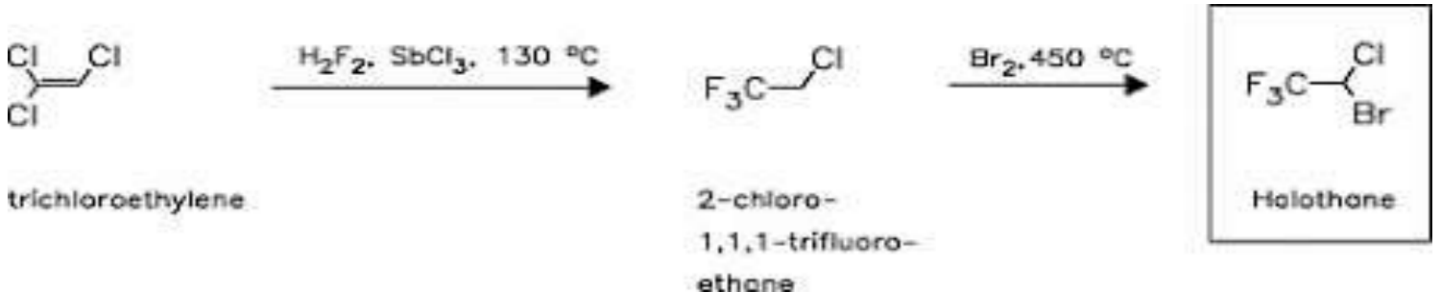
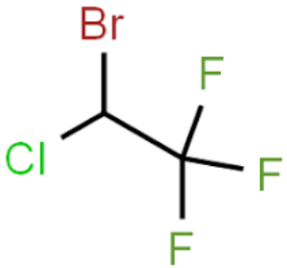
Drugs acting on Central Nervous System General anesthetics:

Inhalation anesthetics: Halothane*, Methoxyflurane, Enflurane, Sevoflurane, Isoflurane, Desflurane.

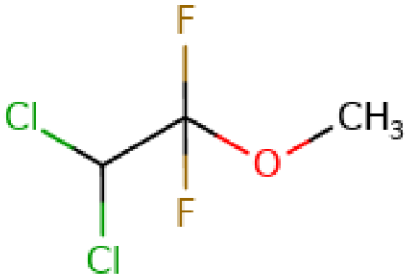
Halothane : 2-bromo-2-chloro-1,1,1-trifluoroethane





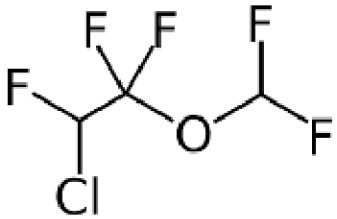
Uses: Halothane is a general inhalation anesthetic used for induction and maintenance of general anesthesia. It reduces the blood pressure and frequently decreases the pulse rate and depresses respiration. It induces muscle relaxation and reduces pains sensitivity by altering tissue excitability. It does so by decreasing the extent of gap junction mediated cell-cell coupling and altering the activity of the channels that underlie the action potential.

Methoxyflurane: 2,2-dichloro-1,1-difluoro-1-methoxyethane



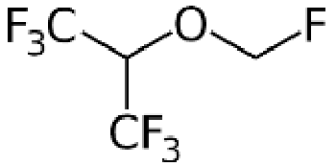
Uses: Methoxyflurane is a general inhalation anesthetic used for induction and maintenance of general anesthesia. It induces muscle relaxation and reduces pains sensitivity by altering tissue excitability. It does so by decreasing the extent of gap junction mediated cell-cell coupling and altering the activity of the channels that underlie the action potential.

Enflurane : 2-chloro-1-(difluoromethoxy)-1,1,2-trifluoroethane



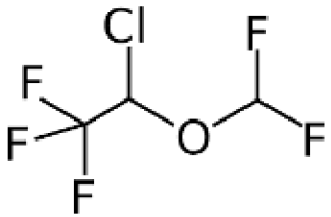
Uses: Enflurane is a fluorinated ether and very potent and stable general anaesthetic agent. The mechanism through which enflurane exerts its effect is not clear, it probably acts on nerve cell membranes to disrupt neuronal transmission in the brain, probably via an action at the lipid matrix of the neuronal membrane. Enflurane may also enhance the activity of the inhibitory neurotransmitter gamma-aminobutyric acid on synaptic transmission. Enflurane may also inhibit glutamatergic excitatory transmission.

