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Review Article

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PHARMACOKINETIC, SOLUBILITY AND DISSOLUTION PROFILE OF ANTI-PARKINSONISAM DRUGS.

AchhrishGoel[1]*, Shaweta Sharma[2], HimaniGoel[3],Yogesh Sharma[4]

1.*RachetPharma Ltd, Baddi, Himachal Pradesh,
2.Teerthaker Mahaveer College of Pharmacy, TMU, Moradabad
3.GRD Institute of Management, Dehradun
4.Chaudhary Devi Lal College of Pharmacy, Jagadhri

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 Antiparkinsonisam drugs at one place.

Keywords: Solubility profile, pharmacokinetic parameters, Antiparkinsonisam.

Introduction

Classification: - [1]

1. Drugs affecting brain dopaminergic system: -

(a) Dopamine precursor: - Levodopa**[2]**

(b) Peripheral decarboxylase inhibitors: - Carbidopa**[14]**, Benserazide**[27]**.

(C) Dopaminergic agonists: - Bromocriptine**[40]**, Ropinirole**[54]**, Pramiprexole**[68]**.

(d) MAO-B inhibitor: - Selegiline**[89]**.

(e) COMT inhibotors: - Entacapone**[108]**, Tolcapone**[121]**.

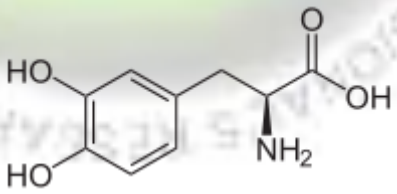
(f) Dopamine facilitator: - Amantadine**[137]**.

2. Druga affecting brain cholinergic system:

(a) Central antocholinergics: - Trihexyphenidyl**[158]**, Benzhexol, Procyclidine**[174]**, Biperiden**[201]**.

(b) Antihistaminics: - Orphenadrine**[202]**, Promethazine**[215]**.

1. Levodopa: - [2]



Systematic (IUPAC) name: - (S)-2-amino-3-(3,4-dihydroxyphenyl)propanoic acid.

Chemical data: -

Boiling Point: - 447.00 to 449.00 °C. **[3]**

Melting point : 295℃. **[4]**

Molecular formula: - C9H11NO4. **[5]**

Molecular weight: - 226.3. **[6]**

Mechanism of action: - Striatal dopamine levels in symptomatic Parkinson's disease are decreased by 60 to 80%, striatal dopaminergic neurotransmission may be enhanced by exogenous supplementation of dopamine through administration of dopamine's precursor, levodopa. A small percentage of each levodopa dose crosses the blood-brain barrier and is decarboxylated to dopamine. This newly formed dopamine then is available to stimulate dopaminergic receptors, thus compensating for the depleted supply of endogenous dopamine.**[7]**

Description: - White to off white, odourless crystalline powder. **[U.S.P][8]**

Solubility profile: - Slightly soluble in water, freely soluble in 3N hydrochloric acid and insoluble in alcohol.**[U.S.P][8]**

Pharmacokinetic data. [1]

Bioavailability: -30%.

Metabolism : - Aromatic-L-amino-acid decarboxylase.

Half-life : - 0.75–1.5 hours

Excretion: - renal 70–80%

Nature: - Hydrophillic. **[9]**

Pka: - 2.30, 8.11, and 9.92. **[10]**

pH: -3-9. **[11]**

logP: -1.8. **[7]**

Dissolution Profile: - Levodopa tablet. **[12]**

Medium: -0.1 N hydrochloric acid, 900ml

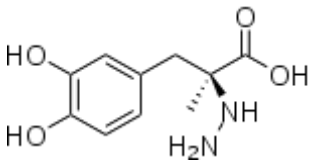
Apparatus: - 1

RPM: -100

Time: - 30

Use: -This medication is used to treat symptoms of Parkinson's disease. Eat food shortly after taking medicine unless your doctor directs you otherwise. Take this drug as directed. It may take a few weeks before the full benefits of this medication are observed. **[13]**

Carbidopa. [14]



Systematic (IUPAC) name: - 2*S*)-3-(3,4-dihydroxyphenyl)-2-hydrazino-2-methylpropanoic acid.

Chemical data: -

Boiling point: - 528.7°C at 760 mmHg. **[15]**

Melting point: - 203-205 °C. **[16]**

Molecular formula: - C10H14N2O4. **[17]**

Molecular weight: - 244.3. **[18]**

Mechanism of action: - When mixed with levodopa, carbidopa inhibits the peripheral conversion of levodopa to dopamine and the decarboxylation of oxitriptan to serotonin by aromatic L-amino acid decarboxylase. This results in increased amount of levodopa and oxitriptan available for transport to the CNS. Carbidopa also inhibits the metabolism of levodopa in the GI tract, thus, increasing the bioavailability of levodopa. **[19]**

Description: - white or off-white crystalline powder. **[20]**

Solubility profile: - [21]

Solubility profile: - [22]

Pharmacokinetic data . [14]

Protein binding: - 76%

Metabolism: - decarboxylated to dopamine in extracerebral tissues

Half-life: - 2 hours

pH: - 5.0. **[23]**

Nature: - Hydrophilic. **[24]**

Pka: - 9.29. **[19]**

Dissolution Profile: - Carbidopa tablet. **[25]**

Medium: - 0.1 N hydrochloric acid, 900ml

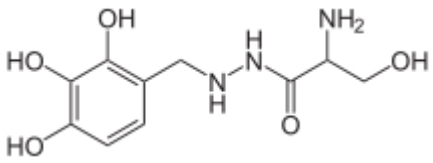
Apparatus: - 1

RPM: - 100

Time: - 30

Uses: - Carbidopa is used with levodopa or the combination levodopa/carbidopa to treat the symptoms of Parkinson's disease or Parkinson-like symptoms (e.g., shakiness, stiffness, difficulty moving). Carbidopa must be taken together with levodopa to be effective. Used alone, carbidopa has no effect on Parkinson's symptoms. It is used to improve the effect of levodopa and reduce some levodopa side effects (e.g., nausea, vomiting).Carbidopa is known as an enzyme blocker. It works by preventing the breakdown of levodopa in the bloodstream. This allows more levodopa to enter the brain, where it can decrease Parkinson's symptoms. By helping more levodopa get into the brain so that less stays in the bloodstream, carbidopa can reduce some of levodopa's side effects such as nausea. This may allow your doctor to increase your dose of levodopa more quickly to find the best dose for you. **[26]**

Benserazide. [27]



Systematic (IUPAC) name: - (*RS*)-2-amino-3-hydroxy-*N*′-(2,3,4-trihydroxybenzyl)propanehydrazide.

Chemical data: -

Boiling point: - 574.2 °C at 760 mmHg. **[28]**

Melting point: - 146-148 °C. **[29]**

Molecular weight: - 257.2432. **[30]**

Molecular formula: - C10H15N3O5.HCl. **[31]**

Mechanism of Action: - It is a peripheral dopa-decarboxylase inhibitor with little or no pharmacological activity when used alone. It inhibits peripheral decarboxylation of L-dopa to dopamine, thus effective brain concentrations of dopamine are produced with lower doses of L-dopa. It is used as an adjunct to levodopa in the treatment of parkinsonism. **[32]**

Description: - White or similar to white crystalline powder. **[33]**

Solubility profile: - freely *soluble in water*, very slightly *soluble* in ethanol, practically *insoluble* in acetone. **[34]**

Pharmacokinetic data

Excretion: - Renal and fecal

Elimination Half life: - 1.5hr.**[35]**

Protein binding: - Less protein binding due to less half life. **[36]**

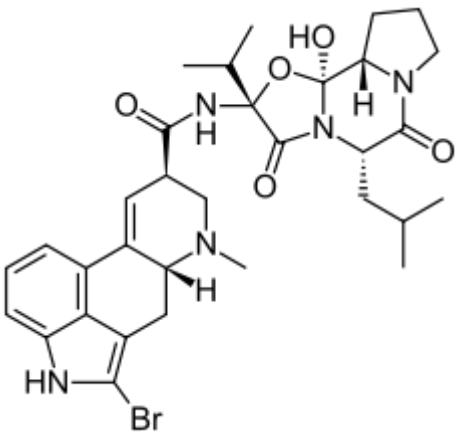
pH: - 4.0-5.0. **[37]**

Log P: - 5.3. **[38]**

Nature: - Acidic. **[39]**

Dissolution profile: - Not available.

