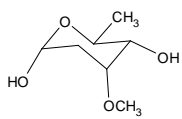
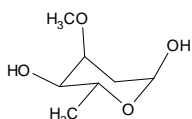


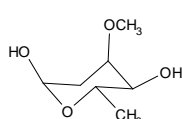
Which ones are α -isomers and which ones are β -isomers?



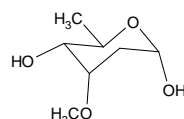
(a)



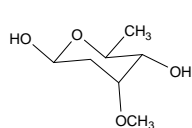
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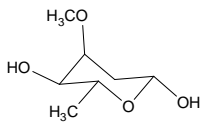
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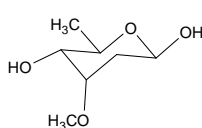
(d)



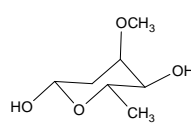
(e)



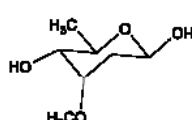
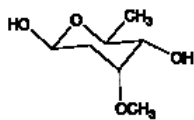
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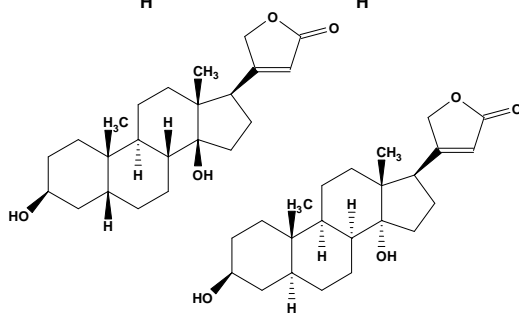
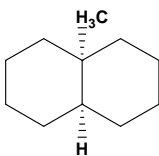
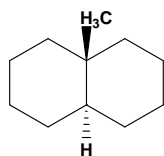
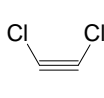
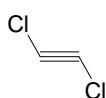
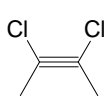
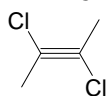
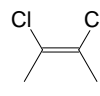
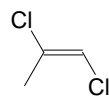
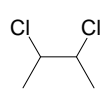
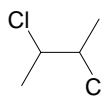
(g)



(h)

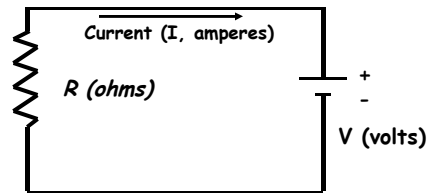


Which one is a cis isomer? Which one is a trans isomer?



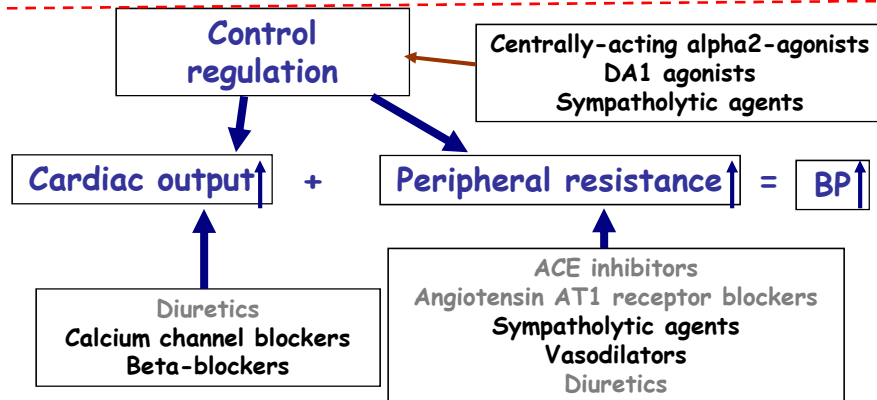
I. Review of anti hypertensive drug therapies

(a) "Ohm's law"



Electrical circuits (Ohm's law):

Current (amperes) \times Resistance (ohms) = Potential Difference (Volts)



(b) Adrenergic receptors and the blood pressure

Subtype	Endogenous agonist potency order	BP-related actions of agonist
α_1	Epinephrine \geq norepinephrine \gg isoprenaline	Smooth muscle contraction
α_2	Norepinephrine \geq epinephrine \gg isoprenaline	Smooth muscle constriction and neurotransmitter inhibition
β_1	Isoprenaline $>$ epinephrine \gg norepinephrine	Heart muscle contraction
β_2	Isoprenaline $>$ epinephrine \gg norepinephrine	Smooth muscle relaxation
β_3	Isoprenaline = norepinephrine $>$ epinephrine	Enhance lipolysis

