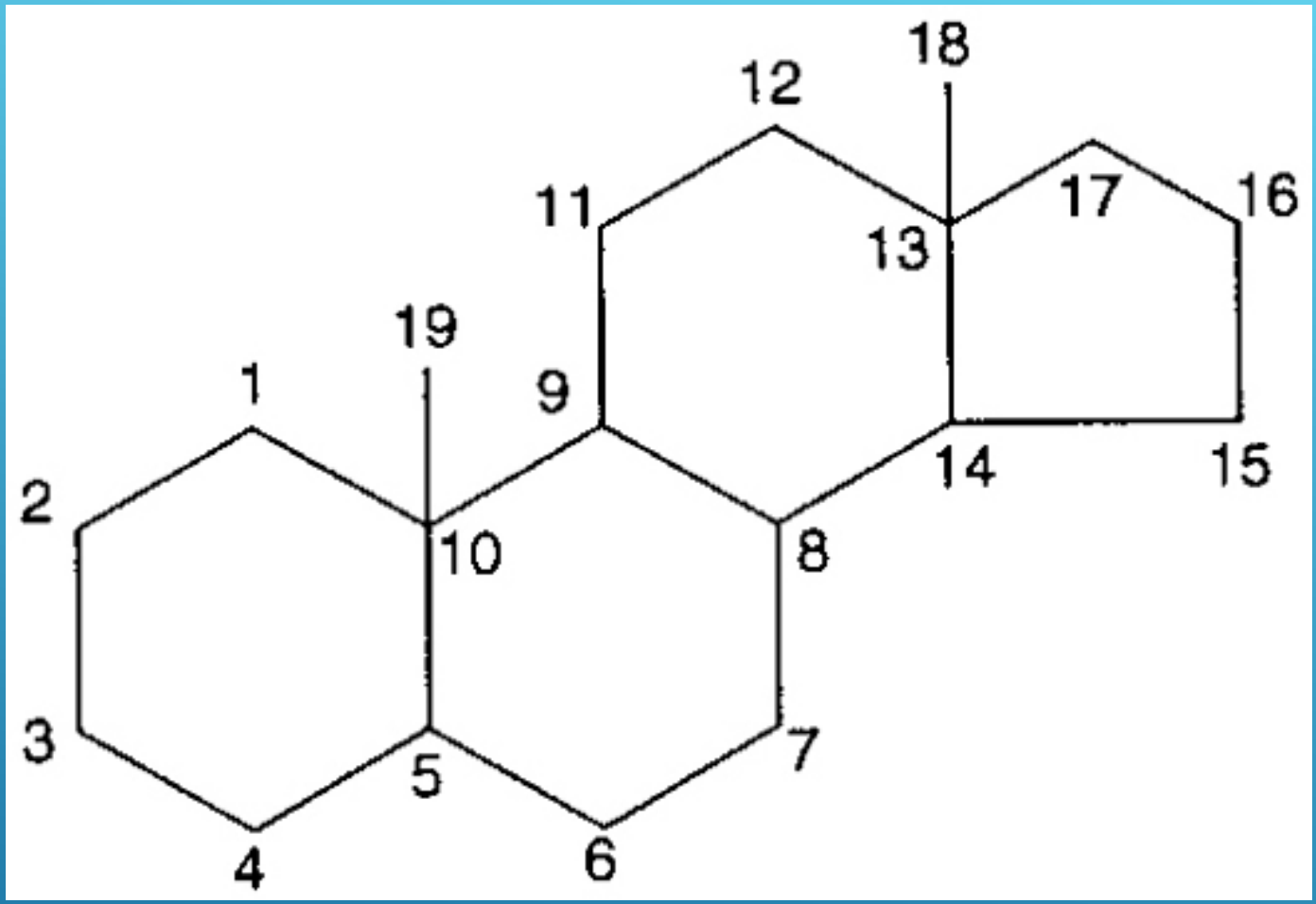
Steroidal Alkaloids

Steroidal alkaloids are biosynthesized by the inclusion of one or two nitrogen atoms into a preformed steroid molecule. *Solanum* and *Veratrum* alkaloids are representatives of this class of alkaloid, and are perceived as pharmacologically important alkaloids, and also as precursors of semisynthetic steroid derivatives. They are distinguished by their tetracyclic cyclopentanophenanthrene backbone that marks their close relationship with sterols.