Bromocriptine.[40]



Systematic (IUPAC) name:- (5′α)-2-bromo-12′-hydroxy-5′-(2-methylpropyl)-3′,6′,18-trioxo-2′-(propan-2-yl)ergotaman.

Chemical Data: -

Boiling point: - 608.7 °C at 760 mmHg. **[41]**

Melting point: - 192-196 °C. **[42]**

Molecular formula: - C32H40BrN5O5. **[43]**

Molecular weight : - 654.594482. **[44]**

Mechanism of action: - The dopamine D_2 receptor is a 7-transmembrane G-protein coupled receptor associated with G_i proteins. In lactotrophs, stimulation of dopamine D_2 receptor causes inhibition of adenylyl cyclase, which decreases intracellular cAMP concentrations and blocks IP3-dependent release of Ca^{2+} from intracellular stores. Decreases in intracellular calcium levels may also be brought about via inhibition of calcium influx through voltage-gated calcium channels, rather than via inhibition of adenylyl cyclase. Additionally, receptor activation blocks phosphorylation of p42/p44 MAPK and decreases MAPK/ERK kinase phosphorylation. Inhibition of MAPK appears to be mediated by c-Raf and B-Raf-dependent inhibition of MAPK/ERK kinase. Dopamine-stimulated growth hormone release from the pituitary gland is mediated by a decrease in intracellular calcium influx through voltage-gated calcium channels rather than via adenylyl cyclase inhibition. Stimulation of dopamine D_2 receptors in the nigrostriatal pathway leads to improvements in coordinated muscle activity in those with movement disorders. **[45]**

Description: - White or slightly coloured fine crystalline powder, odorless or having a weak chracterstic odor. **[46]**

Solubility profile: - sparingly soluble in ethanol (95), very slightly soluble in acetic anhydride, in dichloromethane and in chloroform, and practically insoluble in water. **[47]**

Pharmacokinetic data

Bioavailability : - 28% of oral dose absorbed

Half-life: - 12-14 hours

Excretion: - 85% bile (faeces)

pH: -5.0–5.5. **[48]**

Pka: - 4.9. **[49]**

Log P: - 6.62. **[50]**

Nature: - acidic. **[51]**

Dissolution Profile: - Bronocriptine mesylate tablet. **[52]**

Medium: - 0.1 N hydrochloric acid, 500ml

Apparatus: - 1

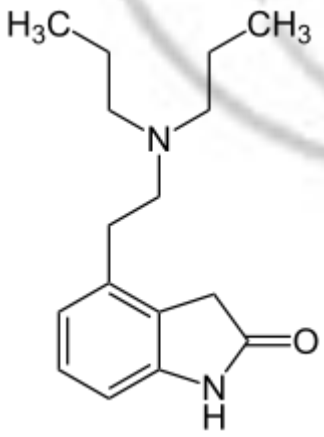
RPM: - 120

Time: - 60

Uses: - This medication is used alone or with other medications (e.g., levodopa) to treat Parkinson's disease. It can improve your ability to move and decrease shakiness (tremor), stiffness, slowed movement, and unsteadiness. It may also decrease the number of episodes of not being able to move ("on-off

syndrome").Bromocriptine is also used to treat hormonal problems caused by high levels of a certain chemical made by the body (prolactin). Such problems include unwanted breast milk, missed/stopped periods, difficulty becoming pregnant, decreased sperm production, and decreased sexual ability. Because of possible serious side effects (e.g., high blood pressure, seizure, heart attack, stroke), bromocriptine is not recommended for stopping unwanted breast milk after pregnancy, miscarriage, or abortion.This medication is also used alone or with other treatments to lower high growth hormone levels (acromegaly). Bromocriptine is also used to treat prolactin-secreting tumors. It may be used to reduce the tumor size before surgery or to control symptoms until other treatments start working.Bromocriptine is an ergot medication that works by helping to restore the balance of a certain natural substance (dopamine) in the brain. It also prevents the release of certain hormones (growth hormone, prolactin). Bromocriptine can lower these hormone levels, but it does not cure the causes of the increased levels. **[53]**

Ropinirole. **[54]**



Systematic (IUPAC) name: - 4-[2-(dipropylamino)ethyl]-1,3-dihydro-2*H*-indol-2-one.

CAS no: - 91374-21-9. **[55]**

Chemical data: -

Boiling Point: - 410.5 °C at 760 mmHg. **[56]**

Melting Point: - 243-250 C. **[57]**

Molecular weight: - 296.84. **[58]**

Molecular Formula: - C16H24N2O.HCl. **[59]**

Mechanism of action: -Ropinirole binds the dopamine receptors D_3 and D_2. Although the precise mechanism of action of ropinirole as a treatment for Parkinson's disease is unknown, it is believed to be related to its ability to stimulate these receptors in the striatum. This conclusion is supported by electrophysiologic studies in animals that have demonstrated that ropinirole influences striatal neuronal firing rates via activation of dopamine receptors in the striatum and the substantia nigra, the site of neurons that send projections to the striatum. **[60]**

Description: -light yellow crystallinity powder**. [61]**

Solubility: - Soluble in water and methanol, very slightly soluble in ethyl alcohol. **[62]**

Pharmacokinetic data

Bioavailability : - 50%

Metabolism: - Hepatic

Half-life: - 5-6 hours

pH: - 9.0-9.2. **[63]**

Pka: - 9.5. **[64]**

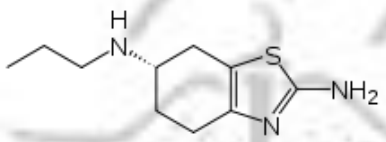
Log P: - 3.19. **[65]**

Nature: - Hydrophillic. **[66]**

Dissolution profile: - Not available.

Uses: -This medication is used alone or with other medications to treat Parkinson's disease. It can improve your ability to move and decrease shakiness (tremor), stiffness, slowed movement, and unsteadiness. It may also decrease the number of episodes of not being able to move ("on-off syndrome").Ropinirole is also used to treat restless legs syndrome (RLS). It may improve your sleep by decreasing the urge to move your legs and decreasing uncomfortable/unpleasant feelings in the legs.This medication works by helping to restore the balance of a certain natural substance (dopamine) in the brain **[67]**

Pramipexole. [68]



Systematic (IUPAC) name: - (*S*)-N^6-propyl-4,5,6,7-tetrahydro-1,3-benzothiazole-2,6-diamine.