Sevoflurane : 1,1,1,3,3,3-hexafluoro-2-(fluoromethoxy)propane



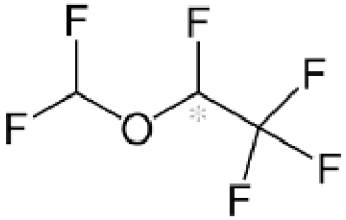
Uses: Sevoflurane is a fluorinated isopropyl ether with general anesthetic property. Although the mechanism of action has not been fully elucidated, sevoflurane may act by interfering with the release and re-uptake of neurotransmitters at post-synaptic terminals, and/or alter ionic conductance following receptor activation by a neurotransmitter. Sevoflurane may also interact directly with lipid matrix of neuronal membranes, thereby affecting gating properties of ion channels. In addition, this agent may activate gamma-aminobutyric acid (GABA) receptors hyperpolarizing cell membranes. This results in a general anesthetic effect, a decrease in myocardial contractility and mean arterial pressure as well as an increased respiratory rate.

Isoflurane : 2-chloro-2-(difluoromethoxy)-1,1,1-trifluoroethane



Uses: Isoflurane is a general inhalation anesthetic used for induction and maintenance of general anesthesia. It induces muscle relaxation and reduces pains sensitivity by altering tissue excitability. It does so by decreasing the extent of gap junction mediated cell-cell coupling and altering the activity of the channels that underlie the action potential.

Desflurane : 2-(difluoromethoxy)-1,1,1,2-tetrafluoroethane

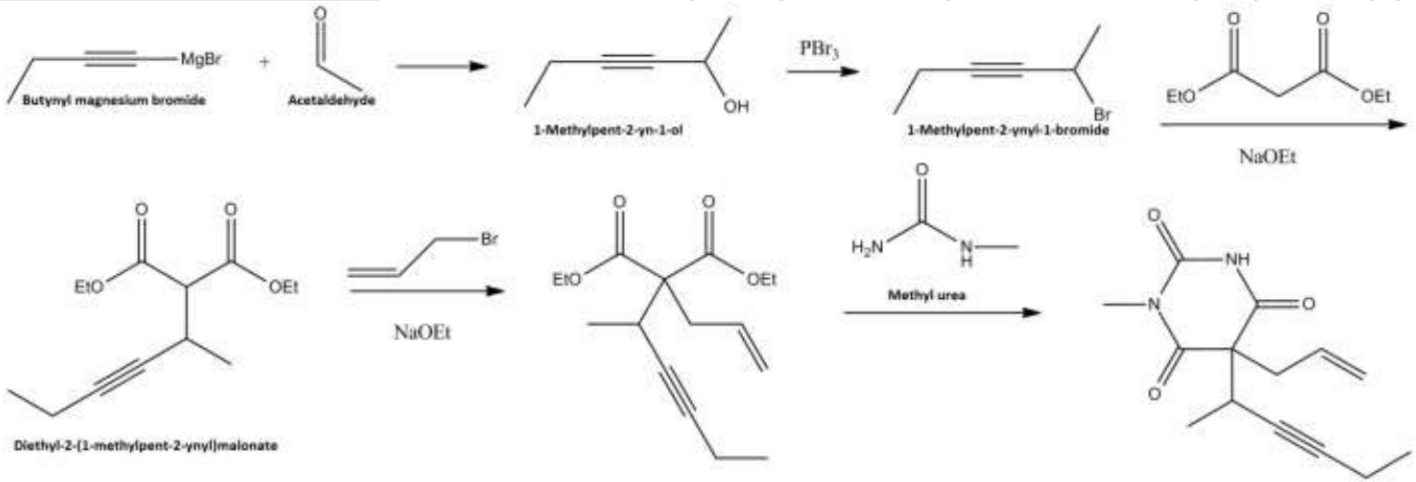


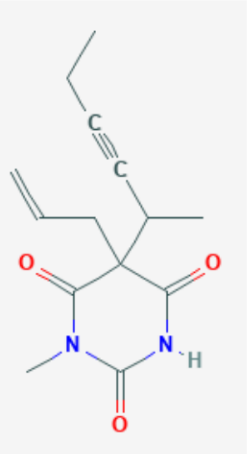
Uses: Desflurane is a fluorinated ether with general anesthetic and muscle relaxant activities. Although the exact mechanism of action has not been established, desflurane, administered by inhalation, appears to act on the lipid matrix of the neuronal membrane, resulting in disruption of neuronal transmission in the brain. This agent may also enhance the synaptic activity of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA).

Drugs acting on Central Nervous System General anesthetics:

Ultra short acting barbitutrates: Methohexital sodium*, Thiamylal sodium, Thiopental sodium.

