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Review Article

PHARMACOKINETIC, SOLUBILITY AND DISSOLUTION PROFILE Of ANTIARRYTHMIC DRUGS

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Abstract
Pharmacokinetic data and Solubility Profile Of drugs are the basic requirement of any researcher, for selecting an appropriate drug for any kind of formulation development. To get such data of all drugs of any category at one place is very difficult task: we by our review article have tried to give all such data of Antiarrhythmic drugs at one place.

Keywords:- Antiarrhythmic, Solubilty, dissolution

Introduction
These are drugs used to prevent or treat irregularities of cardiac rhythm.

Classification

Membrane stabilizing agents(Na channel blockers)

Moderately decrease dv/dt of 0 phase
Quinidine
Procainamide
Disopyranide
Moricizine

Little decreasw in dv/dt of 0 phase
Lignocaine
Mexiletine
Phenytoin

Marked decrease in dv/dt of 0 phase
Propafenone
Flecainide

Antiadrenergic agents
Propranolol
Esmolol
Sotalol

Agents widening AP
Amiloride
Bretylium
Dofetilide

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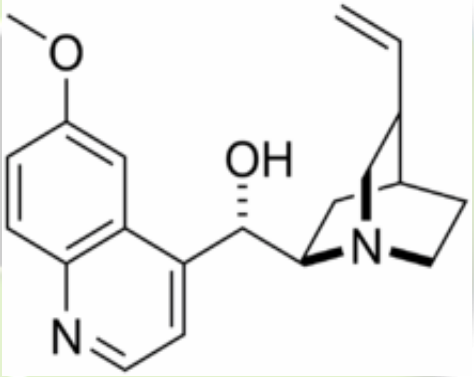
4. Calcium channel blockers
Verapamil
Diltiazem.

Quinidine[2]



Systematic (IUPAC) name: - (9S)-6'-methoxycinchonan- 9-ol

Chemical data:-

Formula: - $C_{20}H_{24}N_2O_2$

Mol. Mass: - 324.417 g/mol

Boiling point: - 495.9 °C at 760 mmHg. **[3]**

Melting point: - 168°. **[4]**

Synonyms: - (2-ethenyl- 4-azabicyclo [2.2.2] oct- 5-yl)- (6-methoxyquinolin- 4-yl)- methanol, 6'-methoxy- α-(5-vinyl- 2-quinuclidinyl)- 4-quinoline methanol,(S)- (6-methoxyquinolin- 4-yl) ((2R,4S,5R)- 5-vinylquinuclidin- 2-yl) methanol

Description: - white powder is odorless and has a very bitter taste. **[USP]**

Solubility profile: - Free soluble in water,slightly soluble in alcohol**[USP][5]**

Quinidine sulphate: - Fine,needle like white crystals,freqently cohering in masses,or fine,white powder is odorless and darkens on exposure ti light.its

solution are neutral or alkaline to litmus.slightly soluble in water,soluble in alcohol,speringly soluble in chlorofom,insoluble in ether. **[USP] [5]**

Solubility profile: - Soluble in ethanol and in chlorofom,sparingly soluble in water,practically insoluble in ether. **[IP] [6]**

Mechanism of action: - Quinidine acts on sodium channels on the neuronal cell membrane, limiting the spread of seizure activity and reducing seizure propagation. The antiarrhythmic actions are mediated through effects on sodium channels in Purkinje fibers. Quinidine may also act on the slow inward calcium current (ICa), the rapid (IKr) and slow (IKs) components of the delayed potassium rectifier current, the inward potassium rectifier current (IKI), the ATP-sensitive potassium channel (IKATP) and Ito. **[7]**

Pharmacokinetic data:-

Bioavailability: - 70-80%

Metabolism: - 50-90**%**

Half-life: - 6-8h

Excretion: - Renal

Pka: - 4.2. **[8]**

logP: - 2.79 to 2.84. **[9]**

Narture: - Hydrophillic. **[10]**

Dissolution:-

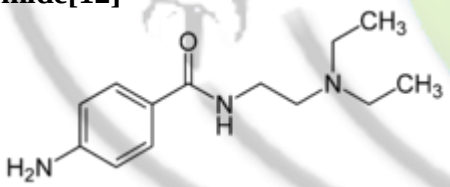
Quinidine sulfate Tablet

Medium: - Dilute hydrochloric acid(0.01 N),900ml

Apparatus: - 1[USP]