II. Classification of the antihypertensive drugs included in CH29 (based on MOA)

A. Peripherally acting sympatholytics

- (1). β -adrenergic receptor blockers
- (2). α -adrenergic blockers
- (3). Mixed α/β -blockers

B. Centrally acting sympatholytics

- (1). Methyldopa and methyldopate ester hydrochloride
- (2). α_2 -adrenergic agonists

C. Vasodilators

- (1). Direct-acting vasodilators
- (2). Potassium channel openers
- (3). Phosphodiesterase inhibitors
- (4). Nitrodilators
- (5). Ganglionic blockers

III. Peripherally acting sympatholytics

A. Mechanism of action

B. Drug development

(a) Mechanism of adrenergic agonist selectivity

(b) First generation

- ☐ Nonselective

(c) Second generation

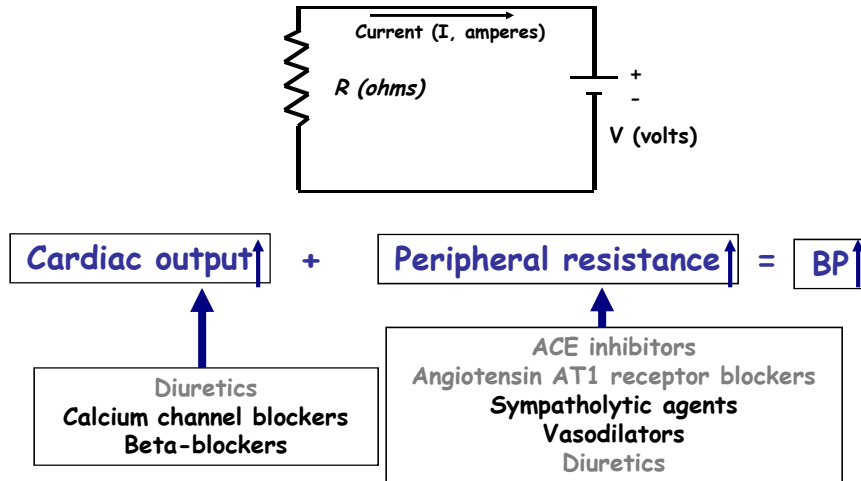
- ☐ Cardio selective (Relatively β_1 -selective)

(d) Third generation

- ☐ Mixed α_1/β_1 adrenergic blockers

A. Mechanism of action

- (a) Inhibition of normal sympathetic effects
- (b) Reducing cardiac output



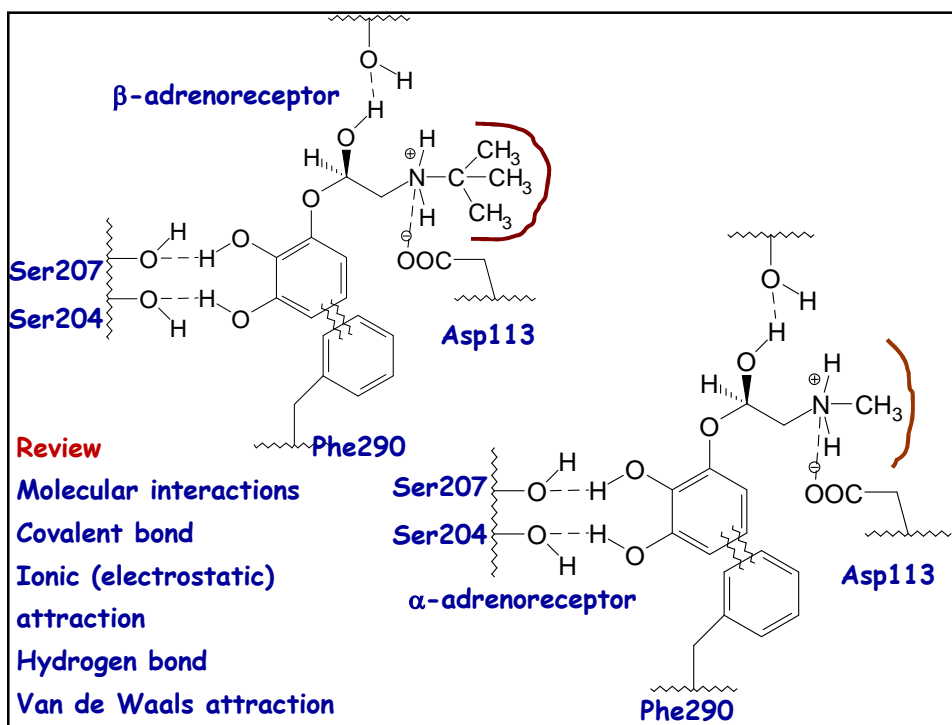
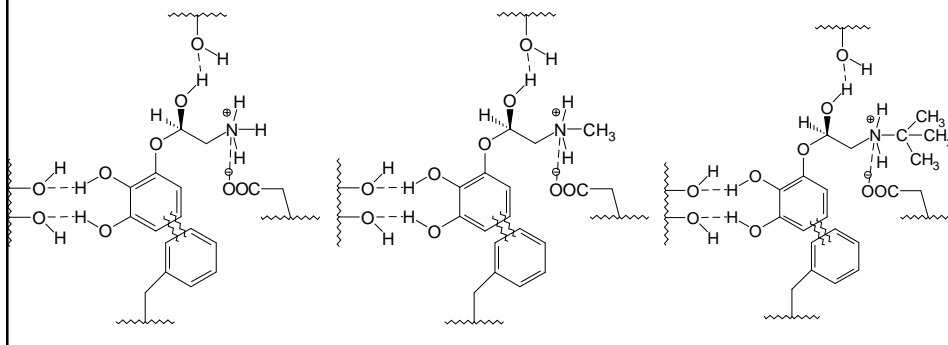
C. Drug development