CAS No: - 104632-26-0. **[69]**

Chemical data: -

Boiling point: - 378 ºC. **[70]**

Melting point: - 127-128 °C. **[71]**

Molecular formula: - C10H17N3S. **[72]**

Molecular weight: - 211.113998. **[73]**

Mechanism of action: - The precise mechanism of action of Pramipexole as a treatment for Parkinson's disease is unknown, although it is believed to be related to its ability to stimulate dopamine receptors in the striatum.**[74]**

Description: - white to off-white powder. **[75]**

Solubility profile: - freely *soluble* in *water* in a pH- independent way, *soluble* in methanol, slightly soluble in ethanol. **[76]**

Pharmacokinetic data

Bioavailability: ->90%

Protein binding: - 15%

Half-life: - 8-12 hours

Excretion: - Urine (90%), Feces (2%)

pH: -2.8 to 3.4. **[77]**

Pka: - 7.2. **[78]**

Log P: - 0.87. **[79]**

Nature: - Hydrophilic**. [80]**

Dose: - 125 micrograms daily. **[81]**

Dissolution Profile: - Pramipexole hydrochloride extended release tablet. **[82]**

Medium: - 0.1 N hydrochloric acid, 900ml

Apparatus: - 1

RPM: - 100

Time: - 30

Uses: Pramipexole is used alone or with other medications to treat Parkinson's disease. It can improve your ability to move and decrease shakiness (tremor), stiffness, slowed movement, and unsteadiness. It may also decrease the number of episodes of not being able to move ("on-off syndrome").This medication is also used to treat a certain medical condition (restless legs syndrome - RLS) that causes an unusual urge to move the legs. Symptoms usually occur at night along with uncomfortable/unpleasant feelings in the legs. This medication can decrease these symptoms and thereby improve sleep. Pramipexole is a dopamine agonist that works by helping to restore the balance of a certain natural substance (dopamine) in the brain.**[83]**

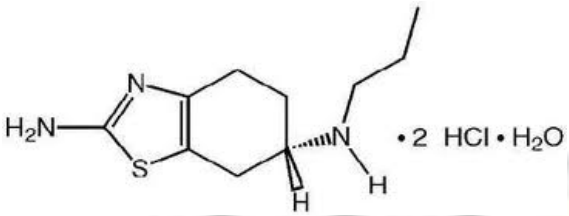
Pramipexole dihydrochloride

CAS No: - 104632-25-9. **[84]**

Molecular formula: - C10H17N3S•2HCl•H2O. **[85]**

Molecular weight: -302.27**. [86]**

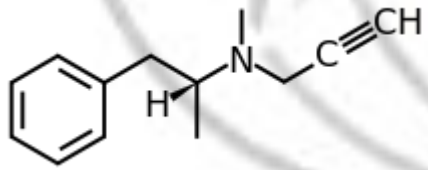
Structure: -



IUPAC Name: - (S)-2-Amino-4,5,6,7-tetrahydro-6-(propylamino)benzothiazole dihydrochloride**. [87]**

Solubility profile: - *Pramipexole dihydrochloride* is more than 20% *soluble* in water, about 8% in methanol, about 0.5% in ethanol, and practically insoluble in dichloromethane **[88]**

Selegiline. [89]



Systematic (IUPAC) name: - (*R*)-*N*-methyl-*N*-(1-phenylpropan-2-yl)prop-1-yn-3-amine

CAS No: -14611-51-9. **[90]**

Chemical data: -

Boiling point: - 272.5 °C. **[91]**

Melting point: - 141-142 ^{o}C. **[92]**

Mlecular formula: - C13H17N. **[93]**

Molecular weight: - 187.281 g/mol. **[94]**

Mechanism of action: - Although the mechanisms for selegiline's beneficial action in the treatment of Parkinson's disease are not fully understood, the selective, irreversible inhibition of monoamine oxidase type B (MAO-B) is thought to be of primary importance. MAO-B is involved in the oxidative deamination of dopamine in the brain. Selegiline binds to MAO-B within the nigrostriatal pathways in the central nervous system, thus blocking microsomal metabolism of dopamine and enhancing the dopaminergic activity in the substantial nigra. Selegiline may also increase dopaminergic activity through mechanisms other than inhibition of MAO-B. At higher doses, selegiline can also inhibit monozmine oxidase type A (MAO-A), allowing it to be used for the treatment of depression. **[95]**

Description: - white to near white crystalline powder. **[96]**

Solubility profile: - Freely soluble in water, in cloroform and in methanol. **[97][USP]**

Pharmacokinetic data

Bioavailability: - 4.4% (oral, fasted), 20% (oral, after food), 18% (patch)

Protein binding: - 90%

Metabolism: - liver

Half-life: - 1.5 hours (oral, single dose), 9 hours (oral, chronic)

Excretion: - urine

pH: -7.4. **[98]**

Pka: -6.88. **[99]**

Log P: -2.9. **[100]**

Dissolution Profile: - Selegiline hcl tablet. **[101]**

Medium: - water, 500ml

Apparatus: - 1

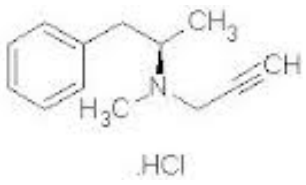
RPM: - 50

Time: - 20

USES: This medication is used to treat movement disorders caused by Parkinson's disease. It does not cure Parkinson's disease, but it may improve shakiness (tremor), muscle stiffness, loss of normal movement as your dose of other Parkinson's medication wears off (end-of-dose failure), and sudden switching between normal movement and stiffness ("on-off" problems). It may improve your range of motion and ability to walk, dress, and exercise. Selegiline is usually used in combination with other medicines (e.g., levodopa, carbidopa).Selegiline is an enzyme blocker (MAO inhibitor) that works by slowing the breakdown of certain natural substances in the brain (neurotransmitters such as dopamine, norepinephrine, and serotonin). **[102]**

Dose: - 5-20 mg daily. **[103]**

Selegiline hydrochloride. [104]

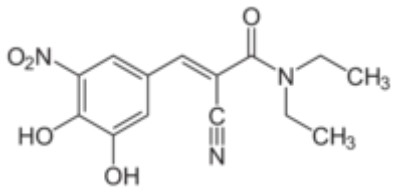


CAS No: - 14611-52-0. **[105]**

Molecular formula: - C13H17N• HCl. **[106]**

Molecular Weight: - 223.77. **[107]**

Entacapone. [108]



Systematic (IUPAC) name: - (2*E*)-2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)-*N*,*N*-diethylprop-2-enamide.

CAS NO: - 130929-57-6. **[109]**

Chemical data: -

Boiling point: - 526.6 ^{o}C. **[110]**

Melting point: - 162-163 °C. **[111]**

Molecular formula: - C14H15N3O5. **[112]**

Moleular weight: - 305.29.**[113]**

Mechanism of action: - The mechanism of action of entacapone is believed to be through its ability to inhibit COMT in peripheral tissues, altering the plasma pharmacokinetics of levodopa. When entacapone is given in conjunction with levodopa and an aromatic amino acid decarboxylase inhibitor, such as carbidopa, plasma levels of levodopa are greater and more sustained than after administration of levodopa and an aromatic amino acid decarboxylase inhibitor alone. It is believed that at a given frequency of levodopa administration, these more sustained plasma levels of levodopa result in more constant dopaminergic stimulation in the brain, leading to a greater reduction in the manifestations of parkinsonian syndrome. **[114]**

Descriotion: - yellow or greenish yellow crystalline powder. **[115]**

Solubility profile: - practically insoluble in water. **[116]**

Pharmacokinetic data

Bioavailability: - 35%

Protein binding: - 98% (binds to serum albumin)

Metabolism: - Hepatic

Half-life: - 0.4-0.7 hour

Excretion: - 90% feces, 10% urine

pH: - 5.0 to 7.4. **[117]**

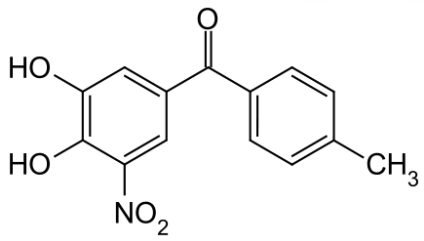
Pka: - 4.5. **[118]**

LogP: - 2.8. **[114]**

USES: This medication is used with other medications (levodopa/carbidopa) to treat Parkinson's disease. Entacapone belongs to a class of drugs known as COMT inhibitors. Many people taking levodopa for Parkinson's have problems with the effects of the levodopa wearing off between scheduled doses, causing symptoms to return or worsen. Entacapone blocks a certain natural substance (COMT enzyme) that breaks down the levodopa in the body. This effect allows the levodopa to last longer in the system so that it doesn't wear off before the next dose. **[119]**

Dose: -50-800 mg. **[120]**

Tolcapone [121]



Systematic (IUPAC) name: - (3,4-dihydroxy-5-nitrophenyl)(4-methylphenyl)methanone.