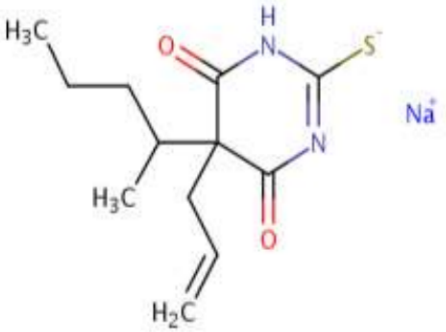
Methohexital sodium : sodium;5-hex-3-yn-2-yl-1-methyl-4,6-dioxo-5-prop-2-enylpyrimidin-2-olate





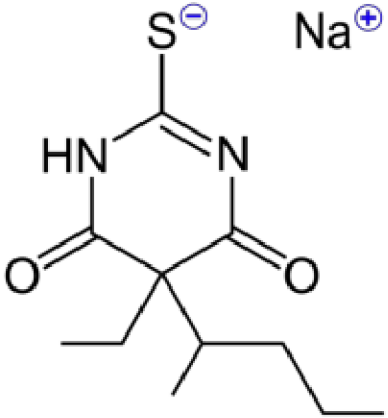
Uses: Methohexital Sodium is the sodium salt of methohexital, a rapid, short-acting barbituric acid derivative, with anesthetic activity. Methohexital binds to the chloride ionophore site of the gamma-aminobutyric acid (GABA)-A/chloride ionophore receptor complex, thereby enhancing the inhibitory actions of GABA-A in the brain. This leads to synaptic inhibition, decreased neuronal excitability and induction of anesthesia. In addition, this agent decreases glutamate (Glu) responses.

Thiamylal sodium: sodium;4,6-dioxo-5-pentan-2-yl-5-prop-2-enyl-1*H*-pyrimidine-2-thiolate



Uses: Ultrashort-acting anesthetics that are used for induction. Loss of consciousness is rapid and induction is pleasant, but there is no muscle relaxation and reflexes frequently are not reduced adequately. Repeated administration results in accumulation and prolongs the recovery time. Since these agents have little if any analgesic activity, they are seldom used alone except in brief minor procedures.

<u>Thiopental sodium</u>: sodium;5-ethyl-5-[(2R)-pentan-2-yl]-2-sulfanylidenepyrimidin-3-ide-4,6-dione

