**PYRIDINE - PIPERIDINE ALKALOIDS**

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On reduction, the tertiary base, pyridine, is converted into the secondary base, piperidine .These two nuclei form the basis of this group, which is sometirnel divided into three subgroups :

(I) Derivatives of piperidine ,including lobeline from lobelia.

(2) Derivatives of nicotinic acid , including arecoline from areca .

(3) Derivatives of both pyridine and pynolidine, including nicotine from

tobacco .

The important alkaloidal drugs and their alkaloids that are classified in

this group are areca, arecoline hydrobromide , lobelia ,lobeline and icotine.

**Biosynthesis of Pyridine-Piperidine Alkaloids**

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Tracer studics have shown that ornithine is incorporated

into nicotine by tobacco plants.

This incorporation resuitsi n a symmetric labeling pattern of nicotine .

Nicotine is primarily a product of root metabolism, but the formation of small amounts , as well as subsequent reactions such as the demethylation of nicotine , can occur in the leaves of plants .

**Areca**

Areca , areca nut , or betel nut is the dried , ripe seed of*Areca catechu* L.

Areca contains several alkaloids that are reduced pyridine derivatives .

duced pyridinen derivatives. Among them are arecoline, arecaidine, guvacine ,and guvacoline . The total alkaloid content can reach 0.45%.

Arecoline,t he most abundant and physiologically

most active alkaloid, is a liquid occurring to the extent of about 0.2% .

Areca also contains tannin( abourl -15%) , lipids , volatile oils,

and gum. Areca is classified as an anthelmintic in veterinary practice and is employed as a vermicide and taeniafuge.

**Lobelia**

**Lobelia or Indian tobacco** consists ofthe dried leaves and rops of *Lobelia inflata* **L.** The drug contains 14 alkaloids, of which lobelineis the major and most important. a pungent volatile oil, resin, lipids, and gum.

**Lobeline** occurs a colorless crystals that are slightly soluble

in water but readily soluble in hot alcohol. Lobeline produces similar, but weaker, pharmacologic effects to those of nicotine on the peripheral circulation; neuromuscular junctions,

and the central nervous system. For this reason, lobeline sulfate was formerly incorporated in tablets or lozenges that were intended to aid in

breaking the tobacco habit (smokingd eterrent) .

The majority of controlled studies showed that Lobeline had only a placebo effect on decreasing the physical craving for cigarettes, so these products were removed from the market.

**Nicotine**

Nicotine is a pyridinea lkaloido btained from the dried

Leaves of the tobacco plant *Nicotiana tabacum* L. (Fam. Solanaceae).

Nicotinei s colorless to pale yellow very hygroscopic, oily , volatilel iquid with an unpleasant. pungent odor and a sharp, burning, persistent taste .

Nicotine is a ganglionic ( nicot inic ) cholinergic – receptor agonist with

Complex pharmacologic actions that include effects mediated by binding to rcceptors in autonomic ganglia , the adrenal medulla , the neuromuscular junction, and the brain . Chronic use of nicotine may result in psychologic and physical dependence . As a temporary aid for the cessation of cigarettesmoking , the drug is available in transdermal system , and it also available bound to an ion exchange resin in a chewing gum base . These alternative sources of nicotine help reduce the withdrawal symptoms associated with nicotine addiction.

**TROPANE ALKALOIDS**

Tropane is a dicyclic compound forme by the condensation of a pyrrolidine precursor( ornithine) with three acetate\_derived carbon atoms..Both pyrrolidine and piperidine ring systems can be discerned in the molecule .

The important drugs and alkaloids in this group are belladonna leaf, Hyoscyamus, stramonium , atropine , hyoscyamine , scopolamine , coca , and cocaine .

**Belladonna**

Belladonna leaf. belladonna herb, or deadly nightshade leaf consists of thedried leaf and flowering or fruiting top of *Atropa belladonna* L.

The poisonous character of the plant has been known for many years, it has a mydriatic and analgesic properties , the leaves were used earlier than the root , the leaf yields alkaloids in conc. Ranging up to more than (1%) , about ¾ of the isolated alkaloid mix. Is Hyoscyamine ; the reminder is atropine . Atropine found in the root but not in the leaf. These include apoatropine, belladonnine, cuscohygrine, and scopolamine .

Belladonna acts as an antimuscarinic agent. which accounts for its use as a spasmolytic drug. It is used as adjunctive therapy in the treatrnent of peptic ulcer; functional digestive disorders, including spastic, mucous, and ulcerative colitis; and diarrhea, diverticulitis, and pancreatitis. It possesses anticholinergic properties and is used to control excess motor activity of the gastrointestinal tract and spasm of the urinary ract.