CAS NO: -134308-13-7. **[122]**

Chemical data: -

Molecular formula: - C14H11NO5. **[123]**

Molecular weight: - 273.25. **[124]**

Boiling point: - 485.6 °C at 760 mmHg. **[125]**

Melting point: - 126-128^{0}C. **[126]**

Mechanism of action: - The precise mechanism of action of tolcapone is unknown, but it is believed to be related to its ability to inhibit COMT and alter the plasma pharmacokinetics of levodopa, resulting in an increase in plasma levodopa concentrations. The inhibition of COMT also causes a reduction in circulating 3-OMD as a result of decreased peripheral metabolism of levodopa. This may lead to an increase distribution of levodopa into the CNS through the reduction of its competitive substrate, 3-OMD, for transport mechanisms. Sustained levodopa concentrations presumably result in more consistent dopaminergic stimulation, resulting in greater reduction in the manifestations of parkinsonian syndrome. **[127]**

Description: - Yellow to red-brown powder. **[128]**

Solubility profile: - Freely soluble in acetone and in tetrahydrofuran, soluble in methanol and in ethyl acetate, sparingly soluble in chloroform and in dichloromethane, insoluble in water and in n-hexane. **[USP][129]**

Pharmacokinetic data

Bioavailability: - 65%

Protein binding: ->99.9%

Half-life: - 2-3.5 hours

pH range: -5.0 to 7.4. **[130]**

Pka: - 10.8. **[131]**

Log P: - 2.6. **[132]**

Nature: - Hydrophobic. **[133]**

Dissolution Profile: - Tolcapone tablet. **[134]**

Medium: - ph 6.8 phosphate buffer containing 1% of sodium laurayl sulphate, 900ml

Apparatus: - 2

RPM: - 75

Time: - 30

Use & Warning:-Tolcapone has caused a severe (sometimes fatal) liver problem (liver failure). Tolcapone should not be used if you have even mild liver disease. You should only use tolcapone if you are experiencing problems with your levodopa wearing off between doses. If you show no benefit from tolcapone after 3 weeks of using it, your doctor may choose to stop it.

Before and during treatment with tolcapone, you will have certain blood tests (liver function tests) every few weeks to monitor for liver problems. Keep all medical and lab test appointments. Tell your doctor immediately if you experience symptoms of liver problems (such as persistent nausea/vomiting, abdominal pain, dark urine, severe tiredness, loss of appetite, itchiness). If you experience liver problems from taking tolcapone, you should not take it again. **[135]**

Dose range: -50 mg to 400 mg. **[136]**

Amantadine. [137]

Systematic (IUPAC) name: - adamantan-1-amine.

CAS NO: - 768-94-5. **[138]**

Chemical data: -

Molecular formula: - C10H17N. **[139]**

Molecular weight: - 151.28. **[140]**

Boiling point: - 225.7°C at 760 mmHg. **[141]**

Melting point: - 206-208°C. **[142]**

Mechanism of action: - The mechanism of its antiparkinsonic effect is not fully understood, but it appears to be releasing dopamine from the nerve endings of the brain cells, together with stimulation of norepinephrine response. It also has NMDA receptor antagonistic effects. The antiviral mechanism seems to be unrelated. The drug interferes with a viral protein, M2 (an ion channel), which is needed for the viral particle to become "uncoated" once it is taken inside the cell by endocytosis. **[143]**

Pharmacokinetic data

Bioavailability: - well absorbed

Protein binding: - approx 67%

Metabolism: - negligible

Half-life: - 10–14 hours, in renal impairment up to 7–10 days

Excretion: - renal

pH: - 4.8 to 5.4. **[144]**

Pka: - 9.0. **[145]**

Log P: -1.903. **[146]**

Nature: -Amphiphile. **[147]**

Description: - white or nearly white crystalline powder. **[148]**

Amantadine hydrochloride

Solubility profile: - freely soluble in water and in ethanol, soluble in chloroform, practically insoluble in ether. **[IP][149]**

Solubility profile: - Freely soluble in water, soluble in alcohol and in chloroform. **[USP][150]**

Dissolution Profile: - Amantadine capsule. **[151]**

Medium: - water, 900ml

Apparatus: - 1

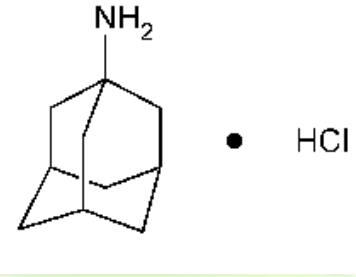
RPM: - 100

Time: - 45

Uses: - Amantadine is used to prevent or treat a certain type of flu (influenza A). If you have been infected with the flu, this medication may help make your symptoms less severe and shorten the time it will take you to get better. Taking amantadine if you have been or will be exposed to the flu may help to prevent you from getting the flu. This medication is an antiviral that is believed to work by stopping growth of the flu virus. This medication is not a vaccine. To increase the chance that you will not get the flu, it is important to get a flu shot once a year at the beginning of every flu season, if possible.Based on the recommendation from the Centers for Disease Control (CDC) in the US, amantadine should not be used to treat or prevent influenza A because the current influenza A virus in the United States and Canada is resistant to this medication. For more details, talk to your doctor or pharmacist.Amantadine is also used to treat Parkinson's disease, as well as side effects caused by drugs (e.g., drug-induced extrapyramidal symptoms), chemicals, other medical conditions. In these cases, this medication may help to improve your range of motion and ability to exercise. For the treatment of these conditions, amantadine is believed to work by restoring the balance of natural chemicals (neurotransmitters) in the brain. **[152]**

Dose range: - 50 to 300 mg. **[153]**

Amantadine hydrochloride. [154]

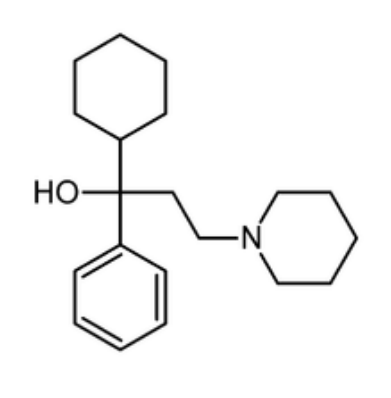


Molecular formula: - C10H17N · Hcl. **[155]**

Molecular weight: - 187.71. **[156]**

CAS NO: - 665-66-7. **[157]**

Trihexyphenidyl. [158]



Systematic (IUPAC) name: - (*RS*)-1-cyclohexyl-1-phenyl-3-(1-piperidyl)propan-1-ol.