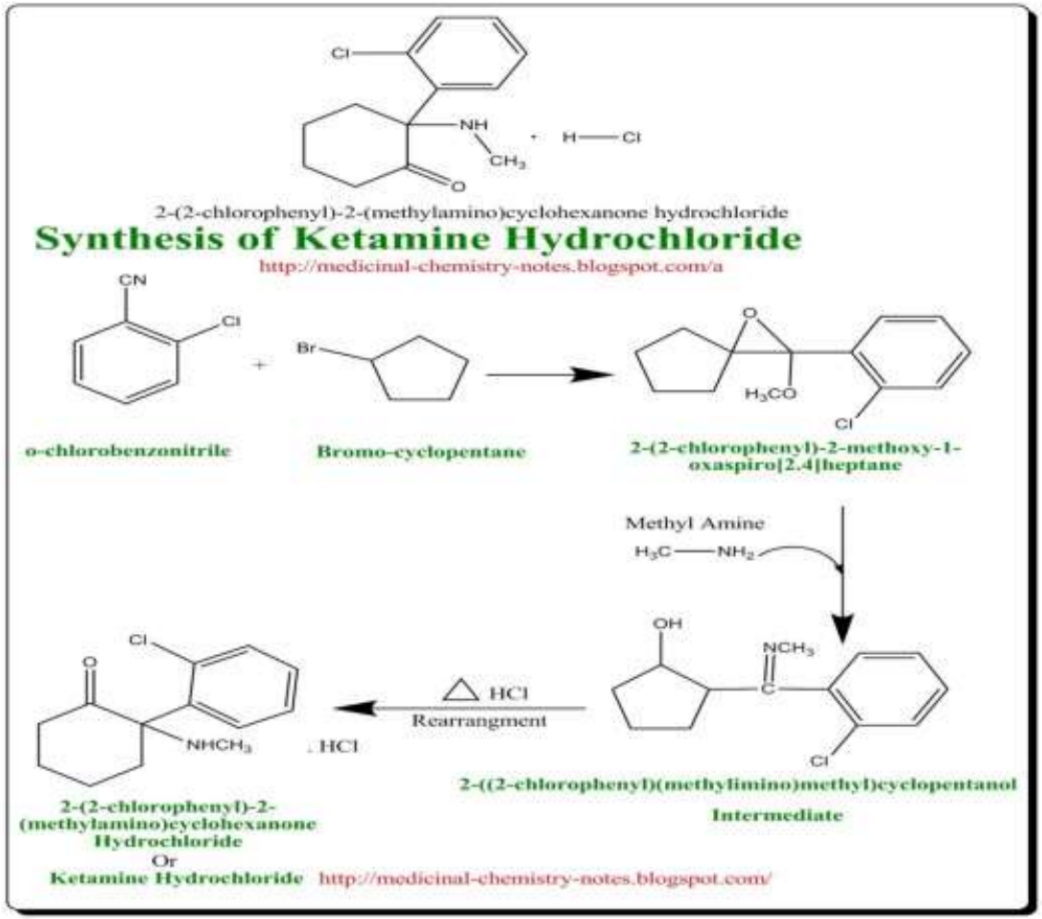


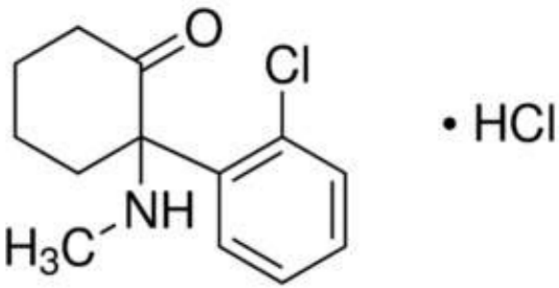
Uses: Thiopental, a barbiturate, is used for the induction of anesthesia prior to the use of other general anesthetic agents and for induction of anesthesia for short surgical, diagnostic, or therapeutic procedures associated with minimal painful stimuli. Thiopental is an ultrashort-acting depressant of the central nervous system which induces hypnosis and anesthesia, but not analgesia.

Drugs acting on Central Nervous System General anesthetics:

Dissociative anesthetics: Ketamine hydrochloride.*

<u>Ketamine hydrochloride</u>: 2-(2-chlorophenyl)-2-(methylamino)cyclohexan-1-one;hydrochloride





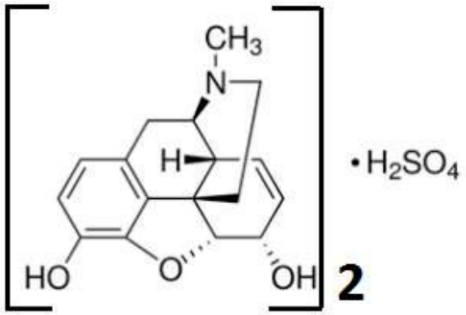
Uses: Ketamine Hydrochloride is the hydrochloride salt of a synthetic derivative of cyclohexanone with analgesic and anesthetic activities. Although its mechanism of action is not well understood, ketamine appears to non-competitively block N-methyl-D-aspartate (NMDA) receptors and may interact with opioid mu receptors and sigma receptors, thereby reducing pain perception, inducing sedation, and producing dissociative anesthesia.

Narcotic and non-narcotic analgesics

Morphine and related drugs: Morphine sulphate, Codeine, Meperidine hydrochloride, Anilerdine hydrochloride, Diphenoxylate hydrochloride, Loperamide hydrochloride, Fentanyl citrate*, Methadone hydrochloride*, Propoxyphene hydrochloride, Pentazocine, Levorphanol tartarate.

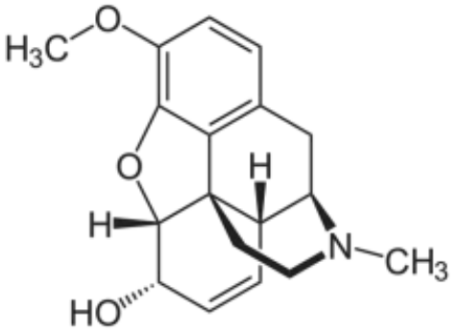
Morphine sulphate: (4R,4aR,7S,7aR,12bS)-3-methyl-2,4,4a,7,7a,13-hexahydro-1H-4,12-methanobenzofuro [3,2-e] isoquinoline-7,9-diol;sulfuric acid

Uses: Morphine Sulfate is the sulfate salt of morphine, an opiate alkaloid isolated from the plant Papaver somniferum and produced synthetically. Morphine binds to and activates specific opiate receptors (delta, mu and kappa), each of which are involved in controlling different brain functions. In the central nervous and gastrointestinal systems, this agent has widespread effects including analgesia, anxiolysis, euphoria, sedation, respiratory depression, and gastrointestinal system smooth muscle contraction.