Time: - 30 minutes.**[11]**

Procainamide[12]



Systematic (IUPAC) name: - 4-amino-N-(2-diethylaminoethyl) benzamide

Chemical data

Formula: - $C_{13}H_{21}N_3O$

Mol. Mass: - 235.325 g/mol

Boiling Point: - 421.8 °C at 760 mmHg. **[13]**

Melting point: - 165 to 169 °C. **[14]**

Solubility profile: - Colorless or having not more than a slight yellow color**. [USP] [15]**

Solubility profile: - very soluble in water, freely soluble in ethanol, slightly soluble in acetone & in chlorofom, practically insoluble in ether**. [IP] [16]**

Mechanism of action: - Procainamide is sodium channel blocker. It stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses thereby effecting local anesthetic action. **[17]**

Pharmacokinetic data

Bioavailability: - 85% (oral)

Protein binding: - 15 to 20%

Metabolism : - Hepatic (CYP2D6-mediated)

Half-life: - 2.5 to 4.5 hours

Excretion: - Renal

pKa : - 9.2. 2. **[18]**

log P: - 1.3. **[19]**

Nature: - Hydrophillic. **[20]**

Dissolution:-[21]

Procanamide hydrochloride Tablet

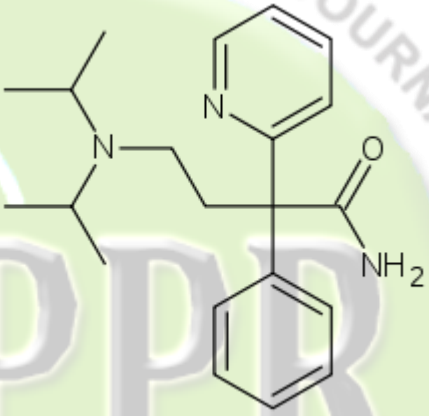
Medium: - Dilute hydrochloric acid(0.01 N),900ml

Apparatus: - 2[USP]

Time: - 30 minutes.

Rpm: - 50

Disopyramide[22]



Systematic (IUPAC) name: - 4-(diisopropylamino)-2-phenyl-2-(pyridin-2-yl)butanamide

Chemical data

Formula: - $C_{21}H_{29}N_3O$

Mol. Mass: - 339.475 g/mol

Boiling point: - 505.2°C at 760 mmHg. **[23]**

Melting Point: - 94.5-95^{0}C. **[24]**

Solubility profile: - white or practically white odorless powder.melt at about 205 degree with decomposition.freely soluble in water,slightly soluble in alcohol.practically insoluble in chlorofom& in ether**. [USP] [25]**

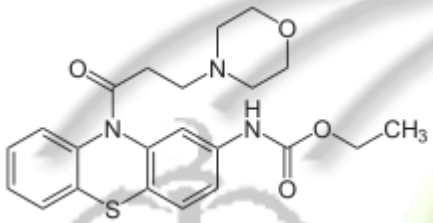
Mechanism of action: - Disopyramide is a Type 1A antiarrhythmic drug (ie, similar to procainamide and quinidine). It inhibits the fast sodium channels. In animal studies Disopyramide decreases the rate of diastolic depolarization (phase 4) in cells with augmented automaticity, decreases the upstroke velocity (phase 0) and increases the action potential duration of normal cardiac cells, decreases the disparity in refractoriness between infarcted and adjacent normally perfused myocardium, and has no effect on alpha- or beta-adrenergic receptors. **[26]**