CAS NO: - 52-49-3. **[159]**

Chemical data: -

Molecular formula: - C20H31NO. **[160]**

Molecular weight: - 301.466 g/mol. **[161]**

Boiling point: - 447.9Cat760mmHg. **[162]**

Melting point: - 258.5 C. **[163]**

Mechanism of action: - Trihexyphenidyl is a selective M1 muscarinic acetylcholine receptor antagonist. It is able to discriminate between the M1 (cortical or neuronal) and the peripheral muscarinic subtypes (cardiac and glandular). Trihexyphenidyl partially blocks cholinergic activity in the CNS, which is responsible for the symptoms of Parkinson's disease. It is also thought to increase the availability of dopamine, a brain chemical that is critical in the initiation and smooth control of voluntary muscle movement. **[164]**

Description: - white or slightly off white, crystalline powder. **[165]**

Solubility profile: - slightly soluble in *water* and soluble in methanol. **[166]**

Pharmacokinetic data

Half-life: - 3.3-4.1 hours

Absorption: - Orally, absorbed in GIT. **[167]**

Distribution: - Brain, heart & lung. **[168]**

pH range:-2.0 and 3.0. **[169]**

***pKa*: -** 8.7. **[170]**

Log P: - 4.5[164]

Nature: - Hydrophillic. **[171]**

Dissolution Profile: -Trihexyphenidyl tablet. **[172]**

Medium: - pH 4.8 acetate buffer

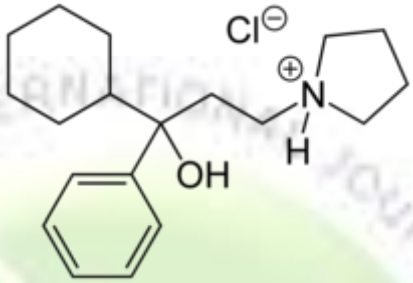
Apparatus: - 1

RPM: - 100

Time: - 45

Use: - Trihexyphenidyl HCl tablets are indicated as an adjunct in the treatment of all forms of parkinsonism (postencephalitic, arteriosclerotic, and idiopathic). It is often useful as adjuvant therapy when treating these forms of parkinsonism with levodopa. Additionally, it is indicated for the control of extrapyramidal disorders caused by central nervous system drugs such as the dibenzoxazepines, phenothiazines, thioxanthenes, and butyrophenones. **[173]**

Procyclidine. [174]



Systematic (IUPAC) name: - 1-cyclohexyl-1-phenyl-3-pyrrolidin-1-yl-propan-1-ol hydrochloride.

CAS NO: - 77-37-2. **[175]**

Chemical data: -

Molecular formula:- C19H29NO. **[176]**

Molecular weight: - 287.43966. **[177]**

Boiling point: - 433.5 °C. **[178]**

Melting point: - 86.00 °C. **[179]**

Mechanism of action: - The mechanism of action is unknown. It is thought that Procyclidine acts by blocking central cholinergic receptors, and thus balancing cholinergic and dopaminergic activity in the basal ganglia. Many of its effects are due to its pharmacologic similarities with atropine. Procyclidine exerts an antispasmodic effect on smooth muscle, and may produce mydriasis and reduction in salivation. **[180]**

Description: - White crystalline *powder*. ***[181]***

Solubility: - Sparingly *soluble* in *water*, *soluble* in ethanol (96%) practically *soluble* in acetone and ether. **[182]**

Pharmacokinetic data

Protein binding: - ~100%-albumin

Half-life: - ~12 h

pH: - 5.0 to 6.5**. [183]**

Pka: - 10.7. **[184]**

Log P: - 4.37. **[185]**

Dissolution Profile: -Procyclidine hcl tablet. **[186]**

Medium: - water, 900ml

Apparatus: - 2

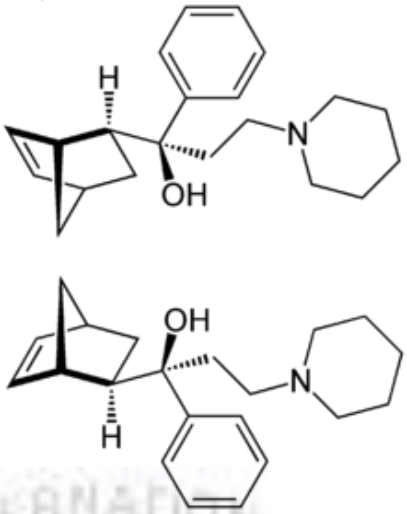
RPM: - 50

Time: - 45

Use: - Procyclidine is used to treat symptoms of Parkinson's disease or involuntary movements due to the side effects of certain psychiatric drugs (antipsychotics such as chlorpromazine/haloperidol). Procyclidine belongs to a class of medication called anticholinergics that work by blocking a certain natural substance (acetylcholine). This helps decrease muscle stiffness, sweating, and the production of saliva, and helps improve walking ability in people with Parkinson's disease.

Anticholinergics can stop severe muscle spasms of the back, neck, and eyes that are sometimes caused by psychiatric drugs. It can also decrease other side effects such as muscle stiffness/rigidity (extrapyramidal signs-EPS). It is not helpful in treating movement problems caused by tardive dyskinesia and may worsen them. **[187]**

Biperidin. [188]



Systematic (IUPAC) name: - (1*RS*,2*SR*,4*RS*)-1-(bicyclo[2.2.1]hept-5-en-2-yl)-1-phenyl-3-(piperidin- 1-yl)propan-1-ol.

CAS No:- 514-65-8. **[189]**

Chemical data: -

Molecular formula: - C21H29NO. **[190]**

Molecular weight: - 312. **[191]**

Boiling point: -142 ºC. **[192]**

Melting point: - 42-47 ºC. **[192]**

Mechanism of action: - Parkinsonism is thought to result from an imbalance between the excitatory (cholinergic) and inhibitory (dopaminergic) systems in the corpus striatum. The mechanism of action of centrally active anticholinergic drugs such as biperiden is considered to relate to competitive antagonism of acetylcholine at cholinergic receptors in the corpus striatum, which then restores the balance. **[193]**

Description:- white, practically odorless, crystalline powder.**[194]**

Solubility profile: - Slightly soluble in water and in ethanol. Very slightly soluble in dichloromethane. Practically insoluble in ether. **[IP][195]**

Solubility profile: - Slightly soluble in water, in ether, in alcohol and in chloroform, sparingly soluble in methanol. **[USP][196]**

Pharmacokinetic data

Bioavailability: - 33 ± 5% (oral)

Protein binding: - 60%

Metabolism: - Hepatic hydroxylation

Half-life: - 18 to 24 hours

Excretion: - Renal

pH range: -2.0-7.0. **[197]**

Pka: - 4.90. **[198]**

LogP: - 3.85. **[199]**

Dissolution Profile: -Biperidin hcl tablet. **[200]**

Medium: -0.1 N Hydrochloric acid, 900ml

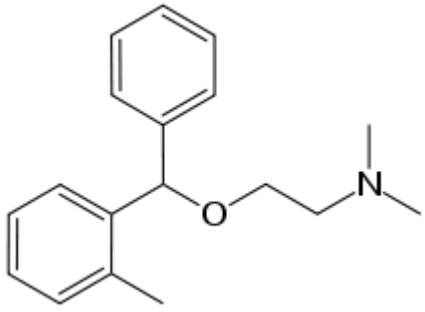
Apparatus: - 2

RPM: - 50

Time: - 45

Dose: - 12.5 to 50 mg daily. **[201]**

Orphenadrine. [202]



Systematic (IUPAC) name: - *N*,*N*-dimethyl-2-[(2-methylphenyl)- phenyl-methoxy]-ethanamine.