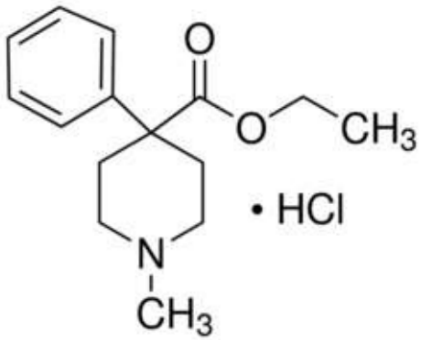


Codeine: (4*R*,4*aR*,7*S*,7*aR*,12*bS*)-9-methoxy-3-methyl-2,4,4*a*,7,7*a*,13-hexahydro-1*H*-4,12-methanobenzofuro[3,2-e]isoquinolin-7-ol

Uses: Codeine is a naturally occurring phenanthrene alkaloid and opioid agonist with analgesic, antidiarrheal and antitussive activities. Codeine mimics the actions of endogenous opioids by binding to the opioid receptors at many sites within the central nervous system (CNS). Stimulation of μ-subtype opioid receptors results in a decrease in the release of nociceptive neurotransmitters such as substance P, GABA, dopamine, acetylcholine and noradrenaline; in addition, the codeine metabolite morphine induces opening of G-protein-coupled inwardly rectifying potassium (GIRK) channels and blocks the opening of N-type voltage-gated calcium channels, resulting in hyperpolarization and reduced neuronal excitability.

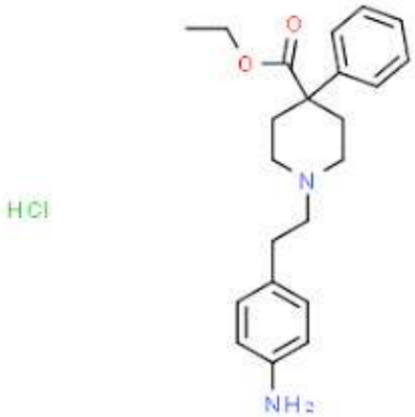


Narcotic and non-narcotic analgesics



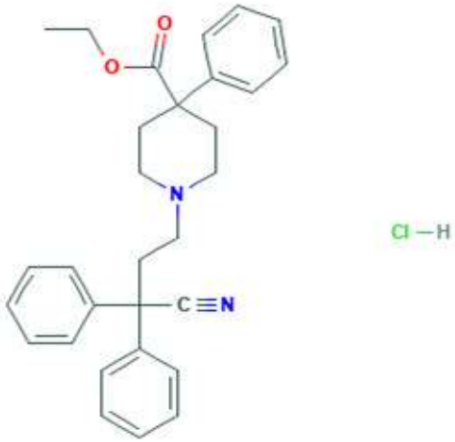
Meperidine hydrochloride: ethyl 1-methyl-4-phenylpiperidine-4-carboxylate;hydrochloride

Uses: Meperidine Hydrochloride is the hydrochloride salt of a synthetic piperidine ester with opioid analgesic activity. Meperidine mimics the actions of endogenous neuropeptides via opioid receptors such as the mu-opioid receptor, thereby producing characteristic morphine-like effects including analgesia, euphoria, sedation, respiratory depression, miosis, bradycardia and physical dependence.



Anilerdine hydrochloride: Ethyl 1-[2-(4-aminophenyl)ethyl]-4-phenylpiperidine-4-carboxylate

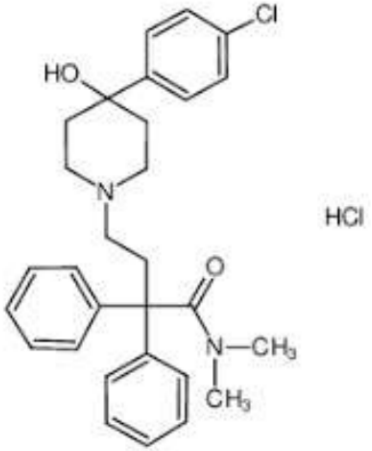
Uses: Anileridine is an opioid receptor agonist belonging to the piperidine class with analgesic activity. By binding to and activating opioid receptors in the central nervous sytem (CNS), anileridine mimics the endogenous opioids resulting in a decrease of nociceptve neurotransmitters and eventually an analgesic effect.



Diphenoxylate hydrochloride: Ethyl 1-(3-cyano-3,3-diphenylpropyl)-4-phenylpiperidine-4-carboxylate;hydrochloride

Uses: Diphenoxylate Hydrochloride is the hydrochloride salt form of diphenoxylate, a piperidine derivate, chemically related to narcotic meperidine, with antidiarrheal activity and devoid of central nervous system (CNS) activity. Diphenoxylate acts on opioid receptors in the gastrointestinal tract, thereby decreasing gastrointestinal motility and causing constipation or preventing diarrhea.