Molecular structure→ steroid core

3 groups:

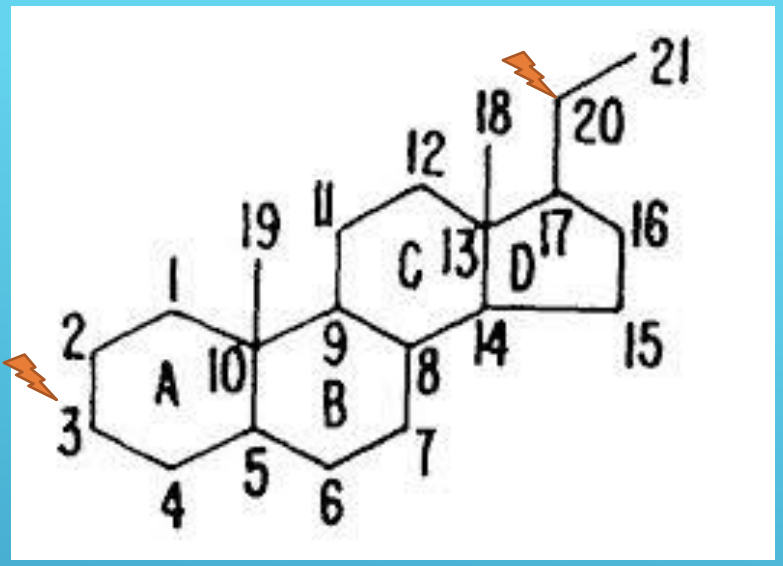
1. 21 C
2. 24 C
3. 27 C



Main steroid structure

Steroidal alkaloids:
1) Alkaloids with 21 C

N??



