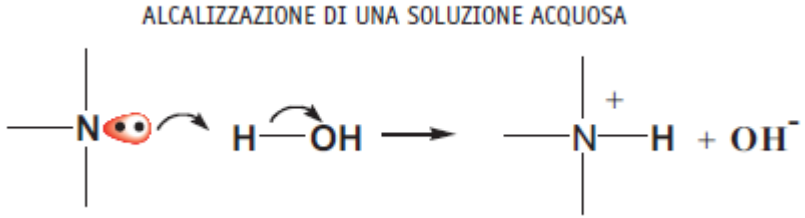
ALCALOIDI

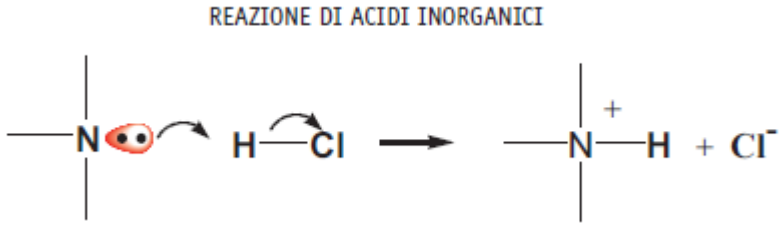
ALCALOIDI: CARATTERE GENERALE

❖SOSTANZE A CARATTERE BASICO

1. pH alcalino delle soluzioni acquose di **alcaloidi solubili** in acqua



2. Reazione con sostanze acide

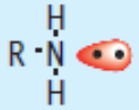
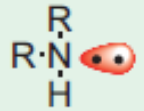
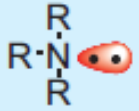
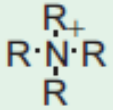


Formazione del **SALE** che rende solubile in acqua anche un alcaloide che di per sè è insolubile

COMPOSTI ORGANICI AZOTATI

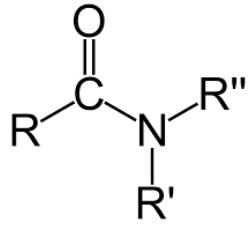
AMMINE e sali

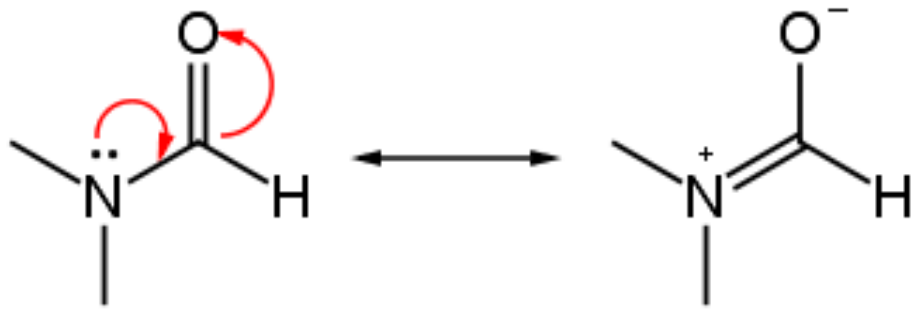
LE CLASSI DELLE AMMINE

AMMINA	STRUTTURA GENERALE	FORMULA GENERALE
PRIMARIA	RNH_2	
SECONDARIA	R_2NH	
TERZIARIA	R_3N	
QUATERNARIA	R_4N^+	

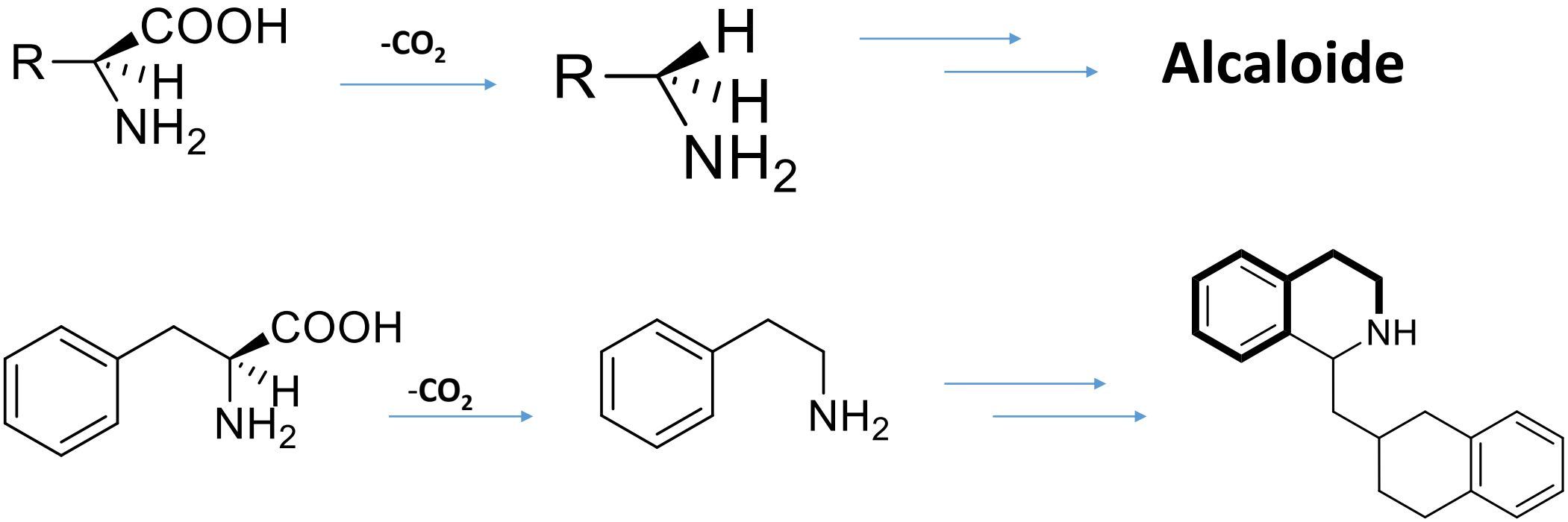
- In base al numero di C legati all'azoto
- Carattere basico (*lone pair* disponibile)

AMMIDI (derivato da ammina)





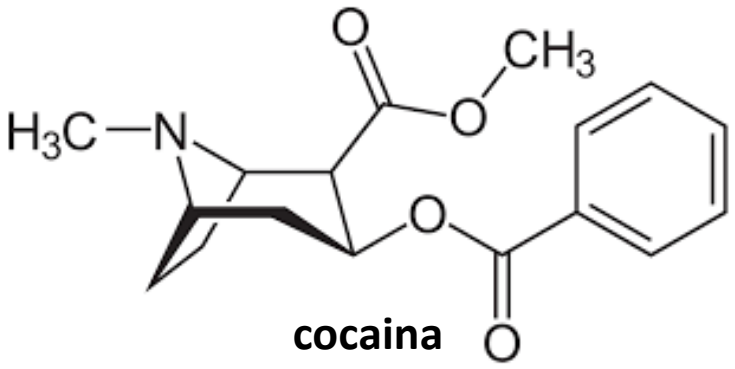
Biosintesi degli alcaloidi



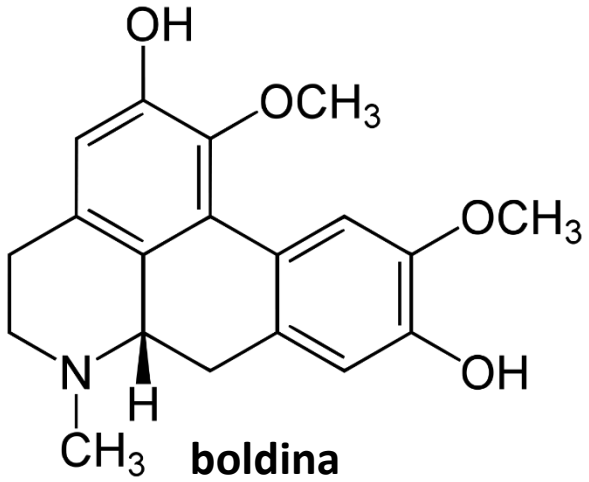
Gli alcaloidi si formano dalla decarbossilazione degli AA

Reattività **alcalina**
Anello **eterociclico** contenente azoto
Derivazione biosintetica degli **AA**

alcaloidi **in senso stretto**

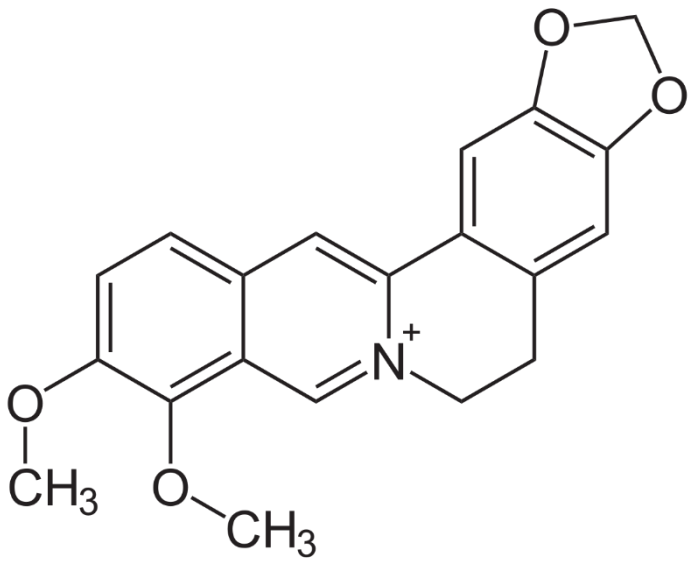


cocaina



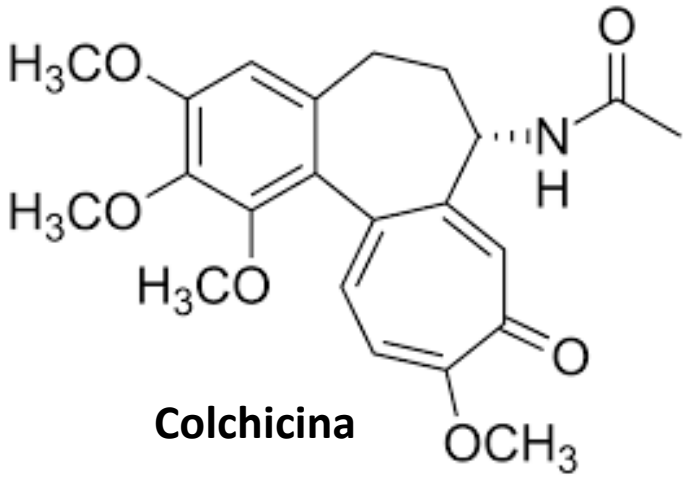
boldina

Esempi di ALCALOIDI IN SENSO LATO



Berberina

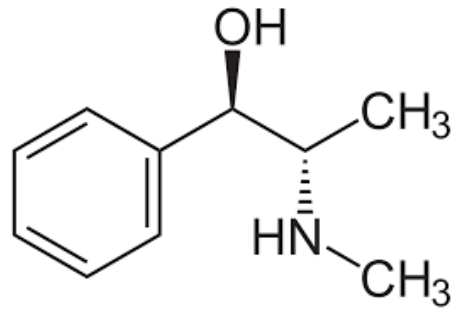
Non è basico



Colchicina

Non è basico

Non-eterociclico

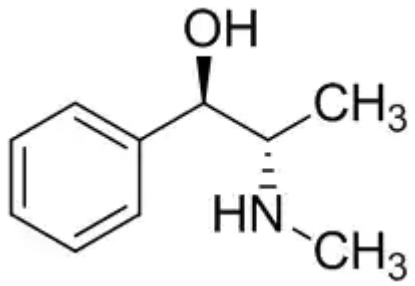


Efedrina

Non-eterociclico

- **PROTOALCALOIDI**

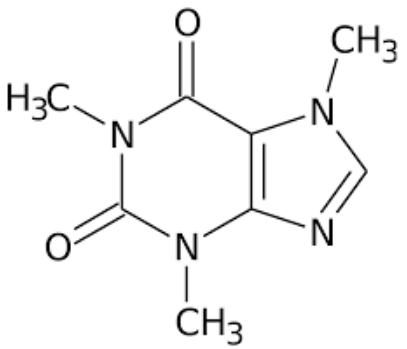
ammine semplici direttamente derivate dagli amminoacidi