Pharmacokinetic data

Bioavailability: - High

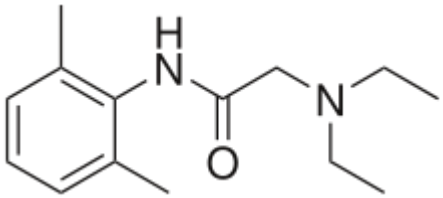
Protein binding: - 50% to 65% (concentration-dependent)
Metabolism: - Hepatic (CYP3A4-mediated)
Half-life: - 6.7 hours (range 4 to 10 hours)
Excretion: - Renal (80%)
Pka: - 8.6 and 10.2. **[27]**
Log P: - –5 to 7.5. **[28]**
Nature: - Hydrophillic. **[29]**
Dissolution:-[30]
Disopryamide extended release capsule
Medium: - ph 2.5, 0.1 M phosphate buffer.
Apparatus: - 1[USP]
Time: - 1 , 2, 4, 5 hours.
Rpm: - 100

Moricizine [31]

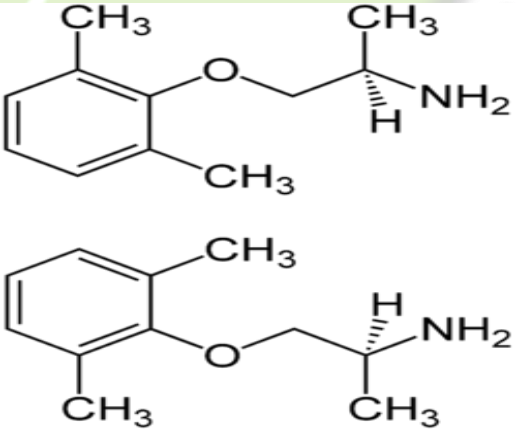


Systematic (IUPAC) name ethyl [10-(3-morpholin-4-ylpropanoyl)-10H-phenothiazin-2-yl]carbamate
Chemical data
Formula $C_{22}H_{25}N_3O_4S$
Mol. mass 427.518 g/mol
Boiling point: - 625°C at 760 mmHg. **[32]**
Melting point: - 165 to 169 °C. **[33]**
Solubility profile:-white to off white crystalline powder .melt at about 189 degree with decomposition.soluble in water & in alcohol**[USP] [34]**
Mechanism of action: - Procainamide is sodium channel blocker. It stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses thereby effecting local anesthetic action. **[35]**
Pharmacokinetic data
Bioavailability 38%
Protein binding 95%
Half-life 3-4 hours (healthy volunteers), 6-13 hours (cardiac disease)
Pka: - 6.26. **[36]**
Log P: - 2.73, 2.98. **[37]**
Nature: - Hydrophillic. **[38]**
Dissolution:-[39]
Moricizine hydrochloride tablet
Medium: - Dilute hydrochloric acid(0.01 N),900ml
Apparatus: - 2[USP]
Time: - 30 minutes.
Rpm: - 50

Lidocaine[40]



Systematic (IUPAC) name: - 2-(diethylamino)-N-(2,6-dimethylphenyl)acetamide
Chemical data
Formula: - $C_{14}H_{22}N_2O$
Mol. Mass: - 234.34 g/mol
Boiling Point: - 350.8 °C at 760 mmHg. **[41]**
Melting Point: - 68.5°C. **[42]**
Solubility profile: - white to slightly yellow,crysaline powder, has a characterstic powder and is stable in air, practically insoluble in water, very soluble in alcohol and in choloroform,freely solubule in benzene and in in ether, dissolve in oil**[USP][43]**
Lidocaine hydrochloride: - white odorless crystalline powder, having a slightly bitter taste, very soluble in water and in alcohol, soluble in chloroform and in insoluble in ether. **[USP][43]**
Pharmacokinetic data
Bioavailability: - 35% (oral) 3% (topical)
Metabolism: - Hepatic, 90% CYP1A2-mediated
Half-life: - 1.5–2 hours
Excretion: - renal
Pka: - 7.94, 10.50. **[44]**
logP: - 2.26. **[45]**
Nature: - Hydrophobic. **[46]**
Mexiletine[47]