CAS No: - 83-98-7. **[203]**

Chemical data

Molecular formula: - C18H23NO. **[204]**

Molecular weight: - 305.80. **[205]**

Boiling point: - 363 °C at 760 mmHg. **[206]**

Melting point: - 132-1340°C. **[207]**

Mechanism of action: - Orphenadrine binds and inhibits both histamine H1 receptors and NMDA receptors. It restores the motor disturbances induced by neuroleptics, in particular the hyperkinesia. The dopamine deficiency in the striatum increases the stimulating effects of the cholinergic system. This stimulation is counteracted by the anticholinergic effect of orphenadrine. It may have a relaxing effect on skeletal muscle spasms and it has a mood elevating effect. **[208]**

Description: - white, crystalline *powder* having a bitter taste. **[209]**

Solubility: - It is sparingly *soluble* in *water*, slightly *soluble* in alcohol. **[210]**

Pharmacokinetic data

Bioavailability: - 90%

Protein binding: -95%

Metabolism: -Hepatic demethylation

Half-life: -13-20 hours

Excretion: -Renal and biliary

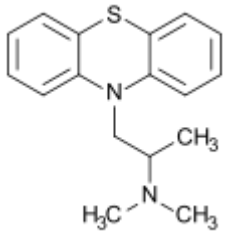
PH range: -4-7. **[211]**

Pka: - 8.71. **[212]**

Log P: - 3.6. **[213]**

Dose range: - 150–300 mg. **[214]**

Promethazine. [215]



Systematic (IUPAC) name: - (*RS*)-*N*,*N*-dimethyl-1-(10*H*-phenothiazin-10-yl)propan-2-amine.

CAS no: - 58-33-3. **[216]**

Chemical data: -

Molecular formula: - C17 H20 N2 S.Hcl**[217]**

Molecular weight: - 320.88. **[218]**

Boiling point: - 403.7 °C at 760 mmHg. **[219]**

Melting point: - 230-232 ºC. **[220]**

Mechanism of action: - Like other H1-antagonists, promethazine competes with free histamine for binding at H1-receptor sites in the GI tract, uterus, large blood vessels, and bronchial muscle. The relief of nausea appears to be related to central anticholinergic actions and may implicate activity on the medullary chemoreceptor trigger zone. **[221]**

Description: - white to faint yellow, practically odorless, crystalline *powder. [222]*

Solubility profile: - Very soluble in water, freely soluble in chloroform and in ethanol, practically insoluble in ether. **[IP][223]**

Solubility profile: - White to faint yellow, practically odorless, crystalline powder slowly oxidizes and aquire a blue color on prolonged exposure to air. **[USP][224]**

Pharmacokinetic data

Bioavailability: - 88% absorbed but after first-pass metabolism reduced to 25% absolute bioavailability.

Protein binding: - 93%

Metabolism: - Hepatic glucuronidation and sulfoxidation

Half-life: - 16-19 hours

Excretion: -Renal and biliary

Ph range: - 4.0 to 5.5. **[225]**

Log P: - 4.78. **[226]**

Pka: - 9.1. **[227]**

Dissolution Profile: -Promethazine Hcl tablet. **[228]**

Medium: - 0.1 N Hydrochloric acid, 900ml

Apparatus: - 1

RPM: - 100

Time: - 45

Dose: - 6.25 to 12.5 mg 3 times/day. **[229]**

USE: - Promethazine is used to treat allergy symptoms such as itching, runny nose, sneezing, itchy or watery eyes, hives, and itchy skin rashes **[230]**

Referances

1. Tripathi et al "Text Book of pharmacology, 4th Edition. Page no-414
2. http://en.wikipedia.org/wiki/L-DOPA
3. http://www.thegoodscentscompany.com/data/rw1253531.html
4. http://zelang.encphi.cn/product/13619/CAS+59927+Levodopa+(Mucuna+pruriens+extract.html
5. http://www.inchem.org/documents/pims/pharm/levedopa.htm

6. http://www.chemspider.com/Chemical-Structure.5824.html
7. http://www.drugbank.ca/drugs/DB01235
8. United state pharmacopeia 32. 2009, volume1, Page no.914
9. http://www.nature.com/nrn/journal/v2/n8/abs/nrn0801_577a.html
10. http://www.ncbi.nlm.nih.gov/pubmed/15352719
11. http://www.faqs.org/patents/app/20080255235
12. http://www.pharmacopeia.cn/v29240/usp29nf24s0_m44760.html
13. http://www.medicinenet.com/levodopa-oral/article.htm
14. http://en.wikipedia.org/wiki/Carbidopa
15. http://www1.chemnet.com/sell/chemdetail/2925221/Carbidopa.html
16. http://www.scbt.com/sv/datasheet-200749-s--carbidopa.html
17. http://www.chemspider.com/Chemical-Structure.31640.html
18. http://www.rxlist.com/sinemet-drug.htm
19. http://www.drugbank.ca/drugs/DB00190
20. http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=83379
21. Indian pharmacopeia 2007, volume1, Page no.146
22. United state pharmacopeia 32. 2009, volume1, Page no.897
23. http://connection.ebscohost.com/c/articles/75238680/electroanalytical-characterisation-dopa-decarboxylase-inhibitors-carbidopa-benserazide-multiwalled-carbon-nanotube-poly-nile-blue-a-modified-glassy-carbon-electrodes
24. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2778405/
25. http://www.pharmacopeia.cn/v29240/usp29nf24s0_m12870.html
26. http://www.medicinenet.com/carbidopa-oral/article.htm
27. http://en.wikipedia.org/wiki/Benserazide
28. http://www.scbt.com/datasheet-200723-benserazide-hcl-ro-4-4602.html
29. http://www.chemblink.com/products/14919-77-8.htm
30. http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=2327
31. http://www.lookchem.com/cas-149/14919-77-8.html
32. http://www.mims.com/India/drug/info/benserazide/?type=full&mtype=generic#Actions
33. http://www.tradesparq.com/products/833527/Benserazide-Hydrochloride-manufacturers
34. EUROPEAN PHARMACOPOEIA. 7th edition, Page no.1067
35. http://www.mims.com/Philippines/drug/info/benserazide%20%2B%20levodopa/?q=isoniazid&type=full&mtype=generic
36. http://www.chemspider.com/Chemical-Structure.2237.html
37. http://www.scielo.br/scielo.php?pid=S0103-50532010000800024&script=sci_arttext
38. http://books.google.co.in/books?id=413qJVovODcC&pg=PA30&lpg=PA30&dq=log+p+of+benserazide&source=bl&ots=FeeO_Bgkax&sig=RSMsk5b49m9KZiodouBD3kHH3p8&hl=en&sa=X&ei=RywCUZu3NM7-rAeN8oHQDQ&ved=0CGEQ6AEwCTgU#v=onepage&q=log%20p%20of%20benserazide&f=false
39. http://www.eje-online.org/content/91/3/410.abstract
40. http://en.wikipedia.org/wiki/Bromocriptine
41. http://www.lookchem.com/Bromocriptine/
42. http://www.scbt.com/datasheet-200395-bromocriptine-mesylate.html
43. http://www.sigmaaldrich.com/catalog/product/sigma/b2134?lang=en&region=IN
44. http://www.chemspider.com/Chemical-Structure.28858.html