Pregnane derivative →

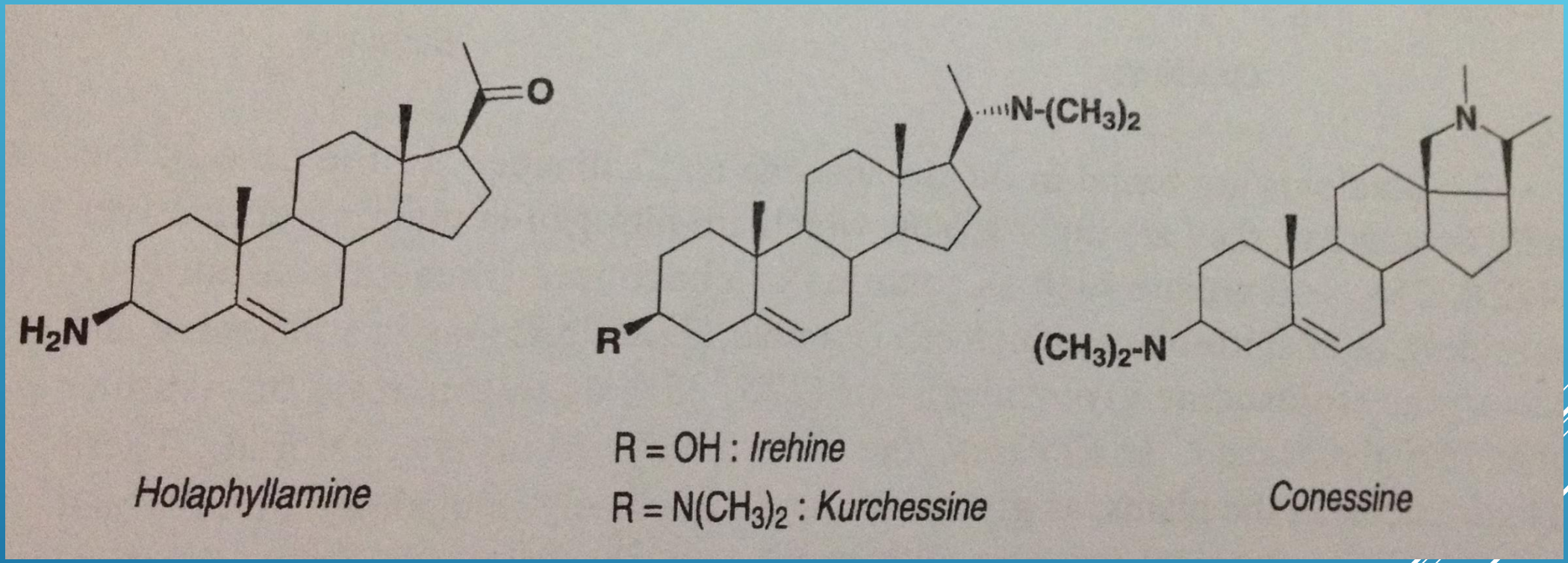
N → 3, 20; 3rd and 20th position

Characteristic for Apocynaceae family.

Holaphyllamine, kurchessine, irehine and conessine are the examples of this group.

Also this type of alkaloids are placed in Buxaceae family.