- (a) Mechanism of adrenergic receptor selectivity
- (b) First generation
 - Nonselective
- (c) Second generation
 - Cardio selective (Relatively β_1 -selective)
- (d) Third generation
 - Mixed α_1/β_1 adrenergic blockers

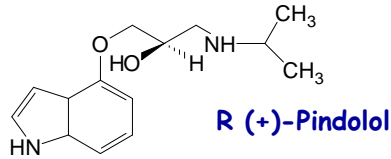
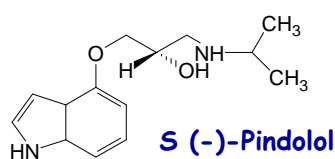
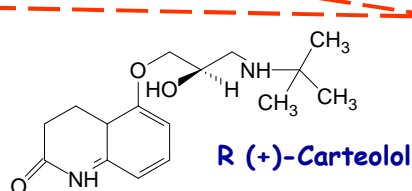
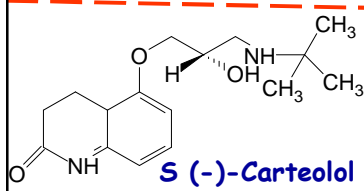
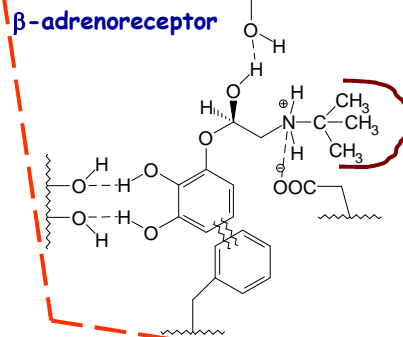
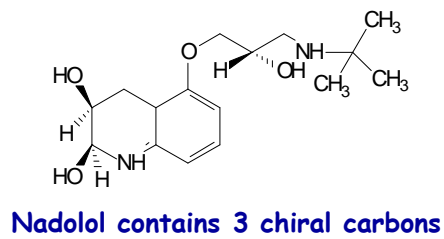
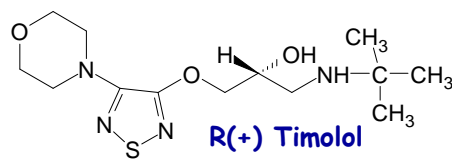
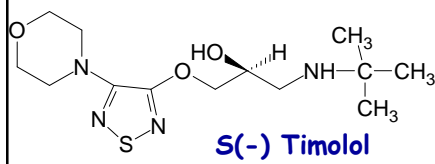
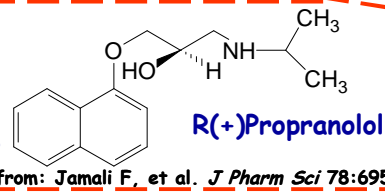
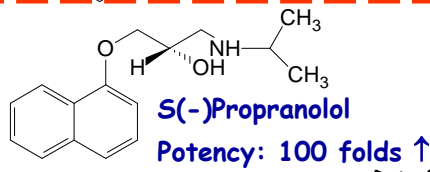
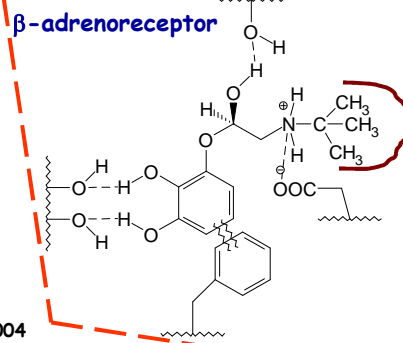
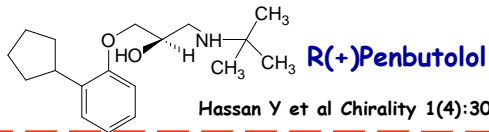
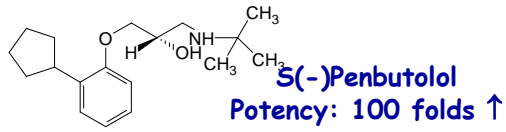
Subtype	BP-related actions of agonist
α_1	Smooth muscle contraction
α_2	Smooth muscle constriction and neurotransmitter inhibition
β_1	Heart muscle contraction
β_2	Smooth muscle relaxation
β_3	Enhance lipolysis

