ANTI - ARRYTHMATICS

By

Mr. Y Pradeep Kumar

Associate Professor

Annamacharrya College of Pharmacy.

Subject Name : Medicinal Chemistry

ANTI ARRYTHMATICS

Anti arrhythmics ???? –

In a textbook - Interesting but sedative.

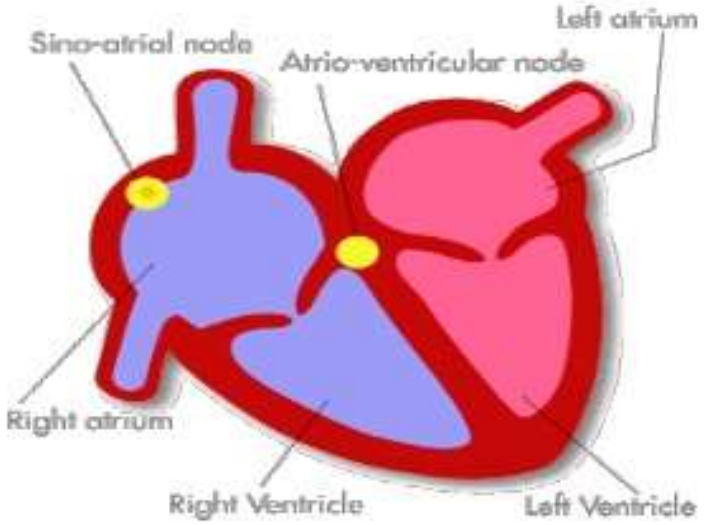
Try it if you have insomnia

–In the lecture Confusion ??????????? •

As always –

In the exam hall Panic! • Don’t worry rarely asked

- A-RHYTHM –IA
- *Defn-* Arrhythmia is deviation of heart from normal RHYTHM.



- *RHYTHM*

1) HR- 60-100
2) Should origin from SAN
3) Cardiac impulse should propagate through normal conduction pathway with normal velocity.

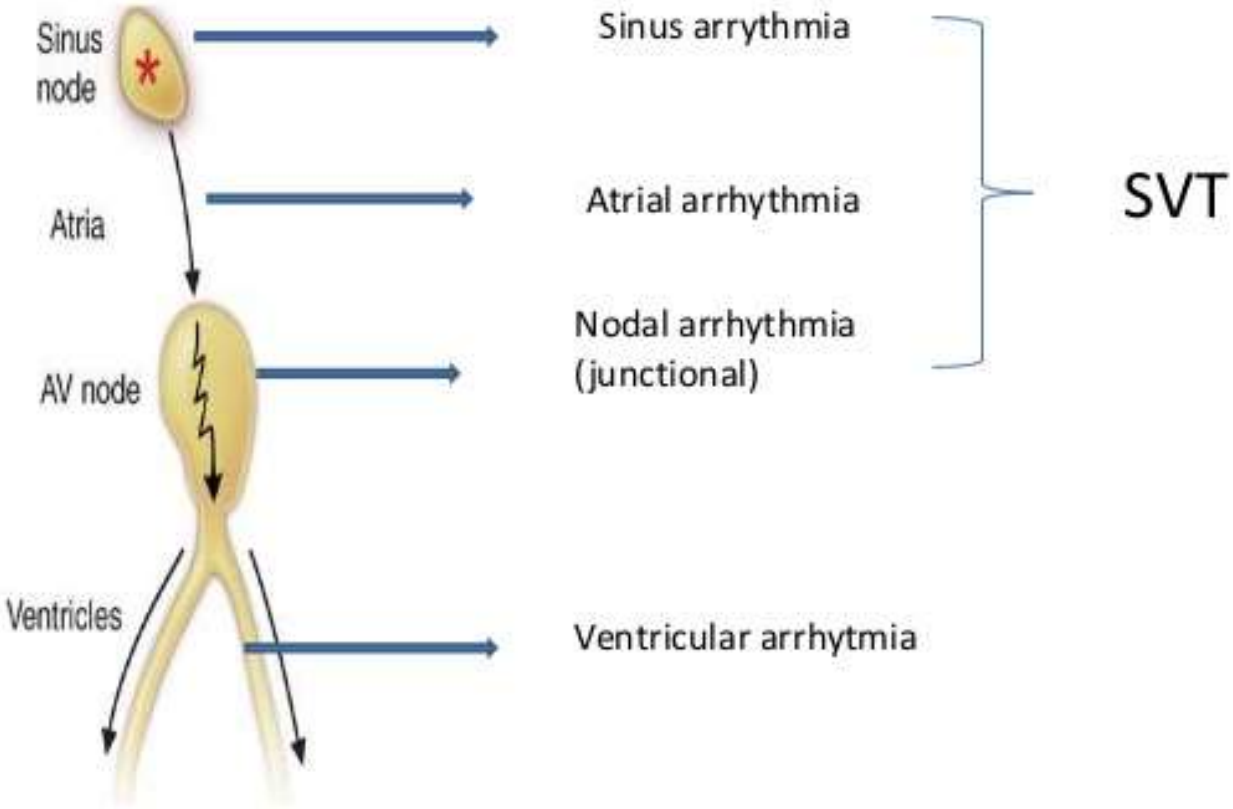
Arrhythmia

- Arrhythmia is an abnormality of rate, regularity, or site of origin of the cardiac impulse or a disturbance in conduction.
- These symptoms cause an alteration in the normal sequence of activation of the atria and ventricles. Ventricular arrhythmias are
- Benign, potentially malignant and malignant based on the risk of their causing sudden death.

