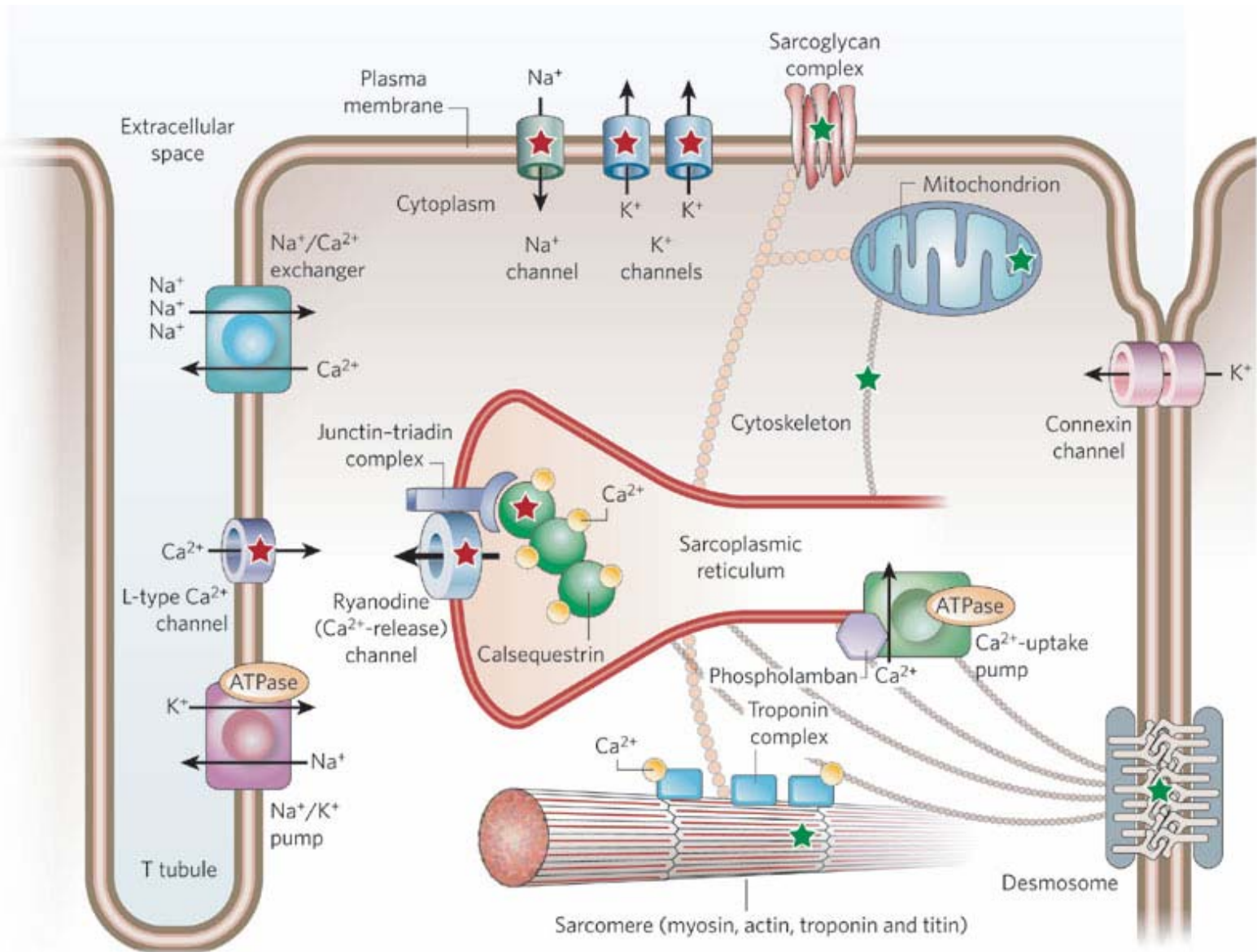


Cardiotonics

Tomáš Goněc

14.11.2011

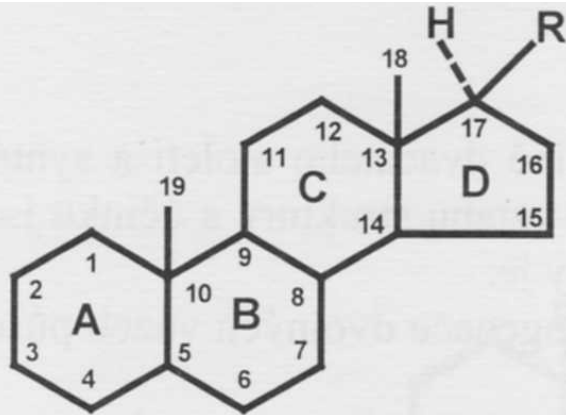
Cardiomyocyte contraction



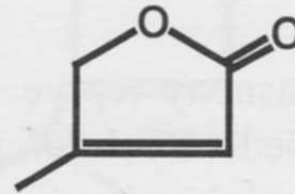
Therapy of heart failure: inotropic agents