Steroidal alkaloids:
1) Alkaloids with 21 C



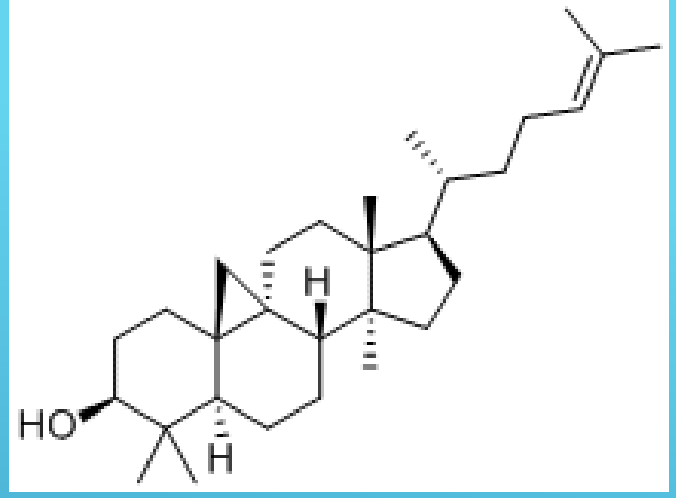
Holaphyllamine

R = OH : *Irehine*

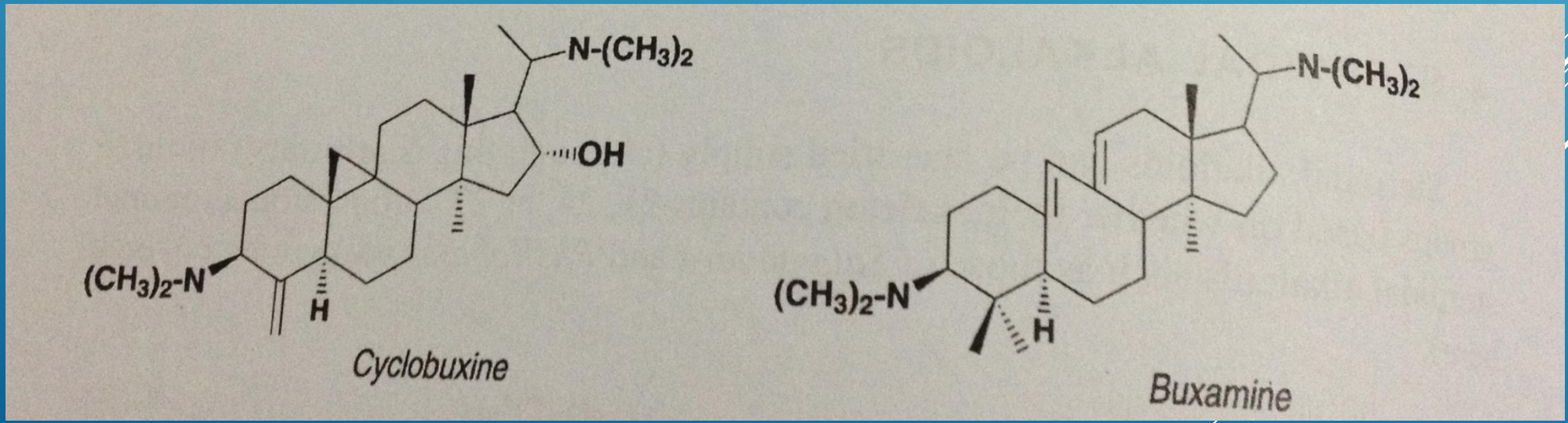
R = $N(CH_3)_2$: *Kurchessine*

Conessine

Steroidal alkaloids:
2) Alkaloids with 24 C



- ✓ Derivatives of cycloartenole, unique to Buxaceae family. Buxamine is a good example for this group.
- ✓ N → 3rd and 20th position



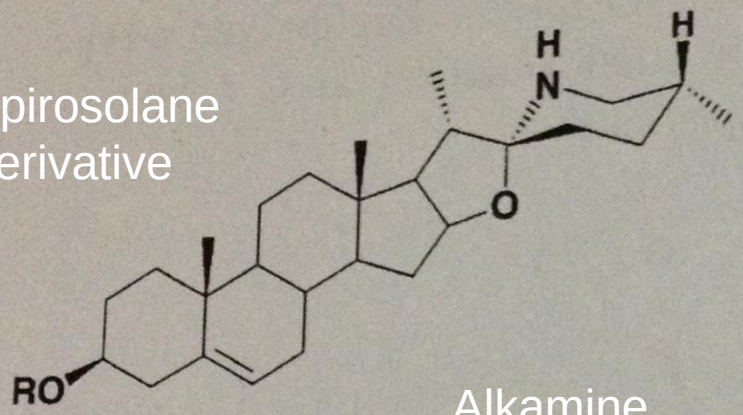
Steroidal alkaloids:
3) Alkaloids with 27 C

They are mainly placed in Solanaceae and Liliaceae families.

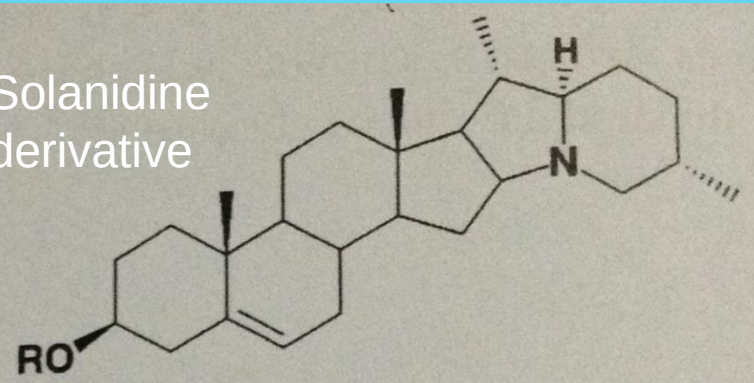
Solanaceae → solanidine derivative (solanine) or spirosolane derivative (solasodine)

These compounds can also be employed in the partial synthesis of steroidal drugs, and a number of companies have devoted considerable attention to commercial production.