TYPES OF ARRYTHMIAS

500	Atrial fibrillation
350	Atrial flutter
200	Paroxysmal TA
150	Simple tachyarrythmia
100 60	Normal range
40	Mild bradyarrhythmias
20	moderate BA
	Severe BA

ARRHYTHMIAS



Electrophysiology of cardiac tissue

- Impulse generation and transmission
- Myocardial action potential
- Depolarization and repolarization waves as seen in ECG

TYPES OF CARDIAC TISSUE (ON THE BASIS OF IMPULSE GENERATION)

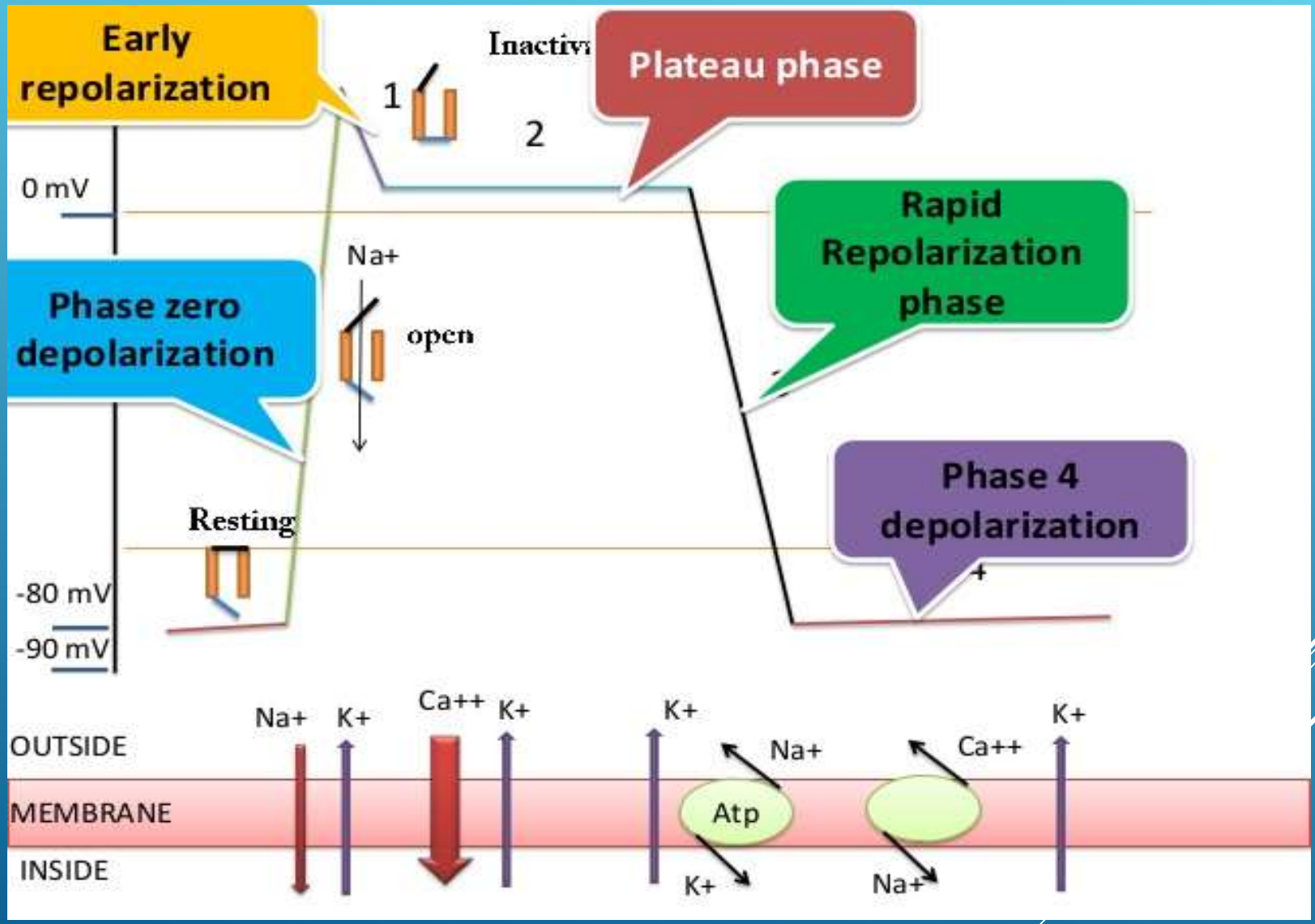
- AUTOMATIC/ PACEMAKER/ CONDUCTING FIBRES (Ca++ driven tissues)

  - Includes SA node, AV node, bundle of His, Purkinje fibres
  - Capable of generating their own impulse
  - Normally SA node acts as Pacemaker of heart