(a). Mechanism of adrenergic agonist selectivity

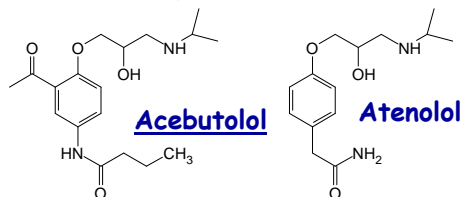
Subtype	Endogenous agonist potency order
α_1	Epinephrine \geq norepinephrine \gg isoprenaline
α_2	Norepinephrine \geq epinephrine \gg isoprenaline
β_1	Isoprenaline $>$ epinephrine \gg norepinephrine
β_2	Isoprenaline $>$ epinephrine \gg norepinephrine
β_3	Isoprenaline = norepinephrine $>$ epinephrine



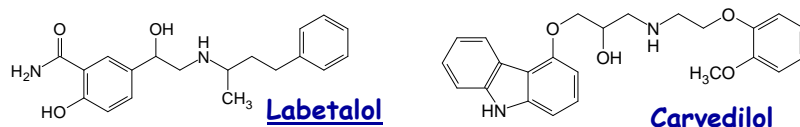
(b) First generation
Nonselective β -blockers



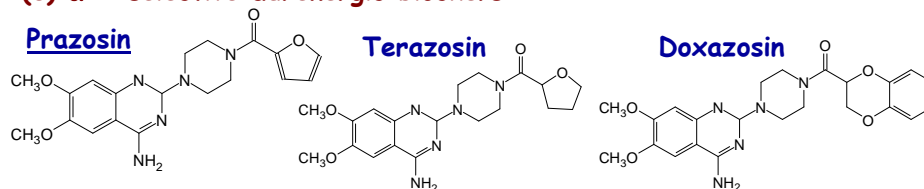
(c) Second generation-Cardio selective (Relatively β_1 -selective)