Spirosolane derivative



Solanidine derivative



Alkamine (aglycone)

R = H : *Solasodine*

R = β-D-Glc (1—>3)-β-D-Gal (1—>) : *Solasonine*

(1—>2) ↑

α-L-Rha

R = H : *Solanidine*

R = β-D-Glc (1—>3)-β-D-Gal (1—>) : α-*Solanine*

(1—>2) ↑

α-L-Rha

R = α-L-Rha (1—>4)-β-D-Glc (1—>) : *Solamargine*

(1—>2) ↑

α-L-Rha

Glc(Rha)-Gal = solatriose

solatriose – rhamose = solabiose

Rha(Rha)-Glc = chacotriose

chacotriose – rhamose = chacobio se

R = β-D-Glc (1—>3)-β-D-Gal (1—>) : β-*Solanine*

R = β-D-Gal (1—>) : γ-*Solanine*

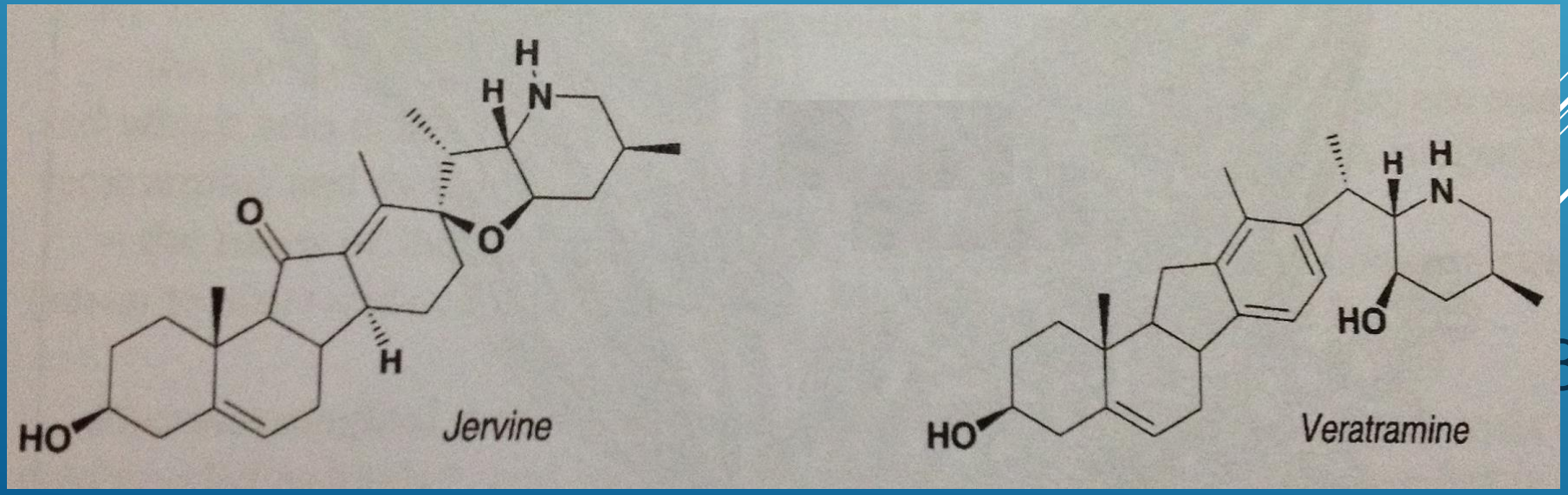
R = α-L-Rha (1—>4)-β-D-Glc (1—>) : α-*Chaconine*

(1—>2) ↑

α-L-Rha

(– Rha-1 = β-*chaconines* ; – Rha-1 et -2 : γ-*Chaconine*)

- Liliaceae → Solanidine derivative; differentiation in the cyclic structure: C-nor-D-homo-steroid → One carbon lacks in C ring; one carbon increses in D ring→ Abnormal steroidal alkaloids
- Veratrae subfamily and *Buxus* species contain these type of alkaloids.



Rhizoma Veratri albi
Veratrum album - Akçöpleme

A herbaceous, perennial plant growing naturally in Europe and North Anatolia mountains. Rhizomes are short with dark brown colour.

The rhizomes are not used so far, that it can not be mixed with Radix Valerianae.