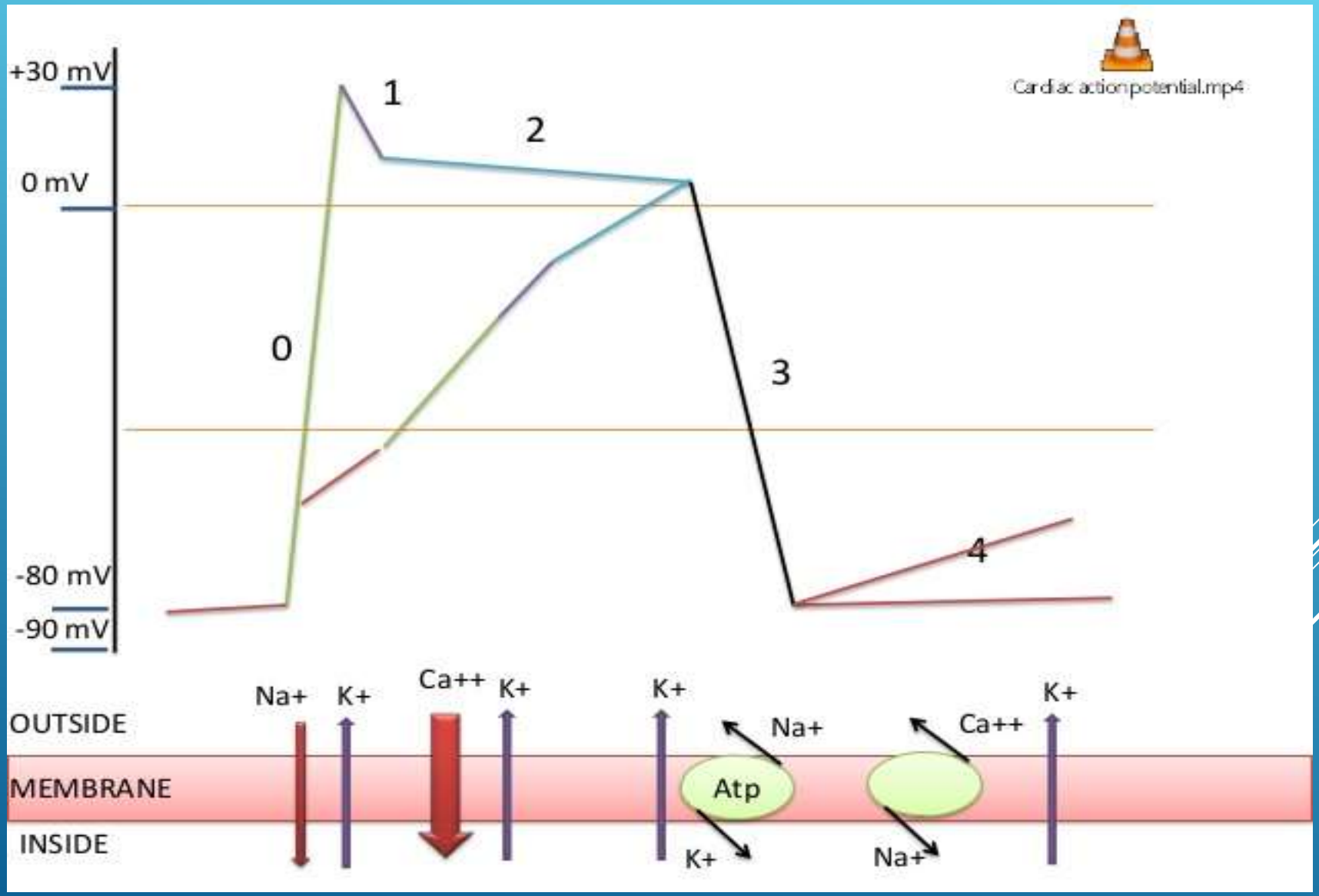
- NON-AUTOMATIC MYOCARDIAL CONTRACTILE FIBRES (Na+ driven tissues)

  - Cannot generate own impulse
  - Includes atria and ventricles

ACTION POTENTIAL IN NON AUTONOMIC MYOCARDIAL TISSUE



ACTION POTENTIAL IN NODAL TISSUE



Fast channel Vs slow channel AP

Fast channel AP

- Occurs in atria, ventricles, PF
- Predominant ion in phase-0 is Na+
- Conduction velocity more
- Selective channel blocker is tetradotoxin , LA

Slow channel AP

- Occurs in SA node, A-V node
- Predominant ion in phase-0 is Ca^{2+}
- Less
- Selective channel blockers are calcium channel blockers

COMMON TERMS

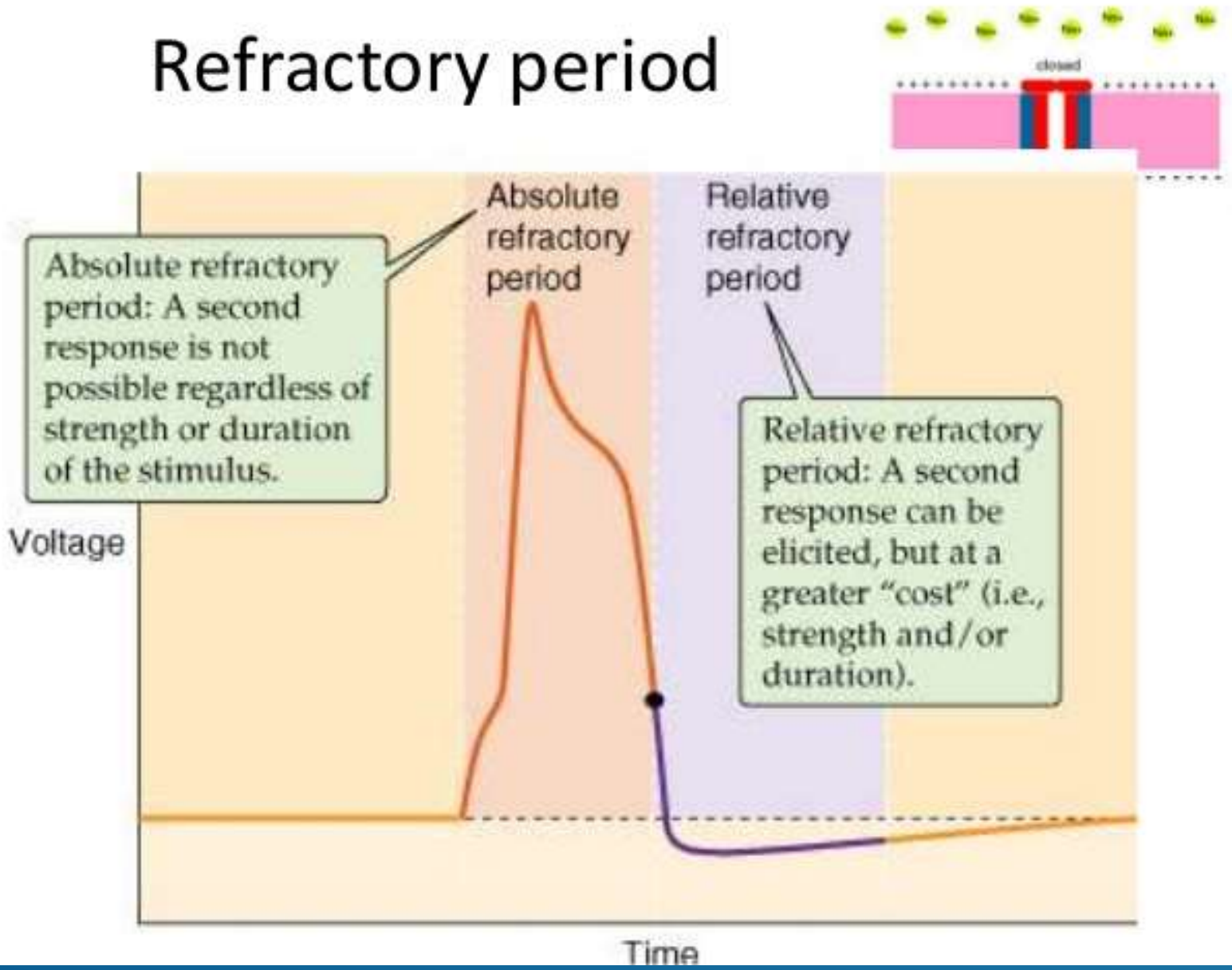
Automaticity – Capacity of a cell to undergo spontaneous diastolic depolarization