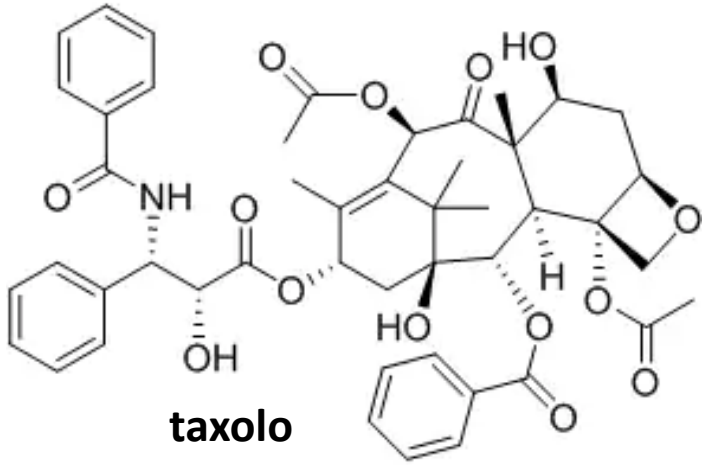
efedrina

- **PSEUDOALCALOIDI**

derivano da purine o terpeni

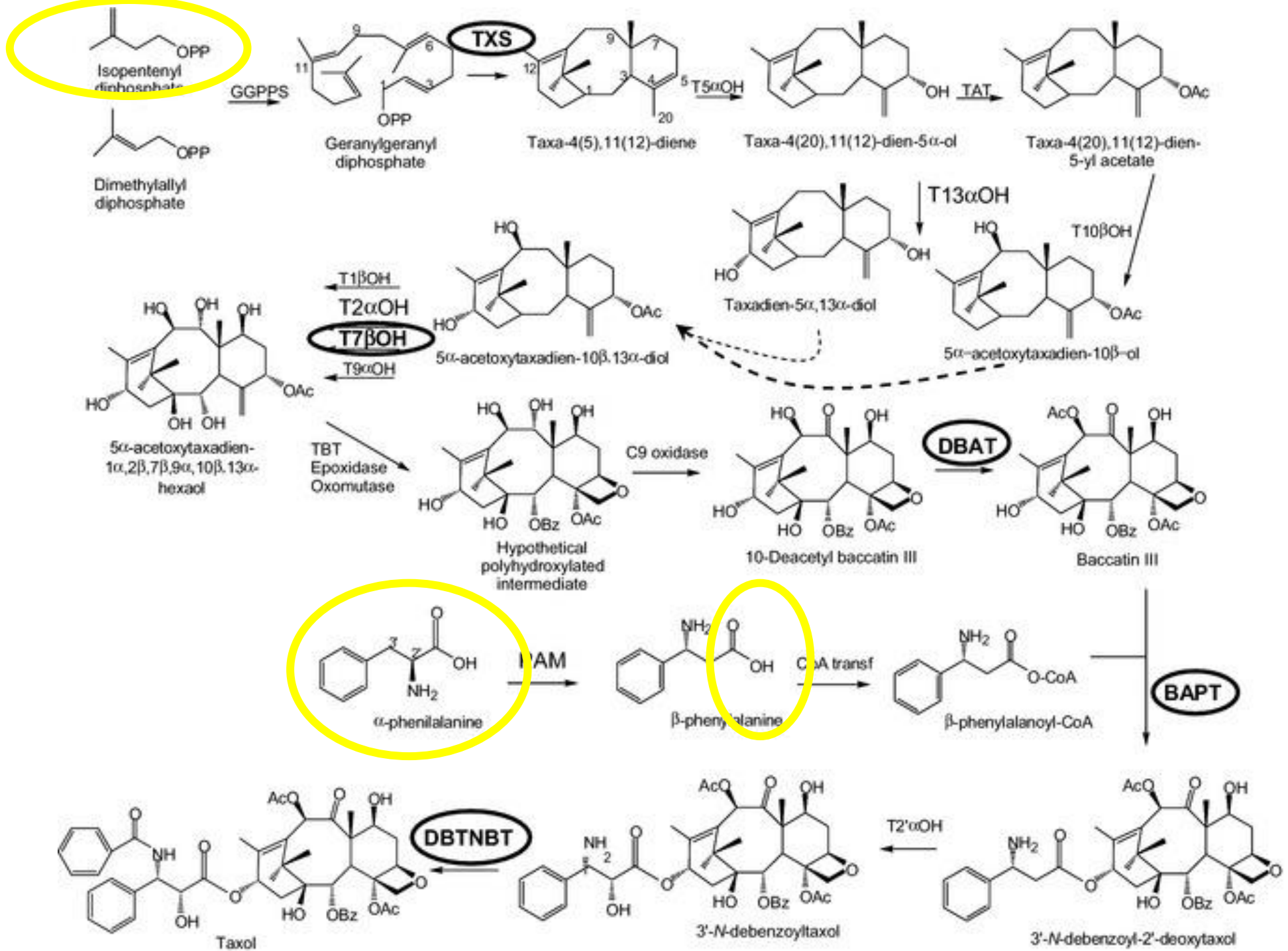


caffeina

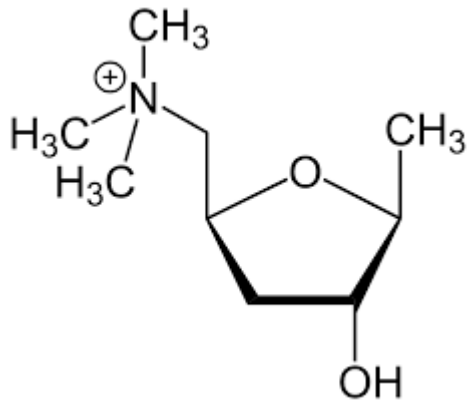


taxolo

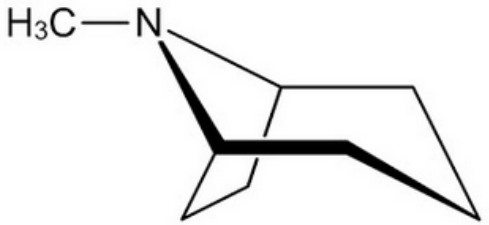
Sono esempi di alcaloidi in senso lato


Isopentenyl diphosphate
Dimethylallyl diphosphate
GGPPS
Geranylgeranyl diphosphate
TXS
Taxa-4(5),11(12)-diene
T5αOH
Taxa-4(20),11(12)-dien-5α-ol
TAT
Taxa-4(20),11(12)-dien-5-yl acetate
T13αOH
Taxadien-5α,13α-diol
T10βOH
5α-acetoxytaxadien-10β-ol
T1βOH
T2αOH
T7βOH
T9αOH
5α-acetoxytaxadien-10β,13α-diol
5α-acetoxytaxadien-1α,2β,7β,9α,10β,13α-hexaol
TBT
Epoxidase
Oxomutase
Hypothetical polyhydroxylated intermediate
C9 oxidase
10-Deacetyl baccatin III
DBAT
Baccatin III
α-phenilalanine
PAM
β-phenylalanine
CoA transf
β-phenylalanoyl-CoA
BAPT
3'-N-debenzoyltaxol
T2'αOH
3'-N-debenzoyl-2'-deoxytaxol
DBTNBT
Taxol

