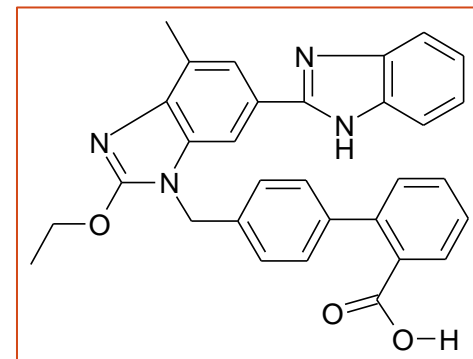
AgII Receptor Blockers



Losartan

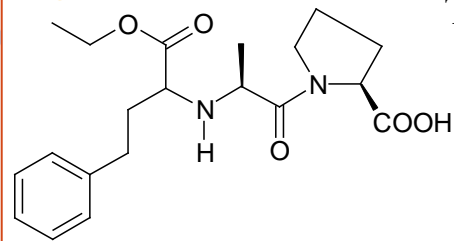


Valsartan

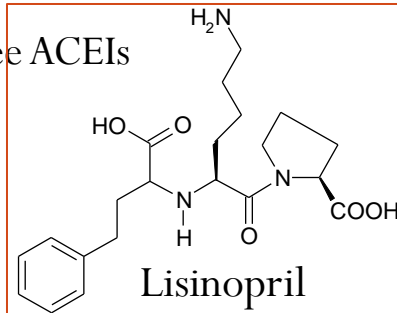


Telmisartan

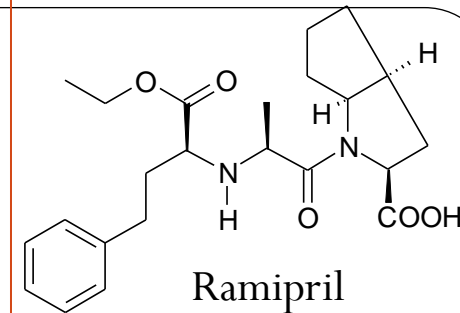
Thiol Free ACEIs



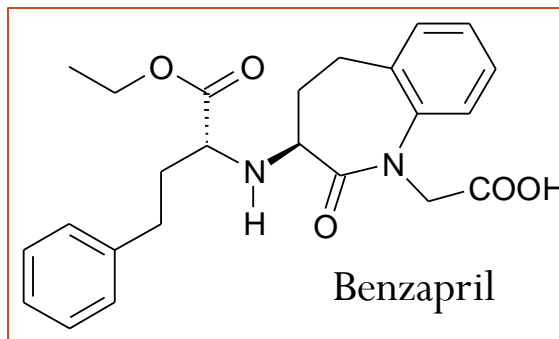
Enalapril



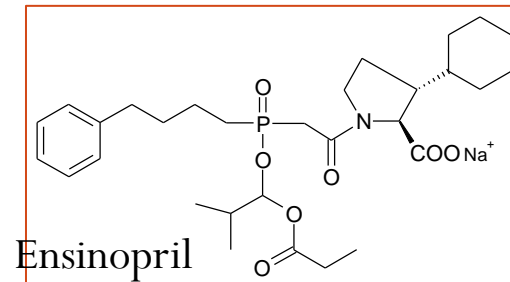
Lisinopril



Ramipril



Benzapril

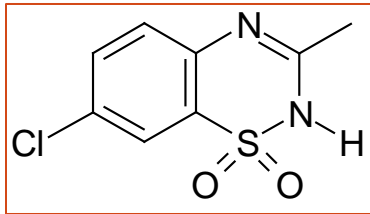


Ensinopril

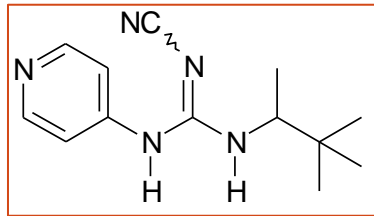
iv- VASODILATORS

- Potassium Channels Openers (PCOs)
- Calcium Channels Blockers (CCBs)
- Other Vasodilators

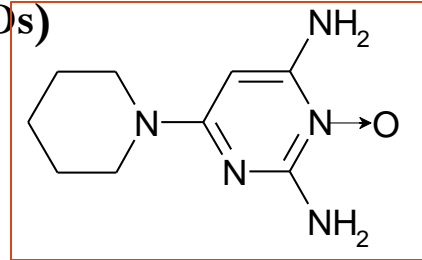
I. Potassium Channels Openers (PCOs)



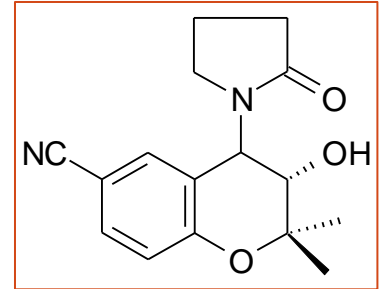
Diazoxide



Pinacidil



Minoxidil



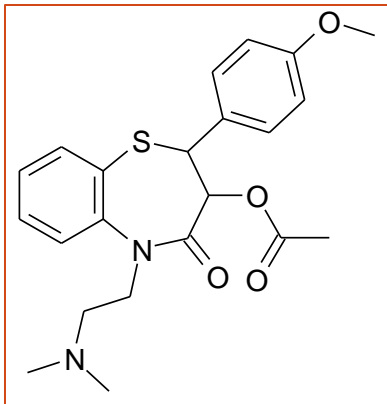
Cromakalim

II. Calcium Channels Blockers (CCBs)

Three Prototypes:

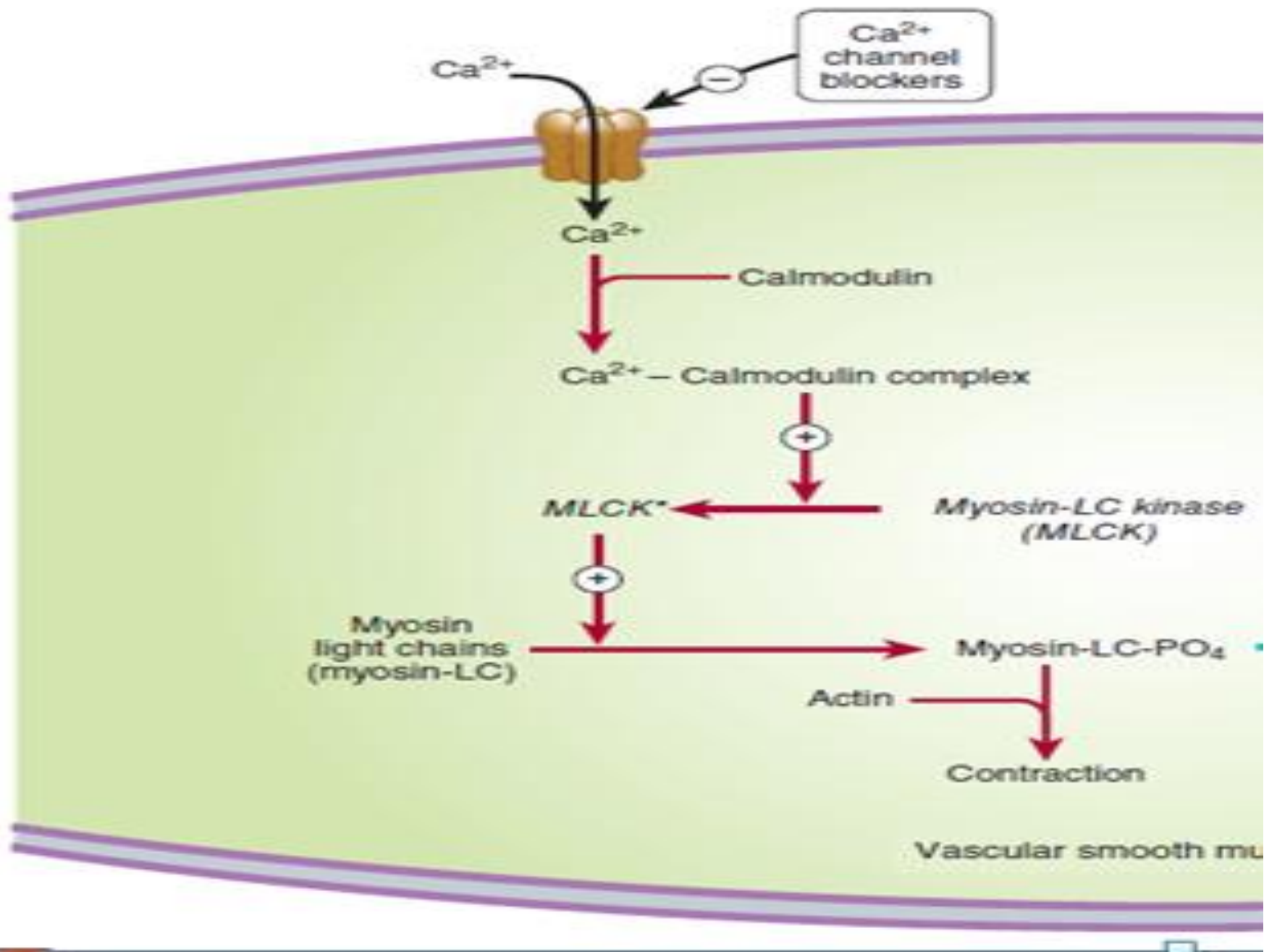
1. Benzothiazepines. (Diltiazem)

Diltiazem

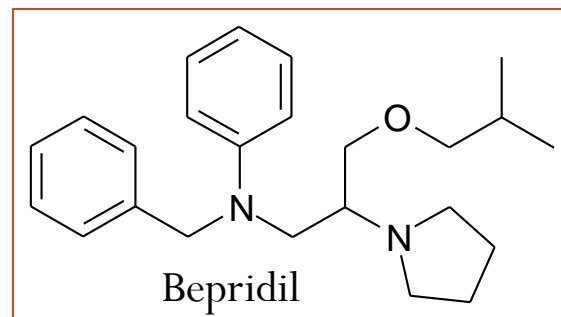
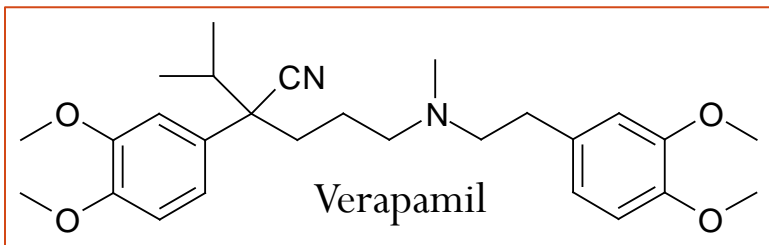


Calcium channel blockers

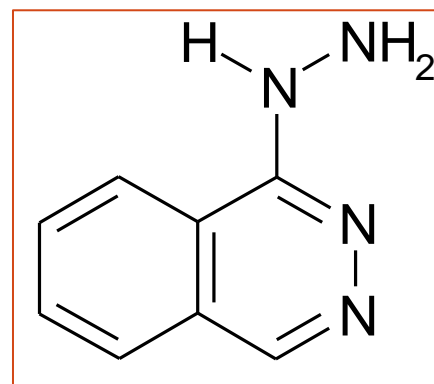
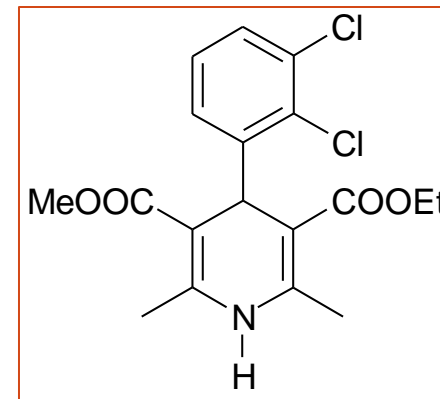
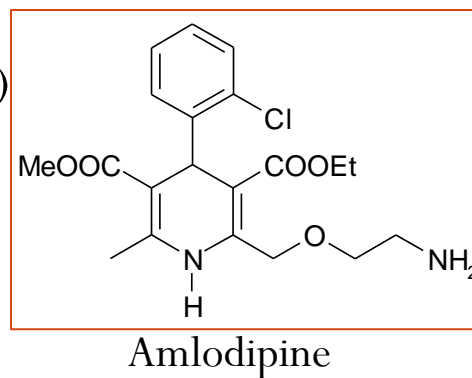
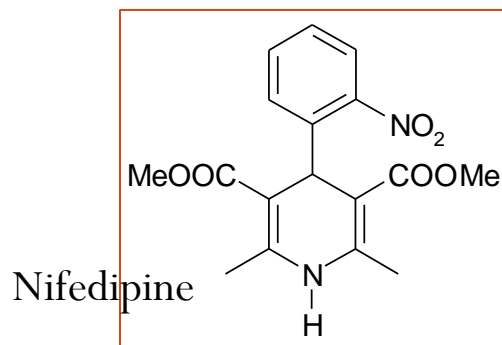
predictably cause vasodilation because they reduce intracellular Ca²⁺, a major modulator of the activation of **myosin light chain Kinase** in smooth muscle.



