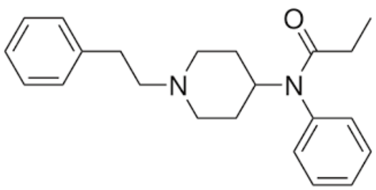
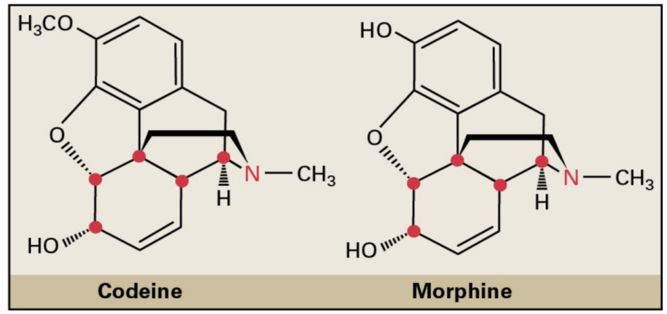
# Alkaloids – Introduction and Importance to Humans

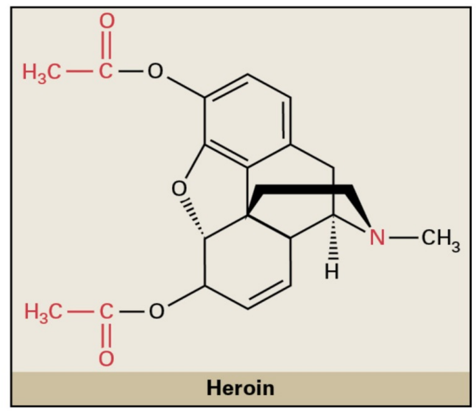
fentanyl




*Papaver somniferum*

A




C

A B

**FIGURE 24.26** *(A) Maturing capsule of the opium poppy* Papaver somniferum. *When the capsule is wounded, a white, milky latex is exuded. Poppy latex contains morphine and related alkaloids, such as codeine. When the exuded latex is allowed to dry, a hard, brown substance called opium is formed. (B) Statuette from Gazi of a goddess of sleep crowned with capsules of the opium poppy (1250–1200 BC).* *Source*: (A) Kutchan, Liebnitz Institut für Pflanzenbiochemie, Halle, Germany; previously unpublished; (B) Ministry of Culture Archaeological Receipts Fund, Athens, Greece.

*ɔm the opium poppy* Papaver somniferum. *Asymmetric (chiral) carbons*
*considerable amount of morphine in its skin. (C) Structure of diacetyl*

hed.



WILEY Blackwell

*Biochemistry & Molecular Biology of Plants*, Second Edition. Edited by Bob B. Buchanan, Wilhelm Gruissem, and Russell L. Jones.
© 2015 John Wiley & Sons, Ltd. Published 2015 by John Wiley & Sons, Ltd.
Companion website: www.wiley.com/go/buchanan/biochem

WILEY Blackwell

# Alkaloids – Introduction and Importance to Humans

(alkaloids are pharmaceutically and ecologically significant)

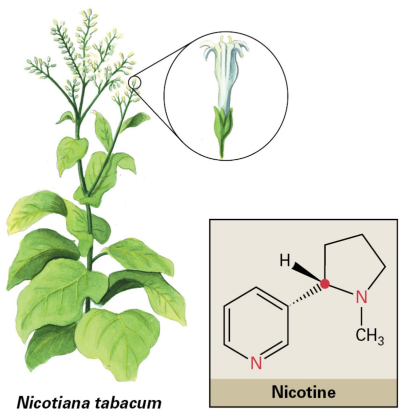



FIGURE 24.32 *Structure of nicotine from* Nicotiana tabacum.



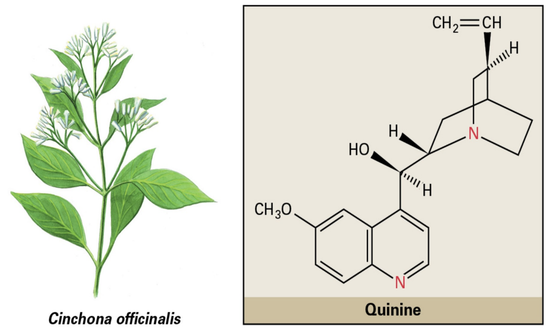



FIGURE 24.30 *Structure of the monoterpenoid indole alkaloid-derived quinine from* Cinchona officinalis. *An antimalarial quinine-containing tonic prepared from the bark of* C. officinalis *greatly facilitated European exploration and inhabitation of the tropics during the past two centuries.*



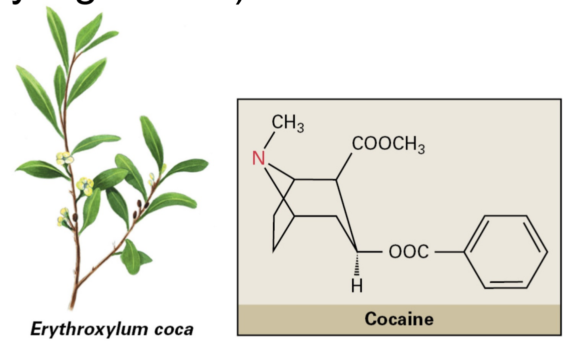



FIGURE 24.31 *Structure of the tropane alkaloid cocaine, a central nervous system stimulant derived from* Erythroxylum coca.



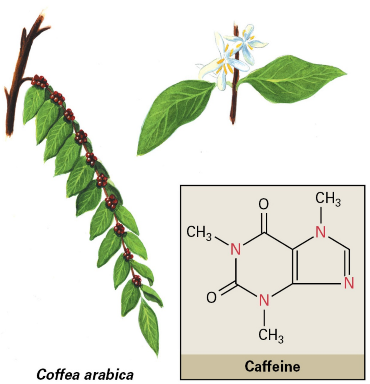



FIGURE 24.33 *Structure of the purine alkaloid caffeine from* Coffea arabica.



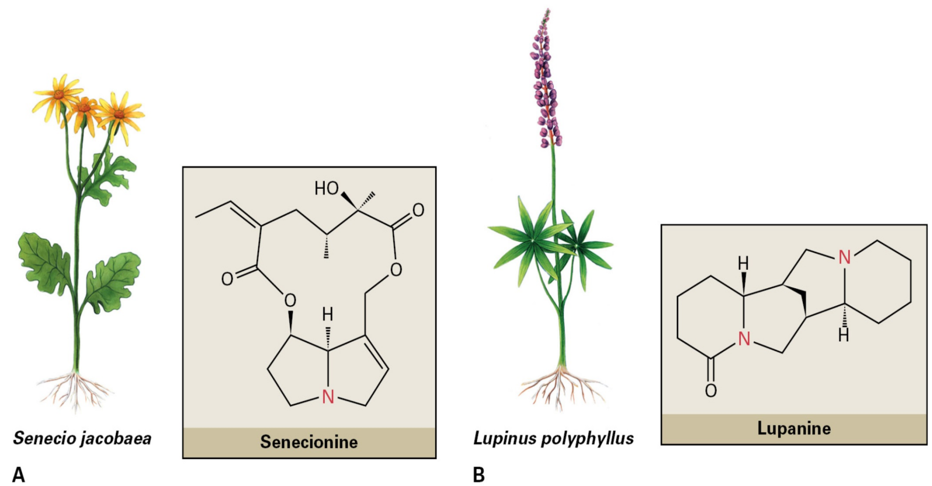



FIGURE 24.35 *Pyrrolizidine and quinolizidine alkaloids. (A) Structure of the pyrrolizidine alkaloid senecionine from ragwort* (Senecio jacobaea). *(B) Structure of the quinolizidine alkaloid lupanine from the bitter lupine* Lupinus polyphyllus. *Lupanine is a bitter compound that functions as a feeding deterrent.*

## Introduction to alkaloids, and importance to humans

**Define:** *= small organic molecules (secondary metabolites) of plants which* ***contain nitrogen*** *(typically in a ring)*

- **alkaloids are pharmaceutically significant**

- traditional and modern uses (25%/75% of drugs are plant derived, mostly alkaloids)

- many have neurological effects - presumed due to the presence of nitrogen (mimic neutrotransmitters)

- potent toxins and defenses - many highly toxic compounds, and with strong biological effects

- interesting chemical ecology and co-evolution with insects

**Alkaloid physiological effects are diverse:**

**Quinine** (*Cinchona officinalis*) -**antibiotics** (anti-malarial)

**Morphine** (*Papaver somniferum* - painkiller (**analgesic**)

**Taxol** - (*Taxus brevifolia*)

**Vinblastine** (*Catharanthus roseus*) - **anticancer** drug

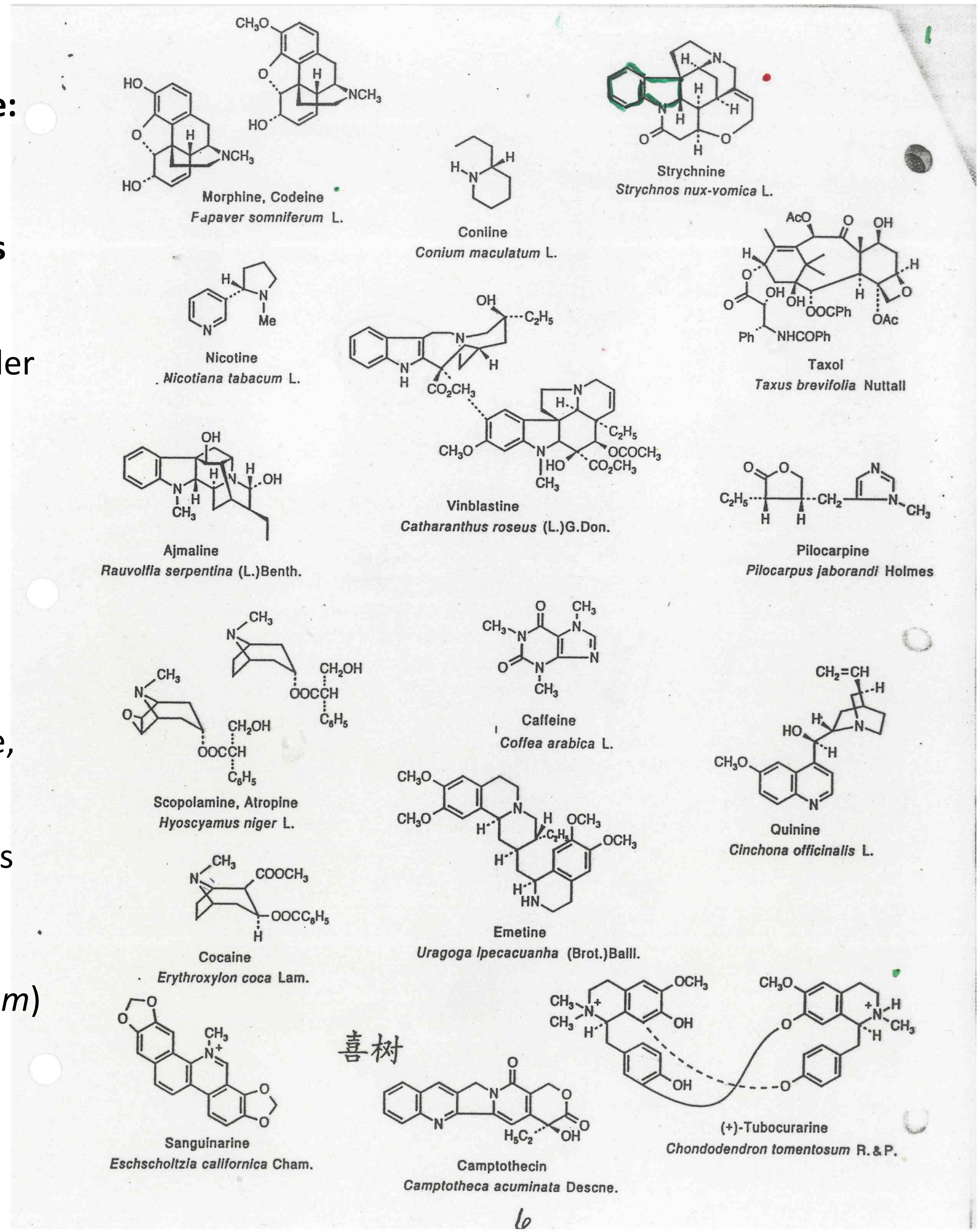
**Coniine** (*Conium maculatum*) - toxin

**Nicotine** (*Nicotiana tabacum*) insecticide, stimulant

**Atropine**(*Atropa belladonna*) dilate pupils

**Cocaine** (*Erythroxylon coca*) –

**Tubocurarine** (*Chondodenron tomentosum*) - muscle relaxant



**General Features and Characteristics**

- N makes them basic in solution -> called ***alkaloids*** for this reason

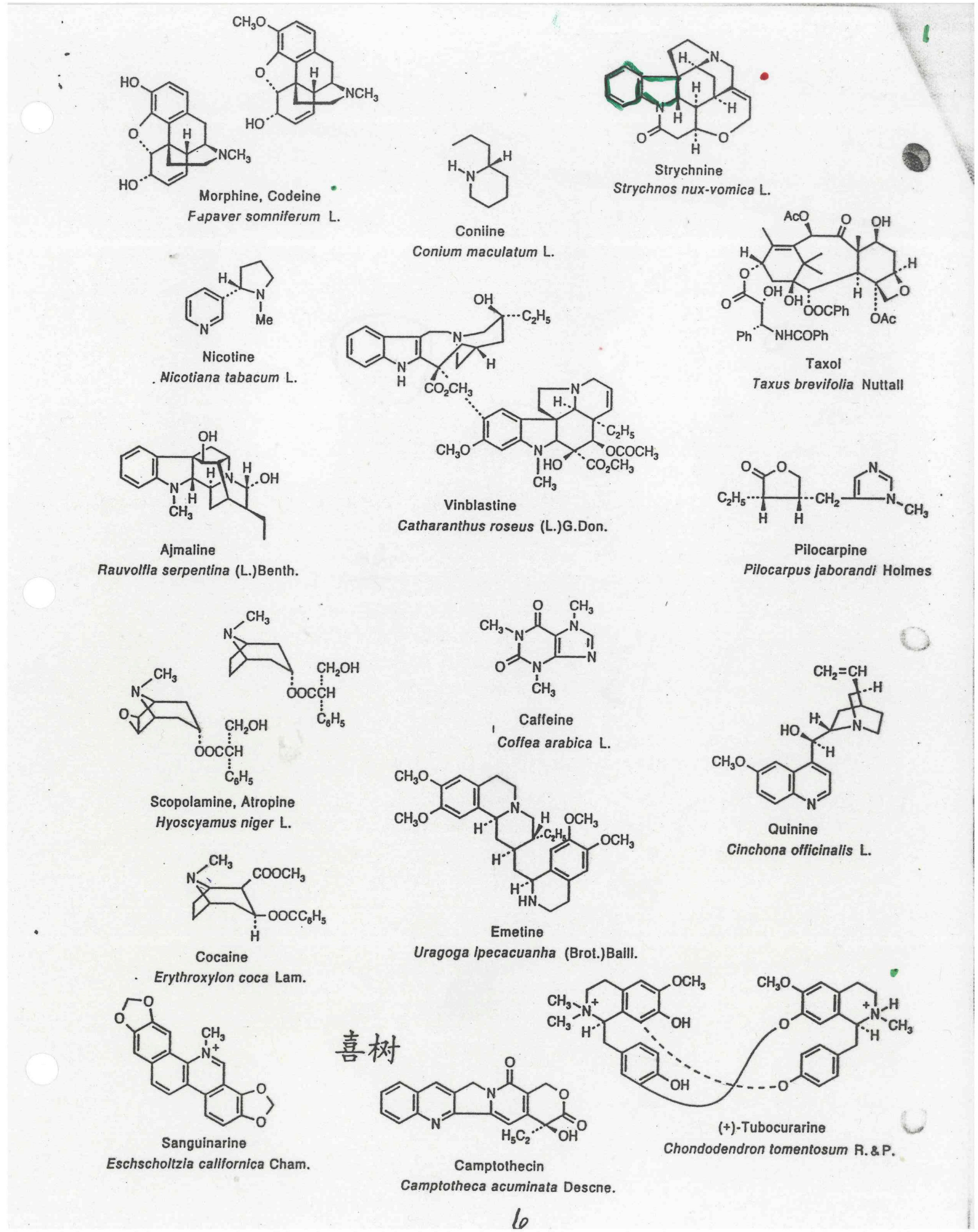
- structurally diverse:  12,000+ structures

-  20% of all plant species have alkaloids

- concentrated in specific plant taxa (families, genera, species), but are 'scattered around' the plant kingdom (independent evolution)

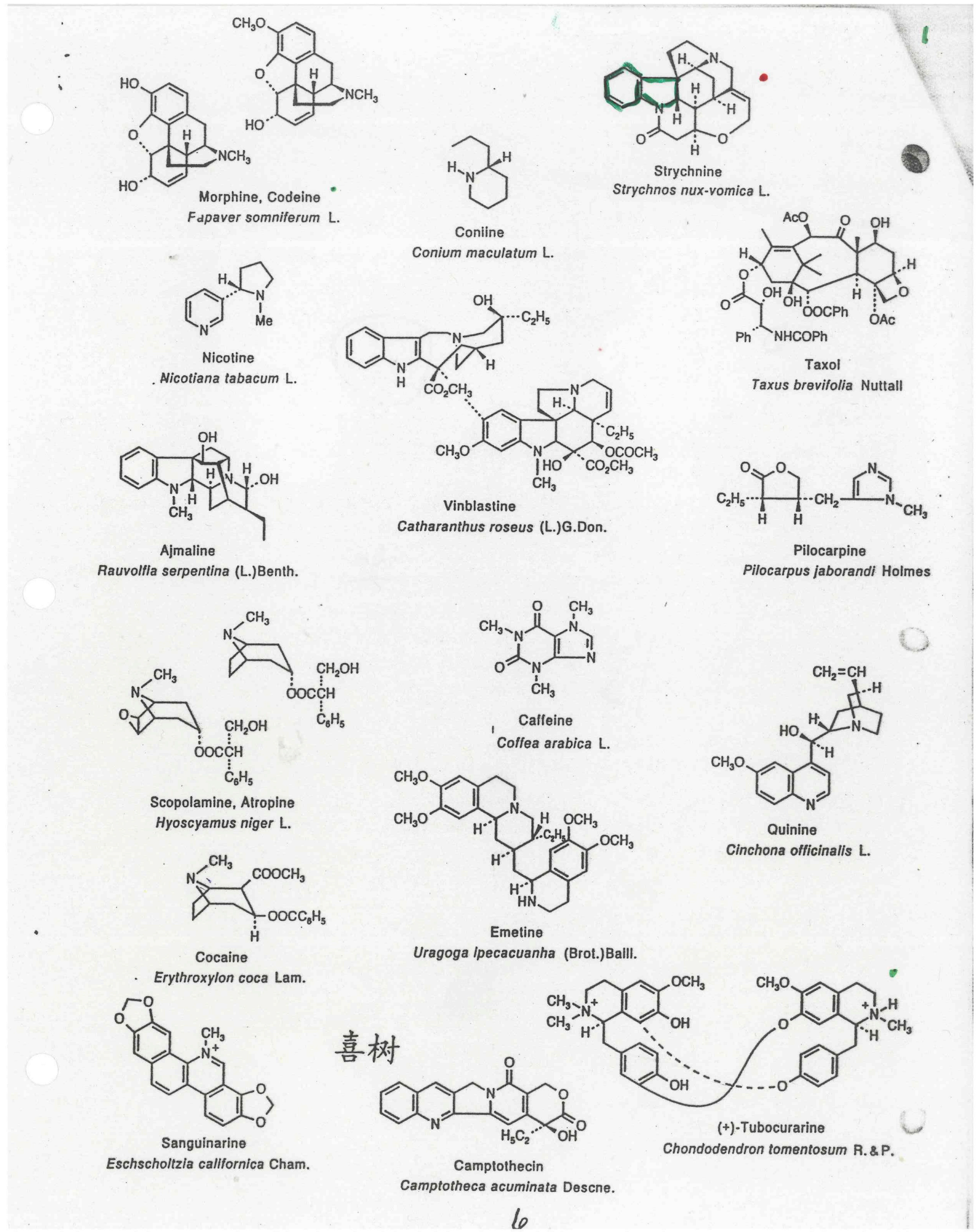
- biosynthetically diverse (arise from different amino acids)

- strong biological effects (see ecological examples)



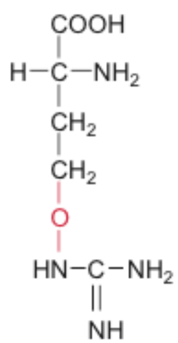
**Examples of diverse mechanisms of action:**

- **bind/block** neuroreceptors (morphine, codeine)
- **block reuptake** of neuroreceptor (cocaine-dopamine)
- **disrupt cytoskeleton** - tubulin (taxol)
- mimic **neurotransmitter action** (nicotine - acetylcholine)
- **block cellular signaling** (cAMP phosphodiesterase - caffeine)

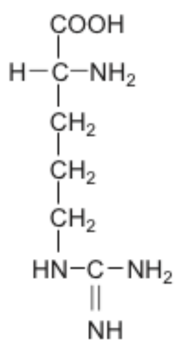


# Alkaloid Families and Biosynthesis
(mostly derived from amino acids)

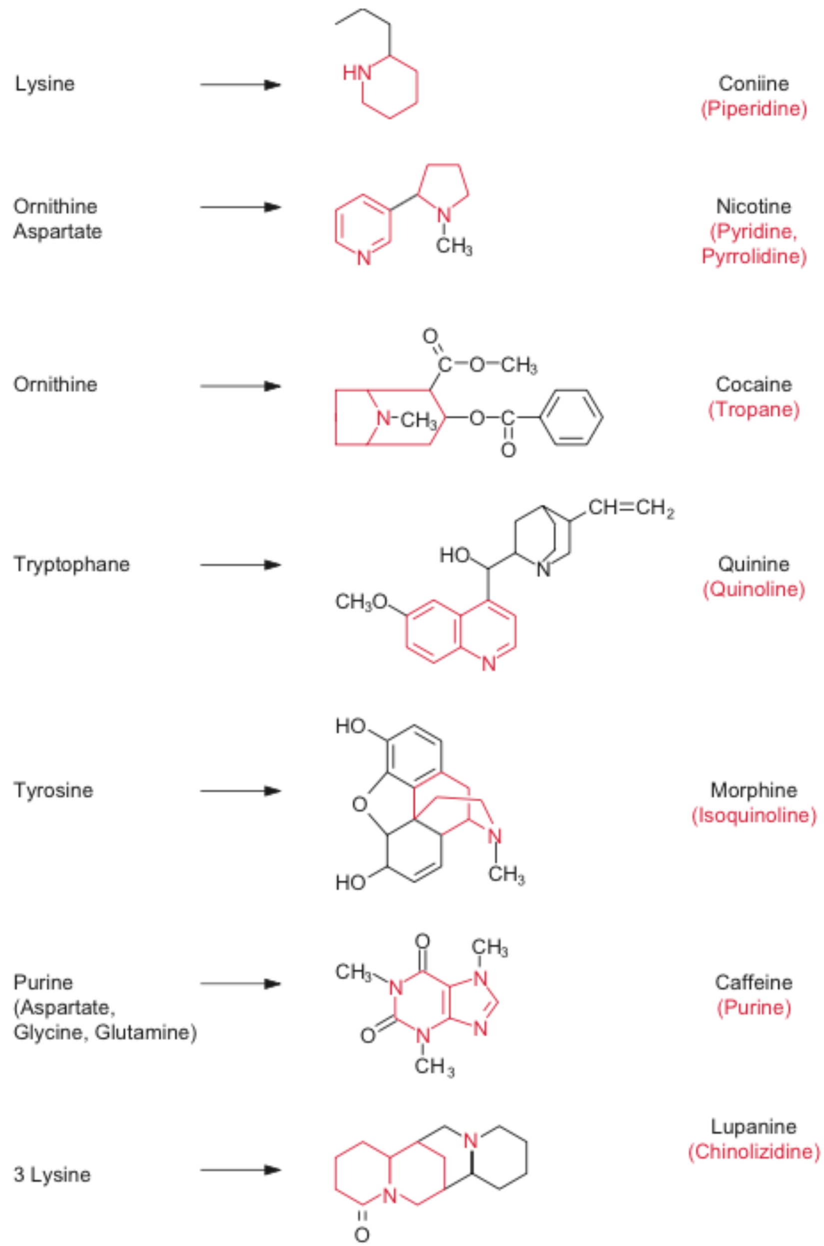
Non-protein amino acids:
– not considered alkaloids
but also toxins



Canavanine



Arginine




Heldt, Fig 16.1

Pseudoalkaloids: N added late in biosynthesis

Protoalkaloids: N not in ring

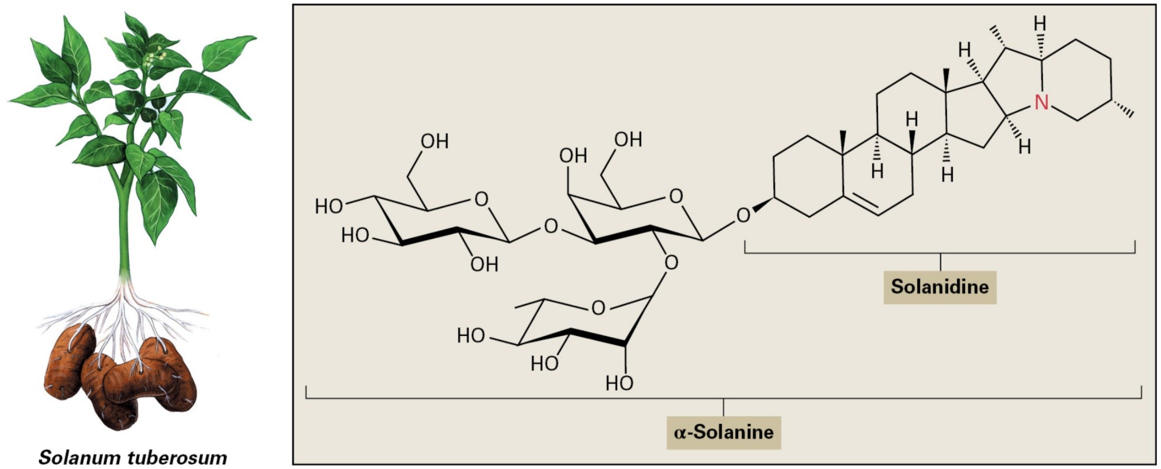



**FIGURE 24.34** *Structure of the steroid alkaloid glycoside α-solanine from* Solanum tuberosum *(potato). The aglycone solanidine is derived from cholesterol.*

**α-solanidine** (tripterpene alkaloid of potato)

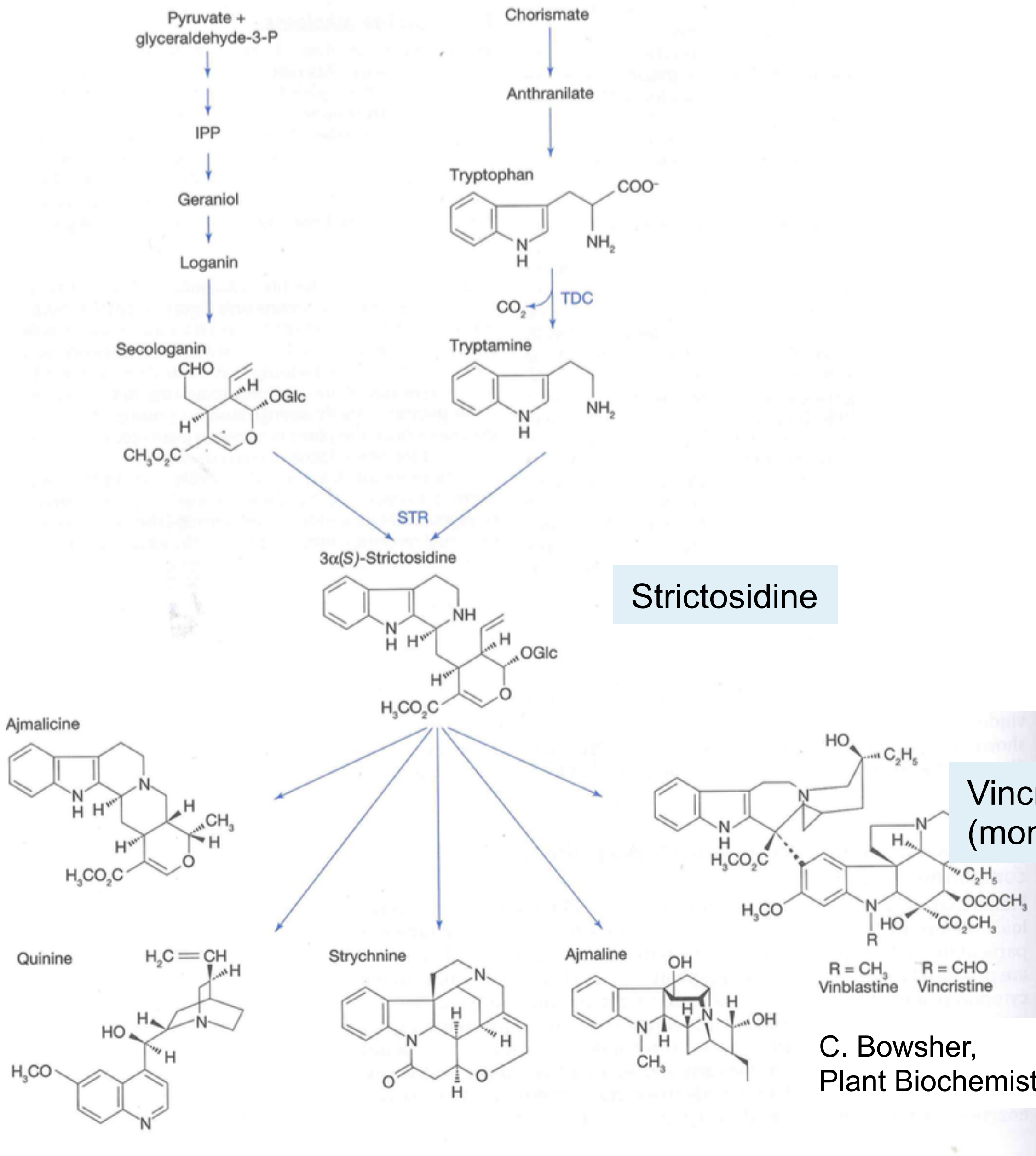
B
©
C

# Biosynthesis of Alkaloids

**General features of alkaloid biosynthesis:**

- many biosynthetic steps are required -> complex structures
- any one plant typically accumulates a mix of related alkaloids
- usually begins with **decarboxylation** of amino acid (eg) tyr -> tyramine, trp -> tryptamine
- **central intermediate** can give rise to different final products: (**strictosidine** for diverse quinoline alkaloids, **reticuline** for isoquinoline and poppy alkaloids)

# Biosynthesis of **Quinoline** Alkaloids & Central Position of **Strictosidine**

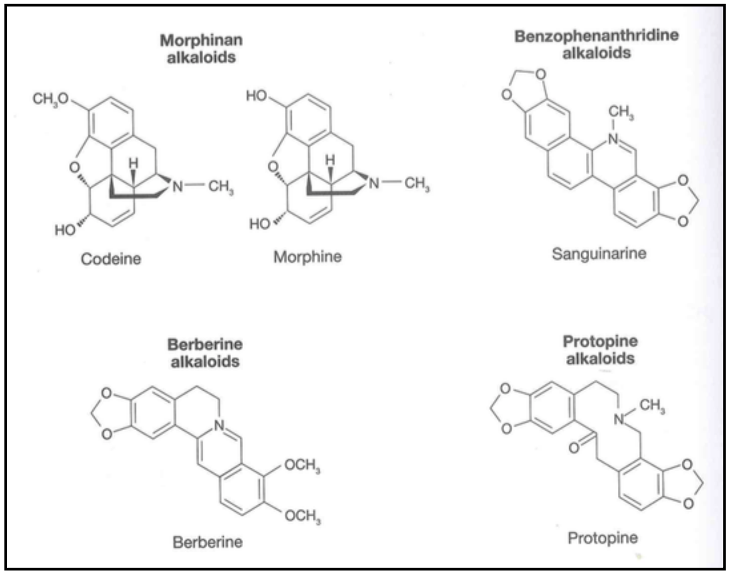



Strictosidine

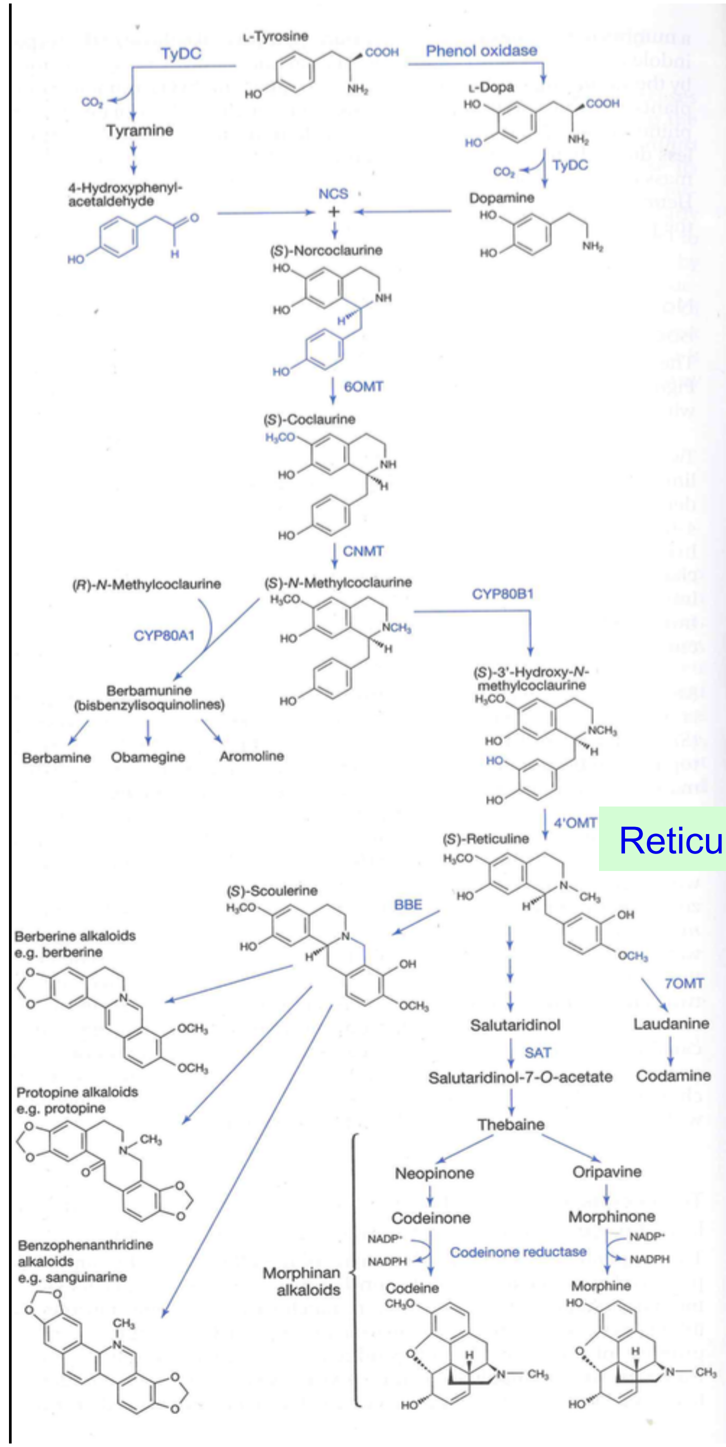
Vincristine/ Vinblastine
(monoterpene indole alkaloids

C. Bowsher,
Plant Biochemistry p. 342

# Central Position of **Reticuline** in Isoquinoline Alkaloid Synthesis




*Isoquinoline Alkaloids*




Reticuline

C. Bowsher, *Plant Biochemistry* p. 344-46

# Biosynthesis of Alkaloids

Alkaloids can have **organ-specific synthesis** and **storage:**

i.e., bark, roots, flowers

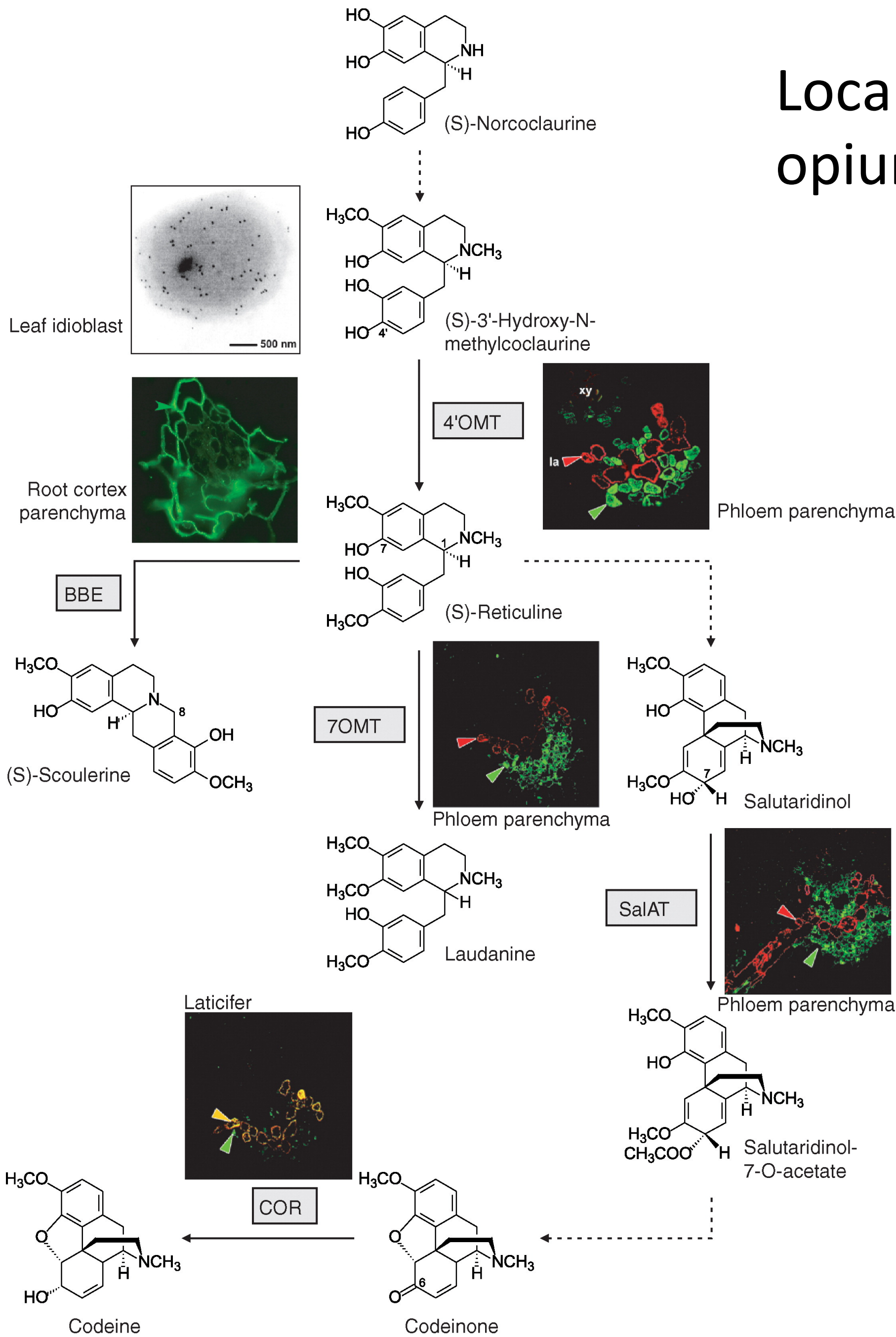
There is also **cell-specific synthesis** / **storage**:

- latex ducts and laticifers for poppy alkaloids
- epidermis, **idioblasts** for *Vinca* alkaloids

Madagascar periwinkle
*(Catharanthus roseus)*

Opium poppy
*(Papaver somniferum)*

# Localization of alkaloid synthesis opium poppy



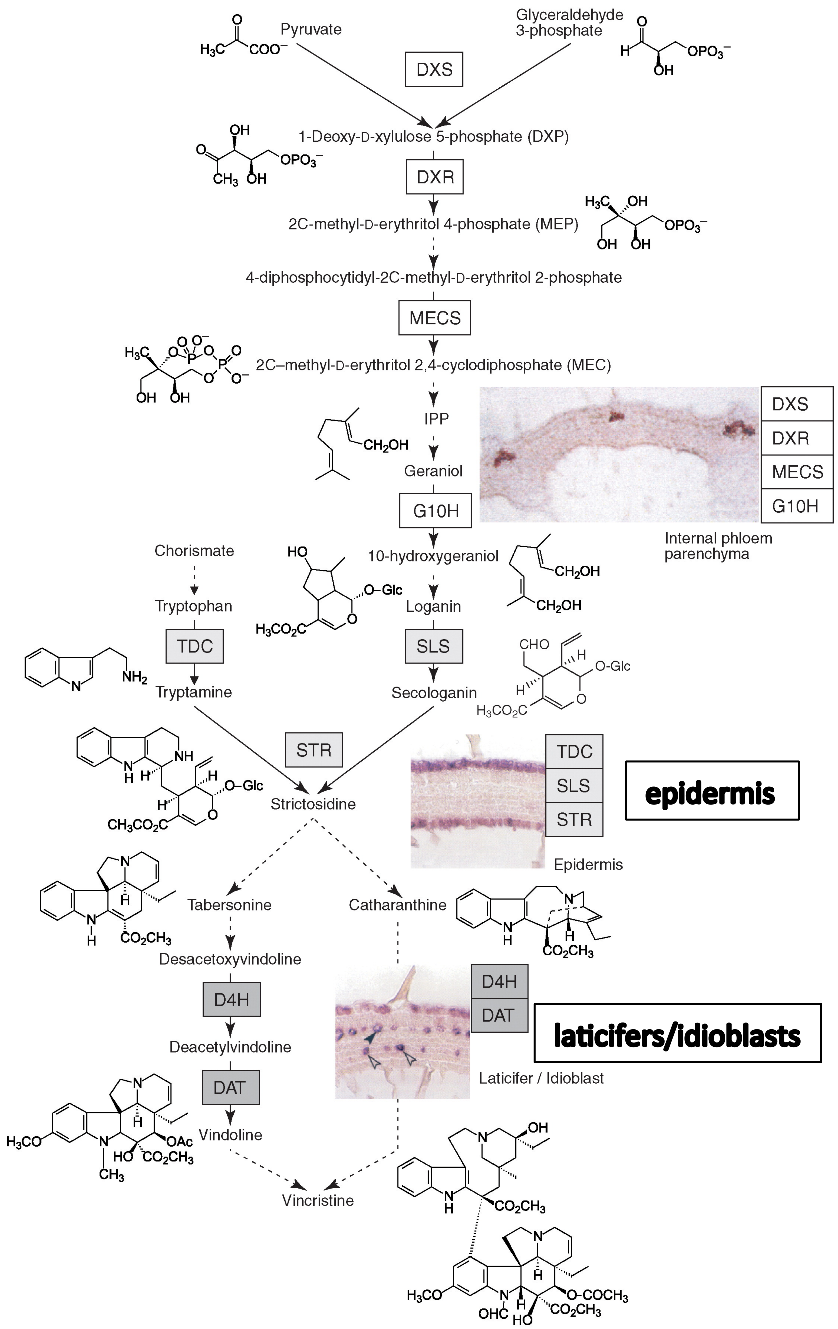

Current Opinion in Plant Biology

Biosynthesis of components in ***different*** cell types:

- root and phloem parenchyma cell
- laticifers and idioblasts (DAT)

# Localization of Vinca alkaloid synthesis in Madagascar periwinkle (*Catharantus roseus)*

**internal** phloem parenchyma cells



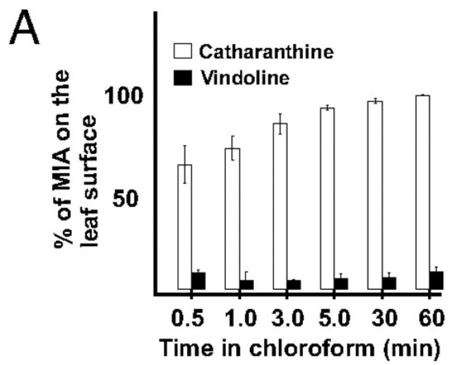

Current Opinion in Plant Biology

Biosynthesis of components in ***different*** cell types:

- phloem parenchyma cells (DXS, DXR)
- epidermis (TDC, STR)
- laticifers and idioblasts (DAT)

# Catharanthine accumulates almost entirely in leaf wax exudates outside of the leaf epidermis, whereas vindoline is found within leaf cells.

leaf surface
(chloroform wash)

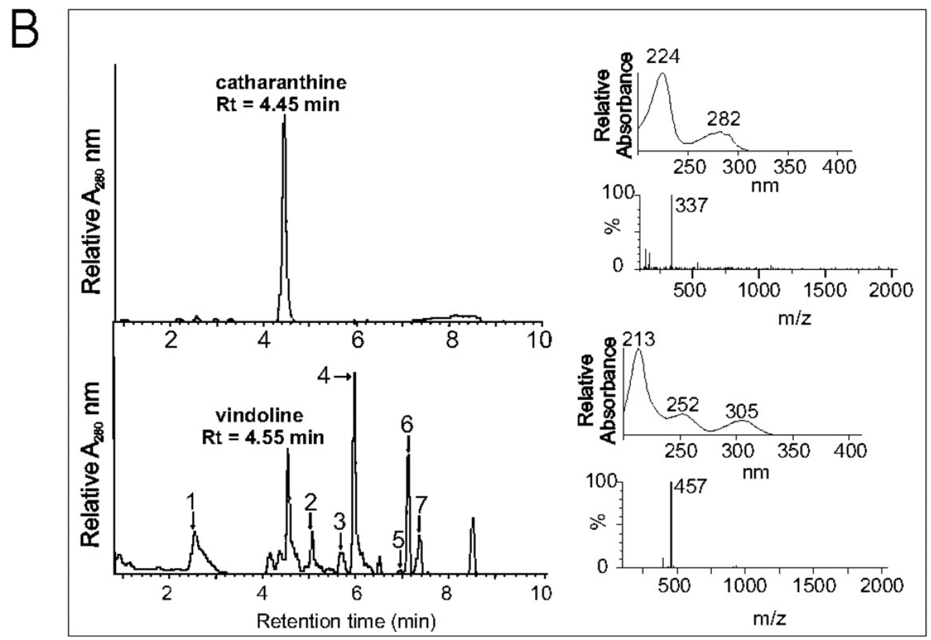



C

| | % of metabolite on leaf surface |
|---|---|
| Ursolic acid | 98 ± 0.5 |
| Catharanthine | 99 ± 1.5 |
| Vindoline | 3.8 ± 1.8 |
| Chlorogenic acid | 9.7 ± 5 |
| Chlorophyll | 0.033 ± 0.012 |

chloroform wash

whole leaf extract after
chloroform wash

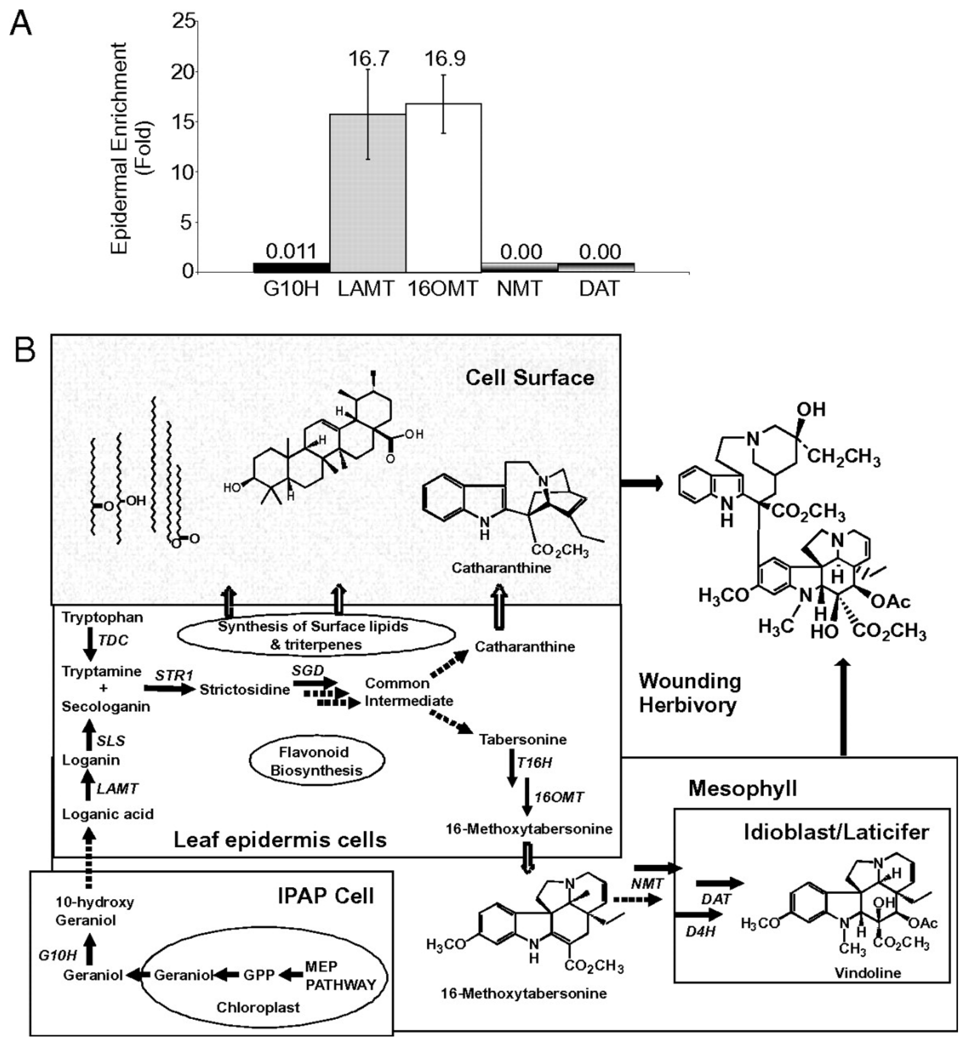



**Roepke J et al. PNAS 2010;107:15287-15292**



PNAS

Model for biosynthesis and secretion of secondary metabolites produced in the epidermis of C. roseus leaves.




Roepke J et al. PNAS 2010;107:15287-15292

# Catharanthine is toxic to insect larvae (silk worm)

**Table 2. Effect of catharanthine concentration on fifth-instar *B. mori* larvae**

| Treatment* | Catharanthine, μg | Days before death |
|---|---|---|
| No food | 0 | 2 ± 1 |
| Mulberry diet | 0 | 7 |
| Mulberry diet + 2/3 catharanthus leaf | 92.1 ± 8.6 | 5.3 ± 0.6 |
| Mulberry diet + 1 catharanthus leaf | 138.1 ± 12.8 | 4 ± 1 |
| Mulberry diet + 2 catharanthus leaves | 276.3 ± 25.7 | 3.3 ± 0.6 |
| Mulberry diet + chloroform extracts of Leaf surface | 180.5 ± 39.6 | 2 ± 0 |
| Mulberry diet + extracts of chloroform treated leaf | 1.4 ± 0.4 | 4.3 ± 0.6 |
| Mulberry diet + catharanthine | 50 | 4.7 ± 0.6 |
| Mulberry diet + catharanthine | 250 | 2.4 ± 1.5 |
| Mulberry diet + catharanthine | 500 | 1.7 ± 0.6 |

*Fifth-instar *B. mori* larvae were fed various diets in triplicate for a 1-wk period. Larvae not provided food died within 2 d of initiating the experiment compared with larvae fed a Mulberry diet that did not die during 7 d of observation.

*Catharanthine is also toxic to pathogenic fungi (not shown)*