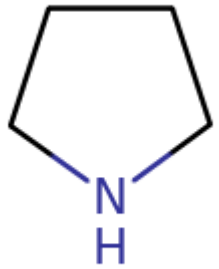
ALCALOIDI DI ORIGINE ANIMALE O FUNGINA



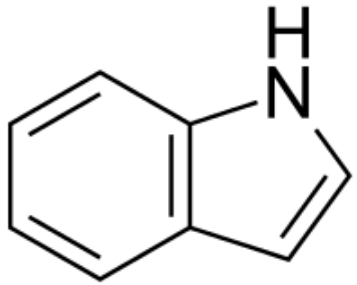
CLASSIFICAZIONE SULLA BASE DELL'ETEROCICLO



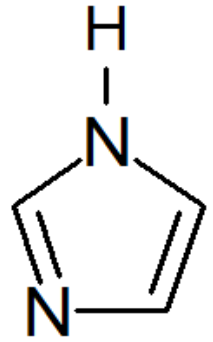
tropano



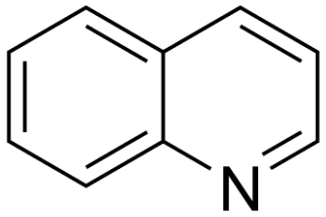
pirrolidina



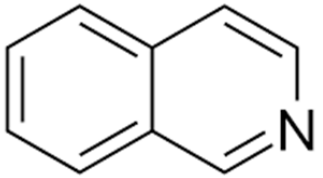
indolo



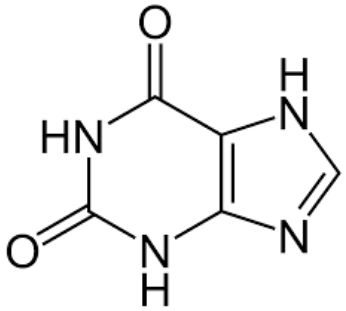
imidazolo



chinolina



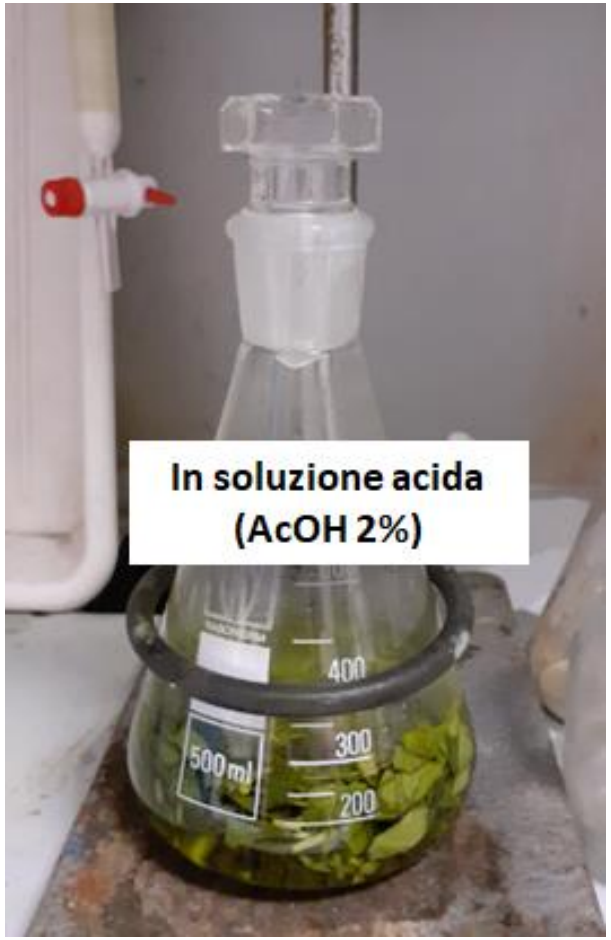
isochinolina



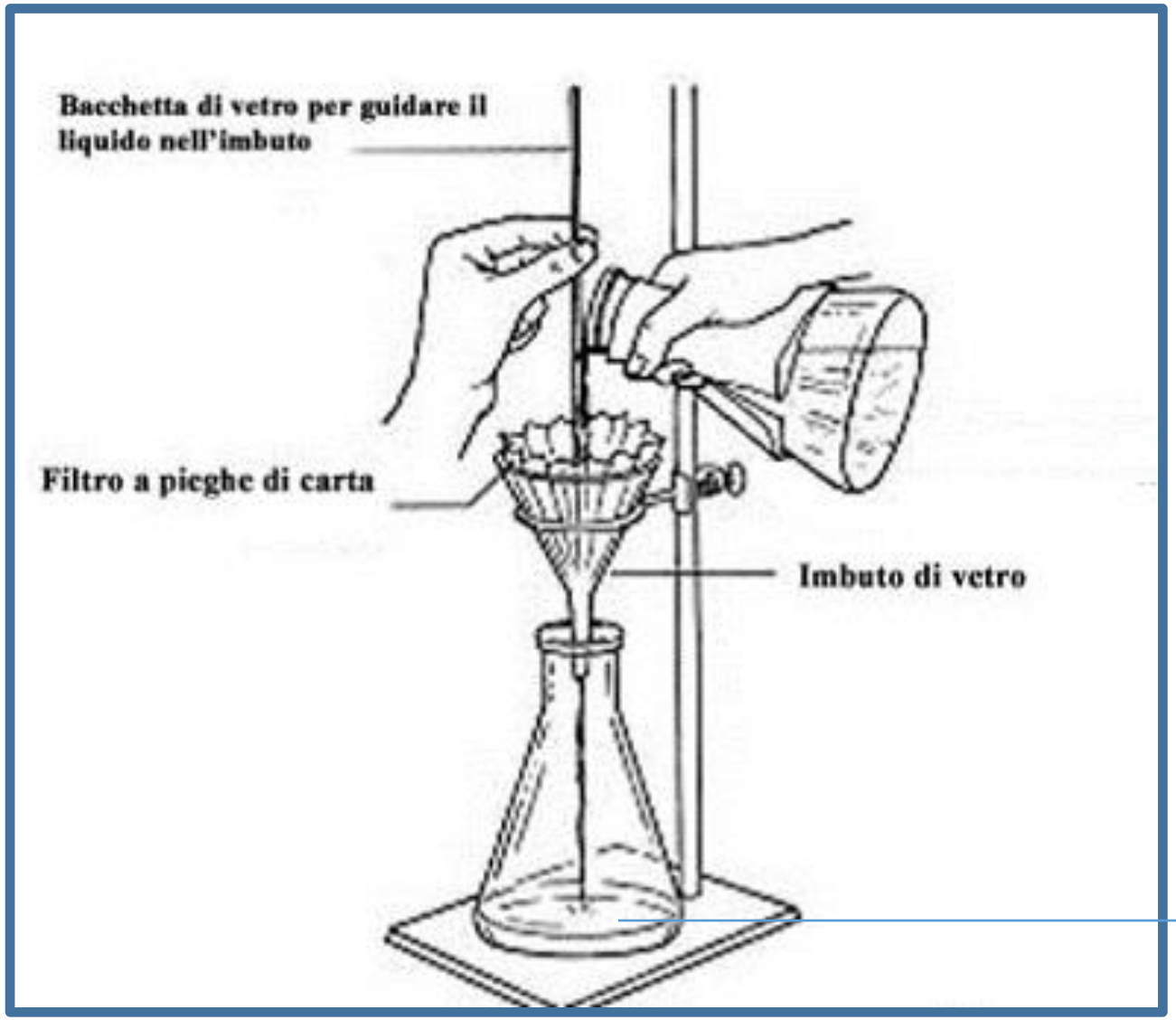
xantina

ALCALOIDI: ESTRAZIONE

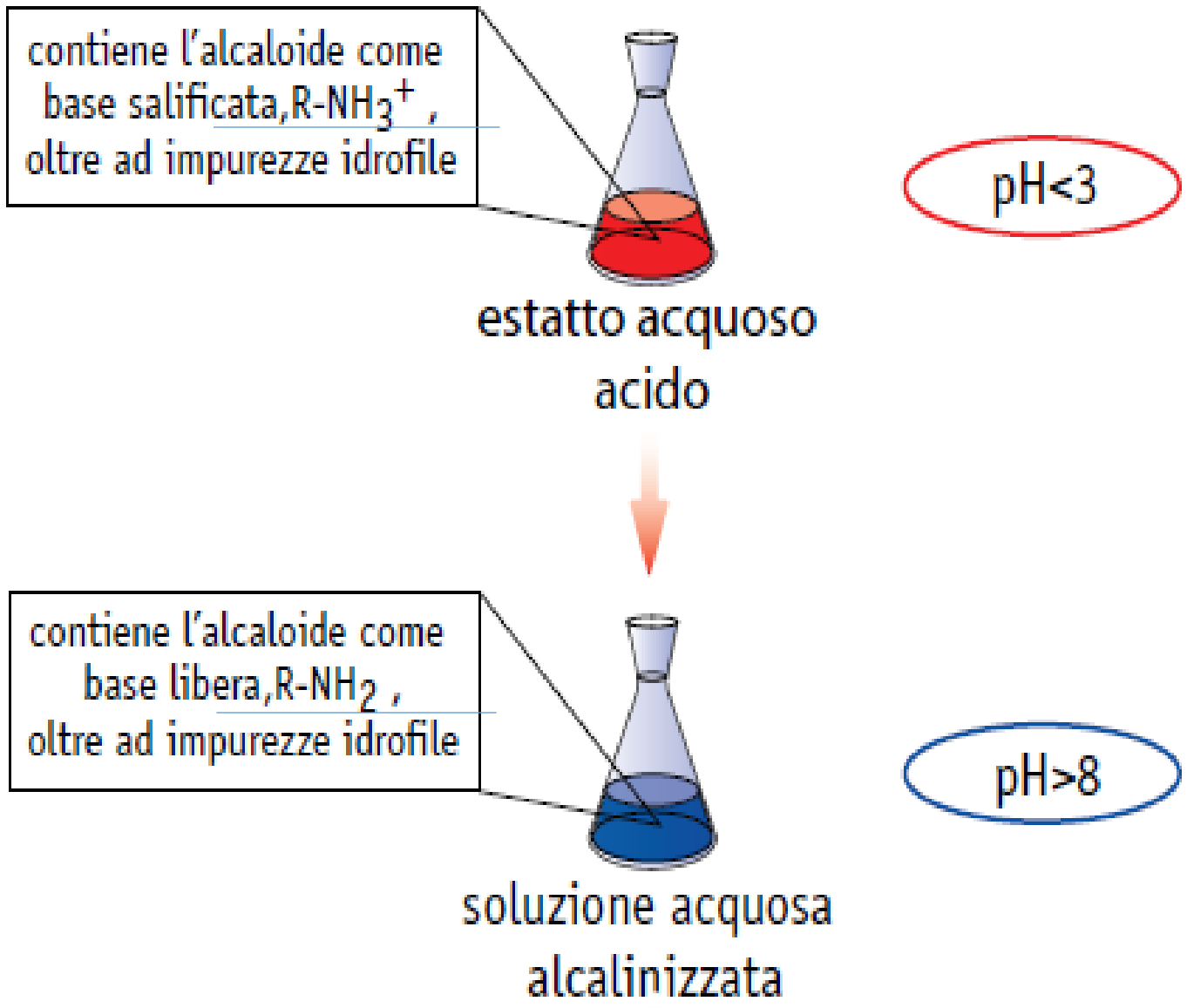
PREPARAZIONE DEL CAMPIONE



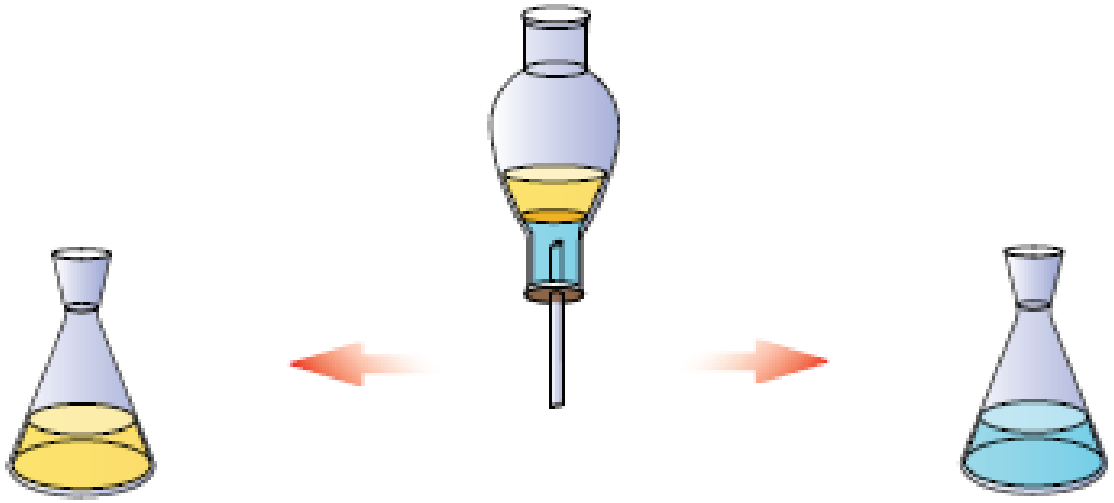
FASE DI ESTRAZIONE IN ACQUA ACIDULATA



FASE LIQUIDA
SOLUZIONE ACIDA CONTENENTE GLI
ALCALOIDI SOTTO FORMA DI SALE



SI FA RITORNARE L'ALCALOIDE NELLA SUA **FORMA BASICA** ALCALINIZZANDO LA FASE ACQUOSA



soluzione organica

contiene l'alcaloide come base libera, R-NH_2

soluzione acquosa

contiene le impurezze idrofile

Identificazione: reattivo di Dragendorff

$KBiI_4$ (in ambiente acido)