2. Phenylalkylamines. (Verapamil)



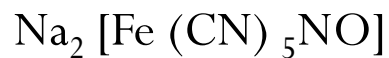
3. Dihydropyridines. (Nifedipine)



Felodipin

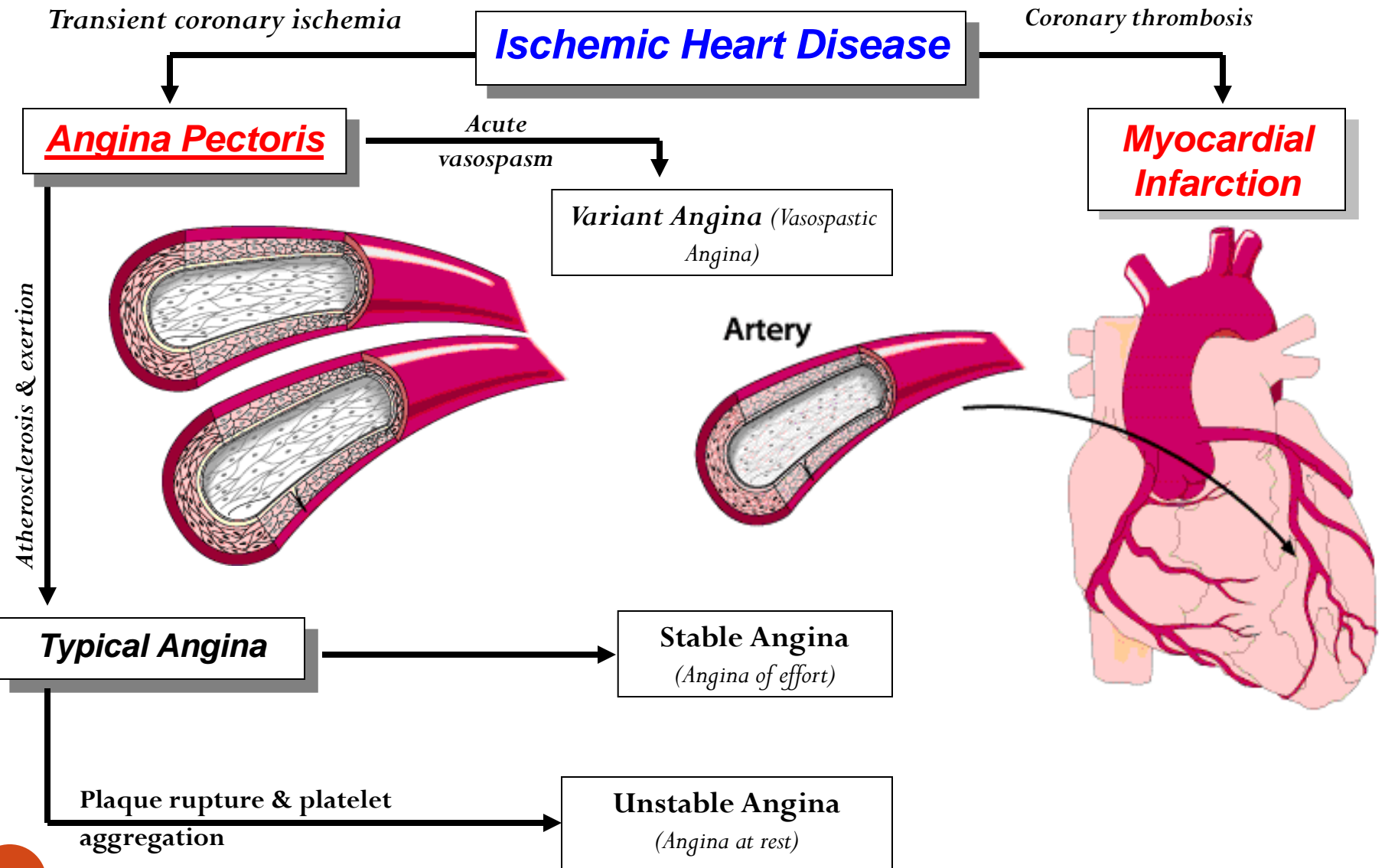
Hydralazine

III. Other Vasodilators

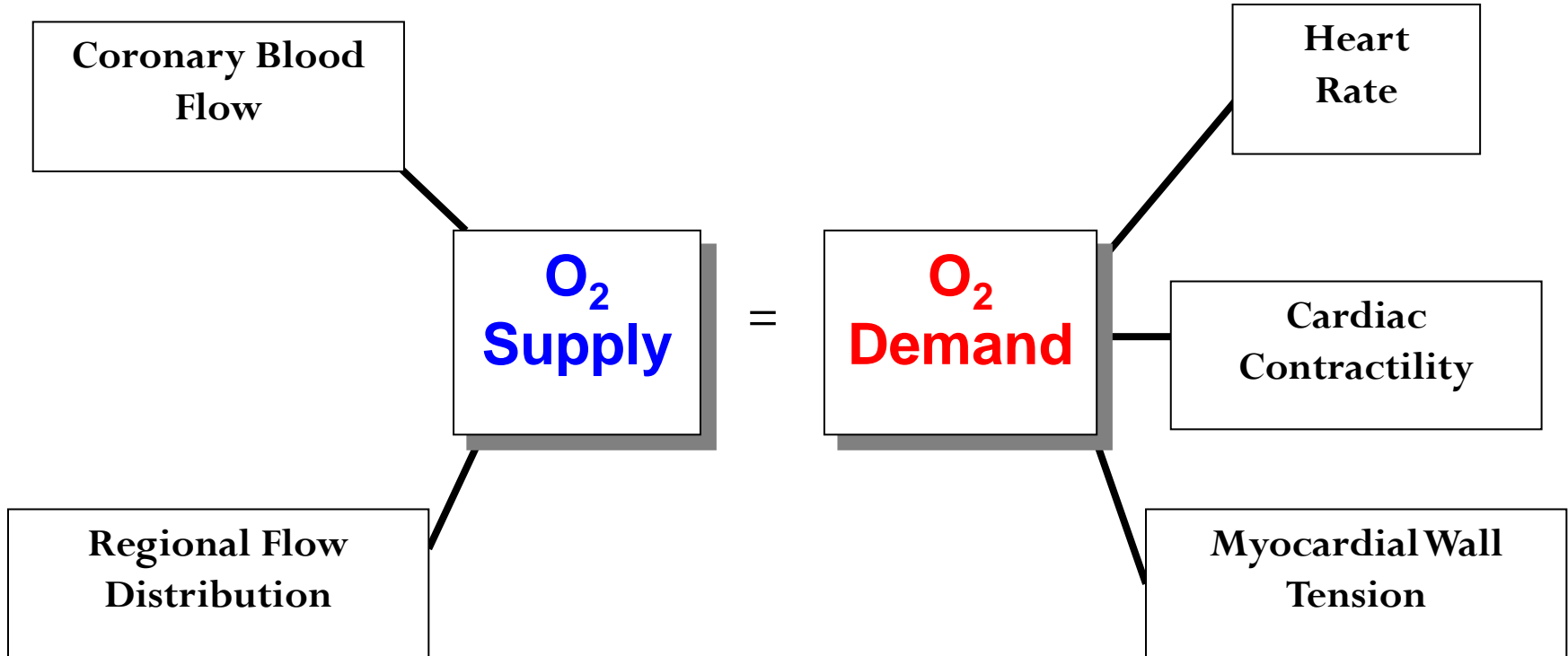


Sodium Nitroprusside

ANTIANGINAL DRUGS



Goal Of Antianginal Drugs: To restore balance between
Myocardial O₂ Demand and Supply



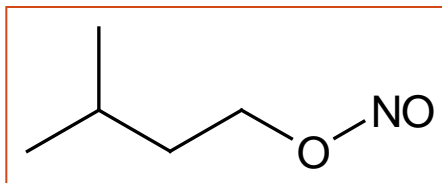
1. Organic Nitrates

2. CCBs

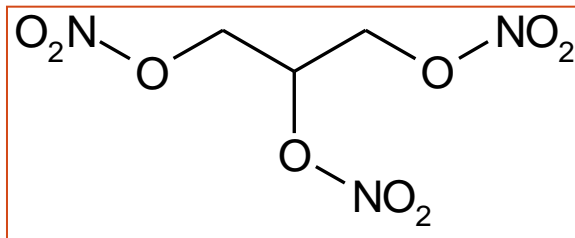
3. β -Bs

4. VDs

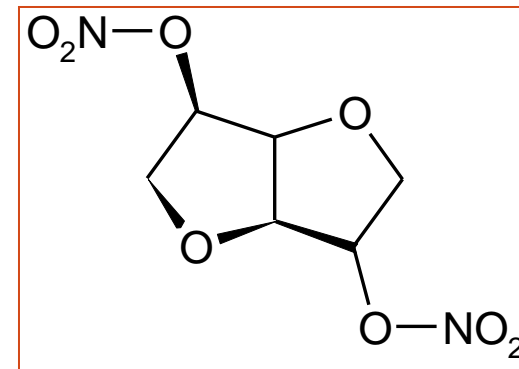
1. Organic Nitrates



Isopentyl Nitrite, *Amyl Nitrite*



Glyceryl Trinitrate, *Nitroglycerin*



Isosorbid Drinitrate, *Isordil*

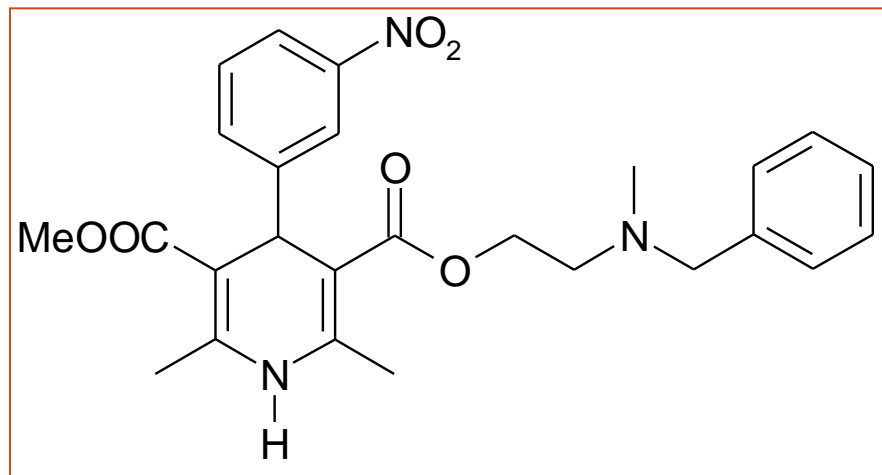
2. CCBs

Verapamil, Bepridil

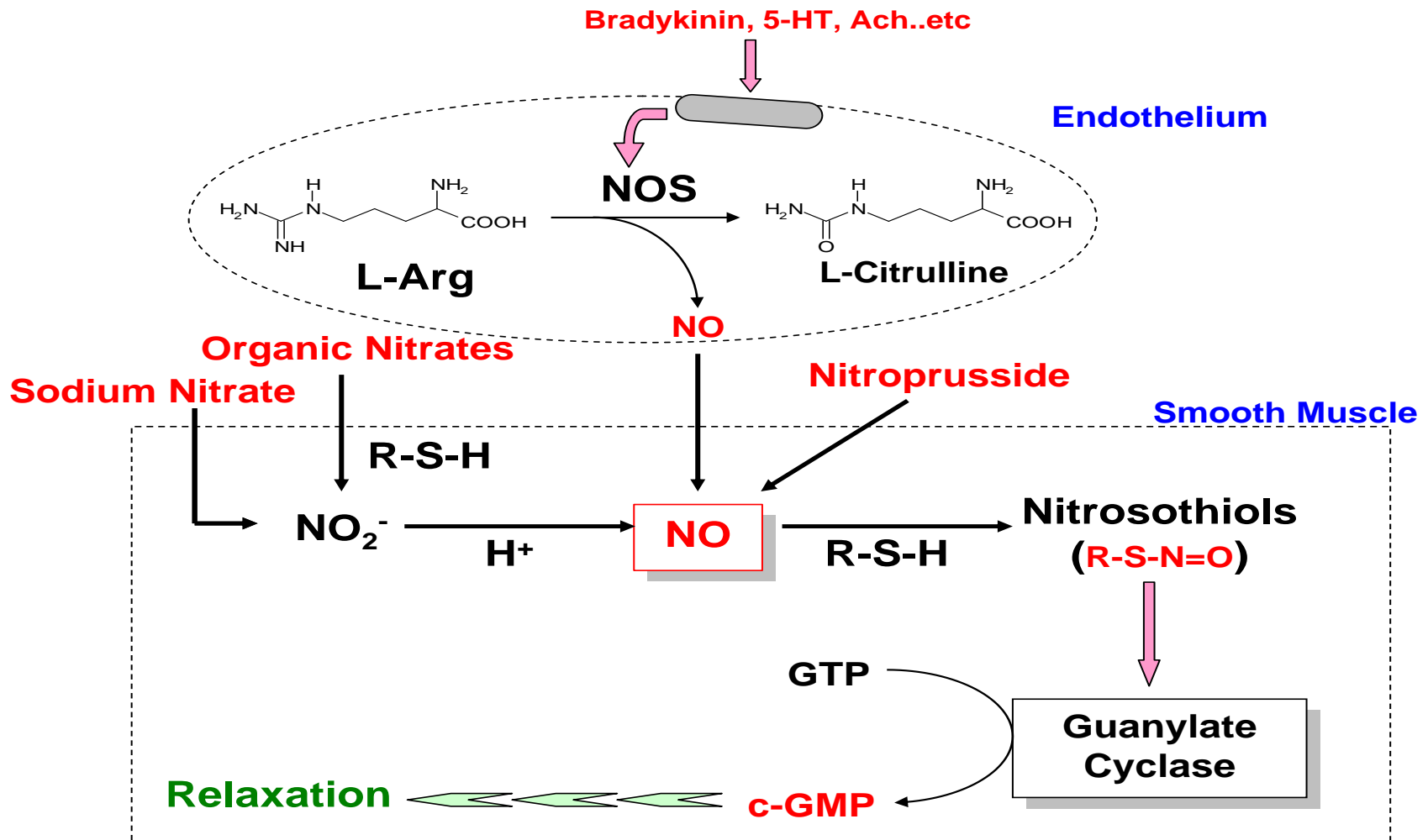
Diltiazem

Nefidipine, Amlodipine &

Nicardipine



Nicardipine, *Cardene*



- cGMP facilitates the **dephosphorylation** of myosin light chains, preventing the interaction of myosin with **actin**.