Rhizoma Veratri albi
Veratrum album - Akçöpleme

Mixture of complex alkaloids (1.5%) and divided into two groups.

1-Jeveratrum group alkaloids; jervine, rubjervine, veratramine and pseudojervine

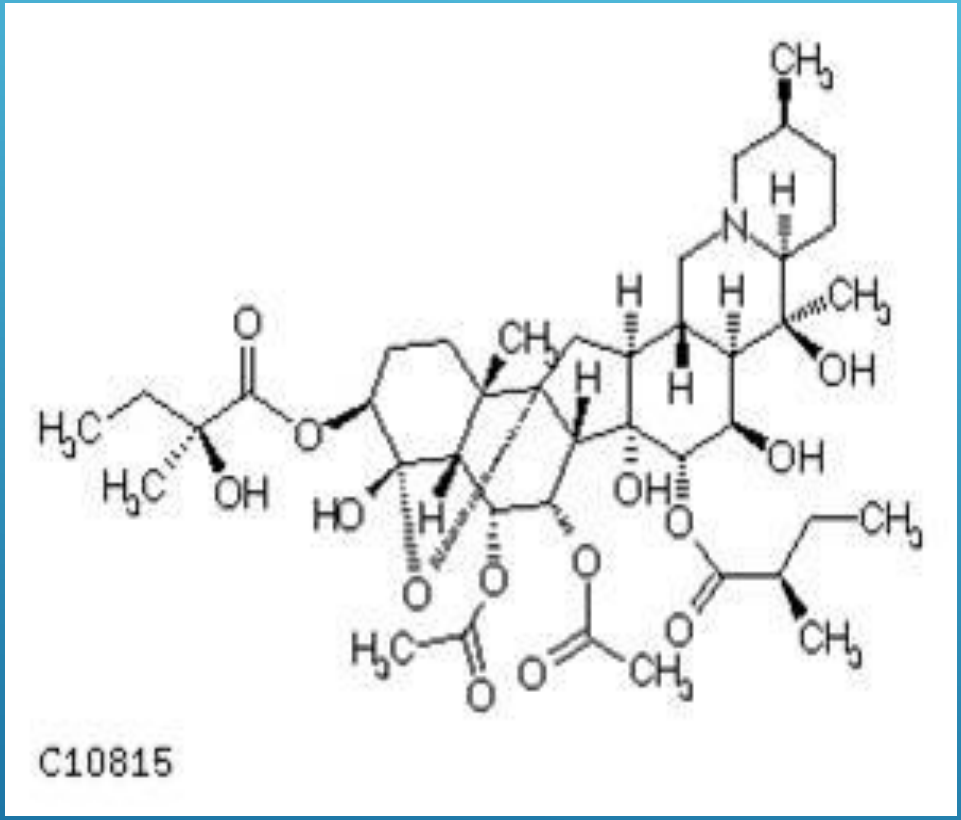
2-Ceveratrum Alkaloids e.g. Protoveratrines A and B, veratridine, germine

Proveratrines are used as an antihypertensive agent. They also possess emetic action and used in the treatment of toxemia of pregnancy.