- Excitability – Ability of a cell to respond to external stimulus by depolariztion
- Threshold potential – Level of intracellular negativity at which abrupt and complete depolarization occurs.

Conduction velocity of impulse – Determined primarily by slope of action potential and amplitude of phase-0, any reduction in slope leads to depression of conduction

- Propagation of impulse – Depends on ERP & Conduction velocity

Refractory period



MECHANISMS OF CARDIAC ARRYTHMIA

- Abnormal impulse generation:
- Depressed automaticity
- Enhanced automaticity
- Triggered activity (after depolarization):
- Delayed after depolarization
- Early after depolarization
- Abnormal impulse conduction:
- Conduction block
- Re-entry phenomenon
- Accessory tract pathways

CLASSIFICATION BASED ON CLINICAL USE

- **Drugs used for supraventricular arrhythmia`s**
  - Adenosine, verapamil, diltiazem
- **Drugs used for ventricular arrhythmias**
  - Lignocaine, mexelitine, bretylium
- **Drugs used for supraventricular as well as ventricular arrhythmias**
  - Amiodarone, - blockers, disopyramide, procainamide

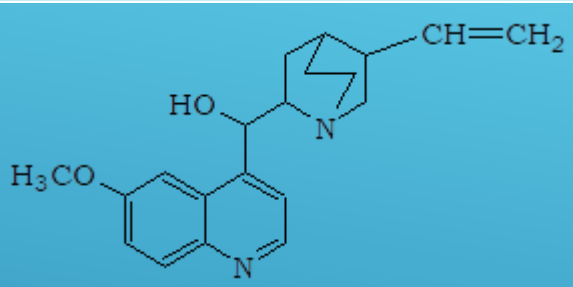
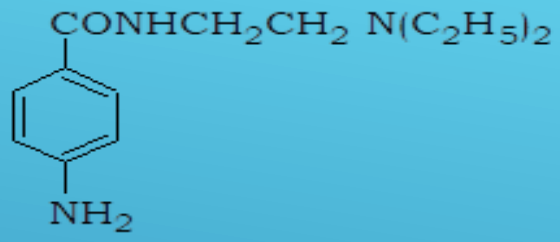
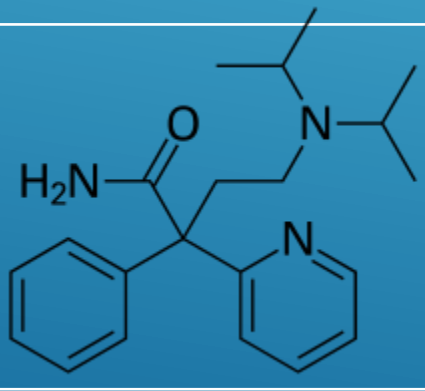
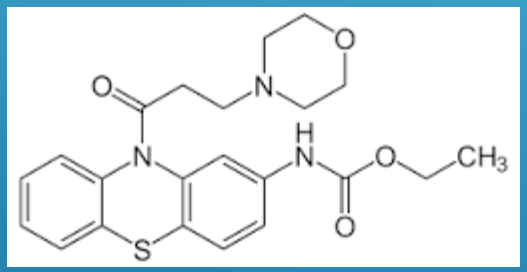
CLASSIFICATION

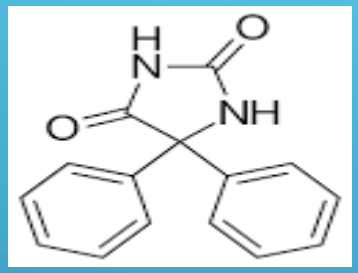
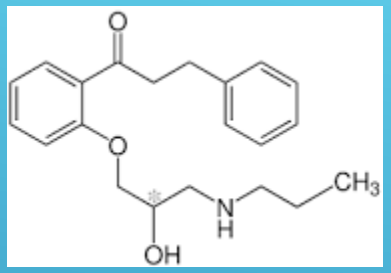
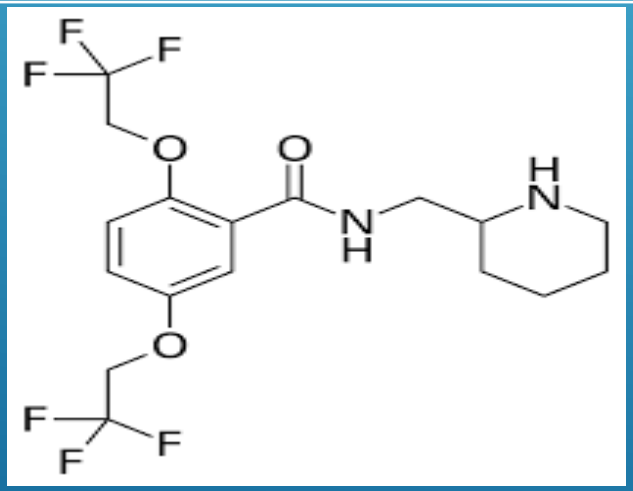
Class-I: Membrane stabilizing agents (Na^+ channel blockers)