Systematic (IUPAC) name: - (RS)-1-(2,6-dimethylphenoxy)propan-2-amineOR2-(2-aminopropoxy)-1,3-dimethylbenzene
Chemical data
Formula: - $C_{11}H_{17}NO$
Mol. Mass: - 179.259 g/mol
Boiling Point: - 271.5°C at 760 mmHg. **[48]**
Melting Point: - 203-205^{0}C. **[49]**

Solubility profile:- white powder,freely soluble in dehydrated alchol an in water,slaigtly sloible in acetonitrile,practically insoluble in ether ,optically inactive**[USP][50]**

Solubility profile:- freely soluble in water and in methanol, sparingly solublein dicholoromethane,practicaly insoluble in ether**.[IP][51]**

Mechanism of action: - Mexiletine, like lidocaine, inhibits the inward sodium current required for the initiation and conduction of impulses, thus reducing the rate of rise of the action potential, Phase 0. It achieves this reduced sodium current by inhibiting sodium channels. Mexiletine decreases the effective refractory period (ERP) in Purkinje fibers in the heart. The decrease in ERP is of lesser magnitude than the decrease in action potential duration (APD), which results in an increase in the ERP/APD ratio. It does not significantly affect resting membrane potential or sinus node automaticity, left ventricular function, systolic arterial blood pressure, atrioventricular (AV) conduction velocity, or QRS or QT intervals. **[52]**

Pharmacokinetic data

Bioavailability: - 90%

Protein binding: - 50-60%

Metabolism: - Hepatic (CYP2D6 and 1A2-mediated)

Half-life: - 10-12 hours

Excretion: - Renal (10%)

Pka: - 9.2. **[53]**

log P: - 2.8 1. **[54]**

Nature: - Hydrophillic. **[55]**

Dissolution:-[56]

Mexilitine hydrochloride capsule

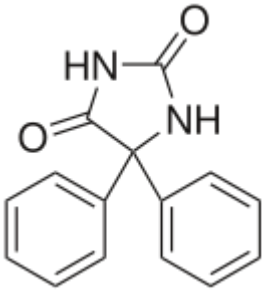
Medium: - Water 900ml.

Apparatus: - 2[USP]

Time: - 3o minute.

Rpm: - 50

Phenytoin[57]



Systematic (IUPAC) name: - 5,5-diphenylimidazolidine-2,4-dione

Chemical data

Formula: - $C_{15}H_{12}N_2O_2$

Mol. Mass: - 252.268 g/mol

Boiling Point: - 428.2 °C. **[58]**

Melting point: - 295-298°C. **[59]**

Solubility profile: - White, odorless powder,melt at at about 295 degree, practically insoluble in water,soluble im hot alcohol.sligthly soluble in cold acohol , in choloroform and in ether.**[USP][60]**

Phentoin sodium: - White,odorless powder is some what hygroscopic and on exposure to air gradually absorb carbondioxide**[USP][60]**

Solubility profile: - Soluble in water, the solution showing somw turbidity due to partial hydrolysis,soluble in ethanol(95%), practically insoluble in dicholoromethane in ether.**[IP][61]**

Mechanism of action: - Phenytoin acts on sodium channels on the neuronal cell membrane, limiting the spread of seizure activity and reducing seizure propagation. By promoting sodium efflux from neurons, phenytoin tends to stabilize the threshold against hyperexcitability caused by excessive stimulation or environmental changes capable of reducing membrane sodium gradient. This includes the reduction of post-tetanic potentiation at synapses. Loss of post-tetanic potentiation prevents cortical seizure foci from detonating adjacent cortical areas. **[62]**

Pharmacokinetic data

Bioavailability: - 70-100% oral, 24.4% for rectal and intravenous administration

Protein binding: - 90%

Metabolism: - hepatic.

