Pharmacognosy

ALKALOIDS

Unit 4th (1)

Naturally occurring chemical compounds containing basic nitrogen atoms Physiologically active Insoluble or sparingly soluble in water Crystalline solids; a few are amorphous Usually classified according to the nature of the basic chemical structures from which they are derived Form double-salts with compounds of Hg, Au, Pt, and other heavy metals. Reagents: Wagner's (Iodine in Potassium iodide), Mayer's (Potassium mercuric iodide), Dragendorff's (Potassium bismuth iodide)

Named from:

the generic name of the plant yielding them the specific name of the plant yielding them the common name of the drug yielding them their physiologic activity the discoverer

Possible functions:

- 1. Poisonous agents protecting the plant against insects and herbivores
- 2. End products of detoxification reactions representing a metabolic locking up of compounds otherwise harmful to the plant
- 3. Regulatory growth factors
- 4. Reserve substances capable of supplying nitrogen or other elements necessary to the plants economy.

Common amino acid precursors: Phenylalanine Tyrosine Tryptophan Histidine Anthranilic acid Lysine Ornithine Important general reactions involved: Decarboxylation The process of removing a carboxyl group from a chemical compound Transamination The process of transposing an amino group within a chemical compound

Classification based on the ring structure or nucleus of the chief alkaloid group in the plant drug: Pyridine-Piperidine Tropane Quinoline Isoquinoline Indole Imidazole Steroid Alkaloidal amines Purine

PYRIDINE - PIPERIDINE ALKALOIDS

TROPANE ALKALOIDS

QUINOLINE ALKALOIDS

ISOQUINOLINE ALKALOIDS

Contain the isoquinoline ring structure

Sources:	Alkaloid(s)
Ipecac	emetine
hydrastis	berberine, hydrastine
sanguinaria	sanguinarine
curare	tubocurarine
opium	morphine, codeine, thebaine

BIOSYNTHESIS OF OPIUM ALKALOIDS:

Tyrosine ----- L Dopa ----- Dopamine

3,4 – dipydroxyphenylpyruvic acid

PAPAVERINE ------ norlaudanosoline (ket intermediate) Reticuline Salut<u>eridine</u> Saluteredinol THEBALNE Codeinone CODEINE **MORPHINE**

IPECAC

Rhizomes and roots of *Cephaelis ipecacuanha*Contains 5 alkaloids
3 principal alkaloids
1.emetine
2. elphaeline
3.psychotrine



Ipecac syrup Treatment of drug overdose and some poisonings procedure emesis central medullary effect by stimulation of chemoreceptor

Ipecac fluidextract

Dover's powder Dipecac +opium Diaphoretic

Emetine/ methylcephaeline

HN

Emetine hydrochloride hydrated hydrochloride of emetine turns yellow when exposed to light Uses: Antiamebic Expectorant Emetic SANGUINARIA Bloodroot Rhizome of Sanguinaria canadensis Other sources: Ranunculaceae Berberidaceae Menispermaceae Papaveraceae Alkaloids (protopine series): sanguinarine chelerythrine protopine allocryptopine

sanguinarine

Alkaloids (protopine series): are colorless but tend to form colored salts:

> HNO3 sanguinarine------> reddish salts HSO4 chelerythrine-----> yellowish salts

Uses: stimulating expectorant emetic

CURARE

First drug
South American arrow poison from bark and stem of Strychnos castelnaei
Early preparations:

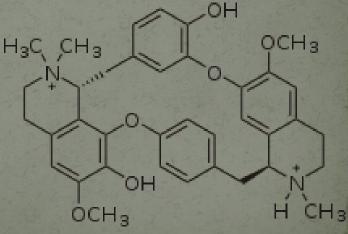
Calabash (gournd)
tube (bamboo)
pot curare (clay pot)
-brownish or black, shiny, resinoid mass with a bitter taste

Alkaloids:

Tubocurarine most important quaternary compound contains

bis-benzylisoquinoline structure





Curariform effect Paralyzing effect on voluntary muscle exhibit by the crude extract Toxic action blood vessels Histamine like effect

Tubocurarine Cl Salt; white, yellowish white to grayish white, odorless crystalline powder

Uses:

Skeletal muscle relaxant

Control convulsions of strychnine poisoning and of tetanus

Adjunct to shock therapy in neuropsyhiatry Diagnostic aid in myasthenia gravis

OPIUM

> Gum opium

- Milky exudate (air-dried) obtained by incising the riped capsule of *Papaver somniferum*
- Opium poppy plantsource

Alkaloids: 1. morphine – 4-12% 2. codeine – 0.8 – 2.5% 3. noscapine (formerly narcotine) – 4- 8% 4. papaverine – 0.5 – 2.5% 5. thebaine – 0.5- 2% 6. meconic acid – 3-5%



Uses:

Stimulant-depressant (first stimulates and then depresses nerve response) analgesic narcotic checks excessive peristalsis miotic Powdered opium used in making Dover's powder and camphorated opium tincture combined with antidiarrheal preparations Paregoric or camphorated opium tincture antiperistaltic Laudanum, opium tincture, deodorized opium tincture antiperistaltic Maw or poppyseed bluish black or yellowish white contains no significant quantity of alkaloids

Morphine

DIDEHYDROXYEPOXY METHYLMORPHINANDIOL
most important of the opiumalkaloids
narcotic analgesic
strongly hypnotic and narcotic
induces vomiting, constipation and b
formation

structural features CNS acting analgesic:
quaternary- central carbon atom with no H substitution
a phenyl group or isostere attached to central C atom
tertiary nitrogen atom
2 – carbon bridge separating (3) and (1)

Codeine

most widely used opiumalkaloid a methylmorphine in which the methyl group replaces the hydrogen of the phenolic hydroxyl group occurs as fine needles or white crystalline powder

Uses:

Narcotic analgesic Antitussive Sedatives in allaying coughs Less toxic and involves lesser danger of habit formation compared to codeine Diacetylmorphine or heroin formed by acetylation of morphine action is similar, yet more pronounced than that f morphine

Apomorphine HCl
morphine treated with HCl
one water molecule is lost
emetic; used subcutaneously in cases of poisoning

Paparavine HCl

muscle relaxant antitussive in combination with codeine sulfate

Hydromorphone HCl or dihydroxymorphine HCl one of the hydroxyl groups of morphine is replaced by **k**etone group; adjacent double bond is removed prepared by reducing morphine in HCl solution with H in the presence of a catalyst powerful narcotic analgesic strongly depresses reeperatory mechanism

Hydrocodone bitartrate or dihydrocodeine bitartrate antitussive

Noscapine

commonly called narcotine exists as free base in opium no narcotic properties (anarcotine) H₃C antitussive H

Ē

*Opioid*Synthetic morphinelike compounds
nonhabit forming
others areantitussive

INDOLE ALKALOIDS

1.Rauwolfia -reserpine -rescinamine -deserpidine 2. Catharanthus (vinca) -vinblastine -vincristine 3. Nux vomica -strychnine -brucine

4. physostigma
-physostigmine
5. Ergot
-ergotamine
-ergonovine

Biosynthesis

Tryptamine ◇ ajmaline ◇ + Corynanthe-type (monoterpenoid precursor)

Serpentine

reserpine

RAUWOLFIA SERPENTINA -dried roots of rauwolfia serpentine

ALKALOID SERIES: 1. weakly basic indole alkaloids -reserpine -rescinamine } PRINcipal alkaloids -desperidine -8-yohimbine -reserpiline 2.indoline alkaloids of intermediate basicity -ajmaline -isoajmaline } NO TRANQUILIZING EFFECT -rauwolfinine 3.strong anhydronium bases -serpentine -serpentinine -alstonine

PACKAGING & STORING

must be packaged and stored in a well-closed container in a cool,dry place that is secure against insect attack.