(d) Third generation-Mixed α_1/β_1 adrenergic blockers

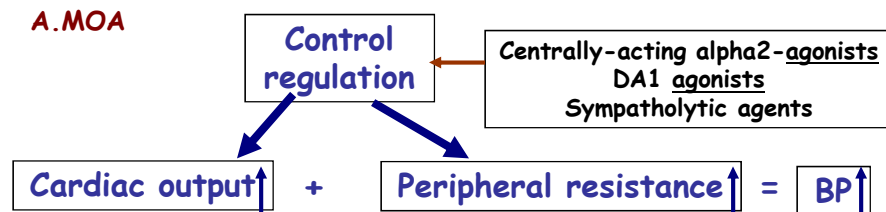


(e) α_1 - selective adrenergic blockers

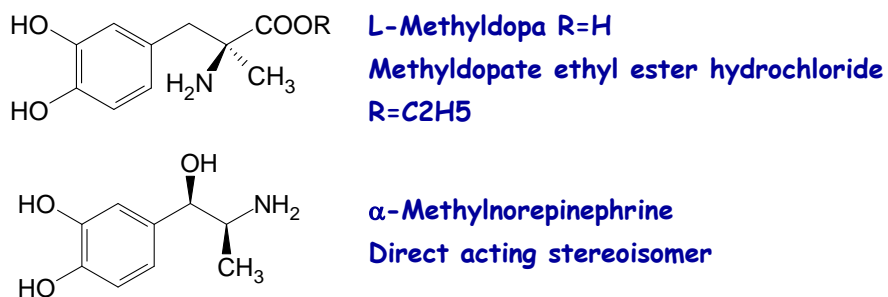


IV. Centrally acting sympatholytics

A.MOA

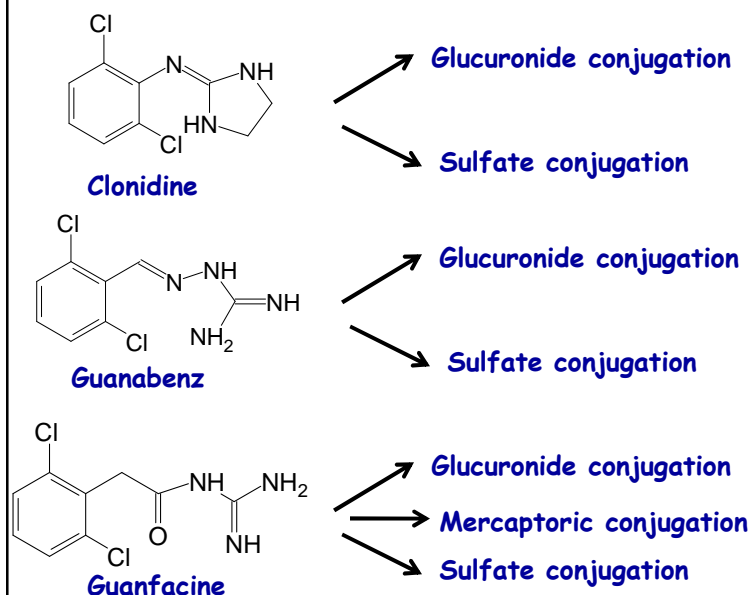


B. Methyldopa and methyldopate ester hydrochloride

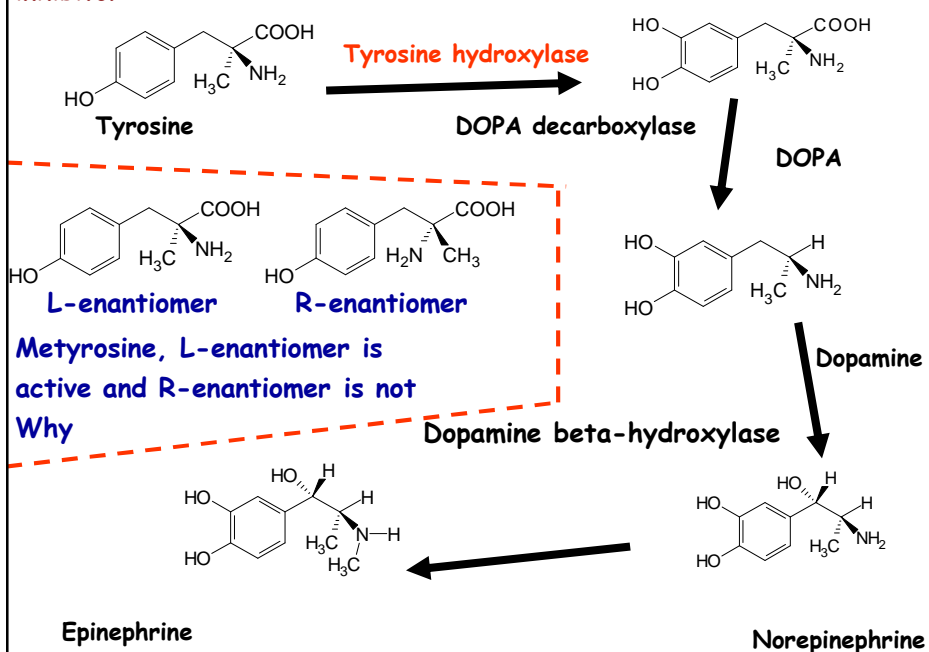


C. α_2 - selective adrenergic agonists

☐ Centrally acting sympatholytics

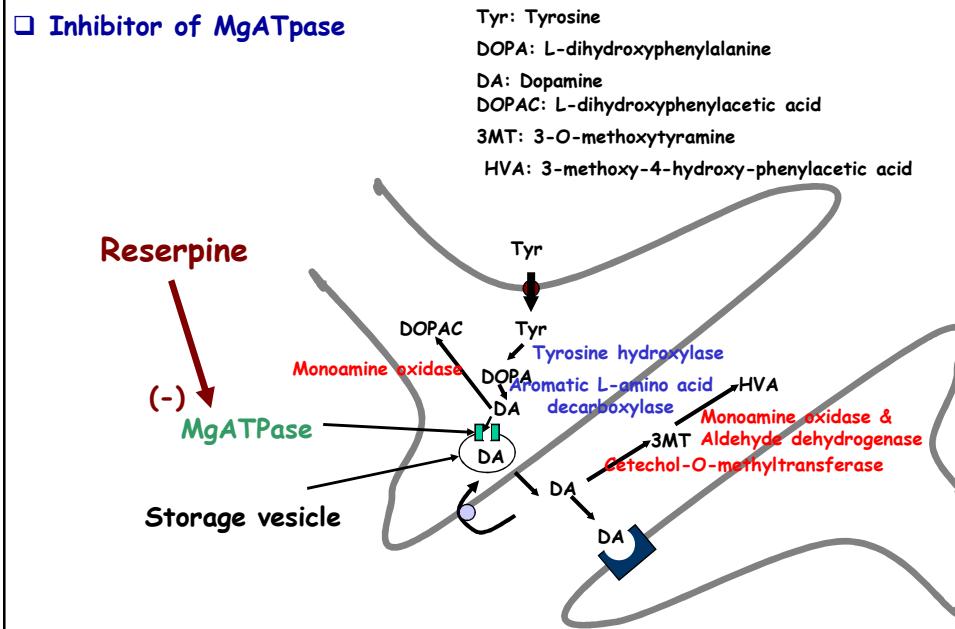