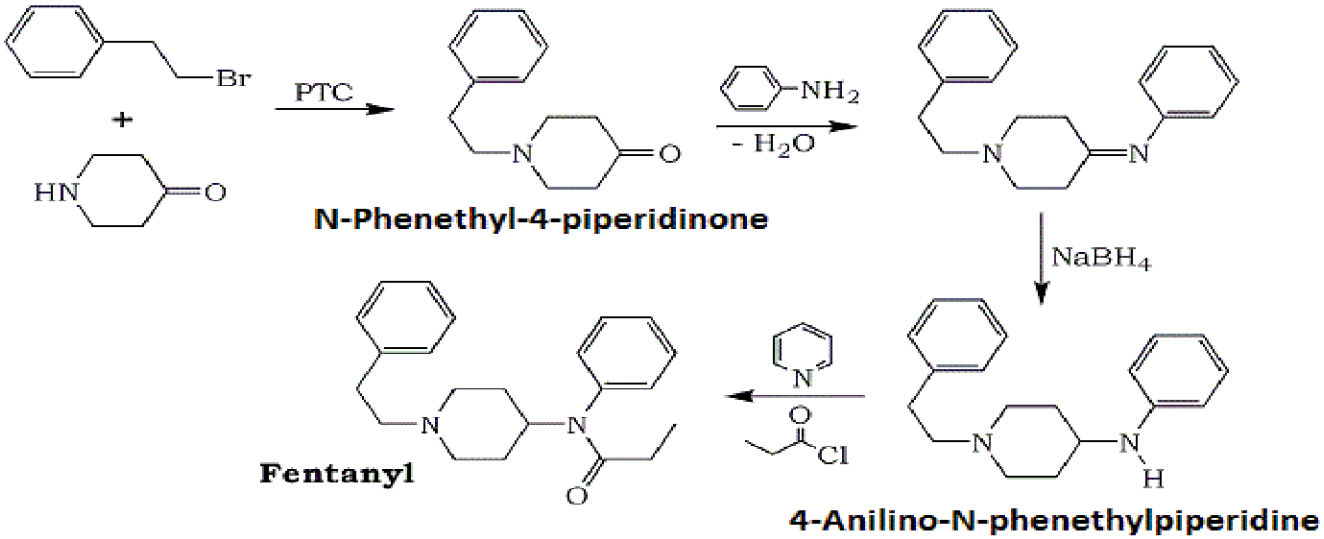
Narcotic and non-narcotic analgesics

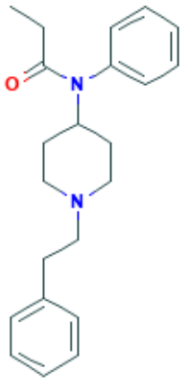


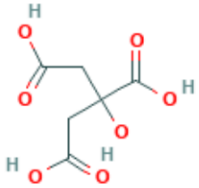
Loperamide hydrochloride: 4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]-*N*,*N*-dimethyl-2,2-diphenylbutanamide;hydrochloride

Uses: Loperamide Hydrochloride is the hydrochloride salt form of loperamide, a synthetic, piperidine derivative and opioid agonist with antidiarrheal activity. Loperamide acts on the mu-receptors in the intestinal mucosa. This leads to a decrease in gastrointestinal motility by decreasing the circular and longitudinal smooth muscle activity of the intestinal wall. This slows intestinal transit and allows for more water and electrolyte absorption from the intestines.

Fentanyl citrate: Ethyl 1-[2-(4-aminophenyl)ethyl]-4-phenylpiperidine-4-carboxylate