RESERPINE – is the chief alkaloid and has a strong hypotensive and sedative activity - white or pale buff to slightly yellow crystalline powder; darkens slowly when exposed to light

USES: antihypertensive and tranquilizer

RESCINNAMINE Methyl reserpate ester of 3,4,5-trimethoxy cinnamic acid Uses: antihypertensive

DESERPIDINE: -is an alkaloid from roots of *Rauwolfia canescens* -11-desmethoxyreserpine USES: -antihypertensive -tranquilizer CATHARANTHUS -vinca and periwinkle -dried whole plant of *catharanthus rosea* -have anticancer potential

ALKALOIDS: -ajmalicine,tetrahydroalstonine,serpentine,lochnerine **U.S ADOPTED** Scientific name **DRUG NAMES** -Vinblastine Vincaleukoblastine(VLB) leurosine -Vinleurosine -Vinrosidine leurosidine -vincristine leuocristine(LC) = posses demonstrable ancolytic activity

VINBLASTINE SULFATE -antineoplastic

-recommended for generalized Hodgkin's disease,lymphocytic lymphoma,histiocytic lymphoma,mycosis fungoides,advanced testicular carcinoma,kaposi's sarcoma,and choriocarcinoma and breast cancer unresponsive to other therapies.

VINCRISTINE SULFATE treatment for acute leukemia combination therapy in Hodgkin's disease,lymphosarcoma,reticulum sarcoma,rhabdomyosarcoma,neuroblastoma,and Wilma's tumor.

VINDESINE -semisynthetic derivative of vinblastine

NUX VOMICA dried ripe seed of strychnos nux vomica ALKALOIDS; -strychnine -brucine

USES: Serve as a commercial source of strychnine and brucine

STRYCHNINE: -extremely toxic -CNS stimulant -blocks inhibitory spinal impulses at the postsynaptic level. -results in tonic convulsion

USES: vermine killer BRUCINE -less toxic -alcohol denaturant

PHYSOSTIGMINE -physostigma or calabar bean or ordeal bean -dried ripe seed of *physostigma venenosum* Alkaloids: -physostigmine(eserine) -eseramine -geneserine -physovenine

Physostigmine or eserine -acquires red tint when exposed to heat, light, air or metal -reversible inhibitor of cholinesterase
-enhances effects of achetylcholine
-used in open-angle glaucoma, decreases intraocular pressure
PHYSOSTIGMINE SALICYLATE OR ESERPINE SALICYLATE
-it is a white powdered that also acquires a red tint

-it is a white powdered that also acquires a red tint when exposed to the conditions described under physostigmine.

-cholinergic (ophthalmic)-IV antidote for poisoning caused by anticholinergic

PHYSOSTIGMINE SULFATE -cholinergic -applied topically to conjunctiva -white microcrystalline powder is deliquescent in moist air and acquires the red tint previously described.

ERGOT

-rye ergot or secale cornutum
Dried sclerotium of *claviceps purpurea* developed on plants of rye
-not less than 0.15% alkaloids (ergotoxine)
-0.01% water soluble (ergonovine)

Spurred eye- common name of the drug

Mycellium-mass of tissue formed with the hyphae

1.sphacelial stage- asexual stage of the ergot fungi where the spores are being transferred from one plant to the other by insects in honeydew

Sclerotium-resting body, hardened ovary

2.ascigerous stage-sexual stage

-production of sexual spores or ascospores

Ergotism-outbreak in old times before moderns agriculture practices a. in France- gangrene

-restricted blood flow due to vasoconstricting action of alkaloids

-previously called ST.ANTHONY's FIRE b. in Rhine and Germany- convulsion

constituents of ergot: 1.ergonovine-most important 2.ergotoxine-3.ergoloxine-ergoristine + ergokryptine + ergocornine Lysergic acid-precursor of medicinal useful alkaloids from ergot Derivatives of isolysergic acid-physiologically inert

Histamine and tyramine- contribute to physiologic activity of crude drug

USES:

oxytocic properties

ERGONOVINE MALEATE OR ERGOMETRINE MALEATE -white or faintly yellow, coloress, microcrystalline powder

Ergobasine- Switzerland -first isolation

Uses: oxytocic vasoconstrictor

Ergometrinine-isolysergic acid isomer of ergonovine

METHLYERGONOVINE MALEATE

-semisynthetic homolog of ergonovine
-lysergic acid + 2-aminobutanol
-white to pinkish tan,microcrystalline powder

Uses; oxytocic slightly more active and longer than ergonovine ERGOTAMINE TARTRATE -specific analgesic in treatment of migrain by reducing extracranial blood flow and decreases the amplitude of pulsations -enhanced by caffeine