Metyrosine, a competitive tyrosine hydroxylase inhibitor

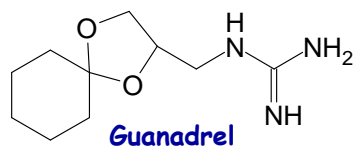
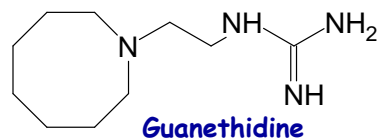


Reserpine

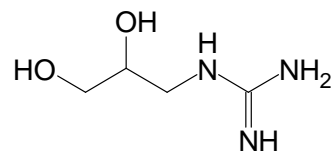
- ❑ A natural product
- ❑ Inhibitor of MgATPase



Structural similarity between guanethidine and guanadrel



Guanadrel metabolism

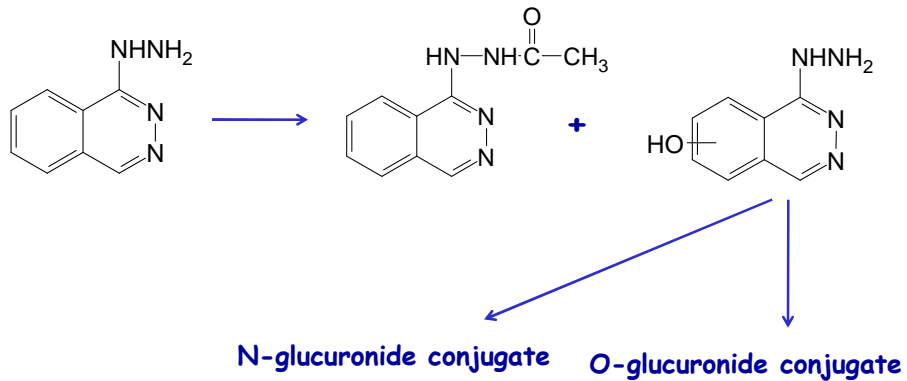


V. Vasodilators

- A. Direct-acting vasodilators
- B. Potassium channel openers
- C. Phosphodiesterase inhibitors
- D. Nitrodilators
- E. Ganglionic blockers