45. http://www.drugbank.ca/drugs/DB01200
46. United state pharmacopeia 32. 2009, volume1, Page no.895
47. http://www.sinoapi.com/Pharmacopoeia/jp15/JP22260-51-1.pdf
48. http://content.karger.com/ProdukteDB/produkte.asp?Doi=136814
49. http://druginfosys.com/Drug.aspx?drugCode=104&drugName=Bromocriptine%20(Mesylate)&type=0
50. http://chrom.tutms.tut.ac.jp/JINNO/DRUGDATA/61bromocriptine.html
51. http://www.soulcysters.net/showthread.php/31443-Vitex-and-the-effects-of-taking-bromocriptine-for-high-prolactin-levels
52. http://www.pharmacopeia.cn/v29240/usp29nf24s0_m10260.html
53. http://www.medicinenet.com/bromocriptine-oral/article.htm
54. http://en.wikipedia.org/wiki/Ropinirole
55. http://www.chemindustry.com/chemicals/598672.html
56. http://www.lookchem.com/Ropinirole/
57. http://www.t3db.org/toxins/T3D2731
58. http://www.rxlist.com/requip-drug.htm
59. http://www.chemblink.com/products/91374-20-8.htm
60. http://www.drugbank.ca/drugs/DB00268
61. http://www.tradeindia.com/fp547604/Ropinirole-Hydrochloride.html
62. http://www.mhra.gov.uk/home/groups/par/documents/websiteresources/con111727.pdf
63. http://www.google.com/patents/EP2513055A1?cl=en
64. http://proj3.sinica.edu.tw/~chem/servxx6/files/paper_13432_1278666133.pdf
65. http://www.lookchem.com/Ropinirole-hydrochloride/
66. http://www.google.com/patents/EP1272167B1?cl=en
67. http://www.medicinenet.com/ropinirole-oral/article.htm
68. http://en.wikipedia.org/wiki/Pramipexole
69. http://www.sinoapi.com/product-view.asp?cas=104632-26-0
70. http://www.guidechem.com/dictionary/de/191217-81-9.html
71. http://www.scbt.com/datasheet-358729.html
72. http://www.chemblink.com/products/104632-26-0.htm
73. http://www.chemspider.com/Chemical-Structure.54002.html
74. http://www.drugbank.ca/drugs/DB00413
75. http://www.healthmash.com/health/pramipexole.html
76. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000133/WC500049949.pdf
77. http://pelagiaresearchlibrary.com/der-pharmacia-sinica/vol2-iss4/DPS-2011-2-4-125-135.pdf
78. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/002291/WC500116760.pdf
79. http://mtnviewfarm.net/drugs-poisons-1367.html
80. *www.ijprs.com/download.php?file=1340800366.pdf*
81. http://www.nps.org.au/publications/health-professional/nps-radar/2009/april-2009/pramipexole
82. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM220199.pdf
83. http://www.medicinenet.com/pramipexole-oral/article.htm
84. http://www.chemicalbook.com/ChemicalProductProperty_EN_CB6291554.htm
85. http://www.rxlist.com/mirapex-drug.htm
86. http://mtnviewfarm.net/drugs-poisons-1367.html
87. http://www.chemblink.com/products/104632-25-9.htm
88. http://www.rxlist.com/mirapex-er-drug.htm

89. http://en.wikipedia.org/wiki/Selegiline
90. http://acccorporation.com/API0009080.aspx
91. http://www.lookchem.com/cas-146/14611-52-0.html
92. http://pharmacycode.com/Selegiline_Hcl.html
93. http://www.erowid.org/smarts/selegiline/selegiline_chemistry.shtml
94. http://pharmacycode.com/Novo-Selegiline.html
95. http://www.drugbank.ca/drugs/DB01037
96. http://www.druglib.com/druginfo/selegiline/description_pharmacology/
97. United state pharmacopeia 32. 2009, volume1, Page no.930
98. http://jpet.aspetjournals.org/content/324/3/992.full
99. http://druginfosys.com/Drug.aspx?drugCode=1007&drugName=Selegiline%20%28HCl%29&type=0
100. http://sitem.herts.ac.uk/aeru/vsdb/Reports/1868.htm
101. http://www.uspbpep.com/usp31/v31261/usp31nf26s1_m74756.asp
102. http://www.medicinenet.com/selegiline-oral/article.htm
103. http://www.longecity.org/forum/topic/24732-selegiline-safety-efficacy-what-does-science-say/
104. http://www.chemicalbook.com/ChemicalProductProperty_EN_CB5137451.htm
105. http://28432.vvchem.com/show-3188960.html
106. http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=23491
107. http://www.lookchem.com/Selegiline-hydrochloride/
108. http://en.wikipedia.org/wiki/Entacapone
109. http://livertox.nih.gov/Entacapone.htm
110. http://www.yipengchem.com/130929-57-6.htm
111. http://www.lookchem.com/Entacapone/
112. http://www.rxlist.com/comtan-drug.htm
113. http://www.chemblink.com/products/130929-57-6.htm
114. http://www.drugbank.ca/drugs/DB00494
115. www.novartis.com.au/DownloadFile.aspx?t=p&f=com.pdf
116. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_Public_assessment_report/human/002075/WC500102610.pdf
117. http://www.ncbi.nlm.nih.gov/pubmed/15784340
118. http://books.google.co.in/books?id=qkjHxX5TgHEC&pg=PA188&lpg=PA188&dq=pka+of+Entacapone&source=bl&ots=NFE8tPGkJc&sig=v0Ol0LYkN8QfigpM3y_qwrnmhrg&hl=en&sa=X&ei=JAQIUabRPMeUrgeL-4CgCg&ved=0CD0Q6AEwAg#v=onepage&q=pka%20of%20Entacapone&f=false
119. http://www.medicinenet.com/entacapone-oral/article.htm
120. http://books.google.co.in/books?id=51ozlZRBvQwC&pg=PA82&lpg=PA82&dq=basic+dose+range+of+entacapone&source=bl&ots=9YS8rLVWp3&sig=tjqhPSaMaCmc1yPmWBMIShMEslo&hl=en&sa=X&ei=wjIOUYSBFMPWrQfCv4CwDg&ved=0CEQQ6AEwBA#v=onepage&q=basic%20dose%20range%20of%20entacapone&f=false
121. http://en.wikipedia.org/wiki/Tolcapone
122. http://www.scbt.com/datasheet-220266-tolcapone.html
123. http://www.rxlist.com/tasmar-drug.htm
124. http://www.chem.ox.ac.uk/mom/tolcapone/tolcapone.html
125. http://www.lookchem.com/Tolcapone/
126. http://13445.vvchem.com/show-2615674.html
127. http://www.drugbank.ca/drugs/DB00323
128. http://www.aksci.com/item_detail.php?cat=71884
129. United state pharmacopeia 32. 2009, volume1, Page no.936

130. http://www.ncbi.nlm.nih.gov/pubmed/15784340
131. http://books.google.co.in/books?id=Sd6ot9ul-bUC&pg=PA435&lpg=PA435&dq=pka+of+tolcapone&source=bl&ots=TLSFOBcKPl&sig=2K7t-zVIM0NPOPVcvyOwmWjgfKg&hl=en&sa=X&ei=EW8OUfnPJsvQrQeP5oHwCQ&ved=0CFgQ6AEwBw#v=onepage&q=pka%20of%20tolcapone&f=false
132. http://books.google.co.in/books?id=bkUdEiPJ4EAC&pg=PA99&lpg=PA99&dq=log+p+of+tolcapone&source=bl&ots=WeauIS-VSQ&sig=t-urmV8cjuU7vIBYgRfCfw5UImg&hl=en&sa=X&ei=PHAOUc69LIntrQe5l4HoDw&ved=0CDMQ6AEwAQ#v=onepage&q=log%20p%20of%20tolcapone&f=false.
133. http://www.jbc.org/content/285/20/14941.full.pdf
134. http://www.pharmacopeia.cn/v29240/usp29nf24s0_m84105.html
135. http://www.medicinenet.com/tolcapone-oral/article.htm
136. http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=23520
137. http://en.wikipedia.org/wiki/Amantadine
138. http://www.chemsynthesis.com/base/chemical-structure-6122.html
139. http://www.chemspider.com/Chemical-Structure.2045.html
140. http://www.lookchem.com/Amantadine/
141. http://bjgk.en.alibaba.com/product/717615305215602615/amantadine_CAS_Registry_Number_768_94_5.html
142. http://www.chemnet.com/cas/en/768-94-5/amantadine.html
143. http://www.drugbank.ca/drugs/DB00915
144. http://vir.sgmjournals.org/content/75/4/945.full.pdf
145. http://www.ncbi.nlm.nih.gov/pubmed/3346834
146. http://pharmacycode.com/Gen-Amantadine.html
147. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2818718/
148. http://www.rxlist.com/symmetrel-drug.htm
149. Indian pharmacopeia 2007, volume1, Page no.144
150. United state pharmacopeia 32. 2009, volume1, Page no.895
151. http://www.pharmacopeia.cn/v29240/usp29nf24s0_m2390.html
152. http://www.medicinenet.com/amantadine-oral/article.htm
153. http://books.google.co.in/books?id=i5zrVD1PAwEC&pg=PA314&lpg=PA314&dq=dose+range+of++amantadine&source=bl&ots=VsIdxqtHp6&sig=GX0wmM48ZL0wOUKSKBCONyBwt4g&hl=en&sa=X&ei=mI8OUeb8OJGHrAfHjICoDw&ved=0CEQQ6AEwAw#v=onepage&q=dose%20range%20of%20%20amantadine&f=false
154. http://www.newdruginfo.com/pharmacopeia/usp28/v28230/usp28nf23s0_m2380.htm
155. http://www.sigmaaldrich.com/catalog/product/sigma/a1260?lang=en&region=US
156. http://dailymed.nlm.nih.gov/dailymed/archives/fdaDrugInfo.cfm?archiveid=7072
157. http://www.scbt.com/datasheet-217619-amantadine-hydrochloride.html
158. http://en.wikipedia.org/wiki/Trihexyphenidyl
159. http://www.chemindustry.com/chemicals/0155449.html
160. http://www.chemspider.com/Chemical-Structure.5371.html
161. http://psychology.wikia.com/wiki/Trihexyphenidyl
162. http://www.whyckj.com/en/product/pharmaceutical_raw_materials_and_interm/2010/1103/88597.html
163. http://www.t3db.org/toxins/T3D2770
164. http://www.drugbank.ca/drugs/DB00376