HYDROERGOTAMINE MESYLATE

-semisynthetic alkaloid ergotamine by hydrogenation -migraine treatment, more effective and tolerated compared to ergotamine

ERGOTOXINE -mixture of alkaloid ergocristine ergokyptine ergocornine -formely employed as ergotoxine extranisulfunate

Ergoloid-methanisulfonate

-for elderly patients

-vasorelaxant,increased cerebral blood flow lower BP and causes bradycardia

METHYsergide maleate -semisynthesized from lysergic acid -serotonin antagonist -for prophylaxis of vascular headache

LYSERGIC ACID DIETHYLAMIDE (LSD) produces a predominant central sympathetic stimulation to parallel slight depression most active and specific psychotomemitic agent

drugs related to ergot: Ololiuqui -ancient ajtec hallucinogec drug -from seed of rovea corymbosa ipomomea spp and arygyreia

IMIDAZOLE ALKALOIDS

Contain imidazole (glyoxaline) rings <u>PILOCARPINE</u>

PILOCARPUS
AKA jaborandi
Consists of leaflets of:
Pilocarpus jaborandi Holmes
Pilocarpus microphyllus Stapf
Pilocarpus pinatifolius
Lamaire
Indigenous to Brazil

PILOCARPINE

the lactone of pilocarpic acid, an acid with glyoxaline nucleus Oily, syrupy liquid, though its salts crystallize easily May be obtained by treating the powdered leaves with sodium carbonate Extracting with benzene Shaking the benzene extract with dilute hydrochloric or nitric acid Aqueous solution is made alkaline and shaken with chloroform The chloroform is shaken with acid The alkaloidal salt is allowed to crystallize.

PILOCARPINE

MOA:

It directly stimulates the muscarinic receptors in the eye, causing constriction of the pupil and contraction of the ciliary muscle.

In narrow-angle glaucoma

Miosis opens the anterior chamber angle to improve the outflow of aqueous humor.

In chronic open-angle glaucoma

The increase in outflow is independent of the miotic effect. Contraction of the ciliary muscle enhances the outflow of aqeous humor via indirect effects on the trabecular system.

PILOCARPINE

Salts
 Pilocarpine hydrochloride - crystals of the hydrochloride of Pilocarpine
 Colorless
 Translucent
 Odorless
 faintly bitter

Pilocarpine nitrate – crystals of the nitrate of Pilocarpine

Shiny
White
Stable inair
Light-sensitive

Hygroscopic

Uses:

Ophthalmic drugs for treatment of galucoma Applied topically

Dosage: o.o5-o.1mL of a o.25 to 10% solution of Pilocarpine hyrdochloride OR o.o5-o.1mL of a o.5 to 6% solution of Pilocarpine nitrate Applied to the conjunctiva, 1-6x a day

EPatients should be advised to wash hands immediately after application.



Pilocar®



Isopto-carpine®

STEROIDAL ALKALOIDS

Characterized by the cyclopentanophenanthrene nucleus either formed from cholesterol or have a common precursor with cholesterol

VERATRUM VIRIDE

- AKA American hellebore or greenhellebore
- Veratum: "vere" = truly, "ater" = black
- Viride = green
- Consists of the dried rhizome and roots of *Veratum viride* Alton

VERATRUM VIRIDE

Grows in wet meadows in the mountainous section of New England and the Eastern United States, North Carolina, Tennessee, and northern Georgia

Veratum: "vere" = truly, "ater" = black

Obtained by: Idigging therhizomes ICleaning ICutting longitudinally Idrying



VERATRUM VIRIDE

Contains a large no. of alkaloids customarily classified in 3 groups, with their chemical constituents as basis.

Group 1	Group 2	Group 3
consists of esters of the steroidal bases (alkamines) with organic acids	consists of lucosides of of the alkamines	Consists of the alkamines
Includes: •Cevadine •Germidine •Germitrine •Neogermitrine •Neoprotoveratrine •Protoveratrine •Veratridine	Includes: •Pseudojervine •Veratrosine	Includes: •Germine •Jervine •Rubijervine •veratramine

The ester alkaloids, germidine and germitrine are probably the most important therapeutically.