A. Moderately decrease dv/dt of 0 phase
   - QUINIDINE
   - PROCAINAMIDE
   - DISOPYRAMIDE
   - MORICIZINE

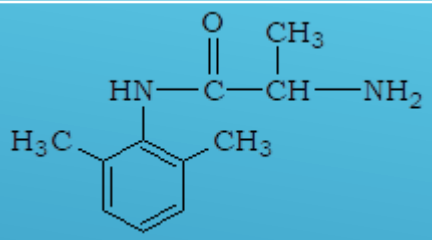
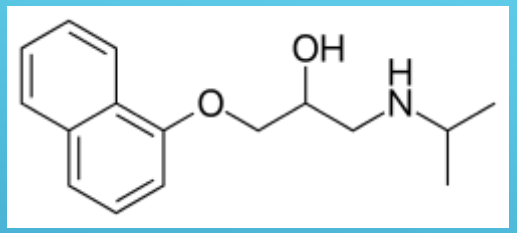
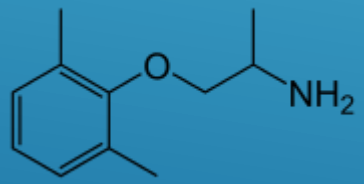
A. Little decrease dv/dt of 0 phase
   - PHENYTOIN

A. Marked decrease dv/dt of 0 phase
   - PROPAFENONE
   - FLECANIDE

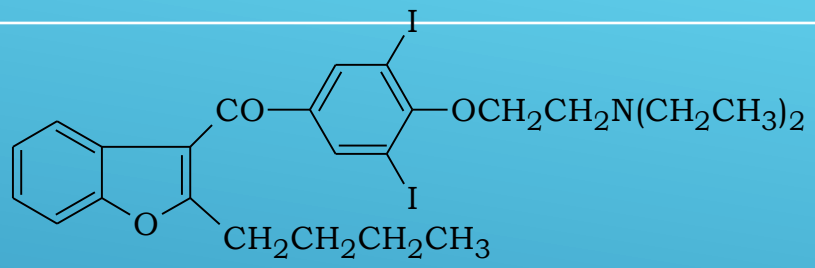
	
Quinidine	Procainamide
	
Disopyramide	Moricizine

	
Phenytoin	**Propaphenone**
	
Flecanide	

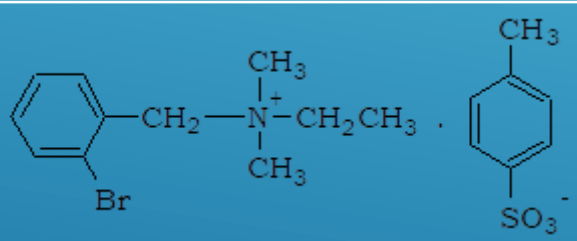
CLASS-II: ANTIADRENERGIC DRUGS (B-BLOCKERS)