Half-life: - 6-24 hours

Excretion: - Primarily through the bile, urinary

pKa: - 8.3. **[63]**

log P: - 2.47. **[64]**

Nature: - Hydrophillic. **[65]**

Dissolution:-[66]

Phenytoin chewable tablet

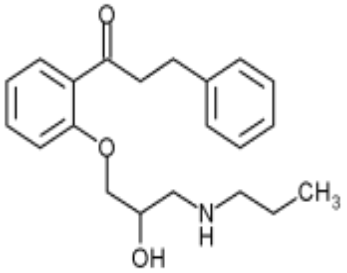
Medium: - 0.05 M tris buffer, 900 ml

Apparatus: - 2[USP]

Time: - 120 minute.

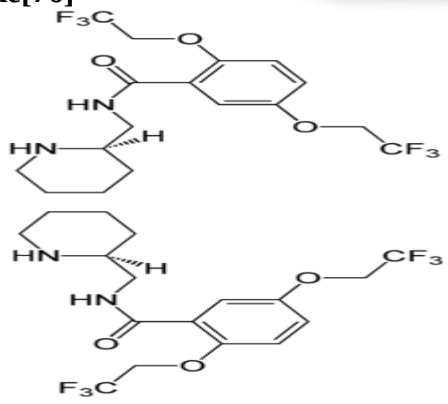
Rpm: - 100

Propafenone[67]

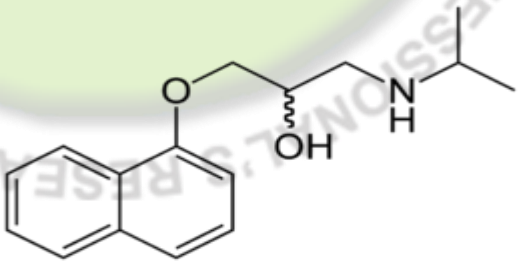


Systematc (IUPAC) name1-{2-[2-hydroxy-3-(propylamino)propoxy]phenyl}-3-phenylpropan-1-one

Chemical data
Formula: - $C_{21}H_{27}NO_3$
Mol. Mass: - 341.444 g/mol
Boiling point: - 519.6°C at 760 mmHg. **[68]**
Melting Point: - 171 - 174 C. **[69]**
Solubility profile: - White powder. Soluble in methanol and in hot water. Slightly soluble in alcohol and in chloroform. Very slightly soluble in acetone, insoluble in diethyl ether and in toluene**.[USP][70]**
Mechanism of action: - The electrophysiological effect of propafenone manifests itself in a reduction of upstroke velocity (Phase 0) of the monophasic action potential. In Purkinje fibers, and to a lesser extent myocardial fibers, propafenone reduces the fast inward current carried by sodium ions, which is responsible for the drugs antiarrhythmic actions. Diastolic excitability threshold is increased and effective refractory period prolonged. Propafenone reduces spontaneous automaticity and depresses triggered activity. At very high concentrations in vitro, propafenone can inhibit the slow inward current carried by calcium but this calcium antagonist effect probably does not contribute to antiarrhythmic efficacy. **[71]**
Pharmacokinetic data
Bioavailability: - Not available.
Protein binding: - 97%
Half-life: - 2-10 hours
Pka: - 9.30, 11.10. **[72]**
LogP: - 3.351. **[73]**
Nature: - Hydrophiillic. **[74]**
Dissolution:-[75]
Propafenone HCL Tablet
Medium: - 0.1 N HCL, 900 ml
Apparatus: - 2[FDA]
Time: - 10,20,30,45 minute.
Rpm: - 75
Flecainide[76]



Systematic (IUPAC) name: - (RS)-N-(piperidin-2-ylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)benzamide
Chemical data
Formula: - $C_{17}H_{20}F_6N_2O_3$
Mol. Mass: - 414.343 g/mol
Boiling Point: - 434.9ºC at 760 mmHg. **[77]**
Melting Point: - 105-107ºC. **[78]**
Solubility profile: - white to slightly off white, crystalline powder. Freely soluble in alcohol, soluble in water.pka is 9.3**[USP][79]**
Mechanism of action: - Flecainide acts on sodium channels on the neuronal cell membrane, limiting the spread of seizure activity and reducing seizure propagation. The antiarrhythmic actions are mediated through effects on sodium channels in Purkinje fibers. Flecainide is a sodium channel blocker, binding to voltage gated sodium channels. It stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses. Ventricular excitability is depressed and the stimulation threshold of the ventricle is increased during diastole. **[80]**
Pharmacokinetic data
Bioavailability: - 95%
Protein binding: - 40%
Metabolism: - CYP2D6 (limited)
Half-life: - 20 hours (range 12-27 hours)
Excretion: - Renal
pKa: - 9.3. **[81]**
logP: - 3.1881419053333335. **[82]**
Nature: - Hydrophillic. **[83]**
Dissolution:-[84]
Flecianide acetate tablet
Medium: - 0.075 Hydrochloric acid, 900ml
Apparatus: - 2
Time: - 30 minutes.
Rpm: - 50
Propranolol[85]