VERATRUM VIRIDE Uses: Antihypertensive Small doses principally affect blood pressure without notably changing respiratory or cardiac rate Cardiac-depressant In tincture form Sedative Insecticide VERATRUM ALBUM AKA European hellebore or white hellebore Indigenous to central and southern Europe Similar in appearance and structure with V. viride, though its external color is lighter

VERATRUM ALBUM

Contains a complex mixture of ester alkaloids, grycoalkaloids, and alkamines similar to those occuring in *V. viride*.

Ester alkaloids protoveratrine A and protoveratrine B are the most active

Upon hydrolysis, both yield protoverine, acetic acid, methylbutyric acid, and methylhydroxybutyric acid (in protoveratrine A) or methyldihydroxybutyric acid (in protoveratrine B)

Uses:

Antihypertensive Insecticide



ALKALOIDALAMINES

Do not contain heterocyclic nitrogen atoms Mostly are simple derivatives of phenylethylamine

EPHEDRINE

- AKA (-)-erythro-α-[1(methyl-amino)ethyl]benzyl alcohol
- Obtained from Ephedra or ma huang (*Ephedra sinica* Stapf)
- "ma"=astringent, "huang"=yellow
- Used as a medicine in China for more than 5000 years

EPHEDRINE Produced commercially by: Extraction of the plant material Chemical procedure involving a reductive condensation between L-1-phenyl-1-acetylcarbinol and methylamine Occurs as white, rosette or needle crystals, or as a unctuous mass Soluble in water, alcohol, chloroform, ether, and liquid petrolatum Melts between 33 and 40°C, depending on its water content

EPHEDRINE Uses: Sympathomimetic (stimulates α, β1, & β2 adrenergic receptors)

Salts

Ephedrine Sulfate – crystals of the sulfate of Ephedrine
Fine, white, odorless
Darkens when exposed to light
Used to combat hypotensive states, for allergic disorders, and for nasal decongestion
Usual dose is:
25-50mg, 6-8x a day as necessary (oral & parenteral)
0.1-0.15mL of a 1-3% solution, 2-3x a day (intranasal)
Readily soluble in water and in hot alcohol but not in ether

EPHEDRINE

Ephedrine hydrochloride – crystals of the hydrochloride of Ephedrine

Fine, white, odorless
Affected by light
Used as a symphatomimetic

Usual dose is 25-50mg, every 3-4 hrs

Readily soluble in water and in hot alcohol but not in ether

Dainite KI, Quadrinal, Tedral, Bronkotabs, Bronkaid

COLCHICINE

- extracted from plants belonging to the Colchicum genus
- has one amino nitrogen atom
- lacks pronounced basicity and does not form a well-defined series of salts
- pale yellow, amorphous scales or powder that gradually turns darker when exposed to light
- soluble in water and ether; freely soluble in alcohol and chloroform
- inhibits leukocyte migration and reduces lactic acid production by leukocytes, resulting in a decreased deposition of uric acid
- causes reduction in phagocytosis which decreases inflammatory response

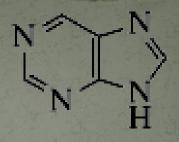
Colchicum seed - dried, ripe seed of C. autumnale

Colchicum corm – dried corm (stalk) of C. autumnale

Use: -suppressant for gout

Dosage: -500-650µg, 1-3x a day (oral) -500µg-1mg, 1-2x a day (intravenous)

PURINE BASES



Derivatives of a heterocyclic nucleus consisting of the 6-memebered pyrimidine ring fused to the 5-membered imidazole ring purine Does not occur in nature, but numerous derivatices are biologically significant

EXanthine – source of the most important purine bases eg caffeine (1,3,7-trimethylxanthine), theophylline (1,3dimethylxanthine), & theobromine (3,7-dimethylxanthine)

MOA: The methylxanthines competitively inhibit phosphodiesterase, which results in an increase of cyclic adenosine monophosphate with a subsequent release of endogenous epinephrine. This results in a direct relaxation of the smooth muscles of the bronchi and pulmonary vessels, a stimulation of the CNS, an induction of diuresis, an increase in gastric acid secretion, an inhibition of uterine contractions, and a weak positive inotropic effect on the heart.