- cardioglycosides
- β -adrenergic agonists
- phosphodiesterase inhibitors
- Ca^{2+} channel sensitizer

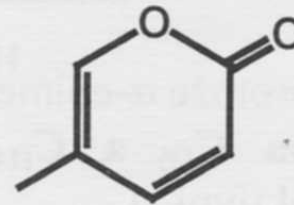
Cardiac glycosides



R =

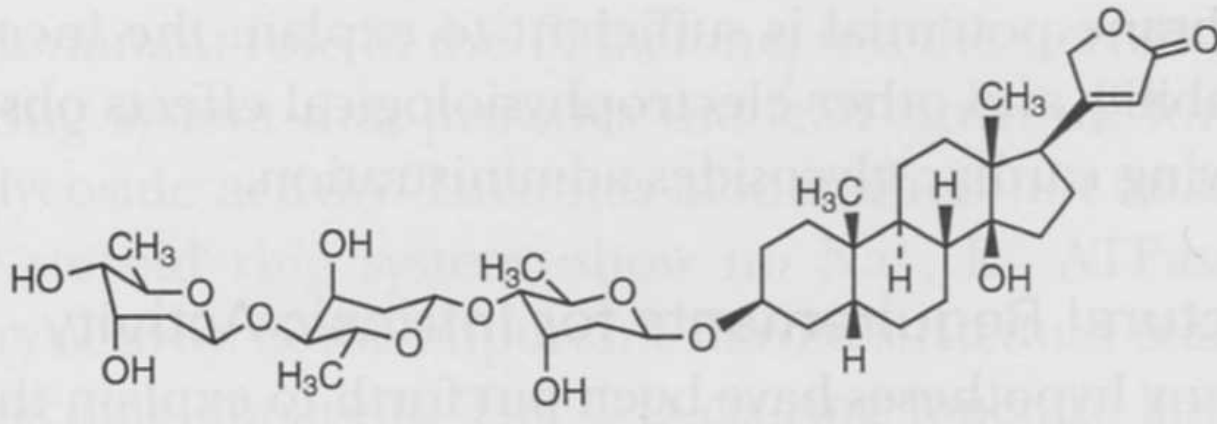


kardenolid

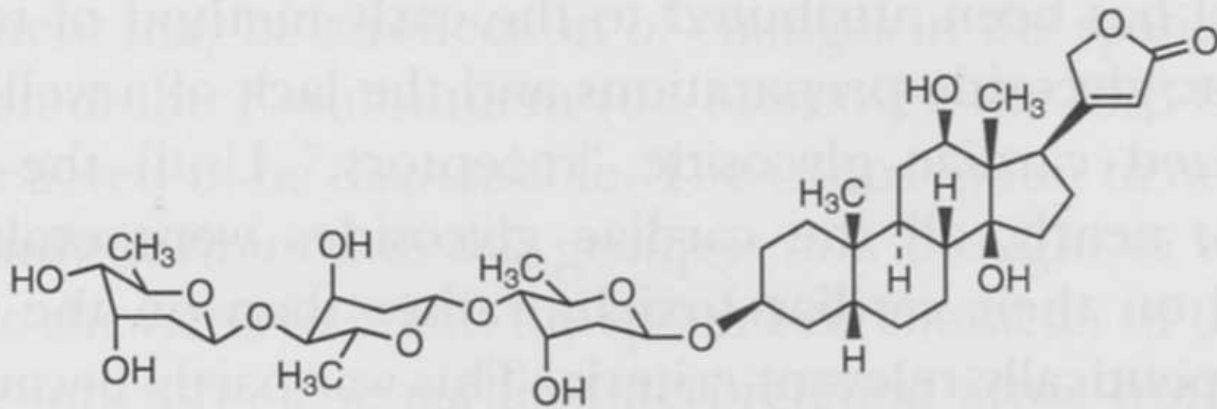


bufanolid

Cardiac glycosides



Digitoxin



Digoxin



Cardiac glycosides – mechanism of action

- Na^+/K^+ -ATPase inhibitors
- Na^+ ions intracellular retention
- due to ion substitution also Ca^{2+} intracellular retention
- positive inotropic effect