A. Direct-acting vasodilators

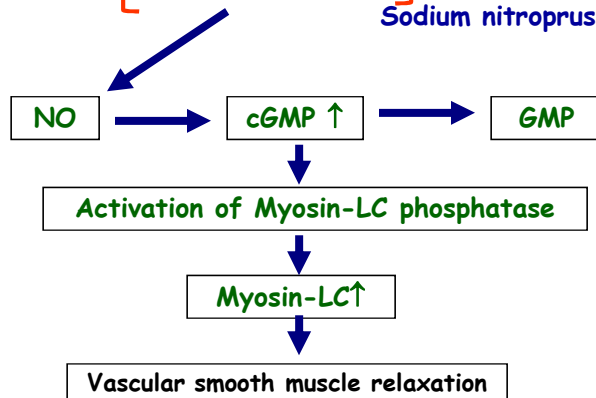
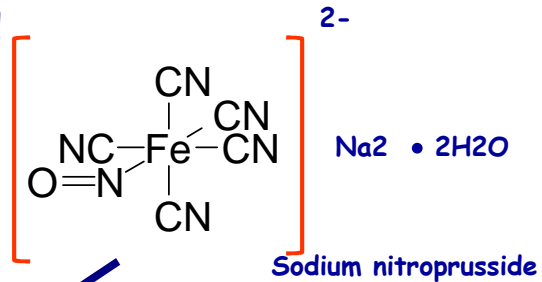
Hydralazine hydrochloride
(Metabolism of hydralazine)



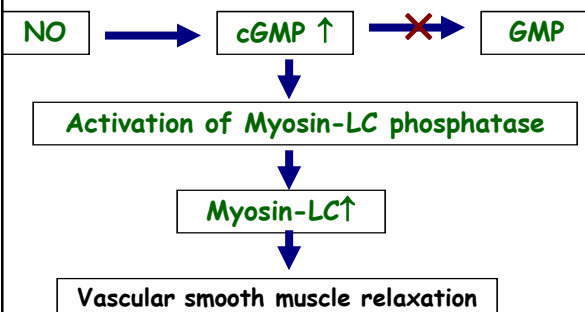
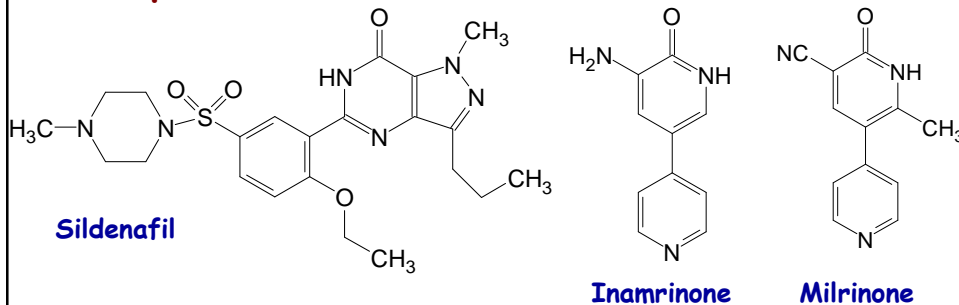
B. Nitrodilators-Sodium nitroprusside