3. β -Blockers

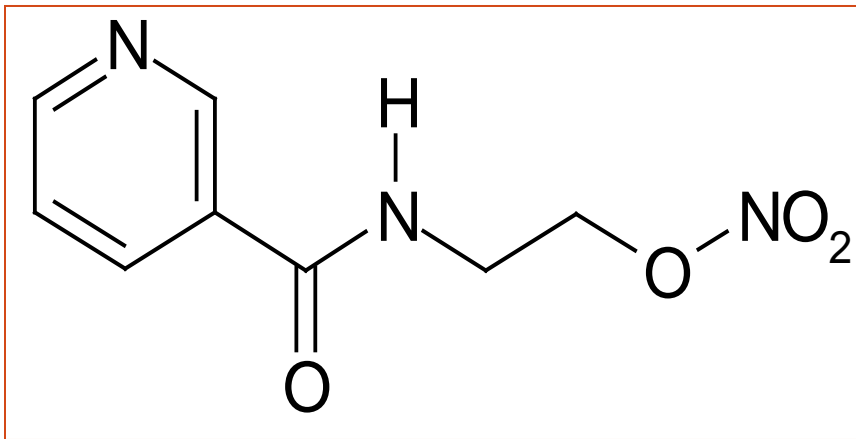
Propranolol

Atenolol

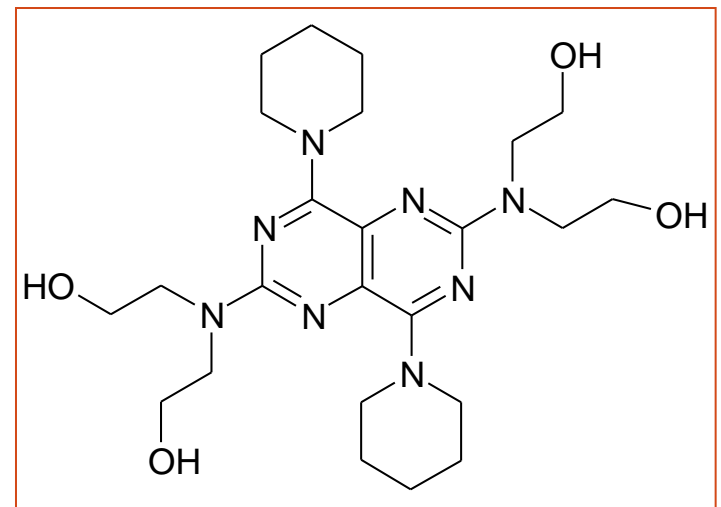
Metoprolol

Nadolol

4. Other Antianginal Drugs (Coronary VDs):



Nicorandil., *Icorel*



Dipyridamol, *Persantin*

3. DRUGS FOR HEART FAILURE

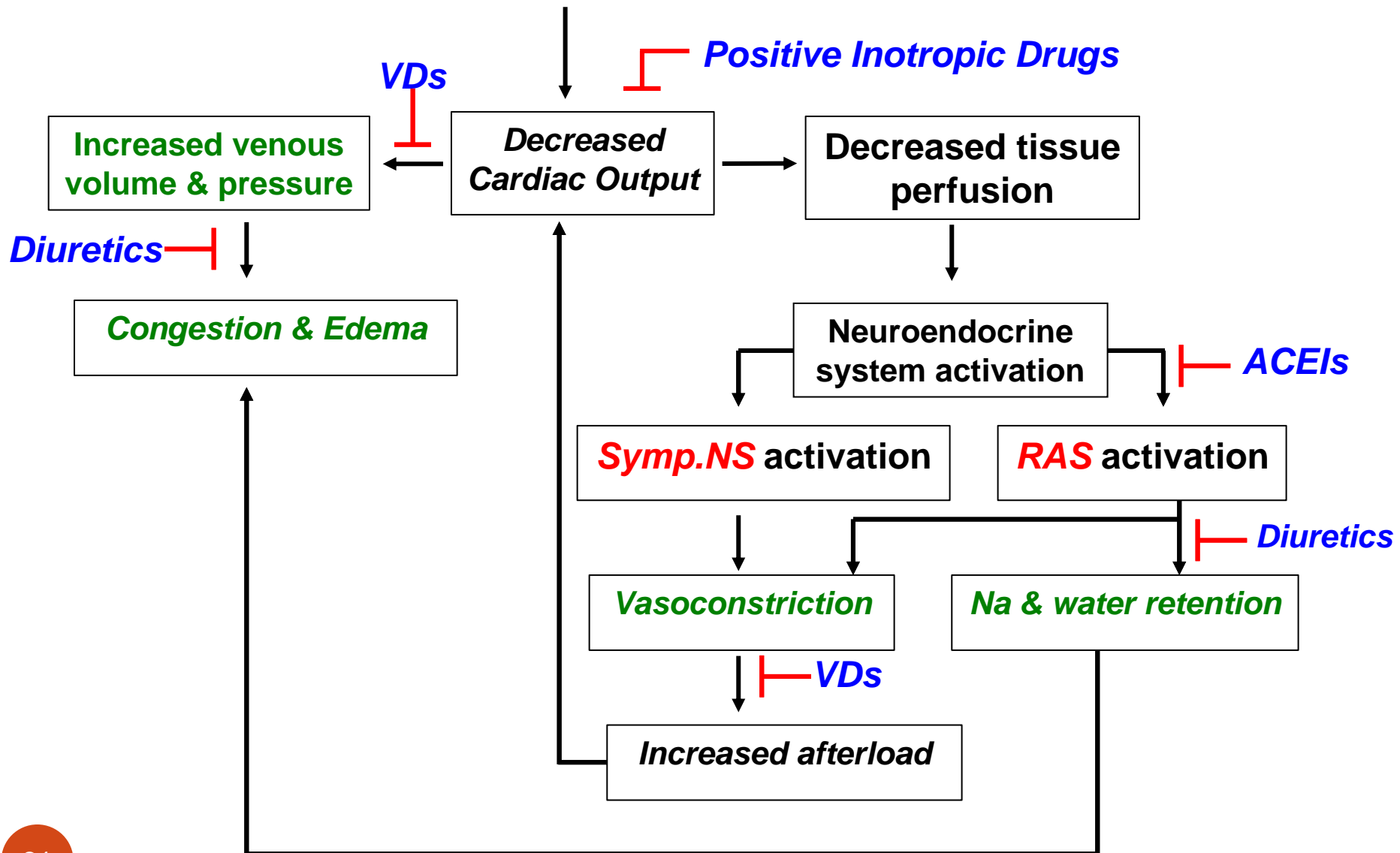
Congestive heart failure **CHF** is a complex clinical syndrome characterized by impaired ventricular performance (**impaired cardiac output**), exercise intolerance, a high incidence of ventricular arrhythmias, and shortened life expectancy.

The signs and symptoms of heart failure include tachycardia, decreased exercise tolerance and shortness of breath, peripheral and **pulmonary edema**, and **cardiac hypertrophy**.

Virtually all forms of heart disease can lead to heart failure, with coronary artery disease, hypertension, and diabetes mellitus being the most common.

The primary goal in treating heart failure is **to improve the patient's quality of life** by reliving the symptoms and to decrease the mortality rate.

HEART FAILURE



Three categories of drugs are used in the treatment of **CHF**:

1. Positively Inotropic Drugs:

- a. Cardiac Glycosides.
- b. Adrenergic Receptors Agonists.
- c. Phosphodiesterase Inhibitors

2. Vasodilators:

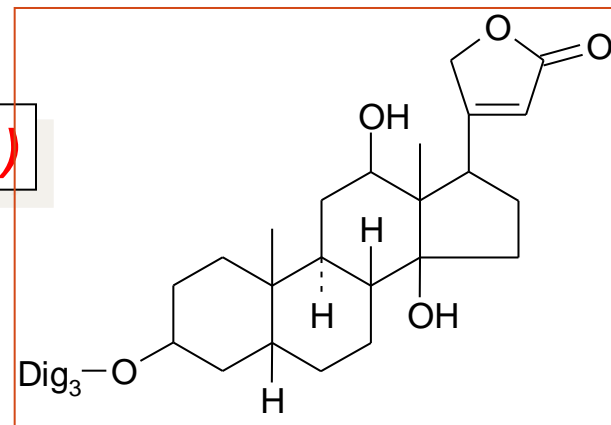
- a. *ACEIs*.
- b. *CCBs* (vasoselective only, why?).
- c. *Organic Nitrates*.

3. Diuretics (*mainly potassium sparing*).

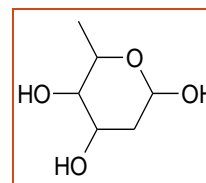
1. Positively Inotropic Drugs (Cardiotonics)

a. Cardiac Glycosides

The cardiac glycosides inhibit the Na^+/K^+ -*ATPase* pump, which causes an increase in intracellular Na^+ , slowing the rate of the $\text{Na}^+/\text{Ca}^{++}$ -exchanger, thereby causing an increase in intracellular Ca^{++} leading to greater **myofibril** shortening (*contraction*).



Digoxin, *Lanoxine*[®]



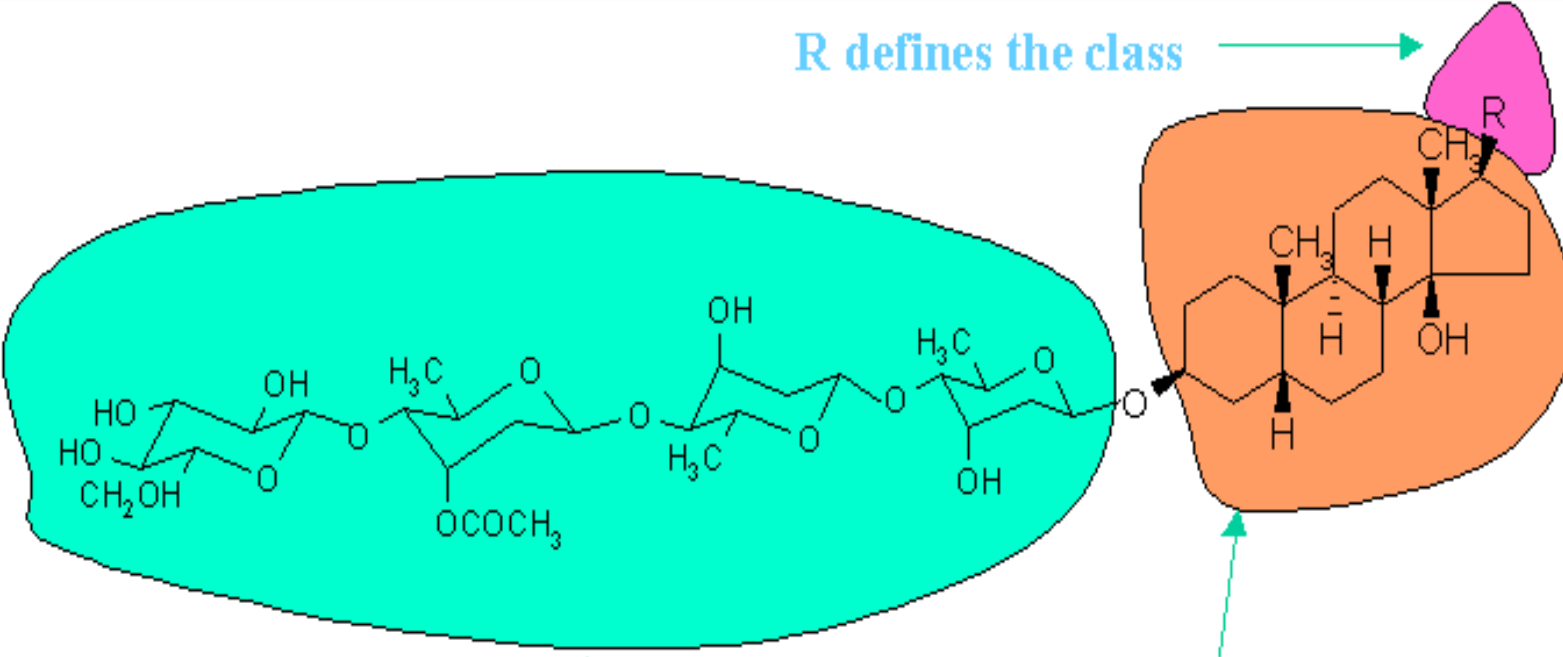
Digitoxose (Dig)

- **Cardiac Glycosides**

- Increasing the **force of contraction** of the heart (positive inotropic activity) is very important for most heart failure patients.
- Cardiac steroids are perhaps the most useful drugs that increase heart contractility.
- The cardiac glycosides are an important class of naturally occurring drugs whose actions include both beneficial and toxic effects on the heart.

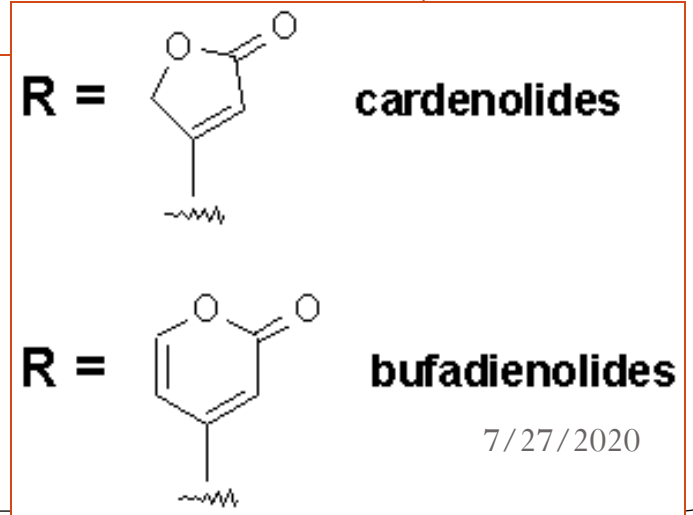
- Cardiac steroids are widely used in the modern treatment of CHF and for treatment of **atrial fibrillation** and **flutter**.
 - Yet their toxicity remains a serious problem.
- **Structure**
 - Cardiac glycosides are composed of two structural features :
 - The sugar (glycoside) moiety
 - The non-sugar (aglycone - steroid) moieties.