Cardiac glycosides used in therapy

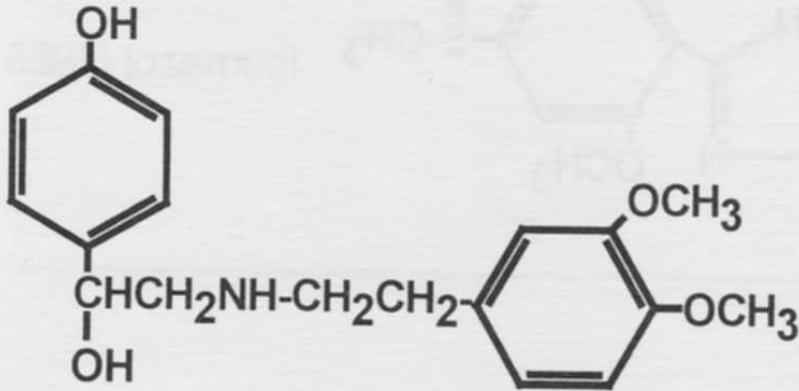
- Lanatosides A, B, C; purpureaglycosides A, B
digitoxin, gitoxin, digoxin – secondary
glycosides with cleavaged terminal sugar
- Ouabain, k-strophanthoside
- Proscillaridine, meproscillarine
(buffadienolides)

Cardiac glycosides

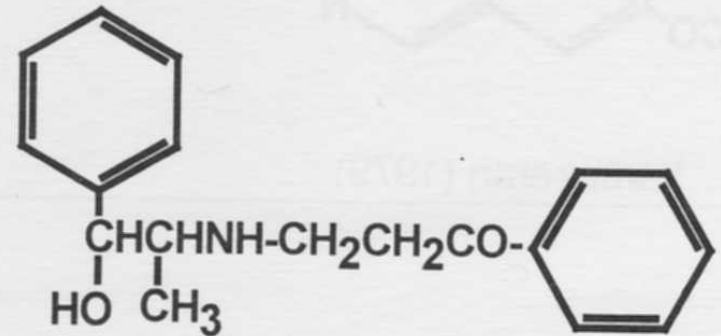
- narrow therapeutic-toxic window
- high plasma proteins binding
- monitoring during therapy necessary
- long-term administration increases mortality –
therapeutic use in future questionable

β_1 -adrenergic receptor agonists

- stimulation of adenylatecyclase, increase of intracellular cAMP, positive inotropic effect

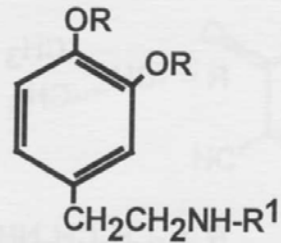


denopamin



oxyfedrin

β_1 -adrenergic receptor agonists



R	R ¹	léčivo
H	H	dopamin
H	$\text{-CH(CH}_3\text{)CH}_2\text{CH}_2\text{-}$	dobutamin
H	$\text{-(CH}_2\text{)}_6\text{NHCH}_2\text{CH}_2\text{-}$	dopexamin
$\text{-COCH(CH}_3\text{)}_2$	-CH_3	ibopamin
$\text{-COOCH}_2\text{CH}_3$	-COCHNHCOCH_3 $\text{CH}_2\text{CH}_2\text{-S-CH}_3$	dokarpamin

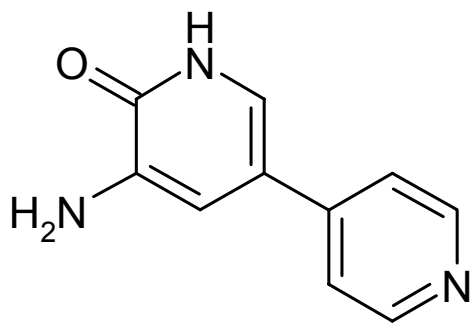
Phosphodiesterase inhibitors

- xanthine derivatives
- bipyridine derivatives
- 3-pyridazinone derivatives
- chinolin-2-one derivatives

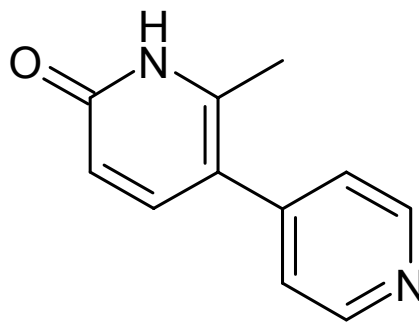
Xanthine derivatives

- Theophylline
 - Aminophylline
 - Etophylline
- * see coronary vasodilators presentation

