

## **Anti –Angina drugs: Drugs for Angina Pectoris**

**Angina pectoris** : is defined as sudden pain beneath the sternum, often radiating to the left shoulder and arm. Anginal pain is precipitated when the oxygen supply to the heart is insufficient to meet oxygen demand.

Most often, angina occurs secondary to atherosclerosis of the coronary arteries. Hence, angina should be seen as a symptom of a disease and not as a disease in its own right.

In the United States, over 7 million people have chronic stable angina; about 350,000 new cases develop annually.

### **Goal of Angina therapy**

Drug therapy of angina has two goals :

- (1) Prevention of myocardial ischemia and Anginal pain.
- (2) Prevention of myocardial infarction (MI) and death

Anti-anginal drugs (ie, drugs that prevent myocardial ischemia and angina pain).

### **There are three main families of Antianginal agents:**

- 1-Organic nitrates (eg, nitroglycerin),
- 2-Beta blockers (eg, propranolol),
- 3- Calcium channel blockers (eg, verapamil).

In addition, a fourth agent— Ranolazine—can be combined with these drugs to supplement their effects.

**Ranolazine**, a new drug with limited indications

<b>β-BLOCKERS</b>
<i>Atenolol</i> TENORMIN
<i>Bisoprolol</i> ZEBETA
<i>Metoprolol</i> LOPRESSOR, TOPROL XL
<i>Propranolol</i> INDERAL, INDERAL LA
<b>CALCIUM CHANNEL BLOCKERS (DIHYDROPYRIDINES)</b>
<i>Amlodipine</i> NORVASC
<i>Felodipine</i> PLENDIL
<i>Nifedipine</i> PROCARDIA XL
<b>CALCIUM CHANNEL BLOCKERS (NONDIHYDROPYRIDINE)</b>
<i>Diltiazem</i> CARDIZEM
<i>Verapamil</i> CALAN, ISOPTIN
<b>NITRATES</b>
<i>Nitroglycerin</i> NITRO-BID, NITRO-DUR, NITROLINGUAL, NITROSTAT
<i>Isosorbide dinitrate</i> DILATRATE-SR, ISORDIL
<i>Isosorbide mononitrate</i> IMDUR, ISMO
<b>SODIUM CHANNEL BLOCKER</b>
<i>Ranolazine</i> RANEXA

**Figure 21.1**  
Summary of antianginal drugs.

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## ORGANIC NITRATES

The organic nitrates are the oldest and most frequently used antianginal drugs.

These agents relieve angina by causing vasodilation.

- ❖ **Nitroglycerin**
- ❖ **Isosorbide mono nitrate**
- ❖ **Isosorbide Dinitrate**
- ❖ Nitroglycerin, the most familiar organic nitrate, will serve as our prototype.

### **B-Mechanism of Vasodilator Actions**

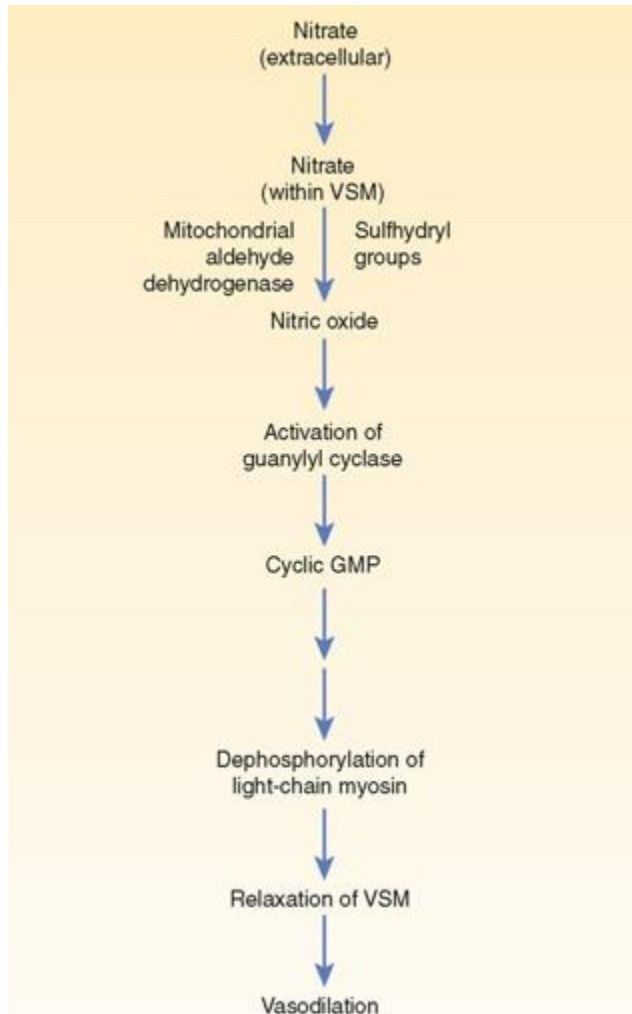
Nitroglycerin acts directly on vascular smooth muscle (VSM) to promote vasodilation. At usual therapeutic doses, the drug acts primarily on veins; dilation of arterioles is only modest.

The biochemical events that lead to vasodilation are outlined in Figure 50-2.

The process begins with uptake of nitrate by VSM, followed by conversion of nitrate to its active form: nitric oxide.