Systematic (IUPAC) name: - (RS)-1-(isopropylamino)-3-(1-naphthyloxy)propan-2-o
Chemical data
Formula: - $C_{16}H_{21}NO_2$
Mol. mass: - 259.34 g/mol
Boiling Point: - 434.9 ºC at 760 mmHg. **[86]**
Melting Point: - 163-164 ºC. **[87]**
Solubility profile: - white to slightly off white, crystalline powder. Is odorless and has a bitter taste. Melt at about 164 degree.

Soluble in water and in alcohol, slightly soluble in chloroform, practically insoluble in ether**. [USP][88]**

Solubility profile: - soluble in water and in ethanol, slightly soluble in chloroform, practically insoluble in ether**[IP][89]**

Mechanism of action: - Propranolol competes with sympathomimetic neurotransmitters such as catecholamines for binding at beta(1)-adrenergic receptors in the heart, inhibiting sympathetic stimulation. This results in a reduction in resting heart rate, cardiac output, systolic and diastolic blood pressure, and reflex orthostatic hypotension. **[90]**

Pharmacokinetic data

Bioavailability: - 26%

Metabolism: - hepatic (extensive)

Half-life: - 4-5 hours

Excretion: - renal <1%

Pka: - 9.50, 11.10. **[91]**

log P: - 3.56. **[92]**

Nature: - Hydrophobic. **[93]**

Dissolution:-[94]

Propanolol hydrochloride extended release capsule

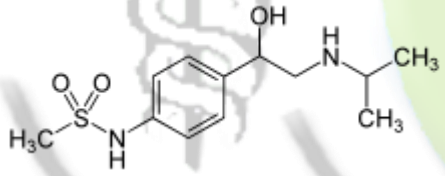
Medium: - ph 1.2 and 6.8 buffer,900 ml.

Apparatus: - 1[FDA]

Time: - 1.5,4,8,14 and 24 minutes.

Rpm: - 100

Sotalol[95]



Systematic (IUPAC) name: - (RS)-N-{4-[1-hydroxy-2-(propan-2-ylamino)ethyl]phenyl}methanesulfonamide

Chemical data

Formula: - $C_{12}H_{20}N_2O_3S$

Mol. mass: - 272.3624 g/mol

Boiling point: - 443.3°C at 760 mmHg. **[96]**

Melting Point: - 206.5-207oC. **[97]**

Solubility profile: - white to off white powder, freely soluble in water, soluble in alcohol, very slightly soluble in chloroform**.[USP][98]**

Mechanism of action: - Sotalol has both beta-adrenoreceptor blocking (Vaughan Williams Class I) and cardiac action potential duration prolongation (Vaughan Williams Class I) antiarrhythmic properties. Sotalol is a racemic mixture of d- and l-sotalol. Both isomers have similar Class I antiarrhythmic effects, while the l-isomer is responsible for virtually all of the beta-blocking activity. Sotalol inhibits response to adrenergic stimuli by competitively blocking β_1-adrenergic receptors within the myocardium and β_2-adrenergic receptors within bronchial and vascular smooth muscle. The electrophysiologic effects of sotalol may be due to its selective inhibition of the rapidly activating component of the potassium channel involved in the repolarization of cardiac cells. The class II electrophysiologic effects are caused by an increase in sinus cycle length (slowed heart rate), decreased AV nodal conduction, and increased AV nodal refractoriness, while the class III electrophysiological effects include prolongation of the atrial and ventricular monophasic action potentials, and effective refractory period prolongation of atrial muscle, ventricular muscle, and atrio-ventricular accessory pathways (where present) in both the anterograde and retrograde directions. **[99]**