	
Lignocaine	**Propronolol**
	
mexelitine	

CLASS – III – REPOLARISATION PROLONGATORS

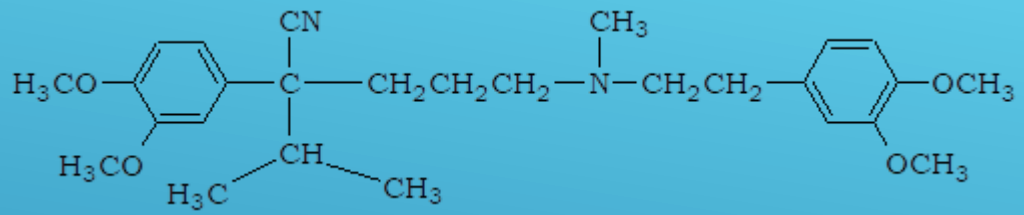


Amaidarone

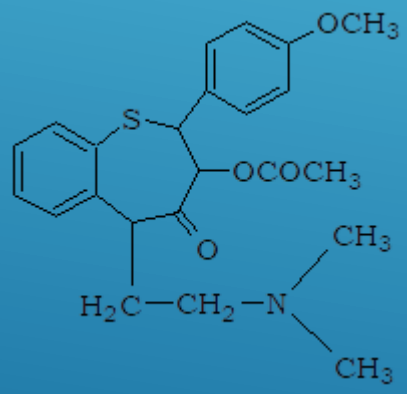


Bretylium Tosylate

CLASS – IV – CALCIUM CHANNEL BLOCKERS

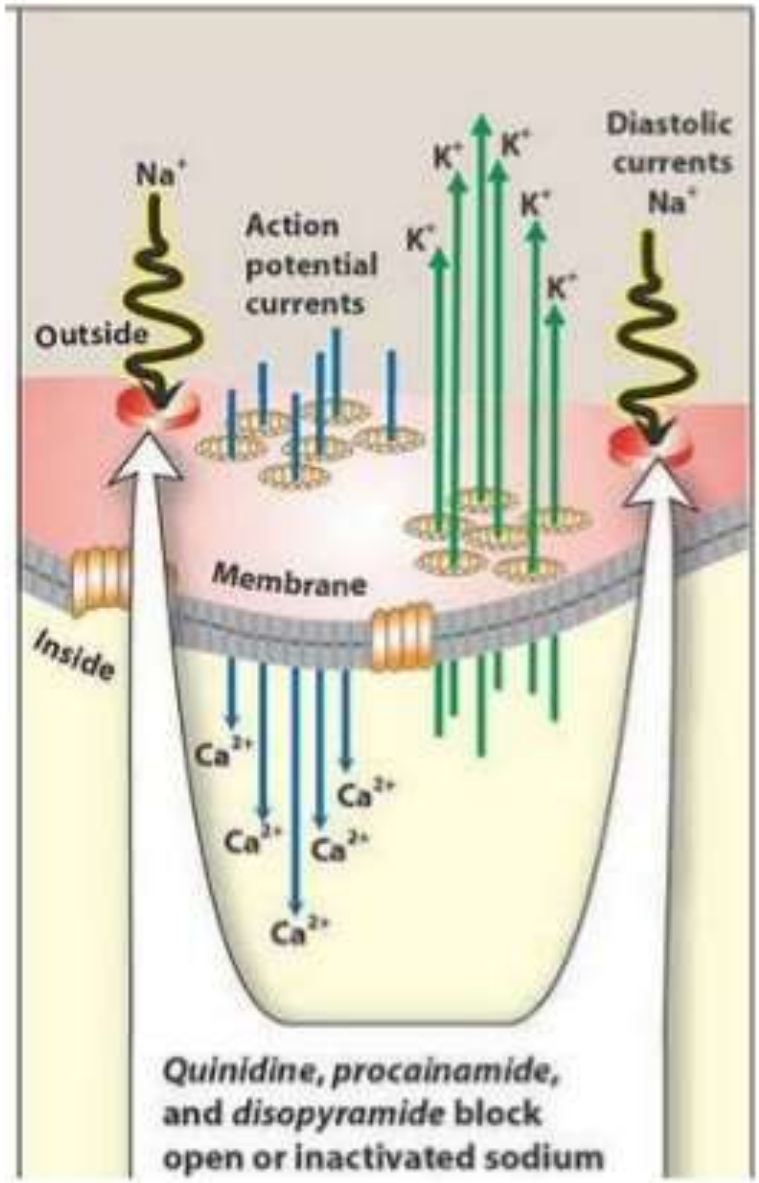


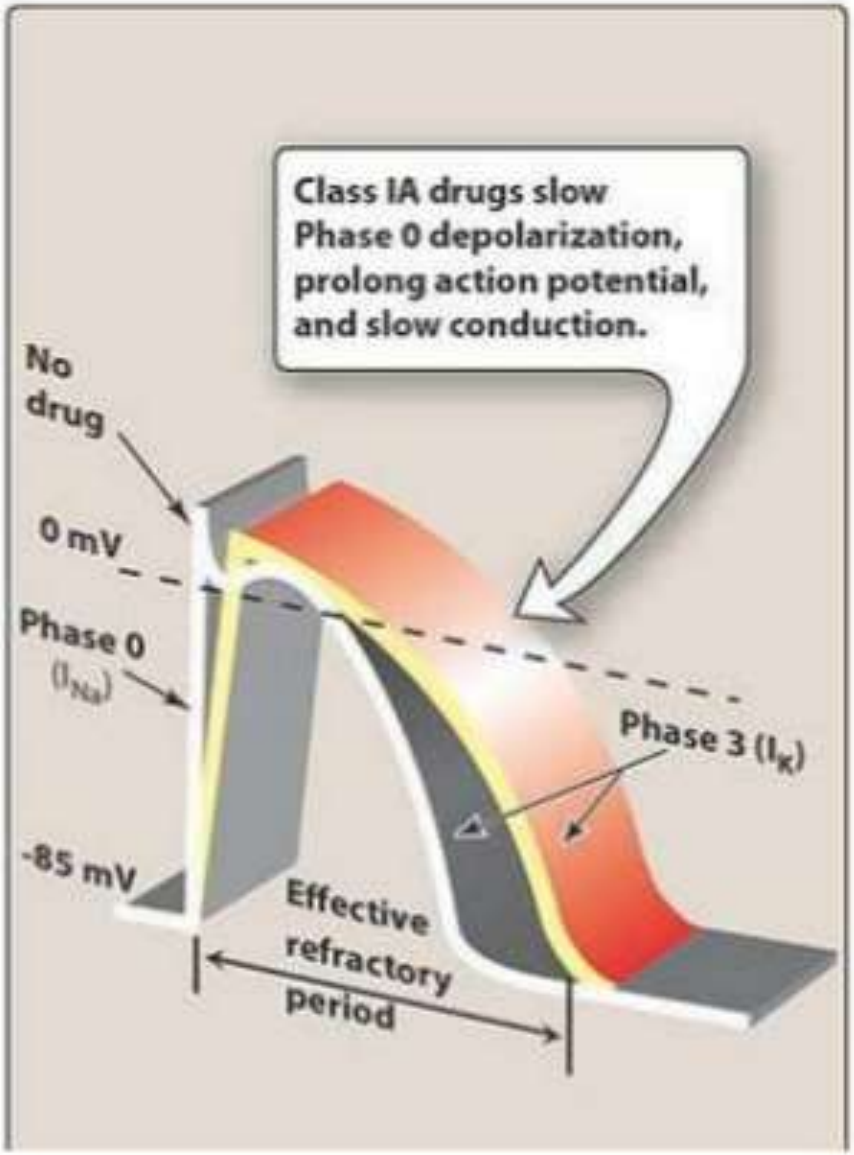
Verapamil



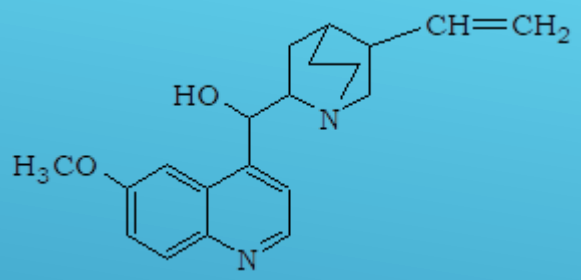
Diltiazem

Class IA


Na+
Action potential currents
K+
Diastolic currents Na+
Outside
Membrane
Inside
Ca2+
Quinidine, procainamide, and disopyramide block open or inactivated sodium


Class IA drugs slow Phase 0 depolarization, prolong action potential, and slow conduction.
No drug
0 mV
Phase 0 (I_{Na})
Phase 3 (I_K)
-85 mV
Effective refractory period