In ambiente , l'azoto si protona quindi si forma la coppia ionica $[R_3NH]^+$ ed $[BiI_4]^-$

Ammine terziarie: **intensa colorazione** rossastra
Ammine secondarie: **minore colorazione**
Ammine primarie: raramente si colarano

ALCALOIDI: funzioni

NELLE PIANTE

- Sostanze di ***rifiuto*** (**IPOTESI ABBANDONATA**!!)
- ***Difesa*** contro erbivori (sapore amaro)

Progressione barriere difensive nei riguardi del predatore
Sapore sgradevole > fastidio, disorientamento > morte

NELL'UOMO

- **SNC**
- **SNP**
- Azione antitumorale
- Azione antimalarica
- Digestione

IN GENERALE (con delle eccezioni) le **proprietà** dipendono dalla dose

BASSE DOSI: potere amaricante → digestione

ALTE DOSI: effetti tossici → morte

ALCALOIDI: dove si trovano

*Frequenti in **Angiosperme** dicotiledoni*

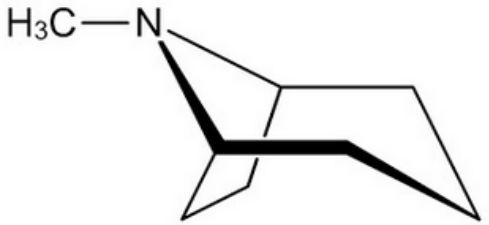
- ✓Papaveraceae
- ✓Solanaceae
- ✓Apocynaceae

Ma abbiamo alcuni esempi anche tra le monocotiledoni

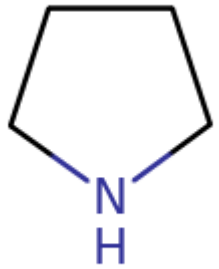
LOCALIZZAZIONE

- ❖ confinati all'interno dei **vacuoli** (pH acido)
- ❖ spesso trasportati all'esterno tramite apposite vescicole extracellulari (**esempio lattice papavero da oppio**)

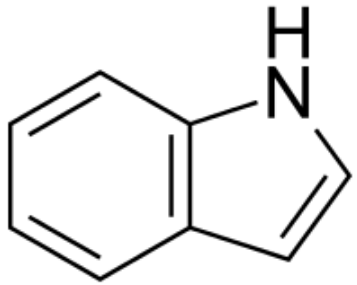
CLASSIFICAZIONE SULLA BASE DELL'ETEROCICLO



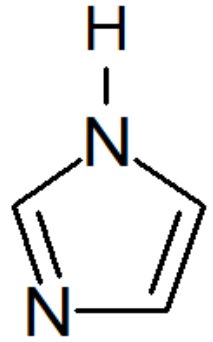
tropano



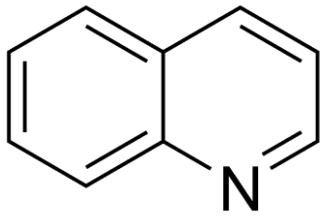
pirrolidina



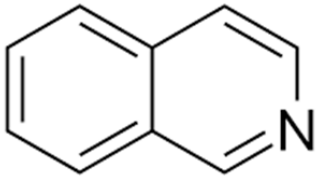
indolo



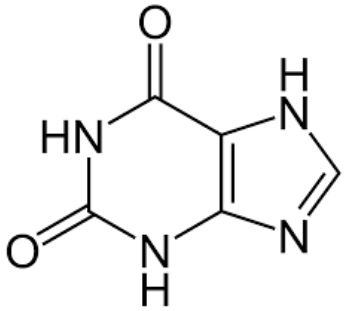
imidazolo



chinolina

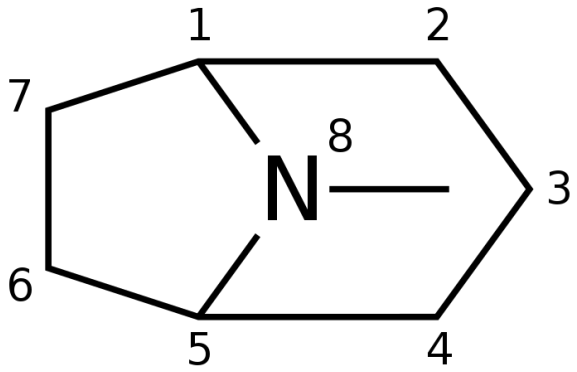


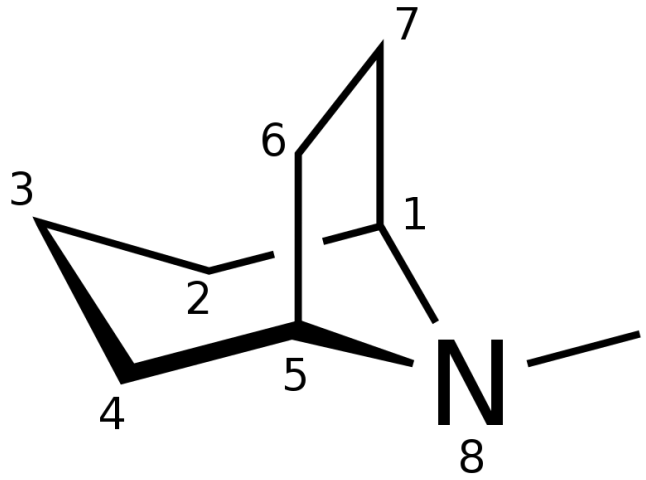
isochinolina

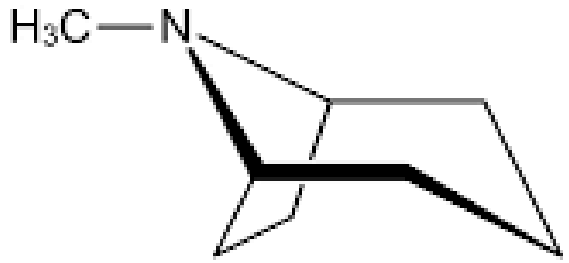


xantina

Alcaloidi tropanici







tropano

Diversi modi di rappresentare il tropano

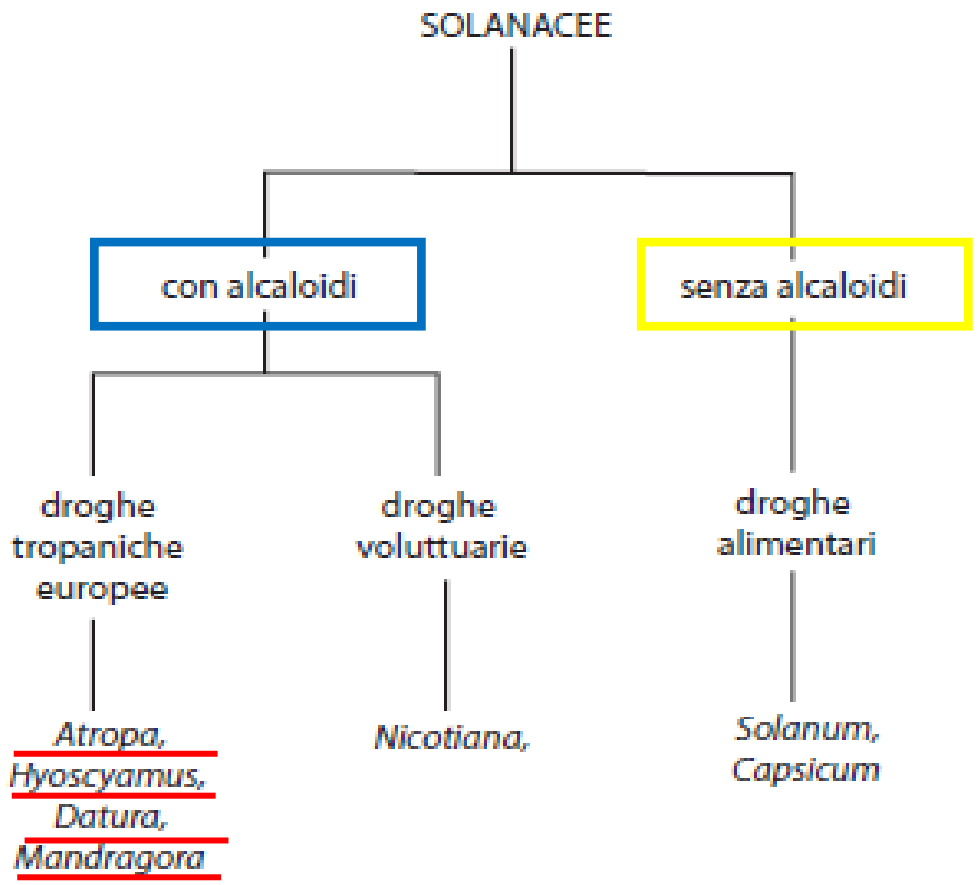
Famiglie con alcaloidi a nucleo tropanico

- **Solanaceae**
- Eritroxilaceae (*Erytroxylon coca*)
- Sporadicamente in qualche genere isolato

Piante medicinali tossiche

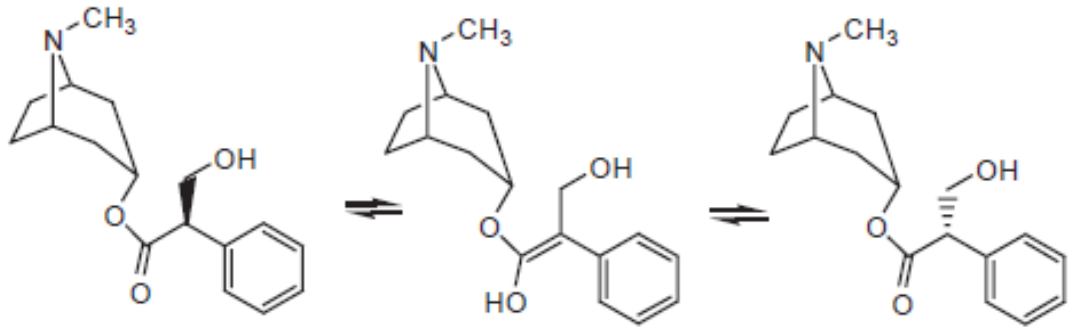
Belladonna
Stramonio
Giusquiamo
Mandragora