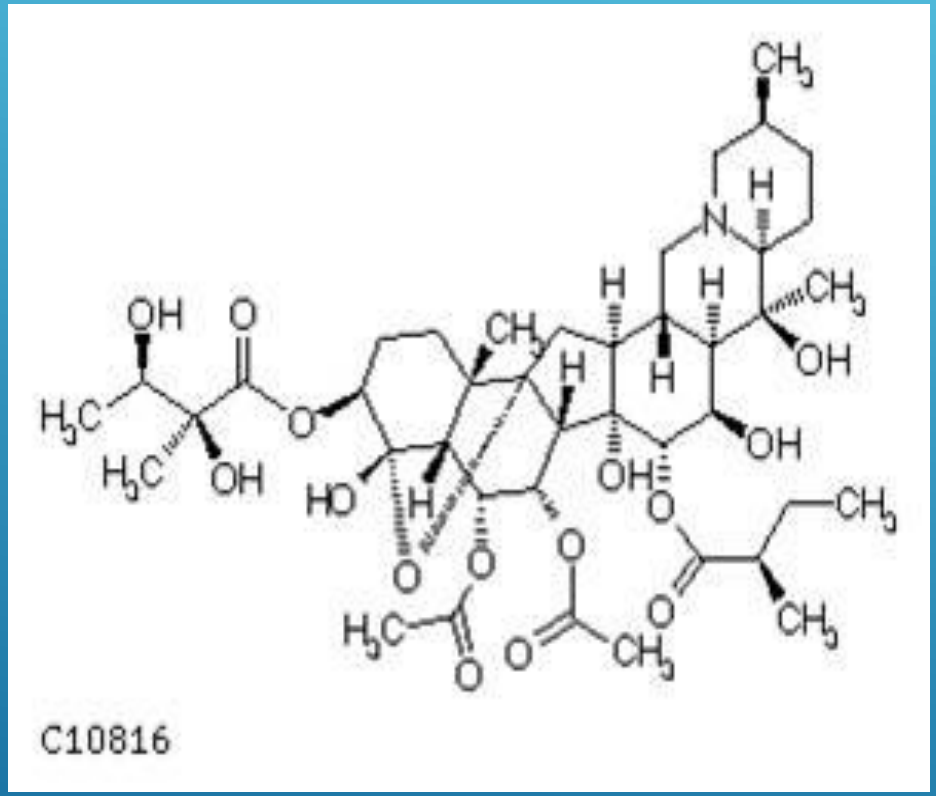
Rhizoma Veratri albi
Veratrum album - Akçöpleme

- It causes serious hypotension.
- Veratrum alkaloids are emetic.
- Toxic for some parasites.

Protoveratrine A



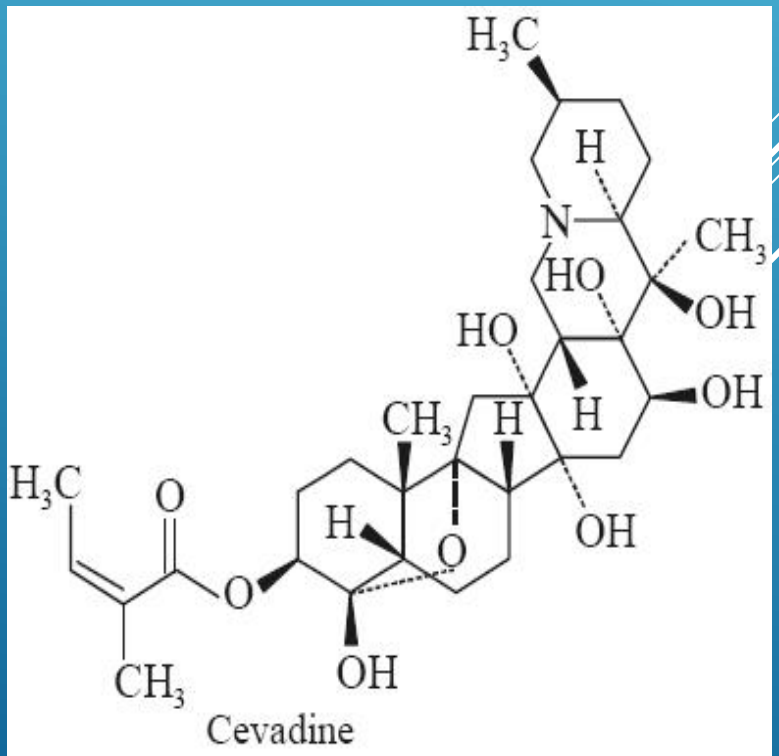
Protoveratrine B



Veratrinum

- *Sabadilla officinarum* (*Schoenocaulon officinale*) (Liliaceae)
- The ethanolic extract obtained from the seeds of Mexicanian plant.