Caffeine-containing drugs □Kola

AKA cola orkolanuts Dried cotyledon of *Cola nitida* or other sp. of *Cola* Yields not less than 1% of anhydrous caffeine Impt. because of its caffeine content and flavor Contains up to 3.5% caffeine, and less than % theobromine

Bound to the tannin kolacatechin in freshnuts

Uses:

Stimulant

Ingredient in several carbonated beverages

Coffee bean
AKA coffee seed
Dried, ripe seed of *Coffea arabica* or *C. liberica*Contains about 1-2% caffeine, 0.25% trigonelline, 3-5% tannin, about 15% glucose and dextrin, 10-13% fatty oil (mainly olein and palmitin), and 10-13% proteins.

Roasted coffee – coffee roasted until it acquires a dark brown color and develops the characteristic aroma

Caffeol – oil that causes the aroma - consists about 50% furfurol with traces of valerianic acid, phenol, and pyridine -produced during the roasting process Decaffeinated coffee – prep. by extracting the most of the caffeine from the coffee bean, yet retaining the pleasant characteristic aroma

-contain up to 0.08% caffeine

Methods of freeing the seeds from the parchmentlike endocarp:

The fruits are allowed to dry and are then broken
 The wet method in which the sarcocarp is removed by

means of a machine, and the 2 seeds with the parchmentlike endocarp are allowed to dry in such a manner as to undergo a fermentation. After drying, the endocarp is removed. Caffeine content comparison: A cup of brewed coffee : 100-150mg instant coffee : 85-100mg tea: 60-75mg cocoa: 5-40mg 120z cola drink: 40-60mg

Est. max. daily dose: 1.5g

Uses: Dietetic Stimulant Diuretic Guarana

Dried paste composed chiefly of the crushed seed of *Paullinia cupana* Contains 2.5-5% caffeine, and 25% cathechutannic acid Uses: Stimulant Astringent

Maté
AKA Paraguay tea
Consists of the leaves of *Ilex paraguariensis*Contains 2% caffeine and tannin Uses:
Stimulant
Laxative/purgative
Diaphoretic
Diuretic

Caffeine

- 1,3,7-trimethylxanthine
- Usually prep. from tea, tea dust, or tea sweeping, or recovered from coffee roasters
- Anhydrous or contains 1 molecule of water of hydration White powder or white glistening neededs matted together in fleecy masses
- Bitter
- May be sublimed without decomposition when heated Uses:
 - CNS stimulant

caffeine

Caffeine and sodium benzoate for IM inj. as an analeptic in the treatment of poisoning Stimulant in acute circulatory failure diuretic

Tea

AKA thea

Consists of leaves and leaf buds of Camellia sinensis Occurs as more or less crumpled, bright green or blackish **g** masses

Smells agreeable and aromatic

Tastes pleasantly astringent and bitter

Contains 1-4% caffeine (theine) and small amounts of adenine, theobromine, theophylline, and xanthine

Green tea – prep. by rapidly drying the freshly-picked leaves in copper pans over a mild artificial heat. The leaves are often rolled in the palm of the hand as they dry.

Black tea – prep. by heaping the fresh leaves until fermentation has begun. They are then rapidly dried artificially with heat. Uses:

Stimulant (due to caffeine)

Astringent (due to the tannin)

Theophylline

Isomeric with theobromine
White, odorless, bitter crystalline powder
Soluble in about 120 parts of water, rendered
more soluble in basic compounds

Uses:

Smooth muscle relaxants for the symptomatic relief or prevention of bronchial asthma and treatment of reversible bronchospasm associated with chronic bronchitis and emphysema Diuretic

Aminophylline - valuable diuretic - exhibits dilating action on the pulmonary vessels in relieving asthma and can lower venous pressure in certain cases of heart failure

Theobromine

3,7-dimethylxanthine

Prep from the dried, ripe seed of *Theobroma cacao* White, crystalline powder with bitter taste and sublimes **a** about 260°C.

Uses:

Diuretic

Smooth muscle relaxant

Preferred over caffeine in the treatment of cardiac edema and angina pectoris, since it has little stimulant action

Thanking you