QUINIDINE



↑ Pharmacological effects
threshold for excitability

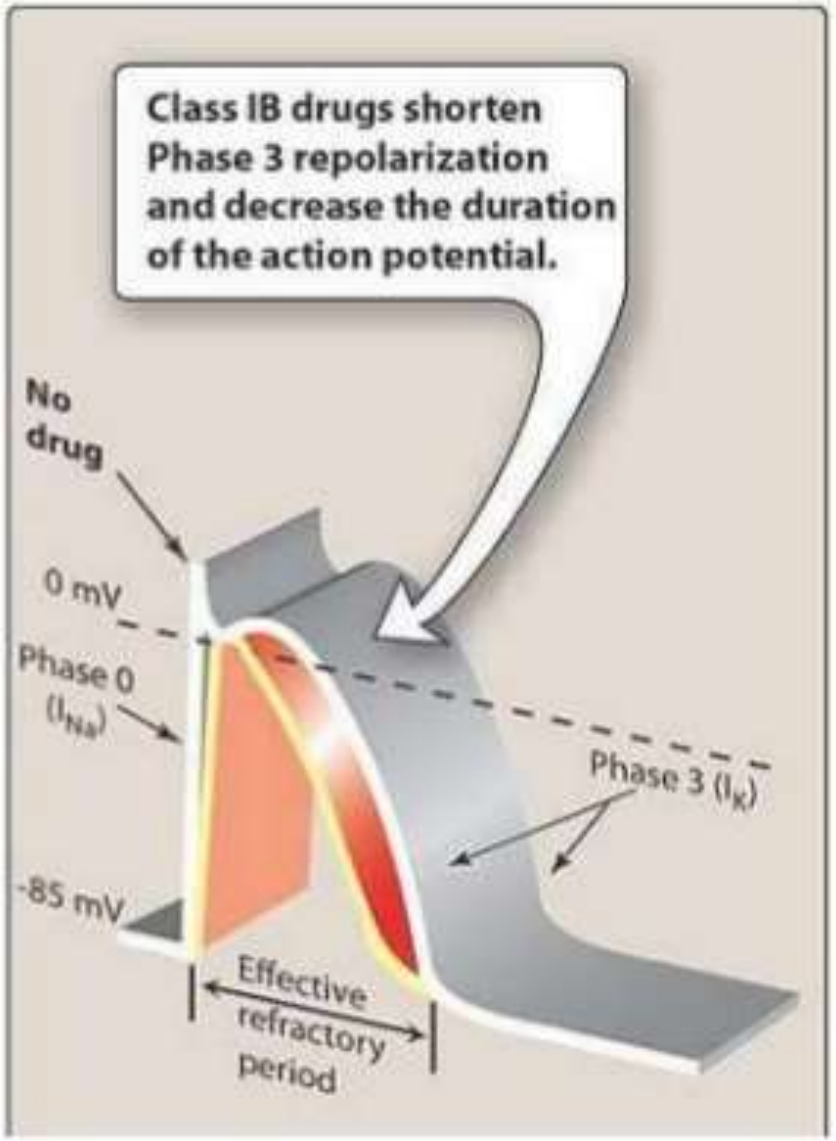
↓ automaticity prolongs AP

1. Used to maintain sinus rhythm after cardioversion of atrial fibrillation.
2. Suppression of supraventricular and ventricular arrhythmias.

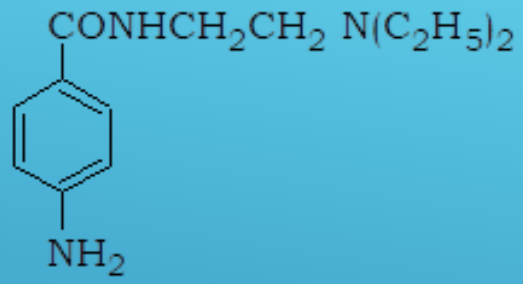
Class IB drugs

Lignocaine, phenytoin, mexiletine

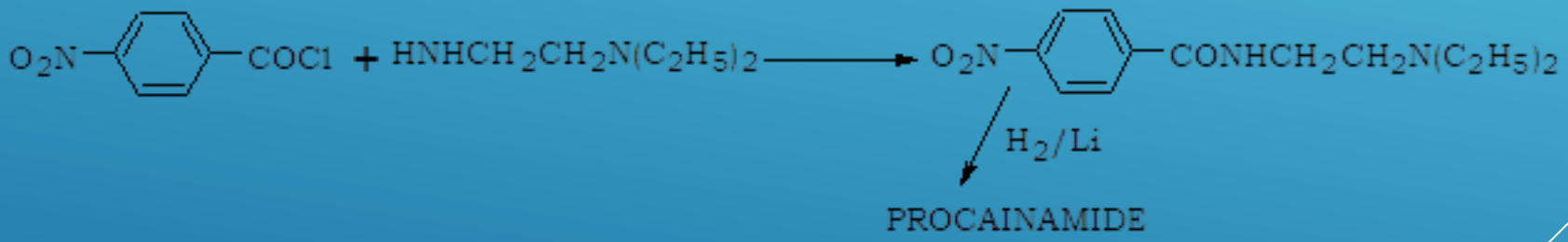
Block sodium channels also shorten repolarization