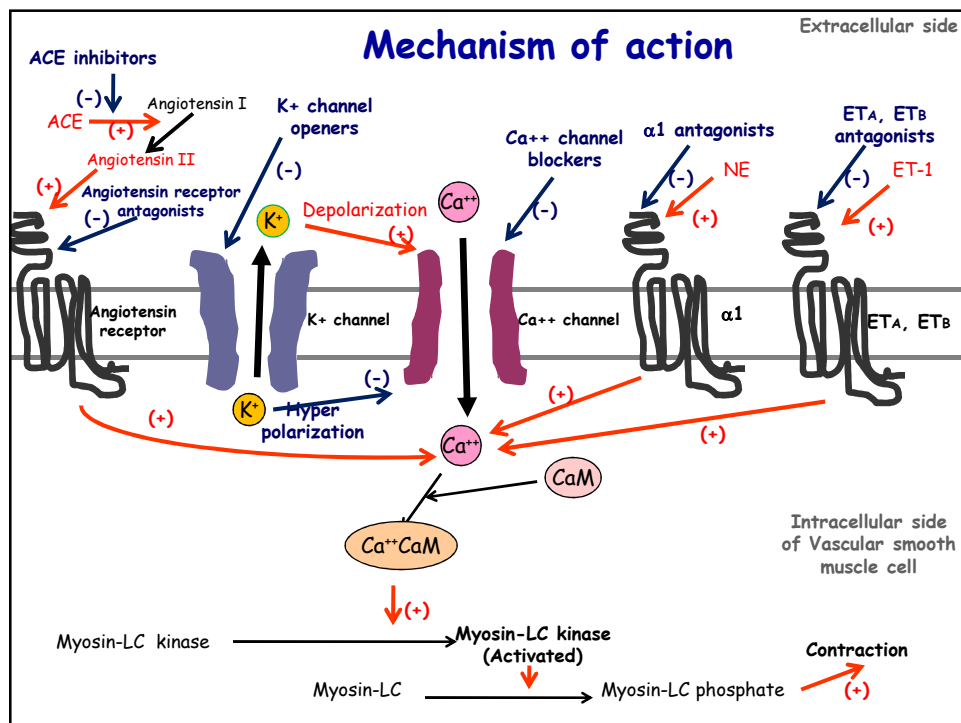
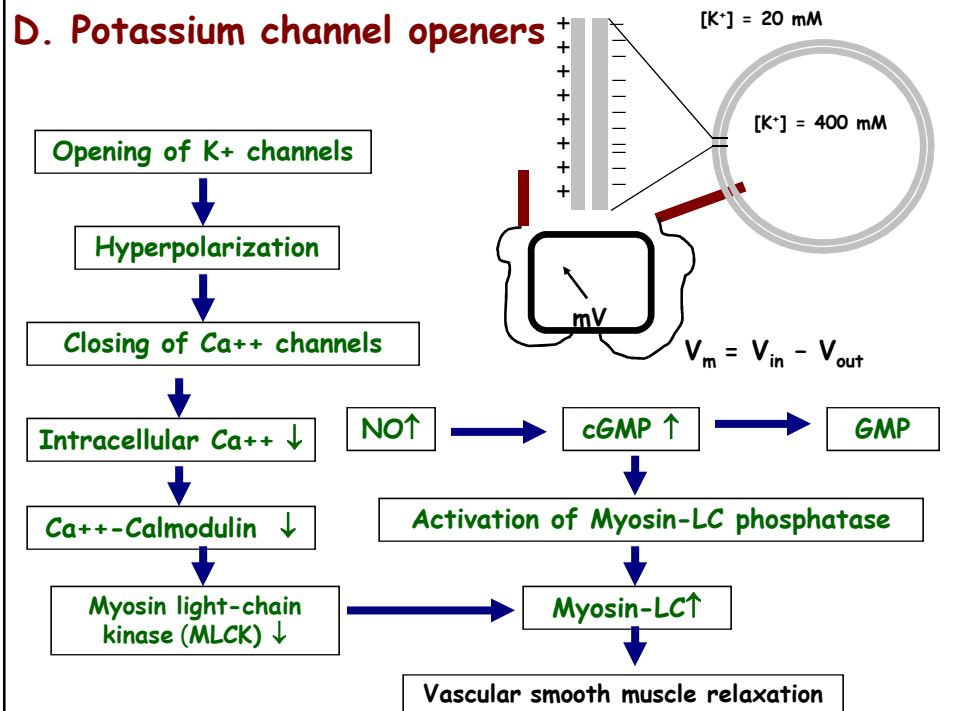
☐ Inorganic compound

☐ Generating NO

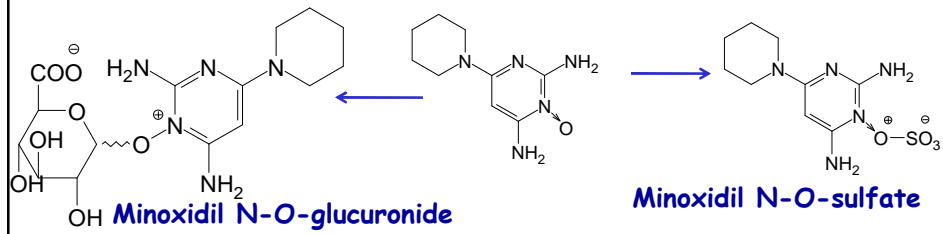


C. Phosphodiesterase inhibitors

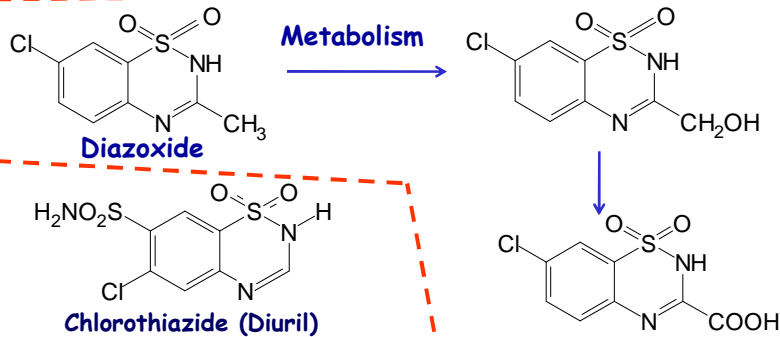




Minoxidil and minoxidil metabolism



Diazoxide (Potassium channel openers) and diazoxide metabolism



E. Ganglionic blockers

Mecamylamine and Trimethaphan

Acetylcholine receptor antagonists