Solanaceae

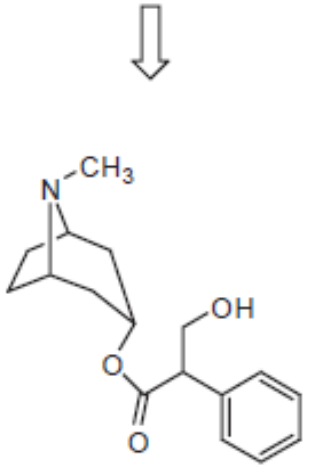


NB: nella famiglia delle Solanacee possiamo trovare sia alcaloidi tropanici che non tropanici **(dipende dal genere)**

Conversione della iosciamina in atropina

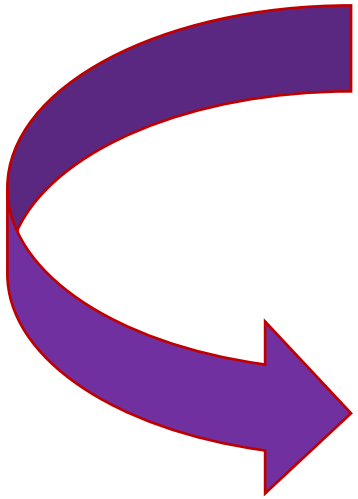


(-)-iosciamina forma enolica (+)-iosciamina



atropina

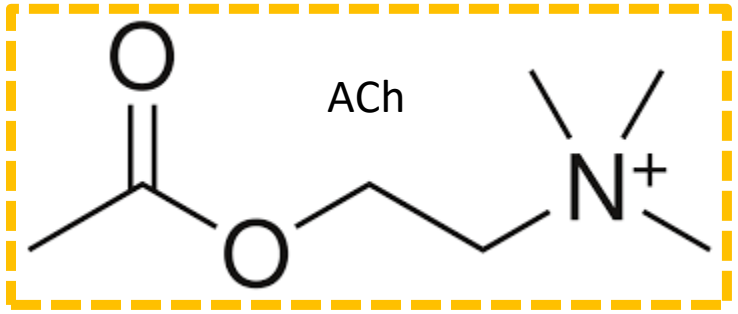
Proprietà delle droghe tropaniche: **attività antimuscarinica**

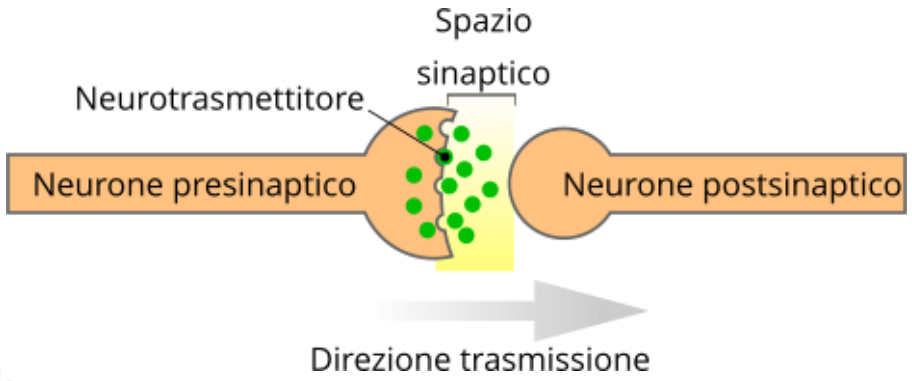


Interferenza con la trasmissione **colinergica** tramite interazione con i recettori **MUSCARINICI**

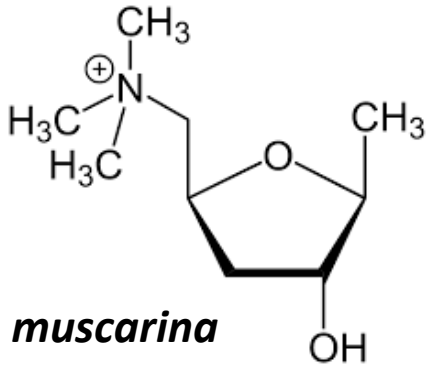
Trasmissione **colinergica**

Mediata dall'**ACETILCOLINA** (Ach) a livello del SNC e SNP



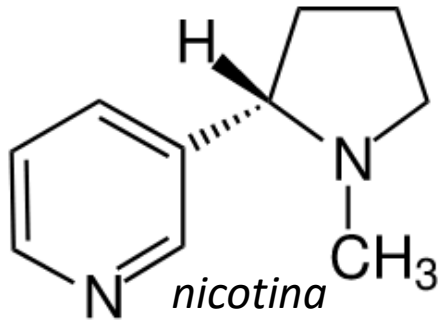


Recettori *muscarinici*:



muscarina

Recettori *nicotinici*:



nicotina

RECETTORI MUSCARINICI (M1-M5)

LOCALIZZAZIONE	RISPOSTA FISIOLOGICA
SNC	Memoria, attenzione
GHIANDOLE	Aumento secrezione gastrica e salivare
OCCHIO	Contrazione pupilla
CUORE	Inibizione cardiaca
MUSCOLATURA LISCIA	Contrazione muscolatura intestino, vie urinarie, vie aeree

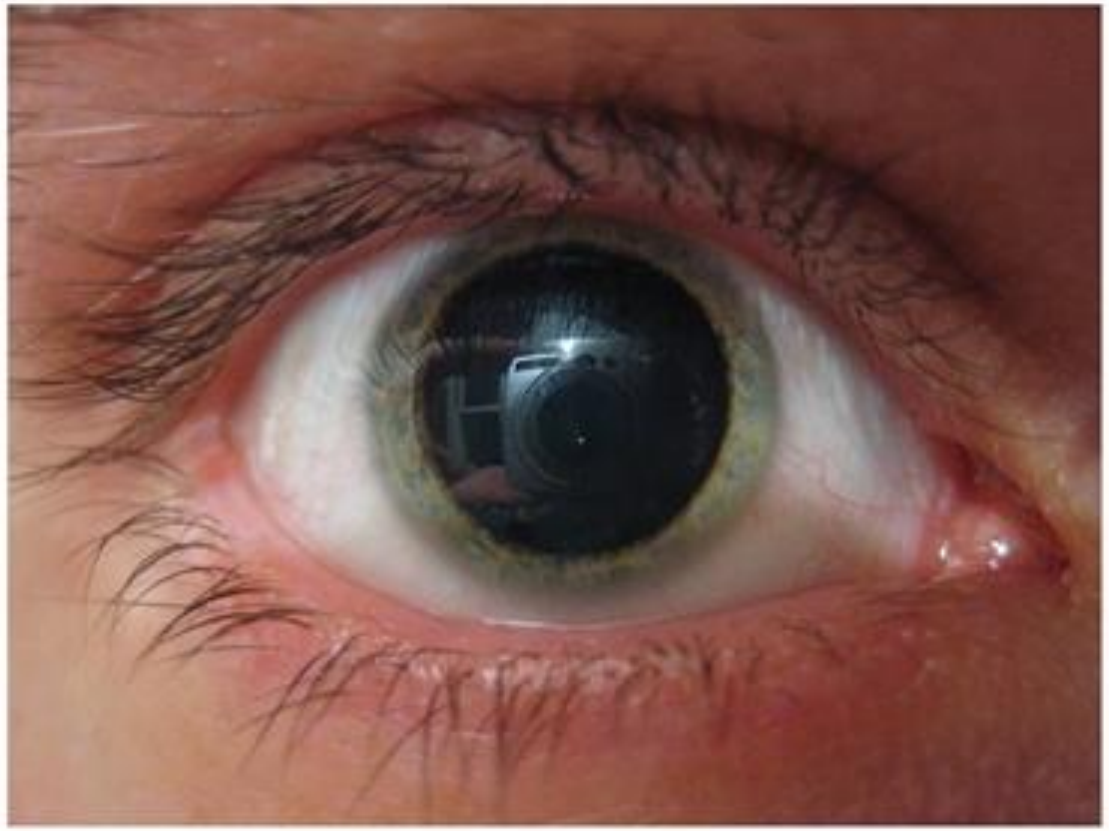
ANTAGONISTI MUSCARINICI

LOCALIZZAZIONE	RISPOSTA
SNC	Sedativo, disturbo memoria, allucinazioni (ad alte dosi)
GHIANDOLE	diminuzione secrezione gastrica e salivare
OCCHIO	dilatazione pupilla
CUORE	attivazione cardiaca
MUSCOLATURA LISCIA	rilassamento muscolatura intestino, vie urinarie, vie aeree

Un uso della scopolamina

Modello animale della malattia di Alzheimer

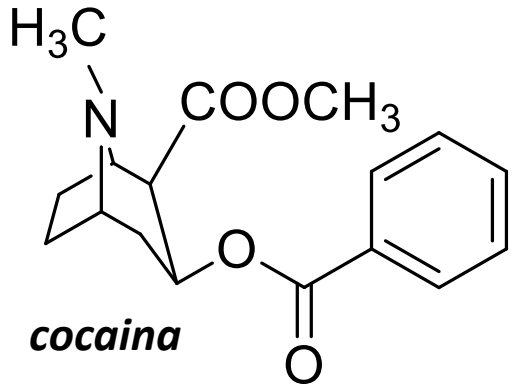
ioscina = scopolamina



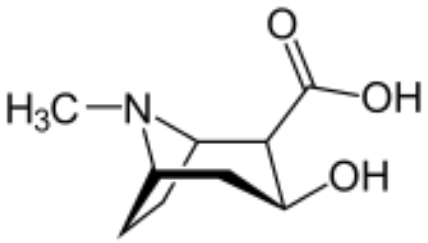
Dilatazione della pupilla

L'atropina è indicata nell'arresto cardiaco

COCAINA



cocaina



ecgonina

- Viene estratta dalle foglie di coca
- Impiego delle foglie dal 2500 a.c. nelle regioni delle Ande → a Freud
- Le foglie masticate vengono lasciate in bocca per ~1h (rilascio lento ed idrolisi influenzano l'effetto)

Diminuisce la fame ed il senso di fatica
Aiuta a superare le condizioni dovute all'altitudine