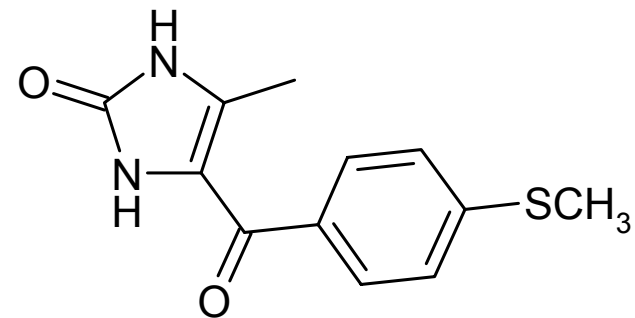
Bipyridine derivatives



amrinon

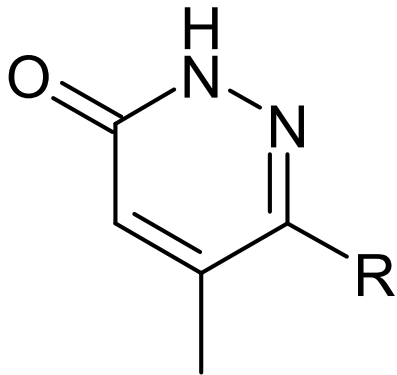


Milrinon

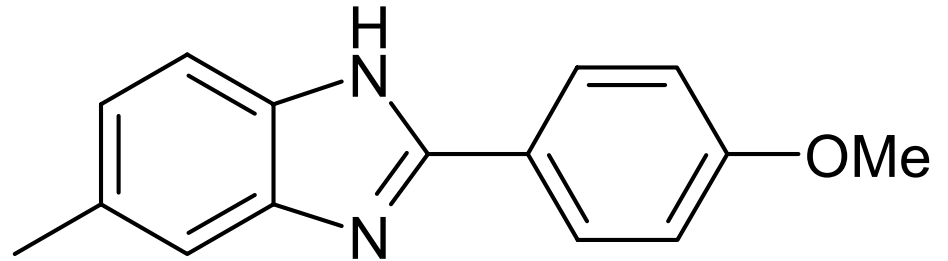


Enoximion

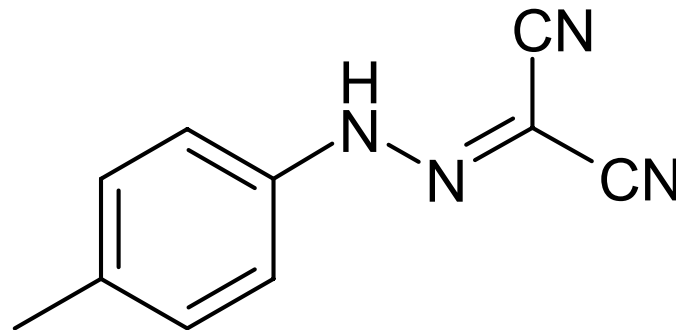
3-pyridazinone derivatives



R:

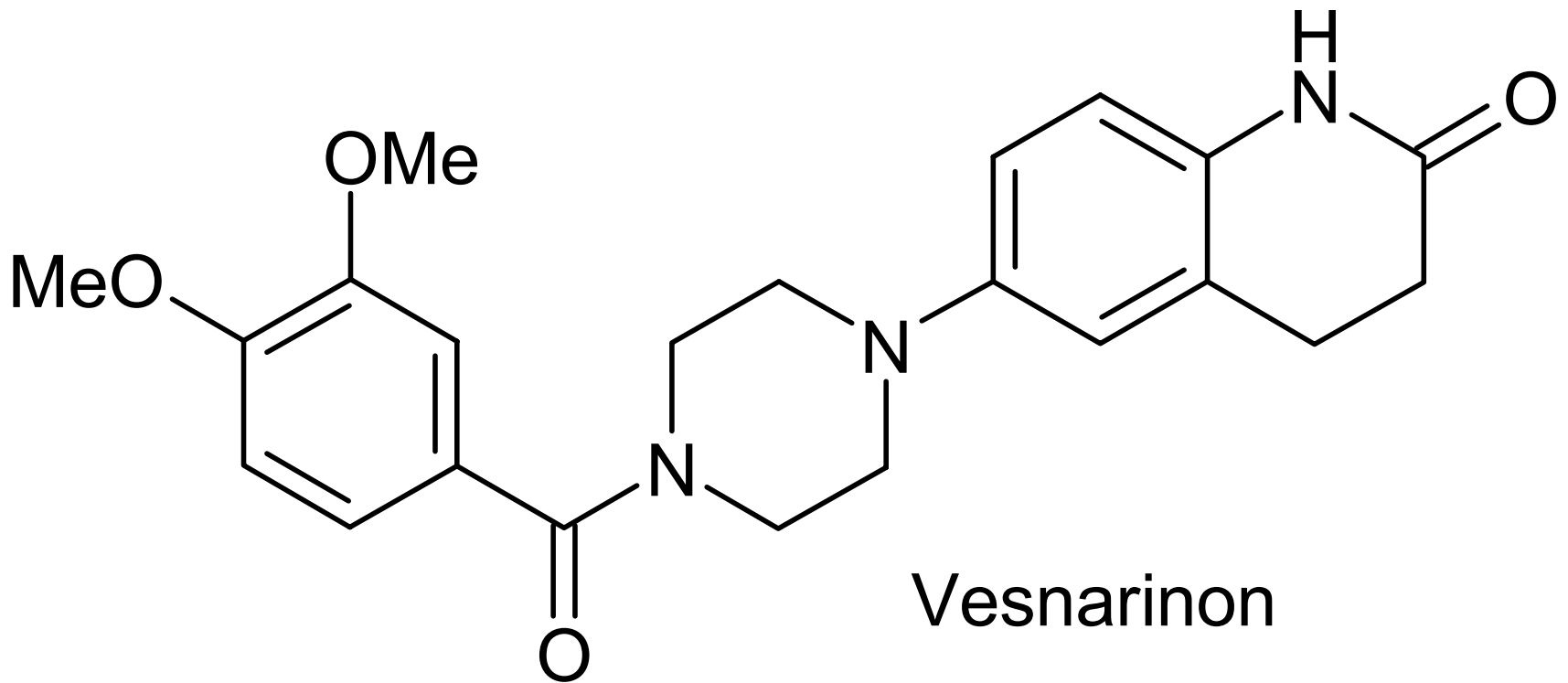


Pimobendan



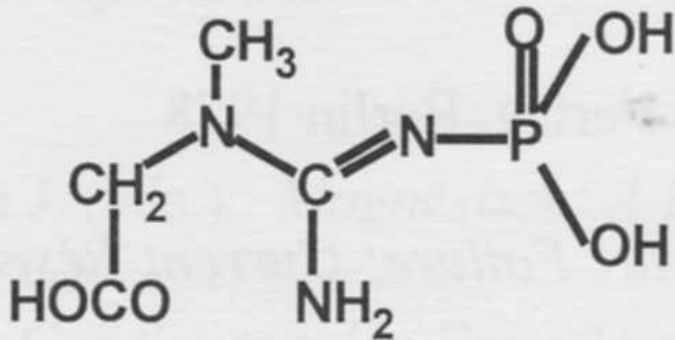
Simendan

Chinolin-2-one derivatives

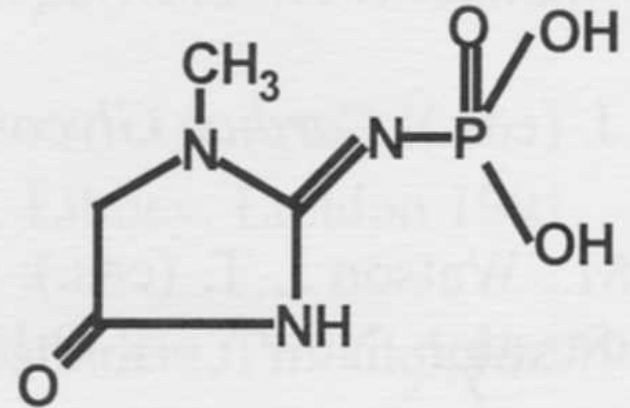


Cardioprotectives

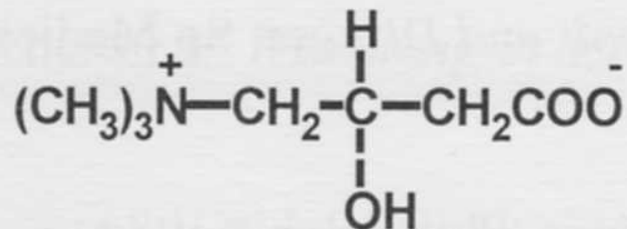
- detoxication of free radicals (NO, OO, OH)



fosfokreatin



fosfokreatinin



levokarnitin