R defines the class



Sugar portion
(glycone)

Aglycone portion

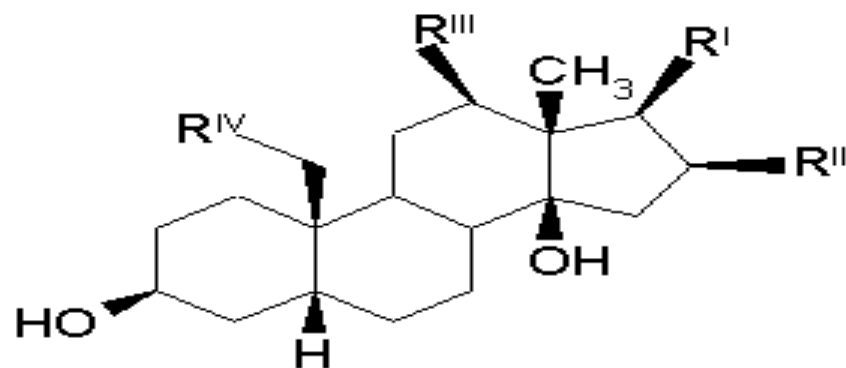


7/27/2020

- The R group at the 17-position defines the class of cardiac glycoside.
- Two classes have been observed in Nature –
 - The cardenolides and the bufadienolides.
 - The cardenolides have an unsaturated **butyrolactone** ring while the bufadienolides have a **pyrone** ring.

- **Nomenclature:** The cardiac glycosides occur mainly in plants from which the names have been derived.
 - *Digitalis purpurea*,
 - *Digitalis lanata*,
 - *Strophanthus gratus*, and
 - *Strophanthus kombe* are the major sources of the cardiac glycosides.

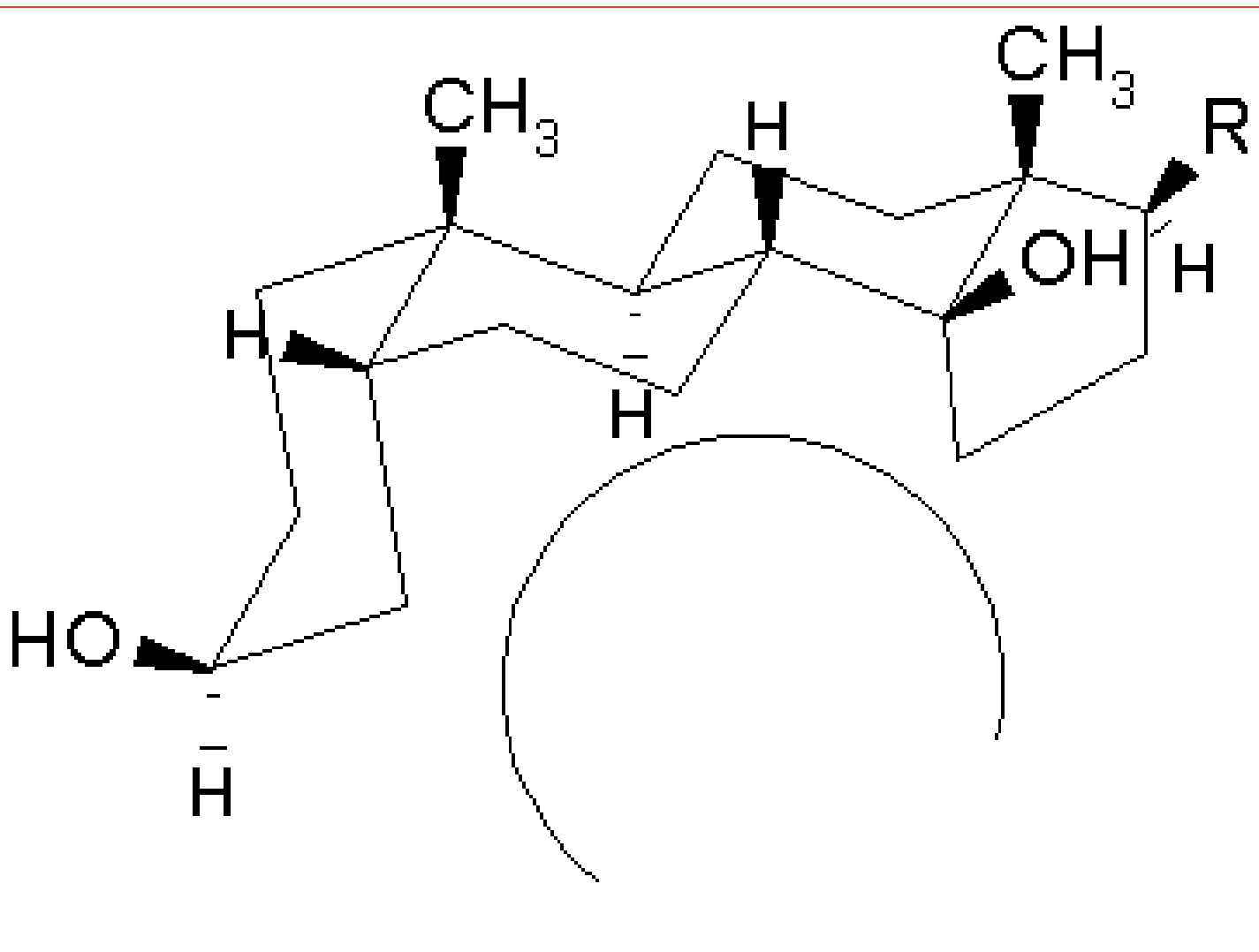
- The term '**genin**' at the end refers to only the **aglycone** portion (without the sugar).
- Thus the word digitoxin refers to an agent consisting of digitoxigenin (aglycone) and sugar moieties (three).
- The aglycone portion of cardiac glycosides is **more important** than the glycone portion.



	R ^I	R ^{II}	R ^{III}	R ^{IV}
Digitoxigenin		H	H	H
Digoxigenin		H	OH	H
Gitoxigenin		OH	H	H
Ouabagenin		H	H	H
Strophanthidin		H	H	=O
Bufalin		H	H	H

- **The aglycone moiety:**

- The steroid nucleus has a unique set of fused ring system that makes the aglycone moiety structurally distinct from the other more common steroid ring systems.
- Rings A/B and C/D are **cis** fused while rings B/C are **trans** fused.
- Such ring fusion gives the aglycone nucleus of cardiac glycosides the characteristic '**U**' shape.



- The steroid nucleus has hydroxyls at 3- and 14- positions of which the sugar attachment uses the 3-OH group.
- 14-OH is normally unsubstituted.
- Many genins have OH groups at 12- and 16- positions.
 - These additional hydroxyl groups influence the partitioning of the cardiac glycosides into the aqueous media and greatly affect the distribution.

- The **lactone** moiety at **C-17** position is an important structural feature.
- The size and degree of unsaturation varies with the source of the glycoside.
- Normally plant sources provide a **5-membered** unsaturated lactone while animal sources give a **6-membered** unsaturated lactone.

Sugar moiety:

- 1 to 4 sugars are found to be present in most cardiac glycosides attached to the 3 β -OH group.
- The sugars most commonly used include:
 - L-rhamnose, D-glucose, D-digitoxose, D-digitalose, D-digginose, D-sarmentose, L-vallarose, and D-fructose.
- These sugars predominantly exist in the cardiac glycosides in the β -conformation.

- The presence of acetyl group on the sugar affects
 - Lipophilic character and the kinetics of the entire glycoside.
- Because the **order of sugars** appears to have little to do with biological activity
 - Nature has synthesized a range of numerous cardiac glycosides with differing sugar skeleton but relatively few **aglycone** structures.

Structure - Activity Relationships

- The sugar moiety appears to be important only for the partitioning and kinetics of action
- It possesses no biological activity.
 - For example, elimination of the aglycone moiety eliminates the activity of alleviating symptoms associated with cardiac failure.
- The "backbone" U " shape of the steroid nucleus appears to be very important. Structures with C/D *trans* fusion are **inactive**.
- Conversion to A/B *trans* system leads to a marked drop in activity. Thus although not mandatory A/B *cis* fusion is important.
- The 14-OH groups are now believed to be **dispensable**. A skeleton without 14-OH group but retaining the **C/D *cis*** ring fusion was found to retain activity.

- Lactones alone, when not attached to the steroid skeleton, are not active.
 - Thus the activity rests in the steroid skeleton.
- The **unsaturated 17-lactone** plays an important role in receptor binding.
 - Saturation of the lactone ring dramatically reduced the biological activity.
- The **lactone** ring is **not** absolutely required.
 - For example, using α,β -unsaturated nitrile ($C=C-CN$ group), the lactone could be replaced with little or no loss in biological activity.

- **Biochemical Mechanism of Action**

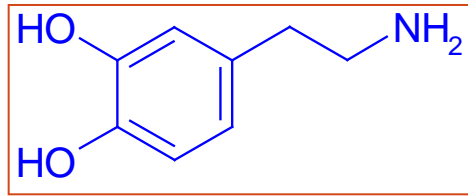
- The mechanism whereby cardiac glycosides cause a positive inotropic effect and electrophysiologic changes is still not completely clear.
- Several mechanisms have been proposed, but the most widely accepted involves
 - The ability of cardiac glycosides to inhibit the membrane bound Na⁺-K⁺-ATPase pump responsible for Na⁺-K⁺ exchange.

- The process of membrane depolarization / repolarization is controlled by the movement of three cations
 - Na^+ , Ca^{+2} , and K^+ , in and out of the cell.
- At the resting stage, the concentration of Na^+ is high on the outside.
- On membrane depolarization sodium fluxes-in leading to an immediate elevation of the action potential.

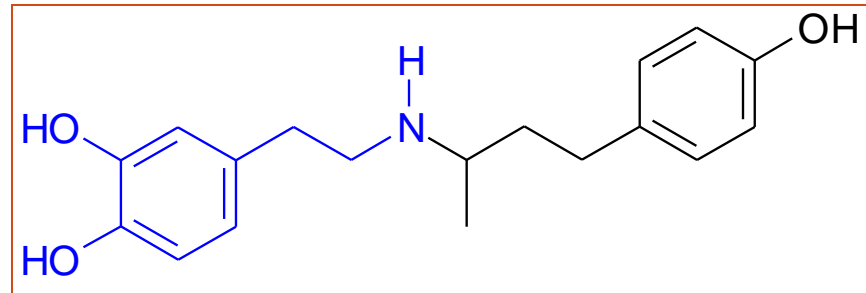
- Elevated intracellular Na^+ triggers the influx of free of Ca^{++} that occurs more slowly.
 - The higher intracellular $[\text{Ca}^{++}]$ results in the efflux of K^+ .
- The re-establishment of the action potential occurs later by the reverse of the $\text{Na}^+ - \text{K}^+$ exchange.
- The Na^+ / K^+ exchange requires energy which is provided by an enzyme $\text{Na}^+ - \text{K}^+ - \text{ATPase}$.

- Cardiac glycosides are proposed to inhibit this enzyme with a net result of reduced sodium exchange with potassium that leaves increased intracellular Na^+ .
 - This results in increased intracellular $[\text{Ca}^{++}]$.
- Elevated intracellular calcium concentration triggers a series of intracellular biochemical events that ultimately result in an increase in the force of the myocardial contraction or a **positive inotropic effect**.

b- β -Adrenergic Agonists

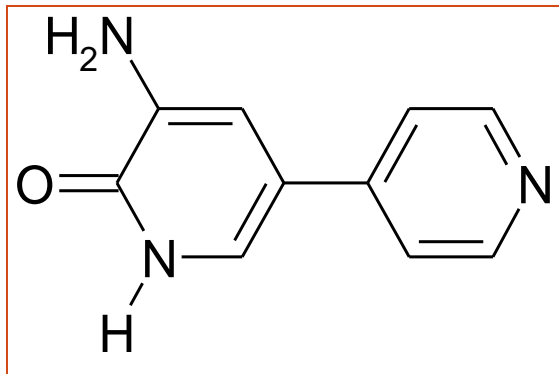


Dopamine, *Intoropin*[®]

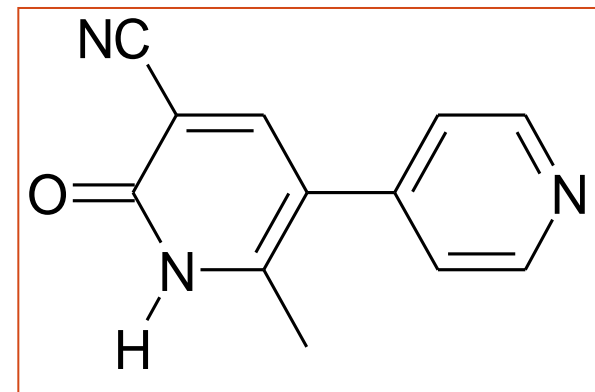


Dobutamine, *Dobutrex*[®]

c- Phosphodiesterase Inhibitors



Inamrinone



Milrinone, *Primacor*[®]

decrease the rate of cyclic AMP degradation. The ensuing increase in cyclic AMP concentration leads to enhanced calcium influx into the cell, a rise in cell calcium concentration, and increased contractility.