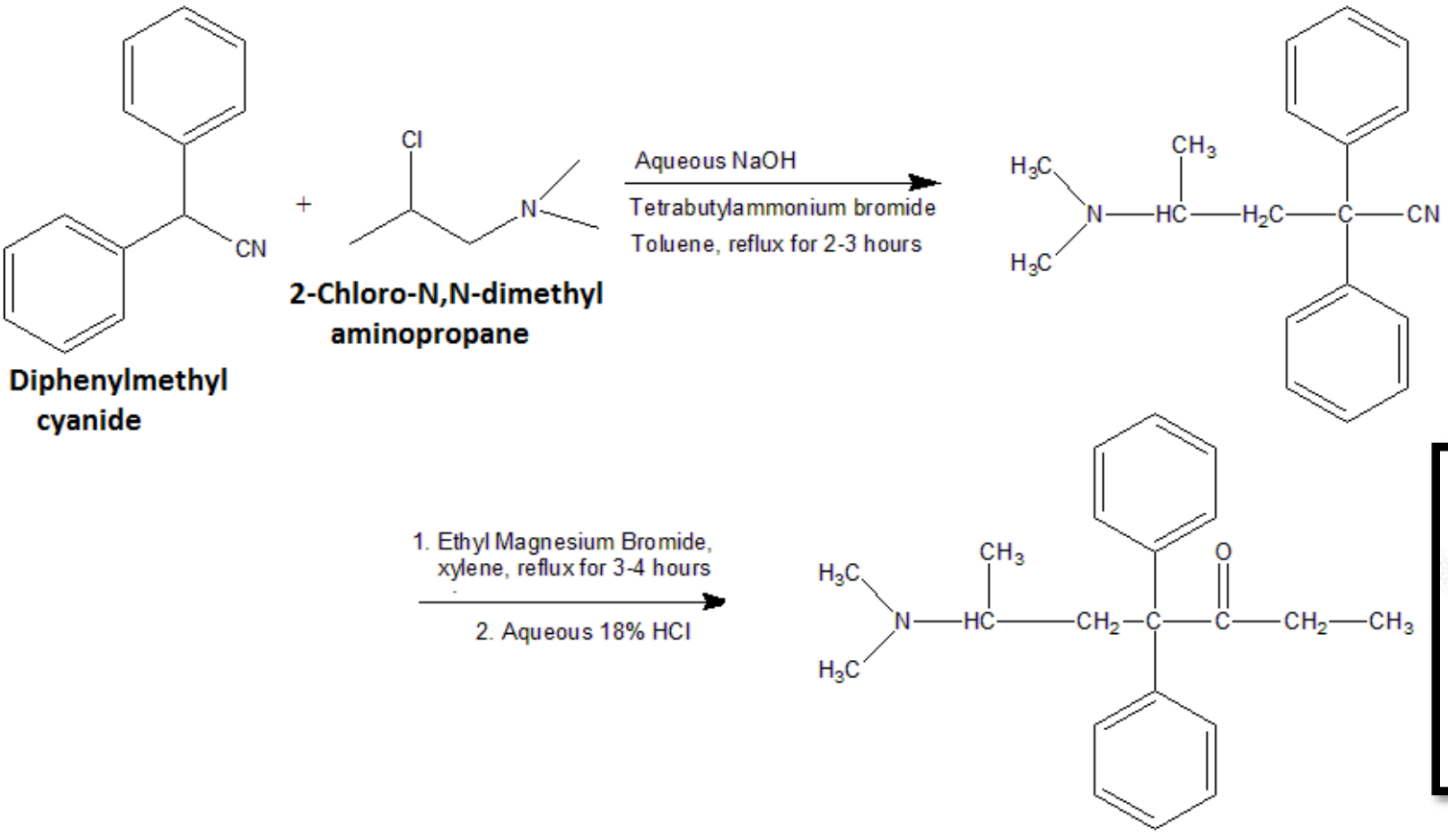


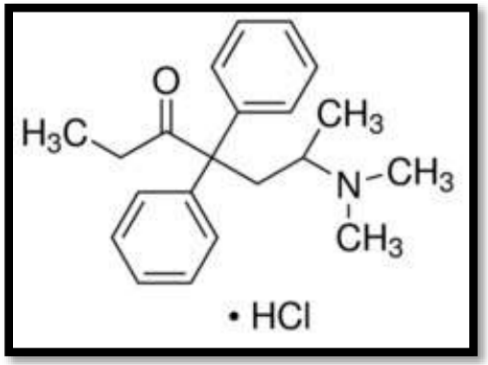


Uses: Anileridine is an opioid receptor agonist belonging to the piperidine class with analgesic activity. By binding to and activating opioid receptors in the central nervous sytem (CNS), anileridine mimics the endogenous opioids resulting in a decrease of nociceptve neurotransmitters and eventually an analgesic effect.

Narcotic and non-narcotic analgesics

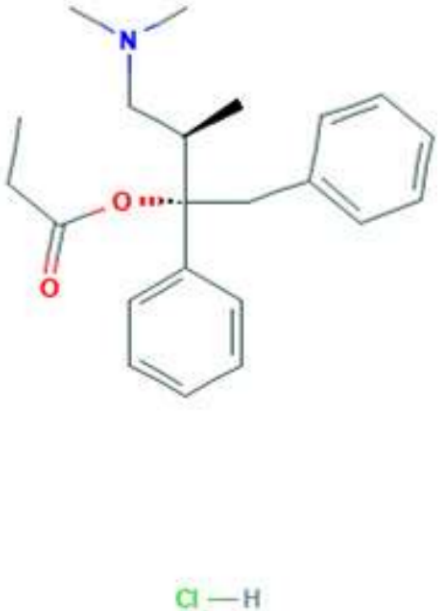
Methadone hydrochloride: 6-(dimethylamino)-4,4-diphenylheptan-3-one;hydrochloride