Nitric oxide then activates guanylyl cyclase, an enzyme that catalyzes the formation of cyclic GMP (cGMP). Through a series of reactions, elevation of cGMP leads to dephosphorylation of light-chain myosin in VSM. (Recall that, in all muscles, phosphorylated myosin interacts with actin to produce contraction.) As a result of de phosphorylation, myosin is unable to interact with actin, and hence VSM relaxes, causing vasodilation.

**Nitroglycerin** decreases the pain of exertional angina primarily by decreasing cardiac oxygen demand. Oxygen demand is decreased as follows: By dilating veins, nitroglycerin decreases venous return to the heart, and thereby decreases ventricular filling; the resultant decrease in wall tension (preload) decreases oxygen demand.



**Fig : scheme diagram Effects of nitrates and nitrites on smooth muscle. cGMP, = cyclic guanosine 3',5'-monophosphate**

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### **Adverse effects**

- ✓ Headache is the most common adverse effect of nitrates.
- ✓ High doses of nitrates can also cause postural hypotension
- ✓ Facial flushing
- ✓ Reflex Tachycardia—occur secondary to vasodilation.
- ❖

### **Isosorbide Mononitrate and Isosorbide Di nitrate**

## BETA BLOCKERS

Beta blockers are first-line drugs for angina of effort, **but are not effective against vasospastic angina.**

When administered on a fixed schedule, beta blockers can provide sustained protection against effort induced anginal pain. Exercise tolerance is increased and the frequency and intensity of anginal attacks are lowered.

### Drugs used in Angina

- ❖ **Propranolol**
- ❖ **Bisoprolol**
- ❖ **Metoprolol**
- ❖ **Atenolol**

## CALCIUM CHANNEL BLOCKERS

The calcium channel blockers (CCBs) used most frequently are verapamil, diltiazem, and nifedipine (a dihydropyridine-type calcium channel blocker).

### SODIUM CHANNEL BLOCKER : Ranolazine

**Mechanism of action** : inhibits the late phase of the sodium current improving

the oxygen supply and demand equation, reduces intracellular sodium and calcium overload, thereby improving diastolic function

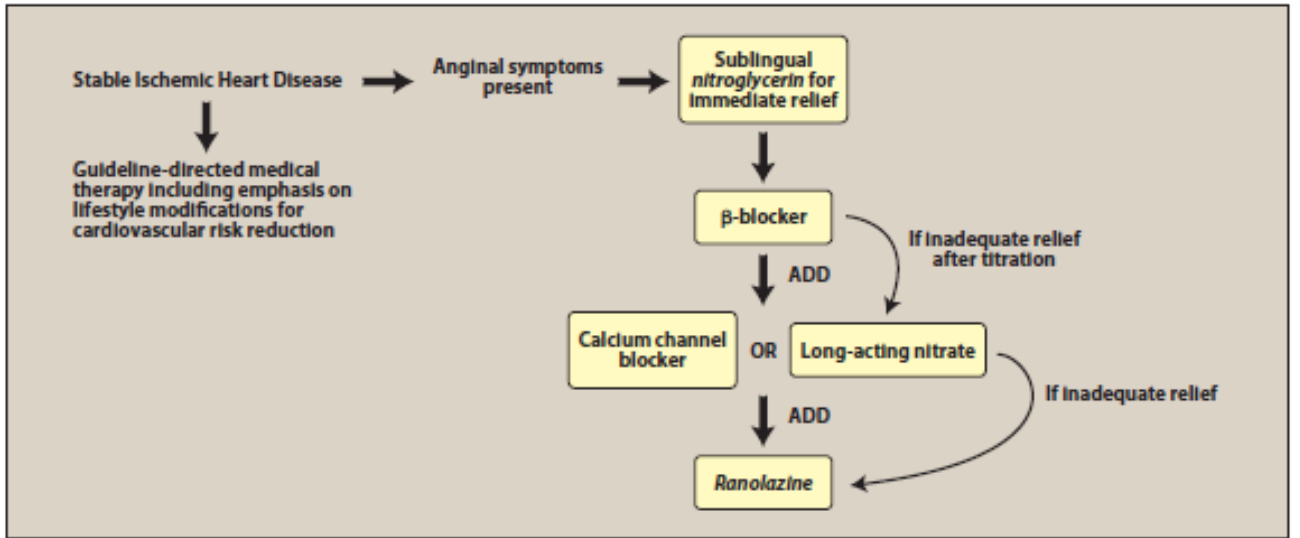
it can reduce accumulation of sodium and calcium in myocardial cells, and might thereby help the myocardium use energy more efficiently.

Unlike most other antianginal drugs, ranolazine does not reduce heart rate, blood pressure, or vascular resistance. However, it can prolong the QT interval

### Therapeutic uses & Adverse effects

Ranolazine has antianginal as well as antiarrhythmic properties, It is indicated for the treatment of chronic angina and may be used alone or in combination with other traditional therapies.

It is most often used in patients who have failed other antianginal therapies , should be reserved for patients who have not responded adequately to nitrates, beta blockers, or CCBs, and should always be combined with at least one of these agents.



**Figure 21.4**  
Treatment algorithm for improving symptoms in patients with stable angina.

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