4. ANTIARRHYTHMIC DRUGS

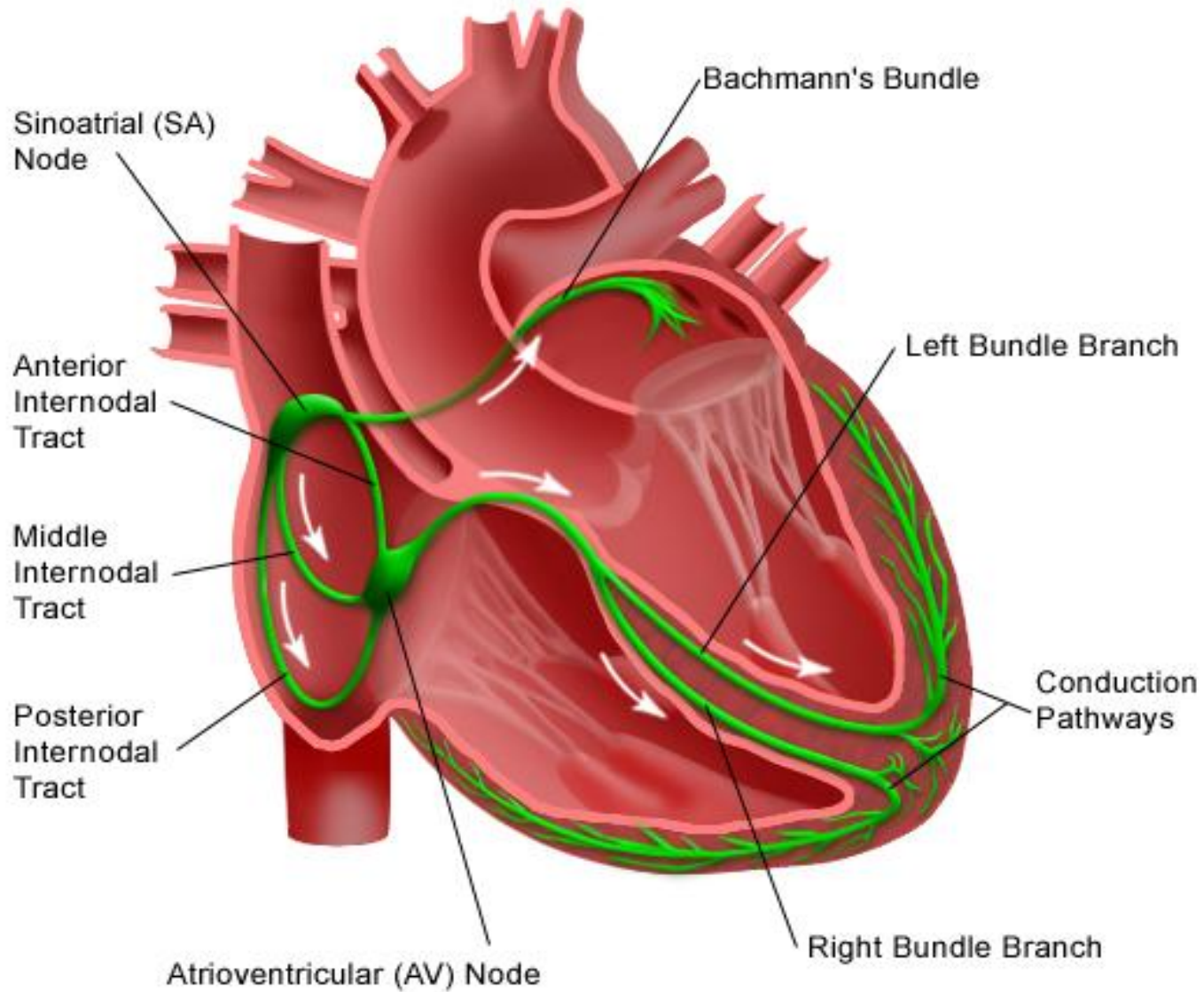
Normal Heart beat

- A normal 'sinus rhythm' starts in the sino atrial (SA) node and spreads down to the atrioventricular (AV) node as the atria contract and force blood into the ventricles.
- The ventricles then contract and pump blood out of the heart as electrical signals reach ventricular muscle cells.

❖ An **Arrhythmia** is an abnormal rhythm of the heart and is caused by problems with your heart's electrical system.

❖ The electrical impulses may happen too fast, too slowly, or erratically - causing the heart to beat too fast, too slowly, or erratically.

Electrical System of the Heart



All of the *antiarrhythmic drugs* act by *altering ion fluxes* within excitable tissues in the myocardium. The three ions of primary importance are Na^+ , Ca^{2+} , and K^+ . *Antiarrhythmic drugs* can be classified by their ability to *directly or indirectly block flux of one or more of these ions* across the membranes of excitable cardiac muscle cells

Therapeutic Classes

Four classes of drugs are used in the treatment of *arrhythmia*:

Class-I: (sodium channels blockers).

Class-II (β -adrenergic blockers)

Class-III (potassium channels blockers)

Class-IV (cardioselective **CCBs**)

Class-I Antiarrhythmic Drugs:

They are called *membrane stabilizing* (*depressant*) drugs, act on sodium channels and block the depolarizing inward Na^+ current. They bind Na^+ channels in the *open* or *inactivated* state and dissociate from the channels in the *resting* state. They affect arrhythmic hearts more than normal hearts (use dependent channels blockade).

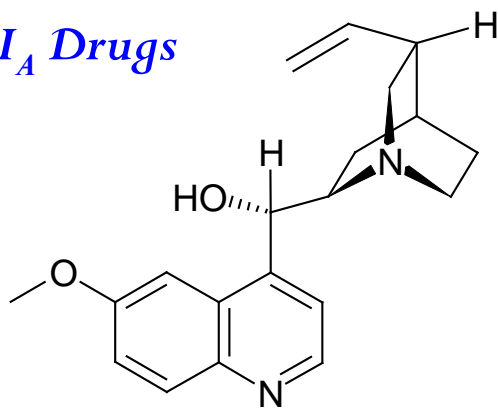
According to the rate of dissociation from the sodium channels, **Class-I** drugs could be subdivided into:

Class-I_A (intermediate rate of dissociation)

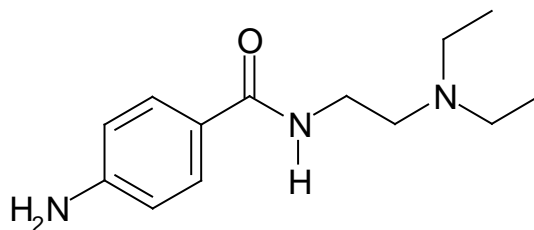
Class-I_B (rapid rate of dissociation)

Class-I_C (slow rate of dissociation)

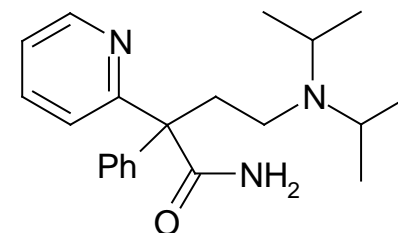
Class-I_A Drugs



Quinidine

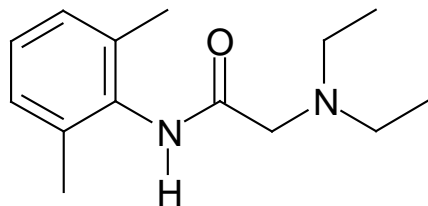


Procainamide, *Pronestyl*

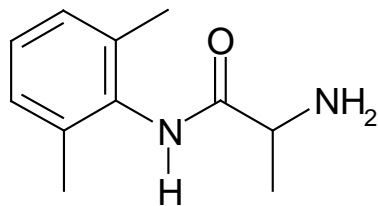


Disopyramide, *Norpace*

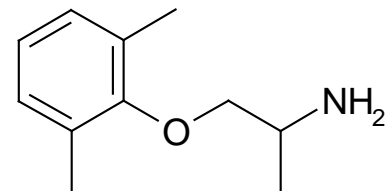
Class-I_B Drugs



Lidocaine, *Xylocaine*

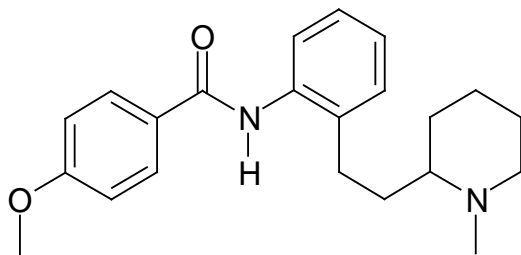


Tocainide, *Tonocard*

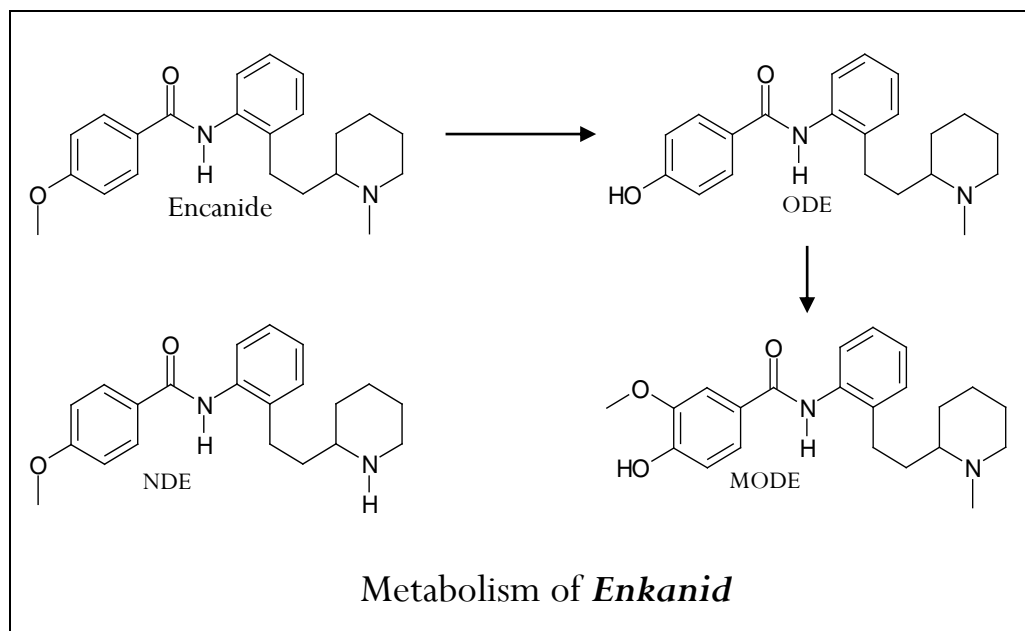


Mexiletine, *Mexitil*

Class-I_C Drugs



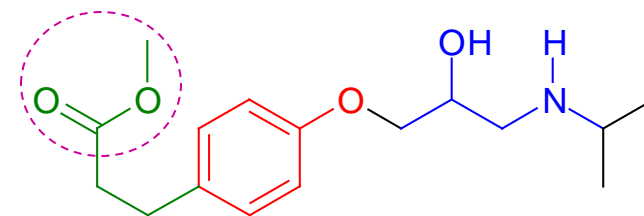
Encainide *Enkaid*



Class-II Antiarrhythmic Drugs:

They decrease inward calcium current by blocking the β -adrenergic receptors and inhibiting sympathetic activation of cardiac automaticity and conduction.

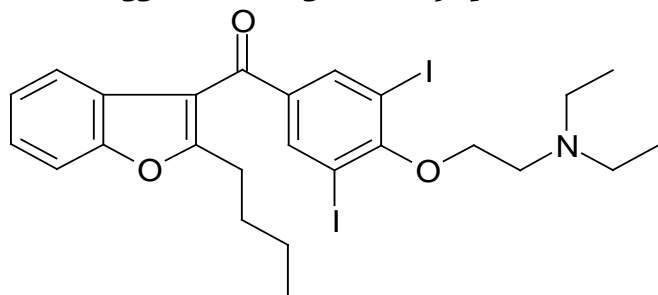
Propranolol, Acebutolol, Metoprolol and Esmolol,



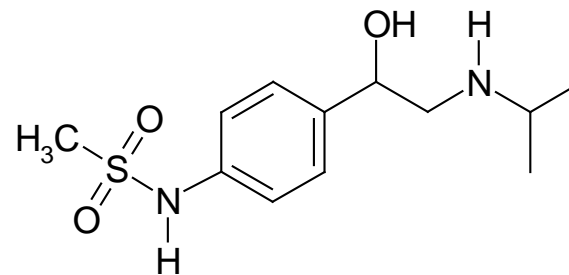
Esmolol, *Brevibloc*

Class-III Antiarrhythmic Drugs:

Drugs from this class share the ability to block *potassium channels*; some members are able to block other channels as well. Potassium channels are activated during the repolarization (Phase 3) of the action potential; thus, their blockade *prolongs action potential duration* resulting in an *increase in effective refractory period*



Amiodarone, *Cordarone*



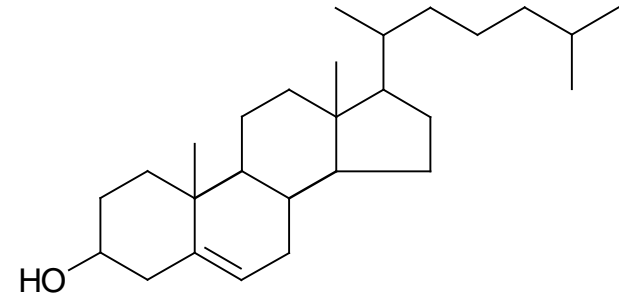
Sotalol, *Betapace*

Class-IV Antiarrhythmic Drugs:

These are the cardioselective **CCBs** namely *Verapamil, Biperidil* and *Diltiazem* they decrease the conduction velocity and increase the refractory period

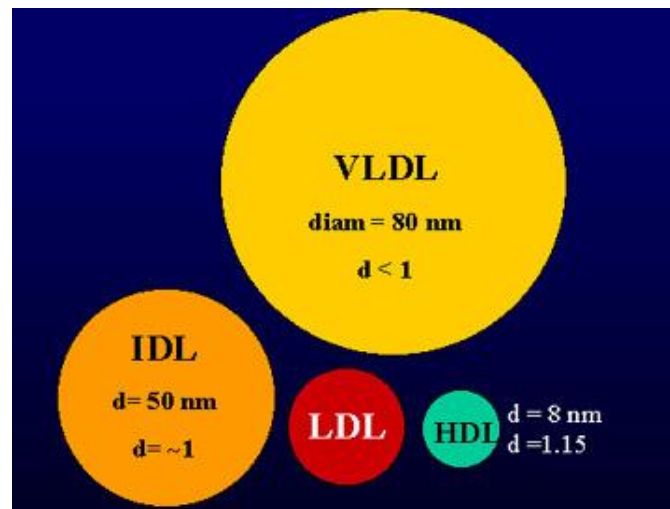
5. ANTIHYPERLIPIDEMIC DRUGS

• **Hyperlipidemia**, which is a general term describing elevated concentration of **lipids** in the blood, is the major cause of atherosclerotic and coronary heart diseases. **Lipids** are essential molecules for human life, they are either **Cholesterol esters or Triglycerides**. **Cholesterol** is a steroid alcohol that is an essential component of cells membranes and myelin sheaths. It also serves as a precursor for *steroid hormones and bile acids*. Most of the body cholesterol is made by the *liver* from **acetyl-CoA**, the rest is absorbed from diet.