Belladonna leaf is commonly administered in the form of the tincture ( 30 mg alkaloids / 100 ml ) or the extract (1.25g alkaloids/100g ) .

**Solanaceous Alkaloids**

The principal alkaloids of this group are hyoscyamine , atropine and scopolamine(hyoscine).These are tropine derivatives and esters and rnay be prepared synthetically but are usually obtained by extraction from plants of the Solanaceae.These include *Atropa beliadonna*, *Datura strantonium*,

*Hyoscyamus niger ,* and *Hyoscyamus muticus ,* another important source is the dried leaves of Duboisia plants of Australia .Atropine and scopolamine have clinically useful effects as antispasmodic which used principaliy to relieve spasms of thc bowel in the treatrnent of Spastic colitis, gastroenteritis,and peptic ulcer ; an antisecretory effect used to reduce respiratory secretions in anesthesia , gastric secretions in peptic ulcer therapy, and nasal and sinus secretions in common cold and allergy medications ; and a mydriatic and cycloplegic effect used to prevent adhesions between the iris and lens of the eye in cases of iritis.

Atropine is an antidote in cases of poisoning caused by cholinesterase inhibitors such as physostigmine and organophosphate insecticides.

Scopolamine has a depressanat ctivity on the central nervoui system end is used to treat motion sickness.I t is also employed for preanesthctic sedation and for obstetric amncsia in conjunction with analgesics ,and to calm delirium.

**Toxicify symptoms** that can occur during the therapeutic use of atropine. Scopolamine and belladonna tincture are skin rash,s kin flushing,

mouth dryness, difficulty in urination, eye pain, blurred vision.and light sensitiviry.The patient should also be advised that such a ntacids as a umina gels may interfere with absorption of these drugs when taken simultaneously.

**Hyoscyamine sulfate** is extremely poisonous its an anticholinergic. It

is used to aid in the control of gastric sccretion. Visceral spasm. hypermotility in spastic colitis.pyl orospasm and associated abdominal cramps.

ln parkinsonism it is used to reduce rigidity and tremors and to control associated sialorrhea and hyperhidrosis.

Atropine sulfate is an antichoiinergic.Used in surgery as an antisialogogue to control bronchial, nasal,pharyngeal and salivary secretions, it is usually injected intramuscularly prior to induction of anesthesia During surgery, the drug is given intravenously when reduction in pulse range and cessation of cardiac action are attributable to increased vagal activity. It is also useful

in pylorospasm ard other spastic conditions of the gastrointestinal tract and for ureteral and biliary colic when administered concomitantly with mrorphine.

Scopolamine or hyoscine is an alkaloid that is particularly abundant in

*Datura fastuosa var.alba* and in D. metel. It is an ester that, upon hydrolysis,yields tropic acid and scopoline,a base resembling tropine.

At usual therapeutic doses,scopolamine is a central nervous depressant whereas atropine is a stimulant. For this reason, scopolamine hydrobromide is used for preanesthetic sedation and for obstetric amnesia in conjunction with analgcsics ; it is also employed for calming delirium.

It is administered subcutaneously or intramuscularly in a single dose.

In addition to its systemic anticholinergic effects, scopolamine is effective in the prevention of nausea and vomiting associated with motion sickness.

Hyoscyamus

Hyoscyamus or henbane is the dried leaf, with or without the stem and flowering or fruiting top, of *Hyoscyamus niger* L. (Fam. Solanaceae)

and contains not less than 0.04% of the alkafoids of hyoscyamus.

The alkaloids hyoscyamine and scopolamine,0.05 to 0.I5% of which 3/4 is hyoscyamine, are the active principles.

Stramonium

Strarnonium, jimson weed, or Jamestown

weedc onsistso f the dried leaf and flowering or fruiting tops with branches of *Datura stramonium* L . or of its variety tatula (Linne.) , (Fam. Solanaceac) It yields not less than 0.25% of alkaloids .

Stramonium seed is the ripe seed of Datura stramonium . The ripening capsules are gathered and dried until the seeds shak out .

Stramonium seed contains about 0.4% of alkaloids, principally

hyoscyamine with a small proportion of scopolamine and traces of atropine.

Stramonium is genendly regarded as'a noxious weed and has frequently caused poisoning in children when seeds were ingested . The chief toxic symptoms are those of atropine poisoning .