165. http://en.diagnosispro.com/drug_information-for/trihexyphenidyl-hydrochloride-tablets-usp-qualitest-pharmaceuticals-description/4625-388697.html
166. http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=43300
167. http://www.parkinsons-information-exchange-network-online.com/drugdb/133.html
168. http://www.ncbi.nlm.nih.gov/pubmed/9477171
169. http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=76898
170. *.downloads.hindawi.com/journals/chem/2010/529386.pdf*
171. http://www.academia.edu/511331/An_overview_of_phytosomes_as_an_advanced_herbal_drug_delivery_system
172. http://www.pharmacopeia.cn/v29240/usp29nf24s0_m85500.html
173. http://www.drugs.com/pro/trihexyphenidyl.html
174. http://en.wikipedia.org/wiki/Procyclidine
175. http://www.chemnet.com/cas/en/77-37-2/procyclidine.html
176. http://www.flexyx.com/T/Triciclidina.html
177. http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=4919
178. http://www.lookchem.com/cas-150/1508-76-5.html
179. http://lxsrv7.oru.edu/~alang/meltingpoints/meltingpointof.php?csid=4750&prediction=yes
180. http://www.drugbank.ca/drugs/DB00387
181. http://yashicapharma.trustpass.alibaba.com/product/239237782-0/PROCYCLIDINE.html
182. http://www.pharmarawmaterials.com/procyclidine-hcl.html
183. http://www.newdruginfo.com/pharmacopeia/usp28/v28230/usp28nf23s0_m69790.htm
184. http://druginfosys.com/Drug.aspx?drugCode=617&drugName=Procyclidine%20%28HCl%29&type=0
185. http://pharmacycode.com/Procyclidine.html
186. http://www.pharmacopeia.cn/v29240/usp29nf24s0_m69820.html
187. http://www.webmd.com/drugs/drug-14104-procyclidine+oral.aspx?drugid=14104&drugname=procyclidine+oral
188. http://en.wikipedia.org/wiki/Biperiden
189. http://www.caslab.com/Biperiden_CAS_514-65-8/
190. http://www.chemspider.com/Chemical-Structure.2289.html
191. http://drugline.sophilabs.com/search?query=mesh:%22biperidin%20-%20AE%22
192. http://www.b2bage.com/the-biperidin-lactate/
193. http://www.drugbank.ca/drugs/DB00810
194. http://www.tradeim.com/search.html?method=product&pagesize=16&page=10&keyword=Lactate&nomap=false&meta=Lactate
195. Indian pharmacopeia 2007, volume1, Page no.145
196. United state pharmacopeia 32. 2009, volume1, Page no.895
197. **197.**http://lib.bioinfo.pl/meid:100412/pmid/pmi
198. http://books.google.co.in/books?id=NFGSSSbaWjwC&pg=PA1418&lpg=PA1418&dq=pka+value+of+biperiden&source=bl&ots=V71QMadvxr&sig=O1hfZOdyWF1LTaUkmLvabywWMfc&hl=en&sa=X&ei=v0UiUciiH4PJrQf12IAw&ved=0CDMQ6AEwAQ#v=onepage&q=pka%20value%20of%20biperiden&f=false
199. http://pharmacycode.com/Biperiden.html
200. http://www.pharmacopeia.cn/v29240/usp29nf24s0_m9580.html
201. http://www.rxmed.com/b.main/b2.pharmaceutical/b2.1.monographs/CPS-%20Monographs/CPS-

%20%28General%20Monographs-%20H%29/HYGROTON.html
202. http://en.wikipedia.org/wiki/Orphenadrine
203. http://www.tlcpharmachem.com/tlc_item.php?upc=O-051&li=le_21&sub=O
204. http://www.chemspider.com/Chemical-Structure.4440.html
205. http://druginfosys.com/Drug.aspx?drugCode=536&drugName=&type=0
206. http://www.lookchem.com/Orphenadrine-Hydrochloride/
207. http://www.scbt.com/datasheet-212481-orphenadrine-citrate-salt.html
208. http://www.drugbank.ca/drugs/DB01173
209. http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=54601
210. http://www.rxlist.com/orphengesic-drug.htm
211. http://www.scielo.gpeari.mctes.pt/scielo.php?pid=S0872-19042011000300003&script=sci_arttext
212. http://www.homeopathswithoutborders.gr/index.php?option=com_content&view=category&id=48&layout=blog&Itemid=55&lang=en&limitstart=2017
213. http://tcm.zju.edu.cn/ptd/category/show_wdrug/1162
214. http://orphenadrine-citrate-100mg.blogspot.in/
215. http://en.wikipedia.org/wiki/Promethazine
216. http://www.inchem.org/documents/pims/pharm/prometha.htm
217. http://medlibrary.org/lib/rx/meds/promethazine-hydrochloride-71/
218. http://www.druglib.com/druginfo/promethazine-dm/description_pharmacology/
219. http://www.lookchem.com/Promethazine-hydrochloride/
220. http://www.chemblink.com/products/58-33-3.htm
221. http://www.drugbank.ca/drugs/DB01069
222. http://www.rxlist.com/phenergan-drug.htm
223. Indian pharmacopeia 2007, volume1, Page no.158
224. United state pharmacopeia 32. 2009, volume1, Page no.927
225. http://www.rxlist.com/promethazine-hcl-injection-drug.htm
226. http://www.lookchem.com/Promethazine-theoclate/
227. http://chrom.tutms.tut.ac.jp/JINNO/DRUGDATA/44promethazine.html
228. http://www.pharmacopeia.cn/v29240/usp29nf24s0_m70170.html
229. http://reference.medscape.com/drug/phenergan-phenadoz-promethazine-342056
230. http://www.drugs.com/promethazine.htm

Correspondence Address:

AchhrishGoel,

Rachet Pharma Ltd, Baddi, Himachal Pradesh,

achhrishgoel@yahoo.com

Contact no. 09736430991.