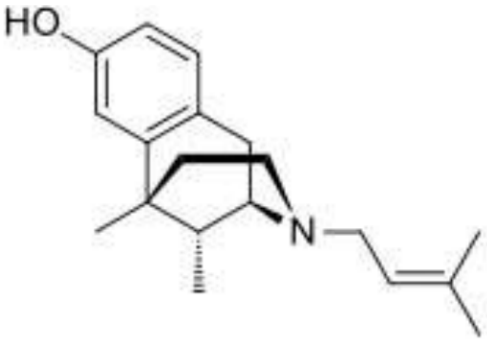
Uses: Methadone Hydrochloride is the hydrochloride salt of methadone, a synthetic opioid with analgesic activity. Similar to morphine and other morphine-like agents, methadone mimics the actions of endogenous peptides at CNS opioid receptors, primarily the mu-receptor, resulting in characteristic morphine-like effects including analgesia, euphoria, sedation, respiratory depression, miosis, bradycardia and physical dependence. Because of the prolonged half-life of methadone compared to other morphine-like agents such as heroin, the onset of opiate withdrawal symptoms is slower, the duration of opiate withdrawal is prolonged, and opiate withdrawal symptoms are less severe.

Narcotic and non-narcotic analgesics



Propoxyphene hydrochloride: [(2*S*,3*R*)-4-(dimethylamino)-3-methyl-1,2-diphenylbutan-2-yl] propanoate;hydrochloride

Uses: Propoxyphene Hydrochloride is the hydrochloride salt form of the d-isomer of synthetic diphenyl propionate derivative propoxyphene, with narcotic analgesic effect. This agent mimics the effects of the endogenous opiate dextropropoxyphene, by binding to mu receptors located throughout the central nervous system. The binding results in GTP to GDP exchanges on the mu-G-protein complex, by which effector adenylate cyclase is inactivated thereby decreasing intracellular cAMP. This, in turn, inhibits the release of various nociceptive neurotransmitters, such as substance P, gamma-aminobutyric acid (GABA), dopamine, acetylcholine, noradrenaline, vasopressin, and somatostatin. In addition, dextropropoxyphene closes N-type voltage-gated calcium channels and opens calcium-dependent inwardly rectifying potassium channels. This results in hyperpolarization, thereby reducing neuronal excitability, which further decreases the perception of pain..

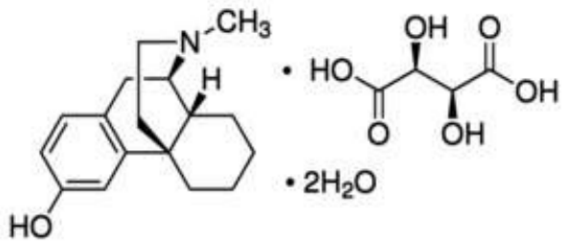


Pentazocine: (1*R*,9*R*,13*S*)-1,13-dimethyl-10-(3-methylbut-2-enyl)-10-azatricyclo [7.3.1.0]trideca-2(7),3,5-trien-4-ol

Uses: Pentazocine, a benzomorphan narcotic agonist-antagonist. Pentazocine binds to and activates kappa- and sigma-opioid receptors, resulting in sedation and analgesia. In addition, this agent antagonizes the mu-receptor. Pentazocine partially reverses opiate-induced cardiovascular, respiratory, and behavioral depression.

Narcotic and non-narcotic analgesics

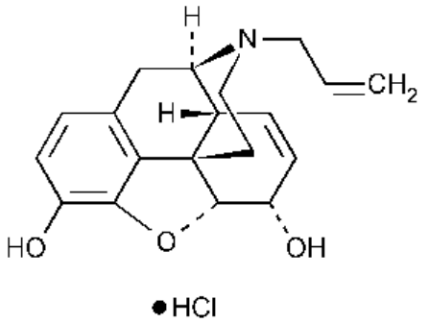
Levorphanol tartarate: (2*R*,3*R*)-2,3-dihydroxybutanedioic acid;(1*R*,9*R*,10*R*)-17-methyl-17-azatetracyclo[7.5.3.0.0]heptadeca-2(7),3,5-trien-4-ol;dihydrate



Uses: Levorphanol Tartrate is the tartrate salt form of levorphanol, a synthetic phenanthrene with potent opioid analgesic activity. Levorphanol tartrate mimics the actions of endogenous peptides at CNS opioid receptors, thereby producing the characteristic morphine-like effects on the mu-opioid receptor, including analgesia, euphoria, sedation, respiratory depression, miosis, bradycardia and physical dependence.

<u>Narcotic antagonists:</u> Nalorphine hydrochloride, Levallorphan tartarate, Naloxone

Nalorphine hydrochloride: (4*R*,4*aR*,7*S*,7*aR*,12*bS*)-3-prop-2-enyl-2,4,4*a*,7,7*a*,13-hexahydro-1*H*-4,12-methanobenzofuro[3,2-e]isoquinoline-7,9-diol;hydrochloride



Uses: Narcotic Antagonists Agents inhibiting the effect of narcotics on the central nervous system.

, Levallorphan tartarate, Naloxone hydrochloride.