Pharmacokinetic data

Bioavailability: - >95%

Metabolism: - Not metabolized

Half-life: - 12 hours

Excretion: - Renal

Lactic (In lactating females)

Pka: - 8.80 and 9.80. **[100]**

Log P: - -0.79. **[101]**

Nature: - Hydrophillic. **[102]**

Dissolution:-[103]

Sotalol hydrochloride tablet

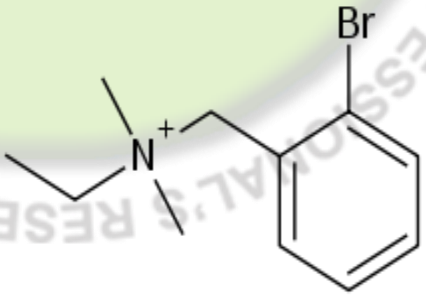
Medium: - Water,900 ml.

Apparatus: - 2[usp]

Time: - 30 minutes.

Rpm: - 50

Bretylium[104]



Systematic (IUPAC) name: - N-(2-bromobenzyl)-N,N-dimethylethanaminium

Chemical data

Formula: - $C_{11}H_{17}BrN^+$

Mol. mass: - 243.163 g/mol

Boiling Point: - 330.9 °C at 760 mmHg. **[105]**

Melting Point: - 97°C. **[106]**

Solubility profile: - white crystalline powder. Is hygroscopic. Freely soluble in water, in methanol, and in alcohol, practically insoluble in ether, in ethyl acetate, and in hexane. **. [USP][107]**

Mechanism of action: - Bretylium inhibits norepinephrine release by depressing adrenergic nerve terminal excitability. The mechanisms of the antifibrillatory and antiarrhythmic actions of bretylium are not established. In efforts to define these mechanisms, the following electrophysiologic actions of bretylium have been demonstrated in animal experiments: increase in ventricular fibrillation threshold, increase in action potential duration and effective refractory period without changes in heart rate, little effect on the rate of rise or amplitude of the cardiac action potential (Phase 0) or in resting membrane potential (Phase 4) in normal myocardium, decrease in the disparity in action potential duration between normal and infarcted regions, and increase in impulse formation and spontaneous firing rate of pacemaker tissue as well as increase ventricular conduction velocity. **[108]**

Pharmacokinetic data

Bioavailability: - NA

Protein binding: - NA

Metabolism: - None

Half-life: - 7-8 hours

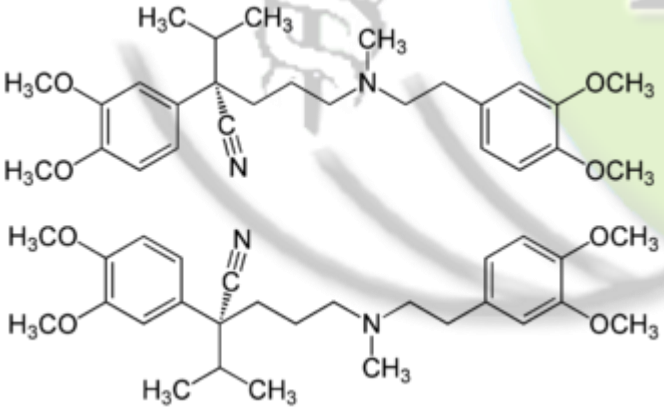
Excretion: - Renal

Pka : - 8.86 and 10.5. **[109]**

logP: - -1.122133453471745. **[108]**

Nature: - Hydrophobic. **[110]**

Verapamil[111]



Systematic (IUPAC) name: - (RS)-2-(3,4-dimethoxyphenyl)-5-{[2-(3,4-dimethoxyphenyl)ethyl](methyl)amino}-2-prop-2-ylpentanenitrile