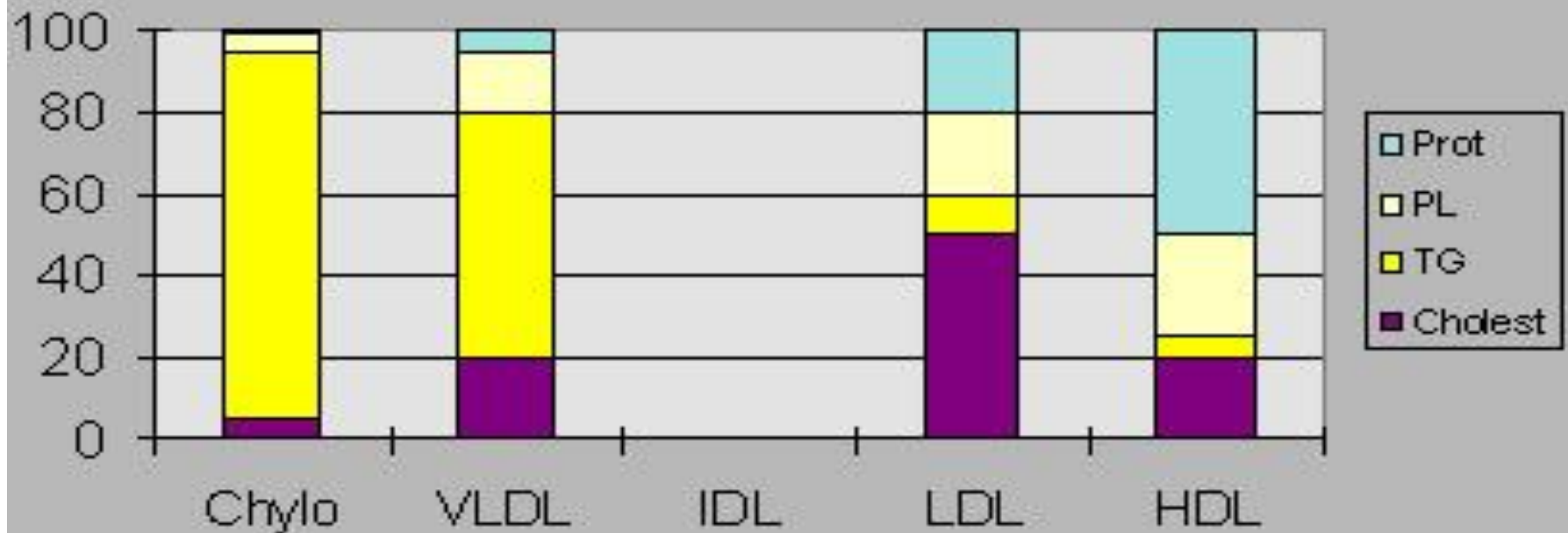


Cholesterol

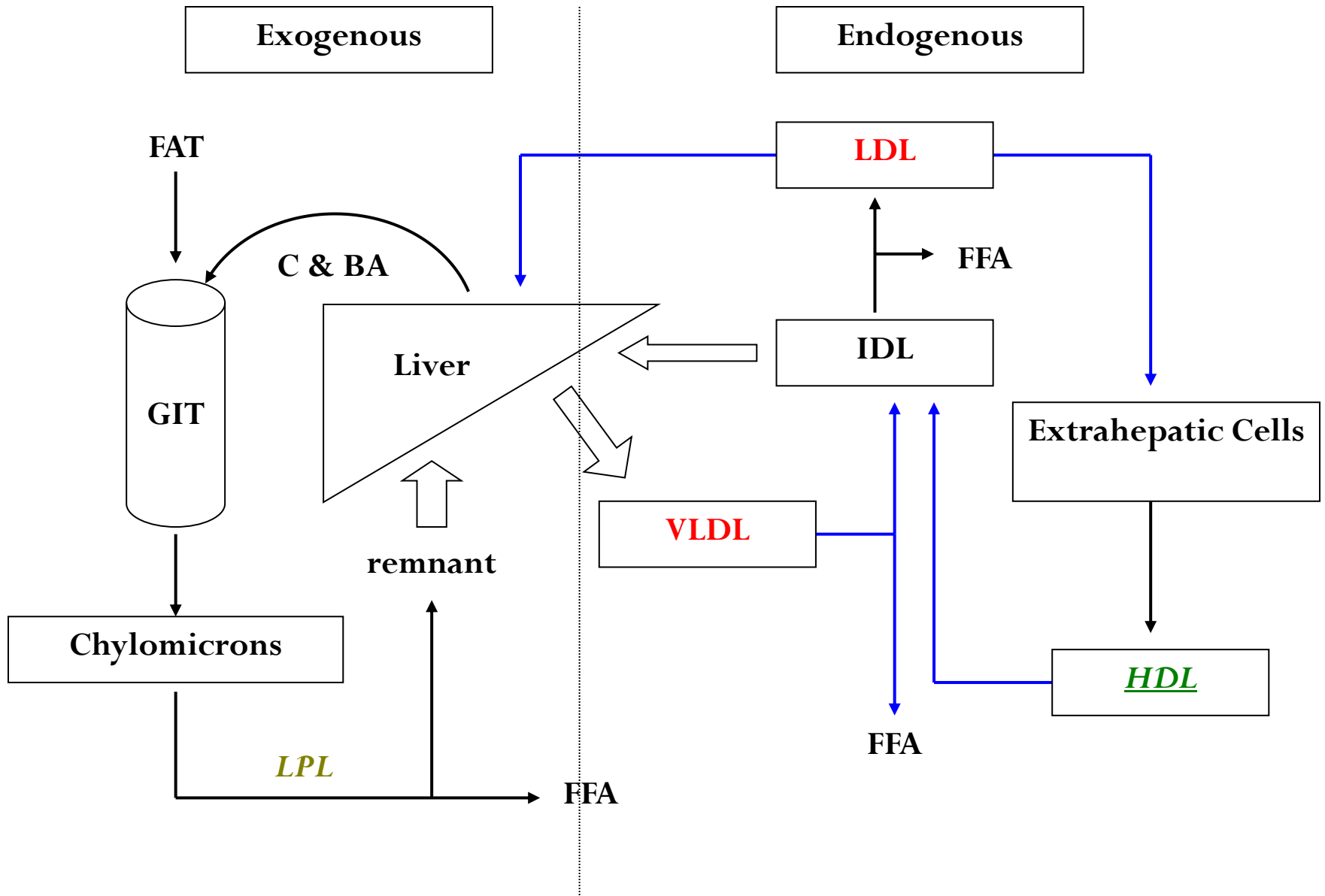
- *Triglycerides* (*TGs*, fats) are the main storage form of fuel to support the generation of high-energy compounds in the body.
- Excess food intake is converted to fat (*TGs*) and deposited in adipose tissue to be mobilized when the need arises.
- Because lipid molecules (*cholesterol* and *TGs*) are water insoluble, they must be packaged with hydrophilic proteins and carbohydrates in special molecular complexes known as *lipoproteins* in order to be transported in plasma.
- There are at least five main lipoproteins differing in size, composition, density, and function namely: *chylomicrons*, very low density lipoproteins (*VLDL*), intermediate density lipoproteins (*IDL*), low density lipoproteins (*LDL*) and high density lipoproteins (*HDL*).



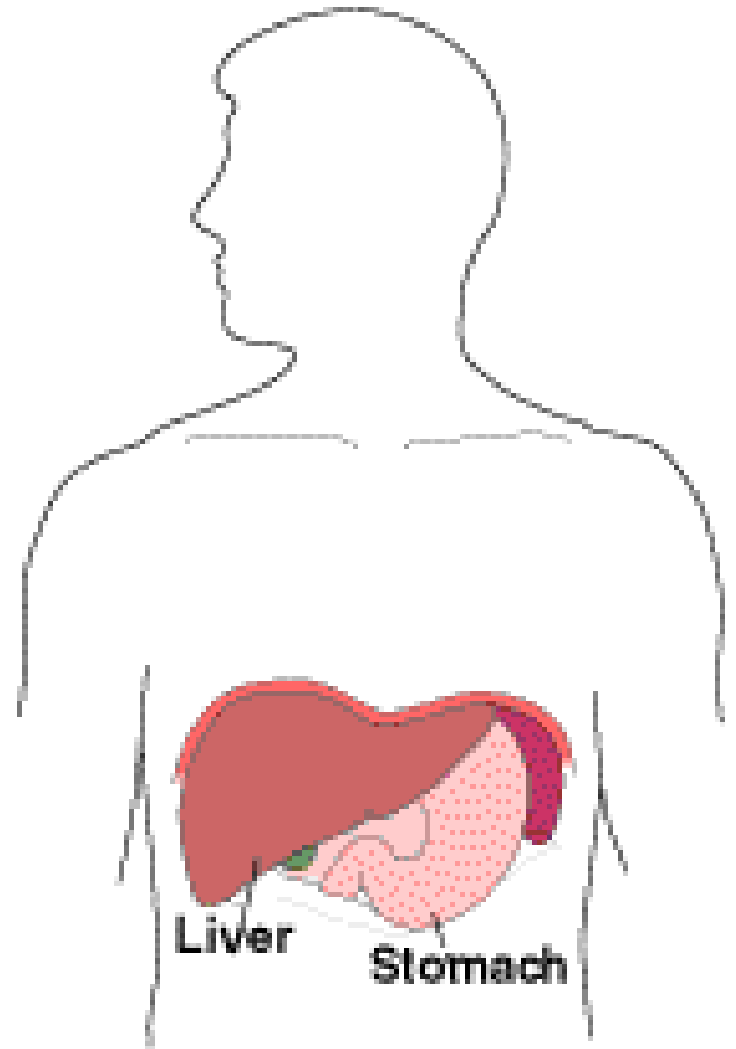
Composition of Lipoproteins



Cholesterol & Lipoproteins Transport and Metabolism



"bad" cholesterol (**LDLP**) is shown being deposited in the blood vessel walls, while "good" cholesterol (**HDLP**) takes it away. The amount of cholesterol taken in through the diet, and the activity of the liver and other organs which metabolize fats and cholesterol are very important determinants of how your body handles cholesterol.



Causes and Types of Hyperlipidemia

It could be a result of **biochemical defects** in lipoprotein metabolism, **excessive dietary intake of lipids** or **endocrine abnormalities** (*primary hyperlipidemia*). Or it could be due to the use of drugs that perturb lipoprotein formation or catabolism such as β -blockers, certain oral contraceptives, glucocorticoids or thiazide diuretics or as a result of diabetes mellitus, hyperthyroidism, hepatitis or uremia (*secondary hyperlipidemia*).

Treatment Strategy

Decrease Fat & Cholesterol Intake (diet control)
Enhance Cholesterol Excretion
Inhibit Cholesterol Biosynthesis
Increase HDL
Decrease LDL or increase their uptake by the liver

Therapeutic Classes

Antihypercholesterolemic only Drugs

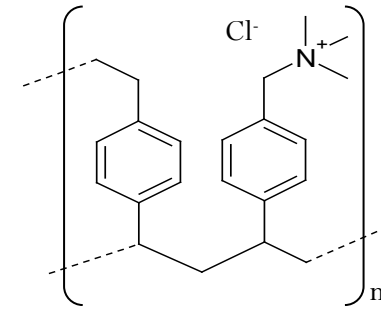
This includes **HMG-CoA reductase inhibitors** and **bile acid binding resins**.

Antihypercholesterolemic and Hypertriglyceridemic Drugs

This group is mainly **Fibric acid** derivatives

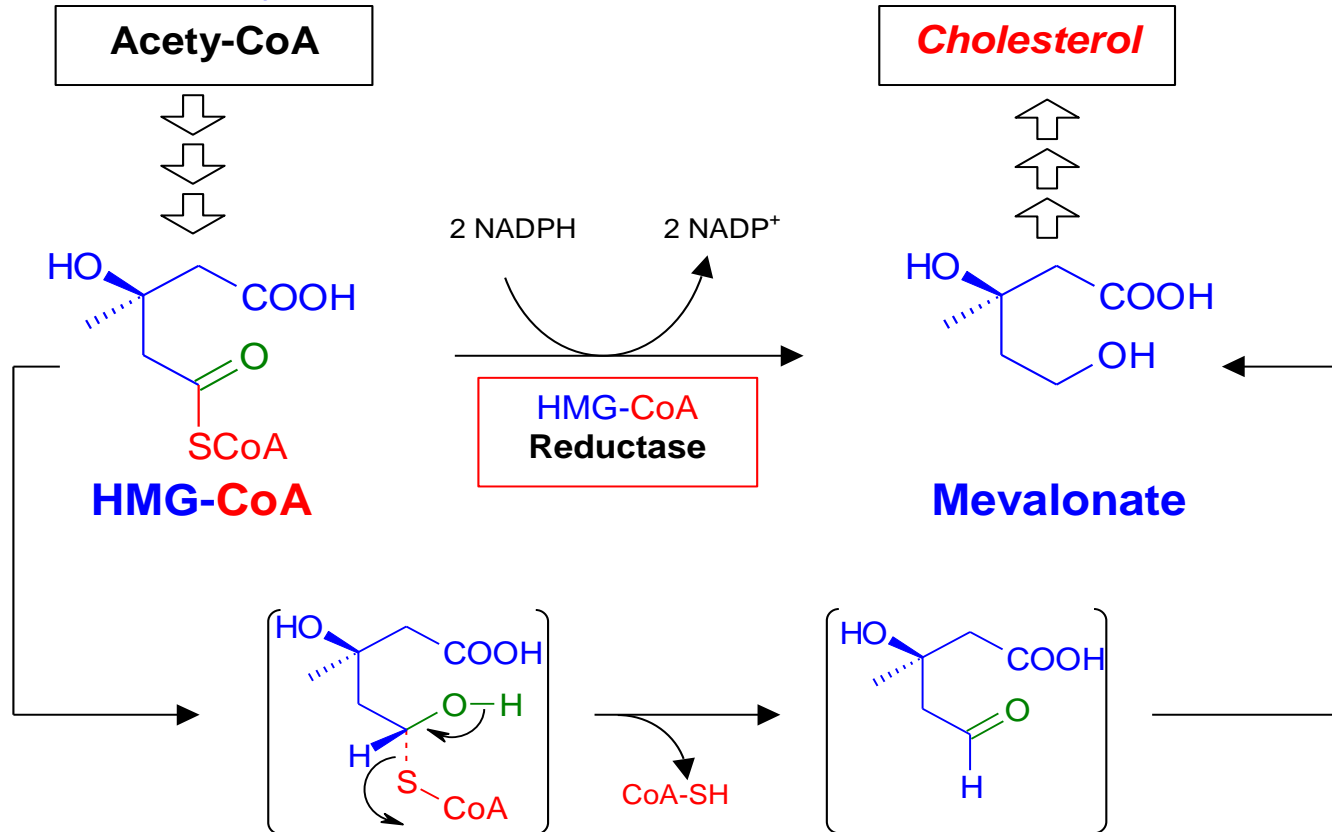
Bile Acid Binding Resins

Cholestyramine (*Questran*) is a non-absorbable strongly basic anion exchange resin that exchange chlorides for bile acids and increases its fecal excretion.