Si masticano 60 grammi di foglie/die (4mg/die), quindi non inducono dipendenza (30-40 mg necessari per indurre dipendenza)

mate di coca

Contenuto basso di **cocaina**, ma consumarlo può dare esito positivo ad un test antidroga

Può essere **decocainizzato**

Attività

SN

Azione locale

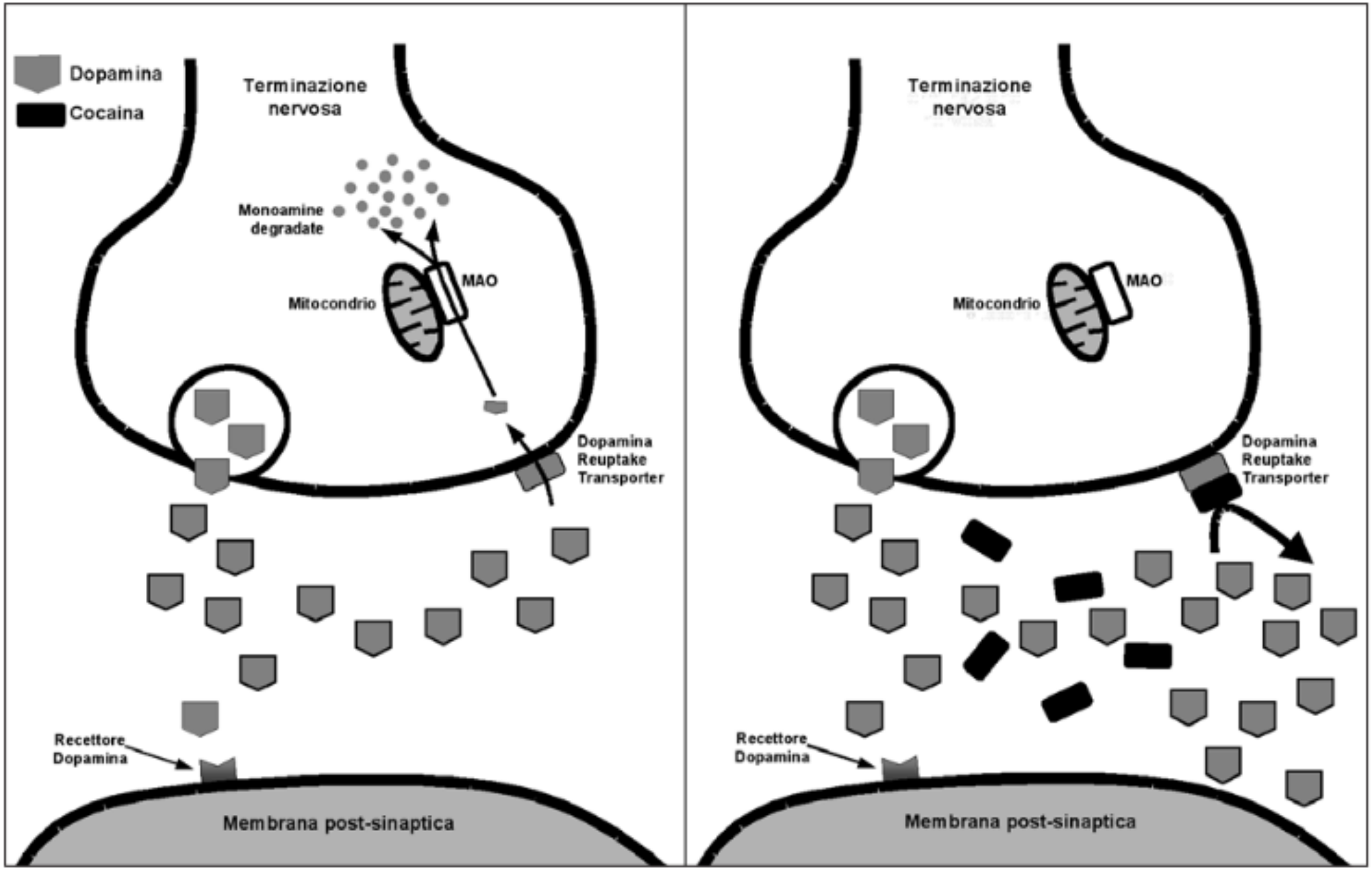
INIBIZIONE DEL REUPTAKE DELLE CATECOLAMINE (soprattutto DOPAMINA, in misura inferiore NA) NELLE TERMINAZIONI NERVOSE PRESINAPTICHE

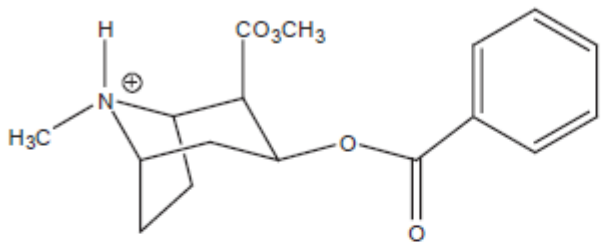
EUFORIA- ECCITAZIONE- IPERATTIVITÀ MOTORIA (livello centrale)

TACHICARDIA, AUMENTO PRESSIONE E VASOCOSTRIZIONE (livello PERIFERICO)

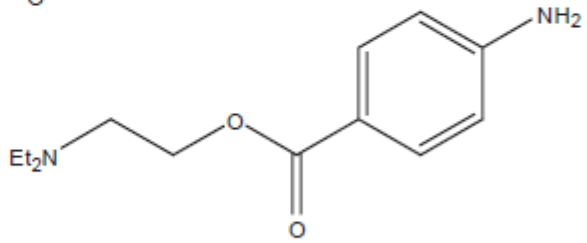
BLOCCO IMPULSO NERVOSO

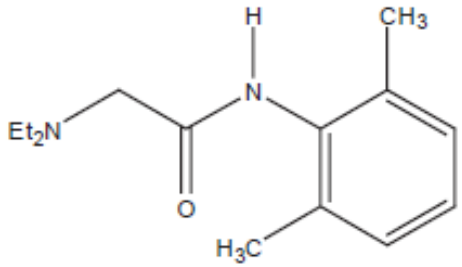
SI LEGA AI CANALI DEL Na^+, BLOCCANDO INGRESSO Na^+ E LA DEPOLARIZZAZIONE


Dopamina
Cocaina
Terminazione nervosa
Monoamine degradate
MAO
Mitocondrio
Dopamina Reuptake Transporter
Recettore Dopamina
Membrana post-sinaptica
Terminazione nervosa
MAO
Mitocondrio
Dopamina Reuptake Transporter
Recettore Dopamina
Membrana post-sinaptica