Chemical data

Formula: - $C_{27}H_{38}N_2O_4$

Mol. mass: - 454.602 g/mol

Boiling Point: - 586.1 °C at 760 mmHg. **[112]**

Melting point: - 141 to 144 °C. **[113]**

Solubility profile: - white to practically white, crystalline powder. Is practically odorless and has a bitter taste. Soluble in water, freely soluble in chloroform, sparingly soluble in alcohol, practically insoluble in ether**.[USP][114]**

Solubility profile: - freely soluble in chloroform, soluble in water, sparingly soluble in ethanol, practically insoluble in ether**.[IP][115]**

Mechanism of action: - Verapamil inhibits voltage-dependent calcium channels. Specifically, its effect on L-type calcium channels in the heart causes a reduction in ionotropy and chronotropy, thuis reducing heart rate and blood pressure. Verapamil's mechanism of effect in cluster headache is thought to be linked to its calcium-channel blocker effect, but which channel subtypes are involved is presently not known. **[116]**

Pharmacokinetic data

Bioavailability 35.1%

Metabolism Hepatic

Half-life 2.8-7.4 hours

Excretion Renal: 11%

Pka: - 9.04, 10.30. **[117]**

log P: - 4.6. **[118]**

Dissolution:-[119]

Verapamil hydrochloride tablet

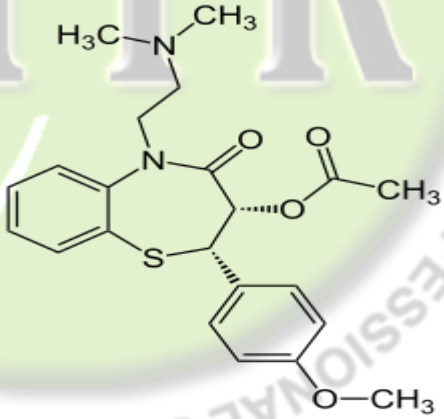
Medium: - 0.1 N Hydrochloric acid,900 ml.

Apparatus: - 2[usp]

Time: - 30 minutes.

Rpm: - 50

Diltiazem[120]



Systematic (IUPAC) name cis-(+)-[2-(2-dimethylaminoethyl)-5-(4-methoxyphenyl)-3-oxo-6-thia-2-azabicyclo[5.4.0]undeca-7,9, 11-trien-4-yl]ethanoate

Chemical data

Formula $C_{22}H_{26}N_2O_4S$

Mol. mass 414.519 g/mol

Boiling Point: - 594.4 °C at 760 mmHg. **[121]**

Melting Point: - 212°C. **[122]**

Solubility profile: - white odorless , crystalline powder or small crystals, freely soluble in chloroform, in formic acid, in methanol and in water, sparingly soluble in dehydrated alcohol, insoluble in ether. Mealt at about 210 degree with decomposition. **[USP][123]**

Solubility profile: - freely soluble in chloroform, in formic acid, in methanol and in water, sparingly soluble in ethanol ,insoluble in ether**.[IP][124]**

Mechanism of action: - Possibly by deforming the channel, inhibiting ion-control gating mechanisms, and/or interfering with the release of calcium from the sarcoplasmic reticulum, diltiazem, like verapamil, inhibits the influx of extracellular calcium across both the myocardial and vascular smooth muscle cell membranes. The resultant inhibition of the contractile processes of the myocardial smooth muscle cells leads to dilation of the coronary and systemic arteries and improved oxygen delivery to the myocardial tissue. **[125]**

Pharmacokinetic data

Bioavailability 40%

Metabolism Hepatic

Half-life 3-4.5 hours

Excretion Renal BiliaryLactic (in lactiferous females)

Pka: - 8.91, 10.10. **[126]**

logP: - 2.7272518843333335. **[125]**

Dissolution:-[127]

Dilitiazem HCL Extended release tablet

Medium: - Phosphate buffer ph 5.8,900ml.

Apparatus: - 2[usp]

Time: - 2,8,14,24 minutes.

Rpm: - 100

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