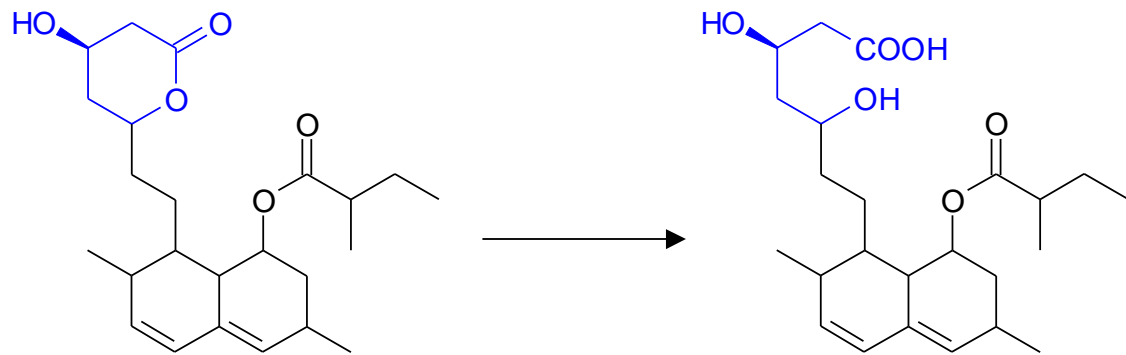


Cholestyramine, *Questran*

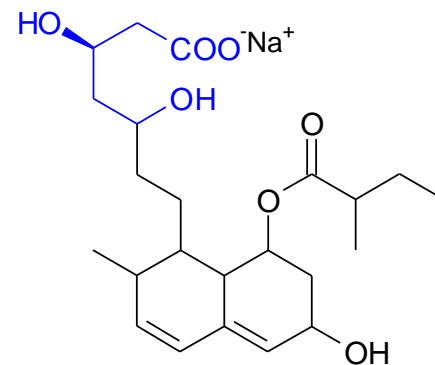
HMG-CoA Reductase & the Biosynthesis of Cholesterol



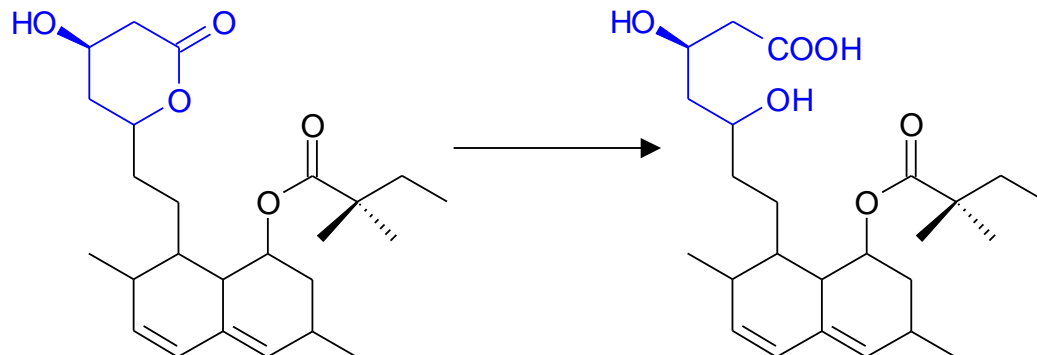
HMG-CoA Reductase Inhibitors



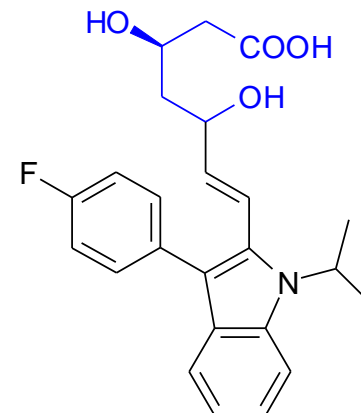
Luvastatin, *Mevacor*



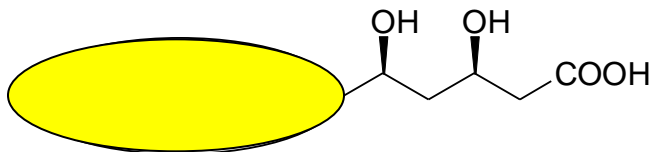
Pravastatin, *Pravachol*



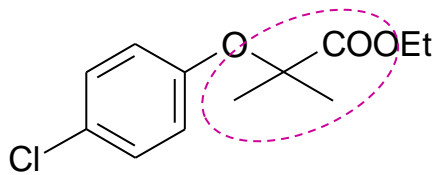
Simvastatin, *Zocor*



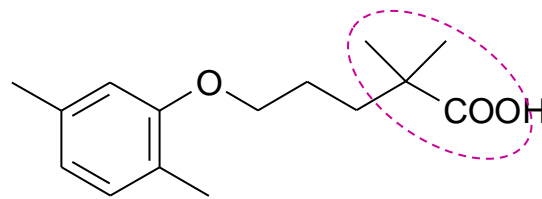
Fluvastatin, *Lesecol*



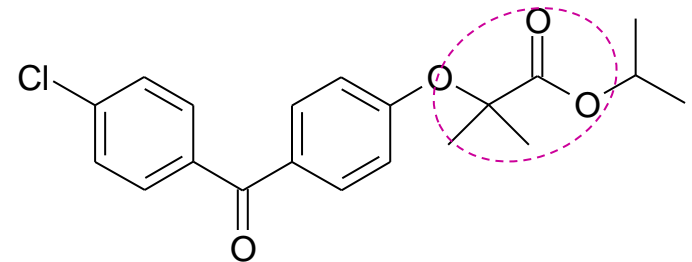
Fibric acid Derivatives



Clofibrate, *Atromid-S*



Gemfibrozil, *Lopid*

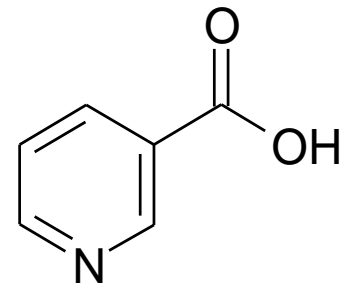


Fenofibrate, *Tricor*

The prototype drug of this group is **Clofibrate**. These drugs are mainly used for *hypertri-glyceridemia* or marked **HDL** deficiency. They activate lipoprotein lipase (**LPL**) thereby promote delivery of **TGs** to the adipose tissue. **Fibrates** also decrease cholesterol levels by inhibiting its biosynthesis at a step before HMG-CoA formation.

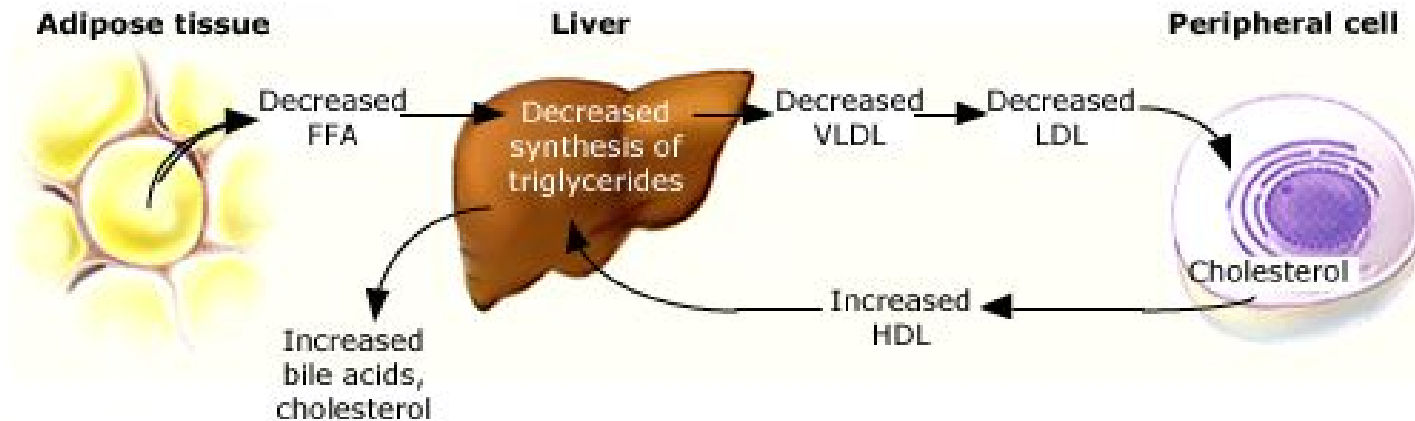
Niacin

Chemically it is nicotinic acid, this vitamin is an effective treatment of almost all types of hyperlipoproteinemia at doses above those given as a vitamin supplement (3-6g/day). It inhibits lipolysis in adipose tissue and activates the action of lipoprotein lipase



Nicotinic acid, *Niacin*

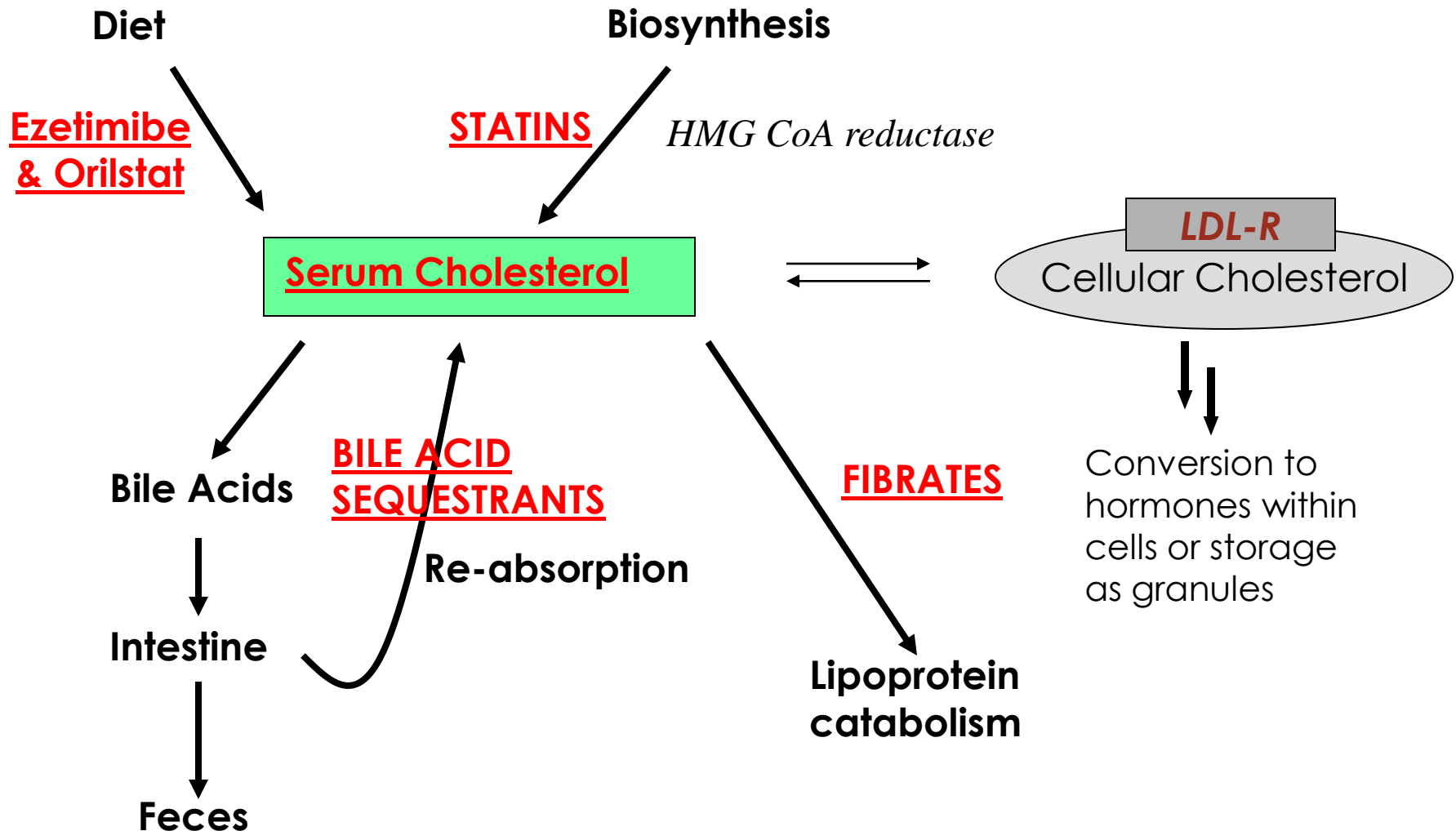
Mechanisms of action of nicotinic acid



Nicotinic acid inhibits the mobilization of free fatty acids (FFA) from peripheral adipose tissue to the liver. As a consequence of this decrease or an additional hepatic effect, the synthesis and secretion of very low density lipoprotein (VLDL) are reduced, and the conversion of VLDL to low density lipoprotein (LDL) is decreased. Nicotinic acid can also increase serum high-density lipoprotein (HDL) cholesterol concentrations by up to 30 percent; the mechanism responsible for this effect is a reduction in lipid transfer of cholesterol from HDL to VLDL and delayed HDL clearance.