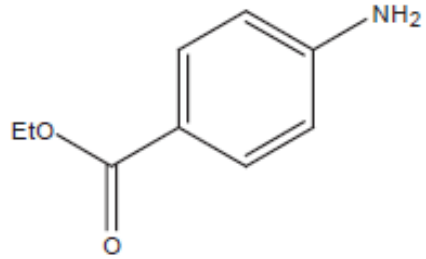


cocaina





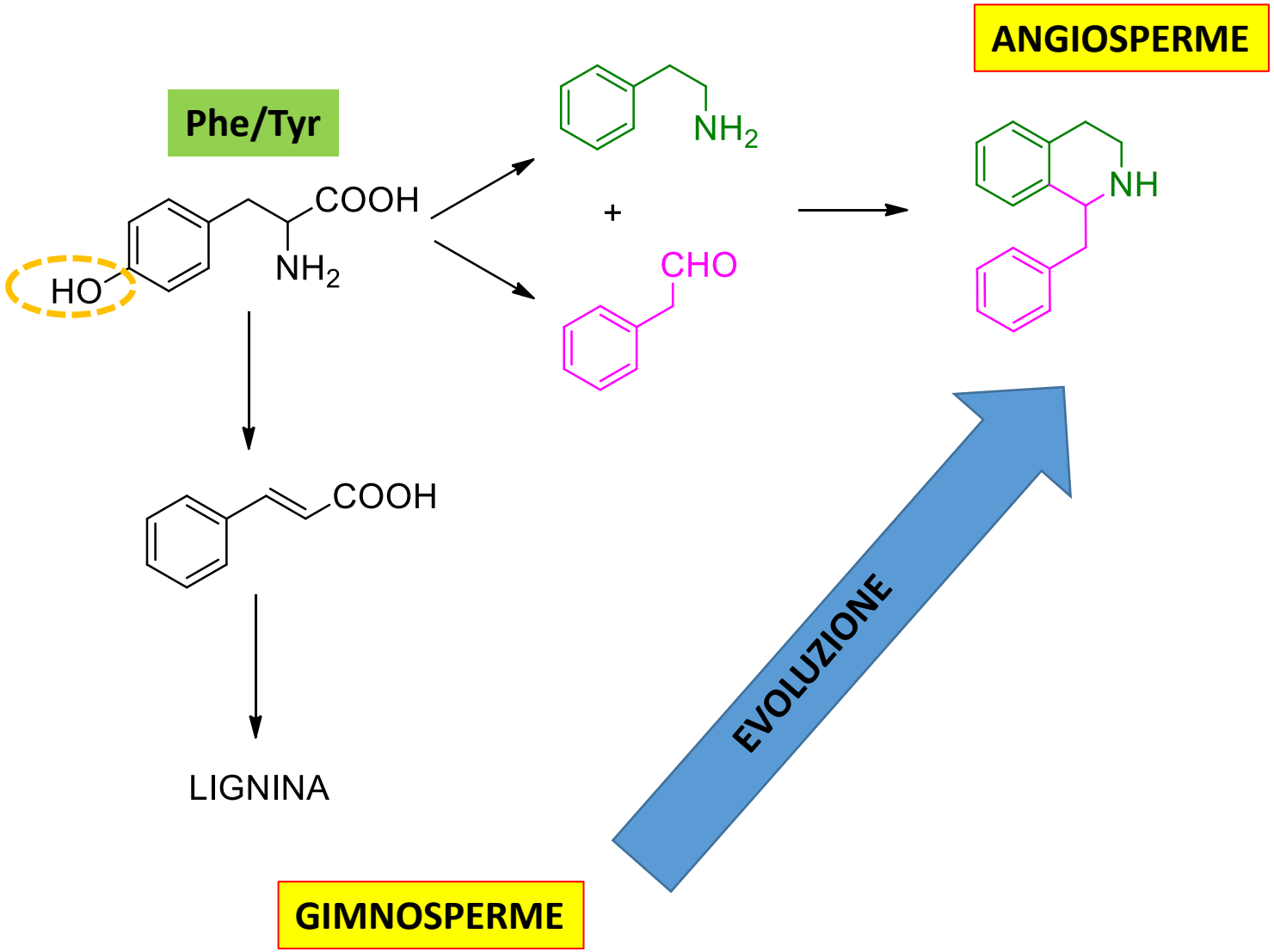
lidocaina

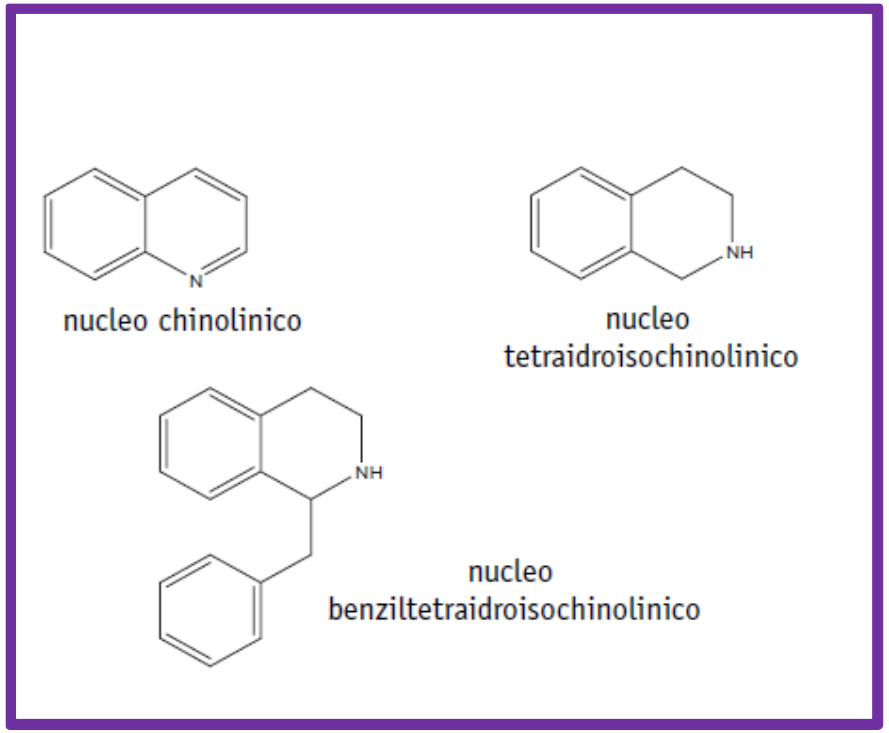


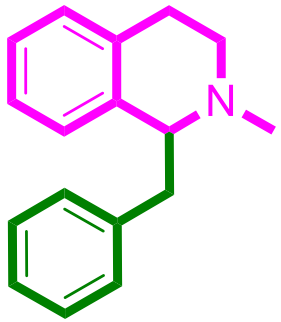
benzocaina

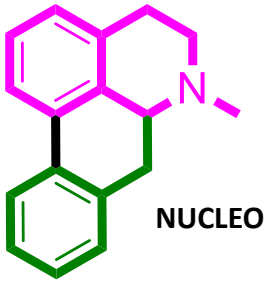
ALCALOIDI ISOCHINOLINICI

SCHEMA BIOSINTETICO DEGLI ALCALOIDI ISOCHINOLINICI

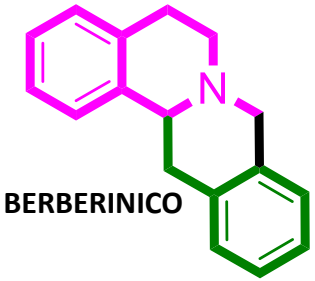




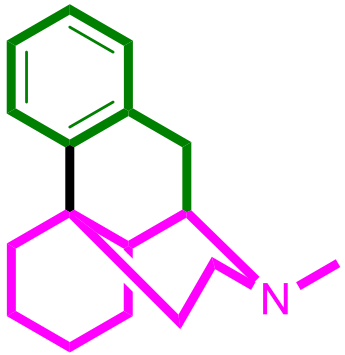




NUCLEO APORFINICO



NUCLEO BERBERINICO



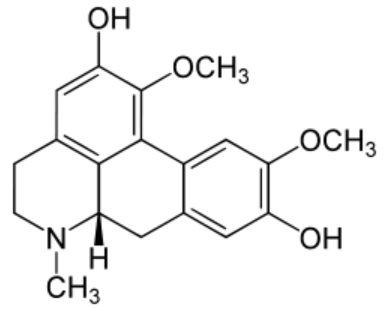
NUCLEO MORFINICO

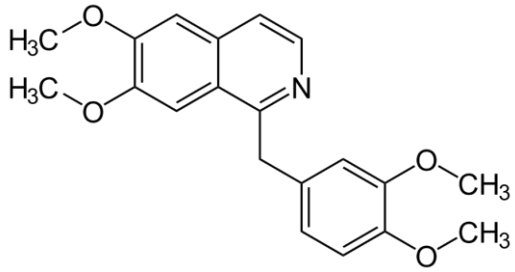
FAMIGLIE CON A. ISOCHINOLINICI

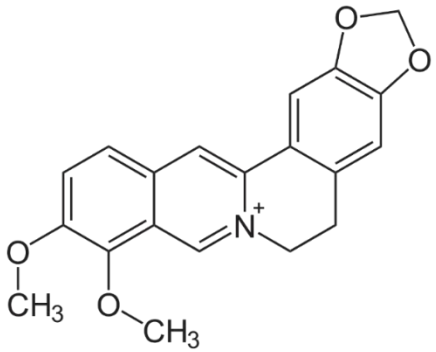
Papaveracee

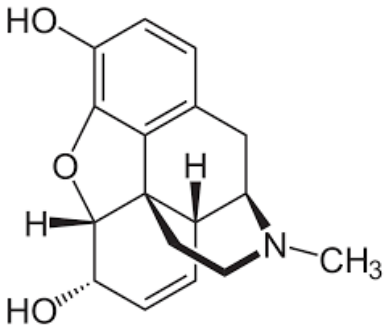
Berberidacee

Monimiaceae

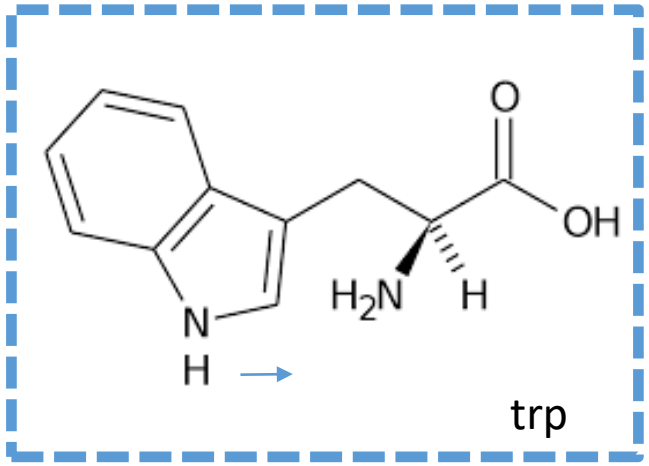






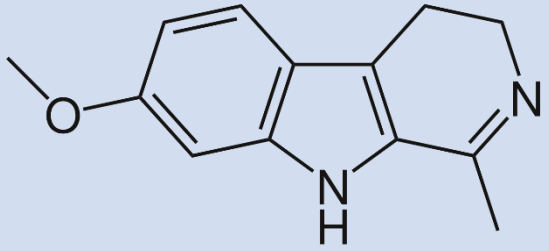
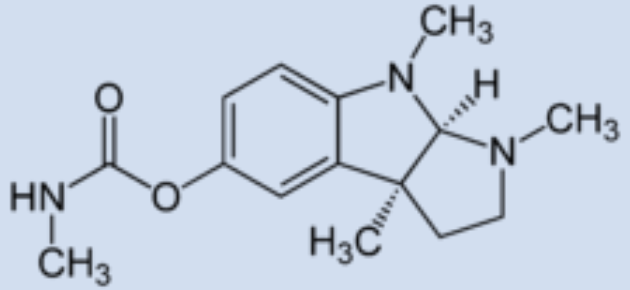
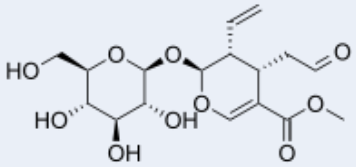
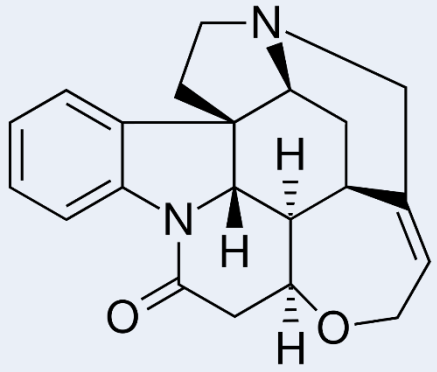
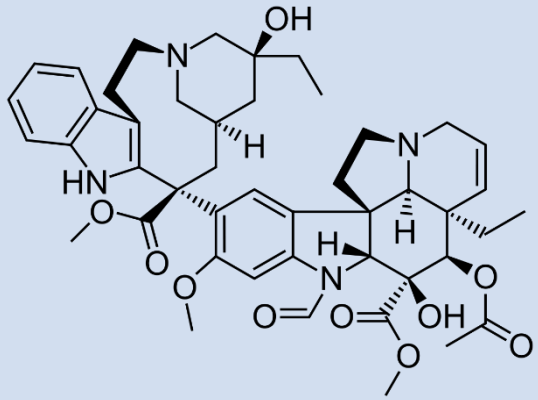


ALCALOIDI INDOLICI



trp

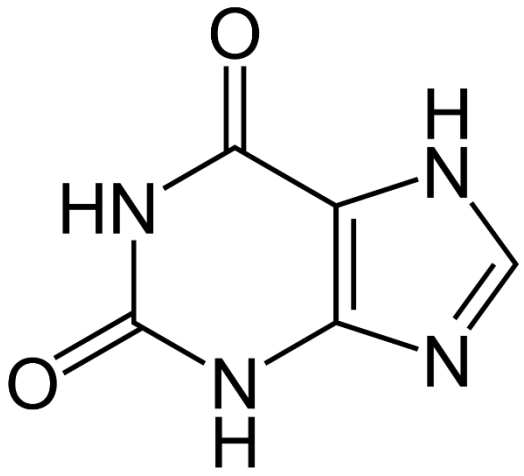
Tre tipi di alcaloidi indolici

TIPO DI ALCALOIDE	ESEMPI
ALCALOIDE INDOLICO **SEMPLICE** PRECURSORE: **TRIPTOFANO**	 **ARMALINA** (PASSIFLORA)  **FISOSTIGMINA** (FAVA DEL CALABAR)
ALCALOIDE INDOLICO **TERPENOIDICO** PRECURSORE: **TRIPTOFANO + SECOLOGANINA** 	 **STRICNINA** (NOCE VOMICA)
ALCALOIDE **BISINDOLICO** PRECURSORE: 2 ALCALOIDI INDOLICII TERPENOIDICI	 **VINCRISTINA** (VINCA ROSEA)

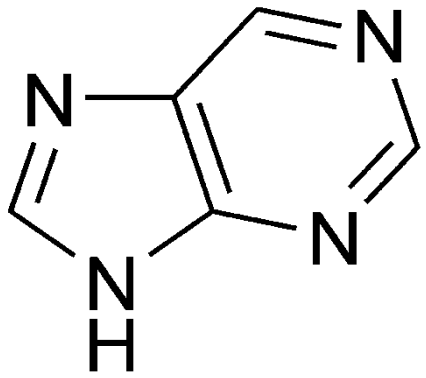
ALCALOIDI XANTINICI

PRECURSORI: 3 diversi AA (**biosintesi complessa**)

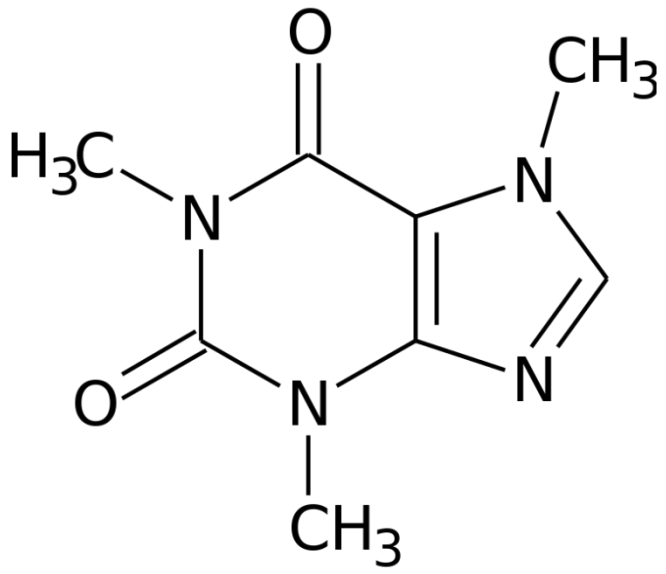
CARATTERISTICHE: possiedono il nucleo xantinico, un derivato purinico



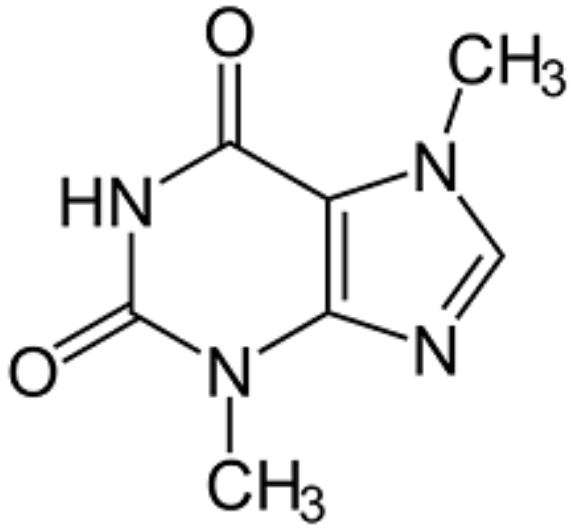
XANTINA



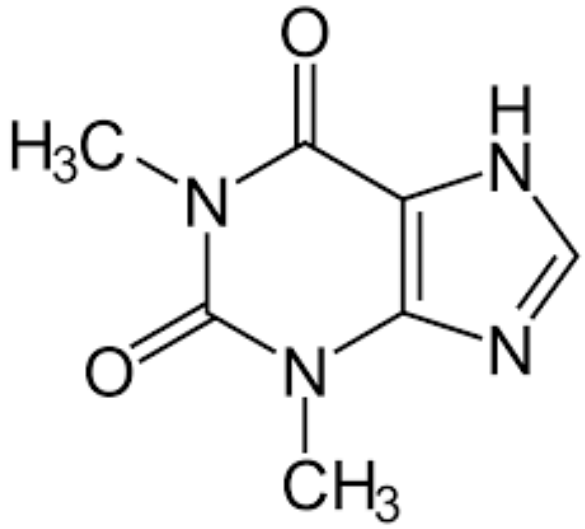
PURINA



CAFFEINA



TEOBROMINA



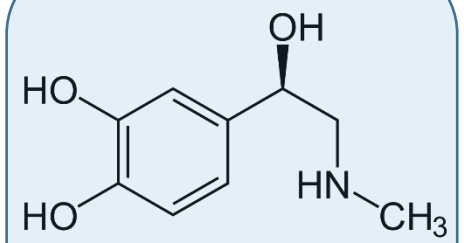
TEOFILLINA

ALTRI ALCALOIDI

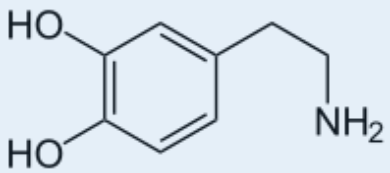
ALCALOIDI FENILALCHILAMINICI

- ✓ STRUTTURA SEMPLICE (*protoalcaloidi*: ammine semplici direttamente derivate dagli amminoacidi)

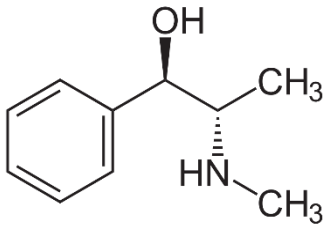
- ✓ SOMIGLIANZA CON CATECOLAMMINE (ADRENALINA, DOPAMINA)



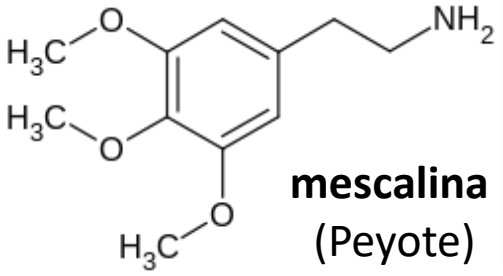
adrenalina



dopamina



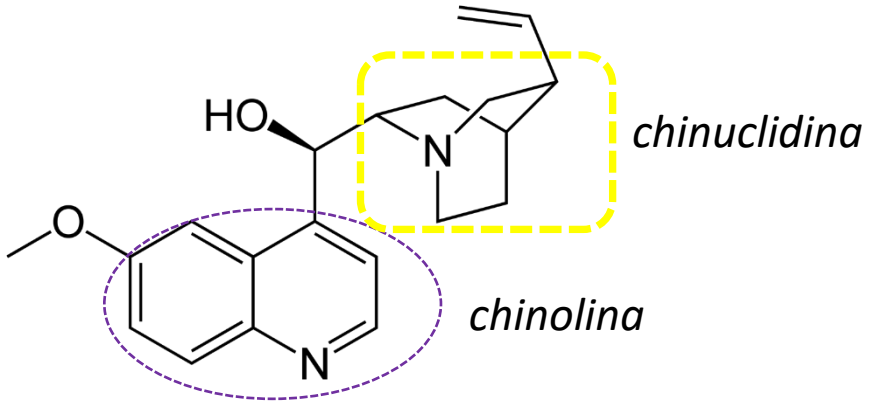
efedrina
(*Efedra* spp.)



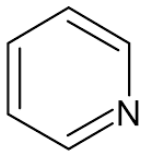
mescalina
(Peyote)

ALCALOIDI CHINOLINICI

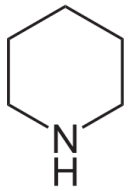
CHININA
(CHINA)



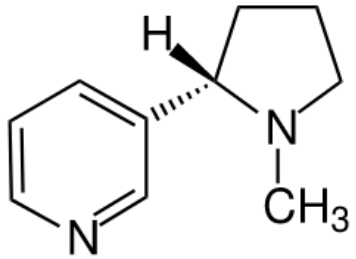
ALCALOIDI PIRIDINICI, PIPERIDINICI ED IMIDAZOLICI



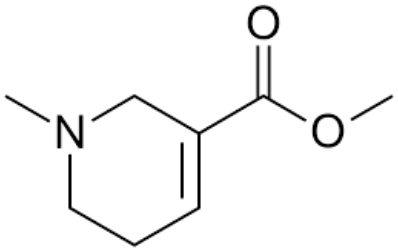
PIRIDINA



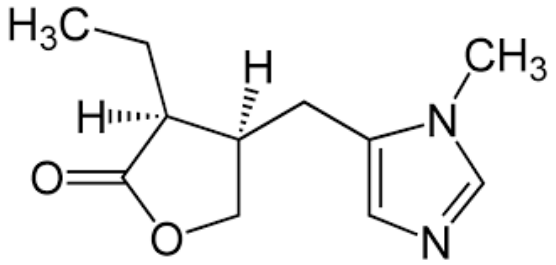
PIPERIDINA



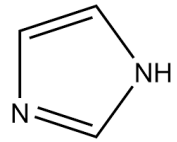
NICOTINA
(da AA ornitina)
v. Alcaloidi del tabacco



ARECOLINA
(da AA lisina)



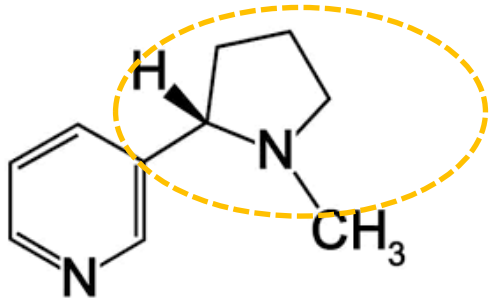
PILOCARPINA
(da AA istidina)



IMIDAZOLO

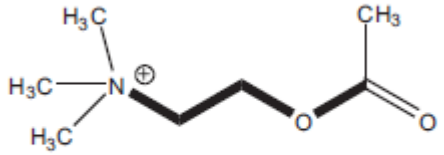
ALCALOIDI DEL TABACCO

NICOTINA



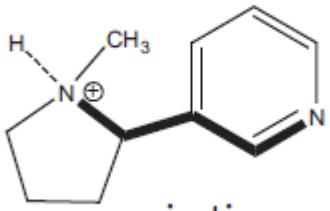
RECETTORI NICOTINICI (SNC e placca neuromuscolare)

Idrolizzabile



acetilcolina

Non idrolizzabile



nicotina

La nicotina agisce sui centri nervosi ***in competizione con l'acetilcolina***

- MOLTO TOSSICA
- ASSORBIMENTO RAPIDO
- IN PARTE COMBUSTA
- 0,06 g dose mortale per l'uomo


NiQuitin®
21mg/24 ore Cerotti Transdermici
nicotina
FASE 1 2 3
7 CEROTTI
AIUTA A SMETTERE DI FUMARE
PER CHI FUMA 10 O PIÙ SIGARETTE AL GIORNO
INIZIARE DALLA FASE 1