PROCAINAMIDE

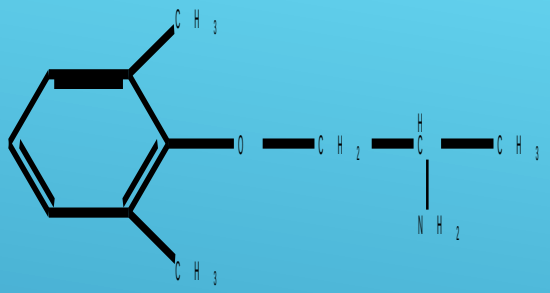


4-amino-N-(2-diethylaminoethyl) benzamide hydrochloride



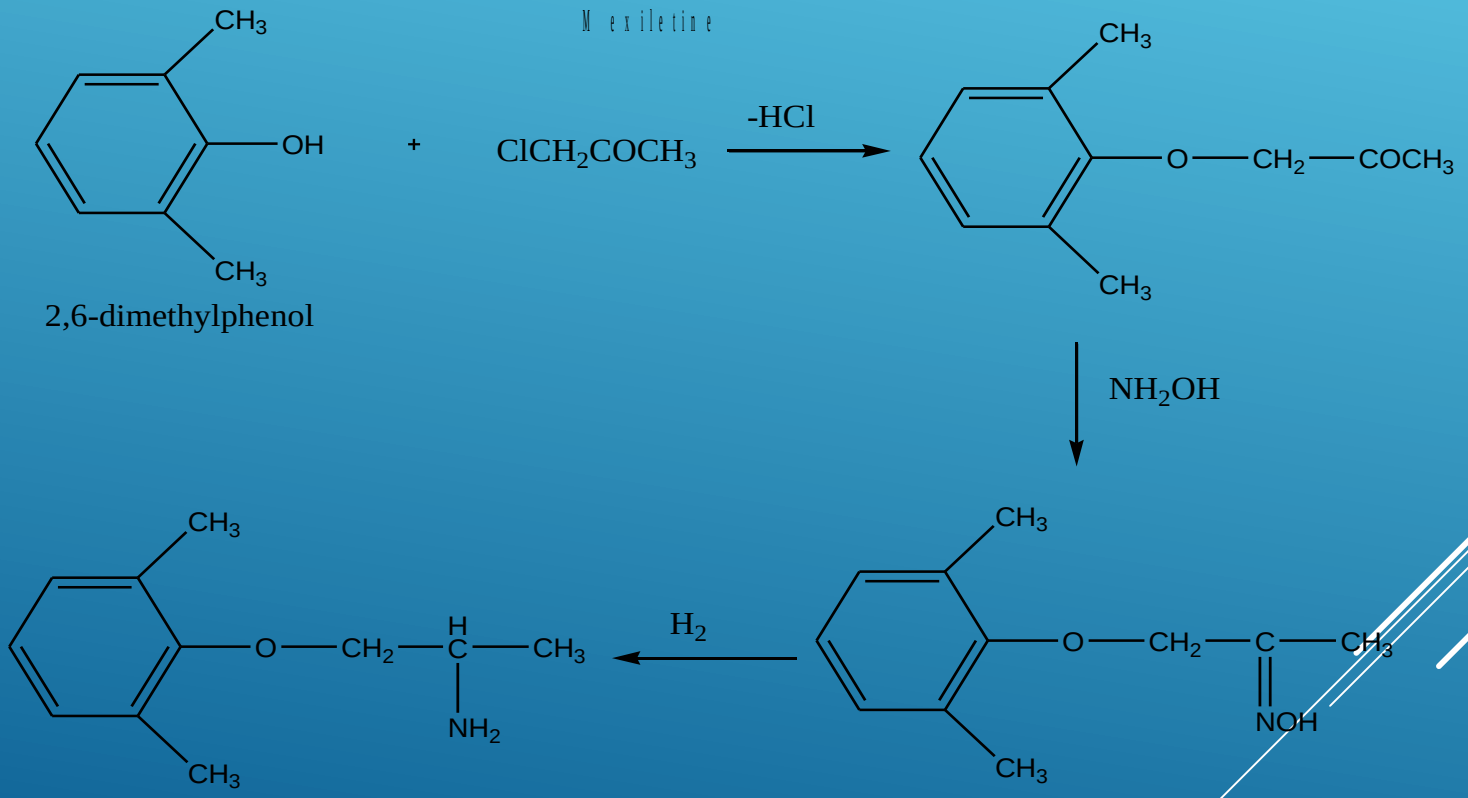
1. In the treatment of ventricular arrythmias, this is resistant to lignocaine and those of following myocardial infarction.
2. Employed to maintain sinus rhythm after cardioversion of atrial fibrillation.

MEXELETINE



1-(2,6-dimethylphenoxy)propan-2-amine

Mexiletine



2,6-dimethylphenol

1-(2,6-dimethylphenoxy)propan-2-amine

Mexiletine

MEXILETINE

Oral analogue of lignocaine

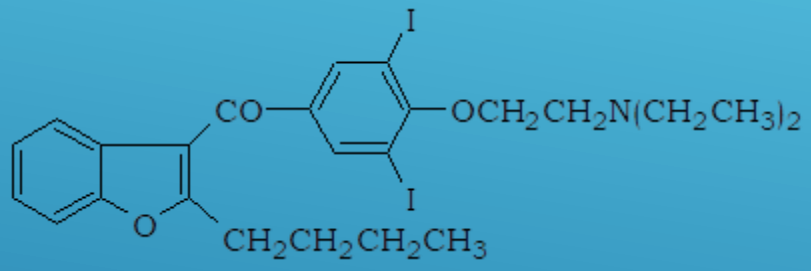
No first pass metabolism in liver

- **Use: – chronic treatment of ventricular arrhythmias associated with previous MI – Unlabelled use in diabetic neuropathy**
- **• Tremor is early sign of mexiletine toxicity**
- **• Hypotension, bradycardia, widened QRS , dizziness, nystagmus may occur**

AMIODARONE

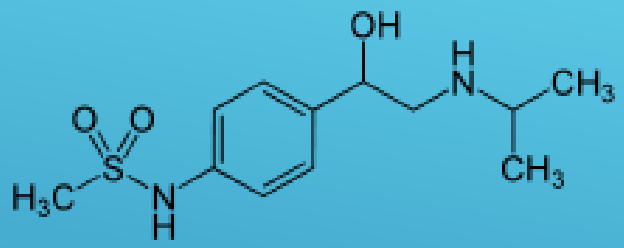
Class – III – Repolarisation prolongators

Prolongs ventricular repolarisation and the effective refractory period.



In the treatment of supraventricular and ventricular arrythmias

SOTOLOL



is a medication used to treat and prevent abnormal heart rhythms.
It is only recommended in those with significant abnormal heart rhythms due to potentially serious side effects.
Evidence does not support a decreased risk of death with long term use.