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Strategy for Controlling Hyperlipidemia



6. Anticoagulants, Antiplatelets & Fibrinolytic Drugs

Blood Coagulation (Normal Haemostasis)

There are 3 mechanisms that work together to stop the flow of blood, namely:
Vasoconstriction, platelet plug formation and clotting of blood

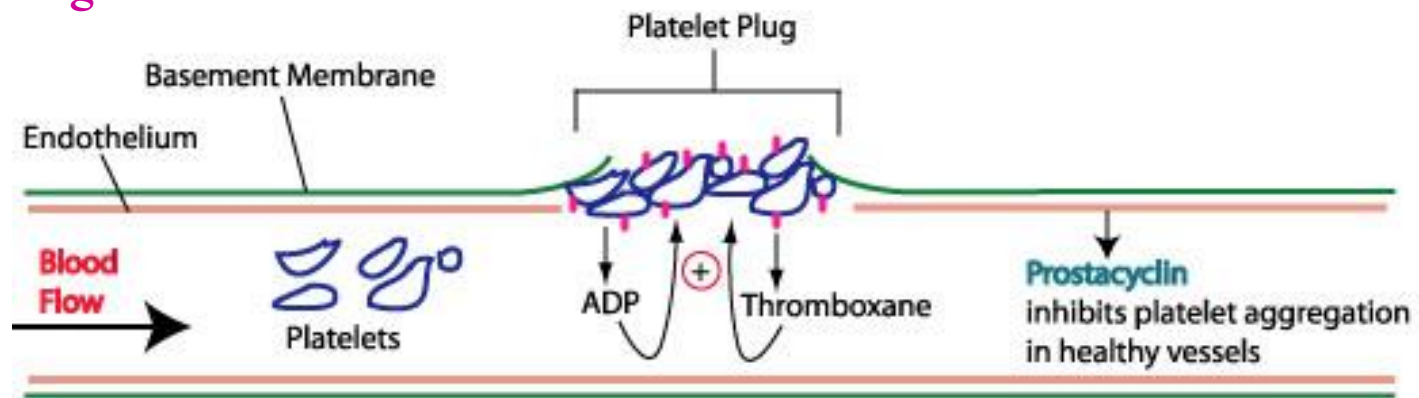
Vasoconstriction

Vasoconstriction of a damaged blood vessel slows the flow of blood and thus helps to limit blood loss. This process is mediated by:

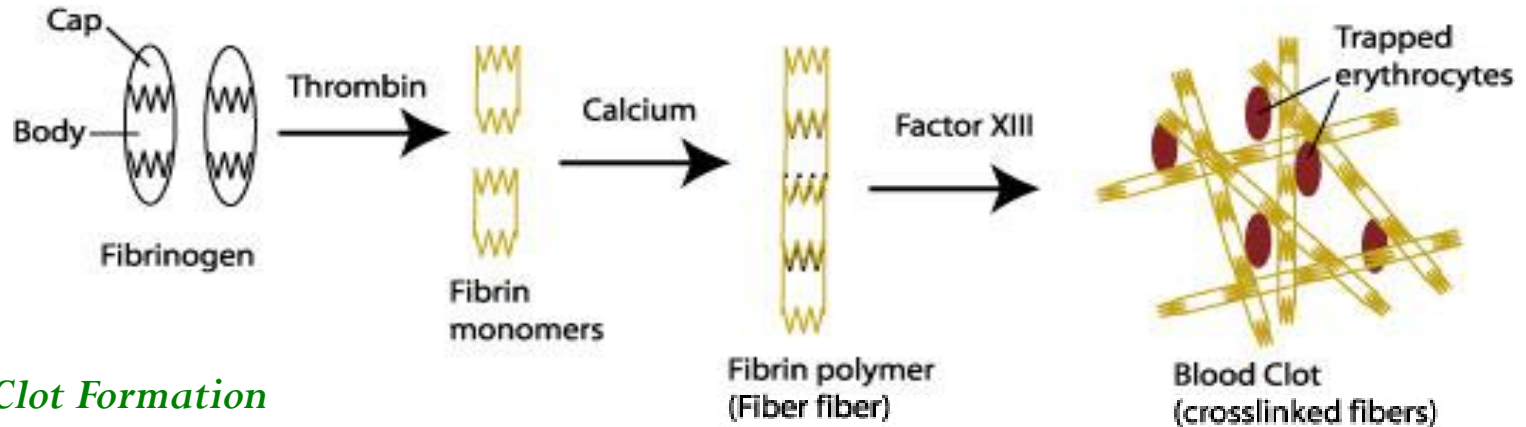
Local controls. Vasoconstrictors such as **thromboxane** are released at the site of the injury.

Systemic control. **Epinephrine** released by the adrenal glands stimulates general vasoconstriction.

Platelet Plug Formation

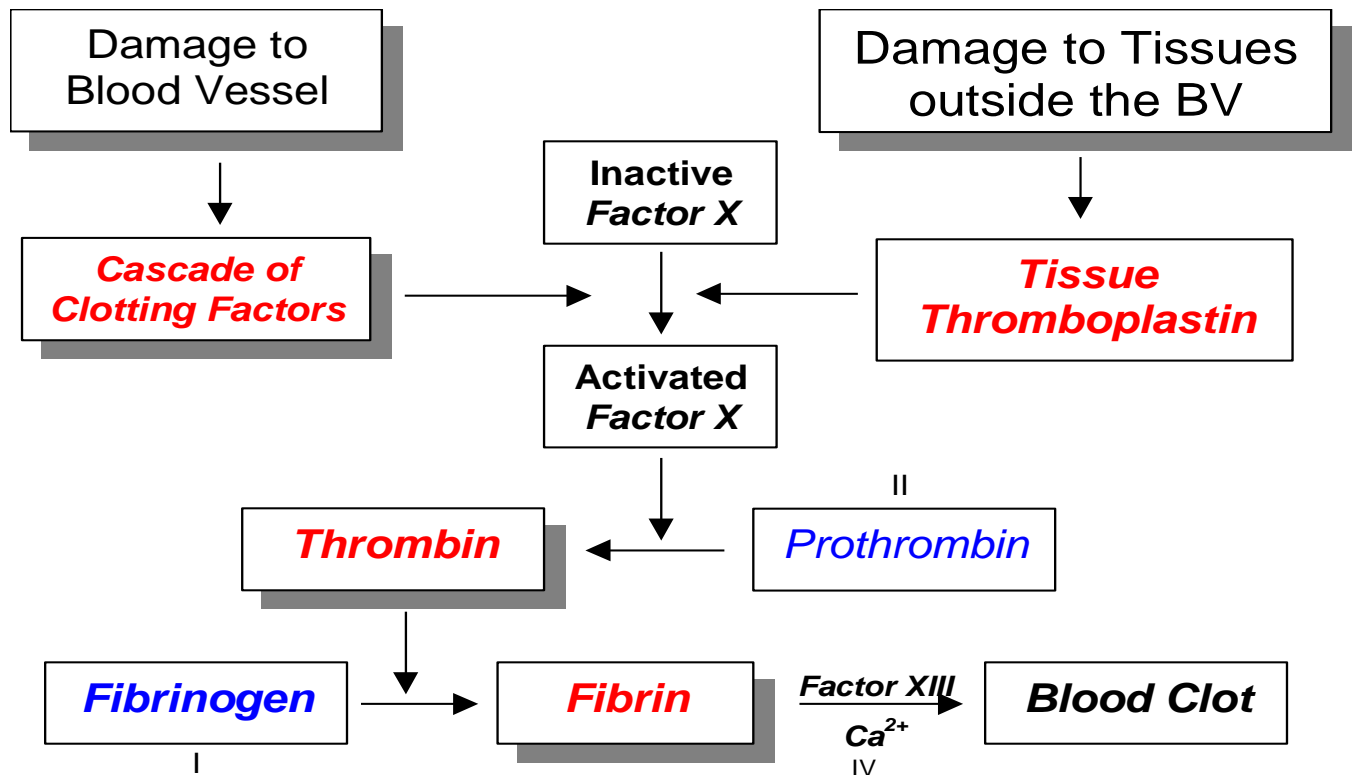


3. Clotting of Blood

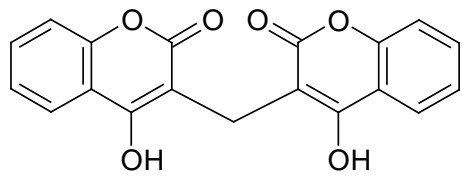


Blood Clot Formation

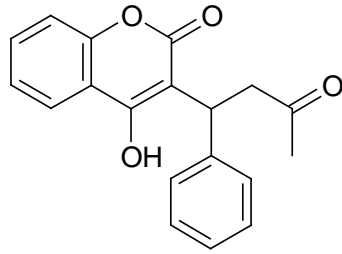
Blood Clot Cascade



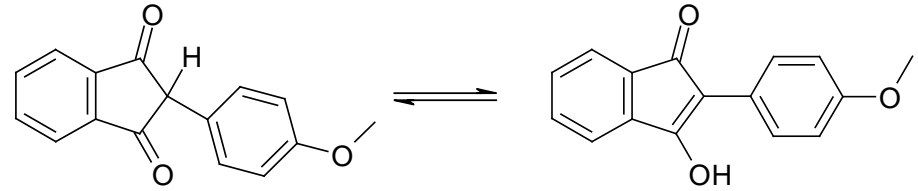
Oral Anticoagulants



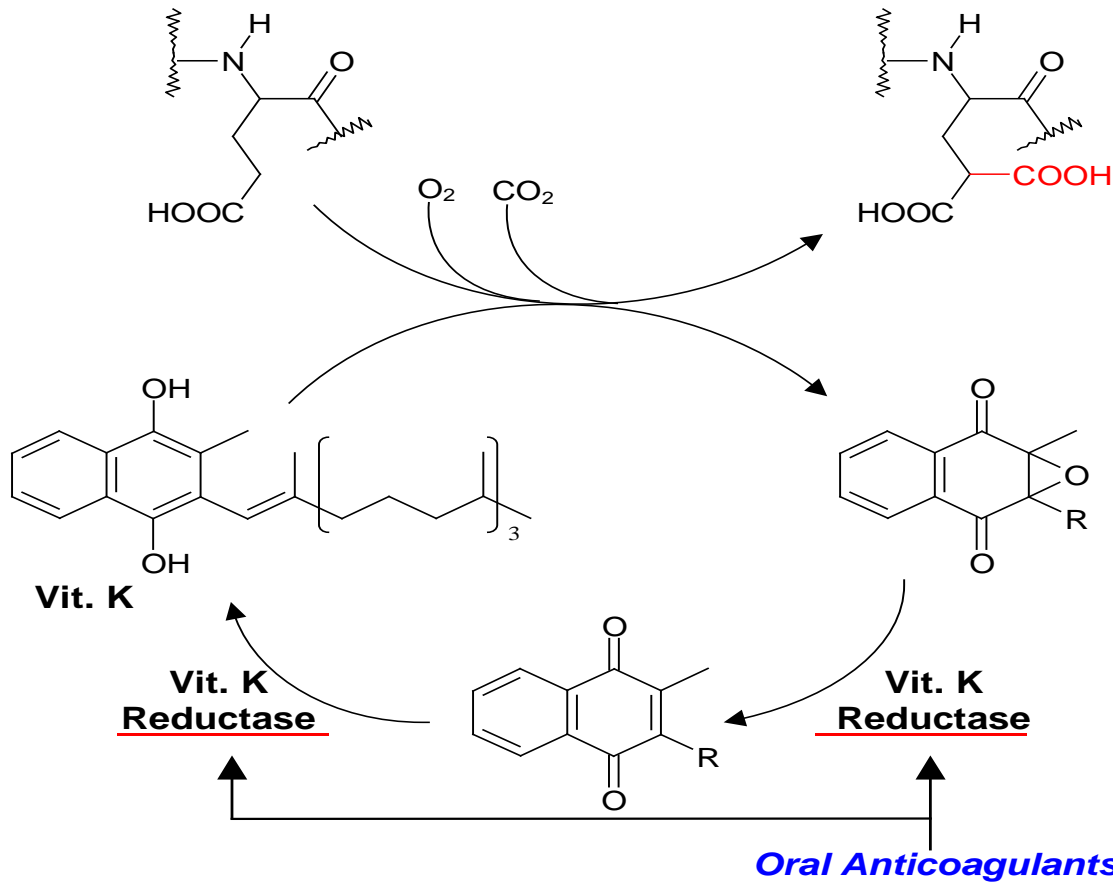
Bishydroxycumarin,
Dicumarol



Warfarin,
Coumadin

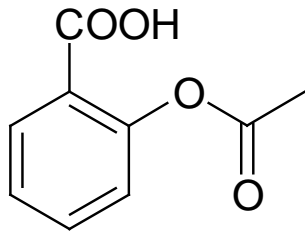


Anisindione, *Miradon*

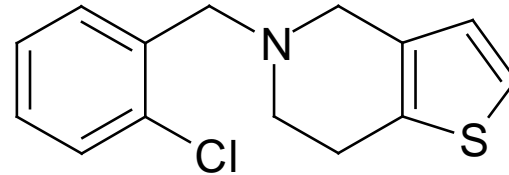


Antiplatelet Drugs

Platelets do not bind to intact endothelial cells but they do adhere to the collagen of the subendothelial tissues and attract other platelets by releasing **ADP**, they then start secreting **Thromboxane A₂ (TXA₂)** and **ADP** to promote further aggregation



Acetylsalicylic acid, **Aspirin**



Ticlopidine, **Ticlid**

Clot Busting Drugs

Tissue Plasminogen Activator (TPA)

It was recently cloned and is now produced as **Alteplase** or **Reteplase**

Streptokinase

It is an enzyme that directly dissolves blood clots. It is produced by streptococcus bacteria