- ✓ 2-4% alkaloid ratio. Main alkaloids are veracevine alkamine esthers; cevadine, veratridine, cevasine
- ✓ Antiparasidic activity, and should be used for the treatment of gout and rheumatism diseases.



Cevadine

SOLANACEAE STEROIDAL ALKALOIDS

- These alkaloids are biosynthetically formed by cholesterole. Mostly in glycosidic form. The aglycone of these alkaolids are called as alkamine/alkylamine.
- They can be hydrolised by boiling with 5% HCl for 3 h.

SOLANACEAE STEROIDAL ALKALOIDS

The Solanaceae family is widely distributed in tropical zones around the world; it contains about 96 genera (about 1500 species), which includes the large genus *Solanum*. The genus is well represented in the tropical and warmer temperate regions. About 20 of these *Solanum* species are endemic to the northeastern region. Many *Solanum* species are widely used in popular medicine or as vegetables. But they also have wide range of biological activities such as antimicrobial, antirheumatics, anticonvulsant, anti-inflammatory, antioxidant and anticancer.

These are toxic alkaloids and they hemolyse the blood like saponins. They are water-soluble and are surfactants similar to saponins. These are toxic and irritable substances, symptoms of intoxication like headache, nausea, vomiting, diarrhea, and some neurological symptoms that occur for several hours.

Shows various activities;

Tomatine, antibiotic

Solanine, antimitotic

Solanocapsine, slow downs the heart rate

Solasodine, accelerates the heart rate.

Solanaceae steroidal alkaloids can be classified in two groups.

1-Solanidine type

2-Spirosolane type

Solanum dulcamara

***Solanum dulca*mara- it üzümü**

The herbaceous climber plant; The leaves are easily recognizable with 3-lobed, yellow-stained purple color and 5 petals flowers and small red soft fruits. The amount of alkaloids is different in different parts of the plant. The immature fruit has the maximum amount.

Plant contains spirosolane alkaloids. Soladulcidine, tomatidenol.

Toxicity is very low.

Solanum nigrum – köpek üzümü

It is a wild plant that grows in the fields of North America and Europe. It is a perennial herb with dark green leaves and small white flowers in the form of a bunch that reminds the potato plant. Fruits are greenish yellow grapes that turn black when they ripen. All parts of the plant contain solasonine and solasodine glycosides, solasonine and solamargine. Alkaloit content of immature fruits is high as 1.3%. Eating this grape may cause minor symptoms such as nausea, flushing.

Solanum aviculare (*S. laciniatum*)

- Growing in Australia and New Zeland.
- Fruits have yellowish green colour.
- Carry 2-3% solasodine in the leaves.
- Precursor for the steroids semisynthesis.

Solanum pseusocapsicum - Kudüs kiraz ağacı

All parts of the plant carry 2 nitrogen alkaloids, such as solanocapsine. The fruit is often eaten by children. At the beginning of poisoning, nausea, vomiting, abdominal pain and drowsiness are observed.

Solanum tuberosum - Patates

Steroidal alkaloids are found in the leaves, roots, fruits and especially flowers. α-solanine, α-chachonine and partially hydrolysed homologues are found. Potato shoots have high amount of alkaloids, also exposure to light and trauma (cut) increase the alkaloid/s concentration. These alkaloids are indestructible and also toxic by cooking. It causes necrosis of the stomach and intestine mucosa and is cholinesterase inhibitors.

Kurchi, Holarrhena bark

The stem-bark of *Holarrhena antidysenterica(H. pubescens)* (Apocynaceae) has long been valued for its antidysenteric properties. The plant is a small tree found in many parts of India and up to about 1250 m in the Himalayas. The drug should be obtained from trees about 8–12 years old, which yield a stem bark about 6–12 mm in thickness.

Small trees growing in India.

Carry1,8-4,5% steroidal alkaloids
Conessine, norconessine, isoconessine, kurchine

Used for